Found 4606 Records

CONTROL ID: 3690421
SUBMITTER (NAME ONLY): Christoph Spartalis
TITLE: The challenge of treating the severest forms of chronic non-infectious posterior and panuveitis
SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Spartalis, N. Stübiger, M. Spitzer, U. Bartsch, Y. Atiskova, Department of Ophthalmology, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|
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ABSTRACT BODY:

Purpose: The aim of the study was to evaluate a cohort of patients, suffering from the severest forms of NIUP or panuveitis, with a special focus on therapy efficacy, therapy-associated adverse side effects and the need of medication switch.

Methods: In the present study a cohort of 18 patients (35 eyes) presenting with the severest forms of chronic non-infectious posterior or panuveitis (ocular Behçet's syndrome, Birdshot Chorioretinopathy, Vogt-Koyanagi-Harada syndrome and Serpiginous Choroiditis) were included. All patients were evaluated regarding the clinical course of the disease with a particular focus on best-corrected visual acuity, treatment duration, remission rates, reported negative side effects and the necessity of switching the medication.

The study was performed in accordance with the Declaration of Helsinki and approved by the medical ethics committee of the General Medical Council Hamburg, Germany (2020-10344-BO-ff)

Results: The cohort's mean age was 45.4 years, twelve patients were male, six were female. The mean follow-up period was 27.8 months. The best-corrected visual acuity improved significantly from baseline to end of follow-up ($p=0.048$). However, complete or partial remission was observed in only 66.7%. 72.2% of the patients underwent a switch of the medical treatment due to either adverse events or inefficacy of medication.

Conclusions: Despite new immunosuppressive therapies, effective treatment of severe non-infectious posterior and panuveitis remains a major challenge. As several therapy changes were necessary in the presented cohort for achieving partial or complete remission. The data shows the urgent need for additional and novel treatment strategies, to prevent systemic adverse effects, and to effectively improve visual outcome and prevent blindness.

CONTROL ID: 3690422

SUBMITTER (NAME ONLY): Gulgun Tezel

TITLE: Immunomodulatory Outcomes of Astroglial p65 Deletion in Experimental Mouse Glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Tezel, X. Yang, Q. Zeng, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Gulgun Tezel: Commercial Relationship: Code N (No Commercial Relationship) | Xiangjun Yang: Commercial Relationship: Code N (No Commercial Relationship) | Qun Zeng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent studies of IκKβ deletion in astroglia showed an essential role of NF-κB for the regulation of neurodegenerative inflammation in glaucoma that besides astroglia responses, astroglial NF-κB can shape microglia responses by regulating the astroglia-microglia crosstalk. This study sought a temporal analysis of the overall impacts of astroglial p65 deletion on neuroinflammation in experimental mouse glaucoma.

Methods: Bead occlusion-induced ocular hypertension was modeled in mice with conditional p65 deletion in astroglia (crossbreds of $p65^{f/f}$ and GFAP-cre/ERT2) and $p65^{f/f}$ controls. Through an ocular hypertensive period of 12-weeks, cytokines/chemokines were profiled in the retina, optic nerve, and vitreous samples using multiplex immunoassays. Transgenic effects on glial morphological responses were determined in retinal whole mounts and optic nerve sections by immunolabeling-based quantitative parameters (such as the coverage/intensity of GFAP or Iba1 immunolabeling). Transgenic effects on neurodegeneration were analyzed by counting RGCs and axons.

Results: Pro-inflammatory molecules exhibited a noticeable reduction in samples from ocular hypertensive GFAP/p65 mice, accompanied by protected RGC and axon survival ($P < 0.001$) compared to ocular hypertensive $p65^{f/f}$ controls. The pro-inflammatory cytokines presenting decreased titers with astroglial p65 deletion included transcriptional targets for NF-κB, such as ILs, TNF-α, IFN-γ ($P < 0.01$). The coverage and intensity of GFAP immunolabeling were significantly decreased with astroglial p65 deletion in ocular hypertensive eyes ($P < 0.001$). Similar to recent observations, microglia also exhibited a lessened morphological response to ocular hypertension with p65 deletion in astroglia. A characteristic shift of microglia from ramified morphology to reactive morphology with ocular hypertension was less prominent, and the Iba1 coverage and intensity were over 30% less ($P = 0.002$, $P = 0.01$, respectively) in ocular hypertensive GFAP/p65 mice than ocular hypertensive $p65^{f/f}$ controls.

Conclusions: These findings further support the importance of astroglial NF-κB as a transgenic treatment target to reduce neurodegenerative inflammation in glaucoma. The ability to detect immunomodulatory responses by vitreous cytokine profiling may also be promising to guide future translational studies for predictive, prognostic, and therapeutic testing for personalized patient care.

CONTROL ID: 3690430

SUBMITTER (NAME ONLY): Tsai-Chu Yeh

TITLE: Predicting Visual Outcome in Patients with Idiopathic Epiretinal Membrane Using A Novel Convolutional Neural Network

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yeh, Y. Ko, Y. Chou, S. Chen, Ophthalmology, Taipei Veterans General Hospital, Taipei, TAIWAN|A. Luo, Y. Deng, Industrial technology research institute, TAIWAN|

Commercial Relationships Disclosure: Tsai-Chu Yeh: Commercial Relationship: Code N (No Commercial Relationship) | Yu-Chieh Ko: Commercial Relationship: Code N (No Commercial Relationship) | Yu-Bai Chou: Commercial Relationship: Code N (No Commercial Relationship) | Shih-Jen Chen: Commercial Relationship: Code N (No Commercial Relationship) | An-Chun Luo: Commercial Relationship: Code N (No Commercial Relationship) | Yu-Shan Deng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Vitrectomy with epiretinal membrane (ERM) peeling is considered the current standard treatment for ERM; however, some patients may experience unfavorable prognosis with limited visual improvement. It remains as a challenge to determine a more rational surgical indication and timing but the guidance or predictive model is lacking currently. Thus, we aim to develop a deep convolutional neural network (CNN) that enables prediction of postoperative visual outcomes based on preoperative optical coherence tomography (OCT) images and clinical prognostic factors to refine surgical decision-making.

Methods: A total of 529 patients with idiopathic ERM who received standard vitrectomy with ERM peeling surgery between January 1, 2014 and June 1, 2020 were enrolled. The newly developed CNN model was introduced to predict postoperative visual acuity (VA) outcome (improvement ≥ 2 lines in Snellen chart or not) 12th months after surgery based on preoperative cross section OCT images and clinical factors, including age, gender and preoperative VA.

Results: The model demonstrated an overall accuracy for visual outcome prediction of 90.2% (95% CI, 79.0%-95.7%) with an AUC of 97.8% (95% CI, 86.8%-98.0%), sensitivity of 87.0% (95% CI, 67.9%-95.5%), specificity of 92.9% (95% CI, 77.4%-98.0%), precision of 0.909, recall of 0.870 and F1 score of 0.889. The heatmaps identified the critical area for prediction as the fovea subjected to tangential traction of the proliferative membrane and the adjacent ellipsoid zone of photoreceptors.

Conclusions: The novel CNN model demonstrated high accuracy in automated prediction of visual outcome based on preoperative macular OCT images. Our study suggests that deep learning has the potential to weigh and leverage the complete data of the patient, and simultaneously process a broad range of clinical information including OCT images. The model has the potential to predict visual outcome of ERM surgery through weighing and leveraging clinical information including OCT images. This approach may be helpful in setting personalized therapeutic strategy for ERM management.

CONTROL ID: 3690451

SUBMITTER (NAME ONLY): Stanton Heydinger

TITLE:

Comparison of Surgical Outcomes: Scleral Buckling versus Pars Plana Vitrectomy versus combined Scleral Buckling/Pars Plana Vitrectomy for primary repair of uncomplicated rhegmatogenous retinal detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Heydinger, A. Wang, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Stanton Heydinger: Commercial Relationship: Code N (No Commercial Relationship) | Angeline Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The mainstay of treatment for uncomplicated rhegmatogenous retinal detachment (RRD) has been surgical intervention using various techniques often decided at the level of individual surgeons. While previous research suggests certain approaches may yield better outcomes based upon pre-operative characteristics such as lens status, a superior method has not been elucidated. We performed a retrospective, observational study comparing the outcomes of primary RRD repair using pars plana vitrectomy (PPV), scleral buckling (SB), or combined SB with PPV (SB/PPV).

Methods: 179 patients between 2015-2020 with RRD managed at a large university hospital system were included. Outcome measures included: primary anatomical success rate, improvement in best-corrected visual acuity (BCVA), and functional success rate. Primary success was classified as maintained anatomical integrity of the retina following one intervention measured 6 months postoperatively. Functional success was defined as measuring a postoperative BCVA of 20/200 or better. BCVA was converted to logMAR for comparison between groups. Statistical analysis was performed using the chi-square test and ANOVA. We excluded patients with: less than 6 months of follow-up, previous retinal surgery, giant retinal tears, aphakia, secondary forms of RRD, or extensive proliferative vitreoretinopathy.

Results: SB/PPV yielded the best results in each outcome measure. Primary anatomical success was achieved in 147 of the 179 eyes (82.1%), with SB/PPV showing the greatest success rate (90.3%; p=0.15) amongst the interventions. Functional success was achieved in 125 of the 179 eyes (69.8%), with SB/PPV showing significantly greater functional success (83.9%; p=0.02) than SB (60.0%). SB/PPV showed significantly greater improved mean BCVA (0.87; p=0.04) when compared to SB (0.40); this result held in sub-group analysis of phakic eyes.

Conclusions: SB/PPV yielded the best results for primary anatomical success, functional success, and BCVA improvement out of the three interventions studied. SB/PPV showed significantly better functional success rates (p=0.02) and mean BCVA improvement (p=0.04) when compared to SB. In phakic patients, SB/PPV showed significantly greater BCVA improvement (p=0.03) when compared to SB.

CONTROL ID: 3690457

SUBMITTER (NAME ONLY): William Wong

TITLE: Lycium barbarum polysaccharide promotes corneal re-epithelization upon alkaline injury

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wong, Y. Bu, Y. Chan, K.C. Shih, Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: William Wong: Commercial Relationship: Code N (No Commercial Relationship) | Yashan Bu: Commercial Relationship: Code N (No Commercial Relationship) | Yau Kei Chan: Commercial Relationship: Code N (No Commercial Relationship) | Kendrick Shih: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: 1) To evaluate the effectiveness of Lycium barbarum polysaccharide (LBP) in promoting corneal repair after alkaline injury.

2) To evaluate the role of LBP in suppressing the secretion of pro-inflammatory cytokines in the corneal epithelium.

Methods: The corneas of C57BL/6J mice were pre-treated with topical phosphate-buffered saline or LBP (0.2/ 2/ 20 mg/mL) for 7 days 4 times per day, followed by 0.1M sodium hydroxide injury for 30 seconds and washing with distilled water for another 30 seconds. Area of epithelial defect and thickness of the cornea were evaluated using sodium fluorescein staining and hematoxylin and eosin stain. The proportion of apoptotic cells was assessed by TUNEL assay. Inflammatory cytokines, including interleukin-1 beta (IL-1β), matrix metalloproteinase 12 (MMP12), and platelet-derived growth factor-B (PDGF-BB) levels were assessed using immunohistochemistry and Western blot.

Results: 0.2, 2, 20 mg/mL LBP topical solution induced no significant apoptosis to the corneal cells. No significant difference in the total corneal, epithelium and stromal thickness was found between control and LBP pre-treated groups. Compared to the injury group, mice with 2 mg/mL LBP pre-treatment revealed a significant decrease in the fluorescein-stained area upon injury ($p=0.025$), with increased epithelial layer thickness ($p=0.004$). The corneal opacity was significantly reduced in the group with 2 mg/mL LBP pre-treatment followed by injury ($p=0.02$). The expression of matrix metalloproteinase 12 ($p=0.033$) and platelet derived growth factor-BB ($p=0.03$) resulted in a decrease in expression level in group with 2 mg/mL LBP pre-treatment compared to the injury group.

Conclusions: The study presented the efficacy of topical 2 mg/mL LBP pre-treatment, with a safety profile, in promoting corneal epithelial wound healing. We have also demonstrated the promising therapeutic effect of LBP in promoting the restoration of corneal transparency after injury, which is attributable to its anti-inflammatory effect. Our findings suggest that LBP may be considered as a potential preventative method against the formation of chemical-induced cornea defects, particularly those related to alkali burn injury.

CONTROL ID: 3690473

SUBMITTER (NAME ONLY): David Jimenez-Collado

TITLE: Face-Mask Associated Dry Eye (F-MADE) Symptoms and Ocular Surface Alterations

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Jimenez-Collado, N. Morales, C.A. Müller-Morales, A. Ramírez-Miranda, E.O. Graue-Hernandez, A. Navas, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|D. Jimenez-Collado, Universidad Panamericana, Ciudad de Mexico, Ciudad de México, MEXICO|

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ABSTRACT BODY:

Purpose: Since the onset of the coronavirus disease 19 (COVID-19) pandemic, people's lives have adapted, with the use of face masks becoming a part of our daily routine. Despite being a useful device to prevent disease contagion, a marked increase in dry eye and stye symptoms has been detected. We aimed to perform an observational correlation analysis between face-mask use and to report both objective and subjective ocular surface measurements performed on a multi-purpose advanced corneal topographer and a high-definition camera.

Methods: This study included 25 healthy subjects without any ocular diseases, ages ranging from 19 to 68 years. We measured tear meniscus height, Non-Invasive Tear Breakup Time (NIBUT), overall redness score, and tear film lipid layer characterization using Keratograph 5M (Oculus, Wetzlar, Germany), as well as Ocular Surface Disease Index (OSDI) scores for dry eye symptomatic assessments. Patients were asked the number of hours of mask-use at the moment of enrollment, the average hours of mask use daily, and the type of face mask used. We assessed for differences between OSDI scores and gender and type of mask used, as well as correlation coefficients for all subjective and objective measurements.

Results: The mean age of the subjects was 42.44±14.49 years. OSDI scores had no significant differences according to gender ($p = 0.1664$) or type of mask used ($p = 0.0791$). Correlation between hours of mask use at the time of testing and ocular surface modifications were minimal. Hours of mask-use at the time of the test and OSDI scores were moderately correlated ($r= 0.5047$, $p=0.01$). No correlation was found between the average hours of mask use and any ocular surface measurements or OSDI scores.

Conclusions: The use of face masks increased subjectively dry eye symptoms. Nevertheless, ocular surface objective measurements remain unchanged by mask-wearing.

CONTROL ID: 3690476

SUBMITTER (NAME ONLY): Weiming Mao

TITLE: A novel ex vivo human anterior segment perfusion culture model using dornor corneal rims

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Mao, M. Peng, T.J. Margetts, C.K. Sugali, N. Rayana, J. Dai, T.P. Sharma, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|W. Mao, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|V. Raghunathan, Basic Sciences, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The human anterior segment perfusion culture model is important for trabecular meshwork (TM) and aqueous humor outflow research. The traditional model relies on whole eye globes with high cost and limited availability. Here, we developed a glue-based method which enabled us to use human corneal rims for perfusion culture experiments.

Methods: Human corneal rim perfusion culture plates were designed with CAD and 3D printed. Human corneal rims containing intact TM were attached and sealed to the plate using low viscosity and high viscosity glues, respectively. The human corneal rims were perfused using the constant flow mode, and the pressure changes were recorded using a computerized system. Outflow facility, TM stiffness, and TM morphology were evaluated.

Results: When perfused at rates from 1.2 to 3.6 µl/ml, the outflow facility was 0.359 ± 0.216 µl/min/mmHg among 10 human corneal rims. The stiffness of the TM in naïve human corneal rim was similar to that of perfusion cultured human corneal rim. Also, the stiffness of TM of corneal rims perfused with dexamethasone was significantly higher than the control. Human corneal rims with glue contamination in the TM could be differentiated by high baseline intraocular pressure as well as high TM stiffness. Histology studies showed that the TM tissues perfused with plain medium appeared normal.

Conclusions: We believed that our glued-based method is a useful, low-cost alternative to the traditional anterior segment perfusion culture model using whole eye globes.

CONTROL ID: 3690494

SUBMITTER (NAME ONLY): Chandrani Chattopadhyay

TITLE: Imipridones target mitochondrial oxidative phosphorylation effectors in uveal melanoma to control growth

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Chattopadhyay, F.S. Khan, J. Roszik, E.A. Grimm, Melanoma Medical Oncology-Research, University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES|R. Bhattacharya, Colon & Rectal Surgery, UT MD Anderson cancer Center, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Chandrani Chattopadhyay: Commercial Relationship: Code N (No Commercial Relationship) | Fatima Khan: Commercial Relationship: Code N (No Commercial Relationship) | Rajat Bhattacharya: Commercial Relationship: Code N (No Commercial Relationship) | Jason Roszik: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Grimm: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveal melanoma (UM) arises from melanocytes in the eye and is distinct from skin melanoma. Half of these patients succumb to metastatic disease in the liver. There is currently no approved therapy for metastatic UM (mUM). Experimental therapies have not shown promising outcomes, with poor response to the targeted and immune therapies. There is an urgent need for new therapeutic strategies for mUM patients. We have previously shown upregulated Oxidative Phosphorylation (OXPHOS) effectors in mUM. In this study we aimed to target them in the mitochondria using Imipridones, inducers of the mitochondrial protease ClpP. ClpP controls the degradation of the mitochondrial OXPHOS proteins and regulates their level in the cell.

Methods: We tested the effect of imipridones (ONC201, 206,212) on UM cell survival in in vitro cell survival assays and also on the levels of SDHA, SDHB and other OXPHOS effectors using western blots. We determined the effect of imipridone treatment on proliferation, apoptotic and integrated stress response (ISR) pathway markers from UM cells. We studied the global proteomic and metabolomic profile of UM cells with imipridone-treatment using RPPA analyses and mass spectrometry-based metabolomics profiling respectively.

Results: The imipridones blocked UM cell survival in all UM cell lines tested. SDHA and SDHB protein levels were significantly reduced in imipridone-treated UM cells. The phosphorylation of AMPK increased post treatment, signaling a metabolic stress in the treated cells. Apoptosis was induced, as shown by increased processing of PARP as well as Caspases 9 and 3. ISR markers were also induced post treatment with imipridones. A global metabolic profile of cells post treatment showed reduction in protein biosynthesis pathways and alteration of lipid metabolism.

Conclusions: Treatment with imirpidones reduced UM cell survival, induced apoptosis, ISR and metabolic stress on UM cells. Finally, protein biosynthesis and lipid metabolism were affected with treatment. Taken together, our data show imipridones can target metabolic vulnerabilities of metastatic UM due to elevated mitochondrial OXPHOS and control cell growth. Appropriate validation of these data in a suitable in vivo model can lead to a clinical study in mUM patients to develop new therapeutic avenues.

CONTROL ID: 3690549

SUBMITTER (NAME ONLY): Jingyu Yao

TITLE: Protective effect of Fas inhibition in mouse models of inherited retinal degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yao, T. Wang, L. Jia, D.N. Zacks, Ophthalmology & Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|T. Wang, Ophthalmology, Central South University Xiangya School of Medicine, Changsha, Hunan, CHINA|

Commercial Relationships Disclosure: Jingyu Yao: Commercial Relationship: Code N (No Commercial Relationship) | Tiantian Wang: Commercial Relationship: Code N (No Commercial Relationship) | Lin Jia: Commercial Relationship: Code N (No Commercial Relationship) | David Zacks: Commercial Relationship(s);Code P (Patent):ONL Therapeutics;Code C (Consultant/Contractor):ONL Therapeutics;Code I (Personal Financial Interest):ONL Therapeutics

ABSTRACT BODY:

Purpose: Inherited retinal degeneration (IRD), a common cause of blinding disease in the United States, is a class of retinal diseases resulted from mutations in nearly 300 different genes. This extreme genetic heterogeneity has limited the development of mutation-specific therapies, and there is an urgent need for approaches targeting broadly shared pathophysiologic pathways in IRD patients. The CD95 death receptor, also known as Fas, has been reported as a contributor to retinal cell death and inflammation in a wide variety of ocular diseases. The purpose of the study is to examine the effects of genetic inhibition of Fas on retinal degeneration in 2 distinct IRD mouse models, P23H and rd10, as a proof-of-concept study of targeting Fas pathway as a novel mutation-independent approach to IRD.

Methods: The basal levels of Fas activation and inflammation in the P23H, rd10 and C57 (wild-type) controls were evaluated by TUNEL cell counts, caspase 8 activity assay, rt-PCR, and IHC. Genetic inhibition of Fas was achieved by crossing Fas-lpr, a functionally Fas-deficient mouse line, with P23H or rd10 to generate P23H/Fas-lpr and rd10/Fas-lpr mice. Retinal structure and function were evaluated by IHC, OCT and ERG analysis. The activation of microglia and the production of inflammatory cytokines were also assessed.

Results: Retinas from both P23H and rd10 mice showed elevated transcript and protein levels of Fas receptor, increased caspase 8 activity and TUNEL (+) photoreceptor cells as compared to wild-type C57 mice. Microglial activation and migration to photoreceptor layer was detected in the retinas of both P23H and rd10 mice, consistent with increased levels of inflammatory cytokines in these two models. Genetic Fas deficiency resulted in preservation of photoreceptor viability and retinal functions in both P23H and rd10 mice. Microglial activation and cytokine production was also reduced in both P23H/Fas-lpr and rd10/Fas-lpr mice compared with age-matched controls.

Conclusions: Our observation of protective effect of genetic Fas inhibition in two different mouse models of retinal degeneration suggests that while the individual IRD mutation may be specific, the retina’s response to the different stress appears to be shared and driven by cell death-inducing receptor Fas. Deletion of Fas might represent a potential mutation-independent therapeutic approach to preserve retinal structure and function in patients with IRD.

CONTROL ID: 3690637

SUBMITTER (NAME ONLY): Mukhtar Ullah

TITLE: Genetic causes of congenital cataract in consanguineous pedigrees from Pakistan

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ullah, H.M. Baig, J.H. Han, M. Quinodoz, A. Muhammad, C. Rivolta, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|M. Ullah, J.H. Han, M. Quinodoz, C. Rivolta, Department of Ophthalmology, Universitat Basel, Basel, Basel-Stadt, SWITZERLAND|S. Irshad, N. Saba, S. Gulzar, S. Parveen, School of Biochemistry and Biotechnology, University of the Punjab, Lahore, Punjab, PAKISTAN|A. Muhammad, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|H.M. Baig, Department of Biotechnology, Institute of Biochemistry, Biotechnology and Bioinformatics, The Islamia University of Bahawalpur Pakistan, Bahawalpur, Punjab, PAKISTAN|

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ABSTRACT BODY:

Purpose: Congenital cataracts (CCat) are a major cause of vision impairment in children worldwide, and are caused by mutations in more than 50 genes. The purpose of this study was to identify the genetic causes of CCat in three Pakistani families.

Methods: Three unrelated consanguineous pedigrees (F1, F2 and F3), were recruited from the Punjab region of Pakistan and were genetically studied at the Institute of Molecular and Clinical Ophthalmology Basel by whole-exome sequencing and Sanger sequencing. Clinical examination of probands was performed by standard procedures.

Results: Patients from F1 and F2 families had non-syndromic bilateral cataracts whereas patients from F3 family had CCat with microcytic hypochromic anaemia, B-cell immunodeficiency, physical developmental delay, muscular dystrophy, and speaking difficulties without intellectual disabilities. Fundus examination of all patients showed normal retina. Genetic analysis of patients from F1 revealed a novel homozygous stop-gain mutation (NM_001318327.1:c.988C>T, p.[Arg330*]) in DNMBP, whereas patients from F2 carried a new missense mutation (NM_000786.4:c.268T>A, p.[Phe90Ile]) homozygously, in the CYP51A1 gene. Finally, patients from F3 were found to have compound heterozygous variants in the TRNT1 gene: the previously unreported nonsense variant (NM_182916.2:c.433C>T, p.[Gln145*]) and the known mutation (NM_182916.2:c.1246A>G, p.[Lys396Glu]). All variants co-segregated with disease in the respective families.

Conclusions: Our findings expand the mutational spectrum of congenital cataracts and provide new information for further functional studies on the molecular mechanisms leading to these conditions.

CONTROL ID: 3690648

SUBMITTER (NAME ONLY): Justin Tram

TITLE: Impact of COVID-19 on Glaucoma Patients' Perception of Care

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bu, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|J.K. Tram, K. Lee, S. Gandham, Department of Ophthalmology, Lions Eye Institute, Albany Medical College, Albany, New York, UNITED STATES|

Commercial Relationships Disclosure: Justin Tram: Commercial Relationship: Code N (No Commercial Relationship) | Kathryn Lee: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Bu: Commercial Relationship: Code N (No Commercial Relationship) | Sai Gandham: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The COVID-19 lockdown resulted in appointment cancellations that affected the medical management and visual health of glaucoma patients. This study aimed to examine COVID-related factors leading to decreased patient perception of visual health. We surveyed glaucoma patients to examine the impact of COVID-related office changes on perceived visual health and level of concern with care.

Methods: 65 patients presenting to an Albany outpatient glaucoma practice in June 2021 were orally surveyed prior to appointment. Survey consisted of Y/N questions and Likert Scale responses examining patients' perception of care and concern over condition management during the March 2020 lockdown period. Likert responses from 1 to 5 regarding difficulty scheduling appointments, knowledge of COVID-19, level of concern regarding condition management, and patient reported vision-related quality of life (VRQOL) were used to gauge perceived visual health and level of concern with care. Patients were grouped into one of two cohorts based on whether they reported an institutional appointment cancellation during lockdown, and Mann-Whitney U and Spearman Correlation analysis were used for statistical analysis of cohorts.

Results: Patients with appointment cancellations during lockdown reported significantly greater concern regarding condition management and impacted VRQOL ($p<0.05$). On a Likert scale up to 5, the level of concern regarding VRQOL in the noncancellation group was lower (1.2 ± 0.4) compared to the cancellation group (1.8 ± 1.0). Concern regarding condition management was also lower in the noncancellation group (1.7 ± 0.6) versus the cancellation group (3.0 ± 1.1). There was no significant difference in how informed the two groups felt about COVID-19. Correlation analysis confirmed these trends and showed that increased perceived ease of obtaining appointments was positively correlated with increased patient perception of visual health, represented by impact on VRQOL.

Conclusions: This study demonstrates that COVID-related appointment cancellations caused patient concerns over care to grow and perception of visual health to decrease. Patient-reported visual health and VRQOL may be directly related to the ease of obtaining appointments and maintaining communication with their ophthalmologist, in addition to the medical management of their condition.

CONTROL ID: 3690659

SUBMITTER (NAME ONLY): Bryce Chiang

TITLE: Factors affecting eye preference in a prospective randomized controlled fellow eye study comparing WFG-LASIK and WFO-LASIK treatment

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Chiang, E.E. Manche, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure: Bryce Chiang: Commercial Relationship(s);Code E (Employment):Roche/Genentech | Edward Manche: Commercial Relationship(s);Code C (Consultant/Contractor):vedro, Carl Zeiss Meditec, Johnson & Johnson Vision;Code I (Personal Financial Interest):RxSight, Placid0, VacuSite;Code P (Patent):Vacusite;Code F (Financial Support):Allergan, Alcon, Avedro, , Carl Zeiss Meditec, and Johnson & Johnson Vision, Novarits

ABSTRACT BODY:

Purpose: To better understand the visual experience and ocular symptoms that influence eye preference in individuals that received wavefront-guided (WFG) LASIK and wavefront-optimized (WFO) LASIK treatments in a fellow eye controlled randomized study.

Methods: A prospective randomized controlled clinical trial (NCT02565537) was conducted where 102 myopic individuals were randomly assigned to receive WFO-LASIK in one eye and WFG-LASIK in the contralateral eye. At the pre-operative visit and subsequent post-operative visits, individuals were asked to identify eye preference. The survey responses of individuals who preferred WFG-LASIK were compared with those who did not preferred WFG-LASIK. The same was done for responses to WFO-LASIK treatments.

Results: At POM#12, 45% of subjects did not have an eye preference, 33% preferred WFO-LASIK treated eye, and 22% preferred WFG-LASIK treated eye ($p=0.2$). For individuals who did not prefer the WFG-LASIK eye, they noted significantly worse “hazy vision” and “blurry vision” compared with those who preferred the WFG-LASIK treatment ($p<0.05$). No differences in visual experience or ocular symptoms were reported by individuals who did prefer or did not prefer WFO-LASIK treatment.

Conclusions: At 12 months post WFG-LASIK treatment in one eye and WFO-LASIK treatment in the contralateral eye, most individuals did not have eye preference. Individuals who did not prefer WFG-LASIK noted hazy and blurry vision compared with individuals who preferred the WFG-LASIK treatment.

CONTROL ID: 3690689

SUBMITTER (NAME ONLY): Yigit Akduman

TITLE: Comparison of Concomitant Administration of Dexamethasone in One Eye versus Fluocinolone Acetonide in the Fellow Eye in Patients with Similar Degrees of Diabetic Macular Edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.C. Akduman, Saint Louis University School of Medicine, Saint Louis, Missouri, UNITED STATES|J.D. Grodsky, E.B. Rodrigues, Ophthalmology, Saint Louis University School of Medicine, Saint Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Yigit Akduman: Commercial Relationship: Code N (No Commercial Relationship) | Jacob Grodsky: Commercial Relationship: Code N (No Commercial Relationship) | Eduardo Rodrigues: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In this case series, we outline and analyze the structural and tomographic changes in three cases of individuals that received a dexamethasone intravitreal implant (Ozurdex®) injection in one eye and a fluocinolone acetonide intravitreal implant (Iluvien®) injection in the fellow eye at the same time.

Methods: The three cases were studied retrospectively to evaluate the relative efficacy between the two drugs. Best corrected visual acuity (BCVA), intraocular pressure (IOP), and maximum macular thickness (MMT) with optical coherence tomography (OCT) were taken as measurements along the timeline of follow up for comparison between the treatments.

Results: Ozurdex® appeared to have a more pronounced and prompter effect when compared to Iluvien®. In two cases, Ozurdex® showed a quick onset with decreased MMT and improved BCVA within two months while Iluvien® took 4-6 months to provide a similar effect. The response to Ozurdex® demonstrated by these variables began to decrease by the fourth month of follow up, requiring repeat injection of medication. In the third case, where macular edema was less pronounced prior to treatment, Iluvien® provided a quick response that was sustained throughout a 22-month follow-up period. In this case, Ozurdex® also showed significant response in the fellow eye but required two additional doses to maintain this effect throughout the same 22-month period. In addition, the eyes injected with Ozurdex® appeared to maintain the structural integrity of the external limiting membrane (ELM) and photoreceptor outer segments (OS) throughout the follow-up period, while OCT of the eyes injected with Iluvien® began to demonstrate structural disintegration of these critical layers as soon as four months after injection.

Conclusions: In patients with significant macular edema, intravitreal injection of Ozurdex® appears to provide quicker and more significant improvement in macular thickness, as well as better preservation of the outer retinal layers, when compared to intravitreal injection of Iluvien®. Further controlled studies comparing these two drugs are necessary.

CONTROL ID: 3690691

SUBMITTER (NAME ONLY): Karla Murillo

TITLE: Geographical Barriers to Surgical Treatment for Glaucoma and Cataract among Medicare Beneficiaries in Rural California

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Yu, Statistics, University of California Los Angeles Jonathan and Karin Fielding School of Public Health, Los Angeles, California, UNITED STATES|K. Kitayama, A.L. Coleman, Epidemiology, University of California Los Angeles Jonathan and Karin Fielding School of Public Health, Los Angeles, California, UNITED STATES|K. Murillo, PRIME-LA, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|K. Kitayama, F. Yu, V. Tseng, A.L. Coleman, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Karla Murillo: Commercial Relationship: Code N (No Commercial Relationship) | Ken Kitayama: Commercial Relationship: Code N (No Commercial Relationship) | Fei Yu: Commercial Relationship: Code N (No Commercial Relationship) | Victoria Tseng: Commercial Relationship: Code N (No Commercial Relationship) | Anne Coleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine if geographic access to surgical treatment for glaucoma and cataracts varies among Medicare beneficiaries living in rural or urban California

Methods:

This was a cross-sectional study of the 2017 California (CA) Medicare population. We included beneficiaries with glaucoma or cataracts using ICD-10 diagnosis codes. Beneficiaries were included if they resided in CA in 2017, were 65 years or older, had at least one Part B claim, and a valid CA ZIP code.

Urban or rural residence was determined by ZIP codes using the Health Resources and Services Administration definitions. Distance travelled to eye care providers was measured between patients' and providers' ZIP codes with ArcGIS. Multivariable linear regression models were performed to compare mean distance travelled to surgery by urban versus rural residence, controlling for age, sex, race/ethnicity and Charlson Comorbidity Index score. Multivariable logistic regression models were used to assess the effect of travel distance on the odds of receiving glaucoma or cataract surgery, controlling for the covariates above.

Results: The study sample included 336,117 glaucoma patients, of whom 82,583 (24.6%) were rural residents and 445,164 cataract patients of whom 127,314 (28.6%) were rural residents. A total of 24,324 (7.2%) patients received glaucoma surgery and 93,460 (21.0%) patients received cataract surgery. In adjusted analyses, beneficiaries in rural regions travelled 14.7 miles more (95% confidence interval [CI]: 13.8 to 15.7) for glaucoma surgery and 9.7 miles more (95% CI: 9.3 to 10.2) for cataract surgery than their urban counterparts. For every additional 100 miles travelled, the odds of cataract surgery decreased by 14% (OR: 0.86, 95% CI: 0.84 to 0.87). However, the odds of glaucoma surgery increased by 13% (OR: 1.13, 95% CI: 1.09 to 1.16) for every additional 100 miles travelled.

Conclusions: In 2017, Medicare beneficiaries who resided in rural California travelled farther to undergo their cataract and glaucoma surgery than beneficiaries in non-rural areas. Longer travel distance was associated with lower odds of cataract surgery, and, paradoxically, was also associated with greater odds of glaucoma surgery. This perhaps points toward the lack of glaucoma subspecialists in rural areas which necessitates further travel; however, additional studies are needed to understand such complex relationships.

CONTROL ID: 3690709

SUBMITTER (NAME ONLY): Taiichi Hikichi

TITLE: Sub-Tenon’s capsule triamcinolone acetonide injection to prevent brolucizumab-associated intraocular inflammation

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Hikichi, Hikichi Eye Clinic, Sapporo, JAPAN|

Commercial Relationships Disclosure: Taiichi Hikichi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Since the approval of brolucizumab, a number of post-marketing cases of severe visual acuity loss resulting from severe intraocular inflammation (IOI) and retinal vasculitis and/or retinal artery occlusion have been reported after intravitreal injection (IVI) ofbrolucizumab. To investigate the efficacy of sub-Tenon’s capsule triamcinolone acetonide (STTA) injections for preventing development of IOI related to brolucizumab IVI for neovascular age-related macular degeneration (nAMD).

Methods: Consecutive patients with nAMD treated with brolucizumab IVIs were studied retrospectively. All eyes treated with brolucizumab in the clinic were switched from another anti-vascular endothelial growth factor agent. After the fourth case of IOI related to brolucizumab IVI, all eyes treated with brolucizumab received a STTA injection. The patients were divided into two groups: brolucizumab alone and brolucizumab combined with a STTA injection.

Results: Thirty-three eyes (33 patients) treated with at least one brolucizumab IVI were studied: 14 eyes received brolucizumab IVI alone and 19 eyes received the combination therapy. IOI related to brolucizumab IVIs developed in four (28.6%) of 14 eyes in the brolucizumab group; IOI was severe in one eye, moderate in two eyes, and mild in one eye according to the HAWK and HARRIER trial definition; IOI did not develop in the 19 eyes that received combination therapy, the difference of which reached significance (p=0.025). Regarding combination therapy, intraocular pressure in one (5.3%) eye increased to 22 to about 24 mmHg after the STTA injection and returned to normal range within 2 months without medication; no cataracts developed during this short mean follow-up period follow-up period of 7.8 ± 0.7 months.

Conclusions: The results indicated the possible preventative effect of a STTA injection on development of brolucizumab-associated IOI. The combination therapy of a brolucizumab IVI with a STTA injection may be recommended for patients with apoor or no response to other anti-VEGF agentsor for those who require frequent IVIs of anti-VEGF agents, especially in the dominant eye.

CONTROL ID: 3690733

SUBMITTER (NAME ONLY): Sean McCafferty

TITLE: Intraocular pressure sensitivity and specificity in ocular hypertension and open-angle glaucoma with Goldmann and modified Goldmann tonometry

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.J. McCafferty, Reichert Technologies, Depew, New York, UNITED STATES|S.J. McCafferty, Intuor Technologies, Tucson, Arizona, UNITED STATES|

Commercial Relationships Disclosure: Sean McCafferty: Commercial Relationship(s);Code I (Personal Financial Interest):Intuor Technologies;Code C (Consultant/Contractor):Reichert

ABSTRACT BODY:

Purpose: Evaluate the sensitivity and specificity of IOP in detecting a need for treatment or progression of glaucomatous optic neuropathy by loss of retinal nerve fiber layer (RNFL) in ocular hypertension (OHT) and open-angle glaucoma (OAG) using Goldmann applanation tonometry (IOPg) and modified applanation surface Goldmann tonometry (IOPc)

Methods: A retrospective cross-sectional study was performed in a multi-specialty ophthalmology practice on 1741 eyes in 952 patients: 164 N, 502 GS, 490 OHT,491 POAG, and 89 normal tension glaucoma (NTG) eyes. Primary outcome measures included glaucomatous optic neuropathy (GON) demonstrated by RNFL loss measured by serial OCT over a period of 2.8 years (average of 3.9 visits) to produce receiver operating characteristic (ROC) curves of sensitivity and specificity with paired IOPc and IOPg measurements. Secondary outcome measures were corneal hysteresis (CH), and central corneal thickness (CCT).

Results: Maximum sensitivity and specificity in diagnosing new onset POAG or NTG using IOPc (77%/91%@23mmHg) and using IOPg (70%/86%@22mmHg)($p<0.001$). OHT, being defined by IOP, was included in a separate analysis of those patients with POAG/NTG/OHT requiring treatment (OHT≥26mmHg): IOPc (91%/96%@24mmHg) and IOPg (82%/88%@23mmHg)($p<0.001$). An increase of IOPc ≥ 2mmHg over IOPg indicated a 79% probability of progressive GON by RNFL loss in treated POAG/NTG ($p<0.001$). Likewise, a CH of < 9.0mmHg also indicated 79% probability of progressive GON ($p<0.001$).

Conclusions: IOP is a primary indicator in the diagnosis of OAG but not significantly reliable alone to make a decision to treat or alter treatment. A modified Goldmann prism demonstrated significantly higher sensitivity and specificity diagnosing POAG and NTG as well as directing treatment. IOP remains a valuable leading indicator of GON with significantly high sensitivity and specificity depending upon where in the spectrum of open-angle glaucoma it is measured. The IOP information may be improved by newer methods of measurement.

CONTROL ID: 3690823
SUBMITTER (NAME ONLY): Hashem Ghoraba
TITLE: Electroretinographic findings in retinal vasculitis
SESSION TITLE: Electroretinography: basic mechanisms and disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: H. Ghoraba, W. Matsumiya, P. Patel, C. Or, I. Karaca, J. Regenold, M. Zaidi, H. Khojasteh, J.J. Hwang, S. Lajevardi, N. Yavari, S. Park, A. Akhavanrezayat, A. Mobasserian, Q.D. Nguyen, Ophthalmology, Stanford University Department of Medicine, Palo Alto, California, UNITED STATES|
Commercial Relationships Disclosure: Hashem Ghoraba: Commercial Relationship: Code N (No Commercial Relationship) | Wataru Matsumiya: Commercial Relationship: Code N (No Commercial Relationship) | Prem Patel: Commercial Relationship: Code N (No Commercial Relationship) | Chi Mong Or: Commercial Relationship: Code N (No Commercial Relationship) | Irmak Karaca: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Regenold: Commercial Relationship: Code N (No Commercial Relationship) | Moosa Zaidi: Commercial Relationship: Code N (No Commercial Relationship) | Hassan Khojasteh: Commercial Relationship: Code N (No Commercial Relationship) | Jaclyn Hwang: Commercial Relationship: Code N (No Commercial Relationship) | Sherin Lajevardi: Commercial Relationship: Code N (No Commercial Relationship) | Negin Yavari: Commercial Relationship: Code N (No Commercial Relationship) | SungWho Park: Commercial Relationship: Code N (No Commercial Relationship) | Amir Akhavanrezayat: Commercial Relationship: Code N (No Commercial Relationship) | Azadeh Mobasserian: Commercial Relationship: Code N (No Commercial Relationship) | Quan Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In this case series, we aim to describe electroretinographic responses and assess their correlation with clinical and angiographic findings in retinal vasculitis.

Methods: Medical records of patients who were diagnosed with retinal vasculitis at a tertiary eye center from December 2017 to May 2021 were reviewed. Cases in which both fluorescein angiography (FA) and electroretinography (ERG) were done within one month were included. Cases with other retinal diagnoses or significant media opacities were excluded. FAs were graded according to the Angiography Scoring for Uveitis Working Group scoring system from 0 to 40, where 0 is normal. Individual ERG waves were graded for both timing and amplitude, based on their corresponding Z (standard deviation) scores from 0 to 5, where 5 is normal and 0 is absent response. General ERG score was determined by mean of individual scores plus 1 point if the oscillatory potential was present. Relevant clinical data were obtained. General and individual ERG scores were correlated with FA scores and clinical findings.

Results: 34 eyes of 20 patients were included. Mean age was 43.9 ± 19.8 years; 70% were female. Underlying ocular diagnoses were isolated vasculitis (70%), intermediate uveitis (20%) and panuveitis (10%). Median (range) best corrected visual acuity (BCVA) was 0.8 (0.08-1). Optical coherence tomography was normal in 59% of eyes. Mean FA severity score was 12.6 ± 6.5. Median general ERG score was 5 (0 to 6). 68% and 91% of eyes had responses with general scores ≥ 5 & 4, respectively. Among ERG parameters, flicker timing was the most commonly and severely affected.

FA scores weakly correlated with delayed photopic cone b wave and flicker timing ($P = 0.03$ and 0.016, respectively). FA scores did not correlate with general ERG or any other individual wave scores. Vitreous haze gradings moderately correlated with delayed cone b wave timing ($P < 0.001$), delayed flicker timing ($P = 0.002$) and weakly correlated with lower flicker amplitude ($P = 0.03$). Lower BCVA weakly correlated with delayed cone b wave timing ($P=0.046$).

Conclusions: Retinal vasculitis is not frequently associated with severe retinal dysfunction. Lower BCVA, higher FA scores, and vitreous haze gradings are weakly correlated with cone related ERG abnormalities. ERG may provide functional assessments not otherwise predicted by clinical or angiographic finding in retinal vasculitis.

CONTROL ID: 3690866
SUBMITTER (NAME ONLY): li xuejiao
TITLE: A new USH2A mutation in a Chinese family with retinitis pigmentosa
SESSION TITLE: Retinal metabolism and physiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. xuejiao, Ophthalmology, Sanmenxia Central Hospital, CHINA|
Commercial Relationships Disclosure: li xuejiao: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To detect USH2A mutations in a Chinese family with retinitis pigmentosa (RP).
Methods: A Chinese RP family with four members was enrolled in this study. Genomic DNA was extracted from peripheral blood and Next Generation Sequencing was performed to detect exonic mutations. Sequencing data were aligned and identified for genetic variants using XYGeneRanger2.0. RCR and Sanger sequencing was used to validate the gene mutations. The segregation test and Silico predictive tool were used to predict the pathogenicity of these mutations.
Results: We identified two heterozygous USH2A variations in this family which were c.8559-2 A> G and c.151 A> T (p.ile51phe). The variant c.8559-2 A> G, which was previously reported as a pathogenic mutation, was detected in the three members in this family (the proband, her father, and her daughter), while the proband's father and daughter were without any RP symptom. Another mutation c.151 A> T was detected in the proband and her mother. Both were diagnosed with RP. It was a novel variant located in chr1-216595528, the second exon of the USH2A gene. This mutation changed nucleotide at position 151 from A to T, resulting in the change of amino acid at position 51 from isoleucine to phenylalanine. c.151 A> T (p.ile51phe) was predicted to be benign by Silico predictive tools, however, co-segregation test indicated c.151 A> T (p.ile51phe) might be pathogenic.
Conclusions: We first identified c.151A> T (p.Ile51Phe) as a new mutation for RP, which was probably a pathogenic mutation. This study expands the spectrum of USH2A variants in RP patients.

CONTROL ID: 3690923

SUBMITTER (NAME ONLY): Richard Hertle

TITLE: Clinical Characteristics and Response to Eye Muscle Surgery in 15 Children Patients With Dyschromatopsia and Infantile Nystagmus Syndrome (INS)

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.W. Hertle, I. Boydstun, A. Juric De Paula, Akron Children's Hospital, Akron, Ohio, UNITED STATES|R.W. Hertle, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Richard Hertle: Commercial Relationship: Code N (No Commercial Relationship) | Ian Boydstun: Commercial Relationship: Code N (No Commercial Relationship) | Ana Juric De Paula: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the clinical characteristics and their response to eye muscle surgery in children with dyschromatopsia

Methods: This is a prospective cohort analysis of 15 dyschromatopsic patients who had eye muscle surgery. Data collected included: 1) demography, 2) clinical and electrophysiological findings, 3) associated non-ophthalmic characteristics, 5) special testing findings and 7) treatments and their results.

Results: The data were collected prospectively as an IRB approved registry. Age range 3mos-12yrs (~7.2yrs) (FU 1-10yrs), 53% male, 23% were other than Caucasian, 17% premature, 94% had delayed visual maturation, 100% had INS, 86% (13/15) with a dual jerk waveform, 100% no vergence damping, latent component or periodicity, 53% had strabismus, 40% had amblyopia, 93% had an anomalous head posture (predominant chin-down), 100% had a significant refractive error, 47% with anisometropia. Ellipsoid and/or outer retina dysmorphology was present in 100%. ERG testing showed cone dysfunction in 100% with varied rod dysfunction in 6, (40%). Positive CNGA3, CNGB3 or CAPB4 homozygosity was found in 4 patients. Systemic findings were present in 29%. Optical and amblyopia treatments were completed prior to eye muscle surgery in all patients. Best binocular acuity after eye muscle surgery ranged from Log MAR 0.55-1.2 (~.72) with a group mean improvement of .24 Log MAR ($p<0.01$). In addition, all patients had improvement in contrast sensitivity and their nystagmus characteristics, including; foveation and breadth, depth and position of their eccentric null zones.

Conclusions: A less common waveforms seen in patients with INS is dual jerk (DJ) or dual pendular which are etiologically connected to disruption in the nucleus of the optic tract. DJ INS is a low-amplitude, high-frequency nystagmus whereas typical INS is a high-amplitude, low-frequency nystagmus, the combination of the two is recognized using eye-movement recordings and seems to be characteristic in dyschromatopsia. In addition to confirming some of the typical clinical characteristics of dyschromatopsia-achromatopsia this series analysis has demonstrated a unique, consistent, pattern of novel ocular motor findings and significant improvements nystagmus and visual function after eye muscle surgery.

CONTROL ID: 3690950

SUBMITTER (NAME ONLY): Luisa Silva

TITLE: Integrative omics approach identifies druggable BAP1-dependencies in Uveal Melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Silva, S. Barnett, J. Kenyani, Z. Butt, J. Coulson, Molecular Physiology and Cell Signalling, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Merseyside, UNITED KINGDOM|K. Aughton, J. Sacco, H. Kalirai, S.E. Coupland, Molecular & Clinical Cancer Medicine, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Merseyside, UNITED KINGDOM|D. Hammond, Biochemistry & Systems Biology, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Merseyside, UNITED KINGDOM|A. Taktak, Physics, University of Liverpool Faculty of Science and Engineering, Liverpool, Merseyside, UNITED KINGDOM|

Commercial Relationships Disclosure: Luisa Silva: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Barnett: Commercial Relationship: Code N (No Commercial Relationship) | Jenna Kenyani: Commercial Relationship: Code N (No Commercial Relationship) | Zohra Butt: Commercial Relationship: Code N (No Commercial Relationship) | Karen Aughton: Commercial Relationship: Code N (No Commercial Relationship) | Dean Hammond: Commercial Relationship: Code N (No Commercial Relationship) | Azzam Taktak: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Sacco: Commercial Relationship: Code N (No Commercial Relationship) | Helen Kalirai: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Coupland: Commercial Relationship: Code N (No Commercial Relationship) | Judy Coulson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is the most common intraocular cancer; 50% of patients develop metastases, usually to the liver, that prove fatal within 2-years due to lack of successful therapies. BAP1 mutations are frequently associated with metastatic UM (mUM), and also with malignant pleural mesothelioma (MPM). Through multi-omics analysis to identify common BAP1-dependencies in UM and a gene-edited model of MPM, we tested the hypothesis that adaptation to BAP1 alteration creates therapeutic vulnerabilities in UM.

Methods: A novel function-driven multi-omics analysis, which included pathway-based and gene-based approaches, was used to integrate mRNA, protein and miRNA datasets from isogenic BAP1-mutant mesothelial MeT5A cells with in-house and publicly available UM patient sample transcriptome datasets (Fig 1A). Genes were then filtered (Fig 1B) and candidates validated by qRT-PCR in MeT5A cells and FFPE primary UM (pUM) samples (n=19). Statistical analyses used one-sample or Wilcoxon t-test for MeT5A and two-tailed t-test or Mann Whitney test for UM, depending on whether data were normally distributed.

Results: Multi-omics integration and filtering identified 24 BAP1-dependent candidates: 14 from pathway-based and 17 from gene-based approaches, with 7 in common (Fig 1B). 16 candidates were validated by qRT-PCR ($p<0.05$) in MeT5A cells, whilst qRT-PCR in pUM samples highlighted 3 lead candidates: BIRC3 significantly increased 9.3-fold in BAP1 altered ($4.38\pm5.66\times10^{-2}$ relative to actin) compared to BAP1 normal pUM ($4.69\pm7.57\times10^{-3}$;$p=0.02$), HSP90AB1 decreased 2.3-fold in BAP1 altered ($3.81\pm0.87\times10^{-1}$) compared to BAP1 normal pUM ($8.75\pm2.85\times10^{-1}$;$p=0.0001$), and KCND3 increased 13.2-fold in BAP1 altered ($1.73\pm1.73\times10^{-1}$) compared to BAP1 normal pUM ($1.32\pm1.56\times10^{-2}$;$p=0.0015$).

Conclusions: This function-driven approach identified novel BAP1-dependent adaptations in UM that may provide therapeutic targets for mUM: increase in BIRC3, an anti-apoptotic gene, decrease in HSP90AB1, a pro-apoptotic gene, and increase in KCND3 which has been shown to promote migration. Assessment of protein expression in UM cell lines and UM patient samples is underway. UM cell line viability will be tested in response to drugs targeting these candidates: LCL-161 (BIRC3), polaprezinc (HSP90AB1 agonist) and dronedarone (KCND3).

CONTROL ID: 3691091

SUBMITTER (NAME ONLY): Ahmed Soliman

TITLE: Deep Augmentation Lamellar Keratoplasty (DALK 2.0) for Severe Keratoconus.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.Z. Soliman, Ophthalmology, Southwest Eye Institute, El Paso, Texas, UNITED STATES|

Commercial Relationships Disclosure: Ahmed Soliman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the initial clinical outcomes of Deep Augmentation Lamellar Keratoplasty (DALK 2.0) in eyes with severe keratoconus (KC).

Methods: Six eyes (6 patients) with progressive KC underwent DALK 2.0. Patients were divided into two groups based on the maximum keratometry (Kmax): Group A: patients with Kmax >65 diopters and group B: patients with Kmax <65 diopters. Best-corrected visual acuity, Kmax, central corneal thickness, thinnest point thickness were recorded before and at the last follow up visit after the procedure (minimum follow up of 6 months with the longest follow up period being 24 months). Any surgical complications or progression of KC were documented.

Results: Best contact lens corrected visual acuity improved in both groups postoperatively with no patients losing any vision. An average Kmax reduction of 7.6 D and 4.8 D was noted in groups A and B respectively at the last follow up visit ($P < 0.001$). Contact lens tolerance improved in 4 patients (two in each group) ($P = 0.3$). One eye underwent topography guided photorefractive keratectomy (PRK) 6 months after the surgery (this eye underwent standard epithelial off corneal crosslinking prior to the transplant). No postoperative KC progression was noted in any of the operated eyes thus far. No postoperative complications were observed.

Conclusions: Deep Augmentation Lamellar Keratoplasty improved best contact lens corrected visual acuity, stabilized KC, improved contact lens tolerance and allowed for subsequent topography guided PRK in select cases. More corneal flattening was achieved in patients with more advanced disease. Allogenic stromal corneal augmentation is a promising technique that will hopefully be utilized more frequently in cases of severe keratoconus.

CONTROL ID: 3691116

SUBMITTER (NAME ONLY): Tongalp Tezel

TITLE: SPATIAL FEATURES OF CYSTOID MACULAR EDEMA ACT AS A BIOMARKER FOR THE ANATOMIC AND FUNCTIONAL STATUS OF THE RETINA IN RETINITIS PIGMENTOSA

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.H. Tezel, Ophthalmology, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Tongalp Tezel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the anatomical and functional correlates of intraretinal cysts in retinitis pigmentosa.

Methods: One hundred three patients (196 eyes) with untreated cystoid macular edema (CME) were identified from a pool of 578 genotyped patients with retinitis pigmentosa. Three central horizontal OCT scans were used to calculate the size of the retinal nerve fiber layer, outer retinal, inner retinal area, cysts, and total retinal areas. Ellipsoid zone and outer limiting membrane lengths were also measured. Best-fit curves were used to analyze the factors that play a role in the size of the retinal cysts and the patient's visual acuity. Correlations between the visual acuity, morphometric and clinical data were sought.

Results: Twenty-five percent of the screened patients (103/578) had CME. Patients with autosomal dominant retinitis pigmentosa had the highest incidence of CME (43.6%, $p<0.001$) but also had the best visual acuity (20/34±20/30, $p=0.02$). The total cyst area was 0.14±0.18 mm2. Outer retinal area ($B=0.214$; $p=0.008$), age ($B=-0.003$; $p<0.001$) and retinal nerve fiber area ($B=0.411$; $p=0.005$) were main determinants of the ($r=0.44$; $p<0.001$) cyst size. Cysts resolved with progressing retinal degeneration. Length of the intact ellipsoid zone ($B=-5.16E-5$; $p<0.001$), the inheritance pattern ($B=0.04$; $p=0.028$) and retinal nerve fiber area ($B=0.751$; $p<0.001$) were the main determinants of visual acuity.

Conclusions: Retinal nerve fiber layer emerges as a significant morphologic parameter correlating with the intraretinal cyst size and decreasing visual acuity. This finding suggests axonal compression and subsequent visual loss as a possible complication of intraretinal cysts in retinitis pigmentosa.

CONTROL ID: 3691152

SUBMITTER (NAME ONLY): Janine Yang

TITLE: AIBSE, AZOOR and MEWDS: Longitudinal Clinical Comparison and Documentation of Conversion

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.Y. Yang, J. Rizzo, L. Sobrin, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Janine Yang: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Rizzo: Commercial Relationship: Code N (No Commercial Relationship) | Lucia Sobrin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the clinical characteristics and clinical transitions between acute idiopathic blind spot enlargement (AIBSE), acute zonal occult outer retinopathy (AZOOR), and multiple evanescent white dot syndrome (MEWDS) with longitudinal follow up.

Methods: Patients were identified by searching electronic medical records using diagnostic codes. Testing reviewed included visual fields, ophthalmic imaging and electroretinography. Demographic and clinical characteristics were compared. Charts were reviewed by both a neuro-ophthalmologist and a uveitis/retina specialist. Transition between diseases was defined by new appropriate funduscopic findings or testing that best fit with a different phenotype. Statistical analysis was performed using STATA 17 software.

Results: A total of 43 patients were identified with a distribution of cases as follows: 14 AIBSE, 26 AZOOR, 1 AIBSE to AZOOR transition, 1 AZOOR to MEWDS transition, and 1 co-occurring AZOOR and MEWDS. AIBSE patients (mean age, 33 years) were younger than AZOOR patients (mean age, 41 years) at diagnosis. Women accounted for 93% of AIBSE patients and 77% of AZOOR patients. All transition patients were women. Time from initial diagnosis to clinical transition was 4 years in AIBSE to AZOOR and 0.75 years in AZOOR to MEWDS. AZOOR patients had longer mean follow up time (AIBSE 28 months, AZOOR 44 months) compared to AIBSE patients. Common misdiagnoses at the time of referral were migraines (42% of AIBSE patients, 32% of AZOOR patients) and optic neuritis (29% of AIBSE patients, 23% of AZOOR patients). AZOOR patients were more likely to present bilaterally at initial visit (Fisher's exact test $p < 0.05$). Unilateral to bilateral occurrence (21% AIBSE eyes, 35% AZOOR eyes) and recurrences (14% AIBSE eyes, 38% AZOOR eyes) were more frequently observed in AZOOR patients. By the final visit, 30% of AZOOR eyes experienced worsening scotoma area by 20%, and 5% of AZOOR eyes experienced worsening visual acuity by 2 or more Snellen lines compared to no AIBSE eyes. Treatment was initiated in 8 AZOOR patients (31%), all transition patients and no AIBSE patients.

Conclusions: A greater percentage of AZOOR patients exhibited worsening visual acuity and scotoma area and received immunosuppressive therapy when compared to AIBSE patients. Patients transitioning between these diseases are uncommon. Specifically, only a single case was observed for AIBSE converted to AZOOR.

CONTROL ID: 3691280

SUBMITTER (NAME ONLY): Louis Tong

TITLE: Patient factors determine acceptability of topical immunosuppressives in dry eye

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Tong, Cornea and external eye disease, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|L. Tong, Ocular Surface Research Group, Singapore Eye Research Institute, Singapore, SINGAPORE|S. Ozdemir, J. Lee, A. Bhaskar, E. Finkelstein, Health Services and Systems Research, Duke-NUS Medical School, Singapore, SINGAPORE|S. Ozdemir, E. Finkelstein, Saw Swee Hock School of Public Health, National University of Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Medications can result in side effects which may lead to medication non-adherence and, eventually, to poor outcomes. This study aimed to quantify to what extent the side effects of dry eye disease (DED) medications (burning/stinging sensation and blurring) are important to patients as opposed to medication benefits or costs.

Methods: Patients who were diagnosed with DED were recruited at a referral eye centre in Singapore (n=139). This study utilized a Discrete Choice Experiment where patients were presented with 10 choice tasks where they were asked to choose between their current medication (or no medication), and two hypothetical medications that varied based on five attributes: duration of burning/stinging, duration of blurring, time to medication effectiveness, medication frequency, and out-of-pocket cost. The main outcomes were relative attribute importance and predicted uptake.

Results: Latent class logistic regressions found two groups with distinct preferences. Classes 1 and 2 constituted 62.5% and 37.5% of the sample. For both classes, duration of burning/stinging (Class1=12%, Class2=20%) and cost (Class1=12%, Class2=19%) were the most important attributes while duration of blurring (Class1=8%, Class2=6%) was the least important. The predicted uptake of a medication increased 18 percentage-points when burning/stinging duration decreased from 2 hours to a few minutes. The increase was 41 percentage-points for Class 2 who were more likely to report neutral/poor control of their dry eye symptoms.

Conclusions: This study showed that side effects should be considered, in parallel with therapeutic efficacy, when choosing anti-inflammatory medications in DED. Incorporating patient preferences in treatment decisions could potentially improve patient acceptance of a treatment regimen.

CONTROL ID: 3691415

SUBMITTER (NAME ONLY): Zane Yu

TITLE: Influence of tobacco smoking on developing age-related ectropion and entropion

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z.Z. Yu, P. Rizzuto, Division of Ophthalmology, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|

Commercial Relationships Disclosure: Zane Yu: Commercial Relationship: Code N (No Commercial Relationship) | Philip Rizzuto: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Studies have shown that tobacco smoking significantly impacts general health and well-being. Tobacco smoking also has a multitude of negative consequences on ocular health, increasing the risk of age-related macular degeneration, cataracts, and glaucoma. The purpose of this study was to assess the impact of tobacco smoking on age-related ectropion and entropion.

Methods: Data on ectropion and entropion cases from a clinical practice from the years 2017 to 2019 were analyzed. Ages of non-smoking ectropion and entropion patients were compared with ages of ectropion and entropion smokers using normal distributions.

Results: The null hypothesis was that the average age of a smoker presenting with ectropion or entropion would not be significantly different from that of a non-smoking patient. The alternative hypothesis was the average age of a smoker presenting with ectropion or entropion would be younger. There were 101 non-smokers and 50 smokers in the dataset. The average age of a non-smoking patient presenting with ectropion or entropion was 77.78 with a standard deviation of 10.31. From a sample size of 50, the average age of a smoker presenting with ectropion or entropion was 74.44 with a standard deviation of 11.84. Z-test analysis reveals a Z-statistic of 1.70, giving a p-value of 0.045 for a one-tailed hypothesis. Using a standard confidence interval of 95%, this allows us to reject the null hypothesis.

Conclusions: Given the significantly lower average age of presentation with age-related ectropion or entropion in smokers compared to non-smokers, tobacco smoking is evidently associated with earlier age of onset in cases of age-related ectropion or entropion. The data only includes patients from around the Rhode Island area – potentially including Massachusetts and Connecticut – and cannot be reliably extrapolated to broader populations; additionally, this study did not address potential increases in risk of age-related ectropion or entropion in smokers. More research will need to be done to elucidate the association between tobacco smoking and age-related ectropion and entropion.

CONTROL ID: 3691564

SUBMITTER (NAME ONLY): Vikas Khetan

TITLE: To determine the predictive risk factors for development of Radiation retinopathy following plaque brachytherapy with Iodine- 125 for choroidal melanoma a study from India

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Khetan, S. Mohan, Ocular Oncology, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|

Commercial Relationships Disclosure: Vikas Khetan: Commercial Relationship: Code N (No Commercial Relationship) | Sashwanthi Mohan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To find out the factors that determine the risk of radiation retinopathy development after Plaque radiation treatment.

Methods: Retrospective analysis of all patients who underwent plaque brachytherapy with Iodine-125 for choroidal melanoma between 2004-2020 was done. Forty-eight patients who had minimum follow-up of 12 months post treatment were included in the analysis.

Results: Thirty of the 48 patients developed radiation retinopathy (62.5%) of which 23 patients had non-proliferative retinopathy and 7 patients had proliferative retinopathy. Twenty-five (83.33%) of the 30 patients also developed radiation maculopathy. Kaplan Meir survival analysis showed that proportion of patients free from radiation retinopathy is 50% at 5 years and 20% at 10 years. On univariate analysis, risk factors predictive of radiation retinopathy included increased width of the tumour (Hazard ratio (HR)= 1.14191, p=0.038), surface area of the tumour (HR= 1.0082, p=0.0371), total radiation dose to the apex of the tumour (HR= 1.01413, p=0.0371) and radiation to the optic nerve head (HR=1.0056, p=0.0374). On multivariate analysis, total radiation to the optic nerve head was the best predictor of radiation retinopathy (HR=1.0056, p=0.0380). Risk factors predictive of radiation maculopathy included total radiation dose to the apex of tumour (HR= 1.0468, p=0.0357) and radiation to the optic nerve head (HR= 1.0069, p=0.0182) on univariate analysis and radiation dose to the apex of tumour (HR= 1.0486, p=0.0334) and radiation to the optic nerve head (HR= 1.0067, p=0.0159) on multivariate analysis also.

Eighteen of the 23 patients with radiation maculopathy were treated with Intravitreal-Anti VEGF injections and 1 patient received an intravitreal dexamethasone implant. A mean of 2.4 (Range 1-6) injections were given.

Conclusions: Radiation retinopathy is a common complication of plaque brachytherapy for choroidal melanoma occurring in 50% of the patients at 5 years. The main predictive risk factors for development of radiation retinopathy in our study was total radiation dose to the apex, radiation to the optic nerve head as well as increased width and surface area of the tumour. All patients undergoing plaque brachytherapy for choroidal melanoma should be followed up closely for signs of radiation retinopathy.

CONTROL ID: 3691686
SUBMITTER (NAME ONLY): Varshini Varadaraj
TITLE: Vision impairment and Dementia: Economic hardships for patients and caregivers
SESSION TITLE: Health Economics and Health Care Delivery
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: V. Varadaraj, B.K. Swenor, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M. Eisenberg, E. Garcia-Morales, N. Reed, Johns Hopkins Bloomberg School of Public Health, Maryland, UNITED STATES|O. Sheehan, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|
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ABSTRACT BODY:
Purpose: To examine the economic impact of vision impairment (VI) and dementia on older adults and caregivers
Methods: We used data from the 2011 National Health and Aging Trends Study (NHATS), a nationally representative survey of Medicare beneficiaries, linked to their family/unpaid helpers from the National Study of Caregiving (NSOC). VI was defined as self-reported blindness or difficulty with distance/near vision. Dementia was based on survey-report, interviews, and cognitive tests. Outcomes included (1) having debt, and receiving (2) financial help from relatives, and government-based (3) Supplemental Nutrition Assistance Program (SNAP) (4) other food assistance, and (5) utility assistance, for NHATS older adults, and (6) financial difficulty for NSOC caregivers.
Results: Of 7,608 NHATS older adults, 84% did not have VI or dementia, 6% had VI only, 7% had dementia only, and 3% had VI and dementia. In fully adjusted, logistic regression analyses, older adults with VI and dementia had greater odds of having debt (OR=3.9 [95%CI=2.1, 7.4]), and receiving financial help (OR=2.5 [1.6, 3.7]), SNAP (OR=2.6 [1.7, 4.1]), and other food assistance (OR=3.5 [2.1, 5.9]), but not utility assistance (OR=1.0 [0.6, 1.9], than older adults without either impairment, (Table 1). Of 2,007 NSOC caregivers, 54% cared for older adults without VI or dementia, 13% for VI only, 25% for dementia only, and 12% for VI and dementia. In logistic regression, caregivers to older adults with VI and dementia had greater odds of reporting caregiving-related financial difficulty (OR=2.8 [1.8, 4.3]) than caregivers of those without either impairment.
Conclusions: Older adults with VI and their caregivers experience similar financial outcomes as compared to older adults with dementia and their caregivers, respectively. However, these results are magnified for older adults with co-occurring VI and dementia, and their caregivers.

CONTROL ID: 3692318

SUBMITTER (NAME ONLY): Elena Bastia

TITLE: NCX 470, a nitric oxide (NO)-donating prostaglandin analog, elicits sustained IOP-lowering and modifies aqueous humor dynamic in non-human primates

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Bastia, S. brambilla, C. Galli, F. Impagnatiello, Nicox Research Institute, ITALY|C.B. Toris, S. Fan, University of Nebraska Omaha, Omaha, Nebraska, UNITED STATES|J.L. Boyer, Nicox Ophthalmics Inc, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore the effects of NCX 470, a nitric oxide (NO)-donating prostaglandin analog, on aqueous humor dynamics in ocular normotensive non-human primates.

Methods: Ocular hypotensive activity after topical dosing with NCX 470 ophthalmic solution 0.1% or its vehicle was tested in ocular normotensive non-human primates (n=6-12) using a randomized, investigator-masked, parallel-group design. Baseline intraocular pressure (IOP) was measured (pneumatonometer, Reichert), after which animals were treated twice daily (10:00AM & 4:00PM) for 3 consecutive days and once (AM dose) on day 4 (experimental day). On day 4 IOP measurements were taken at 90, 180 and 300min after the AM dose. Additionally, on day 4, animals were dosed topically with 10% fluorescein and fluorophotometric scans (Fluorotron Master, OcuMetrics) of the cornea and anterior chamber were taken at 45min intervals throughout the experimental period to address changes in aqueous inflow, outflow facility and uveoscleral outflow.

Results: Baseline IOP was similar between groups (23.7±0.9 and 23.3±1.1mmHg in NCX 470 0.1% and vehicle, respectively). On day 4, the IOP reductions with NCX 470 were greater than those with vehicle and were sustained throughout the entire experimental period [Change From Baseline (CFB), $NCX\ 470_{CFB}$ =7.8±0.7, 5.5±0.9 and 6.5±1.0mmHg and VEH_{CFB}=4.8±0.9, 2.9±0.9 and 3.5±1.4mmHg at 90, 180 and 300min post-dosing, respectively]. In addition, NCX 470 increased outflow facility (0.64±0.17 and 0.37±0.09µl/min/mmHg for NCX 470 and vehicle, respectively) and uveoscleral outflow (2.58±0.61 and 1.24±0.26µl/min for NCX 470 and vehicle, respectively) leaving unaltered aqueous inflow (1.93±0.31 and 2.03±0.22µl/min for NCX 470 and vehicle, respectively).

Conclusions: NCX 470 increased uveoscleral outflow and outflow facility in ocular normotensive non-human primates suggesting that changes in both pathways contribute to the IOP-lowering effect of this compound.

CONTROL ID: 3692652

SUBMITTER (NAME ONLY): Andrew Lotery

TITLE: Risk factors for progression of intermediate age-related macular degeneration: A systematic review and meta-analysis

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. Lotery, R. Kaye, V. Hoang, B. Stuart, University of Southampton Faculty of Medicine, Southampton, Southampton, UNITED KINGDOM|A.M. Hagag, S. Sivaprasad, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|S. Riedl, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|P. Anders, H.P. Scholl, G. Traber, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|T. Prevost, King's College London, London, London, UNITED KINGDOM|L. Fritsche, University of Michigan, Ann Arbor, Michigan, UNITED STATES|D. Rueckert, Imperial College London, London, London, UNITED KINGDOM|P. Anders, H.P. Scholl, Department of Ophthalmology, University of Basel, Universitat Basel, Basel, Basel-Stadt, CH, academic, Basel, SWITZERLAND|C. Appenzeller-Herzog, University Medical Library, University of Basel, Universitat Basel, Basel, Basel-Stadt, CH, academic, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To perform a comprehensive review of literature and meta-analysis of risk factors that accelerate progression of intermediate age-related macular degeneration (AMD) to late AMD.

Methods: The full protocol was registered on PROSPERO (CRD42021266710).

The search strategies were developed by an information specialist (C.A.-H.). The electronic databases Embase via Elsevier and Medline via Ovid were searched using text word synonyms and database-specific subject headings for AMD and disease progression (last search November 10, 2020). Records published before 1991 were excluded. No language restrictions were applied. The titles and abstracts of references were screened against eligibility criteria including: only studies with a defined grading system; a clear end point of advanced AMD; yearly follow up; in English and fellow eye AMD status known. Selected references were retrieved in full-text and independently assessed for eligibility by two reviewers. Any disagreements over eligibility were solved by discussion with other team members.

A data extraction sheet was constructed based on the modified checklist for critical appraisal and data extraction for systematic reviews of prediction modelling studies (CHARMS-PF). The risk of bias in each of the included studies was assessed using the quality in prognostic factor studies (QUIPS) tool. Data extraction and risk of bias assessment for each article was performed by two reviewers independently.

Results: Our electronic searches identified 3229 unique records. After initial title/abstract screening, 3130 records were deemed ineligible, and 99 papers were selected for the full-text screening. Eight articles met the inclusion criteria and will proceed to the data extraction and risk of bias assessment stages.

Conclusions: Despite extensive studies assessing progression of early or intermediate AMD to late AMD only 0.3 % met our requirements for inclusion in a systematic review. This reflects the heterogeneity of the assessed studies and suggests further consensus is needed on AMD classification systems and acceptable follow up times for cohort studies to ensure they can be included in future meta-analyses.

CONTROL ID: 3692753

SUBMITTER (NAME ONLY): Liangbo Shen

TITLE: A Hierarchical Bayesian Change Points Method to Study the Long-Term Natural History of Diseases

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.L. Shen, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|L.V. Del Priore, Ophthalmology, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|J. Warren, School of Public Health, Yale University, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Liangbo Shen: Commercial Relationship(s);Code C (Consultant/Contractor):Boehringer Ingelheim | Lucian Del Priore: Commercial Relationship(s);Code C (Consultant/Contractor):Boehringer Ingelheim | Joshua Warren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is often impractical to follow patients over decades to study the long-term natural course of a chronic disease. Here, we developed a statistical method for investigating the long-term natural history of diseases using data from patients followed over short durations.

Methods: We manually delineated geographic atrophy (GA) lesions on 1607 fundus photographs of 318 eyes in the age-related eye disease study (AREDS). We developed Bayesian entry time realignment (BETR), a hierarchical Bayesian change points method (Fig. 1), which estimated a patient's disease progression rate and disease duration at enrollment based on a hypothesized progression model. The best model was selected based on the lowest deviance information criterion (DIC). We tested BETR in 100 rounds of simulated trial data generated from GA data in the AREDS. We then applied BETR in the actual GA data from the AREDS.

Results: BETR identified the correct model in 100 out of 100 simulations when the true disease progression model was the first order, second order, or exponential model. The intraclass correlation coefficient (ICC) between the estimated and true disease duration and progression rate ranged from 0.73 to 0.93. Applying BETR in patients with GA in the AREDS showed that the second order model (DIC = -358) was better than the first order model (DIC = -6) and exponential model (DIC = 365). The results remained the same among 100 rounds of random subsamplings of 159 eyes. BETR reconstructed an approximately 30-year natural history of GA progression among individual eyes (Fig. 2).

Conclusions: BETR could identify the correct long-term disease progression model and estimate patient-level disease progression parameters with high accuracy, demonstrating BETR as a promising method to study long-term natural history of diseases. The square root of GA area enlarged linearly and at different rates among different eyes over approximately 30 years.

CONTROL ID: 3692787

SUBMITTER (NAME ONLY): Young Hyun Kim

TITLE: Protection Against Localized Corneal Hyperosmolarity Spikes with Soft-Contact-Lens Wear

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Kim, M.C. Lin, C.J. Radke, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|Y. Kim, C.J. Radke, Chemical and Biomolecular Engineering Department, University of California Berkeley, Berkeley, California, UNITED STATES|M.C. Lin, Clinical Research Center, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|C. PENG, Coopervision Inc, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent work highlights that lower salt diffusivity (D_s) of a soft contact lens (SCL) can prevent post-lens tear-film (PoLTF) hyperosmolarity and that the PoLTF osmolarity is significantly different from that of the tear meniscus and the pre-lens tear film (PrLTF) [Kim et al. 2021]. That effort focused on the spatially averaged PoLTF osmolarity and did not address localized tear break-up areas, which cause localized PrLTF osmolarity spikes that can be greater than 1000 miliosmolar (mOsM) [Peng et al. 2014]. Here, we assess the effect of localized PrLTF hyperosmotic spikes on PoLTF osmolarity and whether SCL wear can protect the cornea from hyperosmotic spikes.

Methods: SCL and PoLTF were designed with Comsol Multiphysics 5.5 platform and incorporated into a 2D continuum diffusion model to determine the PoLTF osmolarity transiently. Lens-salt partition coefficient (k_s), D_s, and lens thickness (h_{lens}) were varied to assess their effect on PoLTF osmolarity. Localized hyperosmolarity spike follows the time-dependent results of Peng et al. [2014] and were used as the anterior lens-surface boundary-layer condition (Figure 1a). A no-flux boundary was incorporated at the PoLTF/cornea interface. Initial conditions for SCL and tear compartments were obtained from steady-state solutions of Kim et al. [2021] for normal and dry eyes with various D_s, k_s, and h_{lens}.

Results: Figure 1b provides PoLTF osmolarity for normal eye with a given D_s, k_s, and h_{lens} (specified in Figure 1b) during various time points within an interblink while experiencing the PrLTF osmolarity spike of Figure 1a. Localized PoLTF osmotic spike did not occur until ~10 s into the interblink and the spike osmolarity was significantly lower than that of the PrLTF spike. For dry eye, osmolarities in break-up and non-break-up areas were elevated for a given D_s, k_s, and h_{lens}. Change in D_s significantly alters the peak magnitude.

Conclusions: SCL wear can protect the cornea against localized hyperosmolarity caused by tear break-up spots on the PrLTF. The magnitude of protection increases as the value of D_s lowers. Infrequent blinking results in higher hyperosmolarity spikes for the cornea; however, high osmolarity spikes can be prevented by lowering the D_s.

CONTROL ID: 3692981

SUBMITTER (NAME ONLY): Terin Dupre

TITLE: Intriguing linear semi-logarithmic relationships of oxygen permeability with water, silicon, and fluorine contents of silicone-hydrogel contact lens materials

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.E. Dupre, W.J. Benjamin, Vision Science Research Center, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|T.E. Dupre, Nova Southeastern University, Fort Lauderdale, Florida, UNITED STATES|W.J. Benjamin, Material Performance Assessments, LLC, Hoover, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Terin Dupre: Commercial Relationship: Code N (No Commercial Relationship) | William Benjamin: Commercial Relationship(s);Code C (Consultant/Contractor):LenTechs Inc, Mojo Vision Inc;Code O (Owner):Material Performance Assessments LLC;Code F (Financial Support):Professor Emeritus Dr. Benjamin performs research under contract by a great number of companies in the contact lens field as part of his post retirement business Material Performance Assessments LLC.

ABSTRACT BODY:

Purpose: Previously, the quadratic relationships between oxygen permeability (Dk), water (W) content, and combination of silicon and fluorine (Si+F) contents of available silicone-hydrogel (SiHy) contact lens materials were inspected (Dupre & Benjamin: Optom Vis Sci, 2020). Surprisingly, here, the relationships could also be described as linearly semi-logarithmic using the logarithm of Dk.

Methods: Sixteen contact lens brands were obtained on the market in a range of refractive powers from −3 to +6 D in single lots. Sixteen lenses per brand were tested after equilibration at 35°C in a standard saline according to ANSI Z80.20-2016 and ISO 18367-3:2017. W, Si, and F contents were obtained in % (Dupre & Benjamin: Eye & Contact Lens, 2019). Dk and the 3 contents were determined for the same lots of lenses of each lens brand.

Results: The relationships between log (Dk), W content, and (Si+F) content were described linearly: log (Dk) - 0.0098(W) + 2.3643, R2 = -0.7905 and log (Dk) = +0.0277(Si+F) + 1.6932, R2 = 0.6860. A point of equality for water and (Si+F) contents was found at W Content = (Si+F) Content = 17.9%, Dk = 154.5 Dk units and a point of equality for water contents of SiHy and conventional hydrogels (Young & Benjamin: Eye & Contact Lens, 2003) was found at W Content = 72.3%, Dk = 45.2 Dk units. The points of equality were similar to those found using the quadratic analyses.

Conclusions: There was a negative semi-logarithmic relationship between log Dk and W content and a positive linear semi-logarithmic relationship between log (Dk) and (Si+F) content. The coefficients of determination were slightly greater for the semi-log analyses as for the quadratic analyses. Thus, quadratic or linear semi-logarithmic equations can be used to describe the relationships within the ranges of values found in this investigation.

Note: Color digital copies of the publications cited in this abstract are available from Dr. Terin E. Dupre at td936@mynsu.nova.edu.

CONTROL ID: 3693248

SUBMITTER (NAME ONLY): Meihui Wu

TITLE: The primary angle closure glaucoma susceptibility gene EPDR1 may contribute to angle closure phenotype by affecting lens development and endoplasmic reticulum stress in lens epithelial cells

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wu, C. Ho, M. Lynn, M. Wang, A. Veluchamy, T. Aung, E.N. Vithana, A. Chan, Singapore Eye Research Institute, Singapore, SINGAPORE|T. Aung, A. Chan, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: PACG is a major cause of irreversible blindness worldwide. It is characterised by the mechanical apposition of the iris to the trabecular meshwork, resulting in anterior chamber angle narrowing and obstruction of the aqueous outflow, IOP elevation and subsequent optic neuropathy. EPDR1 was previously identified by GWAS to be a susceptibility locus in PACG, but its role in disease pathogenesis remains unknown. Our lab had previously shown EPDR1 expression in human and mouse lens epithelium, and the aim of our current study is to determine the ocular phenotype of Epdr1^{tm1b} knockout (KO) mice and elucidate the function of EPDR1 in human lens epithelial cells (HLECs).

Methods: The ocular phenotype of wildtype (WT) and Epdr1-KO mice was determined by serial IOP measurements and anterior segment OCT imaging. The HLEC line B-3 was transfected with an EPDR1 overexpression vector and the protein localisation was determined by confocal microscopy. Oxidative stress was induced in the cells by treatment with H_2O_2 and the expression of various unfolded protein response markers was analysed by qRT-PCR and western blot.

Results: For mice up to 24 weeks of age, there was a significant correlation between lens vault and age for Epdr1-KO mice but not for WT mice, suggesting that the loss of EPDR1 may cause an increase in lens thickness. No difference in IOP and anterior chamber depth was detected between KO and WT mice. EPDR1 is predominantly localised in the endoplasmic reticulum (ER) of B-3 cells and its overexpression in B-3 cells resulted in an increase in the baseline levels of the ER chaperone protein BiP and the ER stress-regulated transcription factor ATF6, suggesting a role of EPDR1 in ER stress response. Furthermore, B-3 cells treated with H_2O_2 expressed higher levels of BiP in the presence of EPDR1 overexpression, although EPDR1 overexpression did not protect cells from oxidative stress-induced apoptosis.

Conclusions: Our findings suggest that the in vivo loss of EPDR1 expression may affect lens vault and thickness as a potential mechanism in angle closure pathogenesis. BiP may work in tandem with EPDR1 during acute oxidative stress to promote the survival of lens epithelial cells. However, EPDR1 overexpression may not be able to protect against apoptosis during prolonged oxidative stress.

CONTROL ID: 3693292

SUBMITTER (NAME ONLY): Kasey Johnson

TITLE: A 10-Year Review of Management of Ocular Mucous Membrane Pemphigoid: A Private Practice Experience

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Johnson, K.S. Michels, Washington State University Elson S Floyd College of Medicine, Spokane, Washington, UNITED STATES|J.T. Rosenbaum, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|J.T. Rosenbaum, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|J.T. Yarter, University of Washington School of Medicine, Spokane, Washington, UNITED STATES|T. Broadbent, K.S. Michels, Northwest Eyelid & Orbital Specialists, Spokane, Washington, UNITED STATES|

Commercial Relationships Disclosure: Kasey Johnson: Commercial Relationship: Code N (No Commercial Relationship) | James Rosenbaum: Commercial Relationship(s);Code C (Consultant/Contractor):Gilead, Abbvie, Novartis, Roche, Revolo, Corvus, Horizon;Code F (Financial Support):Pfizer, Horizon;Code I (Personal Financial Interest):UpToDate;Code E (Employment):Celgene-Bristol Myers | Jason Yarter: Commercial Relationship: Code N (No Commercial Relationship) | Talmage Broadbent: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Michels: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular mucous membrane pemphigoid (OcMMP) is a rare and potentially blinding condition for which consensus treatment guidelines do not exist. The purpose of this study was to assess the effectiveness and safety of various immunomodulatory agents in the treatment of OcMMP in a private practice setting.

Methods: We conducted a 10-year retrospective chart review of patients managed with OcMMP between 2011 and 2021 (n=22) at Northwest Eyelid & Orbital Specialists (Spokane, WA). Median age at diagnosis was 73 (Range: 35-91) and 59% (13/22) of patients were female. Visual acuity, Foster stage, and adverse effects (AE) were documented. A treatment episode (TE) was defined as initiation of a single immunomodulatory agent or a therapeutic combination of agents. For each TE, treatment outcomes were qualified at 3 months as a complete response (CR), response (R), or failure (F). After 3 months, CR was then further qualified as either sustained CR (CR_s), reactivation after initial CR (CR_r), or AE after initial CR (CR_a). Fisher's exact test p-values were calculated for each TE's outcome and discontinuation rate due to AE in comparison with mycophenolate.

Results: Twenty patients were treated with an immunomodulatory agent for a total of 55 TEs. Treatment outcomes are displayed in Figure 1. In comparison to dapsone, mycophenolate was more likely to achieve CR_s (50% vs. 0%, p=.022) and R (100% vs. 50%, p=.007), and less likely to fail (0% vs. 50%, p=.007). Figure 2 displays a Kaplan-Meier persistence curve for each immunomodulatory agent. Dapsone was also more likely to be discontinued due to AE than mycophenolate (40% vs. 6%, p=.041). Foster stage progression occurred in 14% (6/44) of eyes, and visual acuity worsened in 20% (9/44).

Conclusions: Mycophenolate is a superior first-line agent to dapsone in the treatment of OcMMP. Although not statistically significant, mycophenolate trends toward superiority over methotrexate as well. Mycophenolate is very effective when used in combination with rituximab. Azathioprine remains a reasonable second-line agent.

CONTROL ID: 3693470

SUBMITTER (NAME ONLY): ByungJin Kim

TITLE: Results of office-based air-fluid exchange for post vitrectomy hemorrhage in diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kim, M. Lee, Department of Ophthalmology, Uijeongbu Saint Mary's Hospital, Uijeongbu, Gyeonggi-do, KOREA (THE REPUBLIC OF)|G. Kim, Department of Ophthalmology, Catholic University of Korea Yeouido Saint Mary's Hospital, Yeongdeungpo-gu, Seoul , KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: ByungJin Kim: Commercial Relationship: Code N (No Commercial Relationship) | Gee Hyun Kim: Commercial Relationship: Code N (No Commercial Relationship) | Mee Yon Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the efficacy and clinical outcomes of one-way air-fluid exchange(AFE) procedure for treatment of post vitrectomy diabetic vitreous hemorrhage (PDVH) in patients with proliferative diabetic retinopathy (PDR).

Methods: We performed a retrospective study including 233 patients with PDR who underwent vitrectomy. One-way AFE procedure was performed for 24 eyes of 24 (10.30%) patients with persistent vitreous cavity rebleeding after the operation. Pre-procedural and post-procedural best corrected visual acuity (BCVA) were achieved. Occurrences of intra-procedural and post-procedural complications were analyzed.

Results: Significant visual improvement was observed at one month after the one-way AFE procedure (2.62 ± 0.60 LogMAR at baseline vs. 0.85 ± 0.94 LogMAR at post-procedure, $p < 0.0001$). Nineteen (79.17%) cases needed the procedure only once. Five (20.83%) cases underwent the procedure more than twice. In three (12.50%) cases, reoperation was eventually required due to persistent rebleeding despite several AFEs. No complication was observed during follow-ups.

Conclusions: One-way AFE procedure can be an excellent alternative to re-vitrectomy for patients suffering from PDVH on PDR by removing the bloody content in the vitreous cavity efficiently and permitting rapid visual recovery without causing obvious complications.

CONTROL ID: 3693479

SUBMITTER (NAME ONLY): Michael Whitehead

TITLE: Perioperative prednisolone administration attenuates systemic immune activation following intravitreal injection of AAV2, but fails to enable repeated gene transfer to the inner retina

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Whitehead, P. Yu-Wai-Man, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Michael Whitehead: Commercial Relationship: Code N (No Commercial Relationship) | Patrick Yu-Wai-Man: Commercial Relationship(s);Code C (Consultant/Contractor):GenSight

ABSTRACT BODY:

Purpose: Injection of adeno-associated virus serotype 2 (AAV2) vectors into the vitreous is associated with the induction of innate and adaptive immune responses that may limit therapeutic efficacy and inhibit vector readministration. Prednisolone is a glucocorticosteroid immunosuppressant that is commonly administered alongside intravitreal (IVT) injection of AAV2 in patients to limit the onset, duration and severity of intraocular inflammation. Whether this strategy can be utilised to enable vector readministration via attenuation of humoral immune activation, however, is unclear.

Methods: Adult male C57BL6/J mice were treated with 0.75 mg/kg/day prednisolone or PBS via intraperitoneal injections throughout the study. At 3wk, bilateral IVT injections of 1E10 viral genomes (vg)/eye AAV2.CAG.GFP were performed. At 6wk, mice received a second set of bilateral IVT injections of 1E10 vg/eye AAV2.CMV.mCherry. Mice were sacrificed at 9wk and eyes were processed into cryosections for immunohistochemical analysis. Spleens were extracted and lymphocyte populations were assessed with flow cytometry. Serum samples were collected throughout the study to assess levels of neutralising antibodies (NAbs) and total antigen-binding antibodies (TAbs).

Results: Prednisolone treatment was associated with significant reductions in NAb and TAb synthesis, and attenuated CD4 & CD8 T-cell and activated B-cell infiltration into the retina. Mechanistically, this was correlated with the inhibition of splenic germinal centre reactions and B-cell class-switching, however, regulatory T-cell levels were not changed in immunosuppressed mice. Despite the significant reduction in humoral immune activation exhibited in prednisolone-treated mice, the immunosuppressant alone proved insufficient in enabling vector readministration to the inner retina.

Conclusions: The present study highlights a cellular and molecular basis for perioperative steroid immunosuppression in attenuating anti-AAV2 immune activation when delivered via IVT injection. However, further improvements to circumvent humoral immune responses are likely to be required to enable vector readministration.

CONTROL ID: 3693516

SUBMITTER (NAME ONLY): Nikhil Sharma

TITLE: Practitioners' perspectives on Demodex blepharitis: a comparison between eye care practitioners in India and Australasia

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Sharma, E. Martin, I. Pearce, S. Hagan, Vision Sciences, Glasgow Caledonian University, Glasgow, Glasgow, UNITED KINGDOM|J.P. Craig, The University of Auckland, Auckland, Auckland, NEW ZEALAND|

Commercial Relationships Disclosure: Nikhil Sharma: Commercial Relationship: Code N (No Commercial Relationship) | Eilidh Martin: Commercial Relationship: Code N (No Commercial Relationship) | Ian Pearce: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Hagan: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Craig: Commercial Relationship(s);Code C (Consultant/Contractor): Théa Laboratoires, Azura Ophthalmics, E-Swin, Alcon, Manuka Health NZ

ABSTRACT BODY:

Purpose: Demodex blepharitis remains an under-diagnosed condition, lacking universally-accepted diagnostic and management protocols. The primary aim of this study was to compare how eye care professionals in different regions of the world diagnose and manage Demodex blepharitis.

Methods: Ophthalmologists and optometrists in India and Australia/New Zealand were invited to complete an online survey on Demodex blepharitis. Practitioner demographics and views on eyelid health in general, as well as details of diagnostic and management practices from those reporting that they treat Demodex blepharitis in clinical practice, were collected. Mann-Whitney U, and Fisher's exact tests were used for statistical analysis.

Results: A total of 261 eyecare professionals completed the survey, 207 from India (84% optometrists); 54 from Australia and New Zealand (91% optometrists). Almost 70% of practitioners across the 3 countries considered Demodex blepharitis to be a cause of ocular discomfort, yet only 45% reported attempting to identify Demodex in their patients. There were significant differences in practice patterns between practitioners in Australasia and India. Practitioners' views differed in terms of perceived prevalence of Demodex blepharitis (60% in Australasia vs 27% in India; $p<0.001$), choice of slit lamp magnification used to detect the mites (25x in Australasia vs 16x in India; $p = 0.002$), preferred treatment option to manage Demodex blepharitis (tea tree oil in Australasia vs Standard lid hygiene in India; $p = 0.001$), treatment duration (3-4 weeks to more than 12 weeks in Australasia vs 3-4 weeks in India; $p = 0.002$) and frequency of treatment (once a day in Australasia vs twice a day in India; $p = 0.001$).

Conclusions: This study highlights differences in clinical evaluation and treatment practices between practitioners in India and Australasia. Overall, practitioners in Australia and New Zealand were more rigorous in their investigation and management. However, in both regions interprofessional differences in perceived optimal treatment duration and frequency were reported, highlighting a need for standardised treatment protocols to be developed for Demodex blepharitis.

CONTROL ID: 3693728

SUBMITTER (NAME ONLY): J. Mark Petrash

TITLE: Metformin-mediated suppression of EMT in lens epithelial cells

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Petrash, B. Shieh, M. Pedler, Ophthalmology, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: J. Mark Petrash: Commercial Relationship: Code N (No Commercial Relationship) | Biehuoy Shieh: Commercial Relationship: Code N (No Commercial Relationship) | Michelle Pedler: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In a study of patient outcomes from cataract surgery at our institution, we previously observed that patients with a history of metformin exposure had a lower risk for YAG capsulotomy (PMID: 34415985). This observation indicated that metformin may have a protective effect against development of posterior capsule opacification (PCO). The purpose of the current study is to use a mouse model to test whether metformin protects against early steps of PCO development.

Methods: We carried out extracapsular lens extraction (ECLE) in mice as a model for cataract surgery. Metformin was given in drinking water (10-50 mg/kg/day), starting 2 days prior to ECLE, and continued until animals were euthanized at day 5 after surgery and eyes processed for immunohistochemistry or extraction of RNA and protein. Molecular markers associated with epithelial-to-mesenchymal transition (EMT) were quantified by Western blotting or qRT-PCR. Mouse lens epithelial cells (LEC) cultures produced from lenses of wild type and aldose reductase-transgenic mice (AR-Tg) were also used to probe the effect of metformin on TGF-β-induced changes in markers associated with EMT.

Results: Treatment of primary LEC cultures with TGF-β led to upregulation of αSMA ($p<0.05$) and stimulation of ERK phosphorylation ($p<0.05$), well established markers of early steps in development of PCO. Treatment with 1 mM metformin suppressed activation of Smad2/3 and upregulated the inhibitory Smad7, resulting in downregulation of αSMA ($p<0.01$). Similarly, immunohistochemical staining showed that expression levels of αSMA in lens capsular bags 5 days following ECLE were substantially reduced by metformin in drinking water as compared to surgical eyes from animals provided regular drinking water. In mouse LEC cultures, metformin treatment led to a dose-dependent increase in AMPK activation as evidenced by levels of AMPKα-subunit phosphorylation ($p<0.01$). Levels of αSMA transcripts in capsular bags of ECLE mice remained suppressed for up 9 days following termination of metformin therapy ($p=0.003$), suggesting a durable effect of metformin against EMT during this timeframe.

Conclusions: Metformin, a well established AMPK activator, is an effective inhibitor of signaling pathways known to be activated in the pathogenesis of EMT. Further studies are warranted to determine the utility of this safe and effective drug against the onset and progression of changes leading to PCO following cataract surgery.

CONTROL ID: 3693943

SUBMITTER (NAME ONLY): Matthew Lam

TITLE: Computational Modeling of Soccer Ball Trauma of the Eye and Comparison With Abusive Head Trauma

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lam, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|P. Dong, Y. Shokrollahi, L. Gu, Florida Institute of Technology, Melbourne, Florida, UNITED STATES|D.W. Suh, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Matthew Lam: Commercial Relationship: Code N (No Commercial Relationship) | Pengfei Dong: Commercial Relationship: Code N (No Commercial Relationship) | Yasin Shokrollahi: Commercial Relationship: Code N (No Commercial Relationship) | Donny Suh: Commercial Relationship: Code N (No Commercial Relationship) | Linxia Gu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular pathology from soccer ball-induced trauma to the eye has been documented in detail, but the underlying mechanics are not as well-studied. This study utilized a computer simulation to evaluate the biomechanical events following the collision of a soccer ball with the eye to better understand the pathophysiology of ocular and retinal injuries that commonly arise. These injuries and their mechanisms were also compared to those observed in abusive head trauma (AHT).

Methods: A finite element computer model of the eye containing 140,770 analyzable nodes was simulated and subjected to a collision by a soccer ball simulated with regulation parameters. Resulting changes in intraocular pressure and stress within the ocular tissue and retina were measured.

Results: Impact of the soccer ball with the eye generated a pressure wave in the vitreous. The pressure wave created pockets of high and negative pressure within the vitreous as it traveled posteriorly. Pressure in the vitreous near the posterior pole flucuated between 39.6 kPa and -30.9 kPa before stabilizing. Stress in ocular tissue was greatest near the point of contact and peaked at 66.6 kPa. Stress in the retina was largely concentrated at the vasculature, especially at distal branches where stress rose to 15.4 kPa. On average, the retinal layer that experienced the most stress was the subretinal layer, but when only considering vascular tissue, the preretinal layer experienced the most.

Conclusions: High intraocular pressure and stress in ocular tissue near the point of soccer ball impact suggest that anterior segment injuries can be attributed to direct transmission of force from the ball. The pressure wave that follows likely accounts for injuries to the posterior segment as the positive and negative pressures in the vitreous exert compressive and tractional forces on the retina. The linear movement of the pressure wave may cause the localization of retinal lesions to the posterior pole. This differs from the diffuse distrubution of retinal hemorrhage in AHT, likely due to the presense of repetitive angular force in AHT, which is absent in soccer ball truama. These quantitive findings provide a foundation for future comparisons of the efficacy of protective eyewear models for soccer ball trauma.

CONTROL ID: 3694012

SUBMITTER (NAME ONLY): Arthur Ho

TITLE: Computational evaluation of a novel intraocular lens design for controlling negative peripheral pseudophakic dysphotopsia

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|A. Ho, School of Optometry & Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Arthur Ho: Commercial Relationship(s);Code P (Patent):WO 2021/181300 A1

ABSTRACT BODY:

Purpose: Pseudophakic individuals experiencing negative peripheral dysphotopsia (DYS) report a persistent 'shadow' in their far peripheral visual field. The optical basis of DYS has been identified previously.[1] While some designs have been evaluated[2], no IOL designed specifically for controlling DYS are currently clinically available. In this study, the efficacy of a novel IOL design for controlling DYS is evaluated through computational modelling.

Methods: A 3D model of a pseudophakic eye based on the Escudero-Navarro Eye Model[2] was constructed (Figure 1). For control evaluation, an equiconvex intraocular lens (+22 D power, refractive index 1.55, 6 mm optic diameter) was placed in the model. Non-sequential optical ray-tracing using OpticStudio (Zemax, Kirkland WA) was conducted with incident light angle ranging from 55° to 100° in 0.5° steps. At each incident angle, 10,000 randomly distributed parallel rays were traced through the model. Using an analysis method based on Simpson (2019)[3], the relative retina intensity distribution (RID) was computed from the range of incident angles. The analysis was repeated for all combinations of pupil diameters (PD) from 2.0 mm to 5.0 mm in 0.5 mm steps, and lens axial positions (LAP) from 0.0 mm to 1.0 mm in 0.1 mm steps. The evaluation process was repeated for an IOL comprising the same central optical zone parameters but enhanced with novel peripheral surface contours described using cubic Bezier curves for preventing DYS.

Results: For the control lens, discrete combinations of PD and LAP resulted in illumination gaps in the RID (e.g. Figure 2a), indicating potential presence of DYS. An interplay between PD and LAP was evident leading to DYS at various PD over different LAP (and vice versa). For the novel lens design, RID results show no illumination gaps at any combinations of PD and LAP (e.g. Figure 2b).

Conclusions: The novel IOL design appears to be effective in controlling DYS over a range of PD and LAP. The seemingly quasi-random clinical presentation of DYS may be partially explained by the interplay of PD and LAP on the formation of retina illumination gaps.

References

1. Holladay & Simpson 2017 JCRS
2. Escudero-Sanz & Navarro 1999 JOSA
3. Erie et al 2019 JCRS
4. Simpson 2019 JOSA

CONTROL ID: 3694019

SUBMITTER (NAME ONLY): Justin Muste

TITLE: Novel Lens Correction Method in Flavoprotein Fluorescence Imaging

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Muste, M. Russell, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|C. Rich, K. Riegger, OcuSciences Inc, Michigan, UNITED STATES|M. Russell, R.P. Singh, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Justin Muste: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Russell: Commercial Relationship: Code N (No Commercial Relationship) | Collin Rich: Commercial Relationship(s);Code E (Employment):OcuSciences | Kurt Riegger: Commercial Relationship(s);Code E (Employment):OcuSciences | Rishi Singh: Commercial Relationship(s);Code I (Personal Financial Interest):Genentech/Roche;Code I (Personal Financial Interest):Alcon/Novartis;Code F (Financial Support):Apellis;Code I (Personal Financial Interest):Zeiss;Code I (Personal Financial Interest):Bausch and Lomb;Code I (Personal Financial Interest):Regeneron;Code F (Financial Support):Graybug

ABSTRACT BODY:

Purpose: Flavoprotein fluorescence (FPF) imaging provides a readout of retinal oxidative stress by quantifying natural autofluorescence of oxidized retinal mitochondrial flavoproteins (535 nm) after blue light excitation (467 nm). Natural fluorophores in a patient's lens get brighter with oxidative stress and so may confound the desired retinal FPF signal, resulting in a combined lens and retinal fluorescence signal that elevates the FPF score. At the same time, natural lens aging can attenuate the signal. The purpose of this study was to generate and evaluate a lens correction algorithm (LCA) for use with FPF imaging.

Methods: Lens fluorescence and transmission were accounted for in a two-step process. First, interpolation was used to generate an estimate of lens fluorescence and isolate the retinal component. Second, after an adjustment for instrument calibration, natural lens attenuation was compensated using a third-order model. The efficacy of the LCA was assessed in 544 images of healthy control patients with no ocular pathology from different databases obtained automatically generated by Ocumet ® Image Analysis software at the time of patient presentation. A case study is also presented of a patient with images before and after cataract surgery, highlighting clinical relevance of this application.

Results: After the LCA was applied the raw FPF scores of 554 images, the slope of best fit was attenuated (m= 1.4556 vs m= 0.0584) suggesting the correction algorithm was successful in accounting for native lens autofluorescence. Signals clustered tightly around line of best fit before and after compensation. A positive age-dependent relationship was maintained, although largely adjusted for (R^2= 0.7012 vs 0.0185). After adjustment, FPF intensity scores displayed similar strength positive relationships with age when compared to patients with intraocular lens implants (IOL), which display minimal fluorescence (R^2= 0.0165 vs 0.0193).

Conclusions: The LCA reduced the effects of the aging lens and addressed an important confounder in measuring retinal FPF. Future work may test this algorithm on a large cohort of cataract patients after phacoemulsification and IOL implantation to confirm the FPF signal changes from aging lens fluorescence contribution

CONTROL ID: 3694257
SUBMITTER (NAME ONLY): Pete Williams
TITLE: Targeting NMNAT2 for neuroprotection in glaucoma
SESSION TITLE: Neuroprotection and neuroregeneration
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: P.A. Williams, J.R. Tribble, M. Jöe, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|M. Coleman, J. Gilley, A. Loreto, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|C. Wheelock, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|G. Johannesson, Umea Universitet, Umea, SWEDEN|A. Brancale, C. Varricchio, Cardiff University, Cardiff, South Glamorgan, UNITED KINGDOM|G. Johannesson, Wallenberg Centre for Molecular Medicine, Umea Universitet, Umea, SWEDEN|
Commercial Relationships Disclosure: Pete Williams: Commercial Relationship: Code N (No Commercial Relationship) | James Tribble: Commercial Relationship: Code N (No Commercial Relationship) | Melissa Jöe: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Brancale: Commercial Relationship: Code N (No Commercial Relationship) | Carmine Varricchio: Commercial Relationship: Code N (No Commercial Relationship) | Michael Coleman: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Gilley: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Loreto: Commercial Relationship: Code N (No Commercial Relationship) | Craig Wheelock: Commercial Relationship: Code N (No Commercial Relationship) | Gauti Johannesson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is the leading cause of irreversible blindness. Despite treatments to lower intraocular pressure many patients will continue to go blind. Neuroprotective therapies that target the retina and optic nerve in glaucoma are of great therapeutic need. Repleting NAD robustly protect from glaucoma-related insults in a variety of animal models and improves visual function in existing glaucoma patients.

Methods: The aim of this study is to assess the role of NMNAT2 in glaucomatous neurodegeneration and neuroprotection. NAD production in retinal ganglion cells is controlled through two terminal enzymes; NMNAT1 (localized to the nucleus) and NMNAT2 (localized in the cytoplasm). NMNAT2 is expressed exclusively in neurons and shows high expression in retinal ganglion cells. We used rodent and cellular systems to assess the role of high and low NMNAT2 in retinal ganglion cell susceptibility to neurodegeneration (genetic, viral gene therapy, and pharmacology).

Results: We demonstrate that there is down-regulation of NMNAT2 in models of glaucoma and retinal ganglion cell axon degeneration and confirm this in post-mortem human glaucoma tissue. Gene therapy restoring NMNAT2 levels to retinal ganglion cells robustly protects from glaucoma and axon injury (in vivo and ex vivo models). Supporting this, mice with genetically depleted NMNAT2 show increased susceptibility to glaucoma related injury. To further target NMNAT2 function, we have identified novel NMNAT2 activators that work in an NAD/NMN- and NMNAT2- dependent mechanism (this specificity was confirmed by using pharmacological and genetic inhibition of enzymes in the NAD-salvage pathway in vitro and in vivo). We are now developing novel pharmacology based on this.

Conclusions: NMNAT2 is an important generator of NAD in retinal ganglion cells and low NMNAT2 critically drives retinal ganglion cell susceptibility to glaucoma-related stresses. Targeting NMNAT2 via viral gene therapy or novel small molecule pharmacology generates NAD and protects from neurodegeneration.

CONTROL ID: 3694445

SUBMITTER (NAME ONLY): W. Clay Smith

TITLE: A modified arrestin1 increases lactate production in the retina and slows retinal degeneration

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Smith, T.S. Nelson, C. Simpson, F.M. Dyka, A. Dinculescu, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

Commercial Relationships Disclosure: W. Clay Smith: Commercial Relationship(s);Code P (Patent):PCT/US2021/022899 | Tiffany Nelson: Commercial Relationship: Code N (No Commercial Relationship) | Chiab Simpson: Commercial Relationship: Code N (No Commercial Relationship) | Frank Dyka: Commercial Relationship: Code N (No Commercial Relationship) | Astra Dinculescu: Commercial Relationship(s);Code P (Patent):PCT/US2021/022899

ABSTRACT BODY:

Purpose: Glucose metabolism in the retina is carefully orchestrated, with glucose being delivered to photoreceptors from the choroidal circulation through the RPE. In photoreceptors, glucose is processed principally by aerobic glycolysis, from which the lactate byproduct is provided to the RPE and Müller glia for their energetic needs. In this study, we utilize a modified arrestin1 protein to enhance the glycolytic output of lactate from rod photoreceptors through disinhibition of enolase1 activity with the goal being to use this increased lactate production as a gene-agnostic approach for slowing retinal degeneration.

Methods: Mouse arrestin1 with E362G/D363G amino acid substitutions (referred to “ArrGG”) was packaged into AAV2-quadY-F+T-V serotype and tested for safety and for efficacy in increasing retinal lactate production. The modified arrestin1 was then delivered intravitreally to the P23H rhodopsin knock-in mouse model of retinitis pigmentosa ($Rho^{P23H/+}$) to determine if enhancing glycolysis in photoreceptors can slow retinal degeneration. Retinal health was measured by electroretinograpy, optical coherence tomography, and histology.

Results: Overexpression of ArrGG in C57BL/6J mice did not result in any detectable changes in either ERG function or photoreceptor survival as measured by outer nuclear layer thickness. However, mouse retinas expressing ArrGG showed a ~25% increase in the rate of lactate secretion. In P23H rhodopsin mice, expression of ArrGG slowed the decline of both scotopic and photopic ERG function. Correspondingly, there was significant preservation of ONL thickness in mice treated with ArrGG compared to controls. Furthermore, ArrGG-treated retinas showed a significantly higher rate of lactate secretion compared to controls.

Conclusions: Our studies show that expressing ArrGG in C57BL/6J mouse retina resulted in an increase in lactate production, consistent with an upregulation of glycolysis. In the P23H rhodopsin model of retinitis pigmentosa, the expression of ArrGG led to significant preservation of photoreceptor function and slowing of retinal degeneration. These findings suggest that enhancing glycolysis by targeting increased enolase1 activity with a modified arrestin1 in photoreceptors may offer a gene-independent therapeutic approach to slowing retinal degeneration.

CONTROL ID: 3694585

SUBMITTER (NAME ONLY): Renu Kowluru

TITLE: Role of Mitochondrial Genome-encoded Long Non-coding RNA in Diabetic Retinopathy

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Kowluru, G. Mohammad, Ophthalmology, Visual & Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Renu Kowluru: Commercial Relationship: Code N (No Commercial Relationship) | Ghulam Mohammad: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mitochondrial DNA (mtDNA), a 16.7kb circular DNA, is damaged in diabetic retinopathy and its transcription is impaired, and the electron transport chain is compromised, fueling into the vicious cycle of free radicals. Diabetes also alters expressions of many long non-coding RNAs (LncRNAs), the RNAs with more than 200 nucleotides and no open reading frame for translation. Although most of the LncRNAs are encoded by nuclear genome, mitochondrial genome also encodes three LncRNAs, and the expression of mtDNA-encoded LncRNA Cytochrome B (LnCytB) is decreased in diabetes. The aim of this study was to investigate the role of LncCytB in mtDNA stability in diabetic retinopathy.

Methods: Human retinal endothelial cells, incubated in normal (5mM) or high (20mM) D-glucose for four days, were analyzed for LncCytB expression by qRT-PCR and strand-specific PCR, and its mitochondrial localization by RNA fluorescence in situ hybridization (RNA-FISH)-immunofluorescence technique. Packaging of the mtDNA was determined by Flow Cytometry and by its sensitivity to Micrococcal nuclease digestion. The role of LncCytB in mtDNA stability was confirmed in HRECs transfected with LncCytB by quantifying mtDNA damage (by extended length PCR) and its protective nucleoids (by SYBR green staining).

Results: Compared to normal glucose, high glucose decreased LnCytB levels in the mitochondria. While the sensitivity of mtDNA to Micrococcal nuclease was increased, packaging of mtDNA and its protective nucleoids were decreased. Overexpression of LnCytB ameliorated glucose-induced increase in mtDNA damage and decrease in mtDNA-encoded nucleoids.

Conclusions: Downregulation of LncCytB in the mitochondria in hyperglycemic milieu reduces the protective nucleoids, which makes mtDNA more susceptible to the damage. The damaged mtDNA compromises the electron transport chain and the vicious cycle of free radicals continues to self-propagate. Thus, regulation of LnCytB has potential to prevent mtDNA damage, and the progression of diabetic retinopathy.

CONTROL ID: 3694701

SUBMITTER (NAME ONLY): Yangjiani Li

TITLE: Thickness of ten retinal layers from macular optical coherence tomography (OCT) volume scans in participants with and without diabetes and their relationship with glucose metabolism

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: We investigate the relationship between macular retinal thickness and glucose tolerance in a large population-based study.

Methods: All participants with available measurements (C-peptide, fasting plasma glucose, HbA1c, and OCT scans) from the LIFE-Adult study, a population-based, sex- and age-stratified study, were included. Macular volume scans (97 B-scans by 512 A-scans) from Spectralis OCT were automatically segmented into ten layers after excluding low-quality (< 20 dB) B-scans. The Early Treatment Diabetic Retinopathy Study (ETDRS) grid was used to calculate average sectorial thickness, adjusted by scan length and location of the fovea center. Figure 1 shows the abbreviations of layers and sectors. ANOVA, t-test (significance level: $p<0.05$), and linear regression (Akaike Information Criterion [AIC] difference >6 defining a strong effect) were used to identify and compare impacts on retinal thickness.

Results: Figure 1A shows the average of ETDRS sectorial thickness in ten layers of the selected 13138 eyes (7234 participants), grouped as diabetic, prediabetic, and normal glucose tolerant. As we did not find significant lateral differences, only right-eye results are presented (6597 eyes/participants). Figure 1B-C reveals extensive retinal thinning in the diabetic group compared with the subjects with normal glucose tolerance, especially in inner layers, with stronger effects for males compared to females. Increasing age was significantly associated with retinal thinning in nearly all layers except RNFL, OPL, and IZ, where age had no or opposite effects (Figure 2A). Apart from age, diabetes-related parameters (e.g., C-peptide) exhibited additional effects on retinal thinning (Figure 2B-C). In males, strong effects of C-peptide were observed in the inner sectors of RNFL, GCL, IPL, outer sectors of ONL, and MZ,

while in females, effects were more pronounced in the outer sectors of ONL, MZ, and some sectors in EZ+OS.
Conclusions: In this large population-based sample, participants with diabetes showed extensive retinal thinning compared to normal glucose tolerant subjects. Age had strong effects on retinal thinning. In addition, diabetes-related parameters were linked to thickness of specific layers, with different patterns in males and females.

CONTROL ID: 3694777

SUBMITTER (NAME ONLY): Mengming Hu

TITLE: Srebf2 is necessary for axon regeneration and visual recovery following optic nerve crush in adult zebrafish

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hu, R. Newland, M.B. Veldman, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Failure of retinal ganglion cell (RGC) axon regeneration prevents recovery of vision in optic neuropathy conditions like glaucoma. Due to the poor regenerative capacity of the adult mammalian central nervous system, finding ways to stimulate successful axonal regeneration in humans remains challenging. Unlike patients and mammalian model organisms, adult teleost fish can fully regenerate RGC axons enabling functional recovery from optic nerve injury. We are using the zebrafish model to probe the mechanisms of successful axon regeneration with the hopes of translating these findings to improve regeneration in mammals and eventually patients.

Methods: Laser Capture Microdissection RNA-seq (LCM-seq) was used to determine differentially expressed genes in the retinal ganglion cell layer of adult zebrafish 3 days post optic nerve crush versus uninjured control. Bioinformatic analysis was used to identify pathways and gene sets that are enriched in differentially expressed genes. To test the importance of srebf2 specifically, fatostatin drug treatment and morpholino antisense were used to antagonize its function. Axon regeneration into optic nerve at 3 days and optic tectum at 7 days post injury was analyzed by measuring GFP intensity using gap43:GFP transgenic zebrafish. The dorsal light response test was used to measure visual recovery at multiple times post injury. To assay RGC survival, whole mount retina with Hoechst stain was used to counting cell densities after each treatment.

Results: Retinal ganglion cell layer LCM-seq identified genes in the mevalonate/cholesterol synthesis pathway that are upregulated during axon regeneration. The master transcriptional regulator of this pathway, srebf2, was also highly upregulated. In comparison to untreated or vehicle treated control groups, srebf2 inhibited by either fatostatin or morpholino decreased axon regeneration into the optic tectum at both 3 days and 7 days post injury and delayed recovery of the dorsal light response over the course of normal optic nerve regeneration without causing any significant loss of RGCs.

Conclusions: These data indicate that srebf2 plays an important role in regulating efficient axon regeneration in the zebrafish visual system and suggests that the mevalonate/cholesterol synthesis pathway and its downstream products may have a role in this effect.

CONTROL ID: 3694926

SUBMITTER (NAME ONLY): Cynthia Owsley

TITLE: A Conceptual Framework for Visual Function Impairment from Normal Aging to Early and Intermediate AMD: ALSTAR2 Cross-sectional Results

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Owsley, T.A. Swain, G. McGwin, M. Clark, J. Crosson, C.A. Curcio, Ophthalmology & Visual Sciences, UAB Heersink School of Medicine, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our conceptual framework for how visual function changes from normal aging to early and intermediate AMD specifies that the first visual dysfunction in AMD is delayed rod-mediated dark adaptation (RMDA), impacting photoreceptor sustenance (eg retinoid re-supply), including changes in choriocapillaris and RPE, and appearance of lipoprotein containing deposits. While evaluating this framework requires a longitudinal analysis, this cross-sectional analysis compares RMDA and other visual functions (acuity, contrast sensitivity, light sensitivity) between aged normal, early and intermediate AMD eyes, providing insight as to the validity of our framework.

Methods: ALSTAR2 is a prospective cohort study to examine functionally validated structural endpoints in normal aging and early and intermediate AMD. At baseline participants were recruited based on ICD10 codes in EHR. AMD disease presence and severity was determined via color fundus photos evaluated by a masked grader using the AREDS 9-step system. Visual functions evaluated were RMDA (5° eccentricity, 83% equivalent bleach), acuity and contrast sensitivity (photopic, mesopic), and light sensitivity for a 21-target grid in the macula (scotopic, mesopic, photopic) using S-MAIA and HFA.

Results: N=482 eyes from 482 persons (M age 72, 60-90 years) were evaluated (60% women, 91% white). Delayed RMDA was the most common visual dysfunction present in 36% of eyes in normal aging, increasing in prevalence to 51% and 94% in early and intermediate AMD respectively (Table 1). The difference in the prevalence of other visual dysfunctions was considerably less than for RMDA. Using z-scores to standardize measures, the largest difference in function by AMD status and severity was for RMDA between aged normal and intermediate AMD. While other functions were reduced among intermediates compared to normal, all differences were less than half that of RMDA (e.g., scotopic light sensitivity=0.75 SD). Of all functions, RMDA also had the greatest difference between aged normal and early AMD (0.30 SD).

Conclusions: Among the visual functions considered, the greatest difference between AMD and normal eyes is for RMDA. This finding provides indirect support for the hypothesis that RMDA is the first visual function impacted during the natural history of AMD, which will be examined longitudinally at the ALSTAR2 three-year follow-up visit.

CONTROL ID: 3694928
SUBMITTER (NAME ONLY): Mark Bullimore
TITLE: Final Level of Myopia versus Age of Onset: Effect of Race and Age at Final Refraction
SESSION TITLE: Refractive Error and Social Determinants of Vision Function
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: M.A. Bullimore, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|N.A. Brennan, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|
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ABSTRACT BODY:
Purpose: Myopia severity has a profound impact on visual impairment in later life. A patient's final level of myopia may be lowered by myopia control, but also by delaying onset. Here we evaluate the influence of age of onset on the final recorded level of myopia.
Methods: Data were extracted from the following reports:
- two prospective cohort studies of myopia progression in East Asia where final recorded level of myopia is presented as a function of age of onset (Chua et al., 2016; Hu et al., 2020)
- two retrospective studies of myopia progression in India and the Netherlands (Verkicharla et al., 2004; Polling et al., 2021)
- two cross-sectional studies in Argentina and the UK (Iribarren et al., 2004; Williams et al., 2013).

For the above, age of onset was based on self-report of age at first spectacle prescription and the midpoint was used for all age ranges.
A seventh set of data comprised Finnish subjects originally recruited for a clinical trial and followed into adulthood (Parssinen et al., 2019). Subjects were divided into five groups according to age at recruitment which was used as a surrogate for age of onset.
Results: Figure 1 shows the final recorded level of myopia as a function of age of onset for the seven studies. Figure 1A shows data for the two East Asian studies. The myopia level is different because the reference ages are 11 and 17 years. The slopes are 0.97 and 0.68 D/year, meaning that each year later age of onset is associated with 0.97 or 0.68 D less myopia at the final refraction. Figure 1B shows data for the five non-East Asian studies. For four studies the slopes are substantially flatter, with slopes between 0.23 and 0.35 D/year. In contrast, the slope for the Finnish study was 0.87 D. Among subjects of European descent, increasing age of final refraction tended to be associated with higher levels of myopia.
Conclusions: Among East Asians, delaying onset of myopia by just one year has potential to lower the final level myopia by 0.75 D or more—equivalent to multiple years of myopia control with existing modalities. The benefit is lower, but meaningful, among non-East Asians. The trend linking age of final refraction with final myopia level suggests ongoing adult progression.

CONTROL ID: 3694930

SUBMITTER (NAME ONLY): Benjamin Steren

TITLE: Gender distribution in Ophthalmology Subspecialties between 1992 and 2020

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Steren, N. Kombo, Ophthalmology, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|P. Yee, S. Feng, K.L. Pepple, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe trends in the number of men and women reporting a subspecialty practice focus among American Board of Ophthalmology (ABO) Diplomates.

Methods: The de-identified records of all ABO-certified ophthalmologists between 1992-2020 were obtained. Certification year, gender, and self-reported primary practice area for each ophthalmologist were extracted. Subspecialty was defined as the self-reported primary practice area. The data was then organized (Table 1) and longitudinal trends were graphed using Microsoft Excel. Chi-square analysis was conducted using R (R Foundation, Vienna, Austria).

Results: A total of 12,844 board-certified ophthalmologists were included: 8,459 men (66%) and 4,385 women (34%). Of those, 3,940 (46%) men and 2,102 (48%) women reported a subspecialty. A significantly greater proportion of women than men reported primary practice in pediatrics (9.9% vs. 3.7%, $p < 0.001$) and glaucoma (10.4% vs. 7.4%, $p < 0.0001$). A significantly greater proportion of men than women reported primary practice in vitreoretinal surgery (22.0% vs. 10.6%, $p < 0.0001$). There was no difference between the proportion of men and women reporting cornea ($p=0.15$) or oculoplastics ($p=0.31$). The gender composition of different subspecialties has changed from 1992-2020 (Figure 1). For new ophthalmologists certifying with the ABO, Oculoplastics has shifted from 27% of women certifying in 1992 to 49% in 2020. Specialization of women has increased from 21% certifying in glaucoma and 25% certifying in cornea to almost 56% in 2020 for both specialties. Representation of women certifying per year has increased in surgical retina from 12% to 25%, however, men still outnumber women 3:1, even among ABO diplomates from 2020. Women became the majority in pediatric ophthalmology around the year 2000, and in 2020 they made up 76% of new subspecialists.

Conclusions: The number of men entering ophthalmology outnumbers that of women 2:1 over the time period of this study, hence they remain the majority in ophthalmology and consequently, in most subspecialties. The gender makeup of ophthalmology subspecialties has changed between 1992 and 2020. The changes are not uniform across subspecialties, with some subspecialties closing the gender gap.

CONTROL ID: 3695106

SUBMITTER (NAME ONLY): Bonnie Huang

TITLE: Evaluating different thresholding methods for vessel density calculations in optical coherence tomography angiography scans of diabetic macular edema eyes

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.B. Huang, J.X. Ong, A.A. Fawzi, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Different thresholding methods to remove background noise in optical coherence tomography angiography (OCTA) scans have not been studied in diabetic macular edema (DME) eyes. We tested whether vessel density (VD) values from a built-in AngioVue Analytics software (Method 1) or a deep capillary plexus (DCP) vessel length density (VLD)-based thresholding method (Method 2) would be more accurate for DME eyes.

Methods: We examined 9 DME eyes, each with 5 repeated OCTA scans. For each eye, we performed image segmentation, registration, and averaging to generate an averaged scan for the full retina as well as the SCP, MCP, and DCP slabs. We calculated the parafoveal VD of each averaged scan using an automated method available in ImageJ and used this VD as the ground truth VD. Then, for the best quality scan of each layer, we calculated the VD using both Methods 1 and 2. For statistical analysis, we calculated the mean absolute error (MAE) of each of the two methods (using the averaged scan VD as the ground truth value) and performed the two-sided paired t-test.

Results: For the DCP layer, the MAE of Method 2 was smaller than that of Method 1 ($p=0.042$). For the SCP layer, the opposite was true ($p=0.037$). For the full retina and MCP layer, Method 1 had a smaller MAE than Method 2, but the difference between the two methods was not statistically significant ($p = 0.46, 0.42$ respectively for these two slabs).

Conclusions: For DME eyes, the DCP VLD-based thresholding method (Method 2) is significantly more accurate for the DCP slab, while the AngioVue VD (Method 1) more closely matches the ground truth VD for the SCP layer. The two methods perform similarly for the full retina and MCP slab. This study highlights the importance of validating different thresholding methods for different retinal slabs in order to accurately calculate parameters such as VD for downstream analysis in eyes with different pathologies, including DME.

CONTROL ID: 3695138

SUBMITTER (NAME ONLY): Derek Nankivil

TITLE: Modelling the expected effect of correcting chromatic aberration on visual performance

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Nankivil, Research & Development, Johnson & Johnson Vision, Jacksonville, Florida, UNITED STATES|A. Roorda, N. Ivzan, M. Banks, Herbert Wertheim School of Optometry & Vision Science, University of California at Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Longitudinal Chromatic Aberration (LCA) and Transverse Chromatic Aberration (TCA) adversely affect retinal image quality. Thus, one expects improved visual performance when chromatic aberrations are minimized or eliminated. Systematic evaluation of the impact of LCA and/or TCA correction under broadband illumination is needed. The purpose of this study is to characterize the expected impact of LCA and/or TCA correction under ecologically valid broadband illumination.

Methods: Simulations utilized an ocular wavefront with +3D of spherical error and +0.06D/mm^2 of spherical aberration and a wavefront correction with a spherical aberration of -0.06D/mm^2 and a paraxial power of -2.87D. Entrance pupil diameter was 4.3mm. LCA was modeled using Thibos et al.'s (1992) chromatic eye and TCA was modeled using Thibos's (1987) modified Gullstrand reduced-eye model. Considering the human population, a range of LCA, TCA or both LCA and TCA were modeled, such that low LCA = 1.29D, high LCA = 3.57D, low TCA = 0.4, 0.2 arcmin, and high TCA = 6.3, 3.1 arcmin in the sagittal and transverse meridians from λ = 400 to 700nm. The spectral weighting function was derived considering three OLED stimuli (white, purple, and green). With the purple stimulus, luminance was equal for all three primaries. The normalized cumulative photopic efficacy weighted foveal Point Spread Function (PSF) and Modulation Transfer Function (MTF) were calculated. To provide an estimate of the perceptual impact of chromatic aberrations, the areas of the MTF from 3 to 12cpd with and without LCA and/or TCA correction were compared.

Results: The area of the photopic efficacy weighted MTF is reduced by approximately 4 to 30%, 13 to 57%, and 1 to 16% due to low and high amounts of LCA and 0 to 12%, 0 to 32%, and 0 to 2% due to low and high amounts of TCA for white, purple, and green stimuli, respectively. Collectively, typical ocular LCA and TCA reduces the area of the photopic efficacy weighted MTF by approximately 4 to 33% for white stimuli, 13 to 59% for purple stimuli, and 1 to 18% for green stimuli.

Conclusions: Chromatic aberration varies widely in the population. Many subjects have negligible foveal TCA, while all subjects have a substantial amount of LCA. Thus, LCA correction improves visual performance more than TCA correction. Correction of LCA should result in salient improvements in visual performance with either white or purple stimuli.

CONTROL ID: 3696497

SUBMITTER (NAME ONLY): Aditya Verma

TITLE: Age-related assessment of choroidal angio-architecture over the macular region in healthy eyes using swept-source optical coherence tomography angiography.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Verma, S.R. Sadda, G. Corradetti, Doheny Eye Institute, Pasadena, California, UNITED STATES|K. Magesan, M. Mahalingam, A. T, R. Gnanaraj, P. Sen, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|S.R. Sadda, G. Corradetti, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|A. Alagorie, Department of Ophthalmology, faculty of medicine, Tanta, Tanta, EGYPT|

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ABSTRACT BODY:

Purpose: The angioarchitecture of choroidal tissue exhibits an array of manifestations in healthy eyes. This study analyzed the age-related changes in the macular choroid in healthy eyes using swept-source optical coherence tomography angiography (SS-OCTA) in Indian subjects.

Methods: This was a cross-sectional, prospective, observational study enrolling 222 eyes of 116 healthy participants. SS-OCTA images were captured using the PLEX Elite 9000 (Carl Zeiss Meditec Inc., Dublin, CA, USA) with a 6x6mm pattern centered on the foveal center. Subfoveal choroidal thickness (CT) and choroidal volume (CV) were generated automatically through manufacturer tools available in the ARI hub network. Choroidal vascularity index (CVI) and choriocapillaris flow deficits (CCFD) were computed using ImageJ.

Results: CV was found to be significantly higher in females as compared to males (table). Overall, there was a significant positive correlation of CVI and CCFD, and a significant negative correlation of CT and CV with age. The relationship, however, was more complex, as decade-wise analysis showed that CT and CV increased until the 2^{nd} decade, followed by a decrease until the 6^{th}, and then an increase again in the 7^{th} and 8^{th} decades. CVI was highest in the 7^{th} decade. In contrast, CCFD increased consistently with age and in all the ETDRS rings (figure). CCFD was negatively correlated with CVI from the 3^{rd} to 6^{th} decades of life.

Conclusions: Choroidal parameters can show significant variations with age. While choriocapillaris shows a consistent worsening with age with increasing flow deficits, the relationship between age and the other choroidal parameters is more complex. These differences are not uniform or consistent with age, highlighting the importance of a normative reference database to assess the significance of choroidal alterations associated with disease.

CONTROL ID: 3697204

SUBMITTER (NAME ONLY): Cristina Canavesi

TITLE: Dual optical coherence tomography and microscopy for topographical and cellular evaluation of the cornea

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Canavesi, A. Cogliati, LighTopTech Corp., New York, UNITED STATES|H.B. Hindman, The Eye Care Center, New York, UNITED STATES|

Commercial Relationships Disclosure: Cristina Canavesi: Commercial Relationship(s);Code I (Personal Financial Interest):LighTopTech Corp.;Code P (Patent):LighTopTech Corp. | Andrea Cogliati: Commercial Relationship(s);Code I (Personal Financial Interest):LighTopTech Corp.;Code P (Patent):LighTopTech Corp. | Holly Hindman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We investigate the feasibility of dual imaging of corneal tissue with optical coherence tomography (OCT) and Gabor-Domain Optical Coherence Microscopy (GDOCM) to simultaneously visualize corneal morphology in three dimensions and resolve cellular features.

Methods: Imaging of donor corneal tissues was conducted with the novel dual-mode imaging system. The corneas, which are stored in a PMMA viewing chamber after recovery from donors, were imaged through the container to avoid contamination. The OCT imaging modality was used to quantify corneal thickness and overall topography over a field of view of 10 mm x 10 mm. The GDOCM imaging modality was used to visualize cellular structures including endothelial cells over a maximum field of view of 3.7 x 3.7 mm^2 with isotropic resolution of <3 µm in 3D. A numerical flattening method was applied to the 3D GDOCM images to compensate for the natural curvature of the cornea and produce a view of the endothelial cells in a single en face view, which can be compared to the conventional output of specular microscopes commonly used at eye banks to assess cell count density. Automated cell counting with machine learning methods was applied to the GDOCM images to assess endothelial cell density in an unbiased manner.

Results: The thicknesses of the corneal layers were assessed with the OCT imaging modality; the GDOCM imaging modality demonstrated cellular resolution in all corneal layers. The cell counts automatically obtained with machine learning from the numerically flattened GDOCM images of the endothelium were compared with the gold standard of specular microscopy.

Conclusions: Corneal imaging was conducted for the first time with two modalities (GDOCM and OCT) in the same instrument. Non-contact imaging provides a volumetric field that enables quantification of key cellular features of corneal tissue. This label-free approach to imaging may help us to better understand changes occurring in disease states or with age over time.

CONTROL ID: 3697351
SUBMITTER (NAME ONLY): Niranchana Manivannan
TITLE: Repeatability of swept-source optical coherence tomography angiography (SS-OCTA) metrics in healthy and glaucomatous eyes
SESSION TITLE: OCT Angiography Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Manivannan, G.C. Lee, T. Callan, B. Sandhoefner, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|K.R. Sung, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|G. Beykin, K. Trang, J.L. Goldberg, Byers Eye Institute at Stanford University, Palo Alto, California, UNITED STATES|G. Lai, C. Leung, The University of Hong Kong, Hong Kong, HONG KONG|G. Wollstein, H. Ishikawa, R. Zambrano, E. Ede, J.S. Schuman, NYU Langone Health, New York, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: To evaluate the intra-visit variability of quantitative measurements of SS-OCTA metrics.
Methods: One eye each from subjects with glaucoma and healthy controls were prospectively recruited from four sites. If two eyes were eligible, one eye per subject was designated randomly as the study eye. Each eye was imaged using the Angio 6x6 mm scan centered on the macula and centered on the optic disc on PLEX® Elite 9000 (ZEISS, Dublin, CA). Scans were repeated at each location on each device 3 times per visit, and the subjects were expected to complete 3 visits within one month.

Data were processed on the Advanced Imaging Network Hub using the algorithms: a) “Peripapillary Nerve Fiber Layer Microvasculature Density v0.9”, which quantifies microcirculation (with large vessels removed) in the radial peripapillary capillary layer, summarizing data over an annulus centered at the optic disc and b) “Superficial and GCIPL analysis v0.5”, which quantifies microcirculation in the superficial slab, summarizing data over the ETDRS grid centered on the macula.

Perfusion density (PD) is defined as the total area of perfused microvasculature per unit area. Flux index (FI) is defined as the total weighted area of perfused microvasculature per unit area in a region of measurement. The weight is the normalized flow intensity corresponding to each pixel. Vessel density (VD) is defined as the length of perfused microvasculature per unit area.

Intra-visit variability was determined by averaging the within-subject variance across visits for all eyes. The square root of this variance is the repeatability standard deviation.
Results: 33 healthy eyes (mean age 56.8, SD 11.5 years) and 31 eyes with glaucoma (mean age 61.1, SD 11.5) were imaged.

Table 1 shows the mean and coefficient of variance (CV) for legacy segmentation for disc-centered PD and FI measurements, which ranged from 1.7% to 3.2%. Table 2 shows the mean and CV for macula-centered VD and PD measurements, which ranged from 8.8% to 16.0%.

Conclusions: Coefficients of intra-visit variation are acceptable for both macula-centered and optic disc-centered SS-OCTA metrics, with optic disc-centered metrics showing excellent intra-visit variation. These parameters may have clinical utility for monitoring glaucomatous damage.

CONTROL ID: 3697359

SUBMITTER (NAME ONLY): kotaro tsuboi

TITLE: Automated macular fluid volume as a treatment indicator for diabetic macular edema

SESSION TITLE: Diabetic Macular Edema

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To assess the diagnostic accuracy of an automated macular fluid volume (MFV) quantification for treatment required diabetic macular edema (DME).

Methods: The evaluation included macular structural optical coherence tomography (OCT) raster scans (Spectralis, Heidelberg), and 3x3-mm macular OCT angiography volumetric scans (Avanti, Optovue). Central subfield thickness (CST) was measured on Spectralis OCT scans using the embedded software. A custom deep-learning algorithm automatically quantified MFV within 3x3-mm on the OCTA scans. Physicians treated patients per standard of care based on clinical and Spectralis OCT findings without access to MFV. We calculated the area under the receiver operating characteristic curve (AROC) and sensitivity and specificity of CST, MFV, and visual acuity for treatment decision.

Results: Of 139 eyes, 39 (28%) eyes underwent treatment for DME. The algorithm detected fluid in all eyes with a mean (SD) MFV of 0.062 (0.14) mm^3, but only 54 (39%) eyes met the DRCR.net criteria (CST>=320mm in male or CST>=305mm in female) for center-involved macular edema. The AROC of MFV for a treatment indication (0.81; 95% CI, 0.73 to 0.90) was larger than the AROC of CST (0.67; 95% CI, 0.56 to 0.78; P = 0.0048) (Fig 1). With the specificity fixed at 80%, the sensitivity of MFV for treatment indication was 74.4% (95%CI, 61.5% to 87.2%), higher than that of CST of 41.0% (95%CI, 25.6% to 56.4%, P = 0.0007). The eyes that met the threshold for treatment based on MFV (>0.031 mm^3) but the physicians chose not to treat had better visual acuity (mean [SD], 77.9 [7.3] letters) compared to the eyes that were treated (70.3 [10.8] letters; P = 0.0053). A multivariate logistic regression model showed that MFV (Estimate = 13.6, [95% CI, 6.7 to 22.7], P = 0.0008) and visual acuity (Estimate = -0.082 [95% CI, -0.14 to -0.026], P = 0.0056) were significantly associated with treatment.

Conclusions: MFV may better predict the need for treatment for DME compared to CST. This may make treatment and screening referral decisions more objective in DME.

CONTROL ID: 3698719

SUBMITTER (NAME ONLY): Dongsheng Yang

TITLE: Short-term effect of dark exposure on vision in patients with amblyopia

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Yang, P. Wang, Y. Pan, J. Zhang, D. Li, W. Gong, L. Wang, M. Huang, D. Zhang, M. Guan, Y. Cao, Z. Tang, Ophthalmology, Jinan bright eye hospital, Jinan, Shandong, CHINA|

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ABSTRACT BODY:

Purpose: It has been shown that a period of dark exposure (DE) restored ocular dominance (OD) plasticity in animals. If the DE has any prompting effect on vision in human subjects, it could be an additional method for refractory amblyopia treatment. However, it is unknown whether DE has any effect on vision improvement in patients with amblyopia. We will report effects of 10-day-darkness on vision improvement in patients with amblyopia.

Methods: Eighteen patients (age: 6-28 years old) with 23 amblyopic eyes were recruited. Patients whose best corrected visual acuity (BCVA) is lower than their age-based norms are included. Patients with retinal disorders and mental health conditions were excluded. All subjects stayed in the dark room for 10 days. They were followed for 1-3 weeks after DE while visual training was performed.

Results: A rapid vision improvement was observed after DE. The mean of BCVA from all patients was 0.55 logMAR before DE and became 0.24 logMAR measured after DE & visual training. The difference was significant (P=0.0056). The BCVA is also improved in adult patients. No vision loss was observed in all patients.

Conclusions: DE is a safe and effective approach for vision improvement in amblyopia. Thus, it could be a new way for refractory amblyopia treatment and for further amblyopia research on human patients.

CONTROL ID: 3699139

SUBMITTER (NAME ONLY): Sachi Patil

TITLE: Investigating the Utility of Near Infrared Reflectance (NIR) Imaging for Diabetic Retinopathy Screening

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Patil, S. Pandit, N. Mehta, Y. Modi, Ophthalmology, New York University, New York, New York, UNITED STATES|A. Nair, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: An investigation of the reliability of near infrared reflectance (NIR) imaging as a method of assessing severity and stage of diabetic retinopathy (DR) by quantitative assessment of hyporeflective foci.

Methods: Retrospective cohort study of spectral domain optical coherence tomography (SD-OCT) images from patients with type I and type II diabetes seen at a tertiary academic center. 195 near infrared images were reviewed by 2 independent graders to document the number of hypo reflective foci and presumptive DR staging based on the image. The benchmarked DR staging was made by the retinal specialist in clinic and recorded in the electronic medical record. Interrater reliability was confirmed via one-way random effects model of intraclass correlation coefficients. A third rater was consulted if there were discrepancies in number of hyporeflective spots between the two original raters. Demographic data was collected. Analysis of variance was conducted to estimate differences between sub-groups based on severity. Receiver operating curves were created to validate the reliability of the model.

Results: A statistically significant difference in mean number of hypo-reflective foci was found between none and moderate NPDR ($p<0.0001$*), none and severe NPDR ($p<0.0001$*), none and PDR ($p<0.0001$*), mild and moderate NPDR ($p=0.008$*), mild and severe NPDR ($p<0.001$*), mild NPDR and PDR ($p<0.001$*). A statistically significant difference did not exist between moderate and severe, moderate and proliferative disease, or between severe and proliferative disease. Upon creation of the receiver operating characteristic curve, the area under this curve was 0.849 (CI: 0.792, 0.905). Based on this curve, the ideal threshold for detection of moderate nonproliferative diabetic retinopathy or worse was 4.75 hypo reflective foci, with a sensitivity of 79.0% and a false positive rate of 20.0%.

Conclusions: Near infrared imaging may be a useful adjunct tool in screening for diabetic retinopathy as discrete hyporeflective foci can provide understanding of DR staging. These findings should be established on newly diagnosed DR patients with reading center evaluations of DR staging and hyporeflective foci counts to further establish the validity of NIR imaging as a screening tool.

CONTROL ID: 3700306

SUBMITTER (NAME ONLY): Priya Tailor

TITLE: Robotic Telepresence Consults in Underserved Community-Based Vision Threatening Disease Screenings During COVID-19

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tailor, A. Zhu, R. Verma, E. Kuklinski, C. Ye, B. Szirth, A. Khouri, M. Habiel, Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision Threatening Diseases (VTDs) (age-related macular degeneration, cataracts, diabetic retinopathy, glaucoma) affect 36 million individuals in the United States. 50% are unaware they have a VTD, disproportionally affecting minorities and low-income groups with less access to eye care. While screening programs in underserved communities result in early detection, less than half of subjects with findings follow up with a specialist. This number is four times lower during COVID-19.

Methods: Robotic Telepresence (RT) was implemented in this pilot study during COVID-19 to increase real-time access to specialist care. 58 subjects (age 56, 45% male) underwent a non-mydriatic screening protocol over five screenings. They were divided into three groups for consult: In Person (IP) followed by RT (N = 21), RT followed by IP (N = 19), and IP only (N = 18). IP consult was done by an on-site certified reader. RT consult was done by an off-site glaucoma or retina specialist with access to blood pressure, visual acuity, intraocular pressure, 45° retinal images, and ocular coherence tomography B-scans via cloud-based software. Video connection for RT was established via HIPAA-compliant mobile hotspot. Subject demographics and preferences were collected afterwards via survey.

Results: Of 40 RT consults, 26 were second opinion for VTD suspect and 14 were wellness encounters. 24 reported their last eye care visit >3 years ago or never. Following RT consult, 18 subjects received one or multiple VTD diagnosis and 3 with glaucoma were referred for pressure-lowering eye drops. In the group with IP consult first, preferences were 5% RT, 52% IP, and 43% none. In the group with RT consult first, preferences were 5% RT, 58% IP, and 37% none. There was no significant difference in number of questions asked, wait time, or encounter length between IP and RT consults.

Conclusions: RT consults proved valuable in community-based VTD screenings, particularly during COVID-19 when access to eye care is further limited. Most subjects preferred IP. However subjects with VTD that face socioeconomic barriers benefit from immediate RT consult and management directives from remote subspecialists. Further studies should incorporate consults from additional specialties (endocrinologists, general practitioners, social workers) and include telehealth CPT code for reimbursement.

CONTROL ID: 3700411

SUBMITTER (NAME ONLY): Thaonhi Cung

TITLE: Maternal Uteroplacental Insufficiency Protects Offspring from Oxygen-Induced Vascular Loss Through Erythropoietin Receptor Mediated Signaling

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.H. Cung, E. Kunz, H. Wang, A. Ramshekar, C. Bretz, M. Hartnett, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|T.H. Cung, Texas Tech University Health Sciences Center School of Medicine, Lubbock, Texas, UNITED STATES|A. Brown, C. Fung, University of Utah Health, Salt Lake City, Utah, UNITED STATES|V. Divoky, Univerzita Palackeho v Olomouci, Olomouc, Olomoucký, CZECHIA|

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ABSTRACT BODY:

Purpose: Maternal uteroplacental insufficiency (UPI) has been reported to be associated with lower or greater risk of infant retinopathy of prematurity (ROP). UPI induces erythropoietin (EPO) expression, and EPO, as a ligand, can be vasoprotective against high oxygen in experimental models but was not found to be neuroprotective for premature infants in a recent clinical trial. To dissect the role of ligand and receptor signaling, we tested the hypothesis that signaling through the EPO receptor (EPOR) in the setting of maternal UPI reduced high oxygen-induced retinal vascular loss. We used humanized EPOR knock-in mice (hWT) with hypoactive signaling through the EPOR and littermate control wild-type mice (mWT) in a combined UPI/oxygen-induced retinopathy (OIR) mouse model.

Methods: Heterozygous hWT mice were bred for homozygous hWT and littermate homozygous mWT pups. On embryonic day 12.5, pregnant hWT dams were implanted with microosmotic pumps that released a thromboxane A2 analogue dissolved in 0.5% ethanol to create UPI or 0.5% ethanol (control). After birth, pups were transferred to a foster heterozygous hWT dam. Postnatal day 7 (p7) pups with foster dams were placed into the mouse OIR model (75% O_2) for 5 days. At p12, pups were euthanized, and blood, serum, and retinae were collected. Retinal flat mounts were stained with isolectin, and imaged with a fluorescent microscope. The images were analyzed for avascular to total retinal area (AVA) with ImageJ. Serum EPO was measured by ELISA. Hematocrits were read with a capillary microhematocrit reader. Data were analyzed with 1) a multilevel linear regression model with eyes nested within animals and animals nested within litters for AVA, and 2) a two tailed t-test for serum EPO and hematocrit.

Results: Compared to mWT, hWT mice born to dams with UPI or control dams had reduced hematocrit ($p<0.0001$) despite increased serum EPO ($p<0.0001$). In p12 mWT pups born to dams with UPI (mWt;UPI), there was reduced AVA ($p<0.05$) compared to mWT;control. However, in p12 hWT;UPI, there was no difference in AVA ($p=0.766$) compared to hWT;control.

Conclusions: Maternal UPI-induced endogenous EPOR signaling may provide some retinal vascular protection from hyperoxia-mediated vascular loss. Further studies are needed to determine the mechanisms involved in EPO/EPOR or other receptor mediated vascular protection.

CONTROL ID: 3701172

SUBMITTER (NAME ONLY): Michelle Guo

TITLE: Loss of macrophage chemoattractant protein-1 reduces retinal inflammation and neuron death in hypertensive glaucoma

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Guo, T.D. Schwartz, J. Sterling, J. Wu, A. Alnemri, M. Adetunji, E. Lawrence, A.G. Ross, J.L. Dunaief, Q.N. Cui, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macrophage chemoattractant protein-1 (MCP-1), a potent chemokine for myeloid cells, has been associated with disease progression in patients with normal-tension glaucoma and animal models of age-related macular degeneration and retinitis pigmentosa. Blocking Müller cell MCP-1 expression reduced macrophage/microglia infiltration and activation in a rat model of retinal degeneration. We previously showed that decreasing macrophage/microglia activation reduced astrogliosis and rescued retinal ganglion cells (RGCs) in a mouse model of glaucoma (PMID 33147455). Using the microbead occlusion model of hypertensive glaucoma, we examined the effect genetic knockout of MCP-1 has on RGC survival and function, retinal myeloid cell density, and pro-inflammatory cytokine expression.

Methods: Five-month-old C57BL/6J (WT) or MCP-1 knockout (KO) mice received bilateral injections of either magnetic microbeads to elevate IOP or sterile BSS in the anterior chamber of both eyes. IOP was measured immediately before injection, 3 days post-injection, and then weekly thereafter. After 8 weeks, immunolabeling of retina flat mounts for RBPMS and Iba1 quantified density of RGCs and myeloid cells, respectively. Quantitative PCR was used to assess expression of pro-inflammatory cytokines C1q, IL-1α, and TNF-α in cellular populations enriched for macrophage/microglia (CD11b+). A multiple electrode array (MEA) recording system was used to characterize RGC function.

Results: IOP remained elevated for 7 weeks in bead- but not BSS-injected eyes ($p<0.05$). In WT mice, RGC density was 16% lower in bead vs. BSS eyes while myeloid cell density was 50% higher ($p<0.05$ for both). In contrast, RGC and myeloid cell density did not differ between bead and BSS eyes in KO mice. Expression levels of pro-inflammatory cytokines did not differ between groups in either WT or KO mice at the end of 8 weeks. MEA recordings suggest that RGCs are viable and more sensitive to light in KO mice compared to WT mice after IOP elevation.

Conclusions: Genetic ablation of MCP-1 rescued RGCs and decreased macrophage/microglia density in the retina without altering pro-inflammatory cytokine expression by macrophage/microglia. Results suggest that reduced retinal infiltration by myeloid cells, as opposed to decreased cytokine activation in these cells, improved RGC survival following loss of MCP-1 in the setting of ocular hypertension.

CONTROL ID: 3701628

SUBMITTER (NAME ONLY): Sarah Cheng

TITLE: Vision is required for cell type specification and function in the developing visual cortex

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: That visual experience is important for proper visual system development is known, but its molecular basis is poorly understood. This study examines the role of visual experience in wiring of the visual cortex during the visual critical period at the molecular level.

Methods: We performed single-nucleus RNA sequencing on mouse primary visual cortex during visual cortical development (P8 – P38) under a variety of visual experience perturbations: normal visual experience, dark rearing during the critical period (P21-28, 21-38), and dark rearing followed by light exposure (P21-28, followed by 8 hours of light). A total of 144,725 cells were clustered and parsed using machine learning to uncover novel cell types and map cell type specific transcriptomes across time. Single-cell fluorescent in-situ hybridization was used to examine in vivo localization of cell types. The function of one candidate cell surface protein selectively regulated by light during the critical period was studied in vivo in knockout mice through 2 photon imaging of the cortex in awake animals and by immunohistochemistry.

Results: We discovered three glutamatergic cell types form three sublayers in L2/3 of the visual cortex. Vision is required for the formation and maintenance of these cell types. By contrast, cell types in deeper layers are specified independent of vision. Cell types exhibit a transcriptomic continuum, defined by graded expression of genes that could be split into eight modules which vary dynamically with time. Cell surface proteins were encoded by many of these genes, and one (Igsf9b) stood out as having a layered distribution that increased during the critical period and was activity regulated. Mice lacking Igsf9b had reduced numbers of binocular cells, changes in their responses to visual stimuli and a reduction in inhibitory synapse proteins.

Conclusions: Vision is necessary for the specification of cell types in L2/3 of the visual cortex. Igsf9b, a homophilic cell adhesion molecule, is necessary for cortical wiring, formation of binocular cells, and the responses of excitatory neurons to visual stimuli. Our transcriptomic atlas of visual cortical development from synaptogenesis to the end of the critical period is an important resource for future studies on cortical development.

CONTROL ID: 3701727

SUBMITTER (NAME ONLY): Robyn Guymer

TITLE: Genetic variants in ANO2 may be predictive for treatment response to anti-VEGF in neovascular age-related macular degeneration

SESSION TITLE: AMD Translational Research

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.H. Guymer, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|R.H. Guymer, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|R. Silva, University of Coimbra, Coimbra Institute for Clinical and Biomedical Research Faculty of Medicine (iCBR-FMUC) and Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, PORTUGAL|R. Silva, Association for Innovation and Biomedical Research on Light and Image (AIBILI), Coimbra, PORTUGAL|M. Ghadessi, Bayer US, Whippany, New Jersey, UNITED STATES|S. Leal, K. Rittenhouse, Bayer Consumer Care AG, Basel, SWITZERLAND|I. Gashaw, Bayer AG, Berlin, GERMANY|A. Damask, C. Paulding, Regeneron Pharmaceuticals, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic predisposition can contribute to treatment response, and predictive variants may explain response direction and/or magnitude. In the VIEW 1 and 2 Phase 3 randomized controlled trials (RCTs), intravitreal aflibercept (IVT-AFL) provided rapid and robust gains in visual acuity (VA) in patients (n=2419) with neovascular age-related macular degeneration (nAMD). This analysis aimed to identify any associations between gene variants and clinical endpoints in VIEW 1 and 2.

Methods: A genome-wide association study (GWAS), utilizing the Illumina HumanOmniExpress Exome v1.3 platform, was conducted on a subgroup of patients from VIEW 1 and 2 (NCT00509795/NCT00637377) consenting to the optional pharmacogenetic analysis.

Results: Data were pooled from 780 patients (VIEW 1, n=362; VIEW 2, n=418), who were representative of the overall VIEW 1 and 2 population. After Bonferroni correction for multiplicity and statistical adjustment for baseline risk factors, there were no significant associations between known gene variants and treatment response according to the pre-specified VIEW 1 and 2 endpoints. Genome wide there were no significant genetic associations in participants experiencing gains ≥15 ETDRS letters after 1 or 2 years of treatment. Investigating participants with VA loss ≥5 letters, a cluster of variants in the ANO2 gene on Chromosome 12 reached $p<5x10^{-8}$. Exploring VA scores at Year 1 and 2, the ANO2 rs2110166 single-nucleotide polymorphism (SNP) also reached $p<5x10^{-8}$. Carriers of the rs2110166 TC genotype showed a smaller improvement in VA score in response to IVT-AFL or ranibizumab (effect size 2.19) compared to those without. The minor allele frequency was 3% in VIEW; these participants lost, on average, ≥5 letters at 1 year.

Conclusions: Based on data from two large, robust RCTs, preliminary analyses suggest an association of ANO2 with retinal function, with a potential impact on VA of ~1 line over 1–2 years. Typical associations between known and potential target candidate AMD variants and clinical endpoints were not found. ANO2 encodes anoctamin 2, a calcium-activated chloride channel expressed on photoreceptor cells and is a gene meriting further investigation of its function in retinal pathophysiology. Further studies may elucidate whether the variants identified are predictive or prognostic in nAMD.

CONTROL ID: 3701740

SUBMITTER (NAME ONLY): Imran Yusuf

TITLE: Gene therapy rescues photoreceptor function, morphology and survival in a pre-clinical model of CDHR1-associated retinal degeneration

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the efficacy and safety of retinal gene therapy in a pre-clinical model of CDHR1-associated retinal degeneration – an as yet untreatable, blinding disorder characterised by progressive cone and rod photoreceptor degeneration.

Methods: $Cdhr1^{-/-}$ (n=28) and C57BL/6J control mice (n=23) underwent paired sub-retinal injections of AAV8.GRK1.CDHR1 ($1.5x10^{8}$) and PBS vehicle control in the fellow eye at 4 weeks of age. Dark- and light-adapted electroretinography (ERG) was undertaken to 8 months post-injection. Photoreceptor layer thickness and outer retinal morphology were compared using optical coherence tomography (OCT) imaging to 6 months post-injection.

Results: In $Cdhr1^{-/-}$ mice, sub-retinal AAV8.GRK1.CDHR1 rescued A-wave amplitudes ($p<0.0001$ at all time points) and B-wave amplitudes ($p<0.0001$ from 6 months) on dark-adapted ERG versus PBS-injected control eyes (Fig.1). Light-adapted flicker ERG amplitudes were greater in AAV-treated eyes at 8-months post-injection ($p<0.0001$).

AAV8.GRK1.CDHR1 preserved photoreceptor layer thickness in the superior retina versus PBS-injected eyes at 6-months post-injection (mean: 76.6µm versus 49.7µm; $p<0.0001$; Fig.2). OCT changes consistent with the regeneration of photoreceptor outer segments and restoration of ellipsoid zone reflectivity were only identified in AAV-treated eyes ($p<0.0001$; Fig.2).

In C57BL/6J mice, there was no difference in ERG assessments (A-wave, $p=0.65$; B-wave, $p=0.47$; Cone responses, $p=0.09$; Fig.1) or photoreceptor thickness measurements at 6 months between AAV and PBS-injected eyes ($p=0.19$; Fig.2).

Conclusions: These data provide proof-of-principle of the efficacy and safety of CDHR1 gene therapy in a pre-clinical model of CDHR1-associated retinal degeneration. Rod and cone rescue occur through prevention of photoreceptor cell death and photoreceptor outer segments may regenerate. A follow-on clinical trial in patients with CDHR1-associated retinal degeneration is warranted.

CONTROL ID: 3701764

SUBMITTER (NAME ONLY): Katharina Breher

TITLE: Choroidal thickness changes in response to defocus-free monochromatic light

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Recent studies on humans showed an impact of the light spectrum on ocular growth parameters. However, it deserves further research whether the eye processes chromaticity or rather the defocus being induced by the longitudinal chromatic aberration (LCA) as a growth signal. The current study therefore investigated the influence of defocus-free monochromatic light on choroidal thickness as a rapid biomarker for ocular growth.

Methods: In total, n=19 left eyes were illuminated for 20min with isoluminant short-wavelength light (“S” 450nm), mid-wavelength light (“M” 550nm), long-wavelength light (“L” 650nm) and polychromatic light (“P” 450nm to 680nm). The right eye was occluded while serving as control eye. A custom-built laser-interference setup generated monochromatic and defocus-free grid patterns with changing spatial frequency content between 3cpd and 18cpd. The patterns covered the central 10° of the retina. Choroidal thickness was measured before and after each exposure period in the illuminated and non-illuminated area using swept-source optical coherence tomography (ZEISS PlexElite 9000, Carl Zeiss Meditec Inc., USA). Paired t-tests and two-factor analysis of variance were performed to compare choroidal reactions from baseline, between eyes, illumination conditions and choroidal regions. Numerical results are reported as mean and standard error and were rounded to full microns.

Results: As seen in Figure 1, there were no significant pre-vs-post-illumination changes for any light condition in the central, illuminated choroidal regions (S: 0±2µm, M: 0±1µm, L: +2±2µm, P: +1±1µm, all $p>0.05$). Statistically significant choroidal thinning occurred only in the non-illuminated area after polychromatic light with a mean change of -2±1 µm ($p=0.04$). No significant effect for "color" ($p=0.80$), "region" ($p=0.29$) and the interaction between both factors ($p=0.21$) was revealed. Furthermore, no differing responses between test eye and control eye could be found (all $p>0.05$).

Conclusions: Monochromatic and defocus-free light did not lead to a significant choroidal response after short-term exposure. Therefore, it can be suggested that the LCA-induced defocus, rather than the chromaticity of the light spectrum, presents the primary signal for guiding ocular growth.

CONTROL ID: 3701775

SUBMITTER (NAME ONLY): Anne Xuan-Lan Nguyen

TITLE: Association between heavy metals and diabetic retinopathy in the National Health and Nutrition Examination Surveys (NHANES)

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Landó, Ophthalmology, University of Toronto, Toronto, Ontario, CANADA|X. Trinh, Computer Science, McGill University, Montreal, Quebec, CANADA|A. Nguyen, Faculty of Medicine and Health Sciences, McGill University, Montreal, Quebec, CANADA|J. Kurian, None, Montreal, Quebec, CANADA|A.Y. Wu, Ophthalmology, Stanford University, California, UNITED STATES|V.Q. Trinh, Pathology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: While studies have suggested relationships between neurotoxic heavy metals (HM) and diabetes (DB), they did not correlate such findings with complications like diabetic retinopathy (DR). We performed a retrospective, observational cohort study to assess the relationship between HM and DR.

Methods: We extracted all patient data from CDC's NHANES with DB and ophthalmic parameters, corresponding to NHANES 2005/6 and 2007/8 cycles. We recorded socio-demographic factors, DB-related factors, HM measures and DR severity. To correct for cycle variations in testing, HM levels were transformed into cycle-specific quartiles. We performed statistical tests (Mann-Whitney U, Pearson Chi^2, Spearman's Rho Coefficient (p), Welch's T-test, multivariable logistic regression), in SPSS, v26. Outcome measures included: serum and urine levels of HMs compared to the degree of DR, past medical history and social history.

Results: 884 eligible patients were classified into 4 groups based on their DR severity: no DR (n=565, 46.5% men), mild DR (n=203, 56.7% men), moderate DR (n=85, 56.3% men), and proliferative DR (n=31, 35.5% men). The average age in each group was respectively 63.1±10.6, 65.1±11.0, 61.4±10.2 and 63.4±7.4 years. Mean serum HM levels for lead, cadmium, total mercury and inorganic mercury did not differ significantly in the presence or absence of DR ($p>0.05$, Welch's t-tests). All mean urinary metal levels were not significantly different in the presence or absence of DR, except for thallium (UThal) which had significant lower levels in DR ($p<0.013$). Adjustments for cycle variations confirm the independent association of DR and UThal, and the absence of correlation with other blood and urinary HM levels (Figure 1). UThal was the most significant correlation with a Spearman p of -0.214 (p=0.0003). We then analyzed the population to see which other parameter was associated with UThal levels. UThal was significantly associated with eGFR (p=0.002), hemoglobin (p=0.040), and insulin therapy (p=0.010). Multivariate logistic regression with 3 models are presented in Table 1. UThal was still independently associated with DR in all models (p=0.011-0.042).

Conclusions: UThal is significantly associated to DR severity in the NHANES database. Additional validation for geographic factors are warranted. If validated, these findings suggest a possible role for thallium, a neurotoxic HM, in DR.

CONTROL ID: 3701833

SUBMITTER (NAME ONLY): Jaime Dickerson

TITLE: Intraocular Pressure Following Pre- and Post-Surgical Glaucoma Medication Washout in the GEMINI Study

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Dickerson, K. Dhamdhere, Clinical Research, Sight Sciences Inc, Menlo Park, California, UNITED STATES|J.E. Dickerson, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|K. Dhamdhere, Ophthalmology, Mahatma Gandhi Medical College and Research Institute, Wardha, Wardha, INDIA|

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ABSTRACT BODY:

Purpose: Assess effectiveness of medication regimen in intraocular pressure (IOP) lowering pre/post-surgically in open-angle glaucoma (OAG) patients scheduled for canaloplasty and trabeculotomy combined with cataract surgery; evaluate relationship between medication number (meds) and IOP reduction.

Methods: Prospective, multicenter, clinical study. Subjects were adults with cataract and mild/moderate OAG. Medicated IOP <33 mmHg on 1-4 meds at screening and post-washout mean diurnal IOP (DIOP) ≥21 and ≤36 mmHg. Subjects underwent medication washout (28 days for prostaglandin analogues, beta blockers, and rho kinase inhibitors, two weeks for alpha agonists, and five days for carbonic anhydrase inhibitors) prior to baseline and Month 12 IOP measurements. All IOP measurements were Goldmann (operator/reader protocol). DIOP was the mean of three timepoints (9AM, 12PM, 4PM). Descriptive statistics (Mean, SD) were calculated for screening medicated IOP, baseline DIOP, Month 12 medicated IOP, and washed out DIOP for all subjects and for subgroups on 1, 2, 3, 4 meds. Paired t-tests compared IOP post-washout pre-surgically and at Month 12 for all patients and for the medication subgroups. Simple linear regression evaluated the relationship between medication number and increase in IOP post-washout.

Results: IOP increased 6.5 (2.8) mmHg (n=141) post-washout pre-surgically (p=0), and 6.0 (2.5) mmHg (1 med, n = 71), 5.9 (2.0) mmHg (2 meds, n = 36), 8.1 (3.4) mmHg (3 meds, n = 30), and 8.9 (3.9) mmHg (4 meds, n = 4). Meds were reintroduced for 22 subjects; 1 (n = 16), 2 (n = 5), or 3 (n = 1) meds. Average increases were 4.1 (all; p=.0024), 3.0 (1 med), and 5.8 mmHg (2 meds). A single patient on three meds went from 17.0 to 30.0 mmHg following washout, an increase of 13 mmHg.

Conclusions: Medication washout results in increases in IOP correlated with number of meds in OAG patients. The results agree with independent results from the COMPASS and HORIZON trials (Johnson and Jampel, 2020) but extend the anaysis to medication washout IOP increase post-surgically. There is a diminished increase in IOP following washout post-surgically and an overall lower unmedicated IOP relative to pre-surgical IOP indicating 1) the surgical treatment provided an IOP-lowering benefit independent of the adjunctive medications and 2) that response to medication post-surgically may be diminished compared to surgically naive patients.

CONTROL ID: 3701844

SUBMITTER (NAME ONLY): William Benjamin

TITLE: OXYGEN PERMEABILITY (Dk) OF REFERENCE MATERIALS

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.J. Benjamin, Dk Assessments, Material Performance Assessments LLC, Hoover, Alabama, UNITED STATES|J. Bonafini, W. Ferrar, Dk Assessments, Acuity Polymers Inc., Rochester, New York, UNITED STATES|R. Broad, L. Simpson, Dk Assessments, CooperVision Corporation, Chandler's Ford, Essex, UNITED KINGDOM|L. Cullen, P. Trotto, Dk Assessments, Bausch & Lomb, Inc., Rochester, New York, UNITED STATES|S. Ono, Dk Assessments, Menicon Company Ltd, Aichi, Nagoya, JAPAN|D. Diec, T. Tapper, Dk Assessments, Contamac Ltd UK, Essex, UNITED KINGDOM|S. Zhang, Dk Assessments, Alcon Laboratories, Inc., Johns Creek, Georgia, UNITED STATES|W.J. Benjamin, Vision Science Research Center, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: William Benjamin: Commercial Relationship(s);Code C (Consultant/Contractor):LenTechs Inc, Mojo Vision Inc;Code O (Owner):Material Performance Assessments LLC;Code F (Financial Support):Professor Emeritus Dr. Benjamin performs research under contract by a great number of companies in the contact lens field as part of his post-retirement business Material Performance Assessments LLC | James Bonafini: Commercial Relationship(s);Code E (Employment):Acuity Polymers Inc | Robert Broad: Commercial Relationship(s);Code F (Financial Support):CooperVision Corporation | Lindsey Cullen: Commercial Relationship(s);Code E (Employment):Baush & Lomb, Inc | David Diec: Commercial Relationship(s);Code E (Employment):Contamac Ltd UK | Wayne Ferrar: Commercial Relationship(s);Code E (Employment):Acuity Polymers Inc | Sadanori Ono: Commercial Relationship(s);Code E (Employment):Menicon Company Ltd | Laura Simpson: Commercial Relationship(s);Code E (Employment):CooperVision Corporation | Tristan Tapper: Commercial Relationship(s);Code E (Employment):Contamac Ltd UK | Paul Trotto: Commercial Relationship(s);Code E (Employment):Bausch & Lomb Inc | Steve Zhang: Commercial Relationship(s);Code E (Employment):Alcon Laboratories Inc

ABSTRACT BODY:

Purpose: The Permeability Reference Material Repository is depleted of the original 7 reference materials denoted R1 to R7. Dk values for these materials were reported in Invest. Ophthalmol. Vis. Sci. 2006; 47(13):97. Materials denoted R8 to R12 in single lots were recently supplied by 3 manufacturers of rigid contact lens materials.

Methods: Seven sites having the apparatus, calibrating specimens, and versed in the measurement and calibration of Dk according to the International Organization of Standardization (ISO) 18369-4:2017 and American National Standards Institute (ANSI) Z80.20-2016 determined the Dk of materials R8-R12. A set of R8-R12 reference samples was sent to each of the sites. They were monocentric, uniform-thickness lenses in nominal thicknesses of 0.11, 0.14, 0.18, 0.23, 0.29, and 0.40 mm such that the linearity between oxygen resistance (t/Dk) and thickness (t) could be inspected. Buttons were manufactured into samples by Valley Contax, Inc. (Springfield, Oregon, USA). The diameter was 10.0mm and back curve radius 7.80 or 8.60mm depending on the electrode in use at each site. To reduce fracture during handling, the thinner samples (0.11, 0.14mm) had thicker peripheries produced by a minus carrier and front junction of 8.0mm diameter.

Results: Reference Dk values were taken as the mean calibrated Dk values (n = 7) of the R8 to R12 materials. For R8: mean 68.7, Standard Error of the Mean (SEM) 2.4, 95% Confident Limits (CL) 64.0-73.5 Fatt Dk units; for R9: mean 120.8, SEM 5.9, CL 109.2-132.5 Fatt Dk units; for R10: mean 161.2, SEM 5.4, CL 150.5-171.9 Fatt Dk units; for R11: mean 145.2, SEM 6.5, CL 132.6-157.9 Fatt Dk units; and for R12: mean 171.7, SEM 4.9, CL 162.1-181.3 Fatt Dk units. Linear regressions between the Dk values from each site and the reference Dk values resulted in coefficients of determination (R^2) ranging from 0.9448 to 0.9922. Three of 7 were above 0.9900. The carrier of the 0.11 and 0.14mm samples did not appear to influence the linearity of t/Dk vs. t.

Conclusions: Dk values from different operators and sites assessing different sets of samples were highly correlated linearly with the reference values. The order of Dk progression for the materials from low to high was the same at each site. The spread of Dk values for each material supported the Dk measurement error (±10%) and tolerance (±20%) in the ISO and ANSI standards.

CONTROL ID: 3701850

SUBMITTER (NAME ONLY): Yevgeniya Atiskova

TITLE: Progressive retinal degeneration despite intraventricular enzyme replacement therapy with cerliponase alfa in classic late-infantile CLN2 disease

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Atiskova, C. Schwering, J. Wildner, C. Spartalis, F. Schüttauf, U. Bartsch, E. Wibbeler, M. Nickel, M. Spitzer, A. Schulz, S. Dulz, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|

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ABSTRACT BODY:

Purpose: Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) is a neurodegenerative, blinding lysosomal storage disorder. The purpose of the current study was to characterize the progression of CLN2-associated retinal degeneration in patients under intraventricular enzyme replacement therapy (ERT) with cerliponase alfa.

Methods: We analyzed visual function, retinal morphology and neuropediatric data using preferential looking test (PLT), Weill Cornell Batten Scale (WCBS), OCT imaging and the Hamburg motor-language scores (M-L score).

Results: Fifty-six eyes of 28 patients had baseline PLT, WCBS and OCT. 15 patients underwent serial examinations, resulting in a total of 132 OCT scans and WBCS results, 67 Hamburg M-L scores and 49 PLT results during a mean follow up time of 18.2 months (range 5-40). A negative correlation ($r=-.69$, $p<0.001$) was found between CRT and age at exam with a maximum annual decrease (23 µm) within the time intervals 56-80 months. A significant correlation was observed between the PLT and the age at examination ($r= .46$, $p=0.001$), the WBCS ($r= .62$; $p<0.001$) and CRT ($r=-.64$; $p<0.001$). The M-L score correlated with the ocular measurements (CRT: $r= .58$, $p<0.001$; WCBS $r= -.64$, $p<0.001$; PLT score: $r= -.57$, $p<0.001$).

Conclusions: Despite intraventricular ERT, retinal degeneration associated with CLN2 disease manifests as a progressive decline, which appears to accelerate during a critical period at 56 to 80 months of age. Retina-specific therapy should occur ideally before or as early as possible within this period. PLT, WCBS are valuable outcome measures to monitor disease progression.

CONTROL ID: 3701859

SUBMITTER (NAME ONLY): Pablo Argueso

TITLE: Glycogene expression profile of human limbal epithelial cells with distinct clonogenic potential.

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Argueso, A.M. Woodward, Department of Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Guindolet, E. Gabison, Fondation Ophtalmologique A. de Rothschild, Paris, FRANCE|

Commercial Relationships Disclosure: Pablo Argueso: Commercial Relationship: Code N (No Commercial Relationship) | Damien Guindolet: Commercial Relationship: Code N (No Commercial Relationship) | Ashley Woodward: Commercial Relationship: Code N (No Commercial Relationship) | Eric Gabison: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glycans function as useful markers of stem cells but also regulate the ability of these cells to differentiate. Approximately 1–2% of the human genome encodes for genes involved in the biosynthesis of glycans. In the present study, we evaluated the expression of a small subset of glycogenes in human limbal epithelial cells with distinct clonogenic potential.

Methods: Human postmortem corneoscleral tissues were generously donated by the Lions VisionGift. Epithelial cells were cultured and expanded in vitro using growth-arrested mouse 3T3 fibroblasts. Individual clones were isolated with cloning cylinders and used in parallel for both colony formation and transcriptional assays. The analysis of 84 genes involved in the biosynthesis of glycans was carried out using a human RT2 Profiler PCR Array. Quantification of gene expression in primary cultures of human limbal epithelial cells was achieved by qPCR.

Results: Individual clones were classified as abortive or clonogenic based on the fraction of abortive colonies produced. Clones leading to >99% abortive colonies were referred as abortive while those with 50% or less as clonogenic. Analysis of glycogene expression in clonogenic colonies revealed a high content of transcripts regulating galactose and mannose metabolic pathways. Abortive colonies were characterized by increased levels of GCNT4 and FUCA2, two genes responsible for the branching of mucin-type O-glycans and the hydrolysis of fucose residues on N-glycans, respectively. Expansion of primary cultures of human limbal epithelial cells for 10 days resulted in stratification and a concomitant increase in MUC16, GCNT4 and FUCA2 expression.

Conclusions: These data indicate that the clonogenic potential of human limbal epithelial cells is associated with specific glycosylation pathways. Mucin-type O-glycan branching and increased fucose metabolism are linked to limbal epithelial cell differentiation.

CONTROL ID: 3701862

SUBMITTER (NAME ONLY): Takae Kiyama

TITLE: Pou4f1-mediated regulatory network in the development of retinal ganglion cells

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kiyama, Ophthalmology and Visual Science, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Takae Kiyama: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: POU family transcription factors play pivotal roles in the development of retinal ganglion cells (RGCs). Pou4f1 is a member of the family and is expressed in the newly differentiated RGCs. Although its roles in RGC differentiation and dendritic morphogenesis have been described, it is unclear how Pou4f1 regulates downstream effector genes to promote newly differentiated RGCs into functional RGC subtypes.

Methods: To identify genes regulated directly by Pou4f1, we conducted CUT&TAG sequencing using an anti-Pou4f1 antibody and developing mouse retinas. We performed immunostaining and in situ hybridization on control and Pou4f1-deleted retinas to validate potential targets.

Results: CUT&TAG sequencing revealed ~8000 Pou4f1 binding regions in developing mouse retinas. Many of these Pou4f1-bound regions are located in genes that encode transcription factors, and some of these TFs are known to play a role in retinal development and RGC subtype formation. Additionally, many genes involved in axon guidance and nervous system development are also direct targets of Pou4f1. We have validated some of these candidate targets in control and Pou4f1-deleted retinas. We are currently exploring whether some of these Pou4f1-bound regions can serve as RGC subtype-specific enhancers.

Conclusions: We have revealed a Pou4f1-mediated regulatory network in RGC development through direct and indirect modes. Pou4f1 directly regulates genes involving in axon guidance and neuronal development. Indirectly, Pou4f1 may control transcription factors functioning in RGC subtype specification and differentiation. We have also uncovered the self-regulation of Pou4f1, confirming a previous study. Furthermore, we discovered that Pou4f1 binds to the promoters of several upstream regulators, including Atoh7, Pou4f2 and Isl1, implicating potential feedback regulatory loops between Pou4f1 and these key RGC regulators in RGC formation.

CONTROL ID: 3701866

SUBMITTER (NAME ONLY): Anat Galor

TITLE: OC-01 (varenicline solution) Nasal Spray for the Treatment of Dry Eye Disease Signs and Symptoms in Subjects with Autoimmune Disease: Integrated Data from ONSET-1 and ONSET-2

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Galor, Surgical Services, VA Miami Healthcare System, Miami, Florida, UNITED STATES|A. Gibson, G. Blemker, L. Hendrix, Oyster Point Pharma, Princeton, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Among patients with dry eye disease (DED), those with systemic autoimmune disease (AID) experience signs and symptoms often more serious with worse treatment effect and prognoses. This analysis evaluated the outcome of DED subjects with documented AID treated with OC-01 (varenicline solution) nasal spray (OC-01 VNS), a cholinergic agonist, compared to vehicle control (VC). OC-01 VNS has been shown to activate the trigeminal parasympathetic pathway to produce basal tear film by stimulating the lacrimal functional unit.

Methods: In ONSET-1, 182 patients were randomized 1:1:1:1 to receive 0.006 mg, 0.03 mg, or 0.06 mg OC-01 VNS or VC. In ONSET-2, 758 patients were randomized 1:1:1 to receive 0.03 mg or 0.06 mg OC-01 VNS or VC. Subjects administered OC-01 VNS or VC once to each nostril twice daily for 4 weeks. For this sub-population of interest, a total of 31 AID subjects were analyzed based on OC-01 VNS treated (0.03 mg or 0.06 mg, n=20) and VC (n=11) groups. Respectively, OC-01 VNS treated and VC mean baseline (BL) values were Schirmer's Test Score (STS, mm): 5.6 and 4.2; Eye Dryness Score (EDS, 0-100): 59.2 and 52.7. Outcome measures from BL to Week 4 included STS and mean change in EDS. Differences in OC-01 VNS treated and VC subjects were compared using t-test and chi square tests.

Results: OC-01 VNS treated subjects showed directional benefit in STS and EDS outcomes compared to VC. For OC-01 VNS treated and VC groups from BL to Week 4, respectively, percentage of eyes demonstrating improvement in STS ≥10 mm: 61.1% and 0.0% (95% CI, 46.0-76.2%); mean change in STS: 13.6mm and 1.8mm (6.5-17.1); and mean change in EDS: -19.6 and -10.3 (-26.8-8.2). OC-01 VNS was well tolerated in the trials. Most common adverse reaction in OC-01 VNS treated groups was sneeze (82-84%); the majority (98%) reported it as mild. Other adverse reactions >5% included cough, throat, and instillation site (nose) irritation.

Conclusions: In a sub-population with potential to have worse DED, OC-01 VNS treated AID subjects demonstrated directional signaled benefits in DED signs and symptoms at Week 4 compared to VC despite a limited sample size. OC-01 VNS was shown to have a favorable safety and tolerability profile in the trials. Future prospective studies with larger AID subject sample sizes are recommended.

CONTROL ID: 3701874

SUBMITTER (NAME ONLY): Shwetha Mudalegundi

TITLE: Long-term decrease in intraocular pressure in survivors of Ebola virus disease in the PREVAIL III Study

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ross, Global Retina Institute, Arizona, UNITED STATES|J. Larbelee, Redemption Hospital, LIBERIA|F. Amegashie, Liberian Ministry of Health, LIBERIA|R.F. Dolo, New Sight Eye Centre, LIBERIA|C. Gargu, Y. Sosu, J. Sackor, P.Z. Cooper, A. Wallace, R. Nyain, M. Fallah, Partnership for Research on Ebola Virus in Liberia, LIBERIA|C. Reilly, Division of Biostatistics, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|S. Mudalegundi, R. Bishop, A. Eghrari, Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Survivors of Ebola virus disease (EVD) experience decreased intraocular pressure (IOP) relative to unaffected close contacts during the first year of convalescence. Whether this effect persists over time, and its relationship to intraocular pathology, is unclear. We sought to determine if IOP remained lower in survivors of EVD over four years of follow-up, and to identify associated risk factors.

Methods: PREVAIL III is a 5-year, longitudinal cohort study of survivors of EVD and their close contacts and is a collaboration between the Liberian Ministry of Health and the United States National Institutes of Health. Participants who enrolled in PREVAIL III at John F. Kennedy Medical Center in Liberia, West Africa from June 2015 to March 2016 underwent comprehensive ophthalmic evaluation annually for 5 consecutive visits. IOP was measured at each visit by a handheld rebound tonometer using sterile tips. Comparisons are made between antibody-positive survivors and antibody-negative close contacts. Among survivors, we tested for associations between IOP and findings on physical examination, optical coherence tomography, or diagnosis of uveitis at baseline.

Results: Of 565 antibody-positive survivors and 644 antibody-negative close contacts enrolled in the study at baseline, the majority of participants returned annually, with 383 (67.8%) and 407 (63.2%) participants, respectively, presenting for the final study visit at a median of 60 months after symptom onset. A sustained, relative decrease in IOP was observed in survivors relative to close contacts, with mean difference of -0.87 mmHg (95% confidence interval -1.24 to -0.51) across all follow-up study visits. This difference remained constant over time ($p=0.23$ for interaction over time). Among survivors, physical examination findings of vitreous cell, optical coherence tomography findings of vitreous opacities, and eyes with diagnosis of uveitis all demonstrated a significant association with decreased IOP at baseline ($p<0.05$ for all).

Conclusions: In this study, survivors of EVD experienced a sustained decrease in IOP relative to close contacts over a five-year period following EVD infection. Clinical implications are unknown, but further research is required to elucidate the physiological origin of such changes. The results highlight the importance of considering long-term sequelae of emerging infectious diseases within a population.

CONTROL ID: 3701878

SUBMITTER (NAME ONLY): Mineo Ozaki

TITLE: Effects of endogenous substances on albumin-binding of diclofenac and site inhibitors in the aqueous humor of patients undergoing cataract surgery.

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ozaki, S. Ishii, Ozaki Eye Hospital, Hyuga, Miyazaki, JAPAN|M. Ozaki, Miyazaki Daigaku Igakubu Daigakuin Ikagaku Kangogaku Kenkyuka, Miyazaki-gun, Miyazaki, JAPAN|K. Ogata, J. Tokunaga, N. Takamura, School of Pharmaceutical Sciences, Kyushu Hoken Fukushi Daigaku, Nobeoka, Miyazaki, JAPAN|S. Ishii, R. Ikeda, Miyazaki Daigaku Igakubu Fuzoku Byoin Yakuzaibu, Miyazaki, Miyazaki, JAPAN|

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ABSTRACT BODY:

Purpose: Diclofenac instillation is useful for preventing intraoperative miosis and suppressing postoperative inflammation and macular edema in cataract surgery; however, optimum efficacy is not attained when the instilled diclofenac strongly binds to albumin in patients' aqueous humor. Therefore, a method that inhibits diclofenac binding and increases the concentration of its free fraction is required. We conducted a study regarding the effects of inhibitors on the binding of diclofenac to albumin and endogenous substances in the aqueous humor.

Methods: At the time of cataract surgery, aqueous humor samples from 15 patients with cataract who had received diclofenac instillations were collected and mixed to prepare pooled aqueous humor, from which diclofenac was extracted. The free-fraction and concentrations of diclofenac were measured using ultra-high performance liquid chromatography in various experiments with pooled and mimic aqueous humor samples. The endogenous substances in the aqueous humor were quantified using a BiOLiS 24i premium, gas chromatography-mass spectrometry, and liquid chromatography-mass spectrometry.

Results: The binding of diclofenac, a site-II drug, to albumin in pooled aqueous humor was significantly inhibited by phenylbutazone (PB), a site-I inhibitor; however, no significant inhibition by ibuprofen, a site-II inhibitor, was observed. To unravel this unexpected result, endogenous substances associated with albumin binding in pooled aqueous humor were investigated. The inhibition of diclofenac binding by PB in mimic aqueous humor containing these endogenous substances revealed significant binding inhibition in the presence of palmitic acid (PA) and L- tryptophan (L-Trp) (PA > L-Trp).

Conclusions: The presence of PA and L-Trp in the aqueous humor inhibited diclofenac from binding to site II, the high-affinity binding site on albumin, and induced a conformational change in albumin. This change caused site I, the low-affinity binding site, to become high-affinity; thus, diclofenac was strongly bound to site I. Therefore, PB, a site-I inhibitor, significantly inhibited the albumin binding of diclofenac. Instilling site-I inhibitors prior to diclofenac may increase the free fraction of diclofenac and enhance its effect.

CONTROL ID: 3701926

SUBMITTER (NAME ONLY): Christopher Loh

TITLE: Comparing FA and OCTA evaluation of retinal vascularity of murine eyes with diabetic retinopathy with Contrast-Limited Adaptive Histogram Equalization (CLAHE) and Matched Filter Image Processing Technique

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Loh, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|P. Zhang, R.K. Meleppat, Department of Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|O. Ramos-Soto, S.E. Balderas-Mata, Division de Electronica y Computacion, Universidad de Guadalajara Centro Universitario de Ciencias Exactas e Ingenieria, Guadalajara, Jalisco, MEXICO|R.J. Zawadzki, S.S. Park, Department of Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fluorescein angiography (FA) remains the gold standard used to evaluate the morphology and leakage of retinal vasculature, but it requires an intravenous injection of fluorescein dye and a skilled photographer. OCT angiography (OCTA) is a newer noninvasive (contrast agent free) imaging technique developed to evaluate morphology of the retinal vasculature. This study evaluated whether retinal vascular density noted in murine eyes with diabetic retinopathy using FA is comparable to those observed using OCTA.

Methods: Simultaneous FA and OCTA images were obtained, using custom build mouse retinal OCT/SLO system, from STZ (Streptozotocin)-induced diabetic mice 6 months after induction of diabetes. The acquired images (FA fundus and OCTA enface projections) were processed to obtain a better profile of the vascular parameters. At first, the Contrast-Limited Adaptive Histogram Equalization (CLAHE) was used to improve the background-vessel contrast. Then, a two-dimensional matched filter was applied by using a Gaussian kernel with two different standard deviation values to enhance both thick and thin vessels. Images of total areas of retina were obtained and analyzed using ImageJ software with the Vessel Analysis plugin to quantify the retinal vascular density of the entire imaged retina ~50deg FOV (total) on FA and OCTA.

Results: Retinal vascular density of the total area on standard FA and OCTA images did not correlate significantly (N=14; correlation r=0.081, p value=0.783, using ANOVA regression). However, when analysis was performed on enhanced images using CLAHE and two-dimensional matched filter, vascular density on FA and OCTA images significantly correlated (N=14; correlation r=0.742, p value=0.002, using ANOVA regression).

Conclusions: Retinal vascular density obtained using FA correlates well with retinal vascular density obtained using OCTA in murine eyes with diabetic retinopathy after application of Contrast-Limited Adaptive Histogram Equalization (CLAHE) and two-dimensional matched filter with Gaussian kernel. Vascular density on FA and OCTA was found to correlate better after image enhancement improved contrast of the fine retinal capillaries.

CONTROL ID: 3701931

SUBMITTER (NAME ONLY): Zach Miller

TITLE: Assessment of Average Length of Time Between Various Anti-Vascular Growth Factor Inhibitor (Anti-Vegf) Injections in Retinal Vascular Occlusions

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z.D. Miller, D. Marino, C.W. Miller, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To calculate and compare the average interval between injections of Aflibercept (AFL), Bevacizumab (BEVA), and Ranibizumab (RAN) for patients with retinal vascular occlusions (RVO).

Methods:

A retrospective cohort study was performed at a private retinal practice in Ohio. The Institutional Review Board (Sterling) determined this study consisted of non-human subjects. All data was collected through the practice management of Retina Associates of Cleveland, Inc. Data was collected from patients who received injections of AFL, BEVA, and RAN from July 2020 through June 2021 and includes: patient number, injection service dates, anti-vegf drug injected, procedure codes, and primary diagnoses. The patients were limited to those injected unilaterally and diagnosed with RVO, and the number of days between injection service dates was calculated for each injection. The data set was then organized by primary diagnosis and injection type, and the average number of days between injection service dates was determined for RVO and each corresponding drug. Statistical analysis included calculating the average interval in days between injections for each medication, standard deviation, and two tailed t-test for comparison between medications.

Results: From July 2020 through June 2021, 14,911 injections were placed unilaterally for any diagnosis. There were 2,812 injections for RVO with an average interval between injections of 54 days for all medications. Of the RVO injections, the average interval was BEVA 55 days with standard deviation (SD) +/- 30 days, AFL 55 days SD +/- 32 days , and RAN 46 days SD +/- 19 days. In comparing the interval of BEVA versus AFL, the two-tailed t test yields a p value = 0.85; BEVA vs. RAN p = 0.00003; AFL vs. RAN p= 0.000001.

Conclusions: The results of the study suggest that AFL and BEVA seem to have a longer interval of injection than RAN in patients diagnosed with RVO. There does not appear to be a difference in average injection intervals for BEVA vs. AFL.

CONTROL ID: 3701945

SUBMITTER (NAME ONLY): Shinji Kakihara

TITLE: Transcriptome analysis of the pathophysiological significance of adrenomedullin 2 in the mouse choroidal neovascularization model

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kakihara, Y. Matsuda, K. Hirabayashi, A. Imai, Y. Iesato, T. Murata, Ophthalmology, Shinshu University, Matsumoto, Nagano, JAPAN|S. Kakihara, T. Sakurai, A. Kamiyoshi, M. Tanaka, H. Kawate, Y. Ichikawa-Shindo, Y. Zhao, Y. Matsuda, K. Hirabayashi, A. Imai, Y. Iesato, T. Shindo, Cardiovascular Research, Shinshu University, Matsumoto, Nagano, JAPAN|

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ABSTRACT BODY:

Purpose: We have reported that peptides belonging to the calcitonin superfamily, such as adrenomedullin (AM) and CGRP, have various biological activities, including vasodilation, angiogenesis, and anti-inflammatory effects that play critical roles in interocular vascular diseases. Intermedin, a newly added peptide to the calcitonin superfamily, is also called adrenomedullin 2 (AM2) because of its structural similarity to AM. In our previous study using a laser-induced choroidal neovascularization (LI-CNV) model, we found that pathological angiogenesis, inflammation, and fibrosis were exacerbated in AM2 knockout mice (AM2-/-). In contrast, exogenous administration of AM2 ameliorated these pathological conditions (ARVO 2020, 2021). In the present study, we performed transcriptome analysis to elucidate the mechanism of the ameliorating effects of AM2 on LI-CNV.

Methods: Wild-type mice (WT) were subjected to LI-CNV and systemic administration of PBS, AM, or AM2 using an osmotic pump. One week later, total RNA was extracted from retinal pigment epithelium-choroid-sclera complex specimens, and transcriptome analysis was performed using the Clariom™S Array. We then compared gene expression levels between WT and AM2-/- by quantitative real-time PCR analysis of angiogenesis-, inflammation-, and fibrosis-related genes found in the transcriptome analysis.

Results: There were 113 genes in the AM-treated group and 82 genes in the AM2-treated group whose expression was significantly changed by more than twofold or less than one-half. Of these, 15 genes, including Meox2, were commonly altered in the AM and AM2-treated groups, and 63 genes were differently altered in the two groups. In quantitative real-time PCR analysis, in samples from the early phase of LI-CNV, the expression of CD68, IL-6, VCAM-1, PAI-1, and fibronectin was significantly up-regulated in AM2-/- compared to WT, and the expression of Meox2 and Angpt-1 was significantly down-regulated.

Conclusions: Meox2, a homeobox transcription factor known to repress epithelial-mesenchymal transition (EMT), was up-regulated by AM2 treatment and conversely down-regulated in AM2-/-. Therefore, Meox2 could be a potential factor in the ameliorating effects of AM2 on LI-CNV. Further transcriptome analysis is expected to reveal functional similarities and differentiation between AM and AM2.

CONTROL ID: 3701958

SUBMITTER (NAME ONLY): Nan Zhou

TITLE: Vitreoretinal Amyloidosis:
Clinical Features, OCTA Appearances, Gene Mutations, and Treatment Outcomes of Vitrectomy Surgery

SESSION TITLE: Retinal Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Zhou, W. wei, Beijing Tongren Hospital, Beijing, Beijing, CHINA|

Commercial Relationships Disclosure: Nan Zhou: Commercial Relationship: Code N (No Commercial Relationship) | wenbin wei: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the clinical characteristics and surgical outcomes of vitrectomy encountered in eyes with vitreous amyloidosis. The novel term named vitreoretinal amyloidosis, systemic evaluation and visual outcome after vitrectomy are discussed. Transthyretin gene (TTR) mutations in Asian patients with familial amyloidosis are described.

Methods: Nineteen eyes of 10 Asian patients with a diagnosis of vitreoretinal amyloidosis from January, 2008, to September, 2021. Detailed history, genetic analysis, systemic and ocular examination of 19 eyes of 10 patients were carried out. Vitreous biopsy, followed by 23- to 25-gauge vitrectomy was performed in all patients. Patients were followed up on days 1, 7, and 30 and then every 3 months. The main outcome measures were best-corrected visual acuity (BCVA), intraocular pressure, SD/SS-OCT/OCTA insights, pathology, TTR mutations, treatment and disease course on follow-up outcomes were investigated.

Results: Mean age at presentation was 51 years, with a 1:1 male-to-female distribution. Family history was positive in 4 patients. Eighteen eyes had pseudopodia lentis, whereas all 19 eyes had glass wool-like vitreous. Waxy or cotton-wool vitreous with firm vitreous adhesions beyond major arcades and along retinal vessels was noted during surgery in all eyes. Congo red staining and polarized microscopy demonstrated vitreous amyloidosis. Most of preoperative BCVA was < 20/200, whereas the postoperative BCVA improved to 20/100 to 20/25.

We identified the OCTA features of vertical hyperreflective lesions that appeared as punctate with moderate or high reflectivity affecting all layers of the neuroretina in 18 eyes of 9 patients (18 eyes of 19 eyes [94.7%]), and the subtle needle-shaped patterns in 17 of 19 eyes (89.5%). Gene sequencing revealed the heterozygous Val30 Met TTR mutation in 2 patients of 1 pedigree, a heterozygous mutation G, p.R54G TTR (late-onset) in another 2 patients of 1 pedigree, confirming the diagnosis of familial amyloidosis. No patients subsequently were found to have systemic amyloidosis during the follow-up.

Conclusions: We firstly described and named the novel terms of "vitreoretinal amyloidosis" mainly based on OCT/OCTA features corresponding to the tissue structures. In addition, the heterozygous mutations of TTR in four patients of familial amyloidosis with vitreoretinal amyloidosis from Chinese are reported.

CONTROL ID: 3701978

SUBMITTER (NAME ONLY): Maxwell Su

TITLE: Evidence-Based Screening to Optimize the Yield of Positive Ophthalmologic Examinations in Children Evaluated for Non-accidental Trauma

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Su, M. Recko, Ophthalmology, Baylor Scott and White Central Texas, Temple, Texas, UNITED STATES|C. Shaver, Research, Baylor Scott and White Central Texas, Temple, Texas, UNITED STATES|K. Taylor, J. Stoutin, College of Medicine, Texas A&M University Health Sciences Center, Bryan, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-accidental trauma (NAT) examinations in children are not entirely benign and preclude neurological examination. The majority of ophthalmic exams routinely ordered for patients suspected of NAT are negative. Our study elucidates clinical and imaging factors that correlate to retinal findings to increase the yield of positive exams and decrease the burden of potentially unnecessary exams, validating previous studies and introducing new screening variables.

Methods: Our study is a retrospective chart review from May 2014 - August 2021 at a level-1 trauma center. 274 patients met the inclusion criteria of: 1) children </= 36-months-old, 2) concern for NAT, and 3) an ophthalmology consultation was placed. Through univariate and multivariate logistic regression, our study produces a screening algorithm for ophthalmic workup in NAT.

Results: Due to a strong association of “abnormal neuroimaging” and retinal hemorrhage (RH) (OR of 170 (95% CI (10.245, >999.999)), multivariate logistic regression controlling for “abnormal neuroimaging” was performed to analyze all variables associated with RH. 1 or more abnormal neuroimaging finding had a statistically significant association with retinal hemorrhages and produced the strongest association with a univariate OR of 170. The multivariate model (p-value<0.0001 with a c-statistic of 0.980) proposes using the following variables for predicting retinal hemorrhage on exam: Abnormal neuroimaging, Glasgow coma score (GSC) < 15, altered mental status on examination, seizure activity, vomiting, burising, scalp hematoma/swelling, and skull fractures.

Conclusions: If neuroimaging is obtained in the evaluation of suspected NAT, the yield of positive ophthalmologic findings would increase if certain non-ocular findings are present. If absent, ophthalmologic exams may not be necessary.

CONTROL ID: 3701987

SUBMITTER (NAME ONLY): Arielle Coughlin

TITLE: Atherosclerotic disease and serum risk factors in phenotypes of age-related macular degeneration (AMD)

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Coughlin, J. Jo, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|R.J. Thomson, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|J. Chazaro, Loyola University Chicago, Chicago, Illinois, UNITED STATES|O. Otero-Marquez, G. Ledesma-Gil, Y. Tong, Z.R. Teibel, K. Tai, H. Lloyd, R.B. Rosen, R. Smith, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|L. Yannuzzi, K. Freund, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Attempts to characterize the connection between AMD and atherosclerotic disease (ASD) and its risk factors have yielded conflicting and inconclusive results, but there has been a growing appreciation of the distinction between subretinal drusenoid deposits (SDD) and soft drusen (SD) subtypes in AMD. Here, we investigate whether the SDD and SD subtypes of AMD show differences in prevalence of ASD or levels of vascular serum risk factors.

Methods: Volume spectral-domain optical coherence tomography (SD-OCT) scans, self-reported health history questionnaire, and blood samples were obtained for 200 subjects with AMD. The presence of SDD or SD or mixed subtype was judged by two retina specialists. The presence of ASD was determined by reported history of angina, stroke, transient ischemic attack, amaurosis fugax, stenting or bypass surgery, documented carotid artery stenosis >50%, or abnormal stress test results. Categorical variables were compared across groups using chi-square testing, while continuous variables were compared using Kruskal-Wallis non-parametric testing with posthoc Mann-Whitney U testing for subgroup analysis.

Results: SD-OCT analysis showed that 103 subjects had pure SD, 26 had pure SDD, and 71 subjects had a mixed subtype. The prevalence of ASD was 15.5% for pure SD, 26.8% for mixed subtype, and 38.5% for pure SDD ($p=0.028$ for pure SD vs pure SDD). Subfoveal choroidal thickness in the right eye was 196 (153-240), 148.5 (118.75-189), and 145 (108.5-173.5) for the SD, mixed, and pure SDD groups respectively ($p<0.001$). There was no significant difference in serum lipid levels among the groups; however, there was a significant difference among the groups in high sensitivity C-reactive protein (hsCRP) level ($p=0.042$): hsCRP was 1.17 (0.6-2.4), 1.72 (0.96-3.72) and 2.09 (0.775-4.115) for the pure SD, mixed SD/SDD, and pure SDD groups respectively.

Conclusions: These findings contribute to a growing body of evidence that SDD and SD phenotypes associate with different risk factors, and that the SDD subtype may have a more robust relationship with ASD, potentially through inflammatory processes related to higher levels of hsCRP found in this subtype. Further studies based on AMD subtype may further elucidate separate risk factors and disease mechanisms underlying these different types of AMD.

CONTROL ID: 3702004
SUBMITTER (NAME ONLY): Kajal Sangal
TITLE: COVID-19 Associated Optic Neuritis
SESSION TITLE: Neuro-ophthalmology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Sangal, V. Barquet-Piza, J. Nichols, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|
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ABSTRACT BODY:

Purpose: While severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is well known for its respiratory complications, ocular manifestations are emerging. This case report describes a patient with bilateral optic neuritis associated with coronavirus disease 2019 (COVID-19).

Methods: A 46-year-old male presented with two weeks of pain with eye movement immediately after testing positive for COVID-19 and four days of bilateral blurry vision. Data including history, ocular examination, Humphrey visual field testing (HVF), magnetic resonance imaging (MRI), and serological testing was collected.

Results: Visual acuity (VA) was 20/100 in the right eye (OD) and 20/70 in the left eye (OS) with pinhole VA of 20/40 in each eye. Pupil exam, intraocular pressures, and confrontational visual fields were normal. Ocular motility was full, however the patient endorsed pain with eye movement in all directions. The right optic nerve had blurred disc margins while the left optic nerve was unremarkable on exam. Color vision was decreased to 13/15 by Ishihara testing in each eye. MRI of the brain and orbits revealed bilateral thickening and T2 hyperintensity and hyperenhancement of the intercanalicular and intraorbital optic nerves with sparing of the nerve sheath and no demyelinating lesions (Figure 1). Bilateral central scotomas were seen on HVF (Figure 2). At this point, the patient’s clinical picture was concerning for optic neuritis associated with COVID-19. A complete blood count, comprehensive metabolic panel, myelin-oligodendrocyte glycoprotein antibody, and aquaporin 4 antibody were unremarkable. Testing for tuberculosis, sarcoidosis, syphilis, thyroid disease, and rheumatologic and autoimmune disorders was normal. The patient was treated with corticosteroids. Within three to six weeks, the patient's symptoms and abnormal exam findings resolved.

Conclusions: Infectious pathogens and their subsequent inflammation can cause optic neuritis. It is postulated that T cells release inflammatory mediators and cytokines that cross the blood brain barrier and lead to destruction of myelin, neuronal cell death, axonal degeneration, and vision loss. SARS-CoV-2 could cause a similar inflammatory response leading to optic neuritis and is important to consider in cases without a clear etiology.

CONTROL ID: 3702022

SUBMITTER (NAME ONLY): Guillaume Tardieu

TITLE: MEDICARE randomized trial: intravitreal aflibercept treatment versus pan-retinal photocoagulation in the regression of neovascularisation in proliferative diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Tardieu, M. Bolet, N. Leveziel, Centre Hospitalier Universitaire de Poitiers, Poitiers, FRANCE|M. Saleh, Centre hospitalier regional universitaire de Besancon, Besancon, FRANCE|G. Pebayle, Centre Hospitalier Universitaire de Poitiers, Poitiers, FRANCE|P. Ingrand, Universite de Poitiers UFR Medecine et Pharmacie, Poitiers, FRANCE|

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ABSTRACT BODY:

Purpose: Proliferative diabetic retinopathy (PDR) is a potentially blindness-inducing complication of diabetes that affects 17 million persons worldwide. Since the 1980s, pan-retinal photocoagulation (PRP) has been the reference treatment, but its side effects involve loss of the peripheral field of vision. The main objective of this study was to evaluate neovascularisation regression by means of anti-VEGF intravitreal injections (IVI) of aflibercept (EYLEA®) in uncomplicated proliferative diabetic retinopathy at 12 months.

Methods: Phase II, interventional, prospective, open-label, multicenter pilot study. Randomized into 2 arms (PRP or IVI group) and monitored for 18 months. Participants had type 1 or type 2 diabetes with uncomplicated proliferative diabetic retinopathy, excluding macular oedema greater than 350 µm. As regards the examination, visual acuity assessment was carried out using an ETDRS Log-MAR scale at 4 meters, optical coherence tomography (OCT) for retinal thickness, OCT angiography for the foveal avascular zone (FAZ) and fluoresceine angiography (Spectralis HEIDELBERG) for surface area measurement.

Results: A total of 40 patients were randomized to the 2 groups between May 2014 and August 2018. As regards the primary endpoint, there was a significant difference, with neovessel regression exceeding 50% in 88.9% of the IVI group at 12 months, compared with 26.3% in the PRP group ($p = 0.0002$). As regards variation in macular retinal thickness, the 12-month test was likewise significant, with a mean reduction of 20.8 µm in the IVI group versus a mean increase of 16.9 µm in the PRP group ($p = 0.0004$). There was no significant difference concerning best corrected visual acuity, area of the foveal avascular zone or non-perfusion index.

Conclusions: The study showed greater regression of neovascularisation at 12 months with intravitreal aflibercept compared to PRP in treatment of proliferative diabetic retinopathy. No significant difference in visual acuity gain appeared. Our study is in line with the S Protocol by Gross (2015, JAMA) and the CLARITY study by Sivaprasad (2017, LANCET). However, instead of focusing on visual acuity, the primary endpoint here is neovessel regression on angiography, showing superior efficacy of IVTs that become a valid alternative to RRP and its adverse effects.

CONTROL ID: 3702059

SUBMITTER (NAME ONLY): Matthew Russell

TITLE: Retinal Mitochondrial Flavoprotein Fluorescence in Patients with Genetically Confirmed Retinal Dystrophies

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Oxidative stress and apoptosis have been implicated as drivers of various vision impairing retinal diseases. These stressors increase the pool of oxidized retinal mitochondrial flavoproteins relative to reduced ones. Oxidized flavoproteins display autofluorescence when excited by 467 nm light, emitting 535nm light in response. The emission signal, termed flavoprotein fluorescence (FPF), can be measured and used as a quantifiable marker for oxidative damage-induced mitochondrial dysfunction. In retinal dystrophies there is a high level of oxidative strain in the retina, which has not been characterized by retinal FPF signal measurements and patterns in a large cohort. Furthermore, these measurements may provide physiologically relevant metrics of disease progression that can complement currently utilized fundus autofluorescence (FAF) imaging.

Methods: This prospective cohort study examined 70 eyes from 35 patients with isolated genetically confirmed Cone-rod dystrophies (Retinitis Pigmentosa, Usher Syndrome), Stargardt disease, and Bardet-Biedl syndrome between 2020-2021. Patients with other ocular pathology were excluded. 70 control eyes from 40 patients were healthy age-matched individuals. In instances of bilateral involvement, each eye was considered separately. FPF score intensity and heterogeneity were recorded using the OcuMet Beacon (OcuSciences, Ann Arbor, MI). Statistical analysis was done to compare scores.

Results: The final analysis included 140 images of 75 patients. Mean FPF intensity was significantly increased between age matched controls and patients with confirmed rod-cone dystrophy, Stargardt disease, and Bardet-Biedl syndrome ($P=0.0014$, $P<0.0001$, and $P<0.0001$). Mean FPF heterogeneity was significantly increased between age matched controls and patients with confirmed cone-rod dystrophy, Stargardt disease, and Bardet-Biedl syndrome ($P<0.0001$, $P<0.0001$, and $P<0.0001$). FPF lesions were noted to visually correlate with patterns of FAF signals in cases with macular involvement.

Conclusions: FPF intensity and heterogeneity are significantly increased in patients with retinal dystrophies compared to matched controls. Correlation of the pattern of FPF lesions with FAF lesions suggests FPF has capacity to be explored as a measurable indicator of disease progression in these patient populations.

CONTROL ID: 3702063

SUBMITTER (NAME ONLY): Sandra Hoyek

TITLE: National versus international practice patterns and outcomes of intravitreal anti-VEGF injection for retinopathy of prematurity

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Hoyek, N.A. Patel, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.A. Acaba-Berrocal, Ophthalmology, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|K.C. Fan, A.M. Berrocal, Ophthalmology, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|C.R. Baumal, Ophthalmology, Tufts University, Medford, Massachusetts, UNITED STATES|M. Martinez-Castellanos, Ophthalmology, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, MEXICO|C. Harper III, Ophthalmology, The University of Texas at Austin, Austin, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a lack of consensus guidelines regarding intravitreal anti-vascular endothelial growth factor (VEGF) therapy for retinopathy of prematurity (ROP). This multicenter, retrospective, consecutive series compares national and international practice patterns and outcomes data of intravitreal injections for ROP.

Methods: Subgroup analysis from the ROP Injection Consortium (ROPIC) data from 23 sites (16 national from the USA and 7 international from Canada, Chile, Dominican Republic, Japan, Mexico, Taiwan and Turkey) from 2007 to 2021. Primary outcomes included rates and types of retreatment as well as complications. Secondary outcomes included specifics of the injection protocol.

Results: 1677 eyes (873 national and 804 international) of 918 patients were included. Mean birth weight and gestational age were lower in the national (665.6 g and 24.5 weeks respectively) compared with the international group (912.7 g and 26.9 weeks respectively) ($p<0.0001$). The percentage of APROP and plus disease were higher in the national (26.2% and 88.7%, respectively) compared with the international group (8.7% and 81.9% respectively) ($p=0.0001$). Ranibizumab was used more frequently in the national group (30.9% versus 17.4%; $p<0.0001$) versus Aflibercept in the international group (5.3% versus 0.8%; $p<0.0001$). Ranibizumab dosage was lower in the national (0.15 mg in 75.2%) compared to the international group (0.25 mg in 65.7%). Intravitreal injection was administered with a 32-gauge short needle in 48.2% of national cases versus 5.5% of international cases ($p<0.0001$) where a 30-gauge needle was primarily used (68.2%). Rates of retreatment with anti-VEGF reinjection or laser post-injection were higher in the national compared to the international group (8.5% vs 4.7% [$p=0.0016$] and 55% vs 7.2% [$p<0.001$] respectively). Average time to retreatment with laser was longer nationally (134.2 days vs. 36.4 days, $p<0.0001$). However, retreatment time with injection was similar between both groups (62.2 vs. 48.7; $p=0.082$). There was no difference in the incidence of complications including endophthalmitis between the two geographical subgroups.

Conclusions: ROP treatment paradigms vary depending on geography. Infants with ROP receiving anti-VEGF injection nationally tended to be younger, smaller, treated earlier, and have more anti-VEGF retreatments compared to international neonates with ROP.

CONTROL ID: 3702067

SUBMITTER (NAME ONLY): Anne Zebitz Eriksen

TITLE: Active Transport of Cationic Liposomes Across the Retina

SESSION TITLE: Drug delivery

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Drug delivery to the retina remain a challenge, limiting the therapeutic possibilities for a myriad of blinding diseases. Ocular barriers and fast clearing of intravitreally injected drugs are recognized as the main obstacles for efficient retinal drug delivery. Encapsulation of drugs into nano-sized vehicles hold the promise of prolonging retention times and enhancing delivery to the retina, however, poor understanding of clearing mechanisms limits the clinical realization of nano-sized drug delivery systems (DDS) for intravitreal injection. Here we investigate the involvement of active transport in clearing intravitreally injected liposomes.

Methods: Liposomes were formulated with 10% cationic lipid (DSTAP) and 5% lipid anchored poly-ethylene-glycol (DSPE-PEG). The metal tracer drug Oxaliplatin (OxPt) was loaded in the core of the liposomes. Liposomes were intravitreally injected in 6-10-week-old female C57BL/6JrJ mice. A subset of 4 mice were pre-injected with chloroquine to inhibit active transport. 24h post injection eyes were harvested and dissected into tissue fractions. The amount of Pt in the tissues were quantified by induced coupled plasma mass spectrometry.

Results: The resulting liposomes were unilamellar, had a diameter of 120.2±2nm and slight positive zeta-potential of 7.6±2mV (Figure 1 A and B). The liposomes showed a clear tendency of retaining OxPt in the vitreous, compared to free OxPt (Figure 1C). Interestingly, free OxPt resulted in the highest retinal concentration of OxPt, while liposomal OxPt by-pass the retina and is transported to the RPE/Sclera. Pre-treatment with chloroquine, an inhibitor of active endosomal transport, significantly reduced the clearing of the cationic liposomes to the RPE/Sclera.

Conclusions: The liposomes enhanced the retention of OxPt after intravitreal injection, however, led to significant lower retinal concentrations compared to free drug, due to active transport from the vitreous to the RPE/Sclera. Active transport mechanisms significantly impact the biodistribution of intravitreally injected liposomes and needs consideration when designing DDS targeting the posterior eye.

CONTROL ID: 3702107

SUBMITTER (NAME ONLY): Yongcheng Li

TITLE: Lipid surface area, emulsion stability and clinical performance of Blink® Triple Care lipid eye drop

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zhuk, J. Martin, Johnson & Johnson Consumer Companies Inc, Skillman, New Jersey, UNITED STATES|Y. Li, M. Bishop, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: When creating a lipid eye drop, there is a desire to have a small oil droplet size. This allows a more uniform and stable product and a higher surface area leading to higher bioavailability. In vitro testing was conducted to analyze the oil droplet size and emulsion stability profile of the Blink Triple Care lipid eye drop and 4 marketed lipid eye drops. Additionally, a clinical study was done to evaluate the improvement in overall ocular comfort and overall quality of vision after 30 days of use of Blink® Triple Care lipid eye drop.

Methods: The droplet size of the lipid phase was measured using a Dynamic light scattering instrument (Malvern Zetasizer Nano). The clinical study was a double masked, bilateral, multi-site, 30 day dispensing trial. Subjects 18-69 years of age were dispensed eye drops for 30 days of use. Endpoints included change from baseline in overall ocular comfort, end of day comfort, overall vision, and end of day vision, all on a 0-100 visual analog scale (VAS).

Results: Blink Triple Care shows a bimodal distribution of the lipid phase, with 83.8% (V) at 25nm & 16.2% at 195nm. Systane Complete shows a peak at 105nm, Systane Balance at 226nm, Refresh Optive Advanced at 309nm. Soothe XP has a size of ~ 8880 nm using a leaser diffraction technique. The surface areas of the lipid estimated from droplet size and lipid concentration were: Blink Triple Care 6.45, Systane Complete 5.71, Systane Balance 2.65, Refresh Optive Advanced 0.49 and Soothe XP 0.34 cm^2 per ml of eye drop. Emulsion instability, expressed as changes in transparency after a sample was centrifuged for 24 hours at 40^oC, was 1.4% for the Blink Triple Care, 4.3% for Systane Complete, 121.8% for Systane Balance, 282% for Refresh Optive Advanced, and 4096% for Soothe XP. Sixty-three subjects successfully completed the clinical study. The mean (std) change from baseline after 30 days us of Blink Triple Care was 21.4 (24.5) for overall comfort, 34.6 (26.8) end of the day comfort, 14.2 (22.5) overall vision, and 24.4 (26.0) end of the day vision.

Conclusions: Blink® Triple Care has the smallest oil droplet size among the lipid eye drops tested, yielding the highest lipid surface area as well as the highest emulsion stability. There was a large improvement in comfort and quality of vision scores, particularly at the end of day after a month of using the Blink® Triple Care lipid drop in a clinical study.

CONTROL ID: 3702116

SUBMITTER (NAME ONLY): Mohammad Mirazul Islam

TITLE: Chemical Crosslinker-free Pro-regenerative Corneal Implants

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Transplantation of the cornea is a standard procedure for the treatment of corneal blindness, but there is a severe scarcity of donor corneas. The development of an artificial cornea could help to quell the demand. Collagen-based artificial corneas, in which the collagen has been chemically crosslinked, have shown promise in human trials. However, most crosslinking agents are cytotoxic. In the absence of crosslinking, collagen implants are mechanically weak and susceptible to enzymatic degradation. In this work, we successfully fabricated transparent hydrogels as corneal substitutes from collagen, without using any crosslinkers or modifying the native collagen structure.

Methods: We developed a pyrene conjugated dipeptide amphiphile PyKC consisting of lysine and cysteine for supramolecular gelation where collagen molecules are intertwined inside the PyKC network without any alteration of the collagen. Hydrogels of 10% and 15% collagen (as controls), 10% collagen-1% PyKC, 10% collagen-2% PyKC, 15% collagen-1% PyKC, and 15% collagen-2% PyKC, are referred to as $Coll_{10}$, $Coll_{15}$, $Coll_{10}$-$PyKC_1$, $Coll_{10}$-$PyKC_2$, $Coll_{15}$-$PyKC_1$ and $Coll_{15}$-$PyKC_2$, respectively. We measured physicochemical properties, biocompatibility, immunogenicity and antiviral property of the hydrogels. One-way ANOVA with Tukey post hoc test was performed to compare between groups.

Results: Light transmission studies showed the hydrogels are transparent in visible light and block UV light. The hydrogels were mechanically comparable with controls ($Coll_{10}$ and $Coll_{15}$-$PyKC_2$, $p=0.0555$), enzymatically stable, and the tolerance for sutures was increased compared to controls ($Coll_{10}$ and $Coll_{15}$-$PyKC_2$, $p=0.0128$). The hydrogels also supported the growth and function of corneal epithelial, stromal, and endothelial cells. In vitro immune response studies showed that the hydrogels suppressed the inflammatory differentiation of human monocyte-derived dendritic cells. The hydrogels also restricted adenovirus propagation ($Coll_{15}$ and $Coll_{15}$-$PyKC_1$, $p=0.0007$).

Conclusions: Our newly developed crosslinker-free fabrication strategy may dramatically impact the development of corneal implants. The hydrogels can also be modified to encapsulate cells, drugs, growth factors, and/or antibodies for therapeutic use.

CONTROL ID: 3702139

SUBMITTER (NAME ONLY): David Berntsen

TITLE: Pupil Size and Myopia Progression in the Bifocal Lenses In Nearsighted Kids (BLINK) Study

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Berntsen, A.T. Gostovic, M.A. Chandler, A.G. Giannoni, M. Walker, University of Houston College of Optometry, Houston, Texas, UNITED STATES|L.T. Sinnott, D.J. Orr, L. Jordan, J.J. Walline, D.O. Mutti, The Ohio State University College of Optometry, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The BLINK Study was a 3-year clinical trial that evaluated center-distance multifocal contact lenses (MFCLs) for myopia control and found reduced myopia progression and eye growth with +2.50 add MFCLs compared to single vision contact lenses (SVCLs). This analysis explores whether pupil size influenced the magnitude of the treatment effect.

Methods: Myopic children (n = 294; 7-11 years old; 60% female) were enrolled (mean ± SD age = 10.3 ± 1.2 years) and randomly assigned to one of 3 groups: SVCL, +1.50 MFCL, or +2.50 MFCL. Children had -0.75 D to -5.00 D of myopia (most hyperopic meridian) and <1.00 D astigmatism at enrollment (mean ± SD spherical equivalent = -2.39 ± 1.00 D). Pupil size (right eye) was measured at baseline and each annual visit under photopic (~500 lux) and mesopic (~2 lux) lighting with a NeurOptics VIP-200 pupillometer. Models of the 3-year change (right eye) in cycloplegic spherical equivalent refractive error (RE; measured by autorefraction) and axial length (AL; measured by optical biometry) were fit with mean photopic or mesopic pupil size, either baseline RE or AL, treatment group, sex, study site, and age. Interactions between pupil size and treatment group were evaluated as the main outcome of interest.

Results: Mean (± SD) photopic and mesopic pupil size were 5.0 ± 0.6 mm (range: 3.3 to 6.9 mm) and 6.4 ± 0.7 mm (range: 4.5 to 8.4 mm), respectively, with no difference between treatment groups (photopic p = 0.60; mesopic p = 0.62). When modelling the 3-year change in spherical equivalent RE, neither photopic (p = 0.67; 95% CI: -0.40 to +0.25 D/mm pupil size) nor mesopic pupil size (p = 0.47; 95% CI: -0.41 to +0.19 D/mm pupil size) modified the slowing of myopia progression found in the +2.50 MFCL group (i.e., no treatment by pupil size interaction). With respect to change in AL, neither photopic (p = 0.92; 95% CI: -0.13 to 0.15 mm AL change/mm pupil size) nor mesopic pupil size (p = 0.37; 95% CI: -0.07 to 0.19 mm AL change/mm pupil size) modified the slowing of AL found in the +2.50 MFCL group.

Conclusions: Larger pupils have been hypothesized to have a greater treatment effect with center-distance MFCLs by exposing the retina to additional plus power. Pupil size did not modify the size of the treatment effect when children wore MFCLs in the BLINK Study. These results do not support using pupil size as a criterion when evaluating which myopic children to fit with this MFCL.

CONTROL ID: 3702151

SUBMITTER (NAME ONLY): Yiyi Wang

TITLE: Enhanced S-Cone Syndrome gives rise to enhanced S-cone acuity

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Wang, A. Roorda, W.S. Tuten, Herbert Wertheim School of Optometry and Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|J. Wong, J.L. Duncan, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Enhanced S-Cone Syndrome (ESCS) is a rare retinal degenerative disease mostly caused by pathogenic variants in the NR2E3 gene. Rod photoreceptor differentiation is disrupted during ESCS retinal development, resulting in a retina where short (S) wavelength cones predominate, long (L) and middle (M) wavelength cones are present in reduced numbers, and rods are absent. This study explores the topographic macular cone distribution in ESCS subjects and examines the impact of abnormally high extrafoveal cone density on spatial vision.

Methods: We used an adaptive optics scanning laser ophthalmoscope (AOSLO) to measure cone spacing in 5 ESCS subjects. A custom display channel was added in the AOSLO to measure L/M- and S-cone mediated visual acuity along with retinal imaging. Acuity measurement used a 4-alternative forced choice, tumbling-E paradigm. S- and L/M-cone acuities were measured along the temporal meridian between the fovea and 4° eccentricity. S-cone isolation was achieved using a two-color chromatic adaptation method that was validated on 3 control subjects. L/M acuity was tested by presenting long-pass-filtered (Wratten 16) optotypes on a black background. Quest staircases with 50 trials were used for each experimental condition.

Results: Normal eyes had ~0.5 arcmin cone spacing at the fovea that increased to ~1.5 arcmin at 3° and ~1.9 arcmin at 8°. The 5 ESCS patients had relatively constant cone spacing throughout the macula with arcmin values of 0.9-1.5 for the 4 youngest ESCS subjects, and 1.8-2.2 for subject 10055. The 4 youngest ESCS patients had increased foveal cone spacing (lower cone density) compared to normal, but beyond 2-3°, cone spacing was lower, and cones were more densely packed than normal. In 7 normal subjects, L/M-cone acuity behaved similarly to normal achromatic acuity. Foveal S-cone acuity was about 20/220, and declined with eccentricity. L/M-cone acuity in the ESCS subjects had high intersubject variability, but showed near normal performance at the fovea and got worse with eccentricity. Two of the ESCS subjects had better than normal S-cone acuity across all eccentricities. The third ESCS subject had worse S-cone acuity near the fovea but better than normal S-cone acuity beyond 2° eccentricity.

Conclusions: Higher-than-normal parafoveal cone densities (presumably dominated by S-cones) in ESCS subjects confer better-than-normal S-cone mediated acuity.

CONTROL ID: 3702190
SUBMITTER (NAME ONLY): Yeboah Gyening
TITLE: Deciphering ELOVL4 mutant activity in retinal degeneration
SESSION TITLE: Tissue, drug and genome engineering
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y.K. Gyening, N.K. Chauhan, R.E. Anderson, M.G. Agbaga, Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|V. Ea, M. Tytanic, R.S. Brush, R.E. Anderson, M.G. Agbaga, Ophthalmology and Dean Mcgee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|
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ABSTRACT BODY:

Purpose: ELOngation of Very Long-chain fatty acids-4 (ELOVL4) is an enzyme that catalyzes the biosynthesis of very long chain saturated (VLC-SFA) and polyunsaturated (VLC-PUFA) fatty acids, collectively known as very long chain fatty acids (VLC-FA). ELOVL4 is only expressed in the retina, brain, skin, testis, and Meibomian glands. Different mutations in ELOVL4 affect these tissues in different ways. Some known mutations in humans only affect the retina causing a juvenile form of macular degeneration known as Autosomal Dominant Stargardt-like Macular Dystrophy (STGD3), while other mutations affect the brain and/or skin leading to Spinocerebellar Ataxia-34 (SCA34) and skin lesions. How the different ELOVL4 mutations cause such different tissue-specific pathologies are not well understood. We hypothesize that the various mutant ELOVL4 enzymes synthesize less and varying amounts of VLC-FA in a tissue-specific manner to cause the different tissue-specific pathologies.

Methods: We transduced ELOVL4 variants (L168S, L168F, W246G, and STGD3) in human embryonic kidney cells (HEK 293T) or human retinal epithelial cells (ARPE-19) and treated the cells with VLC-FA precursors lignoceric acid (24:0) and eicosapentaenoic acid (EPA; 20:5n3). The cells were harvested for fatty acid analyses to determine the level of VLC-FA biosynthesis. The effect of the different ELOVL4 variants on cell health was also examined using cell-based assays.

Results: The truncated ELOVL4 mutations that cause STGD3 did not synthesize VLC-FA. However, the SCA34 proteins, although enzymatically active, synthesized lesser quantities of VLC-FA than that of wild-type ELOVL4. Further, the accumulation of mutant ELOVL4 protein triggers endoplasmic reticulum (ER) stress through the eIF2α–ATF4 pathway and leads to cell death. We were able to alleviate the ER stress and cell death by supplementation with unsaturated fatty acids (EPA) while saturated fatty acids (24:0) exacerbated cell death.

Conclusions: The SCA34 ELOVL4 proteins make less VLC-FA product and promote cell death via ER stress, which can be alleviated with EPA supplementation. Future experiments will delve deeper into understanding the mechanisms of retinal degeneration in ELOVL4-related diseases.

CONTROL ID: 3702201

SUBMITTER (NAME ONLY): Clayton Radke

TITLE: Dynamic Salt Accumulation in the Post-Lens Tear Film with Soft-Contact-Lens Wear: Implications for Protection Against Corneal Hyperosmolarity

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Radke, Y. Kim, T. Nguyen, Chemical and Biomolecular Engineering Department, University of California Berkeley, Berkeley, California, UNITED STATES|C.J. Radke, Y. Kim, M.C. Lin, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|M.C. Lin, Clinical Research Center, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|C. PENG, Coopervision Inc, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaporative-salinity increases in the pre-corneal tear film can lead to hyperosmotic stress-induced discomfort [Liu et al. 2013]. By shielding the cornea, soft contact lenses (SCLs) can, in principle, protect the cornea against such hyperosmotic stresses. Because SCLs are hydrogels, salt can permeate through the lens [Guan et al. 2011] and post-lens tear film (PoLTF) to reach the cornea [Kim et al. 2021]. Permeation through the lens requires time for the salt to diffuse across the lens. If the time required for salt to transport across the lens is of order hours, lens wearers could remove and reinsert the lens during the midday to forestall PoLTF hyperosmolarity. Here, to ascertain whether midday reinsertion is suitable method to mitigate PoLTF hyperosmolarity, we determine the time it takes for the PoLTF osmolarity to reach a periodic steady state.

Methods: The SCL osmolarity model of Kim et al. [2021] was modified to determine the time it takes to reach steady state for various lens salt partition coefficients (k_s), lens salt diffusivities (D_s), and lens thicknesses (h_{lens}). The mathematical model is scripted and computed with Matlab R2019b. Modified script counts the number of iterations required to reach periodic steady state and converts iteration number into the time to reach steady state. Analyses are conducted for both normal and dry-eye scenarios.

Results: Figure 1 provides calculated PoLTF osmolarity for normal eye for various D_s and fixed interblink period (t_{ib}), k_s, and h_{lens} (specified in Figure 1). The D_s range in Figure 1 accounts for most commercially available silicone-hydrogel and hydrogel contact lenses today. PoLTF osmolarity reaches steady state within the first 30 min of lens wear. This is also the case for the dry-eye scenario (i.e., increased tear-evaporation and decreased tear-production rates). Time to attain steady state was still less than 30 min even after varying h_{lens} and t_{ib} over physically realistic values.

Conclusions: Time to steady state for the PoLTF osmolarity occurs within the first hour of lens insertion for all adjustable parameters. Therefore, midday lens removal is not a viable way to regulate PoLTF osmolarity. Lowering D_s is the most effective way to mitigate PoLTF hyperosmolarity.

CONTROL ID: 3702212

SUBMITTER (NAME ONLY): Kyong Jin Cho

TITLE: Effect of Minocycline Ointment on Meibomian Gland Dysfunction Rat Model

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) is known to be a major cause of dry eye disease, with various ocular surface disorders. Currently, appropriate eye drops are prescribed to deal with MGD, as well with thermal and mechanical means such as warm compresses or lid scrubs. Minocycline is one of the tetracycline antibiotics, routinely being prescribed to MGD patients for oral administration. It is proven to be effective in dealing with MGD symptoms but has potential risks such as photosensitivity, gastrointestinal disturbances (emesis, diarrhea, and dyspepsia), and genitourinary symptoms, etc. If possible, the use of minocycline ointment may reduce some of the known risks with the same effect. Since there is no study yet regarding the use of minocycline ointment on MGD, the authors aimed to investigate the effect of minocycline ointment in the MGD rat model.

Methods: Cell viability test was conducted using human corneal epithelial cells and the appropriate concentration of minocycline without toxicity was confirmed. Then the proven concentration was compared with the currently available minocycline ointment for in vivo experiment. MGD rat model was established using CFA injection on the nasal and lateral eyelid margin of six-week-old male SD rats. After MGD induction for a week, the rats were treated with minocycline ointment twice a day for three weeks. A total of six experimental groups were used, including control, control with minocycline ointment, MGD, MGD with hyaluronic acid, MGD with oxytetracycline, MGD with cyclosporine, and MGD with minocycline ointment. Symptom scores (tear break-up time, corneal fluorescent staining score, telangiectasia score, and eyelid swelling score) were assessed every week for three weeks, then the rats were sacrificed for immunohistochemistry.

Results: The use of minocycline ointment in MGD rat model alleviated the symptoms showing decreased corneal fluorescent, lid swelling, and telangiectasia scores, as well with increased tear break-up time. Also, the level of inflammatory cytokines, IL-1b, IL-6, and TNF-a, were lowered after minocycline ointment treatment in corneal, conjunctiva, and meibomian gland tissues.

Conclusions: In conclusion, this study confirmed the positive effect of minocycline ointment in the MGD rat model, having lower symptom scores, higher tear break-up time, and showing the reduced level of inflammation in cornea, conjunctiva, and meibomian gland tissues.

CONTROL ID: 3702290

SUBMITTER (NAME ONLY): Emily Warner

TITLE: Design of Novel Multi-Cistronic AAV2 Gene Therapy Constructs for the Treatment of Diabetic Macular Edema

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.F. Warner, K. Boyd, P.S. Widdowson, K. Binley, A. Osborne, Ikarovec Limited, Norwich, UNITED KINGDOM|M. Whitehead, Department of Clinical Neuroscience, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: First-line anti-VEGF therapies for diabetic macular edema (DME) are efficacious in around half of DME patients and repeated administrations are associated with complications.

Anti-VEGF therapies fail to address inflammation and retinal cell loss associated with this disease and furthermore, hemolysis has been observed in primates treated with aflibercept through IgG-Fc gamma receptors. Therefore, we have designed a gene therapy to address the complex pathophysiology of DME that requires a single ocular injection.

Methods: Multi-cistronic plasmids and rAAV2/2 vectors expressing a novel anti-VEGF component and Tie2 receptor agonist together with a retinoprotective PEDF polypeptide were evaluated in HEK293T, ARPE-19 cells and co-cultures of human fibroblast/HUVECs. HUVEC monolayers were grown on transwells to assess permeability (TEER). The lead vectors were evaluated using rodent models.

Results: In a co-culture model of angiogenesis, lead constructs demonstrated significantly reduced capillary length and branch number versus controls equivalent to aflibercept (capillary length (mm); control = 13.7 ± 0.5, IKC113 = 3.8 ± 0.4***, aflibercept = 3.9 ± 0.3***; mean ± SEM of 12 replicates; ***P<0.001 by ANOVA with Bonferroni modified t-tests). A lead construct reduced angiopoietin-2 concentrations (ng/mL) in the co-culture medium (control = 1.29 ± 0.20, IKC113 = 0.09 ± 0.00***, aflibercept = 0.06 ± 0.00***; mean ± SEM of 3 replicates; ***P<0.001). Furthermore, a lead construct, acting through the Tie2 agonist component, attenuated TNF-alpha (TNFα)-induced reduction in TEER (Ohms/cm^2) over 24h in HUVEC monolayers (control minus TNFα = 23.5 ± 0.3, control Null plasmid plus TNFα = 15.1 ± 0.6, IKC113 plasmid plus TNFα = 20.1 ± 0.4; mean ± SEM of 3-6 replicates; **P<0.001 versus Null plasmid with TNFα) demonstrating reduced cytokine-induced vascular permeability. In the laser CNV study a lead tri-cistonic rAAV demonstrated a 60% reduction in CNV leakage compared to the vehicle control.

Conclusions: In addition to robust anti-VEGF activity, we have demonstrated that the multi-cistronic rAAV2/2 gene therapy has the ability to reduce vascular leakage and inflammation through Tie2 receptor activation. These novel gene therapies are set to become a valuable new treatment option for patients with DME.

CONTROL ID: 3702433

SUBMITTER (NAME ONLY): Paul McCann

TITLE: Diagnostic accuracy of optical coherence tomography angiography (OCTA) versus spectral domain optical coherence tomography (SD-OCT) parameters in perimetric glaucoma

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.M. McCann, R.E. Hogg, I. Young, F. Kee, A. Azuara-Blanco, Centre for Public Health, Queen's University Belfast School of Medicine Dentistry and Biomedical Sciences, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To compare the diagnostic accuracy of OCTA parameters and circumpapillary retinal nerve fibre layer thickness (cRNFLT) for perimetric glaucoma.

Methods: Northern Ireland Cohort for the Longitudinal Study of Ageing participants with vertical cup to disc ratio ≥0.7 and/or intraocular pressure ≥25mmHg were invited to clinical examination by a glaucoma expert and full-threshold 24-2 perimetry. Eyes were diagnosed as “glaucoma”, “glaucoma suspect” or “control”. Participants underwent OCTA and SD-OCT scans with Heidelberg Spectralis OCT2 at the same visit. OCTA en face images were segmented using ImageJ and quantitatively analysed using AngioTool. Areas under the receiver operating characteristic (AUROC) curves were calculated for diagnostic parameters using funcs_clusteredROC.R. Comparisons of AUROC curves were made between the mean global OCTA parameters and mean global cRNFLT.

Results: 63 eyes from 46 participants (mean age [SD] 65.33 [7.39]; 43.48% female) were included. Circumpapillary vasuclar flow density (cVFD) was statistically significantly lower in glaucoma eyes (n=20; 23.77%) compared to control eyes (n=16; 26.14%; $p<0.05$) and glaucoma suspect eyes (n=27; 25.65%; $p<0.05$). OCTA total number of vessel junctions was statistically significantly lower in glaucoma eyes (165.10) compared to control eyes (210.18; $p<0.05$) and glaucoma suspect eyes (207.07; $p<0.05$). OCTA mean lacunarity was statistically significantly higher in glaucoma eyes (0.705) compared to control eyes (0.666; $p<0.05$) and glaucoma suspect eyes (0.670; $p<0.05$). Mean global cRNFLT was statistically significantly lower in glaucoma eyes (70.05 µm) compared to control eyes (92.19 µm; $p<0.05$) and glaucoma suspect eyes (88.63 µm; $p<0.05$). AUROC (SE) was 0.83 (0.07) for OCTA cVFD, compared to 0.82 (0.06) for OCTA total number of vessel junctions ($p=0.80$), and 0.81 (0.07) for OCTA mean lacunarity ($p=0.76$). AUROC was 0.85 (0.06) for cRNFLT compared to 0.83 (0.07) for cVFD ($p=0.74$).

Conclusions: In participants referred from a population-based cohort study, OCTA mean global cVFD was the best performing OCTA parameter. Mean global cRNFLT was the overall best performing diagnostic parameter, however, it was not statistically significantly different from OCTA mean global cVFD. Longitudinal studies are required to assess the role of OCTA in detecting glaucoma progression.

CONTROL ID: 3702435

SUBMITTER (NAME ONLY): Nayasha Madhan

TITLE: In Vivo Relationship of Corneal and Scleral Stiffness with Bruch's Membrane Opening Minimum Rim Width in Glaucomatous versus Non-Glaucomatous Eyes

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.S. Madhan, Y. Ma, A. Mahmoud, G. Fleming, C.J. Roberts, Ophthalmology and Visual Sciences, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|S. Buma, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|A. Mahmoud, G. Fleming, C.J. Roberts, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the relationship between Bruch's Membrane Opening Minimum Rim Width (BMO) and ocular biomechanics in glaucomatous and non-glaucomatous eyes.

Methods: A cross-sectional study of prospectively acquired data was used to evaluate 323 eyes of 181 healthy controls (NRL) and 66 eyes of 42 subjects diagnosed with primary open angle glaucoma (GLA). Biomechanical response was characterized using the Corvis ST by comparing the stiffness parameters at first applanation (SP-A1) to indicate corneal stiffness and the stiffness parameter at highest concavity (SP-HC) to quantify scleral stiffness in the seated position. Spectralis OCT imaging was used to measure BMO. Pneumatonometry was used to measure intraocular pressure (IOP) and ocular pulse amplitude (OPA). BMO was compared to IOP by group with univariate regression analysis. BMO was also compared between GLA and NRL using ANCOVA with IOP as a co-variate. Finally, two multiple regression analyses were performed with BMO as the dependent variable, and IOP, age and either SP-A1 or SP-HC as the independent variables, using SAS statistical analysis software with $p<0.05$ as the significance threshold.

Results: Global BMO was significantly smaller in GLA compared to NRL eyes (211 ± 59 µm vs 358 ± 60 µm; $p<0.001$), and significantly negatively related to IOP only in NRL ($p<0.001$). Both corneal and scleral stiffness were significantly greater in GLA (SP-A1 $p<0.001$; SP-HC $p<0.027$). The two multiple regression analyses showed a significant, negative relationship of BMO with SP-A1 ($p<0.001$, $R^2=0.088$) and SP-HC ($p<0.001$, $R^2=0.078$) in NRL but not in GLA.

Conclusions: BMO decreases as IOP increases in NRL, but IOP has no effect on the significantly smaller BMO in GLA. As corneal and/or scleral stiffness increases, the BMO decreases in NRL but has no effect in the significantly stiffer GLA. These in vivo findings indicate that increasing stiffness may be an additional risk factor to increasing IOP for decreased BMO, and to the development of glaucomatous damage. Our results provide insight into the role of ocular biomechanics in glaucoma and identify parameters that may increase the risk of glaucoma development.

CONTROL ID: 3702455

SUBMITTER (NAME ONLY): Yuya Fujii

TITLE: Direct reprogramming of Müller cells into photoreceptor cells in mice by stimulation with small molecule compounds

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Arima, Ophthalmology, Kyushu Daigaku Igakubu Daigakuin Igakukei Gakufu Daigakuin Igaku Kenkyuin, Fukuoka, Fukuoka, JAPAN|Y. Murakami, Ophthalmology, Kyushu Daigaku Igakubu Daigakuin Igakukei Gakufu Daigakuin Igaku Kenkyuin, Fukuoka, Fukuoka, JAPAN|Y. Fujii, K. Sonoda, Ophthalmology, Kyushu Daigaku Igakubu Daigakuin Igakukei Gakufu Daigakuin Igaku Kenkyuin, Fukuoka, Fukuoka, JAPAN|

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ABSTRACT BODY:

Purpose: The aim of this study is to identify small molecule compounds that can reprogram retinal Müller cells (MCs) into photoreceptor cells and to evaluate the recovery of retinal function in animal models of retinal degeneration.

Methods: In vitro, MCs were stimulated with all combinations of candidate compounds, and rhodopsin (Rho) expression was confirmed on day 7 by Polymerase Chain Reaction and immunostaining. In vivo, we used 6-week-old N-methyl-N-nitrosourea [MNU]-treated and 4-week-old rd10 mice, representative models of retinal degeneration. The optimal combination of compounds determined by in vitro screening was injected into the vitreous and the changes in Rho expression were evaluated on day 7. The origin of Rho-positive cells was also validated in td-Tomato reporter mice. PAAV.GFAP.Cre.WPRE.hGH, which is an adeno-associated virus (AAV) containing human GFAP promoter, was injected into the vitreous of 2-week-old B6.Cg-Gt(ROSA)26Sortm14(CAG-tdTomato)Hze/J mice so that MCs could be visualized. On day 7 after MNU administration, co-expression with td-Tomato and Rho in the outer retina was confirmed by immunohistochemistry. Finally, the recovery of retinal function was assessed by electroretinography.

Results: In vitro, mRNA expression of Rho in MCs increased 30-fold, and 25% of MCs expressed Rho protein 7 days after stimulation with the combination of 4 compounds: tumor growth factor-β inhibitor, bone morphogenetic protein inhibitor, glycogen synthase kinase 3 inhibitor, and γ-secretase inhibitor. In vivo, Rho mRNA expression and the number of Rho-positive cells in the outer retina were significantly increased on day 7 after the intravitreal injection of these 4 compounds in both MNU-treated and rd10 mice. Lineage tracing in td-Tomato mice treated with MNU showed that the regenerated Rho-positive cells were originated from endogenous MCs, accompanied with recovery of Rho-derived scotopic function, which suggested Rho-positive cells may have the properties of photoreceptor cells.

Conclusions: These results suggest that photoreceptor cells can be regenerated from endogenous retinal MCs via direct reprogramming by small molecule compounds.

CONTROL ID: 3702459

SUBMITTER (NAME ONLY): Tatsuya Mimura

TITLE: Evaluation of subjective comfort of Verofilcon-A (Precision 1®) in first time contact lens wearing: First report

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Mimura, Y. Inoue, M. Kawashima, E. Watanabe, A. Mizota, Department of Ophthalmology, Teikyo Daigaku Igakubu Daigakuin Igaku Kenkyuka, Itabashi-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Purpose: A new, one-day disposable soft contact lens (SCL), the Verofilcon A (Precision 1®), constructed of silicone hydrogel material, has recently become available in Japan. This SCL has a very smooth surface produced by using the Smart Surface® technology. The purpose of this study was to compare the comfort of wearing eyeglasses and SCL for first time SCL wearers.

Methods: Methods: A total of 10 new SCL wearer were participated in this study. We compared the scores for comfort when wearing spectacles and Verofilcon-A.

Results: Results: The Subjective comfort scores (1-10) for glasses and SCL were (8.2 ± 1.5 vs 8.7 ± 1.3, $p = 0.13$) at insertion, (8.0 ± 1.3 vs 8.7 ± 1.1, $p = 0.07$) at daytime, and (6.0 ± 2.3 vs 8.7 ± 1.2, $p < 0.01$) at the end of the day, and (7.0 ± 1.6 vs 8.8 ± 1.2, $p = 0.02$) throughout the day, which were relatively higher for SCL than for glasses.

Conclusions: Conclusions: These findings indicate that the Verofilcon-A 1DSCL is more comfortable than eyeglasses and may be effective as an introductory lens for SCL initial wear.

CONTROL ID: 3702478

SUBMITTER (NAME ONLY): Katie Binley

TITLE: Novel Gene Therapy for the Regeneration of Schlemm's Canal for Patients with Ocular Hypertension

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Binley, E.F. Warner, K. Boyd, P.S. Widdowson, A. Osborne, Ikarovec Limited, Norwich, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Ocular hypertension (OHT) is a primary risk factor for developing glaucoma. Narrower Schlemm's canal (SC) and reduced SC epithelial cell pores have been observed post-mortem in glaucoma eyes indicating higher aqueous outflow resistance. Lower Tie2 receptor activity resulting from reduced angiopoietin-1 (Ang1) agonist levels may underlie this pathology. We have developed a regenerative gene therapy capable of restoring SC epithelium through release of a novel Tie2 agonist within the anterior chamber. This novel approach for OHT would eradicate the need for regular eye drops that have been hampered by poor adherence.

Methods: Novel plasmids and self-complementary rAAV2/2 vectors were examined for phospho-Tie2 levels using HEK293Ts transiently expressing Tie2 receptors. Intraocular pressure (IOP) was periodically measured by tonometry in normotensive mice and rats following intracameral injection of vector and compared to animals injected with a Null control vector. Expression levels were examined by immunohistochemistry.

Results: A series of proteins were designed based on the fusion of the fibrinogen-like domain of Ang1 and short coiled-coil regions of human proteins that could be accommodated within the capacity-limited scAAV2/2. The lead agonist construct (IKC074) was able to significantly activate Tie2 receptors (ratio of p-Tie2/total Tie2; IKC074 = 2.09 ± 0.35 $P<0.01$, mean ± SEM for n = 4 replicates). Intracameral injection of the IKC074 vector in mice and rats produced a sustained significant reduction in IOP (mmHg) versus animals administered with Null control vector and correlated with transgene expression levels (mouse IOP 14 days after injection controls = 16.3 ± 0.4 versus IKC074 = 13.1 ± 0.7 and at 42 days controls = 16.5 ± 0.5 versus IKC074 = 14.1 ± 0.6; $P<0.001$; Student's t-test, n = 10).

Conclusions: This gene therapy expresses a novel Tie2 agonist that has significant IOP reduction in both normotensive mice and rats through improved SC function and aqueous drainage. This experimental treatment requires only a single intracameral injection with anticipated efficacy to last several years. It would provide a valuable addition to the armamentarium for glaucoma treatment and prevention for patients with poor adherence or tolerance to eye drop medication.

CONTROL ID: 3702488

SUBMITTER (NAME ONLY): Gustav Stålhammar

TITLE: Systematic Review and Meta-Analysis of Long-Term Metastasis-free Survival in Untreated Uveal Melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Stålhammar, St. Erik Eye Hospital, Stockholm, SWEDEN|G. Stålhammar, V.T. Gill, Clinical Neuroscience, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|V.T. Gill, Department of Pathology, Västmanland Hospital Västerås, Västerås, SWEDEN|

Commercial Relationships Disclosure: Gustav Stålhammar: Commercial Relationship: Code N (No Commercial Relationship) | Viktor Gill: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The impact of primary tumor treatment on the survival of patients with uveal melanoma is uncertain and it is debated if a beneficial survival effect exists at all.

Methods: PubMed, Web of Science and Embase were searched for articles published in any language and in any year. Publications were included if they reported patients with primary melanoma of the choroid or ciliary body with ≥ 5-year follow-up for patients without metastases. Studies were excluded if patients had received any kind of treatment for their primary tumor within 5 years from diagnosis. The long-term cumulative metastasis-free and overall survival of the included patients was estimated and contrasted to cohorts of treated tumors.

Results: Seven studies with a total of 19 patients were included. Seven of the patients that initially refused treatment were eventually enucleated at a mean of 13 years after diagnosis (SD 10). Tumor size at diagnosis and last follow-up was available for eight patients. All of these were either small or medium-sized. Five tumors with specified diameter and/or thickness grew to a mean of 2.4 times its original size until last follow-up. The cumulative metastasis-free survival for 17 patients with choroidal or ciliary body melanoma was 71 % at five years (95 % CI 49-93 %), 29 % at 10 years (7-51 %), 18 % at 15 years (0-36 %) and 11 % at 30 years (0-27 %). This was significantly worse than the survival in comparison cohorts of both medium-sized (Log-rank $p<0.001$) and large treated tumors (Log-rank $p<0.01$).

Conclusions: Patients that do not undergo treatment for their primary uveal melanoma are exceedingly rare in the literature. Of the published cases, eight or nine out of ten have eventually developed metastases. This indicates that primary tumor treatment may prevent metastases.

CONTROL ID: 3702492

SUBMITTER (NAME ONLY): Isaiah Junior Osei Duah

TITLE: Bacteria isolates in external ocular and periocular infections and antimicrobial treatment patterns among Ghanaian ophthalmic patients: a multicenter study

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Osei Duah, M. Tchiakpe, D. Ben Kumah, B. Owusu Prempeh, J. Munyaneza, K. Owusu Akuffo, Department of Optometry and Visual Science, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|L. Sheringham Borquaye, Department of Chemistry, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|L. Sheringham Borquaye, Central Laboratory, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|K. Amoah, The Eye Clinic, Kumasi South Hospital, Atonsu-Agogo, Kumasi, GHANA|F. Kwaku Dzideh Amankwah, S. Yao Gbedema, Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|L. Aurelia Ofori, Department of Theoretical and Applied Biology, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|A. Danso-Appiah, Department of Epidemiology and Disease Control, School of Public Health, University of Ghana, Legon, GHANA|A. Danso-Appiah, University of Ghana Centre for Evidence Synthesis and Policy, School of Public Health, University of Ghana, Legon, GHANA|B. Owusu Prempeh, The Anglican Eye Hospital, Jachie, Kumasi, GHANA|C. Amaning Danquah, Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|

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ABSTRACT BODY:

Purpose: Given the surge in global antimicrobial resistance infections, insight into the bacteria etiology is essential in the choice of antibiotic therapy among ophthalmic clinicians in their routine management of eye infections. Considering the paucity of data from Ghana, this study investigated the bacteria etiology of external ocular and periocular infections, and antimicrobial treatment patterns among ophthalmic patients in Ghana.

Methods: The multicenter cross-sectional study enrolled patients from three hospital facilities in Ghana. One hundred and fourteen eligible subjects were enrolled and underwent comprehensive ophthalmic assessments. Clinical profile and demographic characteristics were collated with a pretested structured questionnaire. Ocular specimens including conjunctival swabs and corneal scrapes were obtained from patients' eyes and subjected to microbial analyses. Bacterial pathogens were isolated and characterized by differential media, colony morphology, gram reactions under light microscopy, and biochemical testing. All procedures were performed under aseptic conditions.

Results: About 95% of ocular samples were positive for bacteria culture. The proportion of Gram-negative bacteria was 58.2%, and the predominantly isolated bacteria species were Pseudomonas aeruginosa 38.8% and Staphylococcus aureus 27.6%. Pseudomonas aeruginosa was mostly implicated in cases of conjunctivitis and keratitis and with a proportionate distribution of 40.0% versus 75.0%, respectively. The routinely used antimicrobial therapy in the clinical management of eye infections was polymyxin B 41.2%, neomycin 35.1%, and ciprofloxacin 31.6%. Participants' demographic and clinical characteristics were not associated ($p > 0.05$, for all) with the presence of positive bacteria culture.

Conclusions: Our results demonstrate a markedly high burden of bacteria ocular infections with variations in etiology. Bacterial infection-control and antimicrobial agent management programs should be urgently instituted to prevent the emergence of potential resistant infections.

CONTROL ID: 3702511

SUBMITTER (NAME ONLY): Michael Christensen

TITLE: Racial & Ethnic Disparities in Diagnosis and Management of Keratoconus

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.T. Christensen, J. Kartchner, M. Giegengack, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|J. Kartchner, Arizona Eye Consultants, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Over 150,000 people in the United States are afflicted with keratoconus (KCN)—a corneal ectatic disease characterized by progressive corneal thinning. Until the recent advent of corneal crosslinking (CXL), one of the only treatment options for advanced KCN was corneal transplantation. Early diagnosis of KCN and subsequent CXL treatment has been shown to improve outcomes in patients suffering from KCN. At Wake Forest Baptist Health (WFBH), we have noticed a trend in referral patterns in which black patients often present to our department with more advanced KCN than non-black patients, which may lead to a delay in treatment and poorer outcomes.

Methods: We performed a retrospective review of patients presenting to WFBH between 2018-2020 for KCN evaluation. For each patient, demographic and referral information was collected. Exclusion criterion included prior corneal surgery or CXL. Outcome measures were best corrected visual acuity (BCVA), presence of corneal scarring, keratometry values, ABCD score, and recommended treatment plan. Follow-through with the recommended treatment plan was evaluated between groups within 6-months of initial consultation. Chi squared tests were used to perform statistical analyses.

Results: 128 patients were included the study. According to demographic information collected, black patients presented with a higher BMI and a more evenly distributed (1:1) male-to-female ratio. Tomographic outcomes showed that black patients presented with worse BCVA ($p < 0.0001$), worse tomographic keratoconus staging ($p < 0.0001$), and were more likely to have corneal thinning ($p < 0.0001$) or scarring ($p < 0.0001$) precluding corneal cross-linking when compared to non-black patients. There was no significant difference in the likelihood that black patients would follow through with a proposed treatment plan. However, there were poor follow-up rates among both groups—thus limiting the strength of this conclusion.

Conclusions: When compared to their non-black counterparts, black patients presented to our institution with more advanced KCN which often precluded CXL as a viable treatment option. Black patients were also just as likely to follow through with a proposed treatment plan.

CONTROL ID: 3702522

SUBMITTER (NAME ONLY): Katherine Tsay

TITLE: Does red flash on a blue background result in more eyelid muscle activity compared to white flash on a white background?

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Tsay, S. Safari, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|R.T. Tzekov, Department of Ophthalmology, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|R.T. Tzekov, Department of Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|

Commercial Relationships Disclosure: Katherine Tsay: Commercial Relationship: Code N (No Commercial Relationship) | Sara Safari: Commercial Relationship: Code N (No Commercial Relationship) | Radouil Tzekov: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: According to the extended protocol for the photopic negative response (PhNR) of the full-field electroretinogram from the International Society for Clinical Electrophysiology of Vision (ISCEV), the preferred method of eliciting PhNR is a red flash on a rod saturating blue background (ROB). However, PhNR can also be elicited by a white flash on a white background, under stimulus conditions like the one used to elicit an ISCEV standard Photopic 3.0 ERG (Ph3) response. The purpose of the current study is to compare the baseline noise between the two conditions in patients with various retinal pathologies.

Methods: A retrospective chart review and data analysis of patients aged 18 and over undergoing routine ERG testing at the University of South Florida Eye Institute (Tampa, FL) between July 2018 and October 2021 were conducted. Throughout the study period, Ph3 was recorded in the same way while ROB response was generated in three different ways, resulting in three comparison groups. Group 1 (Gr1) ROB protocol used a ~5 cd•s/m^2 red flash (627 nm) on a 30 cd/m^2 blue background (470 nm), Group 2 (Gr2) protocol used a ~2.5 cd•s/m^2 red flash on a 10 cd/m^2 blue background, while Group 3 (Gr3) protocol used a ~5 cd•s/m^2 red flash on a 10 cd/m^2 blue background. The level of background bioelectrical activity (30 ms before the flash) was compared between the Ph3 and ROB conditions by calculating the root mean square (RMS) of the signal under all three protocols.

Results: The records of 69 patients/138 eyes (19M, 50F, mean age 50.7 +/- 14.5 years) were evaluated (Gr1=14; Gr2=27; Gr3=28). The baseline level of activity was higher in all three ROB conditions compared to Ph3 for both right (OD) and left (OS) eyes. Specifically, in Gr1, OD RMS = 0.95 µV (Ph3) vs. 1.66 µV (ROB) ($p=0.003$, Wilcoxon matched-pairs signed-rank test) and OS RMS = 1.1 vs. 1.7 µV ($p=0.006$); in Gr2, OD RMS = 0.80 vs. 1.98 µV ($p=0.0003$) and OS RMS = 0.90 vs. 1.79 ($p<0.0001$); in Gr3, OD RMS = 0.87 vs. 1.27 µV ($p<0.0001$) and OS RMS = 0.96 vs. 1.14 µV ($p=0.02$).

Conclusions: Baseline activity was higher under ROB stimulation in all conditions compared to Ph3, indicating more eyelid muscle activity and a higher level of visual discomfort consistent with anecdotal patient reports. The results of our study suggest that a white flash on a white background may reduce patient discomfort while generating a comparable PhNR.

CONTROL ID: 3702529

SUBMITTER (NAME ONLY): Mallika Somayajulu

TITLE: Airborne exposure to PM_{10} induces corneal oxidative stress and disrupts Nrf2 mediated anti-oxidant defenses.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Somayajulu, S.A. McClellan, A. Pitchaikannu, R. Wright, B. Croniger, L.D. Hazlett, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effects of whole body animal exposure to airborne particulate with a diameter of <10µm (PM_{10}) in vivo in the mouse cornea and in vitro in immortalized and primary human corneal epithelial cell cultures.

Methods: C57BL/6 mice were exposed to ambient air or an acute, high dose of PM_{10} (500µg/m^3) for 2 weeks for 3h/day/5days/week and rested on the weekends. At 2 weeks, tear levels and corneal sensitivity were measured using phenol treated threads and a Cochet and Bonnet Esthesiometer, respectively. Hematoxylin and eosin staining of paraffin embedded tissue was used to evaluate corneal morphology. Corneal levels of reduced glutathione (GSH) and malondialdehyde (MDA) were evaluated by assay kit or ELISA. RT-PCR and ELISA evaluated levels of Nrf2 pathway molecules and pro-inflammatory markers. SKQ1 (Visomitin), a novel mitochondrial targeted antioxidant, was used to treat the 2 week PM_{10} exposed mice. Ambient air and PM_{10} exposed mice were pretreated with 7.5µM SKQ1 or PBS (control) topically 3 times one day before and then once/day/each day of exposure and tested for oxidative stress and Nrf2 pathway molecules. In vitro, cells were treated with 100µg/ml PM_{10} ± 50nM SKQ1. MDA levels were analyzed by ELISA, Nrf2 protein levels by western blot, mitochondrial ROS by a mitoSOX assay and ATP levels by an assay kit.

Results: No significant changes in tear secretion and sensitivity were observed in PM_{10} vs ambient air exposed mice at 2 weeks. PM_{10} significantly decreased GSH and increased MDA levels in cornea at 2 weeks over controls. Focusing on 2 weeks exposure, PM_{10} exposure caused thinning of the corneal epithelium and stroma. PM_{10} exposed corneas showed significantly higher mRNA levels for Nrf2 pathway and pro-inflammatory molecules over controls. Nrf2 protein was significantly reduced vs controls. SKQ1 treatment restored GSH and Nrf2 protein to control levels and lowered lipid peroxidation. In vitro, in immortalized human corneal epithelial cells, PM_{10} application reduced Nrf2 levels, increased MDA and mitochondrial ROS, but reduced ATP levels; while SKQ1 treatment reversed these effects.

Conclusions: Whole body PM_{10} exposure triggers corneal oxidative stress and disrupts the Nrf2 pathway which regulates antioxidant defenses. SKQ1 treatment reverses these deleterious effects. In vitro corneal epithelial cell data parallel the in vivo effects, suggesting human applicability.

CONTROL ID: 3702531

SUBMITTER (NAME ONLY): Danial Roshandel

TITLE: Localised cone density and retinal sensitivity changes in female carriers of RPGR mutations

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Roshandel, T.M. Lamey, J. Charng, R.C. Heath Jeffery, T.L. McLaren, J.N. De Roach, S. McLenachan, D.A. Mackey, F.K. Chen, Centre for Ophthalmology and Visual Science, The University of Western Australia, Perth, Western Australia, AUSTRALIA|D. Roshandel, J. Charng, R.C. Heath Jeffery, S. McLenachan, D.A. Mackey, F.K. Chen, Ocular Tissue Engineering Laboratory, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|T.M. Lamey, T.L. McLaren, J.A. Thompson, J.N. De Roach, Australian Inherited Retinal Disease Registry and DNA Bank, Department of Medical Technology and Physics, Sir Charles Gairdner Hospital, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Heterozygous RPGR mutations may cause progressive photoreceptor degeneration in female carriers. In this single-center, retrospective, observational study, we assessed retinal structure and function in female carriers of RPGR mutations.

Methods: Adaptive optics (AO) imaging and microperimetry (MAIA) were performed in female carriers of RPGR mutations. Cone density (CD) at 1.4° (4 loci/eye) and 3.2° (8 loci/eye) from the foveal center, and point-wise sensitivity (PWS) at 68 loci spanning central 20° (the 10-2 test grid) were analysed (Figure 1). Normality of measured values was defined against 10 (AO cohort) and 25 (MAIA cohort) age-matched healthy controls: normal < 1 SD, moderate defect 1–2 SD and severe defect > 2 SD from the normal average.

Results: AO and MAIA data were available in 8 and 12 patients, respectively. CD at 1.4° and 3.2° eccentricities showed severe defect in at least 2 locations in 4/8 and 5/8 patients, respectively (overall 38 locations at both eccentricities across the cohort). Severe PWS defect at 1.4° and 3.2° eccentricities was observed in at least 2 locations in 3/12 and 4/12 patients, respectively. Overall, PWS was normal in 25/38 (66%) loci with severe CD defect within the central 3.2° across the cohort (Figure 2). In addition, PWS showed at least moderate defect in ≥ 10/68 loci in 9/12 patients.

Conclusions: AO imaging and microperimetry detected localised defects in cone mosaic and retinal sensitivity in RPGR mutation carriers. Severe cone loss in locations with normal PWS in the parafoveal region suggests that structural damage preceded functional loss in this cohort.

CONTROL ID: 3702551

SUBMITTER (NAME ONLY): Barbara Swiatczak

TITLE: Axial length changes induced by positive defocus correlate with changes in choroidal blood flow

SESSION TITLE: Myopia: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Swiatczak, G. Calzetti, F. Schaeffel, Institute for Molecular and Clinical Ophthalmology IOB, Basel, SWITZERLAND|F. Schaeffel, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: It has previously been shown that imposed positive defocus induces significant changes in axial length and choroidal thickness after only 30 minutes. We investigated in young adult subjects whether these changes result from changes in ocular blood flow.

Methods: Sixteen young adult subjects (average age: 28±3 years, average refraction: -0.75±1.65D withing the range: +1.7 to -6D) watched a movie from a large screen (LG OLED65C9, 65 inch, 2019) at 2 m distance. Fifteen minutes wash-out period (watching a movie in a dark room with habitual refractive error correction) was followed by 30 minutes of watching a movie with a monocular positive defocus (+2.5D) in the right eye and a habitual correction in the left eye. Changes in axial length and blood flow were measured in both eyes before and after the defocus. Eye biometry was measured by using low-coherent interferometer (LS 900 with autopositioning system; Haag-Streit, Switzerland). Blood flow was measured by using a laser speckle flowgraphy (LSFG) RetFlow unit (Nidek Co., LTD, Japan). Two regions were analyzed: (1) the macular area, where choroidal blood flow can be measured, and (2) the optic nerve head.

Results: All subjects responded to imposed positive defocus as previously found: hyperopes and emmetropes displayed eye shortening while myopes showed axial elongation (Pearson's correlation coefficient between axial length change and refractive state: $R2 = 0.50$, $p<0.01$, Figure 1A). Control eyes did not show any significant changes in axial length after 30 minutes of watching a movie. Changes in axial length were significantly correlated with changes in choroidal blood flow in the macular region ($R2 = 0.43$, $p<0.01$, Figure 1B) and in the optic nerve head ($R2 = 0.27$, $p<0.05$, Figure 1C).

Conclusions: Transient changes in axial length induced by positive defocus appear to be linked to changes in choroidal blood flow which may affect the thickness of the choroid. Blood flow in the macular region showed better correlation to the axial length changes than blood flow in the optic nerve probably because the macular LSFG measurement is less affected by the retinal circulation.

CONTROL ID: 3702557

SUBMITTER (NAME ONLY): Sara Safari

TITLE: Correlation between PhNR signal generated by a Photopic 3 ERG vs. red flash on a blue background

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Safari, K. Tsay, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|R.T. Tzekov, Department of Ophthalmology, University of South Florida, Tampa, Florida, UNITED STATES|R.T. Tzekov, Department of Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The photopic negative response (PhNR) is a component of the full-field electroretinogram (ERG) reflecting the function of the retinal ganglion cells. The current recommendation to optimally elicit the PhNR response is with a red flash stimulus on a blue background (ROB) as defined by the International Society for Clinical Electrophysiology of Vision (ISCEV). The purpose of this study was to compare PhNR and b-wave amplitudes in patients between two conditions: ROB and standard Photopic 3.0 ERG (Ph3) under two different protocols.

Methods: A retrospective chart review and data analysis of patients aged 18 and over undergoing routine ERG testing at USF Eye Institute (Tampa, FL) between July 2018 and October 2021 was conducted. Throughout the study period, while Ph3 was recorded in the same way, ROB response was generated in two different ways. Group 1's ROB protocol used a ~2.5 cd.s/m2 red flash (627 nm) on a 10 cd/m2 blue background (470 nm), Group 2 protocol used a 5 cd.s/m2 red flash on a 10 cd/m2 blue background. PhNR was measured before and after the i-wave, as PhNR1 and PhNR2, respectively. Eyes where the average signal did not come from at least 5 individual quality runs or those whose b-wave amplitude responses were less than 10 µV were excluded.

Results: The records of 55 patients / 110 eyes (13 M, 42 F; mean age 50.1 +/- 14.3 years) were selected: 27 patients (Group 1) and 28 patients (Group 2). There was no significant difference between the linear regression slopes of PhNR amplitudes under Ph3 vs. ROB between left and right eyes for either group ($p>0.05$), although the slopes in Group 1 were steeper compared to Group 2 (1.0 vs. 0.44). Furthermore, no significant difference was observed between the slopes of PhNR1 vs. PhNR2 in either group ($p>0.05$), although PhNR2 peaks were less reliably determined compared to PhNR1 (41.7% in Group 1 and 74.5% in Group 2). Similarly, the slopes of the b-wave amplitudes were not significantly different between right and left eyes ($p>0.05$) and appeared to be no different between Group 1 and Group 2 ($p>0.05$).

Conclusions: Consistent and predictable correlations were found between the PhNR responses obtained under Ph3 and ROB recording conditions at two different strengths of ROB stimulation.

CONTROL ID: 3702591

SUBMITTER (NAME ONLY): Kati Tormanen

TITLE: Small non-coding RNA (sncRNA1) within latency associated transcript (LAT) modulates HSV-1 virulence and host immune response during acute but not latent infection

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Tormanen, H. Matundan, U. Jaggi, S. Wang, H. Ghiasi, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: HSV-1 latency associated transcript (LAT) plays a major role in establishing latency and reactivation; however, the mechanism by which LAT controls these processes is largely unknown. The LAT locus contains two sncRNA sequences (sncRNA1 and sncRNA2) that are not miRNAs. We recently reported that sncRNA1 is more important for in vitro activation of the herpes virus entry mediator (HVEM) than sncRNA2, but its in vivo function is not known. In this study, we sought to establish the role of sncRNA1 during HSV-1 ocular infection by constructing a recombinant HSV-1 lacking sncRNA1.

Methods: The 62 bp sncRNA1 sequence in HSV-1 strain McKrae was deleted by homologous recombination using HSV-1 strain McKrae and a plasmid containing the region of LAT from -161 to +1667 relative to the LAT transcription start site and lacking sncRNA1 region, generating recombinant virus ΔsncRNA1. Deletion of the sncRNA1 in ΔsncRNA1 virus was confirmed by complete sequencing of ΔsncRNA1 virus and its parental virus (i.e., McKrae). Mice were ocularly infected with $2x10^5$ PFU HSV-1 McKrae, dLAT2903 (LAT-minus) or ΔsncRNA1 virus. Virus titers in tear films were determined by standard plaque assay. Mouse survival, level of latency and reactivation and extent of eye disease were monitored, and expression of viral and host transcripts were measured by qRT-PCR and Nanostring assays.

Results: Replication of ΔsncRNA1 in tissue culture or in the eyes of infected mice was similar to McKrae and dLAT2903 viruses. Absence of sncRNA1 reduced LAT expression in trigeminal ganglia (TG), but not in corneas of infected mice by day 5 post infection (PI). Levels of eye disease in mice infected with ΔsncRNA1 and McKrae viruses were similar, and absence of sncRNA1 did not affect latency or ex-vivo reactivation. However, mice infected with ΔsncRNA1 virus were more susceptible to ocular infection than their WT counterparts. Expression of host immune response genes in corneas and TG of infected mice during primary infection showed reduced IFNβ and IFNγ expression and altered activation of key innate immune pathways, such as the JAK-STAT pathway in ΔsncRNA1 virus compared with parental WT virus.

Conclusions: Our results reveal novel functions for sncRNA1 in up-regulating host immune response and suggest sncRNA1 has a protective role during primary ocular HSV-1 infection.

CONTROL ID: 3702592

SUBMITTER (NAME ONLY): Anita Kundu

TITLE: Longitudinal Analysis of Retinal Structural and Microvascular Parameters in Parkinson's Disease compared to Controls

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kundu, J. Ma, C. Robbins, P. Pant, S. Soundararajan, S. Stinnett, D.S. Grewal, S. Fekrat, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|B. Scott, K. Moore, Neurology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior cross-sectional studies have revealed decreased macular perfusion density (PFD) and increased peripapillary capillary PFD in Parkinson's disease (PD). We assess longitudinal rate of change of retinal microvascular and structural parameters in PD vs controls with normal cognition.

Methods: Subjects were imaged using Zeiss Cirrus HD-5000 AngioPlex. Those with confounding medical or ocular comorbidities were excluded and image quality was manually reviewed. Superficial capillary plexus PFD, vessel density (VD), and foveal avascular zone (FAZ) were assessed using ETDRS 6x6 zones (circle, inner ring, outer ring), and 3x3 zones (circle, inner ring). PFD, VD, FAZ, peripapillary retinal nerve fiber layer (RNFL) thickness, ganglion cell-inner plexiform layer (GC-IPL) thickness, and central subfield thickness (CST) were measured at 2 time points roughly 1 year apart. Rate of change was calculated per year and compared between groups using generalized estimating equations.

Results: 74 eyes of 40 patients with PD (60% male, mean age 67.4±7.9 years) & 149 eyes of 78 controls (28% male, mean age 70.3±5.8 years) were included. No demographic differences were observed between groups except a higher proportion of females in controls (p=.001). PD had a greater decline in PFD in the 6x6 circle (mean change per year in PD= –0.021, control=0.00; p=.001), 6x6 inner ring (PD= –0.018, control=0.001; p=.007), 6x6 outer ring (PD= –0.022, control=0.00; p=.001), 3x3 circle (PD= –0.016, control=0.002; p<.001), 3x3 inner ring (PD= –0.016, control=0.002; p<.001). PD had greater decline in VD in the 6x6 circle (mean change per year in PD= –.072/mm, control= –0.054/mm; p=.006), 6x6 inner ring (PD= –0.636/mm, control= –0.048/mm; p=.03), 6x6 outer ring (PD= –0.746/mm, control= –0.054/mm; p=.005), 3x3 circle (PD= –0.939/mm, control=0.006/mm; p<.001), 3x3 inner ring (PD= –0.942/mm, control=0.013/mm; p<.001). PD had greater decrease in GC-IPL thickness (mean change per year in PD= –0.403µm, control=0.128µm; p=.01). There were no significant differences in rate of change in FAZ, CST, RNFL thickness, and no significant differences in rate of change when stratified by PD severity.

Conclusions: PD may be associated with more rapid loss of retinal microvascular perfusion and vessel density, and more rapid thinning of the GC-IPL compared to normal aging in healthy controls with normal cognition.

CONTROL ID: 3702599

SUBMITTER (NAME ONLY): Gretchen Johnson

TITLE: Mechanisms of Peptain-mediated Neuroprotection in Retinal Ganglion Cells

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.A. Johnson, J.H. Pham, B. Kodati, R.R. Krishnamoorthy, D.L. Stankowska, Pharmacology and Neuroscience, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|R.H. Nagaraj, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine mechanisms underlying neuroprotective effects of the core peptide of a-B crystallin, peptain-1 (P1) conjugated to a cell-permeable peptide CPP (P1-CPP) in retinal ganglion cells (RGCs) in a rodent model of glaucoma and human retinal explants.

Methods: Ex vivo human retinal explants (n=3 donors) were obtained within 12h postmortem and were incubated with 12.5 µg/ml P1-CPP or vehicle for 7 days. Explants were stained with RGC marker, RBPMS, and surviving RGCs were counted using ImageJ. In a separate set of experiments, intraocular pressure (IOP) was elevated in Brown Norway (BN) rats and intravitreally injected with 2 µl of either P1-CPP or vehicle, once a week for a period of 2 weeks. Rats were euthanized, primary adult RGCs were isolated by the immunopanning method. Total RNA was isolated using the Trizol/column method. RNA-sequencing was performed using an Illumina platform. The resulting FASTQ files were uploaded into Galaxy for analysis with FASTQC, RNASTAR, featureCounts, and finally DESeq2. The results from DESeq2 were then assessed with Qiagen's Ingenuity Pathway Analysis (IPA) to identify significantly upregulated pathways.

Results: P1-CPP treatment, at 7 days significantly ($p<0.005$) prevented RGC loss by 35% compared to the vehicle. RNA-seq analysis from rat RGCs isolated following 2 weeks of IOP-elevation revealed that P1-CPP treated groups had several differentially expressed (DEGs), compared to vehicle-treated groups, including 6343 significantly upregulated and 5960 significantly downregulated. Some significantly upregulated pathways following P1-CPP treatment include phagosome formation, synaptic long-term depression, and CREB signaling in neurons. The IOP and vehicle-treated groups, when compared to the naïve group, demonstrated a decreased expression of members of the CREB signaling pathway (Creb-1, c-RAF, MEK1/2, ERK1/2, and p90RSK). This decline was prevented by P1-CPP treatment. Quantitative PCR further confirmed the RNA-seq findings of the increased expression of Creb-1 in P1-CPP treated rats compared to that of vehicle-treated group.

Conclusions: P1-CPP was neuroprotective against neurotrophic factor deprivation-mediated RGC loss in human retinal explants. Mechanism of action of P1-CPP in a rodent model of glaucoma includes the activation of the pro-survival CREB signaling pathway, phagosome formation, and long-term synaptic depression to prevent cell death and vision loss.

CONTROL ID: 3702609

SUBMITTER (NAME ONLY): Glenn Lobo

TITLE: Motor Protein MYO1C functions in the Pathophysiology of Usher Syndrome

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Usher Syndrome (USH) is an inherited disorder characterized by hearing loss, vestibular dysfunction, and visual impairments. Most of the identified gene loci do not account for all known USH cases. The role of Myosins have been implicated in the pathophysiology of USH. Interestingly, mutations in the motor protein, Myosin 1C (MYO1C) are associated with deafness. We developed a Myo1c-knockout mouse line to investigate a functional role for MYO1C in retinal cell physiology and to confirm its role in hearing.

Methods: Whole-body Myosin 1C knockout (Myo1c-KO) mice were generated and visual function tests using electroretinogram (ERG) and Auditory Brain Response (ABR) tests for hearing were performed on wild-type (WT) and Myo1c-KO animals, at 2-6 months of age. Immunofluorescence and trafficking analysis of key photoreceptor outer segment (OS) proteins were performed on retinal sections from both genotypes. Histology and electron microscopy (TEM) analysis were performed to determine photoreceptor cell structure and to quantify retinal cell layer thickness. Co-immunoprecipitation and reciprocal IP assays were performed to access direct binding of MYO1C to retinal proteins.

Results: Systemic loss of MYO1C in mice specifically affected rhodopsin trafficking, where rhodopsin mislocalized to the rod photoreceptor inner segments and cell bodies, while trafficking of other OS proteins (CNGA1, Arrestin, and Transducin) were largely un-affected. ERG analysis of Myo1c-KO mice showed a progressive loss of visual function. OCT analysis showed thinner photoreceptor cell layer and a reduction of outer nuclear layer thickness, while histological and TEM analysis confirmed shorter photoreceptor OS lengths in Myo1c-KO animals, at the 6-months' time point. ABR thresholds were significantly decreased in Myo1c-KO vs. WT animals, at 6-months of age, indicating that these mice also suffer from deafness.

Conclusions: We have identified a physiological role for the motor protein, Myosin 1C (MYO1C), in the pathophysiology of Usher Syndrome. Our novel Myo1c knockout mouse model mimicked BOTH the visual dysfunction and hearing loss phenotypes observed in Usher Syndrome patients. The study specifically identified rhodopsin as a cargo of MYO1C. The ongoing goals are to identify the precise molecular mechanisms of visual dysfunction and hearing loss in Myo1c-KO animals and to screen for MYO1C variants in patients with syndromic RP and Usher Syndrome.

CONTROL ID: 3702664

SUBMITTER (NAME ONLY): Mari Ogino

TITLE: Clinical Validation of a Novel Smartphone Application for Measuring Visual Acuity in Adults

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure: Mari Ogino: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Hunter: Commercial Relationship: Code N (No Commercial Relationship) | Vincent Hussey: Commercial Relationship: Code N (No Commercial Relationship) | Donny Suh: Commercial Relationship: Code N (No Commercial Relationship) | Rujuta Gore: Commercial Relationship: Code N (No Commercial Relationship) | Rosa Salmerón-Campillo: Commercial Relationship(s);Code E (Employment):Visionapp Solutions S.L. | Norberto López-Gil: Commercial Relationship(s);Code C (Consultant/Contractor):Visionapp Solutions S.L.;Code O (Owner):Visionapp Solutions S.L.;Code P (Patent):Visionapp Solutions S.L. | Matt Jaskulski: Commercial Relationship(s);Code P (Patent):Visionapp Solutions S.L.;Code E (Employment):Visionapp Solutions S.L.;Code O (Owner):Visionapp Solutions S.L. | Daniel Piña-Miguelsanz: Commercial Relationship(s);Code C (Consultant/Contractor):Visionapp Solutions S.L.

ABSTRACT BODY:

Purpose: It is well known that best-corrected visual acuity (BCVA) practically does not change during accommodation. Thus, it should be possible to measure BCVA by situating an appropriately scaled test within the subject's interval of clear vision. This can be achieved by means of a mobile device placed at a handheld distance. In an effort to address the need for an accurate tool for the measurement of BCVA, the purpose of the present study was to clinically validate BCVA measures obtained with VisionApp by comparing them to the gold standard.

Methods: BCVA was measured in n=48 eyes using VisionApp installed in four electronic devices. The app displayed a Landolt C optotype and utilized a 4-force choice procedure loosely based on the FrACT (Freiburg Visual Acuity & Contrast Test). The angular size of the optotype was automatically scaled as a function of the face-to-screen distance, which was continuously measured by means of the front camera. Results were compared to clinical BCVA measurements taken using a standard ETDRS chart placed at 10 feet (3 m). To assess the similarity of measurement methods, a statistical analysis was performed based on a two-tailed, paired t-test.

Results: The t-test revealed no significant difference in measured VA ($p = 0.415$), with a mean difference between clinical and app measurements of less than one letter (0.005 logMAR). The Bland-Altman analysis showed that the mean difference between measurement methods was 0.05 LogMAR (95% CI), with a standard deviation of 0.153.

Conclusions: The high agreement in measurements of BCVA between the app and the gold standard facilitates home monitoring for adult patients providing ophthalmologists with a reliable and accessible method to communicate BCVA results remotely between providers and patients. Further studies are needed to validate the results in children.

CONTROL ID: 3702721

SUBMITTER (NAME ONLY): Raffaele Parrozzani

TITLE: Choroidal Abnormalities in Pediatric NF1: a Cohort Natural History Study

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Parrozzani, L. Frizziero, G. Miglionico, C. De Biasi, E. Midena, Department of Ophthalmology, University of Padova, 35128 Padova, Italy, ITALY|G. Midena, E. Midena, IRCCS—Fondazione Bietti, 00198 Rome, Italy, ITALY|

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ABSTRACT BODY:

Purpose: Choroidal abnormalities (CAs) have recently been introduced as new clinical criteria for the diagnosis of neurofibromatosis type 1 (NF1).The purpose of this study was to assess the long term natural history of CAs in a large pediatric NF1 population, quantifying their progression in number and dimensions.

Methods: Pediatric patients (<16 years old) affected by NF1 with a minimum follow-up of 3 years with at least one CA in one eye were consecutively recruited. Near-infrared (NIR) imaging was performed to identify CAs, which were quantified in number and size using the open-source ImageJ software (National Institutes of Health, Bethesda, Maryland, USA)(Fig 1). CAs area and perimeter were normalized for the optic disc dimensions, to avoid possible bias related to the growing process of the eye.

Results: This study enrolled 99 eyes of 53 patients (31 males and 22 females), with a mean age of 7.1 ± 3.8 years old. All 99 eyes were examined at baseline and at least at 3-years follow-up (T3); 1-year follow-up (T1) was available for 80 eyes, 5-years follow-up (T5) for 59 eyes and 7-years follow-up (T7) for 36 eyes. Mean number of CAs increased from baseline (3.6 ± 3.2) to different follow-up visits (4.6 ± 3.5 at T1, 6.4 ± 4.1 at T3, 8.1 ± 4.8 at T5 and 9.6 ± 5.3 at T7), with a statistically significant trend ($p<0.0001$), and an estimated growth rate of 0.82 CAs per year, adjusted for age and for CAs number at baseline ($p<0.0001$). CAs area and perimeter also significantly increased during follow-up ($p<0.0001$ for each parameter). Patient age at baseline was inversely correlated with CAs number along time (coefficient=-0.1313, $p=0.0068$), while no correlation was found between patient age and CAs progression in size.

Conclusions: In NF1 pediatric patients CAs increased both in number and dimensions, independently from the physiological growth of the eye. While the increase of CAs number occurs particularly at an earlier age, the increase in CAs dimensions is a slow process that remains constant during childhood.

CONTROL ID: 3702728

SUBMITTER (NAME ONLY): Monika Grudzinska Pechhacker

TITLE: SCLT1-related disease as a rare cause of cone dystrophy with subtle systemic associations resembling ciliopathy.

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Grudzinska Pechhacker, A. Molnar, U. Birkeldh, L. Querat, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|M. Grudzinska Pechhacker, A. Molnar, U. Birkeldh, L. Querat, St Erik Eye Hospital, SWEDEN|A. Lindstrand, Clinical Genetics, Karolinska Universitetssjukhuset, Stockholm, SWEDEN|A. Lindstrand, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: SCLT1 gene has been reported in the pathogenesis of oral-facial-digital syndrome, Senior-Loken syndrome and Bardet-Biedl syndrome. SCLT1 encodes a linker protein associated with the sodium voltage-gated channel alpha subunit 10 and clathrin, and was identified as one of the component proteins involved in ciliogenesis. Only few patients with SCLT1-related rod-cone dystrophy have been reported. Here, we present two siblings with cone dystrophy and some features resembling ciliopathy.

Methods: Comprehensive eye exam was performed together with fundus images, fundus autofluorescence (FAF), optical coherence tomography (OCT), color vision test, visual fields, full-field electroretinography (ffERG) and multifocal ERG. The patients were assessed for ciliopathy features including echocardiography, ultrasonography of abdomen, and blood tests for liver and kidney function, and glucose levels. Genetic testing (NGS retinal dystrophy panel, 285 genes) was performed for probands and parental testing of SCLT1 variants.

Results: Two male children, age 10 and 8 years, were affected with ADHD and well-controlled obesity. Abnormalities of the heart, liver or kidneys, and postaxial polydactyly were not present. Children had mild light sensitivity and esotropia. Cycloplegic refraction revealed moderate hyperopia and significant astigmatism. BCVA was reduced (0.4 right eye/0.5 left eye logMAR in older patient; 0.3 logMAR both eyes in younger one) and moderate red-green color vision defects were noticed. Fundus exam was largely normal. FAF revealed decreased foveal FAF surrounded by increased FAF signal. OCT macula showed retinal thinning. Central visual field defects were observed. Further ffERG confirmed cone dystrophy. Ciliopathy was suggested as a possible diagnosis. Retinal dystrophy panel showed homozygous likely pathogenic, splice-site variant in SCLT1 gene NM_144643.3: c.1439+1del. This variant was not reported in ClinVar or gnomAD, and was heterozygous in the healthy parents.

Conclusions: In this report, we highlight the importance of extensive diagnostics in patients with unexplained reduced vision, strabismus, refractive errors and autism/ADHD spectrum disorders. Ciliopathies may present with milder systemic and ocular phenotype and thereby can be underdiagnosed. SCLT1-related retinal degeneration is rare and cone dystrophy was not observed until now.

CONTROL ID: 3702738

SUBMITTER (NAME ONLY): Tim Dorweiler

TITLE: Anti-ceramide immunotherapy for diabetic retinopathy

SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.F. Dorweiler, P. Nolan, J.V. Busik, Physiology, Michigan State University, East Lansing, Michigan, UNITED STATES|R.N. Kolesnick, Department of Molecular Pharmacology, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Tim Dorweiler: Commercial Relationship: Code N (No Commercial Relationship) | Peter Nolan: Commercial Relationship: Code N (No Commercial Relationship) | Richard Kolesnick: Commercial Relationship(s);Code O (Owner):Ceramedix | Julia Busik: Commercial Relationship(s);Code C (Consultant/Contractor):Ceramedix

ABSTRACT BODY:

Purpose: Previous work highlights the detrimental effects of increased ceramide generation in diabetic retinopathy (DR) progression. We have shown that ASM mediated ceramide generation leads to chronic low-grade inflammation in various cell types such as endothelial cells. We hypothesize that underlying mechanism is based on the formation of pro-inflammatory ceramide rich platforms (CRP). The focus of this project is to address the novel concept of functional and highly-specific ceramide inhibition using cutting edge anti-ceramide immunotherapy to prevent early onset diabetes induced pro-inflammatory and pro-apoptotic changes in the retinal vasculature.

Methods: Ischemia reperfusion (I/R) studies were utilized to mimic acute vascular degeneration in mice as observed in DR. Streptozotocin was utilized to induce hyperglycemia-induced vascular degeneration as a type-1 diabetes model. Anti-ceramide single chain variable fragment (scFv) treatment was administered via a 2 ug single dose into the vitreous. Pro-inflammatory markers (IL-1β, VEGF and ICAM-1) as well as ASM expression levels were analyzed via qRT-PCR. Ceramide species were analyzed via lipidomics (nESI-MS/MS). Vascular degeneration was captured using FITC-albumin technique and confocal microcopy and quantified using MetaMorph software.

Results: In vivo I/R studies in $asm^{+/+}$ and $asm^{-/-}$ mice identified significant upregulation of ASM, C16 and C18 ceramide production, as well as IL-1β, VEGF and ICAM-1 gene expression in $asm^{+/+}$ but not in $asm^{-/-}$ mice (n=6 per group; $p<0.05$). To determine feasibility of anti-ceramide immunotherapy, intravitreal injection of anti-ceramide scFv was first performed in the mouse I/R model. We found significant upregulation of IL-1β, VEGF and ICAM-1 gene expression in WT untreated retinas injured by I/R. These pro-inflammatory changes were inhibited by a single injection of anti-ceramide scFv 12 hours prior to I/R injury (n=6-8 per group; $p<0.05$). Impact of intravitreal injection of scFv was next tested in STZ-induced Wistar rat diabetes model. A single injection of scFv at the onset of hyperglycemia prevented diabetes-induced increase in retinal vascular permeability (n=3-10 per group; $p=0.08$).

Conclusions: These results suggest that anti-ceramide scFv immunotherapy may represent a novel approach to targeting deleterious ceramide-rich platform mediated pro-inflammatory and pro-apoptotic changes prevalent in the early stages of vasculopathy in the diabetic retina.

CONTROL ID: 3702763

SUBMITTER (NAME ONLY): Frank Schaeffel

TITLE: Dynamic OFF stimulation reduces perceived saturation of red color, similarly in myopes and emmetropes

SESSION TITLE: Myopia: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Schaeffel, B. Swiatczak, Myopia Research Group, Institute of Molecular and Clinical Ophthalmology Basel, Basel, SWITZERLAND|F. Schaeffel, Section Neurobiology of the Eye, Ophthalmic Research Institute University of Tuebingen, Tuebingen, GERMANY|

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ABSTRACT BODY:

Purpose: It has previously been shown that predominant activation of OFF pathways in the retina induces choroidal thinning and transient axial eye elongation, while stimulation of ON pathways can thicken the choroid. Because the balance between ON and OFF input strength has been linked to refractive error development, we developed a novel psychophysical procedure to quantify ON vs. OFF input strength in emmetropes and myopes.

Methods: Sixteen young healthy subjects (7 males, average age: 28±3 years, average refraction: -1.0±1.9D, range: +1.6 to -5.5D) were asked to match the saturation of a red bar presented on the computer screen with the perceived saturation of red squares (RGB(255,0,0) that randomly appeared inside a dynamic ON or OFF stimulus field (Figure 1A). The field consisted of 1400 grey squares with saw–tooth shaped temporal luminance profiles that could be reversed by the user. Cycle repetition frequency was 7.5 Hz. Temporal profiles in each field were randomly phase shifted with respect to each other. Each stimulus (ON or OFF) was repeated four times in each subject in random order. Subjects were blinded regarding the type of stimulation.

Results: Dynamic OFF stimulation severely reduced perceived saturation of the red squares in 13 out of 16 subjects. They appeared darker and pale. In contrast, red squares appeared fully saturated with dynamic ON stimulation (ON: matched red pixel values 202±20; OFF: 154±11, $p<0.001$). Three subjects (2 emmetropes and 1 myope) did not perceive changes in red saturation between ON and OFF (gray bars, Figure 1B, left). However, no trend was observed that OFF stimulation was more effective in myopes than in emmetropes (Figure 1B, right).

Conclusions: Perceived saturation of small red squares in a field with dynamic OFF stimuli was considerably reduced, suggesting an interaction of chromatic pathways and OFF pathways. The effect was not dependent on refractive error, suggesting that ON and OFF pathways are not affected in myopic subjects. This is in line with previous findings showing that the choroid in emmetropic and myopic eyes responds similarly to reading of text with normal and inverted contrast.

CONTROL ID: 3702765
SUBMITTER (NAME ONLY): Manmohan Singh
TITLE: Single-Shot Optical Coherence Elastography at 11.5 MHz
SESSION TITLE: Keratoconus and corneal biomechanics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Singh, A.W. Schill, A. Nair, K. Larin, Biomedical Engineering, University of Houston, Houston, Texas, UNITED STATES|I.V. Larina, K. Larin, Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, UNITED STATES|S.R. Aglyamov, Mechanical Engineering, University of Houston, Houston, Texas, UNITED STATES|
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ABSTRACT BODY:
Purpose: Corneal biomechanical properties are inherently tied to its shape and function but noncontact measurements of corneal biomechanical properties can be difficult due to physiological motion. In this work, we developed and tested an ultra-fast line-field optical coherence elastography (LFOCE) system capable of single-shot measurements of wave propagation in the cornea.
Methods: We developed a parallel line-field spectral domain optical coherence tomography system based on a supercontinuum laser (EXR-9 OCT, NKT Photonics) and a line-field Michelson interferometer. The spectral interference was imaged onto a high speed 2D camera (Phantom v2512, Vision Research). An air-pulse induced elastic waves, which were imaged by the LFOCE system. Figure 1 is a schematic of the system. The equivalent A-scan rate was 11.5 MHz based on 460 spatial pixels with a framerate of 25 kHz.
Validation measurements with LFOCE and uniaxial mechanical testing were made in tissue-mimicking gelatin phantoms (8%, 10%, and 12% w/w, N=3 of each type). Measurements were made in in situ and in vivo rabbit corneas. In vivo measurements were made in an anesthetized rabbit, and all procedures were approved by the University of Houston Institutional Animal Care and Use Committee.
Results: The LFOCE-measured elasticity of the 8%, 10%, and 12% phantoms was 13.8 ± 1.5 kPa, 21.4 ± 2.8 kPa, and 32.5 ± 3.1 kPa, respectively. Mechanical testing measured the stiffness of the 8%, 10%, and 12% phantoms as 15.6 ± 1.8 kPa, 23.7± 2.1 kPa, and 36.1 ± 1.6 kPa, respectively. Figure 2 shows the elastic wave propagation in the in situ rabbit cornea at 10 mmHg IOP at the noted times after excitation. The average wave speed of 3 repeated measurements in the in situ cornea at 10, 15, and 20 mmHg IOP was 3.03 ± 0.05 m/s, 4.66 ± 0.03 m/s, and 8.85 ± 0.08 m/s, respectively. In the in vivo rabbit cornea, the wave speed was 11.10 ± 0.32 m/s.
Conclusions: The LFOCE system was capable of imaging the wave propagation in the cornea successfully in a single shot. Future work will focus on improving the system sensitivity, incorporating a scanner for 3D imaging, and reducing the spectral band imaged by the camera to adhere to safety limits.

CONTROL ID: 3702809

SUBMITTER (NAME ONLY): Conor Delaney

TITLE: Transcriptional landscapes of the retina and RPE/choroid in the Cldn5-inducible model of retinal degeneration

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Delaney, N. Hudson, A. Reddy, K. Byrne, M. Campbell, The University of Dublin Trinity College, Dublin, IRELAND|

Commercial Relationships Disclosure: Conor Delaney: Commercial Relationship: Code N (No Commercial Relationship) | Natalie Hudson: Commercial Relationship: Code N (No Commercial Relationship) | Avril Reddy: Commercial Relationship: Code N (No Commercial Relationship) | Kieva Byrne: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Campbell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study aimed to examine transcriptional changes with progression of age-related macular degeneration (AMD)-like phenotypes in a novel mouse model of retinal degeneration, examining the retinal and retinal pigment epithelium(RPE)/choroid transcriptomes.

Methods: Inducible Cldn5 downregulation mice were fed a specialized high cholesterol diet (HCD) and retinas imaged using optical coherence tomography and fundus fluorescein angiography to monitor pathology progression. Control groups consisted of animals on normal diet and Cre-negative mice on HCD. Two bulk RNA-seq datasets were generated using mRNA isolated from retina and RPE/choroid, and sequenced using the Illumina NextSeq550 platform.

Results: RNA-seq analyses revealed distinct pathological processes occurring in the retina and RPE/choroid. Within the retina, 398 genes were identified to have significant expression changes unique to the pathology cohort. Pathway analyses revealed significant decreases in lens structural and extracellular matrix (ECM) gene expression networks, accompanied by upregulation of wound healing and cell motility pathways. The apical cell junction and cell leading edge were identified as GO cellular compartments enriched for increased gene expression.

A total of 661 genes displayed significantly altered expression in the RPE/choroid. In contrast to the structural and extracellular changes of the retina, decreased immune activation, angiogenesis and signalling receptor activity were observed. Gene networks governing neurotransmission increased, particularly those regulating ion channels. The synaptic membrane and external plasma membrane were identified as GO cellular compartments enriched and depleted respectively within the cohort.

Conclusions: The etiology of retinal degeneration in AMD has yet to be fully elucidated, and we have previously proposed inner-retinal vasculature dysfunction as an initiator of early AMD progression. Here we demonstrate unique responses of the retina and RPE/choroid to endothelial Cldn5 downregulation and HCD. Loss of ECM integrity and changes in cell localization may represent actions of infiltrating leukocytes driving wound healing pathways within the retina. This immune response is absent from RPE/choroid. Understanding molecular changes unique to each compartment of the eye will be essential for targeting therapeutic intervention for retinal degeneration and AMD.

CONTROL ID: 3702812

SUBMITTER (NAME ONLY): Owen Bowie

TITLE: ATP-induced retinal damage in cone-dominant 13-lined ground squirrel throughout euthermia

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Bowie, H.M. Follett, C. Yu, N. Manfredonia, C. Guillaume, P. Summerfelt, J. Carroll, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D. Merriman, University of Wisconsin Oshkosh, Oshkosh, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The 13-lined ground squirrel (13-LGS), a cone-dominant hibernator, has emerged as an accessible animal model for vision research. Induction of cone degeneration through exposure to cytotoxic chemicals has revealed variable effectiveness in the 13-LGS. Here, we sought to examine how the time of year (relative to hibernation emergence) influenced the degree of cone damage in 13-LGS following intravitreal injection of adenosine triphosphate (ATP).

Methods: Eighteen (9M,9F) 13-LGS were placed into three active season experimental groups, early-season (N=6), mid-season (N=6), and late-season (N=6), to determine the time of intravitreal ATP injection. Each animal underwent baseline imaging OU using near-infrared reflectance and short wavelength autofluorescence scanning light ophthalmoscopy (SLO) as well as optical coherence tomography (OCT). Animals then received a 10µL intravitreal injection of 0.723M ATP in one eye, followed by OCT and SLO imaging at 1, 3, 10, and 21 days post-injection. Among mid-season and late-season animals where no retinal damage was observed in follow-up imaging, adaptive optics SLO (AOSLO) was performed. Retinal thickness and cone density measures from the late-season cohort were compared to values from a control group of wild-type animals (N=12 eyes, OCT; N=6 eyes, AOSLO).

Results: Five animals showed retinal damage following ATP injection, including 4/6 early-season, 0/6 mid-season, & 1/6 late-season (Fisher’s exact test, p= 0.065). A two-way ANOVA showed significant differences in axial length between early-season & mid/late season cohorts (p = 0.029; p = 0.035). All animals with retinal damage displayed lesions on SLO and disrupted retinal lamination on OCT. Follow-up imaging with AOSLO on mid-season and late-season animals without observed retinal damage showed no evidence of photoreceptor disruption at any of the 97 ROIs analyzed. In late-season animals, 518 of 528 eccentricity matched locations imaged by OCT were within the normative range (mean +/- 2SD) from the control group, consistent with no ATP-induced damage.

Conclusions: The 13-LGS retina may be more susceptible to retinal damage by intravitreal ATP injection during the early season. However, differences in both axial length and vitreous volume between groups may impact the effective dose. Future studies adjusting dose based on ocular biometry may help elucidate the impact of time of year on chemical response.

CONTROL ID: 3702814

SUBMITTER (NAME ONLY): Garrett Grissim

TITLE: Longitudinal Assessment of Cone Structure in Achromatopsia

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Grissim, School of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|R. Linderman, Wisconsin Reading Center, Ophthalmology & Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Garrett Grissim: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Linderman: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Carroll: Commercial Relationship(s);Code F (Financial Support):OptoVue;Code C (Consultant/Contractor):AGTC;Code F (Financial Support):AGTC;Code F (Financial Support):MeiraGTX;Code I (Personal Financial Interest):Translational Imaging Innovations

ABSTRACT BODY:

Purpose: Achromatopsia (ACHM) is an autosomal recessive disease that results in reduced or absent cone function. There is controversy regarding the extent to which cone structure shows progressive degeneration in ACHM. Here we performed a retrospective review of optical coherence tomography (OCT) images to evaluate cone structure over time in patients with genetically confirmed ACHM.

Methods: Sixty-three patients with ACHM (due to CNGA3, CNGB3, or ATF6 mutations) with Bioptigen or Cirrus OCT images from multiple time points stored in the Advanced Ocular Imaging Program Bank were included. Integrity of the ellipsoid zone (EZ) was assessed twice by a single grader (GG) in a masked fashion using the grading scale from Sundaram et al (2014).[1] Images with disparate grades between the two assessments were finalized by a second grader (JC).

Results: A total of 457 OCT images were processed and graded, 236 OD and 221 OS. The baseline distribution of EZ grades was highly symmetrical between eyes (OD: I=8, II=33, III=2, IV=17, V=3; OS: I=8, II=32, III=2, IV=17, V=2). The average patient age was 23.01 years at the first visit and 25.99 at the last visit, with an average time between visits of 2.88 years for OD images and 2.56 years for OS images (range from 5 months to 10 years). A total of five eyes showed change in EZ grade (OD: n=3, OS: n=2) across follow-up from a grade II (EZ disruption) to grade IV (hyporeflective zone). These eyes belonged to three individuals (aged 24, 29, & 35 years), representing 4.76% of the total study group. The remaining 60 subjects, 95.24% of the total study group, retained the same EZ grade throughout the follow-up period.

Conclusions: ACHM appears to be a generally stable condition, at least over the follow-up period assessed here. Even with stable EZ appearance there may be other factors that impact the therapeutic potential of a given ACHM retina, which may change/progress over time.

CONTROL ID: 3702815

SUBMITTER (NAME ONLY): Polina Prokhoda

TITLE: The Effect of Tyrosinase Hypomorphic Alleles on Visual Acuity in Patients with Albinism

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Prokhoda, E. Woertz, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|E. Woertz, J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|E. Curran, D. Costakos, J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the effect of hypomorphic alleles in the tyrosinase gene (TYR) on best corrected visual acuity (BCVA) in patients with albinism.

Methods: We retrospectively analyzed BCVA and genetic data from 75 individuals with suspected albinism. We did not include individuals with a history of premature birth or retinal pathology, or those who had mutations in multiple albinism genes. Patients were organized by albinism subtype and number of mutations. For individuals with OCA1, 16 had a single pathogenic TYR mutation, while 25 had two or more pathogenic TYR mutations. For individuals with OCA2, 10 had a single pathogenic mutation and 17 had two pathogenic mutations. Seven individuals had OA1 caused by hemizygous mutations in GPR143. For each albinism subtype, we further grouped individuals based on the number of TYR hypomorphic alleles that were identified. One-way ANOVA and Tukey's multiple comparisons tests were performed to assess the difference in BCVA within groups.

Results: For patients with OCA1 who had two or more pathogenic mutations, we observed a significant difference in BCVA between the TYR hypomorphic allele groups (p=0.0013). Post hoc testing revealed significant differences between patients with zero versus two hypomorphic alleles (p=0.04) and one versus two hypomorphic alleles (p=0.001). For subjects with OCA1 who had one pathogenic mutation, there was no significant difference in BCVA between the TYR hypomorphic allele groups (p=0.56). For subjects with OCA2 who had either one or two pathogenic mutations, there was no significant difference in BCVA between the TYR hypomorphic allele groups (p=0.96 and p=0.22, respectively). For subjects with OA1, there was no significant difference in BCVA between the TYR hypomorphic allele groups (p=0.67).

Conclusions: In patients with OCA1 with two or more pathogenic mutations, the presence of hypomorphic alleles in TYR is associated with worse visual acuity, which could be due to further reduced tyrosinase function. While TYR hypomorphic alleles have been shown to alter foveal structure in individuals with normal vision,[1] it remains to be seen if the hypomorphic allele-related changes in visual acuity described here are also associated with changes in foveal structure in albinism.

1: PMC8143408

CONTROL ID: 3702820

SUBMITTER (NAME ONLY): Ching Tzu Yu

TITLE: Exploring the survival of transplanted hiPSC-derived photoreceptors in the 13-lined ground squirrel

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To assess the survival of transplanted human induced pluripotent stem cell (hiPSC)-derived photoreceptors in the cone dominant 13-lined ground squirrel (13-LGS; Ictidomys tridecemlineatus).

Methods: Cone-rich 3D-retinal organoids were differentiated from hiPSC with GFP knocked in at the AAVS1 safe harbor locus. 13-LGS retinas were degenerated via experimental retinal detachment (RD, n=18) or by intravitreal chemical injection of either adenosine triphosphate (ATP, n=16) or tunicamycin (Tm, n=6). 13-LGS were immunosuppressed using cyclosporine A for 14 days. Organoids were dissociated with papain and cell viability was assessed by flow cytometry. Cells were transplanted into the subretinal space of all eyes ($0.7\text{-}1.4\text{x}10^6$ cells/eye) at least two weeks post-damage. To track survival of transplanted cells, eyes were imaged in vivo immediately post-transplantation and at 1 week, and 1-,2-,3-, and 4-months later, using SLO, OCT, and AOSLO. AOSLO images were acquired at 3-mo to capture high resolution images of the cell patches. After the 4-mo imaging time point, retinas were analyzed by immunohistochemistry (IHC) with marker antibodies to GFP (reporter), Otx2 (photoreceptor), and HuNu and LMNB2 (human-specific).

Results: Cell viability using flow cytometry was 61.2%-93.5%. Locations of transplanted cells were observed with OCT, and initial transplantation was deemed successful when cells were deposited and retained subretinally. 15 of 40 transplants failed for technical reasons: reflux of cells into the vitreous space (ATP, RD; n=3); degeneration of GFP signal over time (ATP, RD; n=7); and hemorrhage that obstructed imaging (Tm; n=5). GFP signal was detected with SLO at all time points post-transplantation in 25 of 40 eyes (ATP, n=11; Tm, n=1; RD, n=13), demonstrating survival of transplanted cells. AOSLO showed clumps of transplanted cells settled above the surviving cones of the host retina. IHC confirmed the expression of GFP, Otx2, HuNu, and LMNB2 in the transplanted cells. Integration of cells in RD retinas was restricted to the outer retina/subretinal space, whereas chemically degenerated retinas exhibited additional signal integration into the inner retina.

Conclusions: hiPSC-derived photoreceptors survived in the outer retina of 13-LGS eyes for up to 4-mo post-transplantation. Further studies are needed to examine the functional properties of these cells.

CONTROL ID: 3702821

SUBMITTER (NAME ONLY): Hannah Follett

TITLE: Non-invasive assessment of retinal structure in the elderly 13-lined ground squirrel

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.M. Follett, C. Yu, J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|C. Guillaume, P. Summerfelt, J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|O. Bowie, School of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D. Merriman, Biology, University of Wisconsin Oshkosh, Oshkosh, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize retinal phenotypes in elderly thirteen-lined ground squirrel (13-LGS) eyes.

Methods: Eleven (2M, 9F) elderly 13-LGS (> 5 years old) were included. OCT imaging was used to assess anterior segment structure (22 eyes) and retinal morphology (20 eyes). NIR reflectance and SW-AF imaging were used to assess retinal and RPE health (22 eyes). Adaptive optics scanning light ophthalmoscopy (AOSLO) images were used to examine the cone mosaic (8 eyes). Retinal thickness and cone density measurements of elderly animals were compared to a control group of 1 year old animals (n=12 eyes, OCT; n=6 eyes, AOSLO).

Results: NIR images showed abnormal expansion of the hyperreflective optic nerve head (ONH) signal, with a concomitant hypofluorescent signal on SW-AF images in 14 eyes. Hypofluorescent puncta were observed on SW-AF images in 10 eyes. Anterior segment OCT revealed lens opacifications in 19/22 eyes, obviating AOSLO imaging of 2 animals and precluding AOSLO analysis for 1 other animal. Posterior chamber OCT showed numerous abnormal phenotypes including hyperreflective vitreous laminations (20/20 eyes), hyperreflective inner retinal puncta (6/20 eyes), and a hyporeflective outer retinal cavity (1 eye). Disrupted outer retinal lamination adjacent to the optic nerve head (ONH) was observed in 17/20 eyes. Retinal and choroidal thickness values were within normative ranges for 5/20 eyes - the remaining 15 eyes had at least one retinal location with altered thickness of at least one layer, with 54% of the outliers being associated with disrupted retinal lamination within 5° of the ONH (Fig. 1). AOSLO images from 2 eyes showed a loss of discernable structure within 2.5° inferior of the ONH. The cone mosaic was otherwise normal, appearing contiguous with 91% of locations having density values within the normative range (Fig 2).

Conclusions: Elderly 13-LGS have abnormal lamination surrounding the optic nerve head and variable differences in retinal thickness when compared to young adult 13-LGS controls. In addition, the anterior segment findings can impose challenges with high quality imaging in all animals. It will be important to control for age in cross-sectional studies of 13-LGS retinal structure.

CONTROL ID: 3702823

SUBMITTER (NAME ONLY): Dina Abusamra

TITLE: Galectin-3 modulates monocyte infiltration in the injured cornea by inducing sialyl Lewis^X expression

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Abusamra, P. Argueso, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M. Anastasiou, P. Alcaide, Immunology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|N.A. Panjwani, Ophthalmology, New England Eye Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Galectin-3 has been associated with many proinflammatory functions by triggering the migration of monocytes; nevertheless, the mechanism underlying this process has not been fully established. Monocyte recruitment is initiated by multiple adhesive interactions between vascular selectins and the sialyl Lewis^X (sLe^X) glycan on circulating monocytes. Here, we investigated whether galectin-3 regulates the expression of sLe^X in activated monocytes and, therefore, their recruitment following injury.

Methods: Human monocytes were purified from the blood of healthy donors. Mouse monocytes were purified from the bone marrow of galectin-3 knockout (Gal3$^{-/-}$) and wild-type (WT) mice. Galectin-3 expression and binding in human monocytes were inhibited using galectin-3 siRNA (siGal3) and the thiodigalactoside analog TD139, respectively. Competitive migration assays were carried out in immunocompromised WT chimera by intravenous injection with fluorescently labeled WT and Gal3$^{-/-}$ monocytes. The glycogene expression profile of mouse monocytes was evaluated using real-time PCR array. Parallel plate flow chamber assays were performed on vascular endothelial cells using galectin-3 deficient monocytes glycoengineered to express human FUT7.

Results: Inhibition of galectin-3 expression or binding in activated human and murine monocytes led to impaired biosynthesis of sLe^X. Conversely, the addition of human recombinant galectin-3 led to increased levels of sLe^X. Injured corneas of Gal3$^{-/-}$ mice displayed lower numbers of CD45$^+$ CD11b$^+$ sLe^X cells compared to WT mice. Deficiency in sLe^X expression was concomitant with impaired recruitment of Gal3$^{-/-}$ monocytes into wounded corneas of WT chimeric mice. Using a PCR array, we found that galectin-3 regulates the biosynthesis of sLe^X on activated monocytes by inducing the expression of FUT7. Enforced fucosylation of human galectin-3 deficient monocytes resulted in augmented rolling capability on activated endothelial cells under flow conditions in vitro.

Conclusions: Overall, these data demonstrate a novel mechanism by which galectin-3 positively regulates the recruitment of monocytes into inflamed tissues by inducing the expression of FUT7.

CONTROL ID: 3702827

SUBMITTER (NAME ONLY): Nathan Hall

TITLE: Demographic Differences of Dry-Eye Disease Between Pediatric and Adult Patients in the IRIS Registry

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Hall, V. Douglas, C. Ross, J.W. Miller, A.C. Lorch, A. Traish, Ophthalmology, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|N. Hall, V. Douglas, C. Ross, J.W. Miller, A.C. Lorch, A. Traish, Ophthalmology, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry-eye disease (DED) is a chronic progressive ocular surface disorder that has been extensively investigated in the adult population, but in the pediatric population, DED prevalence and its characteristics remains largely unstudied. It is a significant healthcare problem which impairs visual functioning and can severely affect patients' quality of life at any age. The American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) was used to investigate differences in demographics and prevalence of DED between pediatric and adult patients.

Methods: A total of 4,795,979 patients with at least one diagnosis of DED between 2013-2019 was identified by ICD code in the IRIS Registry. Of these, 203,171 were pediatric patients, defined as patients under the age of 18 (PDED) at the time of initial diagnosis, while 4,592,808 were adults, defined as patients aged 18 or older (ADED). The earliest-recorded diagnosis of DED for each patient was included, and demographics that were investigated included biological sex, race, ethnicity, and U.S. geographical region. Descriptive statistics, Pearson's chi-squared tests, and two-sample proportions tests were conducted to compare key demographic distributions between the ADED and PDED cohorts.

Results: Demographic characteristics were compared between the ADED and PDED groups. The average age at onset for ADED patients was 61.06 (±14.75) years, while the average age at onset for PDED patients was 12.51 (±3.86) years. Characteristics with the largest discrepancies between ADED and PDED patients included female sex (68.12% vs. 58.08%), male sex (31.55% vs. 41.58%), White race (67.06% vs. 50.24%), Hispanic/Latino ethnicity (9.03% vs. 17.04%), and Northeast region residency (21.04% vs. 32.20%), respectively. Comparisons of each category within each demographic between ADED and PDED patients were statistically significant (all $p<0.01$), with the exception of unreported sex ($p=0.48$).

Conclusions: Our results characterize significant differences within major demographic factors between pediatric DED patients and adult DED patients in the IRIS Registry. There was a significantly higher proportion of females and Whites in adults with DED as compared to pediatric patients with DED, and a significantly lower proportion of Hispanic/Latino individuals and Northeast region-dwelling individuals in adults with DED as compared to pediatric patients with DED.

CONTROL ID: 3702832

SUBMITTER (NAME ONLY): Thomas Chang

TITLE: Effects of glycemic control on anti-VEGF regimens in the management of diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chang, R.A. Adelman, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Thomas Chang: Commercial Relationship: Code N (No Commercial Relationship) | Ron Adelman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study whether patients with diabetic retinopathy (DR) who have lower mean hemoglobin A1c levels had either a decrease of total anti-VEGF intravitreal injections, or an increase in interval between injections.

Methods: Retrospective chart review of DR patients at the Yale Eye Center including Hb A1c values, the number of anti-VEGF injections, and the intervals between anti-VEGF injections. Inclusion criteria were adults with DR who received anti-VEGF injections and regular A1c tests. Exclusion criteria were other retinal pathologies, inconsistent follow-up, or deferment of anti-VEGF treatment. Patients were divided up into two groups, those with anti-VEGF treatment and those with both anti-VEGF and panretinal photocoagulation (PRP) therapy. These two groups were further divided with mean A1c either > or < 7%, and into A1c tertiles. Welch's t-test was performed.

Results: In patients who received only anti-VEGF treatment (n=60), there was a significant difference in the number of injections (p=0.006) between the middle (7.7 inj.) and top (3 inj.) tertiles of average A1c. There was also a difference (p=0.024) in interval between the bottom (1.3 months) and middle (1.8 months) tertiles of A1c. There was no statistically significant differences in either mean number of injections or mean interval between injections when comparing groups with mean A1c<7 and >7. In the group who received anti-VEGF and PRP (n=79), there were no significant differences in mean number of injections or mean interval between injections in groups with A1c<7 and >7 or when comparing tertiles.

Conclusions: Individuals with average A1c below 7 did not have a decrease in number of anti-VEGF injections when compared with those with A1c>7. Surprisingly, in some cases the higher tertiles of A1c were found to have a lower mean of injections, as well as increased time between injections. One possible explanation is that those with poor glycemic control may refuse treatment and are less likely to follow up with care regularly.

CONTROL ID: 3702835

SUBMITTER (NAME ONLY): Jenna Grieshop

TITLE: Towards uniform cone reflectivity in confocal adaptive optics scanning light ophthalmoscope retinal images

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Grieshop, J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|H. Heitkotter, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Grieshop, R. Woehlke, M. Gaffney, R.F. Cooper, Biomedical Engineering, Medical College of Wisconsin and Marquette University, Milwaukee, Wisconsin, UNITED STATES|J.A. Kuchenbecker, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The appearance of cone photoreceptors in confocal adaptive optics scanning light ophthalmoscope (AOSLO) images is highly variable, which can present challenges for cone detection algorithms. We sought to develop a method to induce intra-video variability in cone reflectance whereby processed images would have less intercell variability in cone reflectance.

Methods: Six individuals with no known eye disease were recruited. One eye from each individual was imaged nine times in a single session with a confocal AOSLO (772±13nm source). Six videos had a 3-second 30Hz stimulus presented halfway through acquisition (three using 450nm light and three using 550nm light), and three videos were acquired with no stimulus. Videos were collected in a randomized order. Videos were then trimmed into two separate videos: frames from the first half of the video and frames from the second half of the video (i.e., before and after the stimulus presentation). These trimmed videos were processed, averaged, and co-aligned for analysis. Cone coordinates identified using a semi-automated program and cone reflectance values were extracted. The change in cone reflectance between before and after stimulus presentation was calculated for each stimulus condition.

Results: With no stimulus, cones changed reflectivity by an average of 20.4% (range:12.8-30.1%). Greater changes in reflectivity were observed for the 450nm stimulus (average=25.9, range:14.4-45.4%) and for the 550nm stimulus (average=28.4%, range:17.7-45.8%). Of the 36 total stimulus videos, 27 (75%) had a greater average change in reflectivity than the no stimulus condition. Standard deviation (SD) of the percent difference for individual cones was also greater for the stimulus conditions: 450nm average SD = 18.3% (range:12.0-24.1%), 550nm average SD = 20.1% (range:15.6-25.1%), no stimulus average SD = 15.9% (range:10.9-19.4%). Of the 36 total stimulus videos, 28 (78%) had a greater SD across cone reflectivity changes than observed for the no stimulus condition.

Conclusions: The presentation of a stimulus during AOSLO imaging increases the amount of change in reflectance of individual cones over the course of a single video. Leveraging this variable cone reflectance across an AOSLO stimulus video may result in processed images with more uniform cone appearance and thus easier detection of cones by either automated algorithms or manual graders.

CONTROL ID: 3702839

SUBMITTER (NAME ONLY): Shaden Yassin

TITLE: Prevalence of Refractive Error in Inherited Retinal Dystrophies

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yassin, E. Walker, S. Borooah, Ophthalmology, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure: Shaden Yassin: Commercial Relationship: Code N (No Commercial Relationship) | Evan Walker: Commercial Relationship: Code N (No Commercial Relationship) | Shyamanga Borooah: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ametropia has been associated with Inherited Retinal Dystrophies (IRDs). However, the prevalence of ametropia in IRDs and its genetic associations is poorly studied. We aim to address this knowledge gap by studying refractive error in a cohort of IRD patients at an academic ophthalmology referral center.

Methods: We performed a single center cross-sectional retrospective study of cases identified from the IRD database of the Shiley Eye Institute, University of California San Diego, containing all patients seen in the dystrophy clinic. Patients were included with clinical and molecular confirmed IRD. Demographic and clinical data retrieved from medical records included age, gender, disease phenotype, best corrected visual acuity, objective and subjective refraction. Distributions and mean spherical equivalent (SE) were calculated for causal genes. Analysis of SE was conducted on a per subject eye level through Linear Mixed Effects modeling. Statistical analyses were performed using R statistical software (R Version 3.6.3).

Results: The database contained 571 patients with IRD. We represent 162 patients with clinical and molecular confirmed IRD, 82 (51%) were males, mean age was 37.6 years (SD +/-2.4). Of these, 112 patients had refractive data, 61 (54%) were ametropic (Fig. 1). Investigating genes associated with myopia, RPGR (n=10, 6%) had the highest odds ratio of myopia 403.43 (P<0.02; SE 1.90 D [SD 34.20]); followed by NYX (n=3, 2%)(78.02, P<0.04; SE 2.59 D [SD 46.62]); and ABCA4 (n= 15, 9%)(54.60, P<0.03; SE 2.92 D [SD 52.56]). For genes associated with hyperopia, NMNAT-1 (n= 3, 2%) had the highest odds ratio of hyperopia 971.57 (P<0.001; SE 2.81 D [SD 50.58]); followed by AIPL1 (n= 2, 1%)(405.45, P<0.001; SE 2.92 D [SD 52.56]); and CNGB3 (n= 3, 2%)(40.04, P<0.001; SE 3.17 D [SD 57.06]). n=number of subjects, 2 eyes per subject was used for SE analysis.

Conclusions: Ametropia was commonly seen in IRD patients and appears similarly prevalent as in the unaffected US population which contrasts previous reports. The pattern of error of refraction varied widely by causal gene. Our findings confirm previous reports in some genes such as myopia associated with NYX. However, in our cohort, AIPL1 variants were associated with hyperopia contrasting with previous reports of myopia. Genes identified require further validation in larger cohorts but are candidates for more in-depth investigation in functional studies of refractive error.

CONTROL ID: 3702846

SUBMITTER (NAME ONLY): Brea Brennan

TITLE: AOSLO Image Quality: Quantifying the Good, the Bad and the Ugly

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.D. Brennan, R.F. Cooper, Joint Department of Biomedical Engineering, Medical College of Wisconsin and Marquette University, Milwaukee, Wisconsin, UNITED STATES|H. Heitkotter, J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Carroll, R.F. Cooper, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics scanning light ophthalmoscopes (AOSLO) are a valuable tool for assessing retinal health. AOSLO image quality can degrade from factors such as poor media quality and eye motion, resulting in lost subject and analysis time. Here we assess the performance of a novel image quality metric against human graders.

Methods: We retrospectively obtained confocal and split-detection images of normative and pathological retinas (>8 diseases) from two AOSLOs with similar designs (Denoted as AOSLO 1 and 2). The dataset was comprised of 125 images from each modality and AOSLO (500 images total) at 1, 2, 4, and 8° from the fovea with field of views between 1 and 3°. For each image, we first determined its quality using a custom algorithm: First, the radial average of the log power spectrum of each image was obtained and differentiated. Next, the differentiated radial average was divided into “signal” and “noise” ranges by selecting a cutoff based on the plausible frequency range of photoreceptors. Finally, a signal to noise ratio (SNR) was determined as the ratio of the summed “signal” and “noise” ranges in decibels. For comparison to a gold standard, three individuals graded the same images (randomized, masked) for cell identifiability on a scale from 0-5, where 0 was considered unanalyzable and 5 easily identifiable. We examined the correlation between log-transformed SNR and grader scores and assessed grader agreement using intra-class correlation (ICC; R package: irr).

Results: On average (±std dev), confocal images had SNR values of 56.2±3.1 and 38.2±6.9 and split-detection images had SNR values of 72.2±1.3 and 30.2±6.4 for AOSLO 1 and 2, respectively. On average, grader scores for confocal images were 3.5±1.3 and 2.4±1.3, and grader scores for split-detection images were 2.5±1.3 and 1.5±1.2 for AOSLO 1 and 2, respectively. These data are summarized in Table 1. All SNR and grader scores exhibited weak (r^2 <0.35), but significant correlations ($p<0.01$). Grader ICC was 0.71, implying moderate agreement amongst the graders.

Conclusions: The algorithm presented here successfully quantifies image quality in both confocal and split-detection AOSLO images. On average, graders showed agreement with our algorithm, and moderate agreement with each other.

CONTROL ID: 3702852

SUBMITTER (NAME ONLY): Sarah Rahman

TITLE: The Impact of Travel Distance on Rhegmatogenous Retinal Detachment Presentation and Outcomes

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rahman, M. Russell, J. Joo, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|M. Russell, C. Carvalho Soares Valentim, R.P. Singh, Center for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rhegmatogenous retinal detachment (RRD) often requires urgent surgery to restore vision.Studies have found variation in RRD presentation and outcomes by age,gender,race,and income.However,the impact of patients' residential location on RRD severity remains unclear.

Methods: Retrospective chart review of adult patients who underwent an RRD repair at Cole Eye Institute from 2012 to 2020.Patients were excluded for previous penetrating trauma, posterior intraocular segment surgery to the presenting eye, or outliers in travel distance above 95th percentile.Demographic differences were characterized. Google Maps was used to calculate the travel distance in miles from the residential zip code to the presenting and surgery location addresses.Multivariable logistic and univariable linear regressions were used to compare macula-off status and Best Visual Acuity (BVA) in ETDRS letters at presentation and 6-month follow-up with patient travel distance by tertile or continuously.

Results: 1063 patients were identified for the study. Demographics and baseline ocular characteristics are shown in Table 1.Average distance to the presenting location was 25.22 mi and to the surgery location was 31.38 mi.Average (SD) BVA at 6-month follow-up for patients with data available was 60.96 (23.36),n=705.The reattachment rate was 95.8% for closest tertile, 96.3% for second tertile, and 94.9% for furthest tertile (p=0.66).In multivariable analysis including age,race,gender,ethnicity,median household income,insurance,and smoking status,distance tertile to presenting location was not predictive of macula-off status (OR 0.9978,95% CI 0.992,1.003,p=.25,n= 1061) or BVA at follow-up (first tertile 0.19 letters more than third tertile,95% CI -2.68,3.06,p=.896,n= 690).A subset analysis of patients with median household income less than$25,000 revealed that further distance to surgical location was associated with longer time to surgery (0.69 days longer per mile of distance, 95% CI 0.41,0.97,p<.0001,n=28),but was not associated with BVA at follow-up (-0.13 letters,95% CI -0.51,0.24,p=.25,n=21).

Conclusions: Further distance is significantly associated with a delay in time from diagnosis to surgery for low-income patients, but distance does not impact macula-off status or BVA at follow-up. This suggests that patients who are further from the hospital may be able to achieve equivalent outcomes from RRD repair, despite delays in surgery.

CONTROL ID: 3702853

SUBMITTER (NAME ONLY): Martina Herwig-Carl

TITLE: Mass spectrometry-based profiling of histone posttranslational modifications in human melanocytes and uveal melanoma cell lines

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.C. Herwig-Carl, K.U. Loeffler, F.G. Holz, A. Sharma, Ophthalmology, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|R. Noberini, T. Bonaldi, Experimental Oncology, European Institute of Oncology IRCCS, Milan, ITALY|M. Zeschnigk, human genetics, Universitatsklinikum Essen, Essen, Nordrhein-Westfalen, GERMANY|S. Landreville, Ophthalmology and Otolaryngology, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|A. Sharma, Neurosurgery, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M.C. Herwig-Carl, Center of Integrated Oncology, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: While genetic alterations in uveal melanoma (UM) have been extensively studied, epigenetic factors of UM are still not well understood. It is also evident that UM differs significantly from skin melanoma regarding clinical behaviour, genetic profile as well as responsiveness to various therapies. However, differences between skin and uveal melanocytes are not obvious. We therefore studied histone posttranslational modifications (hPTMs) which are epigenetic mechanisms regulating gene expression. HPTMs were analyzed in different UM cell lines and healthy melanocytes (from skin and uvea) to provide a deeper insight into the pathogenesis of UM.

Methods: Human skin (n=6) and uveal melanocytes (n=2) as well as human UM cell lines (n=7) were analyzed by quantitative mass spectrometry for 52 histone modifications involved in the dynamics of active and repressive chromatin.

Results: Hierarchical clustering showed clear differences between melanocytes and UM cell lines. Uveal melanocytes showed a different hPTM pattern than skin melanocytes. With regard to the UM cell lines, those with a monosomy 3 signature (MP65 and UPMM1) were distinguishable from cell lines with a disomy 3 signature (Mel 202, 92.1, UPMD1, UPMD2). The BAP1-associated mark H3K27me3 was unaltered in melanocytes and non-specifically altered in UM cell lines.

Conclusions: Our study demonstrated different hPTM patterns between skin and uveal melanocytes which both originate initally from the same precursor of melanocytes. Since the potential neoplasms arising from these melanocytes (skin and uveal melanoma, respectively) differ in their clinical behaviour and their genetic profile, hPTM may be a step towards understanding the differences between these two melanocyte subtypes. In addition, healthy uveal melanocytes were distinct from UM cell lines which could be further subgrouped with regard to chromosome 3 status. Thus, hPTM signature may be an additional prognostic marker and further studies on human tissues are warranted.

CONTROL ID: 3702854
SUBMITTER (NAME ONLY): Len Zheleznyak
TITLE: The anisotropy of retinal blur in the human periphery
SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Zheleznyak, Clerio Vision, Inc., New York, UNITED STATES|
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ABSTRACT BODY:
Purpose: Retinal image blur in the periphery varies remarkably between individuals and their refractive state. Furthermore, the sign and shape of peripheral blur may provide a cue for the sign of defocus, and hence may play a role in accommodation and emmetropization. This study sought to investigate the peripheral image quality through-focus and how it depends on the eye's refractive error.
Methods: Previously published [1] Zernike coefficients across retinal eccentricity (0, 10, 20 and 30 deg horizontal visual field) were used to compute the monochromatic modulation transfer function (MTF) at 555 nm for a 4 mm pupil. Two-dimensional MTF was computed through-focus, from -3 to +3 D in 0.1 D steps at each eccentricity and used to define two metrics of image quality: (1) overall image quality defined as the volume under the MTF (vMTF) and (2) blur anisotropy defined as the ratio of the horizontal to vertical meridians of the MTF (HVRatio).

[1] Romashchenko, D, R. Rosén, and L. Lundström. "Peripheral refraction and higher order aberrations." Clinical and Experimental Optometry 103.1 (2020): 86-94.
Results: Across the horizontal visual field (at 10, 20, 30 deg), through-focus vMTF revealed best focus (max vMTF) close to the retina in emmetropes (-0.3, -0.3, 0.0 D, respectively), as opposed to myopes whose best focus was behind the retina (-0.1, 0.4, 1.5 D, respectively) and hyperopes in front of the retina (-0.5, -0.6, -0.6 D). At 0.0 D (on the retina), emmetropes and hyperopes both exhibited radially elongated blur, whereas myopes had circumferentially elongated blur (HVRatio = 0.3, 0.7 and 2.8, respectively, at 30 deg eccentricity). In all groups, peak vMTF (best focus) coincided with radially elongated blur.
Conclusions: Blur in the peripheral retina is dominated by so-called "odd-error" blur signals, primarily due to oblique astigmatism. Thus orientation of peripheral blur (radial vs circumferential) provides the eye with an optical cue for the sign of defocus and may play a role in mechanisms of accommodation and emmetropization. All subject groups had anisotropic blur in the periphery: myopes exhibited a circumferentially elongated peripheral blur, whereas emmetropes and hyperopes exhibited radial blur. These differences may be due to the interaction between peripheral wavefront aberrations and field dependent axial length (i.e. globe shape).

CONTROL ID: 3702877

SUBMITTER (NAME ONLY): Mahasweta Nayak

TITLE: Availability of Social Determinants of Health Data for Ophthalmology Patients in Electronic Health Records

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nayak, T.C. Lee, B. Radha Saseendrakumar, A. Chan, J. McDermott IV, B. Shahrvini, G. Ye, C. Nebeker, S. Baxter, University of California San Diego, La Jolla, California, UNITED STATES|M. Nayak, T.C. Lee, B. Radha Saseendrakumar, A. Chan, J. McDermott IV, B. Shahrvini, G. Ye, A. Sitapati, S. Baxter, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|A. Sitapati, University of California San Diego Department of Medicine, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Social Determinants of Health (SDoH) have been shown to play a substantial role in the development and treatment of eye conditions. Electronic health records (EHRs) offer a potential source for obtaining information regarding social determinants, but missing data are a known limitation of EHRs. In this study, we aimed to quantify the availability of SDoH data in our institutional EHR system for patients with common eye conditions.

Methods: Based on diagnosis codes, we identified adult patients (18 years and older) in the University of California San Diego (UCSD) EHR with the following conditions: cataracts, glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy (DR). For each cohort, we extracted SDoH data from the EHR. SDoH variables included demographics (age, race, ethnicity, gender), social history (alcohol, tobacco, drug use), and other relevant variables (income, education, housing security, food insecurity, stress levels, physical activity). We calculated data coverage per variable (i.e. the proportion of patients with available data for that variable) and analyzed the distribution of data coverage across variables within each cohort. We evaluated whether SDoH data coverage differed significantly among cohorts using chi-squared analyses, defining statistical significance as $p<0.05$. All analyses were performed using R.

Results: We identified 40,429 patients with cataracts, 26,794 patients with glaucoma, 6,713 patients with AMD, and 6,616 patients with DR. Demographic data across all cohorts had the highest rate of coverage at 98%. Tobacco-related variables had 80-90% coverage across all cohorts, while alcohol-related variables had 40-90% coverage. All remaining SDoH variables such as education, food insecurity, and income had an average of approximately 2-5% coverage (Figure 1). SDoH variables had low rates of data coverage across all cohorts.

Conclusions: There is increasing interest in understanding how social determinants influence the risk of eye disease and outcome. However, our study demonstrates that coverage of SDoH in our institutional EHR was highly variable, with large amounts of missing data. This highlights the need to develop standard practices for collecting SDoH data as well as to understand how to overcome potential barriers to data collection.

CONTROL ID: 3702882

SUBMITTER (NAME ONLY): Rodney Fong

TITLE: Efficacy of the Treat-and-Extend Regimen in the Management of Neovascular Age-related Macular Degeneration: 8-year Results of the RENO Study

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.D. Fong, M. Thomas, A.A. Aziz, F. Siddiqui, N. Mojumder, M. Hagen, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|C. Romero, J. Vannavong, A. Wadsworth, A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|P. Shappell, University of Southern California, Los Angeles, California, UNITED STATES|G.M. Gahn, The University of Arizona Department of Ophthalmology and Vision Science, Tucson, Arizona, UNITED STATES|W. Yang, University of Nevada Reno Division of Health Sciences, Reno, Nevada, UNITED STATES|J. Chhablani, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|J.M. Dang, Internal Medicine, University of Nevada Las Vegas Kirk Kerkorian School of Medicine, Las Vegas, Nevada, UNITED STATES|M. Koci, Ophthalmology, University of Missouri School of Medicine, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Treat-and-Extend (T&E) regimen with anti-VEGF agents is often used by retina specialists in clinical settings in the treatment of neovascular age-related macular degeneration (nAMD). This study evaluated the real-world long-term eight-year visual acuity outcomes of regular intravitreal anti-VEGF agents in patients with nAMD in the United States.

Methods: This is a retrospective, interventional, consecutive case series. 165 eyes from 137 treatment-naïve patients diagnosed with nAMD after August 2010 were treated at a single site by one physician with ranibizumab, aflibercept, bevacizumab, or brolucizumab for ≥1 year using a T&E regimen. Patients needed to receive ≥6 injections in the first year and ≥3 injections in the following years to be included in this study. Snellen best-corrected visual acuity (BCVA) was converted to ETDRS letters using a standardized formula. The main outcome measures were: BCVA change from baseline to end of patient follow-up; mean number of injections per year, and percentage of eyes losing ≥15 letters, gaining ≥15 letters or maintaining vision within 15 letters.

Results: The average (standard deviation [SD]) baseline patient age was 78 years (8.5); 60% of patients were female. The mean follow-up period was 5.4 years, with 165, 158, 143, 126, 102, 78, 48, and 26 eyes completing 1, 2, 3, 4, 5, 6, 7, and 8 years of follow up, respectively. The average BCVA at baseline was 53 letters. Mean (SD) changes from baseline in BCVA were 8.3 (21.8) letters, 7.1 (25.0) letters, 4.7 (26.5) letters, 4.5 (27.1) letters, 4.5 (28.3) letters, 5.1 (26.5) letters, and -0.5 (34.8) letters and -4.3 (38.9) letters for years 1-8 respectively. Mean number of injections during years 1-8 were 7.9, 6.1, 5.8, 6.0, 6.2, 5.9, 6.2, and 6.0, respectively. At the final follow-up, 24.2% of eyes had lost ≥15 letters, 26.1% of eyes had gained ≥15 letters and 49.7% of eyes had maintained vision within 15 letters.

Conclusions: 75.8% of patients on the T&E regimen either maintained or improved their vision at the final follow up. The T&E regimen has been effective in maintaining visual acuity in nAMD patients treated with ranibizumab, aflibercept, bevacizumab, or brolucizumab for up to six years of treatment. Patients lost vision in the 7th and 8th year

of treatment and further analysis is needed to evaluate the cause of vision loss.

CONTROL ID: 3702903

SUBMITTER (NAME ONLY): Hong-An Nguyen

TITLE: The Incidence and Characteristics of Charles Bonnet Syndrome in a Large Cohort of Leber's Hereditary Optic Neuropathy Patients

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Nguyen, M. Kreimei, E. Mollanji, R. Karanjia, Ophthalmology, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|L. Poincenot, LHON.org, California, UNITED STATES|R. Karanjia, Dohney Eye Institute, California, UNITED STATES|H. Nguyen, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Charles Bonnet Syndrome (CBS) is a condition involving visual hallucinations as a result of vision loss, but it is not well characterized nor routinely assessed for. Some patients with Leber's Hereditary Optic Neuropathy (LHON) experience CBS, but there is limited published data. This is the first study screening for and characterizing CBS in a large cohort of the LHON patient population.

Methods: A recently validated French-Canadian CBS screening questionnaire was adapted to an online bilingual (English-French) format, tailored to LHON patients (Cantin et al. CJO, 2019;54:323–7). The 59-item questionnaire was distributed to numerous mailing lists, online communities and social media platforms consisting of LHON patients. Quantitative and qualitative response data was used for cross-sectional analysis.

Results: A total of 155 affected LHON patients, 59% male and 41% female with over 85% of participants between the ages of 18 to 65, completed the questionnaire – with 54% screening positive for CBS. Of the participants who screened positive for CBS, 55% were affected by the 11778G>A mutation, 13.3% by 14484T>C, 14.5% by 3460G>A, 8.4% by other mutations and 8.4% by an unknown mutation. In addition, 41% of these participants have been diagnosed with LHON for more than 10 years while 38.5% have been diagnosed for less than 5 years.

Among CBS-positive patients, 90% of patients reported experiencing the hallucinations within the past year. Furthermore, 39% of patients reported that the images disturb their sleep, while 53% reported that the images negatively affect their mood. Additionally, only 55% had heard of CBS before and only 12% (10 participants) had been diagnosed with CBS by a health-care professional.

Conclusions: Our results yielded a high proportion of LHON patients screening positive for CBS (54%), indicating the condition may be a lot more common than previously suspected, and only a minority of LHON patients are being adequately assessed and managed for the condition. There is also an indication that their CBS tends to be long-lasting and can be associated with various negative health outcomes. Overall, this study provides a better understanding of the prevalence of CBS in LHON and the need for proactive discussions by health care providers.

CONTROL ID: 3702916

SUBMITTER (NAME ONLY): Ahmad Al Moujahed

TITLE: A Novel ATF6-Achromatopsia Allele Regulated by Nonsense-Mediated mRNA Decay

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Al Moujahed, L. Safarta, D. Vollrath, J. Lin, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Achromatopsia is an autosomal recessive form of cone dysfunction that is characterized by reduction of visual acuity, photophobia, nystagmus, and poor color vision. To date, six genes have been found to cause achromatopsia. ATF6 is the most recent of these genes to be identified with multiple types of mutations affecting it, including single-nucleotide changes, small deletions and duplications of the gene, and large multi-exon deletions. The purpose of this study is to describe a novel ATF6 mutation in 2 patients diagnosed with achromatopsia.

Methods: Patients were clinically evaluated and retinal images were obtained using standard methods with findings that were consistent with achromatopsia. Genetic testing of the two patients was performed using an inherited retinal degeneration disease gene panel. All ATF6 exons were further amplified by polymerase chain reaction (PCR) and analyzed by direct sequencing. The resulting sequence data were compared to the human ATF6 gene reference sequence NM_007348.3.

Results: Two siblings from a consanguineous family of Arab descent were diagnosed with ACHM. We identified a homozygous mutation in the exon 10 of the ATF6 gene c.1243dup, which leads to introduction of a premature stop codon p.(Arg415Lysfs*10) in the new coding frame. This premature stop codon is located 534 nucleotides from the last exon-exon (exon 15-exon 16?) or (exon 17-exon 18?) junction and satisfies the >60-65 nucleotide criteria for transcripts that are subject to nonsense-mediated decay (NMD).

Conclusions: This is the first report of a new homozygous single-nucleotide duplication mutation in the ATF6 gene c.1243dup in 2 patients with achromatopsia that leads to a premature stop codon. We also show the predicted regulation of this ATF6-achromatopsia allele by NMD of the variant transcript mRNA.

CONTROL ID: 3702940

SUBMITTER (NAME ONLY): Jung Woo Han

TITLE:

Role of mTORC1 activity on early retinal devleopment and lamination in human induced pluripotent stem cell derived-retinal organoids

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Han, S. Lee, E. Choi, T. Park, Soonchunhyang University Hospital Bucheon, Bucheon, Gyeonggi-do, KOREA (THE REPUBLIC OF)|J. Bang, H. Shin, Department of Interdisciplinary Program in Biomedical Science, Soonchunhyang Graduate School, KOREA (THE REPUBLIC OF)|H. Chang, Department of Anatomy and BK21 Four Project, College of Medicine, Soonchunhyang University, KOREA (THE REPUBLIC OF)|J. Choi, H. Jun, Laboratory for Translational Research on Retinal and Macular Degeneration, Soonchunhyang University Hospital Bucheon,, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To identify a time-dependent role of mTORC1 in retinal development using hiPSC-derived retinal organoids, especially retinal ganglion cell (RGC) differentiation, and retinal lamination process during early stages of retinal organoids (ROs).

Methods: We utilized American Type Culture Collection (ATCC)-DYR0100 hiPSCs for retinal organoid differentiation. Rapamycin and MHY1485 were prepared at final concentrations of 100 nM and 10 μM, respectively. From 35 days of differentiation, organoids were transferred to the wells of a 96 well plate and treated with rapamycin and MHY1485 until 40 days of differentiation. The development of RGCs was assessed by the expression of various specific markers (HuC/D, AtoH7, Islet-1, and Brn3b) We examined the relative expression of total mTOR, Raptor, and Rictor, S6K1 to investigate the dynamics of mTOR activity in ROs. RGC markers HuC/D, AtoH7 and mTORC1 marker S2448, ps6 were detected in ROs by immunofluorescence staining.

Results: mTORC1 activity in ROs was the highest at 40 days of differentiation. Hyperactivation of mTORC1 during this period using MHY1485 resulted in the significantly increased overall size of ROs compared to untreated controls and rapamycin-treated ROs, while showing markedly increased proliferative activity both in inner and outer layers of ROs. Also, MHY1485-treated ROs showed a significantly increased number of ectopic RGCs in outer layers, indicating disruption of retinal laminar structure, with robust expression of HuC/D in inner layers

Conclusions: mTORC1 plays a critical role in the development of hiPSC-derived ROs, especially during the early stages of differentiation. Moreover, our results also outline the feasibility of using hiPSC-derived ROs as a tool for translational research on retinal development.

CONTROL ID: 3702952

SUBMITTER (NAME ONLY): Karen Peynshaert

TITLE: Photodisruption of the ILM to enhance retinal drug delivery after intravitreal injection

SESSION TITLE: Drug delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Peynshaert, K. De Clerck, H. Vanluchene, F. Sauvage, A. Minnaert, K. Braeckmans, S. De Smedt, K. Remaut, Laboratory of General Biochemistry and Physical Pharmacy, Universiteit Gent, Ghent, East-Flanders, BELGIUM|G. Accou, Departement of Ophthalmology, Universiteit Gent, Ghent, East-Flanders, BELGIUM|

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ABSTRACT BODY:

Purpose: The development of many therapies involving retinal delivery of biologics or cells by intravitreal injection is greatly hampered by obstruction of the therapeutics at the inner limiting membrane (ILM). Therefore, we explore photodisruption of the ILM to generate therapeutic entryways that can greatly enhance retinal delivery. To this end, the photothermal dye indocyanine green (ICG) is applied to the ILM and irradiated with pulsed laser light in order to create vapor nanobubbles (VNBs) which upon their collapse can disrupt the ILM (Fig 1).

Methods: To perforate the ILM, we applied varying concentrations of ICG (0,1 mg – 1mg/ml) on top of bovine retinal explants followed by scanning of the laser beam at lower and higher laser energies (0,24 or 0,4 J/cm^2). For the latter, an Nd:YLF laser was applied to generate 800 nm single laser pulses of a 2 picosecond pulse width and frequency of 1 kHz. Propidium iodide staining was applied to assess retinal cell death right after treatment and after 24 hours in retinal cryosections (n=3). To assess the impact on delivery, 120nm-sized Lipid Nanoparticles (LNPs) loaded with luciferase-mRNA were dripped on top of explants (according with a dose of 1 µg of mRNA) prior to their culture for 24 hours after which retinal luciferase expression was measured in intact explants using an IVIS sytem (n=4). During these experiments, untreated, ICG-only and laser-only controls were added. Finally, dark-field microscopy was applied to image VNB formation upon laser pulse irradiation in patient-derived isolated human ILM (n=2).

Results: The strongest conditions (1 mg/ml ICG; 0,43 J/cm2) elicited significant cell death, especially in the GCL and INL layer, yet, milder conditions (0,1 mg/ml ICG; 0,43 J/cm2) did not affect retinal viability, even after 24 hours. Strikingly, the latter conditions elicited a nearly 5-fold increase (4.7 ± 0.4 SD, $p<0001$) in retinal luciferase expression when compared to explants treated with LNPs only. Dark-field microscopy on the human ILM confirmed that this effect is based on pore formation owing to VNB generation.

Conclusions: This ex vivo study reveals that ICG-mediated photodisruption of the ILM can greatly enhance delivery of nanoparticles into the retina in a safe manner. Driven by this positive outcome, future plans include assessment of the safety and efficacy of our technology in vivo.

CONTROL ID: 3703002

SUBMITTER (NAME ONLY): Cyril Eleftheriou

TITLE: Retinoschisin deficiency induces persistent aberrant waves of activity affecting neuroglial signaling in the developing retina

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: X-linked juvenile retinoschisis (XLRS) is an early onset inherited condition characterized by abnormal retinoschisin (RS1) expression, early visual deficiencies and cystic retinal lesions. We characterize a series of novel dysfunctions at the cellular level of the developing retina of mice lacking RS1.

Methods: We studied spontaneous intracellular calcium dynamics in male mice expressing GCaMP6f in neuronal, glial, and vascular cells and compared results from Rs1 knockouts ($Rs1^{-/Y}$) and controls ($Rs1^{+/Y}$). Optophysiological assessment was carried out in live wholemount retinal explants of cohorts aged P10-11, P14-15, P20-22, and P60-65. Additionally, we performed in vivo OCT imaging of retinal cysts and immunohistochemical characterization of retinoschisin expression in the retina.

Results: The development of retinal cysts imaged in vivo by OCT is paralleled by the appearance of aberrant spontaneous neuro-glial signals after postnatal day 13. These presented as glutamate-driven wavelets of neuronal and Müller glia activity spanning all retinal layers that disrupt light-induced signaling.

Conclusions: This study highlights the critical role that RS1 plays in early retinal development. Additionally, it confers a functional role to RS1 beyond the scope of an adhesion molecule and identifies a tight bracket for the onset of dysfunction, a potential temporal target for therapeutic intervention.

CONTROL ID: 3703021

SUBMITTER (NAME ONLY): William Swanson

TITLE: Predicting Deep Perimetric Defects from Retinal Nerve Fiber Layer (RNFL) Reflectance at the Optic Disc

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.H. Swanson, B. King, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|M.S. Alluwimi, Optometry, Qassim University, Buraidah, Al Qassim, SAUDI ARABIA|R. Malik, Ophthalmology, University of Alberta Faculty of Medicine & Dentistry, Edmonton, Alberta, CANADA|

Commercial Relationships Disclosure: William Swanson: Commercial Relationship: Code N (No Commercial Relationship) | Muhammed Alluwimi: Commercial Relationship: Code N (No Commercial Relationship) | Rizwan Malik: Commercial Relationship: Code N (No Commercial Relationship) | Brett King: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To use RNFL reflectance at the optic disc to distinguish hemifields with deep perimetric defects from hemifields with no perimetric defect.

Methods: Volume scans for a 30° x 15° scan covering the optic disc were gathered on one eye per person with Spectralis optical coherence tomography (OCT), and used to compute en face maps of log attenuation coefficient (AC) at 24 μm below the inner limiting membrane (ILM). The analysis method was developed by analyzing results for 15 patients with glaucoma and 15 age-similar controls recruited and tested at Indiana University School of Optometry (IUSO) in the United States. Then this method was applied to an independent data set for 23 patients with glaucoma and 10 age-similar controls recruited and tested at King Khaled Eye Specialist Hospital (KKESH) in Saudi Arabia. For each eye, both superior and inferior visual hemifields were scored as having a deep defect when the location with deepest total deviation had a value of -24 dB or worse. A grid of 338 square cells was overlaid on an en face image, pixels containing vasculature and/or optic disc were excluded and mean AC was computed for each cell. For each eye, the 85th percentile for AC was computed as a reference value and cells for which mean AC fell 0.3 log unit or more below the reference value were scored as abnormal. A hemifield was considered abnormal if there was a cluster of defects corresponding to inferior temporal or superior temporal RNFL sectors.

Results: For the hemifields in the IUSO dataset, all 11 hemifields with deep perimetric defects were identified and none of the 38 hemifields with no perimetric defect. For the KKESH dataset, 17 of the 23 hemifields with deep perimetric defects were identified and none of the 22 hemifields with no perimetric defect. The 95% confidence limit for specificity for perimetrically normal hemifields was 91%-100% for the IUSO dataset and 85%-100% for the KKESH dataset. The 95% confidence limit for sensitivity for hemifields with deep perimetric defects was 74%-100% for the IUSO dataset and 54%-87% for the KKESH dataset.

Conclusions: A method with good specificity and sensitivity was developed, and then tested on an independent dataset. Specificity remained high, but sensitivity was at the lower end of the 95% confidence interval for the first data set. Further work is needed to improve sensitivity of en face reflectance analysis at high specificity.

CONTROL ID: 3703028

SUBMITTER (NAME ONLY): Siggi Trier

TITLE: Ocular Surface Pain: Online medical education can significantly improve ophthalmologists' knowledge on causative factors, diagnostic methods and emerging therapies and increase confidence for patient assessment

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Trier, P. Aboulsaoud, P. Schoonheim, Education Global, Medscape LLC, New York, New York, UNITED STATES|A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|M. Labetoulle, Hopital Bicetre, Le Kremlin-Bicetre, Île-de-France, FRANCE|E. Messmer, Ophthalmology, Ludwig-Maximilians-Universitat Munchen, Munchen, Bayern, GERMANY|

Commercial Relationships Disclosure: Siggi Trier: Commercial Relationship(s);Code C (Consultant/Contractor):Medscape LLC;Code I (Personal Financial Interest):Glaxo Smith Kline (own shares) | Pakinam Aboulsaoud: Commercial Relationship(s);Code E (Employment):Medscape LLC | Peter Schoonheim: Commercial Relationship(s);Code E (Employment):Medscape LLC | Anat Galor: Commercial Relationship(s);Code C (Consultant/Contractor):Dompe, Novaliq, Novartis, Oyster Point;Code F (Financial Support):Sjögren's Syndrome Foundation | Marc Labetoulle: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon, Allergan, Bausch & Lomb, DMG, Dompe, GlaxoSmithKline, Horus, Merck Sharpe and Dohme, Novartis, Quantel, Santen, Shire, Thea, Topivert;Code R (Recipient):Alcon, Allergan, Bausch & Lomb, DMG, Dompe, GlaxoSmithKline, Horus, Merck Sharpe and Dohme, Novartis, Quantel, Santen, Shire, Thea, Topivert;Code F (Financial Support):Thea | Elisabeth Messmer: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon, DMG, Dompé, Kala, Novartis, Pharm-Allergan, Santen, Shire, Sun, Thea Pharma, TRB Chemedica, Visufarma;Code R (Recipient):Alcon, Dompe, Novartis, Pharm-Allergan, Santen, Thea, TRB Chemedica, Ursapharm, Visufarma, Chiesi;Code F (Financial Support):DMG, Dompé, Kala, Novartis, Pharm-Allergan, Santen, Shire, Sun, Thea Pharma, TRB Chemedica, Visufarma

ABSTRACT BODY:

Purpose: To determine if online medical education for ophthalmologists (Opht) could improve their knowledge and confidence to assess patients with ocular surface pain, in particular those with a neuropathic component and recall new mechanisms of action for emerging treatments

Methods: Opht participated in an online 30 min video, 3 expert roundtable discussion with accompanying slides. A repeated pairs pre-/post-assessment study design was used, assessing 3 multiple choice knowledge and one confidence question. Statistical significance tests: McNemar's test for individual questions (5% significance level, $P < .05$), paired sample t-test for overall average correct responses and confidence rating; data collected Apr 16, 2021 to Jul 15, 2021. Test completers: 441

Results: At baseline, 38% of Opht (n=441) answered all 3 questions correctly, increasing to 71% ($P < 0.01$) on post-assessment. 49% of Opht reported improved confidence in their ability to assess patients with ocular surface pain. The activity significantly increased knowledge on neuropathic causes as contributing factor to ocular surface pain (pre: 81%, post: 89%, $p<.001$), on selecting assessment methods to differentiate between neuropathic corneal pain of central and peripheral origin (pre: 68%, post: 88% $p<0.001$) as well as recalling the mechanism of action for an emerging therapy inhibiting transient receptor potential cation channel subfamily V member 1 (TRPV1) which plays a key role in ocular surface pain. (pre: 60%, post: 82%, $p<.001$). 93% of test completers polled stated a need for new therapies to treat chronic ocular surface pain.

Conclusions: Online medical education in the form of expert roundtable discussions with accompanying slides can significantly improve ophthalmologists' knowledge and confidence on assessing patients with ocular surface pain to raise awareness and improve diagnosis of peripheral and central neuropathic pain and increase knowledge on emerging treatments, such as topical TRPV-1 inhibitors. Polling confirmed a high unmet need for new treatments to better control chronic ocular surface pain. Additional education is warranted to shorten time to diagnosis for neuropathic ocular pain, disseminate latest clinical data for emerging treatments and evidence based patient selection guidance for clinical practice.

CONTROL ID: 3703050

SUBMITTER (NAME ONLY): Joe Rappon

TITLE: TWO-YEAR EFFECTIVENESS OF A NOVEL MYOPIA MANAGEMENT SPECTACLE LENS WITH FULL-TIME WEARERS

SESSION TITLE: Myopia: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Rappon, T.W. Chalberg, SightGlass Vision, Palo Alto, California, UNITED STATES|J. Neitz, M. Neitz, University of Washington, Seattle, Washington, UNITED STATES|C. Chung, Carol Chung Statistics Consulting Inc., California, UNITED STATES|

Commercial Relationships Disclosure: Joe Rappon: Commercial Relationship(s);Code E (Employment):SightGlass Vision;Code P (Patent):SightGlass Vision;Code I (Personal Financial Interest):SightGlass Vision | Jay Neitz: Commercial Relationship(s);Code P (Patent):SightGlass Vision;Code I (Personal Financial Interest):SightGlass Vision | Maureen Neitz: Commercial Relationship(s);Code P (Patent):SightGlass Vision;Code F (Financial Support):SightGlass Vision;Code I (Personal Financial Interest):SightGlass Vision | Carol Chung: Commercial Relationship(s);Code C (Consultant/Contractor):SightGlass Vision, Adverum Biotechnologies, Stargazer Pharmaceutical, Annexon, 4DMT, iRenix | Thomas Chalberg: Commercial Relationship(s);Code E (Employment):SightGlass Vision;Code I (Personal Financial Interest):SightGlass Vision;Code P (Patent):SightGlass Vision

ABSTRACT BODY:

Purpose: New therapies are urgently needed to slow or stop myopia progression in children, and therefore reduce the risk of long-term, sight-threatening complications from myopia. The discovery that polymorphisms at the myopia genetic locus, MYP1, are associated with splicing-defective cone opsin genes (OPN1LW and OPN1MW) led to the hypothesis that contrast signaling in the retina plays an important role in myopia development and progression. This hypothesis predicted that reducing the contrast of images on the retina could slow myopia progression. Novel spectacle lenses (DOT lenses) were developed to evaluate this hypothesis, and a multi-center, double-masked, randomized, controlled clinical trial was initiated.

Methods: CYPRESS (NCT03623074) evaluated two investigational spectacle lenses (Test 1, Test 2) designed to slightly reduce contrast compared to control spectacle lenses for the ability to reduce myopia progression in children 6-10 years of age over a period of 3 years. Two hundred and fifty-six (256) eligible myopic subjects were randomized and dispensed spectacles at 14 clinical sites in North America. Subjects were asked to wear the study spectacles constantly, except for activities in which standard spectacle wear would be inappropriate, such as contact sports and swimming. “Full time wearers” were defined as those subjects whose parents reported that they did not remove the study spectacles for near vision activities. Axial length (AL) and cycloplegic autorefraction (SER) were measured at baseline and annual follow-up visits, now through 24-months.

Results: Approximately two-thirds of study subjects (61, 45, and 66 in Test 1, Test 2, and Control, respectively) met criteria for “full-time wearers”. After 24-months, the mean (± SD) change from baseline in AL was 0.33 ± 0.23, 0.34 ± 0.39, and 0.53 ± 0.33 mm for Test 1, Test 2, and Control respectively. The mean change from baseline in SER after 24-months of usage was -0.36 ± 0.54, -0.48 ± 0.85, and -0.88 ± 0.77 D for Test 1, Test 2, and Control, respectively. The difference in means (Test 1 minus Control) for change from baseline of AL (-0.21 mm) and SER (0.52 D) were statistically significant ($p<0.0001$).

Conclusions: DOT spectacle lenses were designed to reduce retinal contrast to slow the progression of myopia. After 24-months of usage, subjects who wore DOT lenses full-time had less myopia progression than control subjects.

CONTROL ID: 3703107

SUBMITTER (NAME ONLY): Joseph Demer

TITLE: Masquerading Superior Oblique Palsy Mimics All Features of Congenital and Acquired Superior Oblique (SO) Muscle Weakness

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.L. Demer, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|J.L. Demer, Neurology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Joseph Demer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Unilateral SO palsy is typically diagnosed by the 3-step test criteria requiring ipsilateral hypertropia, that increases in contralateral gaze, and with ipsilateral head tilt. I asked if this pattern, in congenital & acquired cases, is specific for SO atrophy that occurs reliably after SO denervation.

Methods: In a prospective study of head-position dependent hypertropia, quasi-coronal, surface coil MRI was performed in central gaze, and in some cases supraduction, and infraduction. The hypertropic SO of 57 subjects had max. cross section <80% of contralateral, indicating unilateral SOP: 22 subjects had congenital (mean age 29±19 yrs, standard deviation, SD) & 35 had acquired strabismus onset (age 46±19 yrs, symptoms for 6±7 yrs). There were 26 similarly hypertropic subjects with normal SO muscles that were considered masquerading cases: 8 subjects had congenital (mean age 36±16 yrs) & 18 had acquired onset (age 34±18 yrs, symptoms for 6±9 yrs). Alignment was measured using prisms in diagnostic positions with & without head tilt, & with double Maddox rods.

Results: Maximum SO cross section averaged 7.7±3.8mm^2 in congenital & 10.7±3.5mm^2 in acquired SOP (P=0.003), significantly less than contralesionally at 17.9±3.7 mm^2 & 18.9±3.9mm^2, respectively (P<10^{-9}). Maximum hypertropic SO cross section in congenital (18.4±3.0 mm^2) & acquired (20.7±3.1mm^2) masquerading cases was statistically identical to contralateral in all groups (P>0.4). The contractile increase in SO cross section from up to down gaze was statistically similar in hypertropic & fellow eyes of masquerades (P>0.6). The 3-step test was fulfilled in all congenital but only 72% of acquired SO atrophy, tending even less than 81% in masquerades (P=0.27). Alignment & torsion measures were statistically indistinguishable in all diagnostic positions between cases of SO atrophy & masquerades, except that hypertropia in infraversion was slightly larger at 14.5±11.5Δ in SO palsy than 9.2±9.1Δ in masquerades (P=0.04). There were supranormal vertical fusional amplitudes of up to 27Δ in 56% of masquerading cases.

Conclusions: Masquerading SO palsy occurs in the presence of normal SO morphology and contractile function, quantitatively mimicking all alignment features of actual SO unilateral weakness manifested by SO atrophy, including supranormal vertical fusional amplitudes with both congenital & acquired onset.

CONTROL ID: 3703119

SUBMITTER (NAME ONLY): Yu-Chi Liu

TITLE: Neuropathic Ocular Surface Changes, Corneal Nerve Imaging and neuromediator Profiles in Small Incision Lenticule Extraction (SMILE) and Femtosecond Laser-Assisted in-situ Keratomileusis (LASIK)

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, M. Lin, I. Lee, Singapore Eye Research Institute, Singapore, SINGAPORE|J.S. Mehta, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Yu-Chi Liu: Commercial Relationship: Code N (No Commercial Relationship) | Molly Tzu-Yu Lin: Commercial Relationship: Code N (No Commercial Relationship) | Isabelle Xin Yu Lee: Commercial Relationship: Code N (No Commercial Relationship) | Jodhbir Mehta: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate and compare the neuropathic ocular surface changes, corneal nerve imaging and neuromediator profiles in small incision lenticule extraction (SMILE) and femtosecond laser-assisted in-situ keratomileusis (LASIK)

Methods: In this prospective study, 25 SMILE patients (n=50 eyes) and 25 LASIK (n=50 eyes) were followed up for 1 year. Five clinical neuropathic ocular surface assessments, 7 corneal nerve parameters evaluated by ACCMetrics software, OSDI questionnaire, and the levels of 4 tear neuromediators, were evaluated preoperatively, and 1 week, 1, 3, 6, and 12 months postoperatively.

Results: SMILE, compared to LASIK, had significantly better corneal sensitivity at 1 week, 1, 3 and 6 months, better tear break-up time (TBUT) at 3 months, lower corneal NEI scores at 1 week, 6 and 12 months, and lower ocular surface Oxford scores 1 week. SMILE had significantly better corneal nerve fiber length (CNFL), density (CNFD), total branch density, fiber area, fiber width (CNFW) and fiber fractal dimension (CFracDim) than LASIK throughout 1year. At 1 year, the nerve metrics were significantly impaired in LASIK, while fiber area and width had been restored in SMILE. There were significant increase in nerve growth factor at 1 month, and decrease in substance P (SP) at 1 month in LASIK, while the changes were insignificant in SMILE. CNFL, CNFD, CNFW, CFracDim and tear SP level were significantly associated with TBUT. Tear SP, neuropeptide Y (NPY) and calcitonin gene-related peptide (CGRP) concentrations were significantly correlated all the nerve parameters, except CNFW.

Conclusions: This is the first study comprehensively evaluate and correlate the molecular profiles, morphological changes and clinical functional changes in patients with refractive surgery. The postoperative corneal denervation was long-lasting, with faster restoration in SMILE. SMILE was also associated with less negative impact on ocular surface clinically, as well as less fluctuations in neuroinflammatory reaction. Even though clinical symptoms and signs have subsided, significant alterations in corneal neurobiological status, nerve morphology and quantity were still observed. Our study provides new insights into the biological responses on the ocular surface after refractive surgery.

CONTROL ID: 3703142

SUBMITTER (NAME ONLY): Nikhil Gupta

TITLE: Preclinical Animal Model for Functional Biocompatibility of a Novel VEGF and Ang-2 Bispecific Protein (RO-634) Using ERG Analysis

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Gupta, Glenwood High School, Chatham, Illinois, UNITED STATES|J.L. Olson, A. Jones, J. Morgenstern, A. Strong, S. Droho, N. Mueller, M. Huvard, Sue Anschutz Rodgers Eye Center, University of Colorado, Aurora, Colorado, UNITED STATES|P.K. Kaiser, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|A.M. Khanani, University of Nevada, Reno School of Medicine, Reno, Nevada, UNITED STATES|J.S. Heier, OCB, Boston, Massachusetts, UNITED STATES|E. Sembell, Southern Illinois University School of Medicine, Springfield, Illinois, UNITED STATES|R. Bhandari, Springfield Clinic Eye Institute, Springfield, Illinois, UNITED STATES|S. Bevers, Structural Biology and Biochemistry, University of Colorado, Aurora, Colorado, UNITED STATES|L. Xu, Independent Research Consultant, California, UNITED STATES|A. Sinha, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the in vivo ocular biocompatibility of a novel intravitreal bispecific protein, RO-634, designed to target Vascular Endothelial Growth Factor-A (VEGF-A) and Angiopoietin-2 (Ang-2) using electroretinogram (ERG).

Methods: All experiments were performed in accordance with the ARVO statement for Use of Animals in Ophthalmic and Vision Research. Five Brown Norway rats received intravitreal injections of RO-634 in the right eye and balanced saline solution (BSS) in the left eye to evaluate for possible retinal toxicity. One month after intravitreal injection, ERGs were performed to assess potential damage to the retina. Animals were dark-adapted overnight prior to the ERG. ERGs were performed on the Celeris device (Diagnosys LLC, Lowell, MA). The test consisted of flash stimuli at 0.01, 0.1, 1.0, and 3.0 cd-s/m^2. Student Paired T-test was used for statistical comparison of the amplitude and peak times between the control and experimental eye at each level of stimuli.

Results: RO-634 was well tolerated in brown Norway rats, demonstrating biocompatibility. ERG analysis of scotopic and photopic light response showed cone and rod functional activity with no statistically significant difference in the A and B wave amplitudes and peak times between the control and the experimental eye. Figure 1 is an illustration of similar ERG response in the experiment and control arm at flash stimuli of 3.0 cd-s/m^2.

Conclusions: In this preclinical animal study, the novel bispecific, RO-634, showed physiologic ocular compatibility as measured by ERG. Future studies are needed to evaluate the clinical potential of this novel and promising agent for treatment of back of the eye disease.

CONTROL ID: 3703145

SUBMITTER (NAME ONLY): Shuizhen Shi

TITLE: Tauopathy induces degeneration and impairs regeneration of sensory nerves in the cornea

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shi, S. Li, B. Luo, F. Xia, Y. Ha, K. Merkley, M. Motamedi, W. Zhang, H. Liu, Ophthalmology & Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|S. Li, Ophthalmology, the second Xiangya Hospital of Central South University, Changsha, Hunan, CHINA|

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ABSTRACT BODY:

Purpose: The cornea is transparent and innervated by a dense collection of sensory nerves originating from the ocular branch of the trigeminal nerve. This study was designed to comprehensively analyze alterations of corneal sub-basal nerve plexus in a mouse model of tauopathy (P301L transgenic mice) to test the possibility of using corneal nerves as a biomarker for tauopathy and to investigate its potential underlying mechanisms.

Methods: Corneal sensitivity, thickness and epithelial wound healing were measured non-invasively by aeshesiometer, optical coherence tomography and fluorescein staining, respectively. Tau, corneal nerves and immune cells were examined by immunohistochemistry or Western blot. Transcriptome changes in the trigeminal ganglion (TG) were determined by RNAseq.

Results: At the early stage of tauopathy, although corneal sensitivity, thickness and nerve fiber density were not greatly altered, corneal nerve abnormalities were observed in the peripheral region of young P301L mice. With aging, the density of abnormal nerves increased, while corneal sensitivity, epithelial thickness, nerve fiber density and length decreased in middle-aged P301L mice compared with WT mice. After corneal epithelial injury in young mice, no difference in reepithelialization was observed between two groups of mice, however, the regeneration of corneal nerves in P301L mice lagged behind WT mice, which was reflected by delayed recovery of corneal sensitivity, decreased corneal nerve density and length and density of $CD45^{+}$ dendriform cells in P301L mice. RNAseq analysis revealed that gene sets related with ribosome, proteasome and protein export were significantly downregulated in TGs from 3-month old P301L mice compared with those from age-matched WT mice.

Conclusions: Our data provide compelling evidence that corneal nerves were changed in a mouse model of tauopathy in an age-dependent manner. Moreover, tau overexpression impairs corneal nerve regeneration, which may involve tauopathy-induced decreases in de novo protein synthesis and transportation. These results suggest that cornea may serve as a promising ocular site for the early diagnosis of tauopathy.

CONTROL ID: 3703160
SUBMITTER (NAME ONLY): Luke Harrison
TITLE: Pointwise Comparison of the 24-2C and 10-2 for Central Field Defects
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Harrison, A. Chen, P.P. Chen, P. Luong, University of Washington, Seattle, Washington, UNITED STATES|
Commercial Relationships Disclosure: Luke Harrison: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Chen: Commercial Relationship: Code N (No Commercial Relationship) | Philip Chen: Commercial Relationship: Code N (No Commercial Relationship) | Preston Luong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The 24-2C SITA Faster on the Humphrey Field Analyzer is a relatively newly introduced visual field-testing algorithm. Preliminary studies demonstrate agreement of global metrics between the 10-2 and 24-2C. We conducted a retrospective, observational study to perform pointwise comparisons of the 24-2C and 10-2 visual field at their 14 points of overlap.

Methods: Chart review was performed for glaucoma patients who had visual testing between 2019 and 2020. Inclusion criteria included diagnosis of POAG, pigmentary glaucoma, or NTG, and refraction between -8.00 and + 8.00. The exclusion criteria included BCVA < 20/60, ocular surgery other than uncomplicated cataract, SLT, YAG or ALT, age < 18 yrs, neurological disease, angle closure glaucoma. The following statistical tests were used: paired T test for pointwise threshold decibel data, McNemar's test for defect probabilities and Wilcoxon's signed rank test for pointwise comparison of defect probabilities.

Results: Figure 1 depicts the overlay of the 10-2 and 24-2C. There were 39 eyes included with testing separated by 219 ± 281 days. Average MD and PSD were -6.66 ± 7.01, 6.41 ± 4.13 and -6.55 ± 6.98, 6.74 ± 5.03 for the 24-2C and 10-2 respectively. For threshold sensitivity, the mean difference (24-2C dB – 10-2 dB) and paired T-test p-value for each point are listed. Statistically significant points: 43 (2.56 dB, p=0.03), 47 (-1.69 dB, p=0.0038), 50 (-2.95 dB, p=0.005), 60 (2.05 dB, p=0.02), and 61 (2.59 dB, p=0.027). The remaining points are: 3 (1.31 dB, p=0.26), 9 (0.85 dB, p=0.54), 12 (3.38 dB, p=0.13), 19 (0.02 dB, p=0.98), 22 (-0.56 dB, p=0.70), 32 (2.05 dB, p=0.17), 57 (1.59 dB, p=0.17), and 67 (1.56 dB, p=0.089). Probability comparison is displayed in figure 2, points 32 (p=0.016) and 43 (p=0.026) were statistically significant. The 24-2C and 10-2 were significantly different across all points with (p=0.044).

Conclusions: The threshold sensitivities of the 24-2C and 10-2 visual field tests are statistically different at 5 points of overlap. In contrast, the probability plots of the 24-2C and 10-2 are different at only 2 points. When comparing the 14 points of overlap in aggregate, for defect probability, we found that the 24-2C and 10-2 were different. These results suggest that the 24-2C can "miss" defects that would otherwise be appreciated on the 10-2. However, the 24-2C could still be a valuable screening tool for central defects.

CONTROL ID: 3703173

SUBMITTER (NAME ONLY): Grant Justin

TITLE: Quality Improvement of Retinopathy of Prematurity Care in the Department of Defense Universal Healthcare System: Epidemiology, Follow-up, and Early Childhood Visual Sequelae

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Justin, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|A. Cox, G. Gorman, Walter Reed National Military Medical Center, Bethesda, Maryland, UNITED STATES|L. Peterson, Naval Medical Center San Diego, San Diego, California, UNITED STATES|G. Justin, M. Colyer, Uniformed Services University of the Health Sciences, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Grant Justin: Commercial Relationship: Code N (No Commercial Relationship) | Anthony Cox: Commercial Relationship: Code N (No Commercial Relationship) | Lisa Peterson: Commercial Relationship: Code N (No Commercial Relationship) | Marcus Colyer: Commercial Relationship: Code N (No Commercial Relationship) | Gregory Gorman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To establish baseline performance data for a process/quality improvement (PI/QI) program for detection and follow-up of Military Health System (MHS)-eligible infants at risk for retinopathy of prematurity (ROP).

Methods: All births in the MHS from 2016-2019 were identified in the M2 database. Demographic information and gestational age were extracted, and ROP diagnosis, laterality, and stage were determined by ICD-10 codes. Infants at risk for sequelae of ROP were defined as those born <31 weeks GA and/or were diagnosed with ROP during the birth admission. Outpatient claims from military and civilian providers were linked to each at-risk infant, and the timing and diagnoses of each claim determined. Secondary visual diagnoses were determined by ICD-10 code. Chi-squared tests determined differences in percentages, and non-parametric tests determined differences in medians.

Results: 1,457 (91.6% of all at-risk infants) could be matched to outpatient claims and formed the population for analysis. 404 infants (27.7%) were diagnosed with ROP. 114 (28.2%) were initially diagnosed with Stage 0, 127 (31.4%) with stage 1, 77 (19.1%) with stage 2, 31 (7.7%) with stage 3, 13 (3.2%) with stage 4 and 5 (1.2%) with stage 5. 37 (9.2%) had unknown stage. The 50^{th} percentile time from birth to first ophthalmic examination was 34 days (IQR 29-48 days). The median first follow-up after discharge for patients with ROP occurred at 18.5 days.

Compared to at-risk patients not diagnosed with ROP, ROP patients had a higher prevalence of strabismus (16% vs 9.6%; p<0.001), refractive error (41% vs 28%, p<0.001), and visual disturbance (12% vs 9.0%; p=0.04). There was no significant difference in the prevalence of blindness and low vision (0.3% vs 0.5%; p=0.73) and nystagmus (1.5% vs 1.2%; p=0.35). Only one patient in the ROP group developed a retinal detachment and none in the non-ROP group (p=0.05).

Conclusions: Retinopathy of prematurity is a high risk, low volume ophthalmic condition for which many MHS-eligible beneficiaries are at risk. The incidence of ROP in infants born in the MHS is similar to infants in other large single payer systems although the incidence of severe ROP stage 4 and 5 may be higher. These patients are at increased risk for strabismus and refractive error and require frequent long-term outpatient follow-up.

CONTROL ID: 3703176

SUBMITTER (NAME ONLY): Nirali Shah

TITLE: Patient Satisfaction with the Symfony Intraocular Lens

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Shah, M.E. Rauser, Ophthalmology, Loma Linda University, Loma Linda, California, UNITED STATES|

Commercial Relationships Disclosure: Nirali Shah: Commercial Relationship: Code N (No Commercial Relationship) | Michael Rauser: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Achieving independence from spectacles and overall satisfaction are challenging goals after cataract surgery. The purpose of this investigator-initiated study is to assess patient satisfaction over one year after implantation of the Tecnis Symfony intraocular lens during cataract surgery. These results assist future patients and surgeons in choosing the intraocular lens that will provide the most benefit long term.

Methods: This was a prospective study of patients who had cataract extraction with Symfony intraocular lens placement between 2015 and 2019 at Loma Linda University Eye Institute by one experienced surgeon. These patients were called by the investigator over one year after their surgery. The patients proceeded with a subjective questionnaire via telephone to assess spectacle independence, photic phenomenon, and satisfaction with vision. The data were recorded using a Google Sheets spreadsheet and analyzed using SPSS software.

Results: 92 patients who had cataract surgery with the Symfony intraocular lens over one year prior were called. Of these subjects, 40 patients agreed to participate in the telephone questionnaire. 82.1% of patients did not require spectacles for distance vision, 70% of patients did not require spectacles for intermediate vision, and 20% did not require spectacles for near vision. 60% of patients never experienced glare, and 25% experienced mild glare. 47.5% of patients never experienced halos, and 45% experienced mild halos. 77.5% of patients never experienced starbursts of light, and 20% experienced mild starbursts. In terms of overall satisfaction, 47.5% of patients were extremely satisfied and 40% were satisfied. 87.2% would choose the same intraocular lens again.

Conclusions: This study demonstrates that after at least one year, patients continue to have high levels of spectacle independence, minimal photic phenomenon, and good overall satisfaction with the Symfony intraocular lens. This information should assist patients in choosing this lens in the future.

CONTROL ID: 3703187

SUBMITTER (NAME ONLY): Yuichi Hori

TITLE: Reduction of mask-associated dry eye by using surgical tape to secure the top edge of the mask

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Hori, T. Itokawa, Y. Okajima, H. Iwashita, K. Kakisu, T. Suzuki, Ophthalmology, Toho Daigaku Iryo Center Omori Byoin, Ota-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: During the COVID-19 pandemic, mask-associated dry eye (MADE) has increased worldwide possibly because the breath leaks from the top of the masks changes the ocular surface conditions. We tested the hypothesis that surgical taping of the top edge of the mask to the skin reduces the risk of ocular surface damage.

Methods: We enrolled 60 volunteers (30 females, 30 males; mean age, 27.1±5.2 years) who wear face masks over 5 hours a day. We measured the fluorescein tear break-up time (FBUT), ocular surface temperature, and conjunctival blood flow before wearing masks, after wearing masks taped on the top edge, and after wearing masks without tape. We used the Ocular Surface Disease Index (OSDI) to record participants' symptoms of MADE and measured their corneal tactile and pain sensitivity using a Cochet-Bonnet esthesiometer.

Results: The FBUT with masks without tape (4.4±2.4 seconds) was significantly shorter than that without masks (6.4±3.1 seconds) and with taped masks (5.8±3.2 seconds) ($P<0.01$ and $P=0.05$, respectively, Tukey HSD test). There was no significant difference in the FBUT between use of no masks and taped masks ($P>0.05$). The differences in the corneal and conjunctival temperatures after wearing masks without tape (0.19±0.28 and 0.13±0.28°C, respectively) were significantly higher than after wearing taped masks (0.05±0.27 and 0.06±0.24°C, respectively, $P<0.01$, paired t-test). The conjunctival blood flow with masks without tape was significantly higher than that of taped masks ($P<0.01$). Of the 60 subjects, 13 (21.7%) subjects reported MADE symptoms. In the MADE group, the OSDI ($P=0.001$, analysis of covariance) was significantly higher and the FBUT of masks without tape ($P=0.006$) was significantly shorter than in the non-MADE group. Pain sensitivity in the MADE group was significantly higher than in the non-MADE group ($P<0.01$), indicating that subjects in the MADE group were significantly hypersensitive to corneal pain.

Conclusions: Wearing masks decreased FBUT and increased ocular surface temperature and blood flow. Taping the top edge of the mask prevented those changes. Fitting masks tightly to the nose or applying tape over the mask may reduce the MADE risk, which can be associated with ocular surface hypersensitivity.

CONTROL ID: 3703234

SUBMITTER (NAME ONLY): Philip Enders

TITLE: Short-term changes in Bruch's Membrane Opening-Based Morphometrics during the first week after trabeculectomy

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Enders, J. Lüke, T.S. Dietlein, A. Lappas, V. Prokosch, S. Roters, L.M. Heindl, C. Cursiefen, C. Gietzelt, Department of Ophthalmology, Universitat zu Koln, Koeln, Nordrhein-Westfalen, GERMANY|P. Enders, Glaucoma Imaging Center University of Cologne, Universitat zu Koln, Koeln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: To evaluate the dynamics of Bruch's membrane opening-based morphometrics of the optic nerve head (ONH) using spectral domain optical coherence tomography (SD-OCT) during the first week after glaucoma surgery by trabeculectomy with mitomycin C.

Methods: Prospective, longitudinal analysis of 25 eyes of 25 patients treated by trabeculectomy. Twenty-four eyes had evaluable postoperative SD-OCT examinations. Bruch's membrane opening minimum rim width (BMO-MRW) and peripapillary retinal nerve fiber layer (RNFL) thickness were analyzed at baseline before surgery, one day, two to three days and one week after surgery. Changes compared to baseline were correlated to intraocular pressure (IOP).

Results: One day after surgery, BMO-MRW changed on average by +24.0%, p=0.002 (IOP reduction by 5.4±13.9 mmHg). This increase persisted on day 2-3 with a mean increase of BMO-MRW of +19.8%, p<0.001 (IOP reduction by 9.2±14.7 mmHg) and by week 1 with a mean BMO-MRW increase of+25.3%, p=0.002 (IOP reduction by 9.9±16.1mmHg). The increase in BMO-MRW correlated significantly with the reduction of IOP on day 1 (Spearman's rho ρ=0.656, p=0.003) and d2-3 (Spearman's rho ρ=0.479, p=0.038). There was no statistically significant correlation found between the IOP and the increase in BMO-MRW in week 1. RNFL thickness showed no significant changes at all three follow up intervals (p≥0.096 respectively).

Conclusions: Structural reversal of disc cupping in BMO-MRW occurs as early as one day after trabeculectomy and correlates to the extent of the IOP reduction. During the whole first week after surgery a strong increase in BMO-MRW can be noted. The changes in BMO-based parameters need to be considered when evaluating patients' longitudinal follow-up.

CONTROL ID: 3703280

SUBMITTER (NAME ONLY): Peter King-Smith

TITLE: Tear film breakup and dynamics analyzed and displayed with pseudo-color images

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.E. King-Smith, Optometry, Ohio State University, Columbus, Ohio, UNITED STATES|R.J. Braun, Mathematical Sciences, University of Delaware, Newark, Delaware, UNITED STATES|C.G. Begley, Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Peter King-Smith: Commercial Relationship: Code N (No Commercial Relationship) | Carolyn Begley: Commercial Relationship: Code N (No Commercial Relationship) | Richard Braun: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In this study, we describe a method to demonstrate tear film dynamics using pseudo-color images to provide information about underlying mechanisms of tear breakup. Pseudo-color images, superimposing two or three grayscale images in different colors have had many applications in analyzing and displaying scientific findings. Here we show the use of pseudo-color images in studying a particularly complex pattern of tear breakup and dynamics.
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Methods: Fig. 1 shows the how a pseudo-color image can be generated by superimposition of two grayscale fluorescein images captured at different times after a blink. Fig. 1A was captured 0.2 s after a blink and colored green, while Fig. 1B was captured 6.5 s after the same blink and colored magenta. Fig. 1C shows the superimposition of these two images after alignment of the images using punctate stains indicated by arrows. Grey indicates no intensity change of an area over the time interval, black indicates probable breakup, green indicates dimming, whereas magenta indicates brightening, e.g., convergent flow of the tear film or a dark object has moved out of the area.

Results: Just after a blink, Fig. 1A, the pattern is dominated by round dark ‘globs’, g, thought to be generated by the expansion of thick globs of lipid; they are often surrounded by a lighter grey halo. Later, Fig. 1B, many vertical ‘squiggles’, s, have formed, together with a horizontal ‘rising tide’, rt.

Fig. 2 shows pseudo-color images for the indicated intervals; color contrast has been increased to emphasize changes in fluorescent intensity. Insets are enlargements of two globs. Magenta borders beneath globs, g, are seen initially, Fig. 2A, indicated thickening of the surrounding haloes, but these borders become narrower, Fig. 2B and eventually disappear, Fig. 2C. While the dark centers of the four upper globs retain their original position and shape, the two lower globs move upwards, Fig. 2A, and give rise to squiggles, Fig. 2C. The squiggles in Fig. 2C, s, are black inferiorly indicating breakup, but are green superiorly indicating thinning, presumably triggered by the inferior breakup. The rising tide, rt, becomes prominent later, Fig. 2D, and is at the level of the top of the squiggles.

Conclusions: Pseudo-color images demonstrate changes that are not evident from viewing a video recording and so provide additional evidence about tear film dynamics and breakup.

CONTROL ID: 3703303

SUBMITTER (NAME ONLY): YUAN ZONG

TITLE: Safety of aflibercept for the eye under HTLV-1 infection status in vitro

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. ZONG, K. Kamoi, H. Kurozumi-Karube, K. Ohno-Matsui, Ophthalmology & Visual Science, Tokyo Medical and Dental University, JAPAN|

Commercial Relationships Disclosure: YUAN ZONG: Commercial Relationship: Code N (No Commercial Relationship) | Koju Kamoi: Commercial Relationship: Code N (No Commercial Relationship) | Hisako Kurozumi-Karube: Commercial Relationship: Code N (No Commercial Relationship) | Kyoko Ohno-Matsui: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To clarify the safety of aflibercept for the eye under HTLV-1 infectious conditions in vitro.

Methods: Human retinal pigment epithelial cell line (HRPE) cell line was used as ocular resident cells, and MT2 and TL-Om1 were used as HTLV-1-infected cells. HRPE and MT2/TL-Om1 were co-cultured, and then aflibercept was administered. Production of cytokines and chemokines, HTLV-1 proviral load, cell growth rate and apoptosis of HRPE cells were measured to assess the effects of Aflibercept.

Results: When HRPE and MT2 or TL-Om1 were co-cultured, the secretion of inflammatory cytokine IL-6, IL-8, IFN-γ and chemokines MCP-1, IP-10, RANTES, MIG was increased significantly. The addition of aflibercept did not affect the level of IL-8, IFN-γ, MCP-1, IP-10, RANTES, MIG. IL-6 secretion in HRPE and TL-om1 co-culture was significantly increased. HTLV-1 proviral load of MT2 and TL-Om1was not significantly changed with treatment. No change in cell growth rate or apoptotic rate of HRPE was seen with the addition of Aflibercept.

Conclusions: Aflibercept could be used safely for the eye under HTLV-1 infectious conditions from the perspective of in vitro assessment.

CONTROL ID: 3703314

SUBMITTER (NAME ONLY): Keiichiro Minami

TITLE: Development of a porcine eye holder for observing intraocular temperature changes during cataract surgery

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Minami, S. Yaguchi, H. Bissen-Miyajima, Department of Ophthalmology, Tokyo Dental College Suidobashi Hospital, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: In cataract surgery, intraocular temperature changes when irrigating fluid and ophthalmic viscosurgical devices (OVD) are injected, and this temperature variation affects the unfolding of the intraocular lens (IOL). Extracted porcine eyes are used for experimental observation, which are unsuitable for observing the IOL in the capsule due to the low temperature of the eyes. In this study, we developed an eye holder that maintained ocular temperature close to body temperature and allowed the observation of temperature changes during cataract surgery.

Methods: An aluminum holder was designed to fit porcine eyes and to control ocular temperature. The temperature of the eye was set at approximately 36 degrees Celsius. Changes of intraocular temperature were monitored by a sensor placed inside the vitreous cavity. Cataract surgery consisting of anterior capsulotomy, hydrodissection, phacoemulsification and aspiration (PEA), and IOL insertion was performed.

Results: During cataract surgery, intraocular temperature varied. The most significant change was observed at the time of OVD injection into the capsular bag after PEA. The temperature dropped 5 degrees Celsius and remained stable during the unfolding of the IOL. The temperature changes were small during anterior capsulotomy, hydrodissection, and PEA.

Conclusions: The porcine eye holder enabled the observation of temperature changes during cataract surgery under similar conditions as clinical cases. The temperature reduction at the time of IOL implantation may decelerate the IOL unfolding process and cause an axis misalignment in the use of toric IOL.

CONTROL ID: 3703320

SUBMITTER (NAME ONLY): Konstantin Galichanin

TITLE: Exposure to subthreshold dose of UVR-B does not induce apoptosis in the rat lens in vivo during the first 24 hours.

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Galichanin, Z. Yu, Uppsala Universitet, Uppsala, SWEDEN|

Commercial Relationships Disclosure: Konstantin Galichanin: Commercial Relationship: Code N (No Commercial Relationship) | Zhaohua Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this study is to investigate the time evolution of active caspase 3 in the rat lens after in vivo exposure to subthreshold dose of UVR-B.

Methods: Twenty six-week-old female albino Sprague-Dawley rats were exposed to subthreshold dose (1 kJ/m^2) of UVR-B unilaterally and sacrificed at 1, 8, 16 and 24 hours after exposure. Lenses were enucleated and active caspase 3 protein was detected by Western Blot. The time evolution was then plotted as a function of relative mean difference in active caspase 3 between exposed and nonexposed lenses.

Results: There is an expression of active caspase 3 in both exposed and nonexposed lenses but there is no difference in relative mean difference in active caspase 3 between exposed and nonexposed lenses in all four postexposure groups.

Conclusions: Exposure to subthreshold dose of UVR-B does not induce apoptosis in the rat lens in vivo within first 24 hours. Apoptosis occurs in the rat lens independently from the exposure to subthreshold dose of UVR-B.

CONTROL ID: 3703331

SUBMITTER (NAME ONLY): Christina Herrspiegel

TITLE: A Prognostic Liquid Biopsy in Uveal Melanoma: Serum Protein Levels at Diagnosis Predict Metastases

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Herrspiegel, F. Plastino, S. Seregard, H. Andre, G. Stålhammar, Department of Clinical Neuroscience,, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|C. Herrspiegel, S. Seregard, G. Stålhammar, St. Erik Eye Hospital, Stockholm, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: To develop a prognostic test based on serum samples obtained at diagnosis of uveal melanoma.

Methods: Eighty-three patients diagnosed with primary melanoma in the choroid or ciliary body at St. Erik Eye Hospital, Stockholm, Sweden between 1996 and 2000. Serum samples from peripheral blood were obtained at diagnosis and kept at -80 °C until this analysis.

Proteome profiling of 84 different cancer-related proteins was used to screen for potential biomarkers. ELISA was then performed to evaluated serum levels of the best candidates. Receiver operating characteristics were used to define thresholds for metastatic risk. A prognostic test was developed (serUM) in a training cohort and tested in a validation cohort.

Results: Of the 83 included patients, 43 (52 %) were female. Their mean age at diagnosis was 65 years (12.6 SD) their mean tumor diameter and thickness was 9.8 mm (3.7 SD) and 4.9 mm (2.3 SD). In proteome profiling, five proteins (Leptin, Osteopontin, Progranulin, Tenascin C and DLL-1) were included for further analysis. Receiver operating characteristics were used to define thresholds for metastatic risk. serUM, based on Leptin and Osteopontin concentrations, was developed in a training cohort (n=17) and then tested in a validation cohort (n=62) after exclusion of three patients with unreliable total protein fractions. Patients had gradually shorter cumulative metastasis-free survival with each increasing metastatic risk category (Log rank p for trend = 0.01). In multivariate Cox regression, serUM was an independent predictor of metastasis when entering all of tumor diameter, tumor thickness and patient age at diagnosis as covariates (hazard ratio 2.4, 95 % CI 1.0 to 5.3).

Conclusions: serUM, a prognostic test based on serum obtained from a peripheral blood sample at diagnosis of uveal melanoma, is a strong predictor of metastasis. Future prospective studies should aim to validate these findings.

CONTROL ID: 3703362

SUBMITTER (NAME ONLY): Sarah Matta

TITLE: Assessing generalization of an automatic diagnosis system of ocular anomalies

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Matta, M. Lamard, Universite de Bretagne Occidentale, Brest, Bretagne, FRANCE|G. Quellec, UMR1101, INSERM, Brest, F-29200 France, FRANCE|C. Lecat, R. Carette, F. Basset, A. Le Guilcher, Evolucare, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Automatic diagnosis of ocular anomalies using fundus photographs has shown great promises to scale-up screening. However, the generalization of the automated algorithms to new data which are very different from the training data, i.e issued from a different population, is a challenging problem. The objective of this study is to assess the generalizability of an AI algorithm on four datasets. Each dataset was collected from a specific population and annotated for a pre-defined set of ocular anomalies.

Methods: Four datasets were considered: OPHDIAT (France, diabetic population, 77,827 images), OphtaMaine (France, general population, 17,120 images), RIADD (India, general population, 3,200 images) and ODIR (China, general population, 7,000 images). In order to unify the ground-truth annotations, the annotation of each dataset was analyzed and converted into the ODIR annotation class system: Normal, Diabetes, Glaucoma, Cataract, AMD, Hypertension, Myopia and Other anomalies. Each dataset was then split into a training, a validation and a testing subset. Different scenarios were studied: the AI algorithm was trained using one of the four training subset and then tested on all the four testing subsets. In addition, AI was trained on the whole four training subsets (joint model). The AI algorithm was evaluated using the mean Area under the receiver operating characteristic curve (mAUC): the AUC was calculated independently for each pathology and then the average was computed.

Results: On OphtaMaine, the mAUC was 0.8799 for the AI trained on OphtaMaine, the best mAUC obtained without training on OphtaMaine was 0.8341 and the mAUC was 0.9338 for the joint model. On RIADD, the AI trained on RIADD reached a mAUC of 0.9164, the best mAUC obtained without training on RIADD was 0.8680, and the mAUC was 0.9169 for the joint model. On ODIR, the mAUC was 0.8803 for the AI trained on ODIR, the best mAUC obtained without training on ODIR was 0.8284, and the mAUC was 0.8865 for the joint model.

Conclusions:

The performances of the AI algorithm trained on a specific dataset were good when tested on data coming from the same population. However, when tested on different datasets, the performances of the AI algorithm degraded. This highlights the variability of experts interpretations among the four datasets. An AI trained on the four datasets performed better on the small datasets.

CONTROL ID: 3703367

SUBMITTER (NAME ONLY): Josy Augustine

TITLE: 2-Hydrazino-4,6-dimethylpyrimidine (2-HDP) as a novel therapeutic for the neurovascular pathology of diabetic retinopathy

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Augustine, T. Friedel, E.M. Byrne, P. Canning, P. Barabas, A.W. Stitt, T.M. Curtis, Wellcome-Wolfson Institute For Experimental Medicine, Queen's University Belfast, Belfast, UNITED KINGDOM|E.P. Troendle, M.B. Ulmschneider, Department of Chemistry, King's College London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a common neurovascular complication of diabetes. Retinal accumulation of the acrolein-derived advanced lipoxidation end-product, FDP-lysine (N^{ε}-(3-formyl-3,4-dehydropiperidino-lysine), has been implicated in the pathogenesis of this condition. We have identified a new drug called 2-HDP that is effective in scavenging acrolein and preventing retinal FDP-lysine accumulation during diabetes. The aim of this study was to determine whether 2-HDP can protect against neurovascular dysfunction during diabetes.

Methods: Male Sprague-Dawley rats were divided into three groups: (1) non-diabetic; (2) streptozotocin-induced diabetic; and (3) diabetic treated with 2-HDP administrated in their drinking water. In vivo analysis of blood pressure, body weights, water intake, HbA1c and electroretinography (ERG) were measured at 1-,3- and 6-months after diabetes induction. Immunolabelling, western blotting, cytokine arrays and the Evan’s blue dye assay were carried out to study the vascular, neuronal, and glial components of the retina. Molecular Dynamics (MD) simulations were performed to investigate 2-HDP drug permeation across cellular membranes.

Results: ERG a- and b-wave amplitudes were significantly reduced in diabetic controls after 3- and 6-months of diabetes and these changes were completely prevented by treatment with 2-HDP ($P<0.01$). This drug also prevented retinal FDP-lysine accumulation, the activation of Müller cells and microglia, and neuro and vasodegenerative changes in the diabetic retina ($P<0.05$). MD simulations have revealed that most 2-HDP molecules are protonated and do not readily cross cell membranes.

Conclusions: Our studies provide strong evidence for a key role of acrolein and FDP-lysine in the development of the neurovascular lesions associated with DR.

CONTROL ID: 3703381

SUBMITTER (NAME ONLY): Lei Siew

TITLE: The effect of past cataract surgery within the medium to long-term period on patients with Dry Eye Disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Siew, L. Tong, Singapore Eye Research Institute, Singapore, SINGAPORE|L. Siew, National University of Singapore, Singapore, SINGAPORE|L. Tong, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Lei Siew: Commercial Relationship: Code N (No Commercial Relationship) | Louis Tong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: With the prevalence of cataract surgery and increased patient expectations of improved vision, side effects increasing morbidity such as tear disorders should not be neglected. Several studies investigating the short-term effect of cataract surgery on Dry Eye Disease (DED) lack evaluation in the medium and longer term (beyond 3 months) and it was uncertain if dry eye parameters had returned to baseline. Hence, this study aims to evaluate the effects of cataract surgery on severity of clinical tear film parameters of patients with DED in the medium to long term period (6 months to 5 years) post-surgery.

Methods: A cross-sectional study was conducted on 448 eyes on first visit to a tertiary clinic (224 eyes with cataract surgery within timeframe, i.e. pseudophakic dry eye group, 224 comparison eyes without such history, i.e. comparison dry eye group). Parameters evaluated include Ocular Surface Disease Index (OSDI), Schirmer's I test score, Tear Break-up Time (TBUT), number of liquid expressing glands in lower lid, cornea fluorescein staining, corneal sensation, meibum character and follicular papillary reaction grade in the upper and lower fornices.

Results: A significantly greater proportion of pseudophakic dry eye group (49%) experienced frequent blurred vision (≥1 episode per week) compared to dry eye control group (37%) (OR=1.57, 95%CI 1.07, 2.31). Those with ocular discomfort before surgery were more likely to experience blurring at least once a day. In addition, a significantly greater proportion of pseudophakic dry eye group (34%) had Schirmer's I >8mm compared to the comparison group (24%) (OR=0.605, 95% CI 0.398, 0.921), though the difference was not clinically significant (7.51mm versus 6.51mm respectively, p>0.05). Other signs such as TBUT, number of liquid expressing glands in lower lid, cornea fluorescein staining, corneal sensation, meibum character and follicle grade did not differ between the two groups.

Conclusions: While uncomplicated cataract surgery does not worsen signs of DED, up to half of participants experienced greater frequency of blurred vision 6 months to 5 years post-cataract surgery, especially in those with ocular discomfort suggestive of dry eyes prior to surgery. Counselling for increased risk of transient blurred vision post-cataract surgery and dry eye prevention measures should be undertaken, especially those with suggestive symptoms pre-operatively.

CONTROL ID: 3703406

SUBMITTER (NAME ONLY): Alice Motschi

TITLE: Depolarization mapping in the retina using polarization-sensitive OCT in a large field of view

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.R. Motschi, S. Desissaire, M. Pircher, C.K. Hitzenberger, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, AUSTRIA|M. Schranz, S. Steiner, P.K. Roberts, C. Vass, Department of Ophthalmology and Optometry, Medical University of Vienna, Vienna, AUSTRIA|H. Bogunovic, Christian Doppler Laboratory for Ophthalmic Image Analysis, Medical University of Vienna, Vienna, AUSTRIA|F. Schwarzhans, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Vienna, AUSTRIA|F. Schwarzhans, Department of Clinical Pharmacology, Medical University of Vienna, Vienna, AUSTRIA|

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ABSTRACT BODY:

Purpose: To quantify depolarization properties of the retinal pigment epithelium (RPE) to gain more insight into its structure and composition.

Methods: A custom-built spectral domain PS-OCT system operating at 860 nm with an A-scan rate of 70 kHz and an integrated retinal tracker was used to image 45 healthy volunteers (43 ± 16 years) and 19 glaucoma patients (62 ± 10 years) three times each at seven distinct regions around the macula (resulting in 21 measurements each consisting of 250 B-scans × 1024 A-scans and covering an area of 8 × 6 mm^2). After standard OCT data processing, the degree of polarization uniformity (DOPU) was calculated and DOPU at the RPE was projected onto an en-face map. The seven maps from the different regions imaged in each subject were averaged over the three measurements per measurement location and stitched together to create a map with a large field of view. On the large maps, a circular grid centered at the fovea, consisting of seven rings with diameters of 0.5, 1, 2, 3, 6, 9, and 12 mm and divided into 8 equal sectors, was placed. The mean DOPU value in each field of the grid was calculated for each participant.

Results: The averaged depolarization map of the 45 healthy volunteers (centered at the fovea) in Fig. 1(a) shows DOPU values at the RPE, where low values indicate stronger depolarization. Fig. 1(c) shows that the depolarization is strongest (lowest DOPU) in the rings next to the center (B, C) and that the depolarization is weaker at the center (A) and decreases towards the periphery (D to G). The results don't seem to differ between men and women, but DOPU values decrease with age.

The averaged depolarization map of the 19 glaucoma patients is shown in Fig. 1(b). It can be observed in Fig. 1(d) that the DOPU distribution in glaucomatous eyes appears to be very similar to healthy eyes, but the DOPU values are in general smaller. Since the glaucoma patients are in average older than the healthy volunteers, this could also be an age effect.

Conclusions: The polarization scrambling properties of the RPE of 45 healthy volunteers and 19 glaucoma patients were displayed in a large field of view map and quantified by calculating DOPU. A varied distribution of depolarization in the fundus could be shown, indicating a heterogeneous distribution of RPE pigmentation and geometry. Glaucomatous eyes showed lower DOPU values but a qualitative distribution similar to healthy eyes.

CONTROL ID: 3703472

SUBMITTER (NAME ONLY): Ella Courtie

TITLE: Skeletonization reduces the reliability of OCTA retinal blood flow analyses.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Courtie, R.J. Blanch, Neuroscience and Ophthalmology research group, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|E. Courtie, A. Kale, N. Capewell, X. Liu, A.K. Denniston, R.J. Blanch, Ophthalmology, Queen Elizabeth Hospital Birmingham, Birmingham, West Midlands, UNITED KINGDOM|X. Liu, Health Data Research UK, London, UNITED KINGDOM|A. Gilani, T. Veenith, Critical Care Unit, Queen Elizabeth Hospital Birmingham, Birmingham, UNITED KINGDOM|A. Gilani, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|T. Veenith, Department of Trauma Sciences, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|G. Montesano, University of London, London, London, UNITED KINGDOM|M. Teussink, Heidelberg Engineering GmbH, Heidelberg, Baden-Württemberg, GERMANY|A.K. Denniston, NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust andUCL Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Variable methods of analysing optical coherence tomography angiography (OCTA) images makes comparing different OCTA studies challenging. We performed a prospective observational study investigating agreement between retinal blood flow metrics calculated using different techniques and within different analysis packages. We hypothesised that measures assessing an underlying physiological parameter would show high agreement, whilst measures that did not relate to the patients' underlying physiology would not.

Methods: We recruited patients undergoing major upper gastrointestinal surgery with planned post-operative care in the intensive therapy unit (ITU) and individuals already admitted to the ITU with sepsis. OCTA scans from 31 right eyes (24 males, 7 females) and 29 left eyes (24 males, 5 females) were included in the final analysis. Custom metrics from MatLab (vessel density [VD], fractal dimension [FD], and their skeletonised analysis [SVD and SFD respectively]) and Heidelberg Engineering ([HE]; Mean vessel length density and Skeletonised analysis) were compared for agreement using intraclass correlation coefficient (ICC).

Results: There was strong agreement between HE Mean and Matlab VD measures, reaching an ICC of 0.84, and moderate agreement between HE Skeleton and Matlab VD with ICCs between 0.48-0.65 depending on eye and vascular layer. There was no agreement between any HE measures and FD with ICCs between 0.24-0.49, or between any of the metrics and Matlab skeletonised values with ICCs as low as 0.04. There was variable agreement between eyes, ranging from 0.28 for SFD to 0.90 for VD.

Conclusions: Our results showed moderate to good agreement between the metrics of the different analysis packages, except for FD, and that skeletonising OCTA scans for retinal blood flow analysis reduced agreement between analysis packages and techniques. The low agreement between HE and FD suggests that these measures assess different and unrelated blood flow parameters. The poor agreement from the skeletonised values suggest that non-skeletonised metrics may be preferred and reported in OCTA studies.

CONTROL ID: 3703474

SUBMITTER (NAME ONLY): Jonathan Lin

TITLE: Monitoring the progression of chemical-induced ocular injury through anterior segment optical coherence tomography (AS-OCT)

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lin, N. Karediya, E.R. Kraft, A. Sharifi, M.E. Schmitz-Brown, K.H. Merkley, P. Gupta, M. Motamedi, Ophthalmology and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|J. Luisi, B.T. Ameredes, Internal Medicine, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Existing clinical assessment methods for ocular chemical exposures are primarily qualitative examinations limited to the surface of the eye and can be subjective. Anterior segment optical coherence tomography (AS-OCT) offers a solution to this issue, allowing for non-invasive and high-resolution imaging of anterior segment structures. AS-OCT thereby provides the ability to quantify pathological changes over time, even in the presence of corneal opacity or fibrosis, which are both considerable hinderances to current methods.

Methods: Following an IACUC-approved protocol, acute injury model of chemical exposure was performed in a mouse model through topical application of a 2 mm diameter circle of filter paper soaked in 2.5 mg/mL acrolein or 1.0M NaOH to the right eye for 30 seconds. AS-OCT was performed on the cornea and iris simultaneously, before the chemical burn and up to 21 days following the burn. OCT angiography (OCTA) was performed using a custom algorithm that is designed to reconstruct the morphological and vascular features of the cornea. Corneal thickness of each eye was measured in ImageJ. Eyes were enucleated on day 21 for histology.

Results: For both chemical agents, AS-OCT/OCTA revealed corneal neovascularization and ulceration by day 21; however, the progression of injury differs significantly. Acrolein exposure initially presents with minor injury (e.g., slight corneal swelling) that apparently recovers until a rebound occurs between 14-21 days, including neovascularization and corneal thickness changes. In contrast, alkali exposure led to an immediate inflammatory response accompanied by severe corneal opacification and swelling (146%) that progressively worsened, peaking at 296% on day 14. Neovascularization was first detectable at day 7 by OCTA and encroached into the central cornea.

Conclusions: AS-OCT was able to clearly visualize the progression of chemical injury and identified qualitative and quantitative image-based biomarkers that assess injury severity and progression, validated through histology. The clinical availability of AS-OCT has the potential to enhance our understanding of ocular injury and different patterns of progression in chemical exposures to improve clinical assessment for better management and treatment development.

CONTROL ID: 3703498

SUBMITTER (NAME ONLY): Yinxi Yu

TITLE: Association of proton pump inhibitors use with severity of dry eye symptoms and signs in the DRy Eye Assessment and Management (DREAM©) Study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yu, P.A. Asbell, G. Ying, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: A recent large population-based hypothesis-free study found that proton pump inhibitors (PPIs) use is highly associated with presence of dry eye disease (DED) symptoms[1]. In this study, we examined the association between PPIs use and severity of DED symptoms and signs among participants in the DREAM© study, a multi-center randomized clinical trial to evaluate the effect of omega-3 fatty acid supplements for the treatment of dry eye.

Methods: At baseline, self-reported PPIs use and the specific drug name were collected using medication log. At baseline, 6 and 12 months, DED symptoms were evaluated using the Ocular Surface Disease Index (OSDI), DED signs in each eye were evaluated for tear break up time (TBUT), Schirmer's test, corneal fluorescein staining, conjunctival lissamine green staining, and Meibomian gland dysfunction (MGD). Generalized linear models were used to compare the scores of DED symptoms and signs between PPIs users and non-users, with adjustment for age, gender, race, visit, history of acid reflux, comorbidities that were previously found to be associated with severity of DED symptoms and signs in the DREAM study. The correlation among repeated measures of DED symptoms and signs at baseline, 6 and 12 months and the inter-eye correlation of DED signs were accounted for by using generalized estimating equations.

Results: Among 535 participants with moderate-to-severe DED, 114 (21.3%) were PPIs users at baseline, with 71 (13.3%) using Omeprazole, and 22 (4.1%) using Pantoprazole. Compared to PPI non-users, PPIs users were significantly older (mean [SD] age 62.7 [10.7] vs. 56.7 [13.5], $p<0.001$), more likely to self-report ongoing acid reflux (82.5% vs. 19.5%, $p<0.001$). When data from baseline, 6 and 12 months were combined, PPIs use at baseline was not associated with severity of dry eye symptoms or signs (Table 1, all adjusted $p\geq0.24$). Specifically, uses of either Omeprazole or Pantoprazole were not associated with severity of DED symptoms or signs compared to non-users (Table 2, all adjusted $p\geq0.08$).

Conclusions: Among DREAM participants with moderate-to-severe DED, PPIs use was not associated with severity of dry eye symptoms and signs.

CONTROL ID: 3703522

SUBMITTER (NAME ONLY): Nathanael Matei

TITLE: Prophylactic Effects of Creatine and Metformin after Incomplete Retinal Ischemia

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Matei, M. Rahimi, S. Leahy, J. Burford, M. Shahidi, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|N.P. Blair, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Nathanael Matei: Commercial Relationship: Code N (No Commercial Relationship) | Mansour Rahimi: Commercial Relationship: Code N (No Commercial Relationship) | Sophie Leahy: Commercial Relationship: Code N (No Commercial Relationship) | James Burford: Commercial Relationship: Code N (No Commercial Relationship) | Norman Blair: Commercial Relationship: Code N (No Commercial Relationship) | Mahnaz Shahidi: Commercial Relationship(s);Code P (Patent):University of Illinois at Chicago

ABSTRACT BODY:

Purpose: Retinal ischemia is implicated in many vision-threatening eye diseases, yet no effective treatment is available. Creatine serves a critical role in protecting tissue during ischemia. We hypothesize that prophylactic treatment with Creatine and Metformin will prevent impairments of retinal oxygen metrics and retinal layer thinning after bilateral common carotid artery occlusion (BCCAO).

Methods: Twenty rats were divided into 3 groups: sham, treatment (Tx), and vehicle. Rats in Tx and vehicle groups received intraperitoneal injections of Creatine + Metformin and saline, respectively. Daily administrations were initiated 7 days prior to and continued 7 days after BCCAO. Multimodal imaging was performed 7 days after BCCAO to measure retinal arterial and venous oxygen contents (O_{2A}, O_{2V}), total retinal blood flow (TRBF), and total retinal thickness (TRT). Arteriovenous oxygen content difference (O_{2AV}), oxygen delivery (DO_2), metabolism (MO_2), and extraction fraction (OEF) were calculated. Retinal sections were stained to measure retinal layer thickness. Linear mixed model analysis and ANOVA were used to compare metrics among groups.

Results: Compared to the sham group, TRBF, DO_2, and MO_2 were reduced, while O_{2AV} was increased in the vehicle group ($P<0.02$). In the Tx group, no differences were detected in O_{2AV}, DO_2, and TRBF compared to the sham group ($P>0.2$), whereas MO_2 was reduced ($P= 0.002$). Compared to the vehicle group, O_{2AV} was decreased in the Tx group ($P=0.04$), whereas no differences were detected in TRBF, DO_2, MO_2, OEF, O_{2A}, and O_{2V} ($P>0.1$). No differences were observed in O_{2A}, O_{2V}, and OEF among groups ($P>0.08$). Compared to the sham group, TRT and thickness of inner retina (IRL) and photoreceptor (PRL) layers were reduced in the vehicle group ($P<0.02$). In the Tx group, TRT and thickness of inner nuclear layer (INL) were not different compared to the sham group ($P>0.4$), whereas thickness of IRL and PRL were reduced ($P<0.03$). Compared to the vehicle group, thickness of retinal ganglion cell + nerve layers (RGC/NFL) was increased in the Tx group ($P=0.04$), whereas no differences were detected in IRL, inner plexiform layer (INL), and PRL ($P>0.1$). No differences were detected in outer plexiform and outer nuclear layers among groups ($P>0.3$).

Conclusions: Prophylactic treatment with Creatine and Metformin prevented elevations in O_{2AV} and increased RGC/NFL thickness after incomplete retinal ischemia.

CONTROL ID: 3703527

SUBMITTER (NAME ONLY): Doug Chung

TITLE: Investigation of the functional impact of CHED- and FECD4-associated SLC4A11 mutations in human corneal endothelial cells

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Chung, A. Chen, C. Choo, W. Zhang, C. Griffis, P. Bonezzi, A.P. Sampath, A.J. Aldave, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the impact of SLC4A11 mutations associated with congenital hereditary endothelial dystrophy (CHED) and Fuchs endothelial corneal dystrophy type 4 (FECD4) on corneal endothelial cell (CEnC) function and SLC4A11 protein localization.

Methods: Human $SLC4A11^{-/-}$ CEnC lines were generated by CRISPR-Cas9 mediated gene editing. SLC4A11 wildtype ($SLC4A11^{WT}$) and SLC4A11 mutant ($SLC4A11^{MU}$) human CEnC lines were generated by stable transduction with lentiviruses containing either $SLC4A11^{WT}$ or $SLC4A11^{MU}$ expression vectors harboring CHED-/FECD4-associated SLC4A11 mutations (CHED: c.374G>A, c.1813C>T, c.2263C>T; FECD4: c.2224G>A). Functional assays were performed to assess cell migration, proliferation, viability after induced oxidative stress and NH_4Cl-induced membrane conductance in the generated $SLC4A11^{WT}$, $SLC4A11^{MU}$ and $SLC4A11^{-/-}$ CEnC lines. Cell barrier function in $SLC4A11^{WT}$ and $SLC4A11^{-/-}$ CEnC were assessed by electric cell-substrate impedance sensing (ECIS). Immunostaining was performed to determine the subcellular localization of SLC4A11 protein in the generated $SLC4A11^{WT}$ and $SLC4A11^{MU}$ CEnC lines and human primary CEnC.

Results: $SLC4A11^{-/-}$ CEnC and the majority of the $SLC4A11^{MU}$ CEnC lines exhibited significantly increased migration rates, altered proliferation, and decreased cell viability under oxidative stress compared to $SLC4A11^{WT}$ CEnC. Induction with 10mM NH_4Cl led $SLC4A11^{WT}$ CEnC to depolarize; conversely, $SLC4A11^{-/-}$ CEnC hyperpolarized and the majority of $SLC4A11^{MU}$ CEnC either hyperpolarized or had minimal membrane potential changes following NH_4Cl induction. Based on ECIS modeling, $SLC4A11^{WT}$ CEnC demonstrated increased cell-substrate adhesion and membrane capacitances compared to $SLC4A11^{-/-}$ CEnC. Immunostaining of primary CEnC and $SLC4A11^{WT}$ CEnC lines for SLC4A11 demonstrated predominately cell surface staining with partial colocalization with mitochondrial marker COX4 within punctate subcellular structures. $SLC4A11^{MU}$ CEnC lines also displayed mainly cell surface staining of SLC4A11, except for $SLC4A11^{MU}$ c.2263C>T CEnC, which exhibited mostly perinuclear staining.

Conclusions: CHED- and FECD4-associated SLC4A11 mutations likely lead to CEnC dysfunction, and ultimately CHED and FECD4, by interfering with cell migration, proliferation, viability, membrane conductance, barrier function, and/or cell surface localization of the SLC4A11 protein in CEnC.

CONTROL ID: 3703555

SUBMITTER (NAME ONLY): Ghulam Mohammad

TITLE: Altered Mitochondrial Dynamics and Diabetic Keratopathy

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Mohammad, R.A. Kowluru, Department of Ophthalmology, Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Ghulam Mohammad: Commercial Relationship: Code N (No Commercial Relationship) | Renu Kowluru: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Keratopathy is one of the most frequent clinical problems faced by diabetic patients, and this potentially sight-threatening condition is caused mainly by corneal epithelial disturbances. Diabetes impairs corneal epithelial cells functionally, morphologically and biochemically, and overproduction of mitochondrial superoxide radicals is considered as a causal link between elevated glucose and the major biochemical pathways implicated in the development of keratopathy. Mitochondria are dynamic structures, and depending on the energy demand, they continuously fuse and divide. An imbalance in the fusion-fission can alter their membrane potential, respiration and bioenergetics. Mitochondria dynamics is regulated by GTPases; fission is mainly controlled by dynamin-related protein1 (Drp1) and fusion by mitofusin-2 (Mfn2) and optic atrophy1. During mitochondrial fission, fission protein 1 (Fis1) and mitochondrial fission factor (Mff) direct Drp1 to the fission site. The aim of this study was to investigate the role of mitochondrial dynamics in the development of diabetic keratopathy.

Methods: Cornea from streptozotocin-induced diabetic rats (3 months duration) were used to quantify mitochondrial reactive oxygen species (ROS) by DCFDA, and expression of Drp1, Fis1, Mff, Mfn2 and OPA1 by quantitative real time PCR (β-actin as a housekeeping gene). Effect of diabetes on the expressions of Drp1 and Mfn2 was confirmed in the corneal cryosections by immunohistochemical technique.

Results: Compared to normal rats, ROS were elevated, and while Drp1, Fis1 and Mff expressions were increased, Mfn2 and OPA1 were decreased in the cornea from diabetic rats. While immunofluorescence of Drp1 was increased in the corneal epithelial cell layer from diabetic rats, that of Mfn2 was significantly decreased.

Conclusions: Our data demonstrate an impaired corneal mitochondria fusion-fission machinery in diabetes, suggesting an important role of mitochondrial dynamics in the development of diabetic keratopathy.

CONTROL ID: 3703557

SUBMITTER (NAME ONLY): Aniket Ramshekar

TITLE: Hierarchical Cluster Analysis of VEGF-induced STAT3-Mediated Genes in Human Retinal Microvascular Endothelial Cells

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ramshekar, C. Bretz, M. Hartnett, Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Aniket Ramshekar: Commercial Relationship: Code N (No Commercial Relationship) | Colin Bretz: Commercial Relationship: Code N (No Commercial Relationship) | Mary Elizabeth Hartnett: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Endothelial signal transducer and activator of transcription 3 (STAT3)-induced intravitreal neovascularization (IVNV) in oxygen-induced retinopathy (OIR) represents retinopathy of prematurity (ROP). To understand pathways involved in endothelial STAT3-induced IVNV, we performed bulk RNA-sequencing of transcripts isolated from human retinal microvascular endothelial cells (HRMECs) transfected with STAT3 siRNA or control siRNA, and treated with vascular endothelial growth factor (VEGF) or vehicle control. We found STAT3 was necessary to differentially regulate genes involved in VEGF-induced mitosis and vascular development signaling pathways. In this study, we used a data-driven approach to cluster the differentially expressed genes based on expression patterns and tested the hypothesis that VEGF-induced STAT3 mediates angiogenic signaling pathways involved in ROP.

Methods: Hierarchical clustering with Ward's linkage method and Euclidean distance metric was performed using scaled regularized log counts of the differentially expressed genes (n=353). Pathway enrichment analysis of the differentially expressed genes within the clusters was assessed by Ingenuity Pathway Analysis (IPA) software. An adjusted p-value < 0.05 was considered statistically significant following Benjamini and Hochberg multiple testing correction.

Results: Hierarchical clustering resulted in the visual identification of 4 clusters of genes. Regardless of VEGF or PBS treatment, knockdown of STAT3 downregulated cluster 1 (n=113) and upregulated cluster 3 (n=116) compared to control. Compared to control, knockdown of STAT3 reduced upregulation of cluster 2 (n=44) by VEGF and reduced downregulation of cluster 4 (n=80) by VEGF. IPA identified significant pathway enrichment in G2/M cell cycle checkpoint regulation, IGF-1 signaling, or JAK/STAT signaling in cluster 1, and glioblastoma multiforme signaling or signaling by Rho family GTPases in cluster 3. No significant pathway enrichment was observed in cluster 2 or 4.

Conclusions: Our results corroborate our previous analysis that STAT3 regulates angiogenesis in HRMECs by mediating transcripts involved in mitosis and identified additional pathways implicated in angiogenesis. Further testing of the identified signaling pathways in cultured HRMECs and the OIR model might lead to a better understanding of the mechanisms involved in IVNV in ROP.

CONTROL ID: 3703559

SUBMITTER (NAME ONLY): Pierre-Henry GABRIELLE

TITLE: Incidence, Risk Factors and Outcomes of Submacular Hemorrhage with Loss of Vision in Neovascular Age-Related Macular Degeneration in Daily Clinical Practice: the Fight Retinal Blindness! Registry

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. GABRIELLE, L. Arnould, C. Creuzot-Garcher, Ophthalmology, Centre Hospitalier Universitaire de Dijon, Dijon, Bourgogne, FRANCE|P. GABRIELLE, V. Nguyen, J. Arnold, D. Barthelmes, M.C. Gillies, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|D. Squirrell, Ophthalmology, The University of Auckland, Auckland, Auckland, NEW ZEALAND|J. Sanchez-Monroy, Hospital Universitario Miguel Servet, Zaragoza, Aragón, SPAIN|F. Viola, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Lombardia, ITALY|L. O' Toole, Mater Private Healthcare Group, Dublin, Leinster, IRELAND|D. Barthelmes, UniversitatsSpital Zurich, Zurich, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To report the estimated incidence, cumulative rate, risk factors, and outcomes of submacular hemorrhage (SMH) with loss of vision in neovascular age-related macular degeneration (nAMD) receiving intravitreal injections (IVT) of vascular endothelial growth factor (VEGF) inhibitor in routine clinical practice.

Methods: Retrospective analysis of treatment-naïve eyes receiving IVT of VEGF inhibitors (ranibizumab, aflibercept, or bevacizumab) for nAMD from 1 January 2010 to 31 December 2020 that were tracked in the Fight Retinal Blindness! registry. Estimated incidence, cumulative rate, and hazard ratios (HR) of SMH with loss of vision were measured using Poisson regression, Kaplan-Meier survival curves, and Cox-proportional hazards models. Locally weighted scatterplot smoothing curves were used to plot visual acuity (VA) between SMH cases and matched controls.

The main outcome measures were the estimated incidence of SMH with loss of vision and change in VA 12 months after SMH.

Results: This study included 7642 eyes (6425 patients) with a total of 135095 IVTs over a 10-year period. One hundred five eyes developed SMH with loss of vision with a rate of 1 per 1283 injections (0.08% 95% confidence interval [95%CI] [0.06; 0.09]). The estimated incidence [95%CI] was 4.6 [3.8; 5.7] SMH with loss of vision per year per 1000 treated patients during the study. The cumulative [95%CI] rate of SMH per patient did not increase significantly with each successive injection ($p = 0.947$). Men (hazard ratio [HR] [95%CI] = 1.71 [1.26; 2.16] vs. women, $p = 0.019$) and patients with disciform scar CNV type (HR = 12.35 [10.76, 13.94] vs. Type 1 CNV; $P = 0.002$) at baseline were significantly more likely to develop SMH with loss of vision in our study. There was little evidence that SMH was related to under-treatment. SMH cases had a mean VA drop of around 6 lines at diagnosis, which then improved moderately to a 4-line loss at one year.

Conclusions: SMH with loss of vision is an uncommon complication that can occur at any time in eyes treated for nAMD in routine clinical practice, with only limited recovery of vision one year later.

CONTROL ID: 3703596

SUBMITTER (NAME ONLY): Andrew Osborne

TITLE: A Novel Bi-cistronic Gene Therapy for Neovascular Age-Related Macular Degeneration in Patients with Developing Subretinal Fibrosis

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Osborne, E.F. Warner, K. Boyd, P.S. Widdowson, K. Binley, Ikarovec Limited, Norwich, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Anti-VEGF therapies for neovascular age-related macular degeneration (nAMD) have significantly revolutionised outcomes for millions of people. However, anti-VEGF drug efficacy and vision deteriorates in a significant proportion of individuals due to subretinal fibrosis. We designed a gene therapy capable of preventing, or reversing, subretinal fibrosis and neutralising pathological VEGF concentrations responsible for neovascularisation.

Methods: Bi-cistronic plasmids and rAAV2/2 vector constructs expressing both anti-VEGF and anti-fibrotic components were examined in HEK293T, ARPE-19 cells and on co-cultures of human fibroblast/HUVECs. The lead constructs were evaluated in rodent models.

Results: The lead constructs express a novel anti-VEGF capture protein that has a reduced affinity for human IgG-Fc gamma receptors than aflibercept. The constructs reduce endogenous VEGF concentrations (ng/mL) in HEK293Ts (control Null plasmid = 663 ± 15, IKC116P = 275 ± 7***, aflibercept = 296 ± 4***; $P<0.001$ by ANOVA followed by Bonferroni modified t-tests, mean ± SEM of 3 replicates) and attenuates capillary formation in co-cultures with equivalent efficacy to aflibercept. The anti-fibrotic component attenuates transforming growth factor (TGF)-beta-induced epithelial-mesenchymal transition, a precursor to subretinal fibrotic scar formation, as shown by the reduction in ARPE-19 fibronectin (control Null plasmid = 2.64 ± 0.32, IKC116P = 1.96 ± 0.26; $P<0.05$, n=4) and release of matrix metalloprotease-2 (control Null plasmid = 1.46 ± 0.09, IKC116P = 0.28 ± 0.04; $P<0.0001$, n=4) by western blot. Intravitreal injection of the lead vectors completely prevented vascular leakage after laser-induced CNV in mice compared to the vehicle controls.

Conclusions: The novel anti-VEGF component is equipotent to aflibercept in VEGF neutralisation. Moreover, the incorporation of an anti-fibrotic transgene reduced TGF-beta induced early scar formation in ARPE-19 cells. This bi-cistronic gene therapy has the potential to address subretinal fibrosis in patients with deteriorating vision currently treated with anti-VEGF therapies.

CONTROL ID: 3703641

SUBMITTER (NAME ONLY): Jonathan Huang

TITLE: Semi-Automated Blood Velocity Determination Using Adaptive Optics Scanning Laser Ophthalmoscopy XT Images

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, N. Konopek, J. Moonjely, A.A. Fawzi, Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Jonathan Huang: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Konopek: Commercial Relationship: Code N (No Commercial Relationship) | Jessica Moonjely: Commercial Relationship: Code N (No Commercial Relationship) | Amani Fawzi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal blood velocity can be determined by measurement of erythrocyte streak angles relative to vessel angles on Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) space-time or XT images, in which successive one-dimensional scans of retinal vessels are stacked. Variability in manual erythrocyte angle determination may contribute error to blood velocity assessment. We evaluated inter-rater concordance between manual and semi-automated measurements of erythrocyte streak angles on AOSLO XT images.

Methods: We implemented a novel semi-automated method in which regions of interest are manually drawn around erythrocyte streaks. An algorithm automatically performs Yen thresholding and weighted least squares regression to determine streak angles measured against the horizontal. The three shallowest angles are averaged to enable maximal blood velocity calculations. For comparison, two reviewers manually measured and averaged the three shallowest angles of each XT image using ImageJ software. Bland-Altman plots and concordance correlation coefficients were evaluated to compare measurement methods.

Results: Our analysis included 16 XT image frames from 4 eyes of 4 patients. The mean difference in average angle measurement was -3.07 and -1.75 degrees for the semi-automated method compared to the first and second reviewers, respectively, indicating that the semi-automated method identified shallower erythrocyte angles than manual reviewers. The mean difference was -0.58 degrees when comparing the semi-automated method with the minimum of the two angles measured between the two manual reviewers. The concordance correlation coefficient was 0.92 for the two manual reviewers, 0.93 and 0.97 for the semi-automated method and the respective manual reviewers, and 0.99 for the semi-automated method and the smaller of the two manual measurements.

Conclusions: By evaluating a range of streaks in an individual AOSLO XT image, the semi-automated method more consistently identified the shallowest erythrocyte streak angles than manual evaluators. Implementation of this semi-automated workflow may improve measurement consistency, increase throughput, and reveal more insights about retinal blood flow metrics.

CONTROL ID: 3703649

SUBMITTER (NAME ONLY): Victoria Blaga

TITLE: Opioid Utilization in Ophthalmology and the Impact of a Decision Support Tool in Reducing Excess Dosing

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Blaga, R.P. Singh, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|A. Kalur, K. Seth, A. Iyer, C. Carvalho Soares Valentim, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Victoria Blaga: Commercial Relationship: Code N (No Commercial Relationship) | Aneesha Kalur: Commercial Relationship: Code N (No Commercial Relationship) | Kanika Seth: Commercial Relationship: Code N (No Commercial Relationship) | Amogh Iyer: Commercial Relationship: Code N (No Commercial Relationship) | Carolina Carvalho Soares Valentim: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Singh: Commercial Relationship(s);Code E (Employment):Ocusciences;Code I (Personal Financial Interest):Genentech/Roche, Alcon/Novartis, Zeiss, Bausch and Lomb, Regeneron, Gyroscope & Asceplix;Code F (Financial Support):Apellis, Grayburg

ABSTRACT BODY:

Purpose: The opioid epidemic remains a public health concern in the United States. This study investigated current opioid dosage rates in ophthalmology based on patient demographics and diagnosis and quantified the effect of an opioid alert system on prescription practices in this retrospective, pre and post implementation study.

Methods: A retrospective chart review was conducted of opioid prescriptions written by ophthalmologists between January 3, 2015, and November 3, 2021. An opioid alert system was implemented in December 2017. The study population was divided into three cohorts based on when an individual's prescription was written: prior to system implementation (cohort 1), while the system was active, but not recorded in the EHR (cohort 2), or while the system was both active and recorded in the EHR (cohort 3). Dosage was measured in morphine equivalent daily dose (MEDD). Mean MEDD per prescription and mean number of prescriptions per patient were compared based on patient demographics, diagnosis, and cohort. For statistical analysis, independent t-tests and linear mixed effects models were completed.

Results: 8014 individuals were included in this study with 4388, 2276, and 1350 individuals in cohorts 1, 2, and 3 respectively. The majority of individuals were female (59.26%) and white (82.31%). There was no significant difference in mean MEDD based on patient demographics when comparing cohorts. However, when considering all cohorts together, black individuals received the highest mean MEDD (33.93 MEDD, $p = 0.03$ compared to white individuals) and male individuals received a higher mean MEDD when compared to females (33.53 MEDD; $p < 0.001$). While not statistically significant, glaucoma was the diagnosis category with the highest mean MEDD per prescription (34.94 MEDD). Mean MEDD per prescription decreased by 15.44 between cohorts 1 and 3 ($p < 0.001$) after implementation of the electronic alert system.

Conclusions: This study demonstrates significant differences in opioid prescription dosage based on patient demographics. The observed decrease in opioid prescription dosage following the alert system may indicate system realization. Patient demographics provide foci for opioid prescription reform in ophthalmology however significant differences between patient diagnosis were not demonstrated.

CONTROL ID: 3703653

SUBMITTER (NAME ONLY): Kaoru Uchida

TITLE: Novel silicone hydrogel surface characteristics of in-vitro contact angle and friction assessment

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Uchida, Medical Affairs, Nihon Alcon Kabushiki Kaisha, Minato-ku, Tokyo, JAPAN|N. Yokoi, Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, JAPAN|P.B. Eftimov, G.A. Georgiev, Department of Cytology, Histology and Embryology, Faculty of Biology, Sofia University “St. Kliment Ohridski”, Sofia , BULGARIA|N. Peev, Faculty of Physics, Sofia University “St. Kliment Ohridski”, Sofia , BULGARIA|Y. Paunski, Institute of Robotics, Bulgarian Academy of Sciences, Sofia , BULGARIA|

Commercial Relationships Disclosure: Kaoru Uchida: Commercial Relationship(s);Code E (Employment):Nihon Alcon | Norihiko Yokoi: Commercial Relationship(s);Code F (Financial Support):Nihon Alcon;Code F (Financial Support):Toray;Code F (Financial Support):Rohto;Code P (Patent):Kowa;Code P (Patent):Menicon;Code P (Patent):Rexxam | Petar Eftimov: Commercial Relationship: Code N (No Commercial Relationship) | Nikola Peev: Commercial Relationship: Code N (No Commercial Relationship) | Yasen Paunski: Commercial Relationship: Code N (No Commercial Relationship) | Georgi Georgiev: Commercial Relationship(s);Code F (Financial Support):Nihon Alcon;Code F (Financial Support):Toray;Code F (Financial Support):Santen S.A.S. ;Code F (Financial Support):Rohto

ABSTRACT BODY:

Purpose: Lens surface properties can contribute to improved contact lens comfort. Herein, in-vitro lens surface characteristics of a novel silicone hydrogel contact lens (SHCL) of verofilcon A and a traditional SHCL of narafilcon A were assessed by both sessile drop contact angle (SDCA) and coefficient of friction (CoF).

Methods: 10 lenses each of verofilcon A and narafilcon A were assessed using both SDCA and a micro-tribometer. Prior to measurement, study lenses were prepared to remove package solution components by using 20 mL of saline solution. This step was repeated until the surface tension demonstrated they were free of surfactants. Each study lens was placed into the cycling machine for 1, 2, 3, 4, 6, 8, 10, 12, 14 and 16 hours (repetitive cycles of 1 sec in saline solution and 10 sec in air). The lens holder was positioned directly beneath the dosing needle of the micro syringe on the sample holder stage of the SDCA equipment. A 3 µL drop of phosphate buffer solution (PBS) was formed on the tip of the dosing needle. Micro-tribometer assessment was performed at both 0.1mm/s and 8cm/s sliding speed with artificial tear solution including lysozyme and PBS. For frictional aging, 50 tribometer cycles were assessed after the saline/air cycling. Statistical analyses were performed using two sample t-test.

Results: For SDCA at 16 hours, verofilcon A was 42.5° and narafilcon A was 91.4°, verofilcon A was superior to narafilcon A including remaining assessment hour ($p<0.0001$). CoF at 8cm/s sliding speed after 50 tribometer cycles and 16 hours showed verofilcon A was 0.8667 and narafilcon A was 1.5251 ($p<0.001$). Assessment after 1 hour to 14 hours also showed verofilcon A was superior to narafilcon A ($p<0.001$). CoF without the 50 cycle frictional aging at both 8cm/s and 0.1mm/s sliding speed showed statistical differences of verofilcon A compared to narafilcon A at 16 hours (each $p<0.0001$).

Conclusions: This is the first in-vitro study for both SDCA and CoF on lens surface assessment with multiple hour blink emulation between verofilcon A and narafilcon A. SMARTSURFACE® Technology in verofilcon A maintained excellent lens surface properties in an assessment of both SDCA and CoF.

CONTROL ID: 3703692

SUBMITTER (NAME ONLY): Kumari Alka

TITLE: Diabetic Retinopathy: Regulation of Ceramide Production and Rac1 Activation

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Alka, R.A. Kowluru, Department of Ophthalmology, Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Kumari Alka: Commercial Relationship: Code N (No Commercial Relationship) | Renu Kowluru: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the development of diabetic retinopathy, cytosolic reactive oxygen species (ROS) are elevated before mitochondrial damage can be observed, and NADPH-oxidase 2 (Nox2) and its regulatory cytosolic component, small molecular weight G protein (Rac1), are considered to play a major role. Hyperglycemia is shown to accelerate and exacerbate transcriptional and functional activation of retinal Rac1, and its promoter undergoes active DNA methylation-hydroxymethylation, leading to increased levels of 5hydroxymethyl cytosine (5hmC). Lipid excess also leads to increased ceramide, and serine palmitoyl-transferase (SPT) is the first and the rate-determining enzyme in its biosynthesis. Our aim was to investigate the mechanism by which ceramide promotes Rac1 activation in diabetic retinopathy in type 2 diabetic (T2D) model.

Methods: C57BL/6 mice were fed high fat diet (45% kcal) for 8 weeks, after which a group of mice were administered a low dose of streptozotocin (30 mg/kg body weight; T2D). Soon after establishment of diabetes, a group of mice received intravitreal administration of 2µg/2µl SPT-siRNA, and these mice were maintained on the same high fat diet for 5 weeks. Age-matched normal mice on a regular mice chow were used as controls. Retinal microvessels (prepared by osmotic shock method) were used to measure Rac1 activity (G-LISA), Nox2 activity (lucigenin) and ROS (DCFDA method). Transcriptional regulation of Rac1 was determined by quantifying 5hmC levels (immuno-capture technique) at its promoter.

Results: Compared with normal mice, the activity of Rac1, Nox2 and ROS were significantly increased in T2D group, and Rac1 transcripts and 5hmC levels at its promoter were also significantly elevated. Administration of SPT-siRNA prevented increase in Rac1, Nox2, ROS, and also ameliorated 5hmC at Rac1 promoter.

Conclusions:

Thus, accumulation of ceramide in diabetes increases ROS production through transcriptional and functional activation of Rac1. This suggests that regulation of ceramide in diabetic patients with hyperlipidemia may be equally important as regulating their blood sugar to prevent the development of retinopathy.

CONTROL ID: 3703718

SUBMITTER (NAME ONLY): Michael Girard

TITLE: 3D Structural Analysis of the Optic Nerve Head to Robustly Discriminate Between Optic Disc Drusen and Papilledema

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.J. Girard, S.K. Panda, Ophthalmic Engineering & Innovation Laboratory, Singapore Eye Research Institute, Singapore, SINGAPORE|T. Tun, R. Najjar, T. Aung, D. Milea, Singapore Eye Research Institute, Singapore, SINGAPORE|A. Thiery, Statistics and Applied Probability, National University of Singapore, Singapore, SINGAPORE|S. Hamann, Ophthalmology, Rigshospitalet, Copenhagen, DENMARK|C.L. Fraser, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: (1) To develop a deep learning algorithm to automatically and simultaneously identify major tissue structures of the optic nerve head (ONH) in 3D optical coherence tomography (OCT) scans; (2) to exploit such information to robustly differentiate among healthy, optic disc drusen (ODD), and papilledema ONHs.

Methods: This was a cross-sectional comparative study including ethnically diverse patients from 3 sites (in Singapore, Australia, Denmark) with confirmed ODDs (105 eyes), papilledema due to high intracranial pressure (51 eyes), and healthy controls (100 eyes). Volume raster scans of the ONHs were acquired using Spectralis OCT, then processed with adaptive compensation to improve deep-tissue visibility. In a first step, a deep learning algorithm was developed using 984 B-scans (from 130 eyes) in order identify: major neural and connective tissues, and ODD regions whenever present. The performance of our segmentation algorithm was assessed (against manual segmentations) using the dice coefficient. In a second step, a classification algorithm (random forest) was designed using 150 OCT volumes to perform 3-class classifications (class 1: ODD, class 2: papilledema, class 3: healthy) strictly from their drusen and prelamina swelling scores that were directly calculated from the segmentations. To assess performance, we reported the area under the receiver operating characteristic curves (AUCs) for each class (one-vs-all).

Results: Our segmentation algorithm was able to simultaneously isolate neural & connective tissues, and ODD regions whenever present (Figure). This was confirmed by an averaged Dice coefficient of 0.93±0.03 on the test set, corresponding to very good segmentation performance. Classification was achieved with very high AUCs, i.e. 0.99±0.01 for the detection of ODD, 0.99±0.01 for the detection of papilledema, and 0.98±0.02 for the detection of healthy ONHs.

Conclusions: A relatively simple AI approach allows to accurately discriminate ODD from papilledema, strictly using a single OCT scan of the ONH. Our classification performance was excellent, with the caveat that validation in a much larger population is warranted for clinical acceptance. Our approach may have the potential to establish OCT as the mainstay of diagnostic imaging for optic nerve disorders in neuro-ophthalmology.

CONTROL ID: 3703774

SUBMITTER (NAME ONLY): David Atchison

TITLE: Accommodation-induced changes in ciliary body length and thickness, peripheral choroidal thickness and peripheral axial length

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Atchison, D. Kaphle, M. Suheimat, K.L. Schmid, Optometry and Vision Science, Queensland University of Technology Faculty of Health, Kelvin Grove, Queensland, AUSTRALIA|

Commercial Relationships Disclosure: David Atchison: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss Vision | Dinesh Kaphle: Commercial Relationship: Code N (No Commercial Relationship) | Marwan Suheimat: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss Vision | Katrina Schmid: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss Vision

ABSTRACT BODY:

Purpose: To determine relationships between accommodation-induced changes in ciliary muscle parameters, peripheral choroidal thickness, peripheral axial length. We hypothesized that changes in ciliary muscle parameters and in choroidal thickness are correlated.

Methods: There were 29 young adults aged 18 and 27 years. All had good ocular and general health. Measurements of right eyes were made for 0 D and 6 D stimuli to accommodation at both nasal and temporal locations.

Axial length AL was measured with a Lenstar LS 900 biometer (Haag-Streit, Switzerland), with an auxiliary system to allow eye rotation in 10° steps to ±30°. Participants turned eyes without head movement to fixate targets and to make the target “as clear as possible” during measurements. Choroidal thickness CTh was measured with the Nidek RS-3000 Advance spectral-domain (SD)-Optical Coherence Tomography (OCT) in 10° steps to ±30°. For peripheral images, the internal cross target on the capture screen was moved from the centre to 17.25° nasal/temporal positions. Ciliary muscle length CML and maximum thickness were determined by imaging ciliary bodies of right eyes with a Carl Zeiss Meditec Visante OCT and an external fixation target placed at 40° to the instrument axis.

Changes in AL, CTh, CML and CMT with accommodation were denoted as ΔAL, ΔCTh, ΔCML and ΔCMT. For each participant, the three ΔCTh on each retinal side were averaged for comparison with corresponding muscle parameters.

Results: Nasal ΔCMT and ΔCML mean±SEs were 88±19 and −89±34μm, respectively. Corresponding temporal changes were 82±20 and −111±57μm.

Fig. 1 shows correlations between ΔCTh and ΔCMT on the nasal (r 0.30, p 0.13) and temporal (r 0.31, p 0.19) sides, neither of which were significant. Neither ΔCTh v. ΔCML correlation was close to significance (p 0.87, 0.89).

Fig. 2 shows ΔAL and ΔCTh as a function of visual field position; error bars are standard errors. ΔAL was greater than −ΔCTh at all positions. Maximum changes occurred on-axis Correlations were non-significant at all positions.

Conclusions: Individual parameters changed in expected directions with accommodation: AL, CMT increased; CTh, CML decreased. However, correlations between changes in parameters were not significant. This may be because of considerable variation between individuals and because individual accommodation responses were not the same for all instruments.

CONTROL ID: 3703864

SUBMITTER (NAME ONLY): Filippo Bonelli

TITLE: Ocular Graft-Versus-Host Disease induces corneal endothelial cell loss and expression of Neurokinin-1 receptor

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Bonelli, R.M. Lasagni Vitar, P. Fonteyne, F.G. Merlo Pich, P. Rama, G. Ferrari, Eye Repair Lab, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|A. Mondino, Lymphocyte Activation Unit, Division of Immunology, Transplantation and Infectious Diseases, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate corneal endothelial cell number and the expression of neurokinin-1 receptor (NK1R) in the endothelium in normal vs. ocular GVHD (oGVHD) corneas and to correlate the density of endothelial cells with clinical and histological inflammatory parameters.

Methods: Pre-conditioning was performed in BALB/c using myeloablative total body irradiation. Subsequently, allogeneic bone marrow transplantation was infused without (BM, n=8) or with mature T cells (BM + T, n=8). BM and normal wild type mice (n=7) were used as controls. Corneal transparency and blepharitis were assessed at the end of the experiment (day 29). After sacrifice, endothelial cell number, corneal thickness, and CD3+ cells were quantified, and the expression of NK1R was investigated in the corneal endothelium through immunofluorescence and quantified by immunohistochemistry.

Results: oGVHD mice showed a significant reduction in the endothelial cell number compared to controls ($p<0.0001$). In addition, NK1R expression was found in the endothelium, and it was significantly increased in oGVHD vs. control mice ($p<0.05$). Corneal transparency and thickness remained unchanged in all groups. An inverse correlation was found between endothelial cell number and the CD3+ cell infiltrate (Pearson $r= -0.8712$, $p<0.05$) and with blepharitis severity (Pearson $r= -0.5959$, $p<0.01$).

Conclusions: Our findings suggest that oGVHD is associated with reduced corneal endothelial cell density and increased expression of endothelial NK1R. Corneal endothelial cell loss correlates with increased expression of clinical and histological markers of inflammation.

CONTROL ID: 3703874

SUBMITTER (NAME ONLY): Zhaohua Yu

TITLE: Evaluating the performance of naive trainees on a virtual reality cataract surgery simulator

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Yu, A. Popa, Uppsala Universitet, Uppsala, SWEDEN|

Commercial Relationships Disclosure: Zhaohua Yu: Commercial Relationship: Code N (No Commercial Relationship) | Alexandru Popa: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the phacoemulsification performance of non-experienced trainees using a virtual reality cataract surgery simulator.

Methods: Ten medical students familiar with the anatomy and physiology of the eye, but naive to cataract surgery, were admitted to the study. Each subject was introduced to the simulator and then registered 40 simulations spanning 10 consecutive days with 4 simulations each day. Each simulation contains two phases, the capsulorhexis plus sculpting phase and the evacuation phase. The simulator automatically measured 38 variables during the simulation. All the variables were converted to performance index previously formulated by Söderberg et al. to assess the performance in both phases.

Results: In the capsulorhexis plus sculpting phase the asymptote of the trainee overall performance index was, estimated as 95% CI, 0.9±0.7 and a number of simulations needed to reach 90% of the asymptote was 37±24, indicating that the performance asymptote of a naive trainee achieves approximately after 40 simulations. An average incidence of capsular damage was 30% for the first 10 simulations whereas 9% for the last 10 simulations. In the evacuation phase the trainee overall performance index of 1 which is equivalent to the reference performance index was reached within the first 5 simulations and quickly plateaued, and less performance variation and better performance correlated with more training on the simulator.

Conclusions: A high-level performance asymptote occurs in the capsulorhexis plus sculpting phase after 40 simulations. In the evacuation phase performance asymptote can be reached at very early stage. Evacuation is less difficult than capsulorhexis plus sculpting.

CONTROL ID: 3703878

SUBMITTER (NAME ONLY): Stephanie McIlwaine

TITLE: Loss of Cone Outer-segments and Thickening of Photoreceptor Layers in Multiple Sclerosis: The Belfast Eye and Multiple Sclerosis Study

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.G. McIlwaine, R. Coey, L. Wang, D. Fitzgerald, J. Moffatt, I. Lengyel, Wellcome Wolfson Institute for Experimental Medicine, Queen's University Belfast Faculty of Medicine Health and Life Sciences, Belfast, Belfast, UNITED KINGDOM|L. Csincsik, T. Peto, Centre for Public Health, Queen's University Belfast Faculty of Medicine Health and Life Sciences, Belfast, Belfast, UNITED KINGDOM|A. Dubis, NIHR Biomedical Resource Centre, Joint Library of Ophthalmology Moorfields Eye Hospital and UCL Institute of Ophthalmology, London, London, UNITED KINGDOM|A. Dubis, Global Business School for Health, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Multiple Sclerosis (MS) causes progressive neurodegeneration characterised by demyelination of neurons and axonal loss. MS also affects the visual system with evidence of inner retinal degeneration; however, this does not fully explain vision loss experienced by patients. The Belfast Eye and Multiple Sclerosis (BEAMS) study aims to investigate if outer retina photoreceptor cells display changes in MS.

Methods: Sixteen patients with MS and 24 controls were enrolled. All patients underwent OCT (Heidelberg Spectralis) and AO (Imagine-Eyes RTX1). OCT analysis used in-built HEYEX automatic segmentation software (aberrations manually corrected) for peripapillary retinal nerve fibre layer (pRNFL), macular ganglion cell layer-inner plexiform layer (GCIPL), and photoreceptor layer (PRL) thicknesses (photoreceptor inner and outer segments). AO images were analysed semi-automatically by the cone segmentation algorithm (AODetect) and manually corrected. Images were captured at 2, 4 and 6-degree eccentricity. Control (ctrl) participants were compared to patients with MS with optic neuritis (MSON) or without optic neuritis (MSnON). Data were analysed using SPSS and GraphPad Prism.

Results: Results identified significant thinning of the pRNFL (Ctrl 106.63±1.60; MSON 89.08±3.94 $p<0.0001$; MSnON 106.54±2.81) and macular GCIPL (Ctrl 73.19±1.24; MSON 61.48±1.91; $p<0.0001$; MSnON 71.21±1.30). No significant differences were observed in MSnON compared to ctrl. In contrast, there was significant thickening of the PRL in patients with MS (Ctrl: 66.24±0.29; MSON 68.76±0.58 $p<0.0001$; MSnON 67.67±0.46 $p=0.011$). After analysing the AO images, we found a significant decrease of cone outer-segment densities in patients with both MSON and MSnON compared to ctrl at 2, 2.5 and 3 degrees (MSON $p<0.0001$; MSnON $p=0.0002$). At >3 degrees the cone densities remained significantly lower in MSON ($p=0.0002$) but not in MSnON ($p=0.0614$).

Conclusions: OCT analysis in the BEAMS study replicates the previously reported thinning of the inner retinal layers. However, we report here for the first time, significant thickening of the photoreceptor layer on OCT, a loss of cone outer segments in patients on images from AO in patients with MS. These results highlight a potential involvement of the outer retina in the pathophysiology of MS changes that could become a marker for monitoring the progression of MS.

CONTROL ID: 3703889

SUBMITTER (NAME ONLY): Sabrina Reinehr

TITLE: Enhanced retinal ganglion cell loss is accompanied by microglia activation in a multifactorial glaucoma model

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: It seems that, among others, immune processes, elevated intraocular pressure (IOP), or a combination of these factors are responsible for glaucomatous damage. Here, we combined two glaucoma models to examine if multifactorial risk factors (IOP and immune response) lead to a more severe damage of retinal ganglion cells (RGCs) and additional microglia activation.

Methods: Six-week-old wildtype (ONA) and βB1-CTGF mice (combination), a genetic OHT model, were immunized with 1 mg ONA (optic nerve antigen). A wildtype (control) and a βB1-CTGF control group (CTGF) received NaCl instead. 6 weeks after immunization, retinae were evaluated for RGCs (RBPMS), microglia/macrophages (Iba1), and microglia (Iba1 and Tmem119) via immunohistology. Further, mRNA levels of corresponding genes were analyzed via RT-qPCR.

Results: A significant RGC loss was noted in ONA ($p=0.02$), but not in CTGF mice ($p=0.60$) compared to controls. In the combination group, significantly fewer RGCs were noted compared to WT ($p<0.001$) and CTGF mice ($p=0.03$). The Pou4f1 mRNA levels (RGCs) were significantly downregulated in CTGF and combination retinae (both: $p=0.04$) compared to controls, while only a trend towards a downregulation was noted in ONA animals ($p=0.055$). The number of $Iba1^+$ cells in the ganglion cell layer (GCL) was significantly increased in CTGF ($p<0.05$) and combination mice ($p<0.001$) compared to control and ONA animals. Significantly more $Iba1^+$ and $Tmem119^+$ microglia were only found in the GCL of combination retinae (1.93±1.30 cells/mm) compared to control (0.29±0.44 cells/mm) and ONA mice (0.38±0.43 cells/mm; both $p<0.001$). The number of $Iba1^+$ and $Tmem119^+$ cells was also increased in the combination group compared to CTGF retinae (0.48±0.64 cells/mm; $p=0.001$). Similar results for $Iba1^+$ and $Iba1^+$ and $Tmem119^+$ cells were observed when counting from GCL to outer plexiform layer. The mRNA expression levels of Iba1 showed no difference within the groups, while a significant upregulation of Tmem119 mRNA could be observed only in CTGF retinae ($p=0.02$).

Conclusions: We revealed an enhanced RGC degeneration accompanied by an increased microglia activation. These results underline the important role of immunological processes, not only in autoimmune glaucoma, but also in IOP-dependent pathologies. Hence, this new model could help to study the pathomechanisms of this multifactorial disease more precisely.

CONTROL ID: 3703912

SUBMITTER (NAME ONLY): Andreas Maunz

TITLE: Machine learning approaches to automated prediction of fibrosis development in neovascular age-related macular degeneration using optical coherence tomography images

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To build and validate machine learning (ML) models using optical coherence tomography (OCT) volume scans for predicting the onset of fibrosis in patients with neovascular age-related macular degeneration (nAMD).

Methods: 935 OCT volume scans from 1097 treatment-naïve eyes with nAMD treated with ranibizumab 0.5 or 2.0 mg on a monthly or as-needed basis over 12 months were selected post hoc from the phase 3, randomized, multicenter HARBOR trial (NCT00891735). Retinal layers and pathological features were automatically detected in the OCT volume scans using a pretrained segmentation model. ML models were trained and evaluated using OCT and/or clinical variables (choroidal neovascularization [CNV] type assessed using fluorescein angiography [FA], baseline visual acuity, and age) in 2 approaches. For feature-based learning, 90 quantitative OCT features were automatically extracted from the segmentations. For end-to-end deep learning (DL), 2 models were trained with raw (DL-raw) and segmented (DL-seg) OCT B-scans.

Results: Binary classification of fibrosis development was assessed as area under the receiver operating characteristic curve (AUC), sensitivity, and specificity, using cross-validation. The DL-seg model predicted fibrosis development with average AUC values of 0.802, similar to the DL-raw model and feature-based learning (AUC = 0.786 for both), and was generally on par with the predictive performance of clinical variables only (AUC = 0.794). Notably, CNV type alone achieved an AUC of 0.747. Adding clinical variables did not considerably improve performance for DL-seg (from 0.802 to 0.809), but improved performance for DL-raw (from 0.786 to 0.808) and feature-based learning (from 0.786 to 0.821).

Conclusions: Fully automated models using OCT segmentation data can predict fibrosis development well. The DL-seg model, DL-raw model, and feature-based learning all achieved comparable performance in predicting fibrosis and were also comparable to the clinical variables only model, which requires invasive procedures and expert training for image interpretation (FA). These findings show that ML using OCT segmentations is a promising noninvasive approach to predicting fibrosis development in nAMD.

CONTROL ID: 3703970

SUBMITTER (NAME ONLY): Paula Liang

TITLE: The modulatory effect of IL11 on retinal angiogenesis

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Liang, J. Rapp, S. Boneva, C. Lange, G.R. Schlunck, H.T. Agostini, F. Bucher, Eye Center, Universitatsklinikum Freiburg, Freiburg, Baden-Württemberg, GERMANY|P. Liang, J. Rapp, S. Boneva, C. Lange, G.R. Schlunck, H.T. Agostini, F. Bucher, Albert-Ludwigs-Universitat Freiburg Medizinische Fakultat, Freiburg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: As a pleiotopic pathway with great angiomodulatory potential, the STAT3 pathway represents an attractive therapeutic target for the treatment of vasoproliferative retinal diseases. IL11, a member of the IL6 cytokine family, is a potent activator of the STAT3 pathway. However, the role of IL11 in the retina is still poorly understood. The aim of this study is to characterize the modulatory effect of IL11 on retinal angiogenesis.

Methods: The concentrations of IL11 and IL11 receptor (IL11R) in human vitreous samples from 16 proliferative diabetic retinopathy (PDR) and 16 control patients were determined by ELISA.

The angiomodulatory effects of VEGF, IL11, soluble IL11R and combinations thereof on human vascular endothelial cells (HUVECs) were determined by spheroid sprouting and migration assays. Transcriptomic shifts were assessed by RNA sequencing.

In the model for oxygen induced retinopathy the retinal vasculature of Bl6/J mice were examined after injection with either IL11, IL11+sIL11R or PBS.

Intracellular signaling pathways in HUVECs and murine Müller cells were studied by Western blot.

Results: While IL11R is significantly upregulated in vitreous samples from PDR patients (ñ=118 pg/mL) compared to the control patients (ñ=1 pg/mL), the concentration of IL-11 showed no significant difference (ñ≈3 pg/mL).

In-vitro, IL11 primarily activated the STAT3 signaling pathway (cis-signaling) and caused a significant reduction of VEGF-induced sprouting in HUVECs (Δ= -15%; $p<0.05$). Interestingly, the combination of IL11 and sIL11R (trans-signaling) enhanced cell sprouting and migration (Δ= +21.6%; $p<0.05$). Western blot analyses revealed that IL11 trans-signaling simultaneously activated STAT3 and STAT1 as well as AKT in HUVECs resulting in a significant transcriptomic shift favoring angiogenesis.

In-vivo, IL11 and IL11+sIL11R both led to a significant reduction in retinal neovascularization (N=15; $p<0.05$). Cryosections of murine eyes after injection suggested that Müller cells respond to IL11 treatment with no differences in intracellular signaling in response to IL11 cis- or trans-signaling.

Conclusions: The different angiogenic properties of IL11 and IL11+sIL11R can be explained by individual signaling responses and associated transcriptomic shifts. The elevated IL11R levels in vitreous samples from PDR patients suggest that IL11 signaling play an important role in PDR pathogenesis, providing an entirely new perspective on its role in angiogenesis.

CONTROL ID: 3704159

SUBMITTER (NAME ONLY): Reza Ladha

TITLE: A model system to define injection pressure and flow characteristics during subretinal drug delivery

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ladha, F. Willermain, Departments of Ophthalmology, CHU St Pierre and Brugmann, Brussels, BELGIUM|R. Ladha, F. Willermain, Universite Libre de Bruxelles, Bruxelles, Bruxelles, BELGIUM|B. Merveille, R. Wyns, Biomedical Department, CHU Saint Pierre, Brussels, BELGIUM|T. Meenink, M.D. De Smet, Preceyes BV, Eindhoven, NETHERLANDS|M.D. De Smet, MicroInvasive Ocular Surgery Center, Lausanne, SWITZERLAND|

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ABSTRACT BODY:

Purpose: The risk of retinal, RPE damage and vitreous reflux increases with increased injection pressure during subretinal injections. Using a model chamber in which injection and chamber pressure can be modulated, this study aims to identify the optimal injection characteristics for subretinal drug delivery.

Methods: A 38 G outer diameter subretinal injection cannula proximally attached to a MicroDose™ Injection device filled with colored water was inserted through a 23 G valved trocar into a 38 cm^3 closed chamber with a defined inner pressure generated by an external compressor. The foot pedal-controlled viscous fluid injection (VFI) modes of two different vitrectomy systems (R-Evolution™ CR from BVI-Optikon and Stellaris Elite™ from Bausch and Lomb) were used to inject the solution with an injection pressure ranging from 1 to 50 psi with predefined chamber pressures of 10 , 20 and 30 mm Hg. Each injection was recorded using a video recording system. The following parameters were analyzed : pressure recording in the model, injection pressure, velocity of the injected solution, presence of an unintentional flow after release of the foot pedal.

Results: The predefined pressure recorded inside the model was constant and unaffected by the different injections pressure levels chosen on the VFI. A minimal pressure of 6 psi was needed to generate a flow inside our model. From 6 to 9 psi, the velocity of the flow was categorized as slow. Higher than 10 psi, we observed a flow with high exit velocity (figure). In all cases, a persistent flow was observed after releasing the foot pedal in VFI mode. The quantity of fluid increased when increasing the level pressure of injection.

Conclusions: Increased Injection pressure are associated with less controlled, high exit velocity flow characteristics. The model appears appropriate to study flow control and its possible role in RPE loss in the context of gene therapy.

CONTROL ID: 3704168

SUBMITTER (NAME ONLY): Ava Bittner

TITLE: An Evolution of Telerehabilitation for Low Vision Follow-ups

SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Bittner, Ophthalmology; Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|N. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Ava Bittner: Commercial Relationship(s);Code C (Consultant/Contractor):jCyte, Inc. | Nicole Ross: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: For studies of telerehabilitation to provide follow-up assessment and training to low vision (LV) patients with newly prescribed magnification devices, we examined whether different approaches to reduce the burden of the technology over the past 5 years had impact on ratings of the telerehabilitation encounter.

Methods: Our previous telerehabilitation studies for follow-ups with LV subjects at home connected loaner Android/iPad tablets to zoom videoconferencing via either remote phone-based support by investigators (phase 1 in 2016-17; n=10) or local Lions Club volunteers who went to participants' homes (phase 2 in 2018-19; n=11), followed by a randomized controlled trial (phase 3 in 2020-21) in which remote control access software connected loaner smartphones to zoom (n=20) or training was provided in-office (control group; n=12). Subjects in all phases completed the same post-telerehabilitation phone survey.

Results: A significantly greater proportion of phase 3 subjects indicated they strongly or mostly agreed that the technology did not interfere with the session (95%) than in phase 1 (60%; OR:3.6; 95%CI:1.1-11.7; p=0.036) or phase 2 (55%; OR:15.8; 95%CI:1.5-164; p=0.02), whereas there was no significant difference in this aspect between phases 1 and 2 (p=0.80). The majority (76%) agreed that telerehabilitation was as accurate as in-person, and 84% strongly or mostly agreed they were interested in another future session, with no significant differences between phases (all p>0.10). Despite only 39% who had previously used any videoconferencing, nearly all (93%) strongly or mostly agreed they were comfortable with evaluation and training via telerehabilitation; there were no significant differences in comfort, prior videoconferencing, or frequency of Internet use between phases (all p>0.10). In phase 3 when comparing ratings for telerehabilitation to in-office training, there were no significant differences for subjects' comfort level (p=0.29), overall satisfaction (p=0.67), whether self-rated magnifier use improved after the session (p=0.22) or interest to have another session (p=0.30).

Conclusions: Study participants across all phases reported high levels of acceptance for telerehabilitation, with less interference of technology when remote control access was used during the pandemic. There were no significant differences in ratings when comparing subjects randomized to telerehabilitation or in-office care during the pandemic.

CONTROL ID: 3704171
SUBMITTER (NAME ONLY): Debarun Dutta
TITLE: APi1775 peptide coated antifouling contact lenses
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D. Dutta, Optometry and Vision Science Research Group, Aston University, Birmingham, Birmingham, UNITED KINGDOM|D. Dutta, M.D. Willcox, P. Kalaiselvan, Y. Mohammad, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|A. Zlotkin, DisperseBio Ltd, Tel Aviv, ISRAEL|
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ABSTRACT BODY:

Purpose: To investigate immobilisation of a novel antifouling cyclic peptide APi1775 (gr14Z-BBC2) onto contact lenses which can produce antifouling activity against ocular pathogenic bacteria P. aeruginosa.

Methods: Increasing concentration (0.1 µM, 1.0 µM and 10 µM) of APi1775 (gr14Z-BBC2) peptide (amino acid sequence Cyclo[Lys-Ser-Val-His-Ser-Phe-Asp-Tyr-Asp-Trp-Tyr-Asn-val-BetaAla]) was immobilized on to Acuvue2® (Etafilcon A) contact lenses using EDC covalent binding as described earlier. Peptide immobilization was characterised by amino acid analysis. Antifouling and antimicrobial activity of the coated contact lenses were tested against Pseudomonas aeruginosa strain 6294 and strain 142 in the presence of saline and tear like fluid over 18 hours by viable plate count. The peptide coated contact lenses were tested for in vitro toxicity towards mammalian cells following ISO standard 10993-5 guidelines.

Results: Amino acid analysis revealed that contact lenses processed with 0.1 µM, 1.0 µM and 10 µM peptide were able to bind 3.71µg, 19.94µg and 23.16µg peptide respectively. The peptide immobilised contact lenses showed a dose-response with respect to antifouling activity against P. aeruginosa adhesion. Inhibition by the peptide coated lenses ranged between 77% (0.8 log) to 96% (1.5log) against P. aeruginosa adhesion when they were processed with 1.0 µM, and 10.0 µM peptide respectively. The cytotoxicity tests confirmed that the peptide coated contact lenses are not toxic to mammalian cells in vitro.

Conclusions: The current study showed that APi1775 peptide coating on commercial contact lenses can demonstrate significant antifouling activity leading to inhibition of bacterial adhesion to contact lenses. The APi1775 peptide coating may have the capacity to reduce microbial eye infections during human contact lens wear.

CONTROL ID: 3704206

SUBMITTER (NAME ONLY): Rahul Iyengar

TITLE: Cost-Effectiveness of a School-Based Screening Program in Indonesia for Identifying and Treating Schoolchildren with Refractive Error

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Iyengar, Ophthalmology - Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|J.R. Ehrlich, Ophthalmology - Kellogg Eye Center, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|M. Krautmann, University of Michigan William Davidson Institute, Ann Arbor, Michigan, UNITED STATES|S. Kotha, J. Macom, N. Kourgialis, Eye Health, Helen Keller International, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Indonesia is a rapidly growing county with over 262 million inhabitants, but among highly populated countries it has one of the lowest concentrations of eye care providers. This study evaluates the cost-effectiveness of a program implemented in South Sulawesi, Indonesia that trained schoolteachers to conduct vision screenings, organized in-school evaluations by opticians, and provided free eyeglasses to schoolchildren with refractive error (RE).

Methods: Schoolteachers across 6 districts in South Sulawesi were trained to screen children with possible RE for subsequent evaluation by opticians. All costs associated with designing and implementing the program (administration, training personnel, labor, service delivery, etc.) were assessed. Expenditures and outcomes data were utilized to calculate the cost per disability-adjusted-life-year (DALY) for this intervention using 2010 and 2016 Global Burden of Disease (GBD) weights.

Results: 521 teachers screened 41,212 students across 172 schools in South Sulawesi. 4,506 (10.9%) students failed screening, 2,652 were seen by optometrists, and 2,038 received glasses. 1,854 (41.1%) students that failed screenings did not follow-up. The total program cost was $97,380, which included glasses (39.6%) and labor (23.3%). In districts with school-based refraction services, the costs per student screened, refracted, and receiving glasses were $2.57, $31.33, and $41.40, respectively; costs were $2.04, $59.80, and $73.22 when district services were instead provided centrally. Assuming an 18.4% prevalence of uncorrected refractive error in South Sulawesi, the estimated cost per DALY averted was $89.04 by GBD 2010 weights.

Conclusions: Treating children with correctable RE in limited resource settings can be done cost-effectively through school-based models.

CONTROL ID: 3704263

SUBMITTER (NAME ONLY): Steven Bernstein

TITLE: Selective elimination and analysis of nestin (+) optic nerve laminar region-neural progenitor cells (ONLR-NPCs)

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Bernstein, Y. Guo, Z. Mehrabyan, Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Steven Bernstein: Commercial Relationship(s);Code C (Consultant/Contractor):Constant Pharmaceuticals;Code P (Patent):PCT/US19/16303 | Yan Guo: Commercial Relationship: Code N (No Commercial Relationship) | Zara Mehrabyan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Dissociating the roles of Nestin(+)/Sox2(+) NPCs present in the optic nerve laminar region (ONLR) from those in the retina are difficult to achieve because: 1) Most current approaches to eliminate Sox2(+) cells result in depletion of these cells in both the retina and ONLR. 2) Most Nestin(+) transgenic animals do not express the nestin-associated transgene in the ONLR. 3) It is difficult to determine whether effective treatments are reaching the target cells. We wanted to identify an appropriate model and approach to selectively deplete ONLR-NPCs, using transgenic mice expressing nestin-promotor drivers.

Methods: The C57BL/6-Tg(Nes-cre/ERT2)KEisc/J strain was crossed with ROSA 26-LoxP (DTA), and following Tamoxifen induction, ONLR's were assayed for elimination of nestin expression. The C57BL/6-Tg(Nes-TK*,-EGFP)145Sker/J) strain constitutively expresses GFP and viral thymidine kinase (Kernie, 2012). GFP(+) cells in the ONLR and retina were evaluated using immunohistochemistry. Nestin(+) cells were eliminated in the latter transgenic strain using either IP injection X 3 weeks of Ganciclovir (50mg/kg/d) or 3 week CNS adminstation of ganciclovir (GCV: Cytovene, 47.5mg/ml) using 2 or 4 week Alzet pumps attached to a intraventricular pump (Alzet pump 3). We evaluated ganciclovir distribution by doping the GCV fill with 0.5-2% fluorescein, and analyzing retinal and optic nerve fluorescence using a Heidelberg SD-OCT instrument with the blue peak fluorescent setting.

Results: No elimination of ONLR-nestin(+) cells occurred in the the Eisch strain. The Kernie strain exhibited scattered GFP(+) cells in the retina and ONLR. Systemic GCV administration resulted in the loss of GFP immunopositivity in both tissues. Administration of GCV by intraventricular pump using both the 2- and 4 week (1/2 the rate of dosing) eliminated GFP(+) NPCs in the ONLR, but not the retina.Positive continuous GCV dosing in the intraventricular cannalized mice was demonstrable best with 1% fluorescein, but also easily detectable with 0.5% fluorescein.

Conclusions: Selective elimination of ONLR-NPCs is possible via intraventricular dosing of GCV, and this can be reproducibly demonstrated at 2-, 3- and 4 weeks administration.The single 4 week Alzet pump used eliminated >90% of GFP(+) cells in the ONLR, while sparing retinal GFP(+) cells. Analysis of isolated ONLR-NPC functions in vivo are possible using this approach.

CONTROL ID: 3704291

SUBMITTER (NAME ONLY): Malik Ladki

TITLE: One-Year Outcome of Ocular Injuries in Survivors of the Beirut Port Ammonium Nitrate Blast

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Ladki, School of Medicine, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|A. Mansour, Department of Ophthalmology, American University of Beirut, Beirut, LEBANON|D. Cherfan, Universite Libanaise, Beirut, LEBANON|D. Cherfan, Universite Saint-Joseph, Beirut, LEBANON|A. Jalkh, Department of Ophthalmology, Universite Saint-Esprit de Kaslik Faculte de Medicine et des Sciences Medicales, Jounieh, LEBANON|F. Kuhn, Department of Ophthalmology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|F. Kuhn, Department of Ophthalmology, Pecsi Tudomanyegyetem Altalanos Orvostudomanyi Kar, Pecs, HUNGARY|

Commercial Relationships Disclosure: Malik Ladki: Commercial Relationship: Code N (No Commercial Relationship) | Ahmad Mansour: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Cherfan: Commercial Relationship: Code N (No Commercial Relationship) | Alex Jalkh: Commercial Relationship: Code N (No Commercial Relationship) | Ferenc Kuhn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ascertain the one-year outcome of patients who sustained open eye injuries from the Beirut Port Ammonium Nitrate (AN) Explosion.

Methods: Retrospective chart review of the operated eyes in 2 major eye hospitals. The recorded data included age, gender, laterality, initial visual acuity, anterior and posterior segment examinations, the type of injury, and the Zone of Injury (Zone 1: wound limited to the cornea, Zone 2: wound of the sclera and no more posterior than 5 mm from the limbus, and Zone 3: wound posterior to anterior 5 mm of sclera).

Results: Out of 42 patients with open globe injury that was originally sutured, 29 patients (34 eyes) were followed at the one-year mark. The initial vision in logMAR (mean±SD) was 2.93±0.87 (hand motion equivalent) and the final vision was 1.80±1.47 (counting finger 2m equivalent). No light perception (NLP) vision was noted in 12 eyes on presentation and 10 eyes remained so, while 2 eyes reached light perception (LP) vision. Eight eyes had an intraoperative expulsive choroidal hemorrhage (7 NLP and 1 LP both pre- and postoperatively), and 6 of the 8 developed phthisis. All eyes that developed phthisis had NLP preoperatively and postoperatively. Ocular Trauma Score (OTS) correlated inversely with both initial and final vision ($p<0.001$). Zone of injury inversely correlated with initial vision ($p=0.02$) and positively with final vision ($p<0.001$). Final vision was significantly worse in Zone 3 vs. Zones 1 and 2 (3.2±0.5) vs. 0.9±1.1) ($p<0.001$) injuries, as was the initial vision (3.3±0.5 vs. 2.7±0.8; $p=0.002$).

Conclusions: The OTS, which provides prognostic information for serious ocular trauma, also yields valuable prognostic information for AN-associated ocular injuries. Expulsive choroidal hemorrhage and NLP vision at presentation remain very poor prognostic signs.

CONTROL ID: 3704302

SUBMITTER (NAME ONLY): Itzam Marin

TITLE: AREDS Supplementation and Complement System Levels in Patients with Intermediate Age-Related Macular Degeneration

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Marin, N. Manoharan, A. Palestine, J.L. Patnaik, M. Mathias, N. Mandava, A.M. Lynch, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|F. Poppelaars, Nephrology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|M. Holers, Immunology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|A. Frazer-Abel, Exera BioLabs, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|B.D. Wagner, University of Colorado School of Public Health Department of Biostatistics & Informatics, Aurora, Colorado, UNITED STATES|I. Marin, B.D. Wagner, N. Manoharan, A. Palestine, J.L. Patnaik, M. Mathias, N. Mandava, A.M. Lynch, Sue Anschutz-Rodgers Eye Center, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a degenerative disease of the retina which can be classified into early, intermediate, and advanced phenotypes. It is recognized that the complement system plays a key role in the pathogenesis of AMD. While advances have been made in the treatment of wet AMD, the only approved therapy for dry AMD to date is AREDS supplementation. There is a paucity of research on the mechanisms behind the effectiveness of AREDS supplementation in reducing the risk of AMD progression. Given the important prognostic and therapeutic value of the intermediate phenotype of AMD (iAMD), the goal of this study was to determine if there was a difference in complement factors among patients with iAMD taking AREDS supplementation compared to those with iAMD not taking AREDS supplementation

Methods: Patients with iAMD were drawn from a biorepository registry of patients with AMD. The diagnosis of iAMD was confirmed with multimodal imaging. Plasma complement factor levels were measured by ELISA and multiplex Luminex immunoassays. Non-parametric Wilcoxon tests were used to compare levels for each analyte by AREDS supplementation

Results: We identified 211 patients with iAMD, of which 92 were on AREDS supplementation at time of study enrollment and 119 were not. The results for all the complement factors measured are shown in Table 1. We found lower levels of C3 ($p=0.05$) and C5a ($p<0.01$) in patients taking AREDS supplementation compared to those not on AREDS supplementation. There were no differences between the groups for the other complement factors measured

Conclusions: We demonstrate significant differences in two important components of the complement system including complement factor C3 and the activation fragment C5a in patients with iAMD taking AREDS supplementation compared to patients not taking AREDS. Our results suggest that further studies are needed in a larger cohort of patient with iAMD to establish the relationship of complement system activity and AREDS supplementation. These results can shed light on the mechanism of action of AREDS supplementation and the reason for reducing risk of progression to advanced AMD forms

CONTROL ID: 3704317

SUBMITTER (NAME ONLY): Levi Todd

TITLE: Inducing regeneration of retinal ganglion-like cells in vivo from Muller glia in the adult mouse using transcription factors.

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Todd, W. Jenkins, M. Hooper, C. Finkbeiner, T. Reh, Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of blindness affecting millions of people worldwide. Glaucoma is characterized by neurodegeneration of retinal ganglion cells (RGCs), the projection neurons of the retina. The mammalian retina lacks an endogenous regenerative capacity so loss of RGCs results in permanent blindness. Therefore, an impetus exists to develop strategies to replace lost neurons to offer therapeutic hope to patients. In this study, we provide evidence that Muller glia (MG) cells in the adult mouse retina can be stimulated to regenerate RGC-like cells.

Methods: To induce retinal regeneration we previously developed a transgenic mouse model that allowed for MG-specific inducible expression of the proneural transcription factor Ascl1 (Glast-CreER/LNL-tTA/TetO-Ascl1-GFP). We developed a regeneration paradigm in which Ascl1 induction followed by NMDA-induced neural toxicity and histone de-acetylase inhibition stimulated MG-mediated regeneration of bipolar neurons in the adult mouse retina. In this project, we sought to regenerate retinal ganglion cells by overexpressing RGC-fate determining factors in combination with Ascl1. We generated a mouse to overexpress the RGC-factors Pou4f2 (Brn3b) and Islet1 in MG in vivo (Glast-CreER/LNL-tTA/TetO-Ascl1-GFP/TetO-Pou4f2-Islet1). We then used our previously established in vivo regeneration paradigm to test whether overexpression of Pou4f2 and Islet1 in Ascl1-expressing MG could alter the fate of regenerated neurons towards the RGC-lineage. We used immunohistochemistry, scRNA-seq, and scATAC-seq to characterize the regenerated neurons.

Results: Following our in vivo regeneration paradigm, immunohistochemistry analysis of MG-lineage traced cells revealed that the combination of Pou4f2/Islet/Ascl1 stimulated around 25% of MG to regenerate neurons expressing RGC markers (Pou4f2, Satb1, HuC/D). This neural phenotype was not observed with Ascl1-alone. Follow up characterization using scRNA-seq, reveal these regenerated neurons express many genes associated with developing RGCs and axon outgrowth. scATAC analysis confirms that Pou4f2/Islet1 shifts the chromatin accessibility of Ascl1-induced neurons to a state more akin to endogenous RGCs

Conclusions: This work demonstrates a strategy to induce endogenous regeneration of RGC-like cells from MG.

CONTROL ID: 3704359

SUBMITTER (NAME ONLY): Dragos Rezeanu

TITLE: A physiologically based simulation of anomalous trichromacy

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Rezeanu, R. Barborek, M. Neitz, J. Neitz, Ophthalmology, UW Medicine, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Red–green color vision deficiency (CVD) is the most common single locus genetic disorder in humans; however, only 25% of CVD individuals are dichromats who rely on two cone types for color vision. 75% are anomalous trichromats whose CVD is milder, being based on three cone types, but who are nevertheless referred to as “colorblind.” Here, we present an algorithm that computes the relative loss of color discrimination in red-green CVD individuals with varying degrees of deficiency and simulates these conditions by transforming the colors in a digital image.

Methods: Our algorithm uses the association between discrimination data from the Nagel anomaloscope and measured spectral separations from anomalous trichromats to simulate color discrimination in anomalous trichromats more generally. Using the measured primaries of an anomaloscope and cone fundamentals derived from a physiologically based photopigment template, we can predict the Rayleigh match and matching range for any pair of middle-to-long wavelength cone photopigments. This information is used to simulate the relative loss in color discrimination of an anomalous trichromat by comparing the predicted matching range against the average color normal range and applying that % loss to a digital image through LMS Daltonization.

Results: The resulting model generates accurate simulations of CVD at any severity, as defined by the spectral separation between the two middle-to-long wavelength cones, with Rayleigh match and matching range values that agree with results from anomalous trichromats who have had their cone photopigments characterized by molecular genetics. We used the model to transform a wide range of test images, all of which illustrate the significant gap in color discrimination between dichromats and even the most severe anomalous trichromats. Even a spectral separation of 2.5 nm, with a corresponding 87.9% loss in color discrimination, leaves sufficient color information to pass the Farnsworth D-15 and identify the primary colors in most real-world scenes.

Conclusions: An accurate simulation of CVD at every level of severity could play an important role in establishing more inclusive employment standards for color critical work by educating the public on the difference between color “deficient” and color “blind.” As our model illustrates, most CVD individuals are very capable of discerning the colors in their environment.

CONTROL ID: 3704367

SUBMITTER (NAME ONLY): Priya Chaudhary

TITLE: Decreased retrolaminar Myelin protein expression in Non-Human Primate (NHP) Early Experimental Glaucoma (EG) is accompanied by increased Iba1(+) cell counts and decreased GFAP signal intensity

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Chaudhary, C. Stowell, J. Reynaud, S.K. Gardiner, G. Williams, I. Williams, C.F. Burgoyne, Devers Eye Institute, Legacy Health System, Portland, Oregon, UNITED STATES|N. Marsh-Armstrong, Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously reported optic nerve head (ONH) lamina cribrosa deformation, thickening and insertion migration in NHP early EG. Here we test the hypothesis that retrolaminar (RL) myelin alterations accompanied by alterations of astrocyte and microglial markers are also present in NHP early EG.

Methods: Four unilateral early EG NHPs were sacrificed by 4% paraformaldehyde perfusion fixation. For each NHP, EG and Control (C) eye ONH tissues were trephined (10 mm circular blade), and cut vertically, embedded in paraffin and serially sectioned 5µm sections (Fig 1). For-each immunohistochemical (IHC) marker, n=4 near-adjacent ONH sections were deparaffinized, stained with the primary antibody [myelin basic protein (MBP), 2',3'-Cyclic-nucleotide 3'-phosphodiesterase, (CNPase), glial fibrillary acidic protein, (GFAP), or ionized calcium binding adaptor molecule 1, (Iba1)] incubated with fluorescent secondary antibodies and cover slipped using a NucBlue mountant. Whole section images were acquired and ONH anatomic landmarks were manually segmented, allowing signal intensity per unit area or cell density to be assessed in consistent RL anatomic regions. Animal specific (AS) and experiment wide (EW) EG versus C eye signal differences were analyzed using a series of linear mixed effects models.

Results: CNPase and MBP decreased significantly in EG versus C eyes (EW, ($p<0.001$)) in both RL regions and in at least 1 RL region of 3 of 4 NHPs individually (AS, $p<0.02$) (Table 1). GFAP decreased and NucBlue and Iba1(+) cell counts increased in both retrolaminar regions (EW, $p<0.01$), and in 3 or 4 NHPs individually for (GFAP and NucBlue only). CNPase, GFAP and MBP expression decreased (EW, $P<0.05$) in the peripheral versus central (Fig 1) RL sub-regions in C eyes. EG vs control eye increases in Iba1(+) expression were greater peripherally than centrally ($p=0.023$).

Conclusions: Decreased myelin–related protein expression within the immediate retrolaminar ONH tissues in NHP early EG is accompanied by decreased GFAP expression and increased NucBlue and Iba1(+) cell counts. Retrolaminar myelin homeostasis may be a neuroprotective target for enhancing axonal survival in glaucoma whether its disruption primarily contributes to axonal injury or is secondary to its occurrence.

CONTROL ID: 3704368

SUBMITTER (NAME ONLY): Jacqueline Shaia

TITLE: A Descriptive Study of Diabetic Retinopathy Disparities among Millions of Patients

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.K. Shaia, Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|D. Kaelber, The MetroHealth System, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Jacqueline Shaia: Commercial Relationship: Code N (No Commercial Relationship) | David Kaelber: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of blindness that affects one third of the diabetic population worldwide. The prevalence of this condition is only expected to grow with estimates of 16 million American's being affected by DR by 2050. The purpose of this study was to complete a descriptive study of patients with DR in the United States among tens of millions of patients.

Methods: 53,287 and 345,420 patients with Type 1 (T1) and Type 2 (T2) DR were identified in the TriNetX database (a combined electronic health records database of over 50 systems) utilizing encounter ICD codes. Data was gathered ondemographics, average body mass index (BMI), and average glycated hemoglobin (A1C) values. Proportions, percentages, and chi-square tests were calculated to evaluate T1 and T2 DR.

Results: Of the 74 million patients, 0.77% and 6.1% of patients had T1 or T2 diabetes. Of those patients, 9.3% of T1 and 7.1% of T2 had DR. When comparing ethnicity among those with T2 DR, the odds of DR among those who were Black was 1.41 times the odds of DR among those who were white (CI 1.40, 1.42). This opposite disparity was found among those with T1 DR who were Black as it was 0.96 times the odds of DR among those who were white (CI 0.94, 0.97). Additionally, when calculating the odds of Black women having T2 DR, they were 1.04 times more likely to have DR then Black men (CI 1.03, 1.05). This was similar in T1 DR patients where Black women were also more likely than Black men to have DR with an odds ratio of 1.08 (CI 1.04, 1.12). When comparing men and women who were white who had T2 DR, the odds ratio was 1 indicating no difference between genders (CI 0.99, 1.01) whereas in T1 DR, the odds of being a white woman was 1.04 (CI 1.04, 1.06). Lastly, the odds of having T1 or T2 diabetes without DR among white women was 0.79 and 0.80 times the odds compared to white men (CI 0.78, 0.79; 0.8, 0.8). A comparison of A1C levels and BMI did not find any significant differences between gender or ethnicity ($p>0.001$).

Conclusions: This large population descriptive study highlights increased odds of DR in Black individuals with T2 diabetes compared to white individuals and an increase in all types of DR in Black women compared to black men. Further research is needed to understand why these differences exist.

CONTROL ID: 3704390

SUBMITTER (NAME ONLY): Gulnoza Azieva

TITLE: Contact lens-induced dry eye in the marmoset model (CLIDEM): central corneal thickness, tear film osmolarity and blink rate.

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Azieva, R.K. Ablordeppey, C. Lin, A. Benavente-Perez, SUNY College of Optometry, New York, New York, UNITED STATES|D. Makrynioti, Panepistemio Patron, Patra, Periféria Dhitikís Elládh, GREECE|

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ABSTRACT BODY:

Purpose: To characterize central corneal thickness (CCT), tear osmolarity and blink rate longitudinally in a non-human primate (NHP) model, the common marmoset (Callithrix Jacchus), in untreated compared to animals treated with contact lenses (CL).

Methods: Longitudinal changes in CCT (N=20; 10CL), osmolarity (N=10; 6CL) and blink rate (N=18; 10CL) were assessed using high frequency A-scan ultrasound (25 MHz, Panametrics, NDT), I-PEN Vet Tear Osmolarity System (I-MED Pharma Inc), and a video recording system (745 frames/minute) from 70 days to 150 days (5 months) at approx. 9am, and again after 9hrs of CL wear (methafilcon A, 55% water content; Capricornia, Australia). Data was assessed for normality. Repeated measures ANOVA and student T-test were used to compare treated to control eyes over time.

Results: At baseline, untreated marmosets had a mean±SD CCT of 0.305±0.008 mm, osmolarity 311.67±11.48 mOsms/L and blink rate 1.83±1.79 blinks per minute (bpm), which remained stable over 5 months, except blink rate that increased to 5.32±1.58 bpm ($p<0.01$) after 5 months. In CL-treated marmosets, CCT increased during the second month of CL wear (baseline: 0.299±0.007 mm; 2 months: 0.307±0.008 mm, $p<0.05$) and stabilized afterwards. Osmolarity progressively decreased after 2, 3 and 4 months of CL wear (baseline: 316.11±13.63; 2 months: 302.63±11.27, $p<0.05$; 3 months: 302.92±14.58, $p<0.05$; 4 months: 301.50±12.90, $p<0.05$). This longitudinal decrease in osmolarity occurred in parallel to an increase in blink rate (baseline: 0.98±1.18 bpm; 1 month: 2.58±2.50 bpm, $p<0.05$; 2 months: 3.46±3.04 bpm, $p<0.05$; 3 months: 3.73±1.50 bpm, $p<0.001$), which later decreased after 4 months (2.11±1.49 bpm, $p<0.05$).

Conclusions: Juvenile untreated marmosets exhibit CCT, osmolarity and blink rates that remain stable from 2 to 7 months of age, except blink rate that increased at 7 months of age. Marmosets treated with CL for 5 months, however, experienced an increase in blink rate and CCT, along with a decrease in osmolarity within the first 3 months of CL treatment. We hypothesize that CL wear might be inducing mild corneal edema and an increased blink rate, in turn delaying the development of hyperosmolarity. These findings support the marmoset as a new animal model for ocular surface research, and its potential to assess CLIDEM.

CONTROL ID: 3704401

SUBMITTER (NAME ONLY): Yulia Pyatova

TITLE: Biofeedback Training to improve visual functions and quality of life post brain injury

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Pyatova, M. Markowitz, S.N. Markowitz, M. Daibert-Nido, Ophthalmology, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Biofeedback training (BT) improves oculomotor control and was never used before in patients with hemianopia post-brain injury. This study analyzes the impact of BT on visual functions and quality of life (QoL) on this population.

Methods: This is a prospective controlled randomized study. The control group did baseline and 1week control measures using a MAIA microperimeter (Centervue, Padova, Italy). Control group patients crossed over to the treated group. Retinal sensitivity, 20" fixation stability (BCEA 63%), reading speed, QoL Massof questionnaire, contrast sensitivity, ETDRS visual acuity (BCVA) and stereopsis were the outcomes. For the treated group, 5 BT weekly sessions of 20' were delivered. BT displaced the visual fields in 1^{0}. Outcome measures were repeated 1 week after BT.

Results: 6 subjects were studied. The average age was 67.5 (± 18.46). 3 patients were in the control group, 2 crossed over, and 5 patients were in the treated group. The control and treatment groups were not significantly different in demographics. 50% were female. Brain injury was from stroke in 4 patients, brain tumor 1, and encephalitis in 1. Time post injury was 9.6 ± 7.7 months. In the treated group, post-BT showed for the BCEA 63% an improvement from 0.72 (± 0.4) to 0.34 s^{02} (± 0.3), p=0.037. QoL showed a significant improvement in visual ability from 0.79 (± 2) to 1.8(± 1.6) p=0.009, reading from 2 (± 2.3) to 3.9 (± 1.5) p=0.02, mobility from -0.2 (± 2.7) to 0.36 (± 2.6) p=0.02, and visual information from 1.2 (± 1.7) to 2.2 (± 1.2) p=0.04. BCVA in the treated eye increased from 0.2 (± 0.2) to 0.1(± 0.08), contrast sensitivity from 1.76 (± 0.25) to 1.87 logMar (± 0.10), reading speed from 106.9 (± 61.6) to 138.8 wpm (± 60.3), and stereopsis from 918 (± 1204) to 708” (± 1291). Retinal sensitivity improved from 16.4 (± 3.4) to 17.2 (± 4). In the control group, outcomes did not change from baseline to control measures.

Conclusions: A significant improvement was noticed in their QoL on visual ability, reading skills, mobility, and visual information post-BT. Oculomotor functions improvement may be involved in this mechanism, as the fixation stability improved significantly. All the variables showed a trend for improvement post-BT.

CONTROL ID: 3704535

SUBMITTER (NAME ONLY): Maximilian Pawloff

TITLE: Comparison of stimulus types for retinotopic cortical mapping of macular disease

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pawloff, D. Linhardt, A. hummer, U. Schmidt-Erfurth, C. Windischberger, M. Ritter, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: Retinotopic maps acquired by fMRI provide a valuable adjunct in the assessment of macular dysfunction at the level of the visual cortex. The present study quantitatively assesses the performance of different visual stimulation approaches for mapping visual field coverage.

Methods: Twelve patients with geographic atrophy (GA) secondary to age-related macular degeneration were examined using high-resolution 7 Tesla fMRI (Siemens Magnetom 7T[CW1]) and microperimetry (MP, Nidek MP-3). We compared pRF-based coverage maps obtained with two stimulus variants (moving bars; rotating wedges and expanding rings) with the results of MP. Correspondence between MP and pRF mapping was quantified by calculating the simple matching coefficient (SMC).

Results: We find that stimulus choice biases the spatial distribution of pRF centres. In addition, eccentricity values and pRF sizes obtained from wedge/ring or bar stimulation runs show systematic differences. Wedge/ring stimulation results show lower eccentricity values and strongly reduced pRF sizes compared to bar stimulation runs. Statistical comparison shows significantly higher pRF centre numbers in the foveal 2.5° region of the visual field for wedge/ring compared to bar stimuli. However, these differences do not have an effect on SMC values when compared to MP (bar below 2.5° : 0,88 plusminus 0,13 bar above 2.5°: 0,88 plusminus 0,11; wedge/ring below 2.5°: 0,89 plusminus 0,12 wedge/ring above 2.5° 0,86 plusminus 0,10) for the peripheral visual field.

Conclusions: Both visual stimulation designs examined in this study can be applied successfully in GA patients. Although the two designs show systematic differences in the distribution of pRF centre locations, this variability has no impact on the SMC when compared to MP outcome.

CONTROL ID: 3704543

SUBMITTER (NAME ONLY): Jessica Karuntu

TITLE: Four-year prospective follow-up in patients with CRB1-associated retinal dystrophies

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Karuntu, X. Nguyen, M. Talib, J. Wijnholds, N.E. Schalij-Delfos, C.J. Boon, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|M.J. van Schooneveld, R.J. Florijn, J.B. ten Brink, A.A. Bergen, C.J. Boon, Amsterdam Universitair Medische Centra, Amsterdam, Noord-Holland, NETHERLANDS|C.C. Klaver, C.C. Hoyng, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|C.C. Klaver, M.M. Meester-Smoor, A.A. Thiadens, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|L.I. van den Born, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|M.M. van Genderen, Bartimeus, Zeist, Utrecht, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Investigate the natural history of CRB1-associated retinal dystrophies (RDs) over the course of 4 years to define optimal clinical endpoints for upcoming gene therapy trials.

Methods: Fifteen patients with genetically confirmed CRB1-associated RDs were included in this prospective study with a mean age of 26.5 years (SD ± 10.2, range 10.5 – 45.5 years) and mean follow-up time of 4.1 years (SD ± 0.2, range 4.0 – 4.7 years). Patients underwent extensive characterization including slit-lamp examination, color fundus photography, spectral-domain OCT, fundus autofluorescence, best-corrected visual acuity (BCVA) using the ETDRS letter chart, Goldmann kinetic perimetry, microperimetry, and full-field stimulus threshold (FST) testing.

Results: Patients were diagnosed with retinitis pigmentosa (13 patients, 86.7%), cone-rod dystrophy (1 patient, 6.7%), or isolated macular dystrophy (1 patient, 6.7%). Analysis revealed a non-significant decrease in BCVA from 0.82 logMAR (Snellen visual acuity 20/132) at baseline to 0.94 logMAR (Snellen visual acuity 20/174) after four years ($p = 0.105$). Furthermore, overall retinal sensitivity using FST was not significantly altered over four years (-0.9 dB; $p = 0.685$). Macular sensitivity, measured using microperimetry, demonstrated a significant reduction in average threshold from 9.7 dB to 7.1 dB (-2.6 dB, $p = 0.001$).

Conclusions: The current analysis of the four-year natural history study in patients with CRB1-associated RD revealed that BCVA and general retinal sensitivity on FST did not change significantly. However, macular sensitivity did show progressive significant decline, and may therefore be a useful and more time-sensitive clinical endpoint for upcoming gene therapy trials for CRB1-associated RDs.

CONTROL ID: 3704553

SUBMITTER (NAME ONLY): Hajrah Sarkar

TITLE: Adult-onset rhodopsin mislocalisation and enlarged phagosomes in rdh12 mutant zebrafish model.

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Sarkar, M. Toms, M. Moosajee, University College London, London, London, UNITED KINGDOM|H. Sarkar, M. Toms, M. Moosajee, The Francis Crick Institute, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Hajrah Sarkar: Commercial Relationship: Code N (No Commercial Relationship) | Maria Toms: Commercial Relationship: Code N (No Commercial Relationship) | Mariya Moosajee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mutations in RDH12 are primarily associated with severe early onset Leber congenital amaurosis, and in rare cases autosomal dominant mutations are linked to late onset retinitis pigmentosa. Aim: to generate a rdh12 zebrafish mutant model and characterise the retinal phenotype to study disease mechanisms.

Methods: CRISPR/Cas9 gene editing was used to generate rdh12 mutant zebrafish. Fish were characterised by retinal histology, TUNEL staining for apoptotic nuclei and immunostaining for rhodopsin and cone opsins. Levels of all-trans retinal were quantified by HPLC. Transmission electron microscopy was used to examine retinal ultrastructure. Expression of oxidative stress and autophagy markers were analysed by RT-qPCR.

Results: The rdh12^{u533} mutant line was generated and carried a 7 base pair (bp) deletion in exon 1 (c.17_23del; p.(Val6AlafsTer5)), which resulted in significantly reduced expression of rdh12 mRNA transcript at 5 days post-fertilisation (5 dpf). Characterisation of rdh12^{u533} fish at 5 dpf did not reveal a retinal phenotype. At 12 mpf, no gross abnormalities were detected in retinal histology and TUNEL staining, however rhodopsin was mislocalised to the inner segments and TEM revealed significantly larger phagosomes in the RPE of mutant fish. Expression of autophagy marker atg12 and oxidative stress marker sod2 were also significantly reduced at 12 mpf.

Conclusions: Mutant rdh12 fish displayed a late onset rod-predominant degeneration, with early indications of disrupted pathways in adult fish. However, stress in the retina is effectively controlled so as not to cause severe disruption. This phenotype corresponds more with the autosomal dominant RP phenotype. Fish are currently being followed up at 24 mpf to assess further degeneration.

CONTROL ID: 3704627

SUBMITTER (NAME ONLY): Irmak Karaca

TITLE: Efficacy of infliximab and tocilizumab in non-infectious retinal vasculitis: 12-month outcomes

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Non-infectious retinal vasculitis (RV) is a rare, heterogeneous clinical condition which may result in sight-threatening consequences. Biologic agents are promising particularly in refractory cases. The index study aimed to evaluate the efficacy of infliximab (IFX) and tocilizumab (TCZ) infusions in non-infectious RV using the Angiographic Scoring for the Uveitis Working Group (ASUWOG) fluorescein angiography (FA) scoring system.

Methods: Records of 15 patients (27 eyes) who received IFX (5-10mg/kg) (Group 1) and 7 patients (10 eyes) who received TCZ (4-8mg/kg) (Group 2) were retrospectively evaluated to assess visual acuity (VA), anterior chamber cell and flare, vitreous haze, central subfield thickness (CST), and FA scoring at baseline and at 12 months of follow-up. The measurements were employed to assess the change in 12 months in each group.

Results: In Group 1 and 2, there was no underlying disease in 9 (60%) and 3 (42.9%) patients, respectively. Three (42.9%) patients in Group 2 had juvenile idiopathic arthritis (JIA) as the most common identified cause. Mean improvement in VA (log MAR) and CST were 0.08±0.25 and 42.2±80.8 μm in Group 1 ($p=0.053$ and <0.001); 0.02±0.24 and 58.9±85.9 μm in Group 2 ($p=0.344$ and 0.492), respectively. Mean FA scores were reduced from 13.3±5.3 and 11.6±4.6 at baseline to 5.3±5.8 and 4.2±2.5 at 12-months in Group 1 and 2 ($p<0.001$ and $p=0.004$), respectively. 15 eyes of 9 patients and 4 eyes of 3 patients had FA score <4 at 12 months in Group 1 and 2, respectively. In Group 2, 8 eyes of 5 patients (71.4%) had been treated with IFX prior to TCZ initiation. There were no significant safety concerns requiring treatment discontinuation during the follow-up in either Group 1 or 2.

Conclusions: IFX and TCZ infusions showed statistically significant improvement of non-infectious RV as shown by ASUWOG FA Scoring System. Both TCZ and IFX are appropriate therapeutic options for non-infectious RV. TCZ seems to be an effective treatment for patients with JIA-associated RV or those who failed IFX therapy.

CONTROL ID: 3704681

SUBMITTER (NAME ONLY): Susanne Roosing

TITLE: Identification of a complex allele in IMPG2 as a cause of adult onset vitelliform macular dystrophy

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Roosing, I. Vázquez-Domínguez, Z. Fadaie, L. Haer-Wigman, F.P. Cremers, A. Garanto, Department of Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|C.H. Li, C.C. Hoyng, Department of Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases are a group of clinically and genetically heterogeneous disorders with ~270 genes involved. IMPG2 is associated with adult onset vitelliform macular dystrophy (VMD). Here, we investigated two unrelated VMD patients in order to identify the underlying genetic cause.

Methods: Whole-exome sequencing identified a rare putative causal complex allele consisting of c.3023-15T>A and c.3023G>A (p.(Gly1008Asp)) in IMPG2 in both individuals. To assess its effect, in vitro splice assays using midigenes were conducted in HEK293T and further characterization of patient-derived iPSC differentiated towards to photoreceptor precursor cells (PPCs) was performed through qPCR and RT-PCR studies.

Results: Clinical assessment showed a typical VMD-features in both patients. The results of the midigene splice assays showed that the complex allele mainly affects splicing by the generation of an in-frame deletion of 48 nt and also the skipping of multiple exons. In contrast, patient-derived PPCs showed a significant increase of out-of-frame transcripts lacking one or multiple exons compared to control. Overall, control PPCs consistently showed low levels of aberrantly spliced IMPG2 transcripts that were highly elevated in patient-derived PPCs. These differences were even more obvious upon inhibition of nonsense-mediated decay with cycloheximide.

Conclusions: We report a heterozygous complex allele in IMPG2 causative for adult-onset VMD in two unrelated individuals with mild visual loss and bilateral vitelliform lesions. The predicted causal missense mutation c.3023G>A, located in the consensus splice acceptor site, enhances the splicing effect of the upstream variant c.3023-15T>A, leading to the generation of aberrant transcripts that decrease the full-length IMPG2 levels. These results suggest an haploinsufficiency mechanism of action and highlights the importance of using different models to functionally assesses splicing defects.

CONTROL ID: 3704727

SUBMITTER (NAME ONLY): Edward Lu

TITLE: Retinal Ischemia Rather than Neovascularization is Associated with Neovascular Glaucoma in Patients with Proliferative Diabetic Retinopathy Using Widefield Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA)

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.S. Lu, Y. Cui, R. Le, Y. Zhu, J.C. Wang, I. Lains, R. Katz, Y. Lu, R. Zeng, I. Garg, D.M. Wu, D. Husain, L.A. Kim, J.B. Miller, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|E.S. Lu, Y. Cui, R. Le, Y. Zhu, I. Lains, R. Katz, Y. Lu, R. Zeng, I. Garg, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate WF SS-OCTA metrics, including nonperfusion area (NPA) and neovascularization (NV), in proliferative diabetic retinopathy (PDR) patients with and without neovascular glaucoma (NVG).

Methods: This prospective, observational, single-center study was conducted from November 2018 to February 2020. A total of 85 eyes of 60 PDR patients without NVG and 9 eyes of 8 PDR patients with NVG were imaged using WF SS-OCTA. Retinal ischemic parameters (NPA; ischemia index [NPA/total retinal area]) and neovascularization features (NV number; NV area; NV vessel density) were evaluated. Foveal avascular zone (FAZ), macular thickness/volume and choroidal thickness/volume were obtained using the Zeiss ARI Network. WF SS-OCTA retinal and choroidal metrics, systemic, and ocular parameters were screened using Least Absolute Shrinkage and Selection Operator (LASSO) logistic regression for variable selection. Firth's Bias-Reduced logistic regression model (outcome: presence of NVG) was subsequently used to identify parameters associated with NVG.

Results: Ischemia index (cutoff 0.406; odds ratio [OR]=77.1, 95% confidence interval [CI]:9.1-1402.4, P<0.001) and BCVA (cutoff 0.185; OR=25.2, 95%CI:1.7-4138.2, P=0.015) were associated with the presence of NVG, and ischemia index remained significantly associated with NVG after exclusion of fellow eyes of NVG and adjustment for sex, age, and diabetes duration. NV metrics, FAZ, and choroidal parameters were not related to NVG.

Conclusions: Retinal ischemia but not neovascularization was associated with the presence of NVG in patients with PDR using WF SS-OCTA. Larger, longitudinal studies are needed to validate imaging biomarkers associated with diabetic NVG.

CONTROL ID: 3704754

SUBMITTER (NAME ONLY): Jing Wang

TITLE: Sigma 1 Receptor (Sig1R) activation attenuates vasculopathy associated with Retinopathy of Prematurity (ROP)

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: ROP, a retinal neurovasculopathy, is a leading cause of childhood blindness. We reported recently that activation of the molecular chaperone, Sig1R, provides a novel rescue of neuronal deficits in the oxygen-induced retinopathy (OIR), model of ROP (Wang et al, ARVO 2020). Here, we focus on Sig1R and its novel therapeutic potential in vascular injury characteristic of ROP.

Methods: C57BL/6J pups (P7 with nursing dam) were subjected to OIR or room air (CT). (+)-Pentazocine ((+)-PTZ), a high affinity Sig1R ligand, was administered starting P7 (0.5 mg/kg, IP, every other day). Retinal vasculature was imaged by fluorescein angiography & vascular tortuosity analyzed by MATLAB at P17& P48. At P17, retinal vascular distribution (neovascularization (NV) and avascular area) & vascular barrier function (Evans blue (EB) leakage assay) were evaluated. Oxidative stress (DHE, 3-NT, 4-HNE), reactive gliosis (anti-GFAP), expression of proteins/cytokines (Sig1R, ZO-1, Occludin, p-STAT3 and VEGF, IL-6, TNFα) were assessed by immunohistochemistry (IMH), Dot/Western blotting (WB) & ELISA.

Results: Vascular tortuosity: Retinal arteries in OIR mice were more tortuous (~1.3) v. CT (1.0), whereas (+)-PTZ significantly reduced arterial tortuosity (~1.1) in OIR mice at P17 & P48. Vascular distribution: Retinal avascular region (OIR-non: ~30% v. OIR+PTZ: ~12%) and NV (OIR-non: ~7.8% v. OIR+PTZ: ~2.5%) were significantly decreased in OIR+PTZ mice. Retinal vascular barrier: EB extravasation was elevated in OIR mice, but decreased significantly in OIR+PTZ mice. ZO-1 & Occludin levels decreased significantly in OIR mice, whereas (+)-PTZ preserved their levels. Oxidative stress and reactive gliosis: Detection of oxidative stress by DHE staining, 4-HNE and 3-NT immunostaining showed that (+)-PTZ attenuated superoxide and lipid peroxide levels in OIR mice. (+)-PTZ treatment diminished reactive gliosis in OIR mice. Exploration of Sig1R-STAT3-Inflammation axis. In OIR mice, we observed a significant decrease of Sig1R, along with increase of p-STAT3, VEGF, IL-6 and TNFα, whereas (+)-PTZ treatment normalized these effects.

Conclusions: (+)-PTZ treatment attenuated OIR-induced vasculopathy, retinal barrier dysfunction, reactive gliosis, oxidative stress and STAT3-mediated inflammation, suggesting that Sig1R is a promising therapeutic target for vascular injury in ROP.

CONTROL ID: 3704764

SUBMITTER (NAME ONLY): Ke-Wei Chen

TITLE: Automatic Blepharoptosis Measurement by Iris Edge Detection with a Deep Learning Model

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Our study proposes a method for margin reflex distances-1 (MRD1) measurement through facial photographs.

Methods: A deep learning U-net based model was trained with 100 external ocular photography to automate segmentation of the iris image. Images were acquired from pre-operative photos of patients prior to ptosis surgery. For each patient's photo, the segmentation result was used to extract the iris edge. A circle of best fit was generated based on the visible iris edges. The margin reflex distance 1 (MRD1) was calculated as the distance between the center of this circle to the margin of the upper eyelid. A fixed size reference marker on the patient's forehead was used to convert pixel measurements to millimeters. The proposed deep-learning-based MRD measurement algorithm was then evaluated with 500 single eye photos by comparing the measurement results from the model with measurements taken by a physician using the same photos. The physician was provided with custom software to enable measurement (available at https://gosienna.github.io/MRD_measurement/)

Results: A total of 500 photos, with MRD's ranging from -3mm to 6.15mm were used to evaluate the performance of the model. Using the physician measurements as the ground truth, we found that 95[1] % of the model measurements were within 1mm[2] of the ground truth. The Pearson's correlation[3] between model measurements and the ground truth was 0.95. The P-value for non-correlation testing was less than 0.001.

The Bland-Altman plot shows good agreement between automatic and manual MRD measurements (95% limits of agreement). Prediction errors occur in images without distinct upper eyelid margins. For example, long eyelashes, severe ptosis or large pterygium can result in difficulty for the model to recognize the iris edge.

Conclusions: Using a deep learning segmentation model, the MRD can be measured from clinical photos with a high degree of accuracy.

CONTROL ID: 3704797

SUBMITTER (NAME ONLY): Aretha Zhu

TITLE: Deep Learning Artificial Intelligence in Vision-Threatening Disease in Clinical and Community Screenings

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zhu, I. Zhang, P. Tailor, R. Verma, C. Ye, E. Kuklinski, B. Szirth, M. Habiel, A. Khouri, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD), diabetic retinopathy (DR), and glaucoma are vision-threatening diseases (VTDs) affecting 36 million people in the USA. With 5.7 ophthalmologists per 100,000 Americans, over 50% of VTDs go undetected. We assessed deep learning Artificial Intelligence (DLAI) in VTD detection in community and clinical settings.

Methods: 223 subjects (mean age 54.6, 58% male) from community screenings (A) and clinic (B) underwent 45-degree retinal imaging. In A (non-dilated), an onsite telemedicine reader (R1) and remote ophthalmologist (R2) graded image quality (gamma and alignment, 1-5 scale) and referable VTD using the international grading scales for AMD and DR, and cup-to-disc ratio and nerve fiber layer for glaucoma. In B (dilated), gradings were collected from R1 and the clinical diagnosis (d). A senior ophthalmologist (R3) adjudicated disputed findings. In A, DLAI VTD referral was compared to R1/R2/R3 consensus (S); in B, overall referral was compared to R1/d/R3 consensus (C). Images were uploaded to a cloud-based DLAI (SELENA+, EyRIS Pte Ltd) (Fig 1). Cohen's kappa assessed intergrader agreement.

Results: R1 and R2 found 4.7% eyes ungradable. DLAI marked 55.6% ungradable; 74.6% of them were for AMD. Of the DLAI ungradable eyes, image quality was ≤ 3, and 56.2% had ≥ 1+ cataract (R1). Compared to in A, in B DLAI had higher sensitivity (97.1% vs. 63.2%) and positive predictive value (69.4% vs. 32%). In A, DLAI had higher specificity (94.5% vs.16.7%) and negative predictive value (98.4% vs. 75.0%) (Table 1). In A, Cohen's kappa was 0.946 between R1 and R2, with a 13% disagreement rate. In 56% of the disagreements, R3 agreed with R1. In B, Cohen's kappa was 0.874 for R1 and d; R1 referred more than d. In A and B, DLAI referred more than R1, R2, and H/C. DLAI referred all eyes with > 1 VTD (1%) for further examination. Grading times for DLAI, R1, and R2 were 30, 129, and 68 seconds.

Conclusions: DLAI performed best in DR and glaucoma detection; a potential solution for the high ungradable rate can be for DLAI to re-center uploaded images. DLAI can increase efficiency and accessibility of screenings for multiple VTDs, in both underserved populations and clinic. The ability to minimize direct contact confers an advantage during COVID-19. Further studies will investigate DLAI use in VTD progression.

CONTROL ID: 3704806

SUBMITTER (NAME ONLY): Jill Sturdivant

TITLE: ROCK'Sters, a novel compound class combining Rho kinase inhibition with corticosteroid anti-inflammatory activity for the treatment of ocular inflammation

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Sturdivant, C. Kelly, D. Clancy, N. Girouard, M. Ina, Q. Wang, D. Cutno, S. Williams, M.A. deLong, C. Kopczynski, D. Hollander, J.C. White, Aerie Pharmaceuticals Inc, Durham, North Carolina, UNITED STATES|M.A. deLong, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Topical corticosteroids are commonly used to treat ocular surface and post-operative inflammation. Topical corticosteroid use is limited by its potential for ocular adverse events, such as elevated intraocular pressure. We have previously described a new class of compounds comprised of a corticosteroid covalently linked to a Rho-kinase inhibitor (ROCKi), termed "ROCK'Sters" that are designed to mitigate steroid-induced intraocular pressure (IOP) elevation. Herein, is described the synthesis, biochemical, and cellular activity of ROCK'Sters as well as a demonstration of their anti-inflammatory efficacy in a rabbit model of post-operative inflammation.

Methods: ROCK'Sters were evaluated for inhibition of ROCK enzyme isoforms in kinase biochemical assays. Steroidal activity of several ROCK'Sters was characterized by inhibition of the pro-inflammatory IL-23 pathway in mouse splenocytes. In vivo, anti-inflammatory efficacy of ROCK'sters was evaluated in a rabbit model of post-operative inflammation after cataract surgery. Post-surgery, ocular examinations evaluated surface morphology and anterior/posterior inflammation using a modified Hackett and McDonald ocular grading system. ROCK'Ster activity in the post-op model was compared to marketed steroids, Pred-Forte® and Durezol®.

Results: Several of the ROCK'Sters demonstrated potent inhibition of Rho kinase activity in enzymatic assays with IC_{50} < 10 nM. In a cellular context, these compounds strongly inhibited the pro-inflammatory IL-23 pathway in mouse splenocytes with IC_{50} values ranging from approximately 1 nM to 30 nM. In a rabbit post-operative inflammation model, ROCK'Sters displayed significant efficacy for resolution of inflammation that was noninferior to both Pred-Forte® and Durezol®.

Conclusions: ROCK'Sters represent a proprietary compound class with in vitro Rho kinase inhibitory activity, cellular steroidal activity, and anti-inflammatory efficacy in an animal model of post-operative inflammation. This class of compounds provides potent efficacy for the treatment of ocular surface and post-operative inflammation coupled with the potential for extended therapeutic use by providing a reduced risk of steroid-induced IOP elevation.

CONTROL ID: 3704823

SUBMITTER (NAME ONLY): Alexander Lieu

TITLE: Assessing Usability and Clinical Utility of GLANCE, an Artificial Intelligence-based Tool for Predicting Glaucoma Visual Field Progression

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lieu, M. Christopher, D.S. Welsbie, J.L. Do, A. Camp, S. Moghimi, S.L. Baxter, L.M. Zangwill, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|S.L. Baxter, Health Department of Biomedical Informatics, University of California San Diego, La Jolla, California, UNITED STATES|A. van den Brandt, Technische Universiteit Eindhoven, Eindhoven, Noord-Brabant, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Artificial intelligence (AI) has the potential to improve risk stratification in glaucoma, but interface design and usability of AI-based clinical decision support tools have been understudied. GLANCE is a visualization tool depicting predicted mean deviation of visual fields (VFs) based on a deep learning model trained on optical coherence tomography (OCT) images, with the potential to reduce VF testing frequency (van den Brandt A, et al., Eurographics Workshop on Visual Computing for Biology and Medicine, 2020). Here, we conducted a pilot study of clinicians using an updated prototype of GLANCE to assess usability, trust in the tool, and utility for clinical management.

Methods: Our updated prototype of GLANCE included dynamic visualization of the AI model output (predicted VF mean deviation) alongside prior VFs and model predictions, intraocular pressure measurements, and clinical history (Fig.1). An online survey consisting of six patient cases with the GLANCE tool was disseminated to clinicians at the University of California San Diego. Participants were asked to comment on whether GLANCE provided additional useful information and whether it impacted their clinical management using 5-point Likert scale items (Fig. 2). They also completed a System Usability Scale (SUS) questionnaire, a standardized instrument for assessing usability.

Results: Seven clinicians (two attendings, two fellows, two residents, and one optometrist) participated in the pilot. The mean SUS score of GLANCE was 62.5/100, which is normalized into the 35th percentile. The mean SUS score among respondents ages 35-44 (75) was greater than ages 65-74 (45). The mean score among female respondents (67.5) was greater than male respondents (57.5). Respondents generally agreed that they trusted GLANCE and that it provided useful information, but disagreed that they would decrease VF testing frequency (Fig.2).

Conclusions: Clinicians agreed that GLANCE provided useful information but were generally not yet willing to allow AI tools to significantly alter their clinical management. Further research is needed to understand how to increase trust in AI models, improve the usability of visualization tools and interfaces, and optimize the integration of AI-based tools into ophthalmic workflows among a diverse group of clinicians.

CONTROL ID: 3704831

SUBMITTER (NAME ONLY): Nitish Mehta

TITLE: Predicting outcomes and treatment frequency following monthly intravitreal aflibercept for macular edema secondary to central retinal vein occlusion: a machine learning model approach

SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To develop machine learning (ML) algorithms to predict visual and anatomic outcomes and treatment frequency in patients with macular edema secondary to central retinal vein occlusion (MEfCRVO) at 52 weeks after undergoing treatment with aflibercept.

Methods: A dataset of 198 patients with MEfCRVO treated with monthly IAI 2 mg for 24 weeks in the COPERNICUS (n=107) and GALILEO (n=91) trials was used to develop ML algorithms. In both trials, patients were switched after 6 monthly intravitreal aflibercept injection (IAI) at week 24 to pro-re-nata (PRN) dosing through Week 52. The ML algorithm was used to predict the absolute and mean change best-corrected visual acuity (BCVA) from baseline to Week 52, the proportion of patients with ≥15-letter gain at Week 52, the absolute and mean change from baseline in central subfield thickness (CST) at Week 52, and IAI frequency during Weeks 24−52. Random Forest was used to develop the ML algorithms. Algorithm performance was assessed using correlation coefficient (r) and area under the curve (AUC) for continuous and categorical variables, respectively. Predictive factors identified with ML algorithms were confirmed using univariate analyses.

Results: The ML algorithm predicted the actual observed values at Week 52 with strong correlation (r) for absolute BCVA (r=0.87), change in BCVA from baseline (r=0.76), gain of ≥15 letters (AUC=0.81), and change in CST from baseline (r=0.76). BCVA at weeks 16, 20, and 24 were predictors of absolute BCVA; BCVA at baseline, week 20 and week 24 were predictors of change in BCVA; BCVA at baseline and at Week 20 were predictors of ≥15-letter gain; and CST and BCVA at baseline were predictors of change in CST. There was no correlation (r=0.07) between predicted and observed absolute CST at Week 52. ML algorithm predicted PRN injection frequency from Week 24 through Week 52 with high accuracy (AUC=0.83). Key factors predicting injection frequency were CST at baseline and at Week 4. Univariate analyses confirmed all predictive factors described herein.

Conclusions: ML algorithms successfully predicted visual and anatomic outcomes as well as dosing frequency with high accuracy, except for absolute CST. ML may help inform patient`s and clinician`s expectations during management of MEfCRVO.

CONTROL ID: 3704851

SUBMITTER (NAME ONLY): Megan Zipperer

TITLE: Toward a Comprehensive Account of Orientation Selectivity in the Retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Zipperer, Anatomical Sciences and Neurobiology, University of Louisville, Louisville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure: Megan Zipperer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While Orientation Selectivity (OS) is a fundamental computation in the visual system, a comprehensive characterization of OS ganglion cell types (OSGCs) in the retina is lacking, the cellular and circuit mechanisms that generate the OS response are incompletely understood, and contributions of OSGCs to subsequent stages of visual processing remain unknown. The purpose of this study was to identify OSGC types in mouse, to investigate the mechanisms that generate their orientation selective selective response, and to identify the contribution of OSGCs to visual processing in downstream thalamic nuclei.

Methods: This study used two-photon fluorescence calcium imaging to survey ganglion cell populations with a genetically encoded calcium indicator in Thy1-GCaMP6f mice, followed by cluster analysis to identify functional types. Innovative intra-experimental analysis of visually-evoked responses allowed targeting of OSGCs for detailed study using electrophysiology and morphological reconstruction. To identify OSGC targets to downstream visual centers, we used state-of-the-art retrograde rabies tracing from thalamus and superior colliculus followed by calcium imaging in the retina.

Results: Our calcium imaging surveys identified six apparent OS types with selectivity for both horizontal and vertically oriented drifting gratings. We identified types that have not been previously described as OS, including a horizontal-preferring RGC matching the 4on type from the Seung Eyewire museum. Amongst these types we identified cells with tuned excitation and tuned inhibition — some with a combination of the two — demonstrating sources for the OS tuning. Preliminary data from retrograde tracing studies implicated one of the vertical-preferring types as synapsing with Wide Field Vertical Cells in superior colliculus (SC), potentially driving OS tuning in SC.

Conclusions: This study identified multiple OSGC types in mouse and provides new insight into the circuit-level tuning mechanisms of these cells. We have begun to resolve correspondences between reported OS RGCs from our dataset and incompletely categorized cell types from previous studies, contributing to a more complete understanding of RGC types and their functional role in the mouse retina. Our novel identification of central targets of OSGCs is an important step toward understanding the role of retinal OS in visual processing of downstream visual centers.

CONTROL ID: 3704884

SUBMITTER (NAME ONLY): Eric Tang

TITLE: Automated instrument-tracking and adaptive-sampling for 4D visualization of ophthalmic surgical maneuvers

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Tang, M. El-Haddad, Y. Tao, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|S. Patel, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Eric Tang: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed El-Haddad: Commercial Relationship(s);Code P (Patent):Vanderbilt University | Shriji Patel: Commercial Relationship: Code N (No Commercial Relationship) | Yuankai Tao: Commercial Relationship(s);Code P (Patent):Vanderbilt University;Code R (Recipient):Leica Microsystems

ABSTRACT BODY:

Purpose: Intraoperative OCT (iOCT) provides real-time imaging data that can be used to aid clinical decision-making and verify completion of surgical goals. However, video-rate 4D iOCT imaging of surgical dynamics is limited by the need to manually align the OCT field-of-view (FOV) to the region-of-interest, thus significantly impacting surgical workflow. Here, we demonstrate automated instrument-tracking at over 120 Hz for 4D imaging and tracking of 25G internal limiting membrane (ILM) forceps at 16 volumes/second.

Methods: A custom spectrally encoded coherence tomography and reflectometry (SECTR) system was used to simultaneously acquire en face spectrally encoded reflectometry (SER) and cross-sectional OCT images. A GPU-accelerated convolutional neural network (CNN) was trained to detect 25G ILM forceps from SER images and corresponding instrument position outputs were used to dynamically modify scan waveforms via a DAQ for tracking. An adaptive-sampling scan protocol was used to densely sample the center of each frame to enhance visualization of tissue interactions (Fig. 1).

Results: Automated instrument-tracking was performed in a retinal phantom with simulated ocular features. SER and OCT images were acquired simultaneously with 1664 x 500 x 50 pix. (spectral x lines x frames) at 16 volumes/second. Images were acquired over a 25 mm x 7 mm lateral FOV and tracking was performed across a 25 mm x 25 mm maximum FOV. Despite out-of-plane motion, the 25G ILM forceps remain centered and localized in the OCT FOV (Fig. 2).

Conclusions: We demonstrate an automated instrument-tracking method that enables video-rate 4D visualization of ophthalmic surgical maneuvers. We believe the proposed methods overcome critical barriers to the adoption of iOCT technology by improving surgical workflow and are broadly applicable for tracking arbitrary surgical instruments during iOCT-guided procedures.

CONTROL ID: 3704948

SUBMITTER (NAME ONLY): Sarunas Daugirdas

TITLE: New Possible Biomarker for Age-Related Macular Degeneration: Increased Retinal Mitochondrial Flavoprotein Fluorescence

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Daugirdas, R.P. Singh, School of Medicine, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S. Daugirdas, J. Muste, K. Seth, A. Iyer, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|M. Russell, Lerner College of Medicine, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|C. Rich, K. Riegger, OcuSciences, Inc., Ann Arbor, California, UNITED STATES|

Commercial Relationships Disclosure: Sarunas Daugirdas: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Russell: Commercial Relationship: Code N (No Commercial Relationship) | Justin Muste: Commercial Relationship: Code N (No Commercial Relationship) | Kanika Seth: Commercial Relationship: Code N (No Commercial Relationship) | Amogh Iyer: Commercial Relationship: Code N (No Commercial Relationship) | Collin Rich: Commercial Relationship(s);Code E (Employment):OcuSciences, Inc. | Kurt Riegger: Commercial Relationship(s);Code E (Employment):OcuSciences, Inc. | Rishi Singh: Commercial Relationship(s);Code I (Personal Financial Interest):Genentech/Roche;Code I (Personal Financial Interest):Alcon/Novartis;Code F (Financial Support):Apellis;Code I (Personal Financial Interest):Zeiss;Code I (Personal Financial Interest):Bausch & Lomb;Code I (Personal Financial Interest):Regeneron;Code F (Financial Support):Graybug

ABSTRACT BODY:

Purpose: Oxidative stress has been implicated as a driver of various vision-impairing retinal diseases, including age-related macular degeneration (AMD). Oxidized retinal mitochondrial flavoproteins emit green light (535 nm) when excited by blue light (467 nm). This flavoprotein fluorescence (FPF) can be measured and used as a quantifiable marker for oxidative damage-induced mitochondrial dysfunction. This study aims to measure FPF average intensity and heterogeneity in patients with early, intermediate, and advanced non-exudative AMD as well as neovascular AMD.

Methods: This prospective cohort study enrolled patients with isolated AMD of any Beckman stage between 2017 and 2021 excluding patients with comorbidities such as glaucoma, ocular hypertension, concomitant retinopathy or uveitis, history of non-cataract ocular surgery, or fluorescein angiogram prior to imaging. Controls were healthy age-matched individuals. In instances of bilateral involvement, each eye was treated separately. FPF average intensity and heterogeneity were recorded using the OcuMet Beacon (OcuSciences, Ann Arbor, MI).

Results: The final analysis included images of 654 eyes (327 AMD eyes, 327 control eyes). The multivariable regression included stage of AMD, age, gender, ethnicity, and smoking status. Intermediate and advanced non-exudative AMD as well as neovascular AMD were correlated with significantly increased FPF average intensity (4.86, CI 2.37-7.34, $p < 0.001$; 11.9, CI 7.70-16.11, $p < 0.001$; 7.24, CI 4.61-9.88, $p < 0.001$, respectively), but early non-exudative AMD was not. Early, intermediate, and advanced non-exudative AMD as well as neovascular AMD were correlated with significantly increased FPF heterogeneity (0.19, CI 0.08–0.30, $p = 0.001$; 0.43, CI 0.36–0.51, $p < 0.001$; 0.59, CI 0.46–0.71, $p < 0.001$; 0.58, CI 0.51–0.66, $p < 0.001$, respectively).

Conclusions: All stages of AMD were associated with increased FPF average intensity and heterogeneity, except early non-exudative AMD, which was only associated with increased heterogeneity. Because FPF imaging provides insight into the health of the retina on a cellular level, this finding of an isolated increase in FPF heterogeneity in early non-exudative AMD could assist with early detection of disease before structural changes are seen on optical coherence tomography.

CONTROL ID: 3704967

SUBMITTER (NAME ONLY): Shaohui Wang

TITLE: Absence of signal peptide peptidase in peripheral sensory neurons affects latency-reactivation in HSV-1 ocularly infected mice

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Wang, U. Jaggi, K. Tormanen, S. Hirose, H. Ghiasi, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Shaohui Wang: Commercial Relationship: Code N (No Commercial Relationship) | Ujjaldeep Jaggi: Commercial Relationship: Code N (No Commercial Relationship) | Kati Tormanen: Commercial Relationship: Code N (No Commercial Relationship) | Satoshi Hirose: Commercial Relationship: Code N (No Commercial Relationship) | Homayon Ghiasi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously reported that HSV-1 glycoprotein K (gK) is involve in exacerbation of eye disease in ocularly infected mice and its binding to signal peptide peptidase (SPP) is required for increased eye disease. In the present study, we investigated the impact of absence of SPP expression in peripheral sensory neurons on HSV-1 infectivity using Avil-SPP$^{-/-}$ mice

Methods: We generated mice lacking SPP specifically in peripheral sensory neurons by crossing Advillin-Cre mice with SPP$^{fl/fl}$ mice. Avil-SPP$^{-/-}$ mice and control mice were infected ocularly with 2 X 10^5 PFU/eye of HSV-1 strain McKrae. Virus replication in the eye and trigeminal ganglia (TG), survival, eye disease, and latency-reactivation were determined in infected mice.

Results: Expression of SPP mRNA and protein were significantly lower in neurons of Avil-SPP$^{-/-}$ mice than in control mice despite similar levels of HSV-1 replication in the eyes of Avil-SPP$^{-/-}$ mice and control mice. Viral transcript levels in isolated neurons of infected mice on day 5 post infection were lower than in control mice. Significantly less LAT, gB, and PD-1 expression was seen during latency in isolated neurons and total trigeminal ganglia (TG) of Avil-SPP$^{-/-}$ mice than in control mice. Finally, reduced latency and reduced T cell exhaustion in infected Avil-SPP$^{-/-}$ mice correlated with slower or no reactivation.

Conclusions: Overall, our results suggest that blocking SPP expression in peripheral sensory neurons does not affect primary virus replication or eye disease but does reduce latency-reactivation. Thus, blocking of gK binding to SPP may be a useful tool to reduce latency-reactivation.

CONTROL ID: 3705004

SUBMITTER (NAME ONLY): Zhihui She

TITLE: Narrow-band, long-wavelength lighting caused hyperopia in normal eyes and retarded minus lens-induced myopia and form deprivation myopia for juvenile tree shrews

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. She, T.T. Norton, T. Gawne, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Zhihui She: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Norton: Commercial Relationship(s);Code P (Patent):University of Alabama at Birmingham | Timothy Gawne: Commercial Relationship(s);Code P (Patent):University of Alabama at Birmingham

ABSTRACT BODY:

Purpose: To examine the effects of narrow-band, long-wavelength (red) ambient light on the maintenance of emmetropization, lens-induced myopia and form-deprivation myopia in juvenile tree shrews.

Methods: Seventeen tree shrews (Tupaia belangeri) were reared in red light (14-hr red, 10-hr dark; peak wavelength = 634 nm, half bandwidth = 9μm; ~600 lux on cage floor) from 24 to 35 days of visual experience either without visual treatment (Binocular Red Controls, n = 7), with concurrent monocular -5D lens (Red -5D, n = 5), or monocular diffuser treatment (Red FD, n = 5). Non-cycloplegic refractions and ocular dimensions were measured in awake animals using an autorefractor and an optical biometer, respectively. Data were compared with those obtained from animals previously reared in colony “white” light without visual treatment (Colony Controls, n = 7), with concurrent monocular -5D lens (Colony -5D, n = 5) or monocular diffuser (Colony FD, n = 10).

Results: Red light produced relative hyperopia in the Binocular Red Controls (closed red circles in both panels. Averaged refraction, Red-Controls vs. Colony-Controls: +3.0 ± 0.7D vs. +1.0 ± 0.4D) and in the untreated eyes of the lens-rearing subjects (panel A: Red -5D vs. Colony -5D, +2.5 ± 0.5D vs. +1.3 ± 0.3D; panel B: Red FD vs. Colony FD, +2.4 ± 0.3D vs. +1.0 ± 0.2D). The hyperopia in the untreated eyes of the Red -5 D and Red FD groups occurred with a two-day delay compared with the Binocular Red Controls and remained about 1 D less hyperopic. Red light slowed the myopic changes in the treated eyes of the Red -5D and Red FD subjects and reduced the final degree of myopia (Red -5D vs. Colony -5D, -1.1 ± 0.9D vs.-3.8 ± 0.3D, $p < 0.05$; Red FD vs. Colony FD, -0.3 ± 0.6D vs. -5.4 ± 0.7D, $p < 0.05$). The degree of lens-induced myopia (treated – untreated eyes, -3.6 ± 0.4D vs. +5.1 ± 0.2D of Colony -5D) and form-deprivation myopia (Red FD vs. Colony FD, -2.7 ± 0.4D vs. -6.4 ± 0.6D) were also reduced ($p < 0.05$). The refractive changes were inversely correlated with the changes in vitreous chamber depth ($r = -0.91$, $p < 0.05$).

Conclusions: For tree shrews, red light slowed ocular growth and caused hyperopic shifts not only in eyes that had previously attained a near-emmetropic refractive state (Gawne et al., 2017), but also in minus-lens-treated eyes and diffuser-treated eyes.

CONTROL ID: 3705029

SUBMITTER (NAME ONLY): Patrick Wang

TITLE: Evaluation of tensile strength and burst pressure of slipknots and surgeon’s knots

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Wang, School of Medicine, Queen's University, Kingston, Ontario, CANADA|D. Johnson, Ophthalmology, Queen's University, Kingston, Ontario, CANADA|

Commercial Relationships Disclosure: Patrick Wang: Commercial Relationship: Code N (No Commercial Relationship) | Davin Johnson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Despite the frequency and importance of corneal suturing by ophthalmologists, there is a paucity of data comparing the tensile strength of these knots. This study aims to compare the tensile strength of the slipknot versus surgeon’s (3-1-1) knot using 10-0 nylon sutures.

Methods: Initial testing of cadaveric phakic eyes was performed by closing a 5mm linear full-thickness corneal wound with either a slipknot or surgeon’s knot using 10-0 nylon suture material. Burst pressure was measured using a cardiac transducer inserted into the vitreous cavity and defined as the intraocular pressure (IOP) at suture failure after constant infusion of saline solution via a 25-gauge needle into the anterior chamber (Fig 1). Follow-up testing of tensile suture strength was performed using a digital force tensiometer. A loop of suture was tied around a tuberculin syringe and the loop was gently removed and mounted on a stand with the tensiometer. Tensile testing was performed at a rate of 0.25mm/s on each type of knot and ultimate tensile strength was measured as the maximum load just prior to knot failure (Fig 2). Light microscopy was used to analyze the site of suture failure. All suture knots were tied by an experienced corneal surgeon and outcome assessors were blinded to each knot type.

Results: 6 cadaveric eyes (3 slipknot, 3 surgeon’s knot) were obtained to assess burst pressure. Minor aqueous leakage through the wound was observed in all cadaveric eyes however both suture knots did not fail despite measured IOP over 300mmHg. A total number of 50 knots (25 surgeon’s knot, 25 slipknot) were tied for tensile testing. The ultimate tensile force upon breakage was higher in the surgeon’s knots compared with that in slipknots (0.75 vs. 0.59 N, $p = 0.02$). After tensile testing, light microscopy revealed that within the collected slipknot sutures (n=8), 3 unraveled and 5 experienced breakage. Of collected surgeon’s knot sutures (n=11), 2 had unraveled and 9 experienced breakage.

Conclusions: Surgeon’s knots provide higher tensile strength compared to slipknots in an experimental model. However, when properly tied, both types of knots provide excellent strength, but it is unclear if this difference is clinically relevant with in vivo conditions.

CONTROL ID: 3705075

SUBMITTER (NAME ONLY): Jianbo Zhou

TITLE: Evaluation of Venturi flow in new phacoemulsification packs with small-bore, dual-durometer aspiration tubing

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zhou, Research and Development, Johnson and Johnson Surgical Vision, Inc., Santa Ana, California, UNITED STATES|

Commercial Relationships Disclosure: Jianbo Zhou: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision, Inc.

ABSTRACT BODY:

Purpose: A relatively large size aspiration tubing in fluidics pack could result in increased flow during cataract surgery when using Venturi mode in a gravity-based phacoemulsification system, causing chamber instability and compromising the balance of holdability and followability. New fluidics packs using small-bore, dual-durometer aspiration tubing were constructed. This study will evaluate aspiration flow of the newly constructed fluidics packs with a new phacoemulsification machine in Venturi mode in a laboratory setup.

Methods: The inner layer of the aspiration tubing of the new fluidics packs uses a stiffer material with a smaller inner diameter than existing products, while the outer layer is soft and maintains flexibility. These packs were tested with a Phaco handpiece and three different Phaco tips (19, 20, and 21 Gauges) in a newly available phacoemulsification machine set to Venturi mode, along with existing packs as the control arm. A glass beaker filled with deionized (DI) water was placed on a weight scale with water level started for each test run at the same height as the vacuum sensor in the Phaco machine. The Phaco tip was submerged in the DI water and the Venturi vacuum was applied for 15 seconds. The loss of the water in the beaker was measured for calculation of the aspiration flow rate with Venturi vacuum ranging from 100 to 600 mmHg in 100 mmHg step. Additionally, the effect of viscous fluid (a water/glycerin mixture) on the aspiration flow rate was also investigated with the 20 Gauge Phaco tip.

Results: The relationship between the aspiration flow and vacuum was nonlinear. The new fluidics packs produced smaller aspiration flow rates than the existing packs, with a 20% reduction for the 20 Gauge Phaco tip configuration. The differences were statistically significant ($p < 0.01$). At least 30% higher vacuum can be used with the new fluidics packs to achieve the same flow rate compared to the existing packs. Using viscous fluid also lowered the flow rate further.

Conclusions: In laboratory test, new fluidics packs with small-bore, dual-durometer aspiration tubing produced markedly smaller aspiration flow rates compared to the existing packs at the same vacuum settings in Venturi mode. The use of the new fluidics packs provides a better flow and vacuum control for improved chamber stability and a more balanced followability and holdability during phacoemulsification.

CONTROL ID: 3705106

SUBMITTER (NAME ONLY): Caroline Awh

TITLE: Long-term visual acuity outcomes of fovea-involving rhegmatogenous retinal detachments following pars plana vitrectomy (PPV) or combined PPV/scleral buckle surgery

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Awh, J. Abraham, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|K.E. Pedersen, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Caroline Awh: Commercial Relationship: Code N (No Commercial Relationship) | Karina Pedersen: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Abraham: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Singh: Commercial Relationship(s);Code C (Consultant/Contractor):Genentech/Roche;Code C (Consultant/Contractor):Alcon/Novartis;Code C (Consultant/Contractor):Apellis;Code C (Consultant/Contractor):Graybug;Code C (Consultant/Contractor):Zeiss;Code C (Consultant/Contractor):Bausch + Lomb;Code C (Consultant/Contractor):Regeneron Pharmeceuticals, Inc

ABSTRACT BODY:

Purpose: Macular involvement is often reported as a poor prognostic factor of rhegmatogenous retinal detachments (RRD). Although patients who undergo RRD repair are reported to reach stable vision 3-6 months after surgery, few studies report visual outcomes longer than 2 years after repair of macula-off RRD with pars plana vitrectomy (PPV), the current preferred method of repair. The purpose of this study is to evaluate visual outcomes of fovea-involving RRD repair with PPV or combined PPV/scleral buckle (SB) in eyes with at least 5 years of post-operative data.

Methods: This retrospective case series evaluated eyes that underwent fovea-involving RRD repair with PPV or PPV/SB at the Cole Eye Institute. Eyes with single operation anatomic success and 5 years or more of follow-up were included. Eyes with other ophthalmic pathology affecting central vision were excluded. Best visual acuity (BVA) was measured in Snellen visual acuity and converted into Early Treatment Diabetic Retinopathy Study (ETDRS) score. Paired t-test analysis compared changes in BVA between two time-points. Multiple linear regression analyses evaluated the impact of age, lens status at baseline, and pre-operative BVA on final BVA and total gain in BVA.

Results: 51 eyes were included. Mean time to final follow-up was 6.55±1.38 years. Mean pre-operatively BVA was 21.47±23.20 (~20/400) and improved to 72.72±16.52 (~20/32) and 78.14±10.16 (~20/25) at the 1-year and final follow-up, respectively ($p<0.001$). Thirteen of 45 eyes (28.89%) had an improvement in BVA of at least 10 letters from the 1-year to the final follow-up. Mean 1-year BVA was significantly different from final BVA ($p=0.002$). Average BVA was 20/40 or better in 35/45 eyes (75.56%) at 1-year and 45/51 eyes (88.24%) at final follow-up. Average BVA was 20/200 or worse in 1/51 (1.97%) eyes at final follow-up. In regression analysis, a greater total gain in BVA was associated with a lower pre-operative BVA ($p<0.001$) but not with age or lens status. In linear regression, no parameter correlated with final BVA.

Conclusions: Patients with fovea-involving RRD successfully repaired with PPV or PPV/SB have favorable long-term visual acuity outcomes. BVA may continue to significantly improve even beyond 1 year after surgery, and the majority of patients have a BVA of 20/40 or better 5 years after surgery.

CONTROL ID: 3705117

SUBMITTER (NAME ONLY): Pamela Capellan

TITLE: Diabetic Retinopathy Screening Experiences among Hispanic, Spanish-Speaking Adults: “¡Trátame Como Familia!”

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Capellan, Weill Cornell Medicine, New York, New York, UNITED STATES|E. Greig, Department of Ophthalmology, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|E. Greig, K.H. Nwanyanwu, R. Gonzalez-Colaso, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Pamela Capellan: Commercial Relationship: Code N (No Commercial Relationship) | Eugenia Greig: Commercial Relationship: Code N (No Commercial Relationship) | Kristen Nwanyanwu: Commercial Relationship: Code N (No Commercial Relationship) | Rosana Gonzalez-Colaso: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To characterize experiences with diabetic retinopathy screening among Spanish-speaking adults living with diabetes.

Methods: Two trained authors conducted in-depth, semi-structured video interviews with 5 Spanish-speaking adults living with diabetes in New Haven, CT between March and June of 2021. Non-Spanish-speaking Hispanic participants were non-eligible for the study. Two independent readers coded each interview transcript and identified thematic categories based on grounded theory and constant comparative methodology. Emerging themes were organized around the socio-ecological framework using unique codes (Figure 1). Themes and quotes were translated to English to facilitate consensus analysis. We achieved thematic saturation for five themes.

Results: Five recurrent cultural and linguistic-sensitive themes emerged in our interviews: personal accountability, reliable support systems, continuity of care, clear communication, and seasonal barriers. 1) At the individual level, participants viewed loss of vision as an act of self-negligence and held themselves accountable for managing their disease. 2). At the interpersonal level, participants relied on a trusting support system that extended outside of their family including their social networks (e.g., friends). 3) At the community level, participants valued long-term familial-like interactions with providers. 4) At the organizational level, participants valued thorough communication with all members of the care team and equated clear communication with provider excellence. 5). At the structural level, inclement weather and transportation were identified as barriers to appointment attendance.

Conclusions: Understanding the specific needs and preferences of Hispanic adults living with diabetes is important to delivering high-quality ophthalmologic care. This is particularly important among patients with limited English proficiency who face further barriers to care, such as language and cultural differences. Understanding the beliefs and attitudes of Hispanic patients can help providers develop behaviors and interventions that specifically motivate this high-risk population to participate in diabetic retinopathy screening.

CONTROL ID: 3705118

SUBMITTER (NAME ONLY): Erin Hisey

TITLE: Antimicrobial Peptide Expression of the Equine Ocular Surface and Amniotic Membrane

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.A. Hisey, B. Da Costa Martins, C.J. Murphy, S.M. Thomasy, B.C. Leonard, Surgical and Radiological Sciences, University of California Davis, Davis, California, UNITED STATES|C.J. Murphy, S.M. Thomasy, Ophthalmology and Vision Science, University of California Davis School of Medicine, Davis, California, UNITED STATES|

Commercial Relationships Disclosure: Erin Hisey: Commercial Relationship: Code N (No Commercial Relationship) | Bianca Da Costa Martins: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Murphy: Commercial Relationship: Code N (No Commercial Relationship) | Sara Thomasy: Commercial Relationship: Code N (No Commercial Relationship) | Brian Leonard: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The antimicrobial peptide (AMP) expression pattern of the equine ocular surface and amniotic membrane are currently undefined. We hypothesized that putative orthologs of both cathelicidins and defensins, two AMP subfamilies, expressed by the ocular surface of humans would be expressed by the equine cornea, conjunctiva and amniotic membrane. This study characterized AMP expression from healthy equine eyes and amniotic membrane to serve as a reference for future investigations of equine microbial keratitis and for the potential use of amniotic membrane for therapeutic corneal grafts.

Methods: RNA was extracted from equine corneal epithelium (n=5), conjunctiva (n=4), amniotic membrane (n=6), testis (n=4) and epididymis (n=4). Testis and epididymis were used as positive controls as they have been shown to highly express AMPs in other species. A targeted qPCR approach was used to investigate the equine orthologs of the three most functionally relevant beta-defensins (DEFB1, DEFB4B, and DEFB103A) of the ocular surface and amniotic membrane of humans. RNA from one sample of corneal epithelium, conjunctiva and amniotic membrane were submitted for 3'Tag-sequencing to further investigate their AMP expression.

Results: Expression of equine orthologs of DEFB1, DEFB4B and DEFB103A were identified in equine corneal epithelium, conjunctiva and amniotic membrane. DEFB103A was expressed at the highest amounts in corneal epithelium, while DEFB4B was most highly expressed in conjunctiva and amniotic membrane. 3'Tag-sequencing confirmed these findings and identified expression of five additional beta-defensins, 11 alpha-defensins and two cathelicidins. The alpha-defensins showed higher normalized read counts than the beta-defensins in these tissues.

Conclusions: This study characterized the AMP expression profile of the equine cornea, conjunctiva and amniotic membrane. We identified high expression of DEFB103A in the cornea suggesting that it plays a key role in the innate immunity of the equine eye. We also determined that equine amniotic membrane expresses a moderate amount of AMPs suggesting it could provide an antimicrobial effect as a surgical corneal graft in structurally compromised eyes. Finally, we identified high expression of alpha-defensins in ocular tissues and amniotic membrane. Future studies will focus on defining the antimicrobial activity of these AMPs and determining their role in microbial keratitis.

CONTROL ID: 3705212

SUBMITTER (NAME ONLY): Amany Tawfik

TITLE: Role of Warburg Effect in Age-Related Macular Degeneration

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Tawfik, William Beaumont School of Medicine, Eye Research Center(OUWB)/ERC, Oakland University, Rochester, Michigan, UNITED STATES|Y. Samra, Department of Biochemistry, Faculty of Pharmacy, Mansoura University, Mansoura, EGYPT|P. Rajpurohit, Augusta University, Augusta, Georgia, UNITED STATES|Y. Zaidi, Augusta University, Augusta, Georgia, UNITED STATES|W. Elkalawozgy, Oakland University, Rochester, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recently impaired glycolysis was reported in patients with age-related macular degeneration (AMD) with a high lactate/pyruvate ratio suggesting that increased lactate levels may be implicated in AMD pathogenesis. Elevated serum homocysteine (Hcy) (known as Hyperhomocysteinemia, HHcy) was reported in many AMD clinical studies, suggesting an association between HHcy and the risk of AMD. We reported a direct impact of HHcy on retinal pigment epithelium (RPE) structure, barrier function, and choroidal neovasularization(CNV). We hypothesis that HHcy contributes to AMD via inducing metabolic switch in the mitochondria, in which cells predominantly produce energy by the high rate of glycolysis simulating cancer cells “Warburg” effect, rather than by comparatively low rate of glycolysis followed by oxidation of pyruvate in mitochondria as in normal cells. Increased glycolysis results in an increase in the rate of glucose uptake and preferential production of lactate, increasing cellular acidity with subsequent activation of angiogenesis, RPE barrier dysfunction, and CNV induction.

Methods: Evaluation of cellular energy production under HHcy was evaluated (both in vivo, using mice with HHcy ($cbs^{+/-}$ & $cbs^{-/-}$) and in vitro, using RPE cells) by Seahorse Analyzer, multitracker-based cytofluorimetry, immunofluorescence, and the western blot (WB) experiments. The Seahorse extracellular flux (XF) analyzer evaluates mitochondrial respiration by measuring oxygen concentration and proton flux in the cell supernatant over time. These measurements are expressed as mitochondrial oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) as indicative of oxidative phosphorylation and glycolysis.

Results: HHcy showed a significant increase of both OCR and ECAR both in CBS mice ($cbs^{+/-}$ &$cbs^{-/-}$) and in vitro (Hcy-treated Human ARPE-19) compared to wild-Type mice retina and untreated ARPE-19 cells. Furthermore, HHcy upregulated glycolytic enzyme in RPE cells and inhibition of Glut1(the main glucose transporter in the RPE) was able to reduce glycolysis in Hcy-treated RPE and improve albumin leakage& CNV induction in Hcy-injected mouse eyes.

Conclusions: The current study suggests that Homocysteine causes a metabolic switch from mitochondrial respiration to glycolysis in RPE during AMD. Resulting in the activation of angiogenesis via activation of VEGF. Therefore, targeting Homocysteine clearance could be a novel therapeutic strategy for AMD.

CONTROL ID: 3705223

SUBMITTER (NAME ONLY): Rajendra Gyawali

TITLE: Clinical indicators for assessment of optometric diabetic eyecare in Australia

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Clinical indicators for diabetic eyecare were previously developed from clinical guidelines published before 2013 and were tested in a nationwide patient record card audit (iCareTrack study), to assess the appropriateness of optometric diabetic eyecare delivery in Australia. To reflect emerging evidence, updated guidelines, and contemporary optometry practice, this study aimed to update the diabetic eyecare clinical indicators.

Methods: Candidate indicators included existing iCareTrack and new indicators derived from nine high-quality evidence-based guidelines identified through a systematic review. A two-round modified Delphi process with an expert panel (eight optometrists and one ophthalmologist) was used for consensus on the candidate indicators. In round-1, the experts rated the impact, acceptability, and feasibility of the indicators on a 9-point scale and voted for inclusion or exclusion. Consensus on inclusion was defined when the median scores for impact, acceptability, and feasibility were ≥7 and >75% of experts voted for inclusion. Any indicator that failed to reach consensus was presented for re-evaluation in round-2, with updated evidence summaries, de-identified group feedback and any modification suggestions from round-1.

Results: Of the 45 candidate indicators presented in the Delphi process, 33 were retained in the final list. The final indicators were grouped in the domains of history taking (13), examination (8), recall (5), referral (6), and patient education (1). All 13 iCareTrack indicators were retained either in the original format or with minor modifications. New history taking indicators included documenting the type of diabetes, serum lipid level, pregnancy status, systemic medications, renal disease, Indigenous status, non-English speaking background, and details of patient's general practitioner. Examination of pupil, intraocular pressure, optical coherence tomography, and diabetic retinopathy grading were added. Recall period for high-risk group without retinopathy, communication with general practitioner, referral of high-risk proliferative retinopathy, and patient education on regular follow up were also added.

Conclusions: The study described a systematic process of updating clinical indicators. These updated indicators will be the basis for a self-audit tool and allow assessment of diabetic eyecare appropriateness in Australia.

CONTROL ID: 3705225
SUBMITTER (NAME ONLY): Abhinav Bheemidi
TITLE: Risk Factors For Cancellation of Ophthalmic Surgery
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Surgery cancellations affect patient satisfaction and ocular health, and negatively impact the efficiency of healthcare systems. By understanding causes of ophthalmic surgery cancellations and related predictive factors, they can be minimized. This study is a retrospective, non-randomized study that aims to determine risk factors for ophthalmic surgery cancellations.

Methods:

The study included a consecutive sample of patients above the age of 18 who had an ophthalmic surgery scheduled at Cole Eye Institute, Cleveland Clinic, OH between January 2012 and December 2019. An automated search pull identified 75,908 scheduled surgeries (63,987 completed and 11,921 cancelled surgeries; Figure 1). Statistical analysis was performed using R (version 3.5.1) to examine factors that impact risk for surgery cancellation.

Results: Analysis was performed on 69,963 scheduled surgeries (57.37% Female, 42.63% Male; Mean age of 62.72 years; 59,959 completed and 10,004 cancelled surgeries). Cataract surgery was the most common surgery scheduled, accounting for 56.32% of scheduled surgeries. Of the 2,384 cancelled surgeries with reasons provided, the most common causes of cancellation were patient refusal (38.42%), patient health condition (18.79%), and reschedule (15.27%). Female sex, black race, patient age less than 50 years, cataract surgeries, regional mean household income greater than $82,900, Medicare insurance, and geographical distance of less than 10 miles from home to the surgery site all significantly increased the risk of surgery cancellation ($p<0.01$; Table 1).

Conclusions: This study successfully identified several factors predicting ophthalmic surgery cancellation. The clinical insights gained from these lines of inquiry may be used to construct models that not only identify patients at greater risk for cancellation but also highlight which interventions would have greatest efficacy in preventing ophthalmic surgery cancellations.

CONTROL ID: 3705252

SUBMITTER (NAME ONLY): Shin Kadomoto

TITLE: Detection of Reticular Pseudodrusen on Embossed Color Fundus Photos

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Near-infrared reflectance (IR) and fundus autofluorescence (FAF) have been shown to be more sensitiive than traditional flash color fundus photographs (CFP) for detection of reticular pseudodrusen (RPD). IR and FAF images, however, are not always available, particularly in historical datasets which may only contain CFP iamges. In this study, we evaluate whether an embossing image processing technique can improve the detection of RPD on CFP.

Methods: Seventy one eyes of 41 subjects (mean age 61.2 ± 5.5 years; range: 53 - 74 years) with RPD were used in this study. Ground truth determination of the presence of RPD in these eyes was established based on the identification of RPD on both IR and FAF images by two independent, masked retinal specialists. A single CFP from the same visit for each case was processed using an embossing technique in which each pixel was replaced by a highlight or a shadow depending on light and dark boundaries present in the original CFP image to yield and embossed photograph (EP). The CFP and EP images were grader separately by two additional masked graders for the presence of RPD. RPD were also classified into two types: dot and ribbon. The dot and ribbon type RPD detection rate on CFP and EP images were assessed indivisually by two other graders. Sensitivity of EP and CFP for detection of RPD was compared to the IR/FAF ground-truth assessment.

Results: Dot type RPD were noted in all 71 eyes in the IR and FAF images, but were detected in only 39 eyes on the CFP images (54.9%), whereas they were detected in 65 eyes from based on the EP images (91.5%). Ribbon type RPD were noted in all 71 eyes in the IR and FAF images, but in only 27 eyes on the CFP images (38.0%) and 14 eyes on the EP images (19.7%). Post-hoc review of the images, confirmed that EP images could visualize dot type RPD lesions not evident on the original CFP image (Figure, arrow). Whereas all 39 eyes in which RPD were noted on CFP also showed RPD on the EP images, EP images demonstrated RPD in 26 of the 32 eyes (81.3%) in which RPD were not visible on the CFP image.

Conclusions: Embossing CFPs can improve the detection of RPD, particurly dot type RPD. As eyes with ribbon type RPD generally also feature dot type RPD, the embossing technique may be a useful tool for better assessing the true frequency of RPD in datasets where only CFP images are available.

CONTROL ID: 3705286

SUBMITTER (NAME ONLY): Line Petersen

TITLE: Retinal vasomotion is increased by increased systemic blood pressure and is reduced by flickering light in normal persons

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal vasomotion is spontaneous oscillations in the diameter of retinal arterioles with consequent changes in retinal blood flow. The phenomenon has been shown to be important for oxygenation and fluid homeostasis, and it has been hypothesized that disturbances in retinal vasomotion may be involved in the pathogenesis of diabetic retinopathy. However, it is unknown how retinal vasomotion is affected by physiological changes in the blood pressure and retinal metabolism.

Methods: 55 normal persons aged 20-30 years were studied. Video recordings (25 frames/sec) were performed over 120 seconds at an upper or lower temporal arteriole at rest, during an increase in the arterial blood pressure induced by lifting a hand weight of 2 kg and during exposure to flickering light at 25 Hz. The arteriolar diameter was determined based on the contrast to the surrounding retina in each of the 3000 consecutive image frames. The diameter changes were subjected to Fourier analysis and the power was calculated for the very low (VLF: <0.04 Hz), low (LF: 0.04-0.15 Hz), high (HF: 0.15-0.4 Hz), very high (VHF: 0.4-2.0 Hz) and the ultra-high (HF: 2-12.5 Hz) frequency bands.

Results: During rest the powers were (mean±SD): VLF: (1.48 ± 0.97), LF: (2.69 ± 1.69), HF: (2.48 ± 1.90), VHF: (5.33 ± 1.94), and UHF: (8.42 ± 2.76). Isometric exercise significantly increased the power of the VLF and the VHF bands ($p<0.0001$ for both comparisons), whereas exposure to flickering light reduced the power to at least the half at all frequency bands ($p<0.0001$ for all comparisons).

Conclusions: The amplitude of spontaneous oscillations in the diameter of retinal vessels are increased by increased blood pressure and reduced by stimulation of retinal metabolism by flickering light. These responses may play a role in the regulation of retinal blood flow under normal conditions. Disturbances in these responses might be involved in the pathogenesis of retinal vascular disease.

CONTROL ID: 3705289

SUBMITTER (NAME ONLY): Xiu Juan Zhang

TITLE: Characteristics of Peripapillary Gamma Zone in Children with Different Refractive Status: The Hong Kong Children Eye Study

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Myopia is the most common ocular disorder worldwide and axial elongation in myopic eyes is accompanied by scleral remodeling of around the optic nerve head (ONH).This study aims to assess the characteristics and the prevalence of the peripapillary gamma zone among the myopic, emmetropic, and hyperopic eyes of Chinese children.

Methods: This is a population-based study. 1274 children aged 6–8 years were recruited from the Hong Kong Children Eye Study (HKCES). All participants completed ocular examinations, including cycloplegic auto-refraction and axial length (AL) measurements. The optic disc was imaged using a Spectralis OCT unit (Heidelberg Engineering, Heidelberg, Germany), adopting a protocol with 24 equally spaced radial B-scans. The peripapillary gamma zone was defined as the region between the Bruch's membrane opening (BMO) and the border of the optic disc, which was defined by the peripapillary border tissue.

Results: The prevalence of the peripapillary gamma zone was much higher in myopic eyes (36.3%) than in emmetropic (16.1%) and hyperopic eyes (11.5%; P<0.001). In the subgroup analysis, the axial length (AL) of eyes with a peripapillary gamma zone was significantly longer than for eyes without a peripapillary gamma zone among the myopia group (24.28mm vs. 23.79mm; P<0.001), but not in the emmetropia (23.21mm vs. 23.15mm; P=0.117) or hyperopia groups (22.79mm vs. 22.67mm; P=0.119). Longer AL was associated with a higher chance of peripapillary gamma zone occurrence in the myopic eyes (OR=1.874, P<0.001), but not in the emmetropic (OR=1.033, P=0.913) or hyperopic eyes (OR=1.044, P=0.883) after adjusting for demographic, systematic, and ocular variables. The locations of the peripapillary gamma zone were different between myopic and non-myopic eyes (P<0.001).

Conclusions: The peripapillary gamma zone was observed in both myopic and non-myopic children, whereas it was associated with an AL elongation only in myopic eyes, suggesting that the mechanisms peripapillary gamma zone were different in myopic and non-myopic eyes.

CONTROL ID: 3705295

SUBMITTER (NAME ONLY): Masakazu Hirota

TITLE: Evaluation of Depth Perception During a Light Field Head-Mounted Display

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Recently, the remote control of machines using virtual reality technology has been attracting wide attention because it avoids the risk of infection and secondary disasters. However, a concern has been identified that conventional three-dimensional (3D) images worsen the accuracy of work due to deterioration in-depth perception. Therefore, since head-mounted displays (HMDs) based on the light field (LF) technology have the advantage of reproducing light flux for each pixel and creating an environment close to natural vision, we compared the depth of LFHMD, 3DHMD, and real space-based visions in this study.

Methods: A total of 25 young healthy volunteers (mean age: 20.6 ± 0.7 years) participated in the study. First, TransRay^{TM} (Toppan Inc.), which can construct a virtual space for both LFHMD and 3DHMD at 0.2–1.2 m in front of the eyes; AS-7JS7 (Kowa Co., Ltd.), was used for depth of vision in real space. Then, the LFHMD depth of vision was measured at a reference distance of 0.5 m. Next, the depth of vision in real space was measured at a reference distance of 2.5 m. Subsequently, bilateral stationary targets were used as cones, the central moving target as a sphere, and three reciprocal measurements were made six times at a speed of 5 cm/s.

Results: As observed, although the deviation from the reference distance was insignificantly different between LFHMD (9.0 ± 22.9 mm) and real space (−6.5 ± 9.3 mm; $P = 0.092$), the deviation from the reference distance was significantly greater in 3DHMD (11.8 ± 32.9 mm) than in real space ($P = 0.038$).

Conclusions: Thus, our findings propose that LFHMD provides better depth perception closer to real space than 3DHMD.

CONTROL ID: 3705308

SUBMITTER (NAME ONLY): Isa van der Veen

TITLE: Clinical and histopathologic characteristics of autosomal dominant cone-rod dystrophy caused by mutations in the CRX gene

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cone-rod homeobox (CRX) is an essential protein for the development and maintenance of rod and cone photoreceptors. Mutations in the gene can lead to several forms of inherited retinal degeneration. In this multicenter study, we describe the phenotypic, genotypic and histopathological characteristics of CRX-associated retinal dystrophies.

Methods: In order to characterize the phenotypic and genotypic features, medical records were reviewed. Clinical data and imaging was collected from multiple European centers to describe the phenotypic and genotypic spectrum. Furthermore, immunohistochemistry was performed on the retina of a patient with CRX-associated retinal dystrophy, to visualize photoreceptor degeneration. Tissue fragments were excised from the macular and peripheral areas of the patient's retina and an age- and gender-matched control. Cryosections were obtained and immunostained for rod, cone and bipolar cell specific proteins and imaged with a confocal microscope.

Results: In 39 patients from 31 families, 21 different autosomal dominant CRX variants were identified, including missense and frameshift mutations. Phenotypes were highly heterogeneous, ranging from mild, late-onset macular dystrophy to Leber congenital amaurosis leading to congenital blindness. Age at onset ranged from at birth to the 8th decade. Mean visual acuity was 0.16±0.21 Snellen at a mean age of 52.3±19.9 years.
Immunohistochemical analysis of the eye of a 17-year-old patient with a deletion of exons three and four in one allele of CRX revealed extensive photoreceptor degeneration and loss of laminar integrity in the neuroretina. The degeneration was concentrated in the central retina, where the thickness of the outer nuclear layer was markedly reduced. Near the macula, complete loss of rods and short-wavelength cones was observed. Mislocalized photoreceptor nuclei and outer segment proteins were observed throughout the retina.

Conclusions: This study found a large phenotypic variation in patients with mutations in CRX. Histopathological analysis demonstrated widespread photoreceptor cell loss, especially in the central retina. These findings mimic features commonly found in animal models for CRX-associated retinal disease and align with clinical observations.

CONTROL ID: 3705312

SUBMITTER (NAME ONLY): Antonia Neumann

TITLE: Visual adaptation to different levels of peripheral optical scattering

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Adaptation to high- or low-contrast is a known process of the visual system. Moreover, adaptation, guided by retinal mechanisms, also influences refractive development. So far, central contrast adaptation has been measured centrally or peripherally after peripheral adaptation, however not centrally after peripheral adaptation. Therefore, this study aimed to investigate the short-term influence of different levels of peripheral optical scattering on central visual performance, by assessing chromatic and achromatic contrast sensitivity (CS).

Methods: In total, 19 participants were included in the study. Each participant performed three blocks of scattering conditions: control, 0.4 and 0.8 Bangerter foil, each with a clear central aperture of 8.0 mm. For each block, CS was tested monocularly at three different adaptation times (at 0 min, 30 min and 90 min) using a 2IFC-modified version of the Tuebingen CS test for 3 cpd and 12 cpd, while the fellow eye was covered. Chromatic stimuli were designed to match the cone type sensitivities of S-, M- and L-cones using the method of silent substitution. During CS testing, pupil size was controlled to ensure a smaller pupil size than the clear central zone of the Bangerter foils. CS changes were analyzed using linear mixed models.

Results: The sensitivity of cone-types differed significantly from each other (all $p<0.05$), except the achromatic and L-cone type ($p=0.87$), where the S-cone type showed the minimum sensitivity across all testing conditions and M-cone CS exhibited the maximum, see Figure 1. Overall, CS was also influenced by the level of peripheral contrast reduction, while the 0.4 Bangerter foil showed a significant reduction compared to the control condition ($p=0.04$) and the 0.8 Bangerter foil condition ($p=0.0008$). Moreover, no central contrast adaptation to peripheral scattering was found, but reversely, a reduction of 0.11 log(CS) after 90 min and of 0.08 log(CS) between 30 min and 90 min (both $p<0.0001$).

Conclusions: Central visual performance depends on the level of peripherally imposed scattering, which affects all cone types equally and non-selective. Adaptation to scattering was not found, but a decrease in CS over the time. Further research is required to determine whether peripheral contrast reduction leads to long-term retinal driven refractive changes.

CONTROL ID: 3705314

SUBMITTER (NAME ONLY): Matthew Pilgrim

TITLE: Correlation of clinical fundus images with molecular and histopathological analyses of calcified Bruch's membrane in patients with pseudoxanthoma elasticum

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Pseudoxanthoma elasticum (PXE) is a rare genetic disorder leading to ectopic calcification of Bruch's membrane (BrM). This can result in a reduced metabolic exchange between the retina and choroid, atrophy of retinal pigment epithelium, and formation of angioid streaks with choroidal neovascularization, all of which can lead to vision loss. Here, we present a histopathological study to investigate the molecular composition and distribution of calcified BrM in eyes with PXE, followed by correlation with clinical images.

Methods: Six cadaveric eyes that were clinically diagnosed with PXE were obtained from the Netherlands Institute for Neuroscience, Amsterdam or the Dutch National Expertise Center for PXE, Utrecht. Eyes were either flat-mounted on to glass slides or embedded in paraffin wax and sectioned to 7 µm. To visualize the distribution of calcified BrM, flat-mounted and cross-sectioned tissues were stained with OsteoSense 680EX, a fluorescent dye specific for the calcium phosphate, hydroxyapatite. The elemental composition of BrM was analysed using energy dispersive x-ray spectroscopy (EDX) whilst time of flight-secondary ion mass spectrometry (TOF-SIMS) was used for mineral composition analysis.

Results: In PXE eyes, the distribution of BrM calcification changes across the central-peripheral axis. On flat-mounted eyes, extensive OsteoSense labelling was observed in the central region with a marked reduction and a patchy distribution towards the periphery. On cross-sections, OsteoSense labelling confirmed the presence of a confluent layer of calcification in the central region with intermittent staining in peripheral regions. EDX analysis confirmed the enrichment of calcium and phosphorus in the BrM of PXE eyes and showed a distribution similar to OsteoSense staining. TOF-SIMS confirmed that some calcifications, at least, were formed of hydroxyapatite.

Conclusions: Extensive calcification is present in the BrM of eyes from PXE patients. Correlation of histopathology and molecular analyses with clinical images suggests that the phenotype observed on fundus imaging modalities is likely associated with the distribution of calcification in the BrM. For example, confluent calcification is associated with angioid streaks whilst the patchy calcification observed in the periphery is likely associated with regions of p'eau d'orange.

CONTROL ID: 3705317

SUBMITTER (NAME ONLY): Kim Schulte

TITLE: Optic nerve degeneration due to complement activation in a combined glaucoma model

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.K. Schulte, R.M. Girbig, H.B. Dick, S.C. Joachim, S. Reinehr, Experimental Eye Research Institute, Ruhr-Universitat Bochum, Bochum, Nordrhein-Westfalen, GERMANY|R. Fuchshofer, Institute of Human Anatomy and Embryology, Universitat Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is the main risk for glaucoma factor, though it is known today that autoimmune factors also contribute to disease development. Likely, a combination of multiple factors is responsible for the damage. Hence, we combined two glaucoma risk factors (IOP and autoimmune response) to examine if the combination leads to greater optic nerve damage.

Methods: For the multifactorial model, six-week-old wildtype mice (ONA) and βB1-CTGF mice (combination) were immunized with 1 mg/ml ONA (=optic nerve antigen). These were compared to wildtype (control) and βB1-CTGF control mice (CTGF). Hence, four groups in total (n=8-10/group). Longitudinal sections were investigated (immuno-)histologically for inflammation (H&E), myelin (LFB), apoptosis (cleaved caspase 3), and the complement system (factor C3). HE and LFB were analyzed using a score to evaluate cell infiltration and demyelination, while cleaved caspase 3^+ and $C3^+$ cells were counted using ImageJ. Further, RT-qPCR analysis of Olig2 mRNA levels were performed.

Results: In comparison to the control group, more inflammatory cells were visible in the other groups ($p<0.001$). Regarding the optic nerve myelin structure, a significantly higher LFB damage score was noted in the combination group compared to controls ($p<0.001$), ONA ($p=0.003$), and CTGF mice ($p=0.01$). Also, more apoptosis was seen in the ONA ($p=0.02$), the CTGF ($p=0.03$), and the combination group ($p=0.04$) compared to controls. The complement system factor C3 was upregulated in the combination group in comparison to the control group (control: 1.43±0.14 cells/mm; combination: 2.18±0.40 cells/mm; $p=0.03$). The mRNA levels of Olig2 were significantly downregulated in ONA, CTGF, and combination optic nerves compared to controls ($p<0.05$). Further, a significant downregulation was noted in the combination group compared ONA optic nerves ($p=0.04$).

Conclusions: Through combining two glaucoma risk a heightened pathological damage could be seen. An increase in demyelination in the combination group and an elevated apoptosis rate was visible. Additionally, the complement factor C3 was upregulated in the combination optic nerves. These results suggest a potential additive role of high IOP and immune factors in glaucoma development, which could be helpful for further investigations of this multifactorial disease.

CONTROL ID: 3705331

SUBMITTER (NAME ONLY): Stephanie Joachim

TITLE: Beneficial impact of primary RPE cells in a porcine organotypic co-cultivation model

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.C. Joachim, N. Wagner, A. Safaei, P. Vogt, M.R. Gammel, H.B. Dick, Ruhr-Universitat Bochum, Bochum, Nordrhein-Westfalen, GERMANY|J. Hurst, S. Schnichels, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: The pathological events of age-related macular degeneration (AMD) are characterized by degenerative processes involving the photoreceptor cells, retinal pigment epithelium (RPE), the Bruch's membrane and choroidal alterations. To examine the interactions between photoreceptor cells and RPE cells ex vivo complex models are required. The aim of this study was to investigate the beneficial effects of a primary RPE cell co-culture or conditioned medium from these cells on neural retina explants.

Methods: Porcine neural retina explants were co-cultured with primary RPE cells (ppRPE) or with medium derived from RPE cells (medium). Individually cultivated neural retina explants served as controls (control). After eight days, RT-qPCR (n=6-7/group) and immunohistology (n=7-10/group) were performed to analyze the amount, condition, and expression of photoreceptors, synapses, macroglia, microglia, complement factors, and pro-inflammatory cytokines (e.g., Il-1β, Il-6, Tnf-α).

Results: The presence of ppRPE cells preserved the expression of photoreceptor specific markers (opsin: $p=0.016$, rhodopsin: $p=0.027$), whereas the medium group only showed a preservation of opsin+ cells in immunohistology ($p<0.001$), but not with RT-qPCR. Only minor differences between the three groups were noted in regard to microglia, $Iba1^+$ cell counts were lower in the ppRPE group ($p=0.042$). Increased Il-6 levels were noted in ppRPE and medium samples, while Tnf-α was only upregulated in the ppRPE group and Il-1β was elevated in medium samples. In regard to synaptic activity, $PSD95^+$ area was increased in ppRPE ($p=0.024$) and medium samples ($p=0.043$).

Conclusions: In conclusion, a co-culture of ppRPE cells and neural retina seems to have a beneficial effect, preserving photoreceptors and synaptic activity in vitro. These organ culture models could be used to mimic the complex interactions between the retina and RPE cells and gain further insights into neurodegenerative pathomechanisms occurring in retinal disease like AMD.

CONTROL ID: 3705334

SUBMITTER (NAME ONLY): Aidan Jackson

TITLE: Fast Progressors in Glaucoma: Prevalence Based on Global and Central Visual Field Loss in a Clinical Population

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.B. Jackson, M.A. Coote, K.R. Martin, Z. Wu, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|A.B. Jackson, M.A. Coote, K.R. Martin, Z. Wu, Ophthalmology, Department of Surgery, University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine the prevalence of fast progressors based on both global and central visual field loss in a clinical cohort of glaucoma patients.

Methods: A retrospective review of patients under routine care at an ophthalmology clinic in Melbourne was undertaken to identify those with glaucoma without any other confounding conditions that had undergone ≥5 visual field tests over a 1–5 year period. The rates of change in the global mean deviation from the entire 24-2 visual field test (MD_{24}) and mean total deviation of the 12 locations in the central 10° (MTD_{10}) were calculated using ordinary least squares regression.

Results: Amongst the 295 eyes from 190 patients with glaucoma included in this study, 6.1% and 9.2% of eyes had a rate of change of <-1.0 dB/year on for MD_{24} and MTD_{10}, and 18.7% and 23.0% had a rate of change <-0.5 dB/year respectively. Furthermore, 17.7% and 21.7% of eyes exhibited a rate of change in the top 5% of the estimated normal distribution (based on the positive slopes) for MD_{24} and MTD_{10} respectively.

Conclusions: Although most patients with glaucoma under routine care in this cohort showed relatively slow rates of global visual field loss, nearly one-quarter of eyes exhibited central visual field loss <-0.5 dB/year, a rate that is relatively fast considering the significance of central vision on functional disability. These findings underscore the need for new management strategies and/or interventions to better prevent functional impairment in patients with glaucoma.

CONTROL ID: 3705361

SUBMITTER (NAME ONLY): Jakob Grauslund

TITLE: Presence and development of diabetic retinopathy in the Danish Registry of Diabetic Retinopathy.

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the prevalence of diabetic retinopathy (DR) and 5-year rates of incident DR, 2-step-or-more progression of DR, as well as progression to proliferative DR along with associated markers in a Danish national cohort.

Methods: We included all persons in the Danish Registry of Diabetic Retinopathy, who had attended at least one episode of DR-screening in 2013-2018. DR was classified by the International Clinical Diabetic Retinopathy Severity Scale with levels 0-4 indicating increasing severity. Data were linked with various national databases to indicate type and duration of diabetes, marital status, comorbidity, systemic medication and screening facility. Baseline DR-level at the worse eye was used for analysis.

Results: Among 170,237 persons with diabetes, mean (with interquartile range) age and duration of diabetes were 65.7 (55.5-73.1) and 5.9 (2.2-11.0) years, respectively, 56.6% were male, and 90.0% had type 2 diabetes. DR-prevalence and 5-year incidences of DR, 2-step-or-more progression of DR and progression to proliferative DR were 12.4%, 4.6%, 0.9% and 0.4%, respectively. The highest rates were found in those below 30 years (21.6%, 13.2%, 2.8%, and 1.2%), with type 1 diabetes (44.2%, 16.0%, 3.4%, and 2.3%), duration of diabetes above 20 years (57.3%, 16.2%, 3.5%, and 2.8%), using insulin (31.8%, 11.0%, 2.4%, and 1.3%), and attending screening at a hospital facility (33.6%, 10.3%, 2.6%, and 1.3%). In multivariable models, use of insulin was identified as a leading marker of all four outcomes (odds ratio 2.24, 95% confidence interval [CI] 2.14-2.34, hazard ratio [HR] 1.90, 95% CI 1.78-2.03, HR 2.23, 95% CI 1.94-2.56, and HR 2.68, 95% CI 2.09-3.43). On the other hand, gender, marital status, Charlson Comorbidity Index score, non-insulin glucose lowering therapy, antihypertensive or cholesterol lowering treatment did not consistenly affect the risk of DR. For patients who entered the registry in the years of 2013, 2014 and 2015, risks of progression to proliferative DR decreased continuously (2.13 vs. 0.97 vs. 0.45, and 2.72 vs. 1.12 vs. 0.70 events per 1,000 person-years for 1- and 3-year progression, respectively).

Conclusions: In a 5-year longitudinal study of a national cohort of persons attending DR-screening, we identified low age, type 1 diabetes, long duration of diabetes, and in particular use of insulin as the most important markers of presence and development of DR.

CONTROL ID: 3705397

SUBMITTER (NAME ONLY): Paris Hanson

TITLE:

TELEMEDICINE AT A UNIVERSITY OPHTHALMOLOGY PRACTICE DURING THE COVID-19 PANDEMIC

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Hanson, A. Oganov, A. Abazari, P. Kung, S. Weissbart, J. Lenoci, R. Honkanen, T. Chou, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze the use of teleophthalmology during the COVID-19 pandemic, with regard to patient demographics, diagnostic precision, therapeutic effectiveness, and patient satisfaction.

Methods: The records of 520 consecutive patients who had telemedicine visits at Stony Brook Ophthalmology between March 30 and June 2, 2020, were reviewed to create a retrospective, cross-sectional analysis. Telemedicine visits were offered to all new patients requesting care and established patients who were scheduled or due for follow-up or postoperative visits. The visits were reviewed and the chief complaint, past medical history, past ocular history, diagnoses, treatment/management, and sub-specialty of the provider were analyzed. Precision was determined by comparing the examination findings and diagnoses of the telemedicine visit with the subsequent in-person, follow-up examination. Progression or resolution of the patients' symptoms was determined by the attending physician's assessment at follow-up visits. A post telemedicine visit satisfaction survey was sent to all patients and the results were analyzed.

Results: Telemedicine visits were offered to 783 patients, 520 (66.4%) of whom accepted (mean age= 34.9 years; range 1-95). Of these 520 patients, 409 (78.7%) were established and 105 (20.2%) had in-person follow-up visits., Overall, the diagnostic precision of the follow-up visits was 89.5%. Of the patients who had in-person follow-up visits, 56.8% remained stable, 32.4% improved, and 10.8% worsened. Established patients presented with more extensive ocular histories/procedures, and experienced a higher percentage of worsening symptoms/disease stage compared to new patients. In total, 78 (15.0%) patients completed the survey. Overall satisfaction was reported by 91.9% of patients, although only 23.0% preferred telemedicine to an in-office visit.

Conclusions: Teleophthalmology provides high levels of precision and patient satisfaction for a wide range of ophthalmologic visits, although most patients still preferred in-office examinations. Employing teleophthalmology for follow-up and emergency care may provide patients with an effective alternative during pandemic situations and beyond.

CONTROL ID: 3705398

SUBMITTER (NAME ONLY): Armin Safaei

TITLE: Apoptotic effects on human RPE cells through $NaIO_3$

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Safaei, J. Brockmann, H.B. Dick, S.C. Joachim, Ruhr-Universitat Bochum, Bochum, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Damage to the retinal pigment epithelium (RPE), a hallmark of AMD, leads to production of oxidative stress and hypoxia which in turn ends in retinal damage. Therefore, the influence of oxidative stress and hypoxia on a human RPE cell line (ARPE-19) was investigated in this study.

Methods: 300 µM $NaIO_3$ or $CoCl_2$ was applied to ARPE-19 cells (3h) to induce oxidative stress or hypoxia. Untreated ARPE-19 cells served as controls. After 4 days of cultivation, RT-qPCRs were performed (n=5/group). Cell samples were analyzed for specific genes relevant to autophagy (MTOR, SQSTM1, BNIP3) or apoptosis (FASLG, CASP3, CASP9). In addition, different concentrations of $NaIO_3$ (0.5 mM, 1 mM, 5 mM and 10 mM) were compared and analyzed by RT-qPCRs (n=10/group). Immunohistochemical stainings were made to visualize apoptotic effects (e.g. cleaved caspase 3) and a cell damage assay was performed (BrdU).

Results: 300 µM $NaIO_3$ or $CoCl_2$ led to increased CASP3 mRNA expression (rel. exp.: 1.44; p=0.018). In addition, a significantly increased FASLG expression was identified in the $NaIO_3$ group (rel. exp.: 4.17; p=0.026). No significant differences were found in regard to autophagy markers. The concentration series with $NaIO_3$ showed apoptotic as well as autophagic effects. An increased FASLG (rel. exp.: 3.77; p=0.008), MTOR (rel. exp.: 3.20; p=0.007), CASP9 (p=0.048), HIF1α (p=0.046), and NFkB expression (p=0.016) was noted with 0.5 mM $NaIO_3$. Additionally, 5 mM $NaIO_3$ led to significantly more FASLG (rel. exp.: 3.12; p=0.037) and NFkB (rel. exp.: 1.70; p=0.031). A higher expression of SQSTM1 (rel. exp.: 2.12; p=0.021) was observed for 10 mM $NaIO_3$. The cleaved caspase 3 staining visualized the apoptotic effect mediated by $NaIO_3$.

Conclusions: The RT-qPCR analyses and stainings suggest that both forms of damage have primarily an apoptotic effect on ARPE-19 cells, but higher concentrations of the stressors also induce autophagic effects. Further investigation at protein level should provide more insight into the effects of the stressors which is important for establishing novel therapeutic approaches.

CONTROL ID: 3705424

SUBMITTER (NAME ONLY): Param Bhatter

TITLE: Treat and Extend Protocol Outcomes in Diabetic Macular Edema: A Meta-Analysis

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Bhatter, J. Muste, S. Wu, M. Elson, University Hospitals, Cleveland, Ohio, UNITED STATES|A. Bheemidi, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|A. Bheemidi, C. Carvalho Soares Valentim, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal injections of anti- vascular endothelial growth factor (anti-VEGF) agents are considered the gold standard for treatment for diabetic macular edema (DME). While monthly and as needed (PRN) injections schemes have been shown to be effective, they constitute a burden for patients and providers in real world clinical settings. Alternatively, treat and extend (T&E) dosing can be used titrate the anti-VEGF dosing based on an individual's clinical response while minimizing treatment burden. This study aims to pool available data on change in visual acuity (VA), number of injections, and change in central subfield thickness (CST) as reported by T&E regimens for DME compared to monthly and PRN regimens.

Methods: PubMed, Science Direct, and EMBASE databases were queried for studies that met the following criteria: retrospective or prospective design, T&E regimen reported in comparison to a monthly or PRN regimen for the treatment of DME, and a 12 month follow up period. After data were extracted, analysis was performed using a random effect model. Publication bias was examined using a funnel plot and Egger's linear regression test. An I^2 test was utilized to determine heterogeneity.

Results: Six total randomized clinical trials were identified. Three studies compared monthly regimens to T&E. The remainder compared PRN regimens to T&E. Comparing monthly and T&E regimens, no significant difference was found between average VA improvement (p=0.30), CST improvement (p=0.28), or number of injections (p=0.20). Comparing PRN and T&E regimens, no significant difference was found between average VA improvement (p=0.64), CST improvement (p=0.11), or number of injections (p=0.89).

Conclusions: In terms of VA and CST, T&E regiments were non-inferior to monthly or PRN regiments. No significant difference in number of injections was detected. These conclusions are limited by study design and outcome: only six studies, which included conservative T&E regimens were included. Furthermore, the criteria did not filter for treatment naïve patients. Future studies need to characterize the long-term reduction of treatment burden in T&E protocols.

CONTROL ID: 3705437

SUBMITTER (NAME ONLY): Amanda Diaz-Garcia

TITLE: HIV-1 Tat-mediated effect on retinal inflammation and homeostasis

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Diaz-Garcia, J. Colón, C. Malpica-Nieves, M. Eaton, S. Skatchkov, Biochemistry, Universidad Central Del Caribe, Bayamon, Puerto Rico, PUERTO RICO|

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ABSTRACT BODY:

Purpose: HIV-1 infection can cause visual impairment in 73% of patients. The HIV viral load is often detected in ocular fluids and the retina. Therefore, understanding the effect of HIV on retinal inflammation and homeostasis is of great importance.

Methods: We used a localized HIV eye model developed by injecting 2.5ng/uL of HIV-Tat protein into the eyes of female Sprague Dawley rats (21 days). After five days, rats were euthanized, and their retinas enucleated. Immunohistochemical analysis and confocal microscopy was used to semi-quantitatively evaluate physiological changes in the BRB components using glial fibrillary acidic protein (GFAP), Aquaporin 4 (AQP4) and potassium channel Kir 4.1 for glial cell markers; intercellular adhesion molecule 1 (ICAM-1) for BRB markers; and Interleukin 1 Beta (IL-1B) and Tumor Necrosis Factor Alpha (TNFa) for inflammation markers. In addition, Western Blot was performed to quantitatively assess differences in Kir 4.1, AQP4 and GFAP expression between sham and HIV-Tat treated eyes.

Results: Immunofluorescence results showed an increased expression of Kir4.1 and AQP4 in Müller glial cells in the retinas treated with HIV-Tat. Additionally, there was also an upregulation of ICAM-1 observed in the outer-BRB/RPE cells. Western Blot analysis showed that Kir 4.1 and AQP4 protein level expression was increased in retinas treated with HIV-Tat compared to sham.

Conclusions: In conclusion, we suggest that such upregulation of Kir 4.1 and AQP4 are rather compensating effects of glial cells to maintain normal potassium and water buffering than commonly expected degradative process. Additionally, results suggests that ICAM-1 could be a promoter of HIV adhesion to the RPE cells by facilitating viral load invasion into the ocular tissues during HIV. Still, further investigation is needed.

CONTROL ID: 3705491

SUBMITTER (NAME ONLY): Peiyao Cheng

TITLE: Visual acuity and full-field stimulus thresholds (FST) over 2 years in the RUSH2A study: annual rates of change from mixed effects modeling

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Best corrected visual acuity (BCVA) and FST are quantitative measures affected by inherited retinal degenerations (IRDs). There are few available estimates for rates of change in IRDs. Here we provide estimates of change over 2 years from the Rate of Progression in USH2A-related Retinal Degeneration (RUSH2A) study using mixed effects models.

Methods: Participants with BCVA ≥ 20/80, stable fixation, and kinetic visual field of ≥ 10° at baseline in the study eye had BCVA (ETDRS letter score) and FST measured at baseline, 1, and 2 years. FST was measured with white, blue and red stimuli in triplicate and was performed only in centers having the required equipment. Mixed effects models were used to estimate the annual rates of change and percentage rates of change using log transformed data with 95% confidence intervals (95% CI). Sensitivity analyses were performed by down-weighting results from eyes with outlier rates of change. Spearman correlation coefficients (r) were calculated among BCVA and FST measures.

Results: The average decline of BCVA score [N=102] was 0.87 (0.48, 1.26) letters/year or 1.1 (0.6,1.6) %/year (Table 1). For FST measures [N=73], the average increase of thresholds was 1.28 (0.85, 1.71) dB/year for white stimulus, 1.25 (0.82, 1.67) dB/year for blue stimulus and 0.76 (0.42, 1.10) dB/year for red stimulus. Models that down-weighted outliers yielded lower rates of decline for BCVA and lower rates of increase for FST measures compared to models that weighted equally all data points. There was no significant correlation between 2-year changes in BCVA letter score and the three FST measures (r between -0.08 and -0.12; Table 2). 2-year changes in the three FST measures were highly correlated with each other (r between 0.61 and 0.77; $p<0.001$). Among eyes [N=65] that had FST testing at baseline and year 2, the response was cone mediated (FST white > -30 dB) in 31 (48%) at both times, rod mediated (FST white ≤ -30 dB) in 29 (45%) at both times and switched from rod- to cone-mediated in 5 (8%).

Conclusions: Based on 2 years of follow-up in RUSH2A, average decline in BCVA was small. Average white and blue FST values deteriorated a similar degree. Sensitivity changed from rod- to cone-mediated in 8% of patients.

CONTROL ID: 3705516

SUBMITTER (NAME ONLY): Nancy Barrett

TITLE: Artificial Intelligence (AI) Enabled Pre-Screening for Diabetic Retinopathy (DR) Clinical Trials

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Barrett, R. Slater, R. Channa, A. Domalpally, B.A. Blodi, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Preventive therapies to reduce progression of non-proliferative DR (NPDR) to proliferative DR are underway. Clinical trial enrollment criteria typically include a baseline DR severity scale (DRSS) of moderately severe (level 47) or severe NPDR (level 53) determined from stereoscopic 7-field retinal color photographs by certified graders at the Wisconsin Reading Center (WRC). The estimated screen failure rate after WRC confirmation is 50% with the most common reason being level < 47. We developed an AI algorithm to enable real-time prescreening of color photographs for DRSS to reduce the screen failure rate.

Methods: Grader training images at WRC were utilized for training the EffcientNetB4 model starting from Imagenet weights and fine tuned to a binary classifier with an input resolution of 768x768 utilizing an 80:20 split for training and internal validation. The dataset included 572 training images stratified across the NPDR scale (levels 35, 43, 47 and 53). 132 images were set aside for internal validation with the same stratification. The algorithm was trained to identify ineligible eyes (levels 35 – 43) and eligible eyes (levels 47-53) using macula centered field 2 images only. WRC graders used the DRSS scale to assess NPDR severity in all 572 eyes.

Results: Of the 37 eyes considered eligible by the AI, the grader agreed on 62.9%. Of 97 eyes considered ineligible by AI, the grader agreed on 90.7%. The best model had an area under the curve (AUC) of 0.91. The overall accuracy (weighted by class) was 83%. The sensitivity of the eligible class was 0.59, specificity of 0.71 giving an F1 score of 0.65. A review of the false positive and negative images showed image quality and an imbalance in DR features between F2 and peripheral fields to be the two largest contributing factors to false results.

Conclusions: The AI algorithm is effective at identifying levels <47 and can exclude them from clinical trial submissions. A tiered approach with AI prescreening for eligible participants followed by WRC grader confirmation reduces the screen failure rate, creating cost efficiency and reduced burden for participants and clinical site staff. Real time automated assessment of potential eligibility could improve enrollment in DR clinical trials.

CONTROL ID: 3705552

SUBMITTER (NAME ONLY): Raymond Warner

TITLE: Reliability and Reciprocity of the Population Cone Optoretinogram

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.L. Warner, J.I. Morgan, Scheie Eye Institute, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|D.H. Brainard, Psychology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|J.I. Morgan, Center for Advanced Retinal and Ocular Therapeutics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optoretinography assesses photoreceptor function. To develop optoretinography as a biomarker for disease affecting cones, we characterize the reliability of the cone optoretinogram in healthy subjects, as well as its dependence on stimulus duration.

Methods: Healthy subjects (N=5, 28-41 years) were imaged with an adaptive optics scanning laser ophthalmoscope (AOSLO). In each session, 270 AOSLO videos were acquired (785 nm, 1° x 1° imaging field, 1.5° temporal retina). A visible light stimulus (545Δ10 nm) was presented 1 s after the start of each video. The confocal reflecances of identified cones were extracted for each video frame, and the optoretinogram reflectance response for that frame was taken as the pooled standard deviation of the reflectances across cones (Cooper et al., 2017). We analyzed the peak response after stimulus initiation, taken from the fit of a smooth curve to the frame-by-frame response. We studied four intensity/exposure duration conditions, each with stimulus energy of 153 nJ/deg^2: 1) 153nW/1s, 2) 306nW/0.5s, 3) 917nW/0.167s, 4) 2.75μW/0.056s. To measure intra-session variation, condition 4 was measured twice per session. For each subject, the full set of measurements was repeated in two sessions separated by at least a week.

Results: Stimulus condition effects were not significant [$F(3,39) = 7.69$, $p = 0.355$]. Peak response varied significantly with subject [three-way ANOVA; subject, session, stimulus condition; $F(4,39) = 9.42$, $p = .025$]. Individual subject mean responses ranged from 2.4 to 4.5 on our response scale (arbiturary units). There was no main effect of session, but there was a significant subject by session interaction [$F(4,39) = 15.75$, $p < .001$]. This size of the session effect was small (mean absolute value 0.63) relative to intersubject differences. Within session variation for condition 4 was not significant in session 1 [one-way ANOVA; $F(1,49) = 0$, $p = 0.975$] nor session 2 [$F(1,49) = 0.06$, $p = 0.810$].

Conclusions: The population cone optoretinogram is reliable for individual subjects, with a single session and a short duration stimulus sufficient for characterizing a subject's response. Though the magnitude of the response varied across subjects, reciprocity between stimulus irradiance and duration held. Future work to establish optoretinography norms in larger numbers of healthy subjects is needed to apply optoretinography in studies of disease.

CONTROL ID: 3705571

SUBMITTER (NAME ONLY): Timothy Gawne

TITLE: Simulated myopic defocus counteracts a myopiagenic environment in juvenile tree shrews producing hyperopia

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Gawne, Z. She, T.T. Norton, Optometry and Vision Science, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the effects of a video display of simulated myopic blur on refractive development (emmetropization) in juvenile tree shrews.

Methods: Seven tree shrews (Tupaia belangeri, diurnal mammals closely related to primates) were removed from standard colony housing at 24 days of visual experience (DVE; days after eye opening) and placed in closed solid-wall cubical cages, 28 cm on a side internal dimension, with black and white patterns on the walls, until 35 DVE. Five animals were placed in the same size cage, but one wall consisted of a video display of simulated myopic blur (see Figure 1) of brightness 147 cd/m2, that was achieved by blurring the blue channel. Non-cycloplegic refractions and ocular dimensions were measured in awake animals using an autorefractor and an optical biometer, respectively. Data were compared with those obtained from seven animals previously reared in standard colony conditions with open-view wire mesh cages.

Results: At the end of the treatment period, the animals in the closed cages without the simulated myopic blur become slightly myopic: -1.0±0.4 (stderr) Diopters (see Figure 2). Animals in the open-view colony caging were slightly hyperopic at this age: 1.0±0.2 Diopters, significantly different from the animals in the closed view cage by t-test ($P<0.001$, $t=4.805$, $df=12$). In contrast, animals exposed to simulated myopic blur were hyperopic: +4.1±0.6 Diopters. The closed cage vs. myopic defocus group difference was 5.1 diopters, significant by t-test ($P<0.001$, $t=7.3638$, $df=10$). Changes in vitreous chamber depth were consistent with the refractive effects.

Conclusions: Cages with restricted viewing distance cause significant myopia in juvenile tree shrews. However, under these conditions simulated myopic blur more than overcomes the effect of restricted viewing distance and causes robust hyperopia. This emphasizes the importance of chromatic cues in emmetropization. This effect could potentially be developed into a powerful anti-myopia visual therapy for children.

CONTROL ID: 3705574
SUBMITTER (NAME ONLY): Noam Sapiens
TITLE: At-Home Refraction Measurement
SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Sapiens, A. Ramic, J. Serri, EyeQue Corp., California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Performing accurate refraction measurement at home will elevate eyecare and increase accessibility for many. The purpose of this study is to determine if the refraction results obtained from measurements in an at-home setting yields Best Corrected Visual Acuity (BCVA) results within 1 line of 20/20 (LogMAR 0.0). the study utilizes the EyeQue VisionCheck which is a smartphone based (figure 1), handheld, ophthalmic refractometer.

Methods: An open-label distributed study to assess the BCVA using glasses with correct PD created from the VisionCheck measurement results included 35 subjects (Female = 13, Male = 22). The age range was between 30-80, with mean 50.4 and SD = 24. Subjects were measured with VisionCheck and had OD Spherical Equivalent (SE) range of -6.0D and +2.25D and OS SE between -6.25D and +1.75D. Each subject performed 3 Visual Acuity tests without correction and 3 tests with glasses made from the VisionCheck results. BCVA measurements were done with the EyeQue Insight, an ETDRS visual acuity screener with logMAR range of 0.0 to 1.0.

Results: Statistical analysis was conducted using a student t-test for each eye separately as well as for both eyes measurement. The analysis included the mean and confidence intervals for both the BCVA measurement without any correction and for that with the VisionCheck based correction. The analysis showed significance for the confidence interval ($p < 0.001$). Table 1 shows a summary of the analysis.

Conclusions: Both the mean acuity and the confidence intervals are significantly lower for the VisionCheck based correction compared to uncorrected vision. The EyeQue VisionCheck refraction measurements on average provides BCVA within 1 letter of 20/20. This study indicates that at home self-refraction is practical and a promising alternative to in office testing.

CONTROL ID: 3705595
SUBMITTER (NAME ONLY): Patrice Hicks
TITLE: The Association between Redlining, Visual Impairment and Blindness
SESSION TITLE: Public Health I
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: P. Hicks, P. Newman-Casey, L. Niziol, M. Lu, L. Kang, O. Jakpor, A. Elam, M.A. Woodward, Ophthalmology and Visual Sciences, Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|B.C. Stagg, Moran Eye Center, Salt Lake City, Utah, UNITED STATES|B.C. Stagg, Population Health Sciences, University of Utah, Salt Lake City, Utah, UNITED STATES|P. Newman-Casey, M.A. Woodward, Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, Michigan, UNITED STATES|
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ABSTRACT BODY:

Purpose: Redlining, a discriminatory practice in the 1930s to 1960s to categorize geographic areas based on investment risk, has negatively impacted communities and individuals. This practice has largely impacted residents of racial and ethnic minority groups and was a form of residential segregation. We hypothesize that neighborhoods with worse redlining scores are associated with visual impairment and blindness (VIB), defined as higher rates of self-reporting blindness or having serious difficulty seeing even when wearing glasses.

Methods: Census tract-level data were obtained from the American Community Survey, including the percent of respondents by tract who had VIB, sex, race, median age, state, and population size. Average redlining scores per census tract (CT) were obtained from OpenICPSR, with scores ranging from 1 to 4 (worst). CTs with missing data or margins of error >15% were excluded. Logistic regression was used to model the effect of redlining on the probability of a CT having a rate of VIB greater than the national average (>2.51%). Results are presented with odds ratios (OR) and 95% confidence intervals (CI). Linear regression was used to estimate the effect of redlining on the logarithm of average VIB. Results are presented with estimates (exponentiated for interpretation on a percentage scale) and 95% CIs.

Results: A total of 12,888 CTs in the US had redlining scores. Of these, 12,227 had complete data meeting inclusion criteria. The average percentage of residents with VIB across our CTs was 2.51% (standard deviation, SD=1.82), and 41% of these CTs had rates of VIB above the national average. The mean redlining score for these tracts was 2.94 (SD=0.78). Logistic regression found worse redlining scores were associated with significantly increased odds of VIB above the national average (OR:1.09; 95% CI:1.08-1.10; p<0.001), after controlling for aggregate measures of age, sex, race, state, and CT population. Similarly, linear regression found that a 1 unit increase in average redlining score was associated with an increase of 10.77% in the percentage of VIB (95% CI: 9.70% -11.85%; p<0.001).

Conclusions: Historical residential segregation through redlining was found to be associated with higher proportions of people living with VIB in these neighborhoods today. This study can aid in the understanding of how geographic area could impact VIB outcomes to inform public health planning and the delivery of eye care.

CONTROL ID: 3705602

SUBMITTER (NAME ONLY): Christopher Brady

TITLE: Development of an Artificial Intelligence Classifier for Follicular Trachoma

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Brady, Surgery/Ophthalmology, University of Vermont College of Medicine, Burlington, Vermont, UNITED STATES|R.C. Cockrell, D. Socia, Surgery/Research, University of Vermont College of Medicine, Burlington, Vermont, UNITED STATES|S.K. West, Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite intensive efforts, trachoma remains the most important infectious cause of vision loss and one of the overall leading causes of global blindness. Current methods for detection may be inadequate for elimination programs, so we sought to develop an artificial intelligence classifier (AI) for follicular trachoma (TF) using conjunctival images to allow for rapid, low-cost remote detection.

Methods: A smartphone camera collected 2614 upper eyelid images during a 2019 district survey in Chamwino, Tanzania. The subset of 2285 gradable images with concordant field and photo grades were re-sized to 224 x 224 pixels and randomly divided into equal training and test sets. To enrich the training set, oversampling of TF cases with data augmentation methods (horizontal flipping, rotation, perspective shift, and color jitter) were applied. Additionally, color space exploration and follicle enhancement methods were employed. Two commonly used pre-trained convolutional neural networks (VGG16 and Resnet101) were further trained on “training set.” Class weighting and batch accumulation were used to improve model performance.

Results: With a goal of maximizing recall, a ResNet101 model generated the best results, with a recall of 89%. This translated to a 75% reduction in skilled grader burden as only positive images require confirmation. Additionally, the misclassification of images in this work is typically due to poor image quality (e.g., failure to capture entire tarsal plate, image focus, etc.).

Conclusions: AI methods show promise in identifying TF, though the training data was limited by low case numbers of TF and non-standardized images. Future studies will retrain the model with larger datasets with more TF and will develop standardized photographic techniques (improved image quality, centration and lighting). While trachoma efforts are decentralized and organized at the country level, we believe photographic standardization using smartphone camera technology is reasonable given the widespread utilization of a single mHealth app (Tropical Data) to support TF prevalence surveys. To allow for practical value in areas of low network connectivity, edge computing strategies such as in-handset classification may be needed.

CONTROL ID: 3705617

SUBMITTER (NAME ONLY): Tae Jin Lee

TITLE: Race and Sex Specific Differences in the Human Aqueous Humor Proteins

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lee, G. Jones, W. Zhi, S. Sharma, A. Sharma, Center for Biotechnology and Genomic Medicine, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|K.E. Bollinger, L. Ulrich, D. Bogorad, A. Estes, S. Sharma, Department of Ophthalmology, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|A. Sharma, Department of Population Health Sciences, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human aqueous humor (AH) plays an important role in maintaining intraocular pressure and metabolic balance in the anterior chamber of the eye. Increasing evidence indicates the incidence of ocular disorders vary by race and sex. Several ocular diseases are more prevalent in females than males. Also, the risk of developing glaucoma is higher among African Americans than Caucasians. In this study, we examined the race and sex-specific differences in human AH proteins.

Methods: Human AH samples from 177 subjects undergoing cataract surgery (without any other ocular disorders) were analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). A total of 233 AH proteins were detected in more than half of the samples. A regression model was used to test the effect of race and sex on the protein levels.

Results: The levels of 21 AH proteins were significantly different between males and females (5 higher and 16 lower in females). The proteins with higher levels in females include retinoschisin X-linked juvenile retinoschisis protein (RS1), extracellular superoxide dismutase (SOD3), and enolase 1 (ENO1). The proteins with lower levels in females include complements C6 and C9, inter-alpha-trypsin inhibitor heavy chain H2, and H4 (ITIH2, ITIH4), and apolipoprotein A-IV (APOA4). The levels of 56 proteins were significantly different between African American and Caucasian subjects (9 higher and 47 with lower levels in African Americans). The proteins with higher levels in African Americans include coagulation factor V (F5), low-density lipoprotein receptor-related protein 2 (LRP2), and several keratins including KRT1, KRT2, KRT10. The proteins with lower levels in African Americans include tetraspanin-14 (TSPAN14), six immunoglobulins (IGHG2, IGHG3, IGHV6-1, IGHLV1-40, IGHLV1-47, IGHLV3-9), and heparan sulfate proteoglycan core protein (HSPG2). Expression of three apolipoproteins (APOA1, APOA2, and APOA4) were significantly lower while SOD3 was higher in both African American and female subjects.

Conclusions: A total of 233 proteins were detected in more than 50% of healthy human AH samples. 69 of these proteins demonstrated race and sex-specific variations. The intra-population variation in AH protein levels highlights the importance of these two factors in future study designs. Additionally, these specific alterations may be associated with higher risks of glaucoma in females and African Americans.

CONTROL ID: 3705628

SUBMITTER (NAME ONLY): wing yip

TITLE: Gender differences in private industry payments to optometrists in 2019

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. yip, M. Schornack, C.B. Nau, M. mahr, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gender inequality in medicine has been well established in literature. Female physicians tend to have lower salary, less representation in academia and research funding. Previous studies have shown that women in ophthalmology are underrepresented in terms of private industry payments and dollar amounts paid. Gender-based disparities in private industry payments to optometrists have not yet been studied. The present study investigates such disparities.

Methods: This study was deemed exempt by the Mayo Clinic IRB because it utilized only publicly available data from Centers for Medicare and Medicaid services (CMS) open payments database. U.S. optometrists listed in the database who had received at least one payment during 2019 were identified. Payments were compared in the following four categories: 1, compensation for non-consulting services (e.g., serving as faculty or speaker at a venue other than a continuing education program), 2, serving as faculty or a speaker for continuing education program, 3, consulting fees, and 4, honoraria were included. The total number of optometrists practicing in 2019 was obtained from a public website using a combination Census Bureau, Bureau of Labor Statistics, and Bureau of Economic Analysis databases. Statistical analysis was completed using RStudio 2021.09.1+372. Independent sample t-test was used to compare means, Wilcox rank-sum test was used to compare medians.

Results: A total of 50,700 practicing optometrists were identified in 2019; 22,100 (43.6%) were female. 630 (2.9%) female and 1033 (3.6%) male optometrists received payments. For all payment categories, mean payment for females was $3354.55 and for males was $7150.60 ($p<0.001$). Median payment for females was $450 and for males was $1238.18 ($p<0.001$).

Conclusions: These results confirm the trend previously reported within ophthalmology is also evident within optometry. Female optometrists are underrepresented in private industry payments. Dollar amounts paid to female optometrists were significantly less in all categories compared amounts paid to male optometrists.

CONTROL ID: 3705630

SUBMITTER (NAME ONLY): Haniah Zaheer

TITLE: Association of patient characteristics with self-reported barriers to eye care at a free community vision screening event

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.A. Zaheer, S. Atta, O. Clinger, P.J. Liu, E.J. Waxman, J.A. Sahel, A. Williams, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|D. McGinnis-Thomas, Department of Business Administration, Marketing and Business Economics Area, Joseph M. Katz Graduate School of Business, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Social determinants of health can limit access to regular eye care, but their role in ophthalmology is underexamined. The purpose of this cross-sectional study is to assess the relationship between patient characteristics and self-reported barriers to eye care among patients attending a free vision screening event.

Methods: We conducted a 12-question survey of adult patients attending a community vision screening event. Our survey queried patients' current general and ocular health status, barriers to obtaining eye care, and demographic information. Associations between patient characteristics and self-reported barriers to eye care were assessed using binary logistic regression and reported as odds ratios (OR).

Results: The survey was completed by 183 of the 269 event attendees (68% response rate), with an average age of 53±15 years. The majority of respondents were women (105, 59%), and most self-identified as black (74, 46%) or white race (67, 41%). The plurality was employed or self-employed (67, 41%), and most others were retired (29, 18%), looking for employment (25, 15%) or unable to work (18, 11%). While about a third of patients reported having no health insurance (60, 34%), most had either public (84, 48%) or private coverage (34, 19%). Only a quarter reported having vision insurance (50, 28%). Three-quarters of respondents indicated at least one barrier to receiving regular eye care (136, 76%), most commonly cost (89, 50%) and insurance issues (73, 41%). Getting time off work (21, 12%) and transportation (13, 7%) were other commonly cited barriers to care. Not having health insurance or vision insurance was strongly associated with reporting at least one barrier to care (OR 5.00, $p=0.002$, and OR 7.463, $p<0.001$). Those with self-reported eye disease had challenges with transportation (OR 4.454, $p=0.013$) and getting time off work was a barrier for younger and employed persons ($p\leq0.01$ for both).

Conclusions: Three quarters of patients at a vision screening event reported at least one barrier to regular eye care. Although most had insurance coverage, medical costs and insurance issues were the leading barriers to receiving an eye exam. Other barriers were associated with specific patient characteristics. Targeted interventions are warranted to address barriers to vision care among underserved communities.

CONTROL ID: 3705655

SUBMITTER (NAME ONLY): Menglu Yang

TITLE: Self-DNA induces inflammation in myoepithelial cells of the lacrimal gland by AIM2 inflammasome activation

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Yang, D.A. Dartt, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Menglu Yang: Commercial Relationship: Code N (No Commercial Relationship) | Darlene Dartt: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Primary Sjögren's Syndrome (pSS) is an autoimmune disease that mainly affects the lacrimal glands and salivary glands. Antibodies against nuclear materials have been found in patients but the mechanism is unclear. When foreign DNA enters the cells, several mechanisms will be activated to defend against viral infection or local tissue damage. In this study, we focus on one of the mechanisms, namely Absent in Melanoma (AIM)2 inflammasome, in myoepithelial cells of the lacrimal gland. AIM2 non-selectively binds the double-stranded DNA in the cytoplasm, causing the formation of the AIM2 inflammasome to activate caspase-1, which cleaves immature pro-IL-1ß to mature IL-1ß that contribute to inflammation. We hypothesize that in pSS patients, self-DNA from the bloodstream of SS patients triggers the activation of AIM2 inflammasome which in turn causes inflammation to damage the healthy lacrimal gland.

Methods: Primary MECs culture was acquired from female wildtype C57Bl/6 mice aged 4-6 weeks. Genomic DNA (gDNA) extracted from the same culture was used to resemble the self-DNA. A random double-stranded DNA poly A:T was used as a positive control for AIM2 activation. Immunofluorescent (IF) was used to detect the assembly of inflammasomes; RT-PCR was used to detect the expression of AIM2. The activation of caspase-1 was measured using FAM-FLICA assay.

Results: The MECs were treated with gDNA for 6 hours, with random double-stranded DNA poly A:T as a positive control. Immunofluorescent (IF) staining result shows the accumulation of AIM2 signals and a speck of Apoptosis-associated speck-like protein containing a CARD (ASC), indicating the assembly of AIM2 inflammasome in both gDNA and poly AT treated groups. RT-PCR showed a significantly increased expression of Aim2 in both gDNA and poly AT treated groups compared to the non-treated group. FAM-FLICA assay showed that the activation of caspase-1 is significantly increased in both poly AT and gDNA treated groups compared to the non-treated group. We next applied the inhibitor of AIM2, A151, to the MECs together with gDNA or poly AT, and the ratio of AIM2 or ASC speck positive cells was measured from each group. We found that A151 significantly terminated the presence of AIM2 and ASC speck compared to the gDNA or poly AT group.

Conclusions: Self-DNA induces caspase-1 activation in MECs through AIM2 inflammasome, which may be a key mechanism in pSS.

CONTROL ID: 3705658

SUBMITTER (NAME ONLY): Cheng-Hui Lin

TITLE: Retinal Müller glia derived ZFP36 regulates the progression of diabetic retinopathy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lin, M. Wu, S. Wang, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Cheng-Hui Lin: Commercial Relationship: Code N (No Commercial Relationship) | Man-Ru Wu: Commercial Relationship: Code N (No Commercial Relationship) | Sui Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We propose to identify mechanisms that underlie the initiation and early progression of diabetic retinopathy (DR) via dissecting the genes and pathways controlling diabetes-induced responses in Müller glial cells (MG), which are one of the first responders of diabetes in the retina. In our studies, we discovered zinc finger protein 36 (ZFP36) are significantly altered by diabetes and contribute to the development of DR.

Methods: Streptozotocin (STZ)-induced diabetic rats were used as models to study DR. RNA-seq, histological immunostaining and fluorescence mRNA in situ hybridization (FISH) were utilized to capture diabetes-induced transcriptomic changes in the retinal MG at early stages. Endogenous ZFP36 gene expression was detected and quantified by quantitative single molecule FISH (smFISH) on rat MG. We also developed novel adeno-associated virus (AAVs) that can specifically and efficiently label and manipulate MG in vivo in rat retinas. These AAVs were used to knock down or overexpress ZFP36 in rat MG in vivo under normal and diabetic conditions. The DR-related retinal phenotypes were characterized as described in the literature, including MG gliosis, RGC survival rate, and vascular permeability and neovascularization.

Results: We detected increased ZFP36 expression in MG starting from 1 month after STZ injection in rats compared to WT controls. The upregulation of ZFP36 diminished at around 3 months after STZ injection. Knocking down ZFP36 in rat MG in vivo using AAVs resulted in accelerated development of DR in diabetic rats, while over-expression can delay the development of the disease.

Conclusions: Diabetes-induced upregulation of ZFP36 in MG plays a beneficial role, and failure to maintain ZFP36 levels contributes to the initiation and early progression of DR.

CONTROL ID: 3705671

SUBMITTER (NAME ONLY): Ivan Lee

TITLE: Prevalence of diabetic retinopathy in a West Virginia sample of patients with inherited retinal diseases.

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Leys, West Virginia University Department of Ophthalmology, Morgantown, West Virginia, UNITED STATES|J. Odom, West Virginia University Department of Ophthalmology, Morgantown, West Virginia, UNITED STATES|I. Lee, West Virginia University Department of Ophthalmology, Morgantown, West Virginia, UNITED STATES|

Commercial Relationships Disclosure: Ivan Lee: Commercial Relationship: Code N (No Commercial Relationship) | J Vernon Odom: Commercial Relationship: Code N (No Commercial Relationship) | Monique Leys: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While it is known that patients with generalized retinal dystrophy are less likely to develop diabetic retinopathy (DR)[JO1] , no prior study in West Virginia has investigated prevalence and severity[JO2] of DR in patients with confirmed molecular diagnosis of inherited retinal diseases (IRD). We performed a retrospective chart review of diabetic IRD patients to determine the prevalence of diabetic retinopathy.

Methods: We identified 415 patients with IRD seen at the West Virginia University Eye Institute between January 2010 and November 2021. 27 of these patients had diabetes (12 males and 15 females of ages 34-85). All 27 had confirmed molecular diagnosis of IRD in themselves or an affected family member.. Their molecular diagnosis, clinical findings, laboratory values, retinal images, and electrodiagnostic tests were reviewed.

Results: Three of the 27 IRD patients with diabetes (11%) were identified to have DR.

A 70-year-old male with type 2 DM and IMPG2 mutation with vitelliform maculopathy presented with moderate NPDR in both eyes. Visual acuity (VA) was 20/40 in both eyes.

A 60-year-old male with type 2 DM and PRDM13 mutation with North Carolina macular dystrophy presented with bilateral tractional retinal detachment with final VA of HM and LP.

A 47-year-old female with type 1 DM and XLRP [RP2] developed tractional retinal detachment bilaterally. Final VA was 20/400 and 20/25.

Conclusions: DR is less frequently observed in diabetic IRD patients with prevalence of 11%, compared to 28.5% in general population. Despite the lower prevalence, it is important to monitor diabetic IRD patients for DR, particularly female XLRP patients or North Carolina macular dystrophy patients.

CONTROL ID: 3705701

SUBMITTER (NAME ONLY): Ye He

TITLE: Ethnic Differences in the Distribution of Diabetic Lesions

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. He, M.G. nittala, A. Verma, H. Esmaeilkhanian, S.B. Velga, I. Tsui, S.R. Sadda, Doheny Eye Institute, Pasadena, California, UNITED STATES|H. Esmaeilkhanian, I. Tsui, S.R. Sadda, Department of Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|Y. He, X. Li, X. Li, Tianjin Medical University Eye Hospital, Tianjin, CHINA|L. Su, X. Li, Tianjin Medical University Second Hospital, Tianjin, Tianjin, CHINA|P. Prasad, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|P. Prasad, Harbor-UCLA Medical Center, Torrance, California, UNITED STATES|C. Jayadev, ophthalmology, Narayana Nethralaya Eye Institute, INDIA|

Commercial Relationships Disclosure: Ye He: Commercial Relationship: Code N (No Commercial Relationship) | Muneeswar nittala: Commercial Relationship: Code N (No Commercial Relationship) | Aditya Verma: Commercial Relationship: Code N (No Commercial Relationship) | Houri Esmaeilkhanian: Commercial Relationship: Code N (No Commercial Relationship) | Swetha Velga: Commercial Relationship: Code N (No Commercial Relationship) | Xiaorong Li: Commercial Relationship: Code N (No Commercial Relationship) | Long Su: Commercial Relationship: Code N (No Commercial Relationship) | Xiao Li: Commercial Relationship: Code N (No Commercial Relationship) | Irena Tsui: Commercial Relationship: Code N (No Commercial Relationship) | Pradeep Prasad: Commercial Relationship: Code N (No Commercial Relationship) | Chaitra Jayadev: Commercial Relationship: Code N (No Commercial Relationship) | Srinivas Sadda: Commercial Relationship(s);Code C (Consultant/Contractor):Amgen, Allergan, Genentech/Roche, Iveric, Oxurion, Novartis, Regeneron, Bayer, 4DMT, Centervue, Heidelberg, Optos, Merck, Apellis, Astellas;Code R (Recipient):Carl Zeiss Meditec, Nidek;Code R (Recipient):Nidek, Topcon, Heidelberg, Carl Zeiss Meditec, Optos, Centervue

ABSTRACT BODY:

Purpose: Ethnic differences in the prevalence of diabetic retinopathy (DR) have been reported but differences in the DR phenotype have not been well described. In this retrospective study, we evaluate the distribution of DR lesions among various ethnicities.

Methods: We enrolled a cohort of 228 eyes with DR consisting of 49 East Asian eyes (Second Hospital of Tianjin Medical University), 103 South Asian eyes (Narayana Nethralaya Eye Institute), 30 Caucasian eyes (UCLA), and 46 Latino eyes (UCLA) with ultrawidefield images. Both treatment naïve and treated cases were included. Images were manually annotated for DR lesions including microaneurysms, hemorrhages, intraretinal microvascular abnormalities, cotton wool spots, neovascularization, and venous beading. The DR severity was assessed according to the International Clinical Diabetic Retinopathy scale. In accordance with previous publications, eyes were classified as having predominantly peripheral or central lesions (PPL or PCL) based on comparing the frequency of lesions in peripheral fields 3 to 7 versus their respective adjacent ETDRS field 3 to 7 (i.e. >50% of lesions in one or more peripheral fields= PPL). The percent of eyes rated to be PPL were compared among the groups.

Results: The proportion of eyes which featured a PPL distribution was highest in East Asians (85.7%) and lowest in South Asians (35.9%) regardless of prior treatment or DR severity. Among treatment naïve eyes, a total of 39 (84.8%) East Asian eyes, 20 (35.7%) South Asian eyes, 12 (57.1%) Caucasian eyes, and 18 (46.2%) Latino eyes were classified as having PPL. For moderate NPDR, treatment naïve eyes, a PPL distribution was observed in 84.8% of East Asian eyes, 34.9% of South Asian eyes, 38.5% of Caucasian eyes, and 44.4% of Latino eyes. This greater PPL distribution among East Asian eyes was significantly different from South Asian eyes ($P<0.0001$), Caucasian eyes ($P=0.0017$), and Latino eyes ($P=0.001$). East Asian eyes were also more likely to have multiple PPL fields.

Conclusions: The distribution of DR lesions appears to vary among different ethnicities. DR lesions tend to be distributed more peripherally in East Asian eyes compared to other ethnicities, particularly South Asian eyes, which tend to have more central lesions. The prognostic implications of these ethnic differences in DR lesion distribution warrant further study.

CONTROL ID: 3705703

SUBMITTER (NAME ONLY): Rui Ji

TITLE: Effect of Lipsome-encapsulated Ripasudil in subretinal fibrosis

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ji, K. Ishikawa, K. Mori, I. Wada, Y. Fukuda, K. Sonoda, Department of Ophthalmology, Kyushu Daigaku, Fukuoka, Fukuoka, JAPAN|N. Matsunaga, S. Ohdo, Faculty of Pharmaceutical Sciences, Kyushu Daigaku, Fukuoka, Fukuoka, JAPAN|

Commercial Relationships Disclosure: Rui Ji: Commercial Relationship: Code N (No Commercial Relationship) | Keijiro Ishikawa: Commercial Relationship: Code N (No Commercial Relationship) | Kenichiro Mori: Commercial Relationship: Code N (No Commercial Relationship) | Naoya Matsunaga: Commercial Relationship: Code N (No Commercial Relationship) | Iori Wada: Commercial Relationship: Code N (No Commercial Relationship) | Yosuke Fukuda: Commercial Relationship: Code N (No Commercial Relationship) | Shigehiro Ohdo: Commercial Relationship: Code N (No Commercial Relationship) | Koh-Hei Sonoda: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the pathogenesis of subretinal fibrosis associated with age-related macular degeneration, epithelial to mesenchymal transition (EMT) of retinal pigment epithelium (RPE) plays a vital role, and we have reported Ripasudil (Ripa) could inhibit EMT of RPE in the subretinal fibrosis related to choroidal neovascularization (CNV). The purpose was to investigate the therapeutic effect of liposome-encapsulated-ripasudil (Lipo-Ripa) on laser-induced CNV model.

Methods: C57BL/6J mice underwent laser photocoagulation to induce CNV-related fibrosis. Single intravitreous injections of BSS, Ripa and Lipo-Ripa in each group were performed at 14^{th} day after laser injury at 28^{th} day. Volume of the CNV and subretinal fibrous tissue (SRF) were measured in choroidal flat mounts. To evaluate the drug distribution in the eyes, localization of FITC-labeled Lipo-Ripa was examined.

Results: In BSS，Ripa and Lipo-Ripa groups，the average volume of CNV were respectively 3.7, 3.2 and 2.9($\times 10^4$ μm^3) while SRF were 11.2, 9.0 and 6.8($\times 10^4$ μm^3). The volume of SRF in Lipo-Ripa group was smaller with statistical significance ($P<0.05$) compared to Ripa group. The accumulation of FITC-signal could be found in the CNV lesions after 48 hours post injection.

Conclusions: Lipsome encapsulation has the therapeutic potential to enhance the suppressive effect of Ripasudil on subretinal fibrosis.

CONTROL ID: 3705710

SUBMITTER (NAME ONLY): Andrew Anderson

TITLE: Investigating the relationship between critical flicker fusion frequency and symptoms of eye strain

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. Anderson, S. Singh, L.E. Downie, Optometry & Vision Sciences, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Andrew Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Sumeer Singh: Commercial Relationship: Code N (No Commercial Relationship) | Laura Downie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Critical flicker fusion frequency (CFF) has been used in clinical studies to measure visual fatigue. Here, we examine the correlation between CFF and subjective reports of eye strain in a group of participants with computer-induced eye strain, to consider whether CFF may be used as a surrogate for subjective measures of strain.

Methods: We analyzed data from a previous randomized controlled trial that examined the effect of blue-blocking lenses on eye strain (Singh et al (2021). Am J Opthalmol, 226: 243). One hundred and twenty adults, aged ≤40 years and diagnosed with computer vision syndrome, had CFF and eye strain symptoms quantified pre- and post- a visually demanding two-hour computer task. Symptoms were assessed using a questionnaire with nine subcomponents that summed to a total score out of 900. CFF (2° diameter green light emitting diode) was measured using a two-interval forced choice method, with flicker rate altered by a computer-controlled staircase procedure. For our primary analysis, we determined Spearman correlation coefficients between post-task symptom scores and CFF, and between change-from-baseline symptom scores and CFF. We also used a bootstrap procedure to consider if symptom score subcomponents were significantly (Bonferroni corrected alpha = 0.0056) different from overall scores with regards to their correlations with CFF.

Results: Although eye strain symptom scores altered significantly post-task (median difference 51 units, $p<0.001$ (Wilcoxon); 96.5% CI: 36 to 99), CFF did not (mean change −0.7 Hz, $p=0.17$ (paired t-test); 95% CI: −1.6 to 0.3). There was no significant correlation between symptoms and CFF either post-task ($r= −0.13$; 95% CI: −0.31 to 0.06) or for the change-from-baseline ($r = −0.17$; 95% CI: −0.34 to 0.02) analysis. Subcomponents of the symptom questionnaire did not show a significantly different correlation with CFF than did the overall symptom score, either for post-task or change-from-baseline values.

Conclusions: CFF is unlikely to be a useful surrogate for symptoms of eye strain, given its low — and insignificant — correlation with scores on an eye strain symptom questionnaire.

CONTROL ID: 3705711

SUBMITTER (NAME ONLY): Sean Adrean

TITLE: Subretinal fibrosis in patients with choroidal neovascularization based on spectral-domain optical coherence tomography classification: findings from the HARBOR trial

SESSION TITLE: Subretinal fibrosis – clinical challenges, mechanism, and diagnostic tools

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Adrean, Retina Consultants of Orange County, Fullerton, California, UNITED STATES|L. Hill, M.J. Amador-Patarroyo, Genentech Inc, South San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Sean Adrean: Commercial Relationship(s);Code R (Recipient):Alimera, RegenXBio;Code F (Financial Support):Genentech, Inc., Regeneron;Code C (Consultant/Contractor):Allergan, Amgen, Apellis, Genentech, Inc., IvericBio, NGM Biopharmaceuticals, Regeneron, RegenXBio | Lauren Hill: Commercial Relationship(s);Code C (Consultant/Contractor):Aerpio, Alimera, Genentech Inc., PolyPhotonix, Recens Medical | Manuel Amador-Patarroyo: Commercial Relationship(s);Code E (Employment):Genentech, Inc.

ABSTRACT BODY:

Purpose: Clinicians increasingly use spectral-domain optical coherence tomography (SD-OCT) to diagnose and follow neovascular age-related macular degeneration (nAMD). The purpose of this analysis of pooled data from HARBOR was to evaluate rates of fibrosis from choroidal neovascularization (CNV) based on SD-OCT classification.

Methods: SD-OCT scans from the phase 3 HARBOR trial (NCT00891735) of ranibizumab in patients with nAMD were reread by Doheny Image Reading and Research Laboratory, and CNV was classified as type 1, 2, and/or 3. Month 24 fibrosis status/location by baseline CNV type were evaluated using pooled observed data.

Results: At month 24, fibrosis was present in 31% (67/216) of eyes with type 1 lesions, 53% (176/332) with type 2 lesions, 45% (120/264) with mixed type 1/2 lesions, and 33% (17/51) with any type 3 lesions (overall $P < 0.0001$; Figure 1). Of those eyes with subretinal fibrosis, the majority had subfoveal involvement at month 24 (% patients for each lesion type: type 1, 75%; type 2, 78%; mixed type 1/2, 73%; type 3, 65%). Results were generally similar when stratified by treatment regimen (monthly vs pro re nata [as-needed]; Figure 2).

Conclusions: These findings demonstrate that eyes with type 2 CNV lesions had higher rates of fibrosis at month 24 than those with other lesion types.

CONTROL ID: 3705718

SUBMITTER (NAME ONLY): Man-Ru Wu

TITLE: Sox9 regulates glutamate homeostasis in the retina

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wu, C. Lin, S. Wang, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Man-Ru Wu: Commercial Relationship: Code N (No Commercial Relationship) | Cheng-Hui Lin: Commercial Relationship: Code N (No Commercial Relationship) | Sui Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The dysregulation of glutamate homeostasis in retina is associated with many retinal diseases, such as glaucoma, diabetic retinopathy and age-related macular degeneration. The study aims to uncover the molecular mechanisms that control retinal glutamate homeostasis via dissecting the regulation of the Glul gene, which is one of the key genes that regulate glutamate homeostasis.

Methods: Retinal Müller glial cells (MG) play key roles in regulating glutamate homeostasis in the retina by converting glutamate into glutamine via glutamine synthetase (GS), which is encoded by the Glul gene. We first examined whether the expression levels of Glul /GS changes in response to different levels of extracellular glutamate in the retina. We then determined how the Glul expression is regulated by identifying novel cis-regulatory modules (enhancer) and revealing the upstream transcription factors.

Results: We found that Glul mRNA levels and GS protein levels were significantly upregulated when we increased the extracellular levels of glutamate in the retina via intravitreally injection of Glutamate or NMDA. Based on ENCODE database, we identified a novel enhancer of Glul gene located in the second intron (referred as M11). We found that Glul expression is regulated via the M11 enhancer, and discovered that Sox9 binds to M11 and positively regulates the expression Glul gene. Notably, over-expression of Sox9 can protect the retina from the damage induced by excessive extracellular glutamate.

Conclusions: Sox9 regulates Glul expression and is essential for glutamate homeostasis in the retina. Elevation of Sox9 levels in MG can protect the retina in acute injury models with excessive extracellular glutamate.

CONTROL ID: 3705734

SUBMITTER (NAME ONLY): Peter Wagner

TITLE: Wide field topographical choroidal thickness measurement following binocular, eye-tracking mapped, short-term optical defocus

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Wagner, A. Ho, R&D, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|P. Wagner, A. Ho, J. Kim, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|J. Kim, Sensory Process Lab, Kensington, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Peter Wagner: Commercial Relationship(s);Code F (Financial Support):BHVI Ltd. | Arthur Ho: Commercial Relationship(s);Code E (Employment):BHVI Ltd. | Juno Kim: Commercial Relationship(s);Code E (Employment):UNSW - Sydney, Australia

ABSTRACT BODY:

Purpose: Changes in choroidal thickness observed after short-term optical defocus support the theory that eye growth is optically guided. Most previous studies used a monocular optical appliance to manipulate the potential myogenic factors, which may introduce confounders by disrupting the natural functionality of the visual system. We explored if optical defocus generated by an ecological environment can predict choroidal thickness changes while habitual binocular vision is maintained.

Methods: A custom 3D eye tracker (Pupil Labs Core, Pupil Labs GmbH, Germany) monitored compliance to fixating the hand-held device (at ~3D, 30min) to estimate dioptric demand over a wide field of view (with magnitudes of ~0.5D up to 4.5D) using a miniature time-of-flight camera (Pico Flexx, PMD Technologies AG, Germany). The spatially diverse peripheral environment around the hand-held device generated an optical defocus at the retinal periphery. Temporal accumulation of dioptric demand was mapped onto a wide field of choroidal locations using gaze direction estimates from the 3D Eye-Tracker. Intra- (3 repeats per participants, pre and post intervention) and inter- participant topographical choroidal maps were landmark matched and subtended a congruent visual field. Local and regional choroidal thickness exposed to different dioptric defocus were evaluated for change with a global, sensitivity enhanced model.

Results: The average intra-participant random error of choroidal thickness estimation (1×s.d. at each pixel within the topographical map, n ~100k) could be reduced by ~20% to 5.2 ± 2.1 μm by truncation of outliers. No significant difference in thickness change was found for choroidal regions exposed to different optical defocus (GLM n=21, eye $p=0.62$, area $p=0.21$, eye*area $p=0.46$). Some apparently randomly positioned loci showed significant difference (Fig. 1).

Conclusions: A change in topographical choroidal thickness consistent with local relative dioptric defocus was not found. The proposed topographical choroidal thickness model showed a sensitivity comparable to theoretical longitudinal resolution of swept-source OCT (wavelength 1060 nm). The presented methods and device can contribute to a better understanding of the ecologically valid dioptric landscape, and with further development, may provide further insight into short-term myopia models.

CONTROL ID: 3705735

SUBMITTER (NAME ONLY): Julia Cluceru

TITLE: Feature discovery using ablation studies for deep learning–based geographic atrophy (GA) progression prediction

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Cluceru, N. Anegondi, Q. Yang, V. Steffen, C. Rabe, M. Friesenhahn, D. Ferrara, S.S. Gao, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although convolutional neural networks (CNN) can accurately predict GA growth rate using fundus autofluorescence images (FAF), what drives the prediction accuracy remains unknown. Here, we ablate different regions of FAF to study their contribution to GA progression prediction.

Methods: The dataset included baseline (BL) FAF of patients with bilateral GA enrolled in NCT02479386, NCT02247479, and NCT02247531. GA progression, measured by annualized lesion growth rate (mm^2/y), was derived as the slope of a linear fit on available measurements of GA lesion area. Data were split into training (n=1041) and holdout (n=255) sets stratified by BL factors. The training set was further split into 5 stratified folds.

GA lesion masks were generated using a segmentation algorithm for each image. Three regions were delineated using the mask: inside the lesion (Lesion), a 500-µm rim around the lesion (Rim), and the remaining region. All possible combinations of these regions were ablated with black pixels to create new datasets. The VGG16 architecture was trained using a random hyperparameter search on each dataset to predict GA progression. The square of the Pearson correlation coefficient (r^2) between predicted and observed GA growth rate was averaged across the 5 folds and used for model selection. The same metric was then used to test performance on the holdout set.

Results: Each 5-fold cross-validation experiment yielded 5 independent models. Fig 1 depicts the holdout r^2 of each of these models for each dataset.

Compared with the full FAF (r^2=0.44), nearly half of the variability in prediction was explained by capturing only shape and size in the Mask Only dataset (r^2=0.24). The No Rim dataset (r^2=0.39) showed a greater decrease in performance compared with the Lesion and Rim (r^2=0.43) or No Lesion (r^2=0.42) datasets. Further, the Rim Only dataset (r^2=0.37) performed better compared with the Lesion Only (r^2=0.33) and No Lesion or Rim (r^2=0.27) datasets.

Conclusions: The intensity and texture within the rim of the FAF contains more predictive features for GA growth rate. We interpret that intensity/texture and morphology have additive contributions to the predictive performance of the CNN. Our findings can be further confirmed by quantifying these features using oculomics and observing predictive performance.

CONTROL ID: 3705738

SUBMITTER (NAME ONLY): Yusuke Kikuchi

TITLE: Predicting optimal treatment regimen for patients with neovascular age-related macular degeneration (nAMD) using machine learning

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kikuchi, J. Dai, C. Quezada Ruiz, Genentech Inc, South San Francisco, California, UNITED STATES|Y. Kikuchi, University of California Berkeley Department of Industrial Engineering and Operations Research, Berkeley, California, UNITED STATES|A. Neubert, Roche Pharma Research and Early Development Informatics, Basel, SWITZERLAND|

Commercial Relationships Disclosure: Yusuke Kikuchi: Commercial Relationship(s);Code E (Employment):Genentech, Inc. | Ales Neubert: Commercial Relationship(s);Code E (Employment):F. Hoffmann-La Roche Ltd. | Jian Dai: Commercial Relationship(s);Code E (Employment):Genentech, Inc. | Carlos Quezada Ruiz: Commercial Relationship(s);Code E (Employment):Genentech, Inc.

ABSTRACT BODY:

Purpose: This pilot study aimed to develop machine learning models to predict the optimal dosing regimen for patients with nAMD using baseline (BL) characteristics for patients treated with faricimab, the first bispecific antibody for intraocular use, in the phase 2 AVENUE (NCT02484690) and STAIRWAY (NCT03038880) trials.

Methods: Predicting optimal regimen, defined as the least frequent dosing regimen that achieves the maximum best-corrected visual acuity (BCVA) potential, is converted to a regression problem on the BCVA ETDRS letter score using treatment regimen as input. Because treatment arm is randomly assigned in clinical trials, we can alternate the treatment regimen feature to predict BCVA letter score for different regimens. To predict an optimal regimen for a new patient, BL characteristics are entered into the trained model together with each possible treatment regimen (Figure 1).

For the regression problem, BCVA at month 9 was set as the target. Linear model, random forest, extreme gradient boosting (XGBoost), and support vector machine are trained and evaluated. Age, sex, BCVA, and central subfield thickness at BL are selected as benchmark features. In addition, image-derived features, such as fluids and layer thickness, obtained by an automated segmentation algorithm on SD-OCT scans, are considered for full models. To evaluate the model's discriminative power between treatment regimens, we define a metric called mean difference, which is the mean difference between the maximum and minimum prediction over all possible treatment regimen assignments.

The methods are applied to a data set consisting of all patients in AVENUE and STAIRWAY, including patients treated with ranibizumab (N = 324).

Results: For the regression problem, XGBoost achieved the highest performance (R^2 = 0.38) with benchmark features and image features (Table 1). The mean difference value varies between models, with no obvious relationship between model performance and discriminative capability of treatment regimens.

Conclusions: The results of this study highlight the potential of a method to predict an optimal treatment regimen for patients with nAMD using a regression model. To fully understand advantages and limitations of this method, validation at a larger scale is warranted.

CONTROL ID: 3705750

SUBMITTER (NAME ONLY): Xiao Liu

TITLE: Later bedtime associated with greater myopic refractive error and variations in axial length rhythms

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure: Xiao Liu: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Naduvilath: Commercial Relationship: Code N (No Commercial Relationship) | Padmaja Sankaridurg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Late bedtime was identified as a risk factor for childhood myopia and disturbance to the sleep/wake cycle was found to induce myopia in chicks accompanied with altered axial length (AL) diurnal rhythms. This study explored the relation between participants' habitual bedtime, diurnal changes in AL and refractive status.

Methods: A total of 25 young, healthy adults (mean age ± SD: 25±4.75 years; 13 myopes, 52%; spherical equivalent mean ± SD: -1.45 ± 1.90D) attended seven consecutive visits over 24 hours. All participants had a best-corrected visual acuity of 20/20 or better, and no history of travelling across different time zones within one month before participating in the study. At each visit, noncycloplegic open-field auto-refraction (NVision-K 5001; Shin-Nippon, Japan) and ocular biometry (LenStar; Haag-Streit, Switzerland) of the right eye was conducted. Myopia was defined as spherical equivalent ≤-0.75D. Sleep habits including usual bedtime were assessed using questionnaires (Pittsburgh Sleep Quality Index, PSQI) at the first visit; those with a usual sleep time of 12am or later were categorised as late sleepers (n=16). Diurnal changes in AL were analysed using repeated measures ANOVA, where repeated visits were modelled as the within-patient factor and usual bedtime categories and refractive status (myopic/non-myopic) were used as between-subjects factors.

Results: Significant time-related differences in AL were observed over the 24-hour period ($p < 0.001$). The diurnal patterns of AL were different between early versus late sleepers ($p = 0.01$). Specifically, while the patterns amongst early sleepers presented a bi-phase rhythm, such characteristic was less apparent for late sleepers. The maximum and minimum values of AL were detected at different times for the two groups, with late sleepers lagging four hours behind (Fig. 1). Additionally, late sleepers were more myopic compared to the early ones (-1.83±2.01D vs -0.78±1.55D, $p = 0.04$) after adjusting for age and gender.

Conclusions: In this adult population, diurnal rhythm in AL varied between early versus late sleepers and late sleepers exhibited greater myopic refractive error. The effect of the variation in sleep and diurnal rhythm in AL needs investigation in children to determine if it has a role to play in the onset of myopia.

CONTROL ID: 3705751

SUBMITTER (NAME ONLY): Pablo Concepcion Grande

TITLE: Evaluation of reading performance with progressive power lenses using eye tracking technology

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Concepcion Grande, A. González, P. Dotor Goytia, E. Chamorro, J. Cleva, J. Alonso, Clinical research department, Indizen Optical Technologies.SL, Madrid, Madrid, SPAIN|J. Alonso, J. Gómez-Pedrero, Applied Optics Complutense Group, Optics Department, Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: The goal of this research is to evaluate the reading performance at different distances when wearing progressive power lenses (PPL) with different power distributions. The reading performance has been assessed by means of eye tracking technology.

Methods: 16 presbyopic subjects participated in a double-masked trial. A wearable eye-tracker system (Tobii-Pro Glasses 3) was used to record gaze position when reading at near and distance vision while using 2 types of PPLs (PPL-D and PPL-N). According to Sheedy's criteria, the distance-vision areas of the PPL-D and PPL-N are 48.2mm^2 and 21.6mm^2 respectively. The near-vision areas are 36.8mm^2 and 54.1mm^2 for PPL-D and PPL-N respectively. Subjects were asked to read a text showed on a digital screen placed at 5.25m and 0.37m when looking through the center and peripheral regions of the lens. Different reading texts with similar difficulty level and same letter size (Visual acuity=0.4logMAR) were used. Reading time and fixations characteristics (count, total duration, and average duration), were analyzed for each reading condition and PPL. Statistical analysis was performed using Statgraphics Centurion XVI.II software.

Results: The analysis of the eye movements at distance-reading showed a statistically significant lower reading time and lower total duration of fixations for PPL-D (Table 1). At near-reading the lens PPL-N provided statistically significant lower reading time, lower total duration of fixations and less fixation count (Table 2).

Conclusions: Reading performance at different distances is affected by the PPL power distribution; a design with wider distance area provides better distance-reading performance while a PPL with wider near area is better for near-reading. This experiment demonstrates that the power distribution of PPLs clearly influences the user performance at vision-based tasks. Henceforth, PPL selection must consider user needs to provide the best visual experience

CONTROL ID: 3705753

SUBMITTER (NAME ONLY): Dimitrios Damopoulos

TITLE: Predicting 5-year progression to vision-threatening complications using machine learning

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Damopoulos, A. Neubert, F. Benmansour, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|L. Mendes, T. Santos, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Dimitrios Damopoulos: Commercial Relationship(s);Code C (Consultant/Contractor):F Hoffmann-La Roche;Code E (Employment):HAYS plc | Luís Mendes: Commercial Relationship: Code N (No Commercial Relationship) | Torcato Santos: Commercial Relationship: Code N (No Commercial Relationship) | Ales Neubert: Commercial Relationship(s);Code E (Employment):F Hoffmann-La Roche | Daniela Ferrara: Commercial Relationship(s);Code E (Employment):Genentech Inc;Code I (Personal Financial Interest):F Hoffmann-La Roche | Jose Cunha-Vaz: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Alimera Sciences, Allergan, Bayer, Gene Signal, Novartis, Pfizer, Oxular, Roche, Sanofi | Fethallah Benmansour: Commercial Relationship(s);Code E (Employment):F Hoffmann-La Roche

ABSTRACT BODY:

Purpose: To develop and evaluate a method for predicting 5-year risk of progression to a vision-threatening complication (VTC) in patients with diabetes and absent or mild diabetic retinopathy (DR).

Methods: Systemic and retinal imaging–based measurements (optical coherence tomography [OCT] and color fundus photographs) were collected from a cohort study (NCT03010397) of 172 patients with diabetes (32% female; mean age at baseline, 63 years). Per inclusion criteria, maximum level of DR at baseline was 35, as classified by the Diabetic Retinopathy Severity Scale. Patients were followed up annually for up to 5 years or until they developed a VTC (OCT-defined centrally involved macular edema, clinically significant macular edema, or proliferative DR). Of 172 patients, 27 (15.7%) progressed to ≥ 1 VTC. Linear regression models were trained and evaluated using 5-fold cross-validation for predicting VTC progression events. Features were either specified via an unsupervised hierarchical clustering method that reduced dimensionality of the feature space or selected manually guided by expert domain knowledge. The selected features of the manual approach consisted of 3 systemic and 5 imaging-based features, summarized in Table 1. Area under the receiver operating characteristic curve (AUC) was used as the performance metric.

Results: The trained models predicted progression to VTC with a mean (SD) AUC of 0.76 (0.04) when using the unsupervised dimensionality reduction approach and 0.78 (0.09) when using the 8 manually selected features. The models performed with a mean (SD) AUC of 0.72 (0.11) when using only the 5 selected imaging–based features versus 0.64 (0.05) when using only the 3 selected systemic features.

Conclusions: In this cohort of patients with absent or mild DR, the models predicted progression events with a mean AUC of 0.78 despite the low progression rate to a VTC and with comparable performance for both the manual and unsupervised approaches. Our results also indicate that imaging features alone are more powerful than systemic features alone in predicting progression to a VTC. With validation from larger and more diverse patient sets, predictive models of VTC in patients with DR could be valuable for informing personalized monitoring and follow-up in both clinical development and clinical practice.

CONTROL ID: 3705754

SUBMITTER (NAME ONLY): Andreas Stahl

TITLE: Intravitreal aflibercept compared with laser photocoagulation for infants with retinopathy of prematurity: A FIREFLEYE subgroup analysis

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Stahl, Department of Ophthalmology, Universitatsmedizin Greifswald, Greifswald, GERMANY|E. Sukgen, Department of Ophthalmology, Adana City Training and Research Hospital, Adana, TURKEY|W. Wu, Department of Ophthalmology, Linkou Chang Gung Memorial Hospital, Taoyuan, TAIWAN|W. Wu, College of Medicine, Chang Gung University, Taoyuan, TAIWAN|D. Lepore, Department of Geriatrics and Neuroscience, Catholic University of the Sacred Heart, A. Gemelli Foundation IRCSS, Rome, ITALY|N. Azuma, Department of Ophthalmology, National Center for Child Health and Development, Tokyo, JAPAN|H. Nakanishi, Research and Development Center for New Medical Frontiers, Department of Advanced Medicine, Division of Neonatal Intensive Care Medicine, Kitasato University School of Medicine, Sagamihara, JAPAN|J. Mazela, Department of Neonatology, Division of Newborn Infectious Diseases, Poznan University of Medical Sciences, Poznan, POLAND|T. Schmelter, E. Koefuencue, Bayer AG, Berlin, GERMANY|S. Leal, Bayer Consumer Care AG, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: FIREFLEYE was the first randomized, controlled, multicenter, international Phase 3 trial of patients with treatment requiring retinopathy of prematurity (ROP) that compared the treatment effects of intravitreal aflibercept (IVT-AFL) to laser. It was also the first ROP study to include Zone II Stage 2+ eyes, permitting unilateral treatment, and using a low injection volume of only 0.01 mL IVT-AFL per eye (20% of the approved adult dose and injection volume). Previously reported primary results demonstrated treatment success (absence of active ROP and unfavorable structural outcomes at Week [W] 24 based on investigator assessment) with IVT-AFL to be numerically higher compared with laser (85.5% versus 82.1%). This was considered clinically relevant, while non-inferiority could not be formally shown. Here, we report a post hoc analysis of the primary endpoint for subgroups stratified by gestational age and weight at treatment.

Methods: FIREFLEYE (NCT04004208) enrolled infants born at gestational age ≤32 weeks or birth weight ≤1500 g, weighing ≥800g at time of first treatment, who had ROP Zone I Stage 1+, 2+, 3+/-; Zone II Stage 2+, 3+; or aggressive posterior ROP in at least one eye. Infants were randomized 2:1 to receive IVT-AFL 0.4 mg or laser photocoagulation. Re-treatment and/or rescue treatment (IVT-AFL rescue for the laser group, laser rescue for the IVT-AFL group) was administered if any of the prespecified criteria were met.

Results: Treatment success in the subgroup of infants with low weight <1500 g at first treatment (n=24) was 87.3% in the IVT-AFL group (n=14) compared to 66.0% in the laser group (n=10). In infants with gestational age <27 weeks (n=77), treatment success was 85.7% for IVT-AFL (n=49) versus 80.0% for laser (n=28). Results for additional subgroups, e.g., infants with Zone II Stage 2+ ROP and infants treated unilaterally, will also be presented.

Conclusions: Overall, FIREFLEYE data consistently show that treatment of ROP patients with IVT-AFL 0.4 mg is clinically efficacious and safe. Subgroup analyses suggest that IVT-AFL may be a sensible alternative to laser treatment particularly for infants born at less than 27 weeks of gestational age and/or weighing less than 1.5 kg at time of first treatment.

CONTROL ID: 3705768

SUBMITTER (NAME ONLY): Hong Liu

TITLE: Activated GABABR Affected Eye Growth in Chickens with Altered Visual Stimuli

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Liu, F. Schaeffel, M.P. Feldkaemper, Section of Neurobiology of the Eye, Ophthalmic Research Institute, University of Tuebingen, Tuebingen, Baden-Wurttemberg, GERMANY|H. Liu, Z. Yang, Aier Institute of Optometry and Vision Science, Aier Eye Hospital Group, Changsha, Hunan, CHINA|F. Schaeffel, Myopia Research Group, Institute of Molecular and Clinical Ophthalmology Basel (IOB), Basel, SWITZERLAND|Z. Yang, Aier School of Ophthalmology, Central South University, Changsha, CHINA|

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ABSTRACT BODY:

Purpose: As an important retinal neurotransmitter, GABA has been proposed to modulate eye growth and refractive development. This study aimed to explore the specific role of GABA B receptors (GABABR) during experimentally induced hyperopia and myopia development.

Methods: Exp. 1: Chicks were intravitreally injected with 25 µg baclofen (GABABR agonist) in one eye and saline into the fellow eye. Choroidal thickness (ChT) was measured by OCT before and 2, 4, 6, 8, 24 hours after injection. Exp. 2: Chicks were monocularly treated with a +7D lens or translucent occluder, respectively, and randomly assigned to baclofen (25 µg) or saline treatment. Drugs were intravitreally injected daily into experimental eyes, for 4 days. Refraction (RE), axial length (AL) and ChT were measured before and after treatment. Dopamine (DA) and its metabolites were analyzed via HPLC.

Results: Experiment 1: ChT decreased strongly at 6 and 8 hours after baclofen injection (-53.5 µm, p = 0.0006; -48 µm, p = 0.002) and returned back to baseline level after 24 hours. Experiment 2: Baclofen inhibited plus lens compensation: eyes got only slightly hyperopic (ΔRE: 1.15 ± 0.67 D), grew significantly more than +L treated saline-injected eyes (ΔAL: 0.32 ± 0.07 mm vs. 0.09 ± 0.07 mm, P = 0.02) and ChT decreased in +7D treated eyes (ΔChT: -78.2 ± 14.1 µm), an effect opposite to the increase in +L saline-treated chicks. Plus lens treatment reduced vitreal DOPAC and DA content in saline (ΔDOPAC: -1.68 ± 0.17 ng/100 mg weight) and baclofen treated eyes compared to fellow eyes (ΔDOPAC: -2.22 ± 0.07 ng/100 mg weight), but significantly more in the baclofen treated eyes. Baclofen also significantly reduced the myopic shift in deprived eyes (ΔRE: -2.83 ± 0.22 D vs -4.30 ± 0.79 D, p = 0.004). However, it did not change ChT compared to deprived saline-injected eyes (ΔChT: -69.7 ± 10.8 µm vs. -65.6 ± 11.6 µm, n.s.). Vitreal DOPAC and DA were reduced in all deprived eyes compared to untreated fellow eyes, with content in the baclofen group decreasing more.

Conclusions: Activation of GABABR downregulated retinal DA release and reduced ChT in chicken eyes. It attenuated the response to modulated visual stimuli, with more eye growth in lens-induced hyperopia and less eye growth in form-deprivation myopia. Since GABA is a ubiquitous transmitter, interference with its signaling may not only interfere with myopia development but also with visual function.

CONTROL ID: 3705778

SUBMITTER (NAME ONLY): Abdelhalim Awidi

TITLE: Comparison of visual and refractive outcomes in simultaneous vs sequential pars plana vitrectomy and cataract surgery

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Awidi, P. Mathews, Y.J. Daoud, Cornea, Cataract and External Disease, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Abdelhalim Awidi: Commercial Relationship: Code N (No Commercial Relationship) | Priya Mathews: Commercial Relationship: Code N (No Commercial Relationship) | Yassine Daoud: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The decision to perform simultaneous versus sequential cataract extraction (CE) surgery and pars plana vitrectomy (PPV) has several implications for both the patient and the surgeon. We performed a retrospective, clinical study to compare outcomes of simultaneous versus sequential CE and PPV surgery in terms of postoperative visual acuity and refractive outcomes.

Methods: We assessed three possible combinations of PPV and CE surgery: simultaneous PPV and cataract surgery (PPV+CE); PPV followed by cataract surgery (PPV/CE), and cataract surgery followed by PPV (CE/PPV). A two-year retrospective chart review of 427 eyes with history of PPV and CE was performed. Assessments of UCVA and BCVA, spherical equivalent (SEQ), and target refraction were done. Outcomes studied were UCVA, BCVA, SEQ and refractive prediction error (RPE) at the 1 month, 3 months, 6 months, 1 year, and 2 years postoperative visits. Only patients with epiretinal membrane (ERM) or vitreous opacity (VO) indications in the PPV+CE and PPV/CE were included in the SEQ and RPE calculations.

Results: In total, 427 eyes of 404 patients were included, of which 113 eyes underwent PPV/CE, 261 eyes underwent PPV+CE, and 53 eyes underwent CE/PPV. Improvement in UCVA and BCVA of the whole patient cohort was seen at every follow-up visit compared to preoperative measures. There was a statistically significant difference in BCVA measures of the PPV/CE, PPV+CE, CE/PPV groups (LogMAR 0.34 ± 0.40, 0.65 ± 0.61, and 0.55 ± 0.60, respectively; $P < 0.001$) at POM1, and at POM12 (LogMAR 0.25 ± 0.34, 0.53 ± 0.68, and 0.44 ± 0.48, respectively; $P = 0.04$). At the POM1+3 visits, RPE was within ± 1.0 D in 11 eyes (65%) in the PPV/CE group, and 44 eyes (86%) in the PPV+CE group, while it was within ± 2D in 16 eyes (94%) in the PPV/CE and 51 eyes (100%) in the PPV+CE group.

Conclusions: Simultaneous PPV and cataract surgery demonstrated a significant improvement in visual and refractive outcomes that were comparable to sequential surgery results. A simultaneous approach may be a suitable option in elective situations as it avoids the gradual deterioration in vision that arises with the progression of cataracts following PPV.

CONTROL ID: 3705783

SUBMITTER (NAME ONLY): Fethallah Benmansour

TITLE: Deep learning (DL) model to identify moderately severe and severe nonproliferative diabetic retinopathy (NPDR) from 7-field color fundus photographs (7F-CFP)

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Benmansour, D. Damopoulos, A. Neubert, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|Q. Yang, N. Sredar, D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|L. Mendes, T. Santos, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: We previously developed and evaluated a DL model to identify eyes with moderately severe and severe NPDR from 7F-CFP leveraging a large cohort of patients with diabetes from the United States.[1] In this study, we evaluate and report performances of the DL model on an independent cohort of patients with DR from Portugal.

Methods: The DL model presented previously[1] was developed using 7F-CFP collected from the eyes of 37,358 patients with diabetes between 1999 and 2016 (Source: Inoveon Corporation, Oklahoma City, OK). DR severity and presence of clinically significant macular edema were assessed from 7F-CFP (Zeiss FF 450+) by expert graders at a centralized reading center using the Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale (DRSS). Prevalence of moderately severe or severe NPDR (DRSS 47–53) in this cohort was 2.2%. The dataset was used to develop a DL Inception v3 model with transfer learning to detect eyes with DRSS 47–53.

The independent evaluation dataset was collected from a natural history study of DR progression (NCT03010397). Enrolled patients had less than mild NPDR at baseline (32% female; mean age at baseline, 63 years) and were followed up annually over 5 years. From 172 patients who completed the study, 635 unique eyes/visits were imaged by 7F-CFP (Topcon TRC-50DX) and had a valid DRSS, of which 14 eyes were identified with DRSS 47–53. Model performance was assessed using the area under the receiver operating characteristic (AUROC) curve, specificity, and sensitivity, using a cutoff computed on the development dataset.

Results: The model performed on the evaluation dataset with an AUROC of 0.900 (95% CI, 0.864, 0.944), sensitivity of 1.0 (95% CI, 1.0, 1.0), and specificity of 0.699 (95% CI, 0.667, 0.734) using a cutoff computed on the development set that maximizes the Youden index.

Conclusions: Despite differences between the development and evaluation datasets in terms of geographic location of patients and CFP imaging instruments used, the DL model rendered good performance and generalizability for identification of eyes with DRSS 47–53. Provided additional validation of this model on more diverse datasets, the model could be used to inform screening of patients at high risk of progression to vision-threatening DR.

Reference:

1. Benmansour F et al. Invest Ophthalmol Vis Sci. 2021;62(8):115.

CONTROL ID: 3705784

SUBMITTER (NAME ONLY): Maliya Delawan

TITLE: Add-On Bolster Element for Temporary Tarsorrhaphy Augmentation

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Delawan, College of Medicine, Gulf Medical University, Ajman, Ajman, UNITED ARAB EMIRATES|S.H. Aljneibi, E. Adami, N. ElShammah, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|R.R. Sayegh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Maliya Delawan: Commercial Relationship: Code N (No Commercial Relationship) | Shaikha Aljneibi: Commercial Relationship: Code N (No Commercial Relationship) | Emma Adami: Commercial Relationship: Code N (No Commercial Relationship) | Nora ElShammah: Commercial Relationship: Code N (No Commercial Relationship) | Rony Sayegh: Commercial Relationship(s);Code R (Recipient):Novartis, Allergan

ABSTRACT BODY:

Purpose: To describe a method of temporary tarsorrhaphy augmentation using an add-on bolster element.

Methods: The add-on bolster was made from 3 plastic tubings of approximately equal length, cut from a pediatric butterfly cannula or other IV tubing. One of the plastic tubings was cut lengthwise on one side. A double-armed non-absorbable suture, such as a 4-0 nylon, silk, or prolene, was passed in a horizontal mattress fashion through one wall of the cut tubing, and through the first uncut tubing. The same procedure is performed on the second uncut tubing, resulting in 3 cylinders connected by the 2 arms of the suture in a parallel fashion. Finally, the 2 needles were passed through the opposite wall of the original tubing, the one with the lengthwise cut, and tied in a horizontal mattress fashion.

Results: The optimal size of the add-on bolster was calculated using a formula which includes the length of the tarsorrhaphy and the size of the palpebral fissure. A 17-year-old corneal graft recipient female with cicatricial lagophthalmos, the add-on bolster was slipped between the original tarsorrhaphy suture and bolster, augmenting its effect and resulting in re-approximation of the eyelid margins and protection of the ocular surface for an additional 2 months. The only complication observed was loss of the add-on bolster that was replaced.

Conclusions: The use of the add-on bolster to augment a temporary tarsorrhaphy is a simple technique to salvage the suture tarsorrhaphy and prolong its usefulness.

CONTROL ID: 3705795

SUBMITTER (NAME ONLY): Eric Kuklinski

TITLE: Agreeability of Tele-ophthalmology and Artificial Intelligence-Based Diagnosis of Diabetic Retinopathy

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.J. Kuklinski, R.K. Henry, M. Shah, P. Tailor, R. Verma, A. Zhu, M.A. Zarbin, B. Szirth, N. Bhagat, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic exposed the need for increased mobilization of tele-ophthalmology resources. Artificial intelligence (AI) may serve as a tool to assist physicians in triaging highest need patients if the AI's assessment of disease is comparable to the physician's assessment. This study assesses the ability of AI software to diagnose diabetic retinopathy (DR) as compared to Tele-ophthalmology and in-person examination by a retina specialist.

Methods: Records of forty patients (average age 55.1±10.9 years) presenting to an urban retina clinic were reviewed retrospectively for factors including demographics, retinal photos taken by Canon CR-2 Plus AF Retinal Imaging camera (Tokyo, Japan), and diagnosis of DR based on the International Clinical Diabetic Retinopathy (ICDR) classification scale during an in-person clinic visit in which a fundus exam was performed. Retinal photos were graded by AI software, EyeArt (EyeNuk, CA), as Normal, Mild DR, or More than Mild DR. Retinal images were also graded remotely by a retina specialist using the ICDR classification scale via TeamViewer software (Tele). Agreement between Tele, AI, and in-person DR diagnosis was assessed using Cohen's Kappa (κ) coefficient using IBM® SPSS® Statistics software.

Results: Among 80 eyes, 33 were diagnosed in-person with no DR, 5 with mild non-proliferative DR (NPDR), 9 with moderate NPDR, 3 with severe NPDR, 7 with proliferative diabetic retinopathy (PDR), and 23 with regressed PDR. Eleven and 26 eyes could not be graded by Tele or AI, respectively. κ±SE for in-Person diagnosis vs Tele was 0.859±0.058 ($p<.001$), in-person vs AI was 0.751±0.082 ($p<.001$), and Tele vs AI was 0.883±0.063 ($p<.001$).

Conclusions: AI is a reliable tool for screening patients for DR and referring them for physician evaluation since AI had a substantial rate of agreement with the in-person diagnosis and near perfect agreement with Tele. Tele grading was in near perfect agreement with the in-person diagnosis, showing that Tele is a reliable option for a physician to remotely screen patients that may be ungradable by AI. However, improvements are needed due to the high number of images that are ungradable via Tele and AI. Further studies should assess ways to reduce the number of ungradable images via Tele and AI and create a trend analysis for multiple visits for a given patient.

CONTROL ID: 3705804

SUBMITTER (NAME ONLY): Jennifer Lim

TITLE: Efficacy, durability, and safety of faricimab in diabetic macular edema: 2-year results from the phase 3 YOSEMITE and RHINE trials

SESSION TITLE: Diabetic Macular Edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.I. Lim, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|J.A. Wells, Palmetto Retina Center, Columbia, South Carolina, UNITED STATES|D.A. Eichenbaum, Retina Vitreous Associates of Florida, St Petersburg, Florida, UNITED STATES|D.A. Eichenbaum, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|C.J. Danzig, Rand Eye Institute, Deerfield Beach, Florida, UNITED STATES|C.J. Danzig, Charles E Schmidt College of Medicine, Florida Atlantic University, Boca Raton, Florida, UNITED STATES|K. Asik, Z. Haskova, S. Mohan, Y. Tang, H. Lin, Genentech Inc, South San Francisco, California, UNITED STATES|D. Silverman, Roche Products Ltd, Welwyn Garden City, UNITED KINGDOM|J.I. Lim, Ophthalmology, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Year 1 data from the phase 3 YOSEMITE/RHINE trials support the hypothesis that dual angiopoietin-2/vascular endothelial growth factor (VEGF)-A pathway inhibition with faricimab, the first bispecific antibody designed for intraocular use, may promote vascular stability and durable efficacy beyond current anti-VEGF therapies for diabetic macular edema (DME). Year 2 of YOSEMITE/RHINE will inform the longer-term efficacy, durability, and safety of faricimab in patients with DME.

Methods: YOSEMITE (NCT03622580) and RHINE (NCT03622593) were randomized, double-masked, active comparator–controlled, 100-week trials of faricimab in treatment-naïve and previously anti-VEGF–treated patients with center-involving DME (YOSEMITE, N = 940; RHINE, N = 951). Patients were randomized 1:1:1 to faricimab 6.0 mg every 8 weeks (Q8W) after 6 initial Q4W doses, faricimab 6.0 mg per personalized treatment interval (PTI) after 4 initial Q4W doses, or aflibercept 2.0 mg Q8W after 5 initial Q4W doses. The PTI algorithm was a protocol-driven treat-and-extend regimen, with dosing intervals extended, maintained, or reduced (from Q4W up to Q16W) based on central subfield thickness (CST) and best-corrected visual acuity (BCVA) change at active dosing visits. The primary efficacy endpoint was mean BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56. Key 2-year outcomes included mean BCVA change from baseline averaged over weeks 92, 96, and 100; the proportion of patients in the faricimab PTI arm who achieved Q4W, Q8W, Q12W, or Q16W dosing at week 96; mean CST change from baseline over 2 years; the proportion of patients with ≥ 2-step Diabetic Retinopathy Severity Scale improvement

from baseline at week 96; and the incidence and severity of adverse events through study end.

Results: At 1 year, faricimab Q8W or per PTI resulted in durable vision gains that were noninferior to aflibercept Q8W and achieved with Q16W dosing in > 50% of patients in the PTI arms. Faricimab Q8W or per PTI demonstrated anatomic improvements compared with aflibercept Q8W and was well tolerated, with low rates of intraocular inflammation. Year 2 results from YOSEMITE/RHINE will be presented at the meeting.

Conclusions: Year 2 data from YOSEMITE/RHINE will examine whether year 1 vision gains, anatomic improvements, and extended (up to Q16W) dosing with faricimab are maintained over 2 years.

CONTROL ID: 3705806

SUBMITTER (NAME ONLY): Brian Vohnsen

TITLE: Geometrical-optics approach to the Stiles-Crawford effect of the first and second kind

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Vohnsen, Q. Kennedy, N. Sharmin, Physics, University College Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The photopic Stiles-Crawford effect of the first kind (SCE-I) is typically described by waveguiding whereas the Stiles-Crawford of the second kind (SCE-II) is attributed to self-screening by visual pigments. Here, both effects are analyzed experimentally and compared to a geometrical-optics absorption model. This will show whether both effects are caused by light leakage rather than waveguiding.

Methods: Light absorption and optical path length in foveal outer segments is simulated for a hexagonal packing foveal cones across a retinal patch of up to 37 cones: 2 S-cones (5%), 11 M-cones (30%) and 24 L-cones (65%), respectively using Comsol^{TM}. Excess light is absorbed by the retinal pigment epithelium layer RPE. Absorption data are fitted to a Gaussian SCE-I and an Airy function representative of the collective light-capture efficiency for stacked visual pigments (Vohnsen, BOE 2014). The SCE-I directionality is evaluated and compared to psychophysical results obtained for two emmetropic subjects using a uniaxial digital micromirror device (DMD) flicker system (Carmichael Martins and Vohnsen, OPO 2018) and a liquid crystal bandpass filter for spectral tuning. Power-weighted absorption in adjacent outer segments is used to calculate an effective SCE-II hue shift as a function of wavelength for oblique light.

Results: Outer segment data in combination with ray optics and absorption can explain the typical Gaussian SCE-I visibility function with directionality parameters in the range of 0.03/mm^2 – 0.10/mm^2. In turn, if all outer segments contain the same class of visual pigment, such as rhodopsin in rods, the directionality becomes negligible confirming the absence of the SCE-I in scotopic conditions. The SCE-II hue shift matches psychophysical observations with no on-axis hue shift but a parabolic hue shift at for oblique incidence. The SCE-II distribution is fully contained within the spectral data of the SCE-I.

Conclusions: The study shows that leakage of light in outer segments can fully explain the SCE-I and crosstalk the related SCE-II without enforcing waveguiding. This shows the visual importance of the retina and photoreceptor optics on par with the optics of the anterior eye and the need for their careful consideration both in Maxwellian and normal Newtonian view. Ultimately, such knowledge may be applied in the development of new ophthalmic optics.

CONTROL ID: 3705811

SUBMITTER (NAME ONLY): Rajashekhar Gangaraju

TITLE: Potential role of exosome associated proteins from iPSC derived MSCs for early complications of diabetic retinopathy

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gangaraju, P. Rasiah, Ophthalmology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|A.P. Shrestha, T. Vaithianathan, Pharmacology, Addiction Science, and Toxicology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|F. Jia, Biochemistry and Molecular Biology, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|J. Rajasingh, Medicine - Cardiology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have developed a consistent and scalable cell source of induced MSCs (iMSCs) generated by differentiating the induced pluripotent stem cells (iPSC) derived from urinary epithelial cells through a non-insertional reprogramming approach. We tested the hypothesis that intravitreal delivery of iMSC exosomes will ameliorate retinal vascular and neuronal damage induced in diabetes.

Methods: Conditioned medium from iMSC that were exposed to TNFα/IFNγ in serum-free media was used to purify exosomes by ultracentrifugation method. Differential expression of proteins was analyzed by proteomic analysis. About 8-month-old $Ins2^{Akita/+}$ mice were intravitreally injected with exosomes (5mg protein/2μL) or saline. Littermate $Ins2^{+/+}$ receiving saline served as control. After 3 weeks post IVT, mice were tested for vascular permeability by FITC-BSA leakage method, visual function by ERG and OKN, and assessed for changes in dendritic complexity and postsynaptic targets by immunohistology.

Results: About 463 proteins were identified in the exosomes. Differential expression analysis revealed ~33 proteins enriched (>1.5 fold) in primed exosomes compared to unprimed exosomes. While $Ins2^{+/+}$ mice had minimal vascular leakage (30.7±6.0 RFU), $Ins2^{+/Akita}$ mice that received saline showed 70.7±10.7 RFU with a significant reduction in $Ins2^{+/Akita}$ mice that received exosomes (38.2±10.8 RFU, $p<0.03$). Similarly, a significant reduction in visual acuity (0.25±0.2 vs. 0.3±0.01 c/d, $p<0.04$), increased in contrast sensitivity threshold (57±8.6 vs. 39.1±6.5 %, $p<0.05$) and decreased b-wave amplitudes (220.2±7.8 vs. 306.2±16.3 mV, $p<0.02$) in $Ins2^{+/Akita}$ mice were improved with exosomes. Finally, immunohistology and confocal microscopy revealed loss of dendrites in cone bipolar (Secretagogin), rod bipolar (PKCα), and horizontal cells (Calbindin D28k) in $Ins2^{+/Akita}$ mice regenerated in mice that received exosomes.

Conclusions: Our data showed that a single intravitreal injection of iMSC-exosomes in $Ins2^{Akita/+}$ mice, reversed the ongoing vascular leakiness, regeneration of dendrite retraction, and re-establishment of synaptic disruption to rescue visual function. Future studies aiming at in-depth analysis of differentially expressed proteins within the exosomes will help establish the molecular processes leading to changes in the diabetic retina post iMSC-exosome transplantation.

CONTROL ID: 3705814

SUBMITTER (NAME ONLY): Viren Rana

TITLE: Treatment of Pediatric Lyme Meningitis with Neuro-Ophthalmic Complications: A Case Series

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Rana, P.B. Greenberg, T. Bakaeva, W. Chen, Ophthalmology, Brown University, Providence, Rhode Island, UNITED STATES|E. Kim, Brown University, Providence, Rhode Island, UNITED STATES|

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ABSTRACT BODY:

Purpose: A recent change in the Red Book: 2018-2021 Report of the Committee on Infectious Diseases now recommends either oral doxycycline (DCN) or intravenous ceftriaxone (IV CTX) for treatment of pediatric Lyme meningitis irrespective of neuro-ophthalmologic involvement. We describe three cases which highlight the challenges of managing pediatric Lyme meningitis with neuro-ophthalmic complications.

Methods: Retrospective case series

Results: Three pediatric patients - < 18 years of age with symptoms suggestive of meningitis, positive 2-tier Lyme serology (ELISA and western blot), +/- cerebrospinal fluid Lyme antibodies, and neuro-ophthalmologic complications (optic nerve edema +/- cranial nerve palsy) - were treated with either DCN or IV CTX initially. Case 1 (Figure 1, A) had optic nerve edema which worsened after 10 days of DCN treatment, necessitating advancement of treatment to IV CTX. Case 2 (Figure 1, B) had persistent grade 4 papilledema and cranial nerve six 6 palsy (CN6P), requiring a prolonged course of treatment with IV CTX. Case 3 (Figure 1, C) developed a new CN6P along with grade 4 papilledema OU after being treated initially with DCN. All three patients ultimately completed treatment with IV CTX to remove the confounding factors associated with use of DCN, and all had resolution of optic nerve edema and CN6P.

Conclusions: Cases of pediatric Lyme meningitis with neuro-ophthalmic complications are difficult to treat. The recent change in treatment recommendations allowing use of DCN as first line therapy further complicates initial treatment and subsequent management of systemic and eye disease associated with Lyme infection.

CONTROL ID: 3705820

SUBMITTER (NAME ONLY): Daniel Hill

TITLE: In vivo Fluorescent Labelling of Retinal Amyloid Beta with Intranasal Curcumin to Detect Alzheimer's Disease Pathology

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hill, V. Luong, L. Guo, M. Cordeiro, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Cordeiro, Western Eye Hospital, Imperial College Healthcare NHS Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: A possible gateway to effective disease-modifying intervention for Alzheimer's disease (AD) is starting treatment pre-symptomatically, facilitated by early-detection. Retinal amyloid beta (Aβ) deposition – reported to predate symptoms by over a decade – has been the subject of experiments investigating the Aβ binding compound curcumin, with controversial findings, partly attributable to the variable absorption from oral administration. Using a novel DMSO-based nasally-applied route of curcumin delivery, we hypothesised that a higher in vivo fluorescent retinal spot-count (using confocal laser scanning ophthalmoscopy) could be used to differentiate transgenic AD model mice from healthy controls, in addition to demonstrating ex vivo Aβ antibody colocalisation with curcumin.

Methods: A total of 10 triple transgenic (3xTg) AD model mice (Jackson labs) and 10 C57 control animals (Jackson labs), aged 2-6 months, were investigated. 10 μL of DMSO-based curcumin formulation was administered intranasally to awake animals. Animals' eyes were imaged using a confocal laser scanning ophthalmoscope at baseline (before curcumin administration) and 2 hours after curcumin, under gas anaesthesia. Whole retinal mounts were immunolabelled for Aβ with the 6E10 antibody, which was fluorescently labelled with a secondary antibody. Colocalisation of nasally delivered curcumin and 6E10 antibody was studied using fluorescent microscopy.

Results: 3xTg animals appeared to have more curcumin staining than controls in vivo. Using a one-way between-subjects ANOVA, a significant ($p<0.05$) effect of transgenic status on spot count was found, revealing that 3xTg animals showed significantly more spots than, and could be differentiated from, healthy animals. Furthermore, histology revealed that curcumin colocalises with 6E10 antibody in the retina.

Conclusions: Intranasally administered curcumin appears to label retinal Aβ, and the resulting fluorescent spots can be used to identify disease state in young transgenic and healthy mice. These results suggest that such an approach may warrant further development and investigation for the early detection of AD.

CONTROL ID: 3705828

SUBMITTER (NAME ONLY): Alvaro Gomariz

TITLE: A unified deep learning approach for OCT segmentation from different devices and retinal diseases

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gomariz, H. Lu, Y. Li, T. Albrecht, A. Maunz, F. Benmansour, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|J. Luu, D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|O. Goksel, Eidgenossische Technische Hochschule Zurich, Zurich, Zürich, SWITZERLAND|O. Goksel, Department of Information Technology, Uppsala Universitet, Uppsala, SWEDEN|

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ABSTRACT BODY:

Purpose: Deep learning–based segmentation models for spectral-domain optical coherence tomography (SD-OCT) images have been used for automatic identification of retinal fluids to support clinicians in patient management. Images from different acquisition devices or retinal diseases, hereafter referred to as domains, typically require distinct models. We propose an effective unified solution applicable to multiple domains.

Methods: SD-OCT images were acquired with Cirrus HD-OCT (Carl Zeiss Meditec), denoted as C, and Spectralis OCT (Heidelberg Engineering), denoted as S, on patients with neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME). The dataset was grouped into 3 domains: S/nAMD (AVENUE, NCT02484690), S/DME (BOULEVARD, NCT02699450), and C/nAMD (HARBOR, NCT00891735), which respectively included 1769, 1686, and 959 B-scans (corresponding to 303, 303, and 160 eyes) with manual pixel-wise annotations. The annotations denote IRF and SRF for patients with DME, as well as PED and SHRM for patients with nAMD (Figure 1). Annotated B-scans from 10% of eyes in each domain were randomly split into a test set for evaluation.
Different domain-specific models with a UNet architecture were trained on each of the 3 domains as a baseline (Figure 1, left). Our cross-domain model was trained collectively on B-scans from all 3 domains (Figure 1, right). Experiments were repeated 5 times to minimize the effect of randomness in network initialization. Performance was measured using the Dice coefficient.

Results: Domain-specific models were confirmed to be superior (5.68 higher Dice overall) when training and evaluation domains were the same (Figure 2). Segmentation results from our cross-domain model were comparable (3/10 cases) or superior (7/10 cases) to any domain-specific alternative for all domains and fluid labels (2.43 higher Dice overall). Training of the cross-domain model was also found to be > 2.5× faster.

Conclusions: Overall, our proposed cross-domain segmentation model is more accurate and faster to train compared with domain-specific models and eliminates the need for customizing models domain-specifically. The benefits of our approach may facilitate automated SD-OCT segmentation in the clinics.

CONTROL ID: 3705845

SUBMITTER (NAME ONLY): Wei Zhang

TITLE: Posttransplant VEGFR1R2 Trap eye drops improve corneal high-risk allograft survival

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Zhang, A.P. Schönberg, F. Bock, C. Cursiefen, Department of Ophthalmology, Universitat zu Koln, Cologen, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Pathological neovascularization of the corneal recipient is one of the main risk factors for graft rejection after corneal transplantation. This study aims to assess whether topical application of VEGFR1R2 Trap eye drops after corneal transplantation can impair the outgrowth of blood vessels (BVs) and lymphatic vessels (LVs) and promote murine high-risk corneal allograft survival.

Methods: Topical VEGFR1R2 Trap or human IgG Fc eye drops (as control) were delivered 3 times per day for 2 weeks after murine high-risk corneal transplantation. VEGFR1R2 Trap in corneal tissue after application was detected by immunohistochemistry. Corneas and draining lymph nodes (dLNs) were excised at week 2 and 8 post-transplantation. Corneal BVs and LVs were quantified by immunohistochemistry and morphological assessment. Dendritic cells (DCs) and regulatory T cells (Tregs) in dLNs were analyzed by flow cytometry. Allograft survival was determined by an 8-week evaluation of corneal opacity scores.

Results: Topically applied VEGFR1R2 Trap penetrated into the corneal bed and graft stroma after high-risk keratoplasty. Additional, postsurgical hemangiogenesis ($P<0.0001$) and lymphangiogenesis ($P<0.01$), and infiltration of CD45+ ($P<0.001$) as well as macrophages ($P<0.01$) in corneas were significantly reduced in the VEGFR1R2 Trap group compared to controls after transplantation. VEGFR1R2 Trap eye drops significantly decreased the frequency of CD11c+ DCs ($P<0.01$), MHC II+CD11c+ DCs ($P<0.01$) and CD40+CD11c+ DCs ($P<0.05$), and enhanced the frequency of CD200R+ regulatory DCs ($P<0.05$) and Tregs in dLNs ($P<0.01$). Moreover, long-term allograft survival was improved ($P<0.05$).

Conclusions: Temporary, posttransplant, topical application of VEGFR1R2 Trap eye drops can achieve sufficient anti-VEGF activity, inhibit additional posttransplant hem- and lymphangiogenesis and significantly improve high-risk corneal allograft survival. VEGFR1R2 Trap eye drops post transplantation may become a new therapeutic option for patients undergoing high-risk corneal transplantation.

CONTROL ID: 3705846

SUBMITTER (NAME ONLY): Jeffrey Cleland

TITLE: Safety and Tolerability of a Single Subcutaneous Dose of Anti-Angiogenesis Drug to Treat Neovascular Age-related Macular Degeneration (wet AMD) and Diabetic Macular Edema (DME)

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cleland, R. Sharma, S. Appiani, Ashvattha Therapeutics, Redwood City, California, UNITED STATES|J. Moore, B. Rogers, PacificBioDevelopment, LLC, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the toxicology, safety, and tolerability of D-4517.2 in rats, dogs and humans at doses anticipated to be efficacious in the treatment of wet AMD and DME.

Methods: D-4517.2 is comprised of a hydroxyl dendrimer covalently linked to a potent inhibitor of vascular endothelial growth factor receptor (VEGFR) tyrosine kinases. A single subcutaneous (SC) or oral dose of D-4517.2 inhibited choroidal neovascularization (CNV) comparable or better than a single intravitreal injection of aflibercept in laser-induced CNV mice[1]. Single-dose GLP toxicology, safety pharmacology studies (rat neurobehavioral and pulmonary studies, dog cardiovascular study, in vitro hERG ionic conductance study) and genotoxicology studies were conducted. A healthy volunteer Phase 1 study has been initiated with regulatory approval to enroll single ascending SC cohorts (n=4/cohort) from 0.25 to 2 mg/kg D-4517.2.

Results: A single SC dose of D-4517.2 was generally well tolerated in rats at levels up to 1000 mg/kg and at levels up to 200 mg/kg in dogs with a no-observed-adverse-effect level of 200 mg/kg. In vitro and rat genotoxicity tests conducted up to limit doses were negative. No findings of toxicologic importance were obtained in safety pharmacology evaluations in rats or dogs treated with D-4517.2 up to doses of 1000 mg/kg and 200 mg/kg, respectively. Analysis of the pharmacokinetics in mice, rats and dogs enabled allometric scaling to determine that the potential efficacious human doses are 0.25 to 2 mg/kg. A Phase 1 study is ongoing and the safety, tolerability, and pharmacokinetics of a single SC dose of D-4517.2 in healthy volunteers will be presented.

Conclusions: The GLP toxicology and safety pharmacology studies conducted in rats and dogs indicated a 100-fold safety margin above the maximum proposed human single SC dose (2.0 mg/kg D-4517.2). Allometric scaling of the D-4517.2 efficacious SC doses in the laser-induced CNV mouse model indicated that a SC dose of D-4517.2 of 0.25 to 2 mg/kg may be effective in treating patients with wet AMD or DME. Although D-4517.2 is renally cleared within 24 hours in animals, CNV lesion formation was suppressed for 2 weeks after a single SC in the CNV mouse model[1]. D-4517.2 may provide a safe SC administered chronic anti-angiogenesis treatment.

[1]Cleland et al, 2021, IOVS vol 62, 205

CONTROL ID: 3705852

SUBMITTER (NAME ONLY): Cheyanne Godwin

TITLE: Targeting Cholesterol Homeostasis Improves Recovery In Experimental Optic Neuritis

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Godwin, J. Anders, B. Elwood, R.H. Kardon, O.W. Gramlich, Ophthalmology, University of Iowa, Iowa City, Iowa, UNITED STATES|L. Cheng, J. Anders, B. Elwood, R.H. Kardon, O.W. Gramlich, Center for the Prevention and Treatment of Visual Loss, Iowa City VA Medical Center, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Magnitude of cholesterol rich myelin debris clearance after demyelination in Multiple Sclerosis (MS) limits recovery. The purpose of our study is to determine if augmentation of cholesterol efflux transporter 1 (Abca1) by gentisic acid (GA) influences synaptogenesis, myelination, and rescue of the ocular phenotype in an experimental autoimmune encephalomyelitis (EAE) optic neuritis model.

Methods: Brain organoids and Brn3a-GFP expressing retinal organoids were grown with or without 400μM GA. Organoids were analyzed for Abca1, PSD95, NG2, and Olig2 expression. EAE-related optic neuritis was induced in 52 female C57BL6 mice by immunization with MOG33-55, complete Freund's Adjuvant and pertussis toxin. 22 EAE mice received intraperitoneal GA weekly (EAE+GA), another 25 naïve mice served as controls. Clinical progression was monitored using a 5-point EAE scoring scheme. At day 60, visual acuity, pattern electroretinography (PERG) and retinal ganglion cell (RGC) complex thickness were measured. Grades of demyelination and cell infiltration in optic nerves were determined. Differences were evaluated using Tukey's post-hoc test.

Results: Retinal organoids+GA show accelerated maturation, evident by increased number of Brn3a+RGC and increased expression of PSD95. Brain organoids+GA demonstrated a 10-fold increase in NG2 and Olig2 expression as well as a 4-fold increase in PLP. EAE+GA animals show significantly lower motor-sensory impairment (EAE:122±4 vs. EAE+GA: 78±5; p=0.0001). Treatment also preserved visual acuity (EAE:0.23±0.08c/d vs. EAE+GA: 0.34±0.09c/d; p=0.0001), improved the PERG amplitude (EAE:16±4 vs. EAE+GA:20±4 μV; p=0.03) and slightly diminished RGC complex thinning (EAE:59±4μm vs. EAE+GA:62±3μm; p=0.2) when compared to untreated EAE mice. Grades of demyelination in the optic nerve was less severe in EAE+GA mice (EAE:2.1±0.8 vs. EAE+GA: 1.1±0.6; p=0.0001) and fewer infiltrating cells were observed (EAE:2.2±1 vs. EAE+GA: 1±0.5; p=0.0001).

Conclusions: GA supplementation in organ specific organoids accelerates retinal development and myelination. In EAE mice, GA administration significantly lessens motor-sensory deficits and promotes visual system recovery that is related to increased clearing of myelin debris and preservation of synaptic plasticity. In summary, this study suggests that interventions to improve cholesterol homeostasis might be a viable approach to promote rehabilitation in MS.

CONTROL ID: 3705868

SUBMITTER (NAME ONLY): Sydney Zhang

TITLE: Point of Care Diagnosis of Dry Eye Disease with Sensitive Dual Biomarker Detection

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.D. Zhang, D. Wang, Westview Optometry and Eye Institute, San Diego, California, UNITED STATES|

Commercial Relationships Disclosure: Sydney Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Dorothy Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Current diagnosis of dry eye disease (DED) has significant challenges with limited accuracy and poor correlation of clinical symptoms. The goal of this study is to develop a sensitive lateral flow immunoassay (LFIA) for point of care (POC) diagnosis of DED. The authors tested the hypothesis of targeting dual biomarkers Interleukin-6 (IL-6) and lactoferrin in tears for multiplexing detection, as to increase the accuracy of POC diagnosis for DED. A standardized tear collection protocol was also developed with the use of disposed contact lenses. The initial trial of 20 tear samples provided positive LFIA results for future clinical studies.

Methods: 1. Production of LFIA paper strips printed with gold nanoparticle conjugates, antibodies against human IL-6 or lactoferrin & antimouse antibody.

2. Determination of lowest detection limits of LFIA with serial diluted concentrations of rIL-6 or lactoferrin solutions

3. Confirmation of LFIA results with the conventional ELISA method

4. De-identified and discarded contact lens were collected with the consent of the patients

5. Application of 50 µL tear samples onto a LFIA paper strip for detection of tear IL-6 or lactoferrin

6. Image capture of LFIA paper strips 10 minutes after LFIA test

7. Quantitative data analysis of LFIA paper strips with ImageJ software

8. Student t test was used for statistical analysis

Results: A paper-based LFIA was successfully developed in a double-antibody sandwich fashion with gold nanoparticles acting as probes. The minimal detection concentrations were 0.1 ng/ml and 10 ng/ml for IL-6 and lactoferrin, respectively. Separated ELISA tests were also performed with data confirming results from LFIA tests. A trial study was conducted with 20 tear samples. Compared to the controls, all 10 DED tears exhibited statistically significantly higher levels of IL-6 and decreased levels of lactoferrin. A quantitative analysis of LFIA images was carried out using ImageJ software for an accurate data interpretation. A smartphone-based platform is being developed for LFIA imaging, data reporting and storage.

Conclusions: In summary, a POC enabled DED diagnostic kit has been successfully developed by targeting two important biomarkers. Tear testing of IL-6 and lectoferrin demonstrated a positive correlation of LFIA results with DED symptoms. Further investigations are warranted to improve its accuracy for clincal diagnosis of DED

CONTROL ID: 3705869

SUBMITTER (NAME ONLY): Dylan Pham

TITLE: Peptide Lv promotes angiogenesis through intermediate conductance calcium-dependent potassium (K_{Ca} 3.1) channels in endothelial cells

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Pham, A. Niemi, G.Y. Ko, Veterinary Integrative Biosciences, Texas A&M University, College Station, Texas, UNITED STATES|

Commercial Relationships Disclosure: Dylan Pham: Commercial Relationship: Code N (No Commercial Relationship) | Autumn Niemi: Commercial Relationship: Code N (No Commercial Relationship) | Gladys Ko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Peptide Lv is an endogenous pro-angiogenic peptide that is upregulated in the retina of diabetic animals and patients with early diabetic retinopathy. Although peptide Lv promotes pathological angiogenesis, the mechanisms of its angiogenic action remains unclear. Activation of endothelial potassium channels, including intermediate conductance calcium-dependent potassium (K_{Ca}3.1) channels, promotes angiogenesis. We hypothesize that peptide Lv augments endothelial K_{Ca}3.1 to promote endothelial proliferation and pathological angiogenesis.

Methods: Membrane potentials and K_{Ca}3.1 currents were recorded from human umbilical vein endothelial cells (HUVEC) treated with peptide Lv (500 ng/ml). TRAM 34 was perfused at the end of each recording to isolate the K_{Ca} 3.1 current from other outward currents. Western blots for K_{Ca}3.1, small conductance calcium-dependent potassium (K_{Ca}2.3), and ATP-sensitive potassium (Kir6.1) were performed after HUVECs and human retinal endothelial cells (HRECs) were treated with peptide Lv (500 ng/ml) or PBS (vehicle control) for 4 hours. For testing the endothelial proliferation, HUVECs were seeded onto 24-well plates and allowed to adhere overnight. Peptide Lv (500 ng/ml), VEGF (5 ng/ml), DMH4 (5 μM), TRAM 34 (10 μM) and PBS/0.1% DMSO (vehicle controls) were added to cultures for another 48 hrs. Then the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) colorimetric assays were performed on these cultures. The absorbance at 560 nm was measured using the Chromate microplate reader.

Results: Endothelial cells treated with peptide Lv had significant increase in the mRNA and protein expression of K_{Ca} 3.1 but not other types of K channels. Peptide Lv hyperpolarized the endothelial cells and increased the K_{Ca}3.1 current densities. Blocking K_{Ca}3.1 with TRAM 34 attenuated peptide Lv-elicited endothelial cell proliferation.

Conclusions: The angiogenic property of peptide Lv is in part through the augmentation of endothelial K_{Ca}3.1.

CONTROL ID: 3705870

SUBMITTER (NAME ONLY): Lorena Perez Gutierrez

TITLE: Establishing the mitogenic potential of oncostatin M on endothelial cells: therapeutic implications for age-related macular degeneration.

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Perez Gutierrez, P. Li, N. Ferrara, Moores Cancer Center, University of California San Diego, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure: Lorena Perez Gutierrez: Commercial Relationship: Code N (No Commercial Relationship) | Pin Li: Commercial Relationship: Code N (No Commercial Relationship) | Napoleone Ferrara: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Development of novel anti-angiogenic therapies distinct from VEGF is critical for the identification of new treatments for blindness-inducing age-related macular degeneration. Leukemia inhibitory factor (LIF), a member of the IL-6 cytokine family, has recently been identified as a potent endothelial cell (EC) mitogen in vitro and in vivo. Surprisingly, although the same results were seen in vitro for oncostatin M (OSM), another member of the IL-6 family, intravitreal (iv) injection of this cytokine decreased vascular density and inhibited laser-induced CNV in vivo. We hypothesize that LIF and OSM act through distinct mechanisms to exert their mitogenic potential on ECs.

Methods: Bovine choroidal, aortic, and retinal ECs were treated with various concentrations of LIF and OSM and key signaling mechanisms were tested by western blot and RT-qPCR. siRNA was used to knock-down the main receptors for LIF and OSM. Retinas from mice subjected to LIF and OSM iv injections were flat mounted, and neovascularization and inflammatory cell infiltration were assessed by confocal microscopy.

Results: OSM promoted proliferation of choroidal and retinal ECs through the JAK-STAT3 pathway. Conversely, OSM inhibited bovine aortic EC growth also via activation of JAK-STAT3 pathway. Interestingly, OSM, but not LIF, was able to upregulate IL-6 mRNA in choroidal and retinal ECs, as opposed to aortic ECs. Moreover, the mitogenic potential of OSM was mediated by different receptors in choroidal and aortic ECs. In vivo, as opposed to LIF, OSM inhibited neovascularization at low concentrations and was associated with an increase macrophage infiltration into the retina. However, high concentrations of OSM were able to stimulate retinal angiogenesis and were associated with reduced macrophage infiltration.

Conclusions: OSM exerts opposing responses in various EC subtypes via activation of the same signaling pathway. Additionally, OSM signals through different receptors, suggesting that different EC types have unique gene expression patterns, which determines their differential responses to the same stimulus. Moreover, our in vivo data points towards a role for OSM in the recruitment of inflammatory cells such as macrophages to the retina in a concentration-dependent manner. Overall, these data demonstrate that LIF and OSM act through distinct mechanisms in ECs.

CONTROL ID: 3705874

SUBMITTER (NAME ONLY): Nimesh Patel

TITLE: Sequential OCTA scans have greater signal variability around venules.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.B. Patel, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Nimesh Patel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) slab projections represent vasculature in which blood flow meets or exceeds threshold. Sequential OCTA scans have regional variability, and averaging slabs improves visualization of capillaries. We hypothesize that some of the regional variability reflects on blood flow physiology. The purpose of this study was to quantify regional OCTA signal variability from sequential scans for vessels in the superficial vascular complex.

Methods: Data were collected from seven non-human primates with no ocular pathology. Prior to imaging, animals were sedated with ketamine and xylazine, and pupils dilated with 1% tropicamide. Six sequential, high speed 384x384 (15°x15°) OCTA raster scans (Spectralis OCT2), centered on the macula, were acquired from one eye of each animal. Scan volumes were imported into Matlab, registered in 3D, and the thresholded signal between the inner limiting membrane and inner plexiform layer isolated. Variability was quantified as the standard deviation of the theresholded signal using a 20x20 A-scan sliding window for identical regions of the six scans. Major vasculature was manually traced on the averaged 2D slab projection, and a 16 pixel dilated region used to compute the average variability surrounding each vessel. Arterioles were identified based on the capillary free zone.

Results: All animals had healthy eyes at the time of imaging, and the mean ganglion cell complex thickness was 103±5.3μm. The average superficial vascular complex slab density was 40.6±3.5%, and volumetric vascular density was 6.9±0.7%. A total of 47 arterioles and 46 venules were identified and traced. The mean standard deviation of OCTA signal was greater around venules (1.11x10-3) compared to arterioles (9.25x10-4, $p<0.01$).

Conclusions: Averaging OCTA scans improves visualization of capillaries. The variability in OCTA signal is greatest around venules, which is likely a reflection of regional differences in blood flow. In addition to vessel density, OCTA signal variability from sequential scans may provide important physiological information when assessing ocular health.

CONTROL ID: 3705881

SUBMITTER (NAME ONLY): Devon Harvey

TITLE: Comparisons of Biomechanical Metrics between eyes of patients with Asymmetric Glaucoma and Symmetric Glaucoma.

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Harvey, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|C.J. Roberts, A. Mahmoud, G. Fleming, Ophthalmology and Visual Sciences, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|C.J. Roberts, A. Mahmoud, G. Fleming, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Devon Harvey: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Roberts: Commercial Relationship(s);Code C (Consultant/Contractor):Zeimer Ophthalmic Systems AG;Code C (Consultant/Contractor):Oculus Optikgeräte GmbH;Code R (Recipient):Heidelberg Engineering, Inc | Ashraf Mahmoud: Commercial Relationship: Code N (No Commercial Relationship) | Gloria Fleming: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare biomechanical metrics between eyes of subjects with asymmetric glaucoma (ASYMM) and those with symmetric glaucoma (SYMM).

Methods: A total of 46 subjects were prospectively recruited. ASYMM was defined as C/D difference > 0.1 between eyes (C/D difference range 0.12 to 0.65) and SYMM was defined as a C/D difference <= 0.1 between eyes (C/D difference range 0 to 0.1). There were 32 eyes of 16 subjects in the ASYMM group and 60 eyes of 30 subjects in the SYMM group. Within the ASYMM group, best eye and worst eye were determined and all parameters were subtracted as worst eye minus best eye. Biomechanical metrics included corneal hysteresis (CH) from the Ocular Response Analyzer, and stiffness parameters at first applanation (SP-A1) and highest concavity (HC), as well as Integrated Inverse Radius and Deformation Amplitude Ratio, all from the Corvis ST. In addition, pulsatile ocular blood volume (POBV) was calculated based on intraocular pressure (IOP) and ocular pulse amplitude (OPA) from pneumatonometry and axial length. Paired T-test comparisons were performed between eyes of both ASYMM and SYMM groups for each variable. Statistical analyses was performed with SAS with the significance threshold set to $p < 0.05$.

Results: Within ASYMM group, CH was significantly different by -0.76 (SD 1.22, $p = 0.025$) with the worst eye having lower CH. POBV was significantly different by -0.38 (SD 0.305, $p = 0.016$) with the worst eye having lower POBV. For SYMM there were no significantly different variables.

Conclusions: Low CH is associated with greater glaucomatous damage between eyes in asymmetric glaucoma, which is consistent with literature reporting CH as a risk factor. In addition, this study showed that the eye with greater glaucomatous damage in asymmetric glaucoma was also associated with lower pulsatile ocular blood volume which may have contributed to the more severe disease.

CONTROL ID: 3705888

SUBMITTER (NAME ONLY): Vaishali Oza

TITLE: Cone contrast testing as an early functional biomarker of age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.H. Oza, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|L. Kurzlechner, S. Stinnett, E.M. Lad, Department of Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|C. Nordstrom, Innova Systems, Inc., Burr Ridge, Illinois, UNITED STATES|U.F. Luhmann, F Hoffmann-La Roche AG Research and Development Division, Basel, Basel-Stadt, SWITZERLAND|

Commercial Relationships Disclosure: Vaishali Oza: Commercial Relationship: Code N (No Commercial Relationship) | Leonie Kurzlechner: Commercial Relationship: Code N (No Commercial Relationship) | Cheryl Nordstrom: Commercial Relationship(s);Code E (Employment):Innova Systems, Inc. | Ulrich Luhmann: Commercial Relationship(s);Code E (Employment):F. Hoffmann – La Roche Ltd. (Basel, Switzerland) | Sandra Stinnett: Commercial Relationship: Code N (No Commercial Relationship) | Eleonora Lad: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis, F. Hoffman – La Roche, Apellis, Annexon Biosciences, Allegro Ophthalmics, Gemini Therapeutics, Galimedix, Retrotope, Alexion Pharmaceuticals, Iveric Bio, Laboratoires Thea;Code F (Financial Support):F. Hoffman La Roche Ltd. (Basel, Switzerland), Apellis, Novartis, Boehringer Ingelheim, LumiThera, Gemini Therapeutics

ABSTRACT BODY:

Purpose: Controversy exists regarding the inclusion of nonexudative age-related macular degeneration (AMD) patients in clinical studies based on structural vs. functional criteria. In a prior analysis, cone contrast testing (CCT) red distinguished intermediate AMD (iAMD) vs. controls at 12 and 24 months. Our goal was to further analyze the longitudinal changes in CCT in normal, early and iAMD participants.

Methods: As part of the single-site, prospective, observational Duke FEATURE study, 69 participants (16 healthy control, 22 early AMD, 31 iAMD) were evaluated. Study participants were assessed at baseline, 12 and 24 months using CCT red and green, dilated exam, and optical coherence tomography. CCT blue was not included in this analysis due to the potential effect of mild cataract on test performance and lack of longitudinal change over 24 months in a prior analysis.

Results: At 12 and 24 months, there was a significant difference across the three groups in the proportion of individuals with no functional deficits based on a normative database (CCT score ≥ 80), moderate deficits (score 50-80), or severe deficits (score ≤ 50) for both CCT red (baseline $p=0.01$; 12 and 24 months $p< 0.01$ Fisher's exact test) and green (12 and 24 months $p< 0.02$). This significant difference between groups was only found at the baseline visit for CCT red ($p=0.01$) but not for CCT green ($p=0.07$).

Compared to normal and early AMD participants, those with iAMD were more likely to show a decrease in total CCT score (red + green) of ≥40 points from any prior visit ($p< 0.05$) throughout the study. Notably, of the control population, 0% had severe CCT red or green, 56% had moderate CCT red and 37% CCT green deficits at baseline. Proportions of control participants with moderate-severe CCT deficits increased over time: 6% progressed to severe and 56% to moderate deficits on CCT red at 24 months, and 6% to severe and 44% to moderate deficits on CCT green at 24 months.

Conclusions: CCT tests for red and green colors represent early functional measures of disease progression in eyes with early-iAMD. We noted a longitudinal decline in CCT function over 24 months. A subgroup of healthy control participants demonstrated functional deficits on CCT red and green, suggesting that both visual function and structural inclusion criteria should be employed in future clinical trials of nonexudative AMD.

CONTROL ID: 3705889
SUBMITTER (NAME ONLY): Christopher Le
TITLE: Outcomes of advanced chronic macula-off retinal detachment repair
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Le, D. Milner, A.I. Marin, J. Smith, N. Manoharan, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|
Commercial Relationships Disclosure: Christopher Le: Commercial Relationship: Code N (No Commercial Relationship) | Dallin Milner: Commercial Relationship: Code N (No Commercial Relationship) | A. Marin: Commercial Relationship: Code N (No Commercial Relationship) | Jesse Smith: Commercial Relationship: Code N (No Commercial Relationship) | Niranjan Manoharan: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: The clinical course and outcomes of patients with advanced chronic retinal detachments (RDs)—detachments greater than one month—have not been well-studied. The goal of this case series was to investigate the outcomes associated with surgical intervention of advanced chronic macula-off RDs.
Methods: Thirty-eight patients that presented to Denver Health Medical Center, a safety-net hospital system, from 2016 to 2021, with a retinal detachment that was not repaired for greater than one month were identified. These patients were analyzed for proliferative vitreoretinopathy (PVR) on presentation, type of surgical intervention, pre-operative and final best-corrected visual acuity (BCVA), initial surgical re-attachment rate, final surgical attachment rate, and occurrence of phthisis. Additionally, post-operative complications were identified and recorded including ocular hypertension and cataract formation.
Results: Mean duration of RD was 153 days. Twenty-eight out of 38 (74%) patients had PVR on initial presentation. Initial surgical intervention included pars plana vitrectomy (PPV) without scleral buckle (SB) (5%), pars plana vitrectomy with scleral buckle (79%), and scleral buckle with cryotherapy (16%). Initial attachment rate was 55.26% and the final attachment rate was 94.74%. Mean number of RD surgeries was 1.50 (SD 0.77). All six patients who underwent SB with cryotherapy failed initial surgery and required PPV. Other post-operative complications included ocular hypertension (76%), cataract formation (66%), and phthisis bulbi (5%). Of patients that developed ocular hypertension, 7/29 (24%) required surgery. Mean final BCVA was 1.60 (0.71) and final globe salvage rate was 38/38 (100%).
Conclusions: We demonstrate the clinical characteristics of advanced chronic RDs with various surgical approaches. We found that initial retinal reattachment in advanced chronic RD was much lower than reported rates of uncomplicated acute RDs. Additionally, a majority of patients developed ocular hypertension and almost a quarter of whom required surgical management. Finally, primary scleral buckle might be less successful in advanced chronic RDs. Poor patient compliance with post-operative positioning and follow-up also appeared to affect patient outcomes. However, most patients had successful final re-attachment, globe salvage, and ambulatory vision. Further studies are needed to optimize surgical outcomes in these patients.

CONTROL ID: 3705890

SUBMITTER (NAME ONLY): Megan Zhao

TITLE: Sex-Related Differences and Hormonal Effects in the Dry Eye Assessment and Management (DREAM) Study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhao, Y. Yu, G. Ying, V.Y. Bunya, Scheie Eye Institute, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|N. Roy, Division of Ophthalmology, Weill Cornell Medicine, New York, New York, UNITED STATES|P.A. Asbell, Hamilton Eye Institute, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Megan Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Yinxi Yu: Commercial Relationship: Code N (No Commercial Relationship) | Neeta Roy: Commercial Relationship: Code N (No Commercial Relationship) | Gui-Shuang Ying: Commercial Relationship: Code N (No Commercial Relationship) | Penny Asbell: Commercial Relationship: Code N (No Commercial Relationship) | Vatinee Bunya: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Sex-related differences in dry eye disease (DED) are acknowledged but are not well-characterized. This study evaluates how DED signs and symptoms differ between men and women, as well as between pre- and post-menopausal women, in the Dry Eye Assessment and Management (DREAM) study.

Methods: This secondary analysis of the data from the DREAM study included 101 male and 434 female participants (59 pre-menopause and 375 post-menopause). Participants self-reported prior medical history and underwent a DED assessment using the Ocular Surface Disease Index (OSDI), Brief Pain Inventory (BODI), Tear Break-Up Time (TBUT)(sec), Schirmer's test (mm/5 min), conjunctival staining, corneal staining, meibomian gland dysfunction evaluation, and tear osmolarity (mOsms/L) at baseline, 6 months, and 12 months. Multivariable linear regression models were used to compare the scores in symptoms and signs between groups while adjusting by age, race, smoking status and existing comorbidities associated with DED signs or symptoms.

Results: In a multivariable analysis of combined data at baseline, 6 months, and 12 months, women had significantly worse DED signs than men with lower Schirmer's test score (9.27 vs 12.16; $p<0.001$), higher corneal staining score (3.59 vs. 2.70; $p=0.006$), and worse composite DED scores (0.52 vs. 0.40; $p<0.001$) [Table 1]. Post-menopausal women experienced significantly worse DED signs than pre-menopausal women with lower TBUT (3.37 vs. 3.93, $p=0.047$), higher corneal staining scores (3.74 vs. 2.58, $p<0.001$), higher conjunctival staining scores (2.80 vs. 2.22, $p<0.001$), worse meibomian gland dysfunction (3.05 vs. 2.62, $p=0.04$), higher tear osmolarity (304 vs. 299, $p=0.004$), and worse composite DED scores (0.54 vs. 0.42, $p<0.001$) [Table 2]. There were no significant differences in DED symptoms between sex and between pre- and post-menopausal women (all $p\geq0.13$) [Tables 1 and 2].

Conclusions: In the DREAM study, women experienced more severe DED signs compared to men, independent of age, race, smoking status and comorbidities. Further, post-menopausal women presented with more severe DED signs compared to pre-menopausal women. These findings may improve DED diagnosis and provide future direction in understanding sex-associated differences in DED.

CONTROL ID: 3705892
SUBMITTER (NAME ONLY): Ngoc Than
TITLE: Flicker ERG findings in posterior uveitis
SESSION TITLE: Applications of adaptive optics and advanced imaging
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Than, H.L. Doan, B. Pham, J. Hwang, J. Regenold, M. Zaidi, Y.H. Khan, W. Matsumiya, S. Park, H. Ghoraba, C. Or, G. Uludag, A. Mobasserian, A. Akhavanrezayat, D.V. Do, Q.D. Nguyen, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|B. Pham, Ophthalmology, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|S. Park, Ophthalmology, Pusan National University, Kumjeong-ku, KOREA (THE REPUBLIC OF)|
Commercial Relationships Disclosure: Ngoc Than: Commercial Relationship: Code N (No Commercial Relationship) | Hien Doan: Commercial Relationship: Code N (No Commercial Relationship) | Brandon Pham: Commercial Relationship: Code N (No Commercial Relationship) | Jaclyn Hwang: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Regenold: Commercial Relationship: Code N (No Commercial Relationship) | Moosa Zaidi: Commercial Relationship: Code N (No Commercial Relationship) | Youan Khan: Commercial Relationship: Code N (No Commercial Relationship) | Wataru Matsumiya: Commercial Relationship: Code N (No Commercial Relationship) | SungWho Park: Commercial Relationship: Code N (No Commercial Relationship) | Hashem Ghoraba: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Or: Commercial Relationship: Code N (No Commercial Relationship) | Gunay Uludag: Commercial Relationship: Code N (No Commercial Relationship) | Azadeh Mobasserian: Commercial Relationship: Code N (No Commercial Relationship) | Amir Akhavanrezayat: Commercial Relationship: Code N (No Commercial Relationship) | Diana Do: Commercial Relationship: Code N (No Commercial Relationship) | Quan Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Electroretinography (ERG), which measures the electrical activity of retinal photoreceptors, has been employed in the management of retinal diseases. Recently, a simplified flicker ERG system has been developed. This cross-sectional study explores whether the Diopsys® flicker ERG system can be used in the monitoring of posterior uveitis patients.

Methods: Patients with posterior uveitis from a single institution were included. Patients with concomitant retinal disease such as diabetic retinopathy or age-related macular degeneration were excluded. Demographic and clinical data, including flicker ERG (Diopsys® NOVA), were collected. Statistical analyses were performed with STATA 16.0 software, and the Student’s t-test was used to compare means of different groups.

Results: A total of 85 patients (134 eyes) were studied. Diagnoses included juvenile idiopathic arthritis associated uveitis, Birdshot, and Behçet’s disease among others. Mean age was 36.89 ± 18.06 years. Fifty-two eyes had retinal vasculitis and 62 eyes had optic disc inflammation. There was a statistically significant difference in magnitude between eyes with (n=52) and without (n=82) retinal vasculitis (p=0.02). In addition, eyes with diffuse (posterior and peripheral) vasculitis (n=13) had reduced magnitude compared to eyes with only peripheral vasculitis (n=39) (p<0.01). However, no significant difference was found between eyes with and without optic disc inflammation (p=0.08).

Conclusions: Based on the index study, the Diopsys® flicker ERG system may aid in the monitoring of eyes with posterior uveitis.

CONTROL ID: 3705893

SUBMITTER (NAME ONLY): Amanur Rahaman

TITLE: Glass Burn Threshold: An Innovative Method to Characterize Refractive Femtosecond Laser Performance

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rahaman, S. Rahaman, H. Fu, Research and Development, Johnson and Johnson Vision, Milpitas, California, UNITED STATES|

Commercial Relationships Disclosure: Amanur Rahaman: Commercial Relationship: Code N (No Commercial Relationship) | Saidur Rahaman: Commercial Relationship(s);Code E (Employment):Johnson & Johnson VIsion | Hong Fu: Commercial Relationship(s);Code E (Employment):Johnson & Johnson VIsion

ABSTRACT BODY:

Purpose: A new femtosecond laser aiming for tissue-bridge-free corneal refractive surgery has been developed. The new laser is designed with the shortest pulse duration, the smallest focal spot, and continuous dissection surface to perform corneal incision at the lowest energy per pulse. Two critical-to-quality characteristics (CTQ) of the new surgical laser are the plasma forming threshold and the accuracy of the cutting-depth baseline. We developed an innovative method to measure these two CTQs simultaneously, which is much more precise, robust, and simpler than the previous gel-cutting method.

Methods: The new femtosecond laser is designed with an Auto-Z detector to measure the reflected light at the laser focal point. By scanning the focus through the patient interface's glass surface, the Auto-Z signal will show a sharp peak if the pulse energy is above the glass plasma threshold, and no peak if the energy is below the plasma threshold. We can measure the threshold energy at sub-nJ precision and measure the glass surface position at sub-μm precision. Using this method, we characterized the system's glass burn threshold and the Auto-Z signal as a function of pulse energy; measured the glass burning position stability for the femtosecond laser for a month; and characterized the impact of pulse energy on the Auto-Z signal's peak position.

Results: First, the new femtosecond laser system can achieve ≤ 50 nJ glass burn threshold. This means that the corneal incision can be achieved at ≤ 70 nJ per pulse. Second, within a month, the system's preset zero depth position can vary by about 15 μm due to laser, optical, and thermal variations. This small drift will be corrected to sub-μm accuracy in each procedure by the Auto-Z device. Third, we found that the glass burn position is a function of pulse energy, indicating that the focal volume of the laser beam that has the light intensity above the glass burn threshold is growing with the increasing pulse energy.

Conclusions: We have developed a precise, robust, and simple-to-operate method to measure the CTQs of the new femtosecond laser. With this method, we can ensure that the new femtosecond laser system can perform tissue incision at the lowest energy per pulse and can ensure that depth variation due to either internal system variation or due to patient interface variation can be corrected to sub-micron accuracy for each procedure.

CONTROL ID: 3705898

SUBMITTER (NAME ONLY): Rajya gurung

TITLE: Genetic biomarkers predicting response to anti-vascular endothelial growth factor injections in diabetic macular edema, a pilot study

SESSION TITLE: Diabetic Macular Edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.L. gurung, L.M. FitzGerald, B.J. McComish, K.P. Burdon, Genetics and Cancer group, University of Tasmania Menzies Institute for Medical Research, Hobart, Tasmania, AUSTRALIA|E. lui, J.E. Craig, Department of Ophthalmology, Flinders University, Adelaide, South Australia, AUSTRALIA|N. Verma, A.W. Hewitt, B.J. Vote, Department of Ophthalmology, University of Tasmania College of Health and Medicine, Hobart, Tasmania, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Intraocular anti-vascular endothelial growth factor (anti-VEGF) therapies are the front-line treatment for diabetic macular edema (DME), however, treatment response varies widely. This study aims to identify genetic determinants associated with anti-VEGF treatment response in DME patients.

Methods: We performed a genome-wide association study on 220 DME patients treated with anti-VEGF therapy, genotyped on Illumina Global Screening Array. Changes in central macular thickness (CMT) and best-corrected visual acuity (BCVA) after 12 months were our primary outcome measures. Association between single nucleotide polymorhphism (SNP) genotypes and DME outcomes were evaluated by linear regression (additive model) using PLINK2.0, adjusting for the first three principal components, age, baseline CMT/BCVA, duration of diabetic retinopathy, and HbA1c.

Results: In the GWAS for CMT change, a single SNP on chromosome 6 (rs78466540, P=1.16E-09) and a locus on chromosome 12 (top SNP rs11614480, P=2.69E-08) reached genome-wide significance (Figure 1A). The chromosome 12 locus was supported by four nearby SNPs rs11615848, rs11614887, rs11615870, rs11615833 in linkage disequilibrium which also showed genome-wide significance (P≤5E-08). For BCVA change we found five SNPs reaching genome-wide significance(Figure 1B), three on chromosome 11, (rs148980760, P=5.30E-09; rs117744949, P= P=6.57E-09 and rs57801753, P= P=1.71E-08), and a SNP each on chromosome 5 (rs187876551, P=1.52E-08) and chromosome 6 (rs118074968, P=4.94E-08). In silico investigations of each locus identify multiple eQTLs and potentially relevant candidate genes warranting further analysis.

Conclusions: Multiple genetic loci predicting treatment outcomes for anti-VEGF therapies in DME have been identified. This work will potentially lead to personalized medicine approaches for managing DME.

CONTROL ID: 3705901

SUBMITTER (NAME ONLY): Monica Jong

TITLE: The Role of Myopia in 2020 Uncorrected Global Visual Impairment

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jong, Professional Education, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|N.A. Brennan, Research and Development, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|M.A. Bullimore, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous estimates of the prevalence of global uncorrectable visual impairment (VI) have not accounted for the increasing prevalence of myopia, particularly in older individuals. We estimate the global prevalence of uncorrectable VI in 2020 accounting for the distribution of both age and myopia.

Methods: Age distribution of the global population in 2020 were taken from www.populationpyramid.net. Overall prevalence of myopia (<–0.50 D) of 33.9% was used, based on Holden et al. (2016). Distribution of myopia, by severity, was calculated using the model of Brennan et al. (2020) Uncorrectable VI as a function of age and refractive error was modelled by multiple linear regression (Bullimore et al., 2021) from a large data set of an advanced European population (Tideman et al., 2016). This data set is agnostic with respect to the disease condition associated with VI. By convolving the distributions of myopia and age with the cumulative risk of VI, the number of individuals with uncorrectable VI in 2020 was calculated.

Results: The 2020 global population is 7.79 billion, of whom 2.64 billion are myopic and 0.46 million have high myopia (<–5D). The cumulative odds of uncorrectable VI (20/40 or worse) is $10^{(0.057Age - 0.122Rx - 4.03)}$ and the estimated global population with uncorrectable VI is 113
million (1.5%). Of these, 60 million are myopes compared with 53 million non-myopes. An estimated 32 million cases of VI (29%) can be directly attributed to increased risk of eye disease associated with myopia; > 40% of cases below 60 years. At 65 years, myopes comprise 60% of individuals with VI, while representing 33.9% of the population. At 81 years, myopes still account for half of the visually impaired.

Conclusions: Assuming that the data from Tideman et al. are applicable to the global population, we estimate that some 29% of global uncorrectable VI is attributable to myopia. Failure to account for the increasing prevalence of myopia among the aging population leads to a substantial underestimate of the prevalence of VI. In our 2020 model each 1% increase in myopia prevalence results in an additional 1.2 million VI. Projecting for 2050, each 1% increase in myopia is associated with 2.7 million increased VI. Approaches that treat diseases associated with myopia are needed to reduce VI, along with programs that reduce myopia prevalence and severity.

CONTROL ID: 3705903

SUBMITTER (NAME ONLY): Claudio Bucolo

TITLE: PHARMACOLOGICAL AND SAFETY PROFILE OF TWO NEW BETAMETHASONE/CHLORAMPHENICOL GEL OPHTHALMIC FORMULATIONS

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bucolo, F. Lazzara, G.L. Romano, F. Conti, F. Drago, Biomedical and Biotechnological Sciences, University of Catania, Catania, ITALY|C. Bucolo, G.L. Romano, F. Drago, Center for Research in Ocular Pharmacology (CERFO), University of Catania, Catania, ITALY|C. Piazza, Unifarm, Catania, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the pharmacological and safety profile of two new betamethasone/chloramphenicol gel formulations with or w/o preservative, versus other steroid/antibiotic combinations.

Methods: Corneal epithelial cells were used. After cell exposure to ocular formulations, cell viability, along with occludin levels, were assessed by ATPlite and WB, respectively. Wound healing was carried out by scratch assay. Cells were exposed to: Ziclor$_P$ gel [0.1% betamethasone (BET)/0.25% chloramphenicol (CHL) with parabens; Alfa Intes], Betabioptal gel (0.1% BET/0.25% CHL with thiomersal; Thea), Netildex eye-drops [0.1% dexamethasone (DEX)/0.3% netilmicin with benzalkonium chloride (BAK); SIFI] and Ducressa eye-drops (0.1% DEX/0.5% levofloxacin; with BAK; Santen). Albino rabbits were used for ocular pharmacokinetic (PK) study (ARVO Statement for Use of Animals in Ophthalmic Vision Research). Two groups of rabbits were treated with a single topical administration (30µl) of 0.1% BET gel formulation w/o parabens (Ziclor$_{PF}$) and 0.1% DEX eye-drops (Ducressa), respectively. Aqueous was collected at 30, 60, 120, 180, and 240 mins after treatment, and levels of steroid detected by LC-MS/MS.

Results: ATP levels were significantly ($p<0.05$) reduced by the three formulations exposure compared to the new gel Ziclor$_{P.}$ A significant ($p<0.05$) wound closure area was observed after the exposure with Ziclor$_P$ compared with the other products. Occludin expression was maintained at physiological levels in the cells exposed to Ziclor$_P$; on the contrary the other formulations elicited a significant ($p<0.05$) protein's reduction. PK study showed no significant difference in terms of AUC and C_{max} between Ziclor$_{PF}$ and Ducressa (AUC_{0-240} 1943 and 1827 ng/ml*min, C_{max} 11.75 and 11.42 ng/ml for gel and eye drops formulations, respectively). However, after 180- and 240-min BET levels were significantly ($p<0.05$) higher compared to DEX.

Conclusions: The new ophthalmic gel formulations have a good pharmacological and safety profile. PK study showed higher levels of steroid in anterior chamber with Ziclor$_{PF}$, suggesting a longer pre-corneal residence time compared to Ducressa eye drops. Cells treated with Ziclor$_P$ showed a better viability and wound healing compared to the other formulations, preserving cell barrier connections, and suggesting that Ziclor$_P$ has a minimum impact on cell repair process.

CONTROL ID: 3705906

SUBMITTER (NAME ONLY): Rachel Xuan

TITLE: A systematic review of laser peripheral iridotomy placement for reducing the incidence of dysphotopsia symptoms in primary-angle closure

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Xuan, K. Ong, University of Sydney, New South Wales, AUSTRALIA|R. Xuan, K. Ong, Royal North Shore Hospital, St Leonards, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Rachel Xuan: Commercial Relationship: Code N (No Commercial Relationship) | Keith Ong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the incidence of dysphotopsia symptoms in patients with priarmy angle-closure glaucoma and/or primary angle-closure suspect with various positions of laser peripheral iridotomies (LPI).

Methods: The authors searched five electronic databases including CENTRAL, MEDLINE, EMBASE and trial registries for randomised controlled trials (RCTs). The search was last conducted on October 4, 2021. Language was not limited to English. Articles were excluded if LPI was compared to other interventions or if the measured outcome did not include dysphotopsia symptoms. Risk ratio was used for binary outcomes.

Results: Five RCTs involving 2364 eyes of 1182 patients were included in the review. Four studies compared superior with nasal/temporal LPIs; one study compared superior with inferior LPIs. The main weakness was potential selection bias for two studies and the lack of blinding for investigative personnel. Risk of bias was assessed at the individual study and outcome level with GRADE approach vigorously applied. Moderate-certainty evidence shows no difference between superior and nasal/temporal LPIs. Low-certainty evidence demonstrated conflicting results.

Conclusions: Various LPI positions used to reduce incidence of dysphotopsia symptoms have been studied. More high-certainty RCTs are needed as clinical decisions currently need to be made based on the available evidence.

CONTROL ID: 3705929

SUBMITTER (NAME ONLY): Xinyi Chen

TITLE: Impact of indeterminant ranges around the cut-off for antibody positivity on the use of serology for trachoma monitoring

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Chen, B. Munoz, S.K. West, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|C. Gaydos, L. Dize, T. Quinn, Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|H. Mkocha, Kongwa Trachoma Project, TANZANIA, UNITED REPUBLIC OF|T. Quinn, Division of Intramural Research, National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Serologic testing for chlamydial antibodies is a potential tool for trachoma surveillance. However, the impact of indeterminate ranges around the cut-off for seropositivity remains unclear. To understand this, we followed a longitudinal cohort of children in a formerly trachoma endemic district.

Methods: A total of 1719 children aged 1-9 years in Kongwa, Tanzania were followed for three years. We assessed their Median Fluorescence Intensity value (MFI-BG) of the antibodies to Chlamydia trachomatis antigen pgp3 at the baseline and three follow-up surveys. The cutoff for seropositivity was determined by receiver operative characteristic (ROC) curve analyses, using sera from children who were positive for both infection and clinical trachoma and a sample of US children who had never been exposed to trachoma. The indeterminate range was defined as the interval between the highest MFI-BG from the negative panel and the lowest MFI-BG from the positive panel.

Results: The overall seropositivity rate was 31.5% at baseline and 36.4% at the last follow-up. The different trajectories of change in serostatus are shown in Table 1. Of the seropositive children at baseline, 12.1% seroreverted; 25.4% of these seroreversions occurred with an MFI-BG in the indeterminate range. Of the seronegatives, 13.0% seroconverted, with 1.9 % of those seroconversions having an MFI-BG in the indeterminant range. Thirty-one children (2% of 1719) experienced a transient seroconversion or seroreversion (Group 3 or 6). Only one child (3% of the 31) had MFI-BG in the indeterminate range for the survey that placed them as a transient change. Eight out of the 1719 children (0.5%) had unstable serostatus. If the serostatus instances where the values fall in the indeterminate range are instead counted as the alternate, then these children would fall into a more regular pattern, and only 3 children were truly alternating between seropositivity and seronegativity at each survey.

Conclusions: The majority of seroconversion and seroreversion was not influenced by indeterminate ranges for antibody levels. Transient changes in serostatus are real and not due to indeterminate values. The indeterminate ranges had the greatest impact on apparent unstable serostatus changes.

CONTROL ID: 3705942

SUBMITTER (NAME ONLY): Scott Sonne

TITLE: Elongation of Axial Length in Older Patients with Degenerative Myopia

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sonne, Y.C. Akduman, Saint Louis University, Saint Louis, Missouri, UNITED STATES|C. Meyer, Augenklinik, SWITZERLAND|S. Saxena, retina service, INDIA|

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ABSTRACT BODY:

Purpose: To investigate the axial length changes in older patients presenting with myopic maculopathy secondary to degenerative myopia.

Methods: Five eyes of three consecutive patients (ages 61-88) with myopic maculopathy secondary to degenerative myopia were studied. All eyes were aphakic or pseudophakic following cataract surgery performed 9-18 years prior. The current axial lengths were compared with the axial lengths measured at the time of cataract surgery.

Results: The follow-up time was between 9-18 (13+/-3.94) years. The initial axial length was between 27.94-30.84 (29.15+/-1.08) mm. The final axial length was between 29.35-32.00 (30.47+/-1.11) mm. The axial length increased by 0.10-2.04 (1.32+/-0.75) mm, which corresponds to an average 3.96 diopter myopic shift, during the average follow-up of 13 years. Initial maculopathy findings were pigment stippling of posterior macular staphyloma, diffuse hypopigmentation, and patchy atrophic scars not involving the fovea. None of these affected the best corrected visual acuity. Additional maculopathy in the final visit included the formation of choroidal neovascular membrane (CNVM), epiretinal membrane (ERM) formation, vitreomacular traction (VMT), and maculoschisis.

Conclusions: Axial length may increase in older patients with degenerative myopia presenting with myopic maculopathy. Determining cause and effect relationship requires further study. The patients' initial axial measurements were made at the time of cataract surgery. They then experienced an undesirable myopic shift averaging 3.96 diopters over a mean of 13 years. Patients with myopic degeneration undergoing cataract surgery should be informed of the potential for increase in their ocular axial length over the following decade and longer; moreover, they may need further attention due to potential development of myopic shift and progression of myopic maculopathy. Some of those maculopathies (such as CNVM formation) may require immediate intervention. The elongation trend seen in degenerative myopia may have been occurring even prior to cataract surgery, but lack of long-term monitoring measurements before surgery makes it difficult to determine.

CONTROL ID: 3705948

SUBMITTER (NAME ONLY): Abdelrahman Fouda

TITLE: Investigation of the retinal metabolic function in type 1 diabetic Akita mice

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Fouda, Pharmacology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, UNITED STATES|E. Shosha, L. Qin, T. Lemtalsi, S.A. Zaidi, M.A. Rojas, Z. xu, R. Caldwell, R.B. Caldwell, Vascular Biology Center, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is the leading cause of vision loss in working-age adults. Understanding the retinal metabolic response to circulating high glucose levels in diabetic patients is critical for development of new therapeutic strategies to treat DR. Measuring retinal metabolic function using the Seahorse analyzer is a promising technique to investigate the effect of hyperglycemia on retinal glycolysis and mitochondrial respiration. Here, we analyzed the retinal metabolic function in young and old diabetic and control mice. We also compared the expression of key glycolytic enzymes between the two groups.

Methods: The Seahorse XF analyzer was used to measure the metabolic function of retina explants from young (7 months) and old (14 months) type 1 diabetic Akita ($Ins2^{Akita/+}$) mice and their control littermates. Rate-limiting glycolytic enzymes were analyzed in retina lysates from the two age groups. Furthermore, retina metabolic function and glycolysis enzyme expression were measured in an acute retinal ischemia-reperfusion (IR) injury model that is routinely used to model the ischemic phase of DR.

Results: Retinas from young adult Akita mice showed a decreased glycolytic response as compared to controls. However, this was not observed in the older mice. Western blotting analysis showed decreased expression of the glycolytic enzyme PFKFB3 (6-Phosphofructo-2-kinase/fructose-2, 6-bisphosphatase, isoform 3) in the young Akita mice retinas. Measurement of the oxygen consumption rate showed no difference in retinal mitochondrial respiration between Akita and WT littermates under normal glucose conditions despite evident mitochondrial fragmentation as examined by electron microscopy. However, Akita mice retinas at both 7 and 14 months showed decreased mitochondrial respiration under glucose-free conditions. Retinal metabolic function and glycolysis enzymes expression did not change in the IR injury model.

Conclusions: This is the first study to our knowledge to examine glycolytic enzyme expression and retinal metabolic function under diabetic conditions. Diabetic retinas display a decreased glycolytic response during the early course of diabetes which is accompanied by a reduction in PFKFB3. Diabetic retinas exhibit decreased mitochondrial respiration under glucose deprivation. Further investigation of the retinal metabolic function in response to hyperglycemia will help elucidate the pathophysiology underlying DR.

CONTROL ID: 3705953

SUBMITTER (NAME ONLY): Blake Cooper

TITLE: Risk of Diabetic Retinopathy (DR) Progression in Patients during 1 year of Semaglutide use

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Cooper, K. Howe, A. Cooper, Retina Associates, LLC, Lenexa, Kansas, UNITED STATES|M. de la Paz, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Blake Cooper: Commercial Relationship(s);Code C (Consultant/Contractor):Genentech, Regeneron | Kellie Howe: Commercial Relationship: Code N (No Commercial Relationship) | Amelia Cooper: Commercial Relationship: Code N (No Commercial Relationship) | Matthew de la Paz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Semaglutide is a medication used for the treatment of type 2 diabetes. Rapid glycemic control and hemoglobin A1c and have been associated with worsening of DR in a preapproval cardiovascular outcomes study with Semaglutide. Paradoxical worsening of DR after a sudden drop in blood glucose is a well-documented phenomenon with other medications; however, for Semaglutide, the long-term effects of acute worsening of DR remain unclear. We hypothesize if worsening of DR occurs with Semaglutide in patients with type 2 diabetes (T2D) it is temporary and not associated with continued DR progression.

Methods: Retrospective data analysis identified 4086 patients with T2D and DR by ICD-10 codes (E11.3XXX) in a Retina only practice from January to June 2020. The use of Semaglutide was found in 116 patients. Inclusion criteria included at least 1 year of Semaglutide and documentation of the level of non-proliferative (NPDR) and proliferative (PDR) retinopathy, visual acuity (VA), and Central Subfield Thickness (CST). 87 patients were included for descriptive analysis.

Results: 87 patients met the inclusion criteria; 36 (41.4%) Female; average age 62.4 years with a range (38-84); baseline level of DR range (10-85); 11.5% mild NPDR (level 10); 38.5% moderate NPDR (level 35-43); 14.4% severe NPDR (level 47-53); 35.6 % PDR (level 61-85). The level of retinopathy progressed over one year in 5.7% of eyes, improved in 8% of eyes, and remained stable in 86.2% of eyes. Over the course of one-year visual acuity remained unchanged in 72.4% of patients while 12.6% of patients lost > 2 lines of vision in at least one eye and 14.9% gained > 2 lines of vision in at least one eye. CST remained unchanged in 44.2%, increased by at least 10% in one eye of 25.6%, and decreased by at least 10% in one eye of 30.2% of patients. Intravitreal injections were required in at least one eye of 63.2% of patients with an average number of injections of 6.1 per patient.

Conclusions: Semaglutide use was not associated with an increased risk of progression of DR, visual loss, or an increased number of intravitreal injections over a 12-month period of time. If confirmed by prospective clinical trials, these findings would offer reassurance the long-term use of Semaglutide does not lead to progression of DR and sight-threatening disease.

CONTROL ID: 3705955
SUBMITTER (NAME ONLY): Richmond Woodward
TITLE: Change in Low Luminance Questionnaire (LLQ) scores in early and intermediate AMD over 24 months
SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Woodward, P. Singh, S. Stinnett, E.M. Lad, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|U.F. Luhmann, Translational Medicine Ophthalmology, F Hoffmann-La Roche AG Research and Development Division, Basel, SWITZERLAND|
Commercial Relationships Disclosure: Richmond Woodward: Commercial Relationship: Code N (No Commercial Relationship) | Pali Singh: Commercial Relationship: Code N (No Commercial Relationship) | Sandra Stinnett: Commercial Relationship: Code N (No Commercial Relationship) | Ulrich Luhmann: Commercial Relationship(s);Code E (Employment):F. Hoffmann-La Roche Ltd. (Basel, Switzerland) | Eleonora Lad: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis, F. Hoffman-La Roche Ltd. (Basel, Switzerland), Apellis, Annexon Biosciences, Allegro Ophthalmics, Gemini Theraputics, Galimedix, Retrotrope, Alexion Pharmaceuticals, Iveric Bio, Laboratories Thea;Code F (Financial Support):F. Hoffman-La Roche Ltd. (Basel, Switzerland), Apellis, Novartis, Boehringer Ingelheim, LumiThera, Gemini Therapeutics

ABSTRACT BODY:

Purpose: Development of new therapeutics to prevent disease progression in early and intermediate dry AMD requires novel endpoints that can be employed in clinical studies. The purpose of this prospective longitudinal observational study was to investigate if the change in Low Luminance Questionnaire (LLQ) scores over time can detect progression of early and intermediate stages of AMD (eAMD and iAMD, respectively).
Methods: As part of the single-center, prospective, longitudinal, observational Duke FEATURE study (Duke study of Functional Endpoints for Age-related Macular Degeneration), 101 subjects (33 eAMD, 47 iAMD, and 21 controls) were administered the LLQ during the baseline visit. 70 (22 eAMD, 31 iAMD, and 17 controls) completed the longitudinal study and received the LLQ instrument at 24 months.
Results: The composite mean LLQ score at baseline was significantly lower in iAMD (75.5, SD 16.7) compared to eAMD (86.8, SD 12.4) or normal control (90.1, SD 8.0). Similar between group differences were found at the 24 months visit (iAMD 72.8, SD 16.7; eAMD 85.3, SD 13.7; control 89.5, SD 7.0). However, the change in mean composite LLQ score from baseline to 24 months for each comparison was not significant.

By defining early or intermediate AMD subjects with an LLQ composite score less than the control baseline mean - 2SD=74.2 as “affected outliers," we identified among subjects with eAMD 5 of 22 (22.7%) as outliers at baseline and at 24 months, while among subjects with iAMD at baseline and at 24 months, 14 of 31 (45.2%) were identified as “affected outliers.”

When pooling the non-outlier participants in eAMD and iAMD groups (n=34), the composite and all subscale scores apart from the emotional distress subscore were significantly lower at 24 months than baseline ($P<0.05$). In contrast, in the "affected outlier" subset (n=19), there was no significant difference in LLQ composite or subscale scores at 24 months and baseline except for the extreme lighting subscore ($p=0.008$).
Conclusions: Our results suggest that the sensitivity of the LLQ to monitor change in function in eAMD and iAMD over time may be limited by a floor effect. LLQ is a useful PRO to detect disease progression in eAMD and iAMD subjects that are not significantly impaired at baseline (composite LLQ score ≥75).

CONTROL ID: 3705957

SUBMITTER (NAME ONLY): Jiawei Zhao

TITLE: Epidemiology of eyelid lacerations presenting to a level I trauma center in the United States: 2018-2020

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zhao, The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES|A. Awidi, X. Li, A. Jensen, F. Rajaii, N. Mahoney, F. Woreta, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|M. Ahmad, University of California San Francisco, San Francisco, California, UNITED STATES|G. Justin, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Eyelid lacerations are a common cause of eye injuries presenting to the Emergency Department (ED), comprising around 10% of all visits. However, the epidemiology of eyelid laceration injuries has not been well documented in the literature. The objective of this study was to investigate the etiologies, demographic factors, and management strategies of patients presenting with eyelid lacerations to a U.S. tertiary academic center ED.

Methods: A retrospective chart review of all patients with eyelid lacerations presenting to the ED of a tertiary academic center from April 2018 to December 2020 was performed. An eyelid laceration was defined as any laceration involving the eyelids, its margins, and/or the canaliculus. Data on demographics, clinical characteristics, and management were analyzed. Variables associated with mechanism of injury in eyelid lacerations were assessed using multivariate logistic regression.

Results: Out of 303 eyelid laceration cases identified, 56% were non-marginal and non-canalicular lacerations, followed by 24% with canalicular involvement and 20% crossing the eyelid margin. Animal bite or scratch was the most common etiology of canalicular involving lacerations (29%), with the majority (66%) of these injuries occurring in children. Mechanical fall was the most common etiology in patients over age 60 (62%). Patients that were assaulted were more likely to present with concomitant ophthalmic injuries (OR 2.25 [95% CI 1.20-4.29]; P = 0.012), with the most common being orbital fracture (25%), corneal abrasion (21%), traumatic iritis (19%) and commotio retinae (17%). Black patients and those with Medicaid insurance were more likely to have an eyelid laceration injury due to assault when compared to Caucasian patients and ones with private insurance (OR 3.57 [95% CI 1.78-7.41]; P = <0.001 and OR 2.66 [95% CI 1.14-6.57]; P = 0.027, respectively). Of all the eyelid lacerations, 78% underwent surgical repair,15% were observed and 3% were repaired by tissue glue.

Conclusions: Animal-related injury was the most frequent cause of canalicular involving eyelid lacerations, occurring mostly in children. The most common etiologies for eyelid lacerations in the elderly and Black patients were fall and assault, respectively. Identifying the most common etiologies for eyelid lacerations can help raise awareness to emphasize preventive measures in specific patient populations.

CONTROL ID: 3705961

SUBMITTER (NAME ONLY): Jason Fan

TITLE: Management Outcomes in Patients with Suprachoroidal Hemorrhage after Anterior Segment Surgery

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fan, J.L. Hudson, P. Pakravan, K.C. Fan, H.W. Flynn, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Suprachoroidal hemorrhage (SCH) remains one of the most devastating complications associated with intraocular surgery. Although advances in surgical technique have been made, the outcomes of SCH management have generally remained poor. The current study reports management outcomes of SCH after anterior segment surgery at a single institution, and identifies clinical features associated with visual prognosis.

Methods: Retrospective chart review of patients with suprachoroidal hemorrhage occurring after anterior segment surgery.

Results: The study includes 112 eyes of 112 patients treated between 2014 and 2020. Factors associated with better visual acuity outcomes included SCH occurring after glaucoma surgery, hypotony at time of presentation, and management by observation. Factors associated with worse visual acuity outcomes included presence of APD (p=0.02), concurrent retinal detachment (p=0.02), appositional SCH (p=0.002), management by delayed drainage (p=0.013), and duration of apposition greater than 7 days (p=0.002). Visual acuity outcomes after management generally remained poor at last follow-up: 58% of patients had a visual acuity (VA) of ≤ 20/200, 17% had light perception (LP), and 10% had no light perception (NLP). Appositional SCH was not found to be associated with worse visual outcome in patients managed with delayed drainage or PPV (n = 66). Both appositional SCH (p=0.01) and duration of apposition (p=0.04) were correlated with worse outcome only in patients that were observed. Regarding management, 53% of patients were observed, 31% underwent delayed drainage, and 31% underwent pars plana vitrectomy (PPV) with or without scleral buckling. Of those with appositional SCH, 12 patients were observed (mean final VA 1.78, SD 1.16), 15 underwent delayed drainage (mean final VA 1.951, SD 0.73), and 13 underwent PPV (mean final VA 1.891, SD 0.73).

Conclusions: Overall visual outcomes in patients with SCH after anterior segment surgery remain poor. The majority of patients with SCH were of advanced age and pseudophakic. Roughly half of all cases occurred after glaucoma surgery (n=59). Appositional SCH is associated with worse VA outcomes when observed (mean difference = 0.859, p= 0.01), but not when delayed drainage or PPV were undertaken. Observation remains a reasonable management strategy for non-appositional SCH.

CONTROL ID: 3705967

SUBMITTER (NAME ONLY): Fatima Iqbal

TITLE: Predictive potential of features of Meibomian glands in determining symptoms of discomfort among contact lens users

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Iqbal, J. Tan, E. Papas, F. Stapleton, School of Optometry & Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Long-term use of contact lens (CL) alters the structure of Meibomian glands (MG), which may lead to discomfort. This study aimed to develop and validate a morphometric automated algorithm to analyse features of MGs and predict symptoms of discomfort among CL wearers

Methods: This retrospective study consisted of 179 (96 upper eyelids & 83 lower eyelids) anonymised meibography images from 69 participants aged ≥18 years to develop and train a morphometric automated algorithm. Images were obtained using the Oculus Keratograph 5M (Oculus GmbH, Wetzlar, Germany) from the database of the School of Optometry & Vision Science, UNSW, Sydney. A custom macro was developed and used to batch-process all images, quantifying gland width and intergland distance at the lid margin, centre, and distal end. A second set of images from participants with contact lens discomfort (CLD) (n=45 CL users with CLDEQ-8 score > 12 and evidence of MG obstruction) were analysed to evaluate associations between these morphological parameters, contact lens dry eye questionnaire score (CLDEQ-8), and ocular surface signs including lid wiper epitheliopathy, non-invasive tear break up time, lipid layer thickness, and telangiectasia. Univariate and multivariate analyses were conducted to develop a multiple regression equation to predict the CLDEQ-8 score. This predictive model was validated on a third independent set of images (n=68 CL users with CLD) using a Bland Altman method comparison between the actual and the predicted CLDEQ-8 score.

Results: In univariate analysis, CLDEQ-8 scores were significantly associated with gland width at the lid margin ($r=0.31$, $p=0.04$), the distal end ($r=0.43$, $p=0.01$), and intergland distance at the upper eyelid margin ($r=-0.48$, $p=0.02$). There were no significant associations between the CLDEQ-8 score and ocular surface signs. Using these variables in multivariate regression, produced a model which accounted for 68% ($R^2=0.68$, $p<0.05$) of the variance in symptoms of discomfort. Bland Altman plot between the predictive and actual CLDEQ-8 score demonstrated ±2.7 limits of agreement around the mean difference of -0.1.

Conclusions: This morphometric algorithm is capable of analysing morphological features of MGs that can predict symptoms of discomfort among contact lens users with reasonable accuracy. This approach may be suitable as a screening tool in the early detection of CLD.

CONTROL ID: 3705970

SUBMITTER (NAME ONLY): Kana Orihara

TITLE: Involvement of calpains and caspases in RGC damage in human iPSCs-derived OV cultured under hypoxia

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Orihara, C. Fukiage, M. Azuma, Senju Pharmaceutical Co., Ltd., JAPAN|T. Yokoi, N. Azuma, National Center for Child Health and Development, JAPAN|

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ABSTRACT BODY:

Purpose: We previously demonstrated calpain activation and retinal ganglion cell (RGC) damage in human retinal explants cultured under hypoxia. Recently, functional RGCs were produced from human pluripotent stem cells (iPSCs)-derived optic vesicles (OV).The purpose of the current experiment was to investigate if human iPSCs-derived OV are suitable experimental models of human retina. For this purpose, activation of calpains and caspases by hypoxia was studied in human iPSCs-derived OV.

Methods: RGCs were induced from human iPSCs as previously described. Dissociated iPSCs were cultured in V-bottomed, 96-well plates. On Day 27, aggregated embryoid bodies were cultured on adhesive substrates. Damage of elongated neurites in OV was evaluated after culture under hypoxia/reoxygenation. When tested, caspase-8 (IETD) and caspase-9 (LEHD) inhibitors, and calpain inhibitor (SNJ1945) were added along with hypoxia. Activation of caspase-3 was assayed by cytochemical staining after dissociation of mechanically isolated OV. Cell lysates were immunoblotted for caspase-3 and α-spectrin.

Results: Hypoxia/reoxygenation induced damage in human iPSC-derived RGCs in a time dependent manner. Activated caspase-3-positive cells were observed after 12 h hypoxia/3 h reoxygenation. Immunoblotting confirmed activation of caspase-3. RGC degeneration and activation of caspase-3 were ameliorated by caspase-8 and caspase-9 inhibitors. Calpain inhibitor inhibited RGC damage, but not caspase-3 activation. Inhibition of caspase-3 was confirmed by observing proteolyzed α-spectrin. Calpain inhibitor ameliorated production of calpain-specific α-spectrin breakdown product (SBDP145), but not caspase-3-specific 120 kDa SBDP. Caspase-9 inhibitor prevented production of caspase specific SBDP, but not calpain-specific SBDP145.

Conclusions: Calpains and caspases are involved in hypoxia/reoxygenation-induced damage to iPSCs-derived RGCs. Human iPSCs derived RGCs are useful for research where access to human eye tissues is limited.

CONTROL ID: 3705972

SUBMITTER (NAME ONLY): Tyler Kaplan

TITLE: The Use of a Convolutional Neural Network Predicted 60-4 Visual Field to Predict the Effect of Facial Contour on Visual Field Defects in Glaucoma Patients

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kaplan, S. Jamali, M. Mousavi, C. Khanna, Ophthalmology, Mayo Foundation for Medical Education and Research, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this paper is to determine if a convolutional neural network (CNN) can be used to predict the contribution of facial contour induced visual field defects in glaucoma patients. This can be utilized to differentiate visual field loss from glaucomatous damage from visual field defects due to facial contour.

Methods: Glaucoma patients were consecutively enrolled and underwent a 60-4 visual field test. A single photograph was taken of each subject. A CNN was used to create a three-dimensional reconstruction based on the two-dimensional image. A map of the intersection between the visual axis and the face on the 3D reconstruction was used to predict the location and extent of visual field defects which corresponded to an individual's facial contour. A python script was then utilized to create a visual field which demonstrated the visual field defects due to facial contour. The predicted 60-4 and the actual 60-4 visual field were superimposed to determine the amount of visual field attributed to glaucoma.

Results: 14 glaucoma patients were included in this study. 28 eyes were included in this study. Each eye completed a 60-4 visual field. The predicted 60-4 visual field related to a patient's facial contour was superimposed on the patient's actual 60-4 visual field. The duration of the 60-4 visual field tests ranged from 8 minutes 17 seconds to 11 minutes 55 seconds. In 27/28 eyes, the predicted visual field loss coincided with areas of visual field loss on their actual 60-4 visual field. The total thresholds, which were generated as a summation of each individual threshold point, ranged from 854-1534 in the right eye and 949-1604 in the left eye. The range of visual field affected by facial contour was 0-7% with an average of 3.14%.

Conclusions: This study demonstrates the utility of a CNN assisted 60-4 visual field in monitoring glaucomatous progression. This tool can help differentiate visual field loss from glaucomatous damage from facial contour. In this study, facial contour commonly corresponded to nasal visual field defects. This methodology may be helpful in determining if a visual field defect is due to glaucoma or facial contour, assist in accurate identification of glaucoma progression, and reduce variability of visual fields by accounting for the role of facial contour in the peripheral field.

CONTROL ID: 3705973

SUBMITTER (NAME ONLY): Gibran Khurshid

TITLE: Common antidiabetic drug metformin reduces the development of age-related macular degeneration

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.S. Khurshid, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

Commercial Relationships Disclosure: Gibran Khurshid: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: AMD is a debilitating disease affecting the elderly. Currently, there are no definitive treatments that clinicians can offer to prevent AMD onset or progression. Metformin is a relatively well-tolerated and widely used medication, proven successful in diabetes treatment. This study examined whether metformin use is associated with decreased risk of AMD development

Methods: This was a retrospective case-control study that included patients over age 55 who were seen at the University of Florida ophthalmology clinics between June 1, 2011, to June 1, 2017. Cases (n=1947) included patients with ICD-9 diagnostic code for macular degeneration who were followed for at least four visits before their diagnosis. Controls (n=5841) were patients who had at least four visits in that time period without the diagnosis of AMD. Cases and controls were propensity score-matched with a 1:3 ratio for variables such as age, CCI, hypertension, and anemia. Univariate regression analysis was used to determine metformin's relationship to the development of AMD. Conditional multivariable logistic regression was used to explore this relationship with consideration of the other covariates of the patients.

Results: Patients on metformin had a statistically significant decreased odds ratio of developing AMD when using univariate analysis (OR, 0.39; 95% CI, 0.31-0.49) as well as conditional multivariable logistic regression (OR, 0.58; 95% CI, 0.43-0.79). Because diabetes can act as a prominent confounder, subgroup analysis was performed studying only patients with diabetes. Through conditional multivariable logistic regression, it was illustrated that metformin use was still associated with decreased odds of developing AMD when diabetes was removed as a confounder (OR, 0.70; 95% CI 0.49-0.98). Other medications assessed such as DPP4 inhibitors, SSRIs, tetracyclic antidepressants, and statins were not found to have a statistically significant relationship with AMD incidence.

Conclusions: In this study we found that metformin decreased the likelihood of developing AMD by 42%, suggesting that this ubiquitous antidiabetic drug may contribute to delaying AMD progression or stopping it altogether. We hope that the relationship between metformin and AMD development will be further established with prospective studies in the future.

CONTROL ID: 3705977

SUBMITTER (NAME ONLY): Mohamed Al-Shabrawey

TITLE: EET Blockade: A New Method to Optimize AT1 Blockade in the Treatment of Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Al-Shabrawey, A.M. Tawfik, Eye Research Center, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|M.A. Al-Shabrawey, A.M. Tawfik, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|N. Sheibani, Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|M. Wang, Physiology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The activation of the renin-angiotensin system (RAS) contributes to the destruction of blood-retinal barrier (BRB) and neovascularization in diabetic retinopathy (DR). Although blocking RAS in clinical studies reduced the incidence of DR, it did not reduce the progression of DR. The goal of this study was to decipher the role of epoxyeicosatrienoic acids (EETs), cytochrome P450 (CYP)-derived eicosanoids, and EETs degrading enzyme soluble epoxide hydrolase (sEH) in angiotensin II (Ang II)- and diabetes-induced retinal microvascular damage. We also determine the interactions between EETs/sEH and angiotensin receptor-1 (AT1) in the retina.

Methods: We induced experimental diabetes in wild-type and sEH knockout mice by intraperitoneal injection of streptozotocin (STZ). Some mice received chronic treatment with Ang II via SC minipump (3 mg/kg/day), with or without AT1 blocker telmisartan (2.5 mg/kg/day). Some mice received intravitreal injection of Ang II with or without 11,12 EET. Integrity of blood retinal barrier (BRB) was assessed by analysis of albumin leakage in the retina. Analysis of the plasma levels of bioactive lipids in normal and diabetic mice was done using LC/MS/MS.

Results: Ang II increases retinal expression of sEH by 2.8-fold (2.84 ± 1.1 vs. 1 ± 0.08, $P < 0.05$, n = 4), which is blunted by AT1 blockade. Moreover, sEH blockade and knockout (KO), which accumulate EETs, enhance Ang II-induced BRB injury as shown by 1.58 folds increase in retinal albumin leakage (1.58 ± 0.4 vs. 1 ± 0.13, $P < 0.05$, n = 4) and 2.8-folds (2.8 ± 1.7 vs. 1 ± 0.09, $P < 0.05$, n = 4), respectively. These results were confirmed by fluorescein angiogram (FA) analysis. Administration of synthetic 11,12-EET enhances intravitreal Ang II-induced retinal albumin leakage by 2.2-fold (2.2 ± 0.5 vs. 1 ± 0.18, $P < 0.05$, n = 4). In addition, 11,12-EET induces retinal hyperpermeability by FA and retinal albumin leakage. Moreover, sEH KO potentiates diabetes-induced retinal damage. This was associated with upregulation of retinal vascular endothelial growth factor (VEGF) and glucose transporter-1 (GLUT-1).

Conclusions: Our data indicate that in DR, the activation of retinal AT1 triggers a compensation mechanism by increasing retinal sEH, thereby reducing the production of EETs. Therefore, the combined use of EETs blockers and AT1 blockers is expected to become a new treatment strategy to prevent or reduce DR.

CONTROL ID: 3705986

SUBMITTER (NAME ONLY): Enzo Maria Vingolo

TITLE: Reaction Time (RT) a new Microperimetry (MP) diagnostic tool, basic evaluation

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Vingolo, E. Rigoni, Ophthalmology, Universita degli Studi di Roma La Sapienza, Rome, Lazio, ITALY|P. Iimoli, Low Vision, Centro studi ipovisione, Milano, Milano, ITALY|

Commercial Relationships Disclosure: Enzo Maria Vingolo: Commercial Relationship: Code N (No Commercial Relationship) | Paolo G Iimoli: Commercial Relationship: Code N (No Commercial Relationship) | Erika Rigoni: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: MP has been used as strong disgnostic tool in several eye diseases. nevertheless its complexity there are functional parameters that are very helpful in evaluating clinical conditions as fixation, scotometry and retinal sensitivity. Reaction time is idefinited as the interval recorded by the device from stimulus presentation and patient's answer. Our goal is tho understand if there are relationships between RT and retinal localization of the stimulus and if this may be as early marker of the disease.

Methods: Using MP3 (Nidek Co. Jpn) mean RT was evaluated in msec. in different retinal areas, 12 points in central 5° area, and 40 point in perpheral retina between 15-20°, tests were performed starting from 0 dB every 10dB, with 31.4 asb background luminance and Goldmann III stimulus (reference value for Humfries), with presentation seen/not seen screening strategy. Were tested 7 healthy subjects and 5 patients with soft drusen (sized >63microns). No statistical differences were found between two groups for age, sex composition and visual acuity.

Results: Average RT value for central area was 549ms. (SD±136ms) for group A while average RT for Group B was 837ms (SD±255ms) differences were statistically significant (p=0.007). RT value for peripheral area was 1003ms. (SD±74ms) for group A while peripheric average RT for Group B was 981ms (SD± 95ms) differences were not significant (p=0.081). Our data underlines that patients in group B patients presented a better performance at higher luminance.

Conclusions: Our interesting data, show very clear difference in central area between healthy people and those presented small soft drusen, this outcome may be due to an irregular intraretinal signaling or neurotransmission as speculated by Curcio, there is a topographic correlation between drusen, cones and rods, that realized exchange pathways among outer retinal cells and across Bruch's membrane and the subretinal space, in service of highly evolved, eye-specific physiology that can slower in these zones retino-cerebral reaction time. In peripheral area soft drusen are ususally more rare due to a slower methabolic speed. Obviously this is a preliminary report of new approach to microperimetry and our intent is to add a new approach to early disease diagnostics with the aim to intercept individuals in which retinal damage may go wider in a short time so that would be possible to start a more efficient treatment.

CONTROL ID: 3705987

SUBMITTER (NAME ONLY): Filippo Locri

TITLE: Combination of Laminin and Nicotinamide accelerates the kinetics of ARPE-19 maturation.

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Locri, J. Bernd, F. Plastino, A. Kvanta, H. Andre, Clinical Neuroscience, Division of Eye and Vision, Karolinska Institutet, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) modulates the exchange of metabolite products to and from the retina, maintains the photoreceptor function by phagocytosis and processing of photoreceptor outer segments allowing their renewal. The human RPE cell-line ARPE-19 is commercially available and widely used as an alternative to primary RPE. However, these cells undergo epithelial-mesenchymal transition losing many features of primary RPE such as polarity, pigmentation, and expression of RPE signature markers. We aimed to determine whether a combination of laminin coating and media supplementation with nicotinamide could improve ARPE-19 expression of genes and proteins, along with morphological phenotype resembling mature RPE.

Methods: ARPE-19 cells were cultured for up to 3 months with or without 10mM nicotinamide supplementation and/or coated with human recombinant laminin 521. Gross cell morphology was evaluated by phase microscopy. Assessment of maturation was performed by immunocytochemistry and gene expression by qPCR.

Results: Laminin 521, in combination with nicotinamide supplementation, promoted cytoskeletal reorganization and expression of differentiation markers such as VMD2, RPE65 and PDGFRB compared to non-supplemented culture condition. Moreover, the combination of nicotinamide media supplementation and laminin 521 coating reduced the expression of the of EMT markers, TNFα and TGF-β1; and NCAM1, an immature phenotype RPE marker.

Conclusions: This study demonstrates that the combination of nicotinamide and laminin 521 coating accelerated the kinetics of expression of mature RPE signature genes, reduced expression of EMT genes, accompanied with improved epithelial cell morphology and cytoskeletal organization, bringing the dedifferentiated ARPE-19 closer to their in vivo phenotype.

CONTROL ID: 3705993

SUBMITTER (NAME ONLY): Francesca Cancellieri

TITLE: Genetic bases of retinoblastoma from liquid biopsies

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Cancellieri, V.G. Peter, M. Quinodoz, C. Rivolta, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|F. Cancellieri, V.G. Peter, M. Quinodoz, C. Rivolta, Department of Ophthalmology, Universitat Basel, Basel, Basel-Stadt, SWITZERLAND|C. Stathopoulos, F.L. Munier, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Retinoblastoma (RB) is the most common ocular tumor of the child, in most instances initiated by mutations in the RB1 gene. Molecular biomarkers determining its aggressiveness and progression have so far only been partially elucidated, due to a significant risk of tumor cells' dissemination following classical biopsies. Recently, the so-called "liquid biopsies" from the aqueous humor (AH) have demonstrated to be a valid alternative to direct tissue sampling for retinoblastoma. By sequencing tumor cell-free DNA (cfDNA) from the AH, we aim to gain insights into the genetic makeup of retinoblastoma and relate specific genotypes to clinical outcomes, such as tumor aggressiveness and therapeutic response.

Methods: Following the collection of approximately 100ul of AH, cfDNA was isolated, and genetic analysis was performed by whole-genome sequencing (WGS) and whole-exome sequencing (WES). Raw data were analyzed with an internal pipeline for the identification of mutations, including single-base variants and genomic copy number variations.

Results: We completed a proof-of-concept analysis on a small set of 5 AHs, and we are now performing the analysis on the bulk of our collection, consisting in approximately 370 samples. Our preliminary results show a considerable genetic heterogeneity of somatic variations in different tumors, despite the relatively small fraction of samples that were sequenced. Nevertheless, we also found some recurrent genomic alterations, such as 1q gain, 16q loss, and 6p gain.

Conclusions: Overall, our data indicate that retinoblastoma is more diverse at the genetic level than previously thought, and that such heterogeneity may shape in the end its clinical characteristics.

CONTROL ID: 3705996

SUBMITTER (NAME ONLY): Ankush Kawali

TITLE: Thermal conduction in posterior scleritis and choroiditis.

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sanjay, P. Mahendradas, Uveitis and Ocular immunology, Narayana Nethralaya, Bangalore, Karnataka, INDIA|A. Khanum, A. Shettigar, J. Rajendran, General Ophthalmology, Narayana Nethralaya, Bangalore, Karnataka, INDIA|A. Kawali, Uveitis and Ocular immunology, Narayana Nethralaya, Bangalore, Karnataka, INDIA|A. Mohan, retina, Narayana Nethralaya, Bangalore, Karnataka, INDIA|R. Shetty, Cornea and refractive surgery, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: To study transmission of thermal energy in posterior scleritis and choroiditis in an experimental model and in practice.

Methods: Model cadaveric eyes for posterior scleritis and choroiditis were created by eviscerating intraocular contents leaving behind scleral strip attached to sclero-corneal button (SCB) and by peeling sclera leaving behind choroidal tissue attached to SCB respectively. (Figure 1) Scleral and choroidal tissue was immersed in hot water and temperature changes on the SCB were noted using a non-contact thermal camera (FLIR Cat S 60 mobile phone). Using same device thermography was done for at least 4 visits between the active and resolved disease for posterior scleritis, VKH disease and control. Difference between the Central Corneal Temperature (CCT) and the ipsilateral temporal eye brow temperature was studied during the follow up and the maximum (Δt Max) and the minimum difference (Δt Min) was calculated. The difference between Δt Max and Δt Min called amplitude of fluctuation (Δt amp). (Figure 2) Comparison of means for all groups was done using the ANOVA test and a p value of <0.05 was considered significant.

Results: In model choroiditis and scleritis eye temperature changed by 3.23°C and 3.52°C respectively at 5 min. Nine eyes of 9 patients of posterior scleritis and VKH disease and 10 eye of 10 controls were studied. Mean highest CCT in scleritis, VKH and the control was 33.2°C (range: 31.5°C – 34.4°C), 33.8°C (range: 32.2°C -35.1°C), and 33.8°C (range: 32.7°C - 35.3°C) respectively. (p: 0.416) Mean Δt Max in scleritis, VKH and control was 2.3 (range: 1.7-3.7), 1.9 (range: 0.4-2.8) and 2.2 (range: 0.8-3.8) respectively. (p: 0.669) Mean Δt Min in scleritis, VKH and control was 0.4 (range: -1.1- 1.1), 0.6 (range: 0-1.4), and 0.1 (range: -0.2 – 2.8) respectively. (p= 0.249) Mean Δt amp in scleritis, VKH and control was 1.8 (range: 0.8-3.2), 1.3 (range: 0.3-1.9) and 1.2 (range: 0.5-1.8) respectively. (p= 0.082).

Conclusions: In model eyes scleral tissue conducted more thermal energy. No significant difference was noted in Δt amp of scleritis, VKH and control eyes. The significance level increased for the parameter ”Δt amp” compared to “Δt Max” or “Δt Min.”

CONTROL ID: 3706004

SUBMITTER (NAME ONLY): Vivian Hawn

TITLE: Additional Resource Utilization Associated with Resident-Performed Cataract Surgeries

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.S. Hawn, D. Flomenbaum, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|G. Kim, J. Kang, W. Yao, Department of Ophthalmology, Montefiore Health System, Bronx, New York, UNITED STATES|E.K. Dackowski, Department of Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare intraoperative material utilization during phacoemulsification surgeries performed by trainees versus experienced surgeons.

Methods: This study included phacoemulsification surgeries performed by three experienced surgeons (EX) and seven resident trainees (RS) over one academic year. Exclusion criteria included prior ocular surgeries or intravitreal injections, combined surgery, preoperative best-corrected visual acuity worse than 20/200, and history of trauma or pseudoexfoliation syndrome. Resources additional to that of routine cataract surgery were enumerated for each case, including viscoelastic, trypan blue, balanced salt solution (BSS), iris expanders, miotic agents, sutures, and capsular support devices. The surgery duration and presence of complications were also noted. Data analysis using rank sum, chi square, Fischer, or student t-tests were used when appropriate.

Results: The 584 EX and 149 RS cases had no significant differences in patient demographics. EX used 23 additional units of resources per 100 cases, while RS used 58 ($p<0.001$). Overall, 111 (19%) EX cases required extra materials compared to 52 (35%) RS cases ($p<0.001$). The majority of these cases required only one additional resource (16% of EX and 23% RS), compared to those that needed two (2.7% EX and 6.7% RS) or more than three additional resources (0.68% EX and 5.4% RS). Additional viscoelastic, trypan blue, BSS, and sutures were used more frequently in the RS cases, whereas there was no statistical difference in the utilization of intracameral miotic agents, iris expander, or capsular support devices between the two groups. Junior residents (PGY-3) consumed more resources than their senior counterparts (PGY-4), 58% versus 22% respectively, ($p<0.001$). More complications occurred in the RS group (2.0%) than in the EX group (0.0%, $p=0.008$). The median surgery duration was 21 minutes [interquartile range: 18-27] for RS compared to 10 minutes [8-12] for EX ($p < 0.001$).

Conclusions: Overall, residents used more intraoperative materials than experienced surgeons did during cataract surgeries. The additional utilization of resources, increased surgery duration, and higher complication rate of resident-performed cataract surgeries are likely associated with increased costs for institutions where trainees perform surgery.

CONTROL ID: 3706007

SUBMITTER (NAME ONLY): Elisabeth Van Aken

TITLE: Fructosamine-3-kinase (FN3K) breaks down advanced glycation end products (AGEs) in human lenses

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Van Aken, S. De Bruyne, J. Himpe, J. Delanghe, Universiteit Gent Faculteit Geneeskunde en Gezondheidswetenschappen, Gent, BELGIUM|L. van Schie, N. Callewaert, Vlaams Instituut voor Biotechnologie, Gent, Oost-Vlaanderen, BELGIUM|

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ABSTRACT BODY:

Purpose: FN3K is a natural intracellular repair enzyme for condensation products of glucose with protein primary amine groups. The enzymes action on AGEs, high molecular weight compounds enhancing oxidative stress and covalent crosslinking, is yet unknown. We produced active recombinant FN3K enzyme (rFN3K) and inactive mutant FN3K (mFN3K) in yeast (Pichia pastoris) and investigated the activity of rFN3K against AGEs in human lenses.

Methods: A DNA construct encoding human FN3K flanked by a N-terminal His-tag with a caspase-cleavable D–E–V–D site was codon-optimized for Pichia pastoris and cloned into the pKai61 vector for intracellular expression. For mFN3K, human FN3K carrying a K41L substitution (FN3K–K41L) in the putative F–V–K catalytic triad was made. After gel filtration, kinase activity (or lack thereof for mFN3K) was tested in vitro. The protein was further characterized on SDS-PAGE and Western blot. Human lens material obtained after phacoemulsification (n=20), was incubated for 3 h with rFN3K or mFN3K. AGEs were measured by Maillard-type autofluorescence (AF) (excitation 365 nm, emission 390–700 nm). Fructose containing AGEs were investigated in the urea-soluble fraction of rFN3K treated human lens material by gel filtration. Individual fractions were photometrically tested (488 nm) by Seliwanoff reaction.

Results: Remarkable decreases of AF were observed for rFN3K compared to mFN3K. Pronounced decrease of AF was found after 1 h incubation (43.6–49.7% decrease compared to baseline). Additional decrease of AF was found after 2 h incubation (56.7–70.8% decrease compared to baseline), and remained stable thereafter. At lower concentration range of rFN3K (12.5 µg/mL, 6.25 µg/mL and 1.25 µg/mL) a more notable time- and dose dependent effect was seen. Gel filtration showed breakdown of fructose-containing AGEs in human lens fragments by rFN3K. Before treatment, presence of AGEs was observed by two peaks with molecular mass of 2500 Da and 1660 Da. After rFN3K treatment, breakdown products with molecular mass ranging between 1500 and 2500 Da were detected.

Conclusions: rFN3K and mFN3K enzyme were successfully produced in Pichia pastoris. AF kinetics on human lens material revealed a dose and time dependent effect of treatment with rFN3K. A breakdown of high molecular mass fructose related AGEs by rFN3K was observed. Further research is needed to identify the exact substrates of rFN3K in human lenses.

CONTROL ID: 3706008

SUBMITTER (NAME ONLY): Yasmin Islam

TITLE: Outcomes of vitreoretinal complications requiring surgery after abusive head trauma

SESSION TITLE: Endophthalmitis & Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Islam, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Florida, UNITED STATES|Y. Islam, S. Khurshid, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Abusive head trauma (AHT) can result in non-clearing vitreous hemorrhages (VHs), retinal detachments (RDs), and retinal tears that require vitreoretinal surgery. There is ample guidance from professional societies emphasizing the importance of urgent ophthalmologic evaluation after AHT, but there is no available literature evaluating the outcomes of vitreoretinal surgery in aggregate and providing guidance on the timing of vitreoretinal intervention in these patients. This case series combined with literature review aims to fill this knowledge gap.

Methods: A case series of three patients from a large academic medical center were combined with cases obtained during a literature search for studies reporting outcomes of vitreoretinal surgery in children with AHT from 2011-2021. Nine studies were included. The visual acuity (VA) and anatomical outcomes were compared between patients who received vitreoretinal surgery within four weeks of diagnosis and those who had delayed surgery.

Results: A total of 78 eyes from 57 patients received interventions ranging from panretinal photocoagulation to pars plana vitrectomy (PPV) and scleral buckling. Most required a PPV (74 eyes/95%). 72 eyes (92%) had a non-clearing VH, while 7 eyes (9%) had an RD. 75 eyes (96%) had anatomical success after surgery, defined as an attached retina without vitreous hemorrhage. Surgery performed within four weeks of injury showed a trend towards improved anatomical and VA outcomes as compared to delayed surgery.

Conclusions: Vitreoretinal surgery after AHT has excellent anatomical success rates, but there is a trend towards improved VA outcomes when surgery is performed within four weeks of diagnosis. This highlights the importance of urgent ophthalmologic evaluation and referral to a pediatric retina specialist for non-clearing VH, RDs, and retinal tears after AHT.

CONTROL ID: 3706019

SUBMITTER (NAME ONLY): Julie Lim

TITLE: Circadian rhythms and glutathione homeostasis in the rat lens

SESSION TITLE: Lens Physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.C. Lim, H. Suzuki-Kerr, T. Nguyen, C. Lim, Physiology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|J.C. Lim, H. Suzuki-Kerr, T. Nguyen, C. Lim, New Zealand National Eye Centre, NEW ZEALAND|R.C. Poulsen, Pharmacology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|

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ABSTRACT BODY:

Purpose: Since circadian clock proteins have been identified in the rat lens, this study aimed to determine whether glutathione homeostasis is controlled in a circadian manner.

Methods: Lenses and aqueous humor were collected every 4 hours over a 24-hour period from 6-week male Wistar rat lenses (n=8 for each time point) and glutathione levels (reduced and oxidised GSH) measured using HPLC. Western blotting and immunohistochemistry were used to confirm and localize the rhythmic expression of circadian clock core proteins (BMAL1 & CLOCK) and confirm if this expression pattern was linked to the rhythmic expression of the glutathione synthesis enzyme, gamma- glutamylcysteine ligase (GCL), the glutathione regeneration enzyme, glutathione reductase (GR) and NRF2, a transcription factor involved in regulating the expression of genes related to GSH homeostasis.

Results: GSH levels in the lens and aqueous humor oscillated throughout the 24-hour period. Western blotting confirmed protein expression of BMAL1, CLOCK and NRF2 in the lens. Immunohistochemistry revealed differences in the localisation and sub-cellular distribution of BMAL1, CLOCK and NRF2. During the day, BMAL1 and CLOCK were present in the germinative zone of the lens with strong labelling present in the nuclei of epithelial and fiber cells. On the other hand, NRF2 labelling was present in the germinative zone but was not co-localised with the nuclei and instead appeared cytoplasmic. These differences in localisation patterns may correlate with fluctuations in GSH synthesis and GSH levels in the lens at different times of the day to protect against oxidative stress.

Conclusions: Collectively, these findings provide preliminary evidence that glutathione levels may be under the control of a circadian clock. In the future, work will be performed on older rats to determine if decreased circadian rhythmicity alters glutathione levels and predisposes lenses to cataract formation.

CONTROL ID: 3706022

SUBMITTER (NAME ONLY): Vivian Roan

TITLE: Intravitreal steroid decreases macular thickness fluctuations in patients with diabetic macular edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Roan, B. Kuo, B. Liu, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|B. Kuo, C. Carvalho Soares Valentim, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fluctuations in macular thickness over time have been shown to be more predictive of visual outcomes than absolute macular thickness in patients with diabetic macular edema (DME) treated with anti- vascular endothelial growth factor (VEGF). However, it is unclear whether this association exists in DME patients treated with intravitreal steroids. We performed a retrospective, non-comparative, observational cohort study to investigate the effect of steroid treatment on macular thickness fluctuations (MTF) and visual outcomes in patients with DME.

Methods: Central subfield thickness (CST) and best visual acuity (BVA) were collected in 4-month intervals over two years for DME patients over the age of 18 without concomitant maculopathies who had at least one intravitreal steroid injection. Paired t-test was used to compare MTF (quantified by CST standard deviation (CST-SD)) before and after initiation of steroid treatment. A mixed-effects linear regression model was used to determine the association between CST-SD and BVA, adjusting for baseline characteristics and treatment patterns.

Results: Of the 108 patients included, 105 (97.2%) received anti-VEGF treatment prior to steroid initiation. Mean 12-month CST-SD after steroid initiation was significantly lower than mean 12-month CST-SD prior (53.469 ± 49.9 vs. 61.139 ± 56.77; $p = 0.04$). Mean BVA after 12 months was not significantly different from baseline (62.717 ± 15.2 vs. 62.997 ± 13.7; $p = 0.4$). There was no significant association between post-steroid CST-SD and 12-month BVA nor any significant differences in post-steroid CST-SD among the different treatment pattern groups.

Conclusions: MTF decreased after initiation of steroid treatment with maintenance of stable visual acuity. There was no significant correlation between decreases in MTF and visual outcomes which is expected in this prior treated DME patient population receiving intravitreally steroid treatment. This reflects the routine clinical practice of using steroids as second-line treatment after anti-VEGF injections. This study demonstrates the efficacy of intravitreal steroids in reducing MTF and maintaining stable visual acuity, confirming its role in the treatment of DME.

CONTROL ID: 3706026

SUBMITTER (NAME ONLY): Sean Berkowitz

TITLE: Economic Impact of the Merit-Based Incentive Payment System for Ophthalmologists

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Berkowitz, J. Siktberg, A. Gupta, A. Finn, S. Patel, Ophthalmology, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|S. Berkowitz, J. Siktberg, A. Gupta, A. Finn, S. Patel, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|D. Portney, Ophthalmology, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|E. Chen, Ophthalmology, UCSF Medical Center, San Francisco, California, UNITED STATES|R. Parikh, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Merit-based Incentive Payment System (MIPS) is intended to promote high value healthcare through quality-related Medicare payment adjustments. We sought to assess the economic impact of MIPS scoring and reporting category on ophthalmology providers.

Methods: A retrospective, cross-sectional economic evaluation of MIPS performance and related payment adjustments was performed for ophthalmology providers registered for Medicare Part B with participation in the Quality Payment Program (QPP) in performance year (PY) 2019 using Centers for Medicare & Medicaid Service (CMS) public data files. Reported CMS methodology and PY 2019 payment percentages were used to estimate payment adjustments in USD for the following categories of MIPS scores: positive MIPS adjustment plus potential additional adjustment for exceptional performance (75.00-100.00 points), positive MIPS adjustment (30.01-74.99 points), neutral payment adjustment (30.00), negative MIPS payment adjustment (7.51-29.99 points), maximum negative MIPS payment adjustment (0-7.50 points).

Results: For PY 2019, roughly 99% of providers received non-negative reimbursement adjustments and 92.6% received positive adjustments. Participants submitted data through MIPS eligibility categories of Advanced Alternative Payment Models (APM) (2102, 15.43%), Group (8369, 61.44%), Individual (3144, 23.08%), and Virtual Group (6, 0.04%). The total average MIPS score differed statistically significantly by filing category for APM, Group, and Individual providers with average scores of 95.39 (3.17), 86.04 (15.12), and 68.72 (28.74), respectively ($p < .001$). Individuals were significantly less likely to achieve exceptional performance (75.00-100.00) than APM and Group participants with OR 0.0003 (95% CI 0.00002- 0.00481) and OR 0.21013 (95% CI 0.19020-0.23215), respectively. The estimated total national payment adjustment ranges for ophthalmology providers for PY 2019 were $2,146,835 to $42,698,167, $0 to $19,960, -$41 to -$28,347, and -$83,544 to -$83,544 for those with exceptional performance, positive performance, negative, and maximum negative performance, respectively.

Conclusions: There are differences in MIPS scores across filing entities, and the specific scoring methodology may be responsible for meaningful economic incentives as performance thresholds become increasingly rigorous in subsequent years.

CONTROL ID: 3706040

SUBMITTER (NAME ONLY): Abdelrahman Elhusseiny

TITLE: Acute Ophthalmic Manifestations in Mycoplasma Induced Rash and Mucositis

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Elhusseiny, Ophthalmology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, UNITED STATES|A.M. Elhusseiny, R. Rashad, S.S. Shanbhag, J. Chodosh, H.N. Saeed, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of the current study is to demonstrate the prevalence of ocular complications in patients suffering with MIRM, an eruption clinically distinct from Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN).

Methods: In this retrospective observational study, we identified all patients in our hospital database who were diagnosed with MIRM. Diagnosis was confirmed by clinical information and a positive Mycoplasma pneumoniae serology. Only patients with available records with formal ophthalmology consults were included. Clinical and laboratory data were collected from our electronic medical record system.

Results: A total of 11 patients were included in our study. The average age was 22 ± 15.2 years, and the majority were male (63.6%). In all 22 eyes, the acute ocular findings were limited to conjunctival hyperemia (n=18, 81.8%), meibomitis (n=2, 9.1%), and conjunctival epithelial defects (n=1, 4.5%). None of the patients were treated with amniotic membrane transplantation in the acute phase. Three patients received follow-up eye examinations; none showed ocular complications.

Conclusions: Ocular complications from MIRM appear to be milder in comparison to ocular complications found in other bullous and inflammatory conditions such as SJS/TEN. Understanding the ocular sequelae of MIRM is important to better inform acute and chronic management.

CONTROL ID: 3706048

SUBMITTER (NAME ONLY): Grant Hom

TITLE: Construction of an Electronic Medical Record-Based Monitoring, Screening, and Referral System for Pentosan Polysulfate Sodium Drug-Induced Maculopathy

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.L. Hom, B.L. Kuo, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|G.L. Hom, R. Sastry, R.P. Singh, S. Sharma, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|J. Ross, G. Chapman, Obstetrics and Gynecology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pentosan polysulfate sodium (PPS) is an oral-based medication used for interstitial cystitis that has recently been linked to retinal toxicity. Recent guidelines indicate that PPS patients should undergo baseline retinal examination upon treatment initiation with periodic monitoring while continuing treatment. This study aims to understand current PPS practice patterns and examine the utility of an EMR alert system for patients on PPS to help non-ophthalmic prescribing providers make appropriate referrals.

Methods: Phase one of this study characterized the population receiving PPS at a single institution with an IRB-approved retrospective study and included patients older than 18 taking PPS from 2005-2020. Variables studied included PPS exposure time and cumulative dosing, demographic information, the presence of ophthalmology monitoring, and the types of physicians prescribing the medication. An automated electronic medical record (EMR) best practice alert (BPA) was developed and implemented to fire upon PPS prescription or renewal. Rates of alert firing, ophthalmic referrals, and imaging were periodically collected.

Results: Our single institution initially identified 1407 patients who have taken PPS for characterization with a majority being female (1220, 86.7%). Starting age was 48.0 ± 15.7 and mean cumulative drug exposure was 669.7 ± 569.2 grams. 151 (10.7%) of PPS users had an eye exam within our institution. Before BPA intervention, 31 (2.2%) had optical coherence tomography (OCT) imaging to document baseline retinal status. 3-month post-BPA intervention results show the alert fired for 12 patients on 14 encounters. Of these 14 visits, ophthalmology was consulted 7 times (50%, $p<0.001$) and OCT macula were ordered 3 times (21.4%, $p<0.001$).

Conclusions: These results indicate that a limited number of patients taking PPS may be receiving appropriate ophthalmic monitoring per recent guidelines. Notwithstanding, many patients fit the criteria for screening for maculopathy onset (e.g., after 500 grams cumulative exposure). An EMR-based alert is a useful tool to improve ophthalmic screening and referral rates for PPS maculopathy. More work needs to be done to explore cross- specialty understanding of PPS drug-induced maculopathy and their role in detecting and minimizing deleterious effects of this condition.

CONTROL ID: 3706050

SUBMITTER (NAME ONLY): Eleonora Lad

TITLE: A Deep Learning Algorithm to Predict Short-term Progression to Geographic Atrophy on Spectral Domain-OCT

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Lad, C.A. Toth, D. Wang, Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|R. Henao, L. Carin, 3.Department of Electrical and Computer Engineering, Duke University Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: the development of a deep learning algorithm to detect OCT-determined geographic atrophy (GA) and to predict the progression from intermediate age-related macular degeneration (AMD) to GA in the short-term on spectral domain optical coherence tomography (SD-OCT) scans.

Methods: We analyzed SD-OCT imaging data from 316 patients with iAMD enrolled in the longitudinal, observational Age-Related Eye Disease Study 2 (AREDS2) Ancillary Spectral-Domain Optical Coherence Tomography (A2A) Study with adequate imaging for repeated measures. We designed an end-to-end, position-aware volumetric image classification model motivated by the observation that scan locations within a SD-OCT have different levels of predictive power for GA progression prediction. The model was developed with a proactive pseudo-intervention learning strategy to jointly allow for robust learning with small sample size and interpretation of predictions via saliency (attention) maps. To improve model performance given the small sample-size of the available dataset, we employed a second publicly available dataset consisting of 108,312 individual OCT B-scans from 4,686 individuals with various retinal diagnoses. The main outcome measure was the predictive performance for GA detection and progression to GA in 1 year, examined based on the area under the curve (AUC) of the receiver operating characteristic.

Results: The proposed deep learning model (multi-scan position-aware model) outperforms simpler image-based models and a model based on qualitative and quantitative features of SD-OCT provided by human experts. The AUC for GA prediction was 0.945 for current year, and 0.937 for the following year. The addition of expert annotated features only improved the AUC for GA prediction by an AUC of 0.008. The method automatically identified and highlighted specific structural features on OCT most predictive of GA, essentially opening the “black box” of this AI algorithm.

Conclusions: Our deep-learning method had excellent performance characteristics for detecting GA and for predicting progression from intermediate AMD to GA in the short-term (one year). Further validation in additional, independent datasets will be needed to determine the utility of this algorithm for prediction of vision-threatening nonexudative AMD and potential modifications for outcome prediction in other retinal diseases.

CONTROL ID: 3706062

SUBMITTER (NAME ONLY): Masahiro Miura

TITLE: Volumetric evaluation of choroidal depigmentation in the eyes with Vogt–Koyanagi–Harada disease using polarization-sensitive OCT

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Miura, T. Iwasaki, R. Nemoto, H. Shimizu, Ophthalmology, Tokyo Ika Daigaku Ibaraki Iryo Center, Inashiki-gun, Ibaraki, JAPAN|S. Makita, Y. Yasuno, Computational Optics Group, Tsukuba Daigaku, Tsukuba, Ibaraki, JAPAN|S. Azuma, T. Mino, T. Yamaguchi, Kabushiki Kaisha Topcon Kenkyu Kaihatsu Center, Itabashi-ku, Tokyo, JAPAN|H. Goto, Ophthalmology, Tokyo Ika Daigaku, Shinjuku-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: The sunset glow fundus (SGF) appearance is an important finding of Vogt–Koyanagi–Harada (VKH) disease, originated from the choroidal depigmentation. We used polarization-sensitive OCT (PS-OCT) for volumetric evaluation of choroidal depigmentation.

Methods: We evaluated 40 eyes (20 patients) with chronic VKH disease and 59 healthy eyes (59 age-matched controls) with 1-μm swept-source PS-OCT. Eyes with VKH disease were divided into three groups according to color fundus images: sunset (17 eyes), potential sunset (13 eyes), non-sunset (10 eyes). The mean thickness of melanin containing tissue in choroid (thickness of MeCh: thickness of low degree of polarization uniformity (<0.8) area within the choroidal interstitial stroma) and the mean choroidal melanin occupancy ratio (occupancy of the low degree of polarization uniformity area within the choroidal interstitial stroma) within a 5-mm circular region from the foveal center were calculated. To evaluate regional variations, the 5-mm circular region was divided into a center area and an outer ring area.

Results: The mean thickness of MeCh was significantly lower in sunset eyes than non-sunset or control eyes ($P = 0.003$). The mean choroidal melanin occupancy ratio of sunset or potential sunset eyes were significantly lower than non-sunset or control eyes ($P = 0.04$). The area under the receiver operating characteristic curves for the combined sunset group (sunset and potential sunset) and the non-sunset group were 0.983 and 0.997 for the thickness of MeCh and the choroidal melanin occupancy ratio, respectively. Regional evaluation of thickness of MeCh and the choroidal melanin occupancy ratio showed that choroidal depigmentation predominantly occurred in the macula's outer ring area ($P = 0.002$). Time course evaluation of 12 eyes for 18 months from disease onset showed that both thickness of MeCh and choroidal melanin occupancy ratio significantly decreased over time.

Conclusions: PS-OCT is useful for objective evaluation of choroidal depigmentation of the SGF in VKH disease.

CONTROL ID: 3706065

SUBMITTER (NAME ONLY): Xinye Qian

TITLE: Systematic Identification of Deep-intronic Splicing Variants in a Large Cohort of Patients with Inherited Retinal Diseases

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Qian, Verna and Marrs McLean Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, Texas, UNITED STATES|X. Qian, R. Chen, Human Genome Sequencing Center, Baylor College of Medicine, Houston, Texas, UNITED STATES|N. Aceves, R. Chen, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Xinye Qian: Commercial Relationship: Code N (No Commercial Relationship) | Nathalie Aceves: Commercial Relationship: Code N (No Commercial Relationship) | Rui Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to better evaluate the contribution of deep intronic splicing mutant alleles to inherited retinal diseases (IRD).

Methods: Whole-genome sequencing was performed for 741 patients who lack a confident molecular diagnosis from a cohort of approximately 7000 IRD patients. We filtered and annotated genomic alterations with a custom pipeline and predicted the effects of intronic variants on splicing using SpliceAI. The candidate splicing variants were restricted to those found in IRD genes and with a SpliceAI score ≧0.02. The candidates were further filtered based on allele population frequency, the distance from the exon-intron junctions, mode of genetic inheritance, and clinical phenotype. To further validate the in silico predictions, we utilized an in vitro minigene system to test a set of 130 candidate deep intronic splicing mutations with a score range of 0.02 to 1. DNA oligos with which sequences include the candidate mutation, SpliceAI-predicted cryptic exon, and flanking regions were synthesized, PCR-amplified, and cloned into a minigene vector. Each construct was separately transfected into HEK293 cells, from which RNA was extracted and RT-PCR was performed to assess the splicing products.

Results: Within the 741 unresolved patients, 18182 candidate deep-intronic splicing mutations were identified with a SpliceAI cutoff score of 0.02, but only 279 candidates have a score above 0.2, which is the cutoff commonly used by clinical labs. Among the selected 130 candidate IRD deep-intronic splicing mutations that were tested in vitro, all high-scored candidates (≧0.5) resulted in the generation of aberrant transcripts. However, for the mid-scored candidates (0.1≦ SpliceAI score <0.5), only half of the candidates affected splicing in vitro, while the majority of candidates with a score less than 0.1 failed to be validated to affect splicing.

Conclusions: Our study is the largest-scale study on deep-intronic splicing variants in IRD diseases. Our findings demonstrated that although there is a good correlation between SpliceAI score and splicing effects, given that many low-scored deep-intronic candidates also generated aberrant transcripts, the contribution of intronic variants, especially those deep within introns, to genetic diseases might be underestimated and further optimization of the prediction tool is needed.

CONTROL ID: 3706066

SUBMITTER (NAME ONLY): Katherine Talcott

TITLE: Three Dimensional Digitally-Enabled Intraoperative OCT Compared with Conventional Microscope-Integrated Intraoperative OCT in Vitreoretinal Surgery: A Post Hoc Analysis of the DISCOVER Study

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Talcott, A. Knapp, S.K. Srivastava, A.V. Rachitskaya, S. Sharma, R.P. Singh, A. Yuan, J. Reese, J.P. Ehlers, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: New digitally-enabled options for high-definition, heads-up stereoscopic visualization during surgery recently became available for an immersive 3D visualization of both the surgical field and the intraoperative OCT (iOCT) datastream. The purpose of this study was to compare conventional microscope-integrated iOCT and digitally-enabled microscope-integrated iOCT surgical platform.

Methods: This was a post-hoc case-control analysis from the DISCOVER study, a prospective, IRB-approved multi-surgeon case series, comparing the use of a conventional microscope-integrated iOCT (Rescan 700; Zeiss, Germany) with a digitally-enabled iOCT (Artevo 800; Zeiss). The two groups were optimally matched for surgeon and preoperative diagnosis. Standardized surgeon questionnaires were collected immediately following surgery. The primary objective was comparative assessment of surgical visualization efficiency [i.e., proportion of surgical field-based visualization (i.e., ocular heads-up display in the conventional group, 3D screen-based visualization in the digitally-enabled group) and non-surgical field-based (e.g., external 2-D monitor)]. Additional variables of comparison included iOCT utility and impact of iOCT on surgical decisions.

Results: 200 eyes from 200 subjects were included with 100 subjects in each arm. The most common indications for surgery were epiretinal membrane (conventional iOCT = 35%; digital iOCT = 33%) followed by retinal detachment and macular holes (conventional iOCT = 21%, 19%; digital iOCT = 21%, 20%, respectively). Surgical field-based visualization of iOCT datastream was significantly higher in the digitally-enabled group compared with conventional iOCT group (88% vs 7%, $p < 0.0001$). Surgeon-perceived utility of iOCT was similar between groups (conventional iOCT = 53%; digital iOCT = 60%, $p = 0.32$). The direct impact of iOCT on surgical decision-making was also similar between both groups (16% vs 21%, $p=0.36$).

Conclusions: Digitally-enabled microscope-integrated iOCT resulted in greater surgical visualization efficiency with a significantly higher proportion of cases with surgical-field based visualization of the iOCT datastream compared to the conventional system. Surgeon-perceived utility of iOCT was high in both groups.

CONTROL ID: 3706067

SUBMITTER (NAME ONLY): Giedre Pakuliene

TITLE: Evaluation of Tear and Anterior Chamber Fluid Samples for Benzalkonium Chloride During Long-Term Glaucoma Treatment

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Benzalkonium chloride (BAK) is a widely used preservative in ophthalmic medications, as well as hygiene and cosmetic products. Experimental studies showed BAK's presence in ocular tissues, however the extent to which it accumulates during chronic topical glaucoma therapy is uncertain. A prospective case-control study was performed to test for the presence of BAK in tear and in anterior chamber fluid (ACF) samples in patients undergoing long-term topical therapy for open angle glaucoma (OAG).

Methods: Study group consisted of 22 cataract patients with OAG who received topical treatment for >2 years and 34 controls free from eye disease (other than cataract) with demographics in Figure 1.

Figure 1. Demographics of study groups.

A full ophthalmic examination and Schirmer's test to collect tear fluid samples were performed in all study patients scheduled for routine cataract surgery, during which 0.1 ml ACF samples of were collected. Analytical sample preparation was carried out by ultrasonic-assisted extraction. Schirmer's test paper strips were placed into the vials containing 1 ml of a mixture of methanol and acetonitrile (50/50) and sonicated for 30 min at 40°C. Extracts were evaporated using nitrogen gas and dry residue dissolved in 100 µl of acetonitrile. Test samples were assayed by LC-MS/MS in positive ionization mode using Acquity UPLC H-Class module and TQD MS detector (Waters, Milford USA). Methanol containing 0.1% of formic acid was used as mobile phase. Empty Schirmer's strips without tear samples were found to have BAK and were used as negative control. A positive result in tear samples was assumed when a higher BAK peak area was detected compared to empty strips. Statistical analysis was performed with SPSS v23.0 program package.

Results: Mean (SD) of glaucoma medication drops/day containing BAK in OAG group was 2.9 (0.7) while the control group did not receive any treatment.

Figure 2. BAK presence in tear fluid samples did not differ significantly between groups (X^2 =3,221, df = 1, p = 0,092). None of the ACF specimens were found to have detectible BAK in either OAG or control groups.

Conclusions: Our data suggests that there is not a significant presence of BAK in tears of OAG patients undergoing long term topical therapy. In addition, no detectible level of BAK was found ACF samples in the for either OAG or control groups.

CONTROL ID: 3706070

SUBMITTER (NAME ONLY): Sze Wan Shan

TITLE: The effect of tissue plasminogen activator on corticosteroid-induced ocular hypertension in guinea pig–a next generation proteomic study

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This project studied the reaction of tissue plasminogen activator (tPA) on corticosteroid-induced ocular hypertension (CIH) and glaucoma using a guinea pig animal model. The molecular mechanism underlying was also explored.

Methods: Ocular hypertension in guinea pigs was induced by sub-conjunctival injection of 5% dexamethasone (DEX) into both eyes. After 6 weeks, tPA was then injected into the treated eyes while PBS was used to inject into contralateral eyes. Trabecular meshwork (TM) tissue in both eyes of the guinea pigs were then collected for proteomic analysis after intraocular pressure (IOP) measurement. Differentially expressed proteins were quantified by liquid chromatography tandem mass spectrometry (LC-MS/MS) using SWATH^{TM} technologies.

Results: The average IOP at baseline was 18.5 ± 2.8 mmHg (mean ± SD) and 18.7 ± 2.8 mmHg (mean ± SD) in both eyes respectively. After 6 weeks of DEX treatment, IOPs increased to 22.9 ± 2.2 mmHg (mean ± SD) and 23.1 ± 2.8 mmHg (mean ± SD) in both eyes respectively. The average inter-ocular difference (IOD, treated minus control IOP) of IOP between 2 eyes was, at day 0 of injection, - 0.2 ± 0.8 mmHg (mean ± SD) while it reached - 6.7 ± 1.6 mmHg (mean ± SD) after 2 days of tPA treatment. IOPs of the tPA-treated eyes were lower than the contralateral eyes. Eight differentially expressed proteins (p-value ≤ 0.05 and fold-change ≥1.3 or ≤ 0.77) were identified by SWATH-MS. Among them, phospholipid scramblase (PLSCR3) was found to be regulated by tPA in CIH TM tissue of guinea pigs. It was found that phospholipid scramblase activity was regulated in a genome-wide association study of glaucoma subjects.

Conclusions: An albino guinea pig CIH model was successfully developed and IOP could be induced after 6 weeks of DEX injection via subconjunctiva. tPA was found to significantly reduce the IOP in CIH guinea pig's eyes. Our results revealed that tPA can also regulate multiple differentially expressed proteins. Furthermore, our result will inform new clinical study to assess the development of a novel therapeutic drug in patients with glaucoma.

CONTROL ID: 3706071

SUBMITTER (NAME ONLY): Yukihiro Miwa

TITLE: Protective effects of a HIF Inhibitor halofuginone on light-induced retinal damage via suppression of HIF/BNIP3 axis

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Miwa, C. Shoda, D. Lee, K. Negishi, T. Kurihara, ophthalmology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|C. Shoda, ophthalmology, Nihon Daigaku, Chiyoda-ku, Tokyo, JAPAN|Y. Miwa, Aichi animal eye clinic, Nagoya, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: Retinal degenerative diseases cause progressive and irreversible visual impairment while effective therapies are still not available. Hypoxia-inducible factors (HIFs) are transcriptional factors that regulate angiogenesis, erythropoiesis, intracellular metabolism, and programmed cell death mainly depending on oxygen availability. In this study, we investigated the therapeutic effects of halofuginone (HF) focussing on HIFs and its target gene BNIP3 in a murine model of light-induced retinopathy (LIR).

Methods: The HIF inhibitory effect of HF on CoCl2-induced HIF activity was confirmed by Luciferase assay and qPCR using a 661W cell line. Eight-week-old male BALB/c mice were exposed to white LED light (3000 Lux) for 1 hour to create an LIR model. Neural retinas were harvested from LIR-treated mice, and qPCR and WB were performed to confirm the expression of HIF-1α and BNIP3. Mice were divided into HF group (0.4 mg/kg/day) and PBS group, and HF or PBS was administered 5 times in total before light exposure. Electroretinography (ERG) and Optical Coherence Tomography (OCT) were performed 7 days after light exposure. TUNEL staining was performed on the retinas of LIR model mice treated with HF or PBS.

Results: Luciferase assay and qPCR using 661W cell line showed that HF significantly suppressed the expression of HIF in a concentration-dependent manner. Light exposure significantly increased the expression of HIF-1α (qPCR: 1.9-fold, $p < 0.001$; WB: 2.9-fold, $p < 0.01$) and BNIP3 (qPCR: 1.3-fold, $p < 0.05$; WB: 1.3-fold, $p < 0.05$) in the retina. OCT results showed a significant inhibitory effect of HF on the retinal damage. TUNEL staining showed an inhibitory effect of HF on apoptosis of photoreceptors.

Conclusions: This study suggests the possibility of therapeutic effects of HF on retinal degeneration via the HIF/BNIP3 axis.

CONTROL ID: 3706073

SUBMITTER (NAME ONLY): Yi Bao

TITLE: Visualization of the inhibition and disruption of immunological synapses by lifitegrast using a live cell imaging assay

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A key factor in the pathophysiology of dry eye disease (DED) is the interaction between intercellular adhesion molecule 1 (ICAM1) on antigen-presenting cells (APCs), such as dendritic cells (DCs), and lymphocyte function-associated antigen 1 (LFA-1) on T cells, resulting in immunological synapse (IS) formation and T cell activation. Previous in vitro studies have shown that lifitegrast may inhibit LFA-1 to ICAM1 interaction, thus preventing IS formation or disrupting established IS's between T cells (CD3+ or CD4+) and human DCs, thereby inhibiting T cell activation. The exact mechanism of action of lifitegrast in DED is unclear. The present analysis aimed to visually demonstrate the kinetics of lifitegrast's effects on APCs to T cell binding using a live cell imaging assay.

Methods: Two cell lines (Raji [as APC] and Jurkat [as T cells]) were used. Raji cells were infected with a lentivirus encoding human ICAM1 fused to enhanced green fluorescent protein, and Jurkat cells were labeled with Hoechst 33258 (blue).To detect prevention of IS formation, live cells were pretreated with either lifitegrast (10μM) or vehicle control followed by staphylococcal enterotoxin B (SEB). Data were captured as time-lapse movies to show kinetic changes and indicate IS formation and the effect of lifitegrast in real-time. Presence of IS's in cells was evaluated using fluorescence microscopy. To detect disruption of established IS, live cells were stimulated with SEB and subsequently treated with lifitegrast and IS was assessed in real-time.

Results: In activated cells, lifitegrast prevented IS formation and disrupted the established IS's (Fig. 1A-C). In control cells, IS formation was evidenced by the green signal unevenly distributed between cells (white arrow; Fig. 1A). Pretreatment with lifitegrast prevented IS formation as shown by the green signal distributed uniformly around cells (Fig. 1B). Post-treatment with lifitegrast disrupted the established IS as evidenced by the green signal (arrow) that became more uniform with the increasing time of lifitegrast action (Fig. 1C).

Conclusions: Our findings show kinetic changes, indicating that lifitegrast can prevent IS formation and disrupt established IS between APCs and T cells. A study with primary cells or LFA-1-labeled T cells is ongoing. These findings may further validate the mechanism of action of lifitegrast in DED.

CONTROL ID: 3706074

SUBMITTER (NAME ONLY): Meng Wang

TITLE: Single cell characterization reveals more frequent IGHV3 and IGHV4 gene usage and the correlation with MYD88 mutation in primary vitreoretinal lymphoma

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Wang, M. Wu, A. Chan, Singapore Eye Research Institute, Singapore, SINGAPORE| M. Wang, Institute of Biomedicine, Turun yliopisto, Turku, Varsinais-Suomi, FINLAND|T. Lim, A. Menarini Biomarkers Singapore Pte Ltd, SINGAPORE|N. Somasundaram, National Cancer Centre Singapore, Singapore, Singapore, SINGAPORE|A. Chan, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To explore whether single cell analysis allows a more detailed characterization of the IGH clonality, gene usage and the correlation with MYD88 mutational status.

Methods: Vitreous fluid or CSF (n = 12) from 9 cases with PVRL and 3 cases with chronic inflammation based on cytological examination and 12 months' follow-up were recruited in accordance with the Singapore Personal Data Protection Act. Single B (CD19/20+, CD3-) cells were isolated using DEPArray™Nxt technology, followed by the single cell IGH sequencing and MYD88 mutation analysis.

Results: Compared with bulk cell sequencing, single cellular characterization displayed more heterogeneous IGH profiles of targeted vitreous/CSF B cells. Higher frequency of the dominant IGH clone in PVRL patients was observed compared with chronic inflammation patients (p=0.0089, Figure 1A). Majority cases (66%) who were diagnosed as PVRL showed the IGHV3 and IGHV4 as dominant clone (Figure 1B). We screened each single B cells (n=61) isolated from PVRL cases for both IGH sequencing and MYD88 mutation. The presence of MYD88 ^{L265P} mutation was more frequently detected in the single B cells with IGHV5 (100%), IGHV4 (71%) and IGHV3-7 (68%) gene sequencing (Figure 1C).

Conclusions: Single cells analysis of vitreous fluid or CSF displayed the complexity of tumor B cell population in PVRL, as well as the bias in the IGH gene sequencing and MYD88 mutational status in cellular level, which adds unique ontogenetic information for disease prognosis and development.

CONTROL ID: 3706095

SUBMITTER (NAME ONLY): Cristina Zappulla

TITLE: Antimicrobial efficacy of netilmicin against Staphylococci administered two or four times a day.

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Zappulla, M. Curatolo, A. Sudano Roccaro, M.G. MAZZONE, C.G. Spoto, Research, Preclinical Development and Patents, SIFI S.p.A., Lavinaio, Aci Sant'Antonio, Catania, ITALY|

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ABSTRACT BODY:

Purpose: Netilmicin is an aminoglycoside antibiotic indicated for the treatment of bacterial ocular infections of the anterior segment of the eye and ocular adnexa. Combined with dexamethasone, it's indicated in inflammatory ocular conditions including post-operative cases. Marketed formulations with netilmicin and dexamethasone have a dosing schedule of 4 administrations per day. To predict clinical efficacy of netilmicin when administered 2 (b.i.d.) or 4 (q.i.d.) times a day, killing kinetic experiments were performed against S. aureus (S.a.) and S. epidermidis (S.e.) using a standard and a pulsed protocol to mimic the posology scheme used in human.

Methods: S.a. 6538 and S.e. 12228 ATCCs grown to reach 10^8 cfu/ml on supplemented Mueller-Hinton (MH) broth were then diluted to 10^6 cfu/ml in the same broth containing 32 µg/ml netilmicin. An antibiotic-free control was similarly inoculated.

Standard protocol: at 0, 1, 2, 6, 12 and 24h, 0.1ml was diluted in phosphate-buffered saline, inoculated onto MH agar plates and incubated at 37°C for 24h, to determine viable cfu/ml.

Pulsed protocol: in the b.i.d. regimen, bacteria were exposed to netilmicin at 0 and 12h while in the q.i.d. regimen, 4 exposures were carried out every 4h along the 12h. In both protocols, contact time of bacteria with netilmicin was 2h. At the end of this period, 0.1ml of each sample were processed as above. Data represent mean±SEM of $\log_{10}$ cfu/ml. Statistical analysis were sought by unpaired t-test.

Results: In the standard protocol, netilmicin showed a bactericidal effect against S.a. at 6h (5 $\log_{10}$ decrease) and this activity is stronger at 12 and 24h (6 $\log_{10}$ decrease). Moreover, netilmicin confirmed bactericidal effect against S.e., and importantly this activity starts 1h after exposure (3 $\log_{10}$ decrease). Data obtained in the pulsed protocol, showed that netilmicin retains its bactericidal effect against S.a. (Fig.1A) and S.e. (Fig.1B) when administered b.i.d. or q.i.d. within 12h (6 $\log_{10}$ decrease) and also at 24h, i.e. after 12h washout.

Conclusions: Interestingly, pulsed protocol demonstrated that bactericidal effect of netilmicin against Staphylococci is maintained unchanged when administered 2 or 4 times a day. Therefore, in order to reduce the antibiotic resistance and improve the patient's compliance, the hypothesis to reduce the posology of marketed products containing netilmicin could be taken into account.

CONTROL ID: 3706102

SUBMITTER (NAME ONLY): Verena Steffen

TITLE: Development and validation of prognostic models to increase power of clinical trials for geographic atrophy (GA)

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Covariate-adjusted clinical trial analysis can improve power and decision making. Here, we report the development, validation, and comparison of different models to predict GA progression and quantify their impact on power.

Methods: This study was performed using data from patients in the lampalizumab program. The outcome was defined as growth rate (mm^2/year) of GA lesion area (measured on fundus autofluorescence [FAF]). The data from the Proxima A (NCT02479386), Chroma (NCT02247479), and Spectri (NCT02247531) trials were split into development (n = 1279) and holdout (n = 443) sets. Three different classes of models were developed: (1) benchmark model: a baseline simple feature-based model using GA area, location, contiguity, and low-luminance deficit; (2) run-in model: uses a 6-month initial lesion growth rate with or without clinical features; and (3) imaging model: a baseline deep learning model using FAF images. These models were validated on 2 additional datasets that were not used for model development: MAHALO (NCT01229215; n = 122) and Proxima B (NCT02479386; n = 175). Performance was evaluated by calculating the squared Pearson correlation coefficient (r^2). Additionally, the effective sample size increase (ESSI) that would result from using the respective model for adjustment in the clinical trial analysis was calculated. ESSI was calculated relative to no adjustment or adjustment with the benchmark model.

Results: The FAF-based imaging model outperformed the feature-based benchmark and run-in models in all datasets, with an r^2 of 0.48 on the holdout set, 0.63 on the MAHALO dataset, and 0.48 on the Proxima B dataset. This translates into ESSIs of 92%, 174%, and 91%, respectively, compared with an unadjusted analysis. Compared with the benchmark model, the imaging model provides an additional effective increase in sample size of 61%, 82%, and 43%, respectively.

Conclusions: These findings suggest that the FAF-based imaging model, using a single image at baseline, is robust and shows a higher prognostic performance than models with simple features derived at baseline and during a run-in phase. These results suggest that the imaging models can significantly improve trial power and decision making.

CONTROL ID: 3706103

SUBMITTER (NAME ONLY): Sandra Gisbert Martinez

TITLE: Effects of the spectral energy distribution of ambient lighting on L-, M- and S-cone abundancies and emmetropization in the chicken

SESSION TITLE: Myopia: Mechanism of Emmetropization and Eye Growth

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Gisbert Martinez, F. Schaeffel, Universitatsklinikum Tubingen Forschungsinstitut fur Augenheilkunde, Tubingen, Baden-Württemberg, GERMANY|S. Wahl, Carl Zeiss Vision GmbH, Aalen, Baden-Württemberg, GERMANY|F. Schaeffel, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: It was previously found that M to L cone ratios were correlated with refraction and ocular length and that chicks develop longer eyes when they have more L-cones. It was also found that less deprivation myopia was induced when chicks were raised in narrow-band blue or UV light, compared to narrow-band red light. Because the spectral composition of ambient lighting can be easily controlled, it may represent a non-invasive and easily applicable intervention of myopia. Therefore, the aim of this study was to find out how light with different spectral compositions interferes with emmetropization and cone ratios.

Methods: Three lighting conditions were used with different energy contributions in the short wavelength range: (1) laboratory light, (2) blue-enriched white light, and (3) white LEDs, all adjusted to approximately 285 (human) lx. Chickens were monocularly treated with diffusers to induce deprivation myopia and exposed to these conditions for a period of one week. Refraction and ocular biometry were determined at the beginning and the end of the experiment and L, M, and S cone photoreceptors were counted in fresh retinal tissue based on the color of their oil droplets.

Results: No differences were found in deprivation myopia among the three lighting conditions. Chickens raised under laboratory light displayed significant correlations of M to L ($p<0.01$) and L to S ($p<0.05$) cone ratios in both eyes. The key finding of this study was that not only M to L but also L to S ($p<0.05$) cone ratios were significantly correlated with refractions in eyes with normal vision. Lower L to S cone ratios were linked to more hyperopic refractions. Unexpectedly, these ratios were inverted when deprivation myopia was induced.

Conclusions: (1) Broadband white light with added energy in the short wavelength range had no effect on deprivation myopia, different from narrow-band short-wavelength light as previously described. (2) Also L to S cone ratios are linked to refractions in eyes with normal vision, in line with the hypothesis that cone photoreceptor densities are linked to refractive development. (3) Inverted correlations of M to L and L to S cone ratios in eyes with deprivation myopia suggest that contrast reduction by the diffusers may affect the mechanism underlying emmetropization. Interesting future questions are why and how.

CONTROL ID: 3706104

SUBMITTER (NAME ONLY): Santa Viola

TITLE: In vitro safety evaluation of two eye drops solutions containing a combination of corticosteroid and antibiotic.

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Viola, G. De Pasquale, M. Curatolo, M.G. MAZZONE, C. Zappulla, Research, Preclinical Development and Patents, SIFI SpA, Lavinaio, Sicilia, ITALY|

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ABSTRACT BODY:

Purpose: The combination of corticosteroid and antibiotic is the most commonly post-operative therapy use to prevent ocular infections. When the epithelial integrity is compromised the composition of the formulation, in terms of active ingredients and excipients, is important for the biocompatibility. The purpose of this study was to evaluate the potential cytotoxic effect of two different marketed preservative-free eye drops solutions containing corticosteroid and antibiotic.

Methods: Human corneal epithelial cells (HCE) were repeatedly exposed (6 times) for 5 min (short time repeated exposure, S.T.R.E.) at 1.5h intervals to Netildex (0.3% netilmicin + 0.1% dexamethasone) or Betabioptal (0.5% chloramphenicol + 0.2% betamethasone) at two different concentrations: undiluted and 1:20 of the marketed concentration. Benzalkonium 0.01% was used as CTRL+. This protocol was designed to simulate the posology and the residence time of eyedrops considering blinking and tearing. Cell viability was assessed in wash and no wash condition by MTT assay. Statistics were by One-way ANOVA.

Results: None of the products tested diluted (1:20) had any significant cytotoxic effect following S.T.R.E. protocol in both wash (Netildex 102.2%±4.3, Betabioptal 103.6%±3.2, respectively, as cell viability) and no wash conditions (Netildex 99.0% ±1.6, Betabioptal 101.2%±4.4, respectively, as cell viability). Interestingly, when tested undiluted, Betabioptal produced significant cytotoxic effects in both wash (24.2%±0.6 of cell viability) and no wash conditions (25.1%±0.3 of cell viability), with respect to Netildex which did not show any cytotoxic effect in both conditions (99.9%±3.5 and 107.8%±2.5, respectively), see figure A-B.

Conclusions: Netildex and Betabioptal, both preservative-free solutions, when used diluted according to Takahashi et. al, 2011, showed no cytotoxic concerns on corneal epithelium. On the contrary, when tested undiluted Betabioptal was found cytotoxic, while Netildex was found to be endowed with an advantageous cytocompatibility profile even at the concentration used in clinical ophthalmological practice.

CONTROL ID: 3706105

SUBMITTER (NAME ONLY): Erin Fahey

TITLE: A novel function for IL-36 cytokines enhancing retinal endothelial cell barrier integrity

SESSION TITLE: Blood flow and ischemia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Fahey, L. Celkova, S.L. Doyle, Trinity College Insititute of Neuroscience, The University of Dublin Trinity College, Dublin, IRELAND|E. Fahey, L. Celkova, P.T. Walsh, S.L. Doyle, School of Medicine, The University of Dublin Trinity College, Dublin, IRELAND|C. Delaney, S.J. Martin, M. Campbell, Smurfit Institute of Genetics Trinity College, Dublin, IRELAND|P.T. Walsh, National Children's Research Centre, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Pathological increases in vascular permeability lead to oedema and swelling, causing a host of retinal and neurological disorders. Few barrier-enhancing factors have been discovered to specifically increase barrier integrity and make vessels resistant to fluid leakage. In this study, we explore the effects of IL-36 on angiogenic processes and vascular permeability in vivo and in vitro.

Methods: The ability of IL-36 cytokines to modulate angiogenic properties in vitro was examined in human retinal microvascular endothelial cells using wound healing, proliferation and tube formation assays. Flux assays were performed to analyse the monolayer integrity of the cells following IL-36 stimulation. RNA sequencing, qPCR and western blot were used to ascertain potential mechanisms underlying these functional readouts. In vivo, laser induced choroidal neovascularisation were performed in C57BL/6J mice injected intravitreally with vehicle or IL-36β. Fluorescein angiography was used to assess the permeability of these CNV and the surrounding retinal microvasculature before tissue was harvested and analysed to ascertain if IL-36 altered the volume of CNV.

Results: IL-36β enhanced endothelial cell barrier function, reducing vascular permeability. IL-36 cytokines also induced primary endothelial cell proliferation, migration, and tube formation in vitro. Importantly, we demonstrate that the IL-36 signalling axis has potential to be useful clinically for reducing microvascular leakage, as the pro-angiogenic features of IL-36 in vitro are uncoupled from the potent ability of IL-36 to enhance vascular integrity in adult mice in vivo in an acute setting. Mechanistically IL-36 regulates endothelial cell tight/adherens junctions, in addition to inducing vessel remodelling and maturation providing a stabilised vascular network. Network analysis of RNA sequencing data support these functional assays.

Conclusions: Our data present IL-36 cytokines as novel promoters of vascular integrity, with barrier enhancing properties that prevent pathological vascular permeability.

CONTROL ID: 3706106

SUBMITTER (NAME ONLY): Simon Salzmann

TITLE: Optical Coherence Tomography Navigated Laser Retinopexy for Retinal Breaks

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Salzmann, C. Burri, C. Meier, HuCE optoLab, Berner Fachhochschule, Biel, SWITZERLAND|C. Burri, Institute of Applied Physics – Biomedical Photonics Group, Universitat Bern, Bern, SWITZERLAND|S. Al-Nawaiseh, Department of Ophthalmology, Universitatsklinikum Munster, Munster, GERMANY|P. Wakili, Eye Clinic Sulzbach, Knappschaftsklinikum Saar GmbH Krankenhaus Sulzbach, Sulzbach, GERMANY|

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ABSTRACT BODY:

Purpose: The prevalent cause of retinal detachment is a full-thickness retinal break, which allows fluid to enter the subretinal space from the vitreous cavity. To prevent progression of the detachment, laser photocoagulation (LPC) lesions are placed around the break in clinical practice to seal the tissue. The treatment is usually performed under indirect ophthalmoscopy. Therefore, the subretinal damage can be difficult to delineate and an experienced operator is required for a successful outcome. In this work, optical coherence tomography (OCT) is used for optimal treatment planning, and LPC is subsequently applied in a navigated and user-friendly procedure.

Methods: The novel method was integrated in a modified OCT diagnostic system (SPECTRALIS OCT, Heidelberg Engineering, Heidelberg, Germany) with integrated treatment laser (Merilas 532 shortpulse, Meridian, Thun, Switzerland). To reliably seal the break, LPC lesions must be applied in regions of still attached retina. Therefore, OCT B-scans were used to manually mark the boundary of the surrounding detachment, which allowed to compute an optimally placed elliptical treatment area. To evaluate the method, artificially provoked retinal breaks were treated accordingly in 10 ex-vivo porcine eyes and the outcome was assessed by fundus photography and OCT imaging.

Results: Ex-vivo experiments showed that OCT-based laser treatment is feasible and the visibility of the subretinal space allows precise treatment planning. A total of 99 to 227 automatically applied lesions per eye at 200 ms and 200 mW were evident as coagulation in color fundus photography. Furthermore, OCT cross-sectional scans showed the required ruptures of the retina at the LPC application sites (Figure 1).

Conclusions: The results indicate the potential of OCT navigated laser retinopexy to achieve high treatment accuracy, efficiency, and safety. Future studies should address treatment of peripheral breaks and the integration of the existing tracking and follow-up functionalities to further enhance and facilitate the treatment.

CONTROL ID: 3706112

SUBMITTER (NAME ONLY): Shuhe Zhang

TITLE: MUTED: Reveal the hidden structures of cataractous retinal images

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zhang, C.A. Webers, T. Berendschot, University Eye Clinic Maastricht, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|A. Mohan, Vasan Eye Care Hospitals Calicut Arayadathupalam, Calicut, Kerala, INDIA|

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ABSTRACT BODY:

Purpose: Diagnosing cataractous retinal images is error-prone due to the severe haze-effect produced by the scattering of cataract layers that decreases the image contrast. To support clinical diagnosing, we propose an image processing algorithm termed multilevel-stimulated denoising (MUTED) that can significantly increase the visual quality and suppresses the haze effect of cataractous retinal images.

Methods: We introduce the double pass fundus reflection model and a multilevel stimulated denoising algorithm. The transmission matrix of the cataract layer is expressed as the superposition of denoised raw images of different levels weighted by stimulated functions. An intensity-based cost function was designed, and the gradient descent with adaptive momentum estimation is used to update the parameters resulting in the final refined transmission matrix of the cataract layer. We tested our methods on a total of 194 images from both public and proprietary databases and compared the performance of our method with other state-of-art enhancement methods. We used fog-ware density estimation (FADE) to evaluate the dehazing quality, and use multiscale contrast to evaluate the contrast of the image. In addition, we collected retinal images before and after cataract surgery to see whether our proposed method leads to unexpected artificial structures and test its reliability.

Results: Figure 1 shows experimental results for visual assessment. MUTED effectively improved the clarity of retinal images as structures like blood vessels that were hidden behind the cataract in the raw image could be observed after enhancement. In addition, by comparing retinal structures presented in pre- and post-cataract surgery images, we found that MUTED did not lead to unexpected artificial structures and maintained the correct information from the images. Table 1, comparing of contrast and FADE scores of the raw and of two methods to enhance images. The MUTED has the highest contrast and the lowest FADE values denoting good dehazing results.

Conclusions: The MUTED is able to reveal the information of cataractous retinal images and significantly increases the visual quality of cataractous retinal images. Both visual and objective assessment using fog-ware density estimation show the superiority of our method.

CONTROL ID: 3706119

SUBMITTER (NAME ONLY): Jeff Henderson

TITLE: Immunohistochemical profiling of the vasculature in visuorecipient brain regions in Rho$^{-/-}$ mice

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Henderson, A. McGlinchey, C. Delaney, N. Hudson, C. Greene, M. Campbell, Smurfit Institute of Genetics Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: While there is evidence that congenital blindness leads to structural and functional brain reorganisation, the impact of blindness on the vasculature in brain regions involved in vision is not well defined. This project aimed to fully characterise the vasculature along the visual pathway in both sighted and genetically blind mice. Immunohistochemistry-based techniques were used to quantify vascular density and integrity; glial and mural cell coverage; and expression of blood-brain barrier (BBB) components across several visuorecipient brain regions in wild-type (WT) mice and the rhodopsin knockout (Rho$^{-/-}$) model of rod photoreceptor degeneration.

Methods: Brain sections were obtained from 12-week old WT and Rho$^{-/-}$ mice, with regions of interest being located by staining with DAPI and comparing anatomical landmarks to the Allen Mouse Brain Reference Atlas. Sections were immunostained for the vascular marker isolectin-IB4; tight junction proteins claudin-5, occludin, and ZO-1; transporter proteins GLUT-1, P-gp, and LRP-1; the pericyte marker PDGFR-ß; the astrocyte marker GFAP; and the microglial marker IBA-1. Vascular density was quantified as the percentage area covered by isolectin-IB4 staining in images of brain regions of interest. Protein expression was quantified by normalising signal intensity for each marker to that of isolectin-IB4. The extravasation of a biotinylated agent (600 Da) and fibrinogen (340 kDa) was quantified as a proxy for BBB integrity.

Results: A distinct profile of BBB protein expression; mural and glial cell coverage; and vascular integrity was observed between WT and Rho$^{-/-}$ mice and between brain regions along the visual pathway in each group. Notably, claudin-5, a key tight junction component, was detected at significantly higher levels in the visual cortex than in thalamic visuorecipient regions, such as the dLGN and the LP in WT mice, with similar trends being observed in Rho$^{-/-}$ group.

Conclusions: Distinct BBB profiles along the visual pathway and between sighted and blind mice highlight the impact that the structural and functional brain reorganisation caused by blindness can have on the neurovascular unit. Given reports that visually impaired individuals are at increased risk of cognitive decline, these results highlight the vasculature as a possible contributing factor to this association, with altered vascular profiles leading to downstream neuronal dysfunction.

CONTROL ID: 3706120
SUBMITTER (NAME ONLY): Giusi Spagnuolo
TITLE: Semi-automatic segmentation for gonioscopic images
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G. Spagnuolo, A. De Giusti, NIDEK Technologies Srl, Albignasego, Padova, ITALY|
Commercial Relationships Disclosure: Giusi Spagnuolo: Commercial Relationship(s);Code E (Employment):NIDEK Technologies Srl | Andrea De Giusti: Commercial Relationship(s);Code E (Employment):NIDEK Technologies Srl
ABSTRACT BODY:
Purpose: NIDEK GS-1 (NIDEK CO., LTD. Japan) collects color images of the Irido-Corneal Angle (ICA) angle split into 16 sectors, each acquired in 17 foci. The manual segmentation of these images could be time consuming and error-prone because the anatomical structures of the ICA have complex boundaries, adjacent tissues are not clearly separated, and some regions may not be in focus. This work proposes a semi-automatic segmentation algorithm based on image processing and prior knowledge of the ICA geometry with the aim of making the user interaction minimal, fast, and effective.
Methods: A boundary is a sequence of curved lines between seed points (i.e., points on the border between two structures) so that the path connecting them has a minimum cost. The cost function is based on 3 components: the gradients of the RGB input image (1280x960) and the optimizer of a geometrical approximation of ICA's anatomical structures. The gradients locate the edges and the geometrical component reinforces the weakest contours. The algorithm's sensitivity to each cost component is automatically evaluated during the segmentation process. A measure of the edges' strength in the neighborhood of the drawn boundary permits to balance the gradient and the geometrical components. The resulting contour is smoothed with a moving average filter.
Results: A qualitative evaluation of the results was assessed on a dataset of 40 GS-1 images. For comparison, images were firstly segmented with a manual tool approximating the regions with polylines based on the user-defined seed points. The same images were then segmented with the proposed algorithm using the same seed points (Fig 1). The outcomes demonstrated that our algorithm permits to trace the tissue boundaries more precisely. Moreover, on average, 19% of seed points, frequently located on strong and complex edges, were redundant (Fig. 2). Finally, the effort for the clinician and both the intra- and inter-user variability were reduced.
Conclusions: The proposed algorithm provides satisfactory segmentations of gonioscopic images and can be also used to collect training data for automatic segmentation and classification algorithms. In fact, it minimizes imperfections due to computer-human interaction, meaning that differences in delineations from multiple experts will only reflect differences in their clinical opinions. Further evaluation should be performed to define a quantitative measure of the algorithm's performance.

CONTROL ID: 3706129

SUBMITTER (NAME ONLY): Kara Boyd

TITLE: Novel bi-cistronic gene therapies for the treatment of dry age-related macular degeneration.

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Boyd, K. Binley, E.F. Warner, A. Osborne, P.S. Widdowson, Ikarovec Limited, Norwich, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: There are no approved treatments for dry age-related macular degeneration (AMD) and advanced geographic atrophy (GA). Experimental anti-complement treatments achieve less than 30% annual reduction in GA progression and some patients develop neovascularisation. We designed a series of novel gene therapy constructs to improve retinal pigment epithelial (RPE) survival via reduced complement activation and prevention of neovascular pathology. Tissue analysis from AMD patients without defined genetic complement factor mutations has revealed early loss of complement regulatory factors and reduced pigment epithelium-derived factor (PEDF). In particular, early loss of complement membrane cofactor CD46, may play a pivotal role in GA progression and PEDF consistently demonstrates anti-neovascular activity in preclinical AMD models. Therefore, enhancing these proteins is an attractive therapeutic approach to treating AMD.

Methods: Bi-cistronic plasmids and rAAV2/2 vectors coding for PEDF and a variety of complement regulatory components were examined in HEK293T and ARPE-19 cells using C3b cleavage assays.

Results: Constructs expressing PEDF in ARPE-19 cells lead to a significant reduction in endogenous VEGF (ng/mL) levels (control = 457 ± 19, IKC030P = 374 ± 12; P=0.01, mean ± SEM n=4, Student's t-test). In a C3b cleavage assay which models the GA retina (e.g., moderate complement factor I (CFI; 11nM) and low cofactors (CFH; 0.5nM), a bi-cistronic plasmid expressing a soluble form of CD46 significantly increased C3b breakdown versus Null control plasmid. In contrast, a plasmid expressing CFI (to further increase CFI concentration) failed to further increase C3b breakdown (% C3b breakdown products/iC3b; Null plasmid = 65 ± 3; sCD46 plasmid = 89 ± 1***; CFI plasmid = 67 ± 1; mean ± SEM, ***P<0.0001 ANOVA/Bonferroni modified t-test). Recombinant C3b degradation by CFI did not occur in the absence of any cofactor.

Conclusions: Lead constructs demonstrate increased endogenous PEDF levels and an ability to reduce VEGF secretion whilst simultaneously attenuating complement activation by enhancing co-factor availability. This multimodal gene therapy approach has the potential to provide greater efficacy against GA progression compared to monotherapies that only target the complement system whilst minimising the risk of developing VEGF-induced neovascular pathology.

CONTROL ID: 3706138

SUBMITTER (NAME ONLY): Heidrun Deissler

TITLE: Disturbances of the retinal endothelial cells' barrier induced by long-term treatment with $VEGFA_{165}$ are independent of the growth factor's action

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.L. Deissler, A. Wolf, Department of Ophthalmology, Universitat Ulm, Ulm, Baden-Württemberg, GERMANY|M. Rehak, Department of Ophthalmology, Justus Liebig Universitat Giessen Fachbereich Medizin, Giessen, Hessen, GERMANY|

Commercial Relationships Disclosure: Heidrun Deissler: Commercial Relationship: Code N (No Commercial Relationship) | Matus Rehak: Commercial Relationship: Code N (No Commercial Relationship) | Armin Wolf: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: $VEGFA_{165}$ induces a persistent dysfunction of the barrier formed by immortalized endothelial cells of the bovine retina (iBREC), completely prevented but only transiently reverted by inhibiting VEGF signaling. Here we investigated how duration of exposure to the growth factor affects the cells' response.

Methods: Confluent iBREC were exposed to 1.2nM $VEGFA_{165}$ for 1 to 9 days. As a measure of barrier function, we continuously determined the cell index (CI) of iBREC cultivated on gold electrodes. Levels of proteins regulating paracellular or transcellular flow, i.e. claudin-1, claudin-5, vascular endothelial cadherin, caveolin-1, plasma lemma vesicle associated protein (PLVAP), of adhesion proteins CD9/TSPAN29, integrins α5 and β1, and of nuclear β-catenin were assessed by Western-blotting; intra- and extracellular VEGFA levels by ELISA.

Results: VEGFA treatment sginificantly reduced CI values still low after 9 days of exposure. Inhibition of VEGFR2 alone or in combination with PDGFRα/β or FGFR1/2/3 by tivozanib or nintedanib led to complete recovery of the low CI values when the inhibitor was added to iBREC pre-treated with VEGFA for 1 day; the effect was stable for 2 days. Reversion of the low CI was not successful when inhibitors were added to cells exposed to the growth factor for more than 3 days. VEGFA concentrations in the cells' supernatant declined from 0.6nM to 0.1nM measured 2 or 9 days after addition, respectively, but its intracellular levels remained stable. Levels of tight junction (TJ)-protein claudin-1 remained low in VEGFA-exposed iBREC from days 1 to 9; those of TJ-protein claudin-5 were elevated, but only on day 6. VEGFA induced expression of PLVAP which was very high on days 2 and 6 after addition, but extremely low on day 9. Levels of integrin α5 - higher on day 2 - declined over time and were lower on day 9 compared to those of control cells; levels of integrin β1 remained slightly elevated at all time points. Only on day 2, VEGFA induced a significant increase of nuclear β-catenin. Levels of the other proteins investigated remained stable.

Conclusions: Only barrier disturbances, i.e.deregulated para- and transcellular flow, observed early during VEGFA exposure depend on the growth factor's action. Changes observed later include impaired TJs and adhesion, and are independent of the presence of the growth factor.

CONTROL ID: 3706139

SUBMITTER (NAME ONLY): Julia Mai

TITLE: GA area measured by SD-OCT shows good correspondence with FAF-based measurements in patients enrolled in the FILLY trial

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mai, D. Lachinov, S. Riedl, G.S. Reiter, W. Vogl, H. Bogunovic, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To compare spectral-domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF) measurements of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) in patients enrolled in the FILLY trial.

Methods: In this post-hoc explorative study, SD-OCT images from the phase 2 FILLY clinical trial were analyzed. The phase 2 FILLY trial was a sham controlled clinical study of intravitreal pegcetacoplan, targeting complement C3, for patients with GA secondary to AMD. A-scan based manual annotation of complete loss of retinal pigment epithelium (RPE) was performed on whole baseline and year one OCT volumes. The RPE-loss measured on OCT was compared to the hypofluorescent GA areas measured on FAF by the centralized reading center of the FILLY trial. The correlation between the GA areas in mm^2 from baseline and year 1 was reported using Pearson's correlation coefficient (r) and coefficient of determination (R^2). In addition the limits of agreement were evaluated with Bland-Altman plots.

Results: 144 OCT volumes of 144 patients at baseline and 111 OCT volumes of 111 patients at year 1 from the FILLY trial were included, resulting in a total of 12 495 manually annotated B-scans. The comparison of GA areas measured on FAF and the RPE-loss measured on OCT revealed a correlation coefficient of r = 0.97 with an R^2 = 0.86 at baseline and r = 0.97 with an R^2 = 0.81 at year 1 (Figure 1). The Bland-Altman plots comparing the GA areas assessed on both imaging modalities show a bias towards higher GA area measurements assessed by FAF as compared to OCT, especially in larger lesions at year 1. Mean difference in measured GA areas between the two imaging modalities was 0.91 ± 0.95 mm^2 at baseline and 1.28 ± 1.23 mm^2 at year 1 (Figure 2).

Conclusions: Our results show a very good correlation of GA measurement between FAF and OCT. Given the fact that OCT has become more established than FAF, this is an essential finding for the design and endpoints in future clinical trials as well as disease monitoring in clinical practice, especially once a treatment will be available.

CONTROL ID: 3706140

SUBMITTER (NAME ONLY): Francesco Impagnatiello

TITLE: NCX 470, a nitric oxide (NO)-donating prostaglandin analog, restores ocular hemodynamic and photoreceptor function after endothelin-1-induced ischemia/reperfusion injury in rabbits

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Impagnatiello, E. Bastia, S. brambilla, C. Galli, Nicox Research Institute, ITALY|S. Sgambellone, L. Lucarini, E. Masini, NEUROFARBA, Section of Pharmacology, University of Florence, ITALY|J.L. Boyer, Nicox Ophthalmic Inc, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: NCX 470 is a nitric oxide (NO)-donating prostaglandin analog in development for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. This work evaluated the ocular hemodynamic effects and neuroprotective activity of NCX 470 in rabbits.

Methods: Endothelin-1 (ET-1)-induced ischemia/reperfusion rabbit model was used. ET-1 was injected next to the optic nerve twice/week for 6 weeks. Animals received NCX 470 (0.1% twice daily, 6 days/week) or vehicle from week 3 until the end of ET-1 treatment. Functional endpoints were IOP, ophthalmic artery resistive index (OA-RI) and photoreceptor function (electroretinogram, ERG). Biochemical endpoints included: oxidative stress markers [manganese superoxide dismutase (MnSOD) and gluthatione GSH)], as well as markers of apoptosis [8-hydroxydeoxyguanosine (8OH-dG)] in retina and iris/ciliary body.

Results: ET-1 increased OA-RI over time [0.30±0.02, 0.39±0.02* and 0.42±0.03* at baseline, week 2 and 6, respectively (*$p<0.05$ vs baseline)]. Treatment with NCX 470 restored baseline OA-RI (0.33±0.02, $p<0.05$ vs vehicle at the same time point) by week 6. Photoreceptor response (dark-adapted 3.0) decreased after treatment with ET-1 (109.8±12.9, 98.6±6.6 and 87.6±10.1μV at baseline, week 2 and 6, respectively) and NCX 470 reversed this effect of ET-1 (122.8±11.4μV, $p<0.05$ vs vehicle). NCX 470 also neutralized ET-1-induced changes in MnSOD ($NAIVE_{MnSOD}$ = 30.1±1.1, VEH_{MnSOD}=18.9±2.3 and NCX 470_{MnSOD}=30.1±3.1mU/mg of protein, $p<0.05$ vs vehicle) and GSH ($NAIVE_{GSH}$= 1301.4±33.6, VEH_{GSH}=371.5±43.7 and NCX 470_{GSH}=1314.6±253.0pmoles/mg protein, $p<0.05$ vs vehicle) in the retina at week 6. Similarly, markers of apoptotic cell death were decreased in the retina from animals receiving NCX 470 compared to vehicle ($NAIVE_{8OHdG}$=18.9±0.7, VEH_{8OHdG}=57.5±6.3 and NCX 470_{8OHdG} =34.1±5.0pg/mg DNA, $p<0.05$ vs vehicle). Similar effects were observed in iris ciliary body.

Conclusions: NCX 470 reduces oxidative stress and apoptosis in the retina after ET-1-induced ischemia/reperfusion and ameliorates ocular perfusion as well as photoreceptor function. Additional studies are needed to establish whether these effects are interdependent.

CONTROL ID: 3706143

SUBMITTER (NAME ONLY): Alessandra Carmichael-Martins

TITLE: Characterization of the human iridocorneal angle in vivo using OCT Gonioscopy

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Carmichael-Martins, B. King, T.J. Gast, B. Walker, S.A. Burns, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the human iridocorneal angle (ICA) in vivo with gonioscopic Optical Coherence Tomography (OCT) imaging using a customized goniolens and a clinically available OCT device (Heidelberg Spectralis). The trabecular meshwork (TM) and Schlemm's canal (SC) located within the ICA are the target for many glaucoma treatments. However, in vivo study of the TM and SC lying at the apex of the ICA is difficult, and most of our knowledge comes from human post-mortem or animal model studies.

Methods: A clinical single-mirrored gonioscopy lens was modified with a 12mm button lens placed on its anterior surface to provide an image plane at the approximate distance of the ICA structures. The subjects' eye was anesthetized with 1 drop of Proparacaine Hydrochloride USP 0.5% . The goniolens was placed on the eye coupled with gonio-gel and aided by a 3D adjustable mount fixed to the head mount of the OCT device to provide additional stability. The waist of the OCT beam was set to fall on the goniolens mirror and steering was available by tilting the OCT device. Radial and tangential dense OCT scans with minimum spacing were performed on 6 young healthy subjects and 1 with pigment dispersion syndrome, focused on the inferior ICA apex.

Results: The TM was seen in all 7 subjects showing more detailed structure of the uveoscleral meshwork, with an average signal penetration depth of 636±116 μm (signal dropped to 2x the noise level). Schlemm's canal was seen in 4 subjects. The penetration depth was 560 μm through the TM and SC for one subject. Schlemm's canal size varied rapidly over space, with the cross-sectional area varying 35% between individual b-scans tangentially and 19% radially.

Conclusions: OCT gonioscopy imaging of the human ICA in vivo has been proved successful, providing both sufficient resolution to depict the structure of the uveoscleral meshwork, and penetration depth past Schlemm's canal.

CONTROL ID: 3706145

SUBMITTER (NAME ONLY): CHIARA RUI

TITLE: Convolutional Neural Network for Glaucoma detection using Compass color fundus images

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare the performance of a Convolutional Neural Network (CNN) model with experienced glaucoma specialists’ grading in detecting glaucomatous optic neuropathy using color images collected with the Compass fundus perimeter (CMP, Centervue, Italy).

Methods: The data used for this project were collected during an international multicentric clinical study. The dataset consisted of 1930 color images of the Optic Nerve Head (ONH, 400x400 pixels) automatically captured by the Compass. Each image was labelled as healthy (NRM) or glaucoma (GLC) based on a glaucoma experts’ evaluation (clinical judgment of the nerve including ophthalmoscopy, fundus image and OCT) performed during the main study, for a total of 1010 NRM and 920 GLC.The original image was resized to 200x200 pixels for the CNN. The CNN model consisted of sequential convolutional and max pooling layers for a total of 1,278,113 trainable parameters. The model was trained using 90% of the dataset (80% train, 10% validation) and tested using the remaining 10% of the data randomly sampled across all study sites. The output of the final sigmoid activation function (AF) was used to build a Receiver Operating Characteristic (ROC) curve. Additionally, two experienced glaucoma specialists (clinician 1 and 2), involved in the main study, were asked to independently grade the test set images with no extra information and no knowledge of group assignment. Their performance was compared to that of the CNN at the same specificity on the ROC curve.

Results: The performance obtained by the CNN, clinician 1 and clinician 2 on the test set (101 NRM, 92 GLC) is shown in Figure 1 and reported in Table 1. The sensitivity of Clinician 2 was just below the 2.5%-Confidence bound of the CNN. The table also reports the performance of the CNN for a threshold of 0.5 on the AF.

Conclusions: The CNN had a performance that ranged from similar to significantly better than the expert graders. The methodology could have applications for automated case finding in glaucoma care.

CONTROL ID: 3706150

SUBMITTER (NAME ONLY): Veeral Sheth

TITLE: Patient Experience with Anti-VEGF Intravitreal Injections in Neovascular Age-related Macular Degeneration and Diabetic Macular Edema: A Multinational Observational Study

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Sheth, University Retina and Macula Associates, Chicago, Illinois, UNITED STATES|T. Peto, Queens University of Belfast, Belfast, UNITED KINGDOM|J. Lambert, V. Barbier, Global Health Economics, Outcomes Research and Epidemiology, ICON plc, Lyon, FRANCE|H. Lewis, Global Health Economics, Outcomes Research and Epidemiology, ICON plc, Reading, UNITED KINGDOM|B. Gentile, G. Chi, Genentech Inc, South San Francisco, California, UNITED STATES|M. Mirt, F. Hoffmann-La Roche, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Anti-vascular endothelial growth factor (anti-VEGF) intravitreal injections are efficacious treatments for neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME), but optimal real-world outcomes require frequent treatment and monitoring that can be burdensome to patients and hinder their ability or willingness to follow their management plan. This study aimed to understand patient treatment experience with anti-VEGF standard of care.

Methods: This observational study employed a cross-sectional quantitative survey comprising de novo questions, patient-reported outcome (PRO) measures and medical chart extraction. Adult patients in the USA, UK and Canada with nAMD or DME, and treated with anti-VEGF injections for ≥12 months, were recruited via 21 (9 USA, 6 UK, 6 Canada) clinical sites.

Results: Between January and August 2021, 148 (67 USA, 33 UK, 48 Canada) DME and 219 (98 USA, 54 UK, 67 Canada) nAMD patients completed their surveys. While 159 (43%) patients had a study eye visual acuity at most recent reading >70 approxETDRS letters, PRO scores indicated that patients across the two conditions had relatively high vision-related functioning (NEI-VFQ-25) and were generally satisfied with their current treatment (MacTSQ and RetTSQ). Eighteen DME patients (12%; 12% in the US, 27% in the UK, 2% in Canadian samples) and 9 nAMD patients (4%; 3% USA, 3% UK, 4% Canada) missed at least 1 injection visit in the past 12 months. Reported barriers were mainly related to treatment, clinic and appointment factors, and the COVID-19 pandemic. Half of the patients reported some level of impairment in their daily activities due to the treatment. Following treatment, the majority recovered within 1 day; however, a sizable portion (24%; 21% USA, 31% UK, 22% Canada) needed >1 day to recover. Among the working patients (N = 55), 34 (62%; 58% USA, 67% UK, 65% Canada) reported some level of productivity impairment in the form of absenteeism.

Conclusions: Despite high adherence and treatment satisfaction levels, patients reported impairment of daily activities, burden, and barriers related to treatment. In general, more DME patients missed at least 1 visit than nAMD patients. More durable treatments with longer intervals could further reduce treatment burden and address the current barriers faced by patients.

CONTROL ID: 3706167

SUBMITTER (NAME ONLY): Ema Ozaki

TITLE: Collagen dynamics in one-stage versus two-stage laser-induced choroidal neovascularization using Collagen-1-YFP reporter mice

SESSION TITLE: Subretinal fibrosis – clinical challenges, mechanism, and diagnostic tools

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Ozaki, S.L. Doyle, Clinical Medicine, The University of Dublin Trinity College, Dublin, IRELAND|E. Ozaki, S.L. Doyle, Trinity College Institute of Neuroscience, The University of Dublin Trinity College, Dublin, IRELAND|P. Westenskow, D. Feenstra, F Hoffmann-La Roche AG Research and Development Division, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Macular fibrosis, observed at the end stage of neovascular AMD, is the leading cause of irreversible blindness in AMD and has been identified as a cause of poor anti-VEGF therapeutic outcomes. Although the pathogenesis of macular fibrosis is still unclear, excessive extracellular matrix deposition by myofibroblasts appears to be a key event. Here, using Collagen-1 (Col1)-YFP reporter mice, we compare the dynamics of collagen production in vivo over time in mice receiving the traditional laser-induced choroidal neovascularization (LiCNV) model to mice receiving the recently described two-stage LiCNV model of subretinal fibrosis, and ex vivo, we examine the CNV tissue for fibrovascular markers in both models.

Methods: LiCNV was carried out using the Micron IV platform (532 nm, 300mW, 100 ms, 50 um spot size, 3 spots per eye) in 8-12 week old Col1-YFP reporter mice. After 7 days, a cohort of the mice received a second laser burn directly over the initial lesion. Mice were fundus imaged every 2-3 days using the YFP filter on the Micron IV to monitor the dynamics of collagen-producing cells infiltrating the CNV lesions. Retinal pigment epithelium flatmounts were harvested 2- and 3-weeks post LiCNV and stained for fibrotic markers, while retinas were harvested for ELISA, RT-PCR and flow cytometry analysis.

Results: Mice that received the two-stage LiCNV showed significantly larger Col1-YFP lesions from 7 days on and YFP was maintained for the 3 weeks post LiCNV induction. In contrast, much smaller Col1-YFP lesions were observed in mice receiving the one-stage LiCNV and YFP was diminished by 3 weeks post induction. Isolectin IB4 staining revealed a more complex networked vasculature in the two-stage lesions, accompanied with enhanced alpha smooth muscle actin and collagen-hybridizing peptide staining, indicative of increased EMT and collagen remodelling, respectively. Interestingly, flow cytometry showed negligible YFP positive cells in the retina in both LiCNV models, indicating that cells involved in collagen production were not in the retina, which was supported by RT-PCR data showing limited changes in EMT and fibrosis markers.

Conclusions: Overall, our in vivo and ex vivo data support the two-stage LiCNV model as a more suitable model for studying subretinal fibrosis over the traditional one-stage LiCNV model, which is better representative of a wound healing model.

CONTROL ID: 3706170
SUBMITTER (NAME ONLY): Luminita Tarita-Nistor
TITLE: Binocularity and PRL location
SESSION TITLE: Mobility, Reading and Driving with Vision Impairment
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Tarita-Nistor, Krembil Research Institute, Toronto, Ontario, CANADA|M.S. Mandelcorn, Ophthalmology, University of Toronto, Toronto, Ontario, CANADA|
Commercial Relationships Disclosure: Luminita Tarita-Nistor: Commercial Relationship: Code N (No Commercial Relationship) | Mark Mandelcorn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is not known what determines the location of the preferred retinal locus (PRL) in patients with macular degeneration. In this study, we tested the hypothesis that binocularity requirements for correspondence play a role in establishing the PRL.

Methods: PRL locations of 101 patients (79±10 years old) with macular degeneration were recorded for both eyes (N=202 eyes) with the MP1 microperimeter, during short fixation tests. The better eye (BE) and the worse eye (WE) were identified from clinical charts. For each eye, the outcome measures were PRL distance from former fovea, polar angle, scotoma size, and fixation stability. Corresponding PRLs were those with the same polar angle and distance from former fovea in the BE and the WE.

Results: Two groups were identified based on the status of the BE: 1) functioning central retina (N=55) and 2) central scotoma (N=46). For group 1, the PRL in the BE was in the foveal proximity (within 1.1±1deg) and that in the WE was: A) on functioning, corresponding location (N=13), B) on functioning, non-corresponding location (N=16), and C) on corresponding, non-functioning location (N=26). No PRL was located further away in eccentricity in the BE to allow for a PRL on functioning and corresponding retinal location in the WE. The BE's outcome measures were equal to those of the WE in subgroup A, different in subgroup B, and different except for polar angle in subgroup C ($p < .05$). For group 2, the PRL in the BE was located eccentrically (6.9±3.4 deg from former fovea) and that in the WE was: A) on functioning, corresponding location in patients with equal scotomas in both eyes (N=15), and B) closer to a location corresponding to the PRL of the BE rather than to the former fovea in patients with unequal scotomas (N=19); C) in those with extensive scotomas in both eyes (size >20deg), the PRLs were generally not in correspondence and at extreme eccentricity suggesting limited functionality (N=12). The BE's outcome measures were equal to those of the WE in subgroup A, different except for polar angle in subgroup B, and different except for the fixation stability in subgroup C ($p < .05$).

Conclusions: In patients with functioning central retina in the BE, the PRL develops in the foveal proximity in this eye and likely drives binocular control. In those with central scotoma in the BE, the PRLs develop to maximize the binocular peripheral inputs from both eyes rather than to be at the closest location from the former fovea.

CONTROL ID: 3706171

SUBMITTER (NAME ONLY): Eli Cehelyk

TITLE: Long-term mortality in patients with neovascular glaucoma following tube-shunt surgery

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the long-term, all-cause mortality rate in patients with neovascular glaucoma (NVG) treated with tube shunt surgery (TS) in a tertiary referral center.

Methods: Retrospective cohort study of 320 eyes of 320 NVG patients who had TS from 1996-2019. Clinical and demographic data were recorded. Death dates were determined using publicly-available Internet data. Kaplan-Meier survival curves were created; subgroups were analyzed with a Bonferroni-corrected $p<.007$ for pre-operative visual acuity (VA), intraocular pressure (IOP), diabetes and complications (i.e. renal, cardiac, stroke, amputation), insulin dependency, and disease control and laterality. Multivariable regression was used to evaluate odds ratios adjusted for these factors.

Results: Median survival after TS was 9.24 years (range 0.00-23.81 years) with 50.7% (151/298 patients) 10-year mortality. Mean±SD patient age at first TS was 59.5±18.5 years; 42% were white, 29% were black. 188 (59%) patients had diabetes. Patients requiring additional ipsilateral treatment had lower mortality (HR=0.45, 95% CI 0.27-0.72; p=.001) and 27.7% (12/45 patients) 10-year mortality. In multivariable analysis, older age (OR= 0.90, 95% CI 0.85-0.94; p<.0001), insulin use (OR=0.25, 95% CI 0.06-0.81; p=.028), and white race (vs. black, OR=0.30, 95% CI 0.10-0.84; p=.028) were associated with increased mortality. Other variables were not associated with mortality in either analysis.

Conclusions: NVG has been suggested to negatively impact mortality. The 10-year, all-cause mortality rate for NVG patients who had TS is greater than 50% with median survival <10 years. This rate is worse than a historical control group of diabetic patients with minimal diabetic retinopathy, better versus ocular ischemic syndrome, and worsens with age and insulin dependency. These results may be useful for pre-operative counseling and decision-making. In conclusion, this retrospective analysis revealed that NVG patients requiring TS have poor long-term survival; older and insulin-dependent individuals exhibit worse mortality rates.

CONTROL ID: 3706173

SUBMITTER (NAME ONLY): Alejandro Navas

TITLE: Accordance between three corneal diagnostic imaging devices in measuring the ocular surface

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Navas, A.L. García-Terraza, D. Jimenez-Collado, F. Sánchez-Sanoja, J.Y. Arteaga-Rivera, N. Morales, S. Pérez-Solórzano, A. Ramírez-Miranda, E.O. Graue-Hernandez, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|D. Jimenez-Collado, Universidad Panamericana, Ciudad de Mexico, Ciudad de México, MEXICO|

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ABSTRACT BODY:

Purpose: To evaluate repeatability, reproducibility, and accordance between NITBUT, tear meniscus and meibography measurements within three different ocular surface imaging devices.

Methods: We performed an observational study on 66 healthy eyes. Tear meniscus, NITBUT (non-invasive tear break-up time) and meibography were measured using 3 types of corneal imaging devices: Keratograph 5M (Oculus, Wetzlar, Germany), Antares (Lumenis, Sidney, Australia) and LacryDiag (Quantel Medical, Cournon d'Auvergne, France). One-way ANOVAs and Welch ANOVAs were used to calculate correlation. Reliability and accordance between the tear meniscus and NITBUT were defined using Tukey Honest Significant Differences, Bonferroni corrections and plotted in Tukey mean difference plots. Accordance from meibography classification was analyzed by calculating Fleiss' Kappa Index and presented visually in Venn diagrams.

Results: We observed discordance between measurements of tear meniscus height between the three devices, $F_{2, 195} = 15.24$, $p<0.01$. Measurements performed with Antares were higher; 0.365±0.0851, than those with both the Keratograph5M and LacryDiag; 0.293±0.0790 and 0.306±0.0731. NITBUT measurements also showed discordance between devices, $F_{2,111} = 13.152$, $p < 0.01$. Measurements performed with LacryDiag were lower (10.4±1.82) compared to those obtained with Keratograph5M (12.6±4.01) and Antares (12.6±4.21). Fleiss' Kappa coefficient showed a value of -0.00487 for the upper lid and 0.128 for the inferior lid Meibography classification, suggesting discrete to poor agreement between measurements.

Conclusions: Depending on the device used and the parameter analyzed, measurements varied between each other, showing difference in image processing.

CONTROL ID: 3706177

SUBMITTER (NAME ONLY): Carmen Canovas

TITLE:

Preclinical evaluation of tolerance to refractive errors with different intraocular lenses

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Canovas, F. Gounou, M.D. Jenkins Sanchez, A. Alarcon, H.A. Weeber, P. Piers, Implant R&D, Johnson and Johnson Surgical Vision, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Literature shows that the tolerance to residual refractive errors (TRE) varies for different intraocular lens (IOL) designs. While patients with multifocal IOLs generally do not tolerate residual astigmatism well, and astigmatism as low as 0.5 D to 0.75 D can affect their visual acuity, extended depth of focus (EDOF) IOLs are less sensitive with an acceptable threshold of residual astigmatism of approximately 1D. The purpose of this study is to preclinically evaluate the TRE of different IOL models.

Methods: Visual performance of an aspheric monofocal (M1), an aspheric monofocal designed to slightly extend depth of focus (M2), a diffractive bifocal (B) (+3.25D add power) and diffractive EDOF IOL designs were evaluated with corrected cylinder and in the presence of up to 1D of residual astigmatism. A set of 46 physiological model eyes that included higher order aberrations were used to predict the clinical defocus curves for the four IOL models. The percentage of eyes with 20/20 or better visual acuity (pVA) in the presence of residual defocus or astigmatism were considered as the metric to evaluate TRE.

Results: When all refractive errors are corrected, the pVA was similar for all lens models. In the presence of 0.5D of residual defocus, both monofocals and the EDOF design showed a greater tolerance, with up to 80%, 100% and 60% of patients having 20/20 VA or better, for M1, M2 and the EDOF IOL, respectively. With the same level of residual defocus, the pVA was reduced to 15% for the multifocal IOL, indicating a lower tolerance to residual defocus. When 0.75D of astigmatism was induced, the pVA was similar (96% for M1, 98% for M2 and 91% for the EDOF), while it was drastically reduced to 35% for the multifocal design, indicating a lower tolerance to astigmatism as well.

Conclusions: This study preclinically assessed the TRE of different IOL models. Computer simulations showed that the monofocal aspheric, the monofocal design to slightly extend depth of focus and diffractive EDOF IOLs preserve high levels of visual acuity in the presence of residual defocus and astigmatism, while multifocal IOLs are more sensitive to them, demonstrating the robustness of the diffractive EDOF IOL and the limited tolerance of multifocal IOLs, as reported in the literature. Therefore, this study validates the use of computer simulations to evaluate the TRE of IOLs.

CONTROL ID: 3706180

SUBMITTER (NAME ONLY): Karina Luiza Dias Teixeira

TITLE: Dissection of the SDC1-GPR87 Coreceptor-Receptor Complex that Captures Tear Lacritin for Promotion and Restoration of Ocular Surface Homeostasis

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Dias Teixeira, G.W. Laurie, Cell Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|M. Adli, Northwestern University, Chicago, Illinois, UNITED STATES|J. Doench, Broad Institute, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Karina Luiza Dias Teixeira: Commercial Relationship: Code N (No Commercial Relationship) | Mazhar Adli: Commercial Relationship: Code N (No Commercial Relationship) | John Doench: Commercial Relationship: Code N (No Commercial Relationship) | Gordon Laurie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Dry Eye Disease affecting 7- 10% of the world’s population is characterized by loss of ocular surface homeostasis yielding chronic inflammation. Lacritin is a prosecretory and regenerative tear (and apparently plasma and CSF) glycoprotein necessary for homeostasis and yet lacking in dry eye. Efficacy was recently validated in a 204-patient phase 2 clinical trial in Primary Sjögren's Syndrome dry eye. We also identified cornea-expressed 'G protein-coupled receptor 87' (GPR87) as the lacritin signaling receptor out of a genome-wide CRISPR/Cas9 death screen using C-terminal lacritin synthetic peptide N-94 as agonist and determined that GPR87 forms an agonist- independent complex with the cell surface heparan sulfate proteoglycan syndecan-1 (SDC1) - an interaction requiring glycosaminoglycan and mutual cytoplasmic domains. Here we further dissect the complex using mutation and peptide inhibition approaches.

Methods: Eleven different synthetic peptides corresponding to or together spanning each of GPR87's extracellular or intracellular strands or loops were introduced as soluble inhibitors at 20, 100 and 400 μM. Binding studies were performed out of GPR87 and SDC1 expressing cells treated with 25-, 50- or 100-mM chlorate to suppress sulfation, or with glycosaminoglycan assembly inhibitor 4-methylumbelliferyl-b-D-xylopyranoside (xyloside) at 0.01, 0.1 or 1 mM. SDC1 lacking 20 ('del 1-21'), 30 ('1-31') or 200 ('del 51-251') N-terminal amino acids was introduced to GPR87.

Results: Outer loop peptides - particularly outer loop 3, but no others, inhibited lacritin-GPR87 targeting. Chlorate and xyloside treatment each inhibited SDC1 - GPR87 coupling, in keeping with lack of binding when heparan sulfate could not be substituted at S15, nor chondroitin sulfate at S184 and S185, and new data pointing to the importance of elements within SDC1 amino acids 1 - 21, 1 - 31 and 51 - 252.

Conclusions: Lacritin targets the outer loop domains of GPR87 (particularly loop 3) as part of a preformed SDC1-GPR87 complex - the latter linked by glycosaminoglycans and by cytoplasmic SDC1 (PDZ binding) and GPR87 ('DRY') domains to regulate ocular surface health.

CONTROL ID: 3706185

SUBMITTER (NAME ONLY): Dawn Meyer

TITLE: Dual Focus Contact Lenses induce Myopic Defocus in Children during Near Viewing

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Meyer, V. Ramasubramanian, M. Jaskulski, M. Rickert, P.S. Kollbaum, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|N.S. Logan, S. Jones, School of Optometry, Aston University, Birmingham, Birmingham, UNITED KINGDOM|A. Bradley, B. Arumugam, P. Chamberlain, Coopervision Inc, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hyperopic defocus can accelerate eye growth in young eyes. Conversely, introduction of myopic defocus can slow eye growth and may counteract the grow signal from simultaneously present hyperopic defocus. Dual focus (DF) lenses for myopia control in children are designed to introduce myopic defocus. This study examined the optical impact of a DF contact lens during near viewing in a sample of children being treated with a DF lens.

Methods: Seventeen myopic children (14 to 18 years, mean ± SD: 16.61 ± 1.63 years) who had completed 3 or 6 years of treatment with a DF lens (MiSight 1 day, CooperVision, Inc., Pleasanton, CA) were fit bilaterally with a DF and a single vision (SV) contact lens (Proclear 1 day, CooperVision, Inc., Pleasanton, CA). Wavefront measurements along the visual axis of the right eye were acquired using a pyramidal aberrometer (Osiris, CSO, Italy) while subjects accommodated binocularly to high contrast letter stimuli (20/40 equivalent) at 6 target vergences (-0.25D, -1D to -5D in 1D steps). Wavefront error data were used to develop pupil maps of refractive error with each lens type.

Results: During near viewing, children fit with SV accommodated to achieve approximate focus in the pupil center but experienced up to 2D of hyperopic defocus in the pupil margins due to increasing levels of negative spherical aberration (C_4^0 changed from -0.27μm at distance to -0.76μm at near) and accommodative lag. With DF, children accommodated similarly achieving approximate focus in the pupil center. The +2D myopic defocus of the DF lens was sufficient to shift the mean defocus in the treatment zone from hyperopia (+0.75D) to myopia (-1.00D) at near (50 cm to 25 cm). The DF lens reduced the % of hyperopic defocus (≥ +0.75D) in the foveal image from 50% to 28% over these target distances leading to an increase in myopic defocus (≤ -0.50D) from 18% to 40%. Lowering the criteria for defocus to > ±0.25D, increased the % of defocused light (65% to 45% for hyperopia and 24% to 47% for myopia), but the shift towards myopic defocus created by the DF lens remained.

Conclusions: The DF contact lens did not alter the accommodative behavior of children. The +2D myopic defocus in the treatment zones successfully removed hyperopic defocus and introduced myopic defocus in the foveal image. These results are consistent with the hypothesis that myopia control with this DF design is achieved by the added myopic defocus.

CONTROL ID: 3706189

SUBMITTER (NAME ONLY): Paul Nderitu

TITLE: Predicting progression to referable diabetic retinopathy from retinal images and screening data using deep learning

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Prior studies report impressive diabetic retinopathy (DR) detection performance using deep learning systems (DLS). However, the utility of DLS for predicting DR and maculopathy progression is unknown. Predicting DR progression could enable individualised, risk-based follow-up or interventions via the early identification of high and low-risk individuals. We aimed to develop multimodal DLS to predict progression to referable DR and maculopathy over 1, 2 and 3 years using curated, two-field retinal images and screening data.

Methods: From 202 928 eyes of 102 446 patients attending the Southeast London Diabetic Eye Screening Programme (Sept 2013 to Dec 2019), 124 418, 89 360 and 71 125 eyes with 1, 2 or 3-year follow-up data were eligible. DLS outcomes were incident (1) referable DR, (2) referable maculopathy or (3) either during follow-up. Detection of any DR at baseline was an auxiliary training task. Inputs were macula/nasal images and screening data (age, gender, ethnicity, diabetes type, diabetes duration, visual acuity and deprivation rank). Data from 68 980 eyes without eligible follow-up were used for DLS pretraining. Image and screening data DLS were developed independently and ensembled for test predictions.

Results: Screening data DLS area-under-the receiver operating characteristic curve (AUROC) for referable DR, maculopathy or either at 2 years were 0.760 (0.684-0.836), 0.733 (0.705-0.761) and 0.733 (0.705-0.760). Image DLS AUROC for referable DR, maculopathy or either at 2 years were 0.898 (0.846-0.951), 0.820 (0.793-0.847) and 0.824 (0.798-0.849). Multimodal DLS AUROC for referable DR, maculopathy or either at 2 years were 0.916 (0.873-0.959), 0.842 (0.819-0.866) and 0.845 (0.823-0.867). Generally, DLS had lower AUROC for all outcomes if initialised without pretraining. Compared to 2-year outcomes, DLS AUROC was higher for 1-year but lower for 3-year intervals.

Conclusions: DLS accurately predicts progression to referable DR and maculopathy using retinal images with modest improvements with additional screening data. Developed DLS for predicting DR or maculopathy progression could enable individualised, risk-based follow-up or interventions with significant time/cost savings for DR screening services/low-risk patients and more timely referrals for high-risk patients.

CONTROL ID: 3706191

SUBMITTER (NAME ONLY): Bailey Hannon

TITLE: The importance of Slc16a8 in light-induced retinal degeneration

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The RPE serves as the blood/retina barrier and facilitates removal of metabolic byproducts from the subretinal space to the choroid. Slc16a8 (Mct3) is an RPE-specific proton coupled monocarboxylate transporter responsible for lactate export identified by human genetic analyses to be associated with age-related macular degeneration (AMD). We investigated the loss of Slc16a8 under constant light exposure (CLE) conditions as a potential stress model, similar to that seen in aging patients, to gain new functional insights into AMD pathobiology.

Methods: Mice with CRISPR mediated deletion of Slc16a8 were used to generate 10-week old $Slc16a8^{-/-}$ (n=6), $Slc16a8^{+/-}$ (n=13), and $Slc16a8^{+/+}$ (n=8) mice. Full-field ERGs (150 $cd*s/m^2$) were measured at baseline and after CLE to determine photoreceptor, bipolar, and RPE cell function using a-, b-, and c-wave amplitudes. OCT was measured at baseline and after CLE to evaluate retinal thickness. Mice were subjected to a CLE of 100k lux for 7 days to induce retinal degeneration.

Results: At baseline (Fig. 1A), eyes from $Slc16a8^{-/-}$ mice had decreased a-, b-, and c-wave amplitudes compared to $Slc16a8^{+/-}$ and $Slc16a8^{+/+}$ eyes (all $p<0.0001$). Eyes from $Slc16a8^{+/-}$ mice had decreased a- ($p=0.0002$) and c-waves ($p=0.01$) compared to $Slc16a8^{+/+}$ eyes. No differences in retinal thickness between genotypes at baseline were found. After CLE, all eyes had decreased a- and b-waves ($p<0.0001$). Retinas from $Slc16a8^{+/-}$ and $Slc16a8^{+/+}$ thinned after CLE ($p<0.0001$), but eyes from $Slc16a8^{-/-}$ slightly thickened ($p=0.011$). Eyes from $Slc16a8^{+/-}$, but not $Slc16a8^{-/-}$, mice showed more loss of a- and c-waves and more retinal thinning compared to eyes from $Slc16a8^{+/+}$ mice (Fig. 1B, $p=0.0002$, 0.002, and <0.0001).

Conclusions: Slc16a8 (Mct3) is necessary for retinal function, but does not affect retinal morphology prior to CLE. After CLE, eyes with complete loss of Slc16a8 do not have increased RPE cell dysfunction, but appear to have retinal edema, perhaps due to proton coupled lactate buildup. Mice with partial loss of Slc16a8 are prone to more photoreceptor and RPE cell dysfunction and more retinal thinning after CLE. These results show that Slc16a8 is key for proper retinal function, both before and after the CLE model of stress-induced retinal degeneration.

CONTROL ID: 3706197

SUBMITTER (NAME ONLY): Madeline D'Aquila

TITLE: Vascular Endothelial Growth Factor-A Signaling Drives Pericyte Coverage in Developing Retinal Blood Vessels

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. D'Aquila, J. Chappell, Virginia Tech Carilion School of Medicine, Roanoke, Virginia, UNITED STATES|M. D'Aquila, J. Chappell, Fralin Biomedical Research Institute at VTC, Roanoke, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor-A (VEGF-A) orchestrates endothelial cell (EC) phenotypic heterogeneity to drive vessel formation; however, we are only beginning to understand how VEGF-A signaling coordinates pericyte (PC) investment. Here, we identify how VEGF-A signaling regulated by VEGF-A decoy receptor Flt-1 (VEGFR-1) affects PC coverage in an in vivo model of angiogenesis, thereby guiding the pursuit of therapeutic targets for sight-threatening diseases. We hypothesize that a VEGF-A signaling gain-of-function, through loss of Flt-1, reduces PC coverage along forming retinal vessels.

Methods: We dissected, stained, imaged, and analyzed postnatal day 7 mouse retinas (N=3) that underwent EC-specific conditional deletion of Flt-1. Presence of a conditional reporter signal, TdTomato, was presumed to correlate with Flt-1 loss. Neural/glial antigen-2 (NG2) antibodies labeled PCs, and platelet-endothelial cell adhesion molecule-1 (PECAM-1) antibodies marked ECs. PC coverage of retinal vessels and TdTomato signals were visualized by confocal. ImageJ facilitated mosaic analysis of (i) TdTomato normalized to PECAM-1 and (ii) NG2 relative to PECAM-1 in regions containing high/low TdTomato. Initial statistical analysis included paired two sample t-tests.

Results: There was a significant difference in the overall TdTomato between areas of high and low TdTomato signal (p-value=0.0025); these differences likely reflect a change in localized Flt-1 deletion within selected regions. PC coverage was significantly higher in regions with high TdTomato and presumed increased Flt-1 deletion compared to areas assumed to lack substantial Flt-1 deletion (i.e., low TdTomato) (p-value=0.035).

Conclusions: In contrast to our initial hypothesis, mosaic analysis of retina areas presumed to contain widespread Flt-1 deletion showed increased PC coverage. VEGF-A signaling, likely elevated by Flt-1 loss, may increase PC investment in remodeling retinal vessels. This observation demonstrates that mis-regulated VEGF-A signaling may aberrantly shift PC coverage, thus, dysregulating vascular growth. Diseases such as diabetic retinopathy are characterized by abnormal VEGF-A signaling and vascular growth, fueling blindness. By investigating context-dependent changes in vascular components, new therapeutic targets may be identified for sight-threatening diseases.

CONTROL ID: 3706200

SUBMITTER (NAME ONLY): Agata Rozanska

TITLE: pRB-depleted pluripotent stem cell retinal organoids mimic retinoblastoma development

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Rozanska, R. Cerna-Chavez, R. Queen, J. Collin, D. Zerti, B. Dorgau, C. Beh, T. Davey, J. Coxhead, R. Hussain, D. Steel, L. Armstrong, M. Lako, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|J. Al-Aama, King Abdulaziz University, SAUDI ARABIA|N. Benvenisty, The Hebrew University of Jerusalem, ISRAEL|M. Parulekar, Birmingham Women's and Children NHS Foundation Trust, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinoblastoma (Rb) is a malignant tumour of developing retina with a typical presentation occurring during the first five years of life. Caused in more than 97% of cases by biallelic inactivation of the RB1 tumour suppressor gene, the frequency of Rb is estimated at about 1 in 15,000 live births. Despite the progress in treatments, and high survival rate in developed countries Rb survivors are left with impaired vision having a negative effect on correct motion processing, depth perception and judging distances. Patients can suffer hearing loss, cataracts, cosmetic deformities as well as a neurocognitive deficit. The urgent need to introduce novel treatments warranted our study to develop and characterise a 3D in vitro model of Rb for drug discovery, repurposing and testing.

Methods: We generated a patient-specific iPSC model (c.2082delC) encompassing the heterozygous ($RB1^{+/-}$), homozygous ($RB1^{-/-}$) and fully corrected isogenic control. We compared the retinal organoids established from the patient-specific iPSC model to those derived from the RB1 knock-out hESC line applying single cell RNA-Seq analysis combined with IHC, TEM, western-blot and colony-forming assay.

Results: Both pRB-depleted models presented significant enrichment in proliferating cone precursors ($RXR\gamma^{+}Ki67^{+}$), defined as Rb clusters by single cell RNA-Seq analysis and displayed tumorigenic features, including mitochondrial cristae aberrations and rosette-like structures. Cells isolated from pRB-deficient organoids were able to undergo growth in an anchorage-independent manner, indicative of cell transformation in vitro. Importantly, the pRB-depleted models, showed an accumulation of retinal progenitor cells at the expense of amacrine, horizontal and retinal ganglion cells, indicating an important role for retinoblastoma protein in the differentiation of these cell lineages. Remarkedly, Rb cells expressed retinal ganglion and horizontal cell markers in addition to cone markers, a novel finding which could help to better characterise these tumours with possible therapeutic implications.

Conclusions: Our data provide robust evidence that pRB-depleted organoids mimic the development and malignant transformation that occurs in vivo, providing a powerful tool for novel drug screening and further retinoblastoma analysis.

CONTROL ID: 3706203

SUBMITTER (NAME ONLY): Stephanie Pietrangelo

TITLE: The impact of a cognitive task and vision impairment on the postural control of older adults

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Older adults, especially those with visual impairments are at risk of falls. Executive functions decline with age and dual-task studies have demonstrated an increase in the postural instability of older adults when performing a cognitive task. However, less is known about the role of cognitive load on the postural stability in visually impaired older adults. The current study examines the separate and combined role of cognitive load and visual impairment on postural stability in older adults.

Methods: A total of 57 normally sighted participants (NSP; M_{age} = 69.7), and 31 visually impaired participants (VIP; M_{age} = 82.5) were included. Measures of postural control (total displacement and mediolateral [ML] movement) were obtained during a static balance task using a Wii Balance Board under normal vision conditions, and by 17 VIP (M_{age} = 80.7), and all 57 NSP while performing a cognitive task (serial-3 subtraction). In addition, the NSP performed all tasks under simulated visual impairment with a visual acuity simulated to either 20/80 (n = 27) or 20/200 (n = 30).

Results: The VIP had greater ML movement compared to NSP under normal vision conditions ($t(39.1) = 3.78$, $p = <.001$, $d = 0.91$) and this difference remained even under simulated impairment conditions (20/80: $p = .001$; 20/200: $p = .002$). With the cognitive task introduced, VIP increased in total displacement ($t(16)$, $p = 0.01$, $d = -0.63$) and NSP increased in both total displacement ($W = 47$, $p = <.001$, $r = -0.94$) and ML movement ($W = 140$, $p = .001$, $r = -0.46$). With the introduction of the cognitive task, the difference in ML movement between VIP and NSP was no longer found regardless of the visual condition NSP were in.

Conclusions: Visually impaired participants had greater ML movement compared to NSP. Movement in the ML direction indicates the use of a hip strategy, which has been associated with increased fall risk. This may point to additional factors contributing to differences in postural control in VIP besides decreased visual function. Given that the NSP experienced a similar increase in ML movement once a cognitive task was introduced, these factors in question may be related to changes in task prioritization and sensory reweighting that the VIP have adopted over time. This can have implications in the type and timing of mobility interventions used for the visually impaired.

CONTROL ID: 3706204

SUBMITTER (NAME ONLY): Vivien Tse

TITLE: Intraocular Pressures Changes at the Central Cornea and Sclera during 5 hours of Scleral Lens Wear

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the impact of scleral lens size and scleral lens wear duration on the intraocular pressure (IOP) of the central cornea and sclera.

Methods: Subjects presenting with no active ocular diseases were recruited for this randomized and crossover study. Each subject wore bilaterally scleral lenses of fluorosilicone acrylate material with two lens diameters (15.6mm and 18.0mm) for 5 hours on two separate days. IOP was measured with the pneumotonometer (Model 30^{TM}, Reichert Technologies, Inc., Buffalo, New York) at the central cornea before and after scleral lens wear, and at the superotemporal sclera 4mm from the limbus before, after, and during 5 hours of scleral lens wear. The primary outcome measure was the change from baseline (i.e., pre-lens insertion) scleral IOP at four predetermined time intervals: 1) immediately after lens insertion, 2) 2.5-hr post-lens insertion, 3) 5-hr post-lens insertion, and 4) immediately after lens removal. Diurnal variations of each subject's corneal and scleral IOP were also determined at a separate day without lens wear.

Results: Seventeen subjects with mean (SD) age of 26.1 (8.5) years completed the study. There was no significant diurnal variability of both IOPs during the 5-hour visit without lens wear ($p>0.05$). The mean [95% CI] changes of corneal IOP after 5 hours of wear for 15.6 mm and 18.0mm lenses were -0.3 [-0.7, 0.1] mmHg and 0.0 [-0.6, 0.6] mmHg, respectively. Both lens diameters did not affect the corneal IOP after 5-hr lens wear ($p>0.05$). The mean [95% CI] changes of scleral IOP were 0.9 [0.2, 1.6] mmHg immediately after lens insertion, 1.6 [0.8, 2.3] mmHg after 2.5-hr lens wear, 1.1 [0.4, 1.9] mmHg after 5-hr lens wear, and 0.2 [-0.4, 0.8] mmHg immediately after lens removal with small-diameter lenses, compared with -0.1 [-1.0, 0.8] mmHg, 1.4 [0.5, 2.3] mmHg, 0.8 [0.0, 1.6] mmHg, and -0.2 [-1.0, 0.6] mmHg with large-diameter lenses. Both lens diameters did not affect the scleral IOP after 5 hours of wear ($p>0.05$). However, 73.5% of the scleral IOP measurements increased at 2.5 hours after lens insertion with 15.6mm lenses ($p=0.021$) and with 18.0mm lenses ($p=0.074$).

Conclusions: The intraocular pressures of healthy eyes restored to the baseline values after 5 hours of scleral lens wear. The smaller scleral lens size induced a statistically but not clinically signficiant increase in scleral IOP at 2.5 hours after lens insertion.

CONTROL ID: 3706211

SUBMITTER (NAME ONLY): Helena Vanluchene

TITLE: Cellulose-based purification enhances the potential of self-amplifying mRNA to induce protein expression in retinal cell types and bovine retinal explants

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal gene therapy using messenger RNA (mRNA) therapeutics is a promising strategy to induce transient (days-months) protein expression in the retina. However, only few mRNA-lipid nanoparticles reach the retina after intravitreal delivery due to the presence of the vitreous and the inner limiting membrane. We explore the use of self-amplifying mRNA (saRNA) that, as a result of its self-replicative nature can be effective at lower doses, making it an interesting candidate to achieve protein expression in difficult to reach tissues, like the retina.

Methods: The ability of mRNA and saRNA to induce protein expression was compared using the carrier MessengerMAX® in a dose titration experiment. Furthermore, two strategies were tested to limit immune activation and enhance protein expression: i) cellulose-based purification to remove double-stranded RNA byproducts, ii) type I IFN decoy receptor B18R. All transfections were performed in ARPE-19 and Müller (MIO-M1) cells (eGFP expression, flow cytometry), and ex vivo on bovine explants (luciferase expression, bioluminescent imaging) (n=3). Immune responses were measured with a LEGENDplex assay.

Results: In the dose titration experiment, we found that a low dose, saRNA outperformed mRNA in terms of eGFP expression, while at a high dose, saRNA seemed to lose its self-replicative advantage as a comparable dose of non-replicative mRNA induced more expression. This was attributed to the immunogenicity of saRNA as a gradual increase in the secretion of innate immune-related cytokines (IL-1β, IL-6, TNF-α, IFN-β, IFN-λ1, IFN-λ2/3) was observed with an increasing dose of saRNA. The immunogenicity of saRNA could be reduced by cellulose purification and addition of B18R. Moreover, cellulose purification of saRNA led to 274x and 66x more eGFP expression in ARPE-19 and MIO-M1 cells respectively, compared to its standardly purified counterpart (silica-membrane columns). B18R increased expression 2.4-times in ARPE-19 cells. Similarly, cellulose purification of saRNA led to a 6-fold increase in retinal luciferase expression in bovine explants.

Conclusions: Overall, saRNA has potential to induce protein expression in the retina provided that measures to temper its innate immune-stimulating activity, like cellulose-based purification and combination with an immune inhibitor (e.g. B18R), are taken into account.

CONTROL ID: 3706216

SUBMITTER (NAME ONLY): Alexandra Sipatchin

TITLE: Assistance for macular degeneration (MD): Different strategies for different augmentations

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sipatchin, M. García García, S. Wahl, Forschungsinstitut fur Augenheilkunde, Universitatsklinikum Tubingen, Tubingen, Baden-Württemberg, GERMANY|S. Wahl, Carl Zeiss Vision GmbH, Aalen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: MD or a simulation of it induces an adaptive eye behaviour to compensate central visual loss: eccentric viewing. Extended reality (XR) tools are currently presented binocularly to assist eccentric viewing. Recent studies showed effective assistance of eccentric viewing behaviour with monocular peripheral assistance. How monocular and binocular peripheral augmentations affect eccentric viewing is unknown.

Methods: Participants played a 2D Pong game in virtual reality (VR) requiring tracking a 3° moving ball. A circular scotoma was gaze-contingently simulated, and it covered 12° of the central visual field. Five different augmentations were concentrically applied at 7.5° away from the simulated scotoma's edges. A 2° broad black ring, an area of 7.5° diameter, either blurred in or out were applied monocularly to the dominant eye. Zoom and fisheye distortions strategies were applied binocularly. Six participants were tested for each augmentation type in three different conditions: control, assisted scotoma, and scotoma simulation. For every condition, the median gaze-target distance was calculated. Kruskal–Wallis and post-hoc Dunn-Šidák tests were used to investigate the effect of condition type over median gaze-target distance. Polar histograms were used to analyse gaze directionality.

Results: All peripheral augmentations tested induced a significant change in gaze-target distance between conditions (ring: χ^2 (2) = 11.47, p = 0.003; blur-out: χ^2 (2) = 8.43, p = 0.01; blur-in: χ^2 (2) = 8.22, p = 0.02; zoom: χ^2 (2) = 11.94, p = 0.003; fisheye: χ^2 (2) = 8.29, p = 0.02). The post-hoc Dunn revealed that the scotoma condition was significantly different from the normal condition when presented after the ring (p=0.006), blur-out (p=0.01), blur-in (0.01), zoom, (p=0.003), and the fisheye (p=0.01) augmentation. Only after the monocular augmentations, the target was always kept visible throughout all blocks during the scotoma condition. Polar histograms indicated an upwards gaze-directionality for the ring and the zoom. Both monocular blurring augmentations had a back-and-forth strategy between the upper left and right hemisphere (Table 1).

Conclusions: Monocular or binocular peripheral assistance differently influenced the eccentric gaze-behaviour of simulated MD participants. Blurring and ring augmentations seem to better improve eccentric viewing over magnification ones, even when applied monocularly.

CONTROL ID: 3706218

SUBMITTER (NAME ONLY): Camille Andre

TITLE: Characterization of the resistome in gram-positive bacteria causing keratitis

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Andre, M. Gilmore, P.J. Bispo, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|M. Gilmore, Harvard Medical School Department of Microbiology and Immunobiology, Boston, Massachusetts, UNITED STATES|C. Andre, P.J. Bispo, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Antimicrobial resistance (AMR) in microbial keratitis is a concerning issue that can result in treatment failure and poor visual outcome. The aim of this study was to characterize phenotypically and genomically the AMR patterns of gram-positive bacteria (GPB) isolated from keratitis at Massachusetts Eye and Ear from 2014 to 2017.

Methods: Whole Genome Sequencing was performed on 161 GPB keratitis isolates using Illumina HiSeq. Molecular typing was performed by MLST. CARD algorithm was used to identify genes and mutations that confer AMR. Minimum inhibitory concentrations were determined by broth microdilution.

Results: Staphylococcus aureus was the most common pathogen (53.4%) and its population structure was dominated by lineages grouped within the clonal complex 5 (32.6%), which includes epidemic MRSA strains commonly associated with multidrug-resistant (MDR) infections. Compared with methicillin-susceptible S. aureus, resistance to other antibiotics was more prevalent among MRSA isolates, with rates of resistance higher than 70% for fluoroquinolones (FQ) and azithromycin. The newest FQ (besifloxacin and moxifloxacin) had lower MIC_{90} overall compared with the earlier ones. More than 30% of coagulase-negative Staphylococcus were resistant to FQ and half of them were resistant to azithromycin (52.9%). We found between 2 and 4 mutations in the quinolone resistance-determining regions (QRDR) of gyrA and parC genes for staphylococci isolates (21.7% of S. epidermidis and 25.0% of S. aureus). 52.1% of S. epidermidis and 22.1% of S. aureus were MDR. CARD analysis revealed that 26.7% of S. aureus co-harbored ant(9)-Ia and ermA genes that confers resistance to aminoglycosides, and to macrolides, lincosamides and streptogramin B, localized in a Tn554 transposon, whereas macrolide resistance in S. epidermidis was frequently associated with mphC/msrA genotype. S. epidermidis were also positive for the dfrC (82.6%) and tetK genes (21.7%) which confers resistance to diaminopyrimidine and tetracycline respectively. Among S. pneumoniae isolates, resistance rates were less than 10% to all antibiotics tested except for ofloxacin (14.4%), azithromycin (30.8%) and penicillin (30.8%).

Conclusions: We provided an overview of current rates of resistance to antibiotics commonly used to treat keratitis caused by GPB and a characterization of the diversity of the associated molecular mechanisms that confer antimicrobial resistance.

CONTROL ID: 3706223

SUBMITTER (NAME ONLY): Catherine Cheng

TITLE: Canonical and non-canonical EphA2 signaling in the lens

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Cheng, School of Optometry and Vision Science Program, Indiana University, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Catherine Cheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Eph-ephrin bidirectional signaling is essential for lens transparency, and mutations in the EphA2 receptor and ligand ephrin-A5 cause a variety of cataracts in humans and mice. Eph receptor canonical signaling is induced by ephrin ligand binding leading to autophosphorylation on tyrosine residues (Y588 on EphA2) and increased kinase activity. EphA2 can also signal in a non-canonical ligand-independent manner that depends on phosphorylation of S897, leading to increased cell invasion and EMT. We determined whether there is canonical and/or non-canonical activation of EphA2 in the lens and whether non-canonical EphA2 signaling is increased in ephrin-A5 knockout (KO) lenses.

Methods: Specific antibodies to detect phosphorylated isoforms of EphA2 were used for capillary electrophoresis Westerns and immunostaining and confocal microscopy to examine control, ephrin-A5 KO and EphA2 KO mouse lenses. Lack of signal in EphA2 KO samples were used to verify antibody specificity.

Results: Capillary electrophoresis Westerns revealed EphA2 is present in the epithelial and cortical fiber lysates from control and ephrin-A5 KO lenses. Canonical ligand-mediated activation of EphA2 due to phosphorylation at Y588 is only detected in the epithelial cell fraction. Surprisingly, non-canonical ligand-independent activation of EphA2 at S897 is detected weakly in the epithelial cell fraction and strongly in the cortical fiber cell fraction. In ephrin-A5 KO samples, we detected increased non-canonical phosphorylation of EphA2 in the epithelial and cortical fiber cell lysates. Using immunofluorescence staining, in control and ephrin-A5 KO lens sections, we found pEphA2-Y558 staining is restricted to epithelial cells while pEphA2-S897 staining is mainly observed in mature lens fibers in the lens cortex.

Conclusions: In summary, both canonical and non-canonical EphA2 signaling are active in the lens. This is the first demonstration of physiological, rather than pathological, non-canonical activation of EphA2 in a normal tissue. Increased non-canonical EphA2 activation due to loss of ephrin-A5 indicates EphA2 and ephrin-A5 may interact in a subpopulation of lens cells, consistent with our recent findings showing EphA2 KO and ephrin-A5 KO lenses have a similar suture patterning defect and lens resilience alteration. Diverse activity EphA2 in different lens cell populations may explain the variability of human lens phenotypes associated with EphA2 mutations.

CONTROL ID: 3706224

SUBMITTER (NAME ONLY): Aixa Alarcon

TITLE: Clinical measurements of peripheral contrast sensitivity in elderly phakic and pseudophakic eyes.

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Alarcon, C. Canovas, M. van der Mooren, P. Janakiraman, R. Rosen, Johnson & Johnson Surgical Vision Inc, Groningen, NETHERLANDS|L. Lundstrom, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN|D.H. Chang, Empire Eye Laser Center, California, UNITED STATES|

Commercial Relationships Disclosure: Aixa Alarcon: Commercial Relationship(s);Code E (Employment):Johnson and Johnson Surgical Vision Inc | Carmen Canovas: Commercial Relationship(s);Code E (Employment):Johnson and Johnson Surgical Vision Inc. | Marrie van der Mooren: Commercial Relationship(s);Code E (Employment):Johnson and Johnson Surgical Vision Inc | Priya Janakiraman: Commercial Relationship(s);Code E (Employment):Johnson and Johnson Surgical Vision Inc | Robert Rosen: Commercial Relationship(s);Code E (Employment):Johnson and Johnson Surgical Vision Inc | Linda Lundstrom: Commercial Relationship(s);Code C (Consultant/Contractor):Johnson and Johnson Surgical Vision Inc | Daniel Chang: Commercial Relationship(s);Code C (Consultant/Contractor):Johnson and Johnson Surgical Vision Inc

ABSTRACT BODY:

Purpose: Previous studies have shown differences in peripheral refractive errors between phakic and pseudophakic eyes and tested the impact on peripheral contrast sensitivity using an adaptive optics (AO) visual simulator. In this study, peripheral contrast sensitivity and peripheral refractive errors were measured in age-matched phakic and pseudophakic human eyes in a clinical setting.

Methods: Peripheral contrast sensitivity at 20 degrees of the nasal field of view was measured monocularly in photopic lighting conditions in two age-matched groups of phakic (29 eyes) and pseudophakic (31 eyes) subjects wearing their best on-axis distance correction. The mean age of the subjects was 64 years (range: 57 to 75 years) and all pseudophakic eyes had the same monofocal IOL model implanted. Central and peripheral refractive errors were measured for the same eyes at 30, 20, 10 and 0 degrees of the nasal and temporal field of view using the Grand Seiko and the Complete Analysis System Aberrometer (COAS).

Results: The difference in peripheral contrast sensitivity between the phakic and the pseudophakic group, 0.21 log units, was statistically significant (p=0.007). The M and J0 values at that eccentricity were -0.5±0.7D and -0.7±0.4D for the phakic group, and -1.1±1.3D and -1.1±0.4D for the pseudophakic group measured with the Grand Seiko. Differences in peripheral aberrations were statistically significant in this study but lower than previously reported in the literature. Peripheral contrast sensitivity was also statistically significantly correlated with the amount of peripheral blur quantified by M+J0 (R2=0.32 and p=0.023). Additionally, good correlation was found between the peripheral refractive errors measured with the Grand-Seiko and the COAS devices (R2 = 0.83 and 0.93 for M and J0 respectively).

Conclusions: This study found a significant correlation between peripheral contrast sensitivity and peripheral refractive errors measured in age-matched phakic and pseudophakic eyes. The results of this study showed a good agreement between the peripheral contrast sensitivity differences measured between phakic and pseudophakic eyes and the value predicted using an AO system to simulate similar optical conditions [Venkataraman et al, BOE 2021].

CONTROL ID: 3706226

SUBMITTER (NAME ONLY): Khaled Elmasry

TITLE: Bone morphogenetic protein 2 contributes to diabetes-induced extracellular matrix deposition and apoptosis in retinal microvasculature

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Elmasry, M. Moustafa, Y. Shin, K. Albishara, M.A. Al-Shabrawey, Eye Research Center, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|K. Elmasry , M. Moustafa, Y. Shin, K. Albishara, M.A. Al-Shabrawey, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|A. S Ibrahim, Department of Ophthalmology and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|A. S Ibrahim, Department of Pharmacology, Wayne State University, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Khaled Elmasry: Commercial Relationship: Code N (No Commercial Relationship) | Ahmed S Ibrahim: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Moustafa: Commercial Relationship: Code N (No Commercial Relationship) | Yunjoo Shin: Commercial Relationship: Code N (No Commercial Relationship) | Kathereen Albishara: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Al-Shabrawey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is the most common cause of blindness in the middle age group. Therapies targeting early stages of DR are urgently needed. One of the earliest changes in DR is endothelial basement membrane thickening, via extracellular matrix (ECM) deposition. The current study tests the hypothesis that bone morphogenetic protein 2 (BMP2) participates in ECM deposition in early DR, representing a possible therapeutic target.

Methods: We evaluated levels of fibronectin in human retinal endothelial cells (HRECs) treated with BMP2 or High glucose (HG) in presence or absence of BMP2 or VEGF inhibitors (LDN1, 100 nM and SU5416, 10μM respectively). We injected wild type mice intravitreally with BMP2 (50ng/ml) or its vehicle (n=4/group). One week later, Western Blot (WB) analysis of retinal fibronectin was performed. Injected mice were also used to prepare flat-mounted retinas co-stained with Isolectin B4 and fibronectin. Conditional endothelial knockout (cKo) mouse model was generated, with deleted BMP receptors (ALK2/3) in endothelial cells. ALK2/3 cKo mice and their littermate controls with/without diabetes of 8 weeks duration (n=3-4 /group) were evaluated with fluorescein angiogram (FA) followed by retinal RT-PCR for inflammatory, apoptotic and fibrotic markers. The results are expressed as means ± SEM. One-way ANOVA or two-tailed t test were used for statistical analysis. Results were considered significant for $p < 0.05$.

Results: BMP2 significantly upregulated fibronectin in HRECs ($p=0.012$). Inhibition of BMP signaling but not VEGF significantly attenuated HG-induced fibronectin production ($p=0.0013$). BMP2 injected mice showed a dense membrane of fibronectin obscuring retinal vessels in flat mounted retinas and also a significant increase of fibronectin levels ($p= 0.0013$) compared to the vehicle injected eyes evaluated by WB. Apoptotic markers; caspase-3 and Fas Ligand mRNA levels were significantly increased with diabetes ($p< 0.05$); however, Fas ligand levels were restored to normal in retinas of diabetic ALK2/3 cKo mice. FA didn't detect any significant vascular changes in diabetic ALK2/3 cKo mice.

Conclusions: BMP2 induces ECM deposition and promote apoptosis which may contribute to microvascular dysfunction and permeability during DR. BMP2 could be a possible therapeutic target for early stage DR.

CONTROL ID: 3706232

SUBMITTER (NAME ONLY): Tae Jun Lee

TITLE: SARM1 Inhibition Protects Photoreceptors from NMNAT1-related Retinal Degeneration and is a Potential Approach to Other Models of Photoreceptor Degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lee, Y. Sasaki, J. Lin, R.S. Apte, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Tae Jun Lee: Commercial Relationship: Code N (No Commercial Relationship) | Yo Sasaki: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Lin: Commercial Relationship: Code N (No Commercial Relationship) | Rajendra Apte: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Leber congenital amaurosis type 9 (LCA9) is a blinding retinal degenerative disease characterized by early childhood onset associated with a mutation in the gene coding for nicotinamide mononucleotide adenylyltransferase 1 (NMNAT1). We demonstrated in mice that a germline NMNAT1 null mutation caused photoreceptor degeneration that was prevented by concurrently knocking out the inducible NAD^+ cleavage enzyme, sterile alpha and TIR motif containing 1 (SARM1). We aim to assess the viability of knocking down SARM1 in other retinal degeneration and NMNAT1 mutation models to explore the relevance of SARM1 as a therapeutic candidate to prevent retinal degeneration.

Methods: SARM1 knockout mice were crossed with NMNAT1 floxed CAG-CreERT2, NMNAT1 E247K, rd10, and RhoP23H mice respectively to create SARM1 double knockout mice with different retinal degeneration models. A SARM1 dominant negative expressing AAV7m8 (SARM1DN) was injected intravitreally as a tractable modality of SARM1 knockdown in the aforementioned models. Mice were characterized for retinal phenotypes using funduscopy/optical coherence tomography (OCT), in vivo electroretinography (ERG), and histology.

Results: ERG (n=7) showed no appreciable scotopic a and b, and photopic b waveforms 33 days post-tamoxifen injection in NMNAT1 KO while NMNAT1/SARM1 KO showed no significant changes compared to wild-types. Hematoxylin and eosin (H&E) staining of retina sections and OCT imaging of NMNAT1 KO mice showed outer nuclear cell loss unseen in imaging of NMNAT1/SARM1 double knockout retinas. NMNAT1 KO mice injected with SARM1DN showed transient preservation of ERG waveforms 1 week after injection that is undetectable 18 days after injection. RhoP23H mice 10 weeks after SARM1DN injection showed no ERG (n=3) significant differences in scotopic waves, but showed significant differences in 15, 20, and 25 dB intensities of photopic measurments by Bonferroni multiple comparisons test. ERG (n=3) of rd10/SARM1 KO showed no appreciable waveforms.

Conclusions: SARM1 inhibition directly plays a role in NMNAT1 null related retinal degeneration. SARM1DN can be a promising tool to test for relevance of SARM1 in models of retinal degeneration. SARM1 may play a role in cone preservation in RhoP23H degeneration. Further investigation is warranted to test the relevance of SARM1 in other models of degeneration.

CONTROL ID: 3706237

SUBMITTER (NAME ONLY): Jamie Choi

TITLE: Social Media Evaluation of Seasonal and Geographic Trends of Corneal Ulcers in the United States

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.H. Choi, E. Ong, W. Munir, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Jamie Choi: Commercial Relationship: Code N (No Commercial Relationship) | Erin Ong: Commercial Relationship: Code N (No Commercial Relationship) | Wuqaas Munir: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Prior studies have examined social media and internet-based search data to study epidemiological factors of infectious eye diseases. None have looked at infectious keratitis. The purpose of this study is to if social media and Google search data could identify seasonal and geographic trends in the incidence of corneal ulcers in the United States.

Methods: This is a case series of all corneal ulcer-related data collected from two major social media websites and Google trends from 2017 to 2021. Instagram and Twitter were searched for posts and hashtags related to “corneal ulcer.” Web and image search volume of “corneal ulcer” were collected from Google trends (https://trends.google.com). Data was compared between seasons, defined by 3-month intervals, and chi-square tests used to determine statistical significance.

Results: 165 individuals (79% female) and 164 individuals (79% female) posted personal new corneal ulcer diagnoses on Twitter and Instagram, respectively. Summer resulted in the highest number of both Twitter (34%, p=0.07) and Instagram (33%, p=0.68) posts. Similarly, summer was the most popular season for Google web and image searches of “corneal ulcer” (search volume average of 58.4 and 41.2, p=0.74 and p=0.01, respectively, with 100 being peak popularity). Of the 66 Twitter posts with available geographic data, 14% comprised New York residents. Of the 71% Instagram posts with available geographic data, 18% were from California residents. Both Google Web and Image searches were evenly distributed between most states, averaging about 2-4%. Across all platforms, the South was the most represented (32% Twitter, 38% Instagram, 32% Google Web, 33% Google Images).

Conclusions: Our results indicate that social media and Google trends may reflect seasonal and geographic patterns of corneal ulcer incidence in the US. However, further study with increased power is needed.

CONTROL ID: 3706240

SUBMITTER (NAME ONLY): RADGONDE AMER

TITLE: Long-term Experience with Anti-Tumor Necrosis Factor- α Therapy in the Treatment of Refractory, Non-infectious Intermediate, Posterior and Panuveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. AMER, B.N. Vofo, J. Corredores, Ophthalmology, Hadassah Medical Center, Jerusalem, ISRAEL|

Commercial Relationships Disclosure: RADGONDE AMER: Commercial Relationship(s);Code R (Recipient):Abbvie | Brice Vofo: Commercial Relationship: Code N (No Commercial Relationship) | Jamel Corredores: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the efficacy and long-term effects of infliximab and adalimumab in patients with active refractory non-infectious intermediate, posterior or panuveitis (NIPPU).

Methods: Retrospective, longitudinal study.

Results: Included were 61 patients (104 eyes) of whom 34 were males (55.74%). Mean age at diagnosis of uveitis was 26.5±16.14 years. All patients had active uveitis at baseline (time of biologic therapy initiatoin). Median interval between start of conventional immunomodulatory therapy (IMT) to introduction of biologic therapy was 13.0 (IQR 26.0) months. Ocular inflammation was effectively controlled in 92 eyes (88.46%).The most commonly used TNF-α inhibitor was adalimumab in 47 patients (77%). In the year preceding the institution of TNF-α inhibitors, average number of flares was 1.5 ±1.1 /year and it decreased to 0.08 ±0.29/year in the first year after baseline ($p<0.0005$). Forty-four eyes (42.30%) experienced flare over the entire period. Mean time to first flare was 14.5±9.26 months. At baseline, mean dose of prednisone was 25.5-±20.8 mg/day. Marked decrease to mean prednisone dose of 7.85±9.7 mg/day was observed at 6 months ($p=0.03$). In patients treated with adalimumab, mean time to prednisone dose of 7.5 mg/day was 4.02±4.89 months compared to 15.64±21.34 months in patients treated with infliximab ($p =0.03$). Eyes treated with adalimumab experienced first flare at a mean time of 14.11±6.29 months whereas eyes treated with infliximab experienced first flare at 18.29±14.24 months after baseline ($p<0.0005$). The risk for moderate and severe visual loss was lower with shorter duration of uveitis before initiating anti-TNF-α treatment (odds ratio, 0.003; 95% CI, 0.000-0.005; $p=0.023$), better presenting logMAR VA (odds ratio, 0.266; 95% CI, 0.172-0.361; $p <0.0005$) and when adalimumab was used (odds ratio, 0.354; 95% CI, 0.190-0.519, $p <0.0005$).

Conclusions: Anti-TNF-α therapy was successful in controlling refractory NIPPU. It significantly reduced flare rate, exerted steroid-sparing effects and preserved visual potential. Both adalimumab and infliximab exhibited similar effectivity in controlling active inflammation and flare-ups with adalimumab exerting faster and bigger steroid-sparing effects. Adalimumab use, better initial visual acuity and earlier introduction of anti-TNF- α therapy were associated with a lower risk of visual loss.

CONTROL ID: 3706246

SUBMITTER (NAME ONLY): Naga pradeep Rayana

TITLE: The role of age and sex in the TGFβ2-induced ocular hypertension mouse model

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Rayana, W. Mao, C.K. Sugali, J. Dai, M. Peng, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Naga pradeep Rayana: Commercial Relationship: Code N (No Commercial Relationship) | Weiming Mao: Commercial Relationship: Code N (No Commercial Relationship) | Chenna Sugali: Commercial Relationship: Code N (No Commercial Relationship) | Jiannong Dai: Commercial Relationship: Code N (No Commercial Relationship) | Michael Peng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is one of the leading causes of blindness. Elevated intraocular pressure (IOP) is the major risk factor of glaucoma. The TGFβ2-induced ocular hypertension mouse model has been widely used to study the pathological changes in the glaucomatous trabecular meshwork (TM). Since most of the published studied used old and female mice with $2.5X10^7$ PFU Ad5-CMV-TGFβ2 virus, in this study, we determined if age and sex affect IOP in this well-established ocular hypertensive mouse model.

Methods: We used young (3 month, n=14) and old (5 month, n=10) male C57BL/6J mice. One eye was injected intravitreally with Adenovirus expressing human TGFβ2 (Ad5-CMV-TGFβ2) at $2.5X10^7$ PFU or $5.0X10^7$ PFU and the fellow eye with the same amount of Ad5-CMV-GFP adenovirus as a control. IOP was measured up to 11 weeks. At the end of the study, the mice were euthanized and the eyes were used for ELISA, qPCR and immunofluorescent staining.

Results: We observed a significant IOP elevation in both 3 and 5 month old male mouse eyes injected with $5.0X10^7$ PFU Ad5-CMV-TGFβ2. However, 5 month old male mice respond early with higher IOP compared to 3 month old male mice. In contrast, no IOP elevation was observed in either groups of mouse eyes treated with $2.5X10^7$ PFU Ad5-CMV-TGFβ2. ELISA and qPCR showed a robust expression of human TGFβ2 expression in the aqueous humor in Ad5-CMV-TGFβ2 injected eyes. Similarly, immunofluorescent staining showed elevated levels of human TGFβ2 and fibronectin in the TM region in Ad5-CMV-TGFβ2 injected eyes.

Conclusions: Male C57BL/6J mice requires high dose of adenoviruses to develop IOP elevation compared to female mice. Also, older male mice are more sensitive to the Ad5-CMV-TGFβ2 virus.

CONTROL ID: 3706249

SUBMITTER (NAME ONLY): Xiaoxin Chen

TITLE: tRNS and exercise do not modulate ocular dominance plasticity

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Chen, B. Thompson, A. Chakraborty, Human Visual Neuroscience Laboratory, School of Optometry & Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|K. Hall, A. Nguyen, G. Sealock, T. Tran, N. Vo, A. Chakraborty, Translational Vision Science Lab, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|B. Thompson, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Xiaoxin Chen: Commercial Relationship: Code N (No Commercial Relationship) | Kennedy Hall: Commercial Relationship: Code N (No Commercial Relationship) | Amy Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Grant Sealock: Commercial Relationship: Code N (No Commercial Relationship) | Tiffany Tran: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Vo: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Arijit Chakraborty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A period of monocular patching (MD) briefly increases the contribution of the previously patched eye to binocular vision. The magnitude of this effect, known as ocular dominance plasticity, provides an index of short-term visual cortex neuroplasticity.

We used ocular dominance plasticity to assess whether physical exercise and/or visual cortex transcranial random noise stimulation (tRNS), a form of non-invasive brain stimulation, enhance short-term visual cortex neuroplasticity in adults with normal vision.

Methods: Participants (n = 10, mean age = 25 ± 2) completed four daily sessions involving two hours of dominant eye patching while watching a movie. Exercise (cycling) and visual cortex tRNS were applied during patching according to the following conditions: 1) cycling and tRNS, 2) cycling and sham (placebo) tRNS, 3) tRNS sitting still, 4) sham tRNS sitting still. Cycling was completed in six 10-minute blocks interleaved with 10-minute rest periods. High-frequency tRNS (100-640 Hz, 1mA) was delivered during the final 20 minutes of patching. Eye dominance was measured using a computerized dichoptic letter luminance judgement test (Bossi et al., 2018) before and after patching.

Results: As expected, MD increased patched eye dominance in most participants. Two-way repeated measures ANOVA revealed that the magnitude of ocular dominance plasticity was not affected by exercise, visual cortex tRNS or their combination.

Conclusions: Physical exercise and tRNS, individually or in combination, do not enhance short-term ocular dominance plasticity in adults with normal vision.

CONTROL ID: 3706259

SUBMITTER (NAME ONLY): Thi Ha Chau Tran

TITLE: Two-year outcome of intravitreal aflibercept injection in vitrectomized eyes with diabetic macular edema.

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Tran, Ophthalmology, Universite Catholique de Lille, Lille, Nord-Pas-de-Calais, FRANCE|S. Verdun, Biostatistics Department-Delegations for Clinical Research and Innovation, Universite Catholique de Lille, Lille, Nord-Pas-de-Calais, FRANCE|J. LE ROUIC, Institut d'Ophtalmologie de l'Ouest, Nantes, FRANCE|J. Uzzan, Clinique Mathilde, Rouen, FRANCE|S. Milazzo, Universite de Picardie Jules Verne, Amiens, Hauts-de-France, FRANCE|L. Kodjikian, Hospices Civils de Lyon, Lyon, Auvergne-Rhône-Alpes , FRANCE|A. Erginay, Ophthalmology, Lariboisiere Hospital, FRANCE|T. Tran, Inserm U1172, Lille, FRANCE|

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ABSTRACT BODY:

Purpose: There is little information with inconsistent results in vitrectomized eyes with DME treated with anti-VEGF. The aim of the study is to evaluate the efficacy of intravitreal aflibercept injection (IAI) for vitrectomized eyes with diabetic macular edema (DME) at two years.

Methods: This is a prospective, non-comparative, multicenter observational study including patients with diabetic macular edema, who have undergone vitrectomy since at least 3 months before the first aflibercept injection. All patients received 5 monthly aflibercept injections during the loading phase followed by a ProReNata until month 12. Participants were then managed at clinician discretion using Treat and Extend or Observe and plan regimen during the second year. Visual acuity, OCT findings and number of IAI were assessed at month 6, one year and two years. Change in visual acuity and central retinal thickness was assessed using Student paired t-test. Chi-squared test was used to compare the frequency of qualitative OCT parameters among eyes between baseline and at 2 years.

Results: 46 previously vitrectomized eyes were enrolled in this study. Median duration of macular edema was 3 years. Median interval between vitrectomy and first visit was 9 months. Data was available for 36 eyes at 6 months, for 34 eyes at 1 year and for 28 eyes at 2 years. Visual gain was significant: +4.6 letters at 6 months, +6 letters at 1 year and +5.4 letters at 2 years. Central macular thickness decreased significantly by 15% (- 65µm) at month 6, by 25% (-108µm) at 1 year, and by 14% (-62µm) at 2 years. Resolution of macular edema allowing discontinuation of aflibercept was observed in 7 eyes (15%). The frequency of eyes with intraretinal cyst decreased significantly from baseline to 2 years (from 89% to 64%, p = 0.046). Proportions of eyes with ellipsoid zone disruption, external limiting membrane disruption did not change significantly thorough the study. Mean number of injections was 9.3 ± 1.8 for the first year and 5.2 ± 3.1 for the second year. Mean interval injections was 1.6 ± 0.3 month for overall 2-year period.

Conclusions: These results suggest that intravitreal Aflibercept Injection is beneficial in vitrectomized eyes leading to improvement of visual and anatomical outcome from baseline to 2 years.

CONTROL ID: 3706260

SUBMITTER (NAME ONLY): Andrew Boal

TITLE: Action potential dynamics underlying depolarization block in retinal ganglion cells are cell type-agnostic

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Boal, Medical Scientist Training Program, Vanderbilt University, Nashville, Tennessee, UNITED STATES|A. Boal, Neuroscience Graduate Program, Vanderbilt University, Nashville, Tennessee, UNITED STATES|N. McGrady, M. Risner, D.J. Calkins, Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Andrew Boal: Commercial Relationship: Code N (No Commercial Relationship) | Nolan McGrady: Commercial Relationship: Code N (No Commercial Relationship) | Michael Risner: Commercial Relationship: Code N (No Commercial Relationship) | David Calkins: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic neuropathies are the leading cause of irreversible blindness, characterized by degeneration of retinal ganglion cells (RGCs) and their axons comprising the optic projection. Not all RGC types appear equally susceptible to disease or injury. Cells with sustained firing to light decrement (OFF-S) appear to be more susceptible than those firing to light increment (ON-S), which may be due to intrinsic physiologic properties. Here, we evaluate if action potential (AP) shape reflects differences in firing dynamics and susceptibility to stress.

Methods: C57Bl6/J mice were sacrificed, and retinas dissected in the dark. Retinas were perfused with glucose-supplemented Ames' medium. Recording pipettes were filled with K-gluconate based solution and Alexa-fluor dye. Whole-cell current clamp signals were amplified and digitized. RGCs were classified by light response and dendritic stratification. 41 ON-S and 34 OFF-S RGCs were recorded during stepwise depolarizing current injections from 0-300pA. An additional 7 ON-S and 6 OFF-S were recorded before and after adding 5mM KCl to the extracellular medium.

Results: OFF-S RGCs had more depolarized resting potentials ($p < 0.001$), higher spontaneous spike rates ($p < 0.001$), and faster spiking to current injections ($p < 0.001$). A plateau of the current-spike rate relationship for OFF-S began at 200pA of current injection, indicating depolarization block, but did not occur at baseline for ON-S. APs widened with increased depolarization for both cells, but more appreciably in OFF-S. However, plots of spike rate vs. measures of AP shape (area, depolarization and repolarization rates) had similar slopes for both RGC types (p range 0.17-0.38). Adding 5mM KCl to the extracellular medium induced depolarization block in ON-S RGCs at 200pA. AP shape analysis showed that K+ significantly altered the repolarization rate of ON-S ($p < 0.001$), and that depolarization block in ON-S + K occurred at similar repolarization rate values as baseline OFF-S RGCs.

Conclusions: Increasing firing rate causes a widening of RGC APs. OFF-S RGCs undergo depolarization block at lower current injections at baseline, but it can be experimentally induced in ON-S. Analyses of AP shape vs. spike rate demonstrate that differences correlate with rate and occur at similar thresholds for both cell types, suggesting that mechanisms underlying depolarization block are cell type-agnostic.

CONTROL ID: 3706262

SUBMITTER (NAME ONLY): Yong Li

TITLE: Discovery and preclinical development of VVN539，a novel ROCK and NO dual MOA agent for the treatment of glaucoma in normotensive rabbits model with minimal hyperemia.

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, L. Yao, K. Dang, Q. Han, C. Lu, E. Xia, W. Shen, VivaVision Biotech, Inc., CHINA|

Commercial Relationships Disclosure: Yong Li: Commercial Relationship: Code N (No Commercial Relationship) | Lili Yao: Commercial Relationship: Code N (No Commercial Relationship) | Kuifeng Dang: Commercial Relationship: Code N (No Commercial Relationship) | Qiao Han: Commercial Relationship: Code N (No Commercial Relationship) | Caroline Lu: Commercial Relationship: Code N (No Commercial Relationship) | Erning Xia: Commercial Relationship: Code N (No Commercial Relationship) | Wang Shen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The inhibitory activities of VVN539 on ROCK were assessed in multiple in vitro studies, demonstrating that both molecules inhibit both ROCK 1 and ROCK2. Additionally, the potency of VVN539 as a NO donator were verified in vitro studies. The objectives of this study were to evaluate the ocular hypotensive activity and tolerability of 0.02% VVN539 ophthalmic solution compared to Netarsudil (coded as VIP-5001) in the same vehicle in normotensive Dutch Belted (DB) rabbits.

Methods: VVN539 was tested in vivo and vitro for its ability to release functionally active NO through analyzing the levels of intracellular cGMP by which many biological actions of NO are mediated. 0.02% VVN539 and 0.02% VIP-5001 formulations were administered topically to one eye of each animal once daily (AM) for 10 consecutive days and the other eye was untreated as control. Intraocular pressure (IOP) was measured daily for both eyes in the conscious animals at pre-dose, 4, 8, 12 and 24 hours after dosing from Day 1 to Day 10. Hyperemia was scored on a scale of 0 to 3 (none to severe) with 0.5 increment by a masked ophthalmologist under slit lamp at 2 hours post dosing on Day 1 to Day 3 and on Day 10.

Results: VVN539 increased intracellular cGMP formation. Peak IOP-lowering effect of 0.02% VVN539 and VIP-5001 formulations in the normotensive rabbits was -5.28±0.40 mmHg and -3.36±0.42 mmHg, respectively. VVN539 produced a about 50% greater peak IOP lowering activity than VIP-5001 at the same concentration on the last dosing day (Day 10). The maximum reduction in IOP was achieved at 4 hours after each dose once per day. The ROCK kinase inhibition combined with another validated IOP lowering mechanism of NO releasing resulted better efficacy vs. the Rho kinase inhibitor, VIP-5001 in ocular normotensive Dutch Belted rabbits.

Conclusions: Topical ocular VVN539 was well tolerated and lowered IOP in normotensive rabbits, demonstrating increased efficacy with only minimal conjunctival hyperemia when compared with topical ocular VIP-5001. Our study indicates that the VVN539, a highly selective Rho-Kinase Inhibitor with dual MOA are superior to VIP-5001 (Netarsudil) in lowering IOP in normotensive rabbit model.

CONTROL ID: 3706264

SUBMITTER (NAME ONLY): Michael De Ieso

TITLE: The role of protein kinase C in the regulation of trabecular meshwork contractile tone via caveolin-1 scaffolding domain.

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. De Ieso, M. Kuhn, D.W. Stamer, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|M.H. Elliott, Department of Ophthalmology and Dean A. McGee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Michael De Ieso: Commercial Relationship: Code N (No Commercial Relationship) | Megan Kuhn: Commercial Relationship: Code N (No Commercial Relationship) | Michael Elliott: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Stamer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Caveolae are specialized invaginations of the plasma membrane. Caveolin-1 (Cav1) is required for caveolae biosynthesis. Polymorphisms at the Cav1/2 gene loci impart increased risk for primary open angle glaucoma. Caveolae are abundant in the trabecular meshwork (TM), serving as mechanosensors that detect and respond to changes in intraocular pressure (IOP). The mechanism by which Cav1 contributes to IOP homeostasis is unknown. Protein kinase C (PKC) interacts with the Cav1 scaffolding domain (CSD), and plays a key role in TM contractility; an important mediator of conventional outflow resistance, and subsequently IOP. Thus, we used the CSD peptide, cavtratin, to test the hypothesis that the CSD regulates TM contractile tone via sequestration and inhibition of PKC.

Methods: Experiments were conducted using 8 different human TM cell strains. Adenoviruses encoding shRNA targeted to Cav1 were used to silence Cav1 expression in TM cells. Western blotting was used to determine relative protein levels, phosphorylation status, and PKC activity. Cells were treated with the CSD mimetic, cavtratin (1μM), a CSD peptide fused to the cell-permeable Antennapedia internalization sequence (AP), and compared to those treated with AP (1μM) alone as a vehicle control. Data are expressed as mean ± SEM.

Results: We used subcellular fractionation to separate the cytosol and membrane portions of lysates from Cav1-competent and Cav1-deficient TM cells. We found a 42% reduction of PKC expression in Cav1-deficient membrane fractions (0.58±0.08, n=4, p=0.013). Additionally, immunohistochemical analysis showed that PKC and Cav1 co-localized at the plasma membrane (3 different TM cell strains). Using phosphorylated myosin light chain (pMLC) as a surrogate indicator for contractile tone, we found that 24 h treatment with PKC inhibitor, Gö6983, reduced pMLC levels in TM cells compared to control (0.74±0.06, n=7, p<0.004). TM cells treated with cavtratin exhibited a 30% reduction in pMLC compared to control (0.7±0.05, n=7, p=0.001). Treatment with cavtratin also resulted in a 9% reduction of PKC activity as compared to control (0.91±0.02, n=7, p=0.008).

Conclusions: Taken together, these data suggest that caveolae act as scaffolds that sequester PKC at the TM cell membrane, inhibiting signal transduction to downstream effectors controlling contractile tone.

CONTROL ID: 3706267

SUBMITTER (NAME ONLY): Ying Zhu

TITLE: Nuclear localized HDAC4 increases retinal ganglion cell survival after optic nerve crush injury

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Zhu, J. Li, M. Bian, X. Xia, M. Nahmou, C. Sun, J.L. Goldberg, M. Kapiloff, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The regulation of retinal ganglion cell (RGC) death and survival in disease is a complex process controlled in part by changes in gene expression, including that regulated by histone deacetylases (HDACs). However, roles of individual HDACs in RGCs remain poorly understood. In this study, we first screened the potential relevance of individual HDACs to RGC death and survival after optic nerve crush injury. Next, we explored the role of class IIa HDAC4 in injured RGCs and further defined underlying molecular mechanisms.

Methods: To study the effect of individual HDACs in RGC after injury, small hairpin RNAs for individual HDAC isoenzymes were expressed using adeno-associated virus (AAV). Optic nerve crush (ONC) injury was used to induce severe axon damage and RGC loss 2 weeks after AAV intravitreal injection in mice. Two weeks after ONC, retina flat mounts were stained with the RGC marker RBPMS to quantify RGC survival. A nuclear localized phosphoablative HDAC4 mutant (3SA) and a truncated HDAC4 mutant (NT) containing only the N-terminal fragment of HDAC4 were also studied. Flag-tagged wildtype and mutant HDAC4 expressed using AAV2 were detected in retina by immunohistochemistry (IHC). Signal intensity in nuclear and cytosol were measured using ImageJ to determine HDAC4 intracellular localization. To test whether nuclear HDAC4 preferentially enhances RGC survival, RGC loss was assessed 2 weeks post ONC by flat mount IHC. Cholera toxin b was intravitreally injected 2 days before endpoint to label regenerated axons.

Results: Inhibited expression of no individual HDAC significantly improved RGC survival after crush injury. Instead, the inhibited expression of only HDAC4 significantly decreased RGC survival. Flag-HDAC4 3SA was localized preferentially to the nucleus, whereas wildtype Flag-HDAC4 was mainly cytosolic. Notably, HDAC4 3SA significantly increased RGC survival and promoted axon regeneration 2 weeks after ONC when compared to GFP control. Overexpression of wild type HDAC4 also tended to increase RGC survival after injury, although not reaching statistical difference. In addition, there was greater RGC survival and axon regeneration following HDAC4 NT expression.

Conclusions: Nuclear localized HDAC4 promotes RGC survival after injury. Enhanced HDAC4 nuclear activity might comprise a new therapy for the prevention of vision loss in diseases like optic nerve injury and glaucoma.

CONTROL ID: 3706271

SUBMITTER (NAME ONLY): Andrew Pucker

TITLE: Treating Symptomatic Heavy Digital Device Users with Systane Hydration PF

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Pucker, Q.X. Franklin, A. Logan, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|C. Lievens, G. Wolfe, Southern College of Optometry, Memphis, Tennessee, UNITED STATES|G. McGwin, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Digital devices are used in nearly every aspect of modern life. While digital devices have improved our lives, some consumers develop bothersome ocular symptoms. The purpose of this investigation was to determine if topical ocular application of a hyaluronic acid- and hydroxypropyl guar-containing artificial tear (Systane Hydration PF) was able to alleviate dryness symptoms and improve the quality of life of patients who have ocular symptoms associated with digital device use.

Methods: This was a 2 week, 3 visit study that recruited participants who used digital devices ≥8 hours per day. Each participant was required to have symptomatic Impact of Dry Eye on Everyday Life (IDEEL) Quality of Life (QoL) Work domain scores (≤80) and Ocular Surface Disease Index (OSDI) scores (13 and 32). All participants were treated with Systane Hydration PF ≥4 times per day. Everyone was randomized to Systane Hydration PF unit-dose or multi-dose system for 1 week. Participants switched to the alterative dosing system at 1 week. The full IDEEL-QoL module and OSDI questionnaire were completed at each visit. A visual analog scale (VAS) home diary was completed to probe ocular comfort. A Likert questionnaire that evaluated dispensing system preferences was completed at the 1- and 2-week visits.

Results: The mean ± SD age of the participants was 28.6 ± 12.0 years (n = 30; 70% female). The mean digital device use at 1 day, 1 week, and 2 weeks was 12.4 ± 3.9, 12.9 ± 5.0, and 10.7 ± 4.2 hours per day, respectively. IDEEL-QoL Daily Activities (83.8 ± 5.4, 88.8 ± 6.1, 91.7 ± 5.6), Feelings (82.9 ± 11.1, 88.1 ± 11.5, 90.0 ± 11.9), and Work (59.0 ± 12.8, 74.0 ± 15.0, 81.4 ± 12.7) scores and OSDI (24.8 ± 6.0, 16.3 ± 7.4, 14.3 ± 8.6) scores all significantly improved across the 3 visits (all $p < 0.0001$). VAS end of day eye comfort significantly improved at 2 weeks compared to 1-day (56.9 ± 21.5 vs. 74.9 ± 19.3; $p < 0.0001$). Participants had a similar preference for the two dosing systems in most respects, though more participants indicated that the multi-dose system was more environmentally friendly than the unit-dose system.

Conclusions: Consistently treating symptomatic heavy digital devices users with Systane Hydration PF for 2 weeks significantly improved dryness symptoms and patient quality of life. Participants were overall equivocal with regards to drop dosing systems suggesting that practitioners should discuss both options with patients.

CONTROL ID: 3706280

SUBMITTER (NAME ONLY): Kazutaka Hirabayashi

TITLE: Optical coherence tomography risk factors for 3-year development of atrophy in eyes with age-related macular degeneration

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hirabayashi, S.R. Sadda, K. Marion, Doheny Eye Institute, Los Angeles, California, UNITED STATES|H. Yu, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|K. Hirabayashi, Hirabayashi Eye Clinic, Matsumoto, Nagano, JAPAN|

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ABSTRACT BODY:

Purpose: To determine the frequency of various optical coherence tomography (OCT) biomarkers of intermediate age-related macular degeneration (int-AMD) and their relationship with the development of complete retinal pigment epithelium and outer retinal atrophy(cRORA) after 3 or more years.

Methods: This retrospective study enrolled 1118 eyes of 765 consecutive patients with int-AMD and at least 12 months of follow-up (including OCT) who were evaluated between October 2016 and October 2020 in Retina Consultant of Houston eye clinics. 250 of these eyes had 36-48 months of follow-up and were included in this analysis. Spectralis OCT 49 slice volume scans at baseline were evaluated for biomarkers including a high central drusen volume (define as ≥ $0.03mm^3$), intraretinal hyperreflective foci (IHRF), subretinal drusenoid deposits (SDD), hyporeflective drusen cores (hDC), incomplete RORA (iRORA), and a thin or thick double layer sign (DLS). Demographic and systemic factors at baseline were also collected. The presence of cRORA was assessed at the final visit between 36 and 48 months. Odds ratios for the baseline features for development of cRORA were assessed using logistic regression and generalized estimating equations.

Results: The frequency of the various OCT biomarkers in this int-AMD cohort is shown in Table 1. Several baseline features were associated with a significantly higher risk for development of cRORA at 3 years including iRORA, IHRF, SDD, hDC, and a thin DLS. (Table 2). Interestingly, hypertension was associated with a significantly lower risk.

Conclusions: Several OCT biomarkers are associated with an increased risk for development of cRORA over three years. These biomarkers may be useful for prognostication and for selecting patients for enrollment into future early intervention clinical trials for AMD.

CONTROL ID: 3706286

SUBMITTER (NAME ONLY): Raju Timsina

TITLE: Association of Alpha-Crystallin with Bovine Lens Lipid Membranes Derived from a Single Lens

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Timsina, N.K. Khadka, L. Mainali, Physics, Boise State University, Boise, Idaho, UNITED STATES|L. Mainali, Biomolecular Sciences Graduate Program, Boise State University, Boise, Idaho, UNITED STATES|

Commercial Relationships Disclosure: Raju Timsina: Commercial Relationship: Code N (No Commercial Relationship) | Nawal Khadka: Commercial Relationship: Code N (No Commercial Relationship) | Laxman Mainali: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the association of α-crystallin with membranes prepared from total lipids isolated from a single bovine eye lens, measure the physical properties of membranes, and illustrate the feasibility that such experiments can be conducted for membranes prepared from total lipids isolated from a single human eye lens.

Methods: Small unilamellar vesicles were prepared with and without decreasing the cholesterol (Chol) content from total lipids isolated from a single lens cortex of two-year-old bovine using the rapid solvent exchange method and probe-tip sonication. Chol content in the cortical membranes was decreased by adding lipid (phospholipids and sphingolipid) mixtures resembling bovine lens lipid composition. The electron paramagnetic resonance spin-labeling method was used to measure the percentage of membrane surface occupied (MSO) by α-crystallin, the association constant (K_a), and the physical properties (hydrophobicity, mobility parameter, and maximum splitting) of membranes.

Results: No association of α-crystallin with bovine lens lipid membranes derived from the single-lens cortex was observed. However, α-crystallin association with cortical membranes with reduced Chol content was observed. The smaller the Chol content in cortical membranes, the larger the MSO and K_a, and vice-versa. These results imply that the membrane Chol is a key component in preventing α-crystallin association with the bovine lens lipid membrane. Hydrophobicity near the surface of cortical membranes increased with the increased α-crystallin association, supporting the hypothesis that α-crystallin association with lens membranes forms a barrier to polar molecules. The profiles of mobility parameters decreased and maximum splitting showed no significant change with the increased α-crystallin concentration, indicating that cortical membranes became less mobile with no significant change in order near the surface with the α-crystallin association.

Conclusions: Results show that the membrane Chol plays a crucial role in inhibiting α-crystallin association with the bovine lens lipid membrane, and such association alters the physical properties of membranes playing a vital role in modulating the integrity of membranes. Moreover, this study demonstrates that it is feasible to investigate the association of α-crystallin with membranes derived from a single human lens.

CONTROL ID: 3706289

SUBMITTER (NAME ONLY): Timothy Xu

TITLE: Population-based Incidence of Ocular Tumors in a Midwestern U.S. Population

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.T. Xu, K.A. Oyemade, J.L. Lopez Dominguez, M.G. Dumbrava, L.A. Dalvin, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|L.J. White, D.O. Hodge, Health Sciences Research, Mayo Clinic in Florida, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the population-based incidence of ocular tumors in a single U.S. Midwestern county population.

Methods: A retrospective review was conducted of all residents of Olmsted County, Minnesota diagnosed with any ocular tumor from January 1, 2006 to December 31, 2015. International Classification of Diseases, 9th and 10th Edition codes associated with ocular tumors were searched using the Rochester Epidemiology Project, a record-linkage system that captures virtually all medical care provided in this single Midwestern U.S. county population. Medical records were reviewed to confirm diagnoses. Age- and sex-adjusted incidence rates were calculated and adjusted to the 2010 U.S. White population.

Results: There were 1,852 incident cases of ocular tumors during the 10-year study period, of which 948 (51.2%) were intraocular, 717 (38.7%) were extraocular/orbital, and 187 (10.1%) were ocular surface. Females accounted for 1,017 (54.9%) cases and 1,685 (91.0%) subjects were White. The overall age- and sex-adjusted incidence rate of all ocular tumors was 142.67 per 100,000 per year (95% confidence interval [CI]: 136.12 to 149.22). Benign tumors accounted for 1,584 (85.5%) cases, while 268 (14.5%) were malignant. Among benign neoplasms, the most frequent intraocular, extraocular/orbital, and ocular surface tumors were choroidal nevus in 837 (52.8%) cases, epidermal inclusion cyst in 264 (16.7%), and conjunctival nevus in 75 (4.7%), respectively. The most common malignant neoplasm was basal cell carcinoma in 182 (67.9%) subjects. The incidence rate of benign tumors was 120.80 per 100,000 per year (95% CI: 114.80 to 126.80), compared to 21.87 per 100,000 per year (95% CI: 19.25 to 24.50) for malignant tumors. Incidence rate for all ocular tumors overall increased with age ($p<0.001$). No difference in ocular tumor incidence rate existed between sexes ($p=0.13$). The incidence rate in adults (≥18 years old) was 137.28 per 100,000 per year (95% CI: 130.83 to 143.73), compared to incidence in pediatric patients of 5.39 per 100,000 per year (95% CI: 4.25 to 6.53).

Conclusions: This population-based investigation may provide a more accurate assessment of ocular oncology epidemiology, demographics, and risk factors compared to referral center or claims data-based studies and may assist clinicians in formulating their differential diagnosis when encountering ocular neoplasms.

CONTROL ID: 3706304

SUBMITTER (NAME ONLY): BROOKE HARKNESS

TITLE: Detection of tear protein biomarkers associated with contact lens use

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. HARKNESS, W. Chamberlain, R. Stutzman, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|D. Hegarty, H. Behrens, L. David, S. Aicher, Chemical Physiology & Biochemistry, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M. Perez-Blanco, J. Betz, A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Betz, A. Galor, Surgical Services, Miami Veterans Affairs Medical Center, Miami, Florida, UNITED STATES|J. Lapidus, OHSU-PSU School of Public Health, Portland, Oregon, UNITED STATES|J. Saugstad, Anesthesiology & Perioperative Medicine, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K. Zientek, Proteomics Shared Resource, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To apply high-sensitivity proteomic analysis to human tears and identify differentially abundant proteins in contact lens wearers.

Methods: Tears were collected from both eyes of 48 volunteers using a 5-min Schirmer’s strip collection then stored individually at -80^{O}C until protein extraction. Volunteers also completed questionnaires about dry eye and ocular pain symptoms. Samples from individuals with features of interest (contact lens use; aqueous production as Schirmer's strip wetting length; ocular symptoms; topical anesthetic) were selected for quantitative proteomic analysis. Proteins were extracted from Schirmer's strips using S-Trap protocol, digested into peptides, and 16-plex Tandem Mass Tag (TMT) analyses were conducted using an Orbitrap Fusion mass spectrometer. Identified peptides were verified with open source databases and results were sorted with quality filters to identify candidates for differential abundance between groups.

Results: For contact lens use analysis, we examined samples from 14 eyes of 14 subjects (5 males; 9 females; age 23-29 years) with no history of ocular surgeries, no current eye infections, and no topical ophthalmic medication use. 5 subjects were contact lens wearers and 9 were not; half were anesthetized with topical 0.5% proparacaine HCl. Over 3000 unique proteins were identified in the volunteers’ tear fluid based on peptide sequence matching from curated databases. Application of the Benjamini-Hochberg multiple-testing correction to limit the false discovery rate and rigorous data quality filtering revealed 4 proteins with differential abundance between contact lens wearers and non-wearers, with cystatin D (CST5) demonstrating the greatest (8-fold higher) differential abundance in contact lens wearers. In addition, we found differential abundance of selected proteins previously reported in the literature, including lipocalin-1, lacritin, S100-A2, cystatins M and C, prolactin-inducible protein and zinc-alpha-2-glycoprotein. Subject age, sex, Schirmer's strip wetting length, dry eye and ocular pain scores, and topical anesthetic use were not different between the groups.

Conclusions: Unbiased TMT proteomics analyses demonstrated highly sensitive and reproducible analysis of human tear protein composition, thus showing promise as a technique in biomarker discovery. Contact lens wear significantly altered the tear proteome, while topical anesthetic use, subject sex and age did not.

CONTROL ID: 3706305

SUBMITTER (NAME ONLY): Ethan Pritikin

TITLE: Average Scleral Lens Lifespan at a Tertiary Care Hospital

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pritikin, G. Chiu, Ophthalmology, Keck Hospital of USC, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Ethan Pritikin: Commercial Relationship: Code N (No Commercial Relationship) | Gloria Chiu: Commercial Relationship(s);Code C (Consultant/Contractor):Glaukos, Acculens, BostonSight

ABSTRACT BODY:

Purpose: Scleral lenses (SLs) have become an effective treatment option for patients (pts) with irregular corneas (IC) and ocular surface disease (OSD). While their popularity has increased over the last decade, the average (avg) lifespan of a SL remains unknown.

Methods: A retrospective study was conducted at the USC Department of Ophthalmology to determine the avg lifespan of a SL. SL wearing pts were identified through evaluation of clinical visits from 01/01/2019 to 12/12/2019 via electronic medical records (EMR). Inclusion criteria included established SL pts fit at USC who had reordered a SL at least once in at least one eye. SL order histories were evaluated to determine the number of SLs ordered and avg days between orders during the pt's duration of care between 12/2009 and 09/2021. Data for OD and OS lenses were combined, and a multivariable mixed methods linear regression model was used to evaluate the effect of independent variables of interest while controlling for other variables. All tests were two-sided and a p-value of <0.05 was considered statistically significant. All analyses were done in R version 4.1.2.

Results: 251 pts (120 males, 131 females; avg age = 57.1±17.4 yrs) and a total of 445 eyes (IC 199, 44.7% and OSD 246, 55.3%) were included in the analysis. The avg lifespan for a SL in this pt cohort was 728.4 ± 434.3 days (1.99 ± 1.19 years; min 5 days, max 7.2 yrs). The avg number of lenses ordered per patient was 2.16 ± 1.47 and the avg duration of care was 2152.0 ± 1033.5 days (5.90 ± 2.83 yrs). There was no statistically significant correlation between avg SL lifespan and gender ($p = 0.67$), primary diagnosis ($p = 0.46$), or brand of SL ($p = 0.14$). Pts with greater SL experience had a statistically significant increase in their avg SL lifespan; for every one year of additional experience wearing SLs, the avg lifespan of SLs increased by 1 month (32.1 days) ($p = 0.001$). The exact reason for lens reordering could not be determined, but included need for updated fit or prescription and lens breakage/loss.

Conclusions: Many factors may affect SL lifespan, including medical indication and individual pt handling and care. The avg SL lifespan in this cohort of IC and OSD pts at a tertiary care hospital was 728.4 ± 434.3 days. There was no significant relationship between SL lifespan and gender, primary diagnosis, or SL brand.

CONTROL ID: 3706310

SUBMITTER (NAME ONLY): Jin Kwon Chung

TITLE: Engineering disease microenvironment of pterygium to elucidate the roles of cell-matrix interaction in cellular dysfunction during disease progression

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although the phenotype of pterygium has known as high levels of proliferation, inflammation, angiogenesis, and extensive amount of extracellular matrix accumulation, the specific molecular mechanism of pterygium pathogenesis is still unclear. Here, we aim to understand the underlying molecular mechanism of pterygium pathogenesis.

Methods: Transcriptome analyses using human pterygium epithelial cells and fibroblasts isolated from primary pterygium tissue. Quantitative polymerase chain reaction (PCR) and wound scratch test were performed to compare characteristics between pterygial and normal conjunctival cells. Traction force microscope (TFM) analysis and migration ability in different matrix stiffness conditions (matrix stiffnesses to mimic normal (~2.5 kPa) and pterygial (~60 kPa) tissue) were compared between pterygial and normal conjunctival cells.

Results: Cell adhesion and migration-associated signaling pathways were significantly upregulated in the pterygium epithelial cells and fibroblasts compared to cells isolated from normal conjunctival tissue, which were validated by quantitative PCR (matrix metalloproteinase, integrin alpha) and wound scratch assays. TFM analyses revealed that pterygium cells showed significantly higher levels of mechano-sensitiveness to their microenvironment and underwent mechanotransduction. Cells cultured on a stiff matrix exhibited increased growth, elongation, and numbers of vinculin, and furthermore, the same cell behaviors were significantly increased in both pterygium-derived cells, compared to cells on soft matrix.

Conclusions: These findings may offer insight into the important roles of cell-matrix interactions in pterygium pathophysiology, which could provide a valid tool to develop potential therapeutic candidates.

CONTROL ID: 3706327

SUBMITTER (NAME ONLY): Biyue Guo

TITLE: Myopia control effect of small back optic zone diameter orthokeratology lenses over two years

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Guo, S. Cheung, P. Cho, School of Optometry, The Hong Kong Polytechnic University, Hung Hum, Kowloon, HONG KONG|R. Kojima, Pacific University, Forest Grove, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the axial elongation (AE) in children wearing orthokeratology (ortho-k) lenses with different back optic zone diameters (BOZD).

Methods: Seventy Chinese children aged 6 to <11 years, with myopia between -4.00 to -0.75 D and astigmatism ≥ -2.50 D, were randomly assigned to use ortho-k lenses with 6mm (6-MM group) and 5mm (5-MM group) BOZD for two years. Corneal topography, sub-foveal choroidal thickness (ChT), and axial length were measured at baseline and 6-monthly visits. Treatment zone (TZ) was defined as the central area of corneal flattening bordered by the circumferential ring, where no dioptric change on the tangential subtractive map (difference between the pre- and the post- treatment) was observed. The horizontal and vertical TZ sizes were determined with the aid of a customized computer software. Linear mixed models were used to investigate factors (TZ sizes and changes of ChT) that may affect AE, considering baseline parameters (sex, age, pupil size, refraction, axial length and visual acuity).

Results: Data of the right eye of 45 subjects (23 in 6-MM and 22 in 5-MM group) who completed the study were analysed. At the 24-month visit, AE and TZ size were significantly reduced in the 5-MM group (AE: 0.15 ± 0.21 mm; horizontal/vertical TZ size: 2.69 ± 0.28/2.65 ± 0.22 mm) compared to the 6-MM group (AE: 0.35 ± 0.23 mm; horizontal/vertical TZ size: 3.84 ± 0.39/3.42 ± 0.34 mm) ($p = 0.005$; $p < 0.001$, respectively). ChT was not significantly changed after 24 months of lens wear in both groups ($p > 0.05$). Linear mixed models showed that the horizontal and vertical TZ sizes ($\beta = 0.130$, $p = 0.001$; $\beta = 0.136$, $p = 0.003$, respectively) and changes in ChT ($\beta = -0.002$, $p < 0.001$) were significantly associated with AE, controlling for the baseline parameters.

Conclusions: The 5-MM group exhibited a smaller TZ size which was associated with smaller AE. The findings also suggested that changes in ChT, although weak, may play a role in regulating myopia progression.

CONTROL ID: 3706333

SUBMITTER (NAME ONLY): María José Ruiz-Pastor

TITLE: The transporter of the omega-3 fatty acid DHA (MFSD2a) is expressed in the human neural retina.

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ruiz-Pastor, X. Sánchez-Sáez, A. Noailles, N. Martínez-Gil, P. Lax, N. Cuenca, Physiology, Genetics, and Microbiology, Universitat d'Alacant, Alicante, SPAIN|V. Maneu, Optics, Pharmacology and Anatomy, Universitat d'Alacant, Alicante, SPAIN|

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ABSTRACT BODY:

Purpose: The omega-3 fatty acid docosahexaenoic acid (DHA) is an essential component of neural membranes and has an anti-inflammatory and neuroprotective effect on the retina. DHA is being widely administered to patients with neurodegenerative diseases, as diminished levels of this fatty acid were found in the central nervous system of these patients and of animal models with neural diseases. Nevertheless, the transport mechanism of DHA remains unclear in the retina. MFSD2a was described as the putative transporter of DHA in the blood-retina barrier, but it is unknown if this protein is expressed in the neurons. We assessed to describe if this transporter is expressed in the neural retina using immunofluorescence.

Methods: We performed immunohistochemistry with anti-MFSD2a and specific markers of retinal populations in cryostat sections of the human retina. We used the transcriptional factors Chx10 for the identification of pan-bipolar cells, Pax6 for amacrine cells, and Brn3a for ganglion cells. For the identification of horizontal cells, we used parvalbumin. We identified the Müller cells and the retinal pigmented epithelium (RPE) with anti-CRALBP, and the cones with anti-cone arrestin. Additionally, we used LaminB2 to detect the nuclear membrane and KDEL and SERCA2 for the immunodetection of the endoplasmic reticulum.

Results: MFSD2a was extensively expressed in the neural retina. We have found that MFSD2a is expressed in the inner segments of photoreceptor cells, as well as in the outer nuclear layer, where somas of photoreceptor cells are localized. We also detected immunostaining in the inner nuclear layer, as well as in the ganglion cell layer. In the double immunostaining with the transcriptional factors Chx10, Pax6, and Brn3a we have found that all bipolar, amacrine, and ganglion cells expressed the DHA transporter. Horizontal cells also expressed MFSD2a in their nucleus. Müller cells showed anti-MFSD2a immunoreaction in the external limiting membrane. However, the RPE did not show immunolabeling with anti-MFSD2a. We have found MFSD2a immunolabelling in the endothelial cells of the blood vessels of the human retina.

Conclusions: MFSD2a is expressed by endothelial cells of the human retina, but also by the neural cells. Photoreceptor cells, Müller cells, and all populations of bipolar, amacrine, horizontal, and ganglion cells expressed MFSD2a in their cytosol and in their nuclear membrane.

CONTROL ID: 3706334

SUBMITTER (NAME ONLY): Penelope Allen

TITLE: Suprachoroidal Retinal prostheses, longterm stability and safety results.

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.J. Allen, C.J. Abbott, M. Kolic, E. Baglin, C.D. Luu, J. Yeoh, Bionic Eye Unit, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|P.J. Allen, C.J. Abbott, C.D. Luu, Surgery (Ophthalmology), University of Melbourne Faculty of Dentistry, Medicine and Health Sciences, Parkville, Victoria, AUSTRALIA|D.A. Nayagam, S. Epp, S. Titchener, C.E. Williams, M. Petoe, Bionics Institute, East Melbourne, Victoria, AUSTRALIA|D.A. Nayagam, The University of Melbourne Department of Clinical Pathology, Melbourne, Victoria, AUSTRALIA|N. Barnes, Research School of Electrical, Energy and Mechanical Engineering, the Australian National University, Canberra, Victoria, AUSTRALIA|R. Briggs, The University of Melbourne, Department of Surgery (Otolaryngology), Melbourne, Victoria, AUSTRALIA|W. Kentler, School of Engineering, University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To report the longterm safety and stability of two suprachoroidal retinal prosthesis trials (NCT01603576, NCT03406416), comprising of seven patients, with followup ranging from two to nine years.

Methods: Three patients with retinitis pigmentosa were implanted with our prototype 24 channel suprachoroidal retinal prosthesis in May - August 2012. One patient had the entire device removed following the trial in 2014 for a medical reason unrelated to the device. The other two patients had the intraocular array left in situ and the percutaneous connector removed, as planned. Ocular followup has continued since that time, albeit interrupted due to the Covid 19 pandemic.

Four patients with retinitis pigmentosa were implanted with our second generation 44 channel fully implantable device in February to August 2018. They continue to use the device in the home enviroment.

Ocular assessments including clinical examination, colour fundus photographs and optical coherence tomography (OCT) have been used to assess stability of the devices and retinal health longitudinally in patients (P) 1-7.

Results: Electrode to retina distance OCT measurements over two to nine years, calculated by comparing group means, showed an increase over time. (Wilcoxon, p=0.03) In the prototype trial, the increase appeared linked to fibrosis and stimulation, with no progression once devices were inactivated, in the second generation trial, it seemed primarily due to passive fibrosis.

Retinal thickness OCT measurements showed a slow reduction in central retinal thickness, as expected, due to progression of dystrophic disease. (Wilcoxon, p=0.11)

Device position compared to the optic nerve head (ONH) was calculated and three patients demonstrated some temporal movement. P1 position returned to baseline over seven years, P2 stabilised over three months and P6 had a temporary choroidal effusion event which settled spontaneously.

Function of the four Generation two fully implantable devices remains stable.

Conclusions: Using fundus photography and OCT measurements we demonstrate that retinal prostheses implanted in the suprachoroidal space for up to nine years are overall stable in position and cause mild progressive fibrosis in the suprachoroidal space. Longterm assessment of the changes in the retina are all consistent with the underlying

retinal dystrophy.
This provides further evidence of the safety of the suprachoroidal surgical approach for retinal prostheses.

CONTROL ID: 3706335

SUBMITTER (NAME ONLY): Tine Van Bergen

TITLE: THR-687, a potent pan-RGD integrin antagonist, protects against retinal vascular permeability, inflammation and reactive gliosis in the diabetic rat

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Van Bergen, A. De Vriese, B. Jonckx, K. Vanhulst, M. Vanhove, M. Porcu, E. Vermassen, P. Barbeaux, A.W. Stitt, Oxurion NV, Leuven, BELGIUM|A.W. Stitt, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Targeting RGD-binding integrins can affect multiple disease hallmarks such as vascular leakage, inflammation, angiogenesis and fibrosis. Therefore, an RGD-integrin inhibitor may have therapeutic benefit for various retinal disorders. In this study, we investigated the therapeutic potential of THR-687, a potent pan-RGD integrin antagonist, in the streptozotocin (STZ)-induced diabetes rat model.

Methods: Following STZ-induced diabetes, different doses of THR-687 (6.7, 16.7 or 75 µg/eye) or its vehicle were administered via 3 consecutive intravitreal injections in both eyes (with 1-week interval, n=7 rats/group). Untreated, non-diabetic rats served as controls (n=5 rats). At 4 weeks after diabetes-induction, the effect of THR-687 was investigated by histological analysis for retinal vascular leakage (using the tracer FITC-BSA), for inflammatory cell activation (Iba1 immunoreactivity) and Müller cell gliosis (vimentin immunoreactivity). Statistical analysis was performed with a one-way analysis of variance using a Bonferroni multiple comparison test.

Results: THR-687 reduced diabetes-induced increases in retinal permeability versus vehicle in a dose-dependent manner. The highest dose (75 µg/eye) completely prevented vascular leakage ($p<0.001$) while the mid dose (16.7 µg/eye) significantly decreased this pathology by 34 ± 21% ($p<0.05$) and the low dose (6.7 µg/eye) had no effect. All doses of THR-687 also significantly reduced the number of inflammatory cells, as compared to vehicle. Indeed, a reduction of 57 ± 12% was seen after administration of the highest dose ($p<0.01$), a decrease of 43 ± 19% for the mid dose ($p<0.05$) and the low dose induced a reduction of 51 ± 13% ($p<0.05$). The highest dose of THR-687 also reduced the diabetes-induced increase in vimentin expression within the Müller cells back to baseline ($p<0.05$ versus vehicle), whereas no significant differences following injections of the mid or low dose were observed.

Conclusions: RGD-integrin antagonism using THR-687 potently inhibits vascular permeability, inflammation and gliosis induced by STZ in the diabetic rat retina. Given its broad mode of action, THR-687 is a promising drug candidate for the treatment of vision-threatening retinal pathologies and is currently in a phase 2 clinical trial in diabetic macular edema patients (INTEGRAL - NCT05063734).

CONTROL ID: 3706336

SUBMITTER (NAME ONLY): Grzegorz Labuz

TITLE: Near-infrared light sensitivity as a new tool to assess retinal function in age-related macular degeneration

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Labuz, A. Rayamajhi, L.J. Kessler, R. Khoramnia, G.U. Auffarth, Department of Ophthalmology, UniversitatsKlinikum Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|G. Labuz, R. Khoramnia, G.U. Auffarth, David J Apple Center for Vision Research, UniversitatsKlinikum Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|A. Zielinska, K. Komar, Institute of Physics, Uniwersytet Mikolaja Kopernika w Toruniu, Torun, Kujawsko-Pomorskie, POLAND|K. Komar, International Centre for Translational Eye Research, Warsaw, POLAND|

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ABSTRACT BODY:

Purpose: Human eye's perception of near-infrared (NIR) light results from the two-photon absorption by retinal photoreceptors. In such a setting, pulsed NIR laser produces color sensation that corresponds (closely but not precisely) to the so-called visible spectrum with half of the wavelength used. The mechanism of NIR vision has recently been elucidated, and its clinical application sought. In this case-control study, we determined retinal sensitivity to NIR in patients with age-related macular degeneration (AMD) and compared it to visible-light microperimetry.

Methods: We recruited 24 AMD patients and 20 healthy controls and measured their visual function in one (better) eye. The NIR threshold was assessed using a two-photon excitation setup, which employs a femtosecond laser to project 1045-nm stimuli with ultrashort pulses. An array of neutral-density filters attenuates the laser power to meet the safety requirements of ANSI Z136.1-2014. Retinal sensitivity to visible light was measured using an MP-1 microperimeter (Nidek Technologies Srl). A customized 12-degree grid consisting of 44 retinal loci was applied. Best-corrected visual acuity (VA) and the logarithm of straylight were secondary outcome measures.

Results: The median (interquartile range) age of AMD and control subjects was 77.2 (71.8 to 79.9) years and 71.3 (67.8 to 78.3) years, respectively. AMD resulted in decreased logMAR VA, i.e., 0.09 (0.04 to 0.22), which in normal eyes was -0.04 (-0.06 to 0.02). A comparable level of straylight was found in the two populations with 1.18 (1.07 to 1.45) log(s) in the study and 1.16 (1.01 to 1.30) log(s) in the healthy group. The NIR threshold of AMD and control groups differed significantly (Mann-Whitney, P=.0001): 7.9 (7.1 to 9.5) dB vs. 10.5 (9.5 to 10.7) dB. In visible-light microperimetry, retinal sensitivity was also significantly decreased (Mann-Whitney, P=.0001) in AMD (14.4; 11.1 to 15.3 dB) compared to the controls (17.5; 16.5 to 18.3 dB).

Conclusions: We demonstrated that NIR retinal sensitivity in AMD patients is significantly impaired compared to healthy subjects, similarly to standard microperimetry. Although further research is needed, this proof-of-concept study suggests that this (new) functional parameter can be used in AMD patients' retinal-function assessment beyond standard VA measurements.

CONTROL ID: 3706339

SUBMITTER (NAME ONLY): Faruque Ghanchi

TITLE: Assessing the effectiveness of intravitreal aflibercept in UK routine clinical practice for treatment-naïve patients with diabetic macular edema: DRAKO 2-year results

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: DRAKO (NCT02850263) is an observational, multicenter study, and is the first study to prospectively evaluate the effectiveness of intravitreal aflibercept (IVT-AFL) for the treatment of patients with diabetic macular edema (DME) within routine clinical practice in the UK. Results are reported for the anti-vascular endothelial growth factor treatment-naïve cohort upon completion of the 2-year follow-up period.

Methods: Adult patients diagnosed with center-involving DME were enrolled and treated according to local practice. Primary endpoints were mean change from baseline in best-corrected visual acuity (BCVA) and central subfield thickness (CST) at 12 months (12M). Secondary endpoints included mean change from baseline in BCVA and CST at 24 months (24M), proportion of patients with ≥5, 10 or 15 letter gain or loss and the number of injections administered.

Results: At 12M (n=388), mean (SD) changes from baseline in BCVA of 2.5 (12.2) letters and CST of -119.1 (116.4) µm were reported. At 24M (n=326), mean (SD) BCVA remained above baseline (0.7 (12.7) letters) and CST was further reduced to -123.3 (104.3) µm from baseline. (24M Baseline; BCVA=71.5 letters; CST=447.6µm). At 24M, 38.0%, 16.6%, and 8.3% of patients gained ≥5, 10, and 15 letters, respectively; 26.1%, 15.3%, and 7.4% of patients lost ≥5, 10, and 15 letters, respectively. Patients received mean (SD) of 6.4 (2.0) injections in year 1 and 3.7 (2.3) injections in year 2. No correlation between the letter gain or loss and number of injections administered was observed. A total of 6.7% patients discontinued IVT-AFL treatment. In the safety population (n=507), 297 serious treatment emergent adverse events (TEAE) were reported, of which 22 were eye disorders. Serious TEAEs with a reasonable causal relationship with the injection procedure (n=4) or IVT-AFL treatment (n=4) were reported in 6 (1.2%) patients. Endophthalmitis was reported in 2 (0.4%) patients.

Conclusions: The DRAKO results indicate that IVT-AFL is an effective and well tolerated treatment for patients with DME in routine clinical practice, preserving or improving functional and anatomical outcomes over the 2-year treatment period. Functional outcomes were not correlated with number of injections administered. The safety profile of IVT-AFL was consistent with previous studies.

CONTROL ID: 3706349

SUBMITTER (NAME ONLY): Catherine Meylan

TITLE: Feasibility study for the use of a low-cost video eye tracker as a tool for eye-movement training.

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Meylan, D. Seidel, R. Gibson, C. Hazelton, Glasgow Caledonian University, Glasgow, Glasgow, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Current rehabilitation for visual field loss frequently involves computer and screen-based visual search tasks. This experiment was conducted to determine if the new generation of low-cost remote video eye trackers are suitable to measure eye movements whilst patients complete visual search tasks and could therefore be considered for use in rehabilitation training.

Methods: Twenty-six visually normal participants aged (mean ± S.D.) 21.36 ± 2.48 years performed a visual search task on a 17” VDU at 60cm without head restraint. The search was conducted under normal viewing (NV) conditions and with a simulated visual field defect (SVFD) of right sided homonymous hemianopia locked to the participant’s binocular eye position. In each condition there were 96 trials with targets which comprised 16 everyday objects presented in 6 different arrangements on a crowded background. During each trial, the eyes binocular position was recorded with a Tobii EyeX video eye tracker at 60 Hz. All trials were conducted under one condition then the other with the order randomised. Search time, maximum saccadic speed and the length of the scanpath were assessed offline.

Results: There was a significant ($p<0.05$) correlation between search time and the length of the scanpath. Search times (SVFD: 1.56 ± 0.03s, NV: 1.00±0.03s) and scanpath lengths (SVFD:72.5±3.2mm NV:51.0±2.9) were significantly longer in the SVFD trials compared to the normal condition ($p<0.01$). This was due to an increase in the length of the scanpath in the hemianopic field while search times between the SVFD and NV condition were similar when the target was in presented the visible part of the field ($p = 0.26$). Maximum velocities of eye movements also varied between the two conditions (SVFD mean±SD: 33.59±0.52°/s, NV: 41.63±1.06) and were significantly lower in the SVFD condition ($p<0.01$). The search time, scanpath and eye movement speed did not improve with practice.

Conclusions: Results of increased search time and scanpath with SVFD match previous research. The low-cost, remote video eye tracker was able to reliably quantify differences in visual search behaviour with a simulated visual field defect. Remote video eye trackers have the potential to improve the visual rehabilitation of patients with VF loss due to their ability to monitor eye movements, provide feedback and quantify progress during the rehabilitation process.

CONTROL ID: 3706364
SUBMITTER (NAME ONLY): Iryna Lobach
TITLE: Voretigene Neparvovec Exploratory Analysis (VNEAN): R-shiny app for the comprehensive and dynamic visualization of voretigene neparvovec clinical trial data
SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: I. Lobach, C. Spera, Novartis Pharma AG, Basel, Basel-Stadt, SWITZERLAND|M. Vacarezza, Novartis Argentina S.A., ARGENTINA|J. Alam, Novartis Pharmaceuticals Corp, East Hanover, New Jersey, UNITED STATES|
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ABSTRACT BODY:
Purpose: R-shiny apps can be useful in maintaining and analyzing data collected in clinical trials of rare diseases, where a suite of measures is used to characterize retinal and visual function, functional vision, and safety courses over time following the treatment.

In a phase 3 trial, participants with biallelic RPE65 mutation-associated inherited retinal dystrophy (IRD), an ultra-rare genetic disorder, received bilateral, subretinal injections of gene augmentation therapy, voretigene neparvovec and followed-up annually.

We explored the development of a novel data visualization tool, VNEAN (R-shiny application), to help in maintenance and analyses of complex trial data into a visual storytelling form that is easier to understand for healthcare audience.
Methods: We developed an interactive and dynamic application using Shiny package for R programming language. This app improves the ability to explore the longitudinal trajectory of main efficacy outcomes (mobility testing and full-field light sensitivity) in concert with other data, including visual function and safety that can be visualized overall and in subsets.
Results: This app has 11 modules of data analyses (Figure 1), including longitudinal visualization, analyses of correlation between changes, and timeline of adverse events. It presents the durability in improvement of functional vision, retinal and visual function, and the safety data at the group, subset and participant levels. The dynamic interface allows the user to define a subset based on the measures at baseline and/or their changes and select measures and/or timepoints.
Conclusions: COVID-19 demonstrated digital engagement at its peak. The R shiny app has the potential to provide alternative data visualization and interpretations of analyses that offer a comprehensive representation of the data generated in rare diseases, not easily achievable via traditional didactic lectures and static data methods. This patient-centric and enduring visualization approach enables health care professionals to learn and retain information for the management and engagement of IRD patients in their clinical practice.

Additionally, this application can progress the knowledge and understanding of treatment effects of rare diseases and help inform the design of future small- or large-scale trials.

CONTROL ID: 3706369

SUBMITTER (NAME ONLY): Raju Sapkota

TITLE: Culturally and linguistically appropriate training intervention program using video clips to improve diabetes knowledge, awareness, lifestyle and retinopathy screening uptake in Nepal: a randomized controlled trial

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sapkota, J. Kidd, S. Pardhan, Vision and Eye Research Institute, Anglia Ruskin University Faculty of Health Education Medicine & Social Care, Cambridge, Cambridgeshire, UNITED KINGDOM|T. Sharma, Department of Medicine, Gandaki Medical College, Pokhara, Kaski, NEPAL|T. Upadhyaya, Department of Medicine, Gandaki Medical College, Pokhara, Kaski, NEPAL|L. Smith, School of Psychology and Sport Science, Anglia Ruskin University Faculty of Science and Engineering, Cambridge, Cambridgeshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To examine the effectiveness of a culturally/linguistically appropriate training program, using video clips (so people who could not read or write could understand) and individual patient-centred reporting, to improve knowledge, awareness, lifestyle and diabetic retinopathy (DR) screening uptake in newly diagnosed diabetic patients in Nepal.

Methods: The training program was developed using video clips by a multidisciplinary team of experts. The training included advice on diabetes, diet, physical activity, the importance of retinal screening etc. A total of 110 participants with newly diagnosed diabetes (mean age=46±11 years) were recruited and divided randomly into two groups: intervention (n=55) and control (n=55). Baseline data on knowledge/awareness, diet, physical activity, glycated haemoglobin (HbA1c), blood pressure (BP), cholesterol, etc. were collected from both groups. All participants received doctor's recommended treatment for diabetes and were followed up after three (n=110) and six (n=41) months. Changes in HbA1c, cholesterol, BP, uptake of DR screening, knowledge/awareness about diabetes, diet, physical activities, etc. were recorded.

Results: Mean age, gender and HbA1c, BP, cholesterol, knowledge/awareness about diabetes, diet and physical activity did not differ significantly between the groups at baseline ($p \geq 0.12$). After three months, a significantly greater number of participants in the intervention group showed: (i) improved knowledge/awareness about diabetes control, physical activity levels and healthy eating ($p \leq 0.05$); (ii) significantly reduced HbA1c, low-density lipoprotein, and systolic BP levels ($p \leq 0.06$). All (100%) participants in the intervention group had retinal screening done as confirmed by their clinical reports (13% had already developed early signs of DR), compared to 0% in the control group. Improvement in knowledge/awareness about diabetes and clinical outcomes in the intervention group were found to be sustained after six months.

Conclusions: A culturally/linguistically appropriate training program using video clips is effective in improving knowledge/awareness about diabetes control, lifestyle, and promoting DR screening uptake in Nepal. This may be vital in reducing the risk of diabetic complications including diabetes-related blindness.

CONTROL ID: 3706372

SUBMITTER (NAME ONLY): Andrea Heredero

TITLE: A comparison of human stem cell-retinal organoid protocols as a way to investigate the timing and regulation of RS1 protein

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Heredero, C.J. Boon, Ophthalmology, Amsterdam UMC, University of Amsterdam (UvA), NETHERLANDS|A. Heredero, P.E. Wagstaff, A.L. Ten Asbroek, J.B. ten Brink, Human Genetics, Amsterdam UMC, University of Amsterdam (UvA), NETHERLANDS|A.A. Bergen, Netherlands Institute for Neuroscience (NIN-KNAW), NETHERLANDS|A.A. Bergen, Human Genetics / Ophthalmology, Amsterdam UMC, University of Amsterdam (UvA), NETHERLANDS|C.J. Boon, Ophthalmology, Leiden University Medical Center (LUMC), NETHERLANDS|

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ABSTRACT BODY:

Purpose:

X-linked juvenile retinoschisis (XLRS) is a degenerative retinopathy characterized by retinal splitting. Although it is well known that the disease is caused by defects in the gene RS1, clinical and genetic heterogeneity hampers early detection and diagnosis. Despite all the efforts, there is no treatment available to prevent vision loss or to delay XLRS progression. Self-organizing 3D in vitro models known as retinal organoids, have emerged as a powerful platform to use in preclinical research for eye diseases. Retinal organoids give us the chance to perform disease modeling, which is also crucial in XLRS since more than 200 mutations have been identified along the RS1 gene and no clear genotype–phenotype correlation has been found. To improve RS1 organoid modeling, we compared three mainstream protocols for retinal organoid development.

Methods:

We use three protocols: Matrigel-embedding protocol established by our group (Wagstaff et al., 2021), Free-floating 96-well plate protocol (Huang et al., 2019) and AMASS protocol (Cowan et al., 2021). Retinal organoids were differentiated up to 180 days. Samples were collected in early stages, as well as multiple time points at later stages to analyse RS1 expression using IHC, PCR and western blot. Functional characterization will be done using multielectrode arrays.

Results:

Free-floating 96-well plate protocol and Matrigel-embedding protocol have both generated long-term XLRS retinal organoids. Both protocols revealed differences in RS1 expression between control and patient, demonstrating the success in mimicking XLRS phenotype. Furthermore, at day 180 the retinal organoids displayed a splitting phenotype characteristic of the disease. We are currently applying the AMASS protocol as well to assess its similarities, strength and limitations.

Conclusions: It is possible to generate long-term retinal organoids with Free-floating 96-well plate and Matrigel-embedding protocols that mimic XLRS pathology. Based on RT-PCR and immunohistochemistry. Differences in RS1 protein expression can be observed comparing patient retinal organoids and controls. This demonstrates that retinal organoids are a suitable model to study XLRS. This will not only allow us to study the molecular mechanisms underlying XLRS, but also will provide us with an excellent in vitro platform to progress for experimental new gene therapy strategies.

CONTROL ID: 3706380

SUBMITTER (NAME ONLY): Wei-Chi Wu

TITLE: Pulmonary function in school-age children following intravitreal injection of bevacizumab for retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wu, Ophthalmology, Chang Gung Medical Foundation, Taoyuan, TAIWAN|

Commercial Relationships Disclosure: Wei-Chi Wu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate pulmonary function in school-age children who have received intravitreal bevacizumab (IVB) for retinopathy of prematurity (ROP).

Methods: In this retrospective, cross-sectional case-control study of 118 school-aged children were separated into three groups: full-term control children (group 1), preterm children who had not received IVB treatment (group 2) and preterm children with ROP who had received IVB treatment (group 3). Pulmonary function, measured by spirometry and impulse oscillometry, was assessed at approximately 7 years of age and compared among the three groups.

Results: One hundred and eighteen children (65 boys and 53 girls; mean age, 6.67±0.52 years) were included in this study. Pulmonary function was significantly better in group 1 than in groups 2 and 3 (all $p < 0.05$ in forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), forced expiratory flow between 25% and 75% of FVC (FEF_{25-75}), resistance of the respiratory system at 5 Hz (R5) and difference between R5 and R20 (R5-R20)). There were no statistically significant differences between group 2 and group 3 in FVC, FEV_1, ratio of FEV_1 to FVC (FEV_1 /FVC), FEF_{25-75}, resistance of the respiratory system at 20 Hz (R20), reactance of the respiratory system at 5 Hz (X5) or R5-R20 after adjusting for important perinatal factors.

Conclusions: By school age, preterm infants with a history of receiving IVB for ROP had comparable pulmonary function to their preterm peers who had not received IVB treatment.

CONTROL ID: 3706381

SUBMITTER (NAME ONLY): Reinier Bakker

TITLE: In vitro modelling of human albinism (OCA1) using patient-derived iPSC-RPE

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Bakker, P.E. Wagstaff, E. Emri, A.A. Bergen, Departments of Human Genetics and Ophthalmology, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|M.M. van Genderen, Diagnostic Center for Complex Visual Disorders, Bartimeus, Zeist, Utrecht, NETHERLANDS|M.M. van Genderen, Department of Ophthalmology, Universitair Medisch Centrum Utrecht, Utrecht, Utrecht, NETHERLANDS|A.A. Bergen, Nederlands Herseninstituut, Amsterdam, Noord-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Albinism is a genetic disorder characterized by absent/reduced melanin pigment in eyes, skin and hair. In addition, the retina exhibits foveal hypoplasia and misrouting of the axonal tracts to the brain, resulting in blurred vision. In (ocular) albinism, the RPE has a melanosomal pigment deficiency. The molecular mechanisms that link pigmentation to neural retinal development and disease are yet unclear. To model the disease in vitro, we compared stem cell derived iRPE of OCA1 patients and controls.

Methods: Human oculocutaneous albinism 1 (OCA1) patient derived iPSCs and controls were embedded in Matrigel for 5 days and cultured in N2B27 medium. The formed embryoid bodies were subsequently plated as single cells on growth factor reduced Matrigel coated trans-well inserts and medium changed to 20% KOSR medium. Produced iRPE was analyzed using RT-PCR and immunohistochemistry (IHC).

Results: As expected, OCA1 patient stem cell-derived RPE showed no pigmentation at all, while control WT iRPE cell lines started to pigment gradually from day 24 onward. To confirm the RPE identity of the differentiated cells, two general mature RPE markers were analyzed: BEST1 and RPE65. BEST1 is a regulator of fluid flux across the RPE and peaks earlier in patient derived iRPE but is lower than controls in later stages. RPE65 is an enzyme involved in the visual cycle and its expression is lower in later stage patient-derived iRPE. At day 60, expression of a number key disease genes involved in human albinism was different between the OCA1 iRPE control derived iRPE. These results were confirmed using IHC.

Conclusions: We created and characterized a new stem cell-derived in vitro model for OCA1. This model has been validated and can be used to study molecular mechanisms and signaling pathways of human albinism in vitro.

CONTROL ID: 3706388

SUBMITTER (NAME ONLY): Mark Buijs

TITLE: Generation of an in vitro stem cell based model for researching gyrate atrophy of the choroid and retina

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Buijs, A.L. Ten Asbroek, A.A. Bergen, Human Genetics, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|B. Balfoort, M. Brands, C. Karnebeek, Paediatrics, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|C.J. Boon, A.A. Bergen, Ophthalmology, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|C.J. Boon, Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|R. Houtkooper, H. Waterham, R. Wanders, Laboratory Genetic Metabolic Diseases, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|M. Wagenmakers, Internal Medicine, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C. Timmer, Endocrinology and Metabolism, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Gyrate atrophy of the choroid and retina (GACR) is an rare autosomal recessive metabolic eye disorder. GACR patients suffer from progressive vision loss, starting with near sightedness and night blindness in the first decade of life which progresses to complete blindness around the age of 50. Mutations in the gene encoding for ornithine amino transferase (OAT) impair the function of the encoded enzyme and thereby the ability of the cell to convert ornithine to 1-Pyrroline-5-carboxylic acid (P5C). It is currently unknown by which mechanism OAT deficiency results in deterioration in vision. In this study we developed GACR in vitro models which can be used to gain a better understanding of the disease mechanism responsible for inducing retinal pigment epithelial (RPE) cell death.

Methods: Skin biopts and blood was collected from 2 clinically well characterized GACR patients, 1 of which has a start codon mutation. From these materials, we generated 2 induced pluripotent stem cell lines (iPSCs). We performed RNA analysis, western blot and immunostainings to determine the presence of OAT in all cell lines. Both patient and healthy control iPSCs were exposed to a range of ornithine and arginine concentrations and subsequently assayed for cell viability.

Results: DNA mutation analysis showed that the patient iPSCs carry the c.1 A>G and c.1058 G>A OAT mutations. Using RT-PCR, western blot and immunostainings we have been able to determine the presence of OAT in our healthy control cell lines. Interestingly, 1 of the patient cell lines showed almost no loss of OAT activity. In contrast, the patient cell line with a start codon mutation showed only residual expression of OAT protein. The cell viability assay demonstrated an increased sensitivity towards ornithine in our patient iPSCs compared to the healthy controls. Similar increased sensitivity was also observed in the patient iPSCs when exposing them to arginine.

Conclusions: We have demonstrated that our patient derived iPSC model displays the key characteristic of GACR, which is toxicity as a result of hyperornithinemia. Our first functional results are promising and encourages further use of the iPSC model to further identify the disease mechanism responsible for ornithine induced toxicity. We are currently differentiating our iPSCs to iRPE cells yielding more specifically relevant information about the effect of OAT deficiency in the eye.

CONTROL ID: 3706396

SUBMITTER (NAME ONLY): Andrew Logan

TITLE: Comparing the effect of AMD on face discrimination and face recognition

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. Logan, G.E. Gordon, G. Loffler, Department of Vision Sciences, Glasgow Caledonian University, Glasgow, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) impairs several aspects of face perception, including face discrimination (identify differences between faces) and face recognition (recognize a previously-viewed face). Both involve processing of face identity, but it is unclear if AMD impairs one more than the other. We aimed to quantitatively compare the effect of AMD on two face perception tasks: one with a memory requirement (recognition) and one without (discrimination).

Methods: 16 patients with non-exudative AMD (VA = 0.12 to 0.6 LogMAR) and 16 age-matched controls (-0.18 to 0.06) completed two computerised face tests. The discrimination task presented four simultaneously-visible faces and required participants to identify the odd-one-out. The recognition task asked participants to identify a previously-viewed face from four alternatives. Both tests measured the face threshold- the minimum difference required between identities for either reliable discrimination or recognition. Thresholds were measured separately for full-faces, internal features (eyes, mouth and nose) and external features (head and hair).

Results: Relative to controls, discrimination (1.71X) and recognition (1.66X) thresholds for full-faces were significantly higher (i.e. poorer sensitivity) in patients with AMD (both $p<0.001$). Thresholds measured with the discrimination and recognition tests were equivalent ($p<0.001$). Compared to the full-face condition, the difference in thresholds between controls and patients with AMD was significantly greater when only the internal features were visible ($p<0.001$). Relative to controls, thresholds for the internal features were 2.24X poorer in patients with AMD. External feature performance was impaired to a lesser extent (1.62X).

Conclusions: AMD impairs both face discrimination and recognition. Face recognition performance (significant memory demand) was equivalent to that on a memory-free discrimination task. Our data indicate that the severity of the face perception impairment in AMD is dependent on the face information available, rather than task memory demands. Specifically, patients with AMD demonstrated the most severe impairment when only the internal features were visible. Overall, these results suggest that impaired encoding of visual information- particularly that from the internal features- underlies the difficulties that patients with AMD experience with both face discrimination and recognition.

CONTROL ID: 3706400

SUBMITTER (NAME ONLY): Wang Jui-Kai

TITLE: Quantifying Spatial Patterns of OCT Total Retinal Thickness (TRT) in Papilledema Over Time using a Deep Learning Variational AutoEncoder

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Jui-Kai, M.K. Garvin, R.H. Kardon, Center for the Prevention and Treatment of Visual Loss, Iowa City VA Health System, Iowa City, Iowa, UNITED STATES|W. Jui-Kai, R.H. Kardon, Ophthalmology and Visual Sciences, University of Iowa, Iowa city, Iowa, UNITED STATES|M.K. Garvin, Electrical and Computer Engineering, University of Iowa, Iowa city, Iowa, UNITED STATES|M.J. Kupersmith, Neurology, Ophthalmology, and Neurosurgery, Icahn School of Medicine at Mount Sinai and New York Eye and Ear Infirmary, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Wang Jui-Kai: Commercial Relationship: Code N (No Commercial Relationship) | Mona Garvin: Commercial Relationship(s);Code P (Patent):University of Iowa | Mark Kupersmith: Commercial Relationship: Code N (No Commercial Relationship) | Randy Kardon: Commercial Relationship(s);Code S (non-remunerative):Fight for Sight;Code S (non-remunerative):Department of Veterans Affairs Research Foundation

ABSTRACT BODY:

Purpose: To describe the continuum of spatial patterns in various levels of papilledema, a deep-learning variational autoencoder (VAE) was proposed to create a 2D latent space map for better visualization (Fig. 1a). We also evaluated the extent that the VAE latent variables can be used to quantify and monitor the pattern of optic nerve swelling over time.

Methods: A paired VAE encoder and decoder were trained using TRT maps from 1509 optic-nerve-head (ONH) optical coherence volume (OCT) volumes from the multiple visits of the 125 subjects in the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT) OCT-substudy. For each input TRT map, the trained encoder computes two latent variables (d1, d2) as a succinct representation of the swelling pattern; the trained decoder reconstructs the input TRT map based on d1 and d2. Longitudinal changes in spatial patterns were quantified and rendered based on d1 and d2 to map the trajectories of improvement over time.

Results: Papilledema swelling pattern trajectories over time were plotted for each of the selected 42 subjects treated with acetazolamide and 37 subjects treated with weight reduction only (Fig. 1b). The distribution of d1 is illustrated in Fig 2a; a significant difference occurred after only three months in the treatment group but took six months in the placebo group (Tukey's analysis). Fig. 2b shows an extremely high correlation between the original and the VAE reconstructed TR volumes, demonstrating the utility of coding the swelling patterns into only two variables.

Conclusions: The VAE latent space (Fig. 1a) can be seen as a visual map to depict the trajectory of improvement of the swelling spatial pattern over time for individual eyes. Latent variable d1 appears to primarily encode a volumetric measure, while latent variable d2 appears to encode the spatial pattern of swelling reflecting which axon bundles are thickened at various levels of severity of papilledema. VAE may provide a robust approach to differentiate causes of optic disc swelling in future studies.

CONTROL ID: 3706405

SUBMITTER (NAME ONLY): Abram Akopian

TITLE: Blockade of Retinal Gap Junctions Provides Significant Neuroprotection in a Non-human Primate Model of Glaucoma

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Akopian, S. Kumar, A. Benavente-Perez, R. Ablordeppey, C. Lin, S. Viswanathan, S.A. Bloomfield, Biological and Vision Sciences, SUNY College of Optometry, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently developed a rigorous and reproducible model of glaucoma in the common marmoset (Callithrix jacchus) (Kumar et al., 2022, TVST). The microbead/occlusion model provides for a consistent elevation of IOP across a 10-week experimental period. Here we tested the hypothesis that the gap junction (GJ)-mediated bystander effect is mechanistically linked to progressive cellular damage in retina and optic nerve associated with glaucoma.

Methods: Experimental glaucoma in marmosets was initiated by IOP elevation induced by an intracameral injection of 10 µm-diameter polystyrene microbeads. The GJ blocker meclofenamic acid (MFA, 50 mM) was delivered by intravitreal injection weekly for 10 weeks. Functional changes were monitored by ERG recordings and structural changes were assayed by immunohistochemistry and SD-OCT imaging.

Results: We found that pretreatment of microbead-injected eyes with MFA largely prevented the loss of RGCs normally seen at 10 weeks after IOP elevation. MFA also prevented the loss of RGC axons and disruption of the mosaic structure of the optic nerve observed in microbead-injected eyes. In electrophysiological experiments, we observed a reduction in the photopic negative response (PhNR) beginning at 8 weeks after microbead injection, but no significant change in the a- and b-waves of the ERG. At 10 weeks, the PhNR amplitude continued to decrease, but there was also a significant reduction in amplitude of the a- and b-waves, suggesting a pattern of late damage to photoreceptors and bipolar cells, respectively. However, following MFA application, all ERG components were maintained at control levels in microbead-injected eyes. Finally, we found that MFA prevented the enlarged optic nerve cupping seen in microbead-injected eyes.

Conclusions: Our results indicate that blockade of GJs offers significant protection of retina and optic nerve in a marmoset model of glaucoma. Taken together with our pervious results from the mouse (Akopian et al., 2017 JCI), the present findings provide further support for our hypothesis that GJs play a critical role in progressive cell death and thereby form novel targets for neuroprotection therapy in glaucoma.

CONTROL ID: 3706438

SUBMITTER (NAME ONLY): Kimberly Wong

TITLE: Dissecting transcriptional networks that regulate retinal ganglion cell survival and axon regeneration after optic nerve injury

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.A. Wong, T. Martheswaran, J. Msaddi, L. Benowitz, Neurosurgery, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|K.A. Wong, L. Benowitz, Harvard Medical School, Boston, Massachusetts, UNITED STATES|D.S. Welsbie, Ophthalmology, Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our limited understanding of the signals that regulate retinal ganglion cell (RGC) death and axon regeneration after axon injury has prevented the development of curative therapies. Inhibiting DLK (MAP3K12) and LZK (MAP3K13) signaling after axonal injury is highly neuroprotective but blocks axonal regenerative capacity even in the presence of a strongly pro-regenerative treatment. The objective of our studies is to investigate the role of transcription factors downstream of DLK and LZK to identify gene regulatory networks (GRNs) that may independently regulate RGC cell death and axon regeneration.

Methods: Conditional deletion of DLK/LZK in RGCs was achieved using intraocular delivery of AAV2-CRE in $DLK^{fl/fl}$;$LZK^{fl/fl}$ mice. Selective knockout of the transcription factors (TFs) known to lie downstream of DLK/LZK was achieved by intraocular delivery of AAV2-gRNAs into mice with RGC-specific Cas9 expression (Vglut2-CRE;ROSA26-LSL-Cas9). Gene manipulation was conducted 2-3 weeks prior to mouse optic nerve injury (ONI). DLK/LZK signaling was assessed via immunofluorescent staining at 1 and 5 days post-injury (dpi), the onset and peak of signaling, respectively. RGC survival and axon regeneration was assessed at 14 dpi.

Results: We found that deletion of both DLK and LZK in RGCs dramatically increased RGC survival at 14 dpi (63.4±6.5% survival in DKO vs 21.5±2.4% in wildtype), but blocked axon regeneration (89±18% reduction) and induction of regeneration associated genes (RAGs), including Gap43, even in the presence of strongly pro-regenerative treatments (incl. Zymosan + CPT-cAMP). We next investigated the roles of the downstream TFs. Independent knockout of Jun, Sox11, Mef2a, and Atf2 in RGCs resulted in significantly increased RGC survival at 14 days after ONI with no improvement of endogenous axon regeneration. However, when axon regeneration was stimulated using pro-regenerative treatments, we identified particular TFs that either enabled or suppressed axon regeneration.

Conclusions: These results show that there are discrete GRNs that independently regulate cell death versus axon regeneration, pointing to novel gene therapies that can function in combination with other well-known treatments to both improve RGC survival while also improving axon regeneration after optic nerve injury.

CONTROL ID: 3706442

SUBMITTER (NAME ONLY): Dennis Akrobetu

TITLE: Intrasession Repeatability of Macular Optical Coherence Tomography Angiography Parameters in Neurodegenerative Disease

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Akrobetu, C. Robbins, M. Quist, S. Stinnett, B. Scott, K.G. Johnson, A. Liu, J. Ma, S. Soundararajan, D.S. Grewal, S. Fekrat, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reliability of OCTA measurements can be affected by various factors including ocular media opacity, imaging artifacts, and patient cooperation during image acquisition. The potential for variation in OCTA measurements may limit its widespread clinical adoption. Studies validating (or refuting) the repeatability of OCTA measurements are essential. In this cross-sectional study, we report the intrasession repeatability and interocular symmetry of macular OCTA parameters in patients with Alzheimer disease (AD), mild cognitive impairment (MCI), and Parkinson disease (PD).

Methods: OCTA images (3x3mm and 6x6mm) centered on the macula were acquired using the Zeiss Cirrus HD-5000 AngioPlex. Perfusion density (PFD), vessel density (VD), and foveal avascular zone (FAZ) area repeatability were assessed using intraclass correlation (ICC) analysis. Interocular symmetry of PFD, VD, and FAZ area were also assessed.

Results: Sixty-one eyes of 36 AD patients, 81 eyes of 52 MCI participants, 55 eyes of 32 PD participants, and 57 eyes of 31 normal cognition participants who underwent 3x3mm OCTA imaging were analyzed. 59 eyes of 35 AD patients, 86 eyes of 53 MCI participants, 63 eyes of 36 PD participants, and 55 eyes of 31 participants with normal cognition who underwent 6x6mm OCTA imaging were analyzed. For 3x3mm OCTA images, ICC values for PFD circle were as follows: AD (0.68; 0.50-0.78 CI), MCI (0.68; 0.53-0.77 CI), PD (0.63; 0.41-0.75 CI), and normal cognition (0.38; 0.22-0.64 CI). For 6x6mm OCTA images, ICC values for PFD circle were as follows: AD (0.64; 0.44-0.76 CI), MCI (0.74; 0.64-0.83 CI), PD (0.57; 0.35-0.70 CI), and normal cognition (0.60; 0.37-0.73 CI). Similar ICC values were observed for VD and FAZ area, although values trended slightly higher for FAZ area. Apart from inner ring PFD on 6x6mm OCTA images in normal cognition participants (0.40; 0.15-0.60 CI) and MCI (0.74; 0.62-0.82 CI), there were no significant differences in repeatability among or between groups. Interocular differences in OCTA parameters were only observed in AD patients who underwent 6x6mm OCTA imaging.

Conclusions: Overall, similar macular OCTA repeatability was observed between normal cognition participants and those with neurodegenerative disease. Regardless of diagnostic group, macular OCTA metrics demonstrated moderate repeatability. On average, FAZ area was more repeatable than VD or PFD.

CONTROL ID: 3706446
SUBMITTER (NAME ONLY): Oluwafeyikemi Okome
TITLE: The Efficacy of Netarsudil - Post-approval Reality
SESSION TITLE: Clinical studies and trials
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: O. Okome, J. Lin, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|S. Wong, Glaucoma, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|J. Song, CareMount Medical PC, Mount Kisco, New York, UNITED STATES|
Commercial Relationships Disclosure: Oluwafeyikemi Okome: Commercial Relationship: Code N (No Commercial Relationship) | Jane Song: Commercial Relationship: Code N (No Commercial Relationship) | Jun Lin: Commercial Relationship: Code N (No Commercial Relationship) | Sze Wong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the real-world efficacy of netarsudil 0.02% ophthalmic solution dosed once daily before bed (q.h.s.) in reducing intraocular pressure (IOP) in eyes on multiple glaucoma medications.

Methods: In this retrospective cohort study subject eyes recruited were patients at the New York Eye and Ear Infirmary of Mount Sinai (NYEEI) resident glaucoma clinic prescribed with netarsudil between November 2020 and February 2021. These eyes were diagnosed with glaucoma and had IOP above target despite being on ≥ 2 ocular hypotensive agents. Subject eyes were excluded if they were unable to tolerate or adhere to netarsudil for a period of 4-8 weeks after initiation of therapy. The main subject measure was the IOP-reducing effect of netarsudil after 4-8 weeks of therapy, with comparisons made between types of glaucoma and between eyes that did and did not have prior glaucoma surgery. Data was further assessed via t-test and interpreted as a percentage change in IOP.

Results: Netarsudil was prescribed for 222 eyes. 50 eyes were excluded from analysis due to lack of adequate follow up or inability to adhere to therapy, leaving 172 eyes for analysis. 114 eyes had open angle glaucoma (OAG) and 17 had mixed mechanism glaucoma (MMG). The mean baseline IOP for eyes with OAG and those with MMG were 21.1 ± 5.8 mm Hg and 19.4 ± 5 mm Hg, respectively. After 4-8 weeks of treatment the mean IOP for eyes with OAG and those with MMG were 16.3 ± 4.8 mm Hg ($p < 0.001$) and 16.2 ± 4.6 mm Hg ($p < 0.001$), respectively. 110 eyes had prior glaucoma surgery and 62 had not. Mean baseline IOPs for eyes that did and did not have glaucoma surgery were 20.7 ± 5.9 mm Hg and 21.6 ± 5.7 mm Hg, respectively. After 4-8 weeks of treatment with netarsudil, the mean IOPs were 16.4 ± 5 mm Hg ($p < 0.001$) and 15.4 ± 4.5 mm Hg ($p < 0.001$), respectively.

Conclusions: This study demonstrates that netarsudil is efficacious in eyes already on multiple glaucoma medications, regardless of the type of glaucoma or whether prior glaucoma surgery was performed and can help delay the need for incisional glaucoma surgery. This efficacy coexists with barriers to accessing and using the medication including cost and the burden of taking multiple ocular hypotensive drops. Patients indoubtedly benefit from the availability of netarsudil and particular attention should be paid to facilitating their ability to access it.

CONTROL ID: 3706451

SUBMITTER (NAME ONLY): Chas Pfeifer

TITLE: Chronic ablation of retinal microglia prevents functional vision loss during early-stage diabetic retinopathy in the mouse

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.W. Pfeifer, R.S. Apte, Ophthalmology and Visual Sciences, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Chas Pfeifer: Commercial Relationship: Code N (No Commercial Relationship) | Rajendra Apte: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Microglia become activated in parallel with neurodegeneration in the retinas of humans with diabetic retinopathy (DR) and in rodent models but their role in mediating functional vision loss remains unclear. This study tested the hypothesis that chronic ablation of activated retinal microglia can prevent visual function deficits during early-stage DR in the mouse.

Methods: Male Cx3cr1$^{YFP\text{-}CreER/+}$; Rosa26$^{DTA/+}$ (TG) mice were given single intraperitoneal (IP) injections of Streptozotocin (STZ; 150mg/kg) delivered in a sodium citrate buffer (pH~4.5) or buffer solution as a control. STZ diabetic (>250mg/dL blood glucose) and non-diabetic mice were transfered to cages containing tamoxifen-infused chow (500mg/kg) or regular chow for 8 weeks to compare control (CTRL), diabetic (STZ), microglia-ablated control (TAM), and microglia-ablated diabetic (TAM+STZ) groups (N=4-5). 9-step scotopic (rod-specific) intensity and 7-step photopic (cone-specific) intensity electroretinography (ERG) assessments were performed on anesthetized mice at 4- and 8-weeks. Retinas were processed post-hoc for immunostaining to assess microglial ablation efficacy. One-way and two-way ANOVA tests were used for statistical analysis.

Results: Tamoxifen-treated TG mice showed reduced microglial density within one week of treatment (Mean±SEM), corresponding to a >93% decrease (14.4±5.4/mm^2 retina; p<.0001) compared to untreated control mice (206.2±6.6) that sustained through 8 weeks of treatment. Comparing STZ to TAM+STZ, the following scotopic measurements showed statistical difference at 4 weeks: (a-wave) 193.9±16.6μV vs. 249.3±14.6 (-4db; p<.0054), 231.0±16.8μV vs. 305.0±15.5 (0db; p<.0001), 307.1±23.3μV vs. 391.0±19.4 (5db; p<.0001); (b-wave) 455.0±48.0μV vs. 589.6±35.8 (0db; p=.0126), 553.6±46.7μV vs. 668.4±32.3 (5db; p=.0499). No significant differences in scotopic measurements were found between TAM+STZ, CTRL, and TAM groups. No significant differences in photopic measurements were found between all groups.

Conclusions: Our results support our hypothesis that ablation of activated retinal microglia can prevent DR-associated functional vision loss during early-stage DR. Further examination of microglial activation in DR will be needed to understand their unique contribution to neuro-retinal dysfunction.

CONTROL ID: 3706453

SUBMITTER (NAME ONLY): David Wirta

TITLE: Dry eye sign, symptom and quality of life improvements associated with administration of AR-15512

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Wirta, Eye Research Foundation, Newport Beach, California, UNITED STATES|M. Senchyna, D. Hollander, Aerie Pharmaceuticals, Inc., Durham, North Carolina, UNITED STATES|D.G. Evans, E.B. McLaurin, Total Eye Care, Memphis, Tennessee, UNITED STATES|A.E. Lewis, Aerie Pharmaceuticals, Inc. (former employee), Durham, North Carolina, UNITED STATES|G.W. Ousler, Ora, Andover, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: David Wirta: Commercial Relationship(s);Code C (Consultant/Contractor):Aerie, Allergan, Eyenovia, Novartis, Oyster Point Pharma, Santen;Code F (Financial Support):Abbvie, Aerie, Allergan, Allysta, Bausch and Lomb, Eyenovia, Jennivision, Nicox, Novaliq, Novartis, Ocuphire, Ora, Orasis, Osmotica, Oyster Point Pharma, Qlaris, Santen, TearCare, Tersus, Visus | Michelle Senchyna: Commercial Relationship(s);Code E (Employment):Aerie | David Evans: Commercial Relationship: Code N (No Commercial Relationship) | Eugene McLaurin: Commercial Relationship: Code N (No Commercial Relationship) | George Ousler: Commercial Relationship(s);Code E (Employment):Ora Inc | Amber Lewis: Commercial Relationship(s);Code E (Employment):Aerie | David Hollander: Commercial Relationship(s);Code E (Employment):Aerie

ABSTRACT BODY:

Purpose: Dry eye disease (DED) is a symptomatic ocular surface condition that imposes a substantial health burden and can affect a patient's daily activities and quality of life (QoL). AR-15512 is a TRPM8 cold thermoreceptor agonist that stimulates both tear production and a cooling sensation across the ocular surface. A phase 2b study was conducted to evaluate DED symptoms and QoL following administration of AR-15512.

Methods: Prospective, double-masked study evaluating two formulations of AR-15512 (0.0014% and 0.003%) versus vehicle dosed twice daily for 84 days in 369 DED subjects. Following vehicle run-in, eligible subjects were randomized 1:1:1 and evaluated where applicable at Days 1, 14, 28 and 84. Outcomes included tear production (unanesthetized Schirmer test, performed at D1 and D14 only), symptoms (Symptom Assessment iN Dry Eye [SANDE] and visual analog scales [VAS] for ocular discomfort [ODS] and eye dryness [EDS]) and QoL (7 VAS questions evaluating activities of daily living: driving, workplace productivity, reading books, reading fine print, using electronic devices, watching TV, and feeling depressed).

Results: Overall, 369 subjects enrolled (mean age 63.7; 72% female) and of these, 345 (93.5%) completed the study. Statistically significant improvements were achieved in the ITT population with 0.003% AR-15512 vs vehicle for both signs and multiple symptoms. Increased tear production was observed after initial dose and repeat dosing (D1: 20.2 vs 8.1mm and D14: 19.5 vs 5.9mm, $p<0.0001$). Symptom improvements were observed as follows: SANDE on D14 (-7.4 vs -2.9, $p=0.0254$), D28 (-12.9 vs -5.0, $p=0.0005$) and D84 (-17.2 vs -8.3, $p=0.0015$), ODS (-20.6 vs -13.6, $p=0.0281$) and EDS (-17.1 vs -10.8, $p=0.0302$) at D84. Lastly, statistically significant improvements ($p<0.05$) from baseline were also seen with 0.003% AR-15512 relative to vehicle on all 7 QoL measures as early as D14, with the magnitude of difference relative to vehicle continuing to widen throughout the 84-day study on most of the measures. AR-15512 was well tolerated, with few discontinuations (n=7; 1.9%) due to adverse events.

Conclusions: In addition to improving signs and symptoms, 0.003% AR-15512 demonstrated improvements in functional vision which were observed within 2 weeks and continued to improve over time. AR-15512 represents a novel treatment for DED with the potential to improve patient quality of life.

CONTROL ID: 3706460

SUBMITTER (NAME ONLY): Bhagwat Alapure

TITLE: Combination ASO therapy improves therapeutic benefits in a mouse model of Usher syndrome

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.V. Alapure, K.N. Robillard, M. Fisher, J.J. Lentz, Neuroscience Center of Excellence, Louisiana State University Health Sciences Centre, New Orleans, Louisiana, UNITED STATES|F. Rigo, Ionis Pharmaceuticals, Inc.,, Carlsbad, California, UNITED STATES|

Commercial Relationships Disclosure: Bhagwat Alapure: Commercial Relationship: Code N (No Commercial Relationship) | Katelyn Robillard: Commercial Relationship: Code N (No Commercial Relationship) | Mark Fisher: Commercial Relationship: Code N (No Commercial Relationship) | Frank Rigo: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Lentz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Morpholino (MO) and 2′ O-methoxyethyl (MOE) are two chemical modifications frequently applied to antisense oligonucleotides (ASOs) that are being used to manipulate gene expression for therapeutic applications. The fate of the ASO-targeted RNA depends on the ASO mechanism of action, which can be influenced by its chemical modifications. MO and MOEs are chemical modifications to the ribose sugar, which, when combined with modifications to the phosphate backbone, significantly improve ASO pharmacokinetic properties, innate immune response, and stability, making them ideal drugs for the treatment of diseases with defined genetic targets. Retinitis pigmentosa (RP) affects 1 in 4000 individuals worldwide, yet there are no effective treatments. In this study, we tested ASOs with MO or MOE modifications for the treatment of visual dysfunction in a mouse model of Usher syndrome (USH). USH is a form of RP that includes hearing impairment. Transgenic mice with a splicing mutation (216A) in the Ush1c gene, which causes USH in humans, have retinal dysfunction characteristic of RP, as well as profound hearing and vestibular deficits. Previously, we showed short-term rescue of hearing, balance, and vision in USH mice treated with a 216A-targeted-MOE-ASO. Here, we demonstrate that a combination of MO- and MOE-ASOs (Combo-ASO) significantly extends the duration of improved visual function in USH mice.

Methods: Juvenile USH mice were treated with MOE-, MO-, or Combo-ASOs by intravitreal injection. Visual function was then measured at 3-12 months of age using electroretinogram (ERG) analysis. Retinal Ush1c and protein expression was measured by Next generation sequencing (NGS) and immunohistochemistry (IHC), respectively.

Results: At 3 months of age, ERGs were significantly increased in all USH mice treated with ASOs compared with untreated USH control mice. The increased ERGs persisted for up to 12 months of age in USH mice treated one time with Combo-ASOs, compared with 3-6 months of age after treatment with MOE- or MO-ASOs alone. Further, NGS and IHC showed significantly improved Ush1c splicing and protein expression in the retinas of ASO-treated USH mice.

Conclusions: These data demonstrate that a single dose of Combo-ASO significantly extends the duration of improved vision in USH mice and the potential for annual administration of ASO therapy for a long-term benefit to vision.

CONTROL ID: 3706462

SUBMITTER (NAME ONLY): Adam Hanif

TITLE: Federated learning for collaborative clinical diagnosis and disease epidemiology in retinopathy of prematurity

SESSION TITLE: Machine Learning and Big Data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.H. Hanif, A.S. Coyner, S. Ostmo, J. Campbell, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|C. Lu, K. Chang, P. Singh, J. Kalpathy-Cramer, Athinoula A Martinos Center for Biomedical Imaging, Charlestown, Massachusetts, UNITED STATES|J. Brown, Computer Science, University of Lincoln, Lincoln, Lincolnshire, UNITED KINGDOM|R. Chan, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|D. Rubin, Biomedical Informatics Research, Stanford University School of Medicine, Stanford, California, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Adam Hanif: Commercial Relationship: Code N (No Commercial Relationship) | Charles Lu: Commercial Relationship: Code N (No Commercial Relationship) | Ken Chang: Commercial Relationship: Code N (No Commercial Relationship) | Praveer Singh: Commercial Relationship: Code N (No Commercial Relationship) | Aaron Coyner: Commercial Relationship: Code N (No Commercial Relationship) | James Brown: Commercial Relationship(s);Code S (non-remunerative):Boston AI Lab | Susan Ostmo: Commercial Relationship: Code N (No Commercial Relationship) | R.V. Paul Chan: Commercial Relationship(s);Code S (non-remunerative):Boston AI Lab;Code F (Financial Support):Genentech;Code C (Consultant/Contractor):Phoenix Technology Group, Alcon;Code O (Owner):Siloam Vision | Daniel Rubin: Commercial Relationship: Code N (No Commercial Relationship) | Michael Chiang: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis;Code I (Personal Financial Interest):InTeleretina;Code F (Financial Support):Genentech | Jayashree Kalpathy-Cramer: Commercial Relationship(s);Code S (non-remunerative):Boston AI Lab;Code F (Financial Support):Genentech | J. Peter Campbell: Commercial Relationship(s);Code F (Financial Support):Genentech;Code C (Consultant/Contractor):Boston AI Lab;Code O (Owner):Siloam Vision

ABSTRACT BODY:

Purpose: To utilize federated learning (FL), a method of collaboratively training deep learning (DL) models without sharing patient data, to differentiate inter-institutional diagnostic patterns and disease epidemiology in retinopathy of prematurity (ROP).

Methods: 5,245 retinal images were obtained from exams of patients in the neonatal intensive care units of 7 institutions. Images were labeled according to both the bedside clinical grading (CL) of plus disease (plus, pre-plus, no plus), and a reference standard diagnosis (RSD) determined by a consensus of three masked graders and the clinical diagnosis. Birthweight (BW), gestational age (GA), and clinical grades for all eye exams were recorded. DL models were trained on clinical labels for plus disease classification using either a centralized multi-institutional dataset, or an FL approach. Area under the receiver operating characteristic curve (ROC) was used as a measure of model performance. A DL-derived vascular severity score (VSS) was calculated for each eye exam. An “institutional VSS” was calculated by averaging the VSS of the most severe eye exam for each baby at each site. Demographics, clinical diagnosis of plus disease, and VSS between institutions were compared with simple linear regression, McNemar-Bowker test and one-way ANOVA.

Results: The performance of FL and central models trained on clinical labels was found to be equivalent (ROC = 0.93±0.06 vs 0.95±0.03, p=0.0175). The proportion of patients diagnosed as no plus and pre-plus by CL and RSD methods varied significantly (p<0.00l). Vascular severity and VSS corresponding to “no plus” diagnoses varied significantly across institutions (p<0.001). We found an inverse relationship between institutional VSS and mean GA (Figure 1, p=0.049, adjusted R^2=0.49).

Conclusions: FL enabled the development of an accurate, DL-derived ROP VSS by drawing from multiple institutions’ labels without inter-institutional sharing of data. We identified differences in the clinical diagnosis of plus disease, and levels of objective ROP severity between institutions. FL has promise for objectively assessing differences in clinician diagnostic paradigms and disease severity across institutions.

CONTROL ID: 3706465

SUBMITTER (NAME ONLY): Ward Fickweiler

TITLE: Elevated Vitreous Retinol Binding Protein 3 Concentrations Are Associated with Decreased Vitreous Inflammatory Cytokines, VEGF, and Progression of Diabetic Retinopathy

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Fickweiler, H. Park, K. Park, T. Chokshi, M. Mitzner, D. Robinson, T. Boumenna, Y. Zaitsu, J. Gautier, I. Wu, Research Division, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|W. Fickweiler, M. Mitzner, D. Robinson, J. Cavallerano, L.P. Aiello, J.K. Sun, Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|J. Cavallerano, L.P. Aiello, J.K. Sun, G. King, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G. King, Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Ward Fickweiler: Commercial Relationship: Code N (No Commercial Relationship) | Hyunseok Park: Commercial Relationship: Code N (No Commercial Relationship) | Kyoungmin Park: Commercial Relationship: Code N (No Commercial Relationship) | Tanvi Chokshi: Commercial Relationship: Code N (No Commercial Relationship) | Margalit Mitzner: Commercial Relationship: Code N (No Commercial Relationship) | Devon Robinson: Commercial Relationship: Code N (No Commercial Relationship) | Tahani Boumenna: Commercial Relationship: Code N (No Commercial Relationship) | Yumi Zaitsu: Commercial Relationship: Code N (No Commercial Relationship) | John Gautier: Commercial Relationship: Code N (No Commercial Relationship) | I-Hsien Wu: Commercial Relationship: Code N (No Commercial Relationship) | Jerry Cavallerano: Commercial Relationship: Code N (No Commercial Relationship) | Lloyd Aiello: Commercial Relationship(s);Code C (Consultant/Contractor):KalVista, Novo Nordisk;Code O (Owner):KalVista | Jennifer Sun: Commercial Relationship(s);Code C (Consultant/Contractor):American Medical Association (JAMA Ophthalmology), American Diabetes Association;Code F (Financial Support):Adaptive Sensory Technologies, Boehringer Ingelheim, Genentech/Roche, Janssen, Physical Sciences, Inc, Novartis, Novo Nordisk, Optovue | George King: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The Joslin Medalist Study found increased concentrations of Retinol Binding Protein 3 (RBP3) in people with type 1 diabetes for 50 years or longer with no to mild non-proliferative diabetic retinopathy (DR) versus those with proliferative DR (PDR). RBP3 potentially protects the retina by inhibiting glucose uptake and inflammation. This study correlated inflammatory cytokines and vascular endothelial growth factor (VEGF) in the vitreous and plasma with vitreous RBP3, DR severity, and DR progression in a diverse population of individuals with type 1 and type 2 diabetes.

Methods: Plasma and vitreous samples (N=205) were collected from individuals undergoing retinal surgery at the Joslin Beetham Eye Institute or as part of the Medalist Study, which collected vitreous postmortem. RBP3 and VEGF concentrations were measured by ELISA, and inflammatory cytokines by multiplex assay. Individual neural retinal layer thicknesses in the foveal area were obtained from optical coherence tomography (OCT) images using automated layer segmentation software (Heidelberg v6.0c) for the Medalist subjects.

Results: Elevated vitreous RBP3 concentrations were associated with less severe DR in all eyes ($p<0.0001$), and in both postmortem Medalist specimens ($P<0.0001$), and surgical samples from type 1 diabetes of shorter duration and type 2 diabetic patients ($P=0.03$). No difference in RBP3 concentration was identified between people with type 1 and type 2 diabetes ($P=0.19$). Higher RBP3 concentration was associated with reduced risk of PDR onset ($N=30$, $P<0.0001$), and with increased photoreceptor layer thickness ($P=0.04$). Higher concentrations of RBP3 were associated with lower levels of TNF-a, TNF-b and VEGF in the vitreous ($P<0.05$). PDR was associated with lower levels of vitreous IFN-γ ($P=0.001$) and IL-10 ($P=0.007$), and higher levels of vitreous IL-6 ($P=0.02$), IL-15 ($P=0.01$), and VEGF ($P<0.0001$), but was not associated with plasma concentrations of these cytokines. Vitreous VEGF levels did not correlate with its plasma levels.

Conclusions: These data suggest that RBP3's association with less severe DR and slower progression to PDR may be mediated by decreasing diabetes-induced inflammatory cytokines and VEGF in the retina. These findings support RBP3's potential as both a diagnostic and therapeutic approach to preventing or delaying progression of DR.

CONTROL ID: 3706467

SUBMITTER (NAME ONLY): Lee Jones

TITLE: Prevalence of Charles Bonnet syndrome among UK visually impaired military veterans and associated impact of visual hallucinations during the COVID-19 pandemic

SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Jones, M. Moosajee, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|L. Jones, M. Lee, R. Gomes, BRAVO VICTOR, London, UNITED KINGDOM|M. Lee, Blind Veterans UK, London, UNITED KINGDOM|R. Gomes, Northumbria University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|M. Moosajee, The Francis Crick Institute, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Lee Jones: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Lee: Commercial Relationship: Code N (No Commercial Relationship) | Renata Gomes: Commercial Relationship: Code N (No Commercial Relationship) | Mariya Moosajee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Charles Bonnet syndrome (CBS) is characterised by visual hallucinations secondary to sight loss. Aside from sight loss, other risk factors associated with CBS include social isolation, loneliness, and post-traumatic stress. The health and lifestyle circumstances of visually impaired military veterans place this profile at an increased risk of developing CBS. The purpose of this study was to estimate the prevalence of CBS through an analysis of health records for members of a UK sight loss charity (Blind Veterans UK) and report experiences of CBS during the COVID-19 pandemic.

Methods: A retrospective analysis and screening/filtering of military veterans' electronic membership records at Blind Veterans UK. Text analysis was used to identify CBS cases. A cross sectional survey of individuals with active CBS was used to measures patient-reported features of hallucinatory experiences during the COVID-19 pandemic and perceived episode triggers.

Results: Analysis was conducted on 4109 members of Blind Veterans UK. Following screening and exclusion of members with non-sight loss related hallucination risk factors (e.g., Alzheimer's disease), 532 members were identified as CBS cases, representing 12.9% (95% CI: 11.1%-14.7%) of the cohort. Forty-five individuals with CBS completed the survey. Loneliness during the pandemic was associated with changes in the nature of visual hallucinations ($p=0.04$). Individuals experiencing greater loneliness were, on average, older than those with no changes to their feelings of loneliness ($p=0.03$). Despite experiencing greater feelings of loneliness (67%), most individuals had not accessed support services.

Conclusions: The relative high prevalence of CBS among visually impaired military veterans indicates that this cohort may be at greater risk of the condition. Approximately half of survey respondents experienced exacerbation of visual hallucinations during the COVID-19 pandemic, which may partly be explained by loneliness and/or environmental triggers.

CONTROL ID: 3706469

SUBMITTER (NAME ONLY): David Brown

TITLE: Evaluation of 8 mg Intravitreal Aflibercept Injection for Neovascular Age-Related Macular Degeneration: Results from the Phase 2 CANDELA Study

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.M. Brown, Retina Consultants of Texas, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: David Brown: Commercial Relationship(s);Code C (Consultant/Contractor):Regeneron, Bayer, Genentech/Roche ;Code F (Financial Support):Regeneron, Bayer, Genentech/Roche

ABSTRACT BODY:

Purpose: Preclinical data suggest that an 8 mg intravitreal aflibercept injection (IAI) may intensify and prolong the therapeutic effect of IAI 2 mg. CANDELA, a phase 2, randomized, single-masked, open-label, 44-week clinical trial (NCT04126317) assessed the safety and efficacy of IAI 8 mg versus IAI 2 mg in patients with neovascular age-related macular degeneration (nAMD).

Methods: Treatment-naïve patients (≥50 years old) with active subfoveal choroidal neovascularization secondary to nAMD and a best corrected visual acuity (BCVA) of 78 to 24 letters (approximately 20/32 to 20/320) in the study eye were enrolled. A total of 106 patients were randomized 1:1 to receive 3 monthly doses of either IAI 2 mg (n=53) or IAI 8 mg (n=53) followed by doses at Week 20 and 32. The primary end points were safety and the proportion of eyes without retinal fluid in the center subfield at Week 16.

Results: Overall, majority of the patients were female (62.3%); the mean (SD) age was 77.4 (8.0) years and mean (SD) baseline BCVA was 58.0 (12.1) letters. The incidence of ocular-related adverse events (AEs) through Week 16 was 17.0% (9/53) for the IAI 8 mg group and 22.6% (12/53) for the IAI 2 mg group. No new safety signals were identified; no AEs of intraocular inflammation, occlusive vasculitis, or anti-platelet trialists' collaboration (APTC)-defined arterial thromboembolic events were reported through Week 16. The proportion of eyes with no retinal fluid in the center subfield at Week 16 was 50.9% (27/53) for the IAI 8 mg group and 34.0% (18/53) for IAI 2 mg group (treatment difference, 17.0% [95% CI, −1.6%, 35.5%]; P=0.0770). Compared to the IAI 2 mg group, eyes in the IAI 8 mg group showed a numerically greater reduction from baseline in median central subfield thickness (−161 µm vs −96 µm), and a numerically higher increase from baseline in mean BCVA (8.4 vs 6.5 letters) at Week 16.

Conclusions: The overall safety of IAI 8 mg was similar to that of IAI 2 mg at Week 16. The observed anatomic and functional improvements with IAI 8 mg suggest potential additional therapeutic benefit over IAI 2 mg in patients with nAMD. The data support further development of IAI 8 mg.

CONTROL ID: 3706472

SUBMITTER (NAME ONLY): Melis Kabaalioglu Guner

TITLE: Optical Coherence Tomography Findings in Choroidal Melanoma-Associated Subretinal Fluid

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kabaalioglu Guner, T.W. Olsen, L.A. Dalvin, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Melis Kabaalioglu Guner: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Olsen: Commercial Relationship: Code N (No Commercial Relationship) | Lauren Dalvin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the optical coherence tomography (OCT) findings of choroidal melanoma with subretinal fluid.

Methods: This is a single center, retrospective review of spectral domain OCT images of treatment naïve choroidal melanoma cases with associated subretinal fluid, presenting between July 2009 and August 2021. Demographic characteristics and tumor features were reviewed. Tumors were grouped according to Collaborative Ocular Melanoma Study (COMS) categories. OCT features were categorized as elongated photoreceptors, photoreceptor/ellipsoid zone (EZ) loss, retinal pigment epithelium (RPE) loss, RPE hyperplasia, intraretinal fluid, retinoschisis (inner layer, outer layer, or both), pigment epithelial detachment (PED), retinal thinning, outer plexiform layer (OPL) splitting, bacillary layer detachment (BALAD) (horizontal, circular or both), and subretinal hyperreflective material (SRHM) (homogenous, heterogenous or both). Statistical analysis was performed using SPSS Statistics Software Version 28 (IBM, Armonk, New York).

Results: OCT features of 236 patients, from the most to least common included: photoreceptor and/or EZ loss or disruption in 174 (73.7%), RPE hyperplasia in 153 (64.8%), photoreceptor elongation in 118 (50.0%), macular subretinal fluid in 92 (39.0%), intraretinal fluid in 84 (35.6%), heterogenous SRHM in 72 (30.5%), BALAD in 67 (28.4%), RPE loss or disruption in 67 (28.4%), retracted photoreceptors in 56 (23.7), retinal thinning in 50 (21.2%), OPL splitting in 50 (21.2%), homogenous SRHM in 48 (20.3%), PED in 38 (16.1%), and retinoschisis in 5 (2.1%) patients. Photoreceptor/EZ loss increased progressively with small vs. medium vs. large tumors (52.0% vs. 86.9% vs. 94.9%, $p<0.001$), and this difference remained significant when further analyzed with subretinal fluid extent as a confounder ($p<0.001$). BALAD was more common in medium compared to small melanomas and was associated with greater extent of subretinal fluid. This difference remained significant when subretinal fluid was considered as a confounding variable ($p=0.006$).

Conclusions: Choroidal melanoma-associated subretinal fluid has many unique OCT features including BALAD and SRHM. Future longitudinal studies are needed to evaluate the diagnostic and prognostic importance of these findings in patients with choroidal melanoma.

CONTROL ID: 3706477

SUBMITTER (NAME ONLY): Roksana Sadeghi

TITLE: Relative brightness and size of electrically induced visual percepts with a visual prosthesis

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Klatzky, Psychology, Carnegie Mellon University, Pittsburgh, Pennsylvania, UNITED STATES|R. Sadeghi, Biomedical Engineering, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|A. Caspi, Jerusalem College of Technology, Jerusalem, Jerusalem, ISRAEL|F. Tenore, B. Christie, S. Billings, Johns Hopkins University Applied Physics Laboratory, Laurel, Maryland, UNITED STATES|A. Kartha, A. Caspi, G. Dagnelie, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The real-time stimulation of electrodes implanted in the visual pathway using a head-mounted camera creates visual perception through the activation of neurons at a close distance of the electrodes. Transferring camera frames to electrical pulses that create a meaningful and uniform percept requires understanding the relationship between the stimulation parameters and different percept properties such as brightness, location, shape, and size. Variable brightness across electrodes would cause images to look "mottled;" variable size could affect blurriness. Here, we studied the relative brightness and size of the percepts created by different Argus II epiretinal electrodes.

Methods: Three people with Argus II implant participated in this study. We tested 10 and 5 electrodes for S1 and S2, respectively, and three groups of 4, 5, and 10 electrodes for S3. The relative brightness and size of the percepts were studied in a 2-AFC task with all pair combinations in the group repeated three times in random order. In each trial, a pair of electrodes was stimulated, one by one, at an amplitude level corresponding to a 0.75 detection rate specific to the given electrode (previously estimated using a Bayesian adaptive threshold test). The participant was asked to choose which electrode in the pair was brighter regardless of the size and which was bigger regardless of brightness. Electrodes were ranked from 0 to 1 based on the percentage of trials in which they were judged brighter or bigger, and ranks were plotted against threshold; the average rank is expected to be 0.5, and the standard deviation (SD) represents uncertainty.

Results: Brightness ranks of all electrodes had a mean of 0.50 and a SD of 0.20 (range: 0.13 - 0.88). The average size rank was 0.50 with a SD of 0.17 (range: 0.07 - 0.81). Across electrodes, brightness ranks show a linear correlation with threshold ($r = 0.45$; $p = 0.007$), but the correlation between the size ranks and thresholds was not significant ($r = 0.27$; $p = 0.1$).

Conclusions: We showed phosphenes size is not affected by threshold differences. However, electrodes with higher thresholds do create brighter percepts. Therefore, uneven brightness may be corrected by scaling stimulus amplitudes according to the threshold, but it is unlikely that the image blur can be reduced. This should be considered when normalizing brightness and size of the percept elicited by implanted electrodes.

CONTROL ID: 3706486

SUBMITTER (NAME ONLY): Evan Sembell

TITLE: Determining the Ocular Biocompatibility of a Novel VEGF-A and Ang-2 Bispecific Protein (RO-634) Through Histological Analysis

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Sembell, J.M. Kunzeman, Southern Illinois University School of Medicine, Springfield, Illinois, UNITED STATES|J.L. Olson, A. Jones, J. Morgenstern, A. Strong, S. Droho, N. Mueller, M. Huvard, Sue Anschutz Rodgers Eye Center, University of Colorado, Aurora, Colorado, UNITED STATES|P.K. Kaiser, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|A.M. Khanani, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|J.S. Heier, OCB, Boston, Massachusetts, UNITED STATES|N. Gupta, Glenwood High School, Chatham, Illinois, UNITED STATES|R. Bhandari, Springfield Clinic Eye Institute, Springfield, Illinois, UNITED STATES|L. Xu, Independent Research Consultant, California, UNITED STATES|S. Bevers, Department of Structural Biology and Biochemistry, University of Colorado School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Antibodies against Vascular Endothelial Growth Factor-A (VEGF-A) and Angiopoietin-2 (Ang-2) are validated targets in the treatment of retinal disease. With the introduction of a novel bispecific protein, RO-634, dual targeting of VEGF-A and Ang-2 is possible. This study investigates the ocular biocompatibility of the bispecific, RO-634, using histological analysis.

Methods: All experiments were performed in accordance with the ARVO statement for Use of Animals in Ophthalmic and Vision Research. Five Brown Norway rats received intravitreal injections of RO-634 in the right eye, and BSS in the left eye to evaluate for potential retinal toxicity. One month post intravitreal injection, the rats were sacrificed, and retinal tissue was collected for histological analysis. The tissues were sectioned, stained, and analyzed via Imagepro software to quantify the number of cells present in ganglion, inner nuclear, and outer nuclear cell layers. Each layer was identified by the software in three distinct areas to increase accuracy in quantification. Following automated check, a manual count was conducted to ensure all cells were counted. Those samples that did not have adequate

sectioning and fixation were discarded.

Results: RO-634 was well tolerated in the Brown Norway rats. Histological analysis between RO-634 and BSS did not demonstrate a statistically significant difference in cell count between ganglion cell layer (L=17.90 ± 1.31, R = 16.33 ± 1.11, T test = 0.40), outer nuclear cell layer (L= 156.04 ± 2.49, R = 153.09 ± 3.19, T test = 0.42) or inner nuclear cell layers (L=56.33 ± 2.11, R = 56.38 ± 1.42, T test = 0.98) within the retina (Figure 1), suggesting biocompatibility of RO-634.

Conclusions: The novel VEGF-A and Ang-2 bispecific protein (RO-634) demonstrates biocompatibility in this animal model. Further studies are needed to understand the therapeutic potential of this bispecific protein in retinal disease.

CONTROL ID: 3706492

SUBMITTER (NAME ONLY): Oliver Gramlich

TITLE: Novel Autoantibody Models of NMOSD and MOGAD Optic Neuritis Demonstrate Distinct Clinicopathologic Features

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O.W. Gramlich, C. Godwin, B. Elwood, J. Anders, R.H. Kardon, Dept. of Ophthalmology, University of Iowa, Iowa City, Iowa, UNITED STATES|O.W. Gramlich, C. Godwin, B. Elwood, J. Anders, R.H. Kardon, Center for the Prevention and Treatment of Visual Loss, VA Health Care Iowa City, Iowa City, Iowa, UNITED STATES|J.L. Bennett, Depts. of Neurology and Ophthalmology, University of Colorado, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optic neuritis (ON) is a common manifestation of auto-immune demyelinating disorders such as myelin oligodendrocyte glycoprotein associated disease (MOGAD) and neuromyelitis optica spectrum disorder (NMOSD). The purpose of our study was to establish an animal model that replicates the clinical and histopathologic features of each disorder via injection of disease-specific autoantibodies under the optic nerve sheath of rats.

Methods: Long Evans rats (n=12/group) received a unilateral injection of NMO patient derived recombinant Aquaporin4 (rAQP4) autoantibodies or MOGAD serum IgG (MOGIgG) into the subarachnoidal space of the optic nerve. Changes in pattern electroretinography (PERG) and visual evoked potential (VEP) recordings, retinal ganglion cell (RGC) complex thickness, and optic nerve histopathology were determined. Results were compared to naïve rats using ANOVA and Tukey's test.

Results: Impaired RGC function was evident by significant declines in the P1 and P1 to N2 PERG amplitude in both MOGIgG (P1:7.6±2.9 µV, p=0.007; P1 to N2:-7.4±2 µV, p=0.001) and rAQP4-injected optic nerves (P1:6.0±1.3 µV, p=0.001; P1 to N2:-6.7±1.4 µV, p=0.001) when compared to naïve rats (P1:11.2±2.3 µV; P1 to N2:-11.3±1.5 µV). Rats having received antibodies displayed a similarly decreased P1 to N2 amplitude in the pattern VEP (naïve:8.3±1.7 µV; MOGIgG:5.1±1.1 µV, p=0.001; rAQP4:3.0±0.7 µV, p=0.001). While PERG indicates notable delays in conduction speed, flash VEP demonstrates significantly prolonged P2 latency in rAQP4-injected optic nerves (102±126 ms, p=0.003), but not after MOGIgG injection (73±19 ms, p=0.84), compared to naïve controls (69±7 ms). Optical coherence tomography reveals RGC complex thinning in both cohorts 21 days after antibody administration which was more severe in eyes from animals with rAQP4 injected optic nerve (naïve:99±8 µm; MOGIgG:92±6 µm, p=0.13; rAQP4:87±6 µm, p=0.005). Optic nerve histopathology revealed distinct patterns of demyelination and presence of anti-human IgG and complement deposition.

Conclusions: Structural and functional analysis of the visual system after MOGIgG or rAQP4 optic nerve injection shows disease-specific patterns of degeneration, with a more progressive nature in NMO-like ON, which parallels the human condition. This novel model of autoantibody-induced ON will provide an invaluable resource for future translational and therapeutic studies.

CONTROL ID: 3706495

SUBMITTER (NAME ONLY): Murali Subramani

TITLE: Human Retinal Ganglion Cell Response to Intra-retinal Guidance Cues

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Subramani, M.J. Van Hook, I. Ahmad, Ophthalmology and Visual Science, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma disease modeling and ex-vivo stem cell approach to RGC degeneration require that human pluripotent stem cell derived RGCs are capable of responding to intra- and extra-retinal guidance cues to reach, recognize and connect with their targets. Here, we demonstrate that human RGCs generated from embryonic stem (ES) cells respond to the evolutionarily conserved intra-retinal cues for the guidance of axons towards the optic disc.

Methods: Human RGCs were generated from RGC reporter hES cells (Sluch et al., 2017, Stem Cells 6:1972) using a modified chemical induction protocol, which recapitulates RGC development. hRGCs were co-cultured with the central/peripheral retinal cells, isolated from embryonic day 16 (E16) rat embryos in the presence of IgG/anti- DCC, IgG/anti-Robo2, or after treatment of cells with chondroitinase. RGC morphology was examined by immunofluorescence coupled Sholl analysis, RGC function by electrophysiology, and transcriptional response by RNA seq analysis.

Results: The ES cell derived RGCs expressed transcripts corresponding to guidance receptors (eg. DCC, Robo2, EPHs and NRP1). When cultured on central retinal cells hRGCs elaborated long and complex neurites. The length and complexity of neurites were compromised when hRGCs were pre-incubated with DCC-antibody. There were more collapsed growth cones (GC) and decrease in Na currents amplitude in DCC antibody treated groups versus controls. In contrast, those co-cultured with peripheral retinal cells displayed short and simple neurites. The length and complexity of neurites improved significantly when peripheral retinal cells were treated with chondroitinase or hRGCs were pre-incubated with Robo2 antibody versus controls. There were more active GCs (increased number of filopodia) and significantly improved amplitude of Na currents in chondroitinase/Robo2 antibody treated groups compared to controls. The transcriptional response to intra-retinal guidance cues will be presented.

Conclusions: The human ES cell derived RGCs recognize the intra-retinal central versus peripheral guidance cues that restrain and guide RGCs axons towards the optic disc. These cues are evolutionarily conserved and may underlie the possible spatial physiological and transcriptional characteristics of RGCs.

CONTROL ID: 3706496

SUBMITTER (NAME ONLY): Rashika Verma

TITLE: Community Based Eye Screenings Using Retinal and OCT-B Combination Imaging in Glaucoma During COVID-19

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Verma, P. Tailor, A. Zhu, C. Ye, E.J. Kuklinski, N. Bhagat, B. Szirth, M. Habiel, Ophthalmology, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal imaging is the gold standard in tele-ophthalmology. Limitations in two-dimensional imaging can lead to poor triage or unnecessary clinical referrals, especially during COVID-19. Combined retinal imaging with Optical Coherence Tomography-B scan (OCT-B) in detecting vision threatening diseases (VTDs) such as glaucoma in community-based screenings adds a third dimension to subject data.

Methods: A non-mydriatic Topcon 3D Maestro1 imaging system was deployed in this pilot study to screen 120 subjects (43.3% male, mean age 55.1) in community-based screenings. Measurements of vertical cup-to-disc ratio (VCDR), nerve fiber layer (NFL) thickness and macular and ganglion cell layer (GCL) thickness were collected along with color retinal images by the Maestro1. Visual acuity and intraocular pressures (IOP) were obtained as part of the screening protocol. Four types of OCTs were acquired: 78.33% 3D Wide, 13.33% 3D Macula, 5.83% 3D Disc, and 2.51% 5-Line Cross. An on-site certified reader (CR) interpreted results and provided consultation follow-up to a remote ophthalmic subspecialist.

Results: Of 222 eyes, OCT-B confirmed follow-up in 86.94%. 88.3% of subjects had referable eye pathology: 23.33% to general or specialty eye clinic and 65% to telemedicine. CR glaucoma referral based on OCT-B scan, VCDR and NFL defects was compared to OCT-B referral based on VCDR ≥0.65. Cohen's kappa was 0.546 with 30% disagreement. Compared to CR, OCT-B generated VCDR had a 91.1% specificity and 42.3% sensitivity in detecting glaucoma. VCDR, IOP, NFL, and GCL measurements were significantly correlated with CR glaucoma referral ($p<0.05$). Only VCDR, NFL, and GCL were significantly correlated with Maestro 1 glaucoma referral ($p<0.05$).

Conclusions: OCT-B images provide valuable added diagnostic information about referrals in glaucoma. Its ability to capture greater depth of information about the eye, such as NFL and GCL measurements, compared to traditional two-dimensional retinal photography, warrants consideration for OCT-B as a replacement for non-mydriatic retinal photography as the gold standard in ophthalmic diagnostics. Further studies can investigate the utility trend analysis of OCT-B in predicting VTD's progression over time.

CONTROL ID: 3706497

SUBMITTER (NAME ONLY): Marian Blazes

TITLE: Higher rates of strabismus surgery and residual amblyopia in children with Medicaid using the IRIS Registry

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Blazes, M. Lacy, A.Y. Lee, C.S. Lee, K. Tarczy-Hornoch, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|K. Tarczy-Hornoch, Seattle Children's Hospital, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Timely strabismus diagnosis may improve amblyopia outcomes or prevent need for surgery. We assessed factors associated with delayed diagnoses and worse outcomes in pediatric strabismus.

Methods: We analyzed electronic health record data from the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight), including children ≤10 years with exotropia or esotropia diagnosis codes. Primary outcome was age at strabismus diagnosis. Associations between strabismus surgery or residual amblyopia and race/ethnicity, insurance, population density, and access to pediatric ophthalmology were analyzed using multivariable linear, logistic regression, and survival analysis.

Results:

Of 161,600 children with new diagnosis of esotropia (107,005) or exotropia (54,595), 43.5% were diagnosed before age of 4. Esotropic Hispanic, Black, and Asian children were diagnosed an average of 5.2 (95% CI: 2.8, 7.5),14.1 (11.2, 17.1) and 8.2 (3.2,13.3) weeks earlier compared to White children, and those with Medicaid were diagnosed 9.5 (7.9,11.2) weeks earlier compared to those with commercial insurance. Exotropic Hispanic and Asian children were diagnosed 10.6 (7.4, 13.8) and 40.9 weeks (35.3, 46.6) later than White children, and Medicaid patients (vs. commercial insurance) 12 weeks earlier (9.5, 14.4). The hazard ratio of strabismus surgery for Medicaid vs. commercial insurance was 1.28 (1.23, 1.32) for esotropia and 1.22 (1.17, 1.27) for exotropia.(Figure) Odds of developing residual amblyopia were significantly higher in children with Medicaid vs. commercial insurance both for esotropia [OR 1.75; 95%CI 1.68, 1.8] and exotropia (1.57; 1.46, 1.69).(Table) Controlling for age of strabismus diagnosis had minimal impact on our results.

Conclusions:

Strabismic children with Medicaid did not appear to have a delayed diagnosis yet were more likely to require surgery and develop residual amblyopia.

CONTROL ID: 3706503

SUBMITTER (NAME ONLY): Mohamed Moustafa

TITLE: 12/15-Lipoxygenase Contributes to Retinal Neuronal Dysfunction in Diabetic Retinopathy

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a neurovascular complication of diabetes with limited therapeutic options due to lack of neuroprotection. We have established the role of 12/15Lipoxygenase (12/15-LO) in inducing microvascular dysfunction in DR. The purpose of this work was to characterize the role of 12/15-LO- metabolite 12-hydroxyeicosatetraenoic acids (12-HETE) in retinal neuronal dysfunction in DR.

Methods: We generated diabetic mouse model that lacks 12/15-LO ($Ins2^{Akita}$/12/15-$LO^{-/-}$). The functional alterations of retinal ganglion cells (RGCs) in diabetic ($Ins2^{Akita}$) mice were assessed using Electroretinogram (ERG) compared to control and ($Ins2^{Akita}$/12/15-$LO^{-/-}$). We also evaluated retinal thickness in hematoxylin and eosin stained retinal sections from various mouse groups using image-J. To understand the pathological role of 12-HETE in diabetes-induced visual impairment, we characterized retinal expression of the 12-HETE receptor G-protein coupled receptor 31 (GPR31) in retinal sections using specific antibody. Colocalization of GPR31 with RBPMS marker of RGCs was also performed. Moreover, we evaluated specific RGC protein Brn3 in retinas of various groups by Western blots. N=3-8.

Results: The total thickness of retina (from the inner limiting membrane or ILM to retinal pigment epithelium or RPE) was significantly reduced in central and peripheral retina of diabetic mice compared to the age-matched control retina (207± 7 vs 254±29 μm in central retina and 172±12 vs 216±31 μm in peripheral retina). While the thickness of inner retina (from ILM to outer plexiform layer or OPL) was also significantly reduced in diabetic mice compared to control (97 +5 vs 133+4 mm), the thickness of outer retina (from OPL to RPE) was not altered. Deletion of 12/15-LO preserved total and inner retina thickness in $Ins2^{Akita}$/12/15-$LO^{-/-}$ mice (258+14 and 125+10 mm respectively in central retina). ERG studies showed significant decrease of the peak amplitudes of pSTRs elicited by moderately high stimuli in diabetic mice. Deletion of 12/15-LO KO partially reversed the reduced amplitudes of pSTRs across a range of light intensities. Immunostaining manifest GPR31 is primarily localized in RGCs and Muller cells. Western blot showed 12/15-LO deletion restored retinal expression of Brn3 in diabetic mice.

Conclusions: 12/15-LO contributes to neuronal dysfunction and could be a therapeutic target to prevent visual impairment in DR.

CONTROL ID: 3706506
SUBMITTER (NAME ONLY): Alisa Patton
TITLE: Survey of Alternative Treatments for Glaucoma
Patton, A.; Pandher, M.; Khouri, AS
SESSION TITLE: Pharmacology/cellular mechanisms
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Patton, M. Pandher, A. Khouri, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|
Commercial Relationships Disclosure: Alisa Patton: Commercial Relationship: Code N (No Commercial Relationship) | Meher Pandher: Commercial Relationship: Code N (No Commercial Relationship) | Albert Khouri: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Glaucoma is a common cause of irreversible blindness worldwide and new treatments are still being developed. Interest in and use of “alternative” treatments for many diseases by adults in the US has grown. The purpose of this study is to evaluate the prevalence of patient use of alternative treatments for glaucoma.
Methods: A survey was adapted from two prior surveys on alternative treatments, one validated and one published in an AAO study. Surveys were administered from November-December 2021 to patients of the Rutgers Department of Ophthalmology and Visual Science glaucoma clinic. Surveys were administered in an interview format with medical students reading survey questions to patients in a private room.
Results: A total of 100 survey results were collected and analyzed. Average age of respondents was in their 60s, with the majority having glaucoma for 10 years or less (Table 1). Of respondents, 95% use at least 1 prescription eyedrop for glaucoma and 68% had prior surgery to treat their glaucoma. Data showed that 32% reported using nonconventional therapies to treat their glaucoma. Of those who use nonconventional therapies, the most common were use of vitamins (84.4%), changes to diet (28.1%), exercise (12.5%) and use of cannabis (18.8%) (Table 2). Common vitamin supplements used included Vitamins A, B, C, D, Vitamin B12, multivitamins, Turmeric, Omega 3, CoQ10, AREDS 2 (Age-Related Eye Disease Vitamins), and an eye specific formulation with bilberry, lutein and antioxidants. When asked if patients believed their use of nonconventional therapies lowered eye pressure, halted worsening of glaucoma, improved vision, or worked in general, most patients were unsure (43%, 59%, 53.1%, and 53.1% respectively). Very few patients discussed use of nonconventional therapies with their doctor (6.3%). Patients answered they were only “somewhat confident” that their dietary supplements would do as they claim (53%) or that their supplements are safe to consume (46.9%).
Conclusions: The most common alternative treatment for glaucoma is vitamins followed by diet changes and cannabis. One in three glaucoma patients use alternative treatments, yet less than a tenth discussed it with their doctor, and most were unsure whether it had a definitive effect on their glaucoma. This indicates a need for increased research in the space as well as patient education on this evolving area of treatment.

CONTROL ID: 3706507

SUBMITTER (NAME ONLY): Diana Moukaddem

TITLE: Comparison of diurnal variations in ocular biometrics and intraocular pressure between hyperopes and non-hyperopes

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Moukaddem, N. Strang, L. Gray, Department of Vision Sciences, Glasgow Caledonian University, Glasgow, UNITED KINGDOM|P. McGraw, C. Scholes, School of Psychology, University of Nottingham, Nottingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Circadian variation in ocular biometry and intraocular pressure (IOP) is well documented and is thought to play an important role in refractive error development. While previous studies have compared emmetropic and myopic subjects, little is known about circadian variation in hyperopia. In this study, we examine the diurnal variation of ocular biometry and intraocular pressure in subjects with and without hyperopia.

Methods: Pre-presbyopic adults (mean (±SD) age 24.00 ±3.89 years) participated; 18 subjects were hyperopic (MSE ≥ +1.25 DS; mean group MSE = +4.33 ± 2.24 DS) and 17 were non-hyperopes (MSE < +1.25 DS; group mean MSE = -1.44 ± 2.27 DS). Nine of the non-hyperopes were myopes. Subjects had the following ocular parameters measured at 6 equally spaced time points between 8am and 9pm: Choroidal thickness (ChT) in the nine regions defined by the EDTRS protocol across the central 30° of fundus, axial length (AL) and IOP.

Results: Group mean AL increased through the morning until 1:12pm ± 13min, and decreased throughout the rest of the day, in both groups. Group mean IOP decreased throughout the day in both groups as well. Group mean sub-foveal ChT reached a minimum value at 3:41pm ±14 min in both groups. However, peripheral ChT was different between the groups: in the hyperopic group, mean peripheral ChT reached a minimum at 6:15pm±13min, while in the non-hyperopic group it reached a minimum at 1:12pm±13min. Diurnal variation amplitudes was not statistically different between hyperopes and non- hyperopes for AL (33.89 ± 16.85μm vs 35.29 ± 29.18μm), sub-foveal ChT (19.72 ± 9.29 μm vs 22.77 ± 11.44μm), peripheral ChT (15.12 ± 9.43μm vs 13.26 ± 5.8μm), or IOP (4.17 ± 1.82mmHg vs 4.82 ± 2.1mmHg).

Conclusions: Diurnal variation of peripheral ChT in hyperopic subjects shows a phase-delay when compared to the non-hyperopic group. This phase-delay aligns the peripheral diurnal variation in ChT more closely to the diurnal variation in AL. This is consistent with ocular growth studies in young chicks (Nickla, 2006) and pre-presbyopic humans (Chakraborty et al., 2012) where ChT and AL cycles phase-align in order to slow their growth response to ocular defocus.

CONTROL ID: 3706512

SUBMITTER (NAME ONLY): Eunice Sze Yin Ng

TITLE: Impaired Cathepsin D evidenced in iPSC-derived RPE cells of STGD1 patients

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Ng, J. Hu, K. Frei, Z. Jiang, M.B. Gorin, A. Matynia, R.A. Radu, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|E. Ng, J. Hu, K. Frei, Z. Jiang, M.B. Gorin, A. Matynia, R.A. Radu, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recessive Stargardt disease (STGD1) is an inherited maculopathy caused predominantly by mutations in the ABCA4 gene. The buildup of auto-fluorescent lipofuscin within the retinal pigment epithelium (RPE) is a pathological hallmark of STGD1. Daily phagocytosis of outer-segments membranes requires a functional endolysosomal system to prevent additional stress on the RPE. Cathepsin D (CatD) is a primary lysosomal protease responsible for protein degradation in the RPE. Both CatD activity and protein maturation are dependent on acidic pH in the endolysosomal compartments. We previously reported impaired maturation and reduced activity of CatD in the STGD1 mouse model ($Abca4^{-/-}$). Here, we sought to investigate CatD activity using induced pluripotent stem cell (iPSC)-derived RPE cells from three STGD1 patients.

Methods: Immature CatD protein was evaluated by immunostaining in iPSC-RPE cells from STGD1 patients with confirmed ABCA4 mutations, and unaffected control (no ABCA4 mutations) at 1-and 2-mo in-culture. Distribution of immature CatD with endolysosomal markers was assessed in iPSC-RPE cells by immunocytochemistry using super-resolution and confocal microscopy. Lysosomal pH was measured using LysoSensor Yellow/Blue DND-160 ratiometric probe (n=3), and CatD functional activity by fluorometric assay (n=4-7) in iPSC-RPE cells. Statistical significance was determined by ANOVA testing with Tukey-Kramer post-hoc analysis.

Results: At 1- and 2-mo, STGD1 iPSC-RPE cells exhibit aggregation of immature CatD. Interestingly, immature CatD in STGD1 iPSC-RPE cells co-localizes with both Rab5 and Lamp1 endo-lysosomal markers respectively. In contrast, immature CatD only co-localizes with the early endosome marker Rab5 in control iPSC-RPE cells. Lysosomal pH was elevated in all three STGD1 patients' iPSC-RPE cells vs control ($p<0.05$). Notably, CatD functional activity was significantly reduced ($p<0.05$) in two of the donor STGD1 iPSC-RPE cell lines compared to control.

Conclusions: Consistent with studies in the STGD1 mouse model, we provide further evidence for endo-lysosomal dysfunction in STGD1 patient-derived iPSC-RPE cells, mediated by CatD deficiency. Improper localization of immature CatD coupled with reduced functional activity indicates an amplified degrative burden in STGD1 RPE cells. These findings support the contribution of CatD in developing a STGD1 phenotype and suggest its potential as a therapeutic target.

CONTROL ID: 3706520

SUBMITTER (NAME ONLY): Michelle Ko

TITLE: Demographic Factors Associated with Treatment Modalities in California Medicare Beneficiaries with Diabetic Retinopathy

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.Y. Ko, C. Felix, A.L. Coleman, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|F. Yu, H. Hosseini, A.L. Coleman, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the association of demographic factors with the use of diabetic retinopathy (DR) treatments in the 2017 California Medicare beneficiaries diagnosed with DR.

Methods: The study population included all Medicare beneficiaries diagnosed with DR with at least one part B claim in California in 2017, using data obtained from the Centers for Medicare & Medicaid Services (CMS). The diagnosis of DR was based on the International Classification of Diseases 10th Revision, Clinical Modification (ICD-10-CM) diagnosis codes. The demographic factors included sex (male, female) and race (White, Black, Asian, Hispanic, Other). The outcomes of interest were major DR treatment modalities, including anti-VEGF intravitreal injections (IVI), laser photocoagulation, panretinal photocoagulation (PRP), and vitrectomy, which were identified based on the Healthcare Common Procedure Coding System (HCPCS) codes or the Current Procedural Terminology (CPT) codes. Multivariable logistic regression modeling was performed to examine the association between demographic predictors and use of DR treatments, adjusting for age, sex, race, and presence of hypertension.

Results: There were 83,085 Californian Medicare DR patients, of which the majority had type 2 DR (78,233, 94.2%). Compared with White DR patients, all other racial groups were less likely to receive the IVI treatment in the adjusted analysis: Asian (odds ratio[OR]=0.65, $p<0.001$), Black (OR=0.83, $p<0.001$), and Other (OR=0.83, $p=0.005$); but were more likely to receive laser photocoagulation: Hispanic (OR=1.84, $p<0.001$), Other (OR=1.34 $p=0.0035$), Black (OR=1.23, $p=0.0245$), and Asian (OR=1.19, $p=0.0033$), and to receive PRP: Hispanic (OR=2.27, $p<0.001$), Black (OR=1.68, $p<0.001$), Other (OR=1.44, $p=0.0004$), and Asian (OR=1.40, $p<0.001$). Compared with male DR patients, females were less likely to receive all types of DR treatment: OR=0.89 ($p<0.001$) for IVI, OR=0.85 ($p<0.001$) for PRP, and OR=0.58 ($p=0.0002$) for vitrectomy, except for laser photocoagulation (OR=1.0, $p=0.95$).

Conclusions: Among all California Medicare DR patients in 2017, Black, Asian, Hispanic, or Other -identifying patients were generally less likely to receive IVI but more likely to receive laser photocoagulation, and PRP compared to their White counterparts. Female patients were less likely to receive IVI, PRP, and vitrectomy compared to their male counterparts.

CONTROL ID: 3706521

SUBMITTER (NAME ONLY): Cynthia Yu-Wai-Man

TITLE: High concentration of adrenaline blocks key cell cycle genes and exhibits potent antifibrotic and vasoconstrictor effects in glaucoma surgery

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Yu-Wai-Man, K. Thong, P. Andriesei, J. Ng, P.G. Hysi, King's College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Adrenaline is a sympathomimetic that is used in the irrigating solution to maintain pupil dilation during cataract surgery, and as a vasoconstrictor to decrease the risk of bleeding (Xylocaine- Adrenaline 0.0005%). It is less cytotoxic than Mitomycin-C and 5-Fluorouracil, which are currently used to prevent scarring in glaucoma surgery. We hypothesise that adrenaline could also have antifibrotic effects in glaucoma surgery.

Methods: Adrenaline (0% to 0.05%) was tested in fibroblast-populated collagen contraction and cell viability assays. Human Tenon's fibroblasts were treated with Adrenaline 0%, 0.0005%, 0.01% for 24 hours and mRNA was sequenced on the Illumina NextSeq 2000. FASTQ files were aligned to the human genome UCSC hg38 using RNA-STAR 2.5.2b. Differential expression was carried out using DESeq2. Adrenaline 0.05% (0.1 ml) was also injected subconjunctivally in 3 patients during trabeculectomy, Baerveldt tube and Microshunt surgeries, and the patients were monitored for ocular and systemic adverse effects. Two-tailed Student's t-test was used for statistical analyses.

Results: There was a dose-response decrease in fibroblast contractility: matrices decreased to 47.4% ($p=0.0002$) and 86.6% ($p<0.0001$) with Adrenaline 0.0005% and 0.01%, respectively, compared to control (0%) where matrices decreased to 25.2%. There was no significant decrease in cell viability even at high drug concentrations ($p>0.05$). High quality RNA was extracted (RIN≥ 9.4) and principal component analysis revealed tight clustering for each drug concentration. Adrenaline 0.01% significantly upregulated 25 G1/S genes and 11 S-phase genes, and downregulated 23 G2-phase and 17 M-phase genes ($p<0.05$) (Fig 1A). Adrenaline 0.05% also caused a significant decrease in conjunctival vascularity and there was no significant change in pupil size, pulse, blood pressure, and respiratory rate during glaucoma surgery ($p>0.05$) (Fig 1B).

Conclusions: Adrenaline is a safe and cheap antifibrotic drug (£1 per vial) that significantly blocks key cell cycle genes when used at high concentrations. Adrenaline inhibits the proliferation of fibroblasts, which enter a period of growth arrest but do not die. Unless contraindicated, we recommend subconjunctival injections of Adrenaline 0.05% to 0.1% in all glaucoma surgeries. Future aim is to include adrenaline in clinical trials of new antifibrotic drugs.

CONTROL ID: 3706522

SUBMITTER (NAME ONLY): Eli Peli

TITLE: Scotoma Replacement: simulation of vision with photoreceptor scotoma

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Peli, R. Goldstein, J. Jung, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Most simulations of vision with scotomas are wrongly represented as black patches over the image. While paracentral scotomas are not explicitly observable by patients, central scotomas due to photoreceptor damage are reported as “blurred” vision. Pyramidal models representing the multiscale contrast processing of the visual system have been used to simulate vision with field loss. However, these simulations blended the low frequency image content, without completely removing it. Here, we present a physiologically plausible computation scheme for scene appearance with photoreceptor scotomas.

Methods: After the pixel values in scotomatous areas in an image are replaced with “not a number” (NaN), we apply a pyramidal model (Peli, JOSA 1991, 2001) in the spatial domain. The interaction of the NaN with the pyramidal structure results in a simulated image that replaces the scotoma.

Results: Content from outside the scotomatous area is drawn into the scotoma by the response of cells higher in the visual pathway centered within the scotoma but with wide receptive fields extending outside the scotoma. The resulting simulation with no black patch is consistent with patients’ descriptions (Figs 1 & 2). Due to the high spatial correlation typical of natural images, the replacement image is highly consistent with the elided part of the scene. The areas outside the scotomatous area are seen by the residual functioning normal peripheral low-resolution retina. The result is a filling-in like effect without any cortical processing or adaptation.

Conclusions: The simulations provide insight into the lack of visibility of scotomas and further point to possible distinctions between field loss due to photoreceptor loss and higher cells loss (Peli, ARVO 2020).

CONTROL ID: 3706525

SUBMITTER (NAME ONLY): Georgie Hollitt

TITLE: Attitudes towards glaucoma genetic risk assessment in unaffected individuals

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Genetic testing for diseases with complex inheritance such as glaucoma will become increasingly accessible with the development of polygenic risk scores (PRS) testing. Integrating polygenic risk scores (PRS) into healthcare has the potential to stratify an individual's risk of glaucoma across a broad population. Glaucoma is the most common cause of irreversible blindness worldwide, therefore effective screening for glaucoma endorsed by the population is highly important. Public acceptability is crucial before PRS testing can be integrated into clinical practice.

Methods: This study assessed the attitude of unaffected individuals towards PRS testing for glaucoma, and sought to identify factors associated with interest in testing. We performed a cross-sectional, questionnaire based survey of 418 unaffected individuals including those with a first-degree relative with glaucoma (n=193), those who had a recent eye examination (n=117), and general members of the community (n=108).

Results: Overall, 71.3% indicated an interest in taking a polygenic risk test for glaucoma. Interest was more likely in those who believed glaucoma to be a severe medical condition (OR 14.58, 95%CI (1.15-185.50), p=0.039), those concerned about developing glaucoma (OR 4.37, 95%CI (2.32-8.25), p<0.001), those with an intention to take appropriate measures regarding eye health (OR 2.39, 95%CI (1.16-4.95), p=0.019), and those preferring to know if considered to be at-risk or not (OR 4.52, 95%CI (2.32-8.83), p<0.001). These findings represent a valuable assessment of general public interest in glaucoma polygenic risk testing, which will be integral to the implementation and uptake of novel PRS based tests into clinical practice.

Conclusions: PRS has the potential to stratify individual risk across a broad population for many common conditions, including glaucoma. We found positive interest toward glaucoma PRS testing among three different groups of unaffected individuals from the community and have identified possible target populations for initial clinical implementation. These findings support the clinical implementation of polygenic risk scores for glaucoma to reduce irreversible vision loss.

CONTROL ID: 3706541

SUBMITTER (NAME ONLY): Marcus Turner

TITLE: Long Term Clinical and Visual Field Outcomes Following Minimally Invasive Glaucoma Surgery Combined with Cataract Surgery

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Turner, S. Yonamine, A. Taha, M. Saifee, Y. Han, J. Oatts, University of California San Francisco, San Francisco, California, UNITED STATES|G. Ying, Penn Medicine, Philadelphia, Pennsylvania, UNITED STATES|M. Yang, Prism Eye Institute, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The use of minimally invasive glaucoma surgery (MIGS) during cataract surgery for patients with glaucoma has increased, accelerated by shorter surgical times and potentially less complications compared to glaucoma drainage device (GDD) implantation or trabeculectomy. Additionally, MIGS may help decrease eye drop burden, which is limited by patient adherence and can cause ocular surface toxicity. While several studies have evaluated clinical parameters following MIGS, information about longer term visual field (VF) outcomes is not widely available. The goal of this study is to evaluate long term clinical and VF outcomes following MIGS combined with cataract surgery.

Methods: This is a retrospective single-center case series of patients with glaucoma who had MIGS during cataract surgery between 11/2015 and 10/2019. Inclusion criteria were at least a 1-year of post-operative follow up, no history of prior incisional surgery, a reliable pre-operative VF, and a reliable post-operative VF at least 1 year after surgery. Clinical and VF metrics were assessed pre-operatively and at 1, 2, and 3 years post-operatively. Data collected included visual acuity (VA), intraocular pressure (IOP), number of glaucoma medications, VF mean deviation (MD), pattern standard deviation (PSD), and visual field index (VFI).

Results: 73 eyes of 60 patients were included, 50% male. The most common glaucoma diagnosis was primary open angle glaucoma (81%). MIGS devices included iStent, Trabectome, and Cypass Micro-Stent. Mean±SD IOP before surgery was 16.8±3.6 mmHg on 2.4±1.3 medications. At 3-year follow up (n=34 eyes), mean IOP was 16.4±2.9 mmHg (P=0.07) on 1.5± 1.4 glaucoma medications (P<0.001). Baseline VF metrics included MD of -6.2±5.9 dB, PSD of 5.3±4.0 dB, and VFI of 84±19%. There were no significant changes in MD, PSD, or VFI over time compared to baseline. VA improved from LogMAR 0.19±0.14 pre-operatively to 0.08±0.15 post-operatively (P<0.001).

Conclusions: Over the 3 year post-operative period of our cohort, MIGS combined with cataract surgery was associated with stable VF metrics as well as stable IOP with significant reduction in the number of glaucoma medications.

CONTROL ID: 3706544

SUBMITTER (NAME ONLY): Daniel Hass

TITLE: Metabolic ecosystems exist between retina and RPE in vivo

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Hass, C. Bisbach, J.B. Hurley, Biochemistry, University of Washington, Seattle, Washington, UNITED STATES|E. Giering, VA Puget Sound Health Care System Seattle Division, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our lab has proposed a working model for a metabolic ecosystem between the retina and retinal pigment epithelium (RPE). In this model, lactate derived from photoreceptor glycolysis fuels energy metabolism and minimizes glycolysis in RPE. We based this model on findings from ex vivo retina tissue and cultured RPE cells. The tissue microenvironment is different in vivo and ex vivo. These differences could influence metabolism and affect the physiological relevance of our model. In this study we directly evaluate the metabolic ecosystem hypothesis in vivo using ^{13}C-labeled glucose infused into the circulation of wild-type mice and mice lacking photoreceptors.

Methods: We infused a 100 mg/kg bolus of $^{13}C_6$-glucose though external jugular catheters in freely moving 3 month-old C57BL/6J or C57BL/6J; AIPL1$^{-/-}$ mice. Photoreceptors degenerate by 1 month of age in AIPL1$^{-/-}$ retinas. We euthanized mice 1-, 2-, 3-, or 5-minutes post-infusion and collected retina and eyecup (RPE, choroid, and sclera) tissue. We extracted and derivatized metabolites from both tissues then assessed metabolite abundance and ^{13}C labeling with gas chromatography-mass spectrometry.

Results: Following the infusion, ^{13}C labeling is saturated at the earliest time points on glycolytic intermediates in retina and eyecup tissue. In contrast, labeling of TCA cycle intermediates accumulates linearly over 5 minutes, suggesting this time period is optimal for assessing differences in ^{13}C flux. We compared ^{13}C labeling on C57BL6/J and AIPL1$^{-/-}$ eyecup tissue 3 minutes following a $^{13}C_6$-glucose infusion. If photoreceptor-derived lactate is a metabolic intermediate in the eyecup, ^{13}C labeling of downstream intermediates should decrease in AIPL1$^{-/-}$ eyecups. In AIPL1$^{-/-}$ eyecups, ^{13}C enrichment is significantly higher in middle glycolytic intermediates and significantly lower on late glycolytic intermediates (lactate, pyruvate) and TCA cycle intermediates.

Conclusions: Our data illustrates that without photoreceptors, flux of glucose through glycolysis to phosphoenolpyruvate increases in eyecup tissue. In contrast, flux of ^{13}C from glucose to lactate, pyruvate, and TCA cycle intermediates decreases. This disconnect in eyecup glucose metabolism in vivo can be explained by shuttling of photoreceptor-derived lactate to feed RPE metabolism. This is the first experimental evidence that a glucose/lactate metabolic ecosystem occurs in a mammalian eye in vivo.

CONTROL ID: 3706556

SUBMITTER (NAME ONLY): Victor Sanchez

TITLE: Ocular Surface Sphingomyelinases, Meibum and Tear Sphingolipids, and Clinical Parameters of Meibomian Gland Dysfunction

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Sanchez, New York University Grossman School of Medicine, New York, New York, UNITED STATES|V. Sanchez, Ophthalmology, Miami Veterans Administration Medical Center, Miami, Florida, UNITED STATES|A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Galor, Ophthalmology, Miami Veterans Administration Medical Center, Miami, Florida, UNITED STATES|K. Jensen, Ophthalmology, Miami Veterans Administration Medical Center, Miami, Florida, UNITED STATES|K. Mondal, N.A. Mandal, The University of Tennessee Health Science Center Department of Ophthalmology Hamilton Eye Institute, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: The lipid composition of meibum and tears is believed to play a role in meibomian gland dysfunction (MGD) and dry eye (DE). Sphingomyelinases (SMase) are enzymes that participate in the metabolism of sphingolipids (SPL), which have structural and bioactive functions on the ocular surface. We prospectively analyzed the tears of individuals with good versus poor meibum quality and quantified the activity of SMases with acidic (aSMase) and neutral (nSMase) pH optimums. We predicted that SMase expression would differ in individuals with good versus poor meibum quality.

Methods:

Participants were grouped by meibum quality (n=25 controls; n=25 with poor quality, MGD group). Meibum was forcefully expressed and collected on a cotton swab and tears were collected on Schirmer strips. Activity of tear SMases were determined by Amplex™ Red Sphingomyelinase Assay Kit (Thermo Fisher). DE symptoms and signs were assessed in a comprehensive manner. First, SMase expression between the MGD and control groups was compared. Next, correlations were conducted to examine relationships between SMases and SPL composition determined previously from meibum and tears. Finally, linear regression analyses examined how DE symptoms/signs relate to SMase expression.

Results: The mean population age was 57 ± 9 years; 84% identified as male, and 38% as white. Demographics were similar between the groups. aSMases (23,748 RFU, IQR=26,392 vs. 4,205 RFU, IQR=13,341, $p<0.001$) and nSMases (30,893 RFU, IQR=51,181 vs. 0 RFU, IQR=6263, $p<0.001$) expression in tears was greater in the control versus MGD group. SMase expression correlated with compositional changes in meibum and tear SPL. In meibum, SMases positively correlated with Sph (aSMase, $\rho=0.45$, $p<0.001$; nSMase, $\rho=0.45$, $p<0.001$). In tears, SMase negatively correlated with SM (aSMase, $\rho=-0.30$, $p<0.05$; nSMase, $\rho=-0.29$, $p<0.05$) and positively with S1P (aSMase, $\rho=0.51$, $p<0.001$; nSmase, $\rho=0.49$, $p<0.001$). Higher nSMase expression correlated with more severe DE symptoms (Dry Eye Questoinnaire-5; $\rho=0.29$, $p<0.05$) but less severe meibomian dropout (nSmase, $\rho=-0.35$, $p<0.05$).

Conclusions: SMase expression was reduced in the tears of individuals with MGD and expression levels were associated with altered concentrations of SPLs in meibum and tears. Enzymes of SPL lipid metabolism, such as SMase, may represent a target of therapeutic intervention in the treatment of MGD.

CONTROL ID: 3706561

SUBMITTER (NAME ONLY): Lauren Dalvin

TITLE: The role of early growth response-1 in uveal melanoma viability and treatment resistance to MEK inhibition

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.A. Dalvin, C. Andrews-Pfannkoch, D.R. Miley, S. Adams, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|J.S. Pulido, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Up to 50% of patients with uveal melanoma will develop metastatic disease, and novel treatments are needed to improve survival. We performed cell culture studies to determine the impact of early growth response-1 (EGR1) expression on uveal melanoma (UM) viability and treatment resistance against MEK inhibitors.

Methods: MP46 primary UM cells were maintained in RPMI media. EGR1 knockdown was accomplished using a lentiviral vector with shRNA against EGR1, and trametinib was used for MEK inhibition. Viability was assessed using an ATP assay, with quantitative real-time PCR and capillary western for gene and protein expression analysis, respectively.

Results: Treatment with trametinib or direct EGR1 knockdown alone reduced UM viability to 75% and 73%, respectively, compared to DMSO control. Combining trametinib and EGR1 knockdown further reduced viability to 50% (Figure 1) with in an approximate 2.5-fold reduction in EGR1 gene expression (n=3, p=0.01) and undetectable EGR1 protein expression compared to scramble plus DMSO control. Associated gene expression changes included upregulation of the metastasis suppressor NDGR1 and upregulation of COL11A1 and COX6A2, two of the top twenty genes downregulated in metastasis-developing uveal melanoma according to a subanalysis of The Cancer Genome Atlas (TCGA) consortium data.

Conclusions: Knockdown of EGR1 reduces viability and overcomes resistance to MEK inhibition in UM cell culture, implicating EGR1 as a key effector molecule in UM survival.

CONTROL ID: 3706562

SUBMITTER (NAME ONLY): Shudan Wang

TITLE: Impact of Neurotrophic Keratopathy on Eye Pain and Quality-of-Life-Related Parameters in Patients with Ocular Graft-Versus-Host Disease

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Wang, R.B. Singh, E. Yuksel, T.H. Dohlman, R. Dana, Cornea, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neurotrophic keratopathy (NK) is a degenerative disorder of the cornea characterized by decreased sensory innervation, epitheliopathy, and impaired epithelial healing. In this study, we performed an objective assessment of ocular pain and quality-of-life-related parameters in ocular graft-versus-host disease (oGVHD) patients with or without NK.

Methods: We included 184 oGVHD patients in this retrospective study, including 29 patients with NK defined as decreased corneal sensation as assessed by Cochet-Bonnet esthesiometer. We assessed their records for ocular pain assessment survey (OPAS) scores and clinical parameters, including corneal sensation, corneal fluorescein staining (CFS) score, Schirmer's test, tear break-up time (TBUT), and ocular surface disease index (OSDI) score.

Results: oGVHD patients with NK had lower corneal sensation (3.4±1.4 vs. 5.9±0.3, p≤0.0001), higher CFS scores (6.4±4.2 vs. 4.7±4.0, p=0.040), and lower TBUT scores (1.2±2.1 vs. 2.2±3.1, p=0.049) compared to oGVHD patients without NK and additionally had significantly higher ocular pain intensity scores (OPAS 24 hour average eye pain intensity: 2.0±2.8 vs. 1.1±1.9, p=0.03). Patients with NK more commonly reported burning (0.2±0.3 vs. 0.3±0.4, p=0.021) and sensitivity to light (0.2±0.3 vs. 0.3±0.4, p=0.049) as compared to patients without NK.

Conclusions: Clinical signs of ocular surface disease are worse in oGVHD patients with NK than in oGVHD patients without NK. These patients experience higher intensity ocular pain and lower quality of life-related parameters.

CONTROL ID: 3706563
SUBMITTER (NAME ONLY): Emily Sherry
TITLE: The Level of Eye Care among Eyecare Professionals Themselves
SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E.G. Sherry, L.S. Azeez, D. Mojica, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|
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ABSTRACT BODY:

Purpose: It is unknown how eyecare professionals take care of their own eye health. This study aims to evaluate the presence of eye diseases and the frequency of eye examinations among eyecare professionals.

Methods: In this cross-sectional study, an anonymous questionnaire survey was distributed among eyecare professionals. The following parameters were evaluated in the survey: demographics, family history, medical and surgical history, refractive error, known eye diseases, previous ocular procedures, and previous eye examinations.

Results: 98 eyecare professionals responded which included 50 ophthalmic technicians, 27 ophthalmologists, 7 ophthalmology residents, 6 optometrists, and 8 ophthalmology clinic administrative staff. These included 36 men and 59 women; 3 preferred not to disclose their sex. The mean age was 41.9 ± 12.2 years (range, 21-75 years). Among these, 7.1% had diabetes. Family history was positive for glaucoma in 22.4%, age-related macular degeneration in 14.3%, and retinal detachment in 4.1%. 25 respondents (25.5%) had previous ocular surgery, including refractive surgery (22.4%), retinal laser surgery (2.0%), and cataract surgery (1.0%). Refractive error in the participants included myopia in 61.2%, hyperopia in 13.3%, and astigmatism in 33.7%. These eyecare professionals were known to have dry eye disease (36.7%), cataract (5.1%), amblyopia (3.1%), strabismus (2.0%), diabetic retinopathy (1.0%), and Fuchs' corneal dystrophy (1.0%). Participants' most recent eye exam was within the past 6 months in 16.3%, 6 to 11 months in 25.5%, 1 year in 14.3%, 2 years in 15.3%, or 3 to 5 years in 14.3%. The last eye exam was over five years ago in 11.2%; 4.1% never had any eye exam before. The average number of eye examinations obtained in the past year was 0.7±0.72. In the past five years, the participants had an average of 2.4±2.0 eye examinations and 6.7±9.4 non-ophthalmic medical examinations.

Conclusions: A significant percentage of eyecare professionals studied had personal or family history of eye diseases, especially dry eye disease and glaucoma, respectively. However, almost half of the participants did not have an eye exam in the past year. Eyecare professionals need to be reminded of the maintenance of their own eye health.

CONTROL ID: 3706576

SUBMITTER (NAME ONLY): Andrew Silva

TITLE: Dorsal and ventral stream associations with autistic traits in children

SESSION TITLE: Vision assessment and Clinical applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.E. Harding, C.J. McKinlay, D.W. Dai, S. Nivins, R.K. Shah, Liggins Institute, The University of Auckland, Auckland, NEW ZEALAND|A.E. Silva, B. Thompson, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|C.J. McKinlay, Kidz First Neonatal Care, Auckland, NEW ZEALAND|B. Thompson, Centre for Eye and Vision Research Limited, HONG KONG|

ABSTRACT BODY:

Purpose: The dorsal stream vulnerability hypothesis posits that dorsal stream function is uniquely susceptible to damage during development. Consistent with this idea, an association between autistic spectrum disorder (ASD) and impaired global motion perception has been reported. We explored associations among dorsal stream functions (global motion perception, fine motor function), ventral stream functions (global form perception), and autism spectrum quotient (AQ), a measure of ASD traits, in 9-year-old children born with neurodevelopmental risk factors. We hypothesized that AQ would be associated with dorsal but not ventral stream functions.

Methods: The Children with Hypoglycaemia and their Later Development (CHYLD) study is a prospective cohort study of children born at risk of neonatal hypoglycaemia. At age 9-10 years, 397 children from the cohort completed measures of AQ, global motion (random dot kinematogram) and global form (Glass pattern) perception, fine motor function (Movement ABC, v2), and visual-motor integration (Beery VMI, v6). We used linear regression to quantify the associations among these measures. All models contained an intercept, and interactions with sex, socio-economic status, academic performance at age 9-10, preterm birth, and hypoglycaemia were assessed.

Results: Motion coherence thresholds ($\beta = 0.10$, $R^2 = 0.01$, $p = 0.045$), Movement ABC score ($\beta = -.30$, $R^2 = 0.09$, $p < 0.001$), and the Beery motor subtest score ($\beta = -.23$, $R^2 = 0.09$, $p < 0.001$), were significantly associated with AQ, but the Beery VMI subtest score was not. Additionally, form coherence thresholds interacted with sex ($\beta = 0.43$, $R^2 = 0.07$, $p = 0.001$), such that boys with higher thresholds (worse performance) exhibited higher AQ scores (more ASD traits; $\beta = 0.28$, $R^2 = 0.08$, $p < 0.001$), but no association was observed for girls.

Conclusions: Most measures of dorsal stream function were significantly associated with AQ, such that worse performance predicted higher AQ scores. Additionally, in boys, worse form perception was associated with higher AQ scores. Therefore, while the results support the presence of abnormal dorsal stream processing in children with high AQ, they also suggest that abnormal visual processing associated with high AQ extends beyond the dorsal stream. Further, the results implicate a sex difference in the association between AQ and visual function.

CONTROL ID: 3706585

SUBMITTER (NAME ONLY): Benedicte Merle

TITLE: B vitamins and incidence of advanced AMD: the Alienor Study

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. Merle, S. BARTHES, A. Cougnard-Gregoire, C. FEART, M. DELYFER, J. Korobelnik, C. Delcourt, Bordeaux Population Health, Bordeaux, Nouvelle-Aquitaine, FRANCE|M. DELYFER, J. Korobelnik, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, Aquitaine, FRANCE|

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ABSTRACT BODY:

Purpose: Nutritional status is linked to onset and progression of advanced forms of age-related macular degeneration (AMD). Among various nutrients, higher dietary and plasma status of B vitamins has been associated with reduced AMD risk in several studies, but prospective studies are scarce. We report the associations of dietary intake and plasma status of B vitamins with the incidence of advanced AMD in French elderly subjects.

Methods: The Alienor study is an ongoing population-based cohort of 963 elderly residents of Bordeaux followed every 2-year since 2006. AMD was classified on the basis of color fundus photographs and spectral domain optical coherence tomography examinations (2006-17), and with self-reported AMD (2001-06). Dietary intakes of vitamins B1, B2, B3, B5, B6, B9 and B12 and total energy intake (TEI) were estimated from a 24-hour dietary recall performed at home by trained dieticians (2001). Plasma status of vitamins B6, B9 and B12 were measured from fasting blood sample (1999). Cox models were used to assess associations between B vitamins and AMD. Models were adjusted for age, sex, smoking status, HDL-cholesterol, genetic risk score, oral supplementation for AMD, BMI and physical activity, with additional adjustment for TEI for dietary B vitamins.

Results: Among 861 participants at risk for advanced AMD with available data for B vitamins, 93 (10.8%) developed advanced AMD. At any time after inclusion, the hazard of advanced AMD onset was significantly 28% lower when the intake of vitamin B5 was 1-SD (1.84mg) higher at inclusion (HR=0.72; 95%CI: 0.53-0.99). The hazard of advanced AMD onset was significantly 10% lower when intake of vitamin B6 was 1-SD (0.60mg) higher at inclusion (HR=0.90; 95%CI: 0.81-0.99). No statistically significant associations were found with intakes of other B vitamins.

At any time after inclusion, participants with a normal status for vitamin B9 (≥10 nmol/L) at inclusion had a 2-fold lower hazard of advanced AMD onset compared with participants with a deficient status for vitamin B9 (HR=0.49, 95%CI: 0.25-0.95). Plasma vitamins B6 and B12 were not significantly associated with AMD.

Conclusions: Higher dietary intake of vitamin B5, B6 and plasma vitamin B9 were associated with a lower risk of AMD. Sufficient intakes of B vitamins, mainly B5 (animal products, whole grains) and B6 (whole grains, liver), as well as a normal status of plasma vitamin B9, may help to prevent development of advanced AMD.

CONTROL ID: 3706586

SUBMITTER (NAME ONLY): Jelena Novosel

TITLE: Detecting patients with ocular comorbidities when screening for diabetic retinopathy (DR): an out-of-distribution (OOD) perspective

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Novosel, F. Benmansour, F. Hoffmann-La Roche Ltd., Basel, SWITZERLAND|J. Dai, D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: When screening for DR in a patient population with diabetes, occurrence of ocular comorbidities, such as glaucoma, neuropathy, or age-related macular degeneration, remains possible. We frame the detection of patients with such ocular comorbidities as an OOD detection problem. Here we evaluated 3 state-of-the-art OOD methods for DR screening by using deep learning (DL) models trained from 7-field color fundus photos (7F-CFP).

Methods: Data, including images, from eyes of 37,358 patients with diabetes were analyzed (Inoveon Corporation). Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale and the presence of referable ocular comorbidities (OOD samples) were assessed from 7F-CFP by professional graders. The prevalence of OOD patients was 1%. The data were split into train:tune:test sets (80:10:10).

A DL ResNet-50 model with transfer learning was trained at the image level using all 7F-CFP for either being more than mild DR (mtmDR) or not. Then, we assessed the ability of ResNet-50 to detect OOD samples by 2 methods: (1) uncertainty estimation (UE) using Monte Carlo Dropout (Gal et al, NIPS 2016), and (2) confidence score (CS) using class-conditional Gaussian distributed feature maps and Mahalanobis distance (Lee et al, NIPS 2018). We also trained an OOD binary classification (BC) model to classify patients as having referable ocular comorbidities or not. Performance was assessed with area under the receiver operating characteristic (AUROC) curve, specificity, sensitivity, and precision.

Results: The OOD BC evaluation results are listed in Table 1 and the method shows high sensitivity and specificity. The UE and CS results are illustrated in Figure 1 and both scores show overlapping values for patients with and without referable ocular comorbidities, making the 2 groups inseparable.

Conclusions: UE and CS render limited ability to identify patients with referable ocular comorbidities when the primary DL model is trained for detecting patients with mtmDR. In contrast, the OOD BC model performed better in detecting OOD samples. This indicates that real-world deployment of DL models for mtmDR detection might require an additional model, such as our OOD BC model, that detects patients with referable ocular comorbidities.

CONTROL ID: 3706593

SUBMITTER (NAME ONLY): John Maddison

TITLE: Characterising DARC (Detecting Apoptosing Retinal Cells) spots in glaucoma and healthy eyes

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Maddison, S. Choi, M. Cordeiro, Novai Ltd, UNITED KINGDOM|S. Choi, M. Cordeiro, Glaucoma & Retinal Neurodegnrtn Res Grp, Imperial College, UCL IOO, Western Eye Hsp London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Apoptosis is recognised as one of the earliest pathological processes in glaucoma. DARC technology is a retinal imaging technique the utilises an intravenous fluorescently labelled annexin 5 (ANX776) to identify cells in stress and apoptosis. We have previously shown, using a convolutional neural network (CNN)-aided algorithm, that the quantification of DARC spots (CNN DARC count) can predict progression of glaucoma up to 18 months ahead of OCT RNFL global changes. Here, we assess the qualitative characteristics of CNN-identified DARC spots by comparing their common descriptive measures (DM) in glaucoma and healthy eyes.

Methods: Anonymised retinal images were used from over-40year old glaucoma (n = 28 eyes) and healthy subjects (n = 68 eyes) from the Phase 2 DARC clinical trial (ISRCTN10751859). These subjects were recruited following informed consent, being obtained according to the Declaration of Helsinki and study approval by the Brent Research Ethics Committee. A previously described CNN-aided automated algorithm was used to identify DARC spots. Assessment of DM characteristics included analysis of mean, std (standard deviation), skew, kurtosis, cv (coefficient of variation), bvdist (Euclidean distance from the nearest blood vessel) and the 7 Hu moments from CNN-algorithm identified DARC spots averaged per eye. These DMs were analysed using single logistic regression (SLR) and bootstrapping (n = 1000) to classify glaucoma and healthy eyes.

Results: SLR identified cv as the best independent DM variable (AUC=0.75), with a log-likelihood ratio (LLR) p-value <0.0001. Then applying bootstrapping (n = 1000) to SLR to obtain confidence intervals gave an AUC of 0.75±0.07.

Conclusions: Our findings suggest that standard DMs of CNN-algorithm identified DARC spots (averaged per eye), may be used to classify glaucoma and healthy subjects. The cv DM appeared most promising using SLR, and can be easily applied to continuing DARC studies. In the future it may be possible to use an increased number of features to improve results. Future analysis of planned larger studies using DMs could further help improve disease classification, but these results support use of DM with CNN DARC for glaucoma diagnosis.

CONTROL ID: 3706595

SUBMITTER (NAME ONLY): Soyoung Choi

TITLE: Characterising DARC (Detecting Apoptosing Retinal Cells) spots in Optic Neuritis (ON) and healthy eyes

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: ON is a common feature of Multiple Sclerosis (MS). Around 25% of MS patients present with ON as their initial symptom and approximately 50% of MS patients experience ON. DARC consists of an intravenously administered fluorescent-tagged annexin V (ANX776) which binds to phosphatidylserine, identifying cell stress and apoptosis, with retinal imaging. Here, we sought to differentiate DARC spots in ON subjects from healthy subjects by observing common descriptive measures (DM) of DARC spots identified by a previously described convolutional neural network (CNN)-aided algorithm.

Methods: DARC images were obtained and anonymised from ON (mean age = 46) and healthy (mean age = 48) participants from the Phase 2 DARC clinical trial (ISRCTN10751859). Recruitment of participants was achieved with informed consent, following the Declaration of Helsinki. The study was approved by the Brent Research Ethics Committee. DARC spots were identified from DARC retinal images obtained at 120 minutes after ANX776 administration in ON (n = 12) and healthy (n = 68) subjects using the CNN-aided algorithm. DM characteristics including the mean, std (standard deviation), skew, kurtosis, cv (coefficient of variation), bvdist (Euclidean distance from the nearest blood vessel) and the 7 Hu moments, were analysed on DARC spots from ON (n = 357) and healthy (n = 2457) eyes using two-tailed student t-tests. The distributions of individual spot metrics were then analysed using the two-sample Kolmogorov-Smirnov (KS) test.

Results: The mean, cv and kurtosis ($p \leq 0.0001$) and hu1 and std ($p \leq 0.001$) were found to be significantly different (using the two-sided t-test) between DARC spots in ON and healthy controls. The distributions of the individual metrics analysed using the two-sample KS test, showed a significant difference ($p \leq 0.0001$) between ON and healthy spots for the same variables (mean, cv, kurtosis, hu1 and std).

Conclusions: Our findings indicate that mean, cv, kurtosis, hu1 and std DM analysis of automatically identified DARC spots, can be used to distinguish DARC spots in ON and healthy subjects. Further planned trials with larger ON groups will involve DMs in the analysis between ON and healthy controls; these early results support use of DARC for ON diagnosis.

CONTROL ID: 3706602

SUBMITTER (NAME ONLY): Hrvoje Bogunovic

TITLE: Artificial Intelligence to Identify Retinal OCT Parameters Predictive of Patient Visual Outcomes under a Treat-and-Extend Regimen

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Bogunovic, G.S. Reiter, O. Leingang, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: Treat-and-extend (T&E) has become a dominant treatment regimen in anti-VEGF therapy in neovascular age-related macular degeneration (nAMD). However, retinal morphology and dynamics predictive of patient outcomes are still unclear. We developed and evaluated a predictive model of one-year visual outcomes based on machine learning to determine predictive optical coherence tomography (OCT)-based quantitative biomarkers.

Methods: Patient visual acuity trajectories were modeled with latent class mixed models (LCMM) parametrized with six classes and being a quadratic function of time. Macular OCT volume scans of treatment-naïve eyes, at baseline and four weeks after the first anti-VEGF injection, were analyzed with artificial intelligence (AI). Intraretinal fluid (IRF), subretinal fluid (SRF), pigment epithelial detachment (PED), and subretinal hyperreflective material (SHRM) were quantified using deep learning. Retinal morphology was represented with Early Treatment Diabetic Retinopathy Study (ETDRS) grid-based quantitative measurements to characterize spatial distribution and its change after the first injection. Using the computed set of biomarkers, a model to predict the responders/non-responders was built using a machine learning classifier, and was evaluated with a ten-fold cross-validation

Results: Pooled clinical trial data of 550 evaluable eyes from as many patients, receiving ranibizumab T&E therapy for one year were used. Based on LCMM analysis of visual acuity trajectories, 23% of eyes were considered as clinical non-responders (Figure 1). The developed machine learning model was able to predict the non-responders with an area under the receiver-operating curve (AUROC) of 0.74 (95% CI: 0.71-0.78), corresponding to a conservative operating point with 0.9 specificity and 0.4 sensitivity. The amount of IRF remaining after the first injection at Month 1 was found to be the most important predictive biomarker.

Conclusions: We proposed and evaluated an AI methodology to predict T&E visual outcomes. Predictive retinal OCT biomarkers help explain the different functional results after treatment between patients having similar baseline visual acuity initially. The result of this study is a promising step toward AI-based prediction of patient outcomes and may help to further personalize and optimize anti-VEGF therapy in clinical practice.

CONTROL ID: 3706605
SUBMITTER (NAME ONLY): Jaan Rauer
TITLE: OCT-A characteristics of uveitic noninfectious macular edema
SESSION TITLE: OCT Angiography Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J.O. Rauer, M. Lövestam Adrian, Eye Clinic, Skanes universitetssjukhus Lund, Lund, Skåne, SWEDEN|J.O. Rauer, M. Lövestam Adrian, Ophthalmology, Lunds Universitet, Lund, SWEDEN|
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ABSTRACT BODY:
Purpose: To evaluate the use of the flow density map in Optical Coherence Tomography Angiography (OCT-A) in noninfectious uveitic macular edema.
Methods: Prospective observational study of 11 consecutive uveitis patients, in 16 eyes with 19 disease episodes, measured with density flow OCT-A in the Topcon DRI OCT Triton plus at edema and at remission. Patient mean age and standard deviation (SD) was 39.1 (20.6) years, where 6/11 (55%) were females. Layers were measured with the built-in automatic software layer segmentation as superficial, deep, outer and choriocapillaris, regardless of edema configuration. Density values in the nasal, central, temporal, superior and inferior macular area were recorded. Main outcome measures were visual acuity (VA) at edema and remission, OCT central retinal thickness (CRT) decrease and difference in layer density OCT-A flow at edema and remission. Mean (SD), median and interquartile range (IQR) as well as Wilcoxon rank sum and rank sum exact test was computed.
Results: The mean (SD) duration of uveitis disease at edema was 7.9 (6.8) years. The uveitis was anterior in 4/11 (36%) and intermediate in 7/11 (64%), where onset was sudden in 5/11 (45%) and insidious in 6/11 (55%). Median (IQR) VA was 0.50 (0.40, 0.75) at edema and 0.90 (0.70, 1.00) at remission, where mean (SD) OCT CRT decreased 154 µm, from mean (SD) 429 (114) µm to 275 (45) µm ($p < 0.001$).

The mean (SD) density flow in the choriocapillaris was significantly lowered $p = 0.001$ in the central macular area in edema 44.31 (5.63), compared to remission 50.59 (5.04), see Table 1.

Table 1: Choriocapillaris density flow in edema and remission per macular area

Macular area	Edema(1)	Remission(1)	p-value(2)
Nasal	51.05 (3.29)	53.58 (2.72)	0.015
Central	44.31 (5.63)	50.59 (5.04)	0.001
Temporal	53.30 (3.91)	53.99 (1.33)	0.48
Superior	52.18 (3.97)	52.97 (2.16)	0.54
Inferior	53.21 (3.36)	53.00 (2.12)	0.75

1 Mean (SD)
2 Wilcoxon rank sum exact test; Wilcoxon rank sum test
Conclusions: In eyes with noninfectious uveitis with macular edema the choriocapillaris density flow in the central macular area is decreased in both anterior and intermediate uveitis. The decreased flow might be a part of the patophysiology of the macula in uveitis. If this reflects the severity or duration of the macular edema, then furhter work can show if it can be used as marker for treatment dosage.

CONTROL ID: 3706609

SUBMITTER (NAME ONLY): Xiaoyuan Ren

TITLE: The potential role of rod-derived cone viability factor long (RdCVFL) in treating retinitis pigmentosa as a thioredoxin-like protein

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Ren, T.D. Leveillard, Department of Genetics, Institut de la vision, Paris, Île-de-France, FRANCE|X. Ren, A. Holmgren, E.S. Arnér, Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is a retinal degenerative disease characterized by the progressive loss of photoreceptors. It affects more than 1 million people worldwide. Despite the genetic heterogeneity, one common phenomenon is shared in RP that the death of rods always precedes the death of cones. The mystery was solved by the discovery of rod-derived cone viability factor (RdCVF) encoded by NXNL1 gene acting as a tropic factor secreted by rods to promote the utilization of glucose by cones, thus sustaining the survival of cones. Interestingly, NXNL1 encodes two proteins due to alternative splicing, the short form RdCVF, and the long-form RdCVFL with a typical thioredoxin (TXN)-like structure. It has been shown by our group that adeno-associated virus (AAV)-mediated expression of RdCVF and RdCVFL could be a potential gene therapy of RP. The short protein, RdCVF, has been well-studied, however, the mechanism of action of RdCVFL remains unclear.

Methods: The RdCVFL was recombinantly purified. Then the biochemical property of RdCVFL as a TXN-like protein was examined by coupling the two major antioxidant systems, the TXN system and the glutathione (GSH) system. The chaperone activity of RdCVFL was also examed.

Results: RdCVFL can be reduced by TXN and GSH systems, and the reduced RdCVFL exhibited an S-denitrosylase activity. However, it is not a highly selective substrate of both systems, showing little activity to reduce cystine, oxidized-GSH, and S-glutathionylated proteins. Interestingly, RdCVFL exhibited a prominent chaperone activity in thermal aggregation assays.

Conclusions: RdCVFL, as a TXN-like protein, may participate in antioxidant defense and redox signaling regulation in the retina. In addition, its chaperone activity may contribute to protein quality control during outer segment renewal or in the prevention of aggregation of the microtubule protein τ (TAU).

CONTROL ID: 3706614

SUBMITTER (NAME ONLY): Magdalena Schneider

TITLE: Induced ablation of scleral TGF-β signaling in mutant mice increases susceptibility to IOP-induced optic nerve damage

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Schneider, A.E. Dillinger, E.R. Tamm, Human Anatmoy and Embryology, Universitat Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Axonal optic nerve (ON) damage in glaucoma is characteristically associated with increased amounts of active Transforming Growth Factor-β2 (TGF-β). Data from Quigley et al., (2015) indicate that TGF-β-signaling promotes IOP-induced ON damage, an effect that involves remodeling of the sclera. In the present study we investigated the functional role of scleral TGF-β-signaling in glaucoma. To this end we induced ocular hypertension (OHT) in mice with an inducible deficiency of TGF-β receptor type II (Tgfbr2) in scleral fibroblasts.

Methods: $Tgfbr2^{fl/fl}$ ($T2^{fl/f}$) mice with a floxed allele of Tgfbr2 were crossed with Col1a2-CreER (Col1) mice. The mouse Col1a2 promoter is specifically active in fibroblasts, including those of the sclera. 14 days after Tamoxifen (TX) treatment OHT was induced in one eye, using the magnetic-microbead-model. IOP was measured by rebound tonometry. After six weeks of OHT, ON axons were PPD-stained and quantified. Somata of retinal ganglion cells (RGC) were quantified on whole mounts by RBPMS-staining. TGFBR2 and its mRNA were analyzed by western blotting and real time RT-PCR. IOP data was analyzed using one-way ANOVA, mRNA expression, protein synthesis, axon loss (Δaxons) and RGC loss (ΔRGC) were compared using two-tailed students t-tests.

Results: Following TX-treatment, scleral TGF-β RII mRNA and protein were significantly decreased ($p \leq 0.05$). IOP was significantly elevated up to six weeks after injection. No difference in IOP of injected and un-injected eyes could be found between $T2^{fl/fl}$ and $Col1xT2^{fl/fl}$ animals at any timepoint. After six weeks of OHT, reduced numbers of ON axons (11±2%, n=17, $p \leq 0.001$) were seen in OHT eyes in comparison to contralateral eyes. Moreover, OHT also led to a decrease of retinal ganglion cell somata (22,87±9,87%; n = 10; $p \leq 0.001$). Axon loss was significantly higher in mice with a fibroblast specific deficiency of TGF-β RII in comparison to control animals (Δaxons $T2^{fl/fl}$ = 9.29±5.76%; n=9; Δaxons $Col1xT2^{fl/fl}$ = 14.89±4.85%; n=8; $p \leq 0.01$). $\Delta RGC/mm^2$ was not changed in $Col1xT2^{fl/fl}$ mice ($\Delta RGC/mm^2$ $T2^{fl/fl}$ = 22.21±6.49%; n=5; $\Delta RGC/mm^2$ $Col1xT2^{fl/fl}$ = 22.37±15.09%; n=5; p=0.88).

Conclusions: We conclude that the ablation of scleral TGF-β signaling increases the susceptibility to IOP-induced optic nerve damage. Scleral TGF-β signaling in mutant mice appears to be beneficial for ON axon survival in experimentally induced OHT.

CONTROL ID: 3706616

SUBMITTER (NAME ONLY): Rebecca Salowe

TITLE: Rates of Structural and Functional Progression of Glaucoma and Their Risk Factors in an African Ancestry Cohort

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the rates of structural and functional progression in an African ancestry cohort and to determine the risk factors for progression.

Methods: Glaucoma cases in the Primary Open-Angle African American Glaucoma Genetics cohort, with ≥2 retinal nerve fiber layer (RNFL) thickness values and ≥2 mean deviation (MD) measurements over ≥6 months follow-up, were examined. The rates of structural progression (change in RNFL thickness/year) and functional progression (change in MD/year) for each eye were calculated from linear mixed effects models, accounting for inter-eye correlation from the same subject and longitudinal correlation for the same eye over time. Eyes were categorized as slow, moderate, and fast progressors (Table 1). Demographic and clinical risk factors for progression rates were assessed using univariate and multivariate regression models.

Results: A total of 1424 eyes were classified as slow, moderate, or fast progressors (Table 1). The median (inter-quartile) rates of progression were -1.60 (-2.05, -1.15) μm/year for RNFL thickness and -0.40 (-0.44, 0.34) dB/year for MD. In multivariate analysis, faster RNFL progression was independently associated with thicker baseline RNFL ($p<0.0001$), lower (worse) baseline MD ($p=0.005$), and beta peripapillary atrophy ($p=0.04$; Table 2). Faster MD progression was independently associated with higher baseline MD ($p<0.0001$), higher cup-to-disc ratio ($p=0.02$), and lower body mass index ($p=0.0004$; Table 2).

Conclusions: This African ancestry cohort had faster median rates of structural and functional progression than other ethnic groups. Higher baseline RNFL thickness and MD values were associated with faster rates of structural and functional progression, respectively, likely due to a “floor effect,” where progression in early disease exhibits a steeper slope before plateauing in advanced stages. Results highlight the importance of monitoring structural and functional glaucoma progression to provide timely treatment in early disease stages.

CONTROL ID: 3706617

SUBMITTER (NAME ONLY): Pooja Shah

TITLE: Racial disparities in retinal detachment presentation and postoperative outcomes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.M. Shah, S. Vadala, E. Rahman, M.A. Greven, Department of Ophthalmology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Differences in sociodemographic factors contribute to health disparities in various ophthalmic conditions. We hypothesized that racial minorities, compared to white patients, have worse visual acuity outcomes following rhegmatogeneous retinal detachment repair. We conducted a retrospective chart review of patients at a tertiary medical center to compare the presentation and outcomes of retinal detachment repair based on race.

Methods: This study included 186 eyes of 181 patients who underwent primary retinal detachment repair at from 2013 to 2021. Eyes with rhegmatogeneous retinal detachment which underwent repair with at least three months of follow-up were included. Eyes with other visually significant pathology were excluded. Baseline characteristics, surgical repair techniques, and final visual acuity outcomes were recorded. Statistical analyses were performed to identify significant differences between the minority and non-minority patient groups.

Results: 144 patients identified their race as white and 42 patients identified with a minority race. Gender and baseline visual acuity were similar between the two groups. Age (p=.0005) and insurance status (p=.011) were statistically significant differences between the two groups. 91% of white patients had health insurance, while 23.8% of non-white patients had health insurance. Time from evaluation to surgery was significantly longer in non-white patients (p=.027). Minority patients were less likely to be pseudophakic at presentation (p=.003) and at final follow-up (p=.005). Visual outcomes were not significantly different between the two groups.

Conclusions: Although the average final visual acuity did not differ between white and non-white patients undergoing retinal detachment surgical repair, minority patients who underwent operative management were of younger age, more likely to be uninsured, less likely to have cataract surgery before and after repair, and experience longer waiting times for surgical treatment following clinical evaluation. These findings may help increase physician awareness of barriers to ophthalmic surgical care associated with race.

CONTROL ID: 3706619

SUBMITTER (NAME ONLY): Felix Bock

TITLE: Injury dependent immune cell recruitment into the cornea

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Bock, W. Zhang, A.P. Schönberg, F. Bassett, C. Cursiefen, Department of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|F. Bock, C. Cursiefen, Center for Molecular Medicine Cologne (CMMC), Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Pathologic insults like chemical burn, transplant rejection or trauma lead to blindness and to a so called “high risk situation” with increased rejection rates after subsequent corneal transplantation.
All these insults cause different immunological tissue responses. Aim of this study was to evaluate the impact of different types of corneal injuries on immune cell recruitment in the cornea.

Methods: We used 5 kinds of corneal injury models and naïve cornea as the control (n=5). The suture model is the corneal intrastromal placement of three nylon sutures. Alkali burn was induced by 1 M NaOH placed on the central corneal. Incision injury was induced in the central cornea with a linear perforating incision with 1 mm length. Corneal grafts were placed either into an avascular recipient bed as the normal-risk keratoplasty (NR-KPL) or a prevascularized recipient as the high-risk keratoplasty (HR-KPL). 1 week after incision and 2 weeks after other different injuries, corneas were excised and stained with F4/80, CD11c, Ly6G, MHC class II, CD3, CD4 and CD8. Furthermore, the draining lymph nodes (dLN) were analyzed by flow cytometry.

Results: HR-KPL and NR-KPL initiated significantly higher recruitment of F4/80+ macrophages (Mφ), CD11c+ dendritic cells (DCs), Ly6G+ neutrophils as well as MHC II expression compared to all other groups. Suture placement and alkali burn induced only a significant increased recruitment of macrophages compared to incision and naïve eyes. The incision model did not induce a significant increase of any immune cells. Regarding T cell recruitment , only HR-KPL and NR- KPL provoked a significant higher invasion of CD3+CD4+ and CD3+CD8+ T cells, whereas in HR-KPL compared to NR-KPL significantly more CD3+CD4+ T cells were recruited. Interestingly, in the dLNs significantly less DC and Mφ could be detected in all groups compared to control. In contrast, MHC II expression was increased in HR-KPL and NR-KPL on DCs and Mφ. Only in NR-KPL CD8+ T cells were significantly increased compared to all groups.

Conclusions: In this study we established for the first time a comparative corneal immune cell profile of different clinically relevant types of corneal injuries. This immune cell profiles will allow the establishment of a more personalized treatment regimen of high risk patients according to their individual preexisting pathologies.

CONTROL ID: 3706622

SUBMITTER (NAME ONLY): Yiyun Zhou

TITLE: Clinical Ophthalmic Findings in Children with Alström Syndrome

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhou, A.V. Levin, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|A.D. Kline, M. Ferguson, J. Billiet, Greater Baltimore Medical Center Harvey Institute for Human Genetics, Baltimore, Maryland, UNITED STATES|M.L. Collins, Ophthalmology, Greater Baltimore Medical Center, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alström syndrome is a rare autosomal recessive disorder affecting multiple systems including the eyes. Despite knowing the causative gene, ALMS1, the spectrum of its clinical manifestations has not been fully characterized, which has been a challenge due to the great variability of presentation, reduced life expectancy, and the less-than-one-per-million prevalence of this disease. This study aims to summarize the clinical ophthalmic findings in children with Alström syndrome using data from the largest known existing cohort, and to familiarize ophthalmologists with these findings.

Methods: Thirty patients of all ages with a known diagnosis of Alström syndrome participated at biannual multidisciplinary Alström syndrome clinics (2015 – 2020) at a centralized academic center. These patients received comprehensive eye examination by a pediatric ophthalmologist. Clinical data were then extracted and summarized from the charts.

Results: Twenty-five pediatric patients had a median age of 7, ranging from 15 months to 16 years. Among these children, nystagmus (22/25) and photophobia (22/25) are not only the most commonly documented ophthalmic findings, but also the most common first presenting symptoms. Retinal vascular attenuation (19/25) and retinal internal limiting membrane changes (15/25) are the most commonly documented retinal findings. In contrast, only 2 children had documented retinal pigment clumps. Previous misdiagnoses included achromatopsia, cone-dystrophy, cone-rod dystrophy, retinitis pigmentosa, and spasmus nutans.

Conclusions: We believe that knowledge of these clinical findings would benefit ophthalmologists to better recognize this potentially vision-threatening and life-threatening condition.

CONTROL ID: 3706625

SUBMITTER (NAME ONLY): Cornelia Peterson

TITLE: Acute and Chronic Proliferative Vitreoretinopathy Characteristics in a Rabbit Model of Rhegmatogenous Retinal Detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is the most common cause of failure of surgically repaired rhegmatogenous retinal detachment (RRD). Chemically-induced and cell-injection PVR models have been developed, but there is an unmet need for translational models in which to evaluate potential therapies specific to RRD-PVR. The objective of this study was to characterize the histologic and immunohistochemical features of a rabbit model of RRD-PVR at acute and chronic time points.

Methods: Posterior segments of enucleated globes from male and female Dutch Belted rabbits were harvested and frozen or formalin-fixed at 6 hours and 2, 14, and 35 days following unilateral induction of RRD-PVR by vitrectomy and retinotomy followed by retinal cryotherapy and intravitreal platelet-rich plasma injection (n = 8 rabbits/time point); contralateral globes served as controls. Routine H&E and Masson’s trichrome staining and immunolabeling for glial fibrillary acidic protein (GFAP), vascular endothelial growth factor receptor 2 (VEGFR2), CD68, retinal pigment epithelium 65 kDa protein (RPE65), and laminin were performed on all sections, and labeling intensity was scored (0: absent, 1: weak, 2: moderate, 3: strong).

Results: Acute histopathologic changes included intravitreal and intraretinal hemorrhage, heterophilic vitritis, chorioretinitis, and retinal necrosis, while chronic lesions included retinal atrophy, gliosis, subretinal fibrotic membranes, and epiretinal fibrovascular proliferation in the region of the medullary streak. Trichrome-positive fibrillar collagen was present in the subretinal fibrocellular and epiretinal fibrovascular membranes at days 14 and 35 along with increased expression of laminin. Moderate to strong GFAP and VEGFR2 labeling was detected in chronic RRD-PVR lesions. RPE65 expression was absent in dedifferentiated subretinal RPE cells in chronic RRD-PVR lesions.

Conclusions: Histologic features of this rabbit model may effectively simulate important late features of human RRD-PVR including epiretinal and subretinal membrane formation. These findings suggest that developing high-fidelity in vivo models for RRD-PVR is essential to enable further research on targeted treatment interventions.

CONTROL ID: 3706631

SUBMITTER (NAME ONLY): Qiuhua Yang

TITLE: Adenosine receptor 2A-mediated HIF signaling enhances endothelial-to-mesenchymal transition (EndMT) and promotes subretinal fibrosis

SESSION TITLE: AMD Translational Research

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: A number of patients with neovascular AMD (nAMD) do not respond well to standard anti-vascular endothelial growth factor (VEGF) therapy. One of underlying mechanisms is development of fibrosis in nAMD lesion. Thus, therapeutic strategies for the inhibition of subretinal fibrosis are imperative. Our past work shows that knockout/blockade of adenosine receptor 2A (ADORA2A for human/Adora2a for rodents) exhibits anti-inflammatory and anti-angiogenic effects. In this study, we examined whether and how knockout/blockade of ADORA2A/Adora2a suppresses the development of subretinal fibrosis.

Methods: Laser injury-induced mouse choroidal neovascularization (CNV) displays subretinal fibrosis lesions. We performed this model in mice deficient in Adora2a globally or in choroidal endothelial cells (CECs) selectively. We collected RPE/choroid complex of mice at day 7, 21- and 35-days post laser injury, and characterized subretinal fibrosis by immunostaining RPE/choroid complex with antibodies against isolectin B4, collagen I and Acta2. In vitro, we initiated EndMT by treating cultured human CECs with TGFβ-2. With loss- and gain-of function approaches, we examined underlying mechanism with quantitative PCR and Western blotting. Two-tailed Student's t-test or One-way ANOVA was used for statistical analysis.

Results: Adora2a/ADORA2A expression was significantly increased in mouse subretinal fibrotic lesions and TGFβ-2-treated CECs. Compared with littermate control mice, mice with deficiency of global and EC-specific Adora2a exhibited 50-60% reduction in the size of CNV and subretinal fibrosis at day 7, 21 and 35 post laser injury. Mechanistically, ADORA2A knockdown in CECs suppressed TGFβ-2-induced EndMT and HIF signaling, and ADORA2A overexpression in CECs increased the levels of HIF and SNAIL1. ADORA2A antagonist KW6002 inhibited TGFB2-induced induction of EndMT, and inhibited subretinal fibrosis in mice of the laser injury-induced CNV model.

Conclusions: Our results demonstrate that ADORA2A-mediated activation of HIF signaling in CECs promotes their transition to mesenchymal cells and then myofibroblasts, and increases production of profibrotic and proinflammatory factors, resulting in formation of subretinal fibrotic lesions. These findings provide the basis for using ADORA2A inhibition as a novel approach in the prevention and treatment of blinding retinal disease.

CONTROL ID: 3706634

SUBMITTER (NAME ONLY): Isabella Palazzo

TITLE: NFkB-signaling promotes glial reactivity and suppresses Müller glia-mediated neuron regeneration in the mammalian retina

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Palazzo, A.J. Fischer, Neuroscience, The Ohio State University, Columbus, Ohio, UNITED STATES|L. Todd, T. Reh, University of Washington, Seattle, Washington, UNITED STATES|T.V. Hoang, S. Blackshaw, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Loss of vision is caused by irreversible death of retinal neurons. Müller glia (MG) are the primary support cell of the retina and are capable of reprogramming into progenitor cells with potential to regenerate neurons following retinal damage. The capacity for MG mediated retinal neuron regeneration varies widely across species. In lower vertebrate species, MG undergo a neurogenic reprogramming event that results in regeneration of functional neurons to restore loss of vision. However, in mammalian systems, MG undergo a “gliotic” response associated with activation of inflammatory gene networks, and fail to regenerate neurons. NFkB signaling is a master regulator of a pro-inflammatory response, and our previous work established that NFkB regulates MG reprogramming in the chick retina. The goal of this study was to investigate the role that NFkB signaling plays in regulating the neurogenic vs. gliotic response in MG after damage in the mammalian retina.

Methods: We investigated patterns of NFkB activation in the mammalian retina after NMDA damage using an NFkB-eGFP reporter mouse line, as well as probing for NFkB signaling components in single cell RNA-seq (scRNAseq) libraries from damaged mouse retinas. Additionally, we utilized an Ascl1 overexpressing mouse line (GlastER-cre/LNL-tTA/tetO-Ascl1-GFP) to investigate neuron regeneration after NMDA damage. We performed intraocular injections of NMDA and a pharmacological inhibitor of NFkB signaling (PGJ2) followed by immunohistochemistry or scRNAseq library preparation to identify retinal neuron regeneration and transcriptomic networks underlying the response, respectively.

Results: We found that NFkB signaling is rapidly activated in Müller glia cells after NMDA damage, and that this activation is dependent on the presence of microglia in the retina. Additionally, inhibition of NFkB signaling decreases macrophage populations within the retina (n=5, p=.03) and promotes Ascl1-mediated retinal neuron regeneration by 30% (n=8, p=.002). Further, scRNA-seq analysis showed that inhibition of NFkB signaling decreases pro-inflammatory and anti-neural gene regulatory networks via coordination with Tgfb signaling and Id factors.

Conclusions: We conclude that NFkB is a key signaling hub that is activated in MG after damage, mediates the accumulation of immune cells, and suppresses the neurogenic potential of MG.

CONTROL ID: 3706646

SUBMITTER (NAME ONLY): Yan Li

TITLE: Use of spatial filters for improved detection of glaucomatous visual field progression

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the benefits of spatial filters in the detection of visual field (VF) progression.

Methods: VF sequences with controlled progression rates were simulated based on the longitudinal VF data of 500 glaucoma patients. One VF per patient was selected as the simulation baseline for stable and progressing sequences (15 fields/sequence, 6 months apart). The number of simulated progressing clusters was determined by the probability distribution of progressing points in the patients' data. Spatial correlations filters based on anatomical and spatial distances of VF test points were applied to the simulated data (Figure 1). Mean deviations (MD), means of total deviation (TD) clusters, and pointwise TD values were analyzed with linear regression (LR) models to monitor global, regional, and local trends, respectively. VF progression was defined as the detection of one negative LR slope (three for local trends) with probability<T. The values of T were adjusted to achieve 95% specificity when testing in stable fields. The time to detect 80% progressing fields and the detection agreements (Fleiss' kappa) between global, regional, and local trends using filtered and unfiltered data were compared.

Results: The mean MD progression rates (±SD) of the simulated stable and progressing VF sequences were -0.03 (±0.05) and -0.21 (±0.10) dB/year. The average time (±SD) to detect 80% progression with filtered data were 7.0 (±0.4), 5.0 (±0.3) and 4.8 (±0.2) years for global, regional, and local trends methods, respectively. The time required for regional and local trends methods to detect progression with unfiltered data (5.5±0.3 and 6.2±0.3 years) was significantly longer ($p<0.001$). With spatial filters, the mean detection agreements (±SD) between the three methods after 2, 3, and 5 years (5, 7, and 11 fields) were 0.47 (±0.03), 0.64 (±0.01) and 0.73 (±0.01), respectively. These were significantly better ($p<0.0001$) than using unfiltered data, which had lower agreements of 0.31 (±0.03), 0.46 (±0.04), 0.59 (±0.03) after 2, 3, and 5 years.

Conclusions: Spatial correlation filters based on anatomical and spatial distances of VF test points can improve the time to detect VF progression with regional and local trends methods, but not with the global trend method. The detection agreements between global, regional, and local trends improve when using such filters.

CONTROL ID: 3706647

SUBMITTER (NAME ONLY): Matthew Van Hook

TITLE: Loss of retinal ganglion cell synaptic outputs to the visual thalamus in the DBA/2J mouse model of glaucoma

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.J. Van Hook, J. Thompson, J.C. Smith, Truhlsen Eye Institute, Ophthalmology & Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|J. Thompson, Pharmacology & Experimental Neuroscience, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|M.J. Van Hook, Cellular & Integrative Physiology, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thalamocortical (TC) relay neurons in the dorsal lateral geniculate nucleus (dLGN) of the thalamus receive convergent retinogeniculate (RG) synaptic input from retinal ganglion cells (RGCs) and convey signals to the primary visual cortex. The goal of this study was to determine how RGC synapses to TC neurons are altered in the DBA/2J (D2) mouse model of glaucoma.

Methods: Experiments were performed with male and female D2 mice at 4-month (m), 6m, 9m, and 12m of age. Controls were the strain-match DBA/2J-gpnmb+ mice. We measured RG synaptic function using optic tract stimulation in parasagittal brain slices while performing whole-cell voltage clamp recordings from post-synaptic TC neurons. Anterograde RGC axon transport was measured as the fraction of dLGN area labeled by a unilateral intravitreal injection of cholera toxin-B-594 (CTB) tracer while microglia activation and RGC synaptic terminal loss was quantified using immunofluorescence staining for Iba1 and vGlut2, respectively. Data were analyzed with a one-way ANOVA and Dunnett's post-hoc multiple comparison tests. Nested statistical tests were used to avoid pitfalls from pseudoreplication. Data are mean±SEM.

Results: CTB transport was reduced in 9m D2 mice (29±10% dLGN labeled, n=7 mice) compared to controls (81±1%, n =14, $p<0.0001$). Microglia showed signs of activation at 9m and 12m including increased cell number and decreased total process length and process endpoints per cell. vGlut2 puncta were reduced at 9m and 12m ($p=0.02$ and $p<0.0001$, respectively). vGlut2 density weakly correlated with microglia activation ($R^2=0.3$; $p=0.0004$ for microglia branch length). There was a statistically significant reduction in the maximum synaptic current amplitude (EPSCmax) detected in slices from 12m D2 mice (822±189 pA; n=31 cells, 9 mice) compared to controls (2269±226 pA; n=35 cells, 12 mice; $p=0.0009$). Reducing stimulus strength to isolate inputs from single RGC axons showed that single-fiber EPSC (EPSCsf) was similar between groups ($p>0.05$). EPSCsf/EPSCmax ratio was higher in slices from 12m D2 mice (0.42±0.07) compared to controls (0.15±0.03; $p=0.004$), indicative of reduced numbers of RGC inputs to each TC neuron.

Conclusions: RGC synaptic loss is functionally detectable in older DBA/2J mice while microglial activation might contribute to pathological synaptic pruning.

CONTROL ID: 3706652
SUBMITTER (NAME ONLY): Galia Issashar Leibovitzh
TITLE: Binocular rivalry of complex stimuli in mild glaucoma
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G. Issashar Leibovitzh, G.E. Trope, Y. Buys, Glaucoma, Toronto Western Hospital, Toronto, Ontario, CANADA|G.E. Trope, Y. Buys, L. Tarita-Nistor, Krembil Research Institute, Toronto, Ontario, CANADA|
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ABSTRACT BODY:

Purpose: Abnormal responses during binocular rivalry have been reported in patients with mild glaucoma when using traditional stimuli. In this study, we tested binocular rivalry using complex images (i.e., face, house) to probe the integrity of higher order visual processing. These stimuli are broadband in spatial frequency and orientation and are processed in stimulus-specific areas: fusiform face area (FFA) for face and parahippocampal place area (PPA) for house.

Methods: Seven patients (4F/3M, 61±7 years old) with mild glaucoma and 9 healthy controls (5F/4M, 51±11 years old) participated. The 2 groups were equivalent in visual acuity and stereo-acuity. Rivalry stimuli were gray-scale images of a house and a face, presented in 4.5 x 6deg rectangular areas, viewed dichoptically. There were 3 stimulus location presentation conditions: centrally, and eccentrically at 3deg in the right (RH) and in the left hemifield (LH), respectively. A 0.5deg fixation cross was presented centrally in all conditions. Participants kept their gaze stable on the cross and used a button-response box to indicate if they perceived the house, the face, or both. The outcome measures were rivalry rate (i.e., switches/min) and time of exclusive dominance of the face or house percept.

Results: A 3 (location: central, LH, RH) x 2 (group: glaucoma, control) mixed factorial ANOVA revealed that rivalry rate was significantly higher for the control group than for the glaucoma group in the LH, $F(2,28) = 3.72$, $p = 0.03$. Compared to central and RH locations, rivalry rate in the LH was highest for the control group (17±6 switches/min) and lowest for the glaucoma group (12±6 switches/min). For the control group, the face dominated 24% longer than the house in the LH location, but the 2 stimuli dominated equally in the central and RH locations. For the glaucoma group, the time dominance for the face percept was 22%, 30%, and 34% longer than the house in the central, LH, and RH conditions, respectively.

Conclusions: Binocular rivalry with complex stimuli produces different pattern of responses compared with traditional stimuli. The control group showed a lateralization of responses that mirrors the FFA's laterality (i.e., FFA is larger in the right hemisphere). Overall, patients with mild glaucoma have stronger responses to faces than to houses, indicating that the function of stimulus-specific areas of FFA and PPA may be unequally affected.

CONTROL ID: 3706653

SUBMITTER (NAME ONLY): Mark Jenkins Sanchez

TITLE: Pre-clinical methods to evaluate photic phenomena in intraocular lenses

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. Jenkins Sanchez, A. Alarcon, L. Franssen, M. van der Mooren, M. Faria Ribeiro, C. Canovas, Implant R&D, Johnson and Johnson Surgical Vison, Groningen, Groningen, NETHERLANDS|E. Thomas, Clinical Science, Johnson and Johnson Vision Surgical, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To introduce and validate a new system and methodology to evaluate photic phenomena (halos, glare and starbursts) induced by different intraocular lens (IOL) technologies using a “see-through” IOL analyzer system in phakic subjects.

Methods: The IOL Telescope Type 1 (IT1) system allows subjects to look through the optics of an IOL. It consists of an eye model into which an IOL is loaded and then attached to a system of relay optics that allows a subject to “look through” the IOL and view a scene including any photic phenomena induced by the IOL.

Twenty subjects looked through the IT1 system under different conditions. Five different IOL designs with different clinical levels of photic phenomena were evaluated by the subjects.

Subjects performed the following tests: First, a subjective rating of the level of bother perceived in a natural scene with a central glare source. After, a ring test was conducted where the size of a ring was adjusted to match the size of the veiling luminance perceived by the subject around the glare source. Two brightness levels were used for the rings, one brighter (Inner) and one dimmer ring (Outer).

The results of this study were compared to the clinical outcomes of the subjective perception of halo, glare and starbursts of implanted cataract patients.

Results: The outer ring test provided results that were well correlated with the clinical questionnaire levels of halo ($R^2 = 0.97$), glare ($R^2 = 0.99$) and starbursts ($R^2 = 0.81$) bother. The inner ring test showed much lower correlation with the clinical levels ($R^2 < 0.48$). Correlations between subjective grading and clinical responses were strongly dependent on the luminance level of the glare source and the photic phenomena evaluated, being $R^2 = 0.72$ in the best of cases.

Conclusions: The results of this study show that the IT1 system can be used to simulate photic phenomena induced by different IOL technologies in phakic eyes. Certain quantitative methods showed a high correlation with the subjective perception of photic phenomena found in cataract patients implanted with the same IOL models. However, exact conditions under which the tests are performed (glare source brightness, scene selection/brightness, subject expectations/variability) can have large effects on test results. The exact visual experience of an implanted subject may not directly map onto the subjective impression in this and similar “see-through” systems.

CONTROL ID: 3706664

SUBMITTER (NAME ONLY): Yaping Jin

TITLE: Predicted backlog in ophthalmic surgeries associated with COVID-19 pandemic in Ontario: a time series modelling analysis

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Jin, S. El-Defrawy, Y. Buys, Dept of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|Y. Jin, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, CANADA|M. Canizares, Schroeder Arthritis Institute, University Health Network, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Health systems' responses to the coronavirus disease 2019 (COVID-19) pandemic created a surgical backlog of unknown size, limiting the ability to develop strategies to effectively address the backlog. We assessed the volume of deferred ophthalmic surgeries associated with the COVID-19 pandemic from March-December 2020 and suggested strategies and duration to clear the backlog in Ontario, Canada.

Methods: Ontario Health Insurance Plan physician billing data from 2017-2020 were analyzed. The ophthalmic surgical backlog associated with the pandemic was estimated using time series forecasting models on training set (115 weeks), validation set (52 weeks) and forecasting set (42 weeks). Clearance time was calculated based on the queuing theory using various scenarios.

Results: In 2020, there were 5.13 million ophthalmologist services, a reduction of 22% compared to the 6.60 million services in 2019. This included a 27% decrease in ophthalmic surgeries that require the use of operating rooms (OR) and a 6% decrease in anti-VEGF (vascular endothelial growth factor) injections (a common procedure for macular degeneration) that can be done in clinics.

From March 16 to December 31, 2020 (a pandemic period), the estimated backlog in ophthalmic surgeries requiring an OR was 92,150 surgeries (95% prediction interval [PI] 71,288-112,841), increasing on average by 2,194 surgeries per week. Roughly 90% of the delayed surgeries were cataract surgeries and 4% were retinal detachment surgeries. Nearly half of the provincial backlog (48%, 44,542/92,150) involved patients from the West health region. Estimated provincial clearance time was 248 weeks (95% confidence interval [CI] 235–260) and 128 weeks (95% CI 121–134) if 10% and 20% of OR surgical capacity per week were added, respectively, based on the weekly ophthalmic surgical volume in 2019. Furthermore, an estimated 23,755 (95% PI 14,656-32,497) anti-VEGF injections were missed.

Conclusions: The magnitude of ophthalmic surgical backlog in Ontario in 2020 alone raises serious concerns for meeting the ophthalmic surgical needs of patients. As the pandemic continues the accrued backlog size is likely increasing. Planning and actions are needed urgently to manage the collateral impact of the pandemic on the ophthalmic surgical backlog in Ontario.

CONTROL ID: 3706665

SUBMITTER (NAME ONLY): Vincent Monnier

TITLE: α-Crystallin chaperone mimetic small molecules as a paradigm for cataract prevention by inhibition of lens γ-crystallin aggregation

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.M. Monnier, S. Islam, M. Do, B. Frank, D.R. Sell, Pathology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S.G. Wheeler, K.J. Lampi, Integrative Biosciences, Oregon Health & Science University, Portland, Oregon, UNITED STATES|X. Fan, Cell Biology and Anatomy, Medical College of Georgia, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: γ-Crystallins play a major role in maintaining age-related lens transparency. Their destabilization by mutations and physical chemical insults is strongly associated with cataract. Therefore, drugs that increase their stability should have anti-cataract properties. To this end we have screened 2560 drugs and natural compounds for their ability to suppress H_2O_2 and/or heat mediated aggregation of bovine γ-crystallins and various recombinant human and mouse γ-crystallins.

Methods: Protein unfolding, aggregation and binding affinity were determined using absorption, fluorescence and CD spectroscopy, dynamic light scattering, transmission electron microscopy and fluorescence quenching. Protein binding sites were determined using AutodockVIna.

Results: The top two drugs, Closantel (C), an antihelmintic drug, and Gambogic Acid (G), a xanthonoid compound prevented or attenuated to variable degree thermal-induced protein unfolding when tested against Human or Mouse recombinant crystallins such as deamidated HγS mutants, wild-type HγD & MγS and their respective mutants W43R, R14C and R58H, and F9S/OPJ. Binding studies using fluorescence quenching and ANS method revealed static binding of drugs C & G to hydrophobic sites of medium to low affinity ranging from -5.9 to -7.9 kcal/mol (HγD) and -4.1 to -8.2 kcal/mol (MγS) with Kb values ranging from $1.34x10^5$ to 6.1×10^5 M^{-1}(HγD) and $0.073 x10^5$ to $1.38 x10^5$ M^{-1} (MγS). Molecular docking to HγD and other γ-crystallin revealed two binding sites, one in the “NC-pocket” including residues in the 50-150 sequence of HgD, and one in the “NC-tail” spanning residues 56-61 from the N-terminal to the residues 168-174 in C-terminal domain. Several of these binding sites overlapped with those of the protective α-crystallin mini-chaperone peptide “MAC”.

Conclusions: These results support the existence of a new class of α-crystallin mimetic drugs with chaperone effect and anti-cataract potential whereby Closantel and Gambogic acid emerge as the most promising candidate compounds. However, their binding activity to gamma crystallins is relatively low and it remains to be tested whether inhibtion of gamma crystallin aggregation can prevent cataract formation in appropriate congenital or environmentally induced animal models of cataract.

CONTROL ID: 3706668

SUBMITTER (NAME ONLY): Manal Benlahbib

TITLE: Treatment of drusen in dry age-related macular degeneration with photobiomodulation : single-center study

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Benlahbib, C. Mehanna, H. Le, E. Souied, ophtalmologie, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To assess the efficacy and safety of photobiomodulation (PBM) treatment for patients with drusen in dry age-related macular degeneration (AMD).

Methods: Thirteen eyes with dry AMD (age related eye disease study (AREDS) categories 3-4) were included in the study and treated with the Valeda Light Delivery System. All subjects underwent two treatments per week for 5 weeks. Outcome mesures included ; best corrected visual acuity (BCVA), microperimetry- scotopic testing, drusen volume (DV), central drusen thickness (CDT), central retinal thickness (CRT) and retinal volume.

Results: BCVA improved in eyes treated with photobiomodulation with a mean score gain of 4 letters at month 6 (M6). Retinal sensitivity increased by 0.70 dB on average. Mean fixation losses decreased by 7.83 % at M6. Drusen volume and retinal volume decreased by 0.28 mm^3 and 0.21 mm^3 on average respectively. Central drusen thickness and central retinal thichness was reduced by a mean of 36.5 µm and 40.16 µm respectively at M6.

Conclusions: This study confirm efficacy and safety of using photobiomudulation for treatment of drusen in dry AMD. The functional and anatomical improvements in our patients support previous reports. PBM may provide a therapeutic option for patients with dry AMD mainly in the earliest stages and may potencially slow the progression of the disease. Further studies are needed to confirm if a repeated PBM treatments are necessary to maintain the benefits.

CONTROL ID: 3706680
SUBMITTER (NAME ONLY): Jun Zhang
TITLE: Epidemiology and burden of astigmatism: a systematic literature review
SESSION TITLE: Anterior Segment and Trauma Epidemiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Zhang, M. Dhariwal, Y. wu, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|M.A. Bullimore, University of Houston, College of Optometry, Texas, UNITED STATES|
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ABSTRACT BODY:
Purpose: To identify published literature on epidemiology, patient and economic burden of astigmatism through a systematic literature review. The unmet needs of astigmatic patients with co-existing ocular conditions (such as cataract, glaucoma, dry eye, presbyopia, or macular degeneration) and the risks associated with untreated astigmatism were also reviewed.
Methods: Using Cochrane methodology, a systematic literature review was conducted in MEDLINE, EMBASE, and Cochrane library (January 1996-May 2021). Studies published in the English language reporting on epidemiology and burden of astigmatism were included. Proceedings (2018-2021) from eye congresses were searched for evidence. A grey literature search was conducted using Google Scholar to identify relevant studies that were not captured by the database searches.
Results: The literature search yielded 6,804 citations, of which 125 met the inclusion criteria (epidemiology: 68; patient burden: 60; economic burden: 6) and were summarized in this SLR. The prevalence of astigmatism in the general population varied from 7.6% to 61.7%, with higher rates in older individuals (≥70 years). The prevalence of with-the-rule astigmatism was higher in the younger population (≤40 years), while rates of against-the-rule and oblique astigmatism increased with age. The prevalence of astigmatism was higher for low levels (<1.5 D: 32.7%-100%) than higher levels (≥1.5 D: 0%-39.1%). Astigmatic patients experienced decreased quality of vision, increased rates of glare (52.9%-77.0%), halos (28.1%-80.0%), night-time driving difficulties (66.0%), risk of falls (particularly with oblique astigmatism), and spectacle dependence (44.8%-85.0%) leading to decreased vision-related quality of life. Astigmatic patients performed vision-related tasks slower (-1 D: 8.9% slower, -2 D: 28.7% slower) and made more errors (-1 D: 38.1% more errors, -2 D: 370% more errors) compared to fully corrected astigmatic patients. In astigmatic patients undergoing cataract surgery, post-operative spectacle cost (mean: $51-$916), outpatient visit cost (mean: $35-$348), travel cost (mean: $14-$21), and informal care cost (mean: $39-$71) contributed to the overall economic burden.
Conclusions: Uncorrected astigmatism decreases patients' vision-related quality of life; increases productivity losses among working-age adults; and poses an economic burden on patients and their families.

CONTROL ID: 3706697

SUBMITTER (NAME ONLY): Tessnim Ahmad

TITLE: Ultra-widefield Imaging versus Ophthalmoscopic Examination in a Routine Patient Population

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.R. Ahmad, W. Au-Yeung, N. Chan, J.D. Keenan, J.M. Stewart, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior studies have established ultra-widefield imaging in the assessment of diabetic retinopathy. The primary aim of this study was to determine its use, compared to slit lamp biomicroscopy, for the detection of fundus pathology in a routine patient population.

Methods: In this prospective randomized study, patients underwent biomicroscopy by certified optometrists and ultra-widefield imaging. Ultra-widefield photos were independently graded by two optometrists. Clinical findings from examiners and photo-graders were coded into themes using inductive thematic analysis, and then clinically significant findings were extracted. Discrepancies between photo-graders were adjudicated by a retinal ophthalmologist to create a consensus interpretation. Cohen’s kappa was used to estimate agreement between the two photo-graders and between the examinations and photo-grades.

Results: Nine-hundred eyes of 450 patients were examined and imaged. Of the clinically significant examination findings, inter-photo-grader agreement was moderate to substantial for most, including optic disc hemorrhage (k = 0.8), macular exudates (k = 0.7), and macular pigmentary changes (k = 0.7). Agreement between examination and photo-grades was moderate to substantial for optic disc hemorrhage (k = 1), indistinct optic disc margins (k = 0.5), macular drusen (k = 0.4), and peripheral retinal pigmentary changes (k = 0.4), drusen (k = 0.4), and hemorrhage (k = 0.8). A total of 187 findings were detected by imaging but not examination, compared with 42 that were detected on examination but not imaging.

Conclusions: Ultra-widefield imaging agreed substantially with standard-of-care examinations in a routine patient population and detected more fundus findings than clinical examination.

CONTROL ID: 3706705

SUBMITTER (NAME ONLY): Sophia Wang

TITLE: Named entity recognition in ophthalmology clinical progress notes: What's in the eye exam?

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.Y. Wang, W. Hu, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|J. Huang, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|H. Hwang, Weill Cornell Medicine, New York, New York, UNITED STATES|T. Hernandez-Boussard, Center for Biomedical Informatics Research, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to develop deep learning models to recognize ophthalmic examination components from free text clinical progress notes in electronic health records (EHR), while using a weak supervision approach to amass a large training corpus.

Methods: A corpus of 39,099 ophthalmology progress notes labeled for 24 anterior and posterior segment anatomical components (named entities) of the ophthalmic examination was assembled from the EHR of a single academic center using a weakly supervised approach that automatically matches labeled EHR fields with corresponding words in the notes. The corpus was split into training, validation, and test sets. Four massively pre-trained transformer-based language models (DistilBert, BioBert, BlueBert, and ClinicalBert) were fine-tuned to this named entity recognition task. Results were compared to a baseline model based on regular expressions. Precision, recall, F1-score were reported for each entity and micro-averaged across the test set. The same metrics were also reported on a sample of human-annotated ground truth notes from the test set, and a sample of human-annotated notes from an independent set of notes.

Results: On the weakly labeled test set, all transformer-based models had micro-averaged recall over 0.92, with precision varying from 0.44-0.85. The baseline model had lower recall (0.77) and comparable precision (0.68). On human-annotated notes from the test set, the baseline model had high recall (0.96) with precision variable depending on the entity (0.11-1.0, micro-averaged 0.57). Bert models had better performance, with recall ranging from 0.77-0.84, and micro-averaged precision >=0.95 for all models. On the independent notes, precision was 0.93 and recall 0.39 for the Bert model, whereas the baseline model had better recall (0.72) but poor precision (0.44).

Conclusions: We have developed the first deep learning system to recognize eye examination components from clinical progress notes, leveraging a novel opportunity for weak supervision to produce a large training corpus from EHR. Transformer-based models had very high precision when evaluated against human-annotated ground truth labels, whereas the baseline model had poor precision but higher recall. This system hold potential to improve ophthalmology cohort design and feature identification using free-text clinical progress notes.

CONTROL ID: 3706709

SUBMITTER (NAME ONLY): Nuria Guardia Ruiz

TITLE: Clinical assessment of the effectiveness of phacoemulsification associated with goniosynechialysis in angle closure treatment

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Guardia Ruiz, J. Juberías, Ophthalmology, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|Y. Diebold, J. Juberías, Instituto de Oftalmobiologia Aplicada, Valladolid, Castilla y León, SPAIN|Y. Diebold, Bioingeniería, Biomateriales y Nanomedicina, Centro de Investigacion Biomedica en Red, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To identify whether there is a decrease in intraocular pressure (IOP) values and the number of hypotensive active principles (AP) required in patients diagnosed with suspected angle closure (SAC), angle closure (AC), and angle closure glaucoma (ACG) who underwent phacoemulsification surgery with intraocular lens (IOL) implantation and goniosynechialysis.

Methods: Retrospective observational study of patients diagnosed of SAC, AC or ACG who received phacoemulsification with IOL implantation and goniosynechialysis by the same glaucoma surgeon in the last 10 years at the Glaucoma Units of the Valladolid Clinic Hospital and the Institute of Applied OphthalmoBiology (University of Valladolid, Valladolid, Spain). We evaluated the difference between baseline and pre-surgical IOP compared to IOP at different times of postoperative follow-up (1, 3 and 12 months), and the difference between numbers of hypotensive AP administered before and after surgery at the same follow-up months.

Results: We analyzed 64 eyes, 31 with AC, 26 with ACG, and 7 with SAC. A statistically significant decrease between baseline and pre-surgical IOP and IOP assessed 1, 3 and 12 months after surgery in AC and ACG patients was observed ($p<0.001$). AC patients showed a 43.6% decrease between baseline and pre-surgical IOP, a 51.3 to 56.6% decrease between baseline and post-surgical IOP, and a 13.3 to 22.9% decrease between pre-surgical and post-surgical IOP. ACG patients showed a 41.5% decrease in pre-surgical IOP compared to baseline IOP, a 53.2 to 56.5% decrease in post-surgical IOP compared to baseline IOP, and a 19.7 to 25.7% decrease in post-surgical IOP compared to pre-surgical IOP. SAC patients showed a 9.47 to 11.74% decrease in postsurgical IOP compared to pre-surgical IOP ($p<0.05$). Regarding numbers of administered AP, we observed a statistically significant decrease in AP at 1, 3, and 12 months after surgery compared to prior to surgery in both AC (53.4 to 61.5%) ($p<0.001$) and ACG (41.9 to 54.5%) ($p<0.05$) patients. In SAC patients, no differences were observed.

Conclusions: Phacoemulsification surgery with IOL implantation, together with goniosinechialysis, significantly lowers the IOP and the AP number required for long-term IOP control in AC and ACG patients. In SAC patients, surgery contributes to a small decrease in IOP, but it does not affect the number of AP required.

CONTROL ID: 3706711

SUBMITTER (NAME ONLY): Eric Kim

TITLE: Analysis of Variability of the Spiral of Tillaux and Corneal Diameters: a Cadaveric Study

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kim, V. Rana, A. Barton, J. Tanzer, J. Schaefer, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|

Commercial Relationships Disclosure: Eric Kim: Commercial Relationship: Code N (No Commercial Relationship) | Viren Rana: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Barton: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Tanzer: Commercial Relationship: Code N (No Commercial Relationship) | Jamie Schaefer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The distances of the extraocular rectus muscle insertions from the limbus and corneal diameters are clinically relevant in surgical ophthalmology. It is widely accepted that the corneal diameters are about 11.7 x 10.6 mm and that the medial, inferior, lateral, and superior recti muscles on average insert 5.5, 6.5, 6.9, and 7.7mm, respectively, from the limbus. This descriptive cadaveric study investigates the measurements of the Spiral of Tillaux and corneal diameters.

Methods: Thirty cadavers were included for a total of 60 eyes. For each eye, a lateral canthotomy and cantholysis followed by a peritomy were performed. Muscle hooks were used to isolate the rectus muscles. Corneal diameters and distances from the midpoint of recti muscle insertions to the limbus were measured using calipers (Fig. 1). Using mixed effects modeling, the mean distance from the limbus to each rectus muscle was found.

Results: Of the 30 cadavers, 50% were female, with a mean age of 81.9 years. Table 1 reports the measurements from the limbus to the rectus muscle insertion (medial rectus = 5.28 mm, inferior rectus = 5.72 mm, lateral rectus = 6.40 mm, superior rectus = 6.78 mm). When compared to the historical benchmarks, nearly all of these measurements in this study were shorter ($p < 0.01$). No meaningful heterogeneity was identified across ages or by right and left eye ($p > 0.05$). Women tended towards approximately half a millimeter shorter measurements on average (limbus to rectus: $t(45.35) = -1.91$, $p = 0.0624$). Mean corneal diameters were found to be 11.7 mm horizontally and 10.7 mm vertically, and were not found to be significantly different from the expected values ($p > 0.05$).

Conclusions: Nearly all measurements from the limbus to rectus muscle insertions demonstrated variations from the accepted Spiral of Tillaux measurements, particularly with females having shorter distances. However, we found that the recti muscles followed the same pattern to the historical Spiral of Tillaux measurements, with the medial rectus inserting most closely to the limbus and the inferior, lateral, and superior rectus inserting successively farther from the limbus. We found no significant differences in the expected corneal diameter measurements.

CONTROL ID: 3706732

SUBMITTER (NAME ONLY): Mateusz Jaskulski

TITLE: Wavefront superposition for predicting retinal image quality with zonal, dual-focus and multifocal contact lenses

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jaskulski, P.S. Kollbaum, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|P. Lazon de la Jara, Research Programs, Coopervision Inc, Pleasanton, California, UNITED STATES|A. Bradley, Research Programs, Coopervision Inc, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Novel zonal, dual-focus contact lenses (CL) for myopia control and multifocal (MF) CLs designed for presbyopia employ spatially separated zones containing different optical properties. While wavefront aberrometry can be used to evaluate CL performance on eye, a novel methodology was evaluated of using pupil-plane superposition of ocular wavefronts with measured and modeled ex-vivo wavefronts to predict retinal image quality of eyes wearing these optics.

Methods: Ocular wavefronts were measured in-vivo using a pyramidal wavefront sensor (Osiris, CSO, Italy) for “eye only” and “eye wearing lens” scenarios. CL wavefronts were measured with a single-pass Shack-Hartmann aberrometer (ClearWave, Lumetrics, Rochester, NY), and modeled using geometrical ray tracing. Numerical superpositions of “eye + measured lens” and “eye + modeled lens” wavefronts were compared to “eye wearing lens” wavefronts for center-distance multifocal (CDMF), center-near multifocal (CNMF), and center-distance dual-focus (CDDF) designs. Point-spread functions (PSF) and corresponding retinal image simulations were computed from the wavefronts.

Results: Peak image quality (VSX) scores for CDMF, CNMF, and CDDF (6.0 mm pupils) were, respectively, 0.15, 0.15; and 0.10 for “eye wearing lens”, 0.12, 0.10; 0.15, for “eye + measured lens”, and 0.13, 0.08; 0.14, for “eye + modeled lens”. Corresponding peak AreaMTF scores were 0.20; 0.16, and 0.15; 0.16; 0.17, 0.15; and 0.14; 0.28, 0.14. The morphology (size, shape, orientation) of the PSFs matched well (Fig. 1).

Conclusions: The three approaches to assess image quality in eyes fit with the different MF and DF lenses reveal a common pattern with the Strehl ratio-based VSX metric with values generally between 10% and 15% of the diffraction limit, and slightly higher values for the AreaMTF metric. The three approaches generally produced similar results, being slightly higher for "eye wearing lens" with the two MF designs, and slightly lower with the DF design. The slight variations in PSF shape can be attributed to differences in lens centration between “eye wearing lens” and “eye + lens” scenarios and data collection interval between “eye alone” and “eye wearing lens” conditions.

CONTROL ID: 3706738

SUBMITTER (NAME ONLY): Mark Rosenfield

TITLE: Effect of scheduled breaks on Digital Eye Strain

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Rosenfield, S. Johnson, SUNY College of Optometry, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Mark Rosenfield: Commercial Relationship: Code N (No Commercial Relationship) | Sophia Johnson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The use of digital devices has increased substantially over the past two decades across all age groups for both vocational and avocational purposes. Today, the use of digital screens is almost universal. Digital eye strain (DES) involves a range of visual and ocular symptoms that can be categorized into oculomotor/refractive abnormalities or dry eye symptoms. There are a wide range of proposed therapeutic and management options for this condition, including optical, medical and ergonomic interventions. Regular breaks are frequently recommended by clinicians. Indeed, the so-called 20-20-20 rule, whereby individuals are advised to fixate on an object at least 20 feet (6m) away for at least 20 seconds every 20 minutes is widely cited. Unfortunately, there is little or no peer-reviewed evidence to support this so-called rule. The aim of the present investigation was to determine whether scheduled breaks are indeed effective in reducing the adverse effects of digital device usage, and if so, to identify the specific schedule that has the greatest success in controlling symptoms.

Methods: The study was performed on 30 young, visually-normal subjects who were required to perform a 40-minute, cognitively demanding reading task from a tablet computer. The task required them to read random words and to identify which began with a specific letter chosen at random by the experimenter. The task was undertaken on four separate occasions, with 20-second breaks being allowed every 5, 10, 20 or 40 (i.e., no break) minutes, respectively. Both before and immediately after each trial, subjects completed a questionnaire regarding ocular and visual symptoms experienced during the session. Additionally, both reading speed and task accuracy was quantified during each trial.

Results: A significant increase in post-task symptoms (with respective to the pre-task value) was observed for all four trials ($p<0.001$). However, there was no significant effect of scheduled breaks on reported symptoms ($p=0.70$), reading speed ($p=0.93$) or task accuracy ($p=0.55$).

Conclusions: While widely cited as a treatment option, these results do not support the proposal of using scheduled breaks as a therapeutic intervention for DES.

CONTROL ID: 3706740

SUBMITTER (NAME ONLY): Andrea Wilson

TITLE: Optimization of novel intraocular pressure measurement system for mice

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Wilson, G. Li, W.D. Stamer, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Andrea Wilson: Commercial Relationship: Code N (No Commercial Relationship) | Guorong Li: Commercial Relationship: Code N (No Commercial Relationship) | William Stamer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mice are widely used to study intraocular pressure (IOP) regulation due to the similarities of their conventional outflow pathway to humans. Elevated IOP is the primary risk factor for glaucoma—a leading cause of irreversible blindness worldwide, but measuring IOP in mice is challenging. The aim of this study is to optimize conditions for reliably measuring IOP using a newly designed system for mice.

Methods: Modeled after a system designed by Dr. Simon John, our system includes an AmScope stereo microscope, custom-designed mouse platform that rotates in two planes, TonoLab rebound tonometer with a mounting clamp, foot pedal trigger, isoflurane anesthesia system, and monitors for heart rate (HR) and oxygen saturation percentage (O2S). For experiments, the same group of C57/B6 mice were used to evaluate two methods of anesthesia: Isoflurane (iso, 2% induction, 1% nosecone) vs. ketamine/xylazine (ket/xy, ~70mg/7mg/kg). Experiments were performed on different days, repeated 9 times for iso and 5 for ket/xy. IOP was measured with and without a microscope for tonometer positioning. IOP, HR, and O2S were recorded at 0 and 5 min after induction of sleep.

Results: For ket/xy vs. iso, IOP was not significantly different (16.19±1.9 vs. 15.32±3.7 mmHg, $p=0.46$), but HR and O2S were significantly lower (HR: 328.57±37.2 vs. 560.35±62.6 per min, $p<0.001$; O2S: 81.68±8.6 vs. 75±7.4, $p=0.01$). After 5 min, IOP dropped 2.5 mmHg with ket/xy (16.19±1.9 vs 13.68±1.9 mmHg, $p<0.001$) but only 0.5 mmHg with iso (15.32±3.7 vs. 14.80±2.3 mmHg, $p=0.68$). HR decreased for both iso and ket/xy but was not significantly different at 5 min. IOP readings with vs. without a microscope did not show a significant difference for iso at 0 and 5 min (0 min: 15.32±3.7 vs. 14.73±1.9 mmHg, $p=0.61$; 5 min: 14.80±2.3 vs. 14.72±2.3 mmHg, $p=0.93$) or ket/xy (0 min: 16.19±1.9 vs. 16.33±1.3 mmHg, $p=0.81$; 5 min: 13.68±1.9 vs. 13.65±2.6 mmHg, $p=0.97$). There was a significant difference between IOPs in iso vs. ket/xy datasets at 0 min without a microscope (14.73± 1.9 vs. 16.33±1.3 mmHg, $p=0.004$).

Conclusions: With our newly designed IOP system, similar IOP readings were obtained using iso or ket/xy, and IOP drops more rapidly with ket/xy than iso. HR is not a determining factor for IOP readings. The use of a microscope for tonometer positioning and consistent time between induction of sleep and IOP collection are the most important parameters for reliable IOP measurements.

CONTROL ID: 3706741

SUBMITTER (NAME ONLY): Jennyffer Smith

TITLE: Local Macular Retinal Oximetry Increases with Disease Duration in Type 2 Diabetes without Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Smith, K. Bisignano, W.W. Harrison, Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Jennyffer Smith: Commercial Relationship: Code N (No Commercial Relationship) | Kelly Bisignano: Commercial Relationship: Code N (No Commercial Relationship) | Wendy Harrison: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetes can have profound effects on vision through changes to the neurons and vasculature in the retina. To prevent these vision threatening changes, such as diabetic retinopathy and edema, early detection of retinal changes is key. One potential biomarker for early change in the retina is alteration in retinal oximetry. The purpose of this study is to characterize differences in retinal tissue oximetry and superficial vascular density in controls and subjects with type 2 diabetes without retinopathy (DM).

Methods: 36 subjects (51.5 ± 9 years) participated in this study; 19 controls and 17 DM with no retinopathy. Duration of DM was noted for all DM subjects. Testing included HbA1c testing (Siemens) and retinal oximetry (Zilia) measurements of the right eye, within the macula at 3.1 degrees from the fovea; with one measurement sup/temp, inf/temp, sup/nasal, inf/nasal, which were averaged together. Also, OCTA imaging (Zeiss Cirrus) was completed, once available, with OCTA completed on 26 of the 36 subjects. Superficial vascular plexus (SVP) slabs were analyzed with ImageJ for density and compared between groups and correlated with oximetry metrics. Foveal avascular zone was measured and considered in SVP analysis.

Results: In DM subjects, increased duration of disease was associated with increased oximetry ($p = 0.038$), but duration was not associated with vessel density changes ($p = 0.351$). Decreased vessel density was associated with increased retinal oximetry overall ($p = 0.036$). There was no correlation with HbA1c and oximetry in controls and DM ($p = 0.244$, $p = 0.832$, respectively) or HbA1c and SVP density in either group ($p = 0.957$, $p = 0.786$). FAZ was controlled for in density measures and not statistically different between groups ($p = 0.58$).

Conclusions: These data suggest that retinal tissue oximetry appears to be correlated to duration of disease in subjects with DM without retinopathy. This may be related to changes in vessel density. This pairs well with literature that has shown duration is also associated with retinopathy development. These data suggest oximetry measurements may be a useful subclinical biomarker in predicting impending retinopathy, but more follow up in longitudinal work is needed.

CONTROL ID: 3706745

SUBMITTER (NAME ONLY): Dun Jack Fu

TITLE: Development and external validation of a novel automatic segmentation model for detection and quantification of geographic atrophy from optical coherence tomography imaging

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Fu, S. Glinton, L. Faes, S. Wagner, G. Zhang, P. Patel, P.A. Keane, K. Balaskas, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|T.D. Keenan, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. McKeown, Apellis Pharmaceuticals Inc, Crestwood, Kentucky, UNITED STATES|B. Liefers, Erasmus Universiteit Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS|

Commercial Relationships Disclosure: Dun Jack Fu: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Abbvie;Code C (Consultant/Contractor):DeepMind | Tiarnan Keenan: Commercial Relationship: Code N (No Commercial Relationship) | Sophie Glinton: Commercial Relationship(s);Code R (Recipient):Moorfields Eye Charity Grant (GR001003), Wellcome Trust Grant (206619_Z_17_Z). | Livia Faes: Commercial Relationship: Code N (No Commercial Relationship) | Siegfried Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Alex McKeown: Commercial Relationship(s);Code E (Employment):Apellis | Gongyu Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Bart Liefers: Commercial Relationship: Code N (No Commercial Relationship) | Praveen Patel: Commercial Relationship(s);Code C (Consultant/Contractor): Bayer, Novartis, Oxford Bioelectronics and Roche | Pearse Keane: Commercial Relationship(s);Code C (Consultant/Contractor):DeepMind, Roche, Novartis, Apellis , BitFount;Code F (Financial Support):Moorfields Eye Charity Career Development Award (R190028A), UK Research & Innovation Future Leaders Fellowship (MR/T019050/1);Code I (Personal Financial Interest):Big Picture Medical | Konstantinos Balaskas: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis, Roche;Code F (Financial Support):Novartis, Bayer, Apellis

ABSTRACT BODY:

Purpose:

Geographic atrophy (GA) is the defining atrophic lesion of advanced non-neovascular age-related macular degeneration (AMD). Detection and segmentation of GA from optical coherence tomography (OCT) imaging is necessary for diagnosis, monitoring, prognosis, and to inform therapy research for this orphan disease. The current standard of segmentation requires specialist manual effort, which is labour intensive and prone to inter-grader variability.

There is a need for validated and fully automated deep-learning approaches to qOCT detection and segmentation of GA that are applicable in clinical care of non-neovascular AMD patients with GA and potential to facilitate therapy research.

Methods:

Deep-learning GA segmentation models were developed for complete GA and its constituent features on 5049 manually segmented optical coherence tomography (OCT) B-scans from 399 eyes (200 patients) with GA secondary to AMD included in the FILLY2 trial (NCT02503332). Predictive performance was validated on an external clinical dataset comprising 884 OCT B-scans from 192 eyes (110 patients) examined at Moorfields Eye Hospital NHS Foundation Trust. The primary outcome was agreement (DSC [dice similarity coefficient] and ICC [intraclass correlation coefficient]) between model GA prediction and consensus of independent graders during external validation.

Results:

Our models accurately segmented GA (median DSC [Dice similarity coefficient] ± SD [standard deviation] 0.96 ± 0.15) and all its constituent features: retinal pigment epithelium (RPE)-loss (0.95 ± 0.21), photoreceptor degeneration (0.96 ± 0.21), hypertransmission (0.97 ± 0.15). Model performance was greater than agreement between specialist human graders (RPE-loss 0.93 ± 0.31, photoreceptor degeneration 0.89 ± 0.20; hypertransmission 0.81 ± 0.30;GA 0.80 ± 0.30). GA segmentation performance remained high in the presence of additional retinal pathologies, including nAMD, PED, and ERM.

Conclusions:

We report development and validation of a scalable deep-learning tool to automatically process OCT scans for

detection and quantification of GA, with a predictive performance equivalent to human specialist graders that is robustly retained beyond the sample used for model development.

CONTROL ID: 3706746

SUBMITTER (NAME ONLY): Aditya Nair

TITLE: Transformers-based retinal nerve fiber layer (RNFL) segmentation in optical coherence tomography (OCT)

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nair, R. Guimares, H. Bagherinia, N. Manivannan, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

Commercial Relationships Disclosure: Aditya Nair: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Rogerio Guimares: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Homayoun Bagherinia: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Niranchana Manivannan: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc.

ABSTRACT BODY:

Purpose: OCT retinal layer analysis is an important diagnostic tool for ocular diseases. In this work we develop an algorithm to predict RNFL layer boundaries using a novel Transformer based deep-learning architecture to improve the performance (accuracy, runtime and memory) of RNFL segmentation. The purpose of this algorithm is to develop a generalized and adaptable algorithm for various scan field of views (FOV).

Methods: Training data consists of 645 volumes of 2mm x 6mm x 6mm CIRRUS^{TM} 4000 HD-OCT (ZEISS, Dublin, CA) data. We used a knowledge-based algorithm to generate the ground truth segmentation for this problem. The ground truth consisted of 2-layer position values each corresponding to every A-scan position as well as 2 confidence of segmentation values. We trained a transformer encoder that takes in an OCT B-scan image patch of 6 mm and outputs the ILM and RNFL segmentations and their confidence values. The input image is passed through a linear projection layer to compress the image in the A-scan direction, then sinusoidal positional encoding is added to retain positional information. Transformer outputs are passed through fully-connected and sigmoid activation layer to output layer position and confidence values. The network setup is shown in figure 1. We also made use of knowledge-based algorithm's confidence value to weigh the loss function (hence learning from noisy training data in a semi-supervised manner). We measured the performance of algorithm on manual segmentation for inferior, superior and central B-scans for held out 35 subjects.

Results: The Transformer-based OCT segmentation provided a better agreement with the ground truth than the knowledge-based algorithm as shown in figure 2. The runtime of this algorithm was 2.12 secs vs the 2.90 secs for the knowledge-based algorithm on Intel(R) Core^{TM} i7-9850H CPU@2.60GHz with a NVIDIA GeForce MX150 GPU. The Transformer method also used significantly lower GPU memory than standard methods (<2 Gigabytes).

Conclusions: We developed a Transformer-based deep learning method to segment the RNFL layer in OCT B-scan. We showed that our method using Transformer performs better than the knowledge-based approach on speed, efficiency, and accuracy while being adaptable to different scan FOV.

CONTROL ID: 3706747

SUBMITTER (NAME ONLY): IAN PURVIS

TITLE: Functional characterization of Otx2 enhancers used in mouse retinal development

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Henry, Clemson University, Clemson, South Carolina, UNITED STATES|A. Haas, Pathology, University of Colorado, Denver, Colorado, UNITED STATES|I. PURVIS, O. Ochoa, K. Park, J.A. Brzezinski, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|M. Kaufman, RNA Bioscience Initiative, University of Colorado, Denver, Colorado, UNITED STATES|

Commercial Relationships Disclosure: IAN PURVIS: Commercial Relationship: Code N (No Commercial Relationship) | Michael Kaufman: Commercial Relationship: Code N (No Commercial Relationship) | Omar Ochoa: Commercial Relationship: Code N (No Commercial Relationship) | Ko Park: Commercial Relationship: Code N (No Commercial Relationship) | Charles Henry: Commercial Relationship: Code N (No Commercial Relationship) | Ami Haas: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Brzezinski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Otx2 is a transcription factor necessary for the development of photoreceptor and bipolar cells in the retina. How Otx2 expression is regulated to produce these cell types is unknown. We identified three enhancers (DHS2, 4, and 15) that potentially explain the spatial and temporal regulation of Otx2 expression and perturbed them to determine how they control retinal development.

Methods: To determine enhancer activity, we constructed plasmids containing enhancer sequences driving a GFP or Cre recombinase reporter. These plasmids were electroporated into retinal explants cultured in vitro or into live newborn mouse retinas. To remove enhancer function, we electroporated CRISPR/Cas9 plasmid systems to delete the targeted sequences. To prevent enhancer activity, we epigenetically silenced the sequences by electroporating a dead Cas9 CRISPRi system. Immunohistochemistry was conducted to determine enhancer activity, OTX2 expression, and changes in cell fate in the electroporated retinas.

Results: Reporter assays and lineage tracing showed that the DHS2 and DHS15 enhancers were expressed in the developing retina, gave rise to photoreceptor and bipolar cells, and remained active in adult photoreceptors. In contrast, DHS4 had an earlier expression pattern that was limited to development. CRISPR-mediated knock-out of DHS4 caused a strong reduction in OTX2 expression embryonically, whereas targeting DHS2 and DHS15 resulted in a pronounced reduction of OTX2 expression postnatally. Targeting DHS4 with CRISPRi caused a strong reduction in OTX2 both embryonically and postnatally and resulted in an increase in amacrine cells.

Conclusions: DHS4 acts early in Otx2 regulation, while DHS2 and DHS15 enhancers act later. Perturbing these enhancers showed that each is important for Otx2 expression. The incomplete phenotypes seen upon deletion suggest that these enhancers act in a partially redundant or compensatory fashion during development, either with each other or with unidentified enhancers. This is supported by the stronger CRISPRi phenotype, which suggests that the Otx2 enhancers are looped in a complex where they can act interchangeably. Ongoing experiments are testing how these enhancers work together to control Otx2 expression and cell fate choice in the developing retina.

CONTROL ID: 3706755

SUBMITTER (NAME ONLY): Geoffrey Nguyen

TITLE: Quality Assessment of Polymer Materials for Human Model Eye Development

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Nguyen, T.H. Balasubramanian, D.M. Shah, J. Palmer, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|A.S. Odolil, University of Maryland at College Park, College Park, Maryland, UNITED STATES|M.R. Levin, R. Swamy, J.L. Alexander, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current commercially available training eye models are expensive while low-cost models have difficulty replicating the feel of real human tissues. In this study, we aim to develop an affordable and accurate model eye that can be used to improve microsurgical skills assessments. We created model eyes using six different polymer materials to determine which materials were the most appropriate in simulating real human sclera and extraocular muscle (EOM).

Methods: Five 3-D printed polymers (FlexFill, PolyFlex, PCTPE, Soft PLA, NinjaFlex) and one silicone material were systematically tested by seventeen board certified ophthalmologists and five PGY-4 ophthalmology residents. Participants performed scleral passes through each material's "sclera" and "EOM" components of their respective eye models. They then completed a questionnaire asking to rank each polymer material from 1-6 (1 = best in the group, 6 = worst in the group) to identify which would be most suitable for simulation training. The Wilcoxon Signed-Rank Test was conducted to determine if there was a statistically significant difference in the distribution of ranks between the polymer materials.

Results: The distribution of ranks for Silicone material's "sclera" and "EOM" components were statistically significantly higher than the distribution of ranks for all other tested polymer materials (all $p < 0.05$). Participants agreed that it effectively simulated real human sclera and EOM.

Conclusions: Silicone model eyes have substantial educational value for incorporation into a microsurgical training curriculum. It provides a low-cost teaching tool that allows for independent practice of microsurgical techniques.

CONTROL ID: 3706756

SUBMITTER (NAME ONLY): Shefali Sood

TITLE: A decision analytic economic model for use in glaucoma management

SESSION TITLE: Health Economics and Health Care Delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Sood, N. Heilenbach, V. Sanchez, L.A. Al-Aswad, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Shefali Sood: Commercial Relationship: Code N (No Commercial Relationship) | Noah Heilenbach: Commercial Relationship: Code N (No Commercial Relationship) | Victor Sanchez: Commercial Relationship: Code N (No Commercial Relationship) | Lama Al-Aswad: Commercial Relationship(s);Code F (Financial Support):Research to Prevent Blindness

ABSTRACT BODY:

Purpose: Given increasing US healthcare costs, decision analysis can help assess various medical and surgical interventions. We aim to build, validate and test a model for open angle glaucoma incorporating current practices.

Methods: Using Markov cycles, progression through 4 glaucoma severity stages (mild (0 to -6 decibels (dB)), moderate (-6.01 to -12 dB), advanced (-12.01 to -20 dB), and severe/unilateral blindness (<-20 dB)) and death was simulated in TreeAge Pro. In the default case, patients entered at age 65 in mild glaucoma and received care per American Academy of Ophthalmology Preferred Practice Patterns. Those with persistently good/moderate adherence progressed following visual field mean deviation decline rates for treated individuals in the Early Manifest Glaucoma Trial (EMGT) while those with poor adherence followed patterns of the untreated. IOP reductions from interventions were converted to glaucoma state transition probabilities using EMGT data. Retinal nerve fiber layer thinning faster than -1.0 µm/year on optical coherence tomography (OCT) imaging related to IOP control was a decision point for further interventions. Whole costs in glaucoma stages were estimated at US Medicare rates and utility values were obtained from previous work. We externally validated the model by comparing the 20-year cumulative incidence of blindness to that reported in a study from Olmsted, Minnesota, which was 13.5% (95% Confidence Interval: 8.8-17.9%.) We further tested the validity and reliability by excluding OCT-based decisions for intervention and instead, substituted progression on visual fields. We conducted test cases of various minimally invasive procedures and varied initial glaucoma severity.

Results: In the default case, 15.5% of the cohort progressed to blindness over 20 years, within the range in Olmsted. Over 35 years, using 10,000 iterations of random draws from parameter distributions, the cohort accrued 10.47 QALY (Standard Deviation (SD): 1.45) at a cost of $51,387.66 (SD: $7,415.93). By excluding OCT-based decisions, 17.0% of the cohort progressed to blindness after 20 years and accrued $46,080.04 (SD: $8,994.55) in cost and 10.45 QALY (SD: 1.44) after 35 years. In the test cases, the 20-year incidences of blindness ranged from 7.9% to 16.6%. Over 35 years, QALYs ranged from 12.09 to 12.27 at costs of $48,025.13 to $64,018.42.

Conclusions: Our model is validated and tested for use in open angle glaucoma cost studies.

CONTROL ID: 3706765

SUBMITTER (NAME ONLY): Catherine Zhu

TITLE: Impact of the dorzolamide/timolol shortage on patients with moderate to severe open-angle glaucoma

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.Q. Zhu, M. Desai, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|J.A. Tran, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Catherine Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Tran: Commercial Relationship: Code N (No Commercial Relationship) | Manishi Desai: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Topical antihypertensives remain the mainstay of treatment for glaucoma, as reduction of intraocular pressure (IOP) is the only proven method to prevent disease progression. We conducted a retrospective, observational study to examine the clinical implications of the limited dorzolamide/timolol supply on patients with moderate to severe primary open angle glaucoma (POAG) at an urban academic safety-net hospital. We predicted that the shortage would increase the mean IOP in our patients as well as the number of medication-related phone encounters.

Methods: Our study included 1,093 patients with a diagnosis of moderate or severe POAG on dorzolamide/timolol. IOP measurements were divided into two groups: those recorded before the FDA-reported shortage date of January 14, 2018 and those recorded following this date. The mean IOPs were calculated from both eyes for each patient. The mean difference between post- and pre-shortage IOPs was calculated using paired t-tests. We also examined data on the number of documented phone encounters; the difference before and after the shortage was calculated using a z-test.

Results: Compared to the mean pre-shortage IOPs, there was no statistically significant change in IOP following the reported shortage onset (pre-shortage IOP 15.9±4.0 mmHg, post-shortage 16.0±3.9 mmHg, $p=0.45$). Notably, only 159 patients had a documented discontinuation of dorzolamide/timolol during the post-shortage period; within this cohort, there was no difference in mean IOPs between the two timeframes (pre-shortage IOP 16.0±4.6 mmHg, post-shortage 16.0±4.6 mmHg, $p=0.87$). There was a significant increase in the proportion of medication-related phone encounters following the reported shortage date (pre-shortage 68/995, post-shortage 97/525, $z = -6.74$, $p<0.001$).

Conclusions: There was no appreciable difference in the outcome measure of IOPs of patients with moderate to severe POAG. This suggests that the detrimental effects of the dorzolamide/timolol shortage may be mitigated with patient education and alternative treatments and medications. Interestingly, there was an increase in the number of medication-related phone encounters following the reported shortage date, implying that there may be negative downstream administrative implications of medication shortages. However, the increase in phone calls may have also helped mitigate detrimental IOP increases through patient education.

CONTROL ID: 3706767

SUBMITTER (NAME ONLY): Anirudh Ashok

TITLE: Periodic axial motion estimation and correction using low-cost optical coherence tomography (OCT)

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ashok, H. Bagherinia, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

Commercial Relationships Disclosure: Anirudh Ashok: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc., Dublin, CA, United States | Homayoun Bagherinia: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc., Dublin, CA, United States

ABSTRACT BODY:

Purpose: Motion artifacts in OCT imaging have been an important topic in OCT data analysis. Periodic motion artifacts during OCT image acquisition of a patient can be caused by various sources such as muscular, peristaltic, cardiovascular, respiratory, as well as mechanical vibration in the instrument. Here we present a new periodic motion correction method for OCT data. We demonstrate the performance of the method by evaluating RPE (retinal pigment epithelium) elevation with and without motion correction.

Methods: Our method uses ILM (internal limiting membrane) and RPE segmentation in low-cost OCT volume scans. The Fourier transformation of ILM layer is used to estimate the periodic motion. The frequency bands associated with periodic pattern were removed prior to the inverse Fourier transformation. The estimated motion is then used to remove periodic motion artifact from the RPE layer. A polynomial surface is fitted to the RPE layer (RPE-fit) to mimic Bruch's membrane. The RPE elevation map is created by measuring the difference between the RPE-fit and RPE surfaces. We evaluated this method using scans from 17 subjects, either left or right eye, with retinal pathology. Each eye was scanned twice using a prototype low-cost OCT device that had a macula scan with 128x512 A-scans over 7x5.8 mm. The RPE elevation map from the 2nd scan was registered to that of the 1st scan. The RPE elevation volumes (in cubic micrometers) were averaged over central 3-mm and 5-mm zones. Regression and Bland-Altman plots were derived to evaluate the agreement of RPE elevation map.

Results: Figure 1 shows the algorithm pipeline and examples of RPE elevation maps with and without periodic motion correction. Figure 2 illustrates the Bland-Altman plots comparing the RPE elevation volume (in cubic micrometers) of the two scans from the same eye in the central 3-mm and 5-mm zones. Our results show that there is a good correlation agreement between the two methods. The method with motion correction shows smaller mean difference and tighter 95% confidence interval, which indicate a more repeatable method.

Conclusions: We presented a method to compensate for periodic motion in low-cost OCT data prior to the RPE elevation map creation. We demonstrated that the motion compensation is essential for visualization of the RPE elevation map as well as better agreement between repeat scans.

CONTROL ID: 3706768

SUBMITTER (NAME ONLY): Sophie Kubach

TITLE: Quality index threshold for optimal measurement repeatability in retinal macular vessel and perfusion density

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kubach, W. Lewis, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

Commercial Relationships Disclosure: Sophie Kubach: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Warren Lewis: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc.;Code E (Employment):Bayside Photonics, Inc.

ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) imaging is known to be prone to artifacts. Floaters, large motion, wavefront error from dry eyes or media opacities when present during the acquisition can reduce the visibility of small capillaries resulting in an inaccurate interpretation and quantification of the images. A flow quality algorithm (AI quantification of OCTA en face image quality – Charles Wu, Luis de Sisternes, IOVS, Aug. 2019, Vol.60, PB099) was recently developed to address the need for a reliable assessment of the quality of OCTA scans. In this study, we analyze how the flow image quality index impacts the repeatability of OCTA measurement to derive a quality index threshold.

Methods: 19 diabetic retinopathy (DR) eyes and 20 heathy eyes (HE) were imaged on PLEX® Elite 9000 swept-source OCT (ZEISS, Dublin, CA) by acquiring 4 consecutive 6×6 mm angiography scans at 100 kHz A-scan rate. For the DR eye cohort, the image quality index, vessel density (VD) and perfusion density (PD) were computed over the 9 ETDRS sectors of the retinal slab. For each eye, the 4 scan values for each ETDRS sector were averaged and the standard deviation from that mean calculated. The mean VD and PD were computer as well on the heathy eye cohort to establish the measurement baseline.

Results: Figure 1 displays the distribution in the image quality index on a 1-5, scale, 5 being the highest quality. Figures 2a and 2b show the VD and PD standard deviation scattered plots as a function of the flow quality index. These plots show a trend for improved measurement repeatability with index quality score. To better visualize this trend, the standard variation computed over a half-unit quality window is shown on Figures 2c and 2d. At a quality index of 3, the standard deviation in VD and PD of 1.3 and 0.027 respectively corresponds to less than 7% deviation from nominal values (VD = 23.2 mm^{-1} and PD = 0.4) obtained from healthy eyes.

Conclusions: The measurement repeatability in vessel and perfusion densities is related to the index quality metric of the flow images. An image quality threshold of 3 is recommended to provide sufficient confidence in the reported flow quality metrics.

CONTROL ID: 3706770

SUBMITTER (NAME ONLY): Jae Yeon Lee

TITLE: Inter-Eye Comparison of Lamina Cribrosa Depth between Eyes with Asymmetrical Severity in Bilateral Normal-Tension Glaucoma Patients

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, J. Kim, ophthalmology, Kangwon National University Hospital, Chuncheon, Kangwon, KOREA (THE REPUBLIC OF)|P.H. Kasani, S. Kwon, bigdata convergence, Kangwon National University, Chuncheon, Gangwon-do, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Jae Yeon Lee: Commercial Relationship: Code N (No Commercial Relationship) | Payam Kasani: Commercial Relationship: Code N (No Commercial Relationship) | Sungok Kwon: Commercial Relationship: Code N (No Commercial Relationship) | Jeong-Ah Kim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the association between lamina cribrosa depth (LCD) and severity of glaucomatous damage in bilateral Normal-Tension Glaucoma (NTG) patients who have more damage in one eye.

Methods: Optic nerve heads (ONH) were scanned using enhanced-depth spectral-domain optical coherence tomography. LCD was measured at the three locations spaced equidistantly across the vertical optic disc diameter using ONH horizontal B-scan images. LCDs were compared between more damaged and contralateral eyes. The association between LCD and the severity of glaucomatous damage was analyzed by using logistic regression analysis. Additionally, the conditional logistic regression analysis was performed to identify the ocular risk factors associated with more damage between both eyes in the individuals.

Results: A total of 72 eyes of 36 bilateral NTG patients were included. The mean age of patients was 66.8 ± 13.0 years, and 21 patients (58.3%) were male. More damaged eyes had thinner global retinal nerve fiber layer thickness ($P < 0.001$), worse visual field mean deviation ($P = 0.032$), and pattern standard deviation than contralateral eyes ($P < 0.001$). In contrast, there were no significant inter-eye differences in intraocular pressure, spherical equivalent, and axial length. Average LCD was significantly larger in more damaged eyes (514.2 ± 129.3 vs. 481.9 ± 114.2 μm, $P = 0.006$). While the severity of the glaucomatous damage was not correlated with the degree of LCD in more and less damaged eyes, the eye with deeper LCD had a higher risk for having severe damage between both eyes with similar systemic condition (odds ratio, 1.017; 95% confidence interval, 1.003-1.301; $P = 0.021$).

Conclusions: Average LCD was significantly larger in eyes with more damage, suggesting that LC deformation would be associated with glaucomatous ONH damage in the NTG eye.

CONTROL ID: 3706771

SUBMITTER (NAME ONLY): Rachel Huckfeldt

TITLE: Findings on visual photosensitivity in two phase 1/2 clinical trials of subretinal gene therapy with AGTC-401 and AGTC-402 for CNGB3 and CNGA3 achromatopsia

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Achromatopsia (ACHM) is an autosomal recessive retinal disorder associated with photosensitivity, absent color discrimination, and decreased visual acuity. We describe the effects of the subretinal gene therapies AGTC-401 and AGTC-402 on photosensitivity at Month(M) 12 and M24 post-treatment.

Methods: Participants with ACHM due to biallelic mutations in either CNGA3 (n=15; 2<18y) or CNGB3 (n=25; 4<18y) were sequentially assigned to one of 5 (CNGA3) or 6 (CNGB3) dose levels before receiving a single subretinal injection of AGTC-402 (rAAV2tYF-PR1.7-hCNGA3) or AGTC-401 (rAAV2tYF-PR1.7-hCNGB3) involving the macula of the study eye (SE). Safety and efficacy assessments included best-corrected visual acuity (BCVA; ETDRS letter score) and photosensitivity, which was measured as the light discomfort threshold (LDT). Two tests assessed LDT: LDT-1 using a full-field light stimulus generated by the Diagnosys ColorDome and LDT-2 using the Ocular Photosensitivity Analyzer. A meaningful post-treatment response in LDT was defined as an increase from baseline >1 loglux.

Results: In these participants with at least 12 months of follow-up, AGTC-401 and AGTC-402 were generally well-tolerated; serious adverse events were related to the surgical procedure (n=1) and steroid-associated elevated intraocular pressure (n=2). Mean BCVA changed by < 3 letters in both trials. Mean LDT at M12 was higher on LDT-1 in the CNGB3 trial (p=0.002) but unchanged on LDT-1 in the CNGA3 trial and on LDT-2 in both trials. The CNGB3 trial had 4 LDT-1 and 9 LDT-2 responders with the greatest number (LDT-1, n=3; LDT-2, n=6) in the pediatric and highest dose groups ($1.1e^{12}$ and $3.2e^{12}$ vg/ml). All LDT-1 responders were also LDT-2 responders. Improved LDT was sustained in 3 of 4 LDT-2 responders with M24 data. Untreated fellow eyes showed >1 loglux change in 75% of LDT-1

and 67% of LDT-2 responders. The CNGA3 trial had 2 LDT-1 and 2 LDT-2 responders among 3 participants with sustained improvement at M24 for the 2 responders for whom data was available.

Conclusions: Subretinal gene therapy with AGTC-401 resulted in clinically-meaningful and sustained improvement in light discomfort in some participants with CNGB3 ACHM. Fewer individuals showed a response after treatment with AGTC-402 in the CNGA3 trial. Further study is needed to understand the bilateral nature of the LDT improvement.

CONTROL ID: 3706772

SUBMITTER (NAME ONLY): Sandra Hammer

TITLE: Intermittent fasting prevents cholesterol accumulation, cholesterol crystal formation and the development of diabetic retinopathy.

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Hammer, J.V. Busik, Physiology, Michigan State University, East Lansing, Michigan, UNITED STATES|M.B. Grant, Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Sandra Hammer: Commercial Relationship: Code N (No Commercial Relationship) | Maria Grant: Commercial Relationship: Code N (No Commercial Relationship) | Julia Busik: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Time restricted feeding has multiple benefits without the detrimental side effects of calorie restriction. However, the mechanism of action in which time the restricted eating paradigm exerts positive outcomes remains inadequately studied. Previously, we showed that a high caloric state in diabetes leads to downregulation of SIRT1/LXRα activity resulting in retinal cholesterol accumulation. Herein, we investigated the retinal specific effects of long term IF using in vitro and in vivo models.

Methods: To model IF, we used human retinal endothelial cells (HREC) and serum depleted the cultures for 24hrs followed by exposure to cholesterol crystals for 24hrs. A type 2 diabetes (T2D) model, the db/db mouse was used and db/m mice was used as controls. Food restriction for 24hrs was followed by a 24hrs feeding period during this time mice had access to water ad libitum. After 6 months of diabetes, animals were sacrificed, and retinas analyzed for cholesterol crystal formation, inflammatory cytokine expression, and levels of SIRT1/LXRα and cholesterol. CC were quantified using ImageJ software analysis. Quantitative Real Time PCR was used to assay inflammatory marker production. Trypan blue exclusion assay was used to measure cell death.

Results: In vitro CC administration resulted in elevated levels of inflammatory markers (IL6, IL8, VCAM1, ICAM1, IL-1ß, n=3; $p<0.001$), complement pathway activation (C5aR, n=3; $p<0.001$) and apoptosis (n=3; $p<0.01$) in HREC which were improved by serum starvation. Long term diabetes resulted in decreased SIRT1 expression (n=5; $p<0.05$), elevated retinal cholesterol levels, CC formation (n=5; $p<0.05$) and inflammation marker expression (n=5; $p<0.05$). While CC were not found in retinas of non-diabetic aged, matched controls, they were observed in db/db mice. Long term IF increased retinal SIRT1/LXRα signaling, cholesterol efflux, prevented retinal cholesterol accumulation, CC formation and inflammation.

Conclusions: IF-mimicking conditions improved HREC response to CC exposure and lowering retinal cholesterol levels via IF prevented formation of CC and DR progression. Thus, this study suggests that IF is an effective and safe therapeutic strategy in combating the deleterious retinal effects associated with long term diabetes by reducing retinal levels of cholesterol, CC formation and deceasing retinal inflammation.

CONTROL ID: 3706778

SUBMITTER (NAME ONLY): Garrett Manion

TITLE: Optimizing patient accessibility: patients with decreased vision prefer educational materials in alternative media formats

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.N. Manion, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|G.N. Manion, M. Pascoe, S. Mian, L. Everett, T.J. Wubben, A. Shah, G. Comer, B. Tannen, N. Nallasamy, C. Hood, B. Young, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|M. Pascoe, Central Michigan University, Mount Pleasant, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Written materials are the dominant medium to convey educational and instructional information to patients. Given the significant proportion of patients with visual impairment in ophthalmology clinics, we hypothesize that these patients would prefer information presented through alternative media formats.

Methods: Patients were recruited from the University of Michigan Kellogg Eye Center Retina clinics (n=60) who had low vision, were scheduled for retina surgery or their first intravitreal injection, or were from the cornea clinic (n=50) at their pre-operative cataract surgery appointment. Best corrected visual acuity (BCVA), age, gender, electronic device usage, and previous usage of educational materials were collected. Each patient completed a Likert scale questionnaire to evaluate preference for written, infographic, audio, and video mediums of education. Data were analyzed through two-tailed Student’s t-test. An institutional review board reviewed this study protocol.

Results: Patients with BCVA of 20/50 or worse comprised 50% of the retina clinic and 30% of the cornea clinic participants. Their most preferred medium was audio while least preferred was written. Lower visual acuity positively correlated with preference for audio ($p<0.001$) and video ($p<0.001$) mediums while negatively correlating with written ($p=0.0004$) and infographic ($p=0.0024$) mediums. Patients with lower visual acuity were also less likely to use written handouts from any physician at prior encounters ($p<0.001$).

For all patients, video was most preferred and audio least preferred. In patients with BCVA 20/40 or better, written was the most preferred medium.

Conclusions: Patients with visual impairment tend to not use written materials from physicians and prefer alternate mediums of receiving information. Low visual acuity was associated with preference for audio and video over written and infographic mediums, with audio being most preferred. The patient population as a whole preferred video. Further investigation will be needed to see if these mediums are effective for educating visually impaired patients. Physicians may consider investing in alternative educational methods to increase accessibility of information to their patients.

CONTROL ID: 3706779

SUBMITTER (NAME ONLY): Matt Trinh

TITLE: Topographical Differences Vary Significantly Across All Retinal Layers in the Early Stages of Age-related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Trinh, M. Kalloniatis, Centre for Eye Health Ltd, Kensington, New South Wales, AUSTRALIA|D. Alonso-Caneiro, Queensland University of Technology Contact Lens and Visual Optics Laboratory, Kelvin Grove, Queensland, AUSTRALIA|L. Nivison-Smith, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Early changes in age-related macular degeneration (AMD) are suggested to extend beyond the outer retina, although locations of these changes are unclear. This study examines anatomical topographical differences across all retinal layers in early/intermediate AMD using high-density OCT analysis.

Methods: OCT macular cube scans of 96 early/intermediate AMD and 96 normal eyes from individual participants propensity-score matched on age, sex, and refraction were retrospectively recruited. High-density (60×60 0.01mm^2) grid thicknesses were custom-extracted and compared between AMD and normal eyes corrected for confounding. 'Normal-differences' were formed and underwent cluster analysis to reveal topography for the retinal nerve fibre (RNFL), ganglion cell (GCL), inner plexiform (IPL), inner nuclear (INL), outer plexiform (OPL), outer nuclear+Henle's fibre (ONL_{+HFL}) layers, inner- and outer-segments (IS/OS), and retinal pigment epithelium-to-Bruch's membrane (RPE-BM).

Results: AMD macular clusters across the inner retina (Fig 1) displayed extensively thinned RNFL, GCL, IPL, and paracentral INL (mean±SD, up to −8.44±1.51μm, P=0.63 to <0.0001) and thickened INL elsewhere. The outer retina (Fig 2) exhibited thinned OPL/ONL_{+HFL} paracentrally, IS/OS centrally, RPE-BM peripherally (up to −2.14±0.48μm, P=0.18 to <0.001), and thickened RPE-BM centrally (up to +5±1.14μm, P<0.01). Effect sizes (−2.74−+18.37SD), cluster sizes (2.2−60.1% area), and eccentricity effects varied.

Conclusions: Anatomical topographical differences are evident across all retinal layers in early/intermediate AMD. These results help define where changes may lie in the early stages of AMD.

CONTROL ID: 3706780

SUBMITTER (NAME ONLY): Melissa Yao

TITLE: Myopia is Associated with Greater Odds of Primary Open Angle Glaucoma Among Minorities in California Medicare Beneficiaries

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Yao, K. Kitayama, F. Yu, A.L. Coleman, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|M. Yao, K. Kitayama, F. Yu, V.L. Tseng, A.L. Coleman, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate for evidence of effect measure modification (EMM) by race/ethnicity on the association between myopia and primary open angle glaucoma (POAG); in other words, to determine whether race/ethnicity modifies the association between myopia and POAG.

Methods: A cross-sectional study was conducted in the 100% sample of 2019 California (CA) Medicare beneficiaries from the Centers for Medicare & Medicaid Services. Inclusion criteria were: age 65 or older, CA residence, and active coverage with Medicare Part B. The outcome of interest was POAG and the primary exposure was myopia, both defined by having International Classification of Diseases, Tenth Revision diagnosis codes for their respective conditions. To test for statistically significant EMM, a multivariable logistic regression model was created with myopia, POAG, and the following covariates: age, sex, race/ethnicity, systemic disease burden defined by Carlson Comorbidity Index (CCI) score, and an interaction term between myopia and race/ethnicity. To compare the effect of myopia on POAG modified by race/ethnicity, separate multivariable models were fitted for the effect of myopia on POAG, stratified by race/ethnicity, and adjusted for age, sex and CCI.

Results: The study population included 2,717,346 CA Medicare beneficiaries. About 1.9% (n = 52,517) of beneficiaries had a diagnosis of myopia and 37.2% (n = 1,010,539) identified as non-White. Subjects with myopia had 2.15 times the adjusted odds of POAG (95% confidence interval [CI], 2.09-2.21) compared to subjects without myopia, and there was evidence of statistical interaction between myopia and race/ethnicity ($p<0.0001$). In our multivariable models stratified by race/ethnicity, myopia was associated with greater adjusted odds of POAG than those without myopia within Black (odds ratio [OR]: 2.49, 95% CI, 2.19-2.82), Hispanic (OR: 3.13, 95% CI, 2.93-3.34), and Asian subjects (OR: 2.22, 95% CI, 2.05-2.41), as compared to White counterparts (OR: 1.92, 95% CI, 1.86-1.99).

Conclusions: In the CA Medicare population, myopia is associated with greater odds of POAG among minorities as compared to White subjects, after adjusting for covariates. There is significant EMM between race/ethnicity and myopia on the likelihood of having POAG. We cannot discern whether this is completely due to health disparities or other factors, such as gene-environment interactions.

CONTROL ID: 3706787

SUBMITTER (NAME ONLY): Alina Miron

TITLE: Studying corneal endothelial cell migration from outer graft rims

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Miron, S. Oellerich, G. Melles, V. Kocaba, R&D, Netherlands Institute for Innovative Ocular Surgery, Rotterdam, NETHERLANDS|A. Miron, Ophthalmology, Leiden University Medical Center (LUMC), Leiden, NETHERLANDS|S. Ní Dhubhghaill, Ophthalmology, Universitair Ziekenhuis Antwerpen, Antwerp, BELGIUM|

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ABSTRACT BODY:

Purpose: Predicting in vivo endothelial cell migration after surgical removal of central diseased endothelium is challenging since the capacity of endothelial cells (EC) to migrate can vary. In this study, outer corneal graft rims were cultured in a temperature-reversible hydrogel matrix to simulate in vitro the EC migration after Descemet stripping only (DSO) with and without ROCK-inhibitor.

Methods: Twenty-one outer rims with the trabecular meshwork still attached were prepared from Descemet membrane-endothelial cell (DM-EC) sheets (from 12 research-grade donors (mean age 76±5 years)) by a 6.5-mm trepanation. For the initial proof-of-concept, 7 outer rims were cultured in a thermo-reversible hydrogel matrix for up to 45 days. To assess the effect of ROCK-inhibitor on the in vitro cell migration, 7 paired outer rims were cultured either with or without ROCK-inhibitor. At the end of culture, tissue was retrieved from the polymer matrix to examine cell viability and expression markers (ZO-1, Na^+/K^+-ATPase, NCAM, glypican and vimentin).

Results: All cultured outer rims remained viable and displayed single regions (n=5/21) or collective (n=16/21) cell migration, regardless of the presence or absence of ROCK-inhibitor. Collective migration started on average after 4±2 days and continued for at least 29 days. Migrated cells showed a more regular cell morphology when cultured in the presence of ROCK-inhibitor than not. Furthermore, 7 outer rims additionally demonstrated a phenotypically distinct late-onset, but fast growing cell population emerging from the far periphery of the endothelium. This occurred after 3 weeks of culture and displayed characteristics for undifferentiated cells. Immunostaining showed that migrated EC maintained the expression patterns of endothelial cell markers.

Conclusions: Using a 3D-culture system, we observed the migration of two morphologically distinct cell populations. The first type was triggered by a broken physical barrier, consistent with disruption of contact inhibition. The second, late-onset type showed a higher proliferative capacity, which appears to be mediated by other stimuli next to cell exposure to free space and ROCK-inhibitor. Further exploration of the differences between these cell types may assist in learning how to selectively stimulate cell migration from DM-EC areas that harbor the latter cell type and may ultimately help to improve DSO outcomes.

CONTROL ID: 3706788

SUBMITTER (NAME ONLY): Norbert Pfeiffer

TITLE: Effect of treatment and frequency of OCT monitoring on quality of life in neovascular age related macular degeneration (nAMD) and diabetic macular edema (DME). ALBATROS Data Collection

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pfeiffer, A. Schuster, Augenklinik, Universitatsmedizin der Johannes Gutenberg-Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|C. Wolfram, Augenklinik, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|T. Hudde, Augenklinik, Eye Hospital Wolfsburg-Fallersleben, GERMANY|A. Klatt, Augenklinik, Eye Center Klatt, GERMANY|B. Schnegelsberg, H. Midani-Oezkam, Augenheilkunde, Novartis Pharma Nürnberg, GERMANY|F. Ziemssen, Augenklinik, Universitatsklinikum Leipzig, Leipzig, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Frequent use of OCT to monitor retinal fluid is essential in the treatment of nAMD and DME. The ALBATROS data collection was set up to measure how the number of sequential OCTs as recommended by 3 German Ophthalmology Societies affects patient quality of life (QoL).

Methods: Parameters collected were BCVA, central retinal thickness (CRT), QoL (NEI-VFQ-25) at baseline and month 12, number of anti-VEGF treatments and number of OCT scans. VFQ-25 was calculated in overall, composite and Rasch-transformed scales.

Results: Data was collected from 102 sites (n=1444 nAMD, n=445 DME). nAMD patients had a mean improvement in vision of 3.4±19.3 (ETDRS letters±SD) from baseline to last visit, DME patients a mean improvement in vision of 4.1±13.3 letters, respectively. For nAMD patients a mean of 7.2 OCTs and 5.2 anti-VEGF injections were performed. For DME patients 7.1 OCTs and 5.0 injections were recorded (median observation time for both groups: 365 days). No relevant change was seen in Rasch-transformed QoL scales for either group. In the nAMD group the VFQ-25 subscale score showed patient relevant improvement (56.4±17.93 to 62.1±17.30) for distance vision, but not for near vision. In DME patients clinically relevant improvement was seen in VFQ-25 subscales for both distance and near vision. In DME higher VFQ-25 scores were seen when more OCT examinations were conducted. Specifically, the general health scale declined by 2.4 when >3 to ≤6 OCTs were done (3.5 injections in this group), but increased by 2.6 with >6 to ≤9 OCTs (5.3 injections) and increased by 6.5 when >9 OCTs (8.3 injections) were completed. In nAMD an increasing injection rate in the 3 OCT subgroups (3.8 vs. 5.5 vs 7.7) was not reflected by a change in VFQ-25 score despite the increase in BCVA in the higher OCT-subgroups (1.4. vs. 4.4 vs 4.1).

Conclusions: Improvement in QoL was seen in both nAMD and DME groups with increasing number of injections and OCT examinations for distance vision and in the DME group for near vision. In DME patients there was a trend for higher scores in the VFQ-25 QoL with increasing number of OCT scans performed although this was not seen in nAMD. Management of these conditions according to the recommendations of the German Ophthalmology Societies results in a reasonable number of OCT examinations and improved patient QoL.

CONTROL ID: 3706793

SUBMITTER (NAME ONLY): Rachel Chong

TITLE: Sector-wise Comparison of Retinal Layer Thickness in High Myopia and Low/Non-Myopia Eyes without Visual Field Defects

SESSION TITLE: Myopia: Structural Changes from Retina to Sclera

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.S. Chong, D. Hoang, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|R.S. Chong, M. Yu, Y. Sim, S. Lor, Q. Wong, S. Majithia, S. Saw, C. Cheng, D. Hoang, L. Schmetterer, J. Chua, Singapore Eye Research Institute, Singapore, SINGAPORE|J. Chia, A. Gan, S. Saw, C. Cheng, National University of Singapore, Singapore, SINGAPORE|L. Schmetterer, Nanyang Technological University, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To compare individual retinal layer thickness in peripapillary (ppOCT) and macula (mOCT) OCT scans in high myopia (HM) and low/non-myopia (NM) eyes without visual field (VF) defects.

Methods: HM was defined as spherical equivalent (SE) of ≤-6D or axial length (AL) of ≥26mm, NM was defined as SE of 0 to -3D and AL of <24 mm. Subjects with diabetes, neurological disease, neuroretinal rim thinning, intraocular pressure of >21mmHg or other ocular disease apart from myopia were excluded. Eyes with indeterminate neuroretinal rim thickness underwent VF testing, and were included if ≥2 reliable VF showed glaucoma hemifield test within normal limits, and VF index ≥97%. Two different 200 x 200 scans were acquired in the same eye using Cirrus spectral-domain OCT: mOCT centered on the macula and ppOCT centered on the optic disc. Poor quality scans were excluded. PpOCT scans were divided into superior (S), nasal (N), inferior (I) and temporal (T) sectors; mOCT scans were divided into S, S-N, S-T, I, I-N and I-T sectors and analyzed using Iowa Reference Algorithms 3.8.0 and MATLAB to delineate individual layer thickness and sectoral boundaries. Ocular magnification was corrected using Littmann's formula, based on axial length. Thickness measurements were compared between HM and NM eyes using linear mixed effect models to account for fellow-eye correlation, after adjusting for age and gender.

Results: 159 eyes from 111 HM subjects and 153 eyes from 98 NM subjects were included. Sector-wise differences were noted in all 10 layers of the retina i.e. RNFL, GCL, IPL, INL, OPL, ONL, IS/OS, OSL, OPR, RPE when considered individually, in both ppOCT and mOCT scans ($p<0.05$). Combining the outer retinal layers into INL to RPE (INL-RPE) however, showed no significant difference between HM and NM eyes at any mOCT sector. Combining the inner retina layers into GCL to IPL (GC-IPL) also showed no significant difference in mOCT, apart from superiorly (mean HM GC-IPL 85.0±1.6μm, NM 82.7±1.4μm, $p=0.03$). HM and NM eyes differed in all ppOCT sectors ($p<0.05$).

Conclusions: HM eyes without VF defects have similar INL-RPE thickness in all macula sectors, and similar GC-IPL thickness apart from superiorly, compared to NM eyes after correcting for magnification error, age and gender. Mapping VF defects in HM to localized INL-RPE or GC-IPL SD-OCT measurements may increase diagnostic accuracy of glaucoma in HM eyes.

CONTROL ID: 3706794

SUBMITTER (NAME ONLY): Indre Vasiliauskaite

TITLE: Effect of surgical indication and disease severity on clinical outcomes and graft survival up to 10 years after Descemet Membrane Endothelial Keratoplasty

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Vasiliauskaite, V. Kocaba, K. van Dijk, L. Baydoun, C. Lanser, D. Lee, G.R. Melles, S. Oellerich, R&D, Netherlands Institute for Innovative Ocular Surgery, Rotterdam, NETHERLANDS|I. Vasiliauskaite, M.J. Jager, Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To evaluate clinical outcomes and graft survival in a large cohort of patients up to 10-years after Descemet Membrane Endothelial Keratoplasty (DMEK) based on surgical indication and Fuchs endothelial corneal dystrophy (FECD) severity.

Methods: In this retrospective cohort, we included 750 eyes (572 patients) which underwent DMEK for FECD (86%), bullous keratopathy (BK, 9%), and other indications (5%). Based on the modified Krachmer grading, 186 eyes (29%) had moderate FECD (Krachmer grade 3 and 4) and 440 eyes (68%) advanced FECD (Krachmer grade 5 and 6). Best-corrected visual acuity (BCVA), central corneal thickness (CCT), endothelial cell density (ECD), endothelial cell loss (ECL), postoperative complications, and graft survival were assessed up to 10-years after DMEK.

Results: BCVA outcomes and CCT remained stable between 1- to 5-years and 5- and 10-years postoperatively (all $P>0.05$). Mean 10-year BCVA was 0.08±0.28 logMAR (n=96) and mean 10-year CCT was 545±39 µm (n=98). Mean ECD was 1136±460 cells/mm^2 (n=460) at 5-years and 890±381 cells/mm^2 (n=96) at 10-years with an ECL of 56% and 66%, respectively ($P<0.05$). Allograft rejection was diagnosed in 3% (n=24) of the eyes. Graft survival rate for the total cohort was 0.85 (95% CI, 0.82-0.89) at 10-years after DMEK. BCVA and ECD differed at 1-5 years between eyes with different surgical indications (all $P<0.05$). Eyes with FECD surgical indication had a higher graft survival rate compared to BK eyes (0.90 vs 0.60, $P=0.001$). Eyes with moderate FECD had better BCVA and ECD outcomes than advanced FECD eyes ($P<0.05$), except for the difference in 10-year ECD where it did not reach statistical significance ($P=0.392$). Furthermore, eyes with moderate FECD stage had a higher graft survival rate compared to advanced FECD eyes (0.94 vs 0.88, $P=0.018$).

Conclusions: Long-term clinical outcomes and graft survival after DMEK are related to surgical indication (FECD versus BK) and to disease severity for FECD eyes. Eyes operated for moderate FECD showed the highest graft survival probability and excellent long-term clinical outcomes.

CONTROL ID: 3706796

SUBMITTER (NAME ONLY): Janika Nättinen

TITLE: Biological processes and clinical variables affecting trabeculectomy surgery outcome

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of the study is to establish what preoperative factors influence the trabeculectomy outcome.

Methods: In this prospective study, we followed 80 glaucomatous eyes for 5 years after trabeculectomy. At baseline, prior to surgery, tear fluid samples and clinical data were collected from the patients. All postoperative complications, i.e., needling, restart of a glaucoma medication and reoperation, were recorded. The patients' postoperative statuses (success (S) vs qualified success (QS) and failure (F)) were then compared against the baseline tear proteomics and clinical variables with Wilcoxon rank sum test. Proteomic pathway analyses were performed using Ingenuity Pathway Analysis (IPA) software.

Results: One year after surgery, 15 (19%) QS+F patients were recorded. Respective numbers 3 and 5 years after surgery were 20 (26%) and 23 (38%). According to pathway analysis results, patients with QS+F status after first year had a decreased generation of reactive oxygen species (ROS) (P=0.02) and an increased development of vasculature and cell movement of immune cells (all P=0.02) at baseline. Patients with QS+F status 1 and 3 years after trabeculectomy had also inhibited estrogen receptor 2 (ESR2) at baseline according to the upstream analysis (P=0.02 and P=0.04, respectively). The patients with QS+F status 1, 3 or 5 years after surgery had statistically higher baseline IOP in comparison to patients with a successful outcome (median IOP value differences were 7 (P=0.003), 3.5 (P=0.008) and 4.5 (P=0.01) mmHg, respectively).

Conclusions: Tear proteomics results revealed that the states of biological functions in the ocular surface are associated with the trabeculectomy outcome. In addition to inflammation, the instability of ROS merits further studies to establish whether they could be used as trabeculectomy outcome indicators or as druggable targets to improve the surgical outcome.

CONTROL ID: 3706801

SUBMITTER (NAME ONLY): Janine Reurink

TITLE: Scrutinizing pathogenicity of the USH2A c.2276G>T; p.(Cys759Phe) variant

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Reurink, K. Neveling, C. Gilissen, L. Haer-Wigman, F.P. Cremers, H. Kremer, S. Roosing, Department of Human Genetics, Radboud University Medical Center, Nijmegen, NETHERLANDS|J. Reurink , E. de Vrieze, C.H. Li, L. Haer-Wigman, C.C. Hoyng, F.P. Cremers, S. Roosing, E. van Wyk, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, NETHERLANDS|E. de Vrieze, S. Broekman, T. Peters, H. Kremer, E. van Wyk, Department of Otorhinolaryngology, Radboud University Medical Center, Nijmegen, NETHERLANDS|C.H. Li, C.C. Hoyng, Department of Ophthalmology, Radboud University Medical Center, Nijmegen, NETHERLANDS|H. Venselaar, Centre for Molecular and Biomolecular Informatics, , Radboud Institute for Molecular Life Sciences, Radboud University Medical Center, Nijmegen, NETHERLANDS|C. Gilissen, Radboud Institute of Molecular Life Sciences, Radboud University Medical Center, Nijmegen, NETHERLANDS|J.J. van Lith-Verhoeven, Department of Ophthalmology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: USH2A variant c.2276G>T (p.(Cys759Phe)) has been described as a frequent cause of autosomal recessive retinitis pigmentosa (arRP). However, its pathogenicity has been a matter of debate since the description of two a-symptomatic individuals homozygous for this variant. In this study, we therefore aimed to assess pathogenicity of the USH2A c.2276G>T variant using extensive genetic and functional analyses.

Methods: Whole genome sequencing and optical genome mapping were performed for three arRP cases homozygous for USH2A c.2276G>T to exclude alternative genetic causes, including variants in potential regulatory regions of USH2A. A minigene splice assay was designed to investigate the effect of c.2276G>T, in the presence or absence of the nearby c.2256T>C variant, on pre-mRNA splicing. A molecular model of the fifth laminin–epidermal growth factor like domain was generated to observe a putative structural effect. Moreover, an ush2a$^{p.(Cys771Phe)}$ zebrafish knock-in model mimicking human p.(Cys759Phe) was generated and phenotypically evaluated using functional and immunohistochemical analyses.

Results: Besides the homozygous c.2276G>T USH2A variant, no other potentially causative DNA variants could be identified with our genetic approaches. Furthermore, p.(Cys759Phe) is predicted to be detrimental for usherin folding and function, based on molecular modeling. Evaluation of the ush2a$^{p.(Cys771Phe)}$ zebrafish model revealed significantly reduced levels of usherin expression at the photoreceptor periciliary membrane, increased levels of rhodopsin localization to the photoreceptor cell body and decreased ERG b-wave amplitudes as compared to wildtype controls.

Conclusions: We confirmed pathogenicity of USH2A c.2276G>T (p.(Cys759Phe)). Consequently, persons homozygous for c.2276G>T can now receive a definite genetic diagnosis and can be considered eligible for QR-421a-mediated exon 13 skipping therapy in the future.

CONTROL ID: 3706804

SUBMITTER (NAME ONLY): Rita Laiginhas

TITLE: Multimodal Imaging, OCT B-Scan Localization, and En face OCT Detection of Macular Hyperpigmentation in Eyes with Intermediate AMD

SESSION TITLE: AMD Imaging

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Multimodal imaging was used to identify and characterize the cause of hyperpigmentation seen on color fundus images (CFIs) in eyes with intermediate age-related macular degeneration (iAMD).

Methods: At the Bascom Palmer Eye Institute, a retrospective review of a prospective observational case series of eyes with iAMD was performed. CFIs with macular hyperpigmentation were compared with same day images obtained using fundus autofluorescence (FAF), near infrared reflectance (NIR) and swept-source optical coherence tomography (SS-OCT) imaging. Two SS-OCT en face slabs were generated for analysis: a retinal slab to identify hyper-reflective foci within the retina and a slab from beneath the retinal pigment epithelium (sub-RPE slab) that was used to detect regions that cause decreased light transmission into the choroid, also known as hypo-transmission defects (hypoTDs). All images were registered to allow for qualitative comparisons by two independent graders.

Results: Six representative cases from this study are shown. Compared with CFIs, FAF imaging appeared to be the least sensitive method for the detection of hyperpigmentation while NIR and SS-OCT imaging reliably detected these foci of hyperpigmentation. While NIR imaging detected most of the hyperpigmentation seen in CFIs, SS-OCT imaging detected all the areas of hyperpigmentation, and these areas were anatomically localized by using both en face and B-scan images. En face OCT slabs of the retina and sub-RPE region were registered to the CFIs and areas of hyperpigmentation were shown to correspond to hyper-reflective foci in the retina and regions of thickened RPE seen on OCT B-scans. While both hyperpigmentation and early atrophic lesions appeared bright on NIR imaging, en face SS-OCT imaging was able to distinguish these lesions since hyper-pigmentation appeared dark and early atrophic lesions appeared bright on the sub-RPE slab.

Conclusions: En face OCT imaging in conjunction with OCT B-scans were able to reliably identify and localize the hyperpigmentation seen on CFIs, and unlike previous reports that associated hyperpigmentation with intra-retinal hyper-reflective foci, we found that this hyperpigmentation could also be associated with a thickened RPE.

CONTROL ID: 3706807

SUBMITTER (NAME ONLY): Tyler Godat

TITLE: In vivo calcium imaging reveals L/M opponent ganglion cells consistent with single cone receptive field centers at the macaque foveal center

SESSION TITLE: Retinal ganglion cells and central processing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Godat, S.S. Patterson, K. Kohout, K. Parkins, Q. Yang, J.M. Strazzeri, J.E. McGregor, W. Merigan, D.R. Williams, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|T. Godat, K. Kohout, D.R. Williams, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|N.P. Cottaris, D.H. Brainard, Department of Psychology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|J.M. Strazzeri, W. Merigan, David & Ilene Flaum Eye Institute, University of Rochester Medical Center, University of Rochester Medical Center, Rochester, NY, US, academic/hospital, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The fovea is specialized for high spatial resolution and color vision, but there is a paucity of recordings that elucidate how retinal ganglion cells (RGCs) at the very center of the fovea facilitate this specialization. Here, we optically record responses to spatial and chromatic stimuli using a calcium indicator in the living eye to characterize the receptive field (RF) properties of RGCs serving the foveal center.

Methods: The calcium indicator GCaMP6s was expressed in the ganglion cell layer of a female macaque. Adaptive optics scanning light ophthalmoscopy (AOSLO) was used to image fluorescence (488nm ex., 520/35nm em.) from RGCs whose RF centers were driven by cones in the central 6 arcmin of the fovea. By recording responses to cone isolating and luminance flicker (1.3deg, 0.15Hz, LED 420nm, 530nm, 660nm), we derived cone weights in 34 RGCs. By recording responses to drifting gratings (1.9deg, 6Hz, 4-50c/deg, 561nm), we derived the spatial frequency responses of 15 L/M chromatic opponent RGCs. Employing computational modeling (ISETbio toolbox, isetbio.org) that accounted for residual blur in the instrument, the eye's optics, cone aperture, and the spacing of individual cones, we inferred the number of cones feeding into RF centers and surrounds.

Results: Of the 34 RGCs, 44% exhibited L/M chromatic opponency, 15% were L+M ON, 6% were -L-M OFF, while the remaining 35% showed only L or only M responses. The spatial frequency response functions of 12/15 L/M opponent cells peaked at high spatial frequencies (25-40c/deg) and had a strong bandpass characteristic. Our model indicates that the responses of at least 9/15 L/M opponent cells are consistent with single cone input to their RF centers [Fig 1].

Conclusions: Using AOSLO to image calcium-mediated responses allows the study of the cone inputs to and spatial frequency responses of the very centermost foveal RGCs in the living primate eye. Our model establishes a framework for estimating sources of optical and neural information loss. The high spatial frequency tuning and single cone inputs we observed in L/M opponent cells emphasize the foveal specialization for spatial and chromatic vision by preserving information at the resolution of the photoreceptor mosaic.

CONTROL ID: 3706809

SUBMITTER (NAME ONLY): Joana Tavares

TITLE: Current management of Inherited Retinal Degenerations (IRD) patients in Europe. Results of a 2 years follow-up multinational survey by EVICR.net and ERN-EYE

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: An increasing number of gene-specific therapies are being developed for IRDs. Identification of well characterised patients is an emerging need. We conducted the second multinational survey among the EVICR.net and ERN-EYE members to understand the management of IRDs in Europe, and compared it to the 2019 survey[1, 2].

Methods: An electronic survey questionnaire was developed and sent to the 126 EVICR.net and ERN-EYE clinical centers (25 countries). Statistical analysis was performed with Excel and R.

Results: The overall response rate was 44% but varied among countries. Only 9% of responding centers do not see IRD patients (1st survey 14%); 42% follow at least 200 patients per year, 18% follow 500-999 and 2% more than 1000. Databases exist in 86% of the centers (local 86%; national web-based 12%). IRD patients are referred to EVICR.net and ERN-EYE centers mainly by general ophthalmologists, patient self-referral, or medical retina specialists. Most IRD patients are first seen as adults. Signs and symptoms depend on age of onset (infancy: nystagmus, older ager night blindness and reduced visual acuity [VA]). Mean time from asking for 1st appointment and clinical diagnosis varies among countries: 36% of centers < 4 weeks, up to 12 months in others (1st survey ≤35 months). Comprehensive ophthalmic examination always includes VA, in 98% visual fields, and imaging (FAF and/or NIRAF, OCT and/or OCTA), in 96% fundus photography and electrophysiology, in 94% color vision testing and in 92% refraction. Identification of genotypes is possible in 72% of centers in 40-80% (1st survey 69%) of cases. The time for confirmation of the genetic diagnosis varies from 2-4 weeks to 24 months (1st survey > 4 weeks and ≤ 10 years). Genetic testing is covered by public health service in 83%, private health insurance in 29%, research funds in 24%; 5% do not have access to genetic testing (1st survey 15%).

Conclusions: This 2nd multinational survey on management of IRDs in Europe highlights important differences in the number of IRD patients managed per center, comparable diagnostic work-up, and increasing genotyping. The data are particularly useful in the era of rapidly increasing gene therapy trials for IRDs.

1. Lorenz B, et al. Ophthalmic Res. 2021;64(4):622-638. doi:10.1159/000514540
2. Lorenz B, et al. Ophthalmic Res. 2021;64(5):740-753. doi:10.1159/000515688

CONTROL ID: 3706810

SUBMITTER (NAME ONLY): Charles Wykoff

TITLE: Brolucizumab for treatment of diabetic macular edema (DME): 100-week results from the KESTREL and KITE studies

SESSION TITLE: Diabetic Macular Edema

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To present the 100-week results from the KESTREL and KITE studies that evaluated efficacy and safety of brolucizumab (BRO) versus aflibercept (AFL) in patients with DME.

Methods: KESTREL (NCT03481634) and KITE (NCT03481660) were two 100-week (W), double-masked, active-controlled, Phase 3 studies. In KESTREL, patient randomization was 1:1:1 to BRO 3mg, BRO 6mg or AFL 2mg; in KITE, randomization was 1:1 to BRO 6mg or AFL 2mg. The BRO arms received 5 loading doses every 6 weeks (q6w) followed by q12w dosing, with an option to adjust to q8w at predefined disease activity assessment visits. At W72 in KITE, based on the disease stability assessment by the masked investigator, there was an option to extend the treatment interval for BRO patients by 4 weeks i.e. from q12w to q16w or q8w to q12w. The AFL arms received 5 monthly loading doses followed by fixed q8w dosing until end of study.

Results: In both studies, BRO 6mg was non-inferior to AFL for the change in BCVA at W52 (primary endpoint) and the VA gains were maintained to W100 (change in BCVA (letters) from baseline: BRO 6mg +8.8 vs AFL+10.6, difference −1.7 [95% CI, −3.8, 0.4] in KESTREL; BRO 6mg +10.9 vs AFL +8.4, difference +2.6 [95% CI, 0.2, 4.9] in

KITE). The change in central subfield thickness (CSFT) from baseline over the period W88 through W100 in BRO 6mg and AFL arms were −171.9µm vs −168.5µm in KESTREL; −196.6µm vs −173.4µm in KITE. Fewer BRO 6mg patients had IRF and/or SRF vs AFL at W100 (KESTREL, 41.8% vs 54.0%; KITE, 40.8% vs 56.9%). Of the BRO 6mg patients who successfully completed the first q12w cycle immediately after the loading phase, 70.2% remained on q12w interval in KESTREL and 69.6% on q12w/q16w interval in KITE up to W100. In KESTREL, intraocular inflammation (IOI) rates were 5.3%, 4.2% and 1.1% in BRO 3mg, BRO 6mg and AFL, respectively; incidence of retinal vascular occlusion (RO) and retinal vasculitis (RV) were 1.6% and 1.6% in BRO 3mg, 1.6% and 0.5% in BRO 6mg and, 0.5% and 0% in AFL arms, respectively. No new RV reported in Year 2 in KESTREL. In KITE, IOI rates were 2.2% in BRO 6mg vs 1.7% AFL; incidence of RO was 0.6% in both BRO 6mg and AFL arms; there were no cases of RV through W100.

Conclusions: The 100-week results from KESTREL and KITE reaffirm the efficacy of brolucizumab for the treatment of DME seen in the Year 1 data. The overall safety profile of BRO 6mg remained unchanged through Year 2.

CONTROL ID: 3706814

SUBMITTER (NAME ONLY): Nobuhiko Shiraki

TITLE: PAX6-positive microglia evolve locally in hiPSC-derived ocular organoids

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Microglia are the resident immune cells of the central nervous system (CNS). Since the immune cells from the general circulation cannot reach the CNS due to the blood-brain barrier, the brain and spinal cord microglial cells provide immune protection for CNS. Also, the microglia provide immune protection to the posterior eye, including the neural retina, and are involved in some sight-threatening conditions, such as age-related macular degeneration, uveitis, glaucoma, and retinal degeneration. However, it is not known how the microglia develop in the eye.

Methods: We studied human-induced pluripotent stem cells (hiPSCs) that had been expanded into a self-formed ectodermal autonomous multi-zone (SEAM) (Hayashi et al. Nature 2016;531:376-380) of cells that partially mimicked the human eye development. We searched and investigated the microglia-like cells, sorted them, and examined them by quantitative polymerase chain reaction (qPCR), cytokine analysis, RNA sequencing (seq), and single-cell RNA seq.

Results: We discovered that they contained immune cells that were significantly similar to the microglia cells in SEAM. Moreover, the RNA-seq data and qPCR showed that the cells were more similar to primary microglia cells than to immortalized human microglia. The results of the functional stimulation assays revealed that the sorted cells are likely govern immune tolerance in the ocular tissue. Furthermore, single-cell RNA seq revealed that the cells resembled yolk sac-derived myeloid progenitors and not macrophages.

Conclusions: Our results showed that microglia-like cells showing characteristics of yolk sac-like linage cells naturally develop in SEAM organoids, which lack vascular components. These cells are unique because they are paired box protein 6 (PAX6)-positive, yet possess some characteristics of the mesoderm. Our data support the possibility of the existence of an isolated and locally developing immune system in the eye, which is independent of the body’s vasculature and general immune system.

CONTROL ID: 3706816

SUBMITTER (NAME ONLY): Veronika Röggla

TITLE: Spatial and temporal distribution of recurrent fluid in neovascular AMD quantified with a deep learning algorithm

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Röggla, G.S. Reiter, P. Fuchs, O. Leingang, L.M. Coulibaly, H. Bogunovic, U. Schmidt-Erfurth, Opthahlmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|D. Barthelmes, Opthahlmology, UniversitatsSpital Zurich, Zurich, SWITZERLAND|

Commercial Relationships Disclosure: Veronika Röggla: Commercial Relationship: Code N (No Commercial Relationship) | Gregor Reiter: Commercial Relationship(s);Code F (Financial Support):RetInSight | Philipp Fuchs: Commercial Relationship: Code N (No Commercial Relationship) | Oliver Leingang: Commercial Relationship: Code N (No Commercial Relationship) | Leonard Coulibaly: Commercial Relationship: Code N (No Commercial Relationship) | Hrvoje Bogunovic: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Barthelmes: Commercial Relationship: Code N (No Commercial Relationship) | Ursula Schmidt-Erfurth: Commercial Relationship(s);Code C (Consultant/Contractor):RetInSight

ABSTRACT BODY:

Purpose: The aim of the study is to investigate the quantity and distribution of fluid in neovascular age-related macular degeneration (nAMD) and the difference between the initial, treatment-naïve, presentation, at the beginning and the end of a treatment break.

Methods: Using data from one site of the Fight Retinal Blindness (FRB) Registry (University of Zurich, Switzerland), the distribution of retinal fluid in treatment-naïve nAMD patients compared to retinal fluid recurrence has been studied in a longitudinal manner. Study eye eligibility required treatment-naïve nAMD, receiving at least three anti-VEGF injections within the first six months of treatment, followed by a treatment pause of at least six months and fluid recurrence afterwards. To quantify fluid, a verified deep learning algorithm was used (Vienna Fluid Monitor, RetInSight, Vienna, Austria). Fluid volumes and proportions were compared between different time points using Friedman test and Wilcoxon signed rank test, respectively.

Results: Fifty-five eyes of 55 patients with the mean age of 76.86 ± 6.04years at baseline matched the inclusion criteria. A median of 12.66 (IQR 11) injections and 18.96 (IQR 22) months of treatment were needed to enable a treatment pause of at least six months. Visual acuity was 0.57 logMar at baseline, 0.47 logMar at start of the break and 0.48 logMar at the end of the break. At baseline, SRF showed a median of 55.29nl (IQR 243.79nl), IRF a median of 1.55nl (IQR 133.37nl) and PED a median of 0nl (IQR 520.73nl) in the central 6 millimeters. At disease recurrence, SRF showed a median of 8.07nl (IQR 86.29nl), IRF a median of 4.88nl (IQR 24.85nl) and PED a median of 0nl (IQR 551.61nl) in the central 6 millimeters (Figure 1). From baseline to start of the break, SRF and IRF decreased significantly ($p<0.01$) and PED did not change significantly ($p=0.215$). At baseline, the proportions of IRF, SRF and PED were 21%, 53% and 26%, respectively, with no significant shift except SRF at end of break to 27%,41% and 32% ($p=0.123$, $p=0.029$ and $p=0.374$), respectively.

Conclusions: Retinal fluid proportions were distributed predominantly in the subretinal compartment in treatment-naïve patients, whereas it was spread more equally between all fluid compartments after a treatment break. These morphological differences may contribute to our understanding of disease activity.

CONTROL ID: 3706823

SUBMITTER (NAME ONLY): Ronald Frenkel

TITLE: Does Intravitreal Anti-VEGF Therapy with Ranibizumab, Bevacizumab, and Aflibercept Cause Rebound Supranormal Systemic VEGF Levels?

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Frenkel, Eye Research Foundation, Stuart, Florida, UNITED STATES|R. Frenkel, East Florida Eye Institute, Stuart, Florida, UNITED STATES|

Commercial Relationships Disclosure: Ronald Frenkel: Commercial Relationship(s);Code C (Consultant/Contractor):Regeneron;Code C (Consultant/Contractor):Opthea;Code C (Consultant/Contractor):Apellis;Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Santen;Code C (Consultant/Contractor):Gemini;Code C (Consultant/Contractor):Sandoz;Code C (Consultant/Contractor):Iveric

ABSTRACT BODY:

Purpose: To determine PK and plasma VEGF evels at baseline, 4 weeks, 6 weeks, or 8 weeks from intravitreal administration of bevacizumab, ranibizumab, or aflibercept and compare them to untreated controls.

Methods: 77 patients, including 8 untreated controls, who were treated with bevacizumab, ranibizumab, or aflibercept at a precedent time interval of 4, 6, or 8 weeks continued to receive the same drug at the same interval and had serum PK and plasma VEGF levels measured at baseline, 4 weeks, and 6 or 8 weeks.

Results: Untreated controls had little variability in plasma VEGF levels which were almost uniformly <20 pg/ml. (Fig1). Following intravitreal administration of bevacizumab, ranibizumab, or aflibercept as the dosing interval increased there were in general more pronounced decreases of the mean plasma VEGF levels as drug concentration increased, especially in the bevacizumab and aflibercept 6 week and 8 week treatment groups. Mean plasma VEGF levels were less affected by ranibizumab than bevacizumab and aflibercept; the drug concentration effect was most marked in the bevacizumab and aflibercept 6 and 8-week treatment groups. Bevacizumab in the 4-week group induced the lowest mean plasma VEGF levels. Surprisingly many treated patients, as exemplfied in the 4 week groups, at times had much higher plasma VEGF levels (up to 47 pg/ml) than individuals in the control group (Fig. 2). This was also true in the 6 and 8 week groups.

Conclusions: Aflibercept and bevacizumab, 6 and 8 week groups showed the most pronounced decrement in mean plasma VEGF as drug concentration increased. Paradoxically, plasma VEGF levels were sometimes much higher in treated individuals than in the control group suggesting an attempted homeostatic influence; this is of unknown significance. Perhaps there is up-regulation of systemic VEGF production in response to the anti-VEGF drug challenge. Ranibizumab disturbed mean plasma VEGF levels the least, as did monthly dosing with all agents, and minimizing systemic VEGF disturbances may be beneficial in terms of systemic homeostasis. A more “regular” anti-VEGF drug effect might be more easily compensated than large loads of anti-VEGF that occur irregularly, and theoretically this may have homeostatic benefits both in the eye and systemically.

CONTROL ID: 3706828

SUBMITTER (NAME ONLY): Patrick Wu

TITLE: A Comparison of the XEN Gel Stent and Ahmed Valve Devices in Preventing Postoperative Hypotony in Patients with Primary Open Angle Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.B. Wu, F.J. Gross, Ophthalmology, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|N. Chaganty, Mathematics and Statistics, Old Dominion University, Norfolk, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Patrick Wu: Commercial Relationship: Code N (No Commercial Relationship) | Fredric Gross: Commercial Relationship: Code N (No Commercial Relationship) | N Rao Chaganty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The XEN gel stent and Ahmed valve are both designed to prevent postoperative hypotony. We performed a retrospective study to compare the efficacy of these devices.

Methods: Patients who had either XEN gel stent or Ahmed valve surgery were screened and those with primary open angle glaucoma (POAG) were identified for further analysis. Patients with low-tension glaucoma, a complicated ocular history, and/or prior glaucoma surgery were excluded. The final study population had 41 eyes from 37 patients with 21 XEN gel stents and 20 Ahmed valves. Pre- and postoperative intraocular pressures (IOP) at day 1 (POD1), week 2 (POW2), and month 1 (POM1) were recorded. We defined hypotony as an IOP < 6.5 mmHg within the first postoperative month. The primary outcome was the rate of hypotony. Secondary outcomes were the mean IOP at each postoperative visit and the rate of short-term failures (defined as an IOP > 21 mmHg at the POM1 visit).

Results: Baseline characteristics were comparable between the XEN gel stent and Ahmed valve groups. At the POD1 visit, hypotony rates were 19.0% and 5.0% for the XEN and Ahmed valve groups, respectively. At the POW2 visit, hypotony rates were 4.8% and 10.5% for the XEN and Ahmed valve groups, respectively. By the POM1 visit, postoperative hypotony had resolved in all eyes in both groups. The differences between the rates of postoperative hypotony of each group were not statistically significant at the specified postoperative visits [p=0.154 (POD1), p=0.494 (POW2), p=N/A (POM1) as there were no cases of hypotony by POM1]. The differences between the mean IOP at each postoperative visit were not statistically significant between the two groups [p=0.887 (POD1), p=0.266 (POW2), p=0.211 (POM1)]. Short-term failures occurred in 23.8% of eyes in the XEN group and there were no short-term failures in the Ahmed valve group.

Conclusions: Both the XEN gel stent and Ahmed valve devices effectively decrease IOP and reduce the risk of early postoperative hypotony in patients with uncontrolled POAG. Any cases of postoperative hypotony were transient and resolved by POM1. Interestingly, all short-term failures occurred in the XEN group and in African American patients only. Additional studies can be performed to determine potential contributing factors.

CONTROL ID: 3706830
SUBMITTER (NAME ONLY): Gary Lee
TITLE: Perimetric simulations of 24-2C SITA Standard visual fields
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G.C. Lee, B. Cunningham, T. Callan, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|L. Chong, School of Medicine (Optometry), Deakin University, Geelong, Victoria, AUSTRALIA|J.G. Flanagan, School of Optometry and Vision, University of California, Berkeley, Berkeley, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|I.A. Falkenstein, Glaucoma Specialists of San Francisco, Oakland, California, UNITED STATES|

ABSTRACT BODY:
Purpose: Perimetric simulators have traditionally been used to develop and optimize visual field (VF) tests. In this preliminary study, we developed and evaluated a new simulator for simulating the relative performance of 24-2C SITA Standard (SS) VFs compared to 24-2C SITA Faster (SFR).
Methods: Retrospective 24-2C SS and 24-2C SFR VFs acquired in a study at each of two visits on one eye each for healthy and glaucomatous subjects on an HFA3 Model 860 perimeter (ZEISS, Dublin, CA) were analyzed. Two SITA 10-2 VFs also acquired at each visit were not used for these analyses.

HFA3 software was modified for use with a simulator [Lee et al. IOVS 2020; 61(7): PB0037] to provide subject responses to SITA VFs. Slopes of frequency of seeing (FOS) responses were modeled as previously described [Henson et al. IOVS 2000; 41(2)]. False answer rates were set to 5%.

Visit 1 data were used as substitutes for true (REF) fields. Mean absolute differences (MAD) between the REF fields and: a) Visit 2 VFs (TEST) and b) simulated VFs (SIM) were calculated for both 24-2C SS and SFR as a measure of “relative accuracy". Analyses were also repeated for the 24-2 test locations and the 10 new central 24-2C test locations.
Results: For 28 healthy eyes, mean age was 57.3 (standard deviation, SD: 7.6; range: 44.3 to 74.7) years and mean 24-2 SS MD was 0.38 (SD: 1.17; range: -1.89 to 2.62) dB. For 28 glaucoma eyes, mean age was 71.3 (SD: 9.0; range 54.0 to 97.9) years and mean MD was -7.92 (SD: 7.72; range: -23.42 to 1.63) dB.

$MAD_{SIM,REF}$ was comparable but slightly lower than $MAD_{TEST,REF}$ overall (see Table 1). $MAD_{SIM,REF}$ and $MAD_{TEST,REF}$ for both SS and SFR were similar in all and healthy eyes. SFR had slightly higher MAD than SS (~0.2 to 0.5 dB) in glaucoma eyes with more and deeper defects. $MAD_{SIM,REF}$ and $MAD_{TEST,REF}$ were more comparable for both SS and SFR in the ten new 24-2C test locations than in all or 24-2 only locations.
Conclusions: Given expected small differences in SS and SFR strategies [Heijl et al. AJO 2019; 198(2)], the study results may support that SS and SFR have similar performance in healthy eyes and SS is marginally better in regions of VF defects. Limitations of this study include the lack of true fields, use of a single representative FOS model, and no fatigue effects. Comprehensive simulations may continue to be a powerful tool in the development of future SITA strategies.

CONTROL ID: 3706831

SUBMITTER (NAME ONLY): Aina Turull Mallofre

TITLE: Behavior of the accommodation response during the subjective refraction

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Turull Mallofre, C. García-Guerra, M. Aldaba, M. Vilaseca, J. Pujol, Centre for Sensors, Instruments and Systems Development, Universitat Politecnica de Catalunya, Barcelona, Catalunya, SPAIN|

Commercial Relationships Disclosure: Aina Turull Mallofre: Commercial Relationship: Code N (No Commercial Relationship) | Carlos E. García-Guerra: Commercial Relationship: Code N (No Commercial Relationship) | Mikel Aldaba: Commercial Relationship: Code N (No Commercial Relationship) | Meritxell Vilaseca: Commercial Relationship: Code N (No Commercial Relationship) | Jaume Pujol: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Subjective refraction is considered the gold standard when assessing refraction. In this method the control of accommodation plays a key role. The purpose of this work was to study the relationship between the subjective refraction and the accommodative response. In particular, we analyzed the residual relative accommodation for the subjective refraction and the relationship between the transition between relaxed and activated accommodation and the subjective refraction.

Methods: The accommodative response of the right eye of 27 young healthy subjects between 18 and 30 years old was obtained with the subjective refraction. The setup used was a system based on a Hartmann-Shack aberrometer coupled to a phoropter that provides an estimation of the accommodative state every 100ms. First, the subjective refraction of each participant was obtained. Then a sweep of spherical lenses (ΔS) from +1.5D to -1.5D, in 0.25D steps, was presented in front of the corrected eye with the subjective refraction while monitoring the accommodation. The residual relative accommodation for the subjective refraction was obtained as the value for ΔS=0 D minus the minimum measured value of accommodation.

The transition between relaxed and activated accommodation within the measured response was obtained as follows: first, two linear fitting were obtained for each spherical power ΔS, one considering the curve between -1.5D and ΔS, and another between ΔS and +1.5D; then, the spherical lens ΔS producing the linear fittings with the best cumulative coefficient of determination was selected as the transition point between relaxed and activated accommodation.

Results: Results showed that the mean relative accommodation ± SD with the subjective refraction was 0.19±0.12D. Bland-Altman analysis was done to determine the agreement between the value of the traditional subjective and the value obtained by finding the transition point of accommodation. The mean ± SD of the differences between methods and 95% limits of agreement were 0.019 ±0.42D (1.01D, -0.64D).

Conclusions: Considering the values of relative accommodation with the subjective refraction a tendency to have a residual activated accommodation can be observed. Moreover, the transition between relaxed and activated accommodation may be a significant information and could be a useful tool to detect accommodative anomalies during subjective refraction.

CONTROL ID: 3706833

SUBMITTER (NAME ONLY): Javier Moreno-Montanes

TITLE: A TRANSCRIPTOMIC STUDY OF A 3D MODEL OF THE HUMAN TRABECULAR MESHWORK CELLS AND ITS RESPONSE TO THE SUBSTRATE STIFFNESS.

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Moreno-Montanes, L. Extramiana, E. Carnero, Ophthalmology, Universidad de Navarra, Pamplona, Navarra, SPAIN|J. Moreno-Montanes, Instituto de Investigacion Sanitaria de Navarra, Pamplona, Navarra, SPAIN|L. Extramiana, E. Carnero, Centro de Investigacion Medica Aplicada, Pamplona, Navarra, SPAIN|M. Bikuña, J. Paredes, Engineering School TECNUN, Donostia-San Sebastian, SPAIN|

Commercial Relationships Disclosure: Javier Moreno-Montanes: Commercial Relationship(s);Code C (Consultant/Contractor):Sylentis, S.A.;Code C (Consultant/Contractor):Horus;Code F (Financial Support):Zeiss;Code F (Financial Support):Alcon;Code F (Financial Support):Bausch & Lomb;Code F (Financial Support):Thea;Code F (Financial Support):Santen | Leire Extramiana: Commercial Relationship: Code N (No Commercial Relationship) | Maria Bikuña: Commercial Relationship: Code N (No Commercial Relationship) | Jacobo Paredes: Commercial Relationship: Code N (No Commercial Relationship) | Elena Carnero: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this study is to create a bio-engineered 3D model of the trabecular meshwork (TM) and to evaluate its response to several external stresses. The morphology and composition of the TM and the mechanical properties were analyzed to evaluate similarities with the physiological features of the human TM and moreover, the effect of the stresses on its growth and functionality.

Methods: The development of the 3D TM polycaprolactone (PCL) material is based on electrospinning techniques combined with fused deposition modeling or Melt electrospinning writing. Different fiber sizes, orientation and deposition density were applied to replicate the micro-anatomy of the human TM. Changes in fiber diameter facilitated the modification of the meshwork cell density and hence, scaffolds with different degrees of stiffness could be obtained. Human TM cells (HTMC) were received from human donors and cultured according to standard protocols. We evaluated the growth, distribution and functionality of HTMC in the 3D model. We used RNA sequencing to assess the HTMC response to increasing stiffness conditions as compared to HTMC cultivated in the classical 2D model.

Results: HTMC demonstrated a fibroblasts-like morphology with slight differences depending on the donor. These cells were expanded according to the confluence observed in the traditional 2D models. HTMC remained functional and responded to dexamethasone stress in the 3D model. RNA sequencing analysis comparing HTMC growth in the 3D model with the 2D model showed changes in genes associated with gene ontology (GO) pathways. These changes included collagen binding, fibronectin binding, microtubule binding, extracellular matrix (ECM) structural constituent conferring compression resistance, among others.

Conclusions: A bioengineered 3D HTM model using electrospinning techniques can reproduce human TM features. We achieved an emulation of the TM in varying degrees of stiffness. HTMCs were able to adhere and grow in the 3D structure. The induction of specific TM markers using dexamethasone demonstrated the functionality of the HTMC in our model. The HTMC responded to the changes in the stiffness by altering the expression of genes implicated in the ECM remodelling. These results facilitate the identification of new target genes associated with ECM remodelling, and other pathways.

CONTROL ID: 3706836

SUBMITTER (NAME ONLY): Riccardo Sangermano

TITLE: Investigating the role of mutational load and cis modifiers of disease severity in RHO P23H autosomal dominant Retinitis Pigmentosa

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sangermano, E. Galdikaite-Braziene, E. Zampaglione, E.A. Pierce, A.V. Segrè, J. Comander, K.M. Bujakowska, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

ABSTRACT BODY:

Purpose: The RHO-P23H mutation is a well-known cause of autosomal dominant Retinitis Pigmentosa. Although affected patients share the same primary sequence defect, their phenotype displays a spectrum of disease severity. We hypothesized that the phenotypic variability could be due to an increased mutational load in the known inherited retinal disease (IRD) genes or to a differentially expressed wild-type RHO allele, that alters the ratio of the wild-type and mutant rhodopsin protein. Therefore, we tested for correlation of: 1) sequence variability in known IRD genes; and 2) wild-type RHO allele haplotypes with RHO-P23H phenotype severity.

Methods: We investigated a cohort of 130 RHO-P23H patients. Variable retinal severity was documented by retrospective analysis of ophthalmological data. We selected electroretinographic (ERG) measurements, in particular the 30Hz flicker ERG amplitude as the most comprehensive single parameter demonstrating phenotypic variability, adjusted for age. Targeted sequencing of all known IRD genes and genotyping of the RHO locus were performed using an in-house sequencing panel and a genotyping array (Illumina GSA), respectively. Deleteriousness of rare IRD variants was assessed using CADD, where for each patient we summed CADD scores for rare (MAF=<0.05) high-impact (loss-of-function) and missense variants. Genotyped variants surrounding the RHO locus (850kb) were phased using Eagle-v2 and samples of European ancestry from the Haplotype Reference Consortium panel.

Results: No significant correlation (r^2<0.01) was observed between retinal disease severity in RHO-P23H patients and the mutational load of rare loss-of-function or missense variants in other known IRD genes. Analysis of the RHO locus confirmed that the RHO-P23H allele is a founder allele in the US population, with only one family showing a different haplotype for the RHO-P23H allele. No particular wild-type allele segregated with mild or severe cases in any of the families.

Conclusions: Our results do not support two of our original hypotheses: 1) that mutational load in IRD genes can lead to the modulation of RHO-P23H disease severity, and 2) that the wild-type RHO allele can have an effect on disease severity. Differences in disease severity in the RHO-P23H patients may be the result of genetic modifiers elsewhere in the genome.

CONTROL ID: 3706840
SUBMITTER (NAME ONLY): Ali Fard
TITLE: Robust macula thickness analysis using low-cost OCT
SESSION TITLE: OCT Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Fard, H. Bagherinia, C. Leahy, S.A. Bello, Carl Zeiss Meditec, Inc., California, UNITED STATES|
Commercial Relationships Disclosure: Ali Fard: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc | Homayoun Bagherinia: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc | Conor Leahy: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc | Simon Bello: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc

ABSTRACT BODY:

Purpose: Remote OCT applications require cost-effective acquisition devices. This challenging constraint often leads to technology choices that provide inferior image quality compared to state-of-the-art clinical devices, and thereby result in unreliable image analysis. The purpose of this work is to demonstrate a strategy for robust macula thickness analysis using low-cost OCT that can navigate data quality limitations and improve correlation of thickness values compared with benchmark clinical systems.

Methods: Our method relies on acquiring multiple OCT scans of the same region and intelligently combining the macula thickness maps generated by individual scans. In this method, inner limiting membrane and retina pigment epithelium are delineated, and the corresponding thickness map and segmentation confidence map (SCM) are generated for each OCT volume. Subsequently, all thickness maps are registered to the thickness map (reference) with highest confidence derived from the SCM. The registration transformation parameters are then used to register and combine the thickness maps into a single map based on the local quality of individual SCMs.

To evaluate this method, we acquired OCT scans over an area of 5.78mm x 5.78mm from each eye, repeated 3 times on a low-cost OCT. 38 patients with retina pathology were enrolled in an IRB-approved study. The OCT macula thickness map was compared to one acquired using CIRRUS^{TM} 5000 HD-OCT (ZEISS, Dublin, CA). Thickness values were compared over an ETDRS grid.

Results: Figure 1 shows examples of thickness maps acquired using the low-cost OCT (before and after combining) and using CIRRUS 5000 HD-OCT. Bland-Altman analysis was performed to compare the results of single acquisition and triple acquisition of the low-cost system with a single acquisition of CIRRUS 5000 HD-OCT. The results are summarized in Table 1. The combined acquisition provides slightly higher mean difference while improving the correlation with the clinical system in the outer ring.

Conclusions: Our analysis suggests that combining macula thickness maps from multiple acquisitions provides an overall improved correlation between the low-cost system and clinical system, and thereby improves the diagnostic utility of the low-cost OCT instrument.

CONTROL ID: 3706841

SUBMITTER (NAME ONLY): Michael Wolek

TITLE: An investigation of the association between metformin use and age-related macular degeneration in type II diabetics with glycemic control held constant

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wolek, B. Wollocko, J. Bansal, N. Ghani, Ophthalmology, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|M. Mackey, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|K. Chaudhary, Ophthalmology, Stony Brook University Hospital, Stony Brook, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies support the use of metformin to prevent the development of age-related macular degeneration (AMD). However, the mechanism by which metformin is protective is unclear. We performed a retrospective, cross-sectional clinical study to assess the association between metformin use and AMD when controlling for glycemic control in patients with diabetes mellitus type II.

Methods: We identified 461 unique patients over the age of 55 years with a diagnosis of diabetes mellitus type II seen in our academic retina clinic in Stony Brook, New York between 12/31/2019 and 12/31/2020. Manual chart review was performed to extract the most recent A1c within 3 months and the presence of an active metformin prescription. The population was split based on presence of AMD diagnosis. A series of multivariate regression analyses was then performed comparing metformin use between groups while controlling for A1c. Secondary endpoints included demographic differences, smoking status, and prevalence of diabetic retinopathy (DR) between groups.

Results: Among the 461 patients, 118 (25.6%) had a diagnosis of AMD. Compared to patients without AMD, patients with AMD were older (69 compared to 66; $p=0.005$) and less likely to have DR (37.3% compared to 59.2%; $p<0.001$). There was no difference in use of metformin and average A1c between groups. After multivariate regression, variables found to be associated with AMD include age (OR 1.05; $p=0.001$) and DR (OR 0.35; $p<0.001$). Metformin use was not found to be associated with AMD and controlling for A1c did not change the association. Stratifying glycemic control using various A1c cutoffs also showed no changes in the relationship between AMD and metformin use.

Conclusions: This is the first reported study assessing the relationship between AMD and metformin use while controlling for glycemic control using A1c. Given our results, the previously described relationship between metformin use and the development of AMD is not likely driven by the antihyperglycemic effects of metformin, but rather by other properties inherent to the drug. Lastly, the use of DR as a surrogate for poor diabetic control in the context of AMD is not ideal, as we found DR to be significantly associated with AMD even after holding A1c constant.

CONTROL ID: 3706842

SUBMITTER (NAME ONLY): Gang Luo

TITLE: Use of Mobile Apps for Vision Assistance - Handheld vs. Head-mounted Modes

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Luo, S. Pundlik, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Gang Luo: Commercial Relationship: Code N (No Commercial Relationship) | Shrinivas Pundlik: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Handheld video magnifiers, such as magnifier apps, are used by visually impaired to assist with daily visual tasks. The same magnification functionality can be implemented in head-mounted devices, to provide hands-free vision assistance. We compared the usage patterns of a handheld mobile app with the head-mounted version, to understand how the two modes may address different visual needs of visually impaired.

Methods: Handheld Supervision Magnifier and head-mounted Supervision Goggles are freely available vision assistance mobile apps intended for people with low vision. Aggregated app use data over 8 months, from Aug. 2020 to Mar. 2021, was collected from the active users, without individually identifiable data. Additionally, the targets in a scene image snapshot viewed during each app launch were tagged in 11 different common object categories via a cloud-based object recognition service. Average launches per user and the distributions of viewing targets over the object categories were compared between the two apps.

Results: There were 40,866(mean)±3372(SD) monthly users of the handheld app and 134±11 for the head-mounted app. The average monthly launches per user were significantly lower ($p<0.001$) for the head-mounted app (4.6±0.91) compared to the handheld app (6.9±0.38). The top 3 target categories with the handheld app were ‘text’ (41%), ‘indoor’ (30%) and ‘art’ (7%), whereas for the head-mounted app the top categories were ‘indoor’ (49%), ‘human’ (14%), and ‘text’ (11%). The chi-square test of independence between the histograms for handheld and head-mounted viewing targets failed to reject the hypothesis that the two distributions were independent ($df=10$, $\chi^2=0.99$, $p = 0.99$), which suggesting they were different.

Conclusions: The relatively low app launch frequency and different viewing targets with the Supervision Goggles app indicate that head-mounted visual aids are probably used for a set of niche visual tasks different for that with handheld visual aids. Head mounted vision assistance may need to be considered as one of options in low vision rehabilitation.

CONTROL ID: 3706848

SUBMITTER (NAME ONLY): Rui Chen

TITLE: Deciphering non-coding genetic variants via integrative single cell multi-omics analysis

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Chen, J. Wang, X. Cheng, Q. Liang, J. Wang, Y. Li, HGSC, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|M.M. DeAngelis, Department of Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic variants located at the non-coding part of the genome, such as enhancers and promoters, can have a significant impact on the cellular state and phenotype of an individual. However, identifying and characterizing functional variants in gene regulatory elements remains challenging. We sought to overcome this challenge by integrating genomic sequencing with recent developed single-cell omics technologies.

Methods: To identify causal genetic variants that affect gene expression in the retina, multi-omics profiling, including whole genome sequencing (WGS), single nuclei RNA-sequencing (snRNA-seq), and single nuclei ATAC-seq (snATAC-seq), were performed on the donor retina. Open chromatin regions in each retinal cell type and potential regulatory elements were identified. Candidate genetic variants that affect gene expression and/or chromatin accessibility in each cell type were identified through integrative analysis of single-cell expression QTLs (sc-eQTLs), single-cell chromatin accessibility QTLs (sc-caQTLs), single-cell allelic specific expression (sc-ASE), and single-cell allelic specific chromatin accessibility (sc-ASCA).

Results: A total of 191,818 and 245,456 nuclei from 20 human donor retinae were profiled with snRNA-seq and snATAC-seq respectively. These data were organized into 11 major cell types in the retina with a total of about 500K open chromatin regions identified. Through co-accessibility and co-expression analysis, 75,477 open chromatin regions were linked to 14,053 genes as candidate regulatory elements. A significant proportion of these elements is cell type specific. Integrative analysis of WGS with the single nuclei multi-omics data leads to the identification of sc-eQTL, sc-caQTL, sc-ASE, sc-ASCA. Strikingly, the majority of these quantitative trait loci are cell type specific. Finally, integration of the single-cell genetic association analyses with GWAS studies leads to the identification of candidate causal variants and genes in cell type context.

Conclusions: Our results indicate that the impact of vast majority of genetic variants on gene regulation is cell context specific. Furthermore, we demonstrated that integrative analysis of genomics and single cell omics data is an effective strategy for genetic fine mapping and casual variant identification underlying human quantitative traits and complex diseases.

CONTROL ID: 3706851

SUBMITTER (NAME ONLY): Anna Wu

TITLE: Characterizing early residual fluid in neovascular age-related macular degeneration using a machine learning algorithm in routine clinical practice

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Wu, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.K. Wu, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|S.W. Perkins, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Treating neovascular age-related macular degeneration (nAMD) often starts with intensive therapy with anti-vascular endothelial growth factor (VEGF) injections. In prior post-hoc studies, early residual fluid (ERF), defined as intraretinal fluid (IRF) and/ or subretinal fluid (SRF) after the loading dose, was associated with poorer long-term visual acuity. This retrospective study examined the impact of ERF on visual acuity using a machine learning (ML) algorithm to quantify fluid on optical coherence tomography (OCT) in routine clinical practice.

Methods: 286 treatment naïve patients with nAMD were identified from a retrospective analysis. Only one eye was included per patient. Best visual acuity (BVA) (ETDRS letters) and OCT data were collected every 3 months from baseline to 12 months. OCTs were analyzed by the Notal OCT analyzer ML algorithm, quantifying IRF, SRF, and total retinal fluid (TRF). The ERF group was defined as those with fluid at week (W) 12. Fluid type at W12 was stratified and volumes were divided into quartiles to see their predictive value for W52 BVA. Paired t-tests and ANOVA compared BVA and fluid changes within and between fluid subgroups.

Results: At W12, 58.4% of patients had ERF. The breakdown of subgroups at W12 were no fluid (41.6%), IRF-only (21.6%), SRF-only (45.5%), and IRF & SRF (32.9%). When comparing long term BVA outcomes according to W12 fluid status, ERF and ERF-free groups had similar mean BVA gains from baseline to W52 (+5.70±15.44 vs. +4.89±17.95; p= 0.69). There was also no significant difference in mean BVA gains from baseline to W52 when comparing the W12 fluid subgroups of no fluid (+4.89±17.95), IRF-only (+4.56±16.36), SRF-only (+5.55±12.49), and IRF & SRF (+6.61±18.45), p=0.93. Quartile analysis of W12 IRF, SRF, and TRF quantities revealed no predictive pattern for W52 BVA.

Conclusions: These results from routine clinical practice diverge from prior post-hoc studies, since there was no significant difference in long-term BVA gains between W12 ERF and ERF-free cohorts, as well as between the various fluid subgroups. In addition, fluid quantifications of ERF did not appear clinically relevant when predicting long term BVA. Thus, the clinical utility of a ML algorithm for predicting visual outcomes of ERF cohorts in nAMD warrants further exploration.

CONTROL ID: 3706852

SUBMITTER (NAME ONLY): Anastasiia Strizhakova

TITLE: βA3/A1-crystallin may link lysosomal clearance and the circadian rhythm in the RPE

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Strizhakova, A. Sreenivas, V. Koontz, P. Shang, H. Liu, S. Ghosh, O. Chowdhury, S.L. Hose, N.A. Stepicheva, D. Sinha, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been well-documented that lysosomal clearance in the retinal pigment epithelial (RPE) cells is tightly regulated by the circadian clock. However, the details of this regulation are still unclear. We hypothesize that βA3/A1-crystallin, a protein known to be important for maintaining lysosomal homeostasis in the RPE, may also provide an important link between lysosomal clearance and the circadian rhythm in the RPE.

Methods: Wild-type (C56Bl/6J) mice (6-8 weeks old) were maintained at LD (light-dark) 12:12 cycle and sacrificed at ZT0, ZT2, ZT8, ZT14, ZT20 (Zeitgeber time; hours after lights on). A second set of mice was kept in complete darkness for 3 days prior to euthanasia. Western blotting and qPCR were performed on WT RPE to detect oscillations in the expression of Cryba1 (gene encoding βA3/A1-crystallin) and known circadian genes. For the in vitro studies, human fetal RPE (fRPE) cells were cultured and entrained with serum shock. Samples were collected every 4 hours after entrainment. qPCR was performed to analyze the expression of Cryba1 and the known circadian genes. Bioinformatic analysis of the Cryba1 gene sequence was performed with MoLoTool and miRDB.

Results: Cryba1 expression oscillates at both mRNA and protein levels during the day in the RPE from WT mice, with the peak of protein expression coinciding with the peak of RPE lysosomal activity. Entrainment of fRPE cells with serum shock resulted in successful entrainment of Cryba1 expression, consistent with the circadian regulation of Cryba1 transcription in the RPE. Bioinformatic analysis revealed potential regulation of Cryba1expression by the circadian machinery (through NR1D1 transcription factor and miR-206).

Conclusions: We have shown that Cryba1 expression is regulated by circadian rhythm. This work contributes to a more complete understanding of the circadian rhythm entrainment in the RPE cells and introduces a novel, RPE-specific member into the circadian network.

CONTROL ID: 3706858

SUBMITTER (NAME ONLY): Arash Kazemi

TITLE: Effect of Supine Position on Episcleral Venous Pressure in Normal Human Eyes using a Portable Electronic Episcleral Venomanometer

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kazemi, A.J. Sit, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been shown that intraocular pressure (IOP) changes with body position, but the mechanism is not well understood. In this study, we evaluated changes in episcleral venous pressure (EVP) between seated and supine positions and compared with changes in IOP and blood pressure in normal subjects.

Methods: Twenty eyes from 10 normal subjects (all females; 30 ± 7 years, mean ± SD) were included in the study. Blood pressure, pulse rate, IOP, and EVP of both eyes were first measured in the seated position. Thirty minutes later and after being in the supine position for 5 minutes, the same measurements were repeated. Systolic and diastolic blood pressures (SBP and DBP), and pulse rate (PR) were determined by a digital monitor. IOP was measured by pneumatonometry. EVP was assessed in a selected episcleral vein by using a computer-controlled portable electronic episcleral venomanometer with video recording and image processing to determine the pressure required to initiate collapse of the vein. Changes in IOP, EVP, systolic and diastolic blood pressures, and pulse rate between 2 body positions and correlations between changes in those variables were analyzed by using generalized estimating equation models and regression analysis, respectively.

Results: Mean IOP increased from 15.5 ± 2.0 mmHg in the seated position to 19.5 ± 2.2 mmHg in the supine position ($P < 0.001$, Table 1) but the change in EVP was smaller in magnitude (from 6.0 ± 1.0 mmHg to 6.9 ± 0.9 mmHg, $P < 0.001$, Table 1). DBP and PR but not SBP were lower in the supine position (Table 1). The change in EVP was not correlated with the change in IOP but showed moderate correlations with blood pressure changes (Table 2). Also, there were no significant correlations between IOP change and BP and PR changes (Table 2).

Conclusions: Both IOP and EVP are higher in the supine position compared to the seated position, but the magnitude of changes is not the same. EVP change is more strongly correlated with blood pressure change than IOP change. Future studies are required to identify the other contributing factors of postural IOP change.

CONTROL ID: 3706861

SUBMITTER (NAME ONLY): Scott Perkins

TITLE: Machine learning prediction of limited early response to anti-VEGF therapy in neovascular age-related macular degeneration in routine clinical practice.

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.W. Perkins, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|A.K. Wu, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.K. Wu, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Scott Perkins: Commercial Relationship: Code N (No Commercial Relationship) | Anna Wu: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Singh: Commercial Relationship(s);Code F (Financial Support):Apellis, Aerie, Graybug;Code I (Personal Financial Interest):Novartis, Genentech, Regeneron, Alcon, Bausch and Lomb, 41 Gyroscope

ABSTRACT BODY:

Purpose: Patients with neovascular age-related macular degeneration (nAMD) have varying responses to anti-vascular endothelial growth factor (anti-VEGF) treatment. Those with residual intraretinal fluid (IRF) and/or subretinal fluid (SRF) after intensive anti-VEGF injections in the first 3 months of therapy have been defined as having limited early response (LER) to treatment. Prior post-hoc studies have associated LER status with reduced long-term visual acuity. Predicting LER from baseline data may be useful in identifying treatment-resistant patients who would benefit from more intensive treatment or targeted selection of anti-VEGF therapy.

Methods: Data was obtained from a retrospective chart review of 286 treatment naïve patients diagnosed with nAMD. Age, best visual acuity (BVA), central subfield thickness (CST), and optical coherence tomography (OCT) data were obtained at baseline, three, six, and twelve months. IRF and SRF were quantified from OCT data using the Notal OCT Analyzer machine learning algorithm (Tel Aviv, Israel). Data were pre-processed by one-hot encoding and min-max scaling. Predictive models were trained and evaluated using a 10-fold cross-validated approach.

Results: LER was predicted from baseline age, BVA, IRF, SRF, and CST by ridge logistic regression, k nearest neighbors classification, and radial basis function kernel support vector classification with 10-fold cross-validated accuracy of 0.66, 0.63, and 0.64, respectively. Area under the cross-validated receiver operating characteristic curve was 0.63, 0.59, and 0.62, respectively. T-distributed stochastic neighbor embedding did not show clusters separated by LER status.

Conclusions: These results demonstrate the potential of machine learning techniques for predicting nAMD outcomes in routine clinical practice. While age, BVA, IRF, SRF, and CST confer predictive accuracy, incorporation of additional variables may further improve predictive models. This would be beneficial for supporting physician decisions regarding anti-VEGF treatment in nAMD. Further studies could incorporate treatment data to determine which anti-VEGF therapies may be most suitable for patients at risk of LER.

CONTROL ID: 3706863

SUBMITTER (NAME ONLY): Raziyeh Mahmoudzadeh

TITLE: Outcomes of Retinectomy without Lensectomy in Eyes with Rhegmatogenous Retinal Detachments with Proliferative Vitreoretinopathy

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Mahmoudzadeh, M. Salabati, A. Chiang, A.E. Kuriyan, O.P. Gupta, S. Mehta, S. Garg, J. Hsu, The Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|N. Mokhashi, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|S. Patel, H. Anderson, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the anatomic and functional outcomes of retinectomy without lensectomy in eyes with rhegmatogenous retinal detachment (RRD) and proliferative vitreoretinopathy (PVR).

Methods: A retrospective review of patients treated with vitrectomy and retinectomy without lensectomy from January 1st 2015 to January 1st 2020 was performed. The primary outcome was the final attachment rate and single surgery anatomic success (SSAS) 3 months after retinectomy. Secondary outcomes included predictors of final visual acuity, the mean number of subsequent operations required for complete retinal reattachment, incidence of cataract surgery, and number of eyes that ultimately had successful silicone oil removal (SOR).

Results: Complete final retinal reattachment was achieved in 111/112 eyes (99.1%), with a mean (SD) follow-up of 29 (14) (range, 8-62) months after retinectomy. The 3-month SSAS was achieved in 84/112 eyes (75%). The final visual acuity improved or stabilized in 76/112 (67.9%) eyes. Silicone oil removal was performed in 72 of 112 patients (64.3%) during the study period, and cataract surgery was performed on 101 (90.2%) eyes before the last follow-up visit.

Conclusions: Retinectomy without lensectomy to repair RRDs complicated by PVR demonstrated anatomic and functional results that were comparable to historical reports of retinectomy with lensectomy. This study suggests that removing the lens when there is no significant cataract may not be necessary in these cases to obtain reasonable outcomes.

CONTROL ID: 3706864

SUBMITTER (NAME ONLY): Fernanda Maria Silveira Souto

TITLE: Changes in quality of life (QoL) in a 24-month interval in patients with non-acute Vogt-Koyanagi-Harada disease (VKHD)

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Silveira Souto, R. Missaka, M.M. Lavezzo, P.F. Nóbrega, B.M. Magalhães, V.M. Caetano, J.T. Takiuti, M.K. Oyamada, C.E. Hirata, J.H. Yamamoto, Ophthalmology, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|V.M. Sakata, Universidade Federal do Parana, Curitiba, PR, BRAZIL|

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ABSTRACT BODY:

Purpose: To analyze the changes in self-reported QoL metrics in a 24-month interval in non-acute VKHD patients and to correlate these changes with visual function, inflammation and treatment

Methods: 22 patients, participants of a prospective ongoing study with a minimum 12-month follow-up since acute disease onset, were evaluated at two 24-month apart time points. They had systematic clinical, multimodal imaging and electroretinogram (ERG) exams with predefined treatment protocols. After acute phase, anterior uveitis and/or macular edema defined clinical inflammation; optic disc or perivascular leakage, dark dots and/or increase in subfoveal choroidal thickness were defined as subclinical inflammation. Visual function was measured by best corrected visual acuity, visual field, contrast sensitivity (CS) and ERG. Self-reported health-related and vision-related QoL were assessed by SF36 and VFQ25 questionnaires, respectively. Visual function and QoL data were collected at 2 moments 24mo apart: Jul-Dec 2017 (M1) and Jul-Dec 2019 (M2). Questionnaire scores were classified as an improvement, unchanged or worsening considering a difference >5 points between M1 and M2 results. Changes in visual function, inflammation and treatment data and significant changes between QoL scores at the 2 time points were compared with likelihood ratio test. This study was approved by Institutional Ethics Committee and followed the Helsinki declaration.

Results: Table represents QoL scores at M1 and M2. Figure shows clinical associations with change on QoL scores. In general health domain on SF-36 questionnaire, patients who remained without systemic treatment or absence of optic disk hyperfluorescence had unchanged or better score at M2. In VFQ25 questionnaire, improvement in binocular CS resulted in better ocular pain score at M2; absence of anterior uveitis relapse, stable fundus findings and absence of intravitreal injections resulted in unchanged or better dependency score, while use of cyclosporin resulted in worse results at M2; absence of intravitreal injection resulted in unchanged or better mental health score.

Conclusions: After 24mo, improvement in QoL scores was associated with less inflammation, better visual function and less need of treatment, reinforcing our previous results (2019, Ocular Immunol Inflamm).

CONTROL ID: 3706870

SUBMITTER (NAME ONLY): Thomas Callan

TITLE: Comparison of vessel density and vessel perfusion measurements in SD-OCT and SS-OCT devices

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Callan, L. De Sisternes, S. Kubach, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|W. Lewis, Bayside Photonics, Inc., Yellow Springs, Ohio, UNITED STATES|S. Bonnin, Université de Paris AP-HP Nord. Lariboisière & Saint Louis Hospitals, France, Paris, FRANCE|T. Santos, J.G. Cunha-Vaz, AIBILI – Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) expands the ability to detect and monitor retinal vascular changes. Both vessel density (VD) and perfusion density (PD) are parameters that can be quantified from OCTA en face images. This study looks at these parameters and compares the results generated by both a spectral domain (SD) and a swept-source (SS) OCT system.

Methods: Subjects were scanned multiple times with the PLEX® Elite 9000 (ZEISS, Dublin, CA) SS-OCT and the CIRRUS™ HD-OCT 5000 (ZEISS, Dublin, CA). Three groups of eyes (41 total) were evaluated: 30 diseased eyes of 15 patients with varying diabetic retinopathy severity were imaged on PLEX Elite with the Angio 6x6 mm at 100 kHz scan and on CIRRUS using the 3x3 mm Angiography scan. One cohort of 6 healthy eyes and another cohort of 5 diseased eyes were imaged 3 times on both PLEX Elite and 3 times on CIRRUS. These results were pooled. VD is the total length of perfused vasculature per unit area in a region. PD is defined as the total area of perfused vasculature per unit area in a region. The inner ETDRS subfields (1-5) these scans have in common were used. The intra-instrument coefficient of variation (COV), defined as the ratio of the standard deviation to the mean, was calculated for each device. In addition, the relative mean difference in measurement between the 2 devices were determined.

Results: Data analysis of these repeated scans showed a similar intra-device coefficient of variation between PLEX Elite and CIRRUS. The COV for vessel density was 3.4% for Plex and 4.7% for CIRRUS. The COV for perfusion density was 3.8% for PLEX Elite and 5.4% for CIRRUS. The relative mean difference in vessel density between CIRRUS and PLEX Elite was 0.02%. The relative mean difference in perfusion density between CIRRUS and PLEX Elite was 1.3%. Both values are smaller than the combined intra-device COVs for the two quantities.

Conclusions: The relative differences in measurement between PLEX Elite and CIRRUS for vessel density and perfusion density are much smaller that the intra-device variability. This indicates the measurement between the two instruments can be considered substantially similar when considering these OCT vascular parameters.

CONTROL ID: 3706872

SUBMITTER (NAME ONLY): Xuesen Cheng

TITLE: A single cell multi-omics atlas of the human retina

SESSION TITLE: Single cell analysis in retinal research in health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Cheng, Q. Liang, J. Wang, Y. Li, R. Chen, Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|Q. Liang, R. Chen, Verna and Marrs McLean Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, Texas, UNITED STATES|L.A. Owen, Department of Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|L.A. Owen, Department of Population Health Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|M.M. DeAngelis, Department of Ophthalmology, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The human retina, as part of the central nerve system and the key light sensing tissue in the eye, has high cell heterogeneity, with an estimate of over 60 distinct cell types distinguished by morphology and physiology. To better understand the gene expression and regulation in each cell type, our study generates the multi-omics atlas at the single-cell level for adult human retina.

Methods: Single-nuclei RNA-seq and single-nuclei ATAC-seq were performed for retinae from human donors using the 10x Genomics technologies. For each donor retina, both the fovea and peripheral regions are profiled. Rare cell types, including the amacrine and retinal ganglion cell, are enriched based on the NeuN gradient. Integrative analysis of transcriptomic and epigenomic data is performed to identify gene regulator networks (GRNs), transcriptional factor binding motif enrichment, and putative gene cis-regulatory elements.

Results: A large single nuclei multi-omics dataset containing over 250K cells with single-nuclei RNA-seq and over 150K cells with single-nuclei ATAC-seq from human adult retina was generated. The atlas contains over 60 distinct cell types with an estimated sensitivity of 0.01%. Cross-species comparison among human, monkey, and mouse retina reveals that cell subtypes are overall conserved with RGCs are most divergent. In contrast, significant difference is observed at the transcriptomic level in corresponding cell types. With a large-scale single-nuclei ATAC-seq, we uncovered 10 times more open chromatin regions than the bulk study. Many of these regions are specific for rare cell types and were not observed in bulk ATAC-seq data. By combining snRNA/ATAC-seq data, 18% of these open chromatin regions (~47K) can be linked to their target genes as putative regulatory elements. Strikingly, a significant portion of these cis regulatory elements are novel and show cell-type-specific activity. Finally, the single nuclei multi-omics data allows fine mapping and functional annotation of genomic variants through integration of eQTL and GWAS results.

Conclusions: Our study represents the most comprehensive transcriptome and epigenome atlas of the human retina to date. This atlas enables in-depth integrative analysis at individual cell type resolution, making it a highly valuable resource for the research community.

CONTROL ID: 3706873

SUBMITTER (NAME ONLY): David Hammond

TITLE: Prior myopia control effects retained upon cessation of dual-focus soft contact lens wear

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.S. Hammond, B. Arumugam, A. Bradley, M. Nguyen, P. Chamberlain, Advanced Development Center, CooperVision International, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Quantify eye growth as a function of age, upon cessation of a dual-focus soft contact lens myopia control treatment. Are the accrued treatment effects retained independent of age?

Methods: Arumugam et al. (ARVO,2021) established models of estimated annualized axial length elongation for children fit with either MiSight 1 day (omafilcon A, dual focus, CooperVision, Inc.; M1d) or Proclear 1 day (omafilcon A, single vision, Coopervision, INC.; P1d) soft contact lenses. Following completion of a 6-year study to assess efficacy of M1d myopia control lenses, 83 subjects were refitted for one year with P1d. Axial elongation rates (mm/yr) observed after cessation of treatment were compared to previously defined age-matched model predictions for both treated and untreated myopic eyes. Annualized post-treatment measures of axial length (age range 14-18 years) were collected from children who were aged 8-12 at study inception.

Results: Average post-treatment growth for eyes following either 6 or 3 years of treatment were below the upper 95% confidence interval of the untreated average control model growth. Post-treatment annual average elongation rates ranged between 0.15 mm/yr, 95% CI [0.11, 0.19] and 0.05 mm/yr, 95% CI [0.03,0.07] for the ages 14 to 18 years. In general, a younger age at cessation of treatment was associated with greater axial elongation rate in the following year when wearing P1d, in concordance with the untreated eye growth model. There was no evidence of a rebound effect in the 14-18 year-old age range upon cessation of M1d wear.

Conclusions: Post treatment return of eye growth to age normal levels reveals that accrued reductions in eye growth from myopia control with M1d were retained following treatment cessation. Data and models reveal that starting myopia control treatment with MiSight 1 day at a younger age and continuing throughout the teenage years will reduce the number of years during which untreated eye growth will occur, maximizing myopia control benefit.

CONTROL ID: 3706876

SUBMITTER (NAME ONLY): Ann Yung

TITLE: Development of a Moxifloxacin Eluting Hydrogel Patch for Sealing Ocular Lacerations

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Full thickness injuries, in particular full thickness lacerations, render the eye susceptible to infection and vision loss. They are particularly difficult to manage in low resource/emergency settings and repair typically requires extensive surgical skill with high frequency post-operative eyedrop regimens. To address these issues, we have developed a hydrogel sealant with the potential to be used as a rapid repair system to stabilize the globe for laceration type injuries while concurrently permitting sustained drug delivery of an antibiotic, Moxifloxacin (MFX), using a nanoparticle (NP) hydrogel system.

Methods: MXF NPs were synthesized and characterized using dynamic light scattering (DLS) to determine particle diameter (PD) and polydispersity index (PDI), and the encapsulation efficiency (EE) was determined. The sealant, composed of gelatin methacryloyl (GelMA) and glycidyl methacrylate-hyaluronic acid (HAGM), was characterized for degree of methacrylation (DM) and biocompatibility. Lastly, free MFX and MFX NPs were loaded into the hydrogel, and drug release profiles were determined via dialysis. Antimicrobial efficacy was assessed by zone of inhibition studies (ZOI) against a gram + (Staphylococcus Aureus; SA) and gram - (Pseudomonas Aeruginosa; PA) bacteria. The MFX NP hydrogel was further assessed in vitro for sealant capabilities via burst pressure testing.

Results: MFX NPs demonstrated a PD of 221 ± 11 nm, PDI of 0.21 ± 0.02, and EE of 93.8 ± 8.2%. Polymers exhibited a 61% and 11% DM for GelMA and HAGM, respectively, and no signs of cytotoxicity. The drug release profiles showed a 74.7 ± 2.38% and 29.65 ± 2.65% burst release within 2 h, with remaining MFX released within 24 h and 5 days respectively for hydrogels loaded with free MFX and MFX NPs. The MFX NP hydrogel demonstrated high antimicrobial efficacy with a ZOI > 30 mm against PA and > 28 mm for SA over 5 days. Lastly, the MFX NP hydrogel showed a high burst pressure of 40.8 ± 4.2 kPa.

Conclusions: The hydrogel sealant is capable of successfully loading NPs containing antibiotic which allows for efficacious levels of drug release for up to 5 days. Furthermore, it was highly adhesive and able to withstand high levels of pressure. Our drug eluting sealant has the potential to address critical factors in emergency ocular injury care by rapidly restoring the globe and concurrently allowing for efficacious levels of antibiotic to prevent infection.

CONTROL ID: 3706878
SUBMITTER (NAME ONLY): Lily Young
TITLE: Utility of Fluorescein Angiogram to Identify Neovascularization in Sickle Cell Retinopathy
SESSION TITLE: Retinal vascular diseases
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Young, A. Rai, U. Mian, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|A. Rai, T. Toribio, U. Mian, Montefiore Medical Center, Bronx, New York, UNITED STATES|
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ABSTRACT BODY:
Purpose: Currently, screening guidelines for sickle cell retinopathy require a dilated fundus exam (DFE). As neovascularization (NVE) is found in the peripheral retina, it may be missed on DFE. Our study compares the identification of NVE by DFE and fluorescein angiogram (FA) in the same patient.
Methods: This is a retrospective chart review of sickle cell patients (N=146) at Montefiore Medical Center (Bronx, New York) between 2016 and 2021. Inclusion criteria: Adult sickle cell patients who have had at least one fluorescein angiogram (FA) and a DFE within six months. Electronic Medical Records were used to identify NVE on DFE and FA reports. Sensitivity and specificity of DFE were calculated to compare to FA. McNemar's test was applied to compare sensitivities of DFE and FA. A kappa coefficient was calculated to compare the agreement of the two tests. Fisher's exact test was used to compare the proportion of patients with NVE across genotypes.
Results: 146 patients met the inclusion criteria. The patient population was predominantly Non-Hispanic Black or African American (75.3%) and a majority female (64.4%). 52.1% of the population had the SS genotype, 37.0% had the SC genotype, and 10.9% were classified as Other (Sß+/Sß0). The average age was 43, with a range from 18 to 74.

Nearly half of the patients had NVE on FA, which was significantly higher than on DFE (49.3% vs.15.8% respectively, $p < .001$). This correlates to a sensitivity of 31.9% and a specificity of 96.0% for DFE. The p-value for McNemar's test was <0.001, indicating that FA is significantly more sensitive than DFE. The agreement between DFE and FA was poor, with a kappa coefficient (95% CI) of 0.2813 (0.1605,0.4622).

SC patients were found to have significantly more NVE on FA than SS patients (71.2% vs. 36%, $p < .001$). The detection rate of NVE on DFE was higher in SC patients than in SS patients (37.8% vs. 25.9%).
Conclusions: Our small, single-center study suggests that FA is a better approach to identifying NVE than DFE in sickle cell patients. This would be clinically important as subsequent treatment with laser therapy, anti-VEGF treatment, or observation with closer follow up typically depends on identification of NVE. Our findings highlight an important improvement in identifying NVE, but more research is required to establish routine FA as part of standard guidelines.

CONTROL ID: 3706882

SUBMITTER (NAME ONLY): Andrea Dillinger

TITLE: Versican GAG-α domain deficiency causes rosette formation and detachment of the sensory retina in the mouse eye

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Dillinger, N. Bauer, M. Schneider, R. Seitz, R. Fuchshofer, E.R. Tamm, Institute of Human Anatomy und Embryology, Universitat Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Versican is a large chrondroitin sulphate proteoglycan and major component of the extracellular matrix. It consists of four isoforms (V0, V1, V2, V3) that show molecular differences in their respective glycosaminoglycan (GAG) attachment domain. To learn more about the specific function of versican and its isoforms in the retina, we analyzed mutant mice with deficiency in V0 and V2.

Methods: $VCAN^{(tm1Zim)}$ mice were investigated with a splice-variant specific gene inactivation of V0 and V2 resulting in GAG-α domain deficiency. Four- and eight-week-old versican$V0/V2^{-/-}$ and versican$V0/V2^{+/-}$ mice were analyzed and compared with wildtype littermates. Semithin sections were investigated by light microscopy. Retinal thickness and the number of optic nerve (ON) axons was quantified. The distribution and expression of GFAP and of the major versican binding partners fibronectin and hyaluronan was investigated by immunohistochemistry.

Results: The loss of V0 and V2 isoforms resulted in the formation of retinal rosettes, affecting the outer nuclear layer, and photoreceptor inner and outer segments. The defects were first seen in 4-week-old homozygous mice. Essentially similar defects were seen in heterozygous mice, though with later onset (8 wks of age). Rosette formation was frequently associated with detachment of the sensory retina. Analysis of the anterior chamber showed a wide-open angle with no obvious structural changes in the trabecular meshwork outflow pathways. GFAP immunoreactivity in Müller cells of mutant mice was identical to that seen in wildtype littermates, even in mutant eyes with rosette formation and retinal detachment. Immunoreactivity for fibronectin was dramatically reduced in the retina of mutant mice but unchanged in the chamber angle. Reactivity for hyaluronan was markedly decreased in the inner plexiform layer but increased in the ganglion cell layer and the vitreous of versican $V0/V2^{-/-}$ mice. Retinal thickness and number of ON axons showed no difference in versican $V0/V2^{-/-}$ mice compared to wildtype littermates.

Conclusions: Deficiency of the versican isoforms V0 and V2 causes retinal changes that indicate its critical role for attachment of the sensory retina to the retinal pigment epithelium.

CONTROL ID: 3706883

SUBMITTER (NAME ONLY): Jun Yang

TITLE: CFAP418 functions in membrane lipid homeostasis through binding phosphatidic acid and cardiolipin during photoreceptor ciliogenesis

SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Yang, A. Clark, D. Yu, D. Zhu, G. Neiswanger, Ophthalmology, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: CFAP418 is a causative gene for several inherited retinal degenerative diseases. Cfap418 knockout in mice leads to photoreceptor cell death by disrupting the membrane disk alignment and reducing the membrane proteins in the outer segment (OS). In this report, we investigated the moculuar mechanism that underlies the retinal phenotypes in Cfap418 knockout mice.

Methods: We systematically examined the protein expression and phosphorylation profiles as well as membrane lipid composition in Cfap418$^{-/-}$ retinas using various quantitative mass spectrometry at the onset and during the robust progress of the phenotypes. Semi-quantitative immunoblotting analysis and standard immunofluorescence were conducted to verify the omics findings. Affinity purifications coupled with mass spectrometry and proten lipid overlay assays were performed to identify CFAP418-binding partners.

Results: We observed differentially expressed proteins that are involved in membrane remodeling and mitochondrial function. In Cfap418$^{-/-}$ photoreceptors, the expression and localization of endosomal sorting complex proteins, mitochondrial morphology, and OS targeting were affected. The phosphorylation of lipid-binding and -activated protein kinase Ca was significantly increased. In addition, a broad range of membrane lipids were altered in abundance. Affinity purifications failed to identify stable CFAP418-interacting proteins, but revealed an indirect associated protein RAB28, which is encoded by another retinal degeneration gene. However, CFAP418 protein binds to lipid metabolism precursor phosphatidic acid and mitochondrial-specific cardiolipin.

Conclusions: Our findings indicate that CFAP418 is a lipid-binding protein and functions in membrane lipid homeostasis, membrane remodeling, and mitochondrial function during photoreceptor OS development.

CONTROL ID: 3706884
SUBMITTER (NAME ONLY): Brian Nguyen
TITLE: The effect of finasteride on dry eye disease
SESSION TITLE: Dry Eye, Clinical
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: B.J. Nguyen, E. Meer, A.S. Gupta, G. Jinpeng, G. Ying, V.Y. Bunya, I. Macchi, M. Massaro-Giordano, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|
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ABSTRACT BODY:

Purpose: The purpose of this retrospective study was to characterize dry eye disease (DED) in patients taking finasteride, a potent targeted anti-androgenic medication.

Methods: An extended case series with retrospective chart review of all cases of patients on finasteride seen in the Scheie Eye Institute Dry Eye Clinic at the University of Pennsylvania from January 1, 2005 to the December 1, 2021. Patient demographics, diagnosis, prior treatment, questionnaire data, and DED clinical exam outcomes were extracted. Statistical analysis was performed to assess clinical characteristics and Ocular Surface Disease Index (OSDI) quality of life measures among patients on varying doses of finasteride.

Results: 116 patients with a history of DED on finasteride were included with an average age of 67.9 years (SD 13.9). The population was predominantly male (95%), and Caucasian (86%). 23 patients were on a finasteride dosage of 1 mg or 2.5 mg, and 93 patients were on a finasteride dosage of 5 mg. Mean follow up was 55.3 months (SD 35.1, range 2.5 to 119.2). When comparing exam findings during initial and followup visit, a significantly greater percent of patients was noted to have meibomian gland disease (MGD) (62.9% [initial] vs 85.3% [followup], $p = 0.0001$), conjunctival abnormalities (21.1% [initial] vs 41.9% [followup], $p = 0.0002$), and corneal abnormalities (26.3% [initial] vs 40.5% [followup], $p = 0.0047$) at final exam. Mean OSDI score was 24.4 (SD 19.6) and was slightly higher in patients taking 5mg, though this was not statistically significant. Lower dose finasteride use was significantly associated with a greater frequency of cyclosporine use at first exam (26.1% vs 6.5%, $p = 0.01$) and last exam (25.0% vs. 3.4%, $p = 0.0168$). Otherwise, treatment modalities were no different between the lower and high dose groups.

Conclusions: To our knowledge, this represents the largest demographic study over 15 years of DED patients on finasteride, demonstrating an association with finasteride usage and MGD, conjunctival, and corneal abnormalities. The androgen sensitive meibomian glands may be altered in those taking anti-androgen medications, and especially finasteride given its unique potency and targeted effects compared to other anti-androgenics. This study reinforces the importance of considering the long-term effects of finasteride use on DED as part of the systemic sequelae of androgen depletion and provides anticipatory guidance for patients and ophthalmologists.

CONTROL ID: 3706887

SUBMITTER (NAME ONLY): Paras Shah

TITLE: Posterior Pole Asymmetry Analysis as a Diagnostic Tool in Glaucoma Suspects: An Electrophysiological Approach

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.P. Shah, A. Tirsi, V. Gliagias, J. Tsai, B. Patel, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|A. Tirsi, C. Tello, Ophthalmology, Manhattan Eye, Ear, and Throat Hospital, New York City, New York, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|S. Tello, Rye High School, Rye, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Posterior pole asymmetry analysis (PPAA) is a spectral domain optical coherence tomography (SD-OCT) software that compares posterior pole retinal thickness measurements between the superior and inferior hemispheres of each eye. We sought to determine whether these structural abnormalities were correlated with functional retinal ganglion cell (RGC) loss, as quantified by steady state pattern electroretinogram (ssPERG) parameters, in glaucoma suspects (GS).

Methods: Twenty GS (34 eyes) were enrolled in a prospective single-center study at the Manhattan Eye, Ear, and Throat Hospital in New York City. All subjects underwent comprehensive ophthalmological examination, including Humphrey visual field, Spectralis (Glaucoma Module Premium Edition) SD-OCT PPAA, and ssPERG testing. The ability of ssPERG parameters (Magnitude [Mag, μv], MagnitudeD [MagD, μv], and MagD/Mag ratio) to predict PPAA thickness measurements (total, superior, and inferior thickness, in μm) was tested via multivariate linear regression analysis.

Results: When total, superior, and inferior PPAA parameters were independently entered as dependent variables, and after controlling for age, spherical equivalent (SE), and central corneal thickness (CCT), Mag explained 8% of variance in total PPAA change ($F(1,29)=6.33$, $B=6.86$, 95% CI: 1.29-12.44, $p=0.018$), 8% in superior PPAA change ($F(1,29)=5.57$, $B=6.92$, 95% CI: 0.92-12.92, $p=0.025$), and 7.1% in inferior PPAA change ($F(1,29)=5.83$, $B=6.80$, 95% CI: 1.04-12.56, $p=0.022$). In the same analysis, MagD explained 9.7% of variance in total PPAA change ($F(1,29)=8.09$, $B=6.47$, 95% CI: 1.82-11.13, $p=0.008$), 10% in superior PPAA change ($F(1,29)=7.33$, $B=6.63$, 95% CI: 1.62-11.63, $p=0.011$), and 8.5% in inferior PPAA change ($F(1,29)=7.25$, $B=6.36$, 95% CI: 1.53-11.18, $p=0.012$). No significant associations between MagD/Mag ratio and PPAA measures were found.

Conclusions: To the best of our knowledge, this is the first report describing the positive relationship between RGC dysfunction and structural retinal changes in the posterior pole. These findings demonstrate possible morphological changes in RGCs prior to cell death, including shrinkage, reductions in the dendritic tree, and thinning of the retinal nerve fiber layer. The detection of asymmetrical structural RGC loss, combined with RGC function assessment using PERG, may be a more informative tool for glaucoma diagnosis in GS.

CONTROL ID: 3706888
SUBMITTER (NAME ONLY): Riaz Qureshi
TITLE: Certainty of evidence in Cochrane Eyes and Vision systematic reviews
SESSION TITLE: Public Health I
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Systematic reviews (SRs) are often considered the highest level of evidence, yet the certainty of the evidence which they present can be low and unusable in practice because the estimates are not precise, the primary study populations are not directly relevant to the target population, the risk of bias of primary studies is high, there may be too much heterogeneity in the estimates, or there may be a potential for publication bias. Grading of Recommendations, Assessment, Development and Evaluation (GRADE), is one approach to assessing the certainty of evidence collected in systematic reviews. Our objective is to assess the distribution of certainty of evidence from SRs published by Cochrane Eyes and Vision (CEV) and to identify reasons for which evidence is commonly downgraded or upgraded.

Methods: So far, we have assessed all CEV systematic reviews that included at least one GRADE Summary of Findings (SoF) table published between January 1, 2008 and February 25, 2020 (N = 275). GRADE was developed, published, and adopted by Cochrane in 2008. We abstracted data from all SRs into a Qualtrics form (single abstraction) and conducted all analyses using Stata 15.

Results: Of the 275 reviews assessed thus far, 149 (54%) presented GRADE SoF tables, which together included 1854 outcomes. Most outcomes were assessed with a median [IQR] of 190 [66 – 551] participants and 2 [1 – 4] studies (Table). Randomized controlled trials were the most common study type used as evidence for outcomes, but 27% (507) of outcomes did not specify the study type (Table). Only 6% (116) of outcomes were judged at a “high” certainty of evidence whereas 47% (869) were either “low” or “very low” certainty, with “risk of bias” and “imprecision” being the most common reasons for downgrading the evidence (Table). Five hundred and fifty-nine (30%) of the outcomes in SoF tables did not have a GRADE rating due to a lack of studies with evidence.

Conclusions: Overall, the certainty of evidence within CEV reviews, according to GRADE, is generally low and SoF tables often failed to report the specific study types contributing to the outcome. Our findings highlight the necessity to improve the quality of primary research: specifically, studies should be properly powered and focus on minimizing their risk of bias. Additionally, future reviewers should ensure their SoF tables are informative and consistent in all aspects to support transparent decisions.

CONTROL ID: 3706889

SUBMITTER (NAME ONLY): Guangying Ma

TITLE: Quantitative optical coherence tomography for longitudinal monitoring of postnatal retinal development

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ma, J. Ding, X. Yao, Biomedical engineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|X. Yao, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Guangying Ma: Commercial Relationship: Code N (No Commercial Relationship) | Jie Ding: Commercial Relationship: Code N (No Commercial Relationship) | Xincheng Yao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study is to validate in vivo optical coherence tomography (OCT) for longitudinal monitoring of postnatal retinal development in developing mouse eyes.

Methods: A custom-designed optical OCT was employed for in vivo retinal imaging of C57BL/6J mice. Three-dimensional (3D) retinal OCT volumetric images were recorded at postnatal 14, 17, 21, 28, and 56 days. The retinal images were manually segmented, and the layer thickness was measured by MATLAB.

Results: Figure 1 and Table 1 shows the longitudinal OCT monitoring of developing retina. After eye-opening, the retinal layer thickness kept changing until 28 days. Figure 1A shows the enface image of the superior quadrant, which indicates the location of the B-scans in Figure 1B. Figure 1B shows the representative B-scans used for layer thickness measurement. The red arrows indicate an hyporeflective layer (HRL) which was unambiguously observed between postnatal day 14 (p14) to p17, and gradually disappeared after p28. Figure 1C shows the reflectance profiles of the B-scans in Figure 1B. Figure 1D1 shows a comparative analysis of inner retinal layer thicknesses with ages from p14 to p56. The nerve fiber (NFL) thickness decreased from p14 to p21 and then remain the same. The HRL thickness kept decreasing after eye-opening and disappeared at about p28. The inner plexiform layer (IPL) thickness did not change significantly between p14 to p56. The INL thickness kept decreasing after eye-opening until p28. Figure 1D2 shows layer thickness change in the outer retina. The outer nuclear layer (ONL) thickness kept decreasing until p28. On the contrary, the external limiting membrane to retinal pigment epithelium (ELM-RPE) thickness kept increasing until p28. Figure 1D3 shows the thickness change of the inner retina, outer retina, and the whole retina. The thickness of the inner retina and the whole retina kept decreasing until p28. On the contrary, the thickness of the outer retina slightly increased after the eye-opening.

Conclusions: In vivo OCT provides a feasible solution for longitudinal monitoring of postnatal retinal development. Quantitative OCT analysis revealed distinct outer and inner retinal layer changes, corresponding to eye development. An HRL between the NFL and IPL was observed in developing eyes and gradually disappeared with aging.

CONTROL ID: 3706890
SUBMITTER (NAME ONLY): Aaron Kho
TITLE: Automated scan quality assessment in low-cost OCT
SESSION TITLE: OCT Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Kho, H. Bagherinia, C. Leahy, S.A. Bello, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) in the remote care setting can be challenging due to self-scanning limitations. Patient-operated OCT systems need to detect the state of patient alignment and determine the OCT image quality for fully automated imaging. Here, we demonstrate an algorithm that automatically assesses the OCT image quality using machine learning.

Methods: A total of 141 volumes were acquired with a prototype low-cost OCT system from 18 subjects using either one or both eyes. The size of each volume was 7.00 mm x 5.78 mm x 2.77 mm and all volumes were centered on the fovea. For each volume, multiple feature maps were created based on signal strength, signal to background ratio, and individual A-scan contrast. These feature maps were then combined into a joint probability map previously presented (Elezaby et al., IOVS, 2020). By placing a threshold on the joint probability map, we generated groups of likelihood functions as inference models for each of the feature maps. The OCT quality map was formed using the likelihood functions and a posterior probability from the inference model. The OCT scan quality was assessed using the ETDRS grid consisting of three concentric circles (radii of 0.5 mm, 1.5 mm, and 2.9 mm) divided into nine subfields. An OCT volume was considered poor quality based on two criteria. The first involved three or more central and inner ETDRS subfields having low confidence. The second involved two or more ETDRS subfields that include at least one outer subfield having low confidence. OCT volumes were assessed manually by an experienced grader to obtain the ground truth.

Results: Out of the 141 volumes, there were 90 true positives (good quality), 44 true negatives (poor quality), 4 false positives, and 3 false negatives. Fig. 1 shows an example for each scenario. The algorithm yielded a sensitivity of 0.97 with 95% confidence interval (CI) [0.91, 0.99], specificity of 0.92 with 95% CI [0.80, 0.98], and success rate of 0.95 with 95% CI [0.90, 0.97].

Conclusions: We demonstrated a new machine learning method that automatically grades OCT volumes with high sensitivity and specificity using the ETDRS grid. This algorithm could help acquire good quality data in the remote care setting.

CONTROL ID: 3706891

SUBMITTER (NAME ONLY): Elizabeth Bolton

TITLE: Optimizing Photorefractive Keratectomy Oucomes in Myopia with Topical Mitomycin C

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Bolton, N. Zhang, P. Bryar, R. Feder, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Elizabeth Bolton: Commercial Relationship: Code N (No Commercial Relationship) | Nigel Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Paul Bryar: Commercial Relationship: Code N (No Commercial Relationship) | Robert Feder: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine the impact of various preoperative characteristics, mitomycin C 0.2 mg/ml (MMC) exposure time, and reduction in refractive correction (backoff) when using topical MMC on the outcome of photorefractive keratectomy (PRK) for myopia.

Methods: In this retrospective analysis, data collected included demographics, pre and postop manifest refraction (MR), preop pachymetry, percent reduction in treatment (sphere reduced by 0 to >10% of SE), MMC exposure time, presence of post PRK haze, and postop uncorrected visual acuities. Outcome measures included uncorrected postop acuity, residual refractive error, and incidence of haze. Inclusion criteria were preoperative myopia defined as > -4.00 D with regular preoperative astigmatism < 5.00 D, with mean of -6.75, [-12.75, -0.50] in patients who underwent PRK with MMC. Patients presenting for enhancement surgery, patients with preexisting corneal disease or tear deficiency were excluded. Linear mixed model and generalized linear mixed model were used to assess the associations between MMC exposure time with 3-month log mar visual acuity and incidence of haze respectively.

Results: A total of 91 eyes from 57 patients were included. The mean (standard deviation, SD) of 3-month log mar visual acuity was 0.06 (0.16). The incidence of haze was 28.6% (30). There was no significant difference in the development of corneal haze with increased MMC exposure time (odds ratio 1.22). There were 71 eyes with 20/25 vision or better defined as group 1, and 20 eyes with 20/30 or worse acuity (up to 20/70) in group 2.The mean (SD) back off in group 1 was 6.6% (4.5) of SE, mean preoperative MR -6.9 (2.3 [-11.75, -1], and mean postop MR -0.4 D (0.67 [-2.25,-0.25]). In group 2, the mean backoff was 9.7% (4.5), the mean preoperative MR -8.9 (2.4 [-12.75, -3.75]), and mean postoperative MR 1.2 D (0.69 [-3.25, 1.75]).

Conclusions: Incidence of haze was higher than expected, but not visually significant. There was no significant difference in refractive outcome even when MMC exposure time was <20 seconds. Extending exposure time beyond 20 seconds was not necessary to prevent visually significant haze. A larger percent backoff of 10% or greater may contribute to undercorrection after PRK.

CONTROL ID: 3706893

SUBMITTER (NAME ONLY): Zain Hussain

TITLE: Rates of Laser Trabeculoplasty by Ophthalmologists and Optometrists: A Comparative Analysis of the Center for Medicare & Medicaid Services Public Use File

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate utilization and payment of Laser Trabeculoplasty (LTP) performed by ophthalmologists and optometrists in three key US states based on CMS Public Use File.

Methods: We analyzed the Medicare Provider Utilization and Payment Data furnished by the CMS to identify LTP (CPT code 65855) claims in three key US states with optometric-expanded surgical authority in 2015 and 2018. We utilized regression, chi-square, and two-way t-tests to compare PUF metrics.

Results: The total sum of Medicare allowed payments to ophthalmologists and optometrists performing LTP amongst Fee-for-Service (FFS) Medicare beneficiaries in the US in 2018 was about 33% lower compared to 2015 while the total sum of Medicare Allowed payments in Kentucky (KY), Louisiana (LA), and Oklahoma (OK) in 2018 was about 26% lower compared to 2015. However, the optometric proportion of total Medicare allowed payments furnished by optometrists in three states increased from 11.3% to 17.9% between 2015 and 2018 (Fig. 1). Additionally, we observed significant increases in optometric-to-ophthalmologic average Medicare allowed payments between 2015 and 2018 in KY, LA, OK, and the tri-state cohort (all $p<0.001$) (Table 1). Significant optometric-to-ophthalmologic ratio increases in summed provider counts ($p=0.007$), summed unique Medicare beneficiary counts ($p<0.001$), and ultimately, summed service counts ($p<0.001$) were observed. Uniquely, we noticed that only one state amongst our tri-state cohort, LA, displayed non-significant differences in all three categories ($p=0.91$, $p=0.35$, $p=0.29$, respectively), despite significantly disproportionate changes in summed Medicare allowed LTP payments ($p<0.001$). Within the ophthalmologic cohort, female-to-male provider ratio significantly increased ($p=0.008$); however, the optometric cohort demonstrated no significant increases ($p=0.99$).

Conclusions: Optometric surgical authority is a continually expanding landscape throughout the United States. We investigated the latest edition of the CMS Medicare database to characterize LTP-associated metrics between ophthalmologists and optometrists in KY, LA, and OK states. Between 2015 and 2018, optometrists significantly increased their share of LTP-associated Medicare-allowed payments, unique beneficiary counts, service provider counts, and provider service counts.

CONTROL ID: 3706897

SUBMITTER (NAME ONLY): Maya Kishimoto

TITLE: One-year results of switching to brolucizumab in exudative age-related macular degeneration.

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kishimoto, A. Miki, A. Chubachi, W. Matsumiya, H. Imai, S. Kusuhara, M. Nakamura, Ophthalmology, Kobe university graduate school of medicine, Hyogo, JAPAN|R. Hara, Ophthalmology, Kakogawa central city hospital, Hyogo, JAPAN|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the functional and anatomical effects of switching to brolucizumab in exudative age-related macular degeneration.

Methods: This retrospective study assessed 41 eyes of 41 patients of exudative age-related macular degeneration cases treated with aflibercept and switched to brolucizumab for one year. We evaluated functional and anatomical parameters including best-corrected visual acuity (BCVA), central retinal thickness(CRT), central choroidal thickness(CCT) and pigment epithelial detachment (PED) height at 1,3,6 and 12 months after the first brolucizumab injection. Change in the interval of anti-VEGF injections between before and after switching to brolucizumab was also evaluated.

Results: The patients did not show a significant change in BCVA at all time points from baseline.CRT was significantly decreased at all time points ($p<0.05$). CCT and PED height decreased significantly at 6 months after the first brolucizumab injection (each $p<0.05$), but not at 12 months. The injection interval was significantly extended from 6.3±3.2 weeks to 13.7±9.2 weeks ($p<0.01$). The mean change of the injection interval was 7.4±8.1. The mean number of brolucizumab injections during the observation period was 5.4±1.9.

Conclusions: Switching from aflibercept to brolucizumab was effective for anatomical improvement and extending injection intervals. Switching to brolucizumab is expected to reduce the burden of frequent injections in patients with exudative age-related macular degeneration.

CONTROL ID: 3706902

SUBMITTER (NAME ONLY): Isis Zhang

TITLE: Provision of Reading Glasses During Underserved Community-Based Tele-Ophthalmology Screenings

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Zhang, P. Tailor, A. Zhu, R. Verma, M. Habiel, A.S. Khouri, B. Szirth, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The most common cause of blurry vision in the United States is refractive error. Despite being a correctable condition, over 8.2 million people are estimated to have their refractive error go undiagnosed or untreated. Minorities and low-income groups in particular have significantly increased odds of inadequate correction and double the rates of near-vision impairment. We aimed to address this gap in care through the provision of refractive glasses during community-based tele-ophthalmology screenings.

Methods: Eight free eye screening events were held in Newark and West New York, NJ. Demographic information, intraocular pressure, visual acuity, auto-refraction, retinal imaging, and optical coherence tomography were obtained from each subject as part of a comprehensive tele-ophthalmology protocol. Reading glasses were provided as needed based on the recommendation of a certified telemedicine reader. Eligible recipients completed surveys on site regarding access to eye care. They were surveyed again by phone after one month to assess degree of satisfaction and vision improvement.

Results: 38 subjects (mean age 53, 47% male) qualified for presbyopia correction and received reading glasses. 97% were Hispanic and 3% were African American. Of the 33 that returned surveys, 88% reported not seeing an eye doctor annually. The most common reason was lack of insurance or inability to pay (71%). Others included having no need to see an eye doctor (10%), disliking eye doctors (7%), not knowing the importance of regular eye exams (3%), and COVID-19 (3%). Of the 25 subjects that were reached for follow-up, 92% reported using the glasses daily. Those that did not reported the power was too strong or they did not feel they needed them. Subjects noted an average improvement in vision of 4.4 out of 5 and an average satisfaction of 4.7 out of 5 (Figure 1).

Conclusions: Glasses distribution is an effective way to address refractive error in underserved communities. Given the gaps in knowledge and utilization of eye care identified in our study, there is an obvious need for continued outreach to these areas. Further studies will include larger populations and evaluate mobile refraction devices to increase ease and reach of glasses provision.

CONTROL ID: 3706903
SUBMITTER (NAME ONLY): Leen Azeez
TITLE: Work-related Musculoskeletal Problems among Eyecare Professionals
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L.S. Azeez, E. Sherry, D. Mojica, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|
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ABSTRACT BODY:
Purpose: Ergonomics are an integral component of eyecare professionals' health. This study reports on the work-related musculoskeletal problems among eyecare professionals.
Methods: In this cross-sectional study, an anonymous questionnaire survey was distributed among eyecare professionals including ophthalmologists, optometrists, ophthalmology residents, ophthalmic technicians, and ophthalmology clinic administrative staff. The following parameters were evaluated in the survey: demographics, musculoskeletal symptoms due to their occupation, and the effects of these symptoms on their work.
Results: 98 eyecare professionals responded which included 50 ophthalmic technicians, 27 ophthalmologists, 7 ophthalmology residents, 6 optometrists, and 8 ophthalmology administrative clinic staff. These included 36 men and 59 women; 3 preferred not to disclose their sex. The mean age was 41.9 ± 12.2 years (range, 21-75 years). Overall, 63 (65.3%) participants had musculoskeletal problems within the past month. These involved the lower back in 38 (38.8%), neck in 36 (36.7%), hand/wrist in 29 (30.0%), shoulder in 24 (24.5%), upper back in 20 (20.4%), and elbow in 8 (8.2%). To manage musculoskeletal problems, the participants had used the following: exercise in 30 (30.6%), analgesics in 21 (21.4%), change of equipment/tools in 12 (12.2%), physical therapy in 10 (10.2%), additional breaks during workdays in 8 (8.2%), taking time off from work in 6 (6.1%), injection of medications in 4 (4.1%), reducing work hours in 2 (2.0%), and 2 (2.0%) with reducing the scheduled cases.
Conclusions: Eyecare professionals have a high prevalence of occupation-related musculoskeletal symptoms, which significantly affect their work. Considering the long-term effects of such musculoskeletal problems on these individuals' health, proper education and work adjustment are necessary to minimize morbidity associated with such problems.

CONTROL ID: 3706904
SUBMITTER (NAME ONLY): Jia Tan
TITLE: The Impact of Open Angle Glaucoma on ON-OFF Perimetry
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Tan, M.W. Dul, V. Moore-Stoll, S. Dellostritto, H.R. Nasrabadi, J.Z. Jin, J. Alonso, SUNY College of Optometry, New York, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: Traditional white-on-white perimetry is limited to the functional assessment of the ON pathway. We investigated visual deficits in both ON and OFF pathways in patients with glaucoma and similarly-aged controls and compared these findings with standard automated perimetry (SAP).

Methods: Fourteen eyes from 14 subjects, 7 with glaucoma (48-76 years old; mean, 64 ± 10.28; severity from MD -0.48 to -18.25) and 7 controls (48-78 years; mean 65.14 ± 9.63) were tested at 8 Michelson contrast levels (5-20%) within the central 30 degrees of the visual field.

A single test included 579 trials (27 catch trials), at 92 locations, repeated 3 times for both light and dark stimuli. Each participant completed 8 tests (4,632 trials) using a head mounted display with eye tracker (HTC Vive Pro Eye, 90 Hz, maximum luminance: 110 cd/m^2). Stimuli were light or dark squares generated with Unity software, presented on a spherical binary noise background, and with their size increasing with eccentricity.

Eye movements were measured at 120 Hz and restricted within 2.5 degrees for controls and 3.5 for glaucoma patients. Correct responses were measured across the entire visual field and within each quadrant. Differences between control and glaucoma subjects were plotted as a function of glaucoma severity.

Results: There was a positive correlation between the control - glaucoma subject difference in percent correct responses measured with ON-OFF perimetry and the visual sensitivity of glaucoma subjects measured with SAP for both the full visual field (r=0.74, p=0.0027) and the quadrant most affected by glaucoma (r=0.58, p=0.0297). Between each pair of subjects, the error rate was greater for glaucoma than control subjects for the full visual field and nasal quadrants, even if the quadrants were not flagged as significantly deviating from the SAP reference data base (see representative example in figure 1).

Conclusions: Glaucoma increases error responses within the central 30 degrees when compared to similarly-aged controls in ON-OFF perimetry, across the entire visual field and within field quadrants most associated with glaucomatous visual loss. Ongoing work is aimed toward the utility of this technology in a clinical setting.

CONTROL ID: 3706905

SUBMITTER (NAME ONLY): Ashley Batchelor

TITLE: Predictors of long-term ophthalmic complications after closed globe injuries using the IRIS® Registry (Intelligent Research in Sight)

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Batchelor, M. Hunt, M. Lacy, C.S. Lee, A.Y. Lee, Y. Chee, S. Saraf, Ophthalmalogy, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|M. Hunt, Ophthalmology, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|C.S. Lee, A.Y. Lee, Karalis Johnson Retina Center, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Closed globe ocular trauma may result in potentially serious injury to vital eye structures. We sought to identify baseline clinical factors associated with ophthalmic complications, including a need for future surgery.

Methods: We analyzed longitudinal data from the American Academy of Ophthalmology IRIS® Registry. We identified patients with a trauma between 2014 and 2019 and performed time-split Cox regression. Demographic factors and the following baseline features were entered as predictors: corneal edema or opacity, traumatic hyphema (TH), iris/angle injury, lens injury (LI), lens displacement, vitreous hemorrhage (VH), retinal break, retinal detachment (RD), commotio retinae, macular scar, macular hole, choroidal injury, and optic nerve injury. Our outcomes of interest included: RD, glaucoma surgery (GS), and cataract surgery (CS). We performed a univariate regression for each feature and selected features with $p <= 0.1$ to be included in the multivariate regressions. For anterior segment complications, we used splits at 60 and 180 days following the date of trauma. For RD, we used a split at 60 days.

Results: A total of 214,163 patients had a trauma diagnosis. The strongest risk factors for CS during the first 60 days were LI (hazard ratio 12.2 95%CI 10.1-14.6), and TH (2.64, 2.32-2.99) (Fig. 1A). The strongest risk factor for GS was TH (8.00, 5.00-12.8), during the first 60 days (Fig. 1B). Baseline TH (4.18, 3.42-5.12), and VH (12.7, 10.3-15.6) were significant risk factors for a subsequent RD and remained significant even after the first 60 days (Fig. 2).

Conclusions: Baseline characteristics at the time of trauma diagnosis are strongly associated with both anterior and posterior segment complications. Regular, long-term follow up is warranted following ocular trauma.

CONTROL ID: 3706909

SUBMITTER (NAME ONLY): M Dominik Fischer

TITLE: PERCEIVE study report: Real-world safety and effectiveness of voretigene neparvovec

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Voretigene neparvovec (VN) is the first approved ocular gene therapy for patients with RPE65-mediated inherited retinal dystrophy and sufficient viable retinal cells. PERCEIVE is a post-authorization safety study assessing long-term safety and effectiveness of VN in a real-world setting.

Methods: PERCEIVE is an ongoing (2019–2029), prospective, longitudinal, multicenter (ex-US), registry-based observational study. All VN-treated patients, including those treated prior to enrollment, were considered eligible. Patients are treated according to local prescribing information and followed-up as per the routine clinical practice for 5 years. The primary objective is to collect adverse events (AEs), including AEs of special interest (AESIs). Secondary objectives include assessment of pregnancy outcomes and visual function over time.

Results: Up to August 2021, 106 patients were enrolled, of whom 103 received VN (mean age [SD]: 19.5 [10.85] years; females: 52 [50.5%]). Mean (SD) duration of follow-up was 0.8 (0.64) years (maximum: 2.3 years). A total of 35 patients (34.0%) reported ≥1 ocular AEs including those with ocular AESIs (number of patients [n] = 17 [16.5%]). Events of chorioretinal atrophic changes (at injection site and/or elsewhere, n = 13) were the most common ocular AEs. Ocular AESIs included foveal degeneration (n = 4), vitritis (n = 4), eye inflammation (n = 3), retinal tear (n = 2) and increased intraocular pressure (IOP; n = 5). Two patients had ocular serious AEs (SAEs: eye inflammation, n = 1; increased IOP, n = 1). Non-ocular AEs occurred in 8 patients; most frequent AE was headache (n = 4). One patient, with no previous history, reported 3 events of psychiatric disorder (non-ocular SAEs). Visual function improved in terms of full-field light sensitivity threshold, and best-corrected visual acuity (LogMAR) at Year 2 with a mean (SD) change from baseline of −13.67 (22.62) decibels and −0.03 (0.55), respectively (Table).

Conclusions: Overall, the safety and effectiveness of VN observed in the PERCEIVE study, with up to 2-years data, are consistent with the findings of VN clinical trials. Chorioretinal atrophy has been identified as a new adverse drug reaction, which so far has not been associated with loss of visual function. These events and overall longer-term safety will be further characterized in the ongoing study.

CONTROL ID: 3706912

SUBMITTER (NAME ONLY): Xiaomeng Wang

TITLE: Secreted frizzled-related protein (SFRP) serves as a potent antiangiogenic factor

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Wang, B. Qiu, A. Tan, A. Veluchamy, S. Ho, L. Zhou, N. Cheung, Singapore Eye Research Institute, Singapore, SINGAPORE|X. Wang, B. Qiu, A. Tan, A. Veluchamy, S. Ho, L. Zhou, G. Ming, T. Wong, Duke-NUS Medical School, Singapore, SINGAPORE|N. Cheung, G. Ming, T. Wong, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|W. Hong, Institute of Molecular and Cell Biology, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Abnormal angiogenesis is a characteristic feature of many blinding eye diseases, including proliferative diabetic retinopathy (PDR) and neovascular age-related macular degeneration (nAMD). Inhibiting excessive blood vessel growth and leakage is effective in preserving vision. Current anti-angiogenic drugs are dominated by vascular endothelial growth factor (VEGF) inhibitors. However, a substantial number of patients do not respond well to anti-VEGF drugs. Targeting VEGF independent pathways may offer an alternative strategy to treat ocular angiogenic diseases.

Methods: Proteomic analysis was performed in vitreous samples collected from PDR and control patients. Human secreted frizzled-related protein (SFRP) and its C-terminal domain were fused to Fc to generate chimera protein SFRP-Fc and SFPRC-Fc. Their impacts on endothelial cell proliferation and tube formation were studied using in vitro cell-based assays. Ex vivo angiogenesis assays including choroid, aortic ring, and metatarsal assays were used to study the anti-angiogenic effect of SFRP-Fc and SFRPC-Fc in a multi-cellular environment. The efficacies of SFRP-Fc and SFRPC-Fc were further evaluated in a mouse model laser-induced choroidal neovascularization (CNV) and a rabbit model of persistent retinal neovascularization (PRNV). Phosphoproteomics, quantitative RT-PCR, and Western bot analysis were used to investigate the mechanism of action of SFRP.

Results: Our study showed that SFRP is expressed at a significantly lower level in the vitreous of PDR patients as compared to that in control patients. SFRP-Fc and SFRPC-Fc strongly inhibit human retinal microvascular endothelial cell (HREC) proliferation, viability, and tube formation as well as vessel outgrowth from the choroid, aortic ring, and metatarsal bones. SFRPC-Fc is able to prevent and reverse laser-induced CNV in mice and demonstrates an additive effect with Aflibercept. In the rabbit model of PRNV, a single intravitreal injection of 2mg SFPRC-Fc could lead to persistent suppression of retinal angiogenesis and leakage for at least six weeks. Mechanistically, SFRP inhibits angiogenesis in a VEGF-independent fashion via Caveolin-1.

Conclusions: This study leads to the discovery of a novel inhibitor of angiogenesis SFRP and confirmed that its functional domain is located at the C-terminal domain of the protein. We further showed that SFRP exerts its anti-angiogenic effect through Caveolin-1.

CONTROL ID: 3706914

SUBMITTER (NAME ONLY): Andrew Lam

TITLE: Repeatability and agreement of multiple neuroretinal rim thickness acquisitions from Cirrus and its ISNT/IST patterns

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Lam, L.H. Lai, W. Lam, C. Tiu, School of Optometry, The Hong Kong Polytechnic University Faculty of Health and Social Sciences, Hong Kong, CHINA|A.K. Lam, Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, CHINA|

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ABSTRACT BODY:

Purpose: Bruch's membrane opening minimum rim width (BMO-MRW) has been popularly used to evaluate and monitor glaucoma. Neuroretinal rim (NRR) thickness also shared good diagnostic ability. This study investigated repeatability and agreement among multiple NRR thickness acquisitions. We also evaluated its ISNT/IST patterns and effect from axial length (AL).

Methods: 100 eyes (100 healthy subjects) had NRR thickness measured 5 times consecutively. Signal strength was at least 7 with no obvious artifacts. NRR thickness and retinal nerve fiber layer (RNFL) thickness were obtained. An average from all 5 acquisitions was considered as reference standard. The first, average from the first 2, first 3, and first 4 acquisitions were compared with the reference standard. AL was measured using partial coherence interferometry. Correlations between AL and NRR thickness, and RNFL thickness were studied. Number of eyes following the ISNT and IST patterns were counted.

Results: 87 eyes fulfilled the inclusion criteria. Table 1 shows repeatability and coefficient of variation among 5 acquisitions. They demonstrated comparable results. Table 2 shows agreement between different averaging methods with the reference standard. Agreement improved with averaging from more acquisitions. There were significant correlations between superior/inferior RNFL thickness and AL ($r=0.28$, $p=0.008$ and $r=0.40$, $p<0.001$, respectively). No significant correlations were found between superior/inferior NRR thickness and AL. There was 5% of the eyes following the ISNT pattern using RNFL thickness, and 36% when referring to IST pattern. There was 20% of the eyes following the ISNT pattern using NRR thickness, and 64% when referring to IST pattern.

Conclusions: One NRR acquisition could provide valid information for clinical use. NRR thickness is less affected by AL for evaluating ganglion cell axons.

CONTROL ID: 3706917

SUBMITTER (NAME ONLY): Miki Takii

TITLE: Optical coherence tomography angiography and wide-field fluorescence angiography for retinal blood vessel evaluation in a rat model of endothelin-1-induced vasoconstriction

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Takii, N. Asai, T. Nakamura, Y. Shinohara, M. Nakatani, T. Ueno, Bioengineering Institute, R&D Div.,, NIDEK CO., LTD, Gamagori, Aichi, JAPAN|T. Kanou, Medical Development Dept., Eye Care Div.,, NIDEK CO., LTD., Gamagori, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: To evaluate vessel density changes using optical coherence tomography angiography (OCTA) and wide-field fluorescence angiography (WF-FA) in a rat model of vasoconstriction induced by intravitreal injection of endothelin-1 (ET-1).

Methods: Vehicle or ET-1 (20 pmol/eye) was injected into the vitreous body in Brown Norway rats. Retinal vessels were observed using OCTA (RS3000A; Nidek) and WF-FA (Mirante; Nidek). OCTA images (20° × 20° field) were taken using a custom-made rat-specific adapter. Retinal layers—the internal limiting membrane and the photoreceptor inner–outer segment junction—were segmented using custom-made software, and en face OCTA images of these volumes were acquired. WF-FA images (Φ110° field) were taken with a wide-field adapter. Retinal vasculature was imaged before, and every 5–10 min until 50 min after, intravitreal injection (n = 4 rats/group). OCTA and WF-FA images were enhanced and vascular binary images were generated by using the Fiji package in the ImageJ software. Vessel density was presented as vessel area/total area*100% and normalized by baseline values (100%).

Results: The binarized WF-FA images showed mainly large vessels. ET-1 caused a significant decrease in vessel density 5 min after injection, peaking at 30 min (vehicle, 97% ± 4%; ET-1, 49% ± 14%, $P < 0.01$) and lasting up to 50 min. The binarized OCTA image detected both capillaries and large vessels. ET-1 significantly decreased vessel density 5 min after injection; most capillaries were invisible by 10 min. Dramatically decreased vessel density was observed by 15 min (Vehicle, 88% ± 10%; ET-1, 16% ± 11%, $P < 0.01$), lasting up to 50 min.

Conclusions: Under the conditions in this study, WF-FA was suitable for evaluating a wide range of large vessels, and OCTA for evaluating large vessels and capillaries. OCTA and WF-FA are useful for different purposes in detailed research evaluation of retinal vasculature.

CONTROL ID: 3706927

SUBMITTER (NAME ONLY): Scott Harris

TITLE: Asymmetries in the vertical optokinetic reflex result from disproportionate excitation to complementary ON direction-selective retinal ganglion cell types

SESSION TITLE: Retinal ganglion cells and central processing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.C. Harris, F.A. Dunn, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|S.C. Harris, Neuroscience Graduate Program, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Scott Harris: Commercial Relationship: Code N (No Commercial Relationship) | Felice Dunn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: An asymmetry exists between the fidelity of the optokinetic reflex (OKR) in the dorsal-to-ventral (“Inferior”) and ventral-to-dorsal (“Superior”) directions. The neural underpinnings of this asymmetry are unknown. We made electrophysiological recordings from mouse ON direction-selective retinal ganglion cells (oDSGCs) to test the hypothesis that behavioral asymmetries in vertical OKR are associated with physiological asymmetries between oDSGCs that prefer Inferior and Superior motion.

Methods: A retrograde tracer was injected into the projection nucleus of Inferior and Superior oDSGCs in adult, wild-type mice of both sexes (N=33). Following dark-adaptation, retinas were harvested for electrophysiology. We compared the direction tuning of Inferior and Superior oDSGCs by making patch-clamp recordings from labeled cells in response to a drifting bar. Direction selectivity indices (DSIs) and tuning curve widths were compared across cell types and recording conditions (mean±SEM, rank sum). A computational model was built to examine the relationship between input currents and spike tuning curves. Vertical OKR was measured in a separate cohort of head-fixed mice.

Results: Our data indicate that Inferior oDSGCs spike less (spikes per stimulus: Inf. 27.40±1.57, Sup. 38.71±2.04, $p<0.0001$), are more direction-selective (DSI: Inf. 0.37±0.01, Sup. 0.28±0.01, $p<0.001$), and have narrower tuning curves (width at half maximum (degrees): Inf. 213.89±6.36, Sup. 258.49±6.12, $p<0.0001$) than Superior oDSGCs (n = 155 Inf., 115 Sup.). Voltage-clamp recordings demonstrated that this asymmetry is not explained by the canonical model of retinal direction selectivity, as there was no difference in inhibitory inputs across cell types ($p>0.05$ for peak IPSC of each stimulus direction). Instead, we found a difference in the magnitude of directionally untuned excitation across oDSGC types ($p<0.02$ for peak EPSC of each stimulus direction). Current-clamp experiments and modeling revealed a mechanism by which such excitation influences tuning curve shape. Finally, we found an analogous asymmetry in the vertical OKR of behaving mice.

Conclusions: Our results demonstrate that Inferior and Superior oDSGCs encode motion asymmetrically due to disproportionate excitatory input, and link this phenomenon to corresponding behavioral asymmetries in vertical OKR.

CONTROL ID: 3706928

SUBMITTER (NAME ONLY): Elena Salami

TITLE: Evidence of epithelial remodeling but not epithelial mesenchymal transition in vernal keratoconjunctivitis.

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Salami, F. Cavarzeran, A. Leonardi, Neuroscienze, Universita degli Studi di Padova Scuola di Medicina e Chirurgia, Padova, Veneto, ITALY|U. Rosani, of Biology, Universita degli studi di Padova Scuola di Scienze, Padova, Veneto, ITALY|A. Di Stefano, Istituti Clinici Scientifici Maugeri SpA IRCCS Veruno, Veruno, Piemonte, ITALY|P. Daull, J. Garrigue, Santen SAS, FRANCE|B. Paola, Universita degli Studi di Padova Dipartimento di Medicina Molecolare, Padova, Veneto, ITALY|

Commercial Relationships Disclosure: Elena Salami: Commercial Relationship: Code N (No Commercial Relationship) | Umberto Rosani: Commercial Relationship: Code N (No Commercial Relationship) | Philippe Daull: Commercial Relationship(s);Code E (Employment):Santen SAS | Fabiano Cavarzeran: Commercial Relationship: Code N (No Commercial Relationship) | Jean-Sebastien Garrigue: Commercial Relationship(s);Code E (Employment):Santen SAS | Antonino Di Stefano: Commercial Relationship: Code N (No Commercial Relationship) | Brun Paola: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Leonardi: Commercial Relationship(s);Code C (Consultant/Contractor):Santen SAS

ABSTRACT BODY:

Purpose: Vernal keratoconjunctivitis (VKC) is a recurrent bilateral ocular allergic inflammatory disease characterized by severe type 2 inflammation and tissue remodeling. Using a transcriptomic analysis, we examined the epithelial conjunctival gene expression related to the barrier function and the potential evolution to epithelial mesenchymal transition (EMT) in VKC.

Methods: Cells from conjunctival imprints from active VKC patients (n=15) and normal subjects (CT; n=5) were collected and their RNA isolated with Qiagen RNeasy Mini kit. 10 ng of RNA were processed with GeneChip Pico Reagent kit prior to a 9-cylcle PCR amplification and reverse transcription. Final cDNA was analyzed with Affymetrix Clarion S arrays system. Differential expression (DE) analysis included comparisons between VKC, VKC-subgroups and CT. Enrichment analyses on DE genes (adjusted p <0.05 and absolute log2 fold change >1) and regression analysis genes (p value<0.05) was performed using Gene Ontology Biological Process (GOBP) and Reactome.

Results: The difference between VKC and CT showed 333 probes (325 genes) significantly DE: 92 over-expressed and 241 down-regulated. Considering all VKC samples vs CT, 169 out of 325 identifiers were found in Reactome, where 646 pathways were hit by at least one of them. In tarsal VKC several GOBP were related to tissue remodeling, cytokine production and B cells regulation while in limbal VKC the ribonucleoprotein complex biogenesis was the most represented. We found a significant overexpression of MUC1, MUC3A, MUC4, MUC16, LGALS3BP, KRT23, GJB2, TJP1, PCDH, a significant reduced expression of CLDN8, CLDN34, CLDND1, CTNNAL1, SPINK2, EDIL3, and LUM. Many other genes of the cadherin, cingulin, occludin, MARVEL domain, lectin and actin families were either significantly up- or downregulated. We found up-regulation of epithelial marker E-cadherin, a non-increased expression of genes encoding for N-cadherin, vimentin and squamous cell carcinoma antigen (SCCA/SERPINB3) as EMT markers and a significant downregulation of the transcription factors required for EMT, SNAI-1, SNAI-2 and TWIST.

Conclusions: Several biological processes are associated to the pathogenesis of VKC in addition to an epithelial barrier remodeling. EMT is inhibited in VKC, explaining the finding that the majority of VKC patients, after the resolution of the disease, have mild cicatricial consequences.

CONTROL ID: 3706932

SUBMITTER (NAME ONLY): Malavika Harikrishnan Nambiar

TITLE: Patient-specific simulation of refractive surgery:
Biomechanics and modeling of CLEAR human lenticules

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nambiar, L. Liechti, P. Büchler, ARTORG Center for Biomedical Engineering Research, Universitat Bern, Bern, Bern, SWITZERLAND|T. Seiler, Dept. of Ophthalmology, Universitat Bern Medizinische Fakultat, Bern, Bern, SWITZERLAND|T. Seiler, Institut für Refraktive und Ophthalmo-Chirurgie, SWITZERLAND|

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ABSTRACT BODY:

Purpose: The purpose of this study is to characterize and simulate patient-specific corneal biomechanics to improve the planning of refractive procedures such as LASIK, CLEAR and PRK. The major drawback in surgical planning of these procedures is the lack of patient-specific biomechanical information. In this study, we propose to address this problem by building a simulation platform that combines in vivo Brillouin measurements with mechanical characterization of the imaged corneal tissue. A material model developed based on patient-specific data will then allow the simulation platform to be used to predict the outcomes of these different interventions.

Methods: Experimental: Corneal lenticules extracted from CLEAR surgeries (KEK approval 2021-00145) were tested by uniaxial extension in the nasal-temporal direction or at an angle 45° to it. The tissue was pre-stretched with a force of 10mN and preconditioned with 4 cycles of 15 % strain. The last cycle of force displacement data was recorded for analysis.

Computational: The lenticules were numerically modeled using an in-house algorithm that can accurately build a finite element mesh from the elevation maps obtained from the pre-operative Pentacam data. These lenticules were modelled with orthogonal collagen fibers. A Bayesian optimization procedure was used to identify the material parameters that best fit the experimental data.

Results: The corneal curvature measured from the Pentacam data and the model showed good agreement (figure 1). Parameter identification performed on three patients showed that the model could accurately reproduce the experimental data (figure 2).

Conclusions: Corneal geometry can be accurately replicated, and mechanical characterization of CLEAR lenticules leads to good parameter estimates across patient data. The current limitation of the characterization is that it is only performed ex vivo and on 3 patients. In addition, the lenticules represent only the most anterior part of the cornea. These results need to be complemented by in vivo biomechanical measurements with Brillouin scattering to account for patient-specific corneal biomechanics in surgical planning.

CONTROL ID: 3706935

SUBMITTER (NAME ONLY): Eric Moulton

TITLE: Clinical functional magnetic resonance imaging of photophobia in individuals with chronic ocular pain: provisional analysis

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Moulton, Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|A. Choudhury, D. Mehra, E. Felix, A. Galor, Research Service, Miami Veterans Administration Medical Center, Miami, Florida, UNITED STATES|A. Choudhury, D. Mehra, E. Felix, A. Galor, Physical Medicine and Rehabilitation, University of Miami School of Medicine, Miami, Florida, UNITED STATES|E. Moulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Eric Moulton: Commercial Relationship: Code N (No Commercial Relationship) | Anjalee Choudhury: Commercial Relationship: Code N (No Commercial Relationship) | Divy Mehra: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Felix: Commercial Relationship: Code N (No Commercial Relationship) | Anat Galor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Individuals with neuropathic ocular pain are similar to those with chronic neurological disorders in that they often report symptoms of sensory hypersensitivity, such as increased corneal sensitivity and evoked pain to light. The latter, often referred to as "photophobia", is a particular topic of interest in the realm of chronic pain. Specifically within ocular pain, patients with discordant symptoms are more likely to report photophobia, which suggests underlying contribution by centrally-sensitized mechanisms in response to light. In this study, we hypothesized that trigeminal sensory processing contributes to photophobia in patients with neuropathic ocular pain.

Methods: fMRI was used to evaluate brain pathways in individuals with neuropathic ocular pain. Subjects were screened to meet criteria for 1 of 2 groups: dry eye symptoms with chronic ocular pain and photophobia (n=8 cases) and no ocular pain or photophobia (n=8 controls). Subjects were presented with intermittent light stimuli during two scans: 1) a control scan after artificial tear instillation, and 2) after pharmacological blockade of afferents in the ocular surface with instillation of 0.5% proparacaine. Pain ratings elicited by light were acquired, and clinical ophthalmic signs and symptoms were recorded.

Results: Light-induced greater group-level activation in cases vs. controls in the somatosensory cortices (S1), spinal trigeminal nucleus, bilateral insula, anterior mid-cingulate cortex (aMCC). Patients with chronic ocular pain and photophobia reported higher pain intensity and unpleasant ratings to light than controls. Correlations between activity and ratings were greater in cases than controls.

Following proparacaine in cases, decreased light-related activation was observed in S1 and MCC. At the group level, cases demonstrated decreased pain intensity and unpleasantness ratings to light following proparacine, but half of cases did not show a decrease in these ratings.

Conclusions: The trigeminal nociceptive system may contribute to photophobia symptoms among individuals suffering from chronic ocular pain. We demonstrate partial modulation of cortical structures in this pathway by means of topically applied anesthetic to the eyes. Further understanding of the modulatory interactions underlying ocular pain and photophobia is critical for developing effective therapies and guiding treatment plans.

CONTROL ID: 3706936

SUBMITTER (NAME ONLY): Ignacio Lopez Minarro

TITLE: Corneal transplantation in year 2019: analysis of results

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Lopez Minarro, J. Herreras Cantalapiedra, L. Cocho Archiles, Ophthalmology, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|

Commercial Relationships Disclosure: Ignacio Lopez Minarro: Commercial Relationship: Code N (No Commercial Relationship) | Jose Maria Herreras Cantalapiedra: Commercial Relationship: Code N (No Commercial Relationship) | Lidia Cocho Archiles: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Results in corneal transplantation vary depending on the type of transplantation performed and the type of disease. Our purpose was to analyze the results in terms of transparency and Best Corrected Visual Acuity (BCVA) in corneal transplants performed in the ophthalmology unit in the Clinic Hospital of Valladolid (Spain) throughout 2019, comparing them with the literature (in particular the latest European reports on corneal transplantation).

Methods: A cross-sectional, observational, retrospective and single-center descriptive study was conducted based on the review of clinical histories of all corneal transplant patients during 2019, their characteristics before and after surgery, and the characteristics of the graft per year, as well as the results in BCVA per year. A descriptive and inferential statistical analysis was performed.

Results: A total of 100 surgeries were analyzed in 92 eyes from 91 patients. The majority of the surgeries were performed in female sex (60.4%), with an average recipient age of 65.6 ±17 years. The most frequent transplant was DMEK (50.5%), followed by Penetrating Keratoplasty (PK) (22.2%), DSAEK (15.2%) and DALK (10.1%). 3 out of 4 were first transplants, with greater frequency of DMEK. The most frequent type of regrafting was PK. The mean endothelial count of donor corneas was 2601.07 ± 355 cells/mm2. The most frequent indication was Fuchs Endothelial Dystrophy (40.7%), followed by regrafting and Bullous Keratopathy. The highest failure rate was obtained in the DSAEK group (32%), and the lowest one in DALK (11%). Overall, there was an average of 1.9±3.9 lines of VA improvement. Worse results in BCVA were obtained when a higher number of transplants performed in the same eye (Chi2, $p<0.05$). Among those who received cataract surgery, no significant differences in graft transparency were found after one year compared with those who did not.

Conclusions: Results obtained in the series of patients who underwent corneal transplantation are very similar to those in the latest European, American and Australian reports. Results vary depending on the type of diagnosis, the number of regrafting, and the technique used. Given its excellent results, DMEK appears to be the probable standard technique for endothelial dystrophies, although DALK and PK hold their own in specific indications with more complex pathology. Combination with cataract surgery has shown good results.

CONTROL ID: 3706938

SUBMITTER (NAME ONLY): David Kleinman

TITLE: PLL-g-PEG inhibits antibody-drug conjugate uptake into human corneal epithelial cells in vitro.

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kleinman, K. Sill, M. Mitchnick, Calm Water Therapeutics LLC, Rochester, New York, UNITED STATES|J.J. Hakkarainen, R&D Division, Experimentica Ltd., Kuopio, FINLAND|A.K. Ghosh, S.D. Ogle, S. Kaja, R&D Division, Experimentica Ltd., Forest Park, Illinois, UNITED STATES|B.A. Mendelsohn, Exelixis, Alameda, California, UNITED STATES|S. Kaja, Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: David Kleinman: Commercial Relationship(s);Code I (Personal Financial Interest):Calm Water Therapeutics LLC, ONL Therapeutics, Inc.;Code O (Owner):Calm Water Therapeutics;Code C (Consultant/Contractor):AGTC, Aprea Therapeutics, Cleave Therapeutics, Coherus BioSciences, Design Therapeutics, Editas Medicine, GSK, Helixmith USA, Kala Pharmaceuticals, Olema Pharmaceuticals, ONL Therapeutics, Revolution Medicines, Triphase Accelerator;Code S (non-remunerative):Calm Water Therapeutics, LLC | Jenni Hakkarainen: Commercial Relationship(s);Code E (Employment):Experimentica Ltd.;Code I (Personal Financial Interest):Experimentica Ltd.;Code S (non-remunerative):Experimentica Ltd. | Anita Ghosh: Commercial Relationship(s);Code I (Personal Financial Interest):eyeNOS Inc.;Code E (Employment):Experimentica Ltd.;Code C (Consultant/Contractor):Experimentica Ltd., K&P Scientific LLC;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code P (Patent):eyeNOS Inc.;Code S (non-remunerative):Experimentica Ltd., eyeNOS Inc. | Sean Ogle: Commercial Relationship(s);Code E (Employment):Experimentica Ltd.;Code C (Consultant/Contractor):eyeNOS Inc. | Kevin Sill: Commercial Relationship(s);Code C (Consultant/Contractor):Calm Water Therapeutics LLC;Code I (Personal Financial Interest):Calm Water Therapeutics LLC | Brian Mendelsohn: Commercial Relationship(s);Code E (Employment):Exelixis;Code I (Personal Financial Interest):Exelixis | Mark Mitchnick: Commercial Relationship(s);Code I (Personal Financial Interest):Calm Water Therapeutics LLC;Code S (non-remunerative):Calm Water Therapeutics LLC | Simon Kaja: Commercial Relationship(s);Code F (Financial Support):Experimentica Ltd., K&P Scientific LLC ;Code I (Personal Financial Interest):Experimentica Ltd., K&P Scientific LLC ;Code C (Consultant/Contractor):Experimentica Ltd.;Code P (Patent):eyeNOS Inc.;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code S (non-remunerative):Experimentica Ltd., K&P Scientific LLC

ABSTRACT BODY:

Purpose: Corneal toxicity secondary to antibody-drug conjugates (ADCs) is a common and clinically significant adverse event that interferes with ADC dosing and could ultimately affect a patient's response to ADC therapy. Effective interventions that either prevent or mitigate this drug-induced keratopathy are lacking. Evidence suggests that ADCs can enter corneal epithelial cells or their precursors indirectly through macropinocytosis, often with no involvement of the targeted receptor. Once internalized, the drug is cleaved from the ADC releasing a cytotoxic small molecule. This present study was based on the rationale that preventing the uptake of an ADC into off-target tissue should mitigate toxicity and the knowledge that charge plays an important role in the interaction of immunoconjugates with cell membranes. The hypothesis that locally delivered poly(L-lysine)-g-poly(ethylene glycol) (PLL-g-PEG) can inhibit ADC uptake into human corneal epithelial cells was tested.

Methods: Rituximab-monomethyl auristatin F (MMAF) was selected as an exemplary ADC that will demonstrate off target corneal epithelial cell toxicity. PLL (not PLL-g-PEG) - coated chamber slides were seeded with human corneal epithelial - transformed (HCE-T) cells (50,000 cells/cm^2). After 48 hours, cells were treated with test article (PLL-g-PEG, or positive control, 5-(N-ethyl-Nisopropyl) amiloride (EIPA)) or vehicle. After 30 minutes, Rituximab-MMAF (75 nM) was added to the wells. The wells were maintained for an additional 3.5 hours before HCE-T cells were fixed and ADC was detected by fluorescent anti-human IgG as viewed under microscopy. Fluorescence intensity was reported utilizing multiple images obtained from multiple replicates. A pilot evaluation was carried out, followed by two validation studies.

Results: The pilot evaluation demonstrated a statistically significant reduction in fluorescence intensity when vehicle was compared to EIPA (150 µmol/L) and PLL-g-PEG 1% solution. Two validation studies demonstrated a dose dependent decrease in fluorescence compared to vehicle for PLL-g-PEG concentrations of 0.05%, 0.1%, 0.5%, and 1% (see images).

Conclusions: PLL-g-PEG exhibited a dose-dependent inhibition of ADC uptake into HCE-T cells. These results suggest PLL-g-PEG may be an effective topical therapy to prevent, mitigate, or otherwise reduce ADC-induced corneal epithelial cell toxicity.

CONTROL ID: 3706940
SUBMITTER (NAME ONLY): Mashael Al-Namaeh
TITLE: DRY EYE SYNDROME PREVALENCE RATE DURING COVID-19
SESSION TITLE: Dry Eye, Clinical
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Al-Namaeh, Eye Research Center, Wilmington, Delaware, UNITED STATES|
Commercial Relationships Disclosure: Mashael Al-Namaeh: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Dry Eye Syndrome (DES) has been increased during the pandemic, as a result of wearing masks using electronic devices and working remotely. During COVID-19, we conducted a survey to determine the prevalence of dry eye syndrome.
Methods: This is a cross-sectional study to determine how frequent DES is during COVID-19 in healthy patients in the United States between the ages of 20 and 45. From October 31, 2021, to December 1, 2021, we administered an Ocular Surface Disease Index (OSDI) questionnaire remotely to 40 subjects. The OSDI survey was used to assess DES.
Results: Subjects had a mean age of 29 years old ± SD 14.14 and 23 of them were males (57.5%), and 17 were females (42.5%). Low DES, moderate DES, and severe DES had a prevalence rate of 15%, 77.5 %, and 7.5 %, respectively, according to the OSDI Survey. 50 % are White, 35 % are African Americans, 7.5 % are Asian, and 7.5% are Hispanic. The prevalence of mild DES during COVID is 77.5%, with 64.50 % of males and 35.50% of females.
Conclusions: The prevalence rate of DES during COVID is high which contribute to the fact of wearing the mask, the use of electronic devices and working remotely.

CONTROL ID: 3706942

SUBMITTER (NAME ONLY): Byron Lam

TITLE: Leber Hereditary Optic Neuropathy Gene Therapy: Adverse Events and Visual Acuity Results of all Patient Groups

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.L. Lam, W.J. Feuer, J.L. Davis, V. Porciatti, H. Yu, E. Vanner, J. Guy, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|R. Levy, Microbiology and Immunology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Byron Lam: Commercial Relationship(s);Code F (Financial Support):AGTC, Biogen. Editas, Janssen, Pixium, ProQR, Spark;Code C (Consultant/Contractor):Biogen, Editas, Janssen, ProQR, Stoke | William Feuer: Commercial Relationship: Code N (No Commercial Relationship) | Janet Davis: Commercial Relationship(s);Code F (Financial Support):AGTC, Biogen, GyroscopeTx;Code C (Consultant/Contractor):Kodiak Sciences, 4DMT | Vittorio Porciatti: Commercial Relationship: Code N (No Commercial Relationship) | Hong Yu: Commercial Relationship: Code N (No Commercial Relationship) | Robert Levy: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Vanner: Commercial Relationship: Code N (No Commercial Relationship) | John Guy: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Leber hereditary optic neuropathy (LHON) is a mitochondrial DNA disease causing severe visual loss. We performed a phase 1 LHON G11778A gene therapy clinical trial (NCT02161380) to assess the safety and tolerability of AAV2(Y444,500,730F)-P1ND4v2 that utilizes allotopic expression.

Methods: The phase 1 open-label clinical trial was designed as a 3+3 dose escalation of unilateral intravitreal gene therapy injection for each group of G11778A LHON patients with visual loss. Setting: single institution. Participants: 28 adult patients (5 females) with G11778A LHON and chronic bilateral visual loss >12 months (Group 1, n=11), acute bilateral visual loss <12 months (Group 2, n=9), or unilateral visual loss (Group 3, n=8). Intervention: unilateral intravitreal AAV2(Y444,500,730F)-P1ND4v2 injection with low (5.0×10^8 vg), medium (2.5×10^9 vg), high (2.4×10^9 vg), or higher (1.0×10^{10} vg) dose to worse eye (20/200 or worse) for Groups 1 and 2 and better eye (20/40 or better) for Group 3. Outcome Measures: Best-corrected visual acuity (BCVA), visual field, pattern electroretinogram. optical coherence tomography, adverse events, and vector antibody responses. BCVAs were compared to our published prospectively natural history cohort with designated surrogate study and fellow eyes. Longitudinal analysis was performed with generalized estimating equation analysis.

Results: Incident uveitis (8/28,29%), the only vector-related adverse event, resulted in no attributable vision sequelae and was related to vector dose, 5/7(71%) higher-dose eyes versus 3/21(14%) low-, medium-, or high-dose eyes ($p<0.001$). Incident uveitis was not associated with anterior chamber or serum AAV2 neutralizing antibody titers, or serum AAV2 PCR. Improvements of >15 letter BCVA occurred in both treated and fellow eyes of Groups 1 and 2 and surrogate study and fellow eyes of natural history subjects. All study eyes (BCVA ≥20/40) in Group 3 lost >15 letters within the first year despite treatment.

Conclusions: G11778A LHON gene therapy has a favorable safety profile. Our results suggest if there is an efficacy effect, it is likely small and not dose-related. Instances of substantial improvement of >15 ETDRS letters were not uncommon in our natural history patients suggesting demonstration of gene therapy efficacy in LHON likely requires randomization of patients to a group not receiving vector in either eye.

CONTROL ID: 3706943

SUBMITTER (NAME ONLY): Etienne Schonbach

TITLE: Secondary surgery after failed macular hole repair in a real-world setting – results from an international, multicenter, retrospective study

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Schonbach, D. Knight, W.R. Freeman, Ophthalmology, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|C. Wu, P. Iyer, W. Smiddy, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Arevalo, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|J. Chhablani, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|K. Delalibera Pacheco, CBV-Centro Brasileiro da Visão, Brasília, BRAZIL|N. Feucht, Augenklinik München Flughafen, GERMANY|I. Kozak, Moorfields Abu Dhabi, UNITED ARAB EMIRATES|N. Feucht, M. Maier, Technische Universitat Munchen, Munchen, Bayern, GERMANY|M. Roizenblatt, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|W. Sobol, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|L. Bittencourt de Souza, A. Maia, Retina Clinic, São Paulo, BRAZIL|

Commercial Relationships Disclosure: Etienne Schonbach: Commercial Relationship: Code N (No Commercial Relationship) | Darren Knight: Commercial Relationship: Code N (No Commercial Relationship) | Chris Wu: Commercial Relationship: Code N (No Commercial Relationship) | J Fernando Arevalo: Commercial Relationship: Code N (No Commercial Relationship) | Luiza Bittencourt de Souza: Commercial Relationship: Code N (No Commercial Relationship) | Jay Chhablani: Commercial Relationship: Code N (No Commercial Relationship) | Kátia Delalibera Pacheco: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon | Nikolaus Feucht: Commercial Relationship: Code N (No Commercial Relationship) | Prashanth Iyer: Commercial Relationship: Code N (No Commercial Relationship) | Igor Kozak: Commercial Relationship: Code N (No Commercial Relationship) | André Maia: Commercial Relationship: Code N (No Commercial Relationship) | Mathias Maier: Commercial Relationship: Code N (No Commercial Relationship) | Marina Roizenblatt: Commercial Relationship: Code N (No Commercial Relationship) | William Smiddy: Commercial Relationship: Code N (No Commercial Relationship) | Warren Sobol: Commercial Relationship: Code N (No Commercial Relationship) | William Freeman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although modern primary macular hole (MH) surgery has excellent closure rates, repair of persistent MHs remains challenging, and numerous surgical approaches have been reported. Given the heterogeneity of techniques, there is a need to investigate how surgeons treat failed MHs, and what the structural and functional outcomes are.

Methods: Anonymized patient records with persistent MHs after primary closure surgery were retrospectively reviewed. All eyes underwent repeat surgery and were grouped in one of three categories based on the surgical approach: 1) manipulation of the internal limiting membrane (ILM) through repeat peeling or ILM translocation, 2) tissue transplantation using amniotic membrane or autologous retina, and 3) other approaches including fibrin glue, induced macular detachment, or autologous blood.

Results: A total of 40 eyes from 40 patients undergoing secondary MH surgeries from 4 continents and 10 centers were included. The average patient age was 63 years, the average number of prior surgeries was 1.6, and 53 % were males. Manipulation of the ILM (N=15) led to MH closure in 53.3% and an improvement of best-correct visual acuity (BCVA) from 20/228 at baseline to 20/156 at month 6 after surgery; tissue transplantation (N= 14) led to MH closure in 85.7 % and an improvement of BCVA from 20/546 to 20/290. Various other approaches (N= 11) led to MH closure in 81.8 % (R^2 = 0.0938) and an improvement of BCVA from 20/235 to 20/84.

Conclusions: Secondary MH closure is possible using various surgical techniques with acceptable anatomical closure rates. We did not observe a meaningful difference in closure rates based on the surgical category but BCVA improved in all groups.

CONTROL ID: 3706948

SUBMITTER (NAME ONLY): William Brock

TITLE: The Minipig as a Model for Intravitreal Injection: Evaluation of a Time Course of Ocular Findings with a Repeated Injection

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Brock, Brock Scientific Consulting LLC, Hilton Head, South Carolina, UNITED STATES|A.J. Kocab, ONL Therapeutics, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: William Brock: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Kocab: Commercial Relationship(s);Code E (Employment):ONL Therapeutics

ABSTRACT BODY:

Purpose: The minipig (MP) has become an accepted animal model for the evaluation of ocular toxicity based on structural and function similarity to humans particularly as the availability of nonhuman primates becomes limited. This study evaluated the ocular effects of a small peptide molecule (MW <5kDa) following two intravitreal (IVT) injections.

Methods: Bilateral injections of 0 (vehicle), 200 or 300 µg/eye were given on Day 1 with a second, unilateral injection given on Day 60. Ocular effects were evaluated with IOP, OCT and fundus imaging, direct and indirect ophthalmoscopy and ERG. The MPs (3/timepoint) were sacrificed on Days 6, 14, 28 and 88 for ocular tissue distribution and histopathological examination.

Results: Vitreal haze without the presence of inflammatory cells was observed at 300 µg/eye. Stable, multiple “black streaks” were observed mostly along the superior retinal vessels in the treated eyes at both doses and controls. OCT scans, fundus images and ophthalmological evaluations did not reveal any morphological changes. The black streaks were likely possible focal pigment deposition, typical for MPs. No drug-related IOP or ERG changes were noted throughout the study. Microscopic findings were limited to the presence of drug-related accumulation in the vitreous at all timepoints at 200 and 300 µg/eye with no adverse pathology. Potential vehicle-related microscopic findings were limited to minimal mononuclear cell infiltration in the vitreous at all timepoints. The drug was detected in the choroid, retina and vitreous humor of the left eye at both doses on Days 6, 14, 28 and 88; retinal levels on Day 88 <LLOQ across all dose groups. Vitreal levels were ~10-fold higher on Day 28 or 88 compared to retinal and choroidal levels.

Conclusions: The results reveal the MP is an acceptable species for evaluation of the ocular effects of single and repeated IVT injection. The findings also demonstrate microscopic findings that were typical of a MP.

CONTROL ID: 3706950

SUBMITTER (NAME ONLY): Mansour Rahimi

TITLE: Alterations in retinal oxygen metrics, thickness, function, and ganglion cell counts after experimental ocular hypertension-induced ischemia/reperfusion injury

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Rahimi, S. Leahy, N. Matei, J. Burford, M. Shahidi, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|N.P. Blair, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Transient elevation of intraocular pressure (IOP) causes both mechanical and ischemic damage to the optic nerve and retina tissues. The purpose of the study was to test the hypothesis that retinal oxygen metrics are impaired and associated with visual dysfunction, retinal thinning, and retinal ganglion cell (RGC) loss after ischemia/reperfusion injury induced by ocular hypertension.

Methods: Right (study) eyes of 10 rats were subjected to anterior chamber cannulation to elevate the IOP for 90 minutes, followed by 7 days of reperfusion. Fellow eyes served as normal controls. Pattern-evoked electroretinography (PERG) and optical coherence tomography (OCT) were performed to measure RGC function and total retinal thickness (TRT), respectively. Retinal arterial and venous oxygen contents (O_{2A} and O_{2V}) were measured using phosphorescence lifetime imaging. Fluorescence and red-free imaging were performed to quantify total retinal blood flow (TRBF). Retinal oxygen delivery (DO_2), metabolism (MO_2), and extraction fraction (OEF) were calculated. RGCs were counted from immunofluorescence-stained retina whole-mounts. Individual retinal layers thicknesses were measured from retinal histology sections.

Results: During ischemia, IOP measurements were 15.7±0.5mmHg and 88.6±6.6mmHg in control and study eyes, respectively ($p<0.0001$). The PERG amplitudes were 5.2±1.5μV and 1.4±0.35μV in control and study eyes, respectively ($p<0.0001$). TRT was 251±7μm and 166±23μm in control and study eyes, respectively ($p\leq0.0001$). TRBF was 6.6±1.0μL/min and 4.0±0.8μL/min in control and study eyes, respectively ($p<0.0003$). DO2 was 912±183nLO2/min and 574±142nLO2/min in control and study eyes, respectively ($p=0.001$). MO2 was 368±81nLO2/min and 222±65nLO2/min in control and study eyes, respectively ($p=0.003$). OEF did not differ significantly between eyes ($p=0.70$). The number of RGCs was 61±23) and 35±12 in control and study eyes, respectively ($p=0.01$). Decreased DO2 and MO2 were correlated with decreased PERG amplitude ($r\geq0.6$, $p\leq0.005$) and decreased TRT ($r=0.7$, $p\leq0.002$). Decreased RGCs counts were correlated with decreased TRT ($r=0.6$, $p=0.04$).

Conclusions: Impairments in retinal oxygen delivery and metabolism and their correlations with visual dysfunction and cell loss were reported for the first time in an experimental ischemia/reperfusion model of glaucoma.

CONTROL ID: 3706951

SUBMITTER (NAME ONLY): Durga Ganesh

TITLE: Effect of Statins on the Age of Onset of Age-Related Macular Degeneration

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Ganesh, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|D. Ganesh, G. Corradetti, S.R. Sadda, Department of Ophthalmology, Doheny Eye Institute, Pasadena, California, UNITED STATES|J.N. Chiang, E. Halperin, Department of Computational Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study evaluated the relationship between statin use and the age of onset of age-related macular degeneration (AMD). Additional covariates such as sex, ethnicity, smoking history, fluoxetine use, obesity, diabetes mellitus (type 1 and type 2), and hypertension were included in the regression model.

Methods: Electronic Health Records (EHR) from 52,840 patients evaluated in the University of California Los Angeles (UCLA) Ophthalmology Clinics between 2014 and 2020 were screened. Subjects with a diagnosis of AMD were included in this study, and their records were reviewed for previously described AMD risk factors: sex, ethnicity, smoking, statins, fluoxetine, obesity, diabetes mellitus, and hypertension. Survival analysis was performed using a Cox proportional hazards regression model and visualized using Kaplan Meier survival curves.

Results: 5,498 of 52,840 patients included in the study (10.4%) were diagnosed with AMD. Statin use appeared to be associated with a later onset of AMD (HR=0.8822, p=0.0006), delaying the age of onset of AMD. However, female sex (HR=1.1382, p=00002), obesity (HR=1.4227, p<0.0001), and usage of fluoxetine (HR=1.3508, p=0.0032) were associated with an earlier onset of AMD. In addition to these factors, when adding ethnicity as a covariate to the model, non-hispanic black ethnicity (HR=0.5687, p<0.0001) and hispanic ethnicity (HR=0.8269, p=0.0028) appeared to be associated with a later onset of AMD. When stratifying for ethnicity, statin use, female sex, obesity, and fluoxetine use were four covariates that appeared to be significant only within the non-hispanic white subjects.

Conclusions: Statin use is associated with a delay in the onset of AMD, particularly in non-hispanic white subjects. Females, obesity, and fluoxetine are associated with an earlier onset of AMD, whereas non-hispanic black and hispanic ethnicities appear to be associated with a later onset of AMD.

CONTROL ID: 3706953

SUBMITTER (NAME ONLY): Nicolas Zarbin

TITLE: Automated Puff Tonometry in Comprehensive Community Based Screening for Vision Threatening Diseases during SARS-CoV-2

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Zarbin, A. Zhu, R. Verma, P. Tailor, M. Habiel, B. Szirth, Ophthalmology, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Over 50% of individuals with vision-threatening disease (VTD) (e.g., diabetic retinopathy, glaucoma, macular degeneration) are unaware of their condition, and once diagnosed, 80% will not follow up for clinical care, especially since the onset of SARS-CoV-2 in 2020. Remote teleophthalmology with real-time robotic teleconsultation was implemented to include automated puff-tonometry (APT) as pre-triage to identify patients who require more detailed clinical assessment and treatment.

Methods: 224 subjects (58% male) of average age 55 years were screened over 8 events. Following COVID-19 protocols screenings took place in New Jersey churches and health fairs featuring a high prevalence of African American and Hispanic subjects. Masked and self-reported vaccinated subjects underwent medical history, blood pressure, visual acuity (with pinhole), automated puff-tonometry (APT) for intraocular pressures (IOP), automated refraction, non-mydriatic retinal imaging, optical coherence tomography (OCT), and wearable visual field device (WVFD) testing. Face masks were fitted with surgical tape on the nose bridge to limit instrument fogging. To minimize equipment contact, all subjects were screened in the standing position, including APT and retinal imaging (Fig.1). Chi-square and t-tests were performed to assess factors associated with glaucoma referral. Subjects without IOP readings were excluded; significance was set at $p<0.05$.

Results: 10.29% of measured eyes had an IOP>18 and underwent additional testing including OCT-B of the optic nerve head, nerve fiber layer, and ganglion cell complex. 31.43% of eyes with IOP>18 underwent teleconsultation with a glaucoma specialist, vs. 8.85% of eyes with IOP≤18 (($p<0.001$), Table 1). The difference in mean age in subjects with glaucoma referral vs. without (57.42 vs. 51.61 years) was significant ($p=0.008$).

Conclusions: APT was useful in supporting on-site OCT-B imaging and WVFD referral (37.67%, 8.52% of total subjects) that yielded 17.94% referral to on-site teleconsultation through a real-time telerobot. Future investigation will include larger and more diverse community-based populations.

CONTROL ID: 3706962

SUBMITTER (NAME ONLY): Shuyi Chen

TITLE: Nyctalopia Due To Severe Liver Cirrhosis-induced Vitamin A Deficiency: A Case Report

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chen, A. Quan, Optometry, VA Medical Center Perry Point, Perry Point, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vitamin A is a micro-nutrient critical to retinal functioning. We report a rare case of night blindness secondary to poor vitamin A metabolism due to severe liver cirrhosis. The purpose of presenting this case is to highlight that even though vitamin A deficiency is very uncommon in developed nations, it should be considered as an etiology of nyctalopia in patients with liver diseases.

Methods: A 62-year-old Caucasian female presented with loss of vision in dim and dark lighting that had gotten progressively worse over the past 8 months. She was asymptomatic in daylight, but almost blind in the dark to the extent that she was unable to navigate and thus afraid to go outside at night. There was no personal or family history of night blindness or retinal disorders. Her ocular health was unremarkable with dilation. Her visual fields were full under bright illumination, but after dark adaptation, there were dense peripheral defects encroaching central fixation in both eyes. The patient had a medical history of stage 4 non-alcoholic liver cirrhosis, which led to a malabsorption of vitamin A, as confirmed by the very low vitamin A level in the serum analysis.

Results: Patient’s primary care physician and endocrinologist were notified of the findings, and vitamin A repletion therapy was implemented to prevent further vision loss. Repeated vitamin A level testings, in addition to visual fields after dark adaptation, were performed periodically to monitor for the resolution of the condition. Subjective improvement in symptoms, along with better performance on visual field, were noted after initiating oral vitamin A supplementation for 6 months.

Conclusions: This case report emphasizes the rare possibility of nyctalopia secondary to severe liver cirrhosis-induced vitamin A deficiency. Due to the presence of abundant storage of vitamin A in the liver, symptoms of vitamin A deficiency, such as nyctalopia, likely do not occur till late stage of liver disease. In the literature, cases of vitamin A deficiency have been reported in patients with a history of gastric and intestinal surgery; to our knowledge, this is the first case of nyctalopia reported in a patient with liver cirrhosis that improved after supplementation with exogenous vitamin A. Although vitamin A deficiency is an extremely rare disorder in the United States, it should be suspected in patients with severe liver disease experiencing a loss of night vision.

CONTROL ID: 3706971

SUBMITTER (NAME ONLY): Peter Kaiser

TITLE: Long term outcomes and pharmacokinetics of the injectable fluocinolone acetonide in the treatment of non-infectious uveitis.

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.M. Kaiser, S. Sharma, C.Y. Lowder, K. Baynes, S.K. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaluate the long-term effectiveness of the injectable fluocinolone acetonide (FA) implant in patients for the treatment of non-infectious uveitis.

Methods: This is a retrospective chart review study of patients enrolled from a single site in 2 multi-centered clinical trials of the FA implant (Psividia 1 and Psivida 6). The number of rescues (defined as intravitreal steroid injections or replacement injectable or surgical FA implants) and the number of flares post implant were collected. Eyes were then categorized into successes if no rescues were required for a minimum of two years.

Results: 14 eyes of 12 patients with noninfectious uveitis were included in analysis. The mean age was 54.6 years (range 39-72). There were 10 females (83%). 2 eyes received a sham injection and were thus removed from analysis. Of the 14 analyzed eyes 9 were successes. Amongst the eyes classified as successes, 5 of the 9 have not required rescues to date, with an average time of follow up of 77.1 months. The average time to first rescue amongst successes was 52 months. The average time to first rescue for all patients was 22 months and 8.5 months for the eyes classified as failures. The two sham eyes had an average time to first rescue of 2.25 months.

Conclusions: The injectable FA implant is an effective treatment for noninfectious uveitis. Approximately two thirds of eyes which received the injectable FA successfully reached two years without rescue and 5 out of 9 (55.5%) of the successes did not require rescues five or more years after initial implant injection with regular follow-up. The injectable FA implant can provide several year control for some patients with chronic non-infectious posterior uveitis.

CONTROL ID: 3706973

SUBMITTER (NAME ONLY): Jessica Song

TITLE: Hemodynamic Retinal Changes on Optical Coherence Tomography Angiography After Anti-Vascular Endothelial Growth Factor Injection in Eyes with Diabetic Macular Edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Song, B.B. Huang, J.X. Ong, N. Konopek, A.A. Fawzi, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate retinal hemodynamic responses to anti-vascular endothelial growth factor injection (anti-VEGF) in eyes with diabetic macular edema (DME) using optical coherence tomography angiography (OCTA).

Methods: 26 eyes of 22 subjects (age 60.2 ± 13.7years) who had prospective OCTA scan before and after anti-vascular endothelial growth factor injection (mean interval between OCTA= 31.1 ± 17.3days). Using previously validated thresholding methods based on the FAZ and on the skeletonized deep capillary plexus (DCP), we analyzed Adjusted Flow Index (AFI), Vessel Density (VD), and Skeletonized Vessel Density (SVD) in the parafoveal area (3mm annulus with 1mm inner circle) as shown in Figure 1. In addition to these parameters, we also assessed the Fovea Avascular Zone area (FAZ) and Central Foveal Thickness (CFT). Longitudinal changes were assessed using a generalized linear model correcting for CFT.

Results: We found significantly decreased AFI in the DCP layer ($p=0.026$). Furthermore, FAZ ($p<0.001$) and CFT ($p<0.001$) showed significant decrease from baseline compared to follow-up OCTA scans. Detailed results in Table 1.

Conclusions: AFI decreased significantly in the DCP layer on follow-up OCTA scan suggesting vascular flow disruption and decreased perfusion after anti-vascular endothelial growth factor injection. Consistent with reduced DME, FAZ and CFT decrease significantly with follow up imaging. These results may have important clinical implications for patients receiving long-term anti-VEGF therapy.

CONTROL ID: 3706981

SUBMITTER (NAME ONLY): Yohei Hashimoto

TITLE: Association between retinal vein occlusion and Life's Simple 7 cardiovascular health metrics: a large claims database study

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Hashimoto, M. Aihara, R. Obata, Ophthalmology, Tokyo Daigaku, Bunkyo-ku, Tokyo, JAPAN|H. Kaneko, Department of Cardiovascular Medicine, Tokyo Daigaku, Bunkyo-ku, Tokyo, JAPAN|A. Okada, Department of Prevention of Diabetes and Lifestyle-Related Diseases, Tokyo Daigaku, Bunkyo-ku, Tokyo, JAPAN|Y. Hashimoto, H. Matsui, H. Yasunaga, Department of Clinical Epidemiology & Health Economics, School of Public Health, Tokyo Daigaku, Bunkyo-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Cardiovascular diseases and retinal vein occlusion (RVO) share many risk factors in common. We aimed to clarify the association between RVO occurrence and cardiovascular health (CVH) metrics called the Life's Simple 7 advocated by the American Heart Association.

Methods: Design: Retrospective cohort study.

Subjects: Individuals undergoing health checkups from 2005 to 2020 in the JMDC Claims Database (JMDC Inc., Tokyo, Japan).

Methods: We set the two exposures: 1) each component of the CVH metrics: body mass index, blood pressure (BP), fasting blood glucose, total cholesterol, smoking, dietary habits, and physical activity; and 2) the number of non-ideal CVH metrics (non-ideal CVH score, ranging from 0 [healthiest] to 7 [unhealthiest]). The outcome was RVO occurrence, identified by the first date of the diagnosis. We performed Cox regression in which RVO occurrence was regressed on the above exposures, age, and sex.

Main Outcome Measures: Hazard ratios for RVO occurrence of 1) each component of the CVH metrics and 2) the non-ideal CVH score.

Results: A total of 2,093,536 individuals were eligible. During a mean follow-up of 1,070 ± 884 days, 3,265 RVO events occurred. Non-ideal BP was most strongly associated with increased risk of RVO occurrence (hazard ratio [HR], 2.25 [95% confidence interval, 2.06–2.46]), followed by non-ideal BMI (HR, 1.30 [1.20–1.40]). Higher non-ideal CVH scores were associated with increased risk of RVO occurrence: adjusted HRs of the groups with non-ideal CVH scores of 6–7, 5 ,4, 3, 2, and 1 were 3.68 (2.61–5.20), 2.83 (2.03–3.95), 2.54 (1.83–3.53), 2.21 (1.59–3.06), 1.78 (1.28–2.47), and 1.39 (0.98–1.95), respectively, compared to the healthiest group with the score 0. This trend was also observed in the subgroups with and without ideal BP.

Conclusions: The strongest risk factor for RVO was non-ideal BP, followed by non-ideal BMI. Non-ideal CVH score, an indicator of unhealthy lifestyle, was dose-dependently associated with RVO occurrence, which also applied to the individuals with ideal-BP. Public health and individual efforts to manage these modifiable risk factors are essential for preventing RVO.

CONTROL ID: 3706982

SUBMITTER (NAME ONLY): John Williamson III

TITLE: Optical Coherence Tomography Findings in Eyes with Spontaneous Reattachment of Macula-off Traction Retinal Detachments

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Williamson III, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|R. Mahmoudzadeh, M. Salabati, R.R. Soares, O.P. Gupta, C. Regillo, A.C. Ho, J. Hsu, Mid Atlantic Retina, The Retina Service of Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the clinical course and optical coherence tomography (OCT) findings in eyes with spontaneous reattachment of macula-off traction retinal detachments (TRD).

Methods: Retrospective case series of eyes with macula-off TRD that had spontaneous reattachment.

Results: Four eyes of 4 patients with macula-off TRD secondary to proliferative diabetic retinopathy (PDR) (n=3) and proliferative sickle cell retinopathy (n=1) were included. Median (IQR) age was 47.5 (22.8) years. Two of 3 PDR eyes each had 1 anti-VEGF injection at the visit prior to the macula-off TRD, with a median time from injection to TRD of 204 days [range 42-365 days]. Two of 3 PDR eyes had prior panretinal photocoagulation before TRD. OCT confirmed spontaneous resolution of the macular retinal detachment (Figure 1) in all eyes. Median (IQR) logMAR VA at the time of macula-off TRD was 0.544 (0.452) [Snellen 20/70] which improved to a median (IQR) logMAR VA of 0.350 (0.156) [Snellen 20/45, p=0.068] at the first visit with reattachment characterized by OCT. Median (IQR) time from TRD diagnosis to OCT measured reattachment was 6 months, (10.25; range 1-12 months). No complete posterior vitreous separation was seen in any of the eyes. One eye had a recurrent TRD 4 months after initial spontaneous reattachment. The macula remained attached until the last visit in the other eyes at a median of 365 days [range 266-469 days] after the TRD diagnosis. The final median logMAR VA of these three eyes was 0.544 (range 0.301-0.544) [Snellen 20/70, p=0.18].

Conclusions: Non-surgical spontaneous retinal reattachment and significant visual acuity improvement may rarely occur in eyes with TRD. In our cases, no OCT evidence of posterior vitreous separation was found, suggesting that some relaxation of the contractile fibrovascular membranes may have occurred to account for macula reattachment.

CONTROL ID: 3706986

SUBMITTER (NAME ONLY): Calesta Hui Yi Teo

TITLE: Investigating the Potential Effects of Peroxisome Proliferator-Activated Receptor (PPAR)-α Agonists on Corneal Nerve Regeneration in Patients with Type II Diabetes Mellitus

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Teo, National University Singapore Yong Loo Lin School of Medicine, SINGAPORE|H. Tan, Department of Endocrinology, Singapore General Hospital, SINGAPORE|M. Lin, I. Lee, J. Mehta, Y. Liu, Singapore Eye Research Institute, SINGAPORE|J. Mehta, Y. Liu, Singapore National Eye Centre, SINGAPORE|

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ABSTRACT BODY:

Purpose: Diabetic neuropathy is one of the most common microvascular complications in diabetes mellitus (DM). Here, we investigate the effects of peroxisome proliferator-activated receptor (PPAR)-α agonists, fenofibrates, on the prevention of corneal nerve degeneration and the stimulation of corneal nerve regeneration in patients with type II DM.

Methods: A single-arm, open-label, single-center interventional study was conducted in Singapore National Eye Centre. Twenty-six patients (80.8% Chinese; 80.8% males; aged 60.8 ± 9.31 years) were prescribed 100mg/day and 300mg/day oral fenofibrate for 30 days. The patients (52 eyes) underwent comprehensive ocular surface assessment, corneal nerve metrics and wing cells epithelium analysis using in-vivo confocal microscopy scans, before and after treatment. Tear neuromediator analysis included substance P, calcitonin gene-related peptide (CGRP), neuropeptide Y (NPY), and β-nerve growth factor (β-NGF).

Results: Corneal nerve fiber density (CNFD) significantly increased from 9.46 ± 6.20 to 12.6 ± 4.36 number of fibers/mm^2 (P=0.01; figure 1), while corneal nerve fiber width significantly decreased from 0.0225 ± 0.00118 to 0.0218 ± 0.00128 mm/mm^2 (P<0.01). Corneal nerve fractal dimension, which measures spatial loss of nerves, also shows a trend of improvement (pre-treatment: 1.39 ± 0.0641; post-treatment: 1.49 ± 0.0371). After treatment, epithelial cells' circularity significantly improved from 0.726 ± 0.0162 to 0.717 ± 0.0213 (P<0.05; figure 1). Tear breakup time significantly improved, and ocular surface staining evaluated by Oxford scores significantly increased after treatment (both p<0.01). Additionally, tear substance P concentrations significantly increased after treatment (pre-treatment: 1239 ± 712 pg/mL; post-treatment: 1668 ± 948 pg/mL; P=0.02), and the changes of tear substance P concentrations were significantly correlated with the increment of CNFD (r = 0.41; P=0.036).

Conclusions: PPAR-α has protective effect on the ocular surface and corneal nerve degeneration, while stimulating corneal nerve regeneration in diabetic corneal neuropathy. These findings may offer novel treatments for diabetic corneas.

CONTROL ID: 3706988

SUBMITTER (NAME ONLY): Yodpong Chantarasorn

TITLE: Treatment Outcome of Wet Age-Related Macular Degeneration Management in Thailand (TOWER) Study Report No. 2: The Fluid Analysis

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chantarasorn, Ophthalmology, Navamindradhiraj University, Dusit, Bangkok, THAILAND|P. Hanutsaha, Ophthalmology, Mahidol University Faculty of Medicine Ramathibodi Hospital, PhayaThai, Bangkok, THAILAND|S. Thoongsuwan, Ophthalmology, Mahidol University Faculty of Medicine Siriraj Hospital, Bangkok, THAILAND|S. Vongkulsiri, Ophthalmology, Phramongkutklao College of Medicine, Bangkok, THAILAND|P. Kungwanpongpun, Novartis Thailand Co Ltd, Bangkok, Bangkok, THAILAND|P. Ruamviboonsuk, Ophthalmology, Rajavithi Hospital, Bangkok, Bangkok, THAILAND|

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ABSTRACT BODY:

Purpose: To identify predictive factors associated with highly fluctuating macular thickness in neovascular age-related macular degeneration (nAMD), and to explore the effects of fluid fluctuation on visual outcomes.

Methods: This was a real-world retrospective cohort study conducted at five tertiary centers in Thailand (2016-2018). We included one eye per each treatment-naïve nAMD patient who received anti-VEGF injections based on a treat-and-extend regimen for a duration ranged from 1 to 3 years. Other maculopathies including macular atrophy and subretinal fibrosis were excluded from the study. The standard deviation (SD) of 1-mm central subfield thickness (CST) from month 3 to 24 in each patient was organized into ascending order from lowest to highest, and thereafter split equally into three groups: low, moderate, and high CST fluctuation group.

Results: Of 558 eyes, baseline CST was 363±137μm, 384±183μm, and 490±210μm in the low, moderate, and high CST fluctuation group (186 eyes in each group), respectively. Correspondingly, the SD of CST from month 3-24 was 11.8± 6.3, 40.6±10.6, and 114.7±59.3. After controlling for age, baseline CST and a total number of injections, the Generalized Estimating Equations showed that eyes with low fluid fluctuation significantly gained more ETDRS letters than those in the moderate and high fluctuation group (mean differences=6.7 and 10.7 letters, respectively) at 12 months follow-up. These differences between the groups increased further at 24 months (10.1 and 14.0 letters, Figure 1). Baseline CST of ≥405 μm was significantly associated with highly fluctuating CST during the maintenance phase (adjusted odds ratio (AOR)=3.27, sensitivity and specificity of detection=62% and 68%). Such correlations were not observed in baseline BCVA, the presence of polypoidal lesion, and Bevacizumab uses. Among different subtypes of retinal fluid, the presence of intraretinal fluid (IRF) coincided with subretinal fluid (SRF) at the baseline visit was the strongest predictor for high CST fluctuation over the treatment course (AOR=2.48) (Table 1).

Conclusions: The presence of baseline SRF and IRF predicted highly fluctuating retinal fluid over the 2-year course of nAMD treatment. Apart from the retinal fluid per se, unstable macular thickness during anti-VEGF therapy may be an additional factor contributing to poor visual outcomes.

CONTROL ID: 3706989

SUBMITTER (NAME ONLY): William Freeman

TITLE: Efficacy of iRGD-Targeted Fusogenic Nanoparticle Delivering VEGF-siRNA to a Rabbit Model of Retinal Angiogenesis

SESSION TITLE: AMD Translational Research

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.R. Freeman, K. Huffman, M. Cavichini Cordeiro, A. Warter, F.P. Kalaw, L. Cheng, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|J.F. Grondek, E. Lee, M.J. Sailor, Chemistry and Biochemistry, University of California San Diego, La Jolla, California, UNITED STATES|R. Fan, M.J. Sailor, Materials Science and Engineering, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Administration of anti-VEGF therapies is the standard of care for the treatment of diseases with the chronic pathology of retinal angiogenesis, such as proliferative diabetic retinopathy, and requires a protracted level of therapeutic intervention to maintain remission. Effective delivery of siRNA would shut down VEGF expression with the potential to extend the therapeutic window of an injection significantly. The purpose of this study was to evaluate an intravitreally injected nanoparticle platform that delivers small interfering RNA (siRNA) targeting vascular endothelial growth factor (VEGF) for its ability to inhibit neovascular leakage.

Methods: We synthesized fusogenic porous silicon nanoparticles (F-pSiNP) containing rabbit VEGF-siRNA and conjugated the surface with iRGD peptide for targeting neovascular and Müller cell surface receptors. The F-pSiNPs were evaluated by intravitreal injection for toxicity and pharmacodynamics in healthy rabbit eyes, and for efficacy in the DL-α-aminoadipic acid (DL-AAA) rabbit model of chronic retinal neovascularization (RNV). Efficacy was measured by a reduction of leakage area and intensity by repeated FA as compared to sham injection controls using ImageJ and by ELISA of VEGF in the vitreous.

Results: The analysis of repeated FA leakage over time (MANOVA) revealed that F-pSiNP treatment significantly inhibited FA leakage from DL-AAA induced RNV compared with the sham control ($p = 0.00137$), which persisted for 12 weeks (Fig. 1A). A corresponding reduction in vitreous VEGF was also observed (Fig. 1B). No toxicity was detected in the healthy F-pSiNP-injected eyes and normal retinal function was observed with ERG. Histological sections revealed penetration of the F-pSiNPs throughout the inner and outer retina and up to the RPE at 72 hr (Fig. 2).

Conclusions: F-pSiNP constructs were observed within Müller cells and throughout the retina, provided a persistent knockdown of VEGF gene expression, and reduced leakage in a rabbit model of RNV. Injection of targeted nanoparticles yielding slow intracellular release of therapeutic anti-VEGF siRNA may be an effective intraocular therapeutic to provide sustained, nontoxic anti-VEGF effects for retinovascular disease.

CONTROL ID: 3706990

SUBMITTER (NAME ONLY): Mak Djulbegovic

TITLE: Conjunctival Papilloma: Surgical vs. Medical Treatment Outcomes

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.B. Djulbegovic, W. Sripawadkul, A. Galor, D. Theotoka, M. Zein, C.L. Karp, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|W. Sripawadkul, Ophthalmology, Srinakharinwirot University, Bangkok, THAILAND|A. Galor, Ophthalmology, VA Miami Healthcare System, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conjunctival papilloma is often resistant to treatment. Various therapies have been reported with no gold standard. This purpose of this study was to compare treatment outcomes after various therapies.

Methods: A retrospective chart review of 30 conjunctival papilloma patients from 2009 - 2020. Data on demographics, tumor characteristics, primary treatment and outcomes were collected. The primary outcome was the frequency of complete tumor resolution and recurrence rate of each primary therapy. The secondary outcome was treatment related side effects.

Results: The mean age was 57.5 years (3-93 years) with male predominance (n=22, 73.3%). Eleven eyes were treated with interferon α-2b (IFN), seven with 5-fluorouracil (5FU), and 10 with excision biopsy and cryotherapy (6 with adjuvant therapy with IFN). The frequency of tumor resolution was 36.4% (4/11), 28.5% (2/7), and 100% (10/10) in each group, respectively. The mean time to resolution was faster in the surgical group compared to the medical group (1 day vs 159 days, $p<0.001$) There was a trend for a higher tumor recurrence with 11% in the surgical vs 0% in the medical group at 6 months and at 12 months, 22% recurrence in the surgical and 0% in the medical group.

Conclusions: Papilloma resolution is faster with surgical excision as compared to medical therapy. However, recurrences are more frequent after surgical vs medical treatment.

CONTROL ID: 3706994

SUBMITTER (NAME ONLY): David Sutter

TITLE: Pilot Study of Retinal Vessel Outgrowth Following Conventional Versus Low-Dose Bevacizumab for Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Sutter, Midwestern University Chicago College of Osteopathic Medicine, Downers Grove, Illinois, UNITED STATES|N. Clarke, K. Anulao, T. Lee, A. Nagiel, Ophthalmology, Children's Hospital Los Angeles Department of Pediatrics, Los Angeles, California, UNITED STATES|T.T. Lima, Ophthalmology, Centro Brasileiro de Cirurgia de Olhos, Goiania, Goiás, BRAZIL|

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ABSTRACT BODY:

Purpose: Recent studies have demonstrated that very low doses of bevacizumab can be used to treat Type I prethreshold retinopathy of prematurity (ROP). We hypothesized that lower doses of intravitreal bevacizumab may promote the normal outgrowth of retinal vessels following injection. The goal of this pilot study is to compare the rate of vessel outgrowth after conventional dose (0.625 mg) and low-dose (0.125 mg) treatment.

Methods: This was an IRB-approved retrospective chart review of patients treated with intravitreal bevacizumab before and after the institution switched to low-dose bevacizumab in September 2019. All eyes had Retcam color and fluorescein angiography (FA) taken at the time of intravitreal bevacizumab injection and at subsequent laser photocoagulation. Gestational age at birth, birthweight, corrected age at injection, and weeks between injection and laser were tabulated. Six eyes of six infants who met these criteria were identified: 3 eyes treated at low dose and 3 eyes treated with conventional dose. Photos were analyzed using MATLAB R2021a. The average distance from optic disc to ridge were calculated using 15 vectors from the nerve to the temporal ridge encompassing one clock hour.

Results: Baseline parameters including birthweight, gestational age at birth, and zone/stage of ROP were comparable between the two groups. Optic nerve to ridge distance at time of injection and laser were used to calculate vessel outgrowth (pixels) and rate of vessel outgrowth (pixels/week) in 6 eyes of 6 patients. Mean vessel outgrowth was 153 pixels for conventional and 260 pixels for low-dose eyes (one-tailed t-test; $p < 0.015$). When corrected for number of weeks since injection, the rate of vessel outgrowth was 32 pixels/week and 30 pixels/week for conventional and low-dose eyes, respectively ($p > 0.64$). The mean interval between injection and laser was 5 weeks for conventional and 9 weeks for low dose eyes ($p > 0.07$).

Conclusions: Low-dose treated eyes had significantly greater vessel outgrowth, but this could be explained by a longer interval between injection and laser treatment in the low-dose group. This pilot study warrants further quantitative analysis of the potential benefits of low-dose bevacizumab treatment in a larger cohort of patients.

CONTROL ID: 3706995

SUBMITTER (NAME ONLY): Xiang Ma

TITLE: The regulation of cGAS-STING signaling by PPARα-mediated autophagy in ischemic retinopathy

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Ma, J. Cai, J. Ma, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|Y. Takahashi, J. Ma, Biochemistry, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ischemia-induced retinopathy is one of the leading causes of irreversible blindness. Overactivated retinal myeloid cells are a crucial driving force of pathological angiogenesis and inflammation in ischemic retinopathy. The cyclic GMP-AMP (cGAMP) synthase (cGAS) and stimulator of interferon genes (STING) pathway is a key regulator of myeloid cell activation. This study investigated both the functions and regulatory mechanisms of cGAS-STING signaling in oxygen-induced retinopathy (OIR).

Methods: WT C57BL/6J mice and Sting$^{-/-}$ mice were used for OIR. Retinal neovascular and avascular areas were quantified in isolectin-stained retinal flat mounts. Retinal leukocyte adhesion was measured by perfusion labeling with concanavalin A lectin. Retinal myeloid cells were isolated from retinas using CD11b^{+} MACS microbeads. The cGAS, STING, peroxisome proliferator-activated receptor α (PPARα), and autophagy markers were measured using Western blot analysis. Surface and activation markers of retinal myeloid cells were measured by flow cytometry.

Results: The protein levels of cGAS-STING signaling were markedly upregulated in retinal CD11b^{+} cells of OIR mice. Sting knockout (KO) alleviated pathologies of OIR, including retinal neovascular areas, avascular areas, and leukostasis. Sting KO reduced the percentages of active M1 (IL1β^{+}) and M2 (CD163) myeloid cells in OIR retinas. In addition, we found that PPARα was downregulated in retinal CD11b^{+} cells of the OIR model. Pparα$^{-/-}$ mice showed higher cGAS-STING levels in retinal CD11b^{+} cells compared to those in WT mice. PPARα agonists suppressed cGAS-STING signaling in the OIR retinas and mitigated the pathologies of OIR. In primary retinal microglial cells, the cGAS-STING levels were decreased in cells with starvation-induced autophagy and increased when autophagy was blocked by chloroquine. Pparα$^{-/-}$ retinal microglial cells showed defective autophagy and increased protein levels of cGAS-STING. Induction of autophagy decreased cGAS-STING levels in Pparα$^{-/-}$ retinal microglial cells.

Conclusions: Overactivation of cGAS-STING signaling in retinal myeloid cells plays a pathogenic role in ischemic retinopathy. PPARα inhibits the overactivated cGAS-STING signaling via the modulation of autophagy.

CONTROL ID: 3707003

SUBMITTER (NAME ONLY): Mustafa Jaffry

TITLE: Monitoring Progression of Optic Nerve Head Drusen with Fundus Auto-Fluorescence

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jaffry, A. Zhu, R. Verma, P. Tailor, A. Khouri, B. Szirth, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|A. Leto, MedStar Health, Columbia, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limited literature exists on Optic Nerve Head Drusen (ONHD) progression. Thought to be benign, ONHD are globules of mucoproteins and mucopolysaccharides that progressively calcify in the optic disc. Found in 2-3% of the population, ONHD can be categorized as superficial, buried, or surface pearl (the most severe). Pearl type progress superficially and may exert mechanical stress on the surrounding vasculature, resulting in peripheral vision loss over time (1.6% per year on VF) due to thinning of the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC), similar to glaucoma.

Methods: Non-mydriatic 45-degree color and fundus autofluorescence (FAF) were captured and grayscale reflectance histograms were determined using Photoshop^{TM} V7. Lipofuscin concentrations in overall ONH as well as targeted single ONHD were measured. Visual Field (VF) was assessed via 30-2 central threshold tests. GCC and RNFL thickness were assessed using Ocular Coherence Tomography (OCT-B). Subject 1 is a 24 y/o female with early signs of pearl ONHD who was followed from 2020 to 2021. Subject 2 is a 53 y/o female with 40 years advanced pearl ONHD with documented FAF and progressive VF loss.

Results: After 14 months, subject 1 Rt FAF intensity index value showed an 11% increase in FAF reflectance (37 to 41) (Fig 1A), while Lt value increased by 89% (37 to 70) (Fig 1B) mirroring the progression seen on OCT-B as the drusen rises to the surface (Fig 1C). Subject 1 had minor increased peripheral VF defects Rt but overall stable VF indices in both eyes. Subject 2 had significant peripheral VF loss Rt/Lt over 40 years with an overall ONHD FAF intensity index value of 96 and a single ONHD intensity index value was 170 FAF reflectance on the surface of the ONH. (Fig 2)

Conclusions: Our findings suggest that over time, pearl ONHD rise superficially to the most anterior portion of the optic disc (Fig 1C). This is shown by an increase in FAF fluorescence of subject 1 Lt, measured by a novel approach of grayscale reflectance quantification. Noninvasive FAF may be a more sensitive marker of early ONHD progression than OCT or VF (Fig 1D) and can be used to screen patients for ONHD. As there is no cure, early detection and protective management of intraocular pressures may be warranted. Further studies will include OCT-B with 1080 nm enhanced depth imaging and 3D volumetric imaging.

CONTROL ID: 3707004

SUBMITTER (NAME ONLY): Saira Khanna

TITLE: Utility of OCT-Angiography in Diagnosis and Management of Atypical Presentations of Macular Telangiectasia Type 2

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Khanna, S. Amin, L.T. Shaw, D. Dao, N. Massamba, D. Skondra, Ophthalmology and Visual Sciences, University of Chicago, Chicago, Illinois, UNITED STATES|J. Moir, The University of Chicago, Chicago, Illinois, UNITED STATES|R. Komati, Georgia Retina, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Idiopathic macular telangiectasia type 2 (MacTel) is a retinal disease characterized by bilateral, asymmetric telangiectatic changes. These findings are often missed or misdiagnosed on optical coherence tomography (OCT) alone especially in the early stages, and fluorescein angiography is an invasive imaging technique. The purpose of this case series is to highlight the use of optical coherence tomography angiography (OCTA) as a non-invasive imaging modality to distinguish early or atypical MacTel from other macular conditions with similar presentations and its utility for longitudinal follow-up.

Methods: Retrospective chart review performed at the University of Chicago from 07/2017-07/2021. Participants included in this study were those diagnosed with MacTel based on clinical examination and imaging criteria on OCTA (Optovue RTVue XR Avanti (Optovue Inc, Fremont, California, USA 2018.1.8.60)).

Results: 15 eyes from eight patients were included in this study. The average follow-up time was 13.6 ± 10.2 months. Six patients were referred with previous diagnoses of macular hole, vitreomacular traction, cystoid macular edema, or diabetic macular edema. OCTA revealed telangiectatic vessels in the parafovea of the deep capillary plexus (DCP), cavitary changes, and ellipsoid zone (EZ) disruption in all 15 eyes. Internal limiting membrane draping was observed in 60% of eyes (n=9), while right-angled vessel branching was observed in 33% of eyes (n=5). OCTA highlighted subretinal neovascularization in 46.67% eyes (n=7). 2 of these eyes (28.6%) were treated with an anti-VEGF injection with improvement in VA, while the other 5 eyes (71.4%) were observed over the entirety of the follow-up period. Finally, one patient with a concurrent macular hole was treated with drop regimen with improvement in VA. At follow-up, VA of eyes was stable or improved with appropriate treatment.

Conclusions: OCTA is an imaging modality that is uniquely suited to detect and facilitate the diagnosis and longitudinal follow up of MacTel. Its repeated B-scans capture neurodegenerative changes in MacTel, while its en face angiograms display characteristic vascular patterns or CNV earlier in disease course than OCT, without needing to use invasive FA. Early diagnosis of MacTel with OCTA can be beneficial in guiding appropriate treatment and treating coexisting diseases to prevent future, irreversible vision loss.

CONTROL ID: 3707005

SUBMITTER (NAME ONLY): Betty Li

TITLE: Stereoscopic 3D videogame play boosts stereoacuity, but not contrast sensitivity

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.Z. Li, C.V. Ngo, M.M. Antonucci, D.M. Levi, Herbert Wertheim School of Optometry and Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|R. Li, College of Optometry, Nova Southeastern University, Fort Lauderdale, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our recent findings suggest that stereoscopic 3-dimensional (3D) videogame play boosts stereoacuity. Here we asked if the immersive 3D video game experience could modify contrast sensitivity.

Methods: Twenty-four healthy young adults with limited previous video game experience were recruited in two groups. In the treatment group (3DVG, n=12), participants were required to play stereoscopic 3D video games for a total of 40 hours (2 hours per session) in 4-5 weeks. First-person shooter action video games were used. In the control group (2DVG, n=12), participants played the same video games but in 2D mode for the same time course. Stereoacuity and contrast sensitivity were measured before and after the video game intervention. (1) Stereoacuity was measured using random dot stereograms. Each random-dot stimulus consisted of a 1-degree central square of random dots embedded in a 3.3-degree square of random dots. The visual task was to determine the stereoscopic depth of the central square (in front of or behind) relative to the outer reference square. (2) Contrast sensitivity was measured binocularly for a range of spatial frequencies (1, 2, 5, 10 & 20 cpd) using a Metropsis system (Cambridge Research Systems, UK). In each trial, a large sinusoidal Gabor patch (Gaussian envelope, SD=1 degree) was displayed randomly at one of four locations on the monitor screen. The visual task was to indicate the target grating location.

Results: After playing 3D video games, the participants in the treatment group showed a significant improvement of 33.5% in stereoacuity (paired t=3.63, p=0.004), but not in contrast sensitivity (two-way repeated measures ANOVA, F=0.18, p=0.95). Note that in the 2DVG control group, we did not observe any significant change in stereoacuity after the intervention (paired t=0.10, p=0.92).

Conclusions: Stereoscopic 3D video game play boosts stereoacuity, but not contrast sensitivity. These findings indicate that the neural alterations for enhanced depth perception might have occurred beyond the early stage of visual processing for contrast perception. Notably, our most recent experiments (Li et al 2018) have shown that these types of video games might have a special benefit for triggering the plasticity of stereo vision in patients with amblyopia.

CONTROL ID: 3707007

SUBMITTER (NAME ONLY): Richard Sather III

TITLE: Prevalence, genetic phenotypic characteristics, and inheritance patterns of patients with retinitis pigmentosa at the referral center clinic of the University of Minnesota (UMN)

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.N. Sather III, T. Khundkar, J. Ihinger, E.J. Van Kuijk, S.R. montezuma, Department of Ophthalmology and Visual Neuroscience, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic factors have a major influence on variable expressivity in gene-phenotype relationships. This study aims to identify potential pathogenic gene variants in patients diagnosed with syndromic and non-syndromic retinitis pigmentosa (RP). A genotype-phenotype correlation is important as there are current and future therapies catered to the genetic inheritance and physical expression for this disease.

Methods: This retrospective series identifies patients with RP who had genetic testing using next generation sequencing panel at the UMN. A database was created to record history and examination, genetic report, and diagnostic imaging. Causative pathogenic genes were recorded. Patient disease status was further characterized by ocular coherence tomography (OCT) and fundus autofluorescence (AF).

Results: 200 patients were included consisting of 154 non-syndromic and 46 syndromic RP. Results were only recorded if stated in the patient's chart. 42.8% of patients first noted eye symptoms before the age of 10. 56.6% had a family history of retinal dystrophy. Presenting symptoms included 85.4% with nyctalopia, 60.2% with photosensitivity/hemeralopia, and 54.7% with decreased color vision measured by the Ishihara's test. On average, 38.5% had visual acuity worse than 20/80. 92.4% had evidence of visual field loss. Ellipsoid zone width on the fovea OCT scan of less than 1500 μm was noted in 73.8%. Approximately 99.0% presented with Fundus AF findings of either macula hypo/hyper AF ring and/or peripheral hypo-AF. The genetic report analysis showed the largest contributed RP genetic finding was VUS at 68.7%. The top identifiable pathogenic variants included USH2A (14.3%), RPGR (7.5%), MYO7A (6.8%), EYS (4.1%), and RP1 (3.4%). 11 patients had X-linked RP, all with RPGR mutation. 13 patients had autosomal dominant RP, including 5 with RP1 mutation and a family of 4 patients with PRPH2 mutation.

Conclusions: The results demonstrated that patients within the UMN are often evaluated for their RP in advanced disease independent of the genetic result. VUS comprised most of the genetic findings. This suggests the need to find either a more encompassing genetic analysis to account for the numerous RP genes and the diversity of our patients or promote testing for other affected RP family members to determine if the VUS is pathogenic.

CONTROL ID: 3707010

SUBMITTER (NAME ONLY): Bliss Cui

TITLE: The Affects of Distortion

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Cui, P.J. Bex, Psychology, Northeastern University College of Science, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Affect and face identification are critical activities of daily living that may be impaired by blur or distortions caused by vision loss and in disorders such as autism, prosopagnosia, and prosopometamorphopsia. Distortions alter the spatial relationships among facial features, disrupting configural information. To examine configural information in face processing, we measure how the spatial scale and amplitude of distortions influence the identification of affect and identity.

Methods: Bandpass filtered noise (Fpeak@1-32 cycles/face) was used to generate pixel shifts to distort faces from the IASLab database. The amplitude of distortion was varied using an adaptive staircase. 8 normally-sighted subjects were given unlimited time to identify which of 4 distorted faces (within 6.5°x9.8°ellipses in a 2x2 grid) matched a word representing 1 of 8 universal emotions: sad, excited, happy, fear, calm, anger, or disgust (affect task) or matched the identity of an undistorted face (ID task). Image cues were removed from each face by equalizing the luminance distribution and chrominance to the average face.

Results: Repeated measures ANOVA showed that observers could tolerate significantly more distortion for face rather than affect identification ($F_{1,35}$=13.3;p=.0083). There was a significant effect of distortion spatial scale ($F_{5,35}$ =6.6;p=.0002) and face inversion ($F_{1,35}$=14.0;p=.0073) on affect identification, with no interaction between these factors ($F_{5,35}$=1.4;p=.2504). There was a significant interaction between distortion scale and inversion for face identification ($F_{5,35}$=4.5;p=.003) such that distortions at coarse and fine scales mediated a face inversion effect, but not when distortions were applied at the middle critical scales (4-16 cycles/face).

Conclusions: These results suggest that the face inversion effect for distortion is present in both affect and face identification, while differences in their spatial tuning imply differences in how our brains process the identity of the face compared to its emotion. This may inform future studies with vision-loss patients and neurodivergent individuals to better understand the impact of their disorder on facial identification and emotion recognition and differentiate potential sites of face processing impairment.

CONTROL ID: 3707012

SUBMITTER (NAME ONLY): Yi Stephanie Zhang

TITLE: Sex-based analysis of vascular alterations on optical coherence tomography angiography in patients with diabetes.

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhang, A. Taha, J. Dickson, I. Thompson, J.D. Keenan, R. Lamy, J.M. Stewart, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|Y. Zhang, A. Taha, J. Dickson, R. Lamy, J.M. Stewart, Ophthalmology, Zuckerberg San Francisco General Hospital and Trauma Center, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Epidemiological studies have found that males with diabetes have a higher incidence of diabetic retinopathy (DR) and higher risk for progression of DR than females. However, there have been limited investigations on vascular manifestations of sex-based differences in DR. We performed a retrospective case-control study using optical coherence tomography angiography (OCTA) to investigate microvascular differences between males and females with diabetes without DR or with mild non-proliferative diabetic retinopathy (NPDR).

Methods: We obtained 3x3mm macular OCTA scans of participants with diabetes without DR or with mild NPDR without other ocular comorbidities or prior DR treatments. Images with significant motion or shadow artifact or signal strength index (SSI) of <8 were excluded. One eye per patient was included in the analysis. Superficial capillary plexus (SCP) and deep capillary plexus (DCP) parameters were analyzed to include parafoveal vessel density (VD), vessel length density (VLD)— a skeletonization of the VD to remove disproportionate influence of large vessels on VD—, and flow index (FI). Multivariable linear regression was used to adjust estimates for potential confounders of age, race, SSI, hypertension, duration of disease, and HbgA1c.

Results: 1548 participants with diabetes without DR and 332 participants with mild NPDR were included in the study with 50.7% male participants. In the multivariable analysis, male sex was associated with lower VD ($P < 0.01$, $\beta = -0.004$), lower VLD ($P < 0.01$, $\beta = -0.196$), and higher flow index ($P < 0.001$, $\beta = -0.013$) in the SCP and lower VD ($P < 0.001$, $\beta = -1.348$) and lower VLD ($P < 0.001$, $\beta = -0.413$) in the DCP.

Conclusions: In a large diabetic population with no or mild DR, OCTA demonstrated a significant association between male sex and multiple reduced vascular parameters. These findings suggest that diabetic males may exhibit more advanced microvascular alterations than females, with implications for further sex-based studies to better understand DR.

CONTROL ID: 3707013

SUBMITTER (NAME ONLY): Minali Prasad

TITLE: STEPWISE UPREGULATION OF BASIC FIBROBLAST GROWTH FACTOR AND MONOCYTE CHEMOATTRACTANT PROTEIN-4 FROM ACUTE TO CHRONIC RHEGMATOGENOUS RETINAL DETACHMENTS

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Prasad, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|J. Agranat, J. Xu, S. Ness, X. Chen, N.H. Siegel, M.L. Subramanian, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|T.D. Stein, Pathology and Laboratory Medicine, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|J. Chung, Medicine (Biomedical Genetics), Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|W. Xia, S. Daley, Pharmacology and Experimental Therapeutics, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|T.D. Stein, Veterans Affairs Boston Healthcare System, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Minali Prasad: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Agranat: Commercial Relationship: Code N (No Commercial Relationship) | Jia Xu: Commercial Relationship: Code N (No Commercial Relationship) | Weiming Xia: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Daley: Commercial Relationship: Code N (No Commercial Relationship) | Steven Ness: Commercial Relationship: Code N (No Commercial Relationship) | Xuejing Chen: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Siegel: Commercial Relationship: Code N (No Commercial Relationship) | Thor Stein: Commercial Relationship: Code N (No Commercial Relationship) | Jaeyoon Chung: Commercial Relationship: Code N (No Commercial Relationship) | Manju Subramanian: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To characterize the pathogenesis of inflammation in rhegmatogenous retinal detachments (RRD) based on duration, and to elucidate inflammatory mediators that may contribute to the development of proliferative vitreoretinopathy (PVR). We report the cytokine profile of patients with RRD ≤2 weeks (acute) and >2 weeks (chronic) and compare them against surgical controls in an observational, case-control study.

Methods: Vitreous humor specimens were collected from 40 patients undergoing pars plana vitrectomy for RRD and noninflammatory vitreoretinal diseases, which served as controls. Quantitative immunoassay was used to measure the levels of 36 cytokine markers on the collected vitreous specimens. We conducted linear regression analyses with duration of detachment symptoms as the predictor and log-transformed cytokine levels as the outcome. The analysis was adjusted for age, sex, and race.

Results: Twenty-seven patients had RRD and 13 were control subjects. We observe significantly elevated levels of monocyte chemoattractant protein-4 (MCP-4) ($p=0.0058$) and basic fibroblast growth factor (bFGF) ($p=0.0007$) between patients with acute RRDs (n=16), chronic RRDs (n=11), and controls. Both cytokines were also significantly elevated (bFGF $p=0.0029$, MCP-4 $p=0.0245$) compared to controls when combining the acute and chronic groups. Additionally, IL-7 was found to be significantly elevated as RRD duration increased from acute to chronic ($p=0.0041$) but was not significant when the acute and chronic groups were combined compared to controls ($p=0.3469$).

Conclusions: MCP-4 and bFGF levels show significant stepwise upregulation as the duration of RRDs increases. While elevated levels of both cytokines have been previously reported, the impact of duration of detachment on its upregulation is unique. The novel increase in IL-7 only from acute to chronic indicates that it may play a role as a late inflammatory marker. Cumulatively, these findings aid in understanding the impact of inflammatory cytokines on RRD and development of complications related to prolonged duration of detachment, such as PVR. This may ultimately serve to identify potential therapeutic targets.

CONTROL ID: 3707017
SUBMITTER (NAME ONLY): Nitya Devireddy
TITLE: Biometric Characteristics of Eyes with a History of Scleral Buckle Surgery
SESSION TITLE: Cataract surgery 1
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Devireddy, E.V. Karakoleva, D. Rosen, N. Cannon, S. Pantanelli, Department of Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|
Commercial Relationships Disclosure: Nitya Devireddy: Commercial Relationship: Code N (No Commercial Relationship) | Ema Karakoleva: Commercial Relationship: Code N (No Commercial Relationship) | David Rosen: Commercial Relationship: Code N (No Commercial Relationship) | Nathan Cannon: Commercial Relationship: Code N (No Commercial Relationship) | Seth Pantanelli: Commercial Relationship(s);Code F (Financial Support):Alcon, Carl Zeiss Meditec, Ocular Therapeutix, Ziemer;Code R (Recipient):Alcon, Carl Zeiss Meditec;Code C (Consultant/Contractor):Bausch and Lomb, Carl Zeiss Meditec

ABSTRACT BODY:

Purpose: The purpose of this study is to investigate biometric changes after scleral buckle (SB) surgery. This is especially important in the age of artificial intelligence IOL power calculation formulas, which depend upon predictable relationships between axial length (AL), anterior chamber depth (ACD), and post-operative effective lens position.
Methods: This is a retrospective, single-center chart review of eyes that had measurements obtained with a swept-source OCT-based optical biometer (IOLMaster 700, Carl Zeiss Meditec) in anticipation of cataract surgery between February 2020 and May 2021. Chart review was conducted to associate the exported biometric data with clinical variables. Eyes with a history of SB at the time of biometry were included in the study as part of the SB group. These eyes were compared to a control group with no history of SB and to contralateral eyes from the same patient that did not have SB. Eyes with any intraocular media opacity other than cataract, abnormal corneal findings, anterior segment pathologies, history of intraocular or corneal surgery [except SB, pars plana vitrectomy, or retinal detachment surgeries], or poor quality biometry measurements as determined by the device's internal image quality metrics were excluded from the study.
Results: There were 7 eyes included in the SB group and 284 eyes in the surgery naive control group. The mean AL in SB and surgery naive eyes was 27.13 ± 2.66 and 23.88 ± 1.21, respectively (p = 0.0029). The mean ACD in SB and surgery naive eyes was 3.444 ± 0.244 and 3.199 ± 0.420, respectively (p = 0.04). The mean ACD/AL ratio in SB and surgery naive eyes was 0.128 ± 0.013 and 0.134 ± 0.016, respectively (p = 0.34).

Of the 7 SB eyes, biometric data was available for 5 contralateral eyes from the same patient. The mean AL of the SB and contralateral eyes was 26.76 ± 3.16 and 25.28 ± 2.06, respectively (p = 0.23). The mean ACD of the SB and contralateral eyes was 3.322 ± 0.157 and 3.505 ± 0.213, respectively (p = 0.08). The mean ACD/AL ratio in SB and contralateral eyes was 0.125 ± 0.015 and 0.139 ± 0.013, respectively (p = 0.13)
Conclusions: Eyes with SB have a longer AL and deeper ACD than surgery naive eyes. However, there was a trend toward shallower ACD in SB eyes when compared with contralateral surgery naive eyes from the same patient. Additional eyes with a history of SB are needed to further explore the unique biometric properties of this group.

CONTROL ID: 3707020

SUBMITTER (NAME ONLY): Igor Kozak

TITLE: Real life analysis of non-compliance with intravitreal injection protocol for retinovascular disease - A patient survey analysis.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Kozak, Moorfields Eye Hospital Dubai, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|I. Al Araj, Cure Medical Center, Abu Dhabi, UNITED ARAB EMIRATES|S. Kakade, Al Ahlia Hospital, Abu Dhabi, UNITED ARAB EMIRATES|P. Rao, Medcare Hospital LLC, Dubai, Dubai, UNITED ARAB EMIRATES|

Commercial Relationships Disclosure: Igor Kozak: Commercial Relationship: Code N (No Commercial Relationship) | Ihab Al Araj: Commercial Relationship: Code N (No Commercial Relationship) | Sathya Kakade: Commercial Relationship: Code N (No Commercial Relationship) | Prasan Rao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intravitreal injection treatment is the standard of care for numerous retinovascular diseases such as diabetic macular edema (DME) and exudative age-related macular degeneration (AMD). Lack of adherence or undertreatment with respect to evidence from clinical trials remains a significant barrier to optimizing real-world outcomes for patients. Contributing factors and strategies to address this are poorly understood. We wish to identify compliance issues with intravitreal anti-VEGF injections treatment.

Methods: A patient survey analysis from multiple retina centers in Abu Dhabi and Dubai, United Arab Emirates. Included were patients receiving intravitreal anti-VEGF injections for AMD or DME willing to participate in the survey. Exclusion was inability to participate in the survey. The 20-minutes question interview (22 questions) took place in the clinic. Proportions for the whole patient group as well as for AMD and DME groups were calculated.

Results: The study included 78 patients (females 32%, males 68%) with average age of 57 years. There were 52 patients with DME and 26 patients with AMD. More than 40% of patients had >7 doctor visits in the last year (46% for AMD patients and 40% for DME patients). More than 50% went to “1 specialist” ever since diagnosed followed by “2-3 specialists” for 35% of patients. Lack of clarity, inconvenience, change of job location and doctor trust were reasons for seeking >3 specialists. Vision improvement was the highest factor for treatment discontinuation followed by visit frequency and costs. Patients regarded treatment visits as “Extremely important” especially AMD patients (65%). 45% of patients never missed a visit, particularly AMD patients (54%). Inconvenient timing was the most significant factor for missing visits followed by fear of treatment. Patients regard the clinic location as “Extremely convenient” especially AMD patients (46%). Physician reputation accounts for 65% of reasons for patients’ clinic choice followed by insurance plan and clinic location.

Conclusions: Vision improvement was the highest factor for treatment discontinuation followed by frequent visits and costs. Inconvenient timing was the most significant factor for missing treatment visits followed by fear of treatment. Physician reputation was a significant reason for patients’ clinic choice followed by insurance plan and clinic location.

CONTROL ID: 3707021

SUBMITTER (NAME ONLY): Edmund Tsui

TITLE: Evaluation of alternative approaches to establishing a standardized laser flare photometry value for patients with uveitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Tsui, J.L. Chen, G.N. Holland, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|N.J. Jackson, Medicine, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Edmund Tsui: Commercial Relationship(s);Code C (Consultant/Contractor):Kowa;Code F (Financial Support):Cylite | Nicholas Jackson: Commercial Relationship: Code N (No Commercial Relationship) | Judy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Gary Holland: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Laser flare photometry (LFP) provides prognostic information about patients with uveitis. The current standard approach for establishing final LFP values is to record the mean of 7 LFP measurements after removal of the highest and lowest measurements. We investigated alternative techniques for establishing a final value, in an attempt to identify a simpler approach to achieve the same standard.

Methods: In a prospective study, LFP was performed on 200 eyes (100 patients with uveitis) using both Kowa FM-500 and FM-700 Laser Flare Photometers. A total of 7 measurements were obtained on each eye. We compared results between devices using 8 statistical methods: (1) all raw data; (2) mean of raw data; (3) mean after removal of highest and lowest values; (4) median of raw data; (5) median absolute deviation (MAD) outlier detection with mean (high threshold of 2.24); (6) MAD outlier detection with mean (low threshold of 1.28); (7) boxplot outlier detection (Carling method) with mean; and (8) boxplot outlier detection (Tukey method) with mean. To simulate fewer LFP measurements, analyses were repeated on the first 5 of 7 values. Intraclass correlation coefficient (ICC) was used to compare results. We also compared final values from different techniques on a per-eye basis. ICC of 0.75-0.90 were considered good.

Results: Mean age of participants was 49.5±19.1 years; 72% were female. Using all 7 LFP measurements, ICC for comparison of the two devices did not vary substantially between techniques; ICC were as follows: (1) all raw data, 0.58; (2) mean of raw data, 0.80; (3) mean after removal of highest and lowest values, 0.81; (4) median of raw data, 0.81; (5) MAD outlier detection with mean (high threshold of 2.24), 0.77; (6) MAD outlier detection with mean (low threshold of 1.28), 0.77; (7) boxplot outlier detection (Carling method) with mean, 0.78; and (8) boxplot outlier detection (Tukey method) with mean, 0.78. ICC using first 5 measurements were similar to those using 7 measurements (range 0.58-0.81).

Conclusions: All statistical methods demonstrated similar results between two devices and final values for alternative techniques were similar to those obtained from the current standard approach. Our study suggests that obtaining fewer LFP measurements and using simpler techniques for calculating final LFP values may be suitable for use in patient care and clinical research.

CONTROL ID: 3707027
SUBMITTER (NAME ONLY): Amar Pujari
TITLE: Defining the role of swept source anterior segment optical coherence tomography in strabismic eyes
SESSION TITLE: Pediatric ophthalmology and imaging
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Pujari, Ophthalmology, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|
Commercial Relationships Disclosure: Amar Pujari: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Purpose: To explore the clinical role of swept source anterior segment optical coherence tomography (SS-ASOCT, CASIA-2, Tomey corp, Nagoya, Japan) in extra ocular muscle imaging under various strabismic conditions.
Methods: Study design: Prospective observational study.

Participants: A total of 1104 extraocular muscles of 150 subjects were imaged. Normal eyes (80 subjects, 640 muscles), eyes undergoing re-operation (30 subjects, 240 muscles), paralytic (4 subjects, 16 muscles) and non-paralytic strabismic eyes (10 subjects, 20 muscles), post-traumatic strabismic eyes (8 subjects, 64 muscles), eyes with thyroid disease (8 subjects, 64 muscles), and other atypical cases (10 subjects, 60 muscles) where extra ocular muscle location was necessary (eyes with rectus muscle hypoplasia or aplasia, eyes with anterior staphyloma, eyes with operated scleral fixated intra ocular lens) were evaluated. In all cases up to four recti muscles were imaged in each eye depending on the need.
Results: Results: Overall, the muscle insertion was comfortably identified in 95% of the subjects, where up to 14 millimetres of the anterior (cross sectional) muscle was studied. The location and prediction on the nature of surgery helped in surgical re-planning in over 90% of the cases. Amongst the four recti, identification of lateral rectus was easy and the medial rectus was technically difficult. Nevertheless, the correlation scanning between vertical and horizontal axis helped in achieving better results than the isolated scanning.
Conclusions: Conclusions: SS-ASOCT with its wider and deeper scanning abilities is able to locate the extra ocular muscles locally. Therefore, this tool can reliably be used for muscle imaging in normal eyes, simple/complex strabismic eyes undergoing routine surgery, surgical planning in re-operations and other technically challenging scenarios where pre-operative muscle localization is necessary.

CONTROL ID: 3707028

SUBMITTER (NAME ONLY): Jeroen Pas

TITLE: Reliability of Quantitative Autofluorescence Imaging in a Multicenter Study Involving Patients with Stargardt Disease

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Pas, P.P. Dhooge, C.C. Hoyng, Radboudumc Afdeling Oogheelkunde, Nijmegen, Gelderland, NETHERLANDS|J.A. Pas, P.P. Dhooge, C.C. Hoyng, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|P.T. Möller, P. Herrmann, F.G. Holz, S. Schmitz-Valckenberg, Department of Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|P.T. Möller, F.G. Holz, S. Schmitz-Valckenberg, GRADE Reading Center, Bonn, GERMANY|K. Stingl, University Eye hospital, Center for Ophthalmology, University of Tuebingen, GERMANY|C.J. Boon, Department of Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|C.J. Boon, Department of Ophthalmology, Amsterdam Universitair Medische Centra, Amsterdam, Noord-Holland, NETHERLANDS|A.J. Lotery, Department of Ophthalmology, University of Southampton, Southampton, Hampshire, UNITED KINGDOM|M. Battaglia Parodi, Department of Ophthalmology, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|P. Herrmann, Center for Rare Diseases Bonn (ZSEB), Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|W. Klein, M.G. Fsadni, Katairo GmbH, Kusterdingen, GERMANY|T.H. Wheeler-Schilling, Center for Ophthalmology and Institute for Ophthalmic Research, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|

Commercial Relationships Disclosure: Jeroen Pas: Commercial Relationship: Code N (No Commercial Relationship) | Patty Dhooge: Commercial Relationship: Code N (No Commercial Relationship) | Philipp Möller: Commercial Relationship: Code N (No Commercial Relationship) | Katarina Stingl: Commercial Relationship: Code N (No Commercial Relationship) | Camiel Boon: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Lotery: Commercial Relationship: Code N (No Commercial Relationship) | Maurizio Battaglia Parodi: Commercial Relationship: Code N (No Commercial Relationship) | Philipp Herrmann: Commercial Relationship: Code N (No Commercial Relationship) | Wolfgang Klein: Commercial Relationship(s);Code F (Financial Support):Katairo GmbH;Code S (non-remunerative):Katairo GmbH;Code I (Personal Financial Interest):Katairo GmbH;Code C (Consultant/Contractor):Katairo GmbH | Mario Fsadni: Commercial Relationship(s);Code C (Consultant/Contractor):paid Consultant to Katairo outworking for International Pharm-Med Ltd in UK | Thomas Wheeler-Schilling: Commercial Relationship: Code N (No Commercial Relationship) | Frank Holz: Commercial Relationship: Code N (No Commercial Relationship) | Carel Hoyng: Commercial Relationship: Code N (No Commercial Relationship) | Steffen Schmitz-Valckenberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this study is to establish the reliability of quantitative autofluorescence (qAF) in a multicenter setting in order to validate qAF as an endpoint for interventional clinical trials in Stargardt disease (STGD1).

Methods: A total of 104 STGD1 patients (208 eyes) underwent qAF imaging at two visits (screening and baseline, mean interval 20 ± 13 days), with two qAF recordings per visit, as part of the Stargardt Remofuscin Treatment Trial (EudraCT No. 2018-001496-20) and according to standardized image acquisition protocol including operator training and certification. qAF_8 values were determined by calculating the mean qAF values within the 8 middle segments of the Delori pattern. Eyes were independently graded by the concerned study site and the central reading center. Intra- and inter-visit as well as interobserver (study site versus reading center) reproducibility of qAF_8 levels were obtained using intraclass correlation (ICC) and coefficient of repeatability (CR) based on the method of Bland-Altman.

Results: At the first visit, there were significant differences in qAF_8 values between the six study sites ($p<0.001$). Overall, the mean qAF_8 value at baseline, 463.55±107.81 units, was not significantly different from the value at screening in the same patients, 467.63±108.53 units ($p=0.753$). qAF_8 reproducibility was ± 26.1% for intra-visit, ± 40.3% for inter-visit, and ± 21.6% for the interobserver reproducibility. Intra-visit and interobserver reliability of qAF_8 was good to excellent for all sites (ICC of 0.84-0.99). However, we observed a significant difference of 8.80 ± 56.18 qAF_8 units between both movies acquired on the same day and 17.49 ± 48.60 between observers ($p=0.007$ and $p<0.001$). Variability between visits was higher with ICC of 0.43-0.83, but there was no significant difference in the

qAF_8 units measured at screening and baseline (p=0.210).

Conclusions: Real-life test-retest variability of qAF is higher in the multicenter setting than previously reported in single center studies. Possible explanations include the demanding imaging protocol, operator variability and differences in patient characteristics. qAF is a successful tool to diagnose STGD1. However, when using qAF as clinical trial endpoint, increased variability must be considered, and larger sample sizes may be required to demonstrate treatment effects.

CONTROL ID: 3707029
SUBMITTER (NAME ONLY): Jaime Tejedor
TITLE: Eye position recording after surgery for large-angle exotropia in adults with deep amblyopia
SESSION TITLE: Strabismus
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Tejedor, Ophthalmology, Hospital Universitario Ramon y Cajal, Madrid, Madrid, SPAIN|J. Tejedor, Neuroscience, Universidad Autonoma de Madrid, Madrid, Madrid, SPAIN|F. Gutiérrez-Carmona, Surgery, Universidad Alfonso X el Sabio, Villanueva de la Canada, Comunidad de Madrid, SPAIN|
Commercial Relationships Disclosure: Jaime Tejedor: Commercial Relationship: Code N (No Commercial Relationship) | Francisco J Gutiérrez-Carmona: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To study change and variability of deviation in operated adult exotropes with deep amblyopia who do not cooperate in cover tests.
Methods: In adult patients (age range: 24-54) who underwent surgery for large angle exotropia (>-40 PD; range: -40 - -60 PD), requiring three-muscle surgery, with deep amblyopia (visual acuity in the amblyopic eye < 0.7 logMAR or 20/100), with or without distance-near disparity, but uncooperative for cover tests, eye movements were recorded 2 months after surgery, using Tobii X120 during near (60 cm) and distance (4 m) fixation. Visual acuity, refraction, ductions, versions, anterior and posterior segment of the eyes, were also examined. Control participants were unoperated age-matched subjects (age range: 26-52).
Results: Ten patients were included in the surgery group and 12 in the control group. Two patients in the surgery group had variable distance angles (range: 0 - -10°) with orthotropia at near, one had variable angle at distance (range: -4° - -12°) and near (range: 0 - -10°), and 7 were orthotropic and stable at distance and near. Peak velocity at 15° eccentricity saccade was slightly lower and latency was larger in the amblyopic compared with the sound eye and eyes of controls in saccades (250°/s vs 305°/s and 296°/s, respectively, p=0.04; 230 ms vs 210 and 205 ms, respectively, p=0.06), whereas pursuit eye movements showed small nonsignificant differences or were difficult to record.
Conclusions: Adult patients with deep amblyopia who undergo surgery for large-angle exotropia have a relatively high likelihood of postoperative variable angle exodeviation, particularly at distance (20-33%).

CONTROL ID: 3707030

SUBMITTER (NAME ONLY): Yeming Yang

TITLE: The m6A writer METTL14 is essential for visual function and retinal photoreceptor survival

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yang, X. Zhu, Medical school, University of Electronic Science and Technology of China, Chengdu, CHINA|

Commercial Relationships Disclosure: Yeming Yang: Commercial Relationship: Code N (No Commercial Relationship) | Xianjun Zhu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: As the most abundant epigenetic modification of eukaryotic mRNA, N6-methyladenosine (m6A) modification has been shown to play a role in mammalian nervous system development and function by regulating mRNA synthesis and degeneration. However, the role of m6A modification in retinal photoreceptors remains unknown.

Methods: We generated the first retina-specific Mettl14-knockout mouse models using the Rho-Cre and HRGP-Cre lines and investigated the functions of Mettl14 in retinal rod and cone photoreceptors. meRIP-seq was employed to explore the underlying pathological mechanism.

Results: Our data showed that loss of Mettl14 in rod cells causes a weakened scotopic photoresponse and rod degeneration. Further study revealed the ectopic accumulation of multiple outer segment (OS) proteins in the inner segment (IS). Deficiency of Mettl14 in cone cells led to the mislocalization of cone opsin proteins and the progressive death of cone cells. Moreover, Mettl14 depletion resulted in drastic decreases in METTL3/WTAP levels and reduced m6A methylation levels. Mechanistically, transcriptomic analyses in combination with MeRIP-seq illustrated that m6A depletion via inactivation of Mettl14 resulted in reduced expression levels of multiple phototransduction- and cilium-associated genes, which subsequently led to compromised ciliogenesis and impaired synthesis and transport of OS-residing proteins in rod cells.

Conclusions: Our data demonstrate that Mettl14 plays an important role in regulating phototransduction and ciliogenesis events and is essential for photoreceptor function and survival.

CONTROL ID: 3707031
SUBMITTER (NAME ONLY): Blake Fortes
TITLE: The Effect of Physician Face Mask Use on Post-injection Endophthalmitis
SESSION TITLE: Endophthalmitis & Trauma
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: B.H. Fortes, K. Astafurov, W.M. Smith, A.J. Barkmeier, T.W. Olsen, R. Iezzi, S.J. Bakri, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|
Commercial Relationships Disclosure: Blake Fortes: Commercial Relationship: Code N (No Commercial Relationship) | Konstantin Astafurov: Commercial Relationship: Code N (No Commercial Relationship) | Wendy Smith: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Barkmeier: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Olsen: Commercial Relationship(s);Code O (Owner):iMacular Regeneration, LLC;Code F (Financial Support):Novartis;Code E (Employment):Secretary of Quality at the American Academy of Ophthalmology | Raymond Iezzi: Commercial Relationship(s);Code C (Consultant/Contractor):Seeing Medicines;Code F (Financial Support):Off-label/Investigation usage: Genentech-Avastin | Sophie Bakri: Commercial Relationship(s);Code C (Consultant/Contractor):Abbvie;Code C (Consultant/Contractor):Allegro;Code C (Consultant/Contractor):Apellis;Code C (Consultant/Contractor):Alimera;Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Kala;Code C (Consultant/Contractor):Genentech;Code C (Consultant/Contractor):Novartis

ABSTRACT BODY:

Purpose: To examine the impact of physician face mask use on the rates and outcomes of postinjection endophthalmitis.

Methods: Design: Retrospective, comparative cohort study. Setting: Multi-center. Study population: Eyes that received intravitreal anti-VEGF injections from January 1, 2005 to January 31, 2020 at Mayo Clinic Rochester (MCR) and at Mayo Clinic Health System (MCHS) sites. Intervention: Cases were divided into the “No Mask” versus “Mask” group depending on whether the ophthalmologist performing the injection wore a mask. Main outcome measures: Rate of endophthalmitis, microbial spectrum, and visual acuity.

Results: 164,824 total injections were performed at MCR and MCHS sites. Of these, 66,098 injections were in the No Mask group and 98,726 injections were in the Mask group. Overall, there were no significant differences in the rates of infectious endophthalmitis in the No Mask vs. Mask cohorts (overall: 0.030% vs. 0.042%; P=0.24; infectious: 0.018% vs. 0.013%; P=0.42). At MCR alone, there was a significant reduction in the infectious endophthalmitis rate between the No Mask vs. Mask groups (0.030% vs. 0.003%; P<0.001). Only 2 cases of infectious endophthalmitis occurred in MCR after the face mask policy was first implemented (1 in 30,000 injections). At presentation and at 6 months, average visual acuity was similar for both groups.

Conclusions: Overall, physician face mask use did not impact the rate or visual outcome of postinjection endophthalmitis. However, there was a significant reduction at MCR after implementation of masks and other quality improvement measures that has led to a low rate of postinjection endophthalmitis.

CONTROL ID: 3707036

SUBMITTER (NAME ONLY): Alexandre Lachance

TITLE: Predicting visual improvement after macular hole surgery: a combined model using deep learning and clinical features

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Lachance, M. Hébert, S. Bourgault, M. Caissie, É. Tourville, A. Dirani, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|A. Lachance, M. Hébert, S. Bourgault, M. Caissie, É. Tourville, A. Dirani, Département d'ophtalmologie et d'oto-rhino-laryngologie – chirurgie cervico-faciale, Centre Universitaire d'Ophtalmologie, Hôpital du Saint-Sacrement, CHU de Quebec-Universite Laval, Quebec, Quebec, CANADA|M. Godbout, A. Durand, Département d'informatique et de génie logiciel, Universite Laval, Quebec, Quebec, CANADA|F. Antaki, Département d'ophtalmologie, Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec, CANADA|A. Durand, Canadian Institute for Advanced Research, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Analysis of preoperative optical coherence tomography (OCT) in patients with macular hole (MH) can provide insight into surgical success and postoperative visual acuity (VA). The aim of this study was to assess the feasibility of deep learning (DL) methods to improve the prediction of VA improvement after MH surgery from a combined model using DL on high-definition (HD) OCT B-scans and clinical features.

Methods: This was a retrospective single-center study (CHU de Québec – Université Laval (Canada)). A DL convolutional neural network (CNN) trained using preoperative HD-OCT B-scans (ZEISS, Dublin, CA) of the macula and combined with a logistic regression model of preoperative clinical features was designed to predict VA increase ≥15 Early Treatment of Diabetic Retinopathy Study letters at 6 months post-vitrectomy in closed MH. A total of 121 MH with 242 HD-OCT B-scans and 484 clinical data points were used to train, validate and test the model. These were randomly split into a training set of 83 eyes (69%), a validation set of 21 eyes (17%), and a held-out test set of 17 eyes (14%). Prediction of VA increase was evaluated using the area under the receiver operating characteristic curve (AUROC) and F1 scores. We also extracted the weight of each input feature in the regression-based hybrid model.

Results: All performances are reported on the held-out test set. Using a regression on clinical features, the AUROC was 80.63, with a F1 score of 79.71. For the CNN, relying solely on the HD-OCT B-scans, the AUROC was 72.83 ± 14.57, with a F1 score of 61.47 ± 23.72. For our hybrid regression model using clinical features and CNN prediction, the AUROC was 81.94 ± 5.22, with a F1 score of 80.35 ± 7.68. In the hybrid model, the baseline VA was the most important feature (59.11 ± 6.94% of the model's weight) while HD-OCT prediction was 9.59 ± 4.17%.

Conclusions: Both the clinical data and HD-OCT models had good discriminative performances. Combining both into a hybrid model did not significantly improve performance.

CONTROL ID: 3707037

SUBMITTER (NAME ONLY): Olivia Chowdhury

TITLE: Activation of mTOR signaling in the RPE cells induces alterations in melanogenesis thereby triggering oxidative stress

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Chowdhury, V. Maddipatla, S. Ghosh, H. Liu, P. SHANG, V. Koontz, N.A. Stepicheva, A. Strizhakova, R. Daley, S.L. Hose, D. Sinha, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, Ophthalmology, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal pigmented epithelium (RPE) is a monolayer of post-mitotic, polarized and highly specialized pigmented cells at the back of the eye. An important and evolutionarily conserved role of the RPE is the absorption of stray light to increase visual acuity and reduce oxidative damage. This activity requires functional melanosomes, which contain enzymes that catalyze the production of melanin. Defective melanosome formation (melanogenesis) causes hypopigmented RPE, leading to RPE cell loss and decline in retinal function. It is known that mTOR plays a key role both in RPE function as well as melanogenesis. We speculated that activation of mTOR specifically in RPE cells by overexpressing mLST8, an important component of both mTOR complexes 1 and 2 (mTORC1 and 2), would have deleterious effects on melanosome formation, resulting in oxidative stress.

Methods: We have generated Best1 (mLST8) constitutive knock-in (KI) mice as a tool for this study. We performed transmission electron microscopy, hematoxylin-eosin (H&E) staining on RPE sections and electroretinography (ERG) on 3- and 9-month-old WT and mLST8 KI mice. Western blot analysis was performed on RPE explants from WT and mLST8 KI mice to evaluate autophagy flux. Expressions of mTORC1 and mTORC2 downstream components, melanosome marker, tyrosinase, and oxidative stress markers, CAT and SOD1 were also determined by western blot.

Results: Our results revealed the presence of abnormal melanosomes, as evident from their marked depigmentation and fragmentation, in the mLST8 KI RPE. H&E staining revealed noticeable hypopigmented patches in the RPE layer along with patchy loss of RPE. ERG analysis also showed a decline in retinal function in mLST8 KI mice, compared to age-matched controls. Western blot analysis indicated reduced autophagy flux, increased expressions (phosphorylation) of mTORC1 and 2 substrates, S6K and Akt2, and oxidative stress markers, SOD1 and CAT, along with decreased expression of tyrosinase in the mLST8 KI RPE, relative to WT. Interestingly, treatment with Torin (mTOR inhibitor) rescued the alterations in phospho- S6K and Akt2, SOD1, CAT and tyrosinase levels in mLST8 KI RPE explants.

Conclusions: Our results suggest that mLST8 overexpression activated both mTORC1 and 2 thereby triggering defects in melanosome formation and leading to oxidative stress in RPE cells.

CONTROL ID: 3707038

SUBMITTER (NAME ONLY): Domenica Marino

TITLE: Comparison of Treatment Intervals for Various Anti-Vascular Growth Factor (Anti-Vegf) Injections in Wet Age-Related Macular Degeneration Patients

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.I. Marino, C.W. Miller, C. McCrossin, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To calculate and compare the average interval between injections of Aflibercept (AFL), Bevacizumab (BEVA), Brolucizumab-Dbll (BROL), and Ranibizumab (RAN) for patients with wet age-related macular degeneration (wAMD).

Methods: All data was collected by the practice management of Retina Associates of Cleveland, Inc. Data was collected from patients who received injections of AFL, BEVA, BROL, and RAN from July 2020 through July 2021 and includes: patient number, injection service dates, injection service ID's, procedure codes, and primary diagnosis. The patients selected were those injected unilaterally and diagnosed with wAMD, and the number of days between injection service dates was calculated for each patient. The data set was then organized by injection type, and the average number of days between injection service dates was determined for each drug. Statistical analysis was performed using a two-tailed t-test to compare the medications.

Results: From July 2020 through July 2021, 10,789 wAMD injections were performed unilaterally with a total average interval between injections of 55 days for all drug types. Within the wAMD patient group, the average injection interval for each medication was as follows: 57 days for BEVA with standard deviation (SD) +/- 33 days, 54 days for BROL SD +/- 23 days, 54 days for AFL SD +/- 29 days, and 56 days for RAN SD +/- 25 days. When comparing the interval of each medication, the two-tailed t-tests calculated a p-value of $p = 0.0003$ for BEVA vs AFL, $p = 0.39$ BEVA vs. RAN, $p = 0.0096$ BEVA vs BROL; $p = 0.003$ AFL vs RAN, $p = 0.99$ AFL vs BROL; $p = 0.05$ BROL vs RAN.

Conclusions: The results of the study suggest that BEVA seems to have a longer interval of time between injections for wAMD patients than BROL and AFL, but not RAN. There does not appear to be a difference between average injection intervals of BROL and AFL.

CONTROL ID: 3707044

SUBMITTER (NAME ONLY): Aden Swayze

TITLE: Monocyte Biomarkers of Early-Intermediate Age-Related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Swayze, L. Kurzlechner, M. Sexton, S. Degan, E.M. Lad, Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|A.D. Proia, Pathology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To employ a flow cytometry gating strategy to investigate blood-based monocyte biomarkers of early-intermediate age-related macular degeneration (AMD) and determine the relationship between monocytes and disease stage on flow cytometry and immunohistochemistry (IHC).

Methods: We recruited 30 study participants: 9 with early AMD (eAMD; category 2 AREDS), 11 with intermediate AMD (iAMD; category 3 AREDS), and 10 normal controls. Samples were matched by age (+/-5 years) and gender. Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood samples and then stained with CD45, CD14, CD16, CD163, CD11a, and CD11b antibodies. We used a flow cytometry gating strategy to identify PBMC subsets (classical, intermediate, and non-classical). In parallel, we performed co-localization IHC studies of CD163+ and CD68+ macrophages in the macula of postmortem eyes with iAMD (stage Sarks 4; N=7) and normal control eyes (stage Sarks 1; N=7).

Results: On flow cytometry, the proportion of CD68+ cells was lowest in the PBMCs from iAMD participants (52.3% vs eAMD 77.7% and normal 60.9%), and there was a significant difference between the early and iAMD groups ($p<0.05$). iAMD samples demonstrated the highest percentage of CD163+ cells (8.7% vs eAMD 2.3%, normal 5.3%; $p= 0.54$) and nonclassical monocytes (5.9% vs eAMD 4.5%, normal 4.4%; $p= 0.62$), although the results did not reach significance. Within CD68+ and CD163+ cells, there were no significant differences between groups with respect to PBMC subsets. However, we found a moderate correlation between CD163-high cells and the intermediate PBMC subset ($r^2= 0.35$).

The quantitative IHC analysis showed a decreased expression of CD163 in the macrophages in the choroid and inner retina of iAMD Sarks 4 postmortem eyes and an increased CD163 expression in the outer retina as compared to normal Sarks 1 eyes (all $p<0.05$). No significant differences in CD68 expression were observed between the iAMD Sarks 4 and normal Sarks 1 groups.

Conclusions: Our data suggest that CD163+ monocytes/macrophages are associated with disease stage in early-intermediate AMD, implicating these cells in the pathobiology and progression of AMD. CD163 may represent a useful clinical blood-based biomarker of disease progression on flow cytometry analysis.

CONTROL ID: 3707045

SUBMITTER (NAME ONLY): Mihir Nemani

TITLE: Inhibiting mTOR-independent TFEB activity in RPE alleviates the early AMD-like phenotype in a mouse model

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nemani, H. Liu, P. SHANG, O. Chowdhury, V. Koontz, N.A. Stepicheva, A. Strizhakova, R. Daley, S.L. Hose, D. Sinha, S. Ghosh, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, Ophthalmology, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision loss from age-related macular degeneration (AMD) is an expanding, major unmet problem due to the aging population worldwide. Retinal pigmented epithelium (RPE) cells are the first to be affected in the dry form of AMD. Phagocytosis and autophagy, two major functions of the RPE, require functional lysosomes. We have previously shown that in the Cryba1 cKO mouse model (lacks Cryba1 gene, which encodes for βA3/A1-crystallin, only in the RPE), there are alterations in TFEB nuclear activity, lysosomal function and autophagy in the RPE. This is accompanied by increased expression of Akt2, mTORC1 activation and an early/dry AMD-like pathology that develops with age. mTORC1 is a critical regulator of TFEB and lysosomal biogenesis in cells. Since targeting mTOR is known to have damaging side-effects, we speculate that inhibiting Akt2, a mTOR-independent regulator of TFEB, with trehalose (a disaccharide Akt inhibitor) might rejuvenate lysosomal function and alleviate the early RPE changes in this mouse model.

Methods: We have generated Best1-Akt2 constitutive knock-in (KI) and Akt2 conditional knockout (cKO) mice as tools to be used in this study. Autophagy flux was estimated in RPE explants from WT, Cryba1 KO (complete knockout), Akt2 KI and Akt2 cKO mice with or without Trehalose (100 mM). In vivo studies to evaluate coordinated lysosomal expression and regulation (CLEAR) network gene expression along with p62/SQSTM1 expression in the RPE, retinal function (electroretinography) and changes in retinal structure were performed on 5 month old Cryba1 cKO mice with or without Trehalose treatment (1 mg/g/day intraperitoneally injected once a day for 2 days, then 2% in the drinking water for 2 months).

Results: We found increased expression of pAkt2 and diminished autophagy flux in RPE cells from Akt2 KI and Cryba1 KO mice relative to controls, but not in Akt2 cKO cells. Trehalose treatment rescued changes in autophagy flux in Cryba1 KO and Akt2 KI cells. Moreover, in vivo Trehalose treatment rescued lysosomal abnormalities, retinal function, and histological abnormalities in the Cryba1 cKO mice.

Conclusions: It can be concluded from our results that inhibiting Akt2-dependent TFEB activation rejuvenates lysosomal function in the RPE of a mouse model and could be employed as a therapeutic approach in treating dry AMD while avoiding the deleterious effects of mTOR inhibitors.

CONTROL ID: 3707046
SUBMITTER (NAME ONLY): Stephen Dellostritto
TITLE: Influence of Myopic Correction and Axial Length on ON-OFF Perimetry
SESSION TITLE: Myopia: Clinical Interventions and Diagnostics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Dellostritto, M.W. Dul, J. Tan, V. Moore-Stoll, H.R. Nasrabadi, J.Z. Jin, J. Alonso, SUNY College of Optometry, New York, New York, UNITED STATES|
Commercial Relationships Disclosure: Stephen Dellostritto: Commercial Relationship: Code N (No Commercial Relationship) | Mitchell Dul: Commercial Relationship: Code N (No Commercial Relationship) | Jia Tan: Commercial Relationship: Code N (No Commercial Relationship) | Veronica Moore-Stoll: Commercial Relationship: Code N (No Commercial Relationship) | Hamed Nasrabadi: Commercial Relationship: Code N (No Commercial Relationship) | Jian Jin: Commercial Relationship: Code N (No Commercial Relationship) | Jose-Manuel Alonso: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:
Purpose: To investigate how the function of ON and OFF visual pathways is affected by myopic refractive error, axial length, and eccentricity.
Methods: Eleven eyes of 11 human subjects (23-30 years old; mean 25.9 +/- 1.9) were tested at 8 Michelson contrast levels (5-20%) out to 30 degrees from fixation.

A single test comprised of 579 trials (27 catch trials), at 92 locations, repeated 3 times for both light and dark stimuli. Each participant completed eight tests (4,632 trials).

Hardware consisted of a head mounted display with an eye tracker (HTC VIVE embedded Tobii) with a refresh rate of 90 Hz, a maximum luminance of 110 cd/m2. Stimuli were light or dark squares on a spherical binary noise background. Stimulus size was increased as a function of eccentricity using a power law relationship.

Unity (version 2017) software was used to generate the stimuli. Eye movements were measured at 120 Hz and restricted within a central 2.5-degree radius circle. Percent of correct responses were measured across the entire visual field and, separately, for each of 6 annual eccentricities 5-10, 11-20, 21-30 degrees from fixation. Percent response errors were plotted as a function of refractive error and axial length for the entire 30 degrees and for each specific eccentricity.
Results: There was no statistically significant correlation between refractive error and percent response errors at any eccentricity or combined over the entire testing area (maximum r value = 0.4015, p = 0.064, between 21-30 degrees). There was a significant positive correlation between axial length and percent response errors across the entire testing area (r= 0.5198, p=0.0132). This was most pronounced at 21-30 eccentricity (r=0.583, p=0.0044). Overall, subjects responded more accurately for dark than light stimuli (14.38 ±8.11 versus 15.98 ± 8.59, p= 0.0127. This was most pronounced at 21-30 eccentricity (p=0.0049).
Conclusions: Decreased accuracy to ON-OFF perimetric stimuli in myopic patients is more closely correlated to axial length than refractive error.

CONTROL ID: 3707047

SUBMITTER (NAME ONLY): Carla Siegfried

TITLE: Oxidative stress and antioxidant protection in human trabecular meshwork cells: Investigating the racial disparity of glaucoma

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Siegfried, Y. Shui, Y. Liu, Department of Ophthalmology and Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|H. Wu, X. Liu, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|H. Wu, College of Pharmacy, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although many studies demonstrate higher prevalence of primary open angle glaucoma (POAG) in those of African descent, no physiologic findings have been identified to explain these phenotypic differences. We tested the hypothesis that there are fundamental differences in mitochondrial function and antioxidant protection between self-reported African American (AA) and White (W) subjects in an in vitro model of trabecular meshwork (TM) from POAG patients and healthy donors (controls).

Methods: TM specimens collected from POAG patients undergoing glaucoma surgery were analyzed by RNA-sequencing (RNA-seq). Control donor and POAG TM tissues, divided by race, were cultured following standard methods and confirmed with specific cell markers. Intracellular reactive oxygen species (ROS) production was measured in live TM cells by CellROX^{TM} Orange after hydrogen peroxide (H_2O_2) challenge. Major antioxidant enzymes superoxide dismutase 2 (SOD2), catalase (CAT), and their transcriptional factor, nuclear factor erythroid 2-related factor 2 (NRF2), were measured at RNA (qPCR) and protein levels (Western blot). Select genes of interest from RNA-seq analysis were also evaluated with qPCR. Student T-Test and Tukey's multiple comparisons test were applied for data analysis.

Results: The most significant expression differences from RNA-seq data were identified in nuclear genes encoding protein components of mitochondrial Complex I, III and IV. POAG TM tissue from AA (n=3) demonstrated higher expression of these genes ($p<0.01$) vs. W (n=4). qPCR assessment of these genes in TM tissues from control donors (6AA, 6W) and POAG patient tissue (4AA, 5W) did not show any racial differential. For the primary cultured TM cells, ROS production in AA TM cells was significantly higher than W ($p=0.004$) following H_2O_2 challenge. qPCR showed NRF2 and SOD2 were significantly lower in AA than W ($p=0.02$, 0.04), with no difference in CAT. Western blot confirmed protein levels of NRF2 and SOD2 were significantly lower in AA TM cells than W ($p=0.003$, 0.04).

Conclusions: Fundamental differences in oxidative stress and antioxidant protection may be important risk factors for racial disparities in POAG risk and severity. The primary TM cell culture model derived from POAG patient tissue and healthy donor controls provides powerful tools to study distinct differences of TM function between AA and W.

CONTROL ID: 3707048

SUBMITTER (NAME ONLY): Ogul Uner

TITLE: Clinical Outcomes of Endophthalmitis in Early and Late Presentation after Intravitreal Anti-VEGF Injection

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.E. Uner, Casey Eye Institute, Department of Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D. Lee, C. Seebruck, Associates In Ophthalmology, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Ogul Uner: Commercial Relationship: Code N (No Commercial Relationship) | Diana Lee: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Seebruck: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intravitreal anti-VEGF injections (IVI) are the most common in-office procedure for retinal diseases. Endophthalmitis is the most feared complication after IVI. Studies suggest that the time elapsed between the causative procedure and diagnosis of endophthalmitis may affect visual potential, but studies investigating timing specifically in the setting IVI are limited. We compared the clinical and microbiological outcomes of endophthalmitis in the setting of early and late presentation after IVI.

Methods: Endophthalmitis cases were identified using ICD-10 codes in 9 clinical practices between January 1, 2017 and October 31, 2021. Patients were defined as presenting early if the elapsed time between IVI and endophthalmitis diagnosis was less than 5 days. Those presenting 5 days or later were placed in the late presenting group. Relationships between elapsed time and visual acuity (VA, logMAR) at baseline, time of diagnosis, and follow-up were analyzed. Culture positivity rates and growth information were also compared between groups.

Results: Among 102,906 IVI, there were 70 (0.07%) cases of endophthalmitis. Forty-one (58.6%) cases presented early and 29 (41.4%) presented late, with median elapsed time (days) of 3 (range 1-4) and 7 (range 5-28). The groups were matched in age, sex, laterality, and baseline VA. The late group had more cases attributable to aflibercept, but this difference was not significant (26.8% in early vs. 48.3% in late, p=0.08). Mean VA at diagnosis was significantly worse for the late group (1.6 in early vs. 2.0 in late, p=0.02). Early and late groups were followed for 2.2 years and 2.1 years, respectively. Mean VA at follow-up was worse for the late group, but the difference was not significant (1.1 for early vs. 1.5 for late, p=0.2). Culture positivity rates were similar between groups (50.0% in early vs. 47.4% in late). Unlike the early group, few cultures in the late group grew gram-negative bacteria (2 cases) and Staphylococcus aureus (2 cases). These patients all had hand motion or worse vision at follow-up.

Conclusions: Compared to early presentation, late presentation for endophthalmitis after IVI is associated with significantly worse vision at time of diagnosis but there seems to be no significant difference in the long term. Though rare, bacteria with higher virulence may be implicated in late presentation and result in poor visual outcomes.

CONTROL ID: 3707050

SUBMITTER (NAME ONLY): Oluchukwu Onwuka

TITLE: Consequences of Real-world Surveillance of Fellow Eyes in Neovascular Age-related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Onwuka, F.S. Akkan, C. Lasalle, D.J. Ramsey, Ophthalmology, Lahey Hospital and Medical Center, Peabody, Massachusetts, UNITED STATES|O. Onwuka, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|J. Saddemi, Rowan University Cooper Medical School, Camden, New Jersey, UNITED STATES|F.S. Akkan, Ankara Sehir Hastanesi, Cankaya, Ankara, TURKEY|

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ABSTRACT BODY:

Purpose: The aim of this study is to determine whether the interval at which fellow eyes are monitored impacts the severity of disease at the time of their conversion in patients with unilateral neovascular age-related macular degeneration (nAMD).

Methods: Cross sectional study of patients with unilateral nAMD who subsequently developed nAMD in their fellow eyes between March 2015 to October 2020. Patients were divided into those who were actively receiving treatment in their first eye at the time of second eye conversion and compared with those who had stopped treatment because of reaching end-stages of the disease. Visit intervals, frequency of monitoring fellow eyes, visual acuity (VA), and central macular thickness (CMT) were abstract from the chart.

Results: At the time of fellow eye conversion, 54 patients (71%) were receiving injections in their first eye and 22 patients (29%) had stopped treatment because of having low vision. VA in the first eyes to develop nAMD in the active treatment group was significantly better compared with the VA in eyes that had ceased treatment by the time of their conversion (logMAR 0.587±0.375 vs. logMAR 1.14±0.531, P<0.001). By contrast, VA was similar both at the time of diagnosis of the first eye (logMAR 0.384±0.436 vs. logMAR 0.367±0.328, P=0.867) and conversion of the fellow eye to nAMD (logMAR 0.492±0.412 vs. logMAR 0.465±0.400, P=0.795). The fellow eyes of patients who were actively receiving injections were monitored much more closely compared with those patients who had stopped treatment. At the visit immediately before second eye conversion, patients who were in the active treatment group had completed their last visit an average of 8.1±5.3 weeks compared with 25.5±24.8 weeks for those patients who had stopped treatment (P=0.004). Finally, the average CMT was similar for the fellow eyes that converted to nAMD in both groups (277±51 µm vs. 265±39 µm, P=0.305).

Conclusions: Patients who stopped treatment for nAMD by the time that their fellow eye developed neovascularization were monitored less frequently compared with patients who continued on treatment for nAMD. This is surprising because a majority of these patients were functionally monocular, and therefore had more to lose from the conversion of their remaining eye. Reassuring, however, visual and structural outcomes were not tied to the interval at which the fellow eyes were being monitored.

CONTROL ID: 3707053

SUBMITTER (NAME ONLY): Neena Singh

TITLE: α-Synuclein modulates extracellular matrix proteins in the trabecular meshwork

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Singh, A. Kritikos, D. McDonald, S. Pillai, S. Chen, M.H. Kang, D. Rhee, E. Lindner, A. Ashok, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: α-Synuclein (α-Syn) is implicated in Parkinson's disease (PD), a neuro-motor disorder with prominent ocular symptoms. Here, we explored whether α-Syn plays a functional role in the anterior segment of the eye, and whether its dysfunction due to aggregation contributes to ocular pathology.

Methods: Primary human trabecular meshwork (TM) cells, cadaveric human and bovine TM tissue and aqueous humor (AH), and human AH collected during cataract surgery were used for this study. Silencing of α-Syn and overexpression of TGFβ2 in TM cells and tissue was achieved by conventional techniques. Expression of fibronectin (FN), α-smooth muscle actin (α-SMA), and ROCK-1 was determined by Western blotting (WB). Binding, uptake, and response of TM cells to extracellular α-Syn was determined by immunostaining and WB.

Results: α-Syn was expressed in the ciliary body and TM, and monomeric and oligomeric α-Syn was present in the AH. Silencing of α-Syn in TM cells downregulated FN, α-SMA, and ROCK-1 expression in the absence and presence of active TGFβ2. Extracellular monomeric and oligomeric α-Syn was internalized by β1-integrin, and upregulated FN, α-SMA, and ROCK-1 in TM cells and TM tissue. Active TGFβ2 was also increased.

Conclusions: Intracellular α-Syn altered the expression of extracellular matrix (ECM) proteins in TM cells through ROCK-1 independently and downstream of TGFβ2, the principal trigger for dysregulation of ECM in primary open angle glaucoma (POAG). Extracellular α-Syn was endocytosed by TM cells through β1-integrin, and likewise, upregulated ECM proteins. These observations have significant implications for POAG, and warrant exploration of the underlying biochemical pathways.

CONTROL ID: 3707067

SUBMITTER (NAME ONLY): Neha Garg

TITLE: The Effect of Leflunomide as Adjunctive Therapy with a TNF Inhibitor in Pediatric Patients with Uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Garg, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|K.C. LaMattina, E. Cohen, Boston Medical Center, Boston, Massachusetts, UNITED STATES|E. Tsui, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Leflunomide (LEF) is a disease-modifying anti-rheumatic drug (DMARD) approved for rheumatoid and psoriatic arthritis in patients over the age of 18. While off-label use has found it to be effective for treatment of childhood conditions such as juvenile idiopathic arthritis (JIA), there has been a lack of literature and good quality evidence on its efficacy in the treatment of noninfectious pediatric uveitis. The aim of this study is to describe the effectiveness of LEF as adjunctive therapy with anti-Tumor Necrosis Factor (anti-TNF) agents in pediatric patients with uveitis who are not able to tolerate methotrexate (MTX).

Methods: A retrospective case series was performed with pediatric patients who were treated with LEF in conjunction with anti-TNF agent therapy after intolerance to a combination of MTX with anti-TNF therapy. Dose and duration of MTX, LEF, and anti-TNF therapy were recorded. Extensive history, laboratory data, demographics, and uveitis flare rate were obtained.

Results: A total of five children were included in the study. Most subjects were initially on MTX and an anti-TNF agent was added subsequently due to inadequate response to monotherapy. After discontinuation of MTX, LEF was initiated with anti-TNF therapy. The replacement of MTX with LEF showed decreased side effects and was associated with lower flare rates and steroid free remission.

Conclusions: LEF was found to be well-tolerated and effective at maintaining uveitis quiescence in conjunction with anti-TNF agents in pediatric patients who do not tolerate MTX.

CONTROL ID: 3707070

SUBMITTER (NAME ONLY): Benjamin Shou

TITLE: Predictors for Non-Diagnostic Images in Real World Deployment of Artificial Intelligence Assisted Diabetic Retinopathy Screening

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.L. Shou, A. Liu, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|K. Venkatesh, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|C. Chen, R. Ghidey, T. Lee, J. Wang, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the pivotal clinical trial that led to FDA approval of the first fully autonomous artificial intelligence (AI) assisted diabetic retinopathy (DR) screening system, 76.4% of patients did not require pharmacological dilation to obtain an AI system disease level output. However, during our real-world, multi-site deployment of this AI system, we found that the non-diagnostic rate was 51% without dilation. We sought to identify patient risk factors associated with non-diagnostic images to strategically identify patients who may require dilation a priori.

Methods: Retrospective chart review of patients who were screened with Digital Diagnostics' IDx-DR® at Johns Hopkins Medicine (8/2020 to 5/2021). No patients underwent dilation. Patients who had a diagnostic result were compared to those with a non-diagnostic result. We used backward stepwise elimination to construct a multivariable logistic regression model for non-diagnostic results. A $p<0.05$ was considered statistically significant.

Results: Of the 241 patients (59% female; median age=59), 123 (51%) were non-diagnostic. Patients with a non-diagnostic result were older (64 years vs. 53, $p<0.001$), had a lower BMI (32.0 kg/m^2 vs. 35.5, $p=0.005$), more likely to be a current smoker (30% vs. 14%, $p=0.002$), and less likely to have type 2 diabetes (T2D) (85% vs. 93%, $p=0.03$) (Table 1). In the multivariable model, every 10-year increase in age was associated with a more than two-fold increased risk for non-diagnosis (adjusted odds ratio/AOR=2.19, 95% CI: 1.67-2.88, $p<0.001$). Type 1 diabetes (T1D) (AOR=4.99, 95% CI: 1.29-19.27, $p=0.02$) and current smoking (AOR=2.74, 95% CI: 1.32-5.69, $p=0.007$) were additional risk factors (Figure 1).

Conclusions: The real-world non-diagnostic imaging rate is much higher than reported in the pivotal clinical trial. Older age, smoking, and T1D were predictive risk factors for non-diagnostic imaging. This information will inform the establishment of a dilation protocol to selectively dilate patients at risk for non-diagnostic testing prior to AI-assisted DR screening, which will decrease the need for dilation after testing has failed and improve screening efficiency and clinic workflow.

CONTROL ID: 3707072

SUBMITTER (NAME ONLY): Vyas Akondi

TITLE: Evaluation of the double-pass wavefront in model and human eyes

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Akondi, X. Huang, A. Dubra, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|X. Huang, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Model eyes are used in adaptive optics (AO) ophthalmoscopy to focus imaging channels, calibrate fields of view, distortion correction, and instrument troubleshooting. We evaluate model retinas and AO control strategies to mitigate the double-pass wavefront and allow stable and converging closed-loop operation when using AO scanning ophthalmoscopes.

Methods: We evaluated model eyes with 19 and 100 mm focal length achromatic doublets, and a variety of flat substrates: protected silver mirror, polished glass, polished opal glass, white diffusers ground with different grits, and paper. The double pass was quantified by poking an off-center actuator in the deformable mirror of the AO ophthalmoscope and comparing the relative heights of the wavefront peaks (see Fig. 1). These measurements were performed with a focused beam of 850 nm light that was at first stationary and then scanned across an ~1.1 deg angle using a 13.8 kHz resonant scanner. The same setup was used to estimate the model eyes field curvature by vertically steering the stationary beam.

Results: Wavefronts from model eyes with paper or rough substrates as retinas (similar to a normal human eye), did not show center-symmetry that can be seen with a mirror retina, irrespective of beam scanning (see Fig. 1). The use of finely polished glass substrates as retinas results in a substantial attenuation of first-pass wavefront. The measured field curvature, with the 100 mm lens is ~7.8 smaller relative to the depth of focus (7.75 mm beam diameter) than for the 19 mm case, consistent with ray tracing. The AO control loop can be successfully operated provided that the first-pass wavefront is less than 100% of the second pass. The first pass wavefront induces AO control oscillations that can be mitigated by lowering the closed loop gain.

Conclusions: Decreasing the AO control gain improves convergence even with highly reflective materials, while the use of model eyes with lower field curvature improves the AO control stability. If the field curvature cannot be changed, then, the AO control stability can be improved by changing the wavefront sensor exposure to match the inverse of the scanning ophthalmoscope frame rate, or if the AO and imaging are synchronized, the exposure.

CONTROL ID: 3707074

SUBMITTER (NAME ONLY): Noor-Ul-Ain Shekoh

TITLE: End Point Management (EPM) in Clinically Significant Diabetic Macular Edema (CSME)

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Shekoh, Valley Retina Institute, McAllen, Texas, UNITED STATES|T. Fatima, Jinnah Sindh Medical University, Karachi, Sindh, PAKISTAN|Q. Shekoh, University of Houston, Houston, Texas, UNITED STATES|V.H. Gonzalez, Valley Retina Institute, McAllen, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes causes release of various inflammatory and angiogenic cytokines, glycosylation causes cell damage and structural changes in blood vessels resulting in microaneurysms and abnormal leaky blood vessels that give rise to CSME. According to ETDRS the risk of development of vision impairment is decreased to 50 % after laser photocoagulation. Laser reduces central subfield thickness (CST) and cause some improvement in visual acuity (VA). However, the disadvantage of threshold Laser photocoagulation is scarring/chorioretinal atrophy, scotoma, and visual field defects. With Topcon Pattern Scanning Laser (PASCAL) system streamline yellow it is possible to calculate and apply the sub threshold energy required to stimulate retinal cells without causing damage to photoreceptors and retinal pigment epithelium (RPE). It applies low power density over large spot size and longer pulse to achieve non damaging end point.

Stimulation of retinal pigment epithelial cells causes formation of heat shock proteins that act as chaperones causing refolding of misfolded proteins, prevent apoptosis and down regulate inflammation, improve RPE function, thereby facilitating absorption of macular edema. The absence of retinal scarring and damage can be evidenced on FAF images.

Methods: We included the 21 eyes of pts. having clinically significant diabetic macular edema (CSME) without ischemia in our study.

Baseline VA measurement, OCT, FAF and fluorescein angiography were done in all patients.

The PASCAL streamline yellow laser was used to apply barely visible burn in mid periphery of retina, then the energy was titrated to 30 percent and subthreshold treatment applied over the CSME in a doughnut shape pattern, with spot size 200 µ, max power 200 mW, duration 15 ms. Pt were followed up after 1, 4 and 12 weeks. VA, FAF and OCT acquisition were done on each visit.

Results: Improvement in CST was seen in 71.4% eyes, 14.2% eyes developed recurrent macular edema after initial improvement and needed retreatment and 14.2% eyes showed no improvement, VA improved in 66.6%, stable in 23.8% and worsened in 9.5% .

Conclusions: EPM with subthreshold laser is a safe and effective way of improvement of CST and VA in CSME. It may reduce the treatment sessions with faster resolution of macular edema if used as an adjunct to intravitreal injections or as a rescue treatment.

CONTROL ID: 3707075

SUBMITTER (NAME ONLY): Michael Dong

TITLE: Differential gene expression by human lens epithelial cells in post vitrectomy cataract vs. steroid induced cataract revealed by RNA sequencing

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.L. Lim, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA| M. Dong, A.J. Hall, Central Clinical School, Monash University Faculty of Medicine Nursing and Health Sciences, Clayton, Victoria, AUSTRALIA|L.L. Lim, Centre for Eye Research Australia, University of Melbourne, East Melbourne, Victoria, AUSTRALIA|J. Shah, T. Khong, A. Spencer, Myeloma Research Group, Australian Centre for Blood Diseases, The Alfred Hospital/Monash University, Melbourne, Victoria, AUSTRALIA|M. Dong, A.J. Hall, Department of Ophthalmology, Alfred Health, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Vitrectomy and corticosteroid-use are known to accelerate cataract development, however, the causative mechanisms are largely unknown. We conducted RNA-sequencing of human lens epithelial cells in steroid-induced and post-vitrectomy cataract to verify and compare gene expression profiles.

Methods: Human anterior lens capsule specimens from post-vitrectomy (n = 8), steroid-induced subcapsular (n = 12) and age-related (n = 2) cataracts were collected from patients following written informed consent from the Alfred Hospital Research and Ethics Committee. Capsulorhexis specimens were collected at the time of cataract surgery for analysis. RNA was isolated using RNeasy Micro Kit and RNA libraries were synthesized using Illumina Stranded Total RNA Prep Ligation with Ribo-Zero Plus followed by sequencing on a NovaSeq S4, 300 cycles at AGRF. Differentially expressed genes (DEGs) were identified and underwent bioinformatics analyses including principal component analysis (PCA).

Results: Approximately 55,000 genes were detected from RNA-seq. We focused on ~15,000 genes with moderate or high average expression of >10 transcripts per million reads sequenced. A dimensionality reduction algorithm known as Principal Component Analysis (PCA) was employed to study gross differences in gene expression profile. PCA clustered steroid induced subcapsular cataract and post-vitrectomy cataract separately (Figure 1), suggesting overall differences in gene expression between the two groups (Figure 2), while age-related cataract samples clustered close to post-vitrectomy samples. Preliminary results indicate a minimum of 28 identified DEGs, 27 were upregulated in post-vitrectomy compared to steroid-induced cataract including IL-33, P2RY6, CAMP, CP, C4B, CFI whilst GPD1 was downregulated.

Conclusions: Our findings suggest that post-vitrectomy cataract and steroid-induced subcapsular cataract have different RNA transcription profiles. Bioinformatics analyses suggest that lens epithelial cells from post-vitrectomy cataract have a similar transcriptome to lens epithelial cells from age-related cataract but the transcriptome from steroid-induced posterior subcapsular cataract lens epithelial cells was quantitatively and qualitatively different.

CONTROL ID: 3707079

SUBMITTER (NAME ONLY): Young Joo Shin

TITLE: Novel ROCK Inhibitors on the Regeneration of Corneal Endothelial Cells

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Shin, Department of Ophthalmology, College of Medicine, Hallym University Medical Center, Hallym University, Seoul, Other, KOREA (THE REPUBLIC OF)|Y. Kim, S.C. Lee, pH Pharma Co., LTD., Seoul, Other, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Young Joo Shin: Commercial Relationship(s);Code C (Consultant/Contractor):pH Pharma Co., LTD | Yoochang Kim: Commercial Relationship(s);Code E (Employment):pH Pharma Co., LTD | Sammy Lee: Commercial Relationship(s);Code E (Employment):pH Pharma Co., LTD

ABSTRACT BODY:

Purpose: The cornea may lose transparency and cause blindness when Human corneal endothelial cells (HCEnCs) are damaged or diseased. Replacing diseased cells with a healthy donor endothelium is the only currently available treatment. There is increasing interest in the development of cultured graft substitutes and artificial corneas due to the global shortage of donor corneas. The aim of the study is to investigate whether novel Rho-kinase (ROCK) inhibitors can aid in the cultivation and regeneration of HCEnCs.

Methods: Human CEnCs were cultured and treated with Y-27632 (Y0503, Sigma-Aldrich), sovesudil (also known as PHP-201; pH Pharma), or PHP-0961 (pH Pharma) for 24h. We observed cellular responses, including cell viability, cytotoxicity, proliferation and Ki67 expression with ROCK inhibitors. We also assessed wound healing and cell adhesion assays. Porcine corneas were used ex vivo to evaluate wound healing and regeneration effects of Y-27632, sovesudil, and PHP-0961. We performed live/dead cell assays and immunofluorescence staining (for SOX2, b-catenin, and ZO-1) on porcine corneas treated with ROCK inhibitors.

Results: Cell viability, BrdU proliferation assay, and number of Ki67-positive cells was higher in Y-27632, sovesudil and PHP-0961 treated compared with control ($p<0.05$). There was no difference in LDH cytotoxicity test between any groups. Cells treated with Y-27632, sovesudil and PHP-0961 showed faster migration, wound healing, and cell adhesion. In the porcine ex vivo experiments, wound healing, the number of live cells, and SOX-positive cells were higher in Y-27632, sovesudil and PHP-0961 treated corneas ($p<0.05$). Across all experiments, the results of sovesudil and PHP-0961 were equal or superior to the results of the gold standard ROCK inhibitor Y-27632.

Conclusions: Novel ROCK inhibitors have a capacity to regenerate HCEnCs through enhancing the cell proliferation and adhesion between cells.

CONTROL ID: 3707088

SUBMITTER (NAME ONLY): Takashi Ono

TITLE: Extended long-term effects of hard contact lens use on the corneal endothelium in healthy eyes: an observational study of 8604 eyes

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ono, Y. Mori, R. Nejima, T. Iwasaki, K. Miyata, Ophthalmology, Miyata Eye Hospital, Miyakonojo, Miyazaki, JAPAN|T. Ono, Ophthalmology, University of Tokyo, Bunkyo-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Contact lens use affects the morphology and density of the corneal endothelial cells, an important factor affecting normal endothelial function and the maintenance of corneal clarity. However, normal corneal endothelial parameters vary among population subsets worldwide. Research assessing the effects of hard contact lens use across populations has been limited in terms of the numbers and duration of use. This study aimed to analyze the effect of extended long-term use of hard contact lens on corneal endothelial cell density and morphology in healthy Japanese individuals.

Methods: This observational study included individuals using hard contact lenses examined at the Miyata Eye Hospital between 1996 and 2015. Eyes with a previous history of ophthalmologic surgery or diseases—except refractive errors—were excluded. Medical information regarding the individual's age, duration of contact lens use, corneal endothelial cell density (ECD), coefficient of variation (CV), rate of appearance of hexagonal cells (6A), and cell area were reviewed retrospectively. The corneal endothelium data were obtained via non-contact specular microscopy.

Results: We included 8604 eyes of 4302 individuals (mean age, 35.6±10.0 years): including 837 male and 3465 female individuals. The mean duration of hard contact lens use was 14.7±9.1 years. Multivariate analysis revealed that ECD was significantly correlated with age ($P<0.001$), but not to duration of use; however, CV, 6A, and cell area correlated significantly with both factors (all $P<0.001$). Univariate analyses revealed that the CV ($Y=29.9+0.24X$, $R^2=0.31$, $P<0.001$), 6A ($Y=60.7-0.26X$, $R^2=0.23$, $P<0.001$), and cell area ($Y=336.1+1.1X$, $R^2=0.26$, $P<0.001$) correlated significantly with the duration of use.

Conclusions: CV, 6A, and cell area significantly correlated with the duration of hard contact lens use in healthy Japanese individuals. It is important to observe the corneal endothelial morphology in long-term contact lens wearers.

CONTROL ID: 3707089

SUBMITTER (NAME ONLY): Hans Lemij

TITLE: Glaucomatous features in fundus photographs of eyes with 'Referable glaucoma' of a large population based labeled data set for training an Artificial Intelligence (AI) algorithm for glaucoma screening

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.G. Lemij, K. Vermeer, Rotterdams Oogheelkundig Instituut, Rotterdam, Zuid Holland, NETHERLANDS|C. de Vente, C. Sánchez, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|C. de Vente, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|J. Cuadros, EyePACS, California, UNITED STATES|N. Jaccard, ORBIS International, New York, New York, UNITED STATES|J. Cuadros, Optometry/Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Too many people in the world are visually impaired by glaucoma, largely because the disease is detected too late. Aim: to build a labeled dataset for training an AI algorithm for glaucoma screening by fundus photography. To assess the accuracy of the graders and to characterize the features of all eyes with referable glaucoma.

Methods: Color fundus photographs of 113,897 eyes were obtained from EyePACS, California, USA, from a population screening program for diabetic retinopathy. Carefully selected graders (ophthalmologists and optometrists) graded the images. To qualify, they had to pass the EODAT[1] optic disc assessment with at least 85% accuracy and 92% specificity. Of 89 candidates, 30 passed. Each image of the EyePACS set was then scored by varying random pairs of graders as 'Referable glaucoma' (RG), 'No referable glaucoma' or 'Ungradable'. In case of disagreement, a glaucoma specialist made the final grading. RG was scored if visual field damage was expected. In case of RG, graders were instructed to mark up to 10 relevant glaucomatous features. [1]Reus N et al.; Ophthal 2010 117(4):717-23.

Results: During the grading, the performance of each grader was monitored; if the sensitivity and specificity dropped below 80 and/or 95%, respectively (the final grade served as reference), they exited the study and their gradings were redone by other graders. In all, 20 graders qualified; their mean sensitivity and specificity (SD) were 85.6 (5.7) % and 96.1 (2.8) %, respectively. The two graders agreed in 92.45% of the images (Gwet's AC2, expressing the inter-rater reliability, was 0.917). Of all gradings, the sensitivity and specificity (95% CI) were 86.0 (85.2 – 86.7)% and 96.4 (96.3 – 96.5)%, respectively. Of all gradable eyes (n = 111183; 97.62 %) the prevalence of RG was 4.38 %. The most common features of RG were the appearance of the neuroretinal rim inferiorly and superiorly (Figure (top) for all features and their probabilities. Conditional probabilities are also shown (bottom)).

Conclusions: The estimated sensitivity and specificity was above our target of 80% and 95%, respectively, and the annotated dataset should therefore be of sufficient quality to develop AI screening solutions.

CONTROL ID: 3707090

SUBMITTER (NAME ONLY): Gyulli Kazakbaeva

TITLE: Association of Vision and Hearing Impairment with Depression, Anxiety and Suicidal Ideas in Populations of Russia: The Ural Eye and Medical Study and the Ural Very Old Study

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Kazakbaeva, M. Bikbov, E. Iakupova, S. Panda-Jonas, J. Jonas, Ufa Eye Research Institute, Ufa, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: To assess prevalence and associated factors of depression, anxiety and suicidal ideas in populations from Russia.

Methods: In rural and urban regions in Bashkortostan/Russia, we conducted two population-based studies (Ural Eye and Medical Study (UEMS), Ural Very Old Study (UVOS)) which included participants aged 40+ years and 85+ years, respectively.

Results: In the UEMS with 5893 individuals (age:59.0±10.7 years;range:40-94 years), higher depression score and higher anxiety score were associated with more marked hearing loss (beta:0.07;P<0.001,and beta:0.07;P<0.0012,respectively) and worse visual acuity (beta:0.04;P=0.02; and beta:0.03;P=0.03,resp.), after adjusting for parameters such as female sex, Russian ethnicity, lower educational level, higher prevalence of alcohol consumption, weaker hand grip strength, less physical activity, and higher prevalence of dry eye disease. Attempted suicide was reported by 88 (1.5%;95%CI:1.2,1.8) participants, with 20 individuals indicating financial reasons for their attempt. Having thought of suicide was reported by 63 (1.1%) individuals. Overall, 131 (2.2%;95%CI:1.9,2.6) individuals attempted or thought of suicide. Out of 1491 UVOS participants (age:88.2±2.8 years;range:85-100 years) with a mean depression score of 20.0±10.3 (median:18;range:0-58), 916/1491 (61.4%;95%CI:59.0,63.9) fulfilled the definition of depression (depressions core ≥16). Higher depression score and higher anxiety score correlated with higher hearing loss score (beta:0.07;P=0.02, and beta:0.06;P=0.04,resp.) and worse visual acuity (beta:0.13;P<0.001, and beta:0.11;P<0.001,resp.), after adjusting for variables such as female sex, urban region of habitation, less physical activity, lower number of days with fruit intake, and lower cognitive function. Overall, 15 (1.0%;95%CI:0.50,1.50) individuals had attempted or thought of suicide.

Conclusions: Besides female sex, lower level of education and lower cognitive function, it was sensory impairment, namely vision and hearing impairment, which belonged to the determinants of depression and anxiety in these populations from Russia. Future studies may explore the role of improvement of vision and hearing impairment in the prevention and therapy of depression and anxiety.

CONTROL ID: 3707092

SUBMITTER (NAME ONLY): Avinash Aher

TITLE: The effect of sinusoidally modulating backgrounds on flash electroretinograms

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. Aher, C.R. Huchzermeyer, J.J. Kremers, University Hospital Erlangen Department of Ophthalmology, Erlangen, GERMANY|

Commercial Relationships Disclosure: Avinash Aher: Commercial Relationship: Code N (No Commercial Relationship) | Cord Huchzermeyer: Commercial Relationship: Code N (No Commercial Relationship) | Jan Kremers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the effect of sinusoidally modulating background on the photopic flash ERGs.

Methods: Four healthy subjects (age: 28-62 years; one female) participated in the study. We measured the response to flashes (500 cd/m^2, 1ms long) on a steady background (50 cd/m^2) as a control and a sinusoidally modulating (50 cd/m^2 mean luminance) background of 1, 5, 10, and 25Hz temporal frequencies. The flashes were presented at 0° (mean luminance), 90° (100 cd/m^2 instantaneous luminance) and 270° (0 cd/m^2 instantaneous luminance) during the carrier sine wave. The responses to the carriers (sine wave only) were also recorded as control measurements and subtracted from the responses to flash plus sine carriers to obtain the flash ERGs at different phases.

Results: The responses to flashes were strongly altered when presented at different phases on the sine wave and particularly at low frequencies. The response was larger for the flash at 270° phase compared to the control flash ERG (flash on steady background) and the flash at 0° and 90° phases. The response to the flash at 90° was smaller than the other responses. The response to the flash at 0° were comparable to the flash ERG on a steady background. The effects of background modulation on the flash ERG decreased with increasing frequency of the background. The amplitudes of the components could be described by the Weber fraction plus saturation and a delay.

Conclusions: The proposed technique can be useful to enhance the flash ERG responses and to increase signal to noise ratio. Weber fraction of the flashes is an adequate quantification of stimulus strength to describe the amplitudes of the flash ERGs.

CONTROL ID: 3707093

SUBMITTER (NAME ONLY): Johannes Iby

TITLE: Encircling scleral buckling for the treatment of retinal detachment: Development in indication and outcome within the last decade

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Iby, M. Hollaus, K.M. Eibenberger, G.S. Reiter, A. Pollreisz, U. Schmidt-Erfurth, M. Georgopoulos, S. Sacu, Ophthalmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To evaluate the use of encircling scleral buckling surgical technique for the treatment of retinal detachment (RD) and its complications as well as success rate within the last decade.

Methods: This retrospective observational study included 116 eyes receiving encircling scleral buckling (ESB) or encircling scleral buckling combined with vitrectomy (SBV) between January 2009 and December 2018. The main outcome measures include the development in usage rate of surgical procedures (either ESB or SBV), indications as well as mean age. Furthermore, intra-/postoperative complications, intraocular tamponades as well as the influences on functional outcome (VA) and central retinal thickness (CRT) were evaluated.

Results: During our 10 years of observation, ESB and SBV surgeries decreased in the first six years from initially 28.9% of all RD-operations to 2.9%, before increasing again to 6.7% between 2017-2018 ($p < 0.001$, Chi-Square test). The mean age for receiving ESB or SBV surgery differed significantly over the years from 56.58 ± 17.33 between 2009 – 2010 to 37.89 ± 28.08 between 2017-2018 ($p < 0.001$, ANOVA). Functional outcome after a mean follow-up time of 1501 ± 1266 days increased from 1.318 ± 0.871 logMar at baseline (BSL) to 0.853 ± 0.845 logMar at the latest follow-up visit. Significant influence on VA was expansion of RD (macula on/off) ($p < 0.001$), significant influences on CRT were postoperative macular edema ($p < 0.001$), surgical technique (ESB or SBV) ($p = 0.022$) and expansion of RD ($p = 0.026$).

Conclusions: After an initial decrease, an increase in SB and SBV surgeries was noticed at the end of the observational period, with a significant reduction in mean age. No significant differences in functional outcome as well as intra- and postoperative complications could be observed over the years.

CONTROL ID: 3707102

SUBMITTER (NAME ONLY): Catherine Kerr-Niermann

TITLE: Evaluating the impact of customized low vision simulator glasses for parents of children with visual impairment

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kerr-Niermann, University of Missouri-St Louis, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Catherine Kerr-Niermann: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Parents of children with visual impairment often express frustration in their lack of clear explanations of what their child can see. Customized simulator glasses created from low vision rehabilitation evaluation measurements may offer a low cost, personalized, and effective method to satisfy this inquiry. This study utilized a quantitative survey to gauge the impact of customized simulator glasses on parental understanding of children's visual impairment.

Methods: Forty-three families received customized simulator glasses as standard of care in a non-profit clinic between April 2021 and October 2021. The simulators layered various filters on clear safety glasses to represent a personalized range of visual acuity, contrast sensitivity, central and peripheral vision fields following a comprehensive low vision rehabilitation evaluation. An emailed link to an IRB approved survey was sent to one parent or guardian per family. Seventeen surveys were completed (44% responded of 39 email addresses collected).

Results: Survey results indicated that parents use multiple sources of information in attempt to understand their child's vision including consulting with optometrists or ophthalmologists (88%), searching the internet (77%), asking their child directly to explain their vision (71%), interpreting eye reports (59%), and using standard (non-customized) simulator glasses (29%). Of those surveyed, 94% agreed that the customized low vision simulator glasses provided were helpful for understanding their child's vision (76% strongly agreed and 18% somewhat agreed). The vision simulated was largely worse than parents expected (82%).

Conclusions: Customized low vision simulator glasses are an effective tool to help parents understand their child's visual impairment. Parents actively seek multiple sources of information in attempt to understand what their child can see. Most parents who received customized simulator glasses following their child's low vision rehabilitation evaluation found them to be helpful and most parents reported the vision simulated was worse than expected. This study raises important questions regarding the validity of simulators, the feasibility of implementing customized simulators as standard of care, and the implication of children's adaptability as a potential contributing factor in the discrepancy of what a child can see compared to parental perception.

CONTROL ID: 3707105

SUBMITTER (NAME ONLY): Ronald Silverman

TITLE: Ultrasound-Activated Perfluorocarbon (PFC) Nanodroplets for Treatment of Glaucoma

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Silverman, R. Urs, G. Tezel, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|M. Burgess, J.A. Ketterling, Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Ronald Silverman: Commercial Relationship: Code N (No Commercial Relationship) | Mark Burgess: Commercial Relationship: Code N (No Commercial Relationship) | Raksha Urs: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Ketterling: Commercial Relationship: Code N (No Commercial Relationship) | Gulgun Tezel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Primary open angle glaucoma (POAG) is the most common form of glaucoma worldwide. Increased stiffness and reduced porosity of Schlemm's canal and juxtacanalicular tissues is known to play a key role in POAG pathogenesis. Ultrasound-induced cavitation has been used to increase porosity of tissues, especially when enhanced by the presence of microbubble contrast agents that serve as cavitation nuclei. In this preliminary study, we introduced PFC nanodroplets (NDs) into the anterior chamber (AC) and exposed eyes to focused ultrasound as a potential means for improving outflow in POAG.

Methods: We synthesized NDs with a liquid perfluoropentane core and lipid shell. NDs averaged approximately 100 nm in diameter. Upon exposure to focused ultrasound of sufficient intensity, NDs undergo a transient phase change from liquid to gas. We introduced 0.1 ml of an ND emulsion into the AC of ex vivo pig eyes and 25 µl into 3 in vivo rat eyes. Using a Verasoncs Vantage-128 ultrasound system, eyes were then imaged and NDs activated with linear array ultrasound probes with center frequencies of 18 MHz and 28 MHz at a series of increasing acoustic intensities.

Results: At diagnostic acoustic intensities, scanned focused ultrasound beams provided visualization of anatomy with minimal activation of NDs. At 28 MHz, NDs in the rat AC activated at a peak negative pressure of 5 MPa (mechanical index, MI=1.2), undergoing rapid phase transition from liquid to gas. Acoustic reflection from transient gas microbubbles produced high imaging contrast and microbubble collapse produced cavitation. Ultrasound and OCT Images showed NDs to be distributed widely within the AC, settling into the angle and entering Schlemm's canal. Two days after treatment, rat eyes showed no sign of inflammation, but a few small gas bubbles were present in the AC.

Conclusions: In this application, NDs are advantageous with respect to conventional microbubble ultrasound contrast agents because of their higher density and smaller diameter (< $1/10^{th}$ that of microbubble agents), which facilitate entry into the outflow channels. ND activation occured at an MI of 1.2, which exceeds the diagnostic maximum of 0.23. Future preclinical in vivo studies using glaucoma models will assess safety and the effect of treatment on IOP and outflow facility.

CONTROL ID: 3707106

SUBMITTER (NAME ONLY): Jingjing Huang

TITLE: Melatonin Prevents Acute Ocular Hypertension-Induced Oxidative Stress, Senescence, and Inflammation by Inducing Sirtuin 1 in Anterior Segment Tissues of Mice

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, D. Ye, Y. Xu, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Jingjing Huang: Commercial Relationship: Code N (No Commercial Relationship) | Dan Ye: Commercial Relationship: Code N (No Commercial Relationship) | Yue Xu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The mechanisms underlying the causal link between acute ocular hypertension (AOH) and subsequent pathological changes of anterior segment in acute glaucoma remain unclear, preventing improvements in treatments. Our previous study has demonstrated that oxidative stress, senescence, and inflammation were involved in the anterior segment of acute glaucoma patients. This study aimed to explore the role of melatonin in oxidative stress, senescence, and inflammation induced by AOH in anterior segment and its underlying mechanisms.

Methods: A murine AOH model was used in this study. Melatonin, or sirtuin 1 (SIRT1) inhibitor with melatonin were administered by daily intraperitoneal injection to AOH mice. Pathological changes of the anterior segment were recorded by a slit-lamp microscope. Hematoxylin & eosin staining, and optical coherence tomography (OCT) were used to observe the changes of anterior segment structure. Immunofluorescence, western blot, and real-time PCR were performed to evaluate the protein expression level.

Results: Corneal edema, and dilated pupil were observed immediately after the establishment of AOH model, melatonin treatment significantly ameliorated corneal edema at Day 1, as reflected by reducing the central corneal thickness measured by OCT ($p<0.01$). Iris became thin and stiff in shape at Day 7, and melatonin treatment greatly relieved the morphological changes of iris. SIRT1 expression was decreased in cornea, iris, ciliary body, and anterior lens capsule after AOH injury, and increased after melatonin treatment ($p<0.001$). Meanwhile, SIRT1 inhibitor could counteract the effects of melatonin. In addition, the number of positive cells of oxidative stress markers (8-OHdG, γ-H2AX), senescence markers (p16, p21, p53), and inflammation markers (Iba-1, CD68) and related protein expression levels were dramatically increased in the anterior segment of AOH model, and the number of these positive cells and related protein expression levels were decreased after melatonin treatment ($p<0.05$). While inhibiting SIRT1 pathway could predominantly eliminate the effects of melatonin.

Conclusions: Collectively, melatonin ameliorated morphology of anterior segment and exerts anti-oxidative stress, anti-senescence, anti-inflammation effects via activation of SIRT1 pathway in anterior segment tissues of AOH.

CONTROL ID: 3707107

SUBMITTER (NAME ONLY): Christian Mardin

TITLE: Possible Impact of functional active GPCR-autoantibodies on retinal microcirculation in Long-COVID

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.Y. Mardin, F. Raith, T. Schroeder, R. Laemmer, B. Hohberger, Ophthalmology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|M. Lucio, Bioinformatics, Helmholtz Zentrum Munchen Deutsches Forschungszentrum fur Gesundheit und Umwelt, Neuherberg, Bayern, GERMANY|C. Szewczykowski, Ophthalmology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|G. Wallukat, Molecular Medicine, Max-Delbruck-Centrum fur Molekulare Medizin in der Helmholtz-Gemeinschaft, Buch, Berlin, GERMANY|J. Hoffmanns, Ophthalmology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|J. Schottenhamml, Pattern Recognition, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|

Commercial Relationships Disclosure: Christian Mardin: Commercial Relationship: Code N (No Commercial Relationship) | Marianna Lucio: Commercial Relationship: Code N (No Commercial Relationship) | Gerd Wallukat: Commercial Relationship(s);Code O (Owner):Berlin Cures | Charlotte Szewczykowski: Commercial Relationship: Code N (No Commercial Relationship) | Jacob Hoffmanns: Commercial Relationship: Code N (No Commercial Relationship) | Franziska Raith: Commercial Relationship: Code N (No Commercial Relationship) | Thora Schroeder: Commercial Relationship: Code N (No Commercial Relationship) | Julia Schottenhamml: Commercial Relationship: Code N (No Commercial Relationship) | Robert Laemmer: Commercial Relationship: Code N (No Commercial Relationship) | Bettina Hohberger: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Long-COVID is assumed to have an autoimmune component. As a seropositivity of functional active autoantibodies against G-protein coupled receptors (GPCR-AAb) and an impaired retinal microcirculation, measured by OCT-angiography (OCT-A), was observed after COVID-19 infection, it was the aim of the present study to investigate the impact of GPCR-AAbs on retinal microcirculation in patients with Long-COVID.

Methods: Seventy-six patients with Long-COVID (COVID-19 infection was confirmed by real time rt-PCR) were recruited. A seropositivity for GPCR-AAbs (Nociceptin-AAb, ß2-AAb, AT1-AAb, α1-AAb, MAS-AAb, M2-AAb, ETA-AAb) was analyzed by a specific rat cardiomyocyte bioassay in vitro. Macular (superficial vascular plexus (SVP), intermediate capillary plexus (ICP) and deep capillary plexus (DCP)) and peripapillary vessel density (VD) were measured by OCT-A (Spectralis II, Heidelberg, Germany). VD analysis was done by the Erlangen-Angio tool, including an APSifyed and Bruch's membrane opening (BMO) based analysis. Data were analyzed by mixed model (SAS version 9.4). Gender and age were set as covariates. The study was approved by the local ethics committee and was done in accordance with the tenets of the Declaration of Helsinki. Informed consent was achieved.

Results: All patients with Long-COVID showed a seropositivity for GPCR-AAbs (100%). Female patients with Long-COVID showed lower macular and peripapillary VD compared to men. A significant effect of a seropositivity of AT1-AAb on age-corrected least squares means (LS-means) overall VD of DCP ([CI: 0,25; 6.07], p=0.03). A seropositivity of α1-AAb showed a significant effect on age-corrected LS-mean overall VD of SVP ([CI: 0.07; 2.69], p=0.04), of DCP ([CI: 0.36; 3.25], p=0.01), and of PH ([CI: 1.17; 5.59], p=0.01), respectively. A seropositivity of MAS-AAb yielded a significant effect on age-corrected LS-mean overall VD of DH (CI: 1.48; 6.07, p=0.001). A seropositivity of ß2-AAb has a significant effect on age-corrected LS-mean overall VD of MH (CI: 0,02; 1,94, p=0.04). For those effects, the covariate age was significant in the type III tests ($p<0.05$), thus analysis was done considering this age-effect.

Conclusions: As autoimmune mechanisms were reported to be involved in the pathogenesis of Long-COVID, we postulate that functional active GPCR-AAb may have an impact on retinal microcirculation, being a propable correlate to systemic disease.

CONTROL ID: 3707109

SUBMITTER (NAME ONLY): Eiji Murotani

TITLE: Modeling the frequency-of-seeing curves in patients with glaucoma as a weighted sum of typical psychometric functions

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Murotani, Kahoku Eye Clinic, JAPAN|

Commercial Relationships Disclosure: Eiji Murotani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To demonstrate computationally that the frequency-of-seeing (FOS) curves in patients with glaucoma can be modeled as a weighted sum of typical psychometric functions.

Methods: The author prepared a set of psychometric functions that represent each threshold from <0 to 40dB, using zero function (<0dB) and cumulative gaussian function with the same slope (0~40dB) (Fig. 1A). Then, a weighted sum of these functions was calculated based on the following weights assigned to each threshold: λ ($0<\lambda<1$) for <0dB, $(1-\lambda)\varphi(\mu, \sigma)$ for 0~40dB, where $\varphi(\mu, \sigma)$ is the gaussian density function with mean μ and standard deviation σ (Fig. 1B).

Results: The weighted sum resulted in a flat and shallow sigmoid curve, which was similar to the FOS curves at regions with glaucomatous damage (Fig. 1C). The decrease in maximum response probability corresponded to λ, and the steepness of slope was linked to σ. Furthermore, the luminance of inflection point agreed with μ.

Conclusions: This result raises the possibility that a single FOS curve in patients with glaucoma may consist of multiple psychometric functions.

CONTROL ID: 3707112

SUBMITTER (NAME ONLY): Zhengping Hu

TITLE: Endomucin deletion delays retinal vascular development and inhibits neovascularization in oxygen-induced retinopathy

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Hu, I. Cano, M. Saint-Geniez, Y. Ng, P.A. D'Amore, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Z. Hu, M. Saint-Geniez, Y. Ng, P.A. D'Amore, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Zhengping Hu: Commercial Relationship: Code N (No Commercial Relationship) | Issahy Cano: Commercial Relationship: Code N (No Commercial Relationship) | Magali Saint-Geniez: Commercial Relationship: Code N (No Commercial Relationship) | Yin Shan Eric Ng: Commercial Relationship(s);Code O (Owner):Sayht Therapeutics, LLC | Patricia D'Amore: Commercial Relationship(s);Code O (Owner):Sayht Therapeutics, LLC

ABSTRACT BODY:

Purpose: Endomucin (EMCN) is a type I integral membrane glycoprotein selectively expressed by venous and capillary endothelium. We have previously shown that EMCN knockdown in vitro significantly inhibits VEGF165-induced VEGFR2 internalization and downstream activities including proliferation, migration and tube formation. The goal of this study is to characterize the role of EMCN in normal retinal vascular development and in pathologic neovascularization using the EMCN knock-out mice.

Methods: Homozygous EMCN knock-out ($EMCN^{-/-}$) mice were obtained by crossing EMCN-floxed mice with the ROSA26-Cre strain. Eyes from adult (8-16 weeks) $EMCN^{-/-}$ mice and $EMCN^{+/+}$ control littermates were collected and retinas and RPE/choroids complex were dissected for RNA extraction, and qPCR to determine gene expression. Eyes from P5 mice and adult mice (12-16 weeks) were collected for retinal flat mounts; retinal vasculature was stained with Isolectin-B4 (IB4). For the oxygen-induced retinopathy (OIR) model, P7 mice were housed in 75% oxygen for five consecutive days and returned to room air at P12, eyes at P12 and P17 were collected and the retinal vasculature was stained with IB4 and the avascular and neovascular areas were quantified using photoshop.

Results: EMCN mRNA in both retinas and RPE/choroids from the $EMCN^{-/-}$ mice was undetectable ($n>4$, $p<0.0001$), compared to $EMCN^{+/+}$ mice by qPCR. The area of retinal vascularization at P5 was significantly lower in the $EMCN^{-/-}$ pups compared to $EMCN^{+/+}$ controls (0.14±0.01 vs 0.2±0.013, $p<0.0001$, $n>10$ for both groups). Adult retinal vascular density remained lower in the $EMCN^{-/-}$ mice compared to $EMCN^{+/+}$ mice (0.135 0.015± vs 0.154±0.017, $p<0.05$, $n= 13$). In the OIR model, the avascular area generated by high oxygen exposure at P12 was similar in the $EMCN^{-/-}$ and $EMCN^{+/+}$ mice (24.57±1.4% vs 23.18±1.0%, $p=0.9$, $n>6$). However, pathological neovascularization at P17 was significantly reduced in the $EMCN^{-/-}$ mice compared to $EMCN^{+/+}$ (8.98 ± 2.9% vs 11.98±1.4%, $p<0.05$, $n>10$) while the avascular area at P17 was comparable between the $EMCN^{-/-}$ and controls (9.9± 1.5% vs 8.85±1.0%, $p>0.5$, $n>10$).

Conclusions: Genetic ablation of the EMCN gene reduces retinal vascularization under normal and pathological conditions. As a critical regulator of retinal angiogenesis, EMCN represents a novel therapeutic target for ocular diseases characterized by pathological blood vessel growth.

CONTROL ID: 3707113

SUBMITTER (NAME ONLY): Rajkumar Nallour Raveendran

TITLE: Assessment of retinal rods and cones function using mesopic full-field stimulus threshold – a preliminary report

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Nallour Raveendran, R.A. Schuchard, Envision Research Institute, Wichita, Kansas, UNITED STATES|J. Farmer, Diagnosys LLC, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Rajkumar Nallour Raveendran: Commercial Relationship: Code N (No Commercial Relationship) | Jeff Farmer: Commercial Relationship(s);Code E (Employment):Diagnosys LLC | Ronald Schuchard: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The main objective of this preliminary study is to test a protocol of mesopic full-field stimulus threshold (mFST) to assess rod and cone function in controls and individuals with retinitis pigmentosa (RP). Typically, in scotopic background (BG), thresholds for blue and red FST are distinct, and are used to assess the function of rods and cones, respectively. But it requires pupil dilation and dark adaptation for at least 30min. We hypothesized that distinct thresholds for blue and red FSTs can be achieved by performing mFST without either pupil dilation or dark adaptation.

Methods: mFST at 0.1cd/m^2 white BG luminance was measured (ColorDome, Diagnosys LLC) in controls (n=21) and individuals with RP (n=11). In addition, mFST at 1cd/m^2 BG luminance was also measured in 10 controls. After adapting to a room light level for at least 10min, FST in two different wavelengths; blue (448nm) and red (627nm) were measured in a dark room. For each wavelength (λ), FST of one eye, with the other occluded, was measured and the test was repeated three times. The results were analyzed using ANOVA and Tukey HSD.

Results: In controls, there was a significant main effect of BG [$F(1, 10)=257.94$, $p<0.001$], λ [$F(1, 10)=561.88$, $p<0.001$] on mFST measured thresholds. Moreover, threshold difference between blue and red mFST using 0.1cd/m^2 BG (0.95 log cds/m^2) was significantly larger compared to 1cd/m^2 (0.22 log cds/m^2) BG luminance ($p<0.001$). This suggested that mFST at 0.1cd/m^2 has more distinct blue and red mFST thresholds. On comparing individuals with RP and controls, there was a significant main effect of groups [RP vs. controls: $F(1, 19)=18.58$, $p<0.001$]. Individuals with RP had significantly worse thresholds overall compared to controls [blue mFST ($p<0.001$) and red mFST ($p<0.001$)]. In addition, threshold difference between blue and red FST in 0.1cd/m^2 BG luminance in RP (0.47 log cds/m^2) was significantly less than the threshold difference noted in control participants ($p<0.001$).

Conclusions: mFST at 0.1cd/m^2 BG luminance can be used to assess the functions of rods and cones without pupil dilation and dark adaptation. In the future, associations between mFST and other measures such as dark adaptation, low luminance visual acuity and contrast sensitivity should be evaluated for some unique information to consider mFST as an outcome measure in clinical trials and for clinical use.

CONTROL ID: 3707116

SUBMITTER (NAME ONLY): Dan Ye

TITLE: Anti-PANoptosis Is Involved in Neuroprotective Effects of Melatonin in Acute Ocular Hypertension Model

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Ye, Y. Xu, J. Huang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Dan Ye: Commercial Relationship: Code N (No Commercial Relationship) | Yue Xu: Commercial Relationship: Code N (No Commercial Relationship) | Jingjing Huang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Approved effective therapy is still lacking in acute glaucoma. PANoptosis, which is consist of three key modes of programmed cell death—pyroptosis, apoptosis, and necroptosis, may contribute to acute ocular hypertension (AOH)-induced retinal ganglion cell (RGC) death. Previous study has demonstrated that melatonin exerted neuroprotective effects in many retinal degenerative diseases. This study aimed to explore the role of melatonin in PANoptosis after AOH injury, and its underlying mechanisms.

Methods: A murine AOH model was used in this study. Melatonin or the equal volume of saline containing 0.5% ethanol were administered by daily intraperitoneal injection to AOH mice. Hematoxylin & eosin staining, and optical coherence tomography were used to observe the changes of retinal structure. Electroretinogram was used to detect changes in visual function. TUNEL assay and PI assay were used to detect the apoptotic and necrotic cells. Immunofluorescence, western blot and real-time PCR were performed to evaluate the localization and quantitative changes of protein.

Results: Melatonin treatment attenuated the losses of ganglion cell complex thickness, retinal nerve fiber layer thicknesses (both $p<0.05$) and RGCs ($p<0.001$). Meanwhile, melatonin improved the amplitudes of a-wave, b-wave, and oscillatory potentials in the electroretinogram ($p<0.0001$, 0.01, 0.05, respectively). Additionally, melatonin remarkably reduced high IOP-induced RGCs apoptosis by decreasing the number of TUNEL-positive cells and inhibiting the upregulation of cleaved caspase-3, Bax, cleaved caspase-8, p-Bad and downregulation of Bcl-2 induced by AOH injury ($p<0.05$). Moreover, melatonin attenuated high IOP-induced necroptosis in RGCs and microglia, as demonstrated by a diminishing expression of MLKL, RIP1, and RIP3, along with a decline of PI-, RIP3- and p-RIP3-positive cells in RGCs and microglia of melatonin-treated mice ($p<0.05$). Furthermore, melatonin reduced expression of NLRP3, ASC, cleaved caspase-1, GSDMD, and cleaved GSDMD, and decreased the positive cells of Iba-1, and IL-1β in microglia of melatonin-treated mice ($p<0.05$), which means attenuated high IOP-induced pyroptosis and retinal inflammation in microglia.

Conclusions: Collectively, melatonin ameliorated retinal morphology and prevented retinal dysfunction after AOH and exerts neuroprotective effects via inhibition of PANoptosis in AOH retinas.

CONTROL ID: 3707120

SUBMITTER (NAME ONLY): Eileen Birch

TITLE: Monocular visual acuity does not accurately represent function of the amblyopic eye during binocular viewing

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.E. Birch, R.M. Jost, L.A. Hudgins, S.E. Morale, M. Donohoe, Pediatric Vision Laboratory, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|E.E. Birch, K.R. Kelly, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|K.R. Kelly, Vision & Neurodevelopment Laboratory, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Eileen Birch: Commercial Relationship: Code N (No Commercial Relationship) | Reed Jost: Commercial Relationship: Code N (No Commercial Relationship) | Lindsey Hudgins: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Morale: Commercial Relationship: Code N (No Commercial Relationship) | Matt Donohoe: Commercial Relationship: Code N (No Commercial Relationship) | Krista Kelly: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Standard-of care assessment for children with amblyopia includes measuring best-corrected monocular visual acuity (BCVA), with the non-viewing eye occluded. Yet, when visual input from the fellow eye is occluded, the central suppression scotoma that is fundamental to amblyopia may have reduced impact on amblyopic eye (AE) BCVA. As a result, AE BCVA measured with occlusion may not accurately represent AE function during natural binocular viewing. We compared AE BCVA with monocular versus binocular (dichoptic) viewing, and determined whether any differences under the two viewing conditions were associated with performance on tests of fixation instability, reading, and motor skills with natural binocular viewing.

Methods: AE BCVA of 50 children (6-12y) with amblyopia (monocular E-ETDRS AE BCVA: 0.2-0.5 logMAR) was tested under monocular and dichoptic viewing conditions with an Optec Vision Tester. In the monocular condition, 8 Sloan letters were presented to the amblyopic eye on each line. In the dichoptic condition, 4 letters were presented to the fellow eye, 4 letters to both eyes, and 4 letters to the amblyopic eye (8 letters to each eye). In both conditions, AE BCVA was defined as the smallest optotype size at which the child identified >75% of letters presented to the amblyopic eye. Fixation stability was calculated as the 68% bivariate contour ellipse for 20 sec binocular fixation, reading speed was determined with silent binocular reading of age appropriate passages using a Readalyzer, and motor skills were assessed with the Movement Assessment Battery for Children-2.

Results: 72% of children with amblyopia had better AE BCVA when tested in the monocular than dichoptic condition (mean difference+SE=0.12+0.02 logMAR), with 38% of children performing 2-4 lines better in the monocular condition. The difference between conditions was correlated with fixation instability of the amblyopic and fellow eyes (r=0.56 and 0.72, p<0.001), reading speed (r=-0.77, p<.0001), manual dexterity (r=-0.35, p=0.01), and aiming/catching skill (r=-0.41, p=0.01).

Conclusions: AE BCVA measured with occlusion may not accurately represent its function during natural binocular viewing. The difference between dichoptic and monocular AE BCVA is potentially a useful index of suppression, with moderate to strong associations with fixation stability, reading speed, and motor skills.

CONTROL ID: 3707122

SUBMITTER (NAME ONLY): Aindrila Saha

TITLE: Functional development of cone photoreceptors in human stem cell derived retinal organoids

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saha, R. Sinha, Neuroscience, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|D.M. Gamm, McPherson Eye Research Institute, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|A. Saha, Cellular and Molecular Biology Graduate Training Program, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|E. Capowski, M.A. Zepeda, E.C. Nelson, Waisman Center, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|D.M. Gamm, R. Sinha, Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Aindrila Saha: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Capowski: Commercial Relationship: Code N (No Commercial Relationship) | Maria Zepeda: Commercial Relationship: Code N (No Commercial Relationship) | Emma Nelson: Commercial Relationship: Code N (No Commercial Relationship) | David Gamm: Commercial Relationship(s);Code P (Patent):Opsis Therapeutics | Raunak Sinha: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Human stem cell derived retinal organoids (ROs) hold promise for therapy and understanding retinal diseases as well as for studying development of human retina in vitro. In fact, recent gene expression studies show that the developmental timeline in ROs closely matches that of human retina in vivo. During differentiation, ROs can be categorized into three distinct developmental stages. However, not much is known about the functional development of neurons in ROs including photoreceptors. Here, we assess in detail the light sensitivity and electrical properties of cones at distinct time points of RO development. In addition, we determine if lack of a defined retinal pigment epithelium (RPE) limits the availability of chromophore for cone function at different stages of RO development.

Methods: We used electrophysiology to record light responses from >500 cones across 8 distinct developmental time points from ROs (170-340 days in vitro). We treat ROs of different ages with 9 cis-retinal and compare cone light sensitivity with those in untreated ROs.

Results: At d170 (stage 2), we did not observe any light-evoked responses from cones in ROs. This is consistent with previous findings that the photoreceptors are not fully developed at stage 2 and may not have the required phototransduction machinery to elicit light responses. Cones in stage 3 ROs (>d200) exhibit light responses with peak sensitivity between d250-d260. Beyond d300, the fraction of light sensitive cones significantly decreases. Despite the differences in light sensitivity, membrane properties of cones remain comparable across different time points of RO development. Cone light responses also demonstrate adaptation at higher luminance like typical vertebrate cones. Addition of 9-cis retinal significantly improved cone light sensitivity across all time points of RO development probed in this study.

Conclusions: By assaying cone function at various stages of RO development, we identified d250-260 as the timepoint of peak cone sensitivity. The timeline of cone functional maturation suggests that cone phototransduction reaches its maximal sensitivity at later stages of fetal development continuing up to early stages of postnatal development, similar to human retina development in vivo. Our results further show that chromophore availability, most likely from the RPE, plays a significant role in cone light sensitivity in ROs during development.

CONTROL ID: 3707124

SUBMITTER (NAME ONLY): Alexander Shusko

TITLE: Comparison of Birdshot Lesions to Choroidal Lesions Identified on Enhanced-depth Imaging Optical Coherence Tomography in Eyes of individuals with Birdshot Chorioretinitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Sarraf, Retina Disease and Ophthalmic Genetics, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|A. Shusko, E. Tsui, G.N. Holland, Cornea and Uveitis, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Alexander Shusko: Commercial Relationship: Code N (No Commercial Relationship) | Edmund Tsui: Commercial Relationship: Code N (No Commercial Relationship) | David Sarraf: Commercial Relationship: Code N (No Commercial Relationship) | Gary Holland: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Choroidal lesions can be seen on enhanced depth imaging optical coherence tomography (EDI-OCT) of individuals with birdshot chorioretinitis (BSCR). Some clinicians have assumed that these choroidal lesions are the “birdshot (BS) lesions” seen on clinical exam. Studies have shown that choroidal lesions identified by EDI-OCT are related to certain features of BSCR, including vitreous inflammatory reactions and macular edema, while other studies have shown that the clinical characteristics of BS lesions are not related to the same disease features. We sought to determine whether there is a relationship between BS lesions seen on fundus photographs and choroidal lesions seen on EDI-OCT.

Methods: Using co-localization techniques, we compared BS lesions on color fundus photographs to choroidal lesions identified on EDI-OCT (Heidelberg Spectralis) of four eyes (two individuals) with BSCR. A choroidal lesion was defined as a homogenous hyporeflectivity that was present external to the Bruch membrane and internal to the choroidal-scleral border. Two investigators (GNH, ET) agreed on the borders of three random BS lesions for each eye, and outlined the lesions on the color photographs with ImageJ software. Three B-scans, equidistant from the borders of the BS lesions and from each other, were identified and evaluated by a third investigator (ARS) for underlying choroidal lesions. If choroidal lesions were present, the width of BS lesions and the width of underlying choroidal lesions were compared.

Results: Only 10 (83.3%) of 12 BS lesions had underlying choroidal lesions on one or more of the three scans. For only six (60%) of these 10 BS lesions were choroidal lesions identified on all three scans; choroidal lesions were identified on two of three scans for two lesions, and on one of three scans for two lesions. On all 24 EDI-OCT images with choroidal lesions, the width of the choroidal lesion was greater than the width of the overlying BS lesion on fundus photographs.

Conclusions: Clinically apparent BS lesions are not precise representations of choroidal lesions on EDI-OCT images. EDI-OCT may provide information for evaluation and monitoring of BSCR that cannot be derived from clinical examination alone. Study of additional lesion characteristics may identify how BS lesions are related to choroidal findings on EDI-OCT, if at all.

CONTROL ID: 3707128

SUBMITTER (NAME ONLY): Richard Braun

TITLE: Data and Analysis from Tear Breakup (TBU) in Normal Subjects

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.J. Braun, T.A. Driscoll, D. Sinopoli, J. Dorsch, C. Hammond, Dept of Mathematical Sciences, University of Delaware, Newark, Delaware, UNITED STATES|R.A. Luke, Dept of Applied Math and Statistics, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|C.G. Begley, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: A custom computer system was used to generate a large amount of data to estimate evaporation, osmosis, and different types of flow within regions of TBU in tear films (TF) for normal subjects. A convolutional neural network (CNN) automatically identified TBU and non-TBU in fluorescent (FL) images gathered in vivo. FL intensity data in those regions was extracted for fitting by three ordinary differential equations (ODE) models for TBU. Model parameters were optimized to best fit the FL data in order to identify the mechanisms active within TBU regions.

Methods: The FL intensity data was originally recorded from 25 normal subjects with 20 trials taken over two visits (Awisi-Gyau, Indiana University PhD thesis, 2020). We extract the experimental FL image data from the centers of TBU regions identified by the CNN. The data were fit with the ODE models using parameters representing evaporation rate (v), steady tangential flow (strain) rate (a), or decaying flow (b_1) with decay rate (b_2). A least squares minimization of the difference between experimental and computed intensities determined the parameters. Initial FL concentration and localized film thickness was estimated as in previous work (Wu et al IOVS 2015, 56:4211; Luke et al Bull Math Biol 2020, 82:71). All programs were custom using Python, Julia and/or Matlab.

Results: Extraction resulted in N=467 usable instances of TBU from 15 subjects. Evaporation rates fall near or within experimental ranges. Statistical distributions of thickness and osmolarity were computed for individual subjects and for the population. Findings include: (i) The population of normals exhibited a range of mechanisms active in TBU instances. (ii) Individual subjects exhibited different mechanisms in different instances of TBU, even within a single trial. (iii) Individual subjects could in some cases be distinguished from each other based on the distribution of parameters responsible for their TBUs (Fig 1). (iv) Osmolarity increases with increasing evaporation rate at less than a linear rate (Fig 2).

Conclusions: Intensity decay in TBU areas yielded new data on the mechanisms of TBU in many instances. Quantitative estimates for TBU parameters were variable within and between subjects. The data provides a valuable baseline for the mechanisms and spatial distribution of TBU in normal subjects.

CONTROL ID: 3707130

SUBMITTER (NAME ONLY): Caleb Shumway

TITLE: A Novel Suture Device for Anterior Segment Applications

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Shumway, N. Nataneli, M. Mayers, BronxCare Ophthalmology, Icahn School of Medicine at Mount Sinai, Bronx, New York, UNITED STATES|M. Wade, University of California Irvine, Irvine, California, UNITED STATES|J. Andrade, D. Buxton, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Suture breakage and suture degradation are challenges in many anterior segment surgical procedures when corneal sutures are used. We compared the standard of care corneal suture material (10-0 nylon) to a biocompatible novel material (metallic alloy) in an experimental ex-vivo comparison study using porcine eyes.

Methods: Each eye was prepared using an infusion line on a 27 gauge needle placed within the anterior chamber and the bottle height was adjusted to mimic the physiologic intraocular pressure (IOP). A full-thickness wound was created perpendicularly to the central cornea with a 3.2 mm blade to mimic a wound sustained by trauma. The surgeon used the suture material (either 10-0 nylon vs metallic alloy) to achieve closure via a simple interrupted technique on each of the test eyes. The bottle height was then raised to the maximum height, or until failure of the sutures (noted by a positive Seidel test using fluorescein test strip). The IOP at either failure or maximum was recorded.

A total of 7 eyes were tested, 4 of which were included for final statistical analysis. The remaining 3 eyes were excluded due to incomplete closure noted prior to stress testing. The mean IOP at failure was compared (10-0 nylon vs metallic alloy) and compared via Student's t-test.

Results: The mean IOP at baseline prior to stress testing was similar between the 10-0 Nylon vs metallic alloy at 21 mmHg vs 19 mmHg, respectively (with p value=0.2). The mean IOP at failure was also similar between the nylon and metallic alloy groups (86.5 mmHg vs 91 mmHg, respectively) with p value=0.5.

Conclusions: The novel metallic alloy suture device had similar closure efficacy compared to the 10-0 nylon in our study. Future applications for this suture are currently being explored.

CONTROL ID: 3707132
SUBMITTER (NAME ONLY): Sol La Bruna
TITLE: OCT Probability Change Maps for Detection of Early Glaucomatous Progression
SESSION TITLE: Structure-Function Relationship
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. La Bruna, E. Tsamis, D.C. Hood, Department of Psychology, Columbia University, New York, New York, UNITED STATES|A. Rai, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|E. Tsamis, A. Leshno, G. De Moraes, D.C. Hood, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: To develop retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) probability change maps (pc-map) obtained from optical coherence tomography (OCT) scans.

Methods: The study group consisted of 70 early glaucoma or glaucoma suspect (baseline 24-2 mean deviation >-6 dB) and 29 healthy (HC)] from 99 individuals from a longitudinal, prospective study. All eyes had 24-2 and 10-2 visual fields (VFs) and baseline OCT volume scans and follow-up scans at least 1 year from the baseline date (1.8 ± 0.3 yr; range: 1.3-3.4 yr.). The OCT scans were obtained on both Topcon (12x9 mm scan) and Heidelberg (30°x25° scan) instruments. The OCT pc-map (Fig. 1, bottom rows) of the RNFL and the GCL were generated by comparing the difference in thickness (Fig. 1, top rows) between an individual eye's baseline scan to the last follow-up against a short-term variability group (4 mos between scans), which consisted of 135 eyes (942 scans) for Topcon and 179 eyes (745 scan) for Heidelberg. A reference standard (RS) was employed to assess the diagnostic ability of these pc-maps. For the RS, we required an agreement in the region progressing based upon an evaluation of baseline and follow-up OCT and 24-2 and 10-2 VF tests. Based upon this RS, 10 eyes were classified as progressors (P). The pc-maps of the P and HC eyes were compared to identify patterns that distinguish real progression from artifacts.

Results: For Topcon, 8 of the 10 P eyes had abnormal arcuate regions characteristic of glaucoma on both the GCL and RNFL pc-maps (arrows in[HDC1] Fig. 1). In all 8, there was clear topographic agreement between the progression seen on the RNFL and GCL pc-maps. Of the 29 HCs, 4 (14%) had damage that resembled an arcuate on the RNFL pc-map (red arrows in Fig. 2[HDC2]). However, none of these 4 showed topographic consistent change on the GCL pc-map. Additionally, arcuates in P eyes were more temporal and curved towards fixation, while "arcuates" on HCs appeared straighter. The results for Heidelberg scans were similar. 8 out of the 10 P eyes had damage resembling an arcuate with topographic agreement on the RNFL and GCL pc-maps. Only 1 HC had arcuate-like region, and it was not confirmed on the GCL pc-maps.

Conclusions: RNFL and GCL pc-maps for eyes with early glaucoma show topographically corresponding abnormal regions that reveals the location and extent of the region progressing.

CONTROL ID: 3707139

SUBMITTER (NAME ONLY): Katherine Lun

TITLE: Comparison Between Swept-Source and Spectral-Domain Optical Coherence Tomography Angiography in Ocular Hypertension and Glaucoma

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Lun, C. Sng, National University Hospital, Singapore, Singapore, SINGAPORE|L. Schmetterer, J. Chua, Singapore Eye Research Institute, Singapore, SINGAPORE|B. Tan, School of Chemical and Biochemical Engineering, Nanyang Technological University, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: We compared the macular choriocapillaris flow deficit density (FDD) using swept-source (SS) and spectral-domain (SD) optical coherence tomography angiography (OCTA) in healthy participants (normal controls; n=104), individuals having ocular hypertension (OHT; n=41), and primary open-angle glaucoma (POAG; n=112).

Methods: In this prospective cross-sectional study, subjects underwent 3x3 mm^2 imaging using both SS-OCTA (Plex Elite 9000) and SD-OCTA (Cirrus AngioPlex). Choriocapillaris OCTA images were extracted from the respective devices' built-in review software and were subsequently loaded into a customized algorithm that evaluted the choriocapillaris FDD.

Results: When using SS-OCTA, older age was independently associated with higher choriocapillaris FDD (all $P \leq 0.026$), after adjusting for confounders. Specifically, the oldest group (70-82 years old) had 1.11% (95% CI = 0.50 to 1.72; $P < 0.001$) more choriocapillaris FDD compared to the youngest group (24-44 years old). In addition, OHT patients had 0.86% (95% CI = 0.10 to 1.62; $P = 0.026$) more choriocapillaris FDD than normal controls, while it did not reach statistical significance for POAG ($\beta = -0.78$, 95% CI = -1.65 to 0.062; $P = 0.08$). In eyes imaged with SD-OCTA, choriocapillaris FDD was not associated with either age or eye disease.

Conclusions: Imaging with SS-OCTA showed higher choriocapillaris FDD in older patients and patients with OHT when compared with normal subjects, and this was not seen when imaged with SD-OCTA.

CONTROL ID: 3707142

SUBMITTER (NAME ONLY): thibaut Chapron

TITLE: Preterm birth and ophthalmological impairments at $5^{1/2}$ years: EPIPAGE-2 cohort study.

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Chapron, V. Pierrat, M. Letouzey, V. Benhamou, L. Marchand-Martin, P. Ancel, H. Torchin, Obstetrical Perinatal and Pediatric Epidemiology Research Team, EPOPé, INSERM, INRAE, University of Paris, CRESS, Paris, FRANCE|T. Chapron, G. Caputo, A. Barjol, Pediatric ophthalmology department, Rothschild Foundation Hospital, FRANCE|V. Pierrat, Centre Hospitalier Universitaire de Lille Service de Reanimation pediatrique, Loos, Hauts-de-France, FRANCE|M. Letouzey, Department of neonatal medicine, Poissy Saint Germain Hospital, FRANCE|E. Kermorvant, Department of Neonatal medicine, Institut Necker-Enfants Malades, Paris, Île-de-France, FRANCE|G. Le Meur, Clinique ophtalmologique, Nantes CHU, FRANCE|H. Torchin, Department of Neonatal Medicine, Cochin-Port Royal Hospital, FRANCE|

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ABSTRACT BODY:

Purpose: To report prevalence of visual-sensory and oculo-motor impairments at age 5½ among children born preterm.

Methods: Date were extracted from the population based cohort study, EPIPAGE-2 which include preterm born children in France in 2011. At age $5^{1/2}$, 4441 children born at 24-34 Weeks' Gestation (WG) survivied. We included also a sample of 592 term-born children from the cohort ELFE as reference group. All patients were invited to assess complete medical examination in one of the 110 centers specially opened for the assessment.

We reported prevalence of refractive errors, strabismus, amblyopia, nystagmus and binocular visual acuities. Prevalence are reported after multiple imputation for missing data and sub-group analysis on Cerebral Palsy and history of Retinopathy Of Prematurity were performed.

Results: Among 4441 children, 2718 (weighted-percentage 58.7%) were clinically assessed. Refractive errors were reported in 43.1% (95% confidence interval 37.6-48.4), 35.2% (32.7-37.6) and 28.4% (25.0-31.8) of children born at 24-26, 27-31, 32-34 WG, respectively. Strabismus was reported in respectively 19.5% (14.6-24.4), 14.8% (12.9-16.7), 8.3% (6.2-10.4). Both impairments presented a significant increase of prevalence while GA decrease ($p<.001$). Among term-born children, refractive errors prevalence was 24.1% (19.1-29.7) and strabismus prevalence was 2.8% (1.0-5.3). Severe/moderate visual deficiencies (<3.2/10) were present in 1.7% (0.2-3.3) of 24-26WG and in less than 1% for other groups. A 10/10 binocular visual acuity was measured for 28.6% (24.0-33.3) of 24-26WG, 35.1% (32.8-37.4) of 27-31WG and 36.0% (32.5-39.5) of 32-34WG Versus 59.7% (53.9-65.4) of reference group. Presence of a Cerebral Palsy at $5^{1/2}$ had a stronger association with visual deficiencies and sub-optimal visual acuity than ROP during neonatal period.

Conclusions: We report in a large cohort of preterm born children high prevalence of refractive errors and strabismus even in children born very and moderate preterm supporting a specific attention for these children. Low prevalence of 10/10 visual acuity, even with glasses, at the age of reading and writing acquisitions could represent an additional challenge.

CONTROL ID: 3707145

SUBMITTER (NAME ONLY): Jon Hammer

TITLE: Comparison of peripheral visual field defects on static and kinetic visual field testing in Asian versus Caucasian subjects

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Hammer, S. Jamali Dogahe, S. Sadegh Mousavi, C. Khanna, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare peripheral visual field testing in Asian vs. Caucasian subjects without ocular pathology

Methods: Subjects with no identifiable ocular pathology and normal optical coherence tomography tests were included. A previously validated three-dimensional facial reconstruction model was used to predict peripheral visual field defects. Static 60-4 Humphrey visual field testing and kinetic visual field testing were performed, and results were compared between the Asian and Caucasian groups.

Results: Thirty-four eyes from 17 healthy subjects were enrolled including 12 Asians of Chinese descent (5 males, 7 females) and 5 Caucasians (2 males, 3 females). On kinetic visual field testing, the Asian group had significantly increased mean nasal (62.7 vs 57.2 degrees OD, p=0.02; 62.3 vs 55.2 degrees OS, p=0.005), and inferonasal (59.3 vs 52.4 degrees OD, p=0.02; 60.7 vs 55.6 degrees OS, p=0.01) peripheral field of vision compared to the Caucasian group in both right and left eyes. No significant difference was noted temporally and inferotemporally between the two groups. On static 60-4 testing, the Asian group had higher mean inferonasal quadrant threshold values that did not reach statistical significance (443 vs 380 dB OD, p=0.07; 431 vs 385 dB OS, p=0.18) while the inferotemporal quadrant threshold values were very similar between the two groups (504 vs 508 dB OD, p=0.66; 506 vs 511 dB OS, p=0.71).

Conclusions: Caucasian subjects in this study had a reduction in nasal field compared to Asian control patients, likely due to differences in facial contour, specifically a more prominent nasal contour in Caucasian subjects. This difference in facial contour among races may be relevant in development of normative 60-4 data.

CONTROL ID: 3707146

SUBMITTER (NAME ONLY): Angela Gupta

TITLE: Correction of accommodative and non-strabismic binocular visual dysfunction in the treatment of multifactorial dry eye disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Gupta, B.J. Nguyen, V.Y. Bunya, M. Massaro-Giordano, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|D. Zhu, Department of Epidemiology and Biostatistics, Temple University, Philadelphia, Pennsylvania, UNITED STATES|L. Lehman, VisualEyes Optique, Malvern, Pennsylvania, UNITED STATES|J. Zyrina, Pine Vision Care, Philadelphia, Pennsylvania, UNITED STATES|M. Richard, Spectrum Vision Care, Chalfont, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this retrospective study was to determine if correction of non-strabismic binocular visual dysfunction using the Neurolens® system improves symptoms of patients with multifactorial dry eye disease.

Methods: The Neurolens® system measures eye misalignments as small as 0.1 prism diopters using an electronic eye tracking system, and accordingly fits patients with customizable prescription lenses with a specialized contoured prism. A retrospective review was conducted on all patients treated in the Scheie Eye Institute Dry Eye Clinic at the University of Pennsylvania who were also prescribed lenses using the Neurolens® system. Patients held the diagnosis of multifactorial dry eye disease including meibomian gland dysfunction, tear film insufficiency, and/or Sjogren's disease. All patients also received ongoing traditional treatments for dry eye. Data including patient age, sex, visual acuity, clinical exam findings, and symptoms evaluated by the Ocular Surface Disease Index (OSDI) was collected before and after prescription of the lenses.

Results: Thirteen patients were included in the study, and 14 were excluded due to lack of follow up. The average age of patients was 53.5 years old (SD 16.7). 85% of patients were female and 15% male. The average follow up time was 6.3 months (SD 2.63). There was no significant change in visual acuity on follow up (p=0.46). When asked if they felt if the lenses improved their symptoms, 9 out of 13 (69%) of patients reported improvement after prescription of Neurolens®. This was also evidenced by a statistically significant decrease in average OSDI score from baseline to follow-up after prescription of lenses (47.2 vs 38.0, p=0.03). There was no significant difference in conjunctival or corneal staining on slit lamp examination on follow up (p=0.34).

Conclusions: We conclude that correction of non-strabismic binocular visual dysfunction in patients with multifactorial dry eye disease, along with traditional dry eye treatment modalities, results in a statistically significant decrease in OSDI scores. Improvement in OSDI scores without change in conjunctival or corneal staining suggests that correction of misalignment, rather than any modulation of the ocular surface with additional treatments, improved symptoms. This study helps provide supporting evidence for an innovative non-invasive treatment for dry eye patients.

CONTROL ID: 3707149

SUBMITTER (NAME ONLY): Chase Miller

TITLE: Evaluation of the Mean Treatment Intervals for Various Anti-Vegf Injections in the Treatment of Diabetic Retinopathy

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Miller, D.I. Marino, H. Sciulli, C. McCrossin, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Chase Miller: Commercial Relationship: Code N (No Commercial Relationship) | Domenica Marino: Commercial Relationship: Code N (No Commercial Relationship) | Harrison Sciulli: Commercial Relationship: Code N (No Commercial Relationship) | Christina McCrossin: Commercial Relationship: Code N (No Commercial Relationship) | David Miller: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To calculate and compare the average interval between injections of Aflibercept (AFL), Bevacizumab (BEVA), and Ranibizumab (RAN) for patients with diabetic retinopathy (DR).

Methods: A retrospective cohort study was performed at a private retinal practice in Ohio. The Institutional Review Board (Sterling) determined this study consisted of non-human subjects. All data was collected through the practice management of Retina Associates of Cleveland, Inc. Data was collected from patients who received injections of AFL, BEVA, and RAN from July 2020 through June 2021 and includes: patient number, injection service dates, anti-vegf drug injected, procedure codes, and primary diagnoses. The patients were limited to those injected unilaterally and diagnosed with DR, and the number of days between injection service dates was calculated for each injection. The data set was then organized by primary diagnosis and injection type, and the average number of days between injection service dates was determined for DR and each corresponding drug. Statistical analysis included calculating the average interval in days between injections for each medication, standard deviation, and two tailed t-test for comparison between medications.

Results: From July 2020 through June 2021, 14,911 injections were placed unilaterally for any diagnosis. There were 1,313 injections for DR with an average interval between injections of 70 days for all medications. Of the DR injections, the average interval was BEVA 69 days with standard deviation (SD) +/- 56 days, AFL 71 days SD +/- 53 days , and RAN 70 days SD +/- 63 days. In comparing the interval of BEVA versus AFL, the two-tailed t test yields a p value = 0.591; BEVA vs. RAN p = 0.886; AFL vs. RAN p= 0.961.

Conclusions: The results of the study suggest that AFL, RAN and BEVA seem to have similar interval of injections for DR.

CONTROL ID: 3707150

SUBMITTER (NAME ONLY): Laura Johnson

TITLE: Pigmented mouse with a tyrosinase mutation as a model for nystagmus

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Johnson, L.K. McLoon, Ophthalmology and Visual Sciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Laura Johnson: Commercial Relationship: Code N (No Commercial Relationship) | Linda McLoon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Infantile nystagmus syndrome (INS) is a gaze-holding disorder characterized by conjugate, uncontrolled oscillation of the eyes that can result in significant loss of visual acuity. However, a large number of INS patients have no known cause in the absence of known sensory afferent defects or previously identified genetic mutations. Using the albino mouse as a model for nystagmus, we tested the optokinetic nystagmus reflexes (OKN) of a mouse strain developed from C57BL6 mice with a mutation in the tyr gene making them phenotypically albino. We performed RNAseq on the extraocular muscles (EOM) and abducens (CN6) and oculomotor (CN3) neurons from B6(CG)-Tyr(c-2J)/J and C57BL6 mice in an attempt to discover molecular differences that may account for nystagmus.

Methods: OKN was measured in C57BL6 and the B6(CG)-Tyr(c-2J)/J mice using an iSCAN system. EOM, tibialis anterior (TA), neuronal populations from CN3 and CN6 isolated en block were dissected from the C57BL6 and B6(CG)-Tyr(c-2J)/J mouse strains. RNA was isolated using a Qiagen kit, and RNAseq analyses were performed. RNA expression levels were compared between the strains to determine genes that were over or under-expressed in the normal compared to the nystagmus mice. We validated candidate genes with a 2-fold difference using PCR and immunohistochemical staining of mouse and surgical waste tissues in children with INS.

Results: All the B6(CG)-Tyr(c-2J)/J mice tested had a nystagmus phenotype when measured with OKN, while the C57BL6 mice had normal OKN. Differential expression analysis from the RNA isolated from the B6(CG)-Tyr(c-2J)/J mice compared to the C57BL6 showed 286 genes differentially expressed in the EOM, 11 genes differentially expressed in the CNs, and 2 genes differentially expressed in all four tissue types: wdfy1 and nnt. Wdfy1 showed decreased immunostaining in rectus muscle samples from human nystagmus subjects compared to controls.

Conclusions: The B6(CG)-Tyr(c-2J)/J mice have nystagmus but, except for the mutation in the tyr gene, are genetically very similar to the C57BL6 mice. Wdfy1 and nnt have been implicated in mitochondrial dysfunction and in maintenance of stem cells in other systems, but their function in the extraocular muscles is unknown. These studies suggest that this mouse model of nystagmus makes them a prime candidate for studying differentially expressed genes between normal and nystagmus mouse groups.

CONTROL ID: 3707151

SUBMITTER (NAME ONLY): Annika Samuelson

TITLE: Clinical Outcomes of Patients with Endophthalmitis after Dexamethasone Intravitreal Implant

SESSION TITLE: Endophthalmitis & Trauma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To report a series of endophthalmitis cases associated with intravitreal dexamethasone implant injections in a single practice and discuss the clinic findings and visual outcomes associated with each case.

Methods: This retrospective consecutive case series identified all cases of endophthalmitis after intravitreal dexamethasone injection performed from January 1, 2014 to October 20, 2020 using the Wills Eye Hospital / MidAtlantic Retina billing record database. Each case was reviewed to confirm diagnosis of endophthalmitis, demographic and clinical information, and microbiology. Data was analyzed using Excel (Microsoft Excel, Redmond, Washington, USA).

Results: Five cases of endophthalmitis were identified from 3,925 intravitreal dexamethasone injections, resulting in an incidence of 0.13% (1 in 785 injections). Mean age was 82.3 years (range, 63 – 88 years) with a mean of 11.3 intravitreal dexamethasone injections performed (range, 2 – 30 injections) prior to developing endophthalmitis. Cases presented with endophthalmitis a mean (SD) of 3.6 (1.64) days after the causative injection. Three cases grew gram-positive organisms on culture, while the other two cases were culture negative. All five patients responded to a single intravitreal tap and injection of vancomycin and ceftazidime. Mean logMAR visual acuity was 0.44 (20/55) at the time of the causative injection, 2.22 (20/3319) at endophthalmitis presentation, 1.18 (20/303) at three month follow up, and 1.46 (20/577) at last recorded follow up.

Conclusions: Endophthalmitis following intravitreal steroid injections may occur more frequently than after other intravitreal injections. Endophthalmitis following intravitreal dexamethasone implant injection remains an uncommon event. Eyes responded to treatment with intravitreal antibiotics, however the visual outcomes are variable.

CONTROL ID: 3707152

SUBMITTER (NAME ONLY): Michael Morano

TITLE: Incidence and Risk Factors for Retinal Detachments and Tears after Cataract Surgery: An Analysis of the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight)

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the incidence and risk factors for rhegmatogenous retinal detachment (RRD) and retinal tears (RT) following cataract surgery.

Methods: Retrospective, cohort analysis of the IRIS Registry was performed. Eyes of patients aged 40 years or older undergoing cataract surgery from 2014-2017 were included. Eyes with history of RRD or RT were excluded. Incidence of RRD and RT, identified using relevant CPT codes, within one year after cataract surgery were the primary outcomes. Multivariable logistic regression was used to evaluate risk factors for RRD and RT after cataract surgery including demographic features (age, sex, race, ethnicity), ocular comorbidities (lattice degeneration, posterior vitreous detachment (PVD), high myopia), and intraoperative factors (hypermature cataract, pseudoexfoliation, floppy iris syndrome, complex surgery CPT code).

Results: Of 3,177,195 eligible eyes (1,983,712 patients), RRD and RT occurred in 6,690 (0.21%) and 5,489 (0.17%) within one year after cataract surgery. Logistic regression odds ratios (OR; 95% CI) showed increased risk of RRD (OR=3.12; 95% CI=2.96-3.28; P<0.001) and RT (OR=1.88; 95% CI=1.78-1.98; P<0.001) for males vs females. Risk was higher in younger patients compared to older patients (ages > 70 yrs), peaking at ages 40-50 yrs for RRD (OR=9.67; 95% CI=8.71-10.74; P<0.001) and ages 51-60 yrs for RT (OR=4.3; 95% CI=3.96-4.66; P<0.001). RRD and RT risk increased in eyes with lattice degeneration (OR=11.09; 95% CI=10.36-11.87; P<0.001 and OR=44.33; 95% CI=41.88-46.92; P<0.001), high myopia (OR=1.35; 95% CI=1.27-1.42; P<0.001 and OR=1.38; 95% CI=1.3-1.46; P<0.001), and eyes with PVD (OR=1.48; 95% CI=1.38-1.6; P<0.001 and OR=1.53; 95% CI=1.42-1.66; P<0.001). Complex surgery CPT code increased RRD risk (OR=1.33; 95% CI=1.23-1.45; P<0.001).

Conclusions: Analysis of the IRIS Registry revealed RRD and RT incidence are low (0.21% and 0.17%, respectively) within one year after cataract surgery. Lattice degeneration, younger age, male sex, PVD, and high myopia conveyed increased risk for RRD and RT. These low incidence rates and risk factors are consistent with prior studies supporting their validity. These data from a large, national database may aid in pre-operative counseling of prospective cataract surgery patients.

CONTROL ID: 3707155

SUBMITTER (NAME ONLY): Subashree Murugan

TITLE: Mapping the universe of Eph and ephrin transcripts in adult mouse lenses

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Murugan, C. Cheng, School of Optometry and Vision Science Program, Indiana University, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Subashree Murugan: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Cheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The Eph-ephrin bidirectional pathway involves receptor-ligand interaction to initiate intracellular signaling. Transmembrane Eph receptors are divided into two subclasses, EphAs (9 members, A1-8 and A10) and EphBs (5 members, B1-4 and B6), and the membrane-bound ephrin ligands are classified as ephrin-As (5 members, A1-5) and ephrin-Bs (3 members, B1-3). Mutations in EphA2 and ephrin-A5 have been associated with cataractogenesis in humans and mice. Genetic tests reveal that EphA2 and ephrin-A5 are not a receptor-ligand pair in lens epithelial cells, and thus, other isoforms of ephrins and Ephs must interact with EphA2 and ephrin-A5, respectively to maintain lens epithelial cell homeostasis. We determined which isoforms of Ephs and ephrins are expressed in adult mouse lenses.

Methods: Whole lens RNA samples from adult wild-type (WT), EphA2 knockout (KO), and ephrin-A5 KO mice were tested for the expression of different Eph and ephrin transcripts using reverse-transcription, qualitative PCR, and sequencing. Tissues, such as the brain, lungs, liver, that have previously been shown to express specific Eph or ephrin transcripts were used as positive controls. Primer pairs were designed for each Eph and ephrin isoform and known variant expressed in mouse tissues using the NCBI Primer-BLAST tool.

Results: We verified the presence of transcripts from 6 Eph receptors and 5 ephrin ligands in adult mouse whole lens RNA samples. In addition to EphA2, adult mouse lenses express EphA1, EphB2 (variant 2), EphB3, EphB4 (variant 2), and EphB6. In these samples, we also detected ephrin-A1 (variant 1), ephrin-A2, ephrin-A4, ephrin-A5 (variants 1 and 2), and ephrin-B1. EphA3-A8, EphA10, and EphB1 were detected in other positive control tissues, but not in whole lens WT or KO RNA samples. Ephrin-A3, ephrin-B2, and ephrin-B3 were also not detected in these lenses.

Conclusions: This data confirms that, in addition to EphA2 and ephrin-A5, other isoforms of Ephs and ephrins are also expressed in the adult mouse lens. It is highly likely that ephrin-A1 or -A4 interacts with EphA2 to organize equatorial epithelial cells into hexagonal cells aligned into meridional rows, and similarly, it’s possible that EphA1 interacts with ephrin-A5 to maintain the quiescence of the anterior epithelium. We are currently investigating the localization of these Eph and ephrin isoforms in the epithelial and fiber cell compartments of the lens.

CONTROL ID: 3707156

SUBMITTER (NAME ONLY): Tiffany Cheng

TITLE: Normative exophthalmometry values in Hispanic individuals

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Cheng, F. Wang, K. Denisova, A. Barmettler, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Orbital anthropometric values vary among ethnic groups. To date, no studies have established normative exophthalmometry values in individuals of Hispanic descent. The purpose of this prospective, observational study was to establish a set of exophthalmometry values and their correlates in the Hispanic population of the Bronx.

Methods:

Two hundred and thirty-eight Hispanic individuals ranging from 9 to 94 years of age recruited at Montefiore Medical Center outpatient clinics from January 2021 to December 2021 were included in the study. Demographic variables including age, sex, ethnicity/race, height, weight, and BMI were collected. The Hertel exophthalmometer was used to determine the degree of ocular prominence (exophthalmometry value, EV) and the inter-orbital distance (Hertel's base, IOD) in each patient. Differences in EV between sexes were evaluated using two sample t tests. Pearson's R was utilized for correlation determination. Multivariable linear regression was utilized to determine the effect of age, sex, and BMI on exophthalmometry values.

Results:

Of the 238 Hispanic patients included, 160 (67.2%) were female and the mean age was 61.1 years (SD=16.3). The mean Hertel's base for all participants was 92.0 mm (SD=4.1), 94.0 mm (SD=3.8) for men and 91.0 mm (SD=3.9) for women. The mean EV for all Hispanic individuals was 16.7 mm (SD=2.4). The mean EV for men was 17.5 mm (SD=2.6) and for women was 16.2 mm (SD=2.1). Exophthalmometry values for men were statistically significantly higher than women's ($p=0.0001$). EV was significantly associated with female sex ($\beta= -1.58$, $p<0.0001$) and BMI ($\beta= 0.091$, $p=0.001$), but not age.

Conclusions:

It is well-established that the degree of ocular prominence varies between ethnic groups. The mean EV in Hispanic individuals is 16.7 mm, higher than that of most Caucasians and Asians, but less than that of Black patients. EV was significantly associated with sex and BMI. This study is the first to create a set of normative exophthalmometry values in the Hispanic population, which may serve as a valuable tool for clinicians to reference when diagnosing and monitoring orbital disease.

CONTROL ID: 3707157

SUBMITTER (NAME ONLY): Margalit Mitzner

TITLE: Baseline Outer Retinal Layer Thickness is Associated with Response of Diabetic Macular Edema to Anti-VEGF Therapy

SESSION TITLE: Diabetic Macular Edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Mitzner, W. Fickweiler, D. Robinson, L.P. Aiello, J.K. Sun, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|M. Mitzner, W. Fickweiler, D. Robinson, T. Boumenna, Research Division, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|L.P. Aiello, J.K. Sun, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Margalit Mitzner: Commercial Relationship: Code N (No Commercial Relationship) | Ward Fickweiler: Commercial Relationship: Code N (No Commercial Relationship) | Devon Robinson: Commercial Relationship: Code N (No Commercial Relationship) | Tahani Boumenna: Commercial Relationship: Code N (No Commercial Relationship) | Lloyd Aiello: Commercial Relationship(s);Code C (Consultant/Contractor):KalVista, Novo Nordisk;Code O (Owner):KalVista | Jennifer Sun: Commercial Relationship(s);Code C (Consultant/Contractor):American Medical Association (JAMA Ophthalmology), American Diabetes Association ;Code F (Financial Support):Adaptive Sensory Technologies, Boehringer Ingelheim, Genentech/Roche, Janssen, Physical Sciences, Inc, Novartis, Novo Nordisk, Optovue

ABSTRACT BODY:

Purpose: This study evaluated the relationship between retinal thickness parameters and response to anti-VEGF therapy in patients with diabetic macular edema (DME).

Methods: Patients receiving their first anti-VEGF injection for DME between 1/2016-12/2019 with ≥6 months of follow-up were included. Mean change in logMAR equivalent visual acuity (VA) over 6 months was assessed. Thresholds for VA and central retinal thickness (RT) improvement (Table 1) categorized eyes as “good” (VA and RT response), “VA only” (VA response only), “RT only” (RT response only) or “poor” (neither VA nor RT response) responders. Poor responders that received <3 injections were excluded. Inner (IRL) and outer retinal layer (ORL) thickness on optical coherence tomography (OCT) was measured using automated segmentation software (Figure 1, Heidelberg V6.14, Germany).

Results: For the 126 subjects (151 eyes), mean±SD age was 60±13yrs, diabetes duration 22±11yrs, A1c 8.7±2.0%, 71.5% type 2 diabetes, and 46.4% female. Amongst the whole cohort, 57.0% of eyes met thresholds for VA response and 43.7% for RT response: 32.5% good responders, 21.9% VA only, 11.3% RT only and 34.4% poor responders. Improvement in mean VA was associated with younger age (β=.004; 95% CI 0.001-0.007; P=.01), but not with diabetes duration, diastolic or systolic blood pressure, A1c, lipids or baseline diabetic retinopathy severity (all P>.05). Less vision gain was associated with decreased ORL thickness (β=-.003; 95% CI -0.006 to -0.001; P=.01) and increased IRL thickness at baseline (β=.0004; 95% CI 0.0001-0.0007; P=.02). No baseline demographic characteristics were significantly associated with treatment response group. Baseline ORL, but not IRL, thickness was associated with treatment response group at 6 mo (β=-.018; 95% CI -0.03 to -0.01; P=.006). In general, decreased ORL thickness was more likely to be present in eyes with poorer response to anti-VEGF.

Conclusions: In this cohort of patients with DME, ORL thickness was correlated with mean VA gain and likelihood of both VA and RT improvement in response to anti-VEGF therapy. Decreased baseline ORL thickness was associated with less favorable anatomic and functional outcomes after anti-VEGF therapy. These data suggest that baseline outer retinal thickness in patients undergoing anti-VEGF treatment for DME might be a useful biomarker for treatment response.

CONTROL ID: 3707162

SUBMITTER (NAME ONLY): Sadia Islam

TITLE: Non-muscle myosin IIA regulates lens epithelial cell alignment during fiber cell differentiation

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.T. Islam, J. Parreno, V.M. Fowler, Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|C. Cheng, School of Optometry and Vision Science Program, Indiana University, Bloomington, Indiana, UNITED STATES|J. Parreno, V.M. Fowler, Molecular Medicine, Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lifelong transparency and focusing ability of the lens depends on the precise alignment of equatorial epithelial cells that differentiate into secondary fiber cells during lens development and morphogenesis. During this process, the equatorial epithelial cells transform from randomly packed cells into precisely aligned, hexagonally shaped meridional row cells that elongate to form the hexagonally packed, long fiber cells. Here, we investigate the function of Non-muscle Myosin IIA (NMIIA) (Myh9) in regulating equatorial epithelial cell alignment (meridional row cells) & fiber cell morphogenesis.

Methods: We used genetic knock-in mice to study two Myh9 mutations, R702C in the motor domain and E1841K in the rod domain. The R702C mutation impairs motor function and contractility, while the E1841K mutation disrupts bipolar filament assembly. Images of dissected lenses were acquired using a digital camera to check for cataracts. Lens equatorial cryosections and whole mounts were stained with fluorescent phalloidins (actin filaments; F-actin) and Hoechst (nuclei) and imaged by confocal microscopy to investigate the cellular organization.

Results: Neither mutation causes cataracts or opacities, and no major defects in cell organization are observed in R702C mutant mice. By contrast, the E1841K mutation results in disordered fiber cell packing in equatorial cryosections. Imaging of the equatorial epithelium and peripheral fiber cells in E1841K lenses also reveals meridional row misalignment, and peripheral fiber cell disorder, and variable widths. This indicates that epithelial cells with the E1841K mutation become misaligned during their initial rearrangement into meridional rows, with misalignment persisting during fiber cell elongation.

Conclusions: Disrupted bipolar filament assembly, due to the E1841K mutation, causes misaligned meridional row alignment and disordered fiber cells, while impaired force generation, due to the R702C mutation, does not. Since R702C can still exert tension by cross-linking F-actin, we propose that actomyosin organization, conferred by bipolar filaments' cross-linking F-actin, is important for cell tension and meridional row alignment. These results indicate a novel function of NMIIA in regulating the alignment of lens epithelial cells during their transformation into precisely aligned and hexagonally packed fiber cells.

CONTROL ID: 3707166

SUBMITTER (NAME ONLY): Xiaojing Huang

TITLE: Retinal Magnification Factor Derived from Individualized Four-Surface Schematic Eye using Real Ray Tracing

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Huang, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|X. Huang, A. Dubra, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The calculation of the retinal magnification factor (RMF) is a first step towards determining retinal feature sizes in units of length. This is particularly important for the creation of normative databases of adaptive optics (AO) ophthalmoscopy biomarkers, such as cell size, cell density, and vessel diameter. Accurate RMF calculation relies on the individualization of schematic eyes through the incorporation of ocular biometry data. Here we compare four paraxial schematic eyes commonly used in AO retinal imaging, against a new individualized schematic eye, in which each of its four surfaces is estimated from ocular biometry and the media between them is assumed to have homogeneous refractive indices.

Methods: The anterior and posterior surfaces of the cornea and crystalline lens were imaged with an ocular biometer (HP-OCT, Cylite, Notting Hill, Australia), and fitted to a linear combination of ANSI standard Zernike polynomials up to 10th order. Using the optical path length between each surface for each ray returned by the biometer, index-corrected surfaces were generated using real ray tracing. Real ray tracing through these surfaces was then used to calculate the RMF at the preferred retinal locus of fixation (PRL) in individualized four-surface schematic eyes.

Results: Across a sample of 23 eyes of 17 subjects and with spectacle prescription in the -5.5D to +1D, the comparison of the paraxial RMF calculations and the proposed RMF differ by us much as 5.0% (mean 1.5%). Importantly, the incorporation of decentering and tilt of the optical surfaces results in RMF changes with orientation that in our dataset are as large as 2.5%.

Conclusions: A novel RMF calculation method that uses four ocular surfaces estimated using optical biometry is demonstrated and tested in a small subject cohort. The method could be refined by incorporating the refractive index variations within the crystalline lens, whenever these can be experimentally measured in the intact living eye.

CONTROL ID: 3707169

SUBMITTER (NAME ONLY): Tianyu Liu

TITLE: Systematic Review and Meta-Analysis of Massive Suprachoroidal Hemorrhage

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Liu, Z. Tauqeer, Y. Yu, G. Ying, B.J. Kim, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|A.G. Elnahry, Ophthalmology, Cairo University, Giza City, Giza, EGYPT|

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ABSTRACT BODY:

Purpose: To review published peer-reviewed reports of massive suprachoroidal hemorrhage (MSCH) between 1990 and 2021.

Methods: We performed a systematic review and meta-analysis of published reports of MSCH, defined as ≥ 2 quadrant involvement, macular involvement, kissing, expulsive, or otherwise defined as “massive” by authors, published between January 1990 and May 2021. The search terms “suprachoroidal hemorrhage”, “choroidal hemorrhage”, “hemorrhagic choroidal detachment”, and “expulsive choroidal hemorrhage” were used to query PubMed, EMBASE, Web of Science, and Google Scholar, and studies with ≥ 3 patients with MSCH and ≥ 3 months follow up were included. Study- and patient-level data including demographics, risk factors, precipitating event, timing of hemorrhage, treatment, pre- and post-treatment best corrected visual acuity (BCVA), anatomic success, and complications were extracted and analyzed using OpenMeta[Analyst] software.

Results: Sixty-four studies including 1423 eyes of 1409 patients with mean (SD) age 62.4 (17.2) years were included. Precipitating event types included 1279/1412 (90.6%) perioperative, 90/1412 (6.3%), traumatic, and 41/1412 (2.9%) spontaneous. The mean (SD) number of quadrants involved was 3.8 (0.4), with 230/330 (71%, 95% CI 60-81%) macular involving, 312/622 (64%, 95% CI 52-76%) kissing, and 160/383 (40%, 95% CI 24-57%) expulsive. 655/1166 (64%, 95% CI 54-74%) eyes were treated surgically, with mean (SD) time until surgery of 9.5 (9.3) days. Patients were followed for mean (SD) 15.0 (9.4) months. Mean (SD) logMAR BCVA was 2.4 (0.3) pre-treatment and 1.6 (0.6) post-treatment. 176/268 (71%, 95% CI 61-80%) eyes achieved improvement in logMAR BCVA (Figure 1) and 136/223 (67%, 95% CI 55-78%) eyes achieved anatomic success (Figure 2) defined as attached macula at last follow up.

Conclusions: In this meta-analysis of published reports of MSCH, the majority of cases were perioperative, with many cases involving the macula, kissing choroidal detachments, or expulsive hemorrhage. Approximately two-thirds of eyes were treated surgically. A majority of eyes experienced some improvement in logMAR BCVA or anatomic success at last follow up, but vision remained limited. Predictors for BCVA improvement and anatomic success are the subject of ongoing analyses.

CONTROL ID: 3707171

SUBMITTER (NAME ONLY): Giulia Corradetti

TITLE: Automated Identification of Incomplete and Complete Retinal Epithelial Pigment and Outer Retinal Atrophy Using Machine Learning

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Corradetti, F. Corvi, M.G. nittala, S.R. Sadda, Doheny Eye Institute, Pasadena, California, UNITED STATES|G. Corradetti, S.R. Sadda, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|J.N. Chiang, A. Rudas, U. An, S. Sankararaman, E. Halperin, Computational Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|N. Rakocz, B. Durmus, A. Chiu, E. Halperin, Computer Science, University of California Los Angeles, Los Angeles, California, UNITED STATES|S. Sankararaman, Human Genetics, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: To assess and validate a deep learning algorithm to automatically detect incomplete retinal epithelial pigment and outer retina atrophy (iRORA) and complete retinal epithelial pigment and outer retina atrophy (cRORA) in eyes with age-related macular degeneration (AMD).

Methods: Methods: A Resnet18 model was trained to jointly classify the presence of iRORA and cRORA within a given B-scan. The training dataset consisted of OCT B-scans from patients with nonneovascular AMD captured at the Doheny-UCLA Eye Centers were annotated by an experienced grader for the presence of iRORA and/or cRORA: 101 OCT volumes (6,138 OCT B-scans) from subjects with diagnosis of intermediate/late AMD without evidence of macular neovascularization (MNV) and 87 OCT volumes (4,128 OCT B-scans) from 34 subjects with early and intermediate AMD without evidence of iRORA. The algorithm was validated on two separate and independent datasets.

Results: Results: Model performance was quantified in terms of area under the receiver operating characteristic curve (AUROC) and area under the precision-recall curve (AUPRC). On an independently collected test set consisting of 1117 volumes sampled from the general population, the model predicted iRORA and cRORA presence within the entire volume with nearly perfect AUROC performance, and AUPRC scores: iRORA: 0.61, 95% CI (0.45, 0.82), cRORA: 0.83, 95% CI (0.68, 0.95). On another independently collected set of 60 OCT B-scans, which was enriched for iRORA and cRORA lesions, the model performed with AUROC (iRORA: 0.68, 95% CI (0.54, 0.81); cRORA: 0.84, 95% CI (0.75, 0.94)) and AUPRC (iRORA: 0.70, 95% CI (0.55, 0.86); cRORA: 0.82, 95% CI (0.70, 0.93)).

Conclusions: Conclusions: A deep learning model can accurately and precisely identify both iRORA and cRORA lesions within a volume scan, despite the performance not being as good for any single OCT B-scan within volume. Notably, the model can achieve similar or better outcomes compared to human graders, thus potentially obviating a laborious and time-consuming annotation process.

CONTROL ID: 3707172

SUBMITTER (NAME ONLY): Inas Aboobakar

TITLE: A genetic risk score consisting of primary open angle glaucoma (POAG)-associated TXNRD2 and ME3 variants correlates with patient clinical phenotypes

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.F. Aboobakar, B. Fan, J.L. Wiggs, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T. Kinzy, J. Cooke Bailey, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|L.R. Pasquale, Mount Sinai Health System, Mount Sinai Health System, New York, NY, US, health/system, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mitochondrial genes TXNRD2 and ME3 are associated with POAG risk in genome-wide association studies (GWAS). These genes may functionally contribute to POAG by altering NADPH levels and oxidative stress response. To assess the impact of these variants, we investigated whether a genetic risk score (GRS) of TXNRD2 and ME3 variants correlates with patient clinical phenotypes.

Methods: 2617 POAG cases from the NEIGHBORHOOD consortium were included in this study. All single nucleotide polymorphisms (SNPs) in the TXNRD2 and ME3 loci associated with POAG ($p<0.05$) were identified using GWAS data. Of these, 20 TXNRD2 and 24 ME3 SNPs were selected for analysis after adjusting for linkage disequilibrium. After aligning alleles for risk, a GRS was constructed for each POAG case using the unweighted sum of POAG risk alleles; this was performed for TXNRD2 SNPs, ME3 SNPs, and TXNRD2+ME3 SNPs combined. The clinical features of individuals in the top 1, 5, 10 and 25% of genetic risk were compared to individuals in the bottom 1, 5, 10 and 25%, respectively. Clinical features examined included age at diagnosis, intraocular pressure (IOP), cup-to-disc ratio (CDR), visual field mean deviation (MD), incidence of paracentral field loss, and need for glaucoma surgery.

Results: Individuals in the top 1% of TXNRD2 GRS had higher mean maximal IOP compared to the bottom 1% (19.9 mmHg in top 1% vs 15.6 mmHg in bottom 1%, $p<0.05$). Individuals in the top 1% of ME3 and TXNRD2+ME3 GRS had greater incidence of paracentral visual field loss (72.7-89% in top 1% vs 14.3-33% in bottom 1%, $p<0.05$ for both). Individuals in the top 5% of ME3 and top 10% of TXNRD2+ME3 GRS had greater mean maximal CDR (0.83 in top 5/10% vs 0.80 in bottom 5/10%, $p<0.05$). There was a trend toward significance for age at diagnosis in the top 10% of TXNRD2+ME3 GRS (63.8 years in top 10% vs 65.6 years in bottom 10%, $p=0.053$).

Conclusions: POAG patients with higher GRS for TXNRD2 and ME3 variants have greater maximal IOP and CDR as well as greater incidence of paracentral field loss. These data suggest that TXNRD2 and ME3 functionally contribute to POAG development and disease severity, potentially through a mechanism that involves NADPH levels. Future prospective clinical studies and translational mechanistic studies will help enable precision medicine approaches to POAG risk stratification and treatment.

CONTROL ID: 3707179

SUBMITTER (NAME ONLY): Jennifer Seal

TITLE: Plasma pharmacokinetics of pilocarpine in participants administered VUITY^{TM} (pilocarpine HCl ophthalmic solution) 1.25%

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Seal, L.M. Borbridge, M. Attar, Allergan, an AbbVie Company, Irvine, California, UNITED STATES|D. Wirta, David Wirta, M.D. & Associates, Newport Beach, California, UNITED STATES|

Commercial Relationships Disclosure: Jennifer Seal: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Lisa Borbridge: Commercial Relationship(s);Code E (Employment):AbbVie Inc | David Wirta: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan (an AbbVie company), Eyenovia;Code F (Financial Support):Aerpio, Allergan (an AbbVie company), Annexon, Dompe, Eyenovia, Mallinckrodt, Nicox, Novaliq, Novartis, SilTech, Santen | Mayssa Attar: Commercial Relationship(s);Code E (Employment):AbbVie Inc

ABSTRACT BODY:

Purpose: Presbyopia is an age-related condition in which the eye exhibits a diminished ability to focus on near objects. VUITY^{TM} (pilocarpine HCl ophthalmic solution) 1.25% was recently approved in the US as the first and only prescription eye drop to treat presbyopia. The purpose of this study was to evaluate the systemic pharmacokinetics (PK) of pilocarpine following once daily administration of VUITY for 30 days.

Methods: Steady-state systemic PK of pilocarpine was assessed in 22 participants following bilateral, once-daily topical ocular administration of VUITY for 30 days. PK samples were collected on Day 1 at predose and on Day 30 at predose and 0.25, 0.5, 1, 3, 6, 8, and 10 hours postdose. Plasma concentrations of pilocarpine were quantified using a validated liquid-chromatography mass spectrometry (LC-MS/MS) method with an assay range of 25-5000 pg/mL and PK parameters were calculated using standard non-compartmental analysis methods.

Results: Pilocarpine was rapidly absorbed into systemic circulation with a median $T_{max,ss}$ of 0.334 hours. Plasma concentrations of pilocarpine were measurable in most participants up to 8 to 10 hours postdose. The systemic exposure at steady state was low with mean $C_{max,ss}$ and $AUC_{0\text{-}t,ss}$ of 1950 pg/mL and 4140 pg˙hr/mL, respectively. The mean $T_{1/2}$ following 30 days of dosing was 1.74 hours. For most participants, $C_{trough,ss}$ was below the assay LLOQ (< 25 pg/mL), indicating a lack of systemic accumulation of pilocarpine. Systemic exposure to pilocarpine following administration of VUITY for 30 days was lower than the exposure reported for other pilocarpine products available on the market. Mean plasma C_{max} and $AUC_{0\text{-}6hr}$ achieved with VUITY were approximately 2 times lower than steady-state exposure reported after topical ocular administration of 4% Isopto Carpine. C_{max} achieved with VUITY was 21 times lower than the exposure reported with oral use of 10 mg Salagen.

Conclusions: Systemic exposure in participants administered VUITY once daily for 30 days was low and rapidly cleared from the circulation. Plasma concentrations were lower than those reported for other pilocarpine products on the market.

CONTROL ID: 3707180

SUBMITTER (NAME ONLY): Hongli Yang

TITLE: Correlating longitudinal Optical Coherence Tomography (OCT) structural change to retrolaminar myelin-related protein alteration in non-human primate (NHP) early experimental glaucoma (EG)

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Yang, P. Chaudhary, J. Reynaud, S.K. Gardiner, G. Williams, I. Williams, C.F. Burgoyne, Discoveries in Sight, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|H. Yang, P. Chaudhary, J. Reynaud, G. Williams, I. Williams, C.F. Burgoyne, Optic Nerve Head Laboratory, Legacy Research Institute, Portland, Oregon, UNITED STATES|C. Stowell, Health Science, South College - Nashville Campus, Nashville, Tennessee, UNITED STATES|N. Marsh-Armstrong, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: OCT peripapillary retinal nerve fiber layer thickness (pRNFLT) change detection is a standard tool in the management of both human glaucoma and NHP unilateral EG. Here, using a novel approach for consistent anatomical comparisons, we employ quantitative immunohistochemistry (qIHC) to test the hypothesis that retrolaminar myelin-related protein expression alterations correlate to longitudinal OCT structural change in NHP early EG.

Methods: Data from n=4 unilateral early EG NHPs (<30% EG pRNFLT loss) were included. For each EG eye, longitudinal OCT pRNFLT change relative to baseline was quantified within 12 Fovea-BMO (FoBMO axis) 30° sectors (Fig 1). For each NHP, the optic nerve head (ONH) of the EG and Control (C) eye was trephined, (10 mm), 5 µm serial vertical paraffin sections were cut, their clinical location was anatomically estimated (Fig 1a), and n=4 adjacent sections were selected to represent similar FoBMO sectors in both eyes. Sections from all 4 NHPs were deparaffinized and stained with anti 2',3'-Cyclic-nucleotide 3'-phosphodiesterase, (CNPase, a myelin associated enzyme). Localized retrolaminar signal intensity in each section was quantified within the first 4 retrolaminar 50 µm bands of 12 anatomically consistent horizontal regions (Fig 1b). For each NHP, EG vs C eye differences in CNPase intensity within each region and EG vs C CNPase intensity % differences were correlated with longitudinal percent change in OCT pRNFLT in the same OCT sector (Fig 2) using a linear mixed effect model.

Results: CNPase intensity decreased significantly in EG versus C eyes in 26 of 48 qIHC regions where early OCT RNFLT loss had occurred ($p < 0.05$). pRNFLT % change and EG versus C CNPase % intensity difference in the same FoBMO 30° sector were correlated ($p=0.01$, linear mixed effect model, $R^2=0.46$, Fig 2b). EG eyes showed a 49% reduction in CNPase intensity at 0% pRNFLT change.

Conclusions: To our knowledge, this is the first attempt to anatomically link qIHC EG vs C protein expression differences to longitudinally detected OCT pRNFLT change in NHP early EG and demonstrate that myelin loss may occur before RNFLT loss. Linking protein expression change to OCT pRNFLT change may enhance the interpretation of OCT findings and inform our understanding of the pathophysiology of glaucoma.

CONTROL ID: 3707181
SUBMITTER (NAME ONLY): Katharina Foote
TITLE: Structure and function comparison of cup/disc ratio and perimetric mean deviations
SESSION TITLE: Structure-Function Relationship
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K.G. Foote, P. Sha, T. Pahlevan-Chaleshtari, G.C. Lee, T. Callan, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|I.A. Falkenstein, Glaucoma Specialists of San Francisco, Oakland, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|
Commercial Relationships Disclosure: Katharina Foote: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Patricia Sha: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Tara Pahlevan-Chaleshtari: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Iryna Falkenstein: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Todd Severin: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Gary Lee: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Thomas Callan: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc.

ABSTRACT BODY:

Purpose: Structural loss often precedes functional loss in cases of primary open-angle glaucoma, thus driving the importance of early detection and monitoring. While established correlations between structure and function in glaucomatous eyes have been studied in various modalities (particularly in traditional narrow field of view (FOV) cameras which assume a constant pixel to distance mapping), it is vital to establish these correlations in widefield (WF) cameras which are widely available, and have not yet been assessed.

Methods: A WF slit-scanning ophthalmoscope (CLARUS™ 500, ZEISS, Dublin, CA) and automated perimeter (HFA3 Model 860 perimeter, ZEISS, Dublin, CA) were used to acquire color fundus photography images and perimetric data respectively. Both healthy (10 eyes, avg. age 56.4 ± 8.9, 44.3 – 73.1 years) and glaucomatous (14 eyes, avg. age 72.5 ± 9.3, 60.9 – 97.9 years) subjects were used as part of a retrospective analysis. Mean deviation (MD) from 24-2 SITA Standard (SS) visual fields (VFs) (extracted from 24-2C) were used to assess global function. Due to the use of a 90° FOV camera, the constant distance assumptions on narrow FOV cameras are not held. The automated measurements with manual annotations are tracked internally. Cup to disc ratios (CDR) from three independent/blind graders were computed and averaged from manual annotations using the default caliper measurement tool in CLARUS software to annotate horizonal and vertical cup and disc lengths; both ratios (hCDR and vCDR) were compared to 24-2 MDs using Spearman correlations.

Results: Structure/functional correlations were observed for both hCDR (ρ = -0.46) and vCDR (ρ = -0.61) measurements as compared with 24-2 MDs. In Fig 1, glaucomatous eyes prove less consistent as compared with normals. Consistent with literature, this study showed CDRs using the standard measurement tool in CLARUS are larger in glaucomatous eyes.

Conclusions: This study demonstrated a capability of providing structure/function comparisons using a WF fundus imager and perimeter. This measurement technique could be useful for enhancing research in the field of glaucoma. The study also confirms the trend that in the early to medium/advanced stages of glaucoma, the vCDR has a stronger correlation than hCDR and that vCDR is traditionally more useful in determining glaucoma severity.

CONTROL ID: 3707190

SUBMITTER (NAME ONLY): Michael Simpson

TITLE: Nodal Points and the Eye

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Simpson, Simpson Optics LLC, Arlington, Texas, UNITED STATES|

Commercial Relationships Disclosure: Michael Simpson: Commercial Relationship(s);Code E (Employment):Simpson Optics LLC

ABSTRACT BODY:

Purpose: The very concept of “nodal points” probably originated with the eye, because they are only distinct when the refractive index is different on one side. Johann Listing described this in 1845, and the points belong on a paraxial “cardinal point” drawing (Fig 1), though they are often misleadingly sketched alone as the axial intersections of 2 parallel rays. They are meaningful only for small angles, yet it has recently been confirmed that the nodal point can scale the pseudophakic retina at large angles for other reasons. The evaluation is extended here to the phakic eye.

Methods: Raytracing software was used to model an average older eye with a gradient index lens. Input chief ray angles were compared to angles leaving the exit pupil, relative to the visual axis. A 70 year old eye was used because this is a typical age for cataract surgery, where recent questions about “negative dysphotopsia” and “far peripheral vison” have not yet been fully resolved.

Results: The phakic eye was found to have broadly similar properties to the pseudophakic eye, with input chief ray angles being rescaled by a fairly constant factor of 0.81 at the exit pupil over more than 70 degrees (Fig 2). These are actual rays, with angles relative to the visual axis that is rotated 5 degs from the optical axis (angle alpha). They identify image locations on the retina, though the overall image may be slightly defocused and astigmatic. Lines are not drawn to the 2^{nd} nodal point (NP2), to maintain clarity, but a ruler parallel to an input ray can be used to confirm that in addition to the angular rescaling at the pupil, angles from NP2 are approximately the same as input angles to the eye, and that the input angles do not all meet at a single point.

Conclusions: The eye has a remarkably linear relationship between input angle and image location on the retina, with the cornea curving around toward light entering at an angle, and the retina curving around to meet the image. These optical properties have nothing directly to do with the traditional nodal points, which are described for very small angles using a sketch that has only straight lines. At large angles, the relationship comes from ray bundles that pass through the center of the pupil. This discussion also has relevance to fundus cameras, and to wide-field imaging of the retina.

CONTROL ID: 3707192

SUBMITTER (NAME ONLY): Wenjing Wu

TITLE: The interplay of luminance and genetics in the retinopathy induced by the dominant RPE65 mutation

SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Wu, Y. Takahashi, X. Ma, G.P. Moiseyev, J. Ma, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: RPE65 is an essential enzyme that is required for vertebrate vision. In humans, RPE65 mutations cause severe blinding diseases. Up-to-date D477G is the only known mutation of RPE65 that is dominantly inherited. The pathogenic mechanism by which the heterozygous D477G (WT/KI) mutation impairs retinal function remains unknown. A total of 4 groups, including us, previously reported that when raised under dim light vivarium illumination, the retinal phenotypes in the WT/KI mice were mild non-pathogenic. This study investigated if environmental light influences the onset of D477G pathogenicity in the WT/KI mice.

Methods: Retina function and morphology were evaluated using ERG, OCT, and H&E staining in heterozygous WT/KI and heterozygous RPE65KO (WT/KO) mice maintained under ambient or higher cyclic lighting. Isomerase activity and endogenous chromophore were measured using HPLC. Immunostaining was performed on eyecup flat mounts and retina sections. Levels of visual cycle proteins were analyzed via immunoblotting. In vivo, subcellular fractionation and sucrose density sedimentation were performed to analyze protein mislocalization and aggregation. In vitro, pVITRO expression systems were used to detect protein-protein interaction. Cycloheximide and MG132 were used to determine protein half-life and degradation rate.

Results: When maintained under the physiological light intensity 2000 lux, the WT/KI mice displayed degenerative retina features, including reduced ERG amplitudes and retinal layers thinning, recapitulating that observed in human patients. We also detected increased free opsin levels and upregulated GFAP expression in the same retinas. Molecularly, we found reduced RPE65 and LRAT levels, decreased retinol isomerase activity, and altered subcellular localization and membrane association of RPE65 in the RPE of WT/KI mice. Moreover, the D477G mutant, formed protein complexes with WT-RPE65, leading to a reduction of RPE65 protein stability, which could not be completely rescued by the addition of MG132, a proteasome inhibitor of ubiquitin-dependent protein degradation.

Conclusions: Our results suggested that physiological non-pathogenic illumination played an important role in the manifestation of vision loss in certain forms of monogenetic causes of blindness and uncovered the dominant-negative mechanism of D477G mutation.

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CONTROL ID: 3707193

SUBMITTER (NAME ONLY): Randy Lu

TITLE: Transfer Learning from Optical Coherence Tomography Images of MacTel Type II to Predict Retinal Sensitivity for Early-Intermediate Age-Related Macular Degeneration

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lu, Y. Kihara, J. Owen, C.S. Lee, A.Y. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|Z. Wu, R.H. Guymer, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|C.A. Egan, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Microperimetry (MP) is a valuable endpoint in clinical trials for various retinal diseases. Deep learning models that can predict MP from optical coherence tomography (OCT) B-scans may be beneficial given the laborious effort of MP. Transfer learning involves using pre-trained weights on a different but related problem where proficiency in one task may generalize to another. We sought to evaluate a deep learning model pre-trained on OCTs of macular telangiectasia type 2 (MacTel) and fine-tuned on patients with non neovascular age-related macular degeneration (AMD).

Methods: The AMD dataset includes 322 eyes of 161 patients enrolled in the Laser Intervention in the Early Stages of AMD (LEAD) trial at the Centre for Eye Research Australia from 2013 to 2018, partitioned into 110,450 samples for training, 52,858 for validation, and 41,719 for testing. Each sample consists of B-scan window slices and MP sensitivities, for which infrared fundus photos were registered by aligning segmented blood vessels. Three VGGNet models were evaluated: 1) trained on MacTel data (VGG-Mac), 2) trained on AMD data (VGG-AMD), 3) pre-trained with MacTel data and fine-tuned with AMD data (VGG-FT). Primary outcome is the mean absolute error (MAE) of predicted vs. observed MP sensitivity.

Results: All models were evaluated against the same AMD validation set. The fine-tuned model VGG-FT achieved lowest MAE of 2.88 dB (95% CI 2.86, 2.91). VGG-AMD achieved MAE of 3.01 dB (2.99, 3.04), and VGG-Mac achieved MAE of 3.44 dB (3.41, 3.48). Continuous predictions by VGG-FT across B-scan levels were then aggregated to create 2D en-face maps (Figure 2).

Conclusions: The model pretrained on MacTel then fine-tuned on AMD data outperformed the model trained only on AMD data, suggesting that transfer learning between different retinal diseases may increase domain specific performance. Deep learning models to estimate retinal sensitivities using OCTs may be a valuable endpoint in following patients with AMD for clinical trials.

CONTROL ID: 3707198

SUBMITTER (NAME ONLY): Lindsay Williamson

TITLE: Optical Coherence Tomography Angiography and Humphrey Visual Field in Patients with Obstructive Sleep Apnea

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Davanian, A. Harrover, K.E. Bollinger, T. Lee, D.M. Marcus, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|A. Davanian, Q. Chen, Eye Institute, Vanderbilt University, Nashville, Tennessee, UNITED STATES|L. Williamson, C. Taylor, D.M. Marcus, Southeast Retina Center, PC, Augusta, Georgia, UNITED STATES|B. Chaudhary, The Sleep Institute of Augusta, Augusta, Georgia, UNITED STATES|V. Taskar, Sleep Medicine, Augusta University, Augusta, Georgia, UNITED STATES|Y. Liu, Q. Chen, Biostatistics, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if obstructive sleep apnea (OSAS) predisposes patients to glaucoma and macular disease due to vascular compromise by evaluating retinal and optic nerve vasculature and function using optical coherence tomography angiography (OCT-A) and Humphrey visual field testing.

Methods: Forty-five patients undergoing polysomnography ordered per standard of care were enrolled and grouped into three categories based on apnea-hypopnea index (AHI) with control patients having AHI <5 episodes/hr. Medical history, visual acuity testing, 24-2 Humphrey visual field (HVF), intra-ocular pressure measurement, OCT-A studies of the macular and peripapillary retina were obtained. Correlations between polysomnography parameters and imaging data were evaluated.

Results: OCT-A radial peripapillary capillary (RPC) vascular density (VD) demonstrated no relationship to AHI (95% CI (-0.026,0.038)) or severity of OSAS (95% CI: (-0.772, 3.648) for moderate OSAS compared to mild/normal and (-1.295, 3.1421) for severe comparing to mild/normal). OCT-A superficial parafoveal VD (95% CI: (-0.068,0.011), deep parafoveal VD (95% CI: (-0.080,0.009)), and FAZ (95% CI: (-0.001, 0.001)) showed no statistically significant relationship to AHI or OSAS severity after controlling for confounders. OCT retinal nerve fiber layer (RNFL) thickness increased with AHI (p=0.014), but there was no statistically significant correlation with OSAS severity with RNFL thickness (95% CI: (-12.543, 6.792) for moderate comparing to normal and (-2.883, 16.551) for severe comparing to normal). 24-2 HVF parameters were unaffected by OSAS (95% CI: Mean deviation (-0.21,0.29), Pattern standard deviation: (-0.351,0.121), Visual field index: (-0.166, 0.329)). OCT choroidal thickness showed a statistically significant decrease when OSAS was grouped by severity (p=0.0092), but did not correlate with AHI (p=0.129, 95% CI: (-1.210, 0.095))

Conclusions: The severity of OSAS did not show a statistically significant effect on parameters associated with glaucoma or macular vascular disease. Larger cohorts may be required to determine the physiologic consequences of OSAS on the macular and optic nerve vasculature, structure, and function.

CONTROL ID: 3707201

SUBMITTER (NAME ONLY): Elizabeth Li

TITLE: Severity of OCTA Artifacts According to Disease Stage in Glaucoma Patients

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.H. Li, A. Kamalipour, S. Moghimi, T. Nishida, N.W. El-Nimri, E. Micheletti, J. Wu, L.M. Zangwill, R.N. Weinreb, Shiley Eye Institute, Hamilton Glaucoma Center, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the severity of optical coherence tomography angiography (OCTA) artifacts by disease severity in glaucoma suspects and patients.

Methods: 644 OCTA images were included from 409 eyes of 228 healthy, glaucoma suspect and glaucoma patients from the Diagnostic Innovations in Glaucoma Study. Angiovue high-density optic nerve head and macula OCTA images were reviewed for the presence of different subtypes of OCTA artifacts, including eye movement, defocus, decentration, segmentation error, blink, Z offset, and shadow in the superficial vascular layer. The severity of artifacts was quantified based on the percentage of the en-face image or B-scans affected. Artifacts that involved <5% of the OCTA scan were categorized as mild, 5-10% as moderate, and ≥10% as severe. Images with at least 1 severe artifact were classified as poor-quality. Univariable and multivariable mixed effect models were used to evaluate the association of demographic and ocular characteristics with artifact severity.

Results: 31.8% of OCTA images were classified as poor-quality. The prevalence of poor-quality images increased with worsening disease from healthy (13.6%) to glaucoma suspect (23.5%) to glaucoma patients (39.0%). In univariable analyses, diagnosis of glaucoma and worse 24-2 visual field (VF) mean deviation (MD) were significantly associated with poor-quality OCTA images (all P<0.05, Table 1). In the multivariable analysis, older age, male gender, absence of eye tracking and worse 24-2 VF MD were significantly associated with poor-quality OCTA images (all P<0.05). Defocus (21.1%), eye movement (19.6%) and decentration (6.7%) artifacts were the most prevalent subtypes of severe artifacts leading to poor-quality OCTA images. Each was significantly associated with severity of disease including worse 24-2 VF MD (all P<0.05). Compared to healthy subjects, both glaucoma suspect and glaucoma patients were more likely to have moderate to severe eye movement, but only glaucoma patients were more likely to have moderate to severe decentration and defocus artifacts (all P<0.05).

Conclusions: OCTA images of glaucoma patients, particularly those with severe disease, are more likely to be affected by artifacts compared to those of healthy individuals. Quantitative OCTA measurements of glaucoma patients, especially those with advanced disease, must be carefully reviewed to exclude images with artifacts.

CONTROL ID: 3707203

SUBMITTER (NAME ONLY): Mike Zein

TITLE: Long Term Outcomes of Topical Interferon α-2β as Primary Treatment for Ocular Surface Squamous Neoplasia.

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zein, W. Sripawadkul, D. Reyes-Capo, A. Wylegala, G.J. Albayyat, A. Galor, C.L. Karp, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|W. Sripawadkul, Ophthalmology, Srinakharinwirot University Faculty of Medicine, Bangkok, THAILAND|A. Wylegala, Ophthalmology, Slaski Uniwersytet Medyczny w Katowicach, Katowice, Slaskie, POLAND|A. Galor, Ophthalmology, Miami Veterans Medical Center, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the efficacy of topical interferon IFN α-2β(IFN) as a primary treatment for ocular surface squamous neoplasia (OSSN) and evaluate factors that impact response to treatment and recurrence of OSSN.

Methods: A retrospective study of 127 OSSN patients treated with topical IFN(1MIU/ml) from January 2009 to June 2021. The diagnosis was based on clinical examination and anterior segment optical coherence tomography. Histologic confirmation was present in 44% of patients. Data on demographics, tumor characteristics, treatment outcome, and side effects were collected. The primary outcomes assessed were tumor resolution frequency and recurrence rate. Secondary outcomes assessed were predictive factors for resolution and recurrence and side effects of treatment.

Results: Participants were mostly older with a mean age of 69 years (SD 12.4, range 29-97), white (92%) males (76%). Complete tumor resolution was achieved in 78% of individuals with a mean time to resolution of 5 months (SD 4.4, range 1.6-36 months). On multivariable analysis, non-Hispanic ethnicity (HR: 0.48, p=0.003, 95% CI: 0.29 to 0.78) and self-reported sun exposure (HR: 0.55, p=0.02, 95% CI: 0.34-0.91) reduced the risk of tumor resolution, while a prior history of OSSN (HR: 4.26, p<0.001, 95% CI: 1.82-9.97) increased the risk of resolution. With a mean follow-up time of 36.3 months (SD 33.8, 0-124 months), the recurrence rate was 1.2%, 3.8%, and 6.2% at 1, 2, and 5 years respectively. Mild hyperemia (18.2%) and pain (12.1%) were the two most common side effects.

Conclusions: Topical IFN is a safe and effective primary treatment modality for OSSN with a reasonable side effect profile.

CONTROL ID: 3707204

SUBMITTER (NAME ONLY): Donald Hood

TITLE: Identifying and understanding OCT artifacts (“red disease") that resemble arcuate damage due to glaucoma.

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. La Bruna, E. Tsamis, Psychology, Columbia University, Columbia University, New York, NY, US, academic, New York, New York, UNITED STATES|A. Leshno, C.G. DeMoraes, E. Tsamis, Ophthalmology, Columbia University, New York, New York, UNITED STATES|A. Rai, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|D.C. Hood, Psychology & Ophthalmology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Arcuate-like artifacts seen on deviation/probability (p-) maps of healthy eyes are the most common source of OCT false positives and are the primary basis of so-called “red disease”. To better identify and understand these arcuate-like artifacts we tested a simple model.

Methods: The model: Figure 1A shows the average thickness map of healthy control (HC) eyes from a normative database. The black border, between the yellow and green regions in Fig.1A, is an iso-thickness (75 um) contour encompassing the thickest portion of the RNFL thickness map. Figure 1B&C show the thickness map and p-map of a healthy control with an arcuate-like artifact. Notice that the RNFL thickness (Fig. 1C) of this HC eye is relatively normal, but that the thickest portion no longer falls entirely within the black border. The model predicts that the arcuate-like artifact is due to this misalignment, and it will fall largely within the black contour (red arrow, Fig. 1B). However, arcuate regions that are due to glaucoma will typically extend outside these black borders, and often cross the midline (black vertical line) as shown in Fig. 1D-F. The model was tested by superimposing the black borders on the p-maps of 200 HC eyes. In addition, these borders were also superimposed on the RNFL p-maps of 62 glaucoma eyes with early (EG, MD>-6dB, n=32), moderate (MG, MD<-6dB, >-12dB, n=12), and advanced disease (AG, MD <-12 dB, n=18).

Results: Arcuate-like artifacts were seen on the RNFL p-maps of 8 (4%) of the 200 HC eyes. As predicted, all 8 (100%) of these arcuate artifacts fell within the black borders as shown in Fig. 2A (1st column). On the other hand, only 3 of the 62 patient eyes (2 EG and 1 MG) had abnormal regions restricted to within the black border (Fig. 2B). A post-hoc analysis revealed that these 3 eyes can be distinguished from the 8 HC eyes based upon topographical agreement with the abnormal regions of the RNFL thickness map and/or ganglion cell layer (GCL) p-map, as shown in the 2nd and 3rd columns of Figs. 2A&B.

Conclusions: Arcuate-like artifacts on RNFL p-maps, which can be confused with glaucomatous arcuate damage, fall within the borders of the thick arcuate region of the average RNFL thickness map of healthy eyes. Abnormal arcuate regions falling within these borders should be assumed to be artifacts unless confirmed with GCL p-maps and/or RNFL thickness maps.

CONTROL ID: 3707209

SUBMITTER (NAME ONLY): David Linn

TITLE: An alpha7 nicotinic acetylcholine receptor agonist induces new RGCs and ERG recovery in a mouse glaucoma model

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.M. Linn, Biomedical Sciences, Grand Valley State University, Allendale, Michigan, UNITED STATES|D.M. Linn, J.B. Spitsbergen, S. Webster, C.L. Linn, Biological Sciences, Western Michigan University, Kalamazoo, Michigan, UNITED STATES|S. Webster, Western Michigan University Homer Stryker MD School of Medicine, Kalamazoo, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this study, experiments were performed to demonstrate ERG recovery in glaucoma-induced mice after generation of new RGCs following PNU-282987 treatment.

Methods: Both sexes of adult mice (3 to 6 months) were injected with 1.2 M hypertonic saline into the episcleral vein to increase IOP. After the procedure, mouse eyes were treated once daily using eye drops containing 1mM PNU-282987/1mg/ml BrdU and weekly ERGs were recorded using the Celeris Diagnosys ERG System. At different time points, animals were euthanized, and retinas were removed, processed immunocytochemically with antibodies against BrdU and Thy 1.2, counterstained with DAPI, and viewed using a Nikon confocal microscope. Data was analyzed with ANOVA and differences were considered significant at $P<0.05$. N's between 3-6 were obtained under each condition.

Results: Hypertonic saline injections elicited a significant increase in IOP four weeks post injection (an average of 15.8 mmHg ±1.2) compared to an average of 11.2 mmHg (±1.8) measured from the same animals before the procedure. Induction of glaucoma also significantly reduced the cell density of Thy1.2+ RGCs by an average of 28.31% (±1.5) four weeks after injection.To illustrate the regenerative potential of PNU-282987, injected animals were treated with BrdU alone or with PNU-282987/BrdU. In the injected mice treated only with BrdU, no BrdU+ cells appeared despite an average loss of 30.88% (±3.4) RGCs. However, after agonist treatment following saline injection, Thy1.2/BrdU+ neurons appeared in the GCL. After 28 days of agonist treatment, PNU-282987 significantly reduced the loss of Thy1.2+ cells associated with the glaucoma procedure to an average of only 12.4% (±0.8) compared to the near 30% average that are typically lost. In ERG recordings, the amplitude of the photopic PhNR decreased by 71.5% (±6.2) after the glaucoma procedure within 1 week. When treated with the agonist for 3 weeks, the amplitude of the PhNR recovered by 90% (±20.5). Scotopic oscillatory potential amplitudes (OP1, 2 and 3) decreased by an average range of between 80.3 and 85.6% (±16.1) after the glaucoma procedure. When treated with the agonist all OPs recovered by an average range of 65 to 85% (±21.7).

Conclusions: Results from these studies support the hypothesis that PNU-282987 can elicit new RGCs and provide recovery of the ERG PhNR and OP amplitudes after inducing glaucoma.

CONTROL ID: 3707210

SUBMITTER (NAME ONLY): Jenna Tauber

TITLE: A Systematic Review of Electrocautery Use During Ocular and Oculofacial Surgery in Patients with Implantable Electronic Cardiovascular Devices

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tauber, J.P. Tingley, A. Barmettler, Ophthalmology, Montefiore Medical Center, Bronx, New York, UNITED STATES|J. Tauber, J.P. Tingley, A. Barmettler, Ophthalmology, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Implantable electronic cardiac devices (IECDs) such as cardiac pacemakers and implantable defibrillators are common life saving devices. Device-related complications can arise in patients undergoing surgical interventions with electrosurgical tools due to electromagnetic interference. Currently, ophthalmologists and oculofacial plastic surgeons rely on inconsistent protocols, which vary by institution, to guide their use of these devices in patients with IECDs. This systematic literature review assesses existing reports on electrocautery use during ocular and periocular surgery in patients with IECDs.

Methods: This review was designed per Preferred Reporting Items for Systematic and Meta-Analysis guidelines. A literature search of published reports was conducted on all Evidence Based Medicine Reviews, Cochrane Databases and Registers, MEDLINE Ovid, Embase.com, Pubmed, and ClinicalTrials.gov. Search terms included “pacemaker” or “implantable cardioverter defibrillator” and “electrocautery” or “cautery”. Inclusion criteria were full text articles, discussing ocular, oculoplastic, or other facial (including dermatologic and head and neck) surgery. Exclusion criteria included non-English language or surgery focused on other parts of the body. Full-text manuscripts of identified articles were reviewed and relevant data were extracted. Data collected included author, publication year, study design, surgery type, electrosurgery type, IECD type, guidelines or findings.

Results: Of 746 publications, twelve studies met inclusion criteria (Figure 1). A summary of these studies can be seen in Table 1. Different safety approaches were taken with pacemakers (such as applying magnets intraoperatively, converting to asynchronous mode, or performing no alterations) and implantable defibrillators (such as disabling prior to electrocautery or no intervention). Precautions such as preoperative device interrogation and limiting duration of current bursts were recommended more often with monopolar cautery.

Conclusions: There is limited original research specifically focused on electrocautery choice during ocular and oculofacial plastic surgery in patients with IECDs. Existing studies suggest bipolar electrocautery and thermal cautery may be safer options compared to monopolar electrocautery in select patients with IECDs.

CONTROL ID: 3707221

SUBMITTER (NAME ONLY): Agnes Ezekwesili

TITLE: Seeing in Color: Inclusion and Characterization of African Americans in Hereditary Eye Disease Research

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Ezekwesili, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|R. Ionin, Library, National Institutes of Health, Bethesda, Maryland, UNITED STATES|B.P. Brooks, W.M. Zein, Ophthalmic Genetics and Visual Function, National Eye Institute, Bethesda, Maryland, UNITED STATES|L. Huryn, D. Blain, A. Agather, Ophthalmic Clinical Genetics, National Eye Institute, Bethesda, Maryland, UNITED STATES|C.A. Cukras, Clinical Investigation of Retinal Disease, National Eye Institute, Bethesda, Maryland, UNITED STATES|R.B. Hufnagel, Medical Genetics and Ophthalmic Genomics, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hereditary eye diseases (HED) affect millions globally. While the field of study of these disorders, Ophthalmic Genetics, has seen major advances, evidence of inclusion and characterization of HEDs in diverse populations is lacking in current literature. This raises questions on the accuracy and applicability of these findings to diverse populations. A literature review was conducted to assess gaps in the representation of African Americans in genomic research surrounding eight HEDs: oculocutaneous albinism, retinoblastoma, congenital aniridia, congenital glaucoma, congenital cataract, Stargardt disease, retinitis pigmentosa, and optic atrophy.

Methods: A two-pronged approach was utilized to gather review sources. 1) An advanced PubMed® search cross-referencing our research population with a predetermined set of search terms for each HED. 2) Exploration of additional databases including Embase®, Web of Science™, and Scopus® by a medical librarian. Sources were then filtered based on predetermined inclusion criteria (to highlight knowledge in the molecular era) and reviewed for significance of contribution to literature.

Results: Out of thousands of studies on each of these diseases, papers clearly reporting disease characterization in African Americans ranged from 14 addressing oculocutaneous albinism to none in aniridia. Analysis of studies that were inclusive of African American patients demonstrated the known utility of diverse genomics research by: reporting novel disease associated variants, challenging classifications of benign and pathogenic variants, proposing previously unreported genotype-phenotype correlations, and expanding documented manifestations of these diseases in more diverse populations.

Conclusions: Genomic research is more likely to be applicable to patients when conducted in populations that share their ancestral background. HED characterization in diverse participants, specifically African Americans, is identified as a knowledge gap area. Addressing this gap will lead to a better understanding of HEDs in broader populations. Greater inclusion of African Americans in Ophthalmic Genetics research is a scientific imperative and is a needed step in the pursuit of the best possible patient care.

CONTROL ID: 3707224

SUBMITTER (NAME ONLY): Joseph Park

TITLE: Scanning laser ophthalmoscopy (SLO) demonstrates less peripapillary strain in older than younger people during adduction

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Park, S. Lim, J.L. Demer, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|J. Park, Bioengineering, University of California Los Angeles, Los Angeles, California, UNITED STATES|S. Lim, Mechanical Engineering, University of California Los Angeles, Los Angeles, California, UNITED STATES|S. Moon, Ophthalmology, Inje University Busan Paik Hospital, Busan, Busan, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Although optic nerve (ON) tethering occurs beyond ~26° adduction, the distribution of resulting ocular strain is predicted to vary depending on local tissue properties. We measured peripapillary strain by imaging displacements of embedded vessels using SLO during horizontal duction.

Methods: Using azimuth rotation of Heidelberg Spectalis SLO to achieve 35° ab- & adduction from central gaze, we imaged a 8.9X8.9 mm^2 region centered on the optic disc of young (42 eyes, age 27±5 years, ±SD) and older (39 eyes, 65±9 years) healthy adults. A MATLAB algorithm equalized brightness, corrected torsion, & registered globally across gaze positions. The VLFeat Team scale-invariant feature transform detector was used to quantify displacements of corresponding features that were analyzed in nasal vs. temporal sectors at disc radius increments from the disc center. A vessel mask was used to exclude non-vascular corresponding features from analysis.

Results: Vascular features on the disc were displaced temporally in adduction & nasally in abduction. During adduction, nasal hemi-disc vessels were displaced temporally by similar amount of 11.0±23.0 μm in younger & 10.6±16.7 μm in older subjects. This was significantly more than the temporal hemi-disc was displaced nasally at 4.1±14.0 μm in young & 4.7±11.6 μm in older subjects (P=0.005). During adduction, nasally directed displacement of peripapillary vessels located >3 disc radii from center averaged 3.1±13.5 μm for younger, but only 0.5±12.2 μm for older subjects (P=0.02). Peripapillary features located between 2 & 3 disc radii shifted nasally in abduction by 2.4±13.3 μm in older (P<0.001) but not significantly in young adults at 0.0±8.8 μm. There were no significant vertical displacements in either group.

Conclusions: Consistent with ON tethering, SLO demonstrates greater local disc & peripapillary vessel displacements in add- than abduction that are greater in the nasal than temporal hemi-disc. Since vessels are embedded in other tissues, these displacements represent local strains that are quantitatively similar in both younger & older subjects. Lesser peripapillary strain in older subjects during adduction may be due to scleral stiffening, which would increase associated stress during tethering. Lesser deformation in abduction than adduction is consistent with ON tethering in adduction but not abduction.

CONTROL ID: 3707228

SUBMITTER (NAME ONLY): Yiqiao Zheng

TITLE: Deciphering how missense mutations in CRX homeodomain produce distinct dominant retinopathies

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Zheng, C. SUN, X. Zhang, P.A. Ruzycki, S. Chen, Ophthalmology & Visual Sciences, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: CRX is a paired-like homeodomain (HD) transcription factor essential for photoreceptor gene expression, function, and survival. This study focused on three human missense mutations within the CRX HD recognition helix, p.E80A, p.K88N and p.R90W, associated with dominant cone-rod dystrophy (CoRD), dominant Leber congenital amaurosis (LCA), and recessive LCA, respectively. The goal was to uncover how each mutation disrupts CRX regulatory activity to inform disease pathogenesis.

Methods: Spec-seq, a high throughput assay for protein-DNA interactions, established quantitative models of CRX HD-DNA binding specificity. pRho-luc reporter assays in HEK293T cells revealed changes in CRX transactivation potential. Knock-in mouse models were generated by introducing p.E80A and p.K88N into the endogenous Crx locus. Previously published p.R90W model was included for comparison. Retinal ChIPseq and RNAseq at postnatal ages detected changes in CRX chromatin binding and subsequent effects on gene expression in each mutation knock-in mouse model.

Results: R90W and E80A maintained WT binding specificity. While R90W significantly lost binding affinity and transactivation activity, explaining rLCA-like phenotype, E80A mutant increased binding affinity and hyperactivated pRho-luc reporter. In accordance with in vitro results, $Crx^{E80A/+}$ and $Crx^{E80A/A}$ mutants showed hyperactivation of rod genes at postnatal age P10. However, cone genes were not activated, and rod differentiation failed to reach mature state at P21, suggesting a path to CoRD-like phenotypes. In contrast, K88N mutant preferred sequences different from that of WT and failed to activate pRho-luc reporter. In agreement with these results, K88N showed reduced binding at WT sites but gained new binding sites in mutant retinas. Both rod and cone genes failed to be activated in $Crx^{K88N/+}$ and $Crx^{K88N/N}$ retinas while some other genes were ectopically activated, explaining the development of LCA-like phenotypes.

Conclusions: We have identified distinct pathogenic mechanisms for two disease-causing mutations in CRX HD: E80A shows hyperactivity, while K88N is antimorphic and alters DNA binding specificity. Thus, HD mutations, through alteration of DNA binding affinity or specificity, can disrupt gene regulation and cause severe dominant diseases. These findings could shed light on the regulatory mechanisms of other HD proteins and associated diseases.

CONTROL ID: 3707229

SUBMITTER (NAME ONLY): Yanhan Ren

TITLE: Nomenclature in the Multidisciplinary care of Thyroid Eye Disease: A Longitudinal Analysis from 2010 to 2020

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ren, ophthalmology, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|V. Palacios, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|D. Bothun, Carleton College, Northfield, Minnesota, UNITED STATES|J. stokken, otolaryngology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|L. Wagner, ophthalmology, Mayo Foundation for Medical Education and Research, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Standardized nomenclature facilitates collaboration across specialties and institutions, as well as communication with patients. This study sought to analyze whether there is a predominant nomenclature for thyroid eye disease (TED), to identify possible associations of different terms with author and journal characteristics and trends over time from 2010 to 2020.

Methods: A search in the PubMed database was completed for all articles published in 2010 and 2020 that contained TED related keywords identified by our interdisciplinary research team. Nomenclature, author and journal characteristics were extracted and descriptive as well as comparative statistical analysis was performed to identify associations.

Results: The search yielded 324 and 147 publication results for 2020 and 2010 respectively. 303 of the 2020 publications and 141 of the 2010 publications were included for final analysis. Comparing 2020 to 2010 data, use of the term “Thyroid Eye Disease” (TED) saw the biggest increase from 21.3% to 36.6% (+15.3%) with the U.S. being the leading authorship country. Use of “Graves’ Orbitopathy” saw a moderate increase from 26.2% to 34.0% (+7.8%) Use of “Graves’ Ophthalmopathy” dropped from 27.4% to 19.2% (-8.2%). In 2020, ophthalmology journals saw the highest number of publications of 138 with more than 55.8% utilizing TED as the nomenclature. In contrast, in endocrinology journals as the second leading publishing group (78 articles), only 11.5% of the published articles used the term TED ($p<0.01$). Although the change was not statistically significant ($p=0.23$), both ophthalmology and endocrinology journals have seen upward trends in TED in the past decade from 33.8% to 55.8% (+22%) and 3% to 11% (+8%) respectively.

Conclusions: “Thyroid Eye Disease” was the most commonly used term in 2020 not only by ophthalmologists, but also among almost all medical specialties. It also has the highest increase in the ophthalmology literature over the analyzed 10-year period. Based on our review, we propose that Thyroid Eye Disease (TED) would be the most appropriate term to standardize communication between patients and medical professionals, as well as documentation in the medical record. Our research was conducted by a multidisciplinary team and provides a guideline for authors of future scientific publications that is not rooted in personal preference, but in existing consensus.

CONTROL ID: 3707234

SUBMITTER (NAME ONLY): Lei Gu

TITLE: Moderate elevation of intraocular pressure induces DNA and RNA oxidative damage in the retina

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Gu, J. Kwong, J. Caprioli, N. Piri, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress in the pathogenesis of neurodegenerative diseases is generally associated with damage to cellular macromolecules, including DNA and RNA. This study evaluates the level of oxidized nucleosides 8-hydroxydeoxyguanosine (8OHdG) and 8-hydroxyguanosine (8OHG), biomarkers for oxidative damage of DNA and RNA, respectively, in the retinas of rat experimental glaucoma models

Methods: The experimental glaucoma model was generated by trabecular laser photocoagulation in 3-month-old Brown Norway rats. Apoptotic cells in glaucomatous retinas were detected with TUNEL staining. Spatial distribution of 8OHdG/8OHG in control and experimental retinas was analyzed with immunohistochemistry using DNA and RNA Oxidative Damage Marker monoclonal antibodies. The levels of 8OHdG/8OHG in retinal mitochondrial DNA/RNA samples were measured with DNA/RNA Oxidative Damage ELISA Kit

Results: 8OHdG/8OHG in the retina were predominantly localized to retinal ganglion cell (RGC) somas. The immunostaining intensities for these oxidatively damaged DNA/RNA nucleosides were significantly higher at 1 and 2 weeks after intraocular pressure (IOP) elevation compared to controls. Analysis of different cellular fractions indicates that 8OHdG/8OHG is almost exclusively associated with mitochondrial DNA/RNA, with approximately 65% of oxidized product associated with RNA isolated from mitochondrial fraction and the remaining 35% with mitochondrial DNA. Quantitative analysis of 8OHdG/8OHG in mitochondrial DNA/RNA isolated from retinas of experimental animals 1 and 2 weeks after IOP elevation showed approximately a 3.2 and 2.8 fold increase in the levels of oxidized DNA/RNA, respectively, compared to that of control animals

Conclusions: The observed high levels of 8OHdG/8OHG in RGCs of wild-type animals may lead to mitochondrial dysfunction and contribute to cell damage and progressive loss of RGCs during normal aging. Ocular hypertension is associated with a significant increase in the level of oxidatively damaged mitochondrial DNA/RNA, which in turn could contribute to the increased rate of RGC dysfunction and death in glaucoma

CONTROL ID: 3707238

SUBMITTER (NAME ONLY): Ming Yang

TITLE: FSP1 controls retinal pigment epithelium degeneration: role of ferroptosis

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Yang, K. So, A.C. Lo, W. Lam, Department of Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|K. So, GHM Institute of CNS Regeneration, Jinan University, China, CHINA|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) degeneration is central in the pathogenesis of age-related macular degeneration. Ferroptosis is an iron-dependent novel regulated cell death pathway attributed to lipid peroxidation and plays an important role in eye diseases. This study aimed to elucidate the role of ferroptosis suppressor protein-1 (FSP1) in RPE degeneration.

Methods: Primary human retinal pigment epithelial cells (HRPEpiC) and ARPE-19 exposed to sodium iodate (SI) were used as the in vitro RPE degeneration model. C57BL/6J mice receiving intraperitoneal injection of SI were chosen as the in vivo RPE degeneration model. Ferroptosis inhibitors and glutathione peroxidase-4 (GPx-4) silencing RNAs were used to test the involvement of ferroptosis. Levels of intracellular labile iron, lipid peroxidation, glutathione, coenzyme Q_{10} (CoQ_{10}), and nicotinamide adenine dinucleotide hydrogen (NADH) were measured. Protein expressions were assessed by immunohistochemistry and Western blot. Retinal function was assessed by electroretinography (ERG). Statistical analysis was performed using SPSS.

Results: SI triggered RPE cell damage, accompanied by increased levels of intracellular labile iron, glutathione disulfide (GSSG), and lipid peroxidation but decreased amount of cytoplasmic glutathione and GPx-4. Ferroptosis inhibitors significantly alleviated SI-induced cell damage, with the restoration of the aforementioned markers. However, silencing GPx-4 aggravated SI-induced cell damage. Although inhibition of FSP1 aggravated SI-induced cell damage, overexpression of FSP1 ameliorated cell damage with decreased lipid peroxidation accompanied by recovery of CoQ_{10} and NADH. Additionally, SI induced a dramatic reduction in retinal function, retinal thickness, and levels of ferroptosis suppressors, with significantly elevated RPE labile iron, GSSG, and lipid peroxidation in mice. Most notably, ferrostatin-1 markedly restored retinal thickness and ERG function, along with elevated levels of ferroptosis suppressors such as GPx-4 and FSP1. These data further confirmed the distinct role of ferroptosis in RPE degeneration.

Conclusions: FSP1 plays an important role in SI-induced RPE degeneration models in vitro and in vivo. Activation of either FSP1/CoQ_{10}/NADH or GSH/GPx-4 pathway effectively protected SI-induced damages in HRPEpiC cells, ARPE-19 cells, and mouse retina, supporting ferroptosis as a novel target for future AMD treatment.

CONTROL ID: 3707242

SUBMITTER (NAME ONLY): Riley Stroman

TITLE: Compliance with hydroxychloroquine screening guidelines at a large academic medical center

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Stroman, P. Rao, Retina & Vitreous of Texas, Houston, Texas, UNITED STATES|R. Stroman, Y. Islam, A. Steigleman, Ophthalmology, University of Florida Health, Gainesville, Florida, UNITED STATES|

Commercial Relationships Disclosure: Riley Stroman: Commercial Relationship: Code N (No Commercial Relationship) | Yasmin Islam: Commercial Relationship: Code N (No Commercial Relationship) | Allan Steigleman: Commercial Relationship: Code N (No Commercial Relationship) | Prethy Rao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Long-term hydroxychloroquine use can result in irreversible maculopathy and vision loss. New screening guidelines to identify early maculopathy were issued by American Academy of Ophthalmology (AAO) in 2016, but limited studies have evaluated compliance with these updated guidelines. This cross-sectional study evaluated compliance with hydroxychloroquine maculopathy screening exams at a large academic institution.

Methods: A retrospective chart review was performed on patients screened for hydroxychloroquine toxicity between 2011-2021. Compliance with AAO screening guidelines was evaluated based on the 2011 guidelines for patients screened between 2011-2015, and with the 2016 guidelines for patients screened in 2016 and later.

Results: A total of 419 patients were included; 239 patients were evaluated between 2011-2015, and 357 patients were evaluated between 2016-2021. Only 60.7% of patients screened before 2016 met the recommended screening exam frequency, while 40.6% received adequate visual field screenings. Amongst patients screened after 2016, 55.3% met the recommended exam screening frequency, 46.4% received screening with macula ocular coherence tomography (OCT) at the recommended interval, and 21.0% of patients received appropriate visual field screening. One-third of patients were prescribed higher than the recommended 5 mg/kg/day of hydroxychloroquine. Ten out of 419 patients developed definite macular toxicity, most of whom had concomitant risk factors for toxicity.

Conclusions: Despite clear guidelines set forth by the AAO in 2011 and 2016, compliance with screening was suboptimal. Hydroxychloroquine prescribers and eye care providers need to collaborate to ensure patients are not overdosed and that they receive appropriate maculopathy screening.

CONTROL ID: 3707243
SUBMITTER (NAME ONLY): Terri Young
TITLE: PIEZO1 and PIEZO2 pathogenic variants identified in primary congenital glaucoma
SESSION TITLE: Glaucoma Genetics
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: T.L. Young, K. Whisenhunt, S. Martin, S. Tompson, Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|
Commercial Relationships Disclosure: Terri Young: Commercial Relationship: Code N (No Commercial Relationship) | Kristina Whisenhunt: Commercial Relationship: Code N (No Commercial Relationship) | Sean Martin: Commercial Relationship: Code N (No Commercial Relationship) | Stuart Tompson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Primary congenital glaucoma (PCG) is a rare, leading cause of childhood blindness. Increased intraocular pressure (IOP) leads to globe and corneal enlargement, and retinal ganglion cell/optic nerve damage. To date, genetic studies have identified ~25% of PCG molecular etiology. We sought novel variants in glaucoma-implicated genes in a cohort of PCG families lacking mutations in known PCG genes (CYP1B1, LTBP2, TEK, and ANGPT1).
Methods: PCG patients referred to our study were consented, and medical histories and blood samples for DNA extraction were acquired. Probands were exome sequenced using the Sure Select Human All Exon v6 or Roche/Nimblegen SeqCap EZ v2 capture kits on an Illumina HiSeq 2000 platform. Variants that were synonymous, not in coding/splice site regions, or with an allele frequency >0.002 in the gnomAD database were removed using Golden Helix SVS software. Sanger sequencing confirmed the variants in probands and enabled co-segregation analyses in additional family members where available.
Results: Six families with PIEZO1 and/or PIEZO2 variants were identified by exome sequencing. For PIEZO1, two families were identified with compound heterozygous variants (p.Arg351Trp, p.Gln1519Pro; p.Met711Lys, p.Arg1404Trp) and another had a single heterozygous variant (p.Val499Ile). For PIEZO2, two families had a single heterozygous variant (p.Arg2731Gln, p.Val971Ile). Digenic inheritance of PIEZO1 (p.Pro913Ala) and PIEZO2(p.Glu1863Gly) variants were identified in a further family. All variants showed low frequencies in global and all ethnic populations (gnomAD), had CADD scores >20, and involved highly evolutionarily conserved residues, strongly suggesting pathogenicity.
Conclusions: Maintenance of IOP involves regulation of aqueous humor outflow via Schlemm's canal (SC), a unique hybrid vessel in the ocular anterior chamber angle with lymphatic and vascular properties. In mice, PIEZO1 and PIEZO2 proteins form mechanically activated ion channels expressed in lymphatic and vascular endothelial cells. PIEZO1 localizes to SC and is important for lymphatic valve formation in mice. Additionally, PIEZO2 is associated with regulation of aqueous outflow in mice. PIEZO1 expression in human trabecular meshwork cells has also been reported. These findings strongly suggest that PIEZO1 and PIEZO2 are involved in IOP regulation and that rare pathogenic variants are causal for PCG.

CONTROL ID: 3707244

SUBMITTER (NAME ONLY): Sayuri Sekimitsu

TITLE: Retinal optical coherence tomography identifies early biomarkers for neurodegenerative disease and future cognitive decline

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sekimitsu, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|Y. Zhao, A.V. Segrè, J.L. Wiggs, N. Zebardast, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A.V. Segrè, Ocular Genomics Institute, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S. Shareef, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection of neurodegenerative disease could provide opportunities to prevent irreversible damage. Optical coherence tomography (OCT) allows for noninvasive retina visualization, serving as a potential window for assessment of neurological conditions. For complex multifactorial disease, polygenic risk scores (PRS) involving genetic variants of individual small effects, are associated with disease outcomes. Here we investigate the correlation between retinal layer thickness and neurodegenerative disease, polygenic risk of disease, as well as current and future cognitive performance.

Methods: We utilized OCT images from 50,342 UK Biobank participants to calculate retinal layer thicknesses. We associated these thicknesses with ICD-based diagnosis of Alzheimer's disease (AD) or Parkinson's disease (PD) as well as a Lassosum-derived PRS for each disease. Multivariate Cox proportional hazard models were developed to predict future cognitive decline. All models were adjusted for age, sex, and glaucoma.

Results: AD diagnosis was associated with a thinner outer plexiform layer (OPL) (adjusted OR (aOR)=1.69, p=0.027). AD PRS was associated with thicker inner nuclear layer (INL), choroid-sclera interface (CSI), inner plexiform layer (IPL), and photoreceptor inner segment/outer segment junction layer (ISOS) and thinner retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) ($p<0.05$ for all) (Figure 1). PD diagnosis was associated with a thinner ISOS (aOR=2.38, p=0.005) and PD PRS was associated with thinner OPL and CSI ($p<0.05$ for both) (Figure 2).

Worse baseline cognitive performance was associated with thinner RNFL (aOR=1.067, $p<0.001$), OPL (aOR=1.017, $p<0.001$) and ISOS (aOR=1.071, $p<0.001$), and thicker INL (aOR=0.948, $p< 0.001$), retinal pigment epithelium (RPE) (aOR=0.977, p=0.033), and GCL (aOR=0.982, p=0.012). In a stepwise Cox model, thinner RNFL (aHR=0.99, p=0.007) and OPL (aHR=0.99, p=0.02) and thicker IPL (aHR=1.04, p=0.002), as well as higher AD PRS predicted future cognitive decline. The model containing retinal thicknesses and PRS improved prediction of future cognitive decline compared to demographic factors alone.

Conclusions: OCT measurements are associated with diagnosis and genetic risk of neurodegenerative disease, as well as cognitive function suggesting that retinal layers may be used as biomarkers for future cognitive disease and decline.

CONTROL ID: 3707247

SUBMITTER (NAME ONLY): Songhomitra Panda-Jonas

TITLE: Hand Grip Strength and its Ocular Associations: The Ural Eye and Medical Study

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Panda-Jonas, J. Jonas, G. Kazakbaeva, E. Iakupova, M. Bikbov, Ufa Eye Research Institute, Ufa, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: To explore associations between the hand grip strength (HGS) as indicator of general health and ocular parameters and diseases.

Methods: The population-based Ural Eye and Medical Study included 5899 (80.5%) out of 7328 eligible individuals who underwent systemic and ophthalmological examinations including dynamometric HGS measurements.

Results: The study included 5381 (90.4%) individuals (age:58.6±10.6 years;range:40-94 years) with HGS measurements. In multivariable analysis, a higher HGS correlated with better visual acuity (beta:0.05;P<0.001), longer ocular axial length (beta:0.02;P=0.008), higher intraocular pressure (beta:0.03;P=0.001) and lower prevalence of diabetic retinopathy (beta:-0.02;P=0.006) after adjusting for younger age, male sex, Russian ethnicity, higher body height and waist-hip ratio, higher educational level, lower number of smoking package years, lower self-reported salt consumption, higher degree of processing meat, higher physical total score, higher serum concentration of hemoglobin, higher prothrombin index, lower leucocyte cell count, lower prevalence of non-alcoholic fatty liver disease, lower depression score, and lower prevalence of arthritis and previous falls. In that model, HGS was not correlated with the prevalence of any cataract (P=0.24), nuclear cataract (P=0.35), cortical cataract (P=0.88), subcapsular posterior cataract (P=0.87), any glaucoma (P=0.57), open-angle glaucoma (P=0.89), or angle-closure glaucoma (P=0.69).

Conclusions: In addition to parameters such as lower physical activity, higher depression score and worse general health status, a reduced HGS is associated with visual impairment, shorter axial length, lower intraocular pressure and higher prevalence of diabetic retinopathy. HGS dynamometry or a handshake may give additional clinical information for the ophthalmologist about the general health and some ocular parameters of the patient.

CONTROL ID: 3707256

SUBMITTER (NAME ONLY): Yoko Ikeda

TITLE: Seasonal Variation of Intraocular Pressure in Non-Glaucomatous Subjects

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ikeda, K. Mori, M. Ueno, K. Imai, H. Mieno, C. Sotozono, Ophthalmology, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|Y. Ikeda, K. Mori, Oike-Ikeda Eye Clinic, Kyoto, JAPAN|K. Yoshii, Mathematics and Statistics in Medical Sciences, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|M. Nakano, N. Omi, R. Sato, K. Tashiro, Genomic Medical Sciences, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|Y. Maruyama, Japanese Red Cross Society Kyoto Daini Hospital, Kyoto, JAPAN|S. Kinoshita, Frontier Medical Science and Technology for Ophthalmology, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: To evaluate seasonal variation of intraocular pressure (IOP) in non-glaucomatous subjects from records established in two large databases since 1995 and 2005, i.e., the Kyoto Prefectural University of Medicine Glaucoma Registry (KPUM-GR) and the Kyoto Glaucoma Cohort Study (KGC), respectively, for the purpose of glaucoma genome research (i.e., data collected from both glaucoma patients and normal, healthy, non-glaucomatous, control-subject volunteers).

Methods: IOP data meeting the following inclusion criteria extracted from the KPUM-GR or KGC database was obtained: 1) subjects diagnosed as non-glaucomatous with bilateral visual fields within normal limits, 2) applanation (A) IOP (Haag-Streit) of ≤ 21mmHg, and 3) non-contact tonometry (N) (RKT-7700, Nidek) findings measured within 2 hours on the same day with A IOP. In all subjects, right-eye data was used for analysis. IOP seasonal variation was determined via regression-model analysis based on the mean values for each month for both A and N IOP by dividing the data into 12 groups by the month of measurement.

Results: Data-points extracted and later evaluated included 620 from the KPUM-GR and 868 independently derived from and KGC; i.e., a total of 1488 subjects [428 males, 1060 females, mean age: 62.2±11.5 (mean±SD) years]. The A IOP data revealed significant seasonal variation ($P<0.01$), i.e., lower IOP in summer and higher IOP in winter, and the N IOP data also showed significant seasonal variations.

Conclusions: The real-world data of the non-glaucomatous subjects in our two large databases revealed significant seasonal variation of IOP in both A and N.

CONTROL ID: 3707257

SUBMITTER (NAME ONLY): Hiroyuki Shimizu

TITLE: Myopia imaging biomarkers to predict atropine response by optical coherence tomography and fundus photography

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Shimizu, T. Yuasa, H. Inoue, T. Imanaka, Santen Seiyaku Kabushiki Kaisha, Osaka, JAPAN|

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ABSTRACT BODY:

Purpose: Atropine is effective for controlling myopia progression in children. Since the response to atropine differs among patients, identification of biomarkers that can predict drug response before treatment is important. Choroidal thickness is reportedly affected by atropine, implying that the drug exerts effects on the posterior segment. However, whether these effects are associated with drug response remains unclear.

Thus, we aimed to predict atropine response by evaluating the relationship between the posterior segment imaging features and drug response.

Methods: We collected optical coherence tomography (OCT) images and fundus photographs (FPs) from our clinical trial “Phase 2 study of STN1012700” (012701LT) (N=99). This study was approved by the Institutional Review Board at Research Committee of Santen Pharmaceutical Co., Ltd. Myopia patients aged 6 to 11 years were included and categorized into three dose groups and a placebo group. The objective equivalent spherical power (SE), axial length (AL), and changes in the SE and AL from baseline to 12 months were evaluated as endpoints. From the OCT data, we extracted the thicknesses of the ganglion cell layer, inner plexiform layer complex (GCL+), and choroid-sclera interface (CSI) at each region, divided in accordance with the Early Treatment of Diabetic Retinopathy Study (ETDRS) grid. From the FPs, we extracted the steepness of the retinal artery (RA) trajectory and the proportion of R layer (Redness) in the RGB layers. A linear mixed model regression analysis was conducted to identify features that were statistically associated with the endpoints. The OCT or FP factors, baseline value, dose groups, and the interaction between the dose groups and factors were included as explanatory variables.

Results: On OCT analysis, the GCL+ thickness in some regions was significantly associated with the change in AL from baseline, depending on the dose group ($P < 0.05$). However, no significant association with the CSI was noted. On PF analysis, while the RA trajectory showed no association with the changes in SE and AL from baseline, the Redness in some regions showed significant association, depending on the dose group ($P < 0.05$).

Conclusions: Therefore, the GCL+ thickness and Redness may be associated with atropine response, suggesting their potential use as biomarkers to predict drug response before treatment.

CONTROL ID: 3707264

SUBMITTER (NAME ONLY): Yuji Takayanagi

TITLE: Fellow eye comparison between Tanito microhook ab-interno trabeculotomy and iStent implantation combined with cataract surgery

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Takayanagi, S. Ichioka, A. Ishida, A. Tsutsui, M. Tanito, Department of Ophthalmology, Shimane University Faculty of Medicine, JAPAN|

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ABSTRACT BODY:

Purpose: The aim of this study was to compare the efficacy and complications after Tanito microhook ab-interno trabeculotomy (TMH) combined with cataract surgery in one eye and iStent implantation combined with cataract surgery in the fellow eye of a patient.

Methods: Sixty-four eyes of 32 participants (mean age, 75.9 ± 7.6 years; 15 men, 17 women) with primary-open angle glaucoma (65.6 %), exfoliation glaucoma (23.4 %), and other glaucoma types (11.0 %) were included retrospectively. The intraocular pressure (IOP) and number of antiglaucoma medications evaluated preoperatively and postoperatively at 2 weeks, 3, 6, and 12 months were collected by chart review. The postoperative complications including layered hyphema and IOP spike of 30 mmHg or higher also were collected. Comparisons between the two surgical procedures were performed by mixed-effects regression models and followed by Wilcoxon signed-rank test or Fisher's exact probability test.

Results: The preoperative IOP and medications of TMH group (18.8 ± 5.7 mmHg and 3.0 ± 1.2 medications, respectively) were higher than those of iStent group (15.5 ± 3.4 mmHg and 2.7 ± 1.2 medications, respectively) ($p<0.0001$ and $p=0.0437$, respectively); while those of TMH group (12.6 ± 2.3 mmHg and 2.3 ± 0.9 medications, respectively) were identical to those of iStent group (12.8 ± 2.5 mmHg and 2.3 ± 0.9 medications, respectively) ($p=0.0934$ and $p=0.3251$, respectively) at the 12 months postoperatively. By mixed-effects regression analysis, postoperative reduction of IOP and medications were significantly different between the two groups ($p<0.0001$, $p<0.0001$, respectively). At 12 months postoperatively, reduction of IOP in TMH group (6.2 ± 5.6 mmHg, 29.5%) was greater than those in iStent group (2.7 ± 3.2 mmHg, 18.8%) ($p=0.0003$); reduction of medication in TMH group (0.7 ± 1.3, 23.3%) was greater than those of iStent group (0.4 ± 1.1, 14.8%) ($p=0.0437$). Frequency of layered hyphema were significantly higher in TMH group (8 eyes, 25%) than iStent group (0 eye, 0%) ($p=0.0048$); frequency of IOP spike was equivalent between the groups (TMH, 2 eyes, 6%; and iStent, 2 eyes, 6%) ($p=1.0000$).

Conclusions: By fellow-eye comparison, IOP reduction was greater with TMH than with iStent, while achieved levels of IOP was identical between both procedures. The rate of layered hyphema was higher in TMH than iStent.

CONTROL ID: 3707265

SUBMITTER (NAME ONLY): Tsung-Han Chou

TITLE: Autoregulatory dynamics of the PERG in mice with induced and rescued mitochondrial dysfunction

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chou, H. Yu, A. Lazo, V. Porciatti, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|R.D. Koilkonda, Lacerta Therapeutics, Inc., Alachua, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Flickering light around 10 Hz induces rapid dilation of retinal vessels in the inner retina as well as progressive reduction (adaptation) of Pattern Electroretinogram (PERG) amplitude, indicating neuro-vascular-metabolic autoregulation. We measured flicker-PERG adaptation in control mice, in mice with induced mitochondrial dysfunction mimicking Leber Hereditary Optic Neuropathy (LHON) and in mice where induced LHON was rescued with gene-therapy.

Methods: 3-month-old DBA/1J mice were randomly split into three groups and received two intravitreal AAV injections at two-day intervals. The first group (Control, N=17) was injected with AAV/mcherry + AAV/mcherry (4.52 E8 vg/eye); the second group (LHON, N=23) with AAV/mutant ND4 (4.32 E9 vg/eye) + AAV/mcherry (4.52 E8 vg/eye); the third goup (LHON rescue, N=27) with AAV/mutant ND4 (4.32 E9 vg/eye) + AAV/wild-type ND4 (4.4 E8 vg/eye). A group of uninjected mice (naïve control, n=101) was also tested for comparison. In all mice, PERG was recorded from both eyes with superimposed 101 Hz flicker (baseline) and then with 11 Hz flicker (test) and the test minus baseline amplitude was considered as measure of flicker PERG adaptation. Group comparisons were performed using Generalized Estimating Equations (GEE) analysis accounting for the inclusion of both eyes.

Results: In naïve and control groups, the mean PERG adaptation was -4.1 µV (SE=0.42) and -3.2 µV (SE=0.94), respectively; in the LHON group was 0.84 µV (SE=0.89) and in the LHON rescued group was - 2.6 µV (SE=0.94). Multiple comparisons revealed significant ($P<0.05$) differences between control groups and LHON group and between rescued LHON and LHON group but not between control groups and rescued LHON group.

Conclusions: Mitochondrial dysfunction in a mouse model of LHON abolishes the flicker-induced PERG adaptation normally present in control mice. Gene-therapy to rescue mitochondrial function restores, at least in part, PERG adaptation. Flicker-induced PERG adaptation may represent a physiological tool to investigate altered metabolic autoregulation of retinal ganglion cells in optic neuropathies.

CONTROL ID: 3707266

SUBMITTER (NAME ONLY): Masayuki Inuzuka

TITLE: Association between macular perfusion density and central visual field, macular thickness in eyes with open-angle glaucoma.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Inuzuka, A. Sawada, H. Inuzuka, T. Yamamoto, H. Sakaguchi, Gifu University School of Medicine Graduate School of Medicine, JAPAN|T. Yamamoto, KAIJIN Glaucoma Center, KAIYA Eye Hospital, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the association between macular perfusion density and functional or anatomical impairment in various stages of glaucoma.

Methods: We retrospectively examined 147 medically treated primary open-angle glaucoma eyes. All the patients underwent static perimetry using the Humphrey Field Analyzer program Central 10-2, spectral-domain optical coherence tomography (OCT), and 6 × 6-mm optical coherence tomography angiography (OCT-A) centered on the fovea.

Results: The mean age was 64.0 ± 10.9 years (males: 62, females: 85). The mean intraocular pressure was 13.1 ± 2.1 mmHg. Macular perfusion density was positively correlated with sensitivity corresponding to central visual field and macular thickness in all 8 sectors (all $P < 0.05$; Pearson correlation coefficient). In addition, there was a positive correlation between the averaged macular perfusion density and the averaged thickness of the circumpapillary retinal nerve fiber layer (cpRNFL), as well as between the macular ganglion cell layer and the inner plexiform layer (mGCIPL) ($P = 0.001$ and $P < 0.0001$, respectively; Pearson correlation coefficient).

Conclusions: Macular perfusion density by OCT-A is highly correlated with both functional and structural changes in glaucoma, and thus its assessment might be useful for monitoring glaucoma.

CONTROL ID: 3707268

SUBMITTER (NAME ONLY): Johanna Heimbucher

TITLE: Mutant Mice With a Heterozygous Collagen Type I Deficiency Develop a Progressive Loss of Optic Nerve Axons

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Heimbucher, M. Schneider, E.R. Tamm, Anatomy, University of Regensburg, Regensburg, Bavaria, GERMANY|M. Mack, Nephrology, University Hospital Regensburg, Regensburg, Bavaria, GERMANY|

Commercial Relationships Disclosure: Johanna Heimbucher: Commercial Relationship: Code N (No Commercial Relationship) | Magdalena Schneider: Commercial Relationship: Code N (No Commercial Relationship) | Matthias Mack: Commercial Relationship: Code N (No Commercial Relationship) | Ernst Tamm: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mechanical properties of the peripapillary sclera (PPS) likely influence the vulnerability of optic nerve (ON) axons to glaucomatous damage. Here we investigated eyes and optic nerves of mice with a substantial deficiency in collagen type I, the major structural fibrillar molecule of the sclera.

Methods: Ubi-Cre3 col1a1$^{wt/fl}$ mice lacking one allele of Col1a1 were investigated. Col1a1 encodes for the pro-alpha1(I) chain that is essential for formation of triple stranded collagen type I. Knockdown of Col1a1 mRNA expression and protein synthesis was analyzed via real-time RT-PCR and western blot respectively. Ocular phenotypes of mutant mice and their control littermates were analyzed by histological staining of sagittal sections, including measurement of central corneal thickness (CCT) and retinal thickness. Axial length of enucleated native eyes was measured with a digital caliper. Myelinated ON axons were visualized and counted in PPD-stained ON cross-sections, whereas RGC somata were quantified on retinal whole mounts with an immunofluorescence staining against RBPMS.

Results: At three months of age, mutant mice showed a significant 50 % ($p = 0.02$) reduction in Col1a1 mRNA in scleral RNA that resulted in a 75 % reduction ($p = 0.03$) of translated COL1A1 at five months of age. Axial length and retinal thickness of Ubi-Cre3 col1a1$^{wt/fl}$ mice were not different from that of control littermates, while the cornea of mutant mice was thinner (98.9 µm ± 12.2 versus 86.3 µm ± 4.4, $p = 0.015$). Otherwise, there were no obvious light microscopical differences in ocular morphology. At two months of age, myelinated ON axon number was not different between mutant mice and their control littermates (36,918 ± 4310 versus 39,095 ± 5000). This was different in 5-month-old animals that showed a significant ($p = 0.008$) reduction in ON axons (40,215 ± 4854 versus 33,598 ± 7588). The findings correlated with a reduction of RGC somata (2370 ± 315 per mm^2 versus 1139 ± 277, $p = 0.04$).

Conclusions: We conclude that reduction in collagen type I causes a chronic and continuous loss of ON axons like that seen in glaucoma. The changes are likely induced by alteration of the mechanical properties of the sclera.

CONTROL ID: 3707273

SUBMITTER (NAME ONLY): Takashi Itokawa

TITLE: Effect of wind stimulation on ocular surface temperatures and blood flow in soft contact lens wearers

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Itokawa, Toho Daigaku Iryo Center Omori Byoin, Ota-ku, Tokyo, JAPAN|Y. Okajima, Toho Daigaku Iryo Center Omori Byoin, Ota-ku, Tokyo, JAPAN|H. Iwashita, Toho Daigaku Iryo Center Omori Byoin, Ota-ku, Tokyo, JAPAN|K. Kakisu, Toho Daigaku Iryo Center Omori Byoin, Ota-ku, Tokyo, JAPAN|Y. Hori, Toho Daigaku Iryo Center Omori Byoin, Ota-ku, Tokyo, JAPAN|

Commercial Relationships Disclosure: Takashi Itokawa: Commercial Relationship: Code N (No Commercial Relationship) | Yukinobu Okajima: Commercial Relationship: Code N (No Commercial Relationship) | Hiroko Iwashita: Commercial Relationship: Code N (No Commercial Relationship) | Koji Kakisu: Commercial Relationship: Code N (No Commercial Relationship) | Yuichi Hori: Commercial Relationship(s);Code F (Financial Support):Alcon

ABSTRACT BODY:

Purpose: Wind stimulation is an environmental factor that causes contact lens (CL) discomfort. We investigated the changes in ocular surface temperature and blood flow resulting from wind stimulation in soft CL (SCL) wearers.

Methods: We recruited 21 SCL wearers (21 eyes; mean age, 25.3±4.2 years) who wore two 1-day disposable silicone hydrogel lens (narafilcon A and delefilcon A). We measured the conjunctival blood flow, ocular surface temperature, and non-invasive tear break-up time (NIBUT) with/without SCLs after wind stimulation, which was created by a fan that directed wind at the rate of 3.0 meters/second to the volunteers' faces for 10 minutes while wearing and not wearing SCLs. The blood flow was measured as the mean blur rate (MBR) using laser speckle flowgraphy (LSFG-OAS, Softcare). The temperature and NIBUT measurements were conducted using ocular surface thermography (TG-1000, Tomey) and tear film interferometry (DR-1 Alpha, KOWA), respectively. Dryness was evaluated using the visual analog scale (VAS), with 0 indicating no symptoms.

Results: After wind stimulation, the NIBUT and VAS score for dryness symptoms with the delefilcon A lens (3.7±1.7 seconds and 29.4±16.9, respectively) were significantly ($P<0.01$ for both comparisons, paired t-test) longer and lower than with the narafilcon A lens (2.3±1.7 seconds and 35.9±17.0, respectively). Compared with no SCL, the corneal and bulbar conjunctival temperatures with SCLs decreased significantly ($P<0.01$ for both comparisons). The temperature difference between with/without the delefilcon A lens (-0.36±0.35°C) was significantly ($P<0.01$) lower than with the narafilcon A lens (-0.60±0.42°C). Although the bulbar conjunctival blood flow with the narafilcon A lens increased significantly ($P<0.05$) compared with no SCL (174.3±39.6 vs 158.7±33.2), that with the delefilcon A lens (156±42.3) did not reach significance. The rate of blood flow after wearing the narafilcon A lens (1.11±0.21) was significantly ($P<0.05$) higher than with the delefilcon A lens (0.99±0.19).

Conclusions: CLs with a lower NIBUT and more dryness show significantly greater changes in blood flow and temperature after wind stimulation. The wind stimulation test may be useful as a stress test for CL wear.

CONTROL ID: 3707277

SUBMITTER (NAME ONLY): Chao Huang

TITLE: The Role of the STING/Type I IFN Signaling Pathway in Age-Related Macular Degeneration(AMD)

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Huang, G. Widmer, P. Strassburger, M. Lazendic, S. Gruener, P. Westenskow, N. Mitrousis, D. Feenstra, Roche Pharma Research and Early Development, Ophthalmology Discovery, Roche Innovation Center Basel, F Hoffmann-La Roche AG Research and Development Division, Basel, Basel-Stadt, SWITZERLAND|H. Liu, D. Sinha, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|E. Lad, Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|A. Proia, Pathology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|D. Sinha, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Geographic atrophy(GA), an advanced form of age-related macular degeneration(AMD), is characterized by degeneration of the photoreceptors and retinal pigment epithelium(RPE). Prior evidence has implicated senescent retinal cells contribute to the pathogenesis of AMD. Increased activation of cyclic GMP–AMP synthase(cGAS)/ stimulator of interferon genes(STING)/Type I Interferon pathway has been reported in GA patients. However, the role of Type-I IFNβ in chronic retinal degeneration remains elusive. This study aims to investigate the role of STING/IFNβ in chronic retinal degeneration and cellular senescence contributing to the pathogenesis of GA.

Methods: STING protein expression in postmortem eyes with various stages of AMD was measured by immunohistochemistry. Luminex was used to determine the IFNβ production in response to STING agonists in primary human RPEs. To elucidate the role of IFNβ in chronic retinal degeneration in vivo, AAV2-CAG-IFNβ(1x10^9 GC/eye, n=12) was used for chronic(20 weeks) expression of IFNβ in the eyes of C57BL/6J mice via intravitreal injection and AAV2-CAG-Null(1x10^9 GC/eye, n= 12) was injected as a control. Optical coherence tomography(OCT) and fluorescein angiography(FA) imaging were performed to monitor leakage and retinal degeneration. Senescence-associated(SA) β-galactosidase assay and immunohistochemistry were used to analyze the retinal cellular senescence and RPE degeneration.

Results: STING protein expression increased in the RPE of AMD patients. In primary human RPEs, STING agonists led to dose-dependent IFNβ production. In the mouse model, an increase of retinal degeneration was observed in AAV2-CAG-IFNβ injected eyes by OCT and fundus imaging, but not in AAV2-CAG-Null injected eyes. AAV2-CAG-IFNβ injected mouse eyes showed a reduction of RPE65 and CRALBP expression and developed degenerated RPEs with features remarkably similar to GA patients. Furthermore, β-galactosidase and p16INK4a positive retinal cells were upregulated in the murine eyes injected with AAV2-CAG-IFNβ, but not in the AAV2-CAG-Null eyes.

Conclusions: STING activation in RPE occurs in postmortem eyes with all stages of AMD. STING agonists drive IFNβ secretion in primary human RPEs. In the murine model, chronic IFNβ expression by AAV2 increases retinal cell senescence and contributes to RPE degeneration. These results suggest that cGAS/STING induced IFNβ may contribute to the pathogenesis of AMD.

CONTROL ID: 3707280

SUBMITTER (NAME ONLY): Ellina Iakupova

TITLE: Macular Pigment Optical Density and Its Determinants in a Russian population. The Ural Eye and Medical Study

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Iakupova, S. Panda-Jonas, M. Bikbov, G. Kazakbaeva, J. Jonas, Ufa Eye Research Institute, RUSSIAN FEDERATION|

Commercial Relationships Disclosure: Ellina Iakupova: Commercial Relationship: Code N (No Commercial Relationship) | Songhomitra Panda-Jonas: Commercial Relationship: Code N (No Commercial Relationship) | Mukharram Bikbov: Commercial Relationship: Code N (No Commercial Relationship) | Gyulli Kazakbaeva: Commercial Relationship: Code N (No Commercial Relationship) | Jost Jonas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the macular pigment optical density (MPOD) and its associations with ocular and systemic parameters and diseases.

Methods: The Ural Eye and Medical Study included 5899 (80.5%) out of 7328 eligible individuals. As part of ophthalmological and systemic examinations, MPOD was measured by reflectometry.

Results: MPOD data were available for 4889 (82.9%) individuals (mean age:57.8±10.1 years;range:40-94). Mean values for MOPD, maximal MOPD, macular pigment (MP) area and MP volume were 0.13±0.04 d.u. (density units), 0.36±0.09 d.u., 60,791±14,826 pixel, and 8,033±2,888 d.u.pixel, respectively. A higher MP density correlated (regression coefficient r:0.63) with older age (standardized regression coefficient beta:0.59;non-standardized regression coefficient B:0.23;95% confidence interval (CI):0.22,0.23;P<0.001), female sex (beta:0.08;B:0.63;95%CI:0.44,0.83;P<0.001), rural region of habitation (beta:0.13;B:1.02;95%CI:0.0.83,1.22;P<0.001), lower body mass index (beta:-0.04;B:-0.03;95%CI:-0.05,0.01;P=0.004), lower prevalence of chronic obstructive pulmonary disorder (beta:-0.03;B:-0.43;95%CI:-0.79,-0.08;P=0.02), higher erythrocyte sedimentation rate (beta:0.03;B:0.01;95%CI:0.002,0.02;P=0.03), lower leukocyte cell count (beta:-0.04;B:-0.10;95%CI:-0.16,-0.03;P=0.003), thinner temporal parafoveal retinal thickness (beta:-0.06;B:-0.01;95%CI:-0.01,-0.003;P<0.001), thinner central corneal thickness (beta:-0.06;B:-0.006;95%CI:-0.009,-0.004;P<0.001), higher prevalence of previous cataract surgery (beta:0.09;B:2.08;95%CI:1.50,2.65;P<0.001) and reticular pseudo drusen (RPD) (beta:0.03;B:0.56;95%CI:0.13,0.98;P=0.01), and lower stage of open-angle glaucoma (beta:-0.03;B:-0.39;95%CI:-0.74,-0.04;P=0. 03). Prevalence (P=0.44;beta:-0.01) and degree (P=0.70;beta:-0.01) of angle-closure glaucoma, prevalence (P=0.31;beta:0.01) of age-related macular degeneration (AMD) without RPD, and prevalence (P=0.95;beta:0.001) of diabetic retinopathy were not significantly associated with the mean MP density in that model.

Conclusions: After adjusting for age, sex, rural region, body mass index, perifoveal retinal thickness, central corneal thickness and previous cataract surgery, a higher MPOD correlated with a higher RPD prevalence and lower stage of open-angle glaucoma, but not with AMD independently of RPD.

CONTROL ID: 3707295

SUBMITTER (NAME ONLY): Olivia Taylor

TITLE: Sphingosine 1 Phosphate Signaling Enhances NF-κB Activation and Suppresses Muller Glia Reprogramming in the Injured Retina

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Taylor, A.J. Fischer, Neuroscience, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Olivia Taylor: Commercial Relationship: Code N (No Commercial Relationship) | Andy Fischer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Harnessing the regenerative potential of Muller glia (MG) may lead to the development of novel therapies reversing neuronal cell loss in sight-threatening diseases. In this study, we identify sphingosine 1 phosphate (S1P) as a critical activator of NF-κB, an inflammatory signaling pathway shown to suppress both the proliferation of Muller glia-derived progenitor cells (MGPCs) in chick retinas and the reprogramming of Ascl1-overexpressing MG in mouse retinas. We hypothesize that inhibiting S1P signaling may promote the formation of MGPCs in injured retinas.

Methods: NF-κB-eGFP transgenic mice (n=6, P77-144) received intravitreal injections of 2 µg/dose PF543, a sphingosine kinase 1 inhibitor, with 14.72 µg NMDA (an excitotoxin); the contralateral eye received NMDA + vehicle. Eyes were enucleated, fixed, and sectioned. Retinas were immunolabeled for GFP and Sox2. Co-labeled cells were quantified, and statistical analyses were conducted using a two-tailed paired t-test. A similar paradigm was conducted with SEW2871 (S1PR1 agonist) (2 ug/dose, n=7, P91-96).

Young postnatal chicks (n=6, P7) received intraocular injections of 5 µg/dose PF543 with 73 µg NMDA and 2 µg EdU. Fixed retinal sections were immunolabeled for EdU and Sox2, and co-labeled cells were quantified and analyzed with a two-tailed paired t-test. A similar paradigm was conducted with SEW2871 (5 ug/dose, n=6, P7).

Results: NMDA-damaged mouse retinas treated with PF543 had significantly fewer NF-κB+ MG (5.17±2.14) than control retinas (10.17±4.26, p=0.0035). Mouse retinas treated with SEW2871, without damage, had significantly more NF-κB+ MG (8.21±4.68) than control retinas (2.00±1.85, p=0.0091). Chick retinas treated with PF543 and NMDA showed greater proliferation of MGPCs (78.67±8.09) than control damaged retinas (44.5±13.61, p<0.0001). A decrease in proliferation was observed in injured chick retinas treated with SEW2871 (56.5±8.04) compared to control retinas (69.17±17.38, p=0.0296).

Conclusions: These results suggest that S1P signaling may suppress MGPC formation in part through NF-κB. We previously found that S1PR1 inhibition was not sufficient to decrease NF-κB or enhance MGPC formation; other S1P receptors may be compensatory in the absence of S1PR1 signaling. In this study, we found that S1P synthesis and receptor activation may be a critical inhibitor of MG reprogramming in chick and mouse retinas.

CONTROL ID: 3707296

SUBMITTER (NAME ONLY): HYEON JEONG YOON

TITLE: Therapeutic Effect of Oral Administration of Bacillus Derived-Superoxide Dismutase in a Murine Model of Experiment Dry eye

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. YOON, R. Jin, H. Yoon, J. Kim, K. Yoon, Department of Ophthalmology, Chonnam National University Hospital, Gwangju, Gwangju, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: HYEON JEONG YOON: Commercial Relationship: Code N (No Commercial Relationship) | Rujun Jin: Commercial Relationship: Code N (No Commercial Relationship) | Hee Su Yoon: Commercial Relationship: Code N (No Commercial Relationship) | Jonghwa Kim: Commercial Relationship: Code N (No Commercial Relationship) | Kyung Chul Yoon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the efficacy of oral administration of Bacillus derived-superoxide dismutase (SOD) in a murine model of experimental dry eye (EDE)

Methods: Mice were divided into 7 groups according to treatment: un-treated, EDE, vehicle, topical 0.05% cyclosporine (CsA), oral 2.5mg/kg SOD, oral 5.0mg/kg SOD, and oral 10.0mg/kg SOD. After exposure to desiccating stress for 5 days except for the un-treated group, tear volume, tear film break-up time (TBUT), and corneal fluorescein staining scores (CFS) were measured at 0, 5, and 10 days after treatment. Ten days after treatment, 2',7'-dichlorodihydrofluorescein diacetate assay (DCF-DA) for reactive oxygen species (ROS) production, enzyme-linked immunosorbent assay for malondialdehyde (MDA) were measured in the cornea, conjunctiva, and lacrimal gland. Flow cytometry for CD4+interferon-γ+ T cells were evaluated in the cornea and conjunctiva. In addition, periodic acid-Schiff staining for conjunctival goblet cells and TUNEL assay for corneal apoptotic cells were performed.

Results: After 5 and 10 days, treatment groups with topical 0.05% CsA, oral 2.5mg/kg SOD, oral 5.0mg/kg SOD, and oral 10.0mg/kg SOD showed increased tear volume and TBUT, and decreased CFS compared with the EDE and vehicle group. ROS production, MDA for oxidative stress, and corneal apoptosis were decreased in the CsA and 3 concentrations of SOD-treated groups. The number of inflammatory T cells of cornea and conjunctiva was decreased and conjunctival goblet cell density was increased in the treatment groups with topical 0.05% CsA, oral 2.5mg/kg SOD, oral 5.0mg/kg SOD, and oral 10.0mg/kg SOD. In addition, compared to the CsA-treated group, the oral 2.5mg/kg SOD groups showed increased TBUT and decreased inflammatory T cells; the oral 5.0mg/kg SOD groups showed decreased CFS and increased conjunctival goblet cells.

Conclusions: Oral administration of SOD could improve clinical parameters, oxidative damage, and inflammation in the murine EDE model.

CONTROL ID: 3707297

SUBMITTER (NAME ONLY): Maria Vittoria Cicinelli

TITLE: FACTORS ASSOCIATED WITH VISUAL OUTCOMES AND TREATMENT BURDEN OF MYOPIC NEOVASCULARIZATION OVER 10 YEARS

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Cicinelli, E. De Felice, L. La Franca, A. Rabiolo, M. Battaglia Parodi, U. Introini, F. Bandello, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor (VEGF) inhibitors provide excellent functional and morphological benefits in treating myopic macular neovascularization (mMNV) in the short term. We longitudinally investigated the real-life visual outcomes and the treatment burden of mMNV over a decade.

Methods: Retrospective electronic record review of adult patients with myopic refraction (<-1.00 D) and active mMNV undergoing at least one anti-VEGF agents' injection between January 2009 and March 2021. Best-corrected visual acuity (BCVA), optical coherence tomography findings, and number of intravitreal anti-VEGF injections administered were extracted at each visit. Factors associated with BCVA change were identified with linear mixed models. Treatment burden was quantified as number of injections to mMNV inactivation and rate of mMNV recurrences. Risk factors for recurrences were identified using recurring-events regression models.

Results: A total of 327 eyes (69% females; median[interquartile range, IQR] refraction -11 D [-14 to -9]) were included; 123 eyes (38%) had ≥5-year follow-up. mMNV presenting with subretinal fluid at baseline (estimate[SE]=0.84[0.40], p=0.03) required a higher number of injections for inactivation. BCVA returned to baseline at 3 years and then worsened (Figure 1). Central macular mMNV location (estimate[SE]= 0.07[0.06] vs. extrafoveal, p=0.01) had the worst prognostic effect on the visual acuity. In 174 eyes (53%), mMNV activity recurred; cumulative number of recurences was 3 at 10 years (Figure 2). Recurring eyes had a faster rate of vision loss (estimate[SE]=0.001[0.002] LogMAR/year for each recurrence, p=0.001) than non-recurring eyes. Older age (HR[95% CI]= 1.10[1.01-1.20] for each 10-year increase, p=0.04), larger mMNV (HR[95% CI]= 1.07[1.01-1.13] for each 1-mm^2 increase, p=0.02), and juxtafoveal mMNV (HR[95% CI]=1.61[1.04-2.51] vs. extrafoveal, p=0.03) were risk factors for recurrences.

Conclusions: mMNV patients progressively lose vision over the long term, despite intravitreal treatments. Older adults with large, central mMNV lesions have a higher risk of mMNV recurrence and faster rates of vision loss.

CONTROL ID: 3707298

SUBMITTER (NAME ONLY): Joao Nassaralla

TITLE: Aflibercept Intravitreal Injection for Myopic Choroidal Neovascularization - 5 years follow up

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Nassaralla, Retina and Vitreous, Instituto de Olhos de Goiânia, Goiânia, Goiás, BRAZIL|A. Nassaralla, Retina and Vitreous, Centro Oftalmológico de Minas Gerias, Belo Horizonte, Minas Gerais, BRAZIL|

Commercial Relationships Disclosure: Joao Nassaralla: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Nassaralla: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Follow up results of aflibercept intravitreal injecton (AII) in choroidal neovascularization secondary a pathologic myopia (MN) after 5 years.

Methods: 15 eyes wiht MN were trated with 2mg AII. BVVA, macular thickness on OCT and FA were evaluated. Follow-up were 5 years

Results: The mean were: age: 25yrs, refractive error: -10.75D and macular thickness decreased from 352 to 230 micrometers. At 12 months post -treatment mean BCVA increased from 20/100 to 20/50. Only 1 patient lost 35 letters; other 14 increased or stabilized their VA

Conclusions: These short-term results suggest thet AII are effective and safe and useful in patients with MN

CONTROL ID: 3707300

SUBMITTER (NAME ONLY): Jos Rozema

TITLE: Influence of rigid lens position on visual image quality in normal and keratoconic eyes

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Rozema, M. Jiménez-García, C. Koppen, Universiteit Antwerpen, Antwerpen, BELGIUM|J.J. Rozema, M. Jiménez-García, C. Koppen, Universitair Ziekenhuis Antwerpen, Edegem, Antwerp, BELGIUM|G.D. Hastings, Center for Innovation in Optics and Vision, School of Optometry, University of California, Berkeley, Berkeley, California, UNITED STATES|R.A. Applegate, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Jos Rozema: Commercial Relationship: Code N (No Commercial Relationship) | Gareth Hastings: Commercial Relationship: Code N (No Commercial Relationship) | Marta Jiménez-García: Commercial Relationship: Code N (No Commercial Relationship) | Carina Koppen: Commercial Relationship: Code N (No Commercial Relationship) | Raymond Applegate: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Rigid contact lenses are the method of choice to optically correct advanced keratoconus. Such lenses may translate and rotate on-eye, changing the resulting Wavefront Error (WFE). This work assesses how this motion affects acuity in normal and keratoconic eyes.

Methods: Previous SyntEyes models were expanded by adding the ability to shift and rotate a sphero-cylindrical rigid contact lens correction with respect to the center of a 5 mm pupil. More specifically, a simulated through-focus experiment of 20 normal and 20 keratoconic SyntEyes first objectively determined the centered sphero-cylindrical correction which optimized the visual Strehl (VSX). The optimal correction was then allowed to misalign ±1 mm in 0.1 mm steps and rotate ±15° in 1° steps, defining an 'alignment space'. This provided 52 111 resultant WFE for each eye, which were used to calculate VSX, changes in which may be used to predict changes in logMAR acuity.

Results: Keratoconic SyntEyes were significantly less tolerant to lens rotation than normal SyntEyes before potentially noticeable changes of more than 2 logMAR letters occur (t-test, $p < 0.01$), which varied considerably between individual eyes. These variations were not correlated with the amount of uncorrected astigmatism ($p > 0.05$) as the contact lenses dampened the corneal astigmatism. Normal SyntEyes had a significantly larger average tolerance to rotation than keratoconic cases (respectively, -14.1° to +13.4° and -10.5° to 10.6°; $p < 0.01$). Similarly, normal SyntEyes were also significantly more tolerant to decentration than keratoconus (0.39 ± 0.15 mm and 0.27 ± 0.13 mm, respectively).

Perfect alignment did not always provide the best possible optical correction, as in 9/20 keratoconic SyntEyes a gain of 1 or more letters was seen for a shifted or decentered lens position (Figure 1). This was also seen in 2/20 normal SyntEyes.

Conclusions: Keratoconic eyes are more sensitive to smaller amounts of misalignment than normal eyes. In many cases, the best possible visual image quality may be obtained with a certain combination of decentration and rotation, rather than with perfect alignment.

CONTROL ID: 3707301

SUBMITTER (NAME ONLY): Nicolas Blais

TITLE: Comparison of Ocular Health Outcomes Between a Tele-Eye Care Comprehensive Eye Exam and a Gold Standard In-Person Eye Exam

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Blais, F. Brisson, J. Hanssens, School of optometry, Universite de Montreal, Montreal, Quebec, CANADA|

Commercial Relationships Disclosure: Nicolas Blais: Commercial Relationship: Code N (No Commercial Relationship) | Fannie Brisson: Commercial Relationship: Code N (No Commercial Relationship) | Jean-Marie Hanssens: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The lack of data on how tele-eye care comprehensive eye exams compare to the in-person exams in primary eye care settings prevents law makers from clearly outlining the role of tele-eye care. This randomized clinical trial aims to compare the number of ocular health tests results that are outside of clinical norms, compare the confidence level of the eye care provider (ECP) for each of these tests results and compare the eye health diagnoses (Dx) between hybrid tele-eye care and in-person comprehensive eye exam.

Methods: Thirty-five optometry-naïve participants (13 M, 22 F, aged 21-58 years), consulting for routine eye examination were randomly subjected to two comprehensive eye exams. The in-person eye exam was completed by an on-site ECP, while the tele-eye care exam was performed by an in-person technician through DigitalOptometrics™ platform and videoconferencing with a remote ECP. All ocular health tests results were categorized according to their compliance to clinical standards and the ECP scored their confidence level for all exam results. Results of the two modalities were compared with Krippendorff's alpha coefficients (a) and Wilcoxon signed rank tests (p). The number of common and different Dx between both modalities were also analyzed.

Results: No statistically significant difference between both exam modalities was found for all ocular health tests ($a > 0.50$), apart from extra-ocular motilities (EOM) testing ($a = 0.25$; $*p = 0.025$). No abnormal pupils were detected in both modalities. ECP reported significantly better confidence for in-person exams (97 ± 01%) compared to tele-eye care (77 ± 3%) ($p < 0.001$). Twenty-five Dx were found in tele-eye care compared to 23 in-person, among which 14 (29%) did not match between modalities with eight found only in-person and six found only remotely. These had a low morbidity and included conditions such as mild blepharitis and conjunctivochalasis.

Conclusions: Our data suggest that for a sample of people consulting for a routine examination, the levels of confidence of ECP are statistically lower for remote eye exams compared to in-person. However, both exam modalities have a statistically equivalent ability to detect out of standards ocular health findings, apart from EOM testing. To better analyze the difference in total number of ocular health Dx, the ECP should have scored a morbidity level to each Dx they made.

CONTROL ID: 3707302

SUBMITTER (NAME ONLY): Dimitrios Karamichos

TITLE: The Surprising Impact of Hormones on Keratoconus

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Karamichos, P. Escandon, S. Nicholas, R. Cunningham, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|L. Van, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|D. Murphy, K. Riaz, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Keratoconus (KC) is a progressive corneal thinning disease that manifests in puberty and worsens during pregnancy. The onset and progression of KC is considered to be multifactorial and include: environmental, genetics, and hormonal imbalances; however, the pathobiology remains elusive. This study will reveal recent in vitro and in vivo findings related to sex hormones and their receptors in an attempt to establish a causal and contributory relationship to the KC disease process.

Methods: In vitro: An established 3D in vitro self-assembled extracellular matrix (ECM) model was utilized in order to determine the interplay of major androgens/estrogens and the sex hormone receptors present in Healthy/KC corneal stromal cells via Western Blot analysis. In vivo: Ongoing clinical studies, focusing on sex hormones and KC, are discussed. Androgen/Estrogen ELISA expression was measured in a small cohort of KC patients before and after Collagen Cross Linking (CXL) treatment.

Results: In vitro: Significant changes were observed between Healthy and KC corneas, as well as between males and females in the sex hormone receptors tested; androgen receptor (AR), progesterone receptor (PR), estrogen receptor alpha (ERα), and estrogen receptor beta (ERβ). For example, both estrone (E1) and estriol (E3) stimulation in Healthy-Females showed that AR, PR, and ERβ were significantly upregulated compared to Healthy-Males. In contrast, ERα and ERβ had significantly higher expression in HKC-Females, when compared to HKC-Males. In vivo: Using blood (plasma) levels, the levels of three essential sex hormones (DHEA-S, Estrone, and Estriol) were measured. After CXL, DHEA-S levels were lower but Estrone and Estriol levels were higher, suggesting that CXL not only affects the corneal tissue (i.e., locally), but also modulates hormonal levels in the bloodstream. Variability among patients, and changes due to medication/severity will also be discussed.

Conclusions: Our data suggests that the human cornea is a sex-dependent and a hormone-responsive tissue. We posit that KC is a systemic disease, at least initially, and is heavily dependent on systemic and local hormone alterations.

CONTROL ID: 3707306

SUBMITTER (NAME ONLY): Haiyan Li

TITLE: Upregulated YAP activity and histone acetylation modulate glaucomatous trabecular meshwork cell dysfunction

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Li, P.S. Ganapathy, S. Herberg, Ophthalmology & Visual Sciences, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|D.W. Stamer, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The extracellular matrix (ECM) in the glaucomatous trabecular meshwork (GTM) is markedly stiffened. This potent biophysical cue drives progressive cellular dysfunction. Increased Yes-associated protein (YAP) activity is linked to GTM cell pathobiology, and a recent genome-wide study identified YAP1 among novel glaucoma risk loci. Epigenetic modifications such as histone acetylation are further associated with TM failure in glaucoma. Yet, the molecular underpinnings of cellular dysfunction in response to TM stiffening, and the contributions of YAP signaling and epigenetic remodeling remain unclear. Here, we investigate the effects of ECM stiffness modulation on YAP activity and histone acetylation, and how these elements modulate GTM cell dysfunction using ECM hydrogels.

Methods: ECM hydrogels were made by photocrosslinking functionalized collagen type I, elastin-like polypeptide, and hyaluronic acid. Bioinert alginate was incorporated to facilitate stiffening (via Ca^{2+} crosslinking) and dynamic softening (via alginate lyase degradation) of ECM-alginate hydrogels. Donor-derived normal TM (NTM)/GTM cells were plated on/encapsulated in hydrogels and stimulated with histone deacetylase inhibitor trichostatin-A (TSA; 150 nM) or histone acetyltransferase inhibitor garcinol (5 μM). Fibrotic marker level expression, YAP activity, cytoskeletal/nuclear organization, and histone acetylation were quantified.

Results: ECM-alginate hydrogel stiffness was increased ~3-fold upon Ca^{2+} crosslinking ($p<0.001$); alginate lyase treatment restored soft baseline levels. ECM stiffening increased F-actin, alpha-smooth muscle actin, nuclear size/tension, YAP nuclear localization, and histone acetylation in NTM and GTM cells ($p<0.05$). These pathological features were completely reversed in NTM cells by ECM softening, while GTM cells displayed a persistent fibrotic phenotype with elevated histone acetylation. Strikingly, NTM cells in a soft ECM environment treated with TSA showed increased YAP transcriptional activity, nuclear size/tension, and F-actin compared to controls ($p<0.001$). Likewise, GTM cells treated with garcinol exhibited markedly decreased nuclear YAP and expression of fibrotic markers.

Conclusions: Our data suggest that targeting ECM stiffening to interrupt aberrant YAP signaling and histone acetylation is emerging as a promising strategy to permanently restore TM tissue function in glaucoma.

CONTROL ID: 3707310

SUBMITTER (NAME ONLY): Uma Balakrishnan

TITLE: Disrupted Macular Cone Post-Synaptic Circuitry is Related to Poor Vision in Albinism

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Balakrishnan, W. Pfeifer, A.V. Drack, Ophthalmology and Visual Sciences, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|N. Wynne, J. Carroll, Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine whether aberrant macular cone post-synaptic circuitry may underly the decreased best corrected visual acuity (BCVA) seen in albinism.

Methods: Eight patients with albinism underwent multifocal electroretinography (mfERG, VERIS) and retinal imaging with adaptive optics scanning laser ophthalmoscopy (AOSLO). Pearson correlation of peak cone density (CD) with BCVA, mfERG amplitudes, and mfERG “slope” (rate of amplitude decline between the central Ring [R] 2 and peripheral R6) was performed. Parafoveal CDs and their rate of decline were compared to mfERG slope in 4 subjects. Control data was obtained from our previous studies of healthy individuals with peak CD measurements (n=58 [PMC7746960]), parafoveal CD measurements (n=20 [PMC3348369]), or mfERG (n=18 [PMC6754264]).

Results: All subjects had below average peak CD (mean 62,223±34,153; range 22,611-129,576 cones/mm^2 vs. 180,286±25,436; 122,710-247,710 cones/mm^2 in controls), decreased BCVA (mean 20/63; range 20/25-20/150), and flattened mfERG topography (R2-R6 slope: 0.239 vs. 0.312 in controls). Higher peak CD correlated with better logMAR BCVA (r=-0.85, p=0.002) and higher mfERG amplitudes in the periphery (r=0.68, p=0.029), but not centrally (r=-0.08). Parafoveal CDs were low compared to controls within the central 2 degrees, and we did not observe an association between higher CD and steeper mfERG topographies. Interestingly, the 2 subjects with 2 confirmed pathogenic mutations in OCA1 had the steepest mfERG topography and BCVA worse than 20/70 (peak CD: 42,100 and 46,400 cones/mm^2), while the 5 patients with at least one hypomorphic allele had BCVA better than 20/70 despite having flatter mfERG topography (peak CD range 38,399-129,576 cones/mm^2).

Conclusions: Although a wide range of peak foveal cone densities overlapping with the normal range is observed among these patients with albinism, denser cone packing does not result in steeper (more normal) mfERG topography, although it does correlate with better BCVA. Instead, higher cone packing is associated with higher peripheral mfERG amplitudes, suggesting abnormal connections between cone photoreceptors and bipolar cells, which could be similar to the unrefined circuitry seen in fetal retinas. This aberrant post-synaptic circuitry may explain why, even among albinism patients with milder foveal hypoplasia and denser foveal cone packing, optimal visual acuity is often unachievable.

CONTROL ID: 3707329

SUBMITTER (NAME ONLY): Catherine Liu

TITLE: Enhanced Antigen-Presenting Cell Maturation in Diabetic Donor Corneas Leads to Heightened Host Allosensitization

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Liu, T. Blanco, H. Nakagawa, A. Musayeva, S. Wang, T.H. Dohlman, Y. Chen, R. Dana, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously shown that a diabetic state induces an altered corneal microenvironment that alters the immune homeostasis of the cornea, leading to increased APC (antigen-presenting cell) maturation. Herein we examine the host alloimmune response to allografts from diabetic donors, in particular the role of graft-borne APC.

Methods: Type I diabetes mellitus (DM) was induced in C57BL/6 mice by injecting streptozocin (STZ). On day 56, corneas were either harvested and assessed through flow cytometry and immunofluorescence or transplanted into non-DM BALB/c recipient mice. Two weeks after transplantation, grafted corneas and draining lymph nodes (DLN) were analyzed by flow cytometry. In addition, IFNγ production by alloreactive CD4+ Th1 cells was quantified by flow cytometry and ELISPOT assay to evaluate the contribution of graft donor APC to host sensitization.

Results: APC ($CD45^+CD11b^+$) in DM corneas showed higher frequency ($p=0.0001$) and enhanced expression of the maturation markers (MHC-II, CD80, CD86, and CCR7) ($p=0.0001$) when compared to APC from non-DM corneas. Following transplantation, the frequency of mature migratory CD45+CD11b+ APC was significantly increased in the DLN of recipients receiving grafts from DM donors as compared to non-DM donors ($p<0.001$). $IFN\gamma^+$ production by alloreactive $CD4^+$ Th1 cells in hosts receiving grafts from DM donors was higher ($p<0.001$) as compared to non-DM donors. DM graft-derived APC were significantly more potent in sensitizing $CD4^+$ Th1 cells (direct pathway of sensitization) ($p<0.001$) compared to host APC (indirect pathway). Finally, DM allografts had a higher failure rate when compared to non-DM allografts (100% vs. 52%, $p<0.001$).

Conclusions: Our results demonstrate that a donor diabetic state leads to increased homing and maturation of corneal APC, and that following transplantation graft-borne APC swiftly migrate to the DLN to increase host sensitization. Together these changes may lead to increased graft rejection / failure when corneal transplants are derived from diabetic donors.

CONTROL ID: 3707330

SUBMITTER (NAME ONLY): Ghasem Yazdanpanah

TITLE: Change in Blink Rate Following Botulinum Toxin Injection in Benign Essential Blepharospasm

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Yazdanpanah, M.T. Yen, S.C. Pflugfelder, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Ghasem Yazdanpanah: Commercial Relationship: Code N (No Commercial Relationship) | Michael Yen: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Pflugfelder: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Benign essential blepharospasm (BEB) is characterized by involuntary twitching of eyelids, increased blinking, and photophobia. Serial injections of botulinum toxin type A (BTX-A) into the eyelid protractors, including the pretarsal orbicularis oculi muscle and corrugator supercili is the core management for BEB. Here, the blink rate was measured objectively to evaluate the effect of BTX-A injection in BEB patients.

Methods: In this prospective case series, 10 subjects with BEB managed with BTX-A injections were included after informed consent. The study was approved by Baylor College of Medicine IRB. Management history was recorded with chart review. Blink rates were measured while watching a video before injection (at least 3 months after last injection) and at follow-up within 4 weeks. The frequency of blinking and the severity of light-sensitivity were self-graded on a visual analog scale. The results are reported as median (range) and Wilcoxon test is used for non-parametric paired comparison.

Results: Nine subjects are female, and median age was 73.5 (49-81) years. The median follow-up time is 21 (14-28) days after BTX-A injection. The duration of treatment is 70 (5-16) months with a total of 27.5 (2-51) injections. Subject graded frequency of blinking (0, normal and 5, constant blinking) was 4.5 (2-5) before BTX-A injection and decreased to 1.75 (0-4.5) at follow-up (p=0.004, Fig1A). Subject reported light-sensitivity (0, none and 5, severe) decreased from 3.5 (0-5) before injection to 2.75 (0-4) at follow-up (p=0.047, Fig 1B). The blink rate before BTX-A injection is 39 (23-64), and significantly decreased to 18.5 (1-60) blinks per minute at follow-up (p=0.004, Fig1C). The average change in blink rate is -45.2±31.2% (mean±SD, Fig 1D). Blink rate change has a significant correlation with both duration of BTX-A injection treatment (r=-0.659, p=0.037) and number of treatments (r=-0.639, p=0.047).

Conclusions: This is the first known report of objective reduction in blink rate after BTX-A injection in BEB patients. BTX-A injection significantly improved photophobia. Higher duration of BTX-A injection treatment or more numbers of past injections significantly correlates with higher decrease in blink rate after each injection.

CONTROL ID: 3707331

SUBMITTER (NAME ONLY): Szilard Kiss

TITLE: Phase 1 Study of Intravitreal (IVT) Gene Therapy with ADVM-022 for neovascular AMD (OPTIC Trial): the role of neutralizing antibodies (NAbs)

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kiss, Ophthalmology, Weill Cornell Medicine, New York, New York, UNITED STATES|A. Turpcu, K. Bender, M. Friedman, E. Chung, J. Han, Adverum Biotechnologies Inc, Menlo Park, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously reported data from the phase 1 OPTIC study of ADVM-022 (AAV.7m8-aflibercept) in nAMD patients have demonstrated a single IVT injection gene therapy that durably expresses intraocular aflibercept can reduce the need for frequent anti-VEGF injections and improve visual and anatomical outcomes. The potential impact of baseline levels of neutralizing antibodies (NAbs) to AAV.7m8 on efficacy and safety outcomes are reported.

Methods: OPTIC is an open-label, multi-center, dose-ranging study in treatment-experienced nAMD patients administered a single intravitreal injection of ADVM-022 at 6E11 vg/eye (Cohort C1 n=6; C4 n=9) or 2E11 vg/eye (C2 n=6; C3 n=9). NAbs inclusion criteria were a titer level of <1:5 within 6 months prior to ADVM-022 for C1 and <1:125 for C2-4. The impact of baseline NAbs on treatment burden, aflibercept protein expression levels, central subfield thickness (CST) fluctuations and safety outcomes was evaluated.

Results: As of August 27, 2021, median follow-up was 104 weeks (C1&2), 92 weeks (C3) and 60 weeks (C4). In C2-4 8/9 (89%) and 10/15 (67%) of 6E11 and 2E11 vg/eye patients, respectively, had baseline NAbs to AAV.7m8 <1:125. 12/15 patients receiving 6E11 and 8/15 receiving 2E11 vg/eye ADVM-022 remained supplemental anti-VEGF injection free; mean annualized anti-VEGF injection frequency was reduced by 97% (6E11) and 81% (2E11). 4/7 (57%) 2E11 patients requiring supplemental aflibercept injections had NAbs titres > 1:125. The reductions in mean annualized anti-VEGF injection frequency in patients with baseline NAbs <1:125 were 97% and 93% in the 6E11 and 2E11 vg/eye groups, respectively. Patients with NAbs <1:125 at baseline showed more robust aflibercept protein expression levels and sustained improvements in CST with less fluctuations compared with patients with baseline NAbs >1:125. No correlation between NAbs titer and immune response was observed. ADVM-022 continues to be well tolerated with a favourable safety profile in the nAMD population.

Conclusions: These data suggest patients with baseline NAbs to AAV2.7m8 <1:125 were more likely to demonstrate robust aflibercept protein expression, have sustained improvements in CST with minimal fluctuations, and were less likely to require supplemental aflibercept injections. Baseline NAbs were not associated with occurrence nor duration of inflammation.

CONTROL ID: 3707333

SUBMITTER (NAME ONLY): Yelena Bagdasarova

TITLE: Instance Segmentation of Reticular Pseudodrusen (RPD) in Eyes with Intermediate Age-related Macular Degeneration

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Bagdasarova, C.S. Lee, A.Y. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|H. Kumar, R.H. Guymer, Z. Wu, Centre for Eye Research Australia, Royal Victoria Eye and Ear Hospital, University of Melbourne, East Melbourne, Victoria, AUSTRALIA|H. Kumar, R.H. Guymer, Z. Wu, Ophthalmology, Department of Surgery, University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Reticular Pseudodrusen (RPD) is a critical phenotype in age-related macular degeneration. We trained a deep learning model to reliably segment RPD on optical coherence tomography (OCT) B-scans in participants with intermediate AMD.

Methods: OCT volume scans from 120 participants from the Laser Intervention in the Early Stages of AMD Study were used for model development and internal testing. A total of 60 eyes with RPD and 180 eyes without RPD (with 49 scans per eye) were split at the participant level into 6 folds; 5 folds were used for cross-validation model training and fold 6 was reserved for testing. Each of 5 models consisted of a Mask-RCNN head with ResNeXt-101-32x8d-FPN backbone. The final model is a soft-voting ensemble of the 5 models.

Results: The instance-level Precision-Recall curve for the test fold, which contains 10 eyes with RPD and 30 eyes without RPD, is plotted in Figure 1a. At the instance-level the ensemble achieved precision of 0.64 [95% CI: 0.61,0.67], recall of 0.69 [0.66,0.72], and F1 of 0.66 [0.64,0.68] at the Intersection over Union (IoU) threshold of 0.2 and model probability threshold of 50%. The false positive rate (FPR), defined as the number of negative scans for which at least one RPD was predicted, was 4.4% [3.5%,5.5%]. The predicted vs actual RPD count per scan is plotted in Figure 1b.

For classifying RPD at the eye level, the ensemble achieved precision of 0.56 [0.33, 0.75], 0.83 [0.55,0.95], and 1.00 [0.72,1.00] when thresholding on 1 or more, 5 or more, and 10 or more RPD instances per eye, respectively, in the model prediction of the test fold. The ensemble achieved a recall of 1.00 [0.72,1.00] at those instance thresholds.

Conclusions: We successfully trained a model to segment RPD instances in B-scans and have validated the model on an internal test set.

CONTROL ID: 3707334

SUBMITTER (NAME ONLY): Taylor Kolosky

TITLE:

Ultrasound biomicroscopy correlation with corneal diameter in pediatric patients

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kolosky, A.U. Saga, M.R. Levin, J.L. Alexander, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior studies have established ultrasound biomicroscopy (UBM) as a clinically valuable imaging modality for structural anterior segment assessment, but its correlation with standard measures of ocular size, such as corneal diameter (CD), has not been examined. CD evaluation is pertinent to cataract surgery planning, and diagnosis and monitoring for congenital conditions such as microcornea, megalocornea, and congenital glaucoma. CD is typically measured using a ruler, calipers, or gray-scale steps devices. These external CD measurements are subject to error and variability, prompting our investigation of measuring corneal dimensions internally from UBM images.

Using a prospective cohort of healthy controls, we tested the hypothesis that CD correlates with internal corneal span determined from the angle-to-angle (AA) distance measured in UBM images.

Methods:

We collected 45 digital external photos and 86 UBM images of a total of 43 eyes from 24 participants between ages 1 – 12 years without ocular disease. We measured horizontal (H) and vertical (V) CD in each external photo using ImageJ software. We also used ImageJ to measure the internal angle-to-angle (AA) distance in H and V cross-sectional UBM images of each eye.

Results: Horizontal and vertical CD and AA measurements were highly positively correlated, as determined by Pearson correlation coefficients of +0.97 and +0.96, respectively. Bland-Altman plots demonstrated high agreement between methods for both H and V measurements (Fig. 1). Regression analysis revealed a linear relationship between CD and AA for H (Fig. 2A, CD = 0.99 x AA + 0.17, R^2 = 0.94, P<0.0001) and V (Fig. 2B, CD = 0.96 x AA + 0.44, R^2 = 0.92, P<0.0001) measurements.

Conclusions:

UBM image analysis can be used to accurately quantify corneal diameter in children with healthy corneas, as shown by the strong correlation between CD and AA measurements. Given its high resolution and non-invasive nature, UBM may be a useful alternative for determining CD. Further studies are needed to understand the potential to determine CD from AA distance in patients with ocular diseases that may impact the cornea, such as primary congenital glaucoma.

CONTROL ID: 3707337

SUBMITTER (NAME ONLY): Noel Brennan

TITLE: Design Concepts for a Myopia Control Soft Contact Lens

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.A. Brennan, X. Cheng, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|M.J. Collins, School of Optometry, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

Commercial Relationships Disclosure: Noel Brennan: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Vision;Code I (Personal Financial Interest):Johnson & Johnson Vision;Code P (Patent):Johnson & Johnson Vision | Michael Collins: Commercial Relationship(s);Code C (Consultant/Contractor):Johnson & Johnson Vision;Code F (Financial Support):Johnson & Johnson Vision | Xu Cheng: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Vision;Code I (Personal Financial Interest):Johnson & Johnson Vision;Code P (Patent):Johnson & Johnson Vision

ABSTRACT BODY:

Purpose: Increasing power in a myopia control treatment zone (MCTZ) of a multifocal soft contact lens can increase myopia control efficacy but negatively impact vision. The basis of vision compromise is explored with simple optical modelling and a novel approach to break the nexus between efficacy and vision.

Methods: The impact of MCTZ power, size and position on visual acuity, contrast and haloes/ghosting were modelled. Optical designs featured annular MCTZs surrounding a central distance vision correction zone (DZ), typical of dual focus (DF) designs such as Acuvue® Bifocal and MiSight®. To overcome limitations of DF designs, the non-coaxial principle described by Yi et al. (ARVO, 2021) was applied to the annular MCTZ. This was tested empirically with an adaptive optics system.

Results: Composite images comprising the clear image from the DZ and blurred images from the DF MCTZ are consistent with Davis et al (ARVO, 2021), showing VA worsening up to a power of +2 to +3 D and improving beyond that level, but with reduced contrast (Fig 1). Rays from a distant point source passing through the DF MCTZ form a halo at the retina (Fig 2), with increasing power in the MCTZ increasing the size of the halo. Convolving for edges shows that ghosting is a major vision limitation of DF designs, with MCTZ power being the main driver of ghost-image size. Forming the MCTZ from a torus rather than a spherical shape generates a ring focus, which can markedly reduce the halo effect (eg. from 3.3° ± 0.1 with a +10D DF MCTZ to 0.11° ± 0.04 with a +10D torus MCTZ). Adding positive power into the torus MCTZ results in short-term (30 min) reduction (± SD) of axial length comparable to that observed with a +3 D full-field lens (11.4 ± 6.2 µm vs 11.0 ± 8.8 µm, N=17 and 18 respectively, p=NS) while maintaining acceptable vision quality.

Conclusions: This is the first optical characterization of vision compromise versus myopia control efficacy with DF lenses to our knowledge. While treatment efficacy of a myopia control soft lens is related to the local power in the MCTZ, the optical method by which treatment is delivered can have a major impact on the extent of vision compromise.

CONTROL ID: 3707338

SUBMITTER (NAME ONLY): Youssef Maroud

TITLE: Precise monitoring of corneal stroma changes in a murine dry eye disease model using in vivo confocal microscopy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Maroud, M. Chen, X. Simmons, S.C. Yiu, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|C. Le, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|W. Schubert, Bayer AG, Leverkusen, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Although in vivo confocal microscopy (IVCM) is routinely used in clinics, it is challenging to precisely monitor cornea pathophysiological changes, partially due to the complexity of cornea nerve architecture. Double lacrimal gland removal (DLGR) is commonly employed to establish animal dry eye disease, with a substantial change in cornea nerve morphology and inflammatory cell infiltration. Here we describe a new method for monitoring corneal stroma change using the Heidelberg Retina Tomography III (HRT III) in a murine dry eye model.

Methods: Sprague-Dawley rats (8-9 weeks, male) underwent DLGR to remove the infraorbital and extraorbital lacrimal glands. Male rats were chosen in this study due to a lesser hormonal cycle influence. Up to three stroma nerves per eye were selected to image and re-imaged 2 weeks and 6 weeks post-surgery. Image data were acquired as volume acquisition. The sequential images with selected stromal nerve were manually adjusted and stacked into a 3-D nerve reconstruction by Image J. To validate the result, whole rat cornea was harvested post-mortem and nerve fibers were stained with TUBBIII.

Results: Cornea wholemounts image indicated that the stroma nerve acquired by IVCM matched the nerve architecture map. Due to the curvature of the rat cornea, three IVCM images were located within an area of 30% of the whole cornea (Fig 1A, B). In the rat cornea with dry eye disease, we observed various dendritic cells infiltration along nerve trunks. 3-D reconstruction of the corneal nerve architecture showed the differential spatial distribution of those dendritic cells (Fig 1C, D, triangles). Longitudinal follow-up of the stroma nerve after DLGR indicated that nerve reflection increase (tan arrows), nerve sprouting (white arrows). There was more dendritic cell infiltration (triangles) 6 weeks after the double lacrimal gland compared to 2 weeks post-surgery (Fig2A, B). The 3-D reconstruction of stromal nerve architecture revealed different nerve and cellular changes in the cornea stroma between the anterior side (0^0) and posterior side (180^0).

Conclusions: Here we demonstrated the precise mapping and 3-D reconstruction of stroma nerve architecture in a DLGR dry eye model, revealing that nerve and cellular changes exacerbation after model establishment. This work also suggested that this methodology held potential for development into a clinical diagnostic modality.

CONTROL ID: 3707342

SUBMITTER (NAME ONLY): Sara Mayer

TITLE: Drosophila models of SNRNP200-associated retinitis pigmentosa exhibit retinal apoptosis and abnormal electroretinograms

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.K. Mayer, Q. Christenson, L.L. Wallrath, Biochemistry, University of Iowa, Iowa City, Iowa, UNITED STATES|S.K. Mayer, A.V. Drack, Ophthalmology, University of Iowa, Iowa, UNITED STATES|

Commercial Relationships Disclosure: Sara Mayer: Commercial Relationship: Code N (No Commercial Relationship) | Quinton Christenson: Commercial Relationship: Code N (No Commercial Relationship) | Arlene Drack: Commercial Relationship: Code N (No Commercial Relationship) | Lori Wallrath: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: RP33 is a non-syndromic form of RP caused by mutations in the SNRNP200 gene encoding an essential component of the spliceosome that is required for pre-mRNA splicing. SNRNP200 is expressed in nearly all cells, yet defects are only observed in the retina. To understand the function of SNRNP200 in vision, we generated Drosophila models.

Methods: The Drosophila orthologue of human SNRNP200 is lethal(3)72Ab, which we refer to as dSNRNP200. Human SNRNP200 and fly dSNRNP200 have 74% amino acid identity and 89% similarity. To understand disease mechanisms, we analyzed the developing retina and performed electroretinograms (ERG) of adult Drosophila using RNAi knock-down and patient based CRISPR mutant alleles of dSNRNP200.

Results: RNAi knock-down of dSNRNP200 in the developing eye increased apoptosis in the larval eye discs relative to controls and produced an adult “rough eye” phenotype. Similarly, a CRISPR mutant allele increased apoptosis in larval eye discs relative to controls. ERGs performed on young adults bearing the CRISPR mutant alleles exhibited abnormal waveforms indicative of loss of phototransduction and synaptic transmission that progressed with age, similar to the human disease condition. In addition, loss of prolonged depolarizing afterpotential indicated that the “rod-like” cells of the retina were defective. By contrast, the cone-like cells appeared functional, recapitulating early stages of the human disease.

Conclusions: Globally expressed dSNRNP200 is essential for Drosophila photoreceptor function. Modeling RP33 mutations in the fly recapitulated many aspects of the human disease, which will allow for a molecular dissection of disease mechanisms and genetic and pharmacological screens for potential treatments.

CONTROL ID: 3707343
SUBMITTER (NAME ONLY): Wongel Bogale
TITLE: Use of virtual care by Ontario ophthalmologists during the COVID-19 pandemic in 2020
SESSION TITLE: Using Technology for Care Delivery and Improvement
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: W. Bogale, Y. Jin, Institute of Medical Science, University of Toronto, Toronto, Ontario, CANADA|Y. Buys, S. El-Defrawy, Y. Jin, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|M. Canizares, Krembil Research Institute, University Health Network, Toronto, Ontario, CANADA|
Commercial Relationships Disclosure: Wongel Bogale: Commercial Relationship: Code N (No Commercial Relationship) | Yvonne Buys: Commercial Relationship: Code N (No Commercial Relationship) | Mayilee Canizares: Commercial Relationship: Code N (No Commercial Relationship) | Sherif El-Defrawy: Commercial Relationship: Code N (No Commercial Relationship) | Yaping Jin: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To describe the use and trends of virtual care and exam associated factors in Ontario, Canada during the 2020 COVID-19 pandemic.
Methods: Ontario physician billing data from 2017-2020 was analyzed. Virtual care provided by ophthalmologists were identified from fee code and specialty codes. Percentage and adjusted odds ratio (aOR) from logistic regression models were used to assess patients' and ophthalmologists' factors associated with virtual vs in-person visits.
Results: Virtual assessments/consults comprised 0.07%-0.10% of ophthalmology assessments/consults in 2017-2019 and 8.31% in 2020. The weekly uptake of virtual visits increased immediately in the week of the Ontario government's directive to ramp down clinic activities and institution of a new virtual fee code (17.6%, week March 16, 2020), peaked 2 weeks later (55.8%, week March 30, 2020) and reduced immediately after the directive was lifted (24.2%, week May 25, 2020).

During the 2020 pandemic period, use of virtual care was higher in female (11.6%) vs male (10.3%) patients and in patients <20 (16.4%) and 20-39 years (12.3%) vs those aged 40-64 (10.8%) and 65+ (10.6%) years. Patients residing in the poorest/poorer neighbourhood area (10.9%) used virtual care similarly to their counterparts (11.1%). Patients with an acute infectious disease (14.2%) or non-urgent diagnosis (16.2%) had the highest use. Those with a retinal disease diagnosis had the lowest use (4.2%).

Female ophthalmologists provided virtual care more often than male ophthalmologists (15.4% vs 9.9%). Ophthalmologists aged 60-69 (13.1%) provided more virtual care than any other age groups (from 7.7% for 70+ years to 11.3% for <40 years).

Regression analyses indicated a significantly higher chance of virtual care use in female (aOR=1.65) vs male ophthalmologists, in female (aOR=1.13) vs male patients, in patients <20 years (aOR=1.57) and 20-39 years (aOR=1.17) vs 65+, in patients residing in Central (aOR=1.37), East (aOR=1.52) and North (OR=1.13) regions vs those in the Toronto region. Compared with ophthalmologists aged 60-69 years, those in other age groups were less likely to use virtual care (aOR ranged 0.57-0.76).
Conclusions: Virtual care in ophthalmology significantly increased during the initial phase of the pandemic and decreased thereafter. There were significant variations in virtual care use by patient and ophthalmologist characteristics.

CONTROL ID: 3707344

SUBMITTER (NAME ONLY): Emily Eton

TITLE: Trends in retinopathy of prematurity training and future practice intentions among retina and pediatric ophthalmology fellows

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Eton, B. Young, C.G. Besirli, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Emily Eton: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Young: Commercial Relationship: Code N (No Commercial Relationship) | Cagri Besirli: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a leading cause of blindness among preterm and low-birthweight infants. Improved survival of very preterm and very low birth weight babies has led to increased numbers of patients requiring ROP care; however, studies demonstrate a ROP provider shortage. We sought to better understand the future ROP workforce by identifying trends in ROP training and practice interest among pediatric ophthalmology and retina fellows.

Methods: Lists of vitreoretinal surgery, medical retina, and pediatric ophthalmology fellowship programs participating in the SF Match with Association of University Professors of Ophthalmology compliance as of August 2021 were obtained. Surveys were emailed to fellowship program directors and administrators to be distributed to current fellows and those who graduated in the last year. Survey data were collected and analyzed using Qualtrics software.

Results: Of the 56 respondents, 55.4% were male. Vitreoretinal surgery fellows made up the largest cohort (n=30; 53.6%) with 20 (35.7%) pediatric ophthalmology and 6 (10.7%) medical retina fellows responding. A majority of fellows trained at an academic teaching hospital (n=49; 89.1%). Forty-eight (85.7%) respondents received ROP training, of which 22.0% did screening examinations, 25.0% completed follow-up examinations, 23.2% performed laser therapy, 19.6% administered anti-VEGF injections, and 10.1% performed incisional surgery. Six fellows received ROP telemedicine training. Just under half of respondents (n=26; 46.4%) indicated plans to provide ROP care in the future. Of these, most plan to do screening (n=24; 92.3%) or follow-up (n=22; 84.6%) exams, laser treatment (n=21; 80.8%), or anti-VEGF injections (n=21; 80.8%). Four individuals indicated intention to perform incisional surgery for ROP and 5 plan to do telemedicine screening examinations. Among the 53.6% who did not plan to care for ROP patients or were unsure, the most common reasons cited were lack of interest in the disease process, liability concerns, or time-consuming nature of ROP care.

Conclusions: Despite widespread ROP training in fellowship, a minority of surveyed trainees plan to provide ROP care in future practice. Increasing fellowship telehealth training may expand future ROP telemedicine use and help overcome workforce shortages.

CONTROL ID: 3707346

SUBMITTER (NAME ONLY): Cameron Bruner

TITLE: Cone location and corneal stiffness in keratoconus

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bruner, A. Mahmoud, C.J. Roberts, Ophthalmology & Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|A. Mahmoud, C.J. Roberts, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the relationship between central corneal stiffness in keratoconic patients as a function of severity of disease and distance of the keratoconic cone from the center.

Methods: Pentacam tomography and Corvis ST biomechanical response metrics were prospectively acquired in 67 eyes of 41 subjects diagnosed with keratoconus. The severity of disease, represented by the magnitude of the 2mm diameter zone around the steepest point of Kmax (Km spot), and the distance of Kmax from the center of the map (Kmax dist) were independently compared via univariate regression analyses to four biomechanical metrics: stiffness parameter at first applanation (SP-A1) and highest concavity (SP-HC), both of which increase with increasing stiffness, as well as deformation amplitude ratio at 2mm (DA Ratio Max) and integrated inverse radius (Int Inv Radius), both of which decrease with increasing stiffness. Statistical analyses were performed in SAS with significant threshold set at $p < 0.05$.

Results: Km spot was found to have a statistically significant negative relationship to both SP-A1 and SP-HC ($p<0.0001$; $R^2 = 0.483$) and ($p<0.0001$; $R^2 = 0.215$), respectively, and a significantly positive relationship to DA Ratio Max and Int Inv Radius ($p< 0.0001$; $R^2 = 0.588$) and ($p<0.0001$; $R^2 = 0.693$), respectively. In terms of Kmax dist, both SP-A1 and SP-HC yielded a weaker, though significantly positive relationship ($p = 0.013$; $R^2 = 0.091$) and ($p = 0.023$; $R^2 = 0.077$), respectively, while DA Ratio Max and Int Inv Radius yielded a significantly negative relationship ($p = 0.002$; $R^2 = 0.137$) and ($p = 0.0002$; $R^2 = 0.190$), respectively.

Conclusions: In keratoconic patients, the corneal stiffness decreases by all biomechanical metrics as severity of disease increases in a continuous manner. In addition, all biomechanical metrics of central corneal stiffness increase as the distance of the keratoconic cone from the center also increases. This is consistent with the focal nature of the biomechanical weakening in keratoconus.

CONTROL ID: 3707352

SUBMITTER (NAME ONLY): Seher Yuksel

TITLE: Deletion of a cholesteryl ester hydrolase leads to a progressive retinal degeneration in mice

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yuksel, B. Aredo, Y. Zegeye, C.X. Zhao, I.A. Butovich, R. Ufret-Vincenty, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|M. Tang, X. Li, S. Ludwig, B.A. Beutler, Center for the Genetics of Host Defense, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|L. Gautron, Department of Internal Medicine, Center for Hypothalamic Research, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lipid dyshomeostasis has a pathophysiologic role in multiple retinal diseases including age-related macular degeneration and diabetic retinopathy. Cholesteryl ester hydrolases are a family of enzymes found in many tissues, which are needed to convert the biologically inactive cholesteryl esters to their bioactive forms. Our goal was to characterize the role of a specific cholesteryl ester hydrolase (CEH), identified during a forward genetics screen, in retinal physiology.

Methods: We used a semiquantitative scale of fundus spots on retinal photos as a screening tool on a forward genetics pipeline (N-ethyl-N-nitrosourea mutagenesis of C57BL/6J mice). CRISPR/Cas9 technology was then used to generate knockout mice targeting the gene of interest. Fundus photos and Optical Coherence Tomography (OCT) were used to confirm the suspected phenotype. Further characterization of these mice was pursued using light microscopy, immunohistochemistry, in situ hybridization, electron microscopy, electrophysiology and retinal lipid analysis.

Results: We examined 5,793 G3 mice carrying 11,244 coding/splicing mutations in 7,679 genes. This corresponds to a genome saturation of 4.7% when considering predicted damaging mutations occurring in ≥2 mice in the homozygous state. Using the fundus spots scale we were able to identify a specific cholesteryl ester hydrolase as a gene of interest. A CRISPR/Cas9-generated KO mouse line targeting this CEH gene recapitulated the findings from the forward genetics screen. By 4 months of age, these CEH-deficient mice demonstrated accumulation of fundus spots ($p < 0.001$) compared to age and gender matched control mice. By 3 months of age, KO mice showed 7% thinning of the outer nuclear layer on OCT ($p < 0.001$) compared to control mice. These changes increased with aging. We will present anatomical, functional, ultrastructural and biochemical analyses of the retinas of these mice at different time points.

Conclusions: We demonstrate that a CEH enzyme, whose function has not been characterized in the retina before, is essential to retinal homeostasis.

CONTROL ID: 3707353

SUBMITTER (NAME ONLY): Lung Di

TITLE: Repeatability and reproducibility of optic nerve head optical coherence tomography angiography (OCTA) measurements on glaucomatous and normal eyes

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Di, S. Yu, P. Sha, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to determine the repeatability and reproducibility (R&R) of spectral domain OCTA metrics on optic nerve OCTA en face images in normal and glaucomatous eyes.

Methods: Subjects with glaucoma and healthy controls (both >18 years old) were recruited in this study. If two eyes were eligible, one eye per subject was randomly designated as the study eye. Each eye was imaged using the Angiography 4.5x4.5 mm scan centered on the optic disc on CIRRUS™ HD-OCT 5000 with AngioPlex® OCT Angiography (ZEISS, Dublin, CA). Scans were repeated on 3 devices (by 3 different technicians) 3 times in 1 visit.

Data was processed on the AngioPlex Metrix in CIRRUS 11.0 software, which quantifies the density of vasculature. Two measures of blood vessels were used: Perfusion Density (PD), the area of blood vessels, and Flux Index (FI), the weighted intensity of the perfused vessels per unit area. PD is defined as the total area of perfused microvasculature per unit area, and ranges from 0 (no perfusion) to 1 (fully perfused). FI is defined as total weighted area of perfused microvasculature per unit area in a region of measurement. The weight is the normalized flow intensity corresponding to each pixel. Each scan is segmented into 4 sectors (temporal, nasal, superior, and inferior) for analysis, and a mean coefficient of variance (CV%) is calculated for both R&R. All statistics are estimated from two-way random-effect ANOVA model with random effects operator/device, eye and interaction between operator/device and eye.

Results: 22 control eyes (mean age 44.7 years, SD 14.7) and 21 glaucoma eyes (mean age 68.5 years, SD 8.9) were imaged. Table 1 and Table 2 shows FI and PD mean, standard deviation (both R&R), and coefficient of variance (CV%) for normal and glaucomatous eyes. Across all sectors, R&R CV% are below 5% in normal eyes, and no more than 6.1% in diseased eyes. Mean R&R CV% (both FI and PD) are less than 3% for normal eyes, and they are less than 5% for glaucomatous eyes.

Conclusions: All CV% (FI and PD) for normal and glaucomatous eyes are excellent, and no significant CV% difference is observed across all sectors from the scans. Given the R&R results, these parameters may be useful for monitoring disease progression or early detection of diseases. Future studies are needed to determine the clinical utility of these measurements.

CONTROL ID: 3707354

SUBMITTER (NAME ONLY): Eric Nguyen

TITLE: Retinal Pigment Epithelium Modulates Endothelial Cell, Fibroblast, and Pericyte Gene Expression Patterns in 3D Bioprinted Tissues

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Nguyen, M. Song, R. Quinn, T. Park, D. Bose, R. Sharma, A. Ali, R. Hirday, A. Maminishkis, K. Bharti, Ophthalmology and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Song, Y. Chen, C. Tristan, I. Singec, M. Ferrer, National Center for Advancing Translational Sciences, Bethesda, Maryland, UNITED STATES|C. Malley, R. Dejene, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) disease processes are thought to initiate at the Retinal Pigment Epithelial Cell (RPE)/choroid interface. However, how each tissue contributes to disease pathogenesis is not known. We hypothesized that the presence of RPE would reduce gene expression patterns indicative of AMD within 3D bioprinted Outer Blood Retinal Barrier (oBRB) models. Here, we utilized 3D bioprinted oBRB models and single-cell RNA-seq to assess how the presence or absence of RPE affects endothelial cell (EC), fibroblast, and pericyte gene expression patterns within the context of AMD pathogenesis.

Methods: iPSC-derived EC, iPSC-derived fibroblasts, and ocular pericytes were encapsulated in a fibrinogen and gelatin-based hydrogel solution and 3D-printed onto degradable PLGA scaffolds or PET membranes to generate choroid-like tissues. iPSC-RPE were seeded on the apical side of scaffolds 7 days after bioprinting. After 6 weeks of maturation, tissues were digested using dispase, collagenase, and RNAse. Single-cell suspensions were retrieved and fixed to generate barcoded single-cell emulsions and cDNA libraries. The Illumina HiSeq 3000, Cellranger package, the Seurat R package, and the Biowulf computing cluster analyzed single-cell sequencing data. Gene set enrichment analysis was performed using EnrichR and curated using Gene Ontology 2021 ontology sets. EC, fibroblast and pericyte populations were identified within 3D oBRB models using UMAP clustering, EnrichR, and the expression of key signature genes by each cell type.

Results: In EC populations, the presence of RPE in tissues enhanced expression of key choriocapillaris signature genes while the absence of RPE enhanced expression of vascular morphogenesis genes and AMD signature genes. In fibroblast populations, the presence of RPE downregulated senescence and aging genes while enhancing the expression of genes associated with melanin synthesis, phenol synthesis, and retinoid metabolic processes; the absence of RPE enriched genes related to AMD and ECM synthesis. Pericytes demonstrated similar effects on ECM synthesis genes as fibroblasts when RPE were absent.

Conclusions: Combined, these data suggest that the presence of RPE changes EC specification toward choriocapillaris, downregulates senescence and aging in fibroblasts, and downregulates AMD-associated gene expression patterns within oBRB models.

CONTROL ID: 3707358
SUBMITTER (NAME ONLY): Shuibin Ni
TITLE: Handheld ultra-widefield optical coherence tomography
SESSION TITLE: Multidisciplinary Ophthalmic Imaging
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Ni, T. Nguyen, S. Khan, S. Ostmo, Y. Jia, D. Huang, J. Campbell, Y. Jian, Oregon Health & Science University, Portland, Oregon, UNITED STATES|R. Ng, Simon Fraser University, Burnaby, British Columbia, CANADA|M.F. Chiang, National Institutes of Health, Bethesda, Maryland, UNITED STATES|
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ABSTRACT BODY:

Purpose: Developing a flexible handheld ultra-widefield (UWF) OCT system with two interchangeable lens combinations, a non-contact approach with 105° FOV and a contact approach with 140° FOV, for pediatric peripheral retina imaging.

Methods: We demonstrated a flexible handheld probe for UWF OCT system with non-contact 105° FOV and contact 140° FOV for peripheral retina imaging. The novel optical designs [Figs. 1(a)-1(b)] were compatible with our previously established 55° FOV handheld OCT/OCTA system and shared the same mechanical parts, except for the telescope design after the slow axis of the galvanometer scanner [Fig. 1(c)]. The OCT engine employed a 400-kHz VCSEL (Thorlabs, Inc.) with a center wavelength of 1060 nm and 100 nm bandwidth that provides an imaging depth of 6 mm and an axial resolution of 4.96 μm in air. The working distance for the non-contact system was ~5 mm. The incident power on the cornea was 1.68 mW. A programmed motorized reference arm and an electrically tunable lens were rapidly adjusted during the imaging session to match the imaging subject's axial eye length and fine tune focus. OCT images were acquired and processed by our GPU accelerated software which enabled direct real-time feedback and facilitated alignment process and navigation. A high-speed alignment mode (10Hz volume rate) and an OCT scanning mode (800 × 780 A-scans/Volume and 1.56 seconds) were available for the operator to toggle between them.

Results: 3 healthy adult volunteers (24-34 years old) and 57 pediatric patients were successfully imaged, all the imaging sessions were completed within 5 minutes. Two representative en face OCT images with posterior pole and peripheral retina obtained via non-contact 105° FOV and contact 140° FOV respectively from two neonates with retinopathy of prematurity (ROP) were shown in Fig 2. Peripheral pathologies were fully appreciated in these images without pronounced motion artifacts.

Conclusions: We have demonstrated a flexible 400-kHz handheld UWF OCT system that has two interchangeable eyepieces, a non-contact approach with 105° FOV and a contact approach with 140° FOV, which could acquire images from the posterior pole to peripheral retina in a single shot. The implementation of UWF OCT imaging technology has the potential to facilitate the diagnosis and treatment of retinal diseases such as ROP.

CONTROL ID: 3707360

SUBMITTER (NAME ONLY): Yeshumenesh Zegeye

TITLE: Novel association to retinal homeostasis identified for a gene involved in ubiquitination and proteasomal degradation.

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zegeye, B. Aredo, S. Yuksel, C.X. Zhao, R. Ufret-Vincenty, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|S. Ludwig, M. Tang, X. Li, B.A. Beutler, Center for the Genetics of Host Defense, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our goal is to identify and study genes essential to retinal development and homeostasis using an unbiased forward genetics approach. Here we characterize a novel association involving a gene with a known role in the ubiquitin–proteasome system (UPS).

Methods: We used a forward genetics screening pipeline (N-ethyl-N- nitrosourea mutagenesis in C57BL/6J mice) to identify, in an unbiased manner, non-redundant genes leading to the accumulation of fundus spots. All G3 mice used in our screening have been pre-genotyped at all mutant loci, making it possible to instantly determine the causative mutation of a given phenotype. We identified a mutation that led to a phenotype of increased fundus spots, that we termed aegean, and used CRISPR/Cas9 mutagenesis to generate mice deficient in the affected gene. We then characterized the retina in these mice.

Results: The aegean phenotype was recapitulated in the CRISPR-generated KO mouse line. This line showed progressive accumulation of fundus spots with age and a statistically significant thinning of the outer retina. We then used serial fundus photos, optical coherence tomography (OCT), immunohistochemistry (of both retinal sections and flat mounts), and electron microscopy to characterize the retinal phenotype. Functional retinal testing with electrophysiology will also be shown.

Conclusions: A forward genetics screening protocol using a semiquantitative fundus spot scale allowed us to identify a novel gene-retinal phenotype association involving a gene important for the ubiquitin proteasome system. This pathway plays a key role in cell cycle control, signal transduction, and removal of toxic/damaged proteins from the cell. Further studies will be needed to further characterize the specific role of this gene in retinal homeostasis.

CONTROL ID: 3707361

SUBMITTER (NAME ONLY): Sofia Ahsanuddin

TITLE: Flavoprotein Fluorescence (FPF) Elevation Using Retinal Metabolic Analysis Correlates with Decreased Visual Acuity in Patients with Various Retinal Pathologies

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Ahsanuddin, Medical Education, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|S. Ahsanuddin, O. Otero-Marquez, R.B. Rosen, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|R.B. Rosen, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|C. Rich, OcuSciences Inc., Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress linked to mitochondrial dysfunction is implicated in the pathophysiology of several retinal pathological conditions. Previous studies have shown that retinal flavoprotein fluorescence (FPF) can be used as a potential biomarker for oxidative stress. Herein, we hypothesize that FPF is higher in conditions mediated by oxidative stress and inversely correlates with best corrected visual acuity (BCVA).

Methods: 10 eyes from 10 healthy subjects, 3 eyes from 3 central serous retinopathy (CSR) patients, 8 eyes from 8 retinal vein occlusion (RVO) patients, 6 eyes from 6 proliferative diabetic retinopathy (PDR) patients, and 12 eyes from 12 chronic exudative age-related macular degeneration (AMD) patients were included in the present observational study (n=39). Eyes were imaged non-invasively using a specialized fundus camera OcuMet Beacon (OcuSciences, Ann Arbor, MI). During each imaging session, the macula was imaged with a blue light in the narrow emission spectra from 520 to 540 nm. Kruskal-Wallis tests were performed to assess differences in FPF values and BCVA between the five groups. Spearman rank correlation coefficient was calculated to assess the relationship between FPF and BCVA. A $p < 0.05$ was considered to be statistically significant.

Results: FPF values and BCVA of all five groups differed significantly (Kruskal-Wallis Tests, $p < 0.001$ and $p = 0.003$, respectively). Mean FPF values of healthy controls, CSR, RVO, PDR, and wet AMD patients were 29.5 ± 7.8, 51 ± 15.6, 60.7 ± 24.4, 64 ± 25.7, and 65 ± 17.7, respectively. Compared to healthy controls, FPF values were significantly higher in conditions such as RVO, PDR, and wet AMD ($p = 0.010$, $p = 0.012$, and $p < 0.01$, respectively). In contrast, there was no significant difference between FPF values of CSR patients compared to healthy controls ($p = 0.912$). There was an inverse correlation between FPF values and BCVA ($r = -0.547$, $p < 0.01$).

Conclusions: FPF values were significantly greater in diseases known to be mediated by oxidative stress compared to healthy controls. Higher FPF values were seen in conditions such as RVO, PDR, and wet AMD as compared to CSR, indicating that there may be varying degrees of oxidative stress in these conditions. The data is consistent with previously published literature on FPF being inversely correlated with BCVA.

CONTROL ID: 3707363

SUBMITTER (NAME ONLY): Sadi Can Sonmez

TITLE: The Immunohistochemical Analysis of Cellular Auto-Degradative Functions in Epithelial Cells of the Anterior Capsule of Lens in Patients with Pseudo-Exfoliation Syndrome: A Preliminary Report

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sonmez, Z. Kisakurek, School of Medicine, Koc Universitesi, Istanbul, Istanbul, TURKEY|M. Karslioglu, A. Sahin, School of Medicine, Department of Ophtalmology, Koc Universitesi, Istanbul, TURKEY|D. Aydemir, M. Gozel, Research Center for Translational Medicine, Koc Universitesi, Istanbul, Istanbul, TURKEY|

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ABSTRACT BODY:

Purpose: Pseudo-exfoliation syndrome (PXF) is a systemic disease in which fibrillary proteinaceous material is deposited within the tissues such as the eye, which is thought to arise from dysfunctional matrix turnover and intracellular auto-degradation pathways. In this case-control study setting, we aim to evaluate whether defects in mitophagy specifically have a role in PXF etiology and prognosis.

Methods: The anterior lens capsules obtained in microincisional cataract surgery were collected both from patients with PXF (n=6) and age-matched healthy controls (n=10). The samples were embedded in paraffin blocks and sliced into 0.4 µm slides for analysis. The ABC® IHC detection kit was used to stain the samples for PTEN-induced kinase 1 (PINK1), Parkin and LC3B. Stained images were captured with 20x magnification under confocal microscopy. The expression intensity was measured using color deconvolution plug-in and integrated density value was calculated on Fiji® (U. S. National Institutes of Health, Bethesda, MD). The Mann-Whitney U test was used for statistical analysis and the results were shown on Graphpad Prism (Graphpad, San Diego, CA).

Results: The staining intensity of PINK1 and PARKIN were higher in the epithelia of anterior lens capsule in patients with PXF compared to the control samples, which was only statistically significant for PINK1. (p=0.0002, p=0.999 respectively) LC3B intensity was also found to be increased in PXF patients with statistical significance (p=0.0006). (Images 1 and 2)

Conclusions: This increase in the markers of mitophagy, which is the targeted elimination of dysfunctional mitochondria, may be an important indicator of increased oxidative stress in PXF. It can therefore signal an extensive mitochondrial impairment and higher generation of reactive oxygen species, potentially overburdening the cellular clearance and enhancing faulty protein release. Certainly, further in vitro studies with a larger sample number are needed to compare the actual stress responses dynamically in PXF.

CONTROL ID: 3707366

SUBMITTER (NAME ONLY): Siamak Yousefi

TITLE: Staging Structural Damage in Glaucoma Based on Optical Coherence Tomography

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yousefi, X. Huang, The University of Tennessee Health Science Center Department of Ophthalmology Hamilton Eye Institute, Memphis, Tennessee, UNITED STATES|P. Brusini, Department of Ophthalmology, “Città di Udine” Health Center, Udine, ITALY|C.A. Johnson, Department of Ophthalmology & Visual Sciences, University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a glaucoma staging system based on optical coherence tomography (OCT)-derived retinal nerve fiber layer (RNFL) thickness measurements.

Methods: We developed a glaucoma damage classification system based on unsupervised k-means and Bayes minimum error classifier using 6561 RNFL profiles from 2269 eyes of 1171 subjects. We annotated the discovered clusters to different severity levels based on their respective mean global RNFL thickness. To establish an objective criterion for glaucoma staging, we computed optimal global RNFL thickness thresholds that discriminated different severity levels with highest accuracy using Bayes principle. We evaluated the quality of learning based on the area under the receiver operating characteristic curve (AUC).

Results: The k-means discovered four clusters with 1382, 1613, 1727, and 1839 samples and mean global RNFL thickness of 58.3 µm (±8.9:SD), 78.9 µm (±6.7), 87.7 µm (±8.2), and 101.5 µm (±7.9), respectively. The Bayes minimum error classifier identified optimal global RNFL thresholds of 70 µm, 85 µm, and 95 µm for discriminating the severity levels. The AUC was 0.90 and about 4% of normal eyes and 98% of eyes with advanced glaucoma had either global or quadrant RNFL thickness outside of normal limit.

Conclusions: Machine learning discovered optimal OCT-derived RNFL thresholds of about 70 µm, 85 µm, and 95 µm for staging glaucoma to normal, early, moderate, and advanced stages. The proposed staging system is unbiased with no pre-assumption or human expert intervention in the development process. Additionally, it is objective, easy-to-use, and consistent, which may augment glaucoma research and day-to-day clinical practice.

CONTROL ID: 3707368

SUBMITTER (NAME ONLY): Blake Simmons

TITLE: The Impact of Demodex Blepharitis on Patients and Healthcare System: Results from the Atlas Continuation Study

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Simmons, Vision Institute, Colorado, UNITED STATES|W. Whitson, Whitson Vision, Indiana, UNITED STATES|P. Vollmer, Vita Eye Clinic, North Carolina, UNITED STATES|G. Berdy, Ophthalmology Associates, Missouri, UNITED STATES|M. Holdbrook, Tarsus Pharmaceuticals, California, UNITED STATES|S. Baba, Tarsus Pharmaceuticals, California, UNITED STATES|J. Meyer, Eye Care Institute, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Demodex blepharitis (DB) is present in a significant number of eyecare patients, yet many patients continue to suffer due to improper diagnosis, minimized or underappreciated significance of findings by the eye care professional (ECP), inadequate management, and the lack of FDA-approved treatments. The purpose of this study was to further evaluate (as a continuation of 311 patients presented previously) the clinical impact of DB, impact on patients' quality of life and motivations for seeking care.

Methods: Patients 18 years of age and older were recruited from 12 eye care centers in the US to participate in this DB screening study. The investigators examined patients for objective signs of DB: ≥1.0 mite count, >10 collarettes, and ≥mild lid margin erythema. Patients with all three signs were asked to complete a questionnaire about their symptoms, quality of life, and treatment experience. Impact of DB on contact lens wearers was also collected.

Results: Among 129 patients, 32% made at least two visits to their doctor due to signs or symptoms associated with DB. Unfortunately, 63% of the patients have never been previously diagnosed for DB. The most bothersome symptoms reported in this group were itchy eyes (53%), dry eyes (44%), irritated eyes (31%), foreign body sensation (26%), tearing (23%), and red eyes/eyelids (23%). Approaches to mitigate DB symptoms included warm compresses (46%), lid wipes (29%), artificial tears (48%), antibiotics/steroids (25%), and various tea tree oil preparations (21%). Among those who discontinued aforementioned management approaches, 52% discontinued due to ineffectiveness or intolerability. Among contact lens wearers (11%), 79% of patients complained of discomfort and/or blurry/foggy vision while wearing contact lenses.

Conclusions: Demodex blepharitis is underdiagnosed and often misdiagnosed despite chronically persisting signs and symptoms that often require multiple visits to ECP, typically without resolution. More effective treatments for DB are needed, which will clear the signs of DB and have a positive impact on patients' eyelid health and quality of life. Aggregated data with larger sample size upon study completion, to be presented, will corroborate these findings.

CONTROL ID: 3707372

SUBMITTER (NAME ONLY): Alina Sinha

TITLE: The Half Maximal Effective Concentration (EC50) of a Novel VEGF-A and Ang-2 Bispecific Protein (RO-634) for Back of the Eye Disease

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sinha, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|J.L. Olson, A. Jones, J. Morgenstern, A. Strong, S. Droho, S. Bevers, N. Mueller, M. Huvard, University of Colorado Health, Aurora, Colorado, UNITED STATES|L. Xu, Independent Reseach Consultant, California, UNITED STATES|P.K. Kaiser, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.M. Khanani, Sierra Eye Associates, Nevada, UNITED STATES|A.M. Khanani, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|J.S. Heier, OCB, Boston, Massachusetts, UNITED STATES|J.M. Kunzeman, E. Sembell, Southern Illinois University School of Medicine, Springfield, Illinois, UNITED STATES|R. Bhandari, Springfield Clinic Eye Institute, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the half maximal effective concentration (EC50) of a novel bispecific protein, RO-634, to Vascular Endothelial Growth Factor-A (VEGF-A) and Angiopoietin-2 (Ang-2) individually versus in tandem. These findings may have important clinical implications for treatment of retinal disease including diabetic macular edema and exudative macular degeneration.

Methods: An Enzyme-linked Immunoassay (ELISA) was utilized to determine the EC50 of the bispecific RO-634 to recombinant human VEGF-A and human Ang-2 analytes independently and in combination. A polyclonal antibody was used to detect when RO-634 bound individually to VEGF-A or Ang-2, while Streptavidin Horseradish Peroxidase (SA-HRP) was used when RO-634 bound both analytes (Figure 1).

Results: The data demonstrate the bispecific RO-634 has an EC50 for solely VEGF-A of 10.04 pM and an EC50 for solely Ang-2 of 136 pM. The bispecific RO-634 demonstrated a lower EC50 to Ang-2 while bound jointly to VEGF-A of 101.9 pM (Figure 2).

Conclusions: Our data suggests EC50 for RO-634 to Ang-2 decreases when the bispecific is also bound to VEGF-A. This synergistic effect could be due to a conformational change that occurs when RO-634 is bound to VEGF-A. Further testing should be done to assess the pharmacokinetics behind the demonstrated synergistic effect.

CONTROL ID: 3707375

SUBMITTER (NAME ONLY): Parag Majmudar

TITLE: RESULTS OF A PHASE III STUDY OF A NOVEL 0.05% ONCE-DAILY CYCLOSPORINE OPHTHALMIC GEL IN THE TREATMENT OF MODERATE TO SEVERE DRY EYE DISEASE (COSMO)

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Majmudar, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Parag Majmudar: Commercial Relationship(s);Code C (Consultant/Contractor):Zhaoke Ophthalmology

ABSTRACT BODY:

Purpose: The COSMO study aimed to evaluate the efficacy and safety of a novel 0.05% Cyclosporine Ophthalmic Gel compared with vehicle in the treatment of patients with moderate to severe dry eye disease (DED).

Methods: After a 14-day open-label placebo run in period, 644 eligible subjects were randomized 1:1 to receive treatment with either 0.05% Cyclosporine Ophthalmic Gel or vehicle nightly for 84 days. Evaluation was carried out on baseline, day 14, 42 and 84 consisting of objective measures including corneal and conjunctival staining, Schirmer test and Tear Break Up Time (BUT) and subjective measures including Eye Dryness Score (EDS) and 6 other symptoms using visual analog scale (VAS). The primary efficacy endpoint was the proportion of patients with a ≥1-point decrease in inferior corneal fluorescein staining score (ICSS) from baseline on day 84. Secondary efficacy endpoints evaluated mean change from baseline to day 14, 42 and 84 including VAS scores for EDS and 6 other dry eye symptoms (burning/pinching sensation, itching, foreign body sensation, discomfort, photophobia, and pain), ICSS score, corneal and conjunctival staining rating (Oxford grading), Schirmer test value and BUT score.

Results: The study met the primary efficacy endpoint of a ≥1-point decrease in ICSS in 73.7% of the treatment group vs 53.2% of vehicle group ($P<0.0001$) at day 84. The treatment group showed statistically greater improvement of both ICSS scores and corneal conjunctival staining score over vehicle group on day 14 ($P=0.0011$; $P=0.038$), day 42($P<0.0001$; $P=0.021$) and day 84($P<0.0001$; $P=0.008$). Significant improvement in tear secretion was also observed at day 14($P=0.024$) and day 84($P=0.005$). The EDS scores and stability of tear film (BUT score) at each visit improved significantly relative to baseline, however no significant difference between groups was observed.

Conclusions: 0.05% Cyclosporine Ophthalmic Gel once a day significantly reduced corneal and conjunctival staining and improved tear secretion compared with vehicle in moderate to severe DED. It also significantly alleviated symptoms compared with baseline. 0.05% Cyclosporine Ophthalmic Gel will be a new efficacious, safe and well tolerated therapeutic option that might bring additional benefits of convenience and compliance as a once-a-day treatment for moderate to severe dry eye.

CONTROL ID: 3707379

SUBMITTER (NAME ONLY): Alan Kong

TITLE: Thrombospondin-1 is synaptoprotective in a retina explant model

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.W. Kong, T. Garcia Ruiz, Y. Kuo, A.K. Yu, L. Della Santina, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|L. Della Santina, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In several neurodegenerative diseases such as glaucoma, there is evidence that synapse loss is an early biomarker. Identifying synaptoprotective factors that may prevent synapse loss or even regenerate these connections in the context of degenerating retinas and/or cell-based therapies are of great interest. Thrombospondin is a family of astrocyte-secreted proteins that has been shown to be synaptogenic. Here we hypothesize that thombospondin-1 (TSP1) is synaptoprotective in a mouse retina explant model.

Methods: Retina explants from adult CD-1 mice were cultured in serum free medium for 0, 3, and 7 days. Some of the retinas cultured for 7 days also contained 150 ng/mL of TSP1. After culturing, the tissue was fixed and immunolabeled with CtBP2 and PSD95 to quantify pre- and post-synaptic proteins. Z-stacks were acquired using confocal microscopy (0.1x0.1x0.3mm/voxels). Volume and distribution of puncta was evaluated in the inner plexiform layer (IPL) using VolumeCut and ObjectFinder (https://github.com/lucadellasantina/). Statistics were performed using a Wilcoxon Rank Sum Test.

Results: The average CtBP2 density (puncta/μm^3 ± SE) for the control retinas (N = 3) and 7-day cultured retinas (N = 4) was 0.244 (0.015) and 0.162 (0.004), respectively. The retinas cultured for 7-days with TSP1 (N = 4) had an average CtBP2 density of 0.226 (0.021), which was significantly greater than the 7-day group without TSP1 (P = 0.03) and was not different from the 0-day control (P = 0.63). The average PSD95 density for the 0-day, 7-day, and 7-day with TSP1 was 0.190 (0.008), 0.092 (0.004), 0.113 (0.017), respectively. There was a trend towards a significant increase in PSD95 density in the presence of TSP1 compared to without (P = 0.06), and PSD95 density with TSP1 was not different from the 0-day controls (P = 0.34).

Conclusions: In a retina explant model, our results suggest that TSP1 may be synaptoprotective, specifically for presynaptic ribbons. As we have demonstrated in a previous study, presynaptic ribbons are disassembled prior to postsynaptic component loss in experimental glaucoma, and consequently, TSP1 may be an effective therapeutic target.

CONTROL ID: 3707380

SUBMITTER (NAME ONLY): Ashley Fitzgerald

TITLE: Diabetic Retinopathy and Nephropathy Have Discordant Progression: A Cross-sectional Case Control Study in a Type 2 Diabetic New Mexican Population

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Fitzgerald, S.R. Salazar, C.J. Moezzi, R. Mankad, C.R. Qualls, A. Cabrera, F. Monickaraj, A. Das, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) and diabetic nephropathy (DN) are the most common microvascular complications of diabetes and are thought to have strong association. The objective of this study was to examine whether these two complications have significant concordance in terms of progression of severity.

Methods: A cross-sectional, case-control study was performed in two cohorts of type 2 diabetic patients in a New Mexican population: the cases had confirmed end-stage renal disease (ESRD; Stage 5, on dialysis, GFR<15, n=163) and the controls had mild DN (Stage 1 or Stage 2, GFR>60, n=114). Systemic parameters including HbA1C, blood pressure (BP), lipid levels, Albuminuria, GFR, serum Creatinine (CR), protein/CR ratio, Hemoglobin (Hb), Hematocrit (Hct), and retinopathy status by dilated fundus exam were collected by retrospective chart review. Statistical analyses were performed with a two-sample t-test for continuous variables and Chi-squared test or Fisher exact test for categorical variables.

Results: The majority (65%) of the ESRD cohort had advanced eye disease (proliferative diabetic retinopathy; PDR), while 18% of patients had no/mild eye disease (No DR/ mild non-proliferative diabetic retinopathy; NPDR). Conversely, the mild DN cohort included a significant number of PDR cases (38%). The development of ESRD was significantly associated with lower HbA1C levels (p=0.001) and higher systolic BP levels (p=<0.001). In the ESRD cohort, development of PDR was significantly associated with younger age (p=0.0002), higher diastolic BP (p=0.03), and higher LDL (p=0.036). No association was found with HbA1C levels, systolic BP, insulin use, HDL, urine albumin/CR between mild DR and PDR groups within the ESRD cohort. Although prediction of ESRD status from advanced retinopathy status has a significant odds ratio (4.033, p<0.001) the analysis of specificity (0.52) determined this to be a poor predictive tool.

Conclusions: Our findings suggest that there is discordance between progression of retinopathy and nephropathy displayed by varying retinopathy statuses within our ESRD and mild DN cohorts. Other factors such as genetic variability may play a role in the divergent pathogenesis and progression of both diabetic micro-vascular complications.

CONTROL ID: 3707385

SUBMITTER (NAME ONLY): Sneha Dodaballapur

TITLE: Rates of Posterior Capsular Rupture in Ophthalmology Resident Cases after Intravitreal Injections

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dodaballapur, M. Desai, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|V. Govindaraju, J. Chao, C. Gupta, Department of Ophthalmology, Beaumont Health, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been documented that intravitreal injections (IVI) can increase the rate of posterior capsular ruptures (PCR) during cataract surgery, however this has not been studied in resident cases. This study seeks to investigate PCR rates and potential risk factors for PCR in resident cases.

Methods: A retrospective consecutive cohort study was performed on patients of Beaumont Health, Royal Oak, Michigan. This study was done with the approval of the Institutional Review Board and with the standards delineated in the Helsinki Declaration. Using appropriate ICD-10 and CPT codes, a patient list was generated. Inclusion criteria included prior Beaumont Eye Institute patients 50 years of age or older, had prior history of IVI administered by a resident physician and had an intraoperative complication of PCR. Exclusion criteria included no other intraocular surgery for 3 months prior to the cataract surgery and no patient less than 50 years. Cataract surgery (CEIOL) was performed by third year ophthalmology residents. Data were analyzed using Chi-square analysis, Student t-test, and Relative Risk Ratio with GraphPad Prism. Statistical significance was set at $p<0.05$.

Results: 1,013 eyes were examined in this study of which 46 had PCR as an intraoperative complication of CEIOL (4.53%). Patients with prior IVI had 2.56 times the risk of developing PCR than patients with no history of IVI (RR=2.56, 95% CI=1.066-5.775; p=0.035). In the cohort with a PCR event, 10.87% had prior IVIs. Mean age for PCR complication was higher (68.33yrs, SD: 9.9) than the no PCR cohort (65.45yrs, SD 11.45); p=0.032. There was no significant relationship found between gender, laterality, prior retina surgery, or diagnosis for injection and PCR incidence.

Conclusions: Rates of PCR in resident cases of 4.53% is within the reported range of 0.5-16%. In attending cases without IVI the PCR rate is 0.45-3.6% and is as high as 6% in patients with IVI. Thus, both attending and residents experience relative increases in PCR rate with IVI. This study provides concrete evidence of the 2.56 times increased PCR risk in CEIOL with IVI history in resident cases and adds to the discussion of increased CEIOL complications in older patients. Therefore, along with intraoperative floppy iris syndrome, previous IVI may signal for the CEIOL to be performed by senior level residents and prompt added assistance and equipment in case of complications.

CONTROL ID: 3707388

SUBMITTER (NAME ONLY): Sonali Bhanvadia

TITLE: Assessing Usability of Digital Health Devices for Blood Pressure Monitoring among Glaucoma Patients

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bhanvadia, M. Brar, B. Radha Saseendrakumar, S. Baxter, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES| S. Bhanvadia, M. Brar, B. Radha Saseendrakumar, S. Baxter, Health Department of Biomedical Informatics, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blood pressure (BP) dysregulation is a known risk factor for glaucoma and home BP monitoring is increasingly common. However, little is known about glaucoma patients' ability to use digital health devices. We performed a pilot mixed-methods study with glaucoma patients to evaluate digital health literacy and usability of a commercially available BP smartwatch monitor.

Methods: Adult participants were recruited from the Diagnostic Innovations in Glaucoma Study (DIGS) and/or the African Descent and Data Evaluation Study (ADAGES) and were provided a BP monitor (Omron HeartGuide) to use at home. Baseline digital health literacy was assessed using the standardized eHEALS questionnaire. After one week, participants assessed the usability of the BP monitor and related mobile app using the Post-study System Usability Questionnaire (PSSUQ) and the System Usability Scale (SUS), standardized instruments for usability assessments in information technology. Variations in eHEALS and usability scores across demographic groups were evaluated with ANOVA. Open-ended responses about participants' experience were analyzed thematically.

Results: Among 39 participants, the mean (standard deviation, SD) age was 66.6 (8.7) years. Two-thirds (26, 66.6%) identified as female, 11 (28.2%) as African American, and 2 (5.1%) as Hispanic/Latino. The mean (SD) eHEALS score was 31.5 (4.9), reflecting excellent self-perceived eHealth literacy. Mean (SD) usability scores were 75.9 (17.9) and 2.3 (1.9) for the SUS and PSSUQ, respectively, indicating relatively high levels of usability (70-79th percentile). However, usability scores were significantly lower among older participants ($p=0.009$ for SUS, $p=0.02$ for PSSUQ; Fig. 1). Common themes in open-ended responses included difficulty using the monitor due to lack of technological skill, the watch not fitting properly, and not knowing how to troubleshoot problems.

Conclusions: We identified challenges with using commercially available home BP monitors and mobile apps among glaucoma patients, particularly with increasing age. Glaucoma patients present unique considerations for digital health design, such as older age and visual impairment. Understanding glaucoma patients' digital health literacy and user experience is important for inclusive design and future interventions.

CONTROL ID: 3707391

SUBMITTER (NAME ONLY): Mohammad Sabbagh

TITLE: Comparison of Visual Outcomes after Combined Phacovitrectomy versus Sequential Vitrectomy and Phacoemulsification for Epiretinal Membrane

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Sabbagh, J.I. Lim, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Mohammad Sabbagh: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Lim: Commercial Relationship(s);Code F (Financial Support):Aldeyra;Code C (Consultant/Contractor):Aura;Code F (Financial Support):Chengdu;Code C (Consultant/Contractor):Cognition;Code C (Consultant/Contractor):Eyenuk;Code R (Recipient):Iveric Bio;Code C (Consultant/Contractor):Luxa;Code F (Financial Support):NGM Bio

ABSTRACT BODY:

Purpose: To assess the visual outcomes of combined phacoemulsification and vitrectomy versus vitrectomy followed by phacoemulsification for patients with epiretinal membranes.

Methods: A single-center, retrospective chart review of 33 phakic patients who underwent combined phacovitrectomy (COM group) or sequential vitrectomy and phacoemulsification (SEQ group) by a single vitreoretinal surgeon and a total of 6 anterior segment surgeons. Patients were included if they had visually significant ERM and cataracts and excluded if they had other concomitant ocular disease except for mild to moderate correctable refractive errors. Outcome measures included postoperative change in best corrected visual acuity (BCVA) from pre-op BCVA, time to best final BCVA, optical coherence tomography central subfield thickness (CST), and ocular complications.

Results: 25 eyes in the COM group and 8 eyes in the SEQ group were followed a mean of 30 months. The post-operative changes in BCVA and CST between the groups were not statistically significant. 14 of 25 eyes in the COM group achieved a BCVA of 20/30 or better by post-phacovitrectomy month 3 that was sustained through follow up. All 8 eyes in the SEQ group achieved peak vision one month after vitrectomy but had vision decline secondary to cataract development. Average time to phacoemulsification in this group was 9.5 months and 7 of 8 eyes achieved > 20/30 by post-phacoemulsification week 1.

Conclusions: Combined phacovitrectomy for patients with visually significant ERM and cataracts achieves similar results to sequential surgery while providing a more rapid achievement of final BCVA.

CONTROL ID: 3707394

SUBMITTER (NAME ONLY): Don Pham

TITLE: Racial Differences in 1-Year Cataract Surgery Outcomes: A Multi-Healthcare System Analysis

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare race-related differences in 1-year outcomes following cataract surgery in individuals of black and white descent.

Methods: A retrospective cohort study was conducted using the TriNetX national database. Patients who underwent cataract surgery were initially stratified into black (n = 40,764) and white (n = 213,657) cohorts. Cohorts were then matched by demographics and comorbidities (age, gender, BMI, history of hypertension, diabetes mellitus, chronic lower respiratory disease, heart failure, nicotine dependence) using 1:1 propensity score matching (PSM). 40,132 patients in each cohort were included in the study for a total of 80,264. Primary outcome measures were vitreous hemorrhage (VH), choroidal hemorrhage, retinal detachment or tear (RD/RT), iridocyclitis, macular edema (ME), cystoid macular degeneration, epiretinal membrane (ERM) toxic maculopathy, ischemic optic neuropathy (ION), glaucoma, strabismus, hemorrhage of orbit, corneal edema, dry eye syndrome (DES), central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), vitreous opacities, ptosis, dislocation of lens, endophthalmitis, and retinal vascular occlusions (RVO). Risk ratios (RR) using 95% confidence intervals (CI) were used to compare primary outcomes 1 year after cataract surgery.

Results: 80,264 total patients were included with 40,132 patients in each of the black and white cohorts following PSM. The black cohort had a significant greater risk for developing VH (RR, 1.49; 95% CI, 1.28-1.73), RD/RT (1.17; 1.02-1.33), iridocyclitis (4.67; 4.21-5.18), ME (1.48; 1.34-1.65), cystoid macular degeneration (1.73; 1.59-1.88), ION (1.71; 1.13-2.6), glaucoma (2.14; 1.98-2.31), DES (1.21; 1.13-1.28), CRVO(2.86; 2.01-4.08), dislocation of lens (1.63; 1.24-2.13), endophthalmitis (1.64; 1.31-2.06), and RVO (1.81; 1.47-2.24). The white cohort had a significant risk of developing ERM (0.71; 0.64-0.79), corneal edema (0.64; 0.47-0.87), and ptosis (0.8; 0.7-0.92). No significant difference was seen in choroidal hemorrhage, toxic maculopathy, strabismus, CRAO, and vitreous opacities.

Conclusions: Race should be considered when evaluating long-term outcomes following cataract surgery. Blacks were more likely to develop VH, RD, ME, cystoid macular degeneration, ION, glaucoma, DES, CRVO, lens dislocation, endophthalmitis, and RVO whereas whites were more likely to develop ERM, corneal edema, and ptosis.

CONTROL ID: 3707398

SUBMITTER (NAME ONLY): Barsha Lal

TITLE: Longitudinal changes in choroidal optical coherence tomography angiography indices among young adults and children over one year.

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lal, D. Alonso-Caneiro, S. Read, A. Carkeet, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Choroidal microvasculature exhibits a significant association with axial length (AL). AL changes with age and as myopia progresses, so long-term changes in choroidal microvasculature might be expected. We conducted a 1-year prospective longitudinal study to investigate changes in choroidal microvasculature indices using optical coherence tomography angiography (OCT-A) among healthy myopic and non-myopic children and young adults.

Methods: Measurements including 3mm×3mm macular OCT-A enhanced depth scans, AL and refraction were collected at baseline and 1-year follow-up for 22 adults (18-30 years,12 myopes,10 non-myopes) and 21 children (6-15 years,11 myopes,10 non-myopes). Choriocapillaris (29 to 49 μm below retinal pigment epithelium (RPE)) and the deep choroidal layer (64 to 115 μm below RPE) en face OCT-A images were analysed to extract magnification-corrected choriocapillaris flow deficit density (FDD_{cc}) and deep choroidal perfusion density (PD_{ch}) for sub-foveal and parafoveal zones. Changes over 1-year were compared between age groups and between refractive groups within the age groups using Mann-Whitney U.

Results: The FDD_{cc} and PD_{ch} did not change significantly over 1-year or differ between age groups ($P>0.05$), however significant differences between refractive subgroups were observed. AL and spherical equivalent refraction underwent significant changes ($P<0.05$), with larger AL changes in children (0.20±0.27mm) than adults (0.04±0.07mm). Parafoveal FDD_{cc} changes were significantly associated with AL changes ($P=0.01$) (Figure 1) and refractive groups ($P=0.01$) and sub-foveal PD_{ch} changes associated with refractive groups ($P=0.01$) in adults but not in children. Between the refractive groups, changes in sub-foveal FDD_{cc} and PD_{ch} and parafoveal FDD_{cc} were significantly different ($P<0.05$) among adults, but not in children (Figure 2).

Conclusions: Longitudinal changes in choroidal OCT-A indices were significantly associated with AL changes and refractive group only in adults, with myopes and non-myopes showing different magnitudes of change. These relationships were not found in children.

CONTROL ID: 3707399

SUBMITTER (NAME ONLY): Himal Kandel

TITLE: Comparison of standard versus accelerated corneal collagen crosslinking for keratoconus: 5-year outcomes from the Save Sight Keratoconus Registry

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Kandel, S.L. Watson, Save Sight Institute, Sydney Medical School, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Long term-effectiveness of standard (UVA intensity: 3mW/cm^2, duration: 30 minutes) vs accelerated (UVA intensity: 9mW/cm^2, duration: 10 minutes) corneal crosslinking (CXL) for stabilizing progressive keratoconus is unknown. This study aimed to compare the long-term (5 years) efficacy and safety of these protocols in keratoconus using the real-world data from the Save Sight Keratoconus Registry (SSKR).

Methods: Data from the routine clinical practice (15 sites across Australia, New Zealand and Italy) were captured through a web-based registry system for this observational study. A total of 100 eyes (75 patients) who had standard CXL and 76 eyes (66 patients) who had accelerated CXL, with a follow-up visit at five-year post-CXL were included. The mean age of the participants was 24.2±7.7 (standard 24.3 ± 7.3 vs accelerated 23.7±7.7) years, and 35.0% were female (standard 33.3% vs accelerated 34.8%). The outcome measures included changes in visual acuity, keratometry (maximum keratometry, Kmax; and central steepest keratometry, K2), minimum corneal thickness (MCT), and frequency of adverse events. The outcomes were compared using mixed-effects regression models adjusted for age, sex, visual acuity, keratometry, pachymetry, doctor, practice, and eye laterality.

Results: Both CXL protocols were effective and safe in stabilizing keratoconus and improving outcomes (Fig 1). The adjusted mean changes (95% CI) in outcomes were better in standard than in accelerated CXL [habitual visual acuity gain, 10.2 (7.9 to 12.5) vs 4.9 (1.6 to 8.2) logMAR letters; pinhole visual acuity gain, 5.7 (3.5 to 7.8) vs 0.2 (-2.2 to 2.5) logMAR letters; Kmax, -1.8 (-4.3 to 0.6) vs 1.2 (-1.5 to 3.9)D; K2, -0.9 (-2.2 to 0.3) vs 0.1 (-1.3 to 1.6)D; MCT, -3.0 (-13.7 to 7.7) vs -11.8 (-23.9 to 0.4) μm (p values for visual acuity, pinhole visual acuity, Kmax: <0.05; for K2 and MCT: >0.05)]. The frequency of adverse events at the 5-year follow-up visit was low in both groups [standard, 5 (5%; haze 3; scarring 1, epithelial defect 1) and accelerated 3 (3.9%; haze 2, scarring 1)].

Conclusions: This real-world observational study found that both standard and accelerated CXL were safe and effective procedures for stabilising keratoconus in the long term. The standard CXL resulted in greater improvements in visual acuity and keratometry.

CONTROL ID: 3707401

SUBMITTER (NAME ONLY): Vivek Singh

TITLE: A biomimetic hydrogel-based therapeutic approach for preventing corneal scarring

SESSION TITLE: Corneal stromal biology, wound healing modulators, and regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Singh, A. Venuganti, D. Prasad, A. Sahoo, S. Basu, Prof. Brien Holden Eye Research Center, Champalimaud Translational Centre for Eye research, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|V. Singh, A. Venuganti, D. Prasad, A. Sahoo, S. Basu, Center for Ocular Regeneration (CORE), LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S. Chameettachal, F. Pati, Department of Biomedical Engineering, International Institute of Information Technology Hyderabad, Sangareddy, Telangana, INDIA|Y. Parekh, K. Bokara, Centre for Cellular and Molecular Biology CSIR, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Corneal wounding, due to infection, injury or inflammation, heals by stromal scarring and opacification. There is an unmet clinical need for a biomaterial that can prevent the development of corneal stromal scar or as therapeutics to treat these scars. This study reports the possible prophylactic potential of biomimetic hydrogels derived from non-transplant grade human cadaveric and bovine corneas.

Methods: Human (h) and Bovine (b) cornea were decellularized using 1.5M NaCl solution to prepare decellularized corneal extracellular matrix hydrogel (DCMH). In-vitro characterization of retained DNA, sulfated glycosaminoglycans (sGAG) and collagen of native tissue and hDCMH, bDCMH were evaluated. Physical, Chemical and environmental stability of the DCMH was looked into for viscosity profile, shear recovery and gelation property. In-vivo investigation for a scar-free cornea regeneration was conducted by corneal injury model in New Zealand white rabbits (n=6) removal of 200μm depth and 3mm diameter of stromal tissue. DCMH from both sources were topically applied to treat the surgically induced cornea wounds in rabbits, followed by clinical evaluation and comparison with collagen and sham controls. Statistical analyses were performed using ANOVA and Student's t-test.

Results: The total dsDNA, sGAGs and collagen content retained was found to be 2.07 ± 0.23% and 2.12 ± 0.51%; 73.35 ± 7.05% and 66.47 ± 4.01%; 66.47 ± 4.01% and 50.57 ± 4.73% respectively in hDCMH and bDCMH. Viscosity recovered after shear thinning was 307100 mPa.s and 281600 mPa.s for hDCMH and bDCMH. In the in vivo study, the average epithelial thickness recovered was 103.5 ± 12.3 % in the collagen group, 95 ± 11.44% in hDCMH, and 81.95 ± 15.8% for the sham group, significant between collagen and sham control. The central corneal thickness (CCT) regained was 88.85 ± 4.08% collagen group, 78.39 ± 5.059% sham control, 97.07 ± 1.59% hDCMH, 96.52 ± 0.12 % bDCMH with significant difference between hDCMH and bDCMH group.

Conclusions: Our DCMH promotes early re-epithelialization, stromal regeneration, and transparency, indistinguishable from a healthy cornea. These findings suggest that the application of our formulated decellularized corneal matrix hydrogel could be a new promising approach as a minimally invasive and easily performable procedure to prevent scarring followed by traumatic injuries in the cornea.

CONTROL ID: 3707402

SUBMITTER (NAME ONLY): Kasumi Kikuchi

TITLE: Retinal capillary changes and cytokine expression in Spontaneously Diabetic Torii fatty rats

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kikuchi, M. Murata, K. Noda, S. Ishida, Ophthalmology, Hokkaido Daigaku Daigakuin Igaku Kenkyuin, Sapporo, Hokkaido, JAPAN|Y. Kageyama, M. Shinohara, Nihon Clea Kabushiki Kaisha, Meguro-ku, Tokyo, JAPAN|T. Sasase, Nihon Tabako Sangyo Kabushiki Kaisha, Minato-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Spontaneously Diabetic Torii (SDT) fatty rat is a novel animal model for obesity and type 2 diabetes. SDT fatty rat develops hyperglycemia, dyslipidemia and other diabetic complications; however, diabetic ocular complications in the animal model have not been fully investigated. Previously, we reported that SDT fatty rats develop diabetic cataract, which well mimics the cataract formation in patients with diabetes. (Kikuchi et al., J Diabetes Res., 2020). In the current study, we further investigated the diabetic retinal complications in SDT fatty rats.

Methods: SDT fatty rats (24 weeks old, male) and age-matched Sprague Dawley (SD) rats were used in this study. Retinal capillaries were isolated by trypsin digestion, and capillary diameter and the retinal capillary pericyte/endothelial cell (P/E) ratio were assessed. Immunostaining for leukocyte adhesion molecules, intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), was performed.Real-time PCR and Magnetic Luminex assay were performed to investigate the alteration of the inflammation-related molecules, i.e., monocyte chemotactic protein-1 (MCP-1), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α) in the retina of SDT fatty rats.

Results: The retinal capillary diameter significantly increased in SDT fatty rats (7.74±0.16 μm, n=5) compared to SD rats (6.42±0.23 μm, n=5, $p<0.01$). The P/E ratio was significantly lower in the retinal capillaries of SDT fatty rats (0.42±0.04, n=5) than those of SD rats (0.61±0.01, n=5, $p<0.01$). ICAM-1 and VCAM-1 were immunostained in the retinal vessels of SDT fatty rats. mRNA expression levels of Mcp1, Il1b and Tnf were significantly upregulated in the retina of 24-week-old SDT fatty rats (Mcp1, $P<0.01$; Il1b, $P<0.05$; Tnf, $P<0.01$). The protein levels of MCP-1, IL-1β and TNF-α were also significantly increased in the retina of SDT fatty rats than those of SD rats (MCP-1, $P<0.01$; IL-1β, $P<0.05$; TNF-α, $P<0.01$, n=5 each).

Conclusions: The present study demonstrated that SDT fatty rats exhibited early diabetic changes in the retina, indicating that SDT fatty rats serve as a potential animal model in researches on the pathogenesis of human diabetic retinopathy.

CONTROL ID: 3707403

SUBMITTER (NAME ONLY): Madhuri Amulya Koduri

TITLE: Molecular mechanisms in ocular surface disease of chronic Stevens-Johnson syndrome patients using tear proteomics

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Koduri, D. Prasad, A. Kethiri, S. Shanbhag, S. Basu, V. Singh, Prof. Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|M. Koduri, D. Prasad, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|S. Shanbhag, S. Basu, The Cornea Institute, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: The chronic sequelae of Stevens-Johnson syndrome (SJS) can progress to various ocular complications and lead to visual impairment. The exact mechanism of the interplay of protein molecules in chronic ocular surface inflammation is not clearly understood. Therefore, this study aims to explore the underlying molecular signaling pathways to understand the disease process and mechanism of ocular damage using a proteomic approach.

Methods: Tear samples were collected from chronic SJS (n=6) with age-gender matched controls (n=6) and analyzed by liquid chromatography-mass spectroscopy for protein profiling and label-free quantification of tear proteins. Highly differentially regulated proteins were selected by z-score normalization followed by t-test significance using abundance values. The candidate proteins were shortlisted based on their presence in at least five patients with exclusive extracellular expression. Also, performed Ingenuity pathway analysis (IPA) to understand the differentially regulated canonical pathways in chronic SJS patients.

Results: The total tear proteins identified were ~1760, of which the t-test revealed 249 were differentially regulated proteins in chronic SJS tears. The results underline that 63 proteins were identified based on the extracellular expression, of which 33 proteins were significantly upregulated, including Neutrophil elastase ($p<0.0001$), Protein S100-A7 ($p<0.0004$), Neutrophil collagenase ($p<0.0016$), Myeloblastin ($p<0.004$), Myeloperoxidase ($p<0.003$), Matrilysin ($p<0.04$). And other 30 proteins were significantly downregulated, mostly related to lacrimal gland secretions. The IPA analysis of the significantly differentially regulated proteins revealed the IL-8 signaling pathway (p-value 1.24E-06) and inflammatory response (p-value 2.64E-04) as a major player in chronic SJS tears and could be correlated with disease conditions. Additionally, 33 proteins were uniquely expressing including Interleukin-36γ in SJS tear.

Conclusions: The findings of this study will contribute to a better understanding of the molecular mechanisms of chronic SJS ocular surface disease and may unravel new biological insights that help identify a potential therapeutic target for an effective treatment strategy.

CONTROL ID: 3707407

SUBMITTER (NAME ONLY): Amanda Lu

TITLE: Trends in California ophthalmology surgical volume during the COVID pandemic

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lu, J.D. Bartlett, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Amanda Lu: Commercial Relationship: Code N (No Commercial Relationship) | John Bartlett: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pandemic era restrictions on non-essential travel, redistribution of healthcare resources, and nursing shortages have impacted the ability of ophthalmologists to deliver care. California had among the strictest 2020 restrictions during the pandemic with reallocation of non-essential surgical resources. This study assesses changes in surgical volume of common ophthalmic procedures in California since the COVID-pandemic.

Methods: The California Health and Human Services Agency (Office of Statewide Health Planning & Development) maintains ambulatory and emergency room procedural databases. Common ophthalmic procedures and surgical volumes were extracted for 29 CPT codes from 2014-2020. Procedures with fewer than 100 cases were excluded.

Results: Overall, ophthalmology surgical volume decreased by 19% from 2019 to 2020. Greatest declines were for anterior lamellar corneal transplant (39%) and pterygium with graft (38%). Simple cataract surgeries declined by 29% in 2020, compared to an average annual decline of 3% from 2014-2019. Volume increased only for two surgeries: aqueous shunt with graft (2%) and complex retinal detachment (0.2%). Temporal artery biopsies, historically stable with 0.2% average change from 2014-2019, declined by 28% in 2020. Retinal detachment repairs declined by 20% and 17% (with and without vitrectomy, respectively). In comparison, laparoscopic appendectomy only declined by 2% in 2020. Limitations of this study include role of population changes and changes in annual coding practices.

Conclusions: COVID era declines were noted across almost all ophthalmic surgeries with steep drops in perceived non-urgent procedures such as pterygium and cataract. However, delays in cataracts and other conditions can result in increased disease burden and morbidity for patients. Uniquely, tube shunt procedures increased, perhaps due to progression of glaucoma from delayed routine care. For vision-preserving surgeries such as retinal detachment repair, lack of accessible care during the pandemic is especially concerning.

CONTROL ID: 3707410

SUBMITTER (NAME ONLY): Björn Bachmann

TITLE: First-in-Human Clinical Trial of a Fish Scale Based Biomaterial for the Emergency Management of Corneal Perforations

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Bachmann, M. Matthaei, P. Enders, L. Altay, C. Cursiefen, Ophthalmology, Universitat zu Koln, Cologne, Nordrhein-Westfalen, GERMANY|T. Stijnen, Biomedical Data Sciences, Universiteit Leiden, Leiden, Zuid-Holland, NETHERLANDS|J. Schuitmaker, Aeon Astron Europe B.V., Leiden, NETHERLANDS|M. Elling, I. Kersten-Gomez, H.B. Dick, Ophthalmology, Ruhr-Universitat Bochum Medizinische Fakultat, Bochum, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Acute corneal perforations need rapid closure to avoid intraocular infections or suprachoroidal bleeding. The worldwide lack of donor corneas delays the emergency therapy. The current study investigates the efficacy and safety of a fish scale based biomaterial (ologen™ Biocornea) for temporary wound closure for a maximum of 72 hours until a donor cornea is available.

Methods: This is a first-in-human prospective, uncontrolled, interventional, multicenter pilot study (Trial registration number: Eudamed database CIV-15-03-013305). Patients with corneal perforation or laceration with the indication of emergency corneal transplantation were included when a corneal graft was not immediately available. Institutional ethics committee approvals were obtained, the patients provided written informed consent, and the study was performed according to the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice guidelines. Ologen™ Biocornea was applied on the recipient's cornea aligning the center of the ologen™ Biocornea with the corneal defect. The ologen™ Biocornea was then fixed onto the cornea by intrastromal 10-0 nylon single sutures. The main outcome measure was effectiveness in closing the perforated cornea until a donor cornea is available. Primary safety endpoints were severe inflammatory anterior chamber reaction, hypotony, suprachoroidal haemorrhage, choroidal detachment, flat anterior chamber, endophthalmitis and wound leakage.

Results: Seven patients (5 m, 2 f) with corneal perforation due to corneal ulcerations were included. A complete success in closing the perforation was achieved in 7 out of 7 patients. In one patient replacement of loose sutures and anterior chamber tamponade with air were needed to complete wound closure. Further adverse events were conjunctival chemosis and hyperemia, foreign body sensation and intracameral fibrin formation in a patient having infectious keratitis at the time of inclusion. Following keratoplasties were regular in all patients.

Conclusions: Using a fish-scale based "biocornea", corneal perforations can be temporarily closed to bridge the time until a human donor cornea becomes available. This approach may alleviate missing immediate access to allogeneic donor corneas and potentially also be an option for complete long-term corneal replacement.

CONTROL ID: 3707420

SUBMITTER (NAME ONLY): Bowen Wang

TITLE: Oxidative stress initiates RIPK3/MLKL-mediated corneal epithelial necroptosis and NLRP3 inflammasome signaling during fungal keratitis

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Wang, X. Yang, X. Zuo, X. Wang, J. Yuan, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To assess how corneal epithelial necroptosis triggers immune responses against fungal keratitis and determine the underlying mechanisms.

Methods: Immortalized and primary human corneal epithelial cells (HCECs), C57BL/6 (wildtype, WT) mice and RIPK3 knockout (RIPK3-KO), NLRP3 knockout (NLRP3-KO) mice were infected with A. fumigatus to establish fungal keratitis models both in vitro and in vivo. Normal corneas (n = 2) and fungal keratitis corneas (n = 2) from donors and patients were collected separately. Cellular reactive oxygen species (ROS) and mitochondrial membrane potential were detected through flow cytometry. CCK8, LDH assay, TUNEL and PI staining were conducted to quantify cell viability. Morphological changes of necroptotic cell death were observed by electron microscopy (EM). RNA sequencing (RNA-Seq), western blot assay and immunofluorescence staining were performed to investigate the differentially expressed genes. Severity of disease was evaluated via slit-lamp photography, clinical scoring, fungal load and HE staining.

Results: Fungal infection triggered significant corneal epithelial necroptosis in human/mice/in vitro models. Moreover, reduction of excessive ROS release effectively prevent necroptosis. NLRP3 knockout did not affect the occurrence of necroptosis in vivo. In contrast, ablation of necroptosis via RIPK3 significantly delayed recruitment and inhibit NLRP3 inflammasome in macrophages, which enhance the progression of fungal keratitis.

Conclusions: Overproduction of ROS in fungal keratitis leads to significant necroptosis in corneal epithelium. Furthermore, necroptotic stimuli-mediated NLRP3 inflammasome serves as a driving force among host defense against fungal infection.

CONTROL ID: 3707423

SUBMITTER (NAME ONLY): Mohammed Salman

TITLE: Identification and in-silico analysis of SLC4A11 mutations in Indian patients with congenital hereditary endothelial dystrophy (CHED)

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Salman, A. Verma, D. Prasad, V. Singh, Prof. Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|M. Salman, D. Prasad, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|A. Verma, V. Singh, Centre for Ocular Regeneration (CORE), LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S. Chaurasia, M. Ramappa, Cornea and Anterior Segment Services, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|M. Ramappa, The Centre of Excellence for Rare Eye Diseases, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Congenital Hereditary Endothelial Dystrophy (CHED) is a rare form of corneal endothelial dystrophy. Mutations in SLC4A11, an abundant corneal solute transporter, leads to CHED. The purpose of this study is to identify SLC4A11 mutations in familial and non-familial CHED cases and in-silico analysis of the identified mutation.

Methods: The study involved 10 CHED patients (6 females and 4 males) from 2 familial and 5 sporadic cases with mean age around 11 years. Clinical diagnosis of CHED was based on the typical clinical characteristics such as a bilateral ground glass appearance of the cornea with increased corneal thickness assessed clinically and documented using high resolution optical coherence tomography. Blood samples were collected with informed consent, from each participants. Genomic DNA was isolated followed by screening for all coding exons with flanking intronic region of SLC4A11 gene using direct sequencing method. In addition, 80 controls were excluded for the presence of identified variations. Further, in-silico analysis was performed using homology-based modeling (Modeller10.1) for all identified SLC4A11 mutations.

Results: Two familial cases of CHED were identified with novel homozygous c.1514C>G (p.Ser489Trp) and compound heterozygous c.591A>C (p.Arg161Arg) + c.2456insT (p.Val805fs) mutations respectively. Among five non-familial cases, two cases were identified with novel homozygous mutations c.1487G>T (p.Ser480Ile), intronic mutation c.620-2A>G respectively and other with previously reported homozygous c.2653C>T (p.Arg869Cys) mutation. Remaining two cases could not be identified with CHED related pathogenic mutations. Homology modelling based in-silico analysis predicted change in protein stability, protein local flexibility and hydrogen bond interactions caused due to such mutations.

Conclusions: Our study shows a spectrum of SLC4A11 mutations ranging from exonic, intronic, homozygous, heterozygous and compound heterozygous in CHED patients. These mutations showed different grade of deleterious effect in in-silico analysis. In two of the non-familial cases, SLC4A11 mutation was not observed thereby indicating involvement of any other gene or genetic mechanism. Our study aided in the mutational spectrum of SLC4A11 in the pathogenesis of CHED.

CONTROL ID: 3707429
SUBMITTER (NAME ONLY): Ana Filipa Pereira-da-Mota
TITLE: Contact lenses that deliver statins
SESSION TITLE: Drug delivery
SESSION TYPE: Paper Session
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ABSTRACT BODY:

Purpose: The oral administration of statins, 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase inhibitors, has been associated with beneficial effects on eye conditions due to their pleiotropic effects. The efficacy of its use could be improved if efficient ocular formulations are developed reducing the side effects related with the systemic absorption. The objective of the work was to design contact lenses (CLs) as platforms for the prolonged release of statins (pravastatin sodium). A bioinspired strategy was used to mimic the active site of HMG-CoA.

Methods: Bioinspired hydrogels were prepared from mixtures of 2-hydroxyethyl methacrylate (HEMA), ethylene glycol phenyl ether methacrylate (EGPEM), and 2-aminoethyl methacrylamide hydrochloride (APMA). A physicochemical characterization of the hydrogels was carried out. The hydrogels were loaded by soaking in a pravastatin solution during 48h. Drug release was monitored in simulated lacrimal fluid. Ex vivo porcine cornea and sclera permeability was assessed using vertical diffusion cells. Pravastatin was administered as eye drops and as CLs to male New Zealand white rabbits. The levels of pravastatin in tear fluid were collected using Schirmer test strips. The drug accumulated in cornea, sclera, crystalline, aqueous and vitreous humour, and retina was also quantified.

Results: The incorporation of APMA monomer (E200A40 and E0A40 hydrogels) remarkably increased the amount of pravastatin loaded (7.26±0.6 and 6.70±0.2 mg/g, respectively, Figure 1), without altering the swelling, transmittance, mechanical properties and ocular compatibility typical of soft CLs. The CLs sustained the in vitro release for 1 day. In ex vivo permeability tests, pravastatin was detected in the receptor chamber through transscleral permeation. In in vivo tests, the eye drops resulted in measurable pravastatin levels for 1h. The permanence of the drug in tear fluid was prolonged for more than 8h when it was administered as CLs. Among the ocular tissues evaluated, pravastatin was detected in the cornea (158.5±31.8 ng/g), sclera (1.53±0.6 ng/g), aqueous (108.7±47.5 ng/g) and vitreous humour (2.00±0.6 ng/g).

Conclusions: The design of CLs applying a bioinspired strategy allows the incorporation of pravastatin without altering the properties required as a medical device. Pravastatin-loaded CLs have a great potential to serve as a novel delivery system for the treatment of disorders affecting the anterior and posterior segment of the eye.

CONTROL ID: 3707430

SUBMITTER (NAME ONLY): Erdost Yildiz

TITLE: Ruthenium-induced Corneal Collagen Crosslinking under Visible Light

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Corneal collagen crosslinking (CXL) is a commonly used minimally invasive surgical technique to prevent the progression of corneal ectasias, such as keratoconus. Unfortunately, riboflavin and UV-A light-based conventional CXL procedures have not been successfully applied to all patients, and they usually have frequent complications, such as corneal haze and endothelial damage. This study proposes a new method for corneal crosslinking by using ruthenium (Ru) based photoinitiator solution and visible light (430 nm).

Methods: As a ruthenium photoinitiator solution, we applied tris(bipyridine)ruthenium(II) ($[Ru(bpy)_3]^{2+}$) and sodium persulfate (SPS) mixture covalently crosslinks free tyrosine, histidine, and lysine groups under visible light exposure (400-450 nm). Firstly, we demonstrated the effects of the Ru/visible blue light procedure on the viability and toxicity of the human corneal epithelium, limbal, and fibroblast cells via flow cytometry, immunofluorescence staining, and cell toxicity assays. After that, bovine corneas crosslinked with ruthenium mixture and visible blue light were characterized, and their biomechanical properties were compared with the conventional riboflavin/UV-A crosslinking approach.

Results: $[Ru(bpy)_3]^{2+}$ and SPS did not show toxicity under 1 mM in any human corneal cell lines. The crosslinked corneas with the non-toxic ruthenium-based visible light CXL method showed significantly higher Young modulus in the hybrid rheometer, higher mechanical stiffness in uniaxial stress-strain test, and more bonding between collagen fibrils under scanning electron microscopy compared to conventional riboflavin, and UV-A light-based method applied corneas. Additionally, other materialistic characteristics (hydrodynamic behavior, optical transparency, and enzymatic resistance) of ruthenium-based crosslinked corneas were significantly better than riboflavin-based crosslinked corneas.

Conclusions: In all biomechanical tests, the visible light-based crosslinked corneas with non-toxic doses of ruthenium photoinitiator solutions showed better results than conventional UV-A crosslinked corneas. In this way, we prevent UV-A light-induced cytotoxicity in a faster and more effective collagen crosslinking procedure. We foresee that Ru/visible light-based crosslinking treatment could become the standard therapy for all ectatic corneal pathologies because of its superior biocompatibility, safety, and efficiency very soon.

CONTROL ID: 3707432

SUBMITTER (NAME ONLY): Iker Sánchez Navarro

TITLE: Next-Generation Sequencing Panel Results for Inherited Retinal Dystrophy in a Large Pediatric Cohort

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Inherited retinal dystrophies (IRDs) are a genetically heterogenous group of disorders for which an early diagnosis may be essential. Approved therapies and clinical trials for many IRDs are most often contingent on a molecular diagnosis. Here, we report our experience with a comprehensive genetic testing strategy for inherited retinal dystrophy using a next-generation sequencing panel in a pediatric population.

Methods: We carried out a retrospective analysis of test results from 1,612 deidentified patients, aged 0 to 12 years, tested consecutively for IRDs using a retinal dystrophy panel at Blueprint Genetics. The molecular diagnoses of IRDs were based on the detection of variants that included mitochondrial variants, copy number variants (CNVs) including small CNVs defined by exon size, and non-coding variants in intron regions +/-20 bps from exon-intron boundaries. Variant interpretation was performed according to American College of Medical Genetics guidelines.

Results: We extracted information from the internal laboratory database. The median coverage of all target regions was 99.9% at >20X while the median sequencing depth was 208X. The median age at testing was 8 years. Males made up 59.7% (962) of the cohort while females made up 39.9%% (643). Sex was not specified for 7 (0.4%) patients. A molecular diagnosis was made in 906 (56.2%) patients while a variant of unknown significance (VUS) favoring pathogenic was identified in an additional 96 (6.0%). Diagnoses were made involving 114 genes; ABCA4, RS1, CNGB3, RPGR, and CEP290 accounted for 37.3% of diagnoses. Mitochondrial variants were responsible for 3 diagnoses. Copy number variants (CNV) contributed to the diagnosis in 71 patients (4.4%); 28/71 (39.4%) patients had CNVs that were 1 or 2 exons in size. Non-coding variants contributed to 171 (10.6%) diagnoses, 45/171 (26.3%) of which were beyond 10 base pairs from the exon-intron boundary.

Conclusions: These results support the clinical utility of genetic testing for IRDs in pediatric patients. Importantly, approved therapies or clinical trials are available for the 5 most common diagnostic genes. Small CNVs, noncoding variants beyond 10 base pairs from the exon-intron boundary, and mitochondrial variants were responsible for the diagnosis in 4.7% of patients, highlighting the importance of a comprehensive testing approach with high sensitivity to detect these variants.

CONTROL ID: 3707440

SUBMITTER (NAME ONLY): Denis Malaise

TITLE: Development of a preclinical model of retinoblastoma in rats mimicking different clinical presentations

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Retinoblastoma is the most common primary intraocular tumor in children. Its management is still a challenge. If preclinical models are helpful to evaluate new therapies, current retinoblastoma ones usually fail to represent the entire spectrum of the disease.

We thus aim to develop an orthotopic preclinical model of retinoblastoma using patient-derived tumor cells, mimicking different clinical presentations and available for the evaluation of new therapies.

Methods: Subcutaneous retinoblastoma patient-derived (from enucleation) xenografts were established and maintained on immunodeficient Nude mice. To develop the orthotopic model, a suspension of retinoblastoma cells (from subcutaneous mice tumors) were injected in the subretinal space of Nude rat eyes. Tumor growth was assessed in vivo by retinal photographs and optical coherence tomography (OCT). At the end of the follow-up, histopathology analysis was performed. All experiments were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and the institutional guidelines and local ethics committee regarding animal experimentation.

Results: Forty-nine eyes were grafted. Tumoral growth was observed in 49% of the eyes in a median time of 1,9 weeks. Media remained clear in nearly all eyes, allowing a high-quality observation of fundus during follow-up. OCT documented different patterns of tumoral growth: subretinal, intraretinal or vitreous growth. Interestingly, in some cases the tumors initially located under the retina has migrated secondarily into the inner retina, the usual location of emergence of retinoblastoma in children. Histopathology confirmed the presence of retinoblastoma viable cells.

Conclusions: We develop a preclinical model of retinoblastoma in Nude rat eyes, by grafting under the retina patient-derived tumor cells. The rate of tumor growth must be improved but the model demonstrated subretinal, intraretinal or vitreous tumors and is adapted to new retinoblastoma treatment evaluation.

CONTROL ID: 3707442

SUBMITTER (NAME ONLY): Evi Malagise

TITLE: Sigma-2 receptor modulators rescue POS trafficking deficits in RPE cell-based models of dry AMD

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Toxic amyloid-beta oligomers (AβOs) and oxidative stress are hallmarks of dry age-related macular degeneration (dAMD) and can disrupt key homeostatic processes in retinal pigmented epithelium (RPE) cells (Rabin et al. 2013). AβOs disrupt RPE cell function in vivo (Ruozhou et al. 2013) and normal RPE-mediated photoreceptor outer segment (POS) phagocytosis in vitro (Lynn et al. 2021). Sigma-2 receptor (S2R) modulators prevent AβOs from binding to neurons and rescue deficits in neuronal functioning (Izzo et al. 2014). Based on dAMD-related deficits in RPE function and the role of the S2R as a key damage sensor, the hypothesis that S2R modulators could rescue AβO and oxidative stress-induced deficits in the ability of RPE cells to phagocytose POSs was tested.

Methods: A human RPE cell line, ARPE-19 cells, were exposed to AβOs (0.5-2μM) over time (1-8 hr) and AβO binding was assessed via immunocytochemistry (ICC) and high content imaging (n=3-6 experiments). A trafficking assay was used to monitor internalization and degradation of POS over time. ARPE-19s were exposed to AβOs or H_2O_2 in the presence or absence of S2R modulators. The effects of S2R modulators on POS colocalization with lysosomal associated membrane protein 2 (LAMP2) and microtubule-associated proteins 1A/1B light chain 3B (LC3B) were quantified via confocal imaging and unbiased algorithm across time (12-48 hr; n=2 experiments). Statistical significance ($p<0.05$) was determined via Two-Way ANOVA and post hoc Tukey's test.

Results: ICC studies show that AβOs bind to ARPE-19s in time and concentration-dependent manners (EC50=1.86μM). Following exposure of cells to 1μM AβO, POS are retained in LAMP2 positive vesicles and trafficking is diminished to LC3B vesicles when compared to control. S2R modulators from three independent chemical series restored POS trafficking through LAMP2 positive vesicles at 36 and 48 hr ($p<0.0001$) and through LC3B vesicles at 48 hr ($p<0.0001$). The same S2R modulators restored POS trafficking after exposure to 100μM H_2O_2 through LAMP2 positive vesicles at 12 and 48 hr ($p<0.001$) and through LC3B vesicles at 12, 24, and 36 hr ($p<0.001$).

Conclusions: Results point to a role of S2R modulators in rescuing AβO and oxidative stress-induced deficits in RPE cells by normalizing the homeostatic recycling of POSs in RPE cells. These data support S2R modulators as a promising potential therapy for dAMD.

CONTROL ID: 3707446

SUBMITTER (NAME ONLY): Rossen Hazarbassanov

TITLE: Detecting keratoconus on two different populations using an unsupervised hybrid artificial intelligence model.

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Several supervised machine learning models have been proposed to assist in keratoconus (KCN) detection, however, they require numerous well annotated data. Herein, we propose a new unsupervised hybrid artificial intelligence model to detect KCN.

Methods: We have developed an unsupervised model based on the k-means algorithm and adapted flower pollination algorithm (FPA). The proposed model was evaluated using two independent datasets: Pentacam (Oculus Inc., Germany) corneal imaging data collected from 5430 eyes from Department of Ophthalmology and Visual Sciences, Paulista Medical School, Federal University of Sao Paulo, Sao Paulo, Brazil; and CASIA (Tomey, Japan) corneal imaging data of 1531 eyes from Department of Ophthalmology, Jichi Medical University, Tochigi in Japan. Three different clustering scenarios were evaluated: 2 classes (normal vs KCN), 3 classes (normal vs KCN low grade (1-2 stage) vs KCN high grade (3-4 stage) and 5 classes (normal, stage KCN 1, KCN 2, KCN 3 and KCN 4). We compared the proposed method with three other standard unsupervised algorithms including K-means alone, K-medoids, and Spectral cluster (figure 1), following 25 runs. Accuracy (Ac) metrics analyses also included Precision (Pr), Recall (R), F-Score (F), and Purity (Pu).

Results: FPA-K-means outperformed the other algorithms in 2-, 3- and 5-class scenarios, except for Recall and Purity for the 5-class scenario. In the 2-class test, FPA-K-means achieved Ac=96.03, Pr=96.29, R=96.06, F=96.17, and Pu=96.03. When considering a 3-class scenario, FPA-K-means reached Ac=71.02, Pr=53.53, R=75.37, F=64.64, and Pu=80.85. While for the 5-class test, FPA-K-means attained Ac= 75.20, Pr= 35.01, R= 47.70, F= 48.97, and Pu= 53.64, whereas Spectral clustering method achieved R= 55.33 and Pu= 55.12

Conclusions: The proposed model consists of a new unsupervised algorithm that combines two computational learning techniques for detecting KCN from corneal image data. As it is unsupervised, the model is not affected by expert pre-labelling bias. Our study demonstrates that the proposed model can be used in the clinical and scientific setting for detection of KCN. Improvements to this model may be applied in clinics for diagnosing the corneal status of KCN patients.

CONTROL ID: 3707447

SUBMITTER (NAME ONLY): Davide Garzone

TITLE: Inter-device and inter-scan comparability of drusen volume assessments in age-related macular degeneration: A MACUSTAR report

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT)-based drusen volume quantification is a relevant biomarker in age-related macular degeneration (AMD). An FDA-approved automated software for quantifying drusen volume using Cirrus (Zeiss Meditec, Dublin, CA) is available, however the comparability with similar approaches on other devices is largely unknown. Hence, we compared drusen volume measured by a newly developed, automated software running on Spectralis OCT data (Heidelberg Engineering, Heidelberg, Germany) against the above-mentioned software on Cirrus.

Methods: We included 306 eyes from 159 individuals with bilateral intermediate (iAMD, n=133) or early (eAMD, n=26) AMD, both reading center confirmed using multi-modal imaging. The Spectralis imaging protocol included a 20°×20°

(25 B-scans) and a 30°×25° macular volume scan (241 B-scans), while the Cirrus protocol included a 200×200 macular cube. We assessed inter-device and inter-scan differences in 3- and 5mm diameter fovea-centered grid with intra-class correlation coefficients (ICCs) and root mean squared error (RMSE). Furthermore, we calculated the agreement based on exceeding a drusen volume cut-off indicating higher AMD progression risk (previously shown at >0.03mm^3 for Cirrus, set at >0.09mm^3 for Spectralis by adding the mean difference between the two devices to 0.03).
Results: Mean age of participants was 71.3±7.4 years. In the 5-mm diameter grid, no drusen were detected in 2 eyes (0.6%) in the Spectralis 241 B-scans, in 13 eyes (4%) in the 25 B-scans and 75 eyes (23.6%) in Cirrus scans. Agreement on drusen volume measurements was high between the two Spectralis scans (ICC 0.993 [0.991-0.994]). Drusen volume measurements between the denser Spectralis scan and Cirrus showed good reliability (ICC 0.803 [0.76-0.84]); the RMSE was 0.007 in eAMD and 0.106 in iAMD. Considering the cut-off mentioned above, agreement (kappa) between the two Spectralis scans was 97.4 (0.94); while with Cirrus it was 89.3 (0.77) for 241 B-scans and 89.4 (0.77) for 25 B-scans, respectively.
Conclusions: Drusen volume measures across the two softwares are not interchangeable. Comparability improves using a binary cut-off. Less dense scan patterns decrease sensitivity of drusen detection in Spectralis OCT scans.

CONTROL ID: 3707451

SUBMITTER (NAME ONLY): Nancy Holekamp

TITLE: Key clinical pearls for evaluating surgical candidates, and patient preference, for the Port Delivery System with ranibizumab (PDS)

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The PDS is a US Food and Drug Administration–approved drug delivery system that includes a refillable ocular implant for continuous delivery of a customized formulation of ranibizumab, surgically implanted in the superotemporal quadrant at the pars plana. Key clinical pearls for preoperative evaluation of PDS surgical candidates and patient preference for the PDS versus intravitreal injection are reported.

Methods: The phase 3 Archway trial (NCT03677934) evaluated safety and efficacy of the PDS with ranibizumab 100 mg/mL with fixed 24-week refill-exchanges versus intravitreal ranibizumab 0.5 mg injections every 4 weeks in patients with neovascular age-related macular degeneration (nAMD). Treatment preference was assessed in the PDS arm at week 40 using the PDS Patient Preference Questionnaire.

Results: PDS candidates require careful preoperative evaluation, including thorough review of medical and surgical history to identify factors that may negatively affect conjunctival health and impact suitability for PDS implantation. History of prior conjunctival-based surgery may result in conjunctival scarring or poor tissue integrity. Long-term use of topical medications (eg, for glaucoma) may affect conjunctival quality, causing inflammation, scarring, and decreased thickness. Relevant ocular medical history, such as severe ocular surface disease, scleritis, or concomitant conditions, such as scleroderma, pemphigoid, or Sjogren's syndrome, may also affect conjunctival or scleral integrity.

Examination of the conjunctiva and Tenon's capsule should be performed preoperatively at the slit lamp with a cotton swab to assess mobility, scarring, and translucency/thickness. Eyelid health should be evaluated, with attention to lid hygiene, position, and mobility, which may impact postoperative infection risk and wound healing.

In Archway, 93.2% of PDS-treated patients (n = 234) preferred ranibizumab delivered via the PDS compared with intravitreal injection, with top reasons for preference identified as fewer treatments, less discomfort, and less worry/nervousness.

Conclusions: Careful preoperative evaluation is required to ensure optimal surgical outcomes for PDS candidates. PDS patients demonstrate a marked preference for the PDS over intravitreal injection; consistent attention to the clinical pearls described should help to maintain high levels of patient satisfaction.

CONTROL ID: 3707454

SUBMITTER (NAME ONLY): Cherie Nau

TITLE: Patient reported mid-day fogging is not related to central fluid reservoir clearance

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.B. Nau, M. Schornack, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|J. Harthan, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|E. Shorter, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|A.C. Nau, Korb and Associates, Boston, Massachusetts, UNITED STATES|J. Fogt, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mid-day fogging is a common complaint from scleral lens (SL) wearers. We compare self-reported patient fogging to measured fluid reservoir (FR) thickness and central FR optical density after at least 2 hours of continuous wear in established SL patients.

Methods: 22 eyes of 14 patients that had worn SLs for 17 ± 9 months (mean ± SD; range 6 – 33 months) were included in this study. Indication for SL wear was ocular surface disease in 12 eyes and corneal irregularity in 10 eyes. Patients were 53 ± 16 years of age (range: 24-76 years); 8 patients were male. Mean wear time before measurements was 3.6 ± 2 hours (range: 2 – 9 hours). Schleimpflug images were collected by Pentacam (Oculus, Inc). The Pentacam caliper program was used to manually measure central clearance from the 90-degree image. Mid-FR densitometry was recorded from the same image. 7 patients (11 eyes) self-reported fogging, 6 patients (9 eyes) did not. Comparisons were made by t-test.

Results: Average central FR clearance for all eyes (n=22) was 276 ± 115 µm (mean ± SD; range 114 – 560 µm) and average FR densitometry was 6.3 ± 2.4% (range 4.3 – 13.5%). Average FR clearance was not statistically different between foggers 286 ± 124 µm (range 114 -520 µm, n=11) and non-foggers (256 ± 111 µm, range 144 - 560 µm, n=9; P=0.6). FR densitometry was also not statistically different between foggers (8.0 ± 2.7%, range 5.3 to 13.5%) and non-foggers (5.0 ± 0.7%, range 4.3 – 6.7%; P=0.2). When FR clearance was plotted against FR densitometry, no correlation was present for: all eyes (R2 = 0.0003), foggers (R2 = 0.0021) and non-foggers (R2 = 0.008).

Conclusions: No statistical differences in central fluid reservoir clearance or measured fluid reservoir densitometry were found between self-reported foggers or non-foggers wearing scleral lenses. Self-reported scleral lens mid-day fogging is not attributed to central scleral lens fluid reservoir clearance.

CONTROL ID: 3707457

SUBMITTER (NAME ONLY): Loren Lock

TITLE: Analysis of Health System Effect on Diabetic Eye Screening Variability in Rural Versus Urban Underserved Primary Care Clinics

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lock, R. Channa, C. FOWLKES, Y. Liu, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|M. Brennan, Department of Medicine, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|Y. Cao, Department of Population Health Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rural and urban underserved communities experience lower rates of preventive screening, but factors contributing to variability in diabetic eye screening receipt between these communities have not been systematically analyzed. We used a unique, all-payer database covering over 75% of Wisconsin residents (Wisconsin All-Payer Claims Database) to assess factors associated with screening variability in rural vs. urban underserved and advantaged primary care clinics.

Methods: We included adults with diabetes (18-75 years old) with claims billed throughout the baseline (2012-2013) and measurement years (2013-2014). Patients received screening if they had a claim billed for an exam with an eye care provider or telemedicine-based retinal imaging during the measurement year. We created multivariable logistic regression models to assess the impact of age, gender, hierarchical condition category risk score, health system, primary care clinic rurality, and level of disadvantage (following the Wisconsin Collaborative for Healthcare Quality classification) on screening receipt.

Results: A total of 118,707 adults with diabetes from 143 Wisconsin health systems were included. Most (74%) were over 55 years of age (mean: 61 ± 11 years), male (51%), and obtained care from urban primary care clinics (84%). Screening rates varied widely from 32% to 72%, with the least screening among those obtaining care from urban underserved primary care clinics and the greatest screening among those obtaining care from urban advantaged primary care clinics. Before adjusting for health system in the model, and with urban advantaged primary care clinics serving as the reference, patients who obtained care from rural vs. urban underserved primary care clinics were more likely to obtain screening (OR_{rural} 0.79, 95% CI 0.71-0.88 vs. OR_{urban} 0.60, 95% CI 0.58-0.63). However, patients from urban underserved clinics were more likely than their rural counterparts to obtain screening after adjusting for health system (OR_{rural} 0.72, 95% CI 0.62-0.82 vs. OR_{urban} 0.89, 95% CI 0.84-0.94).

Conclusions: There was significant variability in screening based on primary care rurality and level of disadvantage. Health system contributed substantially to this variability. Health system-focused interventions, particularly those serving patients in urban underserved primary care clinics, may increase screening receipt.

CONTROL ID: 3707460

SUBMITTER (NAME ONLY): Kent Anderson

TITLE: Compliance with Documenting the Presence of a Teaching Physician in a Resident Ophthalmology Clinic

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.L. Anderson, A.I. Garcia, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure: Kent Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Angelica Garcia: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Supervision must be documented for every patient encounter during residency training. This is especially indicated when a bill is submitted to a payor for services performed with the involvement of a resident. (1) The teaching physician must include an attestation documenting the level of resident involvement in the patient encounter. (2) When submitted to CMS the GC modifier is also utilized to indicate that a resident, under the direction of a teaching physician, is involved in a patient encounter. We retrospectively reviewed our documentation of the teaching physician in a resident ophthalmology clinic.

Methods: All patient encounters performed by ophthalmology residents over a 5-month period (January thru May 2021) were retrospectively reviewed for appropriate documentation of the teaching physician. All patient encounters were supervised by teaching physicians in an outpatient ambulatory ophthalmology clinic at the Texas Diabetic Institute, San Antonio, TX. Each electronic medical record (EMR) was reviewed for appropriate documentation of the teaching attestation and GC modifier. The data was analyzed using R software.

Results: A total of 1,500 patient encounters were reviewed. All records (100%) documented the teaching attestation. The GC modifier was utilized in 1,388 of patient encounters (92.5%). January (95%) and May (88%) showed the highest and lowest compliance, respectively. The GC modifier was not documented in 7.5% of patient encounters.

Conclusions: All patient encounters included appropriate documentation of the teaching attestation. Residents in clinic have direct supervision by the teaching physician and the EMR sends all notes to teaching physicians to be signed and attested. In addition, all notes are reviewed internally for compliance and are amended if not documented appropriately. Compliance with the GC modifier was significantly lower. This is attributed to inadequate understanding of proper usage and that it may not be required by all payors. With recent increase emphasis on the attestation for all notes, providers are less enthusiastic to also ensure documentation of the GC modifier due to this redundancy. Good practices aim for 100% compliance in documentation. Both teaching and resident physicians should be educated on appropriate supervision and how it should be best documented in the medical record.

CONTROL ID: 3707462

SUBMITTER (NAME ONLY): Richard Tran

TITLE: ASCORBIC ACID ATTENUATES HYDROGEN PEROXIDE INDUCED OXIDATIVE STRESS AND OSTEOBLASTS DEMONSTRATE ANTIOXIDANT RECYCLING POTENTIAL

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Tran, J. Morgenstern, S. Droho, J.L. Olson, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Richard Tran: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Morgenstern: Commercial Relationship: Code N (No Commercial Relationship) | Steven Droho: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Olson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Oxidative stress is strongly implicated in disease progression of age-related macular degeneration. Oral supplements, including ascorbic acid (AA), target this oxidative etiology, yet efficacy is limited due to insufficient ocular distribution. One possible avenue is restoring the antioxidant potential of the vitreous by improving recycling of the inactive oxidized form of AA, dehydroascorbic acid (DHA), back to its active reduced form. Here, we demonstrate the antioxidant potential of AA to improve common retinal pigment epithelium (ARPE-19) cell viability in the setting of H_2O_2 induced oxidative stress and evaluate osteoblasts as a potential source of antioxidant recycling.

Methods: In vitro evaluation was performed by incubating ARPE-19 in culture media containing .2mM H_2O_2 with and without 100uM AA. MTT assay was performed to assess for cell viability. Osteoblast antioxidant recycling potential was tested by exposing MG-63 osteosarcoma cells to culture media containing 100uM DHA. At each time point from 0 to 80 minutes, media was collected and concentrations of DHA and AA were assessed using HPLC. Statistical comparisons were performed using a student's t-test.

Results: AA successfully attenuated the toxic effects of H_2O_2, with 88% of ARPE-19 cells remaining viable after exposure to both $H_2O_2$and AA, compared to 61% viable after incubation with H_2O_2 alone ($P < .001$). Osteoblast antioxidant recycling of DHA was observed with an increase of AA concentration and a concomitant decrease in DHA levels over time. At 80 minutes, the concentration of AA had a 2-fold increase with a paired 2-fold decrease in DHA levels.

Conclusions: These experiments demonstrate the antioxidant potential of AA to attenuate the effects of oxidative stress and its physiologic importance in managing cellular exposure to reactive oxygen species. Osteoblasts exhibited the potential for antioxidant regeneration of AA outside their biological niche. While preliminary, these results demonstrate the promise of an implantable device that continuously recycles antioxidant, eliminating the need for constant injections.

CONTROL ID: 3707463

SUBMITTER (NAME ONLY): Gilad Rabina

TITLE: Safe Delivery Through 20G Trocar of Soft Mono Layer Retinal Pigment Epithelium Implant

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Rabina, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|G. Rabina, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|L. Rosenberg Belmaker, A. Eisenbach, D. Sade, M.M. Maayan.ma@precise-bio.com, M. Marcus, Y. Hayardeni, A. Eitan, Precise Bio, ISRAEL|

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ABSTRACT BODY:

Purpose: Clinical studies suggest that RPE transplant may delay geographic atrophy progression in AMD patients. Our purpose is to examine a novel device for a novel soft monolayer RPE sheet implantation to the subretinal space in a domestic pig in an in vivo study.

Methods: A novel RPE implant comprised of natural biocompatible scaffold with a printed monolayer of polygonal RPE cells was developed. Implants demonstrate high viability, density, morphology, identity to RPE markers such as PMEL17 and potency by measuring PEDF secretion. For safe delivery of the RPE implant into the subretinal space a novel delivery device has been developed. A patented safe folding of the RPE implant into the device allows to transplant a 2x4 mm RPE implant through a standard 20G trocar. In order to insert the RPE implant into the subretinal space a 25G pars plana vitrectomy performed followed by a retinal bleb formation using a 41G canula. A 25G trocar replaced by a 20G trocar, the device is inserted into the subretinal space and the 2x4 mm RPE implant is released, followed by flattening the retina. Animals were followed for eight weeks, during which, OCT imaging and clinical examination took place.

Results: A total of six eyes of six female domestic pigs were included in this prospective study. Four study eyes underwent subretinal RPE transplant (two with systemic and topical immunosuppression and two with short systemic and full topical immunosuppression) and two control eyes (underwent the procedure without RPE transplant). At the end of the follow up period, all eyes were without inflammation signs, retinas were attached with normal neuroretinal layers and without evidence of proliferative vitro retinopathy, intraretinal nor subretinal fluid nor photoreceptor atrophy on OCT. At the end of the follow up period four eyes had clear crystalline lenses and two eyes developed significant cataract.

Histopathological examination demonstrated the presence of human RPE cell monolayer, with no immune cell activity.

Conclusions: A subretinal transplant of a novel printed RPE sheet implant with the aid of a novel 20G delivery device may be a safe method for RPE subretinal transplantation.

CONTROL ID: 3707468

SUBMITTER (NAME ONLY): Dongfeng Cao

TITLE: Human photoreceptor mitochondria (PR-Mit) are molecularly unique in healthy aged retina and outer retinal tubulation (ORT) of age-related macular degeneration (AMD)

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Cao, J.D. Messinger, D. Kar, C.A. Curcio, Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|T. Ach, Ophthalmology, University Hospital Bonn, Bonn, GERMANY|

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ABSTRACT BODY:

Purpose: Mit in inner segments (IS) of photoreceptors (PR) have optical as well as energy-generating and calcium-buffering functions. They guide light to outer segments (OS). PR Mit are the hypothesized reflectivity source for the border of ORT, a scrolling of photoreceptors by Müller glia in advanced AMD, seen in optical coherence tomography (OCT). We immuno-stained Mit in aged-normal and advanced AMD retinas for cytochrome oxidase 4 (COX4), the terminal oxidase of the electron transport chain, and transmembrane protein 119 (TMEM119), a microglia cell-surface marker.

Methods: Twelve µm-thick sections of maculae from 20 eyes including 4 normal, 7 early-or-intermediate (e-i) AMD, 9 advanced AMD (6 atrophic (a), 3 neovascular (nv)) of white donors >80 years were immuno-stained with COX4 (Invitrogen, #459600) and TMEM119 (Abcam, #ab185333) using red-substrate enzymatic detection and scanned with a 40x objective. Positive controls were surgically excised human liver tissue. Negative control experiments used mouse IgG isotope (COX4) and omitted primary antibody (TMEM119).

Results: In neurosensory retina of normal and e-iAMD eyes, punctate COX4 immunoreactivity localized to inner limiting membrane, ganglion cell layer, PR IS, retinal pigment epithelium and cone pedicles/rod spherules in outer plexiform layer. Staining was moderate in other retinal layers and undetectable in PR OS, Bruch's membrane, and sclera. Of these locations, PR IS was also labeled with anti-TMEM119, in fovea and non-fovea regions, indicating labeling in both cones and rods. In advanced AMD eyes with ORT, both COX4 and TMEM119 specifically labeled PR IS in ORT open and closed configurations. In ORT, immunoreactivity in individual IS of PR lacking OS progressively approached and crossed the external limiting membrane.

Conclusions: Data suggest that PR MIT have a unique molecular composition possibly important for optical properties in health and AMD. The hypothesis that mitochondria are reflectivity sources in OCT, initially shown for ORT using electron microscopy of advanced AMD eyes (PMID 25635579), is further supported by the current demonstration of immunoreactivity for TMEM119 and COX4 at all stages of photoreceptor degeneration. Direct contributions of COX4 and TMEM119 to light transmission and reflectance remain to be determined experimentally.

CONTROL ID: 3707470

SUBMITTER (NAME ONLY): Kiersten Snyder

TITLE: Demodex Blepharitis and Coexisting Bacterial Burden in Eye Care Patients: The Pandora Study

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Demodex is a vector for bacteria and the prevalence of bacteria on eyelids has shown to be correlated with Demodex presence. To understand type(s) and/or number of bacteria in those with Demodex blepharitis, the Pandora study evaluated the bacterial flora on the eyelid margin and conjunctival fornices in Demodex blepharitis (DB) and normal or non-Demodex blepharitis (non-DB) patients.

Methods: This is a prospective, observational, multicenter study. Swabs were taken from the eyelid margin and conjunctival fornices of 24 patients with at least 10 collarettes (DB) and 11 patients who have no diagnosis of DB or other forms of blepharitis (patients without collarettes, or signs or symptoms consistent with blepharitis). By study completion, samples from a total of 60 DB patients and at least 40 non-DB patients will be collected. All eyelid/conjunctival swabs were sent for culture on blood, Chocolate and Sabouraud agar plates and gram stain.

Results: Methicillin-resistant Staphylococcus epidermidis (MRSE) were isolated from 29% (7/24) of DB patients while only 2 out of 11 patients (18%) had MRSE in the non-DB group. More than one type of bacteria was found in 63% and 45% of the DB and non-DB patients, respectively. Staphylococcus epidermidis was the most isolated bacteria in both DB and non-DB eyelids but methicillin-sensitive coagulase negative Staphylococcus epidermidis was more commonly isolated in non-DB patients (45% vs 21%).

Conclusions: These preliminary results suggest that more pathogenic (MRSE) and more bacterial strains are found in DB patients compared to normal patients. This signifies the importance of treating Demodex blepharitis to minimize the presence of pathogenic bacteria which can compromise outcomes in patients wearing contact lenses or undergoing refractive or cataract surgery. Larger sample size upon study completion will confirm these preliminary findings.

CONTROL ID: 3707471

SUBMITTER (NAME ONLY): Krati Chauhan

TITLE: Comparing utilization for inflammatory and infectious eye diseases for Medicare and Commercial insurance

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chauhan, Southern Illinois University School of Medicine, Springfield, Illinois, UNITED STATES|J.T. Rosenbaum, Oregon Health & Science University, Portland, Oregon, UNITED STATES|J.T. Rosenbaum, Legacy Health System, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Eye health is influenced by access to eye care. Eye care in the United States is covered by health insurance plans, either private or made available by government. Medicare is provided by government and Marketscan is a private or commercial insurance. Utilization of eye care is impacted by type of insurance a person has. There is lack of data, comparing utilization for infectious and inflammatory eye diseases among those who have Medicare and private insurance. We have conducted a retrospective study, using Medicare and Marketscan to evaluate this comparison

Methods: We have used Medicare and Marketscan data available through National Vision and Eye Health Surveillance System (VEHSS). Medicare is funded by government and covers eye services for nearly the entire US population aged 65 years or older and some < 65 years. The MarketScan Commercial Claims and Encounters (CCAE) data has insurance information from persons with employer-sponsored insurance.

VEHSS uses ICD-10 codes to identify ocular disorders. Each code is categorized in one subgroup and multiple subgroups are combined to form a category. Inflammatory and infectious eye disease category includes subgroups of ocular inflammatory conditions, lacrimal system and orbital inflammation, keratitis, conjunctivitis, eyelid inflammation and infection, and endophthalmitis.

Utilization for Medicare and Marketscan is compared for the year 2016. Utilization for the inflammatory and infectious eye disease category is stratified by age and sex for the two databases

Results: There were 30,423,400 million Medicare beneficiaries and 28,717,700 commercial insurance enrollees in 2016. Annual utilization for Medicare was higher 11% (95% CI: 11.00-11.00) as compared to Marketscan 5.22% (95%:5.21-5.23), and differences remained after stratification by age (data shown in Table).

For both Market scan, females 5.90% (95% CI: 5.89-5.91) vs males 4.50% (95% CI: 4.49- 4.51) and Medicare, females, 13.30% (95% CI: 13.30-3.30) vs. Males, 9.40% (95% CI: 9.30- 9.40), females had higher utilization

Conclusions: Medicare beneficiaries have higher utilization as compared to commercial insurance. This remains when data are stratified by age and sex. Our results are consistent with prior studies that indicate higher utilization in general for Medicare.

CONTROL ID: 3707474

SUBMITTER (NAME ONLY): Jun Liu

TITLE: High-frequency ultrasound detects biomechanical weakening in keratoconus with a decreasing stiffness at higher grades

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Liu, S. Kwok, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Liu, A. Hendershot, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|X. Pan, Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio, UNITED STATES|W. Liu, Department of Computer Science and Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: In vivo biomechanical characterization of the cornea remains a challenge. We have developed a high-resolution ultrasound elastography method to measure corneal axial displacement (CAD) induced by the ocular pulse. Here we compared CAD and a stiffness index derived from CAD between keratoconus patients and normal controls. We also explored the trend of these parameters with keratoconus grade.

Methods: Twenty normal controls (40 eyes) and 20 keratoconus patients (35 eyes) were recruited. Each subject underwent three tests: (1) OCULUS Pentacam for corneal topography; (2) PASCAL Dynamic Contour Tonometry for intraocular pressure (IOP) and ocular pulse amplitude (OPA), and (3) ocular pulse elastography (OPE) for CAD using the Vevo2100 ultrasound system. Corneal topography data was reviewed by a specialist (AH) to determine the presence and grade of keratoconus. Four ultrasound measurements were performed in each eye, and each measurement acquired an 8-second video of the cornea during fixation. This data was processed to obtain the average CAD following published protocols [Kwok et al, TVST, 2020; 9(13):33]. Corneal stiffness index was calculated as OPA/CAD for each eye. Linear mixed models for repeated measures were used to account for association between two eyes of the same subject in data analysis.

Results: Mean CAD (unit: μm) was significantly higher (p=0.0088, Fig. 1A) in keratoconus (46.6, 95% CI: 39.2, 53.9) than normal (34.6, 95% CI: 30.1, 39.1). Mean corneal stiffness (unit: mmHg/μm) was significantly lower (p=0.0068, Fig. 1B) in keratoconus (0.0522, 95% CI: 0.0384, 0.066) than normal (0.0804, 95% CI:0.0666, 0.0942). Age and IOP were not different between groups. Overall, mean CAD increased while corneal stiffness decreased at higher keratoconus grade (p=0.002 and 0.011, Fig. 2).

Conclusions: This study confirmed the biomechanical weakening in keratoconus and suggested that this weakening worsened in more severe cases. Ultrasound elastography may provide a quick (minutes) and safe (no applied forces) biomechanical evaluation of the cornea to aid in keratoconus diagnosis.

CONTROL ID: 3707476

SUBMITTER (NAME ONLY): Bogale Aredo

TITLE: Differential response of Muller cells to retinal injury in the fundus camera-delivered light induced retinal degeneration (FCD-LIRD) model

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Aredo, C.X. Zhao, R. Ufret-Vincenty, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|B. Chen, Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Wuhan, Hubei, CHINA|Y. Ding, The Central Hospital of Wuhan, Wuhan, Hubei, CHINA|A. Kumar, C. Xing, McDermott Center for Human Growth and Development, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Information on retinal recovery from oxidative/photo-inflammatory retinal injury is scarce. Retinal light injury models have been used in understanding the various processes involved in retinal degeneration. Our lab developed the FCD-LIRD model and reported evidence of retinal recovery from the original damage caused by intense light. Now using single cell RNA sequencing we performed cell-type specific analyses to identify retinal responses associated with the recovery processes at different time points post light injury.

Methods: C57BL/6J mice (2-4 m) were exposed to FCD-LIRD. Posterior 2mm central retinae were peeled off from eyes collected at 4 h, 48h and 5d after this injury. Unexposed eyes served as controls. Retinal single-cell suspensions were prepared using a Papain Dissociation System and processed using droplet-based single cell RNA-seq (10X Genomics). Sequencing libraries were analyzed using Cell Ranger 3.0.0. Seurat R package (v3.0.0) was used to generate unsupervised cell clusters which were then assigned to specific retinal cell types/sub-types based on expression of known cell-specific gene markers. Differential and specific gene expression patterns, pathway and trajectory analyses were performed.

Results: Twenty-three discrete clusters representing the major retinal cell classes, types and subtypes were identified with a resolution of 0.5 at each time point post retinal injury. Expression patterns of several genes were significantly altered in each cell type at the three time points post light injury. Using IPA analysis, we were able to identify several differentially regulated pathways in several cell types. At 5d post injury, various classes of signaling pathways were differentially upregulated in a Muller cell cluster suggestive of a role in directing retinal recovery from injury.

Conclusions: Differential cell type-specific responses are generated following photo-oxidative/photo-inflammatory retinal injury in the FCD-LIRD model. The differential activation of signaling pathways in Muller cells at 5d post injury may initiate the retinal recovery process suggesting that Muller cells may play important role in cellular recovery earlier than other cell types. Muller cells could be potential targets in a search for therapeutic approaches to maximize retinal recovery from injury.

CONTROL ID: 3707479

SUBMITTER (NAME ONLY): John Moir

TITLE: Racial differences in optical coherence tomography angiography (OCTA) parameters between older non-diabetics

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Moir, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|J. Moir, S.H. Rodriguez, N. Massamba, L. Chun, L.T. Shaw, D. Dao, A. Farooq, K. Nelson, S. Quan, D. Skondra, Department of Ophthalmology and Visual Science, The University of Chicago Medicine, Chicago, Illinois, UNITED STATES|N. Massamba, Department of Ophthalmology, Handicap, and Vision, Pitie Salpetriere Hospital, Sorbonne Universite, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Black populations face higher rates of diabetes (DM) and vision loss from diabetic retinopathy, even after controlling for known risk factors. While we have found differences in OCTA parameters between young healthy black and white subjects, the effect of aging is unknown. The purpose of this prospective cross-sectional study is to use OCTA to determine if there are differences in the chorioretinal capillaries of older black and white non-DM subjects.

Methods: OCTA (Optovue RTVue XR Avanti) was used to image 40 eyes from 27 black non-DM patients (mean age 56.9±14.4y) and 46 eyes from 30 white non-DM patients (mean age 51.7±16.1y). At baseline, there were no significant differences in age (p=.86), gender (p=.17), or image signal strength (p=.45). Subjects had similar baseline systemic comorbidities including hyperlipidemia, heart disease, smoking pack-years, but not hypertension. Built-in software was used to measure vessel density (VD) at the superficial (SCP), middle (MCP), and deep capillary plexuses (DCP); the foveal avascular zone (FAZ) area, perimeter, acircularity index (AI), and FD-300; and the percentage of blood flow area (%BFA) in the choriocapillaris. A mixed-effects regression model, controlling for 2 eyes of the same patient and hypertension, was used to determine the association between race and OCTA parameters.

Results: Within the SCP and MCP, black subjects had lower foveal VD compared to white subjects (15.03±7.54% vs 21.07±8.07%, p=.02) and (28.03± 8.19% vs 35.44±6.51%, p<.001, respectively). No differences were observed at the DCP. Black subjects had a larger FAZ area (.35±.12mm^2 vs .23±.10mm^2, p<.001), FAZ perimeter (2.38±.39mm vs 1.88±.44mm, p<.001) and larger FD-300, a measurement of VD in a 300 µm wide region around the FAZ (51.21±3.76% vs 49.2±3.53%, p=.001). Black subjects had a lower %BFA at the fovea, parafovea, and the 3x3mm area (p=.04, p=.008, p=.006, respectively).

Conclusions: To our knowledge, this is the first report of differences in OCTA parameters between older black and white non-DM adults. Decreased blood flow in the fovea and choriocapillaris, as well as a larger FAZ in older black adults, may contribute to a higher susceptibility to diabetic vascular damage, while highlighting the need for normative databases and racially diverse clinical studies. Further studies are needed to elucidate the role of racial differences in OCTA parameters.

CONTROL ID: 3707483

SUBMITTER (NAME ONLY): Joby Tsai

TITLE: PERG Parameters as Predictors For 3 Different OCT RNFL Circle Scan Diameters, An Electrophysiological Approach

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tsai, A. Tirsi, B. Patel, S.A. Obstbaum, C. Tello, Ophthalmology, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|A. Tirsi, S.A. Obstbaum, C. Tello, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|D. Kacaj, Cornell University, Ithaca, New York, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|S. Tello, Rye High School, Rye, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies have demonstrated that pattern electroretinogram (PERG) has the ability to detect early retinal ganglion cell (RGC) dysfunction 8 years before glaucomatous structural changes are detected on optical coherence tomography (OCT) scans, which uses the standard 3.4mm circumpapillary scan diameter for glaucoma diagnosis. A new Glaucoma Module Premium Edition (GMPE) software offers 3 different retinal nerve fiber layer (RNFL) circle scans (3.5, 4.1, 4.7mm) to improve glaucoma diagnosis. From our previous research, we determined that 3.5mm circle scan diameter and PERG parameters had the highest area under the curve (AUC) diagnostic capabilities. The purpose of this study was to assess the ability of PERG parameters to best predict change in the 3 RNFL circle scan diameters.

Methods: 49 eyes (26 patients) were enrolled in the study at Manhattan Eye, Ear, and Throat Hospital, and tested with Humphrey Visual Field Test (24-2), Diopsys NOVA PERG device, and Spectralis spectral domain OCT. Linear regression models were used to assess the contribution of each PERG parameter (Magnitude [Mag], MagnitudeD [MagD], MagnitudeD/Magnitude Ratio [MagD/Mag Ratio]) to the RNFL global thickness variance in the 3 circle scan diameters. Age and spherical error (SE) were entered in Step 1 and one PERG parameter was entered in Step 2 for each OCT circle scan diameter.

Results: In a 2-step linear regression model (Table 1), where the RNFLT circle scan of 3.5mm diameter was the independent variable and after controlling for age and SE, Mag, MagD, and MagD/Mag ratio significantly explained OCT variance by 16.8%, 17.9%, and 13%, respectively. Similarly, when the 4.1mm RNFLT circle scan was the independent variable, Mag, MagD, and MagD/Mag ratio significantly explained OCT variance by 16.3%, 16.6%, and 11.8%, respectively. Lastly, when the 4.7mm RNFLT circle scan was the independent variable, Mag, MagD, and MagD/Mag ratio significantly explained OCT variance by 13.6%, 13.3%, and 8.9%, respectively.

Conclusions: All 3 PERG parameters significantly predicted variance in all 3 circle scan diameters with the 3.5 and 4.1mm RNFL circle scan diameters being most significant. This is in line with previous studies showing that 3.5 and 4.1mm circles have better diagnostic capability at distinguishing normal from PrG. This could be due to a high association between PERG and the 3.5 and 4.1mm RNFL circle scans.

CONTROL ID: 3707485

SUBMITTER (NAME ONLY): Nazlee Zebardast

TITLE: Deep unsupervised discovery of OCT phenotypes enables genome-wide analyses

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Zebardast, M. Fazli, S. Kazeminasab Hashemabad, T. Elze, A.V. Segrè, M. Wang, J.L. Wiggs, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Sekimitsu, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a complex and heterogenous disease with structural and functional variation that might reflect underlying pathogensis. We aim to discover hidden structural patterns of optical coherence tomography (OCT) derived macular ganglion cell complex (GCC) thickness using unsupervised deep learning (DL) among subjects with high polygenic risk (PRS) for primary open angle glaucoma (POAG). Subsequently we used these endophenotypes to discover novel genomic loci.

Methods: POAG PRS was constructed for UK Biobank subjects with LDpred2 using genome-wide association study (GWAS) summary statistics from largest cross-ancestry meta-analysis. Macular OCTs from participants with highest PRS were segmented using Topcon Advanced Boundary Segmentation algorithm to extract GCC layer thickness. A hybrid unsupervised artificial intelligence method that combines deep convolutional autoencoders, manifold learning, and Gaussian Mixture Model (GMM) clustering grouped semantically similar GCC thickness patterns. Optimal number of clusters was determined using probabilistic model selection method (AIC/BIC). We performed GWAS for each GMM-identified feature dimension using linear mixed models adjusted for age, sex, and principal components of ancestry.

Results: We identified 11 optimal macular GCC patterns using 26806 OCT scans from 13403 UKBB participants in the top half of the POAG PRS (Fig1). Among all patterns, P1, 7 and 8 had the highest proportion of subjects with self-report or ICD-code for glaucoma (6.25%, 6.37%, 6.53%) and IOPcc > 24 mmHg (5.83%, 5.70%, 5.84%) while pattern 9 had most myopic refractive error (SE -0.3 ±2.4 D). GWAS was performed with hard-call genotypes for 424155 variants after quality control filters (Fig2). There was no evidence of unaccounted stratification ($lambda_{GC}$ 1.000 to 1.011). We identified numerous genomic regions associated ($P < 1e^{-05}$) with at least one feature dimension related to neurologic disease and development (P1, gene: KIRREL3; P3, genes: DENND4B, ARHGEF28; C7 ZDHHC7), immune system and autoimmune disease (P7 HIVEP3, P8 MARK1, P10 MUSK), metabolomics/obesity (P11 CFAP77) and ocular development (P10 MAF).

Conclusions: Here we demonstrate that DL can be used to identify hidden OCT patterns which in turn can be used to identify unexpected genetic associations. Future work is needed to ensure these patterns are disease specific and further explore the impact of identified genetic variants.

CONTROL ID: 3707487

SUBMITTER (NAME ONLY): Deena Dahshan

TITLE: Accessibility and cultural inclusivity of online glaucoma-based video content for patient education

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Dahshan, Marshall University Joan C Edwards School of Medicine, Huntington, West Virginia, UNITED STATES|N. Johnson, Duke Medicine, Durham, North Carolina, UNITED STATES|K. Muir, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Deena Dahshan: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Johnson: Commercial Relationship: Code N (No Commercial Relationship) | Kelly Muir: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Online video content for glaucoma patient education requires evaluation for understandability and accessibility. This study describes the ease of access, readability, actionability, and cultural inclusivity of glaucoma-specific patient education videos found on websites commonly recommended by glaucoma specialists.

Methods: A survey of glaucoma specialists at the Duke Eye Center identified commonly recommended patient education websites. Materials with content for medical providers, dedicated to research, or affiliated with private practices were excluded. Videos that were not glaucoma-specific or longer than 15 minutes were also excluded. Videos were evaluated by two independent reviewers using the Patient Education Materials Assessment Tool (PEMAT) for understandability and actionability as well as cultural inclusivity and accessibility measures. Agreement analysis with a kappa coefficient (k) over 0.6 was established with the first five videos and scoring discrepancies were resolved via a third independent reviewer.

Results: From 10 recommended websites, 22 videos from the AAO and Glaucoma Research Foundation websites met criteria for evaluation. The average PEMAT score was 68.77% (SD = 18.34) for understandability and 100% (SD = 0.00) for actionability (k=0.63). The average video length was 114.32 ± 120.46 seconds. Only three videos were available in another language (Spanish). With regards to representation among actors and images, there were 42% male and 58% female individuals. Most actors and images were White individuals (68.9%), followed by Black (22.1%), then Asian (5.7%) and other/ambiguous (3.3%). Of note, most physicians (85%) were portrayed by White males.

Conclusions: Current educational videos, while actionable, have room to improve with regards to understandability of materials. Lack of language accessibility may pose as a barrier to care for non-English speaking patients seeking video resources for glaucoma. Improving cultural representation of actors and images may also improve patient receptiveness. Recognizing the readability, accessibility, and cultural inclusivity of glaucoma-specific patient education video content on commonly recommended websites may guide future recommendations to improve patient care.

CONTROL ID: 3707492

SUBMITTER (NAME ONLY): Pietro De Angeli

TITLE: Effective splicing restoration of a deep-intronic ABCA4 variant in cone photoreceptor precursor cells by CRISPR/Cas9

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Stingl, Centre for Ophthalmology, Universitatsklinikum Tubingen, Tubingen, Baden-Württemberg, GERMANY|P. De Angeli, P. Reuter, B. Wissinger, S. Kohl, Institute for Ophthalmic Research, Universitatsklinikum Tubingen, Tubingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Several deep-intronic variants (DIVs) in ABCA4 have been classified as causative for Stargardt disease. By strengthening a cryptic splice site, ABCA4 DIV c.5197-557G>T determines the retention of an intronic sequence in the mature mRNA, resulting in a premature termination codon. For the first time, we investigated CRISPR/Cas9 genome editing for the potential to correct a splice defect caused by a DIV in ABCA4 - specifically c.5197-557G>T.

Methods: Three CRISPR/Cas9 approaches, implementing Streptococcus pyogenes Cas9 (SpCas9) or SpCas9-nickase were designed: dual gRNA/SpCas9, utilizing two paired gRNAs designed to target regions flanking the c.5197-557G>T DIV, dual gRNA/SpCas9-nickase rescue based on the use of two paired gRNAs coupled to SpCas9-nickase, and (single) gRNA/SpCas9 rescue employing single gRNAs. Minigene splicing assay in HEK293T of the DIV c.5197-557G>T was used for preliminary testing the rescue potential of sixteen strategies. Subsequently, eight most-promising ones were validated in patient-derived heterozygous ABCA4 c.5197-557G>T cone photoreceptor precursor cells (CPCs).

Results: Splicing rescue in the minigene splicing assay ranged from 10±3% to 100±0%. In CPCs, two gRNA combinations each for dual gRNAs/SpCas9, as well as for dual gRNAs/SpCas9-nickase, and four single gRNAs for gRNA/SpCas9 were validated. Due to the partial degradation of the aberrant transcript via nonsense-mediated mRNA decay, CPCs show 28±2% aberrant transcript. The selected strategies reduced the fraction of aberrant transcript up to 5±2%, corresponding to a splicing rescue of 83±5% achieved by a (single) gRNA/SpCas9 strategy. Upon CRISPR/Cas9 treatment, a significant fold increase up to 1.8±0.2 in ABCA4 transcript levels was also detected. Interestingly, when using two paired gRNAs coupled to SpCas9 to target the DIV in CPCs, the level of editing at the ABCA4 target locus quantified 35 days compared to 7 days after treatment revealed a drop in the percentage of edited cells of around 50%, hinting at potential genotoxicity of this design.

Conclusions: In conclusion, we proved CRISPR/Cas9 effective in addressing a splice defects in ABCA4. This study paves the way to the investigation of CRISPR/Cas9 genome editing as a therapeutic tool to correct the several DIVs in the ABCA4 gene, providing initial evidence of possible permanent splicing correction for Stargardt disease.

CONTROL ID: 3707495

SUBMITTER (NAME ONLY): Andrew Taylor

TITLE: The Effects Of Melanocortin Receptor Agonists On Experimental Autoimmune Uveitis

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.W. Taylor, K. Dawit, T. Ng, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Andrew Taylor: Commercial Relationship(s);Code C (Consultant/Contractor):Palatin Technologies;Code F (Financial Support):Palatin Technologies | Kaleb Dawit: Commercial Relationship: Code N (No Commercial Relationship) | Tat Fong Ng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The melanocortin system plays a vital role in regulating immune activity and retinal cell health within the eye. Augmenting the melanocortin system with α-melanocyte stimulating hormone (α-MSH) during uveitis suppresses inflammation, promotes immune tolerance, and protects the retinal structure. To determine which melanocortin-receptors are important in mediating the beneficial effects of α-MSH-therapy, we assayed different α-MSH-analogs with different functional melanocortin-receptor (MC1r, MC3r, MC4r, and MC5r) specificities.

Methods: Experimental autoimmune uveitis (EAU) was induced in C57BL/6J mice, and the retinas were clinically scored by fundus exam. When the mice reached the chronic stage of EAU, they were injected twice one-day apart with 50 µg of α-MSH (pan-agonist), PL8331 (pan-agonist), PL8177 (potent MC1r-only agonist), PL5000 (same as α-MSH but no MC5r functional activity), MT-II (same as PL5000) or PG901 (MC5r agonist, but an antagonist to MC3r, and MC4r). Clinical EAU scoring was continued until EAU resolution in the α-MSH-treated EAU mice. The eyes were then collected for histology, and spleen cells were collected for retinal-antigen-stimulated IL-17 and IL-10 production.

Results: There was significant EAU suppression with significant retinal structure preservation in EAU mice treated with α-MSH and PL8331. A similar effect was seen in PL8177 treated EAU mice, except the suppression of EAU was temporary. In EAU mice treated with PL5000, MTII, or PG901, there was no suppression of EAU with no preservation of the retinal structure, The stimulated spleen T cells produced IL-10 in mice treated with α-MSH, PL8331, PL8177, PL5000, but continued to produce IL-17 in MT-II, and PG901 treated EAU mice.

Conclusions: In this study, we investigated the effects of α-MSH-analogs in suppressing EAU. Our previous studies showed the importance of the melanocortins in the maintenance of ocular immune privilege and that α-MSH-treatment accelerated recovery and induced retinal-antigen-specific regulatory immunity. Our current results demonstrated that α-MSH-analogs targeting MC1r and MC5r together have a therapeutic potential to suppress uveitis and induce regulatory immunity. Moreover, they can maintain normal retinal structure and prevent retinal cell loss.

CONTROL ID: 3707501

SUBMITTER (NAME ONLY): Sarah Atta

TITLE: Clinical Characterization of Culture-Negative Infectious Keratitis

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Atta, K. Samanthapudi, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|P. Chandrashan, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|R.P. Kowalski, S. Nayyar, V. Jhanji, The Charles T. Campbell Ophthalmic Microbiology Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Infectious keratitis is a leading cause of ocular morbidity globally, and approximately one-third of all cases are culture-negative. We sought to better understand these cases by investigating risk factors, clinical manifestations, and treatment outcomes.

Methods: This single-center, retrospective case series included all culture-negative infectious keratitis cases at the UPMC Eye Center from January 2016 through December 2020. Cases were reviewed for suspected etiology, ocular and systemic risk factors, visual acuity, symptom duration, management, and outcomes.

Results: 256 cases of culture-negative infectious keratitis were identified (55.08% female, 50.11±20.34 years). 167 cases had complete medical records. Antimicrobial medication was used by 59.88% patients prior to presentation. Majority of cases were presumed to be viral at presentation (45.70%). The most prevalent ocular risk factors were history of ocular surface disease (44.14%), contact lens use (32.34%), and prior ocular surgery (36.84%). Mean presenting VA was 0.91±0.87 logMAR with average defect size of 7.81±12.53 mm^2 and hypopyon in 12.57% cases. Most common initial management was with topical moxifloxacin (26.95%). Management was modified in the majority of cases with 29.34% switched to antiviral therapy. Adjunctive treatment was required in 45.51% cases. Average time to defect resolution was 46.15±65.10 days. Cases with presumed viral etiology had the longest treatment duration and follow-up time. Cases with presumed bacterial etiology had significantly younger age at presentation (41.39±22.10 years) ($p=0.004$). Worse final visual acuity was significantly associated with older age at presentation ($p<0.001$), history of ocular surgery ($p=0.005$), topical corticosteroid use ($p=0.008$), history of corneal disease ($p=0.023$).

Conclusions: Management of culture-negative keratitis relies on clinical suspicion. Viral etiology is commonly suspected in culture-negative keratitis cases, however younger age is significantly associated with bacterial etiology. There is significant variability in presentation and management duration depending on type of etiology. These cases generally have favorable outcomes with prompt intervention.

CONTROL ID: 3707502

SUBMITTER (NAME ONLY): Mohamed M Khodeiry

TITLE: Early Corneal Endothelial Changes Following Transscleral Cyclophotocoagulation

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Khodeiry, P. Monsalve Diaz, P. Gordon, K. Khine, R.K. Lee, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Mohamed M Khodeiry: Commercial Relationship: Code N (No Commercial Relationship) | Pedro Monsalve Diaz: Commercial Relationship: Code N (No Commercial Relationship) | Phillip Gordon: Commercial Relationship: Code N (No Commercial Relationship) | Kay T Khine: Commercial Relationship: Code N (No Commercial Relationship) | Richard Lee: Commercial Relationship(s);Code F (Financial Support):The Bascom Palmer Eye Institute is supported by NIH Center Core GrantP30EY014801 and a Research to Prevent Blindness Unrestricted Grant. R.K. Lee is supported by the Walter G. Ross Foundation. This work was partly supported by the Camiener Foundation Glaucoma Research Fund and the Gutierrez Family Research Fund.

ABSTRACT BODY:

Purpose: To evaluate the effect of continuous-wave transscleral cyclophotocoagulation (CW-TSCPC) using the slow coagulation parameters on the corneal endothelium in the early postoperative periods.

Methods: A retrospective study of glaucomatous patients who underwent slow coagulation CW-TSCPC (1250 mv power and 4-second duration). The exclusion criteria were previous ocular surgery except for cataract surgery, any corneal disease, the presence of anterior chamber intraocular lens, aphakia, previous ocular inflammation. In addition to intraocular pressure (IOP) measurements, specular microscopy values were obtained using a Konan Noncon Robo Pachy Sp-9000 noncontact-type specular microscope preoperatively, at week 1 (W1), month 1 (M1), and month 3 (M3) after TSCPC. Corneal endothelial cell density (CECD), percent hexagonality, coefficient of variation in cell area (CV), and central corneal thickness (CCT) were assessed in the central corneal area.

Results: The study included 34 eyes of 34 patients. Mean age of the patients was 69.8±11.1 years, 19 (55.9%) patients were females, and 17 (50%) were Hispanic. Primary open angle glaucoma was the most common glaucoma type in 82.4% of the cohort. Twenty-three (67.6%) patients were pseudophakic. Treated patients received 19.1 ± 1.5 laser spots.

After TSCPC, IOP decreased from 19.2±6.5 mmHg at baseline to 13.6±5.2 mmHg at W1 ($p<0.001$), 14.1±3.7 mmHg at M1 ($p<0.001$), and 13.9±5.5 mmHg at M3 ($p<0.001$).

CECD changed from 2517.2±147.1 cell/mm^2 at baseline to 2590.2±151.7 cells/mm^2 at W1, 2443.3±314.3 cell/mm^2 at M1, and 2394.0±560.6 cell/mm^2 at M3 ($p=0.58$, $p= 0.507$, $p=0.882$ respectively). CV values were 38.3±7.4% at baseline, 37.4±6.6% at W1, 53.0±44.9 at M1, and 51.1±40.9 at M3 (all $p>0.05$). No statically significant changes in the percentage of hexagonal cells were noted during the follow up period ($p=0.192$ at W1, $p=0.977$ at M1 and $p=0754$ at M3). CCT changed from 515.9±37.7 µm at baseline to 561.1±56 µm at W1($p=0.006$), 538±48.7µm at M1 ($p=0. 21$) and 532.5±44.8 µm at M3($p=0.356$).

No major complications were reported during the study.

Conclusions: Slow coagulation TSCPC is an efficient and relatively safe procedure with no significant corneal changes noted in patients during the early postoperative period. Studies with longer follow up periods are required for further evaluation of the long-term effect of cyclophotocoagulation treatment on the cornea.

CONTROL ID: 3707503

SUBMITTER (NAME ONLY): Ning Tian

TITLE: Campana cells relay both rod- and cone-mediated visual signals to multiple RGC types

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Tian, B.K. Young, P. Wang, Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|N. Tian, Research, VA healthcare system Salt Lake City, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Ning Tian: Commercial Relationship: Code N (No Commercial Relationship) | Brent Young: Commercial Relationship: Code N (No Commercial Relationship) | Ping Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We recently described a previously not fully characterized interneuron in the mammalian retina, the Campana cells. The Campana cells share some morphological, physiological, and molecular features with retinal bipolar cells and amacrine cells. Thus, we assume that Campana cells may play atypical roles in vision. To further understand the roles of Campana cells in visual signal processing, we determined the types of RGCs which receive synaptic inputs from Campana cells.

Methods: RGCs are divided into functional groups based on the patterns of their light responses, e.g., rod-, cone-mediated, or mixed ON, OFF, and ON-OFF RGCs. The synaptic connections between Campana cells and RGCs are determined by synaptic responses of RGCs to optogenetic stimulation of a single ChR2-expressing Campana cell. The light/synaptic responses of RGCs are recorded using calcium imaging. Comparison of the light responses of RGCs to the synaptic responses from Campana cells evoked by optogenetic stimulation determines the functional types of RGCs which receive synaptic inputs from Campana cells.

Results: We analyzed the light responses of 88 RGCs from 3 retinas, in which 42 RGCs receive synaptic inputs from Campana cells while 46 RGCs do not receive synaptic inputs from Campana cells. From these 88 RGCs, 4 RGCs only receive rod inputs, 29 RGCs only receive cone inputs, and 55 RGCs receive both rod and cone inputs. 61% RGCs receiving rod-mediated signals receive direct synaptic inputs from Campana cells, while 49% RGCs receiving cone-mediated signals receive direct synaptic inputs from Campana cells ($p = 0.149$, chi test). In the 36 RGCs receiving both rod and Campana cell inputs, 78% are ON cells, 14% are OFF cells, and 8% are ON-OFF cells. This is not different from the RGC type proportion without Campana cell inputs ($p = 0.302$). In the 41 RGCs receiving both cone and Campana cell inputs, 32% are ON cells, 12% are OFF cells, and 56% are ON-OFF cells. This is significantly different from the RGC type proportion of RGCs without Campana cell inputs ($p < 0.0001$).

Conclusions: Campana cells relay rod- and cone-mediated visual signals to multiple functional RGC types. In RGCs receiving rod-mediated inputs, the synaptic connection from Campana cells is independent of the functional types of RGCs. In RGCs receiving cone-mediated inputs, Campana cells preferentially relay synaptic input to ON-OFF RGCs.

CONTROL ID: 3707504

SUBMITTER (NAME ONLY): Roshni Kailar

TITLE: Fluid Fluctuations in Early Responders Versus Limited Early Responders to Anti-VEGF Treatment for Macular Edema Secondary To Retinal Vein Occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Kailar, B. Kuo, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|B. Kuo, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|S.W. Perkins, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with Retinal Vein Occlusion (RVO) have differing degrees of response to anti-VEGF treatment. A retrospective comparative study was performed to determine if response to anti-VEGF treatment at 3 months post-initiation of anti-VEGF treatment could predict RVO outcomes, namely Central Subfield Thickness (CST) and Best Visual Acuity (BVA), at the 12-month time point.

Methods: Patients over age 18 with treatment naïve RVO-related macular edema and treated with anti-VEGF injections were included in the study. A machine learning algorithm (Notal Vision Ltd., Tel Aviv, Israel) quantified total retinal fluid (TRF), intraretinal fluid (IRF), and subretinal fluid (SRF). Patients were categorized as early responders (ER) or limited early responders (LER); LER eyes were defined as having CST reduction < 10%, BVA gain < 5 ETDRS letters, or both at 3-months after anti-VEGF initiation. BVA and CST changes over the 12-month period following first anti-VEGF treatment were compared. Statistical analysis involved Levene test, Welch's t-test, and Welch's ANOVA.

Results: 116 eyes met inclusion criteria (74 ER, 42 LER). Baseline VA differed between ER (45.8 letters) and LER (62.9 letters) ($p < 0.0001$). Both 12-month change in BVA and CST varied significantly between early response statuses. Specifically, change in BVA for ER was 21.4 letters and 0.8 letters for LER ($p < 0.0001$), and the change in CST was -187.1 mm for ER and -104.4 mm for LER ($p < 0.05$). VA (+19.9 letters, $p < 0.0001$) and TRF (-613 nl, $p < 0.01$) significantly improved for ER eyes, but only in the initial 3-month period. Changes in VA and fluid compartments were not significant across all other time points and responder categories.

Conclusions: Functional and anatomical improvements at 12-months were more impressive for ER than LER defined at 3 months. Additionally, this study highlights the potential for 3-month TRF reduction as a marker of early response. Most functional and anatomical gains in ER occurred during the initial 3 months of treatment, with no significant improvements in VA or TRF after the first 3 months. Thus, the 3-month response to anti-VEGF treatments may be a useful biomarker to predict the prognosis of eyes with RVO treated with anti-VEGF.

CONTROL ID: 3707505

SUBMITTER (NAME ONLY): CHRISTIANA FOWLKES

TITLE: Factors influencing eye screening adherence among urban Black patients with diabetes: a qualitative study

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. FOWLKES, L. Lock, J. Hoang, Y. Liu, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|O.O. Shiyanbola, Social and Administrative Sciences Division, University of Wisconsin-Madison School of Pharmacy, Madison, Wisconsin, UNITED STATES|N. Jacobson, Institute for Clinical and Translational Research, University of Wisconsin-Madison School of Nursing, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Black adults are twice as likely as non-Hispanic whites to become blind and are 50% more likely to develop diabetic eye disease. As few as 30% of Black adults with diabetes obtain yearly eye screening. Thus, there is an urgent need to increase screening to prevent vision loss. We aimed to identify factors influencing eye screening adherence among Black patients with diabetes at an urban federally qualified health center (FQHC) in Milwaukee, WI.

Methods: We conducted semi-structured individual interviews with 25 participants (14 patients with diabetes who self-identified as Black or African-American and 11 clinical personnel). Both inductive and deductive content analysis was performed. All interviews were transcribed verbatim and analyzed using QSR NVivo software.

Results: Patients had a mean age of 54 years (range: 27-72 years) and 57% were female. Clinical personnel included 3 primary care clinicians, 3 medical staff, and 5 administrators. We developed a model to understand factors influencing eye screening adherence among urban Black patients with diabetes adapted from the Socio-Ecological Model of Health and National Institutes of Minority Health and Disparities Research Framework. Factors were categorized as individual, social, and environmental. Many factors, such as limited access to healthcare and transportation, financial tradeoffs, anxiety about diabetes complications, and the burden of diabetes management, were similar to those from our prior qualitative study in a rural FQHC serving predominantly non-Hispanic white patients with diabetes. However, urban Black patients with diabetes reported many additional factors influencing diabetic eye screening adherence, including mistrust and discomfort with healthcare providers, experiences of racism and discrimination in healthcare settings, intergenerational trauma from healthcare experiences, and housing instability. Patients also emphasized the importance of patient self-advocacy in navigating the health care system to manage their medical conditions.

Conclusions: Urban Black patients with diabetes and clinical personnel reported several factors influencing patient adherence with eye screening. The effectiveness of interventions targeting eye screening disparities among urban Black patients with diabetes may be enhanced by addressing these factors.

CONTROL ID: 3707509

SUBMITTER (NAME ONLY): Yohei Tomita

TITLE: Cytochrome P450 Oxidase 2J Inhibition Suppresses Choroidal Neovascularization

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Tomita, Y. Gong, M. Ko, J. Yang, H. Yagi, Z. Fu, L.E. Smith, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|Y. Tomita, Z. Fu, L.E. Smith, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M.L. Edin, D.C. Zeldin, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, UNITED STATES|Y. Gong, Biological Repositories, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, CHINA|

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ABSTRACT BODY:

Purpose: Choroidal neovascularization (CNV) in age-related macular degeneration (AMD) can cause blindness. Increased dietary intake of ω-3 long-chain polyunsaturated fatty acids (LCPUFAs) reduces CNV. ω-3 LCPUFA metabolites from most metabolic pathways (COX, LOX) are anti-angiogenic, but ω-3 LCPUFA metabolites of cytochrome P450 oxidase (CYP)2J, promote angiogenesis. We hypothesized that inhibition of CYP2J activity would augment the protective effects of ω-3 LCPUFAs on CNV.

Methods: We investigated the effects of the CYP2J inhibitor (Flunarizine) in the laser-induced CNV mouse model. The plasma levels of CYP2J metabolites were determined by liquid chromatography and tandem mass spectroscopy. Mouse choroidal and aortic explant sprouting assays were used to investigate the effects of CYP2J inhibition and CYP2J metabolites on angiogenesis ex vivo.

Results: CNV was increased in Tie2-driven CYP2J2-overexpressing mice, associated with increased plasma epoxide: diol ratio ($n \geq 25$, both genders, $p < 0.001$). Inhibiting CYP2J activity with flunarizine augmented the protective effects of ω-3 LCPUFAs on CNV by 20% ($n \geq 26$, both genders, $p < 0.05$). In Tie2-driven CYP2J2-overexpressing mice fed a ω-3 LCPUFA diet, flunarizine suppressed choroidal neovascularization by 39% ($n \geq 33$, both genders, $p < 0.001$) and reduced the plasma levels of CYP2J2 metabolites. In addition, the combination therapy of Flunaridine and Montelukast (CYP2C inhibitor) enhanced the prevention of CNV. The proangiogenic role of CYP2J2 was corroborated in choroid and aortic sprouting assays. Exposure to the ω-3 LCPUFA CYP2J metabolite, 19,20-epoxydocosapentaenoic acid, reversed the suppression of angiogenesis ex vivo by the CYP2J inhibitor flunarizine.

Conclusions: CYP2J Inhibition augmented the protective effects of ω-3 LCPUFAs on pathological choroidal angiogenesis. Flunarizine suppressed angiogenesis by inhibiting CYP2J activity, and Montelukast enhanced the effect. CYP2 inhibition may be a viable approach to inhibit CNV in AMD.

CONTROL ID: 3707511

SUBMITTER (NAME ONLY): Mishank Jain

TITLE: Characterizing anti-VEGF treatment patterns for neovascular age-related macular degeneration in the United Kingdom

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jain, Western Eye Hospital, London, London, UNITED KINGDOM|R. Cantrell, Genentech Inc, South San Francisco, California, UNITED STATES|J.D. Chidambaram, D. Judge, Roche Products Ltd, Welwyn Garden City, Hertfordshire, UNITED KINGDOM|M. Dodds, S. McGrory, Medisoft Limited, Leeds, UNITED KINGDOM|C. Bailey, Bristol Eye Hospital, Bristol, Bristol, UNITED KINGDOM|

Commercial Relationships Disclosure: Mishank Jain: Commercial Relationship(s);Code C (Consultant/Contractor):Roche | Ronald Cantrell: Commercial Relationship(s);Code E (Employment):Genentech, Inc.;Code I (Personal Financial Interest):Roche | Jaya Chidambaram: Commercial Relationship(s);Code E (Employment):Roche | Davneet Judge: Commercial Relationship(s);Code E (Employment):Roche | Melanie Dodds: Commercial Relationship(s);Code E (Employment):Medisoft Limited | Sarah McGrory: Commercial Relationship(s);Code E (Employment):Medisoft Limited | Clare Bailey: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis, Bayer, Roche, Alimera Sciences, Janssen, Boehringer Ingelheim

ABSTRACT BODY:

Purpose: Anti–vascular endothelial growth factor (VEGF) treatments for neovascular age-related macular degeneration (nAMD), the leading cause of blindness and visual impairment in the United Kingdom (UK), require frequent intravitreal injections and monitoring. These can pose a substantial burden to patients, caregivers, and health care professionals. This study of routine clinical practice characterized long-term anti-VEGF treatment patterns for nAMD in the UK.

Methods: This was a retrospective analysis of a multicenter electronic medical record (EMR) database that contains data from 9 UK National Health Service ophthalmology sites. A deidentified dataset was constructed from anonymized Medisoft EMR of patients with initial nAMD diagnosis in ≥ 1 eye between January 1, 2014, and December 31, 2018, ≥ 1 anti-VEGF injection (ranibizumab, aflibercept, or bevacizumab), and ≥ 12 months of follow-up. Results are reported by anti-VEGF agent initiated; patients were able to switch anti-VEGF agents.

Results: A cohort of 10,971 patients was analyzed (aflibercept, n = 4908; ranibizumab, n = 5699; bevacizumab, n = 364 [not reported]). In year 1, for patients initiating either aflibercept or ranibizumab, the mean (SD) interval between consecutive injections was 48.4 (21.8) and 46.8 (26.4) days, respectively, and the mean (SD) number of treatment visits was 7.3 (2.5) and 6.4 (2.8), respectively. For aflibercept, the mean (SD; n) treatment interval was 59.0 (27.4; 3523) days in year 2 and 56.6 (26.5; 1812), 55.2 (26.2; 899), and 52.3 (24.6; 409) days in years 3−5, respectively. For ranibizumab, these were 59.9 (29.5; 3128) days in year 2, and 58.7 (27.6; 1791), 58.6 (26.9; 1032), and 56.6 (26.4; 530) days in years 3−5, respectively. The mean (SD) number of treatment visits was also similar for years 2−5 (aflibercept: 5.3 [3.1], 5.5 [3.4], 5.7 [3.5], 5.7 [3.7]); ranibizumab: 5.3 [2.9], 5.5 [2.9], 5.2 [2.9], 4.9 [2.9]) for patients with available data.

Conclusions: Overall, treatment patterns were consistent throughout the follow-up period and data from years 2−5 suggest that patients initiating ranibizumab or aflibercept maintained relatively stable treatment intervals, receiving anti-VEGF injections approximately every 8 weeks.

CONTROL ID: 3707514

SUBMITTER (NAME ONLY): Jason Xiao

TITLE: High-fat diet modulates the retinal pigment epithelium and choroid transcriptome in the absence of gut microbiota

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Xie, M. D'Souza, Center for Research Informatics, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|D. Dao, H.A. Barba, D. Skondra, Department of Ophthalmology and Visual Science, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|J. Xiao, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|A. Movahedan, Department of Ophthalmology and Visual Science, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|E. Chang, Department of Medicine, Microbiome Medicine Program, Knapp Center for Biomedical Discovery, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|B. Xie, D. Sulakhe, Department of Medicine, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|B. Theriault, Department of Surgery, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|M. Spedale, Animal Resources Center, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diet and the gut microbiome are implicated in age-related macular degeneration (AMD). Our team has shown that high-fat diets (HFDs) induce gut dysbiosis, exacerbate laser-induced choroidal neovascularization, and alter retinal transcription in the absence of microbiome. However, the diet-microbiome-transcriptome associations within the choroid/retinal pigment epithelium (RPE) remain unknown. Here, we study how HFDs alter choroid/RPE gene expression and related biological pathways in the absence of microbiome using germ-free (GF) mice.

Methods: RNA was extracted from choroid/RPE tissue (4 mice/group) of 15-weeks old GF C57BL/6J male mice fed normal diet or HFD (23% saturated fat for 8 weeks). RNA was sequenced via paired-end method on NovaSeq6000. Differentially expressed genes (DEGs) were identified (adjusted p-value <0.05) and incorporated in functional enrichment analysis using Toppgene (FDR BH <0.05, logFC >1.5).

Results: After correction of raw data, 1044 DEGs were identified from 24,784 genes. In the GF-HFD cohort, 912 DEGs were upregulated and 132 were downregulated. HFD affected genes involved in inflammation, angiogenesis, immunity, and extracellular matrix (ECM) interactions in the RPE/choroid according to Gene Ontology enrichment. HFD increased expression of Vegfc, Angpt1, Angpt2, Pdgfc, and Pdgfd, which function in concert to regulate angiogenesis and vascular remodeling, and are active targets in clinical trials of AMD. In addition, HFD affected inflammatory and immune-related genes. Some of the most significant DEGs clustered around natural killer T (NKT) cells, including NKT receptors (Cd244a), binding partners (Cd48), cytotoxic effectors (Gzma and Prf1), activators (Cxcl10), and growth factors (IL12b). HFD also upregulated C1qb, C2, C4b, and Cfh of the complement cascade. Finally, ECM components, including collagens Col8a1 and Col10a1, as well as enzymes such as Adamts9, were impacted, all of which correlate with AMD.

Conclusions: This study provides novel data that HFDs alter choroid/RPE biology at the transcriptional level in the absence of gut microbiota. We use the framework of AMD pathogenesis to highlight significant differences in gene expression and pathways, including angiogenesis, inflammation, complement cascade, and ECM interactions. Further studies will help delineate the complex relationships between diet, gut microbiota, and AMD pathobiology.

CONTROL ID: 3707515
SUBMITTER (NAME ONLY): Ellen Shorter
TITLE: Indication for Scleral Lens Wear and Fogging in Established Wearers
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Shorter, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|E. Shorter, Optometry, Jesse Brown VA Chicago Health Care System, Chicago, Illinois, UNITED STATES|J. Fogt, K. Patton, The Ohio State University, Columbus, Ohio, UNITED STATES|M. Schornack, C.B. Nau, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|A.C. Nau, Korb and Associates, Boston, Massachusetts, UNITED STATES|J. Harthan, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|
Commercial Relationships Disclosure: Ellen Shorter: Commercial Relationship(s);Code F (Financial Support):Johnson & Johnson, BostonSight, Contamac, Art Optical, SynergEyes | Jennifer Fogt: Commercial Relationship(s);Code F (Financial Support):Nevakar, EyeNovia, Alcon, Innovega, Contamac;Code C (Consultant/Contractor):Alcon and Contamac | Muriel Schornack: Commercial Relationship: Code N (No Commercial Relationship) | Amy Nau: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Harthan: Commercial Relationship(s);Code F (Financial Support):Bausch and Lomb, Kala Pharmaceuticals, Ocular Therapeutix, Metro Optics;Code C (Consultant/Contractor):Allergan, Essilor, Euclid Systems, International Keratoconus Academy, Metro Optics, SynergEyes, Visioneering Technologies, Inc. | Kimberly Patton: Commercial Relationship: Code N (No Commercial Relationship) | Cherie Nau: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Scleral lenses (SLs) are fit to support the ocular surface in patients with dry eye disease as well as to improve vision in patients with irregular corneal astigmatism or refractive error. Individuals wearing SLs may complain of lens fogging requiring SL removal and reapplication throughout the day.

The purpose of this study was to report indication(s) for SL wear, subjective fogging, mid-day SL removal and reapplication, and clinician observed findings of front surface non-wetting and presence of posterior fluid reservoir (FR) debris.

Methods: Patients who had worn their current SLs for a minimum of 6 months were recruited from 5 sites. After obtaining informed consent, data was collected on patient demographics, indication for SL wear, subjective complaint of fogging, and if SLs were removed and reapplied mid-day. In addition, clinicians recorded the presence or absence of front surface non-wetting, mucus debris, particulate debris, and posterior FR haze.

Results: There were 30 patients enrolled with the following indications for SL wear: corneal irregularity (63.3%), dry eye disease (23.3%), refractive error (10%), and other (3.3%). Slightly more than half complained of lens fogging (56.7%) with 60% reporting removing and reapplying their lenses mid-day.

Of those with subjective fogging 94.1% reported routinely removing and reapplying lenses mid-day compared to only 15.4% of those without fogging complaints.

Clinicians observed SL front surface non-wetting in 34.5% (10/29 eyes) of patients with fogging complaints and only 4.2% (1/24 eyes) of those without.

Particulate debris was noted in 58.6% (17/29 eyes) of those with subjective fogging and 25% (6/24 eyes) of those without which was observed more frequently than mucus debris (10/29 foggers vs 1/24 non fogger eyes) and haze (10/29 fogger vs 0/24 non fogger eyes).

Conclusions: In this series of established SL wearers, most patients with subjective fogging routinely remove and reapply their lenses mid-day. Symptoms described as “fogging” may arise from either front surface non-wetting or post-lens FR debris.

CONTROL ID: 3707516

SUBMITTER (NAME ONLY): Valery Shestopalov

TITLE: Inflammasome facilitates ganglion cell dysfunction and loss in ocular hypertension glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Shestopalov, M. Spurlock, W. An, G. Reshetnikova, T. Chou, G.S. Solis, M. Braha, G. Dvoriantchikova, V. Porciatti, Bascom Palmer Eye Institute, Dept. Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|V. Shestopalov, Cell Biology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Spurlock, Neurology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|A. Pronin, Molecular and Cellular Pharmacology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine molecular pathways facilitating retinal ganglion cell (RGC) dysfunction and death in response to ocular hypertension (OHT)-induced stress. In this study, we sought to establish the contribution of the inflammasome to RGC pathology in a mouse model of OHT-induced glaucoma.

Methods: Glaucomatous degeneration was induced by intracameral injection of the Ad5-MYOC vector that produced a chronic IOP elevation. Inflammasome activation was detected by IL-1β production, changes in casp1, pycard (ASC), nlrp1, and gsdmD gene expression, and protein accumulation using RT-PCR, Western blot, and immunohistochemistry. Wild type and knockout mouse strains were used to determine the role of the inflammasome in ocular hypertension glaucoma. IL-1β cytokine production was assessed by sandwich ELISA in the vitreous fluid; gene expression changes in the retina, by RT-PCR. Changes in RGC functionality were assessed by PERG recordings; RGC loss was assessed at 8 wks post-OHT induction by direct counts in retinal flat mounts.

Results: Activation of the inflammasome became evident in the inner retinal layer and co-localized with $RPBMS^{+}$ RGCs in C57Bl6 (WT) mice at 2-4 wks after glaucoma induction. This correlated in time with RGC dysfunction, where PERG amplitude was reduced 55.8% in WT eyes with chronic OHT glaucoma. RGC density analysis in these animals showed a loss of 32.3±9.2 % in the central and 28.4±9.2 % in the peripheral retina at 6 wks post-OHT-induction. In contrast, mice are deficient in key inflammasome complex proteins NLRP1, Casp1 and GsdmD did not produce statistically significant changes in PERG amplitude. RGC loss was also blocked, averaging 0.7±11.2% increase in the central and no change in the peripheral retina of $NLRP1^{-/-}$ eyes; 7.3± 9.2% decrease in the central and 1.3 ±19.5 % increase in the peripheral retina of $Casp1^{-/-}$ eyes. Immunohistochemistry data in retinal cross-sections showed the absence of Casp1 and a reduction in GsdmD immunolabeling labeling in RGCs in the knockout retinas with induced glaucoma.

Conclusions: Our results show a strong correlation between the elevation of IOP, induction of inflammasome, and RGC pathology in the retina. Our results in mice deficient for inflammasome pathway components revealed the key role of the inflammasome in driving RGC dysfunction and cell death. Drugs inhibitors of inflammasome could protect vision loss in human ocular hypertension glaucoma

CONTROL ID: 3707520

SUBMITTER (NAME ONLY): Sarah Byun

TITLE: Lens thickness in congenital and childhood cataracts: A case control study

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Byun, A. Dolgetta, University of Maryland Baltimore, Baltimore, Maryland, UNITED STATES|M.M. Manrique, I. Dortonne, C. Martinez, M. Bazemore, M. Jaafar, W. Madigan, Children's National Hospital, Washington, District of Columbia, UNITED STATES|M.R. Levin, J.L. Alexander, Ophthalmology and Visual Sciences, University of Maryland Baltimore, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Sarah Byun: Commercial Relationship: Code N (No Commercial Relationship) | Alexandra Dolgetta: Commercial Relationship: Code N (No Commercial Relationship) | Moran Levin: Commercial Relationship: Code N (No Commercial Relationship) | Monica Manrique: Commercial Relationship: Code N (No Commercial Relationship) | Isabelle Dortonne: Commercial Relationship: Code N (No Commercial Relationship) | Camilo Martinez: Commercial Relationship: Code N (No Commercial Relationship) | Marlet Bazemore: Commercial Relationship: Code N (No Commercial Relationship) | Mohamad Jaafar: Commercial Relationship: Code N (No Commercial Relationship) | William Madigan: Commercial Relationship: Code N (No Commercial Relationship) | Janet Alexander: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Childhood cataract is defined as a lens opacity resulting in reduced visual acuity observed in the early years of life. As the most common cause of preventable pediatric vision loss worldwide, early diagnosis is key to achieve good visual function. Literature suggests congenital cataract is associated with altered lens structure, but no quantitative baseline has been established for the difference in lens structure in pediatric cataract versus control eyes. We tested the hypothesis that cataract eyes in children 0-5 years old will have significantly thinner lens thickness compared to age-matched healthy/control eyes by performing a prospective observational case control study.

Methods: 63 subjects, 109 eyes (34 subjects, 53 eyes with cataracts and 40 subjects, 56 eyes as controls) were recruited prospectively at 0-5 years old and imaged using ultrasound biomicroscopy (UBM). Lens thickness was measured using ImageJ and UBM software. Inter-observer agreement of lens measurement techniques was determined by calculating intraclass correlation (ICC) and assessing a Bland-Altman plot. Welch's two-sample two-tailed t-test was used for statistical analysis of lens thickness between groups.

Results: Agreement analysis showed excellent reliability between image measurement tools (ICC = 0.986) and between observers (ICC = 0.989). Cataract eyes had significantly thinner lens (3.17 ± 0.63mm) than control eyes (3.55 ± 0.17mm, p = 0.0008). Stratifying for laterality or prematurity did not yield significant difference in lens thickness within cataract or control groups. Children 0-5 years old with cataracts were 2.9 times more likely to have a lens thickness less than 3.5mm, increasing to 6.6 times if under 7 months of age. Laterality of cataract did not affect odds of having a lens thickness less than 3.5mm. When controlling for age and compensating for correlation between eyes from the same patient, the odds of having cataract decreased by 2.66 for every 1mm increase in lens thickness.

Conclusions: Lens thickness can be measured repeatably and reliably from UBM images in a pediatric population. Cataract eyes in children 0-5 years old have significantly thinner lenses than age-matched control eyes.

CONTROL ID: 3707521

SUBMITTER (NAME ONLY): Judit Horvath

TITLE: Drug release kinetics of the Port Delivery System with ranibizumab (PDS): platform technology for continuous retinal drug delivery

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Horvath, K. Maass, A. Hieb, S. Ranade, Genentech Inc, South San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Judit Horvath: Commercial Relationship(s);Code E (Employment):Genentech, Inc. | Katie Maass: Commercial Relationship(s);Code E (Employment):Genentech, Inc. | Aaron Hieb: Commercial Relationship(s);Code E (Employment):Genentech, Inc. | Shrirang Ranade: Commercial Relationship(s);Code E (Employment):Genentech, Inc.

ABSTRACT BODY:

Purpose: The PDS is an FDA-approved drug delivery system designed for continuous delivery of a customized formulation of ranibizumab into the vitreous. The drug is contained within the implant reservoir and released through the porous release control element (RCE) via passive diffusion. In vitro testing was performed to verify modeled drug release kinetics of the PDS implant; effects of varying drug and implant parameters are reported.

Methods: Release rate profiles from the PDS implant were determined by implant loading (drug concentration, implant volume) and device half-life (dependent on RCE porosity and dimensions, drug diffusion coefficient, and implant volume). Drug-filled implants were regularly transferred to new buffer-containing vials to mimic ocular drug clearance and sustain similar release kinetics. A concentration assay (UV-Vis/Bradford) was used to measure released drug concentrations. Release rate data were fit using an exponential model to mimic the expected release kinetics of diffusion and were compared with predicted release rate kinetics.

Results: PDS release rates decreased over time. Changing initial ranibizumab concentration from 10 mg/mL to 150 mg/mL increased starting drug release rates from 1.75 to 25.2 µg/day, with observed ranibizumab release closely following model predictions over a 6-month period.

The PDS implant volume is currently fixed at ~20 µL; however, a range of implant volumes from 10–100 µL have been evaluated. In model predictions for ranibizumab 100 mg/mL, starting drug release is consistent at 13.9–14.5 µg/day across varying implant volumes, with drug release at 6 months ranging from 1 µg/day (10-µL implant) to 11 µg/day (100-µL implant).

The PDS implant is optimized for ranibizumab release, with an RCE release rate index (RRI) of 0.024 mm. Alteration of RCE pore size or drug diffusion coefficient has a significant effect on implant half-life. Decreasing RRI from 0.024 to 0.008 mm increased implant half-life from 14 to 42 weeks in experimental studies with ranibizumab 100 mg/mL.

Conclusions: Drug release from the PDS implant was demonstrated to be highly predictable and tunable based on a simple diffusion model. The Port Delivery System offers a flexible platform technology, with the ability to tailor implant release kinetics by careful selection of the drug molecule, drug concentration, and specific implant parameters.

CONTROL ID: 3707531

SUBMITTER (NAME ONLY): Mohammad Sharifian Gh.

TITLE: Passage of human basal tears over immobilized lacritin bactericidal peptide N-104 captures ten antimicrobial tear proteins among fifty-eight

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sharifian Gh., F. Norouzi, G.W. Laurie, Cell Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|M.G. Odrich, G.W. Laurie, Ophthalmology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Mohammad Sharifian Gh.: Commercial Relationship: Code N (No Commercial Relationship) | Fatemeh Norouzi: Commercial Relationship: Code N (No Commercial Relationship) | Marc Odrich: Commercial Relationship(s);Code I (Personal Financial Interest):TearSolutions, Inc. ;Code S (non-remunerative):TearSolutions, Inc. ;Code P (Patent):UVA Licensing and Ventures Group | Gordon Laurie: Commercial Relationship(s);Code F (Financial Support):TearSolutions, Inc. ;Code I (Personal Financial Interest):TearSolutions, Inc. ;Code O (Owner):TearSolutions, Inc. ;Code S (non-remunerative):TearSolutions, Inc. ;Code P (Patent):UVA Licensing and Ventures Group

ABSTRACT BODY:

Purpose: Lacritin non-lytic peptides comprising the protease-released 'N-104' domain are a primary source of natural basal tear bactericidal activity that target Gram-negative inner-membrane proteins FeoB and SpuG (PotH) - in part via the outer-membrane lipoprotein YaiW. While N-104 is highly potent (MIC < 2 μM) against ocular surface pathogen P. aeruginosa (PA14), its efficacy is significantly reduced at physiological conditions - as per many cationic antimicrobial peptides. Here, we searched for peptides or proteins in human normal basal tears that might ligate N-104 thereby synergistically enhancing its bactericidal efficacy.

Methods: Normal human basal tears from 0.5% proparacaine-anesthetized eyes were collected onto Schirmer strips for 5 min. Schirmer strips with ≥ 12 mm of wicked tears were eluted in PBS at 4°C for a pooled tear equivalent of 100 mm, and diluted 5-fold in PBS containing protease inhibitor cocktails (cOmplete Mini, 11836153001). Tears were precleared for 5 hours while rocking at 4°C with 100 μl of Pierce™ Control Agarose beads, and then were added in equal amounts to SulfoLink® immobilized Cys-N-104 or to negative control Cys-C-95 beads (each 100 μl) for overnight incubation at 4°C. C-95 is the inactive N-terminus of lacritin. After collection of flow-through, beads were washed with 100 bead volumes of PBS, eluted via a step gradient of 0.3, 0.5 and 1.0 M KCl for SDS-PAGE/silver staining, and then subjected to MS/MS focusing on the 0.5 M KCl eluate. Mass spectra were analyzed using the Sequest against UniProt Human.

Results: Captured by N-104 and absent from C-95 beads were fifty-eight different proteins above a threshold. Threshold of ≥ 0.24% was defined based on a histogram of the percentage over total values of each hit in the N-104 column. Nine are reported to be antimicrobial including: PIGR, F2, GSN, DMBT1, CST4, IGKC, PRR4, SCGB2A1, and LYZ. Also detected was IGLC2 that although also on C95 beads was 2.6x enriched on N-104.

Conclusions: N-104 appears to target numerous antimicrobial proteins/peptides in normal basal tears under physiological conditions. Whether the relationship might be functionally synergistic has yet to be determined. Given that N-104 is non-lytic, potential synergism may occur via enhancement of N-104’s electrostatic interaction with the bacterial surface and/or with YaiW.

CONTROL ID: 3707536

SUBMITTER (NAME ONLY): CHI SUN

TITLE: Phenotypic characterization of murine models with CRX homeodomain mutations

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. SUN, Y. Zheng, S. Chen, Ophthalmology and Visual Sciences, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: CHI SUN: Commercial Relationship: Code N (No Commercial Relationship) | Yiqiao Zheng: Commercial Relationship: Code N (No Commercial Relationship) | Shiming Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: CRX is a transcription factor (TF) essential for photoreceptor functional development and maintenance with an important role in the terminal differentiation of photoreceptors. Missense mutations in CRX homeodomain (HD) are linked to variable human retinopathies. We previously reported a murine model carrying the loss-of-function mutation p.R90W that causes recessive Leber Congenital amaurosis (LCA). This study aims to characterize the retinal phenotypes of new murine models for distinct dominant CRX HD mutations, p.E80A and p.K88N.

Methods: Knockin models were generated by introducing E80A or K88N mutations into the Crx locus. Hematoxylin and eosin (H&E) staining of retinal cross-sections revealed morphological defects at various postnatal (P) ages. Immunostaining of cell-type specific markers reported altered localization and relative abundance of affected cell types. Electroretinography (ERG) detected deficits in visual functions. Quantitative PCR (qPCR) determined differential gene expression of CRX-target genes and photoreceptor-specific TFs.

Results: New models showed retinal morphologies different from those found in published animal models. Irregular whorls and rosettes were detected within the outer nuclear layer of all E80A and K88N mutants at P14, worse in homozygotes than in heterozygotes. This phenotypic abnormality appeared within the window of photoreceptor differentiation and the severity progressed over the time of photoreceptor development. At P30, homozygotes of both mutations failed to develop rod outer segments and differentiated cones, thus showing null ERG responses. K88N heterozygotes also showed null ERG responses. E80A heterozygotes had shorter rod outer segments and few detectable cones, resulting in significantly decreased A- and B-wave amplitudes in rod ERG responses and undetectable cone responses. Gene expression analysis at P21 found that overall Crx levels in E80A and K88N mutants were comparable to that in wildtype control, but the expression of CRX-dependent phototransduction components were downregulated.

Conclusions: The murine models of E80A and K88N mutations display dominant Cone-rod dystrophy and LCA-like phenotypes respectively, which match corresponding clinical features in human patients. These models help to understand the underlying cellular and molecular mechanisms of dominant CRX HD mutations, informing treatment windows and strategy designs.

CONTROL ID: 3707537

SUBMITTER (NAME ONLY): Enny Oyeniran

TITLE: Treatment Outcomes of Anti-VEGF Agents for Non-Infectious Uveitic Macula Edema

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Oyeniran, S. Bhandari, H. Sen, S. Kodati, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Enny Oyeniran: Commercial Relationship: Code N (No Commercial Relationship) | Sanjeeb Bhandari: Commercial Relationship: Code N (No Commercial Relationship) | H Nida Sen: Commercial Relationship(s);Code E (Employment):Janssen | Shilpa Kodati: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the outcomes of intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections for macula edema secondary to non-infectious uveitis.

Methods: The records of patients that received anti-VEGF injections for uveitic macula edema from January 2017 to August 2021, allowing for at least 180 days of follow-up, were reviewed. Excluded were eyes with a history of infectious uveitis and macula edema secondary to non-uveitic conditions. The primary outcomes were mean change in visual acuity (VA) and central subfield thickness (CST) over 6 months [and 12 months if available] from the start of anti-VEGF treatment. Secondary outcomes were the proportion of eyes that required additional local therapy (including periocular/intraocular steroid injections) or escalation in systemic treatment (including oral steroids or immunomodulatory therapy).

Results: A total of 16 eyes (of 12 patients) met the inclusion criteria. Of these, 63% had panuveitis, 6% posterior uveitis, and 31% intermediate uveitis. Three-fourths of eyes (75%) starting anti-VEGF treatment had a history of elevated intraocular pressure secondary to a steroid response. Aflibercept was the most frequently injected anti-VEGF agent (in 88% of eyes) and the remaining received bevacizumab injections (12% of eyes). The mean VA gain at 6 months was 3.2 letters from a mean VA of 62.3 letters at baseline while mean CST improved by 101 µm from 445 µm at baseline. Three-quarters of eyes (75%) demonstrated a reduction in CST after their initial injection. Fourteen eyes had a 12 month visit from the start of treatment. The mean VA at 12 months remained similar to their baseline while the CST improved by a mean of 83 µm. Eyes received a median of 4 injections from 11 visits over 12 months. Only 1 eye required the addition of a dexamethasone implant in 6 months, with an additional eye requiring it over 12 months. One-tenth of eyes (10%) required an escalation in systemic treatment over 6 months [5% of eyes over 12 months]. IOP remained relatively stable (with a mean change of 0.4mm Hg over 6 months and -3.7 mm Hg over 12 months).

Conclusions: Eyes with non-infectious uveitic macula edema, particularly those intolerant to local steroid injections, may benefit from anti-VEGF injections. Larger studies on the long-term outcomes of VEGF inhibition may establish their role in preventing vision loss in patients with uveitic macular edema.

CONTROL ID: 3707539

SUBMITTER (NAME ONLY): Kimberley Yu

TITLE: Characterization of dry eye subtypes and their omega-3 treatment response in the Dry Eye Assessment and Management (DREAM) Study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Yu, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|P.A. Asbell, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|R.M. Shtein, Ophthalmology, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|G. Ying, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) represents a heterogeneous group of conditions with tear film instability and ocular surface irritation. While DED is traditionally classified as aqueous tear deficient vs evaporative, the full spectrum of DED subtypes is poorly characterized. Different etiological subtypes are hypothesized to respond to treatments differently. The DREAM study was a large multi-center randomized clinical trial that did not find omega-3 to be more effective than placebo in treating a broad spectrum of patients with symptomatic DED. We performed secondary analysis of the DREAM data to characterize DED subtypes and their response to omega-3.

Methods: 535 patients with moderate-to-severe DED were 2:1 randomized to receive omega-3 or placebo over one year. We used latent profile analysis to identify subtypes based on baseline DED symptoms, measured via the Ocular Surface Disease Index (OSDI), and 5 DED signs: tear break-up time (TBUT), anesthetized Schirmer's test, corneal staining, conjunctival staining, and meibomian gland dysfunction (MGD). We evaluated the effect of omega-3 on symptom improvement for each subtype using generalized linear regression with false discovery rate (FDR)-adjustment for multiple comparisons.

Results: We identified 5 DED subtypes considered clinically meaningful by dry eye experts (Table 1, Figure 1). Sex ($p<.001$) and race ($p=0.02$) differed significantly among subtypes. Class 1, characterized by the most severe DED signs yet relatively milder symptoms, was significantly associated with a higher proportion of Sjögren's syndrome patients (21%, $p<.001$). Class 5, characterized by severe MGD and TBUT, was significantly associated with rosacea (29%, $p=0.04$). For Class 1 only, the mean OSDI change over one year was greater in patients receiving omega-3 (n=60, -12.2±1.9) than placebo (n=29, -5.3±1.7) (95% CI for difference: [-11.9, -1.9], FDR-adjusted $p=0.03$). However, this was not significant after adjustment for baseline OSDI (-11.3±1.7 vs -7.1±1.9, 95% CI: [-9.2, 0.8], FDR-adjusted $p=0.54$).

Conclusions: Five clinically meaningful DED subtypes identified in the DREAM study differed significantly in demographics, symptoms, signs, and systemic disease associations. Understanding DED subtypes can improve DED classification and targeted management. We did not find omega-3 to be significantly beneficial for the five DED subtypes.

CONTROL ID: 3707544

SUBMITTER (NAME ONLY): Peter Nesper

TITLE: Perfusion Deficits in Diabetes Mellitus without Diabetic Retinopathy Localize to the Perivenular Deep Capillaries in Averaged OCT Angiography

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.L. Nesper, G.O. Bou Ghanem, A.A. Fawzi, Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: We used geometric perfusion deficit (GPD) analysis in OCT angiography (OCTA) to test the hypothesis that early nonperfusion in patients with diabetes mellitus (DM) without diabetic retinopathy (DR) localizes to the deep capillaries near larger vessels.

Methods: After averaging multiple OCTA scans (average 6.7 ± 1.0 scans), we used a semi-automated method to measure GPD, defined as the retinal area located further than 30 μm from the nearest blood vessel, and compared healthy subjects to patients with DM without DR. In the superficial capillary plexus (SCP), deep (DCP) and full retina, we analyzed percent area of GPD in the whole scan as well as in the 100 μm area around arterioles (periarteriolar space), the 100 μm area around venules (perivenular space) and in the area greater than 100 μm from the nearest arteriole or venule (capillary space).

Results: Our initial analysis included 11 eyes of 11 healthy subjects (6 females; age 39.9 ± 11.7 years) and 11 eyes of 11 patients with DM without clinical DR (7 females; age 46.9 ± 16.0 years). The GPD in the DCP was significantly greater in patients with DM without DR compared to healthy subjects (4.0% ± 1.1% versus 3.2% ± 0.8%, respectively; p=0.030), but not in the SCP or full retina (p=0.371 and p=0.094, respectively). Perivenular GPD in the DCP showed the greatest difference (3.0% ± 1.1% in DM versus 2.2% ± 0.7% in healthy; p=0.028), while the periarteriolar and capillary spaces showed no significant difference (p=0.073 and p=0.151, respectively).

Conclusions: We found that perfusion deficits were increased most prominently in the deep capillaries near venules in patients with DM without clinical DR compared to healthy controls. This study suggests that in the macula, early capillary dysfunction in diabetes may preferentially occur in the perivenular compartment of deep capillary plexus.

CONTROL ID: 3707545

SUBMITTER (NAME ONLY): Gareth Leung

TITLE: Diabetes-specific health literacy is associated with increased adherence to diabetic eye examinations in older adults.

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Leung, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|C. Cai, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Gareth Leung: Commercial Relationship: Code N (No Commercial Relationship) | Cindy Cai: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Adherence to recommended annual or biennial diabetic eye exams can prevent vision loss from diabetes. Successful diabetes management including eye care involves a high degree of health literacy and diabetes-specific knowledge. Diabetes-specific health literacy is likely particularly important among older adults who must simultaneously manage other chronic diseases. This study evaluates the role of diabetes-specific health literacy in adherence to diabetic eye exams in a nationally representative sample of older American adults.

Methods: Respondents with self-reported type 2 diabetes mellitus from the Health and Retirement Study (HRS) 2003 Diabetes Study and HRS 2002 Core survey were included. The main outcome was having an eye exam within the past year. The secondary outcome for sensitivity analysis was having an exam within the past two years. The main explanatory variable was diabetes-specific health literacy, an index based on how well respondents understood a series of 10 diabetes care regimen items (e.g., taking insulin, reading nutrition labels). Poisson regression models with robust sandwich variance estimator were constructed to estimate the risk ratio (RR) of diabetes-specific health literacy on adherence to diabetic eye exams, adjusted for age, gender, race and ethnicity, education status, household income, baseline eyesight, and the total illness burden index. Chi-squared tests and Wilcoxon rank sum tests were used to compare groups. All analyses incorporated HRS survey weights.

Results: The analysis included 2060 respondents. Those who had an eye exam within the past year had a higher diabetes-specific health literacy index (mean 3.40 [range 3.00, 3.90] vs. 3.10 [2.80, 3.60], $p<0.001$). On multivariate analysis, having a higher diabetes-specific health literacy index was associated with increased likelihood of an eye exam within the past year (RR 1.14 [95% confidence interval (CI) 1.04, 1.24], $p=0.006$). On sensitivity analysis, the association was borderline (RR 1.05 [95% CI 1.00, 1.10], $p=0.07$).

Conclusions: In an older population of type 2 diabetics, having more diabetes-specific health literacy was associated with increased adherence to diabetic eye exams. This suggests that improving disease-specific health literacy skills could be a means by which to promote vision saving diabetic eye examinations.

CONTROL ID: 3707549

SUBMITTER (NAME ONLY): Samantha Lee

TITLE: Change in peripapillary retinal nerve fibre layer thickness from 20 to 28 years old

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Lee, D.A. Mackey, Centre for Ophthalmology and Visual Science (incorporating the Lions Eye Institute), The University of Western Australia Faculty of Health and Medical Sciences, Perth, Western Australia, AUSTRALIA|A.W. Hewitt, D.A. Mackey, Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, AUSTRALIA|

Commercial Relationships Disclosure: Samantha Lee: Commercial Relationship: Code N (No Commercial Relationship) | Alex Hewitt: Commercial Relationship: Code N (No Commercial Relationship) | David Mackey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma diagnosis almost definitely always lags disease onset by several months if not years. However, it is unclear when exactly does glaucoma start. Moreover, little is known of how the peripapillary retinal nerve fibre layer (pRNFL) thickness change during young adulthood. To address these gaps in our knowledge, we investigated whether pRNFL thinning could be detected at a young age by mapping the 8-year change in pRNFL thickness in a community-based cohort of young adults. We further tested the hypothesis that those with a family history of glaucoma have faster rates of pRNFL thinning than those without a known family history.

Methods: Generation 2 participants from the Raine Study attended an eye examination when they were 20 and 28 years old. The pRNFL thickness globally and at 6 sectors were measured with spectral-domain optical coherence tomography (SD-OCT) imaging. Information on family history of glaucoma was collected using questionnaires administered to the participants and their parents. The 8-year longitudinal change in pRNFL thickness was explored using linear mixed-effect models with random intercept and slope for participants to account for the within-participant correlation between two eyes.

Results: After excluding eyes with pathology and low-quality or erroneous scans, 1,313 eyes of 693 participants were included in the analysis. The pRNFL was thinner at 28 years old than at 20 years globally and at all sectors. The global pRNFL thinned by -0.34µm/year (95% confidence interval= -0.37 to -0.31), with the nasal and superonasal sectors showing the most thinning (-0.46 and -0.45µm/year), followed by the inferotemporal (-0.38µm/year), temporal (-0.29µm/year), superotemporal (-0.22µm/year), and inferonasal (-0.14µm/year) sectors. There was no significant association between family history of glaucoma and rate of pRNFL thinning.

Conclusions: The pRNFL starts to thin at least from the third decade of life, albeit at a very slow rate. There was no evidence that the pRNFL thins at a faster rate in those with a family history of glaucoma. Nonetheless, longer-term follow-up of this cohort is warranted to ascertain the rate of pRNFL thinning in a reference population and in those who eventually develop glaucoma.

CONTROL ID: 3707552

SUBMITTER (NAME ONLY): Adina Kazan

TITLE: Indications and Outcomes for Laser Retinopexy in Patients with Lattice Degeneration

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Kazan, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|R. Mahmoudzadeh, M. Salabati, M. Spirn, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R. Mahmoudzadeh, M. Salabati, M. Spirn, Mid Atlantic Retina, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the characteristics of eyes with lattice degeneration treated with laser retinopexy and to determine the indications, safety, and outcomes of using laser retinopexy in these eyes.

Methods: Single-center, single-surgeon, consecutive retrospective chart review conducted at Wills Eye Hospital between 2014 and 2021. Comprehensive chart reviews documented characteristics and outcomes of these eyes and fellow eyes.

Results: A total of 158 eyes of 139 patients (58.2% female, mean (±SD) age 50 (±17); range 13-79 years) were included in this study. The mean (±SD) follow-up from the lattice diagnosis visit was 880 (±629; range 46-2183) days. The mean time from lattice diagnosis to initial laser was 77 (±263); range 0-2772) days. The mean (± SD) pre-laser logMAR visual acuity was 0.14 (±.27; Snellen equivalent 20/28) and mean post-laser logMAR visual acuity was 0.12 (±.26; Snellen equivalent 20/26, p=0.157). Indications for laser retinopexy were as follows: 54 eyes (35.3%) had retinal detachment of the fellow eye, 69 eyes (45.1%) had an atrophic hole in the lattice, and 36 eyes (23.5%) had an atrophic hole with subretinal fluid. After laser treatment, 20 eyes (12.8%) developed a new posterior vitreous detachment, 13 eyes (8.2%) developed a new epiretinal membrane, and 6 eyes (3.8%) developed a new retinal detachment. Individuals that developed an epiretinal membrane after laser were more likely to be older (60±8 years v 49±17 years, p=0.018). Additionally, eyes that developed epiretinal membranes after laser were also more likely to develop posterior vitreous detachment (OR=6.143 (1.732-21.788, p=0.002). Of eyes that developed a new epiretinal membrane after laser (n=13), no eyes required surgery to fix the epiretinal membrane. Those that developed retinal detachments were more likely to be older (63±5 years vs. 49±17 years) although this did not reach statistical significance (p=0.054). Of eyes that developed retinal detachments after laser (n=6), 4 eyes were treated with laser retinopexy alone, 2 eyes were treated with scleral buckle and pars plana vitrectomy, and all eyes remained attached up to the final visit with one procedure.

Conclusions: Performing laser retinopexy in eyes at higher risk for progression to retinal detachment does not eliminate the risk of further complications, and routine follow-up is recommended. Older patients also tend to have more ERM formation after laser retinopexy.

CONTROL ID: 3707569

SUBMITTER (NAME ONLY): Yunxi Chen

TITLE: The effects of GNAQ mutation and blue light exposure on the malignant transformation of choroidal melanocytes

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, E. Jin, M. Abdouh, T. Tsering, M.N. Burnier, J.V. Burnier, Cancer Research Program, Research Institute - McGill University Health Centre, McGill University, Montreal, Quebec, CANADA|

Commercial Relationships Disclosure: Yunxi Chen: Commercial Relationship: Code N (No Commercial Relationship) | Eva Jin: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Abdouh: Commercial Relationship: Code N (No Commercial Relationship) | Thupten Tsering: Commercial Relationship: Code N (No Commercial Relationship) | Miguel Burnier: Commercial Relationship: Code N (No Commercial Relationship) | Julia Burnier: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is the most common and lethal eye cancer in adults. Most benign nevi harbor the UM driver mutations in GNAQ/GNA11, suggesting additional genetic insults are required for UM initiation. While ultraviolet light, the major risk factor for skin melanoma, is filtered out by the ocular lens and cornea, the blue light (BL) spectra reaches the posterior of the eye. However, the exact role of BL in inducing uveal melanomagenesis is not well understood. In this study, we investigated the impacts of GNAQ mutation and BL irradiation in UM development.

Methods: Using a solar simulator (TSS-156R, OAI), we analyzed the impact of acute (1 sun (1000 W/m^2), 30 min) and chronic (0.3 sun, 3 hours/day, 4 days) BL exposure (400-500 nm) on UM cell lines, normal choroidal melanocytes (NCMs), and GNAQ-mutant CMs (a precursor cell for UM). NCMs were isolated from human donor eyes, and a GNAQ mutation (c.626A>T) was introduced by lentivirus to generate the mutant CMs. The proliferation rate and clonogenicity potential (i.e. soft agar and spheroid assay; in vitro clue of malignant transformation) of NCMs and mutant CMs were compared. The cell viability (CCK8 assay), reactive oxygen species (ROS, DCFDA assay) levels, and proteomic changes (analyzed by mass spectrometry and DAVID database) post BL exposure were assessed. Statistical analyses were performed by Student's t-test. A P value < 0.05 was considered significant.

Results: GNAQ-mutant CMs maintained the expression of melanocyte markers (Vimentin, MelanA, TRP1, HMB-45, S100) and displayed increased proliferation and clonogenicity potential compared to NCMs. Chronic BL irradiation reduced the viability of NCMs but not UM cell lines (i.e. 92.1, MP46 and OMM2.5). Acute BL exposure generated ~100-fold and 7-fold more ROS in 92.1 and NCMs, respectively, compared to non-treated cells. Proteomic analysis identified that BL caused endoplasmic reticulum stress and reduced DNA repair in NCMs, and significant oxidative stress in 92.1 cells.

Conclusions: We report that BL affected the oxidative status of melanocytes and UM cells, which may lead to DNA damage that can accelerate mutation accumulation, thus initiating or facilitating UM development. In addition, GNAQ mutation and BL exposure trigger central clues involved in uveal melanomagenesis, suggesting that BL may represent an additional hit in the process of GNAQ-mutant nevi transformation.

CONTROL ID: 3707570

SUBMITTER (NAME ONLY): Adrit Rao

TITLE: Computationally Efficient Deep Learning Applied to Glaucoma Eye Drop Bottle Detection for Increasing Medication Compliance in Low-Vision Patients

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rao, Palo Alto High School, Palo Alto, California, UNITED STATES|H. Fishman MD PHD, Clinical Research, FishmanVision, California, UNITED STATES|

Commercial Relationships Disclosure: Adrit Rao: Commercial Relationship: Code N (No Commercial Relationship) | Harvey Fishman MD PHD: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Compliance in the usage of prescription eye drops is a major limitation in the management of ocular disease regardless of age, medical condition, or sightedness. However, eye drop medication adherence is particularly challenging in low-vision patients who may have difficulty in differentiating among medications because of small font, and similarities in size, color, and shape. Research has surveyed self-administration of medication in low-vision patients and found that a total of 89% of respondents were unable to read the prescription labels and 96% of these patients did not inform healthcare providers when they faced difficulties in handling their medication. The inability to correctly administer eye drops because of low-vision is a significant subset of eye drop medication non-compliance. We propose a deep learning algorithm which can accurately localize eye drop bottles to aid low-vision patients in recognition.

Methods: Our image dataset was collected from the internet and spans the widely prescribed Latanoprost, Timolol, and Alphagan glaucoma eye drop bottle classes (1500 images). Bounding boxes are placed around the bottles in each image by a trained optometrist. Various image augmentations (sheer, zoom, contrast, flip) are applied. The YOLOv4 tiny computationally efficient object detection algorithm is trained on our annotated coordinate dataset.

Results: The algorithm was trained across 300 epochs with a batch size of 16 and image size of 416x416. It recieved a final mean average precision (mAP) score at a 0.5 IoU threshold of 0.85 and at a 0.5:0.95 IoU threshold of 0.49. The algorithm recieved precision of 0.881 and recall of 0.924 across the test set (20% test split). Figure 1 shows box, objectness, and classification loss across epoch progression along with precision, recall, mAP@0.5 and mAP@0.5:0.95 scores. Bottle localization inference on images averaged at 0.008 seconds on a P-100 GPU.

Conclusions: We have proposed a custom deep learning object detection model which can accurately detect and localize three prescription eye drop bottles. With such a tool, patients can potentially identify and use bottles with more ease, lowering the amount of non-compliance. The proposed system is a proof-of-concept and more testing, a larger dataset, and classes are required before deployment onto a mobile phone.

CONTROL ID: 3707571

SUBMITTER (NAME ONLY): Anil Upreti

TITLE: Vitreous exposure increases global chromatin accessibility in cis-regulatory elements in lens epithelial explants as they undergo fiber cell differentiation

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Upreti, J.A. Tangeman, B.D. Wagner, T.J. Jaquish, R. Palko, C. Gantz, M.L. Robinson, Cell,Molecular and Structural Biology(CMSB), Center for Visual Science at Miami University(CVSMU), Miami University, Oxford, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The lens epithelial explant system represents a powerful, in vitro approach to understand how extracellular signals coordinate fiber cell differentiation. In this system, growth factors present in the vitreous humor elicit widespread transcriptomic changes resulting in proliferation and the production of proteins characteristic of both inflammation and lens fiber cell differentiation (CD). Here, we document how vitreous treatment changes chromatin accessibility (CA) through time in lens epithelial explants.

Methods: Chromatin extracted from 8-day-old FVB/N mouse lens epithelia was subjected to ATAC-sequencing at 5 different time points: immediately after collection, after 1 day in explant culture, and after an additional explant culture period in 50% bovine vitreous/media for 1, 5 and 10 days. The ATAC data was processed to identify open chromatin regions and associated genomic features. Furthermore, the differentially accessible regions (DARs) between different time points were identified and subjected to GO term analysis. Similarly, DARs were analyzed for over-represented motifs to identify candidate transcription factors (TFs) associated with observed accessibility changes. Finally, the ATAC-seq data was integrated with RNA-seq data to identify novel relationships between CA and transcriptomic changes associated with fiber CD.

Results: Genome-wide analysis of CA indicates a general trend toward increased accessibility of cis-regulatory elements (CREs) for vitreous treatment. GO analysis of genes associated with DARs included eye development, inflammatory response, lens development in camera-type eyes, NIK/NF-kappa B signaling and PI3K signaling. Similarly, some of the top overrepresented motifs associated with DARs in the vitreous treated samples include the transcription factors ATF3, JUN, SOX21, SOX3 and TEAD3. These motifs are consistent with a recent report (Zhao et al. Epigenetics & Chromatin 2019) of these TFs in fiber CD. Fiber cell genes Dnase2b, Cryba4, Crybb1, Crygc, Cryba3 and inflammatory response genes Mmp3, Mmp10, Mmp9, Fn1 exhibit increased accessibility in response to vitreous, consistent with their increased transcription.

Conclusions: Vitreous treatment results in TF-mediated chromatin remodeling in CREs and within gene bodies associated with fiber CD and inflammatory response genes.

CONTROL ID: 3707572

SUBMITTER (NAME ONLY): Aziza Dhalai

TITLE: The Use of Capsular Tension Rings in Preventing Toric Intraocular Lens Rotation

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Dhalai, F. Boumelhem, University of Nevada Las Vegas Kirk Kerkorian School of Medicine, Las Vegas, Nevada, UNITED STATES|S. Mowen, A. Johnson, J. David, A. Pan, R. Lieberman, 99th Medical Group Mike O'Callaghan Military Medical Center, Nellis AFB, Nevada, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the rotational stability of toric intraocular lenses (IOL) with and without the use of a capsular tension ring (CTR) in patients undergoing cataract surgery.

Methods: This study is a prospective, randomized clinical trial performed at a military medical center in Las Vegas, Nevada. The eyes of adult patients undergoing cataract surgery with corneal astigmatism greater than or equal to 1.0 diopter were randomized into either the control group or the treatment group. Standard-of-care phacoemulsification cataract surgery was performed using a Tecnis toric lens (Johnson and Johnson Vision) in both groups. In the control group, no CTR was used. In the treatment group, a MORCHER® EYEJET® preloaded single-use CTR was implanted immediately prior to the IOL. Eyes of every axial length were eligible to enroll, and a CTR size 14, 14A, or 14C w used depending on the axial length. Slit lamp photos using retroillumination to document the toric axis were taken on the first day, 1 week, 1 month, 3 months, and 6 months postoperatively. The toric axis was measured by blinded reviewers using computerized image software. The primary outcome was the difference between the preoperative intended toric axis and the measured toric axis on postoperative month 6.

Results: The mean difference between intended and measured toric axis at 6 months postoperatively was 7.4 ± 7.2 degrees in the control group and 4.6 ± 4.7 degrees in the treatment group. The difference was not statistically significant. There were no complications related to the use of the capsular tension ring.

Conclusions: There is a non-significant trend towards fewer degrees of rotation with the addition of the capsular tension ring during cataract surgery. Additional study is needed to determine if this trend will be clinically significant.

CONTROL ID: 3707573

SUBMITTER (NAME ONLY): Liqin Jiang

TITLE: Differences in mRNA to Protein Expression Levels in a Spontaneous Myopia Guinea-Pig Model

SESSION TITLE: Myopia: Mechanism of Emmetropization and Eye Growth

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Jiang, J.F. Busoy, M. Chua, V. BARATHI, Singapore Eye Research Institute, Singapore, SINGAPORE|N.A. Brennan, Johnson & Johnson Vision Jacksonville, Florida, UNITED STATES|Q.V. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS Medical School, Singapore, SINGAPORE|Q.V. Hoang, Dept of Ophthalmology, Columbia University, New York, NY, USA, New York, UNITED STATES|V. BARATHI, ACP in Ophthalmology & Visual Sciences, DUKE-NUS Graduate Medical School, SINGAPORE|

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ABSTRACT BODY:

Purpose: To elucidate the signaling pathway from the retina to sclera (via the choroid), in the regulation of spontaneous axial myopia in an albino guinea pig (GP) model.

Methods: Refraction and biometry measurements were assessed by retinoscopy and Sonomed A-Scan ultrasound respectively. Eighteen Elm Hill albino GPs were divided into two groups, based on post-natal day 14 refraction, as either albino myopia (AM, n=9) or albino hyperopia (AH, n=9). Four GPs from each group were analyzed by RNAseq and the rest were analyzed by proteomics assay. QIAGEN IPA software was used to identify the canonical pathways in the retina, choroid, and sclera from both RNAseq and proteomics data.

Results: The refraction (-5.0±1.5D vs. +3.6±2.4D, $p<0.001$) and axial length (7.4±0.2mm vs. 7.2±0.1mm, $p<0.001$) significantly differed between AM and AH. Around 17,000 gene IDs for GPs were identified from Ensembl, but only 150 genes in the sclera showed significantly different expression between AM and AH with adjusted $p<0.05$. Based on proteomics analysis, >8,000 protein names for GPs were identified from UniProt, and the levels of 274 proteins in the retina, 106 proteins in the choroid, and 125 proteins in the sclera were statistically different between AM and AH with adjusted $p<0.05$. The canonical pathways identified at the gene level were far fewer than at the protein level among all three tissue types.

Conclusions: The combination of differentially expressed mRNA and proteins data can increase the confidence for biological discovery in the spontaneously myopic eye, which can elucidate the genetic basis of individual susceptibility to myopia development and potential pharmaceutical therapeutic targets.

CONTROL ID: 3707579

SUBMITTER (NAME ONLY): John Gonzales

TITLE: Peripheral blood transcriptome in Sjögren Syndrome: Insights from the Sjögren's International Collaborative Clinical Alliance

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Gonzales, J. Nortey, E. Gebreegaziabher, A. Hinterwirth, L. Zhong, C. Chen, T. Doan, Francis I. Proctor Foundation, University of California San Francisco, University of California San Francisco, San Francisco, CA, US, academic, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify a peripheral blood transcriptome that distinguishes Sjögren Syndrome (SS) from non-Sjögren Syndrome. SS is an underdiagnosed condition in patients with dry eye disease.

Methods: Cross-sectional study of participants from Sjögren's International Collaborative Clinical Alliance (SICCA) UCSF sub-cohort returning for up to 15-year follow-up. Participants were classified using the universally accepted American College of Rheumatology/European League Against Rheumatism SS criteria. All participants had slit lamp examination performed including determination of the ocular staining score (corneal staining with fluorescein and conjunctival staining with lissamine green). Additionally, whole peripheral blood was collected into PAXgene RNA tubes (QIAGEN, Germantown, MD) and then submitted for metagenomic sequencing for differential gene expression. Sequenced data were quality filtered and aligned to the ENSEMBL CRCh38 human genome using STAR2. Genes were filtered to include only protein-coding genes that were expressed in at least 25% of the patients. Gene count data were analyzed with DESeq2. Differentially expressed genes with false discovery rate (FDR) <0.01 were considered as notable.

Results: Fourteen participants (10 SS and 4 non-SS) were recruited for up to 15-year follow-up. The ocular staining score remained stable up to 15 years of follow-up in both SS and non-SS groups. However, we identified 6 differentially expressed genes distinguishing SS from non-SS. The genes included OAS3, IFIT1, RSAD2, IFI44L, ISG15, and OASL, all genes that are involved in the canonical interferon pathway.

Conclusions: In those classified as SS, a robust peripheral blood transcriptome distinguishes them from non-SS. The differentially expressed genes, which are related to the interferon pathway, may indicate candidate genes for further study, which could be used as future additional biomarkers of SS and may guide future treatment options.

CONTROL ID: 3707583

SUBMITTER (NAME ONLY): Sabrina Do

TITLE: Glaucoma Medication Non-Compliance in a Vietnamese American Population

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fan, Loma Linda University Medical Center, Loma Linda, California, UNITED STATES|S. Do, C. Do, Pacific Eye Care Center, Westminster, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Higher rates of medication non-compliance in Vietnamese populations have been reported among patients with cardiovascular diseases and diabetes mellitus. Glaucoma medication non-compliance and potential barriers to compliance among Vietnamese Americans have not been reported. This cross-sectional, observational study assesses glaucoma medication non-compliance among a Vietnamese American patient population and identifies the commonly cited barriers which potentially hinder glaucoma medication compliance.

Methods: 206 Vietnamese American patients taking glaucoma medication(s) were recruited from an ophthalmology practice in Westminster, California. All study subjects completed questionnaires on demographics, administration of glaucoma medications, social support, insurances, and commonly reported barriers to medication compliance. Medication non-compliance was determined by criteria established by the MARS-5 questionnaire. Quantitative analyses using descriptive statistics, Chi-square test, t-test, and logistic regression were performed.

Results: 19.4% of the subjects were found to be non-compliant as per the MARS-5 criteria. Decreasing age had a statistically significant association with medication non-compliance (OR=1.05, p=0.02). Increasing frequency of daily administrations of glaucoma medications trended towards non-compliance (OR=1.55, p=0.07). Among non-compliant patients, the most frequently cited barriers were forgetfulness (60%), burning or stinging with drops (47.5%), blurriness from drops (45%), medication cost (32.5%), intolerable medication-induced side effects (32.5%), and busyness with obligations (32.5%).

Conclusions: Non-compliance was found in 19.4% of our survey subjects. Both decreasing age and increasing frequency of administration were correlated with glaucoma medication non-compliance. The most commonly cited barrier was forgetfulness. Knowledge of the factors relevant to non-compliance can guide interventions to improve glaucoma medication compliance.

CONTROL ID: 3707584

SUBMITTER (NAME ONLY): Jeff Win

TITLE: CD177 and PR3 in the pathogenesis of P. aeruginosa-induced keratitis

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Win, A. Stambersky, Y. Wang, T. Carion, E. Abdul Shukkur, E.A. Berger, Department of Ophthalmology, Visual, and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bacterial keratitis is a prevalent eye infection that causes corneal opacification and purulent discharge, especially among contact lens wearers. Such infections recruit innate immune cells into the cornea, predominately neutrophils (PMN). CD177 is a GPI-anchored protein expressed on ~50% of circulating PMN. Proteinase-3 (PR3) is a serine protease that binds CD177 and is shown to be released from PMN granules upon activation or expressed on the plasma membrane (mPR3). $CD177^{+}$ PMN can be protective or pathogenic in various diseases ranging from IBD to COVID-19. On the other hand, elevated PR3 is found in patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated systemic vasculitis. With little known regarding the eye, this study investigates the expression and role(s) of CD177 and PR3 in the cornea following bacterial keratitis.

Methods: This work uses an experimental model of bacterial keratitis carried out in 8-week-old, female susceptible C57BL/6 (B6) and resistant BALB/c mice. The left eye of each mouse was scarified then infected with P. aeruginosa ATCC strain 19660 (5 µL of 1 x 10^{6} CFU). Corneas from naïve, uninfected mice from both strains served as controls. Corneas were harvested at 1, 3, and 5 days post-infection (p.i.). Levels of CD177 and PR3 were determined at the protein level by Western blot and by phenotypic profiling using flow cytometry. In vitro assessment was carried out using HL-60, a human promyelocytic cell line, and siCD177 knockdown.

Results: Results from the in vivo model showed no differences in protein levels at 1 day p.i., but significantly higher levels of both CD177 and PR3 in B6 vs. BALB/c at 3 and 5 days p.i. Flow cytometry data revealed $CD177^{+}$ and $PR3^{+}$ expression on both PMN and macrophages from B6 and BALB/c infected corneas with differential mean fluorescence intensities detected between the strains under normal conditions and following infection. In vitro results indicated that cell activation was altered following CD177 knockdown with differences in downstream signaling.

Conclusions: As one of the first studies to explore the role of CD177 and PR3 in the pathogenesis of bacterial keratitis, our findings reveal strain-specific expression profiles for PMN that may contribute to resistance vs. susceptibility. In addition, we show the presence of $CD177^{+}PR3^{+}$ macrophages. Overall, these findings may uncover novel therapeutic targets to treat bacterial keratitis.

CONTROL ID: 3707591

SUBMITTER (NAME ONLY): Werner Eisenbarth

TITLE: Prevalence of Amblyogenic Risk Factors among Preschool Children in Rural Ghana

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Eisenbarth, M. Lippok, Department of Applied Sciences and Mechatronics, Hochschule Munchen, Munchen, Bayern, GERMANY|L.N. Aduku, C. Apprey, Department of Biochemistry and Biotechnology, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|J.A. Hamidu, Department of Animal Science, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|I. Osei Duah, D. Ben Kumah, K. Owusu Akuffo, Department of Optometry and Visual Science, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|B. Singh, Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|B. Singh, University Hospital, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|E.K. Addo, Department of Ophthalmology and Visual Sciences, Moran Eye Centre, University of Utah Health, Salt Lake City, Utah, UNITED STATES|E.K. Addo, Department of Nutrition and Integrative Physiology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|W. Eisenbarth, M. Lippok, Munich Center for Applied Vision Science, Hochschule Munchen, Munich, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Early childhood vision screening remains paramount in the detection of refractive amblyogenic risk factors. However, in resource-constrained environment the limited number of eye care cadres and disproportionate distribution of eye care services mostly lives the rural areas underserved. Photoscreening is a promising technology with increased specificity and sensitivity to identify these refractive anomalies, and with greater propensity to filling this human resource and service gap. Therefore, using plusoptix vision screener A12 we determined the prevalence of amblyopic risk factors among preschool children in rural communities in the Bosomtwi District of Ghana.

Methods: This was a community-based cross-sectional study. Photoscreening was performed for 169/202 children (response rate 83.7%) aged 2-5 years. Referral for comprehensive ophthalmic assessment by an experienced optometrist was dependent on a prespecified amblyopic risk factors criterion by the American Association for Pediatric Ophthalmology and Strabismus (AAPOS). Vision screening was not performed on sleeping and uncooperative children.

Results: The mean age of children was 3.20 (± 0.98) years, with the majority (53.2%) being males. Mean spherical equivalent (S.E.) for the right and left eyes were 0.47 ± 0.42 and 0.68 ± 0.54 diopter respectively. Out of the 14 subjects referred (8.28%) the proportion of amblyogenic risk factors were as follows: 4.14% (7/169) anisocoria, 1.78% (3/169) myopia, 1.18% (2/169) anisometropia, 0.59% (1/169) hyperopia, 0.59% (1/169) gaze asymmetry and 0.0% astigmatism. Anisocoria was more prevalent in females 85.7% (6/7) compared to males 1 (14.3%).

Conclusions: The prevalence of amblyopia risk factors in this study was 8.28%. Anisocoria and myopia were commonly encountered, and female pediatrics were mostly found of unequal pupil size. This results showed undiagnosed amblyogenic risk cases which merits vision screening among children in these rural areas to enhance early detection and management.

CONTROL ID: 3707599

SUBMITTER (NAME ONLY): Jost Jonas

TITLE: Intravitreal Panitumumab for Prevention of Myopic Axial Elongation in Highly Myopic Adult Eyes with Myopic Macular Degeneration: Phase 1 Study on Safety

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Jonas, G. Kazakbaeva, S. Panda-Jonas, L. Gilemzianova, D. Khakimov, M. Bikbov, Ufa Eye Research Institute, Ufa, RUSSIAN FEDERATION|F.G. Holz, Department of Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Recent histomorphometric studies suggested that axial myopic elongation occurs through an equatorial ocular wall enlargement, changing the eye shape from a sphere to a prolate configuration. The equatorial ocular wall enlargement may be achieved by a growth of the equatorial Bruch's membrane (BM), leading to a backward push of the posterior BM and a secondary thinning of the posterior choroid. Since BM is produced by the retinal pigment epithelium, which contains receptors for the epidermal growth factor (EGF) and the in-vitro proliferation of which is supported by EGF, EGF may be a myopic axial elongation-associated messenger molecule. Subsequently, experimental studies in guinea pigs showed that the intravitreal application of blockers of EGF family members and of the EGF receptor led to a decrease in axial elongation, while the intravitreal injection of EGF family members was associated with an increase in axial elongation. The findings suggest that the intravitreal application of EGF receptor blockers such as panitumumab may prevent further axial elongation in adult highly myopic patients. We here examined the safety and tolerability of intravitreally applied panitumumab (Vectibix®).

Methods: The phase 1 study included highly myopic patients with myopic macular degeneration. The eyes received a single intravitreal injection of 0.6 mg (60 µL) panitumumab in a standardized manner.

Results: The study included two patients: Patient #1: male, age: 56 years, best corrected visual acuity (BCVA): 0.05, axial length: 29.10mm, IOP: 12mmHg.; Patient #2: female, age: 68 years, BCVA: 0.12, axial length: 30.86 mm, IOP: 17 mmHg. The examinations performed at one day after the injection did not show any intraocular inflammation or morphological change. Examined at 7 days after the injection, no change was observed in BCVA, retinal electroretinography, perimetry, optical coherence tomography-based clinical histomorphometry of the retina and optic nerve, and intraocular pressure, nor were intraocular signs of inflammation or tissue destruction observed.

Conclusions: The preliminary observations of the first two patients receiving an intravitreal application of the EGF receptor antibody panitumumab do not contradict the assumption of an intraocular tolerability of panitumumab injected in a dose of 0.6 mg.

CONTROL ID: 3707603

SUBMITTER (NAME ONLY): Yunlu Xue

TITLE: Fat3 deficiency impairs bipolar cell function and fast vision in mice

SESSION TITLE: Photoreceptors and the OPL

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Xue, C. Cepko, Genetics, Harvard Medical School, Boston, Massachusetts, UNITED STATES|E. Avilés, L. Goodrich, Neurobiology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|V. Kefalov, Ophthalmology & Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|V. Kefalov, Gavin Herbert Eye Institute & Center for Translational Vision Research, University of California Irvine, Irvine, California, UNITED STATES|

ABSTRACT BODY:

Purpose: Fat3, a member of the Fat family of atypical cadherins, is critical for the development of retinal circuitry. The deletion of Fat3 from the mouse retina impairs amacrine cell migration, neurite retraction, and the proper location of synapses, resulting in the formation of ectopic synaptic layers. However, it is unknown how retinal function is affected by these developmental cellular defects. To investigate this question, we examined retinal function of Fat3-deficienct mice.

Methods: Mice were dark adapted overnight before being anesthetized for in vivo electroretinography (ERG) recordings. Four types of ERG recordings were performed: 1) scotopic test, 2) photopic test, 3) flicker test up to 50 Hz, and 4) three-second step light test. The photopic visual acuity of $Fat3^{-/-}$ mice was measured using the optomotor behavioral assay. In addition, to test if mice can perceive flickered light, a contextual and vision-cued fear conditioning (CVFC) test was designed and applied to $Fat3^{-/-}$ mice. Additional immunohistochemistry and in vivo ERG experiments were performed on $Grik1^{-/-}$, $Grm6^{-/-}$, and $Grik1^{-/-}Grm6^{-/-}$ mice to look for effects due to perturbations in bipolar cells.

Results: $Fat3^{-/-}$ eyes did not show a significant difference in the scotopic ERG, photopic ERG or photopic visual acuity compared to the controls. However, the flicker ERG tests revealed severely decreased amplitude and delayed implicit time from $Fat3^{-/-}$ eyes at the high temporal frequencies (i.e. >20 Hz) compared to the controls. $Fat3^{-/-}$ mice also presented impaired perception of 33 Hz flashes as measured by the CVFC test. $Fat3^{-/-}$ eyes showed diminished d-wave amplitude in the step ERG test, which correlated with decreased GRIK1 expression in OFF-bipolar cells (BC), in which Fat3 mRNA was enriched. $Grik1^{-/-}$ eyes presented a diminished d-wave, slightly decreased 30 Hz amplitude, and advanced 20 Hz implicit time.

Conclusions: These results suggest that Fat3 is critical for OFF-BC function and for retinal processing of visual signals at high temporal frequency. Fat3 is not required for basic light sensation in dark or daylight conditions. Fat3 also appears not to be critical for normal spatial visual resolution in daylight conditions. Additional results from $Grm6^{-/-}$ and $Grik1^{-/-}Grm6^{-/-}$ mice suggest that the function of ON-BCs, in addition to the function of OFF-BCs, might be compromised by Fat3-deficiency, contributing to the unique fast vision phenotype.

CONTROL ID: 3707604

SUBMITTER (NAME ONLY): Zhiqi Chen

TITLE: Segmentation-Free OCT-Volume-Based Deep Learning Model Improves Point-Wise Visual Field Threshold Estimation

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To overcome the floor effect of OCT measurements, we developed a deep learning model to estimate the functional deterioration directly from 3-dimensional (3D) OCT volumes (segmentation free) and compared the performance with the model trained with 2-dimensional (2D) OCT thickness maps (segmentation dependent) as inputs.

Methods: 8387 24-2 Humphrey visual field (VF) tests were acquired from 1129 patients over multiple visits. 13792 macular and 15026 optic nerve head scans (both 200x200 samplings, Cirrus HD-OCT, Zeiss, Dublin, CA) were acquired within 90 days of the VF visits. To reduce variances caused during imaging, the Bruch's membrane surface was flattened and aligned by adjusting A-scans in the z-direction. Downsampling to 64x64x128 was applied to prevent memory shortage. Two models were trained to estimate the 52 VF threshold values: one was an 18-layer 3D ResNet taking OCT 3D volumes as inputs and the other was an 18-layer 2D ResNet taking 2D macular ganglion cell-inner plexiform layer and retinal nerve fiber layer thickness maps as inputs. A mean square error loss was used to train both models. The 52-point average of the mean absolute error (MAE) and Pearson correlation (PC) between the measured and estimated VF threshold values of each point were used to evaluate the performance.

Results: The MAE was significantly lower in 3D than 2D models (3.41 vs. 3.73 dB, respectively, $p<0.001$, Wilcoxon Signed-rank test). The PC was slightly better in 3D than 2D models (0.76 vs. 0.71, respectively, $p<0.001$, Williams test for equality of correlations). Figure 1 shows the histogram of VF threshold values in the training set with the MAE results. Both models performed better for VF threshold values between 20 and 35 dB, which were most frequently sampled in our dataset. For values under 20 dB, MAE of the 3D model clearly shows a better trend than that of the 2D model, indicating the model using 3D volumes may have less influence from the floor effects.

Conclusions: 3D model shows better accuracy than the 2D model, indicating the possibility of overcoming the floor effects of OCT measurements, although a relatively large error is present due to the under-represented low threshold sensitivity. Further investigation is needed with additional low threshold data.

CONTROL ID: 3707605

SUBMITTER (NAME ONLY): Theodore Spaide

TITLE: Leveraging unlabeled OCT data for training better deep learning vision-transformer models

SESSION TITLE: Machine Learning and Big Data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Spaide, Y. Bagdasarova, C.S. Lee, A.Y. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Deep learning is increasingly used for automating tasks in medicine, such as diagnosis of ophthalmic images. However, most previous approaches to this problem have required the use of time-intensive manual labeling of images. We used self-supervised learning to train a network to extract features from a large number of unlabeled optical coherence tomography (OCT) images, and then used this feature extractor as the backbone of a classification system trained on a small set of labeled images.

Methods: A total of 94,847 OCT volumes from 16,710 patients obtained from University of Washington were used. These were split into an unsupervised training set of 88,834 volumes (15,716 patients), a training set of 4490 volumes (795 patients), and a validation set of 1523 volumes (199 patients). Diagnostic labels were used for the training and validation sets, but not the unsupervised training set. Unsupervised training was done using the DINO framework. The resulting models produced feature vectors from B-scans. The models were then frozen and used to extract features from the labeled training set. Linear regressors were fit on the extracted features to predict age and logMAR, and a k-nearest neighbor (kNN) classifier was fit to diagnose age-related macular degeneration (AMD), diabetic eye disease, and glaucoma (Figure 1).

Results: The OCT-trained network had an R2 of 0.61 for age and 0.32 for LogMAR. Its Average Precisions (AP) for AMD, diabetic eye disease, and glaucoma were 0.87, 0.70, and 0.56, respectively. The age R2 and all three diagnostic scores were higher than for the ImageNet-trained model, and the diagnostic scores for both models were significantly higher than the baseline prevalence (Figure 2).

Conclusions: Here we leverage unlabeled images to perform feature extraction with deep learning and then use a small set of labeled images to train simple algorithms using these features. This approach may be useful for training deep learning models with few labeled examples. Pretraining on ophthalmic images without labels can improve model performance on labeled datasets.

CONTROL ID: 3707606

SUBMITTER (NAME ONLY): merve gözel

TITLE: Communications Between Adipose-Derived Mesenchymal Stem Cells (AdMSCs) and Retinal Pigment Epithelial Cell Line (RPE-1) in Different Stress Environments via Tunneling Nanotubes

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Paracrine supportive effects of MSCs are thought to be at least partially accomplished by TNTs which allow direct intercellular communication and cargo transfer. This study aims to demonstrates formation of TNTs between AdMSCs and RPE-1 and their alterations in response to experimental stress conditions.

Methods: Serum starvation and oxidative stress were used as stress conditions to induce TNTs. Texas Red™-X Phalloidin for binding F-actin of tunneling tubes, anti β-tubulin for cell structure, DAPI for nuclei were used for immunofluorosence staining. Scanning electron microscopy (SEM) imaging determined the average thickness of TNTs. CTG (CellTiter-Glo®) assay determined cell survival due to TNTs. Reactive oxygen species (ROS) quantification within the cells group was performed. Fluo-4AM staining was used to determine Ca^{2+} concentrations.

Results: Fluorescence microscopy revealed that TNTs, which are not anchored to the substratum, regularly connect between cultured RPE-1 and AdMSCs in stress environments and contain F-actin but no microtubules. SEM showed the ultrastructure of TNTs were straight connections between cells with a diameter ranging from 35 to 200 nm and a length of up to 120 mm. We observed that RPE-1 have lower cell viability when seeded under stress without AdMSCs than in the group co-cultured ($p=0.0015$). Decreased total ROS production in RPE-1 under stress conditions was observed with coculture ($p=0.017$) and it suggested that TNT-mediated mitochondrial transport may have occurred. In hypoxic condition, TNTs was determined more widely than in serum starvation ($p=0.0001$). Ca^{2+} imaging has been shown that calcium signals are transmitted by intercellular communication via TNTs and increase in stress environments ($p=0.0001$).

Conclusions: Our observations demostrated the signal trafficking via TNTs between RPE-1 and AdMSCs. This communication may support the ability to survive in response to stress conditions. These results can provide a new perspective on stem cell-based therapy in ophthalmologic diseases that may help develop a new strategy to manipulate direct signal, organelle, or molecule transfer for retinal pigment epithelial damage.

CONTROL ID: 3707613

SUBMITTER (NAME ONLY): Dong LIANG

TITLE: Retinal Thickness and Visual Acuity in Eyes with Different Types of Astigmatism

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the optical coherence tomography (OCT) measured retinal thickness (RT) and best-corrected visual acuity (BCVA) in eyes with different types of astigmatism.

Methods: This retrospective, case-control study was conducted at the Optometry Clinic of Hong Kong Polytechnic University. Subjects were stratified into with-the-rule (WTR), against-the-rule (ATR) and control groups by noncycloplegic subjective refraction. Inclusion criteria were: age between 18-45 years, spherical-equivalent refraction (SE) ≥ -10.00 D, cylindrical power (Cyl) ≤ -0.75 D with cylindrical axes of 0-30°/150-180° for WTR and 60-120° for ATR, and Cyl ≥ -0.25 D for the control group. Those eyes with any ocular disease that may cause retina defect, previous history of ocular surgery, BCVA > 0.1 LogMAR or poor imaging quality were excluded. BCVA were determined with Snellen charts and converted into LogMAR. The fovea-centred 6-mm scan was performed by SD-OCT (Spectralis OCT, Heidelberg), and RT was measured automatically by the inbuilt Heidelberg software, then manually checked and corrected by an experienced operator. Both corneal curvature and SE were used to adjust the magnification factor in OCT imaging.

Results: In total, 101 subjects met the inclusion criteria and only right eyes were analysed (WTR, n=41; ATR, n=25; Controls, n=35). There were no significant differences in age, gender, SE, corneal curvature and intraocular pressure across three groups (all P > 0.05). One-way ANOVA showed a significant difference in both BCVA (P = 0.046) and global RT in 6-mm macula (P = 0.031) among the three groups. Bonferroni's post hoc tests showed that the between-group difference in BCVA (WTR vs Controls, P = 0.041), as well as those differences in RT at inner-nasal (WTR vs ATR, P = 0.034) and outer-temporal (WTR vs Controls, P = 0.042) were statistically significant. BCVA was positively correlated with global RT (r = 0.310, P = 0.002) after adjusting for age, gender, SE, and corneal curvature.

Conclusions: A thicker RT and poorer BCVA were found in eyes with WTR astigmatism in Chinese young adults, compared with the ATR and control groups. Our findings suggest that the effect of astigmatism on ocular morphological and functional characteristics may vary depending on not only magnitude but axes of astigmatism.

CONTROL ID: 3707615

SUBMITTER (NAME ONLY): Viktor Nedelchev

TITLE: Novel fixation target promotes more accurate fixation: initial proof-of-concept

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.V. Nedelchev, F.A. Ennis, L. Mcilreavy, Optometry and Vision Sicences, Cardiff University, Cardiff, UNITED KINGDOM|P.J. Bex, Department of Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: When fixating a target, small eye movements (drift, microsaccades and tremors) cause the eyes to move. We have devised a novel fixation target (a radial sine wave grating) that, when drifting, recruits optokinetic-like responses. We predict that these drift-induced eye movements will either stabilize (contracting) or destabilize (expanding) fixation.

Methods: Five typical observers with normal vision were asked to fixate four different fixation targets for 90s each in random order. The target was either a radial sine wave luminance grating (3° diameter; 1 cpd; 100% contrast) that contracted (2Hz), expanded (2Hz) or was stationary (0Hz). As a control condition, observers fixated a 'bull's eye and cross hair' target (0.6° outer diameter; 0.2° inner diameter) previously reported to improve fixation performance (Thaler et al. 2013). All stimuli were presented against a 53 cd/m^2 mean luminance grey background. Observers viewed the targets binocularly and eye movements were recorded at 1000Hz from the eye with better acuity. Saccades and blinks were excluded from eye movement traces and a bivariate probability density function of target-relative eye position was calculated. The accuracy and precision of gaze were derived from the 68% isocontour that encompassed the eye position data.

Results: There was a significant main effect of stimulus type on the accuracy of eye position [$F(3,12) = 5.979$, $p = 0.010$, $\eta^2 = 0.599$]. The contracting stimulus resulted in more accurate fixation than the typical bull's eye and crosshair stimulus ($p_{bonf} = 0.009$). There were no other significant differences among the different stimuli for fixation stability. Despite our novel fixation target being larger in diameter, there was no significant change in precision compared to the conventional target.

Conclusions: Our results suggest that our novel contracting concentric fixation targets improve the accuracy of fixation over an extended epoch. The constant level of precision with this target further suggests that functional benefits of fixational eye movements (Tulunay-Keesey, 1960) are preserved. We envision that our novel fixation target may be useful in applications where maintaining gaze over long durations is critical, for example during visual field testing, experiments in vision science, or for individuals with impaired central vision (e.g. age-related macular degeneration) when viewing with an eccentric retinal locus.

CONTROL ID: 3707622

SUBMITTER (NAME ONLY): Andrea Gil Ruiz

TITLE: Dynamic Analysis of Retinal Image Quality Metrics for Predicting Manifest Refraction

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Modern autorefractors have demonstrated high accuracy and higher repeatability than manifest refraction in adults yet are not considered precise enough to substitute the gold standard, even in low-resource settings where there is a severe shortage of experienced refractionists. This work evaluates a novel approach that combines dynamic wavefront aberrometry data, acquired using an affordable portable autorefractor, with the analysis of retinal image quality metrics (IQMs) to predict subjective refraction.

Methods: 56 subjects (34±14 years) were recruited for the analysis. Each participant underwent standard clinical refraction followed by a 10-second video acquisition using a QuickSee (QS) wavefront aberrometer (PlenOptika, USA). Shack-Hartmann images of each video for the right eye were processed to obtain Zernike coefficients up to the 4^{th} order. Coefficients obtained for each image were mathematically corrected with the closest sphero-cylindrical correction and the residual wavefront error was used to calculate the Point Spread Function (PSF) and IQMs (e.g., Strehl Ratio) describing some performance parameter of the corrected eye. Since each IQM is part of a dynamic sequence, it is possible to build a dynamic signal for each metric which contains information about fluctuations in image quality during the measurement. The final refraction is obtained as the average of the refractions corresponding to the images whose IMQs provided optimal performance.

To assess this method, we compared the results of the QS with those obtained by the new algorithm (using 6 different IQMs, Table 1) against the standard clinical refraction. Figures of merit were mean bias error (MBE), 95% limits of agreement (LOA), mean absolute error (MAE), and the percentages of agreement (0.25 and 0.5D thresholds) between refractions.

Results: The proposed method reduced the differences between QS and manifest refraction. Specifically, for spherical equivalent refraction (M) (Table 1) a 79% average reduction in MBE together with moderate average improvements for MAE (10.3%), LOA (5%), and percentage of agreement within 0.25D (8.8%) and 0.5D (6.3%) were found for all IQMs evaluated.

Conclusions: The proposed algorithm behaves as an efficient filter which selects those measurements within the dynamic sequence that are more representative of the manifest refraction of the patient.

CONTROL ID: 3707625

SUBMITTER (NAME ONLY): Caroline Brandl

TITLE: Association of photostress recovery time with age-related macular degeneration in old-aged individuals

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Brandl, M.E. Zimmermann, V. Thanner, K.J. Stark, I.M. Heid, Genetic Epidemiology, Universitat Regensburg Fakultat fur Medizin, Regensburg, Bayern, GERMANY|C. Brandl, H. Helbig, Ophthalmology, Universitatsklinikum Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Previous evidence suggests that the time for visual recovery after exposure to glare is commonly slowed in age-related macular degeneration (AMD), even among patients with normal visual acuity, varying by age and extent of disease. However, systematic data from epidemiological studies is lacking. We thus set out to assess photoreceptor function and recovery following photostress in a population-based study of individuals aged 70+ (AugUR), to investigate the association of photostress recovery time (PRT) with age and AMD status.

Methods: Presence and severity of AMD was assessed via manual grading of color fundus images applying the Three Continent AMD Consortium Severity Scale. After assessing visual acuity via ETDRS charts in 4m distance, the full macular region was bleached tor 30 seconds via a bright direct ophthalmoscope and PRT was measured as the seconds of the participants' recovery to regain their visual acuity. The participant's AMD status was derived as their most severe eye-specific AMD status (worse eye), PRT was then analyzed for this worse eye, or a random eye if both had the same AMD stage. As cataract can potentially influence PRT, status after cataract surgery was determined via interview-based questionnaire.

Results: Baseline data on AMD status as well as PRT was available for 1391 AugUR participants, aged 70-95 years (mean age 78.3±4.9), 42.5% male. A total of 289 individuals had early (moderate, mild, severe) and 49 had late AMD. PRT ranged from 2 to 239 seconds (mean 94.6±48.1), increased by age and particularly early AMD (Figure 1A,B). Logistic regression adjusted by age and sex revealed a highly significant association of increasing PRT with any AMD (Odds Ratio [OR]=1.091 per 10 seconds, P-value=$3.2*10^{-11}$). The same association was found when focussing on early AMD (OR=1.091, P=$3.0*10^{-10}$), and when only including participants with cataract surgery (n=483; e.g. any AMD: OR=1.088, P=$7.7*10^{-5}$).

Conclusions: PRT is easy to assess, thus potentially applicable broadly in epidemiological studies and worthwhile for further evaluation longitudinally. In addition to providing unique PRT values for an older population, we demonstrate a significant association with particularly early AMD cross-sectionally, indicating the potential of PRT as a functional biomarker.

CONTROL ID: 3707626

SUBMITTER (NAME ONLY): Thomas Khuu

TITLE: Characterization of refractive error progression in patients with blue cone monochromacy

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.H. Khuu, A.D. Igelman, P. Yang, M.E. Pennesi, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|T.H. Khuu, Elson S. Floyd College of Medicine, Washington State University, Spokane, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blue cone monochromacy (BCM) is associated with a high prevalence of myopia. However, data on the natural history of refractive error in BCM are scarce. The aim of this study is to investigate the refractive error changes in patients with BCM to better characterize its natural progression.

Methods: A retrospective, single-center study of patients with BCM confirmed by genotypic analysis was conducted. Study variables included age, refractive error, and genotype. Refractive error is reported as spherical equivalent of refraction (SER). Patients with at least two SER evaluations measured under 25 years of age and 2 or more years apart were included in the analysis.

Results: Six patients met the study inclusion criteria. The mean patient age ± SD in years at the first and last measurements was 7.00 ± 5.92 (range 0.42–15.00) and 15.50 ± 7.71 (range 7.00–25.00), respectively. The mean SER ± SD at the first and last measurements was -0.58 D ± 7.76 D (range 7.75 D – -13.19 D) and -5.05 D ± 9.61 D (range 3.88 D – -22.94 D), respectively, with an average change in refraction of -4.47 D (range 0.875 D– -9.75 D). Five patients had genotypes consistent with previously described OPN1LW and OPN1MW mutations associated with BCM. One patient had a novel R151T inactivating mutation; this particular mutation demonstrated the highest myopic average SER at the first and last measurements of -13.19 D and -22.94 D, respectively, and the highest average change in refraction of -9.75 D.

Conclusions: Although BCM is commonly associated with myopia, refractive error in this population may vary, with some patients exhibiting hyperopia. However, refractive error generally trended towards increased myopia as patients aged. The R151T variant demonstrated the most severe myopic changes, suggesting that specific genetic mutations may contribute to the degree of myopic progression in BCM.

CONTROL ID: 3707628

SUBMITTER (NAME ONLY): Gregory Tsougranis

TITLE: Optical Coherence Tomography (OCT) Features Associated with Three-Year Changes in Microperimetry Sensitivity in Age-related Macular Degeneration (AMD)

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Tsougranis, I. Lains, A. Nigalye, R. Katz, T. Koch, I.K. Kim, D.G. Vavvas, J.B. Miller, J.W. Miller, D. Husain, Retina Service, Harvard Medical School, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|K.M. Mendez, J. Lasky-Su, Channing Division of Network Medicine, Harvard Medical School, Brigham and Women's Hospital Department of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Average retinal sensitivity measured by microperimetry may be a more sensitive measure of disease progression than standard visual acuity in patients with dry age-related macular degeneration (AMD). Several optical coherence tomography (OCT) structural parameters have been associated with decreased retinal sensitivity across all stages of AMD. However, limited longitudinal work has been published to date. This study aimed to evaluate associations between baseline OCT structural parameters and changes in average retinal sensitivity over three years.

Methods: Prospective, longitudinal study. At baseline and 3 years later, AMD patients and controls (>50 years old) were imaged with color-fundus photographs used for AMD staging (Age-Related Eye Disease Study scale) and spectral domain OCT (Spectralis, Heidelberg, Germany). OCT features were graded by two independent graders using a pre-established protocol. MAIA microperimetry (Centervue, Italy) was used to assess retinal sensitivity, using a full-threshold 37-point protocol (10 degrees diameter). Univariable and multivariable mixed-effect linear regression models were utilized for data analysis.

Results: We included data from 43 eyes with AMD and 22 eyes from age-matched controls. A diagnosis of early AMD at baseline was associated with decreased average retinal sensitivity three years later (p=.03). No associations were found between baseline intermediate or late AMD stages and changes in average retinal sensitivity at three years. Accounting for confounding factors, among the baseline OCT features assessed, the presence of ellipsoid disruption was associated with decreased average retinal sensitivity at three years (p= .04, β= -5.33).

Conclusions: Among several OCT features commonly seen in patients with AMD, the presence of ellipsoid zone disruption at baseline was associated with a decrease in average retinal sensitivity at three years. These results support retinal sensitivity measured by MAIA microperimetry as a potentially useful functional measure in the care of patients with AMD. Longitudinal structure/function correlations like these may improve our ability to provide prognostic information in AMD.

CONTROL ID: 3707629

SUBMITTER (NAME ONLY): Constantin von Medem

TITLE: Long-term results of postoperative viscoelastic installation after trabeculectomy for hypotension management

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. von Medem, M. Saeger, B. Noelle, J. Roider, Christian-Albrechts-Universitat zu Kiel Medizinische Fakultat, Kiel, Schleswig-Holstein, GERMANY|

Commercial Relationships Disclosure: Constantin von Medem: Commercial Relationship: Code N (No Commercial Relationship) | Mark Saeger: Commercial Relationship: Code N (No Commercial Relationship) | Bernhard Noelle: Commercial Relationship: Code N (No Commercial Relationship) | Johann Roider: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Anterior chamber viscoelastic installation is a common procedure for postoperative hypotension after trabeculectomy with mytomycin C (TET). It increases the intraocular pressure (IOP) by reducing flow through the scleral flap. However, it could be supposed that this reduced flow within the critical postoperative healing phase could negatively affect the overall outcome. Therefore, we investigated long-term outcomes.

Methods: Retrospective study of 71 eyes with postoperative viscoelastic filling (cohesive viscoelastic, Healon) and 89 eyes (control group) that underwent TET between 2008-2016. We compared Best-Corrected Visual Acuity (BCVA), IOP, number of antiglaucomatous eye drops and the potential need of an additional operation at seven different times (pre-op, post-op, year 1-5). Failing criteria were defined as the occurrence of one or more of the following: IOP greater than 21mmHg, IOP lower than 5 mmHg, less than 20% reduction of the IOP compared to baseline or the need of an additional IOP-lowering intervention.

Results: The average IOP at baseline was 27.3 mmHg in the Healon group and 24.8 mmHg in the control group (p=0.082). One year after TET, the IOP was reduced to 14.1 mmHg in the Healon group and to 15.0 mmHg in the control group (p=0.365). The number of failed TET (see above-mentioned criteria) at year 1 was n=7 (14%) in the Healon group and n=26 (33.8%) in the control group (p=0.013).

At year 5, the mean IOP was 14.3 mmHg in the remaining 15 patients of the Healon group and 14.1 mmHg in the remaining 33 patients in the control group (p=0.868). The number of failures at year 5 was n=3 (20.0%) in the Healon group and n=11 (33.3%) in the control group (p=0.346).

The need of topic antiglaucomatous medication after operation was reduced from 3.0 to 0.6 (year 1) and 1.4 (year 5) in the Healon group and from 3.0 to 1.0 and 1.4 in the control group (p=0.07 year 1, p=0.851 year 5).

Conclusions: This data shows that the postoperative installation of Healon is a safe way to treat hypotension after TET. Also during a 5 year follow-up no significant difference in BCVA, IOP, antiglaucomatous eyedrops and re-operations could be found between the two groups. Additionally, the number of failures defined due to the above mentioned criteria do not show a significant difference between both groups. Based on this data, Healon does not have a negative effect on the long-term outcome of TET.

CONTROL ID: 3707635

SUBMITTER (NAME ONLY): Mengxi Shen

TITLE: Choroidal Changes in Eyes with Exudative AMD Before and After Anti-VEGF Therapy Imaged with Swept-Source OCT

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shen, X. Jiang, O. Trivizki, R. Laiginhas, J. Liu, J. Li, W.J. Feuer, G. Gregori, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|H. Zhou, Q. Zhang, R.K. Wang, University of Washington, Seattle, Washington, UNITED STATES|L. De Sisternes, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Swept-source optical coherence tomography (SS-OCT) was used to investigate choroidal changes after anti-vascular endothelial growth factor (anti-VEGF) therapy in eyes with exudative age-related macular degeneration (eAMD) that contained three types of macular neovascularization (MNV).

Methods: Treatment-naïve eyes with eAMD undergoing anti-VEGF therapy were included. SS-OCTA images (PLEX® Elite 9000; Carl Zeiss Meditec, Inc, Dublin, CA) were obtained at the first treatment and after anti-VEGF injections. Mean choroidal thickness (MCT) and choroidal vascularity index (CVI) measurements in both 5mm and 11mm foveal centered circles were obtained from the 12X12mm scans. If the choroidal signal was blocked from overlying retinal pigment epithelial detachments (PEDs) or hemorrhage, then these areas were excluded from the CVI measurements. If more than 10% of the 5mm circle region was blocked, then these eyes were excluded from the CVI analysis.

Results: A total of 41 treatment-naïve eAMD eyes from 37 patients were included: 24 eyes with type 1 MNV, 4 eyes with type 2 MNV, and 13 eyes with type 3 MNV. All eyes had two visits that included the day of the first treatment and the first visit after treatment. Seven eyes were excluded from the CVI analysis. For all eyes, the MCT and CVI decreased in both the 5mm and 11mm circles after treatment ($P<0.05$) compared with the first treatment visit. In eyes with both type 1 and type 2 MNV, the decrease in the MCT within the 5mm ($P<0.05$) and 11mm circles ($P<0.05$) were statistically significant, but in eyes with type 3 MNV, the decrease in the 5mm circle MCT was not significant ($P=0.32$), while there was a significant decrease in the 11mm circle after treatment ($P<0.05$).

Conclusions: Due to the decrease in the central MCT observed in eyes with type 1 and type 2 MNV, but not type 3 MNV, we propose that at baseline, the type 1 and type 2 MNV lesions serve as high-volume arteriovenous shunts between the choroidal arterial and venous circulations. Anti-VEGF therapy causes a decrease in exudation and a decrease in flow within the arteriovenous shunt that would exist in any type 1 or type 2 MNV while this type of central choroidal arteriovenous shunt would not exist in the intra-retinal type 3 MNV.

CONTROL ID: 3707636
SUBMITTER (NAME ONLY): Jeffrey Levenson
TITLE: APP13007 (Clobetasol Propionate Ophthalmic Nanosuspension) for the Treatment of Inflammation and Pain after Cataract Surgery
SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Levenson, Levenson Eye Associates, Jacksonville, Florida, UNITED STATES|T.R. Walters, Keystone Research, Austin, Texas, UNITED STATES|J. Martel, Martel Eye Medical Group, Rancho Cordova, California, UNITED STATES|L. Wang, AimMax Therapeutics, Inc., Durham, North Carolina, UNITED STATES|D. Nunez, AimMax Therapeutics, Inc., Durham, North Carolina, UNITED STATES|
Commercial Relationships Disclosure: Jeffrey Levenson: Commercial Relationship(s);Code F (Financial Support):Formosa Pharceuticals Inc | Thomas Walters: Commercial Relationship(s);Code F (Financial Support):Formosa Pharmaceuticals Inc | Joseph Martel: Commercial Relationship(s);Code F (Financial Support):Formosa Pharmaceuticals Inc | Laurene Wang: Commercial Relationship(s);Code E (Employment):AimMax Therapeutics Inc | Derek Nunez: Commercial Relationship(s);Code E (Employment):AimMax Therapeutics Inc
ABSTRACT BODY:
Purpose: To evaluate the safety and efficacy of APP13007 0.05% twice daily (BID) after cataract surgery in a Phase 2 double-masked, placebo-controlled study.
Methods: Subjects with inflammation on the first post-operative day (POD1) following routine, uncomplicated cataract surgery were randomized (1:1) to receive 1 drop of APP13007 0.05% or placebo BID (morning and evening) in the study eye for 21 days. Subjects were evaluated on PODs 4, 8, 15, 22 and 28.
Results: Forty-five (45) male/female subjects (mean age 67.7 yrs, 71.1% females and 73.3% white) were randomized to receive APP13007 (APP) (N=22) or placebo (PBO) (N=23). Subject demographics were comparable between the two groups. Seven (7) subjects discontinued the study before POD22: 1 on APP was withdrawn due to an AE (moderate photophobia and eye pain); 3 on PBO were rescued and 3 on PBO were withdrawn for other reasons.

APP was well-tolerated with a safety profile similar to placebo. There were no treatment-emergent SAEs. The most common AEs were ocular disorders commonly reported after cataract surgery (mild to moderate severity; more frequent in the PBO group). There were no AEs related to IOP elevations, no individual IOP was > 21 mmHg and no IOP elevations were > 10 mmHg while on APP13007.

A higher percent of subjects receiving APP achieved ACC count/Grade = 0 at POD8 sustained through POD22 when compared to PBO. Subjects reporting ocular pain at POD1 had rapid resolution on treatment. When compared to PBO, a higher percent of subjects receiving APP had complete resolution of ocular pain at POD4 sustained through POD22. In addition, visual acuity appeared to improve more rapidly in subjects receiving APP compared to PBO.

Number (%) of Subjects with ACC Count/Grade = 0 at a Visit Sustained to POD22:
POD1 (Baseline): APP = 0; PBO = 0
POD4: APP = 0; PBO = 0
POD8: APP = 7 (31.8%) *; PBO = 1 (4.3%)
POD15: APP = 15 (68.2%) *; PBO = 7 (30.4%)

Number (%) of Subjects with Ocular Pain Grade = 0 at a Visit Sustained to POD22:
POD1 (Baseline): APP = 6 (27.3%); PBO = 6 (26.1%)
POD4: APP = 16 (72.7%); PBO = 11 (47.8%)
POD8: APP = 18 (81.8%); PBO = 13 (56.5%)
POD15: APP = 21 (95.5%) *; PBO = 15 (65.2%)

* $p < 0.05$ (Pearson Chi-Square test)
Conclusions: These data support the development of APP13007 0.05% BID to treat inflammation and pain following ocular surgery.

CONTROL ID: 3707637

SUBMITTER (NAME ONLY): Harald Junge

TITLE: A Norrin mimetic restores vascular and neural functions in Tspan12 mutant mice

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.J. Junge, M. Abedin, H. Jo, J. Levey, Q. Dinh, L. Zhang, OVNS, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|Z. Chen, Neuroscience, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|S. Angers, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Norrin/Frizzled4 signaling plays an important role in the development of retinal blood vessels, blood-retina barrier (BRB) function, and ultimately retinal function. We recently reported that the antibody-based Norrin mimetic F4L5.13, a novel agonist for Frizzled4 and LRP5, promotes angiogenesis and BRB function in the Tspan12 KO model of impaired Norrin/Frizzled4 signaling. Here, we sought to define the pharmacodynamic effects of the agonist in the presence or absence of vascular malformations, determine if the agonist restores visual function, monitor gene expression responses in multiple retinal cell populations, and determine the duration of its barrier promoting effects after intraperitoneal or intravitreal administration.

Methods: ERG, fluorescein angiography, single cell RNA-sequencing, immuno-staining of vascular endothelial cells, and staining with pimonidazole/hypoxyprobe were performed after F4L5.13 administration to Tspan12 systemic KO mice. In addition, Tspan12 endothelial-cell-specific KO mice (ECKO) were generated by activation of Cdh5-CreERT2 at P28, resulting in a BRB disease model without vascular malformations. Effects of F4L5.13 on BRB function in Tspan12 ECKO mice were monitored longitudinally using fluorescein angiography.

Results: Administration of F4L5.13 from P6-28 fully restored the ERG b-wave in Tspan12 KO mice, restored angiogenesis and BRB function, alleviated hypoxia, and largely restored gene expression profiles in the neuroretina of Tspan12 KO mice. Administration after P28 did not restore the ERG b-wave, revert vascular malformations, or establish normoxia, but it resulted in substantial restoration of BRB function. In adult Tspan12 ECKO mice without vascular malformations, F4L5.13 restored BRB function efficiently, and a single intravitreal injection suppressed BRB phenotypes for 2-4 weeks.

Conclusions: Vascular malformations in Tspan12 KO mice, once developed, cannot be resolved by F4L5.13, yet, the agonist partially promotes BRB function even in the malformed vasculature. When F4L5.13 is administered before vascular malformations have formed, it induces the development of a normal vasculature, restores the ERG, and normalizes gene expression profiles. In the Tspan12 ECKO model of BRB dysfunction without vascular malformations, F4L5.13 demonstrates excellent efficacy in promoting BRB function, even after a single intravitreal injection.

CONTROL ID: 3707638

SUBMITTER (NAME ONLY): Maria Pilar Martin Gutierrez

TITLE: ABCA4-alleles bearing two rare cis-variants comprise a significant proportion of those found in affected patients.

SESSION TITLE: Retinal Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Pontikos, M. Simcoe, M. Michaelides, G. Arno, O.A. Mahroo, A.R. Webster, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Martin Gutierrez, S. Vermeirsch, N. Pontikos, M. Michaelides, G. Arno, O.A. Mahroo, A.R. Webster, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Biallelic pathogenic variants in the ABCA4 gene cause a significant proportion of inherited retinal disease worldwide. High allelic heterogeneity partly explains the wide variability in visual outcomes in affected patients. Understanding the pathogenicity of individual alleles is confounded by the co-occurrence on one chromosome of two or more rare variants. Such ‘complex alleles’, due to linkage disequilibrium, often occur in many unrelated probands. Here we explore this phenomenon in a large cohort of molecularly solved and phased probands.

Methods: Patients with genetically confirmed ABCA4-retinopathy seen at a single centre were included. We sought those with 3 or more rare variants; either variants with proven pathogenicity or else rare missense variants, including those scored individually as variants of uncertain pathogenicity (VUP). The reported complex alleles that comprise c.5603A>T, p.(Asn1868Ile) (allele frequency 4%) are the subject of a separate study and not included here.

Results: The full cohort comprised 925 patients. Of these, 106 patients (11.4%) carried 3 protein altering rare variants, and 12 (1.3%) carried 4, such alleles comprising 7% of all disease-associated chromosomes, occurring in 118/925 probands. The most common was c.[1622T>C;3113C>T] (p.[Leu541Pro;Ala1038Val]) accounting for 39 alleles in 36 probands. The allele c.[634C>T;5882G>A] (p.[Arg212Cys;Gly1961Glu]) occurred on 10 alleles of 10 patients of African descent, c.[4222T>C;4918C>T] (p.[Trp1408Arg;Arg1640Trp]) and c.[2588G>C;1715G>A] (p.[Gly863Ala;Arg572Gln]) occurred in 9 and 6 alleles in European patients, respectively, and did not include c.5603T.

Conclusions: Our results show that a significant proportion of patients have complex alleles in which two or more disease-associated variants may be found together. The reporting of such alleles, will help in the scoring of genotypes by clinical labs, reducing those instances in which two variants might be assumed to be in trans, particularly when relatives are unavailable for phasing. The modification of some variants by others occurring in cis will become evident with increasing phased genotypic data from affected patients.

CONTROL ID: 3707639

SUBMITTER (NAME ONLY): Amy Stark

TITLE: Prostanoids are elevated and serve as inflammatory stimuli in diabetes-relevant retinal inflammation in vitro

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Stark, J. Penn, Pharmacology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|J. Penn, Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Amy Stark: Commercial Relationship: Code N (No Commercial Relationship) | John Penn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Evidence since the 1960s indicates retinal inflammation may drive early diabetic retinopathy (DR) progression in a cyclooxygenase (COX)-dependent manner. However, trials of nonsteroidal anti-inflammatory drugs (NSAIDs) as DR treatments have failed largely due to severe cardiovascular and gastrointestinal side effects associated with chronic, broad-spectrum COX inhibition by NSAIDS. Prostanoids, signaling lipids downstream of COX, may offer specific targets for DR therapies that circumvent NSAID side effects. We investigated the prostanoids elevated by DR-relevant inflammation and determined their effects as inflammatory stimuli in select human retinal cells.

Methods: Human Müller cells (hMC) and retinal microvascular endothelial cells (hRMEC) were treated with 1ng/ml IL-1β or control for 24hrs, then media were harvested for mass spectrometry of prostaglandins PGD_2, PGE_2, $PGF_{2\alpha}$, prostacyclin PGI_2, and thromboxane TXA_2. hMC and hRMEC were treated with 1nM-10μM doses of PGE_2, $PGF_{2\alpha}$, or cicaprost (PGI_2 analog) with controls for 6hrs before lysis for qRT-PCR analysis of cytokine or adhesion molecule gene expression.

Results: Mass spectrometry demonstrated increases of 2124% for PGE_2 ($p<0.001$), 615% for $PGF_{2\alpha}$ ($p=0.001$), and 375% for 6-keto-$PGF_{1\alpha}$ (PGI_2 metabolite; $p<0.001$) in IL-1β-treated hMC vs. control. In IL-1β-treated hRMEC, $PGF_{2\alpha}$ increased 288% ($p<0.001$) and 6-keto-$PGF_{1\alpha}$ decreased 66.7% ($p=0.007$) vs. control. 10nM treatments of PGE_2 ($p=0.042$), $PGF_{2\alpha}$($p=0.041$), or cicaprost ($p<0.001$) significantly elevated IL1B expression in hMC. IL6 and CXCL8 also increased dose-dependently. Elevation of ICAM1 in hRMEC was elicited by 1μM $PGF_{2\alpha}$ ($p=0.035$) or 10μM PGE_2 ($p=0.015$), similar for VCAM1 and SELE (E-selectin). Notably, 1μM cicaprost decreased SELE 42.1% ($p=0.035$) while VCAM1 and ICAM1 were not altered.

Conclusions: Our results indicate that IL-1β-induced inflammation of hMC and hRMEC alters the secretion of prostanoids PGE_2, $PGF_{2\alpha}$, and PGI_2. In hMC, stimulation by these prostanoids elevates proinflammatory cytokine gene expression. In hRMEC, PGE_2 and $PGF_{2\alpha}$ elevate gene expression of adhesion molecules, whereas PGI_2 reduces SELE expression, potentially yielding an anti-inflammatory effect. Specific modulation of PGE_2, $PGF_{2\alpha}$, and/or PGI_2 signaling in the retina may be beneficial in slowing early DR progression in a targeted manner, eliminating adverse effects of broad-spectrum COX inhibition.

CONTROL ID: 3707640

SUBMITTER (NAME ONLY): Suzanne Daly

TITLE: Evaluation of lenticular and zonular changes in patients with Marfan syndrome using ultrasound biomicroscopy

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Daly, D. Coleman, R.H. Silverman, A.H. Abdelhakim, L. Park, I.H. Maumenee, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Marfan syndrome (MFS) is a connective tissue disorder with manifestations in the cardiovascular, musculoskeletal and ocular systems. MFS affects approximately 1:3,000 people; it is inherited in autosomal dominant fashion, caused by mutations in the FBN1 gene on chromosome 15. The ocular features consist of lens dislocation, increased axial length, presenile cataract formation, open angle and phacolytic glaucoma, and retinal detachments. The purpose of this study is to evaluate the utility of ultrasound biomicroscopy (UBM) in quantifying lens subluxation and zonular stability.

Methods: We conducted a retrospective review of UBM exams of 8 eyes of 4 patients with MFS aged 21-43 years; diagnosis was confirmed using Ghent II criteria. Eight eyes of 4 age-matched normal patients in our database were measured for comparison. Examinations were performed using Quantel Aviso UBM system with 50 MHz probe. We measured anterior chamber (AC) depth, lens thickness, anterior radius and displacement from the pupil center as well as appearance of the zonules.

Results: Central AC depth averaged 2.59±0.39 mm in MFS versus 2.92±0.38 mm in controls. Lens thickness averaged 4.3±0.6 mm in MFS patients versus 3.9±0.4 for controls and the anterior radius of curvature averaged 6.3±2.1 mm in MFS versus 9.8±1.5 mm in controls. The difference in anterior lens radius from controls was statistically significant (p=.002). The lens was displaced superonasally in 3 eyes, superotemporally in 1 eye and inferotemporally in 2 eyes. There was no displacement in 2 eyes. Zonules were enhanced in all MFS eyes compared to normals, particularly in the quadrant opposite to the direction of lens displacement or herniation.

Conclusions: MFS patients on average showed decreased central AC depth. The lens tended to be greater in thickness than in age-matched controls and its anterior radius was significantly reduced. Ectopia lentis is a diagnostic criterion of MFS and many patients will undergo lens extraction, which may be complicated by weakened zonular support. UBM can be a useful adjunct in evaluating zonular stability and lens size and subluxation.

CONTROL ID: 3707641

SUBMITTER (NAME ONLY): Nadezda Stepicheva

TITLE: Looking for hidden cues: can the function of the moonlighting ocular protein βA3/A1-crystallin be regulated by the signals hidden in its coding sequence?

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.A. Stepicheva, V. Koontz, P. SHANG, H. Liu, S. Ghosh, A. Strizhakova, O. Chowdhury, R. Daley, S.L. Hose, D. Sinha, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|E. Volkova, Pervyj Moskovskij gosudarstvennyj medicinskij universitet imeni I M Secenova, Moskva, Moskva, RUSSIAN FEDERATION|J.S. Zigler, D. Sinha, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: βA3/A1-crystallin (encoded by Cryba1) plays a structural role in the lens but has non-structural functions in the retinal pigment epithelium (RPE). Several isoforms of βA3/A1-crystallin exist, including two peptides (A3 and A1) produced from the same full-length mRNA by leaky ribosomal scanning and a truncated isoform produced from mRNA lacking exon 4. We hypothesize that such isoform plasticity represents a unique mechanism of precise regulation of βA3/A1-crystallin function.

Methods: Phylogenetic analysis of the βA3/A1-crystallin sequence was performed using GeneTree (Ensembl, ENSGT00940000159685). NetPhos3.1 was used for predicting phosphorylation sites. RPE flatmounts and whole lenses (from C57Bl/6J mice) and HPV16 E6/E7 cells were incubated with 100 mg/mL cycloheximide for 3 hours followed by qPCR using Taqman probes designed against different exon junctions of Cryba1 mRNA.

Results: The analysis of the Cryba1 coding sequence (CDS) revealed a CCACC sequence upstream of the second translation initiation site that is used to produce the shorter A1 isoform. This sequence might represent a KOZAK sequence that is “hidden” within the Cryba1 CDS to drive leaky ribosomal scanning. Strikingly, this “hidden” KOZAK translates into threonine residues, which are predicted to be phosphorylated by protein kinase C (PKC, NetPhos score 0.835) and are highly conserved in mammals, except for Marsupials. We also found that the truncated peptide translated from mRNA lacking exon 4 might be produced only to be degraded by nonsense-mediated decay (NMD). Treatment of immortalized mouse RPE cells (but not freshly extracted RPE or lens) with NMD inhibitor cycloheximide, resulted in a reduced proportion of Cryba1 mRNA transcripts that include exon 4, suggesting that NMD may be a primary mechanism involved in shutting down Cryba1 expression as occurs in RPE cell lines.

Conclusions: The finding that the “hidden” KOZAK might not only be responsible for the emerging of a shorter, functionally different A1 isoform but also translates into potentially phosphorylatable threonines may reveal an elegant way to regulate protein function at multiple levels. NMD might offer an additional layer of regulation of Cryba1 expression, however, its mechanism and possible benefits are yet to be studied.

CONTROL ID: 3707642

SUBMITTER (NAME ONLY): Ellen Aagaard

TITLE: Single-Cell Isolation of Morphologically Distinct Cultured Adult Retinal Ganglion Cells

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.J. Aagaard, C.W. Miller, Y.H. Park, B.J. Frankfort, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Ellen Aagaard: Commercial Relationship: Code N (No Commercial Relationship) | Chase Miller: Commercial Relationship: Code N (No Commercial Relationship) | Yong Park: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Frankfort: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Single cell resolution provides insight into a cell's biology. Current methods that provide high throughput isolation of cells are limited to dissociated cells, often at the cost of important morphological features. Thus, methods that allow for the rapid isolation of single cells according to their morphological phenotype are valuable. Previously, our lab successfully isolated and cultured adult retinal ganglion cells (RGCs) from mice and found a wide range of neurite outgrowth capacity. To understand the molecular mechanisms by which certain RGCs inherently regenerate, we have implemented a magnetic microraft array system (QIAscout) to efficiently isolate cells according to morphology.

Methods: Retinas from 6-12-week old transgenic mice expressing tdTomato in Vglut2-Cre+ cells were dissociated and incubated with CD90.2-APC antibody. Cells were sorted using Fluorescence-Activated Cell Sorting (FACS) to isolate RGCs. Following FACS, cells were stained with RBPMS, an RGC-specific marker, to determine purity. Sorted RGCs were seeded onto 96-well plates and onto 200μm^2 microraft arrays, where they were cultured in RGC medium for 7 days. Prior to collection of RGCs, viable cells were stained with Calcein-AM and imaged to identify their distinct morphologies. Each microraft, carrying a single Calcein-AM+/tdTomato+ cell, was extracted using the QIAscout system and subsequently placed in a lysis buffer and stored at -20°C. Images were captured of each raft before, after, and during collection.

Results: FACS collected cells were highly enriched for RGCs, and 99.3% of tdTomato+/APC+ cells were immunolabeled with RBPMS. Additionally, these cells were successfully cultured and showed neurite outgrowth. Using the QIAscout system, viable RGCs were collected at a rate of 1 cell per 3 minutes. Morphologically distinct groups of RGCs were collected according to four general patterns of neurite extension: 1. No neurite outgrowth; 2. Single neurite; 3. Multiple neurites; 4. Complex/branching neurites.

Conclusions: Using the QIAscout system, our lab has successfully collected individually cultured RGCs by their morphological phenotype at an efficient and reproducible rate. Further single cell transcriptomic profiling can be performed on our morphologically distinct populations to provide insight as to why certain cells are more resilient and capable of higher levels of innate neurite outgrowth.

CONTROL ID: 3707645

SUBMITTER (NAME ONLY): Natarajan Perumal

TITLE: Thealoz® Duo eye drops protect the ocular surface of dry eye patients by breaking the inflammatory vicious cycle

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Perumal, E. Jeong, S. Runde, D. Wolter, C. Manicam, N. Pfeiffer, F. Grus, Experimental and Translational Ophthalmology, Universitatsmedizin der Johannes Gutenberg-Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|

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ABSTRACT BODY:

Purpose: Topically administered lubricants are fundamental for treating dry eye syndrome (DES). In this study, the protective mechanism conferred by the Thealoz® Duo eye drops was investigated in dry eye patients by longitudinal clinical examination and, subsequently, the tear proteome changes were characterized employing the mass spectrometry-based proteomics approach.

Methods: A total of 58 participants underwent thorough DES diagnostic steps, namely the ocular surface disease index (OSDI) and, were divided into dry eye (DRY, N=35) and healthy (CTRL, N=23). Only participants in the DRY were subjected to administration of the Thealoz® Duo (hyaluronic acid 0.15% and trehalose 3%). All participants in both groups were scheduled for clinical investigation before the application (day 0, T1) of the Thealoz® Duo and after day 28 ± 4 (T2) and day 56 ± 4 (T3). Descriptive statistical analysis of all the clinical attributes of the participants were investigated. Next, 174 individual tear samples from both groups at three time-points were subjected to proteomics and in-silico bioinformatics analyses.

Results: Application of Thealoz® Duo significantly improved the OSDI score in DRY at T2 vs. T1 ($p=4.1E-3$) and T3 vs. T1 ($p=2.0E-5$) as well as many visual analogue scale parameters. Proteomics analysis resulted in identification of 649 tear proteins (FDR<1%) and 144 were found to be significantly ($p<0.05$) differently abundant between the designated groups. Bioinformatics analysis revealed that in DRY vs. CTRL at T2 due to the usage of the Thealoz® Duo resulted in heightened molecular processes involved in glycolysis ($p=2.3E-5$), cellular homeostasis ($p=2.4E-3$), acute phase response ($p=4.9E-3$), actin cytoskeleton signaling ($p=8.5E-3$) and inhibition of apoptosis ($p=4.1E-4$). The hallmark of this study was that the activated inflammatory process in DRY vs. CTRL at T1 ($p=9.7E-4$) and T2 ($p=8.7E-4$) was inhibited at T3 of Thealoz® Duo use.

Conclusions: In summary, this clinical investigation ascertained that the continual application of Thealoz® Duo significantly improved vision-related functions in DES patients. Notably, for the first time, the proteomics analysis unraveled novel mechanistic changes and expression of specific markers attributed to the efficacy of Thealoz® Duo in breaking the vicious cycle of inflammation and promoting the restoration of homeostasis on the ocular surface of DES patients.

CONTROL ID: 3707646

SUBMITTER (NAME ONLY): Mohamed Abdouh

TITLE: Filtering blue light mitigates the deleterious effects induced by the oxidative stress in primary human retinal pigment epithelial cells

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Abdouh, M. Lu, Y. Chen, A.A. Goyeneche, J.V. Burnier, M.N. Burnier, Research Institute of the McGill University Health Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a major cause of blindness in the elderly population. It is characterized by the loss of central vision due to damaged retinal pigment epithelium (RPE) cells and photoreceptors. Blue Light (BL) exposure was proposed as a risk factor for AMD progression as it triggers RPE cell loss. We undertook this study to determine the effects of BL on the behaviour of RPE cells and their potential mitigation by BL-filtering intraocular lenses (IOL).

Methods: A2E-loaded ARPE-19 cells and human eye-isolated primary RPE cells were exposed or not to BL (400 – 500 nm) under a Solar Simulator (TSS-156R, OAI) set at 100 mW/cm^2, in the absence or presence of either clear ultraviolet (UV)-filtering intraocular lenses (CIOL), or a yellow UV- and BL-filtering IOL (YIOL). RPE cells were analyzed for (i) their oxidative stress by measuring both total cellular and mitochondrial reactive oxygen species (ROS), and (ii) their viability. The involvement of ROS in the cytotoxic effects of BL was investigated following the pre-treatment of RPE cells with the antioxidant N-acetyl cysteine (NAC). All experiments were performed at least 3 times, and data were compared using an ANOVA followed by the Dunnett post-hoc test for multiple comparisons with one control group. A P value < 0.05 was considered statistically significant.

Results: We observed that RPE cells exposure to BL significantly increased the levels of both total cellular ROS ($P < 0.001$) and mitochondrial superoxide anion ($P < 0.001$). While these increases were not affected by placing the CIOL in the BL beam, YIOL decreased the levels of both ROS reservoirs ($P < 0.01$; compared to BL-exposed cells). Increased ROS production induced following BL exposure was accompanied by a significant increase in cell death ($P < 0.001$). Similarly, in contrast to CIOL, YIOL reversed the effects of BL on RPE cell viability ($P < 0.001$). Notably, pre-treatment of cells with NAC abolished the increased cell death, suggesting that the cytotoxic effects of BL on RPE cell were mainly due to increased levels of ROS.

Conclusions: Our data indicate that BL is cytotoxic to RPE cells due to increased oxidative stress. These effects were mitigated by filtering these radiations. The use of BL-filtering devices may represent a strategy to reduce the BL harmful effects on RPE cells and delay the onset of AMD.

CONTROL ID: 3707650

SUBMITTER (NAME ONLY): Michal Turkiewicz

TITLE: Primary ophthalmic hospitalizations among individuals experiencing homelessness in the United States, 2016-2018

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Turkiewicz, N. Arya, Mayo Clinic Alix School of Medicine, Mayo Clinic Minnesota, Phoenix, Arizona, UNITED STATES|A. Bhandarkar, N. Arya, M. Bydon, Department of Neurosurgery, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|J. Shen, Department of Opthalmology, Mayo Clinic Minnesota, Scottsdale, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is little data characterizing ophthalmic illness among individuals experiencing homelessness, who face health hazards distinct from the general population. We quantified rates of hospitalization for ophthalmic disease and injury among individuals experiencing homelessness in the United States, using the National Inpatient Sample(NIS) database.

Methods: We conducted a retrospective cross-sectional analysis using recent data from the NIS database(2016-2018). This database is the largest all-payor inpatient care database and provides a stratified random sample representing 97% of discharges in the United States. Individuals with primary ophthalmic illness were identified by filtering for those with an ICD-10 code related to disease of the eye or adnexa, excluding diabetic eye disease. Housing status was identified using ICD-10 codes for homelessness. Data analysis was conducted using R software.

Results: The most common diagnoses among homeless individuals hospitalized for ophthalmic disease are: corneal ulcer(16.8%), orbital floor fracture(13.4%), laceration of the eyelid(9.1%), orbital cellulitis(5.9%), and endophthalmitis(2.5%). This distribution differs from the most common diagnoses among the general population. Our results show higher rates of trauma-related diagnoses among homeless individuals(38%) when compared to ophthalmic hospitalizations among the general population(23%). In addition, there is a lower proportion of optic neuritis(7.1% to 1.2%), and diplopia/visual disturbances(9.2% to 2.8%) in the homeless population compared to the general population.

Conclusions: This is the first published data on ophthalmologic illness requiring hospitalization among homeless individuals. Our study shows trauma-related hospitalizations at an increased rate among the homeless population, with lower rates of illness with neurological cause. This is attributable to homeless individuals facing greater risk of trauma and infection. An effective intervention might be the development of education materials and programs teaching causes and signs of eye trauma and infection, to enable prevention and quicker treatment.

CONTROL ID: 3707653

SUBMITTER (NAME ONLY): Palak Patel

TITLE: Scleral Buckle Removal: Long-term Patient Outcomes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Patel, A. Shepherd, V. Chaturvedi, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Scleral buckling has been a successful course of management for repairing primary rhegmatogenous retinal detachments. Occasionally, patients require their removal. While outcomes in this subset of patients have been investigated, there have not been any large patient series to be able to reach any conclusions. Long term sequelae of scleral buckle (SB) removal is debated in the literature, specifically around the risk of re-detachment. We performed a retrospective observational study evaluating the clinical indications for and outcomes following scleral buckle removal.

Methods: A retrospective chart review of 87 patients with history of SB removal between June 1st, 2000 and January 1st, 2021 at a large academic center and associated private retina practice in Chicago, IL was completed. Exclusion criteria included unplanned or self-explanted scleral buckle removal. Primary outcomes measured include patient symptoms prior to SB removal, indications for removal, resolution of symptoms following removal, rate of redetachment, rate of additional ocular surgery, and changes in visual acuity and intraocular pressure. Secondary outcomes will include identifying factors associated with poorer outcomes.

Results: A total of 87 eyes with history of SB removal were included with an average follow-up of 4 years. About 60% were males and the mean age at the time of SB removal was 58 years. The leading indications for removal were exposure (53 eyes, 60.9%), infection (18 eyes, 20.7%), and diplopia/strabismus (17 eyes, 19.5%). The average time from SB placement to removal was 12.1 years (SD ±11.2). Most patients presented with symptoms, specifically of pain and discomfort (57 eyes, 65.5%), diplopia (19 eyes, 21.8%), and drainage/discharge (16 eyes, 18.4%). Of these patients, 92.7% experienced symptom resolution following SB removal. Notably, only 5.75% of all eyes (5 eyes) experienced a re-detachment requiring surgery. Within this subset, the average time from SB placement to removal was 1.87 years (SD ±1.78) and time to re-detachment following removal was 13.0 months (SD ±23.2 months). Nine percent of all eyes required additional strabismus or oculoplastic surgery.

Conclusions: Overall, our review demonstrates that the removal of scleral buckle provides a high rate of symptomatic relief and low risk of subsequent detachment. Nonetheless, close monitoring is warranted to monitor for a recurrent retinal detachment.

CONTROL ID: 3707655

SUBMITTER (NAME ONLY): Rohan Chawla

TITLE: A novel, minimally invasive implant for intraocular drug delivery

SESSION TITLE: Drug delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Chawla, L. Moksha, T. Velpandian, S. Kashyap, Ophthalmology, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|D. Kalyanasundaram, J. Bhattacharyya, A. Phour, Biomedical Engineering, Indian Institute of Technology Delhi, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Patients undergoing intravitreal injections experience pain as the needle courses through the unanaesthetised sclera and choroid. We describe the design, development and in-vivo testing in a rabbit model of a titanium implant that allows for intravitreal injections through the implant to minimize patient discomfort.

Methods: Computer aided design of the novel implant was rendered using Solidworks®. Anodized Grade 5 titanium alloy (TiAl6V) implants were machined by conventional turning of blank rods. The holes and slots were machined using a drill press while the conical end of the implant was created by shaping tool. The implant was hand polished using 500 grit sandpaper followed by 1000 grit sandpaper. Both ex-vivo testing of the implant in enucleated goat's eye as well as in-vivo validation in 4 rabbit eyes was carried out. The implant was placed through the pars plana via a minor surgical procedure and was sutured to the sclera and covered with conjunctiva. Subsequent intravitreal injections were administered under topical anaesthesia with a 30 gauge needle through the implant, thus delivering the drug directly into the vitreous cavity. Repeated intravitreal injections were administered every 2 weeks via the implant for 3 months in 4 rabbits. The implants were removed at 5 months and the scleral wound was sutured. One eye was enucleated for histopathological evaluation.

Results: There was no complication during the implantation. Post-implantation, eye opening of rabbits was normal. Subsequent intravitreals were easy to administer. No efflux was observed during injection. Focal cataract adjacent to the implant was observed in 1 rabbit. Complications such as vitreous haemorrhage, retinal detachment or endophthalmitis were not observed. There was no focal erosion of conjunctiva. Following explantation the sclera and overlying conjunctiva healed well. Histopathological analysis did not reveal any inflammation or necrosis.

Conclusions: The current work shows the successful design and implantation of an intraocular device that can be used repeatedly for painless minimally invasive drug delivery. The in-vivo evaluation of the implant shows promising results for future animal and human studies.

CONTROL ID: 3707657

SUBMITTER (NAME ONLY): Owais Aftab

TITLE: Virtual Reality Visual Field Exam in Community Screenings During COVID-19

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.M. Aftab, R. Verma, V.P. Shah, Y. Shah, P. Tailor, A. Zhu, B. Szirth, M. Habiel, Rutgers New Jersey Medical School Institute of Ophthalmology and Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: 57.5 million people worldwide are affected by glaucoma. However, 50% of those with glaucoma are unaware, and 80% of those identified for follow-up in community screenings (CS) fail to do so. Current standards of visual field testing are usually limited to the clinic. As such, a wearable perimetry headset was used to perform Virtual Reality Visual Field Acuity (VRVFA) examination for suspected visual field loss in the community minimizing exposure to COVID-19 and the need for follow-up.

Methods: 31 subjects from 4 CS were screened by an onsite certified telemedicine reader (CR) who considered family history, visual acuity, intraocular pressures, cup-to-disc ratio, nerve fiber layer defects, and ganglion cell complex captured by non-mydriatic photography and ocular coherence tomography (OCT-B). Cataracts were also graded. Supervised VRVFA testing with a multilingual Palmscan VF2000 Analyzer (Fig.1) was performed in 6 minutes on average. Eyes with fixation losses >20% or false positive/negative ratios >0.375 were excluded. Visual field index (VFI), mean deviation (MD), pattern standard deviation (PSD), and mean sensitivity (MS) from VRVFA were compared to CR glaucoma referral and cataract grading. Descriptive statistics, independent samples t-tests, and Mood's median tests were performed. Subjects with positive findings underwent same-day robotic glaucoma specialist telepresence evaluation.

Results: 37 eyes from 31 subjects met inclusion criteria (mean age 51.42 ± 14.57 years, 56.76% male, 94.59% Hispanic). 7 (18.92%) eyes were referred for glaucoma evaluation. Glaucoma referrals had significantly different VFI (66.86% vs 86.40%, p=0.027), MD (-9.60 vs -4.04, p=0.031), and MS (19.94 vs 26.01, p=0.027) (Fig. 2). 30 (81.08%) eyes were 0-1+ in cataract grading, 5 (13.51%) were 2-3+, and 2 (5.41%) were intra-ocular lenses (IOL); respectively, these subgroups were not significantly different in VFI (84.20% vs 92.80% vs 35.00%, p=0.147), MD (-4.70 vs -2.11 vs -18.41, p=0.147), PSD (3.52 vs 2.25 vs 9.69, p=0.053), or MS (25.38 vs 27.75 vs 9.91, p=0.147) (Fig. 2).

Conclusions: VRVFA testing yielded valuable information on the extent of vision loss as a supportive screening tool for glaucoma congruent with referrals. Expanded testing is needed. Future studies may evaluate VRVFA utility in evaluating other peripheral vision threatening diseases.

CONTROL ID: 3707658

SUBMITTER (NAME ONLY): Ana Ripolles-Garcia

TITLE: Triple drug immunosuppression for xenotransplantation of human photoreceptor precursor cells in the canine retina.

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ripolles-Garcia, N. Dolgova, S. Savina, O. Garden, G.D. Aguirre, W.A. Beltran, Division of Experimental Retinal Therapies, Department of Clinical Sciences and Advanced Medicine, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|M. Phillips, A. Ludwig, S. Stuedemann, D.M. Gamm, Waisman Center, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|M. Phillips, A. Ludwig, D.M. Gamm, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|J. Wolfe, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect of a systemic multidrug immunosuppressive protocol on the survival and integration of hESC-derived photoreceptor precursor cells (PRPCs) transplanted into the subretinal space (SRS) of normal and degenerated canine retinas.

Methods: Stage 2 retinal organoids (day 104-151 of differentiation) were generated from a CRX-tdTomato reporter line (WA09 CRX+/tdTomato, WiCell, Madison, WI) and dissociated to produce cell suspension containing fluorescent PRPCs for subretinal injection in 7 normal (12 eyes) and 3 mutant (rcd1/PDE6B) dogs (6 eyes) using a modified subretinal injector (RetinaJect, SurModics, CA). Seven dogs were placed under an immunosuppressive (IS) regimen (prednisolone, cyclosporine A, mycophenolate mofetil), 2 dogs were not medicated, and 1 dog had IS halted after 20 weeks. Survival of PRPCs was monitored by non-invasive multimodal imaging including color and fluorescence photography, cSLO (NIR and BAF modes), cross-sectional and en face OCT. Following termination, survival and integration of PRPCs and involvement of innate and adaptive cellular immune responses were assessed by IHC.

Results: In dogs under IS, loss of transplanted donor cells was seen within the first week post-injection (PI) but remaining cells survived up to 20 weeks PI. In normal retinas, most donor cells remained in the SRS, while in degenerated retinas clusters of cells were found to have migrated into the host's ONL and inner retina. IHC analysis showed that most PRPCs expressed cone markers (hCA, M/L opsin) and some formed neurites and pedicle-like structures. In dogs that were not under IS, or that had IS halted, there was a rapid loss of transplanted cells. In these dogs, IHC revealed a mixed inflammatory infiltrate composed mostly of macrophages ($CD18^+$) and resident microglia ($Iba1^+$) and to a lesser extent of helper (CD4+) and cytotoxic (CD8+) T-cells as well as B-cells ($CD20^+$).

Conclusions: Our triple drug IS regimen provided long-term (up to 5 months) survival of xenotransplanted hESC-derived PRPCs into the canine retina. Additionally, our results confirmed that degenerating retinas are more suitable for integration of donor PRPCs.

CONTROL ID: 3707663

SUBMITTER (NAME ONLY): Mina Gaffney

TITLE: Assessing adaptive optics corrected visual acuity in individuals with fragmented foveal avascular zones

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gaffney, R.F. Cooper, Biomedical Engineering, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|M. Gaffney, R.F. Cooper, Biomedical Engineering, Marquette University, Milwaukee, Wisconsin, UNITED STATES|P. Tiruveedhula, W.S. Tuten, A. Roorda, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|H. Heitkotter, J. Kreis, J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Carroll, Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been suggested that individuals with a fragmented foveal avascular zone (FAZ) have altered foveal photoreceptor distributions which would impact visual function.[1] Here we sought to compare adaptive optics (AO) corrected visual acuity in individuals with fragmented FAZs to those with normal FAZ morphology.

Methods: We recruited five individuals with fragmented FAZs (2M, 3F; Age range: 12 to 45 years, Avg = 27 years) and 16 individuals with normal FAZ morphology (6M, 10F; Age range: 11 to 67 years, Avg = 28 years). Stimuli (black Snellen E's of varying sizes and orientations) were presented using a custom-built AOSLO (mean illumination wavelength 790nm, mean wavefront sensing wavelength 850nm). Individuals were asked to identify the orientation of each E in a four alternative forced-choice task. The orientation of each E was random, and the gap size of the E was driven by the individual's responses by using two interleaved QUEST procedures. Prior to initiating each measurement block, the AO operator specified the number of E's to be presented (typically 30-40 E's per block). After 7-30 (Average = 13) blocks were performed, a psychometric function was fit to the data (using the Palamedes toolbox in MATLAB). The acuity threshold was defined as the log minimum angle of resolution (logMAR) in arc minutes from the psychometric fit function which corresponded to where individuals responded with the correct orientation for 62.5% of the E's presented. Statistical analyses were performed using GraphPad Prism 9.

Results: The mean logMAR acuity for individuals with fragmented FAZs was -0.21 (0.62 MAR, 20/12.5 Snellen) with a standard deviation of 0.063 (range: -0.29 to -0.13). The mean logMAR acuity for individuals with a normal FAZ was -0.23 (0.59 MAR, 20/12 Snellen) with a standard deviation of 0.054 (range: -0.34 to -0.13). No significant difference in AO-corrected acuity estimates (defined as the psychometric fit threshold) was found between control eyes and eyes with a fragmented FAZ. (unpaired t-test; $p = 0.33$)

Conclusions: AO-corrected acuity measured at the fovea does not appear to differ between individuals with and without fragmented FAZs. Our findings are inconsistent with individuals with fragmented FAZs having altered photoreceptor distributions.

[1]PMID: 31274711

CONTROL ID: 3707664

SUBMITTER (NAME ONLY): Sven Schnichels

TITLE: Customized magnetic nanopropellers grant targeted delivery to the retina

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Schnichels, H. Mühl, M. Löscher, J. Hurst, University Eye Hospital Tübingen, GERMANY|F. Peter, V.M. Kadiri, P. Fischer, Max-Planck-Institute Stuttgart, Stuttgart, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: A major challenge in the treatment of retinal eye diseases is the delivery of therapeutic agents to the target site. Traditional intravitreal injection is based on the random, passive diffusion of molecules. Topical drug delivery to the retina is an even more complex challenge. The major hurdle for all medication or drug delivery systems is the narrow macromolecular matrix of the different ocular tissues, which act as a barrier and prevent the penetration of particles and drugs. In order to address specific cells or layers of the retina, the use of micro- or nanoparticles from biomaterial research promises targeted, biocompatible and safer applications. Previously published nanopropellers (NPs) that can be actively controlled through the vitreous body to reach the retina present a chance to reach desired targets in the retina. The propulsion takes place through the spiral shape of the magnetic NPs.

Methods: In the present study, the biocompatibility and degradability of the NPs were adjusted by using different chemical materials. The biocompatibility was evaluated with several ocular cells and cell lines, including primary porcine Müller and RPE cells as well as the 661W, Mio-M1, and ARPE-19 cell line. The changes in the chemical composition of the NPs demand a revaluation of the delivery properties. To this end, the magnetic NP function was assessed with the prior mentioned primary cells and cell lines, porcine retinal organ cultures, and eyes. To investigate the propulsion of the NPs, they were labeled with fluorescent agents for imaging and analyzed with confocal microscopy in vitro, ex vivo, and after histological preparation.

Results: Our studies on retinal cells and retinal organ cultures resulted in excellent biocompatibility of the NPs. Furthermore, since the NPs were now formed out of different degradable materials, the time of degradation could be customized. The still-intact propulsion properties were confirmed with OCT and confocal microscopy. The NPs could be controlled to and into the retina or retinal cells. Histological examinations confirmed that only the magnetic NPs arrived at the region of interest.

Conclusions: The biodegradability and the active navigation of the nanopropellers to aimed positions in the retina promise new possibilities for targeted forms of delivery and therapy.

CONTROL ID: 3707665

SUBMITTER (NAME ONLY): Stephanie Ying

TITLE: Glaucoma Care Practice Changes Triggered by the COVID-19 Pandemic: A Qualitative Study

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ying, H. Liu, S. Kamat, C. Tukel, J.B. Serle, N. Chadha, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|N. Chadha, T.T. Tai, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic led to changes in glaucoma care to ensure patient and provider safety. In this qualitative interview study, we aimed to identify changes perceived as improvements in care that have persisted, even following vaccine rollout and uptrending patient volumes after the pandemic's initial surges.

Methods: From July-December 2021, 20 of 45 (44%) NYC glaucoma specialists contacted were interviewed through semi-structured interviews, utilizing a 15 question guide while allowing for exploration of new topics. Interviews were audio-recorded, transcribed, and thematically analyzed with NVivo qualitative software.

Results: Thematic saturation was reached after 15 transcripts. Participants included 12 women and 8 men from 9 institutions, in practice for 6-41 years. When asked to rate the change their practice experienced during the pandemic's first surge on a scale of 1 to 5 (5 being the most change), physicians reported a 4.26 ± 0.94. Certain changes have persisted [Figure 1]. Almost all physicians reported that infection prevention protocols (e.g. hand washing, mask donning) remain and may persist after the pandemic subsides. 9 [45%] reported that increasing the follow-up window for stable patients (e.g. from every 4 months to 6 months) was also a persistent change. While practices initially switched to disposable tools (e.g. tonometer tips, gonioscopy lenses), 9 of 17 [53%] physicians who reported on disposable tools have continued their usage. While disposable tool usage has declined since the first wave [p value=0.003; Figure 2], physicians who continued their usage shared positive views on safety and efficiency. 8 [47%] discontinued their usage, reporting negative sentiments around inaccuracy and waste. Telemedicine was not a persistent change, with only 1 provider continuing to use telemedicine. Reported rationale for discontinuation was the inability to collect data such as intraocular pressure, visual field testing and ophthalmoscopy.

Conclusions: COVID-19 continues to impact glaucoma care. Persistent practice changes include infection prevention, extended follow-up windows and disposable tool usage, while telemedicine has largely been discontinued. As glaucoma care continues to evolve, these changes have lasting implications for continuity of care, patient safety and care delivery.

CONTROL ID: 3707666

SUBMITTER (NAME ONLY): Luis De Sisternes

TITLE: Uncertainty estimation of a geographic atrophy OCT segmentation algorithm: How do we identify cases where the algorithm may be mistaken?

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We developed a geographic atrophy (GA) segmentation model for OCT data based on deep learning. One of the main obstacles for clinical application of this automated algorithm is understanding for which specific cases we can expect reliable results and when it is likely to fail. This work proposes an approach to estimate the regional uncertainty of a deep learning segmentation model.

Methods: We generated uncertainty maps for GA segmentation using a model ensemble trained through cross-validation. As each model in the ensemble was trained with different data, observing the variance in results across them can be used to estimate epistemic uncertainty (unseen manifestations). Data augmentation in the test phase simulating different signal level conditions can estimate the aleatoric uncertainty (signal levels the model is unfamiliar with). Analyzing both sources of uncertainty, we generated maps that relate to model confidence. These maps were evaluated by analyzing the segmentation performance at different levels of uncertainty compared to two expert graders (R1 and R2), excluding from the analysis those regions with uncertainty higher than a chosen level (Figure 1).

Results: We processed 180 OCT scans (PLEX® Elite 9000, ZEISS, Dublin, CA) from GA eyes and 45 from non-GA AMD eyes. Regions of segmentation disagreement between the automated method and each grader had significantly higher values of uncertainty (Figure 2A). Automated segmentation accuracy (Dice Index) increased with lower uncertainty thresholds (excluding larger image regions from the analysis) while the comparison between two graders did not improve (Figure 2B), showing the ability of the uncertainty maps to indicate regions where the algorithm was not confident. Choosing a threshold producing a segmentation performance similar to the intergrader agreement (Dice=0.91) deemed as uncertain approximately 6% of the image on average while maintaining detection sensitivity. Uncertain regions corresponded primarily to locations without GA where the algorithm might make a false positive decision (Figure 2C).

Conclusions: We introduce a method to generate uncertainty maps for an automated GA segmentation model. These maps inform about segmentation confidence and can be used as feedback for manual review.

CONTROL ID: 3707667

SUBMITTER (NAME ONLY): Xiaoying Zhu

TITLE: Accommodative Behavior during Multifocal Soft Contact Lens Wear Can Predict Myopia Progression in Children

SESSION TITLE: Myopia: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Zhu, Z. Zlatin, D. Troilo, Biological and Vision Sciences, SUNY College of Optometry, New York, New York, UNITED STATES|H. Feng, LensCrafters, Mason, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myopia is a significant public health concern because of its rapidly increasing prevalence and the ocular complications associated with myopia progression. Multifocal soft contact lenses (MFCLs) are used for myopia management, but with variable effectiveness, potentially caused by reduced accommodative responses during MFCLs wear (see Kang 2016 and Gong 2017). In this study we investigated the accommodative response in children during early MFCL wear for myopia management and measured the change in refractive error (RE) and axial length (AL) over one year.

Methods: Ten myopic children (mean age 10.8 ± 2.3 yrs; 5Ms/5Fs) with no history of myopia control and normal binocular functions were fit with Biofinity MFCLs with a +2.00 D ADD. MFCLs were worn for at least 10 hrs/d and 5 d/wk. At the beginning of treatment, accommodative responses to 2, 2.5, and 4 D stimuli, were measured monocularly with a Grand Seiko open field autorefractor while the subjects wore the MFCLs. The gains of the accommodative stimulus-response functions were estimated by the slopes of linear regressions fit to each subject's data. Wet autorefraction and AL were measured at baseline, 6 months, and 12 months using a Grand Seiko autorefractor and Lenstar Biometer, respectively.

Results: The mean (± SEM) wet RE was OD –2.94 ± 0.27 D, OS –2.88 ± 0.37 D at baseline and was –3.35 ± 0.38 D and –3.28 ± 0.47 D one year later, respectively. Greater axial elongation caused more myopia progression in both eyes after wearing MFCLs for one year (R^2, OD 0.65 and OS 0.78; $p < 0.01$ for both). Accommodative gain measured during MFCL wear varied at baseline (OD 0.80 ± 0.14, OS 0.90 ± 0.12) and was a significant predictor of myopia progression and axial elongation: Lower accommodative gain during MFCL wear at baseline was correlated with more myopia and greater axial elongation at 1 yr (see fig for details).

Conclusions: These data support the hypothesis that children with higher accommodative gains during MFCL wear experience more ADD power leading to more effective myopia management. To improve the effectiveness of MFCLs for myopia management, we speculate that accommodative biofeedback training during MFCL wear may be helpful (see Wagner 2020).

CONTROL ID: 3707668
SUBMITTER (NAME ONLY): Zhen Zuo
TITLE: Single-cell Multiomics Analysis of Human Retinal Development
SESSION TITLE: Single cell analysis in retinal research in health and disease
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: Z. Zuo, X. Cheng, Y. Li, S. Ferdous, J. Li, R. Chen, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|Z. Zuo, R. Chen, Graduate Program in Quantitative and Computational Biosciences,, Baylor College of Medicine, Houston, Texas, UNITED STATES|A. Jacobo Lopez, A. Moshiri, Department of Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Development of the retina is under precise temporal and spatial regulation. Although it has been observed that the chromatin state changes dynamically during retinal development, how it changes and its relationship with transcriptomics are unclear. Therefore, we aim at applying the latest single-cell multi-omics and spatial transcriptomics tools to gain insights into this complex development process.

Methods: Samples from foveal and peripheral human fetal retina between 10- and 23-weeks gestational age were collected and subjected to single nuclei multiome profiling using the 10X Genomics platform to generate transcriptomic and open chromatin data from the same nuclei. Batch corrected data obtained from all samples were analyzed together to identify cell types and subtypes. Transcription factors (TFs) and gene regulatory networks (GRNs) that correlate with the developmental process were analyzed based on the multiome dataset. Finally, the single-cell spatial developmental maps will be generated using the massively multiplexed single-molecule RNA in situ hybridization (MERFISH) technology.

Results: In total, single nuclei multiome profiling of 280,000 nuclei has been generated from 24 samples of the peripheral and foveal retina. All major cell types and over 30 cell subtypes have been identified in our dataset. Consistent with the idea that cell differentiation starts from the central retina and progresses toward the periphery, delayed development onset of the peripheral retina was clearly observed. Furthermore, based on pseudotime analysis, the trajectory matched well with the established birth order of all cell types. By analyzing cells close to the branch points among trajectory, known and novel TFs, GRNs that correlate with the developmental process were identified. Both concordant and discordant regulations of transcripts and open chromatin were observed, providing insights on different modes of regulatory switch during development. Finally, the generation of a single-cell spatial developmental map of the retina is underway.

Conclusions: Our study produces a spatial-temporal multi-omics map of the human developing retina. Integrative analysis of this multi-omics dataset reveals candidate TFs and GRNs controlling the developmental process. Comparison between transcriptome and open chromatin profiles reveals the complex dynamics of gene regulation between genomic and epigenomics during retinal development.

CONTROL ID: 3707669

SUBMITTER (NAME ONLY): Jake Spitsbergen

TITLE: Neurogenesis and Functional Recovery of Adult Retinal Neurons in Mice after Blast Exposure

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Spitsbergen, C.L. Linn, Biological Sciences, Western Michigan University, Kalamazoo, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To demonstrate that application of the alpha7 nicotinic acetylcholine receptor selective agonist, PNU-282987, elicits new neurons in a blast damaged retina and recovery of retinal function.

Methods: Ocular blast damage was induced in adult mice (3-8 months old; both sexes) after exposure to a single blast of 35 psi to the left eye. Blast exposed transgenic mice expressing TdTomato Müller glia, were treated daily with an eyedrop solution containing 1mM PNU-282987 post-blast for 4 weeks. Antibody staining studies were performed to study regeneration of new neurons derived from Müller glia and ERGs were obtained each week to examine functional recovery. ERG recordings were obtained from control, blast damaged and mice exposed to blast followed by 4 weeks of PNU-282987 treatment. Recordings were obtained using the Celeris Diagnosis system. Data was analyzed with ANOVA and significant differences were indicated as $P<0.05$. N's between 4-6 were obtained under each condition.

Results: Blast exposure caused a significant loss of cells in all retinal layers after 4 weeks, ranging between 15 and 40% (+/- 8.2) compared to unblasted eyes. Immunohistochemical analysis demonstrated double labeled TdTom positive photoreceptors, bipolar cells, amacrine cells and retinal ganglion cells in blast exposed mice treated with PNU-282987. Scotopic ERG recordings from blast exposed mice had significantly decreased amplitudes in a-waves, b-waves, and oscillatory potentials (OP1,2,3) (between 35 and 47% +/- 6) compared to ERGs obtained from the same mice prior to blast exposure. Significantly decreased amplitudes were also seen from scotopic flicker frequency recordings at 5, 10, 20 and 30 Hz (between 31 and 52% +/-11) following blast exposure. Animals treated with PNU-282987 for 4 weeks after blast showed a significant recovery in a-wave amplitudes by 45% +/-12, in b-waves by 35% +/-11, and in OP1,2 and 3 waves (between 43 to 82% +/-25). Recovery of flicker amplitudes of 5, 10, 20 and 30 Hz were measured between 20 and 48% +/-10 when compared to responses from the same mice under control conditions.

Conclusions: Blast exposure caused a significant loss of cells in all retinal layers and a reduction in ERG waveform amplitudes. After treatment with PNU-282987 for 1 month, newly generated neurons derived from Müller glia were found in all retinal layers, which corresponded with recovery of ERG responses.

CONTROL ID: 3707670

SUBMITTER (NAME ONLY): Jasmyne McCoy

TITLE: Characterization of real-world neovascular age-related macular degeneration (nAMD) switch patients treated with brolucizumab (BROL) alternating with other anti-Vascular Endothelial Growth Factors (VEGF) versus brolucizumab alone

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. McCoy, R. Donkor, C. McCrossin, D.G. Miller, H. Pham, J. Schartman, L. Rao, L.J. Singerman, M. Novak, S. Pendergast, J.M. Coney, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|R. Zubricky, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|S. Buxy Sinha, N. Sonbolian, H. Karcher, Novartis AG, Basel, Basel-Stadt, SWITZERLAND|L. Zhou, KMK Consulting, Morristow, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study real-world nAMD patients' characteristics in two BROL regimens.

Methods: A retrospective cohort study at Retina Associates of Cleveland, Inc. (extracted on December 1, 2021) analyzed two nAMD groups, BROL alone and BROL alternating with other anti-VEGFs. BROL alone switched from a previous anti-VEGF, had at least 12 months follow-up post switch and at least 3 BROL injections and no other anti-VEGF in first 12 months of treatment post switch. BROL alternating switched from a previous anti-VEGF, had at least 12 months follow-up post switch and at least 3 BROL and 1 other anti-VEGF injection in first 12 months of treatment post switch. Injection intervals, visual acuity (VA), and central macular thickness (CMT) were analyzed at baseline (first BROL injection) and last follow-up, along with follow-up times distribution post first BROL injection. Inflammatory events were reported.

Results: BROL alone identified 172 eyes from 152 patients (53.3% females) with mean±standard deviation (SD) age, VA and CMT of 80.7±7.8 years, 1.14±0.87 logMAR and 300.7±118.1 µm respectively at baseline. BROL alternating identified 56 eyes from 49 patients (65.3% females) with similar baseline mean age, VA and CMT (77.5±9.0 years,1.04±0.75 logMAR and 299.3±91.0 µm respectively).

Alternating eyes had shorter pre-switch intervals (33.2±11.9 days) than BROL alone (48.8±25.8 days), and could extend interval by 8.4±20.5 days at last follow-up compared to 32.7±61.1 days for BROL alone (Table 1). Follow-up time (from first BROL injection) in BROL alternating and BROL alone was 564.3±107.0 days and 552.5 ±104.4 days, respectively. BROL alternating had no inflammatory events, 1.7% of BROL alone eyes did.

Mean change from first BROL injection to last follow-up in VA was a gain and CMT reduction in both groups (Table 1). BROL alone group saw largest CMT reduction (-39.6 µm) compared to alternating group (-28.5 µm) (Table 1), consistent with fluids volume reduction within retinal layers (Table 2).

Conclusions: Both regimens had similar baseline characteristics. Alternating group had history of shorter intervals pre-switch and extended interval by fewer days with at least a year follow-up.

CONTROL ID: 3707673

SUBMITTER (NAME ONLY): Mira Sachdeva

TITLE: Single-nuclei RNA sequencing of the diabetic mouse retina reveals novel insights into the pathophysiology of early diabetic retinal disease

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: While increasing evidence from patients and animal models suggests that early diabetic retinal neurodegeneration may precede the retinal vascular abnormalities that currently define diabetic retinopathy (DR), the underlying pathophysiology and relevant cell types affected in early diabetic retinal disease (DRD) remain poorly understood. In order to identify molecular pathways dysregulated in specific retinal neuronal cell types in early DRD, we performed single-nuclei RNA sequencing of the retina in diabetic mice at two time points following disease onset.

Methods: To induce diabetes, male C57BL/6J mice were treated with five daily intraperitoneal injections of 60mg/kg streptozotocin (STZ) or vehicle. Animals with random glucose >250 mg/dL were considered diabetic and the early retinal phenotype was confirmed at 6 weeks after treatment using optical coherence tomography and dark-adapted electroretinogram. At either 6 or 36 weeks following STZ treatment, retinas from control and diabetic mice (n=8 mice per group per time point) were dissected and separated into two batches for methanol fixation, homogenization, and nuclei preparation. Nuclei were subjected to sequential combinatorial labeling using HiFseq and library sequencing was performed using the Illumina NovaSeq6000 S4 platform.

Results: After preprocessing, we selected cells with >300, <2,000 UMIs (unique molecular identifiers) and <5% mitochondrial counts, then normalized the count matrix in the Seurat package. In total, 18,328 and 3,643 cells were identified at the 6- and 36-week time points, respectively. Unsupervised cell-type annotation analyses yielded 6 clusters representing all retinal neuronal cell types, though relative proportions differed from expected likely due to the use of nuclear rather than whole cell transcripts. The most highly differentially-expressed genes were dysregulated across multiple cell types at the early time point. Integration of gene regulatory networks and our dataset to infer transcription factor activity for each cell suggested unique transcriptional programs at different stages of DRD.

Conclusions: Single-nuclei RNA sequencing of the retina in the STZ-induced diabetes mouse model reveals patterns of gene dysregulation in retinal neurons that may underlie the pathogenesis of early diabetic retinal neurodegeneration and contribute to subsequent progression of DR.

CONTROL ID: 3707674

SUBMITTER (NAME ONLY): Santiago Mejia-Freire

TITLE: Optical coherence tomography imaging quality in patients with retinitis pigmentosa without mydriatic eye drops

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mejia-Freire, M. Mateos-Olivares, F.J. Valentín Bravo, S. Pastor, Ophthalmology, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|E.M. Sobas Abad, R. Usategui Martin, J. Pastor, S. Pastor, Instituto de Oftalmobiologia Aplicada, Valladolid, Castilla y León, SPAIN|

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ABSTRACT BODY:

Purpose: Many factors influence the acquisition and interpretation of optical coherence tomography (OCT) and OCT angiography (OCT-A) images, including the state of the pupil. The aim of this observational prospective study was to determine the effect of non-mydriasis when obtaining and interpreting the images in patients with retinitis pigmentosa (RP).

Methods: Seventy-six patients with a diagnosis of RP were enrolled and classified by severity, and 30 healthy individuals were used as controls. All of them underwent a complete ophthalmological examination. Zeiss PLEX Elite 5000® High Definition-OCT was used for imaging, which was performed without pharmacological mydriasis. Main measured parameters were vessel (VD) and perfusion density (PD), foveal avascular zone area (FAZ), signal strength, macular and ganglion cell (GCL) layer thickness, presence and type of artifacts found.

Results: Seventy-nine eyes with RP and 60 eyes as controls were analyzed. Statistically significant differences were observed in most OCT-A parameters between both groups, with a reduction in complete VD (-5.98 mm/mm^2; $p<0.001$), and PD (-16.32%; $p<0.001$) and an increase in FAZ (+ 0.11 mm^2; $p<0.001$) which was measured manually in 76 patient images and 21 of controls. Signal strength was significantly lower in the patient group (7.86 ± 1.79 ($p < 0.002$)), as well as in structural OCT images (central macular thickness: -42.88 µm ($p < 0.001$); GCL thickness: -33.18 µm ($p<0.001$)). Artifacts were found in 76 of the 79 patient images (96%) and in 47 of the controls (78%). Projection artifact was the most frequent in both groups. Seventeen images of the patient group and fourteen images of patients with severe RP had between 3 to 4 artifacts ($p <0.001$).

Conclusions: Non-mydriasis is not a limiting factor for a correct acquisition and interpretation of images in patients with a mild-moderate stage of RP, considering that in severe stages pupillary dilation may be necessary to improve the image quality and reduce artifacts, despite increased glare and photophobia in these patients.

CONTROL ID: 3707678

SUBMITTER (NAME ONLY): Arash Delavar

TITLE: Gender Disparities in Mental Health and Social Support among Glaucoma Patients during the COVID-19 Pandemic

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Delavar, J. Bu, B. Radha Saseendrakumar, S. Baxter, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mental health burden of the COVID-19 pandemic is thought to be substantial. Glaucoma patients are especially vulnerable considering prior reports of higher rates of anxiety and depression than the general population at baseline. In this study, we explore how measures of mental health and social support during the pandemic varied by gender among those diagnosed with glaucoma.

Methods: We obtained a cohort of patients diagnosed with glaucoma (any type) from the NIH All of US Research Program. Answers from the latest COVID-19 Participant Experience (COPE) survey were used. Logistic regression was used to evaluate the association between reported depression (using Patient Health Questionnaire-9 (PHQ-9) scores), stress associated with social distancing, and measures of social support if one became sick with COVID-19 by self-reported gender (male, female, other). Multivariable models were adjusted for age, race/ethnicity, health insurance status, education, and income, with males as the reference group. Observations with missing values for covariates used in the models were dropped.

Results: Of 3,675 glaucoma patients, 56.1% were female, 83.4% were non-Hispanic White, and 95.0% had insurance plans other than Medicaid or none. Many patients had a PHQ-9 score >4 (33.5%), indicating mild, moderate, or severe depression, and 74.4% experienced “a lot” or “some” stress during the pandemic from social distancing. After adjusting for covariates, females were more likely to report depression (OR: 1.40, 95% CI: 1.20-1.62) and stress associated with social distancing (OR: 1.34, 95% CI: 1.14-1.57) than males. Further, females were less likely to report having help if they were sick with COVID-19 and needed someone to prepare meals (OR: 0.78, 95% CI: 0.67-0.92) or help with daily chores (OR: 0.79, 95% CI: 0.67-0.91).

Conclusions: Females with glaucoma were more likely to experience depression, stress due to social distancing, and were less likely to have social support if sick with COVID-19 than their male counterparts. As measures of mental wellbeing and social support are associated with better medication adherence and health outcomes, glaucoma patients identifying as female may represent an especially vulnerable population. Efforts should be made to identify glaucoma patients experiencing hardship during the COVID-19 pandemic.

CONTROL ID: 3707680

SUBMITTER (NAME ONLY): Ryo Terao

TITLE: Roles of adipose tissue metabolism on synthesis of photoreceptors outer segments and retinal senescence

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Terao, M. Yoshida, T. Lee, J. Colasanti, C.W. Pfeifer, J. Lin, A. Santeford, K. Hase, K. Jongshin, R.S. Apte, Department of Ophthalmology & Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|R. Terao, Department of Ophthalmology, The University of Tokyo Graduate School of Medicine Faculty of Medicine, Tokyo Daigaku Daigakuin Igakukei Kenkyuka Igakubu, Bunkyo-ku, Tokyo, JP, academic/medsch, Bunkyo-ku, Tokyo, JAPAN|M. Yoshida, Department of Anesthesiology, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|K. Hase, Department of Ophthalmology, Hokkaido Daigaku Daigakuin Igaku Kenkyuin, Sapporo, Hokkaido, JAPAN|

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ABSTRACT BODY:

Purpose: Adipocytes have lipid droplets in their organelles specialized in fat storage. Free fatty-acids (FFAs) are released from lipid droplets to provide energy substrates. Since some FFAs such as docosahexaenoic acid cannot be synthesized de novo in mammals, adipose tissue is indispensable as a long-term depot of these FFAs. Considering that several FFAs have essential roles in retinal homeostasis, we hypothesized that adipocyte deficiency would promote retinal dysfunction and senescence. We investigated this hypothesis in two genetic mouse models where adipocytes are ablated.

Methods: C57BL/6J expressing an inducible diphtheria toxin receptor (Lox-Stop-Lox-ROSA-DTR) and adiponectin-Cre (DTR^{ADQ}) were used. DTR^{ADQ} mice were treated with diphtheria toxin intraperitoneally to eliminate adipocytes selectively. FAT-ATTAC (fat apoptosis through targeted activation of caspase 8) mice were treated with a dimerizer as another model to induce adipocyte apoptosis. Retinal responses were recorded by electroretinogram (ERG) using littermates that received the same treatments as controls. Transmission electron microscopy (TEM) was used to visualize photoreceptor structure. Senescence-associated (SA) β-galactosidase (Gal) staining was utilized to detect senescent cells which produce acid lysosomal β-Gal in retinal tissue.

Results: Both DTR^{ADQ} and FAT-ATTAC lost fat by postnatal adipocyte ablation. Fat-ablated mice demonstrated significantly decreased a- and b-wave amplitudes measured by ERG, indicating that adipocyte ablation induced retinal dysfunction. TEM images revealed that DTR^{ADQ} had sparse outer disc membrane compared to control suggesting an abnormality in outer segment synthesis. Furthermore, disc membranes at the base of photoreceptor outer segments were disorganized by adipocyte ablation. SA β-Gal staining revealed the increased level of β-Gal in the inner segment of photoreceptor in DTR^{ADQ}mice, where lysosome localizes in photoreceptors.

Conclusions: Adipocytes play an essential role in retinal function and photoreceptor disc membrane synthesis. Ablation of adipocytes causes retinal dysfunction as measured by electrophysiology, and induces photoreceptor senescence.

CONTROL ID: 3707682

SUBMITTER (NAME ONLY): Fernando Abib

TITLE: Corneal Endothelial Mosaic of the Descemet Membrane Tears (Haab Striae)

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.C. Abib, Anatomy, Univerisdade Federal do Paraná, Curitiba, Paraná (PR), BRAZIL| F.C. Abib, Córnea, Clínica de Olhos Prof. Dr. Fernando Abib, Curitiba, Paraná (PR), BRAZIL|

Commercial Relationships Disclosure: Fernando Abib: Commercial Relationship(s);Code P (Patent):Fernando C Abib

ABSTRACT BODY:

Purpose: Otto Haab (1850–1931), Swiss ophthalmologist that contributed with pathological anatomy of the eye, one of than was used to describe tears in the Descemet membrane, thus originated the eponymous Haab striae. The Haab striae are found in congenital glaucoma, trauma as birth injury, contusion, acute hydrops, megalocornea, conical cornea, and with marked AP diameter.

Purpose: to demonstrate the behavior of endothelial mosaic in corneas with Haab striae using contact specular microscopy and compare with normal eye.

Methods: Ten patients with Haab striae: female 6 and male 4, right eye 6 and left 4, age 6 – 54 and mean 27.7±15 years old. BioOptics contact specular microscope and Bambi 2500 software was used.

Haab striae group (HSG) - eyes with Haab striae (central, near of the HS, further of the HS areas); Control group (CG) - contralateral eyes without striae (central area).

The sampling process of the specular microscopy (images and endotelial cells) was guided by the Cells Analyzer software (USA Patent) to obtain a sampling error smaller than 5% for each especular microsocpy exam.

Descriptive cell data from the sample of the endotelial mosaic acquired by specular microscopy exams: image number, total cell number, and calculated sampling error.

Morphometric data of the endothelial cells: endothelial cell density (ECD), coefficient of variation (CV), and percentage of hexagonal cells (HEX).

Descriptive statistics were used to demonstrate endothelial data and the comparison between the studied groups and areas will be compared by the Student t test at 95% significance level.

Results: Endothelial samples: CG: 2.8±1.6 images with 328±169 cells per exam and sampling error 3.12±0.86; HSG: 7.2±2.2 images with 393±90 cells per exame and sampling error 2,87±0.50.

Endothelal data of the studied groups (Figure 1A).

Endothelial mosaic areas compared in eyes with Haab Striae (Figure 1B).

The Figure 2 shows the specular microscopy images of the one of the studied Haab stria due to birth injury.

Conclusions: Haab striae cause continuous and significant loss of endothelial cell density, it's highier at the margins of the Haab striae. The endotelial cell density gradually decreases as it approaches the margins of the Haab striae. Coefficient of variation and percentage of hexagonal cells did not show changes.

CONTROL ID: 3707684

SUBMITTER (NAME ONLY): Bright Asare-Bediako

TITLE: DIFFERENTIAL RECUITMENT OF HEMATOPOIETIC CELLS INTO THE INJURED RPE/CHOROID

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Acute injury to the retina or choroid can mobilize hematopoietic cells to the sites of injury and vascular repair can be performed by a BM population termed myeloid angiogenic cells (MACs). Hematopoietic cells are derived from the bone marrow (BM) present in both long and flat bones such as the tibia and calvarium, respectively. However, whether this injury-induced mobilization of hematopoietic cells to the damaged eye occurs specifically from one BM source or the other is not known. In this study, we investigated the differential contribution of tibial (long bone) and calvarial (flat bone) BM cells to the areas of injury using the mouse model of choroidal neovascularization (CNV).

Methods: BM-derived hematopoietic cells were isolated from the calvarium of adult Rosa-mTmG mice and from the tibia of adult C57BL/6-EGFP mice to obtain td tomato-fluorescent (td^+) calvarial cells and green-fluorescent (gfp^+) tibial cells, respectively. The BM cells were enriched for hematopoietic stem and progenitor cells using EasySep Mouse Hematopoietic Progenitor Cell Isolation Kit (Stemcell Technologies). Adoptive transfer of cells ($1x10^5$) was performed in C57BL/6J wild type. Recipient mice were then subjected to laser photocoagulation in one eye to induce CNV. Uninjured eyes were used as control. Mice were euthanized 24 hours post-injury and their rpe/choroids were harvested for flow cytometry.

Results: CNV resulted in a significant increase in total $CD45^+$ hematopoietic cells in the choroid compared to untreated eyes (0.7% vs. 0.43%, p=0.0143). We observed that the injured choroid recruited more gfp^+ (tibial) monocytes compared to td^+ (calvarial) monocytes (0.36% vs. 0.039%, p=0.0022). However, there were more td^+ neutrophils (0.867% vs 0.1179%, p=0.029) compared to gfp^+ neutrophils in the injured choroid. The injured choroid recruited more td^+ MACs compared to gfp^+ MACs (0.80% vs. 0.01310%, p=0.0022). There was no significant difference in the contribution of tibial or calvarial cells to macrophages 24 hours after CNV injury.

Conclusions: Our study supports dynamic recruitment of hematopoietic cells into the rpe/choroid during acute injury. Our data suggests that mobilization of cells from the hematopoietic system into the injured rpe/choroid is not homogenous. Calvarial marrow cells may provide the optimal source of cells for generating vascular reparative cells in vivo.

CONTROL ID: 3707686

SUBMITTER (NAME ONLY): Susan Vitale

TITLE: Visual field score decline in eyes with untreated diabetic retinopathy: historical data from the Diabetic Retinopathy Study (DRS) randomized clinical trial

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vitale, D. Lee, E. Agron, T.D. Keenan, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies have shown visual field (VF) loss to be greater in eyes treated with pan-retinal photocoagulation (PRP) than in those treated with anti-VEGF for proliferative diabetic retinopathy (PDR); reasons for VF loss in eyes treated with anti-VEGF are yet unknown. To better understand VF loss that occurs after various PDR treatments, studying VF changes in untreated eyes may be helpful. However, after establishment of PRP as standard of care, eyes with PDR are rarely left untreated. This study used data from the Diabetic Retinopathy Study (DRS) to investigate the natural history of VF changes in untreated eyes with nonproliferative diabetic retinopathy (NPDR) or PDR.

Methods: The DRS (1971-1979) was a randomized clinical trial evaluating the efficacy of PRP in persons with PDR in ≥ 1 eye or severe NPDR in both eyes. Participants had one eye randomized to PRP; the fellow eye was assigned to deferred treatment. VF data (Goldmann perimetry, IV4e test stimulus) were collected at baseline, 4 months, and then annually until 6 yrs. VF score was the sum of 12 meridian scores (for each meridian, peripheral extent of the field in degrees minus width of any scotomas). VF scores were analyzed over time among untreated eyes and for the paired difference between (argon)PRP-treated and fellow untreated eyes. Eyes that developed PDR with high-risk characteristics (HRC) in the deferral arm were treated with PRP and subsequently censored in the analyses.

Results: 1660 eyes (18% NPDR, 40% PDR/HRC) of 830 persons (44% female, age 43±14y) were included. Baseline VF score was 729±80. Among untreated eyes, VF score declined 30 /yr (95% CI, -35, -26) after adjustment for age, sex, and baseline PDR status and VF score. Difference in VF score between treated and untreated eyes was negative at 4 months, 1 yr, and 2 yrs (-32, -22, -20, $p<.001$ for all) (i.e., PRP-treated eyes had significantly lower VF scores than untreated eyes). After yr 3, differences were not statistically significant (yrs 3 through 6: 0.5, 11.4, 32.9, 18.4; p-values .96, .31, .05, .68).

Conclusions: VF scores declined significantly in untreated eyes in the DRS, suggesting VF loss progresses over the natural history of PDR. VF loss was initially greater after PRP than in untreated eyes, but this difference diminished after yr 3.

CONTROL ID: 3707688

SUBMITTER (NAME ONLY): Ganeswara Rao Musada

TITLE: Role of non-canonical Wnt signaling in Retinal Ganglion Cell (RGC) neurite growth and optic nerve regeneration

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Musada, T. Carmy-Bennun, G. Dvoriantchikova, D. Ivanov, A. Hackam, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: A primary challenge during optic neuropathies is to promote Retinal Ganglion Cell (RGC) survival and axon growth during or after axon degeneration. Although the role of canonical Wnt ligands such as Wnt3a was studied in RGC axon regeneration, the effect of non-canonical Wnt ligands such as Wnt5a on RGC protection and axon growth and regeneration was not analyzed. In the current study, we explored the role of Wnt5a in RGC protection and optic nerve regeneration in a mouse model of traumatic optic neuropathy.

Methods: Primary RGC cultures were treated with different concentrations of recombinant Wnt5a to identify its effect on RGC neurite growth and complexity. Optic nerve crush mouse model was used to identify the effect of intravitreal injections of Wnt5a on RGC protection and optic nerve regeneration after 2 weeks of injury. Western blots and IHC were performed with Wnt5a intravitreally injected retinal lysates and retinal sections respectively, to identify the induced signaling mechanisms in retinal cells. PERG was used for the functional assessment of RGC.

Results: Primary RGCs treated with 20ng (Average neurite length (ANL); 138±11.6 mean±SD, $p=0.0003$), 50ng (ANL; 236.5±11.9, $p<0.0001$) and 100ng (ANL; 407.6±29.5, $p<0.0001$) concentration of Wnt5a protein showed significantly increased average neurite length and neurite complexity compared to BSA treated RGCs (ANL; 35.16±2.63). The optic nerve sections also showed significant increase in axon length and axon number in Wnt5a injected eyes compared to saline injected eyes. The western blots showed a significant increase in phosphorylation of CamKII ($p<0.0001$), phosphorylation of JNK ($p=0.0007$) and phosphorylation of STAT3 ($p<0.0001$) in Wnt5a 20ng and 50ng injected eyes in comparison with PBS injected eyes. The IHC of retinal sections identified the activation of CamKII and JNK in RGCs.

Conclusions: For the first time, this study identified Wnt5a, a non-canonical Wnt ligand as a regulator of RGC protection, neurite growth and optic nerve regeneration. The induced CamKII and JNK/STAT3 signaling mechanisms in RGC and other retinal cells such as Muller glia by Wnt5a could be responsible for RGC protection and optic nerve regeneration. This study identifies the importance of Wnt5a and non-canonical Wnt signaling mechanisms to induce RGC protection and RGC axon regeneration that could be useful as therapeutic targets.

CONTROL ID: 3707692

SUBMITTER (NAME ONLY): Rachel Wozniak

TITLE: Treatment of Ocular Infections: Consideration for Antibiotic Drug-Drug Interactions

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Wozniak, W. Johnson, E. Dunster, Ophthalmology, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the treatment of ocular infections such as conjunctivitis, keratitis and endophthalmitis, it is common practice to use more than one antibiotic to achieve broad spectrum coverage as well as overcome circulating antibiotic resistance. However, there is the potential for individual compounds to either potentiate or antagonize one another with respect to antimicrobial efficacy when used in combination. Thus, we studied drug-drug interactions using a suite of common ophthalmic antibiotics to aid clinicians in selecting appropriate combination therapies.

Methods: Using standard in vitro microbiologic growth conditions, we measured the minimum inhibitory concentrations (MICs) of 8 ophthalmic antibiotics (vancomycin, tobramycin, gentamicin, moxifloxacin, polymyxin B/trimethoprim, ceftazidime, cefazoline and erythromycin) towards Gram-positive Staphylococcus aureus and Gram-negative Pseudomonas aeruginosa. Next, each drug was systematically tested in combination with each other using standard checkerboard Fractional Inhibitory Concentration (FIC) testing. The formula: [(MIC Drug A in combination/MIC Drug A alone) + (MIC Drug B in combination/MIC Drug B alone) = FICI] was used to classify drug-drug interactions as antagonistic (FICI>4), indifferent (FICI=1-4), additive (FIC=0.5-1) or synergistic (FIC<0.5).

Results: 56 combinations were evaluated for drug-drug interactions (28 in S. aureus and 28 in P. aeruginosa). Towards S. aureus, 19 combinations were indifferent (efficacy was similar alone or in combination). However, 8 combinations demonstrated additive activity (improved efficacy in combination), and 1 displayed synergistic activity (improved activity beyond what may be expected). Similarly, against P. aeruginosa, 20 combinations proved indifferent, 7 were additive and 1 was synergistic. No antibiotic drug combinations were found to be antagonistic towards either S. aureus or P. aeruginosa.

Conclusions: Drug-drug interactions are well known in medicine yet have not been specifically studied with a relevant set of ophthalmic antibiotics. Our data suggest that while the majority of ophthalmic antibiotics had no change in efficacy when used alone vs in combination, there were combinations that displayed improved antimicrobial efficacy. These combinations may represent an improved treatment modality for ocular infections.

CONTROL ID: 3707695

SUBMITTER (NAME ONLY): Seokjoo Lee

TITLE: $CD11b^+Gr\text{-}1^+$MDSC prevent IL-6-induced Treg dysfunction partially through secretion of IL-10

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lee, F. Kahale, A. Musayeva, S. Wang, T. Blanco, T.H. Dohlman, S. Chauhan, Y. Chen, R. Dana, Department of Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Regulatory $FoxP3^+$ T cells (Tregs) are critical in maintaining corneal allograft tolerance. The highly vascularized inflammatory microenvironment in corneal transplantation adversely affects the suppressive function of Tregs. Emerging evidence indicates the functional crosstalk between $CD11b^+Gr\text{-}1^+$ myeloid-derived suppressor cells (MDSCs) and Tregs, but little is known about the impact of $CD11b^+Gr\text{-}1^+$ MDSCs on the rescue of inflammation-induced Treg dysregulation. The purpose of this study is to determine the rescue effect of $CD11b^+Gr\text{-}1^+$ MDSCs on IL-6-mediated Treg dysregulation, and to further elucidate the underlying mechanism by which this rescue occurs.

Methods: BALB/c bone marrow cells were cultured in complete RPMI medium in the presence of IL-6 (20ng/ml) and GM-CSF (20ng/ml) for 4 days to differentiate MDSCs. $CD4^+CD25^+$ Tregs ($2.5x10^5$) were co-cultured either with $CD11b^+Gr\text{-}1^+$ MDSCs or with $CD11b^+$ cells at a ratio of 1:1 in the absence or presence of IL-6 (40ng/ml) for 48 hours. IL-10 knockdown (KD) $CD11b^+Gr\text{-}1^+$ MDSCs were generated by IL-10 siRNA (10nM) transfection for 6 hours prior to co-culture with Tregs. FoxP3 expression and IL-10 secretion of Tregs were analyzed by flow cytometry and immunoblotting.

Results: Flow cytometric quantification showed Tregs cultured with IL-6 had significantly reduced expression of FoxP3 (12.5±0.3% vs. baseline 15.97±0.6%, p=0.0318) and modestly decreased secretion of IL-10 (5.16±1.2% vs. baseline 10.7±1.9%, p=0.0495) as compared to culture without IL-6. Addition of $CD11b^+$ cells to culture partially preserved FoxP3 expression (18.2±0.3%) and IL-10 production (32.63±12.3%) by Tregs in the presence of IL-6. In contrast, addition of $CD11b^+Gr\text{-}1^+$ MDSCs to culture led to significantly higher FoxP3 (32.93±1.9%, p=0.0035) and IL-10 (60.03±13.3%, p=0.0238) expression by Tregs than addition of $CD11b^+$ cells. Furthermore, Tregs co-cultured with IL-10 KD $CD11b^+Gr\text{-}1^+$ MDSCs exhibited significantly reduced $FoxP3^+$ Tregs (23±1.8%) and IL-10-secreting $FoxP3^+$ Tregs (55.93±4.4%) as compared to those co-cultured with WT $CD11b^+Gr\text{-}1^+$ MDSCs (32.3±2.4% and 82.53±3.4%, respectively, p=0.0403 and p=0.0015, respectively).

Conclusions: Our data show that in vitro generated MDSCs are effective in preventing inflammatory cytokine-induced impairment of Treg function, which can be explored as a novel therapeutic approach in ocular alloimmune disorders, including high risk corneal transplantation.

CONTROL ID: 3707696

SUBMITTER (NAME ONLY): Maha Coucha

TITLE: The Impact of COVID-19 Spike Protein on Retinal Microvascular Environment

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Coucha, Pharmaceutical Sciences Department, South University School of Pharmacy, Savannah, Georgia, UNITED STATES|M. Abdelsaid, D. Bolduc, Biomedical Science Department, Mercer University School of Medicine, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Background: Despite being primarily a respiratory disease, COVID-19 can lead to non-respiratory complications, including myocardial infarction and acute ischemic stroke. Moreover, COVID-19 spike protein (SP) was reported in the retina of deceased patients with COVID-19. Retinal microvascular abnormalities as loss of microvasculature and distinct thinning of the microcapillaries were reported in patients who recovered from COVID-19. We are still in the midst of the COVID-19 pandemic, with more deaths and cases every day. Therefore investigating the impact of COVID-19 on the retinal neurovascular environment and the long-term effect of this virus on vision is of great interest.

Purpose: To study the contribution of COVID-19 SP to retinal inflammation and vascular death.

Methods: Methods: COVID-19 SP, a highly glycosylated protein that allows the virus to penetrate the cell and cause infection, was injected intravitreally in 6-8 weeks global h-ACE2 knock-in mice and wild-type mice. Mice were sacrificed after 14 days, then vascular cell death and inflammation were evaluated by the presence of acellular capillaries and the expression of inflammatory and apoptotic markers. To complement our in-vivo studies, Human Microvascular Endothelial Cells (HMEC) were treated with 100 nM COVID-19 SP for 48 hours. The expression of inflammatory and apoptotic markers was assessed by PCR western blot.

Results: Results: Our results showed that HMEC exposed to COVID-19 SP for 48 hours displayed an increase in inflammatory and apoptotic markers expression including TNF-α, IL-1β, IL-6, and cleaved caspase-3 compared to control conditions. Additionally, COVID-19 SP enhanced the oxidative stress in HMEC, evident by the increase in nitro-tyrosine formation, superoxide dismutase, and NADPH oxidase complex 1 (NOX1 and NOX5) expression. The in-vivo findings came in agreement with our in-vitro studies. We found that intravitreal injection of the COVID-19 SP-induced 1) strong activation of the retinal glial cells, assessed by GFAP radial staining, and 2) increased vascular death, assessed by acellular capillaries formation 14 days after the injection.

Conclusions: Conclusions: Our findings highlight the possible role of COVID-19 SP in inducing retinal inflammation and vascular death. Further studies are required to reveal the impact of COVID-19 SP on visual acuity and the possibility of causing visual impairment using various animal models.

CONTROL ID: 3707698

SUBMITTER (NAME ONLY): Warren Lewis

TITLE: Comparison of procedural and neural network algorithms for segmentation of regions of non-perfusion in retinal OCTA scans

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Segmentation of regions of nonperfusion (RNP) with an automated algorithm enables detection of these regions by personnel that have not been trained in interpreting OCTA scans.

The procedural, or conventional, algorithm uses vessel binarization and image processing to detect areas without vessels. This algorithm is subject to error in regions with noise or low signal. The alternative algorithm is a convolutional neural network (CNN) that has been trained with OCTA retina projections and OCT reflectance images as inputs and annotations made by expert clinicians as targets.

Methods: The CNN was trained using 60,000 patches obtained from 14 15x15 and 46 12x12 OCTA scans (PLEX® Elite 9000, ZEISS, Dublin, CA) of eyes having significant areas of ischemia, along with expert segmentations of RNPs. 21 scans not used for the training were segmented using the procedural and DL algorithms. Outputs were compared against annotations of these scans made by expert clinicians. Dice coefficients were calculated for each output vs the expert segmentation for each acquisition.

Results: For the 21 scans in the test dataset, the CNN outperformed the procedural algorithm. Undesired segmentation of the FAZ as RNP was reduced but not eliminated in the CNN output, and some regions of low signal were incorrectly segmented. This may be improved by modifying the CNN training dataset and architecture.

Conclusions: A CNN algorithm for segmentation of RNP compares favorably with one based on binarization and thresholding of OCTA scans.

CONTROL ID: 3707699

SUBMITTER (NAME ONLY): Brian Soetikno

TITLE: Investigating hyalocyte-like cells in epiretinal membranes using serially acquired optical coherence tomography

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Soetikno, J.L. Goldberg, T. Leng, A. Dubra, Spencer Center for Vision Research, Stanford University, Stanford, California, UNITED STATES|D.A. Miller, H. Zhang, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hyalocyte-like cells (HLC), also known as macrophage-like cells, are cells located at the vitreoretinal interface. Recently, HLCs have been imaged in human subjects by averaging several acquisitions of optical coherence tomography (OCT) volumes. In this study, we investigated whether multiple acquisition averaging of OCT volumes could visualize HLCs in patients with epiretinal membranes (ERM).

Methods: Five patients with ERM and three control subjects were recruited for the study. OCT angiography (OCTA) and OCT volumes were simultaneously acquired using the RTVue XR Avanti (Optovue, USA). For each eye, we performed 3x3 mm2 scans at two locations: (1) ~7 degrees temporal to the fovea and (2) ~7 degrees nasal to the fovea. At each location, ten scans were serially acquired for averaging. Rigid followed by non-rigid of the volumes was performed using MATLAB (MathWorks, USA). The B-scans of were then cross-correlated and averaged. OCT volumes were then inspected in ImageJ. A projection of a 3 um slab above the inner limiting membrane (ILM) was used to isolate the HLCs from the underlying retina. Cell counting was performed manually.

Results: Fig. 1A shows a composite image from a control subject's left eye. En face OCTA is shown in red, while the projection of the 3 um slab above the ILM is shown in green. HLC's were numerously observed with a star-shaped appearance and regular spacing (Fig.1B). Fig. 2A shows a composite image from a the right eye of a subject with ERM. The shape of HLCs in ERM eyes appeared more elongated, stretched, and spindle-shaped compared to controls (yellow arrows, Fig. 2B). Additionally, HLCs were far less abundant than in controls (1.92 +/- 1.9 cells/mm2 vs. 50.5 +/- 22 cells/mm2) and irregularly spaced.

Conclusions: Using serial acquisition, image registration, and averaging of OCTA and OCT volumes, we observed HLCs on the surface of ERMs. HLCs were less numerous in patients with ERM than controls and possessed a more elongated, spindle-shaped appearance. Imaging of HLCs with OCT could potentially provide biomarkers for the management of ERMs.

CONTROL ID: 3707700

SUBMITTER (NAME ONLY): Philip Zhou

TITLE: Diagnostic Accuracy of Trained Image Graders in Screening for Retinopathy Among Youth with Diabetes

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zhou, Baylor College of Medicine, Houston, Texas, UNITED STATES|L. Eltemsah, L. Prichett, R. Wolf, Department of Pediatrics, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|A. Liu, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M. Bahrainian, R. Channa, UW Health, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

ABSTRACT BODY:

Purpose: There is a growing prevalence of diabetes mellitus in the pediatric population, which increases the importance of regular screening for complications such as diabetic retinopathy (DR). The use of digital fundus photography and trained image graders can help increase access to DR screening. Our aim was to assess the diagnostic accuracy of trained image graders (with no prior experience in ophthalmology) in detecting retinopathy from digital fundus photos of pediatric patients with diabetes.

Methods: This cross-sectional analysis compared DR evaluations from two fellowship trained retina specialists and two non-ophthalmologist trained graders. The graders evaluated 90 nonmydriatic fundus photos obtained from pediatric patients with type 1 and type 2 diabetes seen at a multidisciplinary pediatric diabetes center. Trained graders took an online course on DR grading and underwent two hours of training with the retina specialists. A reference standard was determined by agreement between the retina specialists, with discrepancies adjudicated by a third fellowship-trained retina specialist and/or in-person eye exam if there continued to be a question regarding presence of DR. The main outcomes measured were percent agreement with the reference standard, and sensitivity and specificity of detecting DR for trained graders and retina specialists.

Results: Among the 90 patients from whom the retinal images were taken, the average age was 13.8 years old, 52% were non-Hispanic white, 52% were female, and 76% had type 1 diabetes. The prevalence of DR was 13% in this sample. Sensitivity for DR detection varied between 83-91% among trained graders compared to 91-92% for retina specialists. Specificity varied between 67-92% for trained graders compared to 71-83% for retina specialists. Agreement with reference standard varied between 70-91% for trained graders and 74-84% for retina specialists.

Conclusions: After undergoing a standardized training program, trained graders (with no prior experience in ophthalmology) can detect DR with high sensitivity from fundus photos of pediatric patients with diabetes, comparable to that of retina specialists. The use of trained graders in teleretinal screening networks for pediatric diabetes may be a feasible option to improve access to DR screening.

CONTROL ID: 3707704

SUBMITTER (NAME ONLY): Carlos Santiago Hernandez Torres

TITLE: Assessment of a machine learning approach to predict subjective sphero-cylindrical correction using wavefront aberrometry data

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hernandez Torres, A. Gil Ruiz, I. Casares, J. Poderoso, E. Lage Negro, Departamento de Tecnología Electrónica y de las Comunicaciones, Universidad Autonoma de Madrid, Madrid, Madrid, SPAIN|C. Hernandez Torres, A. Gil Ruiz, I. Casares, J. Poderoso, A. Wehse, S. Dave, D. Lim, E. Lage Negro, PlenOptika, Inc., Boston, MA, USA, Boston, Massachusetts, UNITED STATES|M. Sánchez Montañés, Department of Computer Science, Universidad Autonoma de Madrid, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Uncorrected Refractive Errors (UREs) is a reversible condition that can be treated with appropriate eyeglasses. UREs affect over 1 billion people globally, with 90% of this population living in low-and-middle-income countries where vision exams can be highly inaccessible due to a shortage of experienced eyecare professionals. This work aims to assess if a machine learning (ML) approach, when applied to data obtained with an affordable handheld autorefractor, could increase access to clinical-quality subjective refraction (SR) when operated by non-experts.

Methods: Data used for this analysis was obtained from a clinical study performed at Aravind Eye Hospital in Madurai, India, using a low-cost portable wavefront aberrometer, an early prototype of the QuickSee (QS) (PlenOptika, Inc., USA). A total of 669 participants were enrolled with ages ranging between 15 and 70 years (35.2 ± 13.7) and spherical equivalent error between -6.0 D and 3.5 D (-0.7 ± 1.67 D). Four ML regressor models were trained and tested for each power vector M, J0 and J45: random forest (RF), gradient boosting (GB), extreme gradient boosting (XGB), and a custom assembly model (ASB) that averages the predictions of RF, GB, and XGB. Algorithms were trained on a dataset of 1,244 samples using as input features: age, gender, Zernike coefficients up to 5th order, and measurement quality related metrics provided by the autorefractor. A smaller subset of 518 unseen samples was used to test the agreement of the predictions against SR using Bland-Altman analysis, overall prediction error in terms of mean absolute error (MAE) and root mean squared error (RMSE), and the percentage of agreement for 0.25 D and 0.5 D thresholds.

Results: All models improved the agreement with SR compared to the baseline autorefraction, but ASB obtained the best results (Table 1). Bland-Altman analysis showed a decrease in the 95% limits of agreement of ±0.63 D, ±0.14 D, and ±0.08 D for M, J0 and J45, respectively. The wavefront-aberrometry related variables had the biggest impact on the prediction, while demographic and measurement quality-related features showed a heterogeneous but consistent predictive value.

Conclusions: These results suggest that ML is effective for improving precision in predicting patient's SR from objective measurements taken with a low-cost portable device.

CONTROL ID: 3707705

SUBMITTER (NAME ONLY): John Demirs

TITLE: Spatial distribution of VEGF-A isoforms in macular retinas with or without wet AMD

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.T. Demirs, T.R. Vollmer, C.W. Wilson, S. Poor, D.S. Rice, C.L. Grosskreutz, Ophthalmology, Novartis AG, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: John Demirs: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Vollmer: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Wilson: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Poor: Commercial Relationship: Code N (No Commercial Relationship) | Dennis Rice: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Grosskreutz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent innovations in in-situ hybridization technologies allows for the distinction between alternatively spliced transcripts of the same gene. VEGF-A is a driving force in choroidal neovascularization and promotes new vessel growth into the sub-retinal and sub-RPE space, but it is unclear if the spatial distribution or expression levels of specific VEGF-A isoform transcripts are a major contributor to pathogenesis. Here, we evaluated the gene expression and distribution of three VEGF-A isoforms (VEGF-A 121, VEGF-A 165, VEGF-A 189) in cross sections of postmortem eyes using BASEscope technology for any wet AMD-associated alteration in VEGF isoform expression levels and spatial distribution.

Methods: Human postmortem globes were collected (< 6 hours post-mortem) in accordance with the Declaration of Helsinki, fixed and processed. AMD grading was performed on H&E sections. Specificity of BASEscope probes was confirmed by in situ hybridization of Calu6 cells transiently transfected with cDNAs encoding the VEGF-A isoforms. In-situ hybridization of probes against donor tissue was performed to assess VEGF mRNA distribution and expression levels in the posterior regions of eyes from control (n = 10) and wet AMD donors (n = 5). Probes against PPIB and POLR2A were used for normalization of VEGF-A expression. Quantification was performed using HALO software.

Results: After quantitation and normalization, no statistically significant difference in VEGF-A isoform transcript expression was observed in the macular regions of sections from wet AMD donor eyes. The spatial distribution of VEGF-A isoforms, throughout the retina layers, was unchanged in sections from both wet AMD and control donor eyes. Similar results were observed in the peripheral retina.

Conclusions: There was no statistically significant difference in the levels of VEGF isoforms between the two study groups. Confounders for this study are age and treatment history of lesions. VEGF synthesis may be transient and highly focal. Evaluating these lesions posthumously may not fully capture the relevant dynamics of the disease. Alternatively, differential regulation of VEGF isoforms that are involved in wet AMD may not be at the level of transcript, and thus there may be differences in protein levels. Isoform specific antibodies are not well characterized and were not tested in this study.

CONTROL ID: 3707706

SUBMITTER (NAME ONLY): Soumya Sahu

TITLE: Optimal Selection of Longitudinally Measured Imaging Biomarkers Affecting Conversion Time to Neovascular AMD Using a Regularized Multivariate Bayesian Joint Model

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. De Sisternes, Carl Zeiss, California, UNITED STATES|T. Leng, D. Rubin, Stanford University, Stanford, California, UNITED STATES|M.N. Alam, Stanford University, Stanford, California, UNITED STATES|S. Sahu, J. Sun, S. Basu, Department of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|S. Sahu, J. Hallak, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|J. Hallak, AbbVie Inc, North Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an interpretable statistical model involving optimally selected spectral-domain optical coherence (SD-OCT) imaging biomarkers related to conversion time from non-neovascular to neovascular age-related macular degeneration (AMD)

Methods: The HARBOR dataset, with 686 fellow eyes and time-varying SD-OCT images, was used for this study. Twenty-one drusen imaging features were extracted at each visit.

A multivariable joint model was implemented which consists of two parts fitted jointly- (1) nonparametric mixed effect models using natural cubic splines of ‘time’ and demographic factors to smoothen longitudinal trajectories of standardized imaging biomarkers, (2) a time-to-conversion model with 5 selected single nucleotide polymorphisms (fixed covariates) and smoothened trajectories of the longitudinal biomarkers (time-dependent covariates). For (2), 3 different models were considered: (a) a model with longitudinal biomarker values, (b) rate of changes in biomarker trajectories, (c) and area under trajectory (AUT).

A Bayesian regularized approach was used for selection among the 21 biomarkers in this multivariable model. A variable importance (VI) measure was defined as the probability of being over .25 in the absolute magnitude of the regularized coefficients of longitudinal variables in the standardized scale.

Results: The top drusen biomarkers based on VI for 3 models were as follows (posterior mean, VI):

(a) value: area (.21, .33) and volume (.16, .26) within 3mm of fovea;

(b) rate of change: area within 3mm (-4.2, 1) and 5mm (-1.5, .54), volume within 3mm (5.8, 1) of fovea, total area within the field of view (FOV) (-.28, .5);

(c) AUT: area within 3mm of fovea (.12, .18), mean area in FOV (.08, .13).

Conclusions: High values and high AUT of drusen area and volume within 3mm of the fovea expedite the conversion to neovascular AMD. However, variations in time for area and volume yield opposite interpretations. Low variations in drusen area over time expedite the conversion, whereas high variations in drusen volume do not. Additionally, as the distance from fovea increases, the impact of drusen area and volume dies out as we observe at 5mm distance, where only drusen area has an impact through its variations over time. Lastly, aggregate and mean area in FOV delay the conversion with higher variations and lower AUT, respectively.

CONTROL ID: 3707713

SUBMITTER (NAME ONLY): Aman Kumar

TITLE: Optical Coherence Tomography Angiography Compared with Indocyanine Green Angiography in Uveitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kumar, W. Kongwattananon, H. Sen, S. Kodati, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. Kumar, Albany Medical College, Albany, New York, UNITED STATES|W. Kongwattananon, Chulalongkorn University, Bangkok, Bangkok, THAILAND|

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ABSTRACT BODY:

Purpose: To compare hypocyanescent lesions on Indocyanine Green Angiography (ICGA) to choriocapillaris flow deficits on Optical Coherence Tomography Angiography (OCTA) in eyes with posterior and panuveitis.

Methods: En-face 6x6 OCTA images of the choriocapillaris and mid-phase ICGA images from patients with posterior and panuveitis were retrospectively reviewed and images were quantitatively compared using ImageJ. Using feature-based image registration, the OCTA image was mapped to the ICGA image. Each lesion was outlined, binarized and then overlapped to determine the Dice similarity coefficient (DSC). Bland-Altman analysis was used to compare measurements of lesion morphology including four primary features: lesion number (LN), lesion density (LD%), lesion circularity (LCi) and mean lesion size (MLS). Lastly, eyes were divided into clinically quiet group and an active group and subgroup comparison of DSC values were conducted.

Results: A total of 36 eyes from 26 patients were analyzed. The overall agreement between lesions from ICG and OCTA was classified as good (mean DSC = 0.744; 95% confidence interval [0.679, 0.809]). No significant differences between the mean LN, LD%, LCi, and MLS were noted. LN and LCi were slightly higher in ICGA compared with OCTA. LD% and MLS were slightly higher on OCTA compared with ICGA. Eyes with active disease (0.642 ± 0.175, n = 12) had a significantly lower DSC compared to those eyes with quiet disease (0.789 ± 0.183, n = 24) (P = 0.028).

Conclusions: OCTA appears to be a reasonably accurate measure of choriocapillaris flow deficits in patients with posterior and panuveitis compared to hypocyanescent lesions on ICGA.

CONTROL ID: 3707715

SUBMITTER (NAME ONLY): Bhakti Patel

TITLE: Pattern Electroretinogram Parameters are associated with inner retinal and foveolar macular thickness layer measurements in glaucoma suspects.

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Patel, J. Tsai, V. Gliagias, P.P. Shah, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|A. Tirsi, S.A. Obstbaum, C. Tello, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|D. Orshan, New York Institute of Technology, Old Westbury, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma has been associated with retinal ganglion cell (RGC) damage and their dysfunction, as well as with thinning of the inner retinal thickness layers; but to the best of our knowledge, no such data is available regarding the involvement of the photoreceptor thickness layer, especially in glaucoma suscepts (GS). The aim is to evaluate the relationships between steady state pattern electroretinogram (ssPERG) with inner and outer retinal layer thicknesses in GS.

Methods: Forty eyes from twenty glaucoma suspects were enrolled in this cross-sectional study conducted at Manhattan Eye Ear Throat Hospital. Subjects underwent comprehensive eye examination, as well as Humphrey visual fields, SD-OCT thickness measurements, and ssPERG testing. Spearman, Pearson, and partial correlation analyses were used.

Results: Spearman's rho analysis showed PERG parameters were significantly correlated with almost all the sectorial retinal thickness measurements ($r_s > 0.352$, $p < 0.03$). As expected, Pearson correlation analysis revealed significant associations between all PERG parameters and the ganglion cell layer (GCL) ($r > 0.352$, $p < 0.041$) and inner plexiform layer (IPL) ($r > 0.356$, $p < 0.039$) thicknesses independently. Additionally, partial correlation showed that Magnitude (Mag) and MagnitudeD (MagD) PERG parameters were significantly and negatively correlated with foveolar outer nuclear layer (ONL) ($r = -0.572$, $p = 0.004$). No other associations between PERG parameters and parafoveal ONL and outer plexiform layer (OPL) were found.

Conclusions: In GS, retinal ganglion cell (RGC) dysfunction, assessed by means of PERG testing, was associated with not only thinning of the ganglion cell layer and inner plexiform layers independently, but also with simultaneous swelling of the foveolar outer nuclear layer demonstrating a possible combined and simultaneous glaucomatous morphological change to the photoreceptors (cone swelling, infiltration of glial cells, and increased extracellular matrix deposition) as well as to the RGCs (reductions in the size of cells, axons, and dendritic tree, apoptosis). More studies are needed to investigate the electrophysiology of the retinal neuronal pathway in glaucoma as well as to determine the possible breakdown of the neurovascular coupling in GS.

CONTROL ID: 3707716

SUBMITTER (NAME ONLY): Hassan khojasteh

TITLE: Spectral-domain optical coherence tomography morphological characteristics in patients with cone dystrophy

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. khojasteh, J. Regenold, A. Akhavanrezayat, I. Karaca, S. Park, G. Uludag, C. Or, H. Ghoraba, Q.D. Nguyen, Byer Eye Institute,Stanford University School of Medicine, Palo Alto, California, UNITED STATES|H. khojasteh, F. Bazvand, M. haidari, A. Mahmoudi, S. Mohammadi, H. Riazi Esfahani, M. Mirghorbani, A. Azarkish, Farabi Eye Hospital, Tehran, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To describe spectral-domain optical coherence tomography (SD-OCT) morphological features of patients with cone dystrophy and to determine the relationship between these findings and visual acuity.

Methods: Forty-two patients (84 eyes) with the diagnosis of cone dystrophy based on clinical findings and electroretinogram (severely reduced or non-recordable cone response with preserved rod function) were included in our study. SD-OCT imaging was performed and images were evaluated regarding the integrity and pattern of hyper-reflective outer retinal bands and other findings. The relationship between these findings, age, central retinal thickness (CRT), and best-corrected visual acuity (BCVA) was assessed.

Results: SD-OCT images of 82 eyes showed outer retinal abnormalities. Five SD-OCT morphological categories were found (figure 1): Outer retinal atrophy (24.4%), undifferentiated outer retinal layers (22.0%), ellipsoid zone (EZ) disruption (19.5%), outer foveal defect (17.1%), and prominent outer retinal layers (17.1%). Also, five isolated OCT findings were found (figure 2) including, foveal hypoplasia (14.6%), trans-retinal hyperreflective dots (THD) (29.3%), outer plexiform layer (OPL) schisis (11.3%), pseudodrusen (9.8%), and EZ bowing (13.4%). Age and CRT were significantly different across the morphological categories ($p<0.001$). Eyes with prominent outer retinal layers and outer retinal atrophy had the best and worst visual acuity, respectively.

Conclusions: SD-OCT imaging shows extensive morphologic findings in cone dystrophy, which can be utilized to evaluate/diagnose these patients and may serve as predictive biomarkers of visual acuity.

CONTROL ID: 3707717

SUBMITTER (NAME ONLY): Yulia Aziza

TITLE: Barrier Function Response to Type I Interferon on Immortalized Human Corneal and Conjunctival Epithelial Cells

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Aziza, Y. Ban, S. Kinoshita, C. Sotozono, Department of Ophthalmology, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|S. Kinoshita, Department of Frontier Medical Science and Technology for Ophthal, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: Interferon β (IFN-β), a subtype of type I IFNs, has an anti-viral effect as part of a response to viral double-stranded RNA (dsRNA) through the Toll-like receptor (TLR) 3 and retinoic acid-inducible gene I (RIG-I) pathways. We previously evaluated the response of synthetic dsRNA stimulation on immortalized human corneal limbal epithelial (HCLE) and conjunctival epithelial (HCjE) cells and found an increased barrier function in those cells. In this study, we investigated the effect of type I IFNs on ocular-surface barrier function in cultured HCLE and HCJE cells.

Methods: HCLE and HCjE cells were cultured on 12-mm Transwell® inserts (Corning®) and stimulated with 0ng/mL (control) and 0.25, 2.5, and 25ng/mL IFN-β, and transepithelial electrical resistance (TER) was measured before stimulation and every 3 hours up until 24-hours post stimulation. Tight junction [claudin (CL)-1, CL4, and CL7] and glycocalyx [mucin (MUC)-1, MUC4, and MUC16] protein expressions were then evaluated via real-time polymerase chain reaction (PCR), western blotting, and immunohistochemistry examinations.

Results: At 24-hours post stimulation with 2.5 and 25ng/ml IFN-β, a significant TER increase of 25.0% and 34.6%, respectively, in the HCLE cells and 10.9% and 15.0%, respectively, in the HCjE cells was observed compared with that in the control cells ($P<0.05$). The TER increase began at 3 hours post stimulation, and remained up until 24 hours. Post stimulation with 2.5ng/mL IFN-β, real-time PCR ($P<0.05$), western blotting ($P<0.05$), and immunohistochemistry findings revealed increased expression of CL1, CL4, MUC1, MUC4, and MUC16, yet no change of CL7 expression, in both the HCLE and HCjE cells compared with the control cells.

Conclusions: In this study, the evaluation of tight junction and glycocalyx protein expression in HCLE and HCjE cells post stimulation with IFN-β revealed that IFN-β stimulation increased the barrier function of those cells, thus illustrating that it plays a significant beneficial role of promoting an anti-viral effect on the ocular surface.

CONTROL ID: 3707718

SUBMITTER (NAME ONLY): Rachel Hutto

TITLE: Generation of an inducible, photoreceptor-specific model of oxidative stress in zebrafish

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Hutto, K.M. Rutter, S.E. Brockerhoff, Biochemistry, University of Washington, Seattle, Washington, UNITED STATES|S.E. Brockerhoff, Opthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress is considered a hallmark of aging and is purported to play a role in many retinal diseases. However, many in vivo models of oxidative stress and damage are limited due to systemic effects or a lack of inducibility. This study aimed to generate an inducible zebrafish model of cone photoreceptor-specific oxidative stress using the KillerRed protein, which generates reactive oxygen species when photobleached.

Methods: We injected plasmid containing mitochondrially-targeted KillerRed under the cone gnat2 promoter into embryos to generate Tg(gnat2:mito-KillerRed) zebrafish. For live imaging of cone mitochondria, Tg(gnat2:mito-KillerRed) fish were crossed with Tg(gnat2:mito-TagBFP) fish and stimulated with 561 nm laser.

An optogenetic stimulus array was constructed using 565nm LED Stars, an aluminum heatsink, an LED driver, and a power supply. LEDs were attached to the heatsink in an array to fit under the 12 wells of a standard 48-well plate fitted to 3D-printed housing. Zebrafish larvae were subject to 15 minute intervals of stimulation from 4 to 6 days of age.

Results: Confocal timelapse stimulation of gnat2:mito-KillerRed in fish co-expressing gnat2:mito-BFP shows an induction of cone mitochondrial migration, a previously reported response to mitochondrial stress (FigA). LED stimulation similarly increases the total number of mislocalized mitochondria in gnat2:mito-KillerRed fish relative to control fish lacking KillerRed and unstimulated gnat2:mito-KillerRed fish (FigB). LED stimulation of gnat2:mito-KillerRed fish caused a specific disruption in mitochondrial morphology in cones while normal morphology of photoreceptors and other retinal cells was maintained (FigC).

Conclusions: Our results demonstrate that the Tg(gnat2:mito-KillerRed) zebrafish model can be used as an inducible tool for monitoring photoreceptor responses to mitochondrial oxidative stress. Future work with this model will evaluate its potential for studying chronic oxidative stress as animals age.

CONTROL ID: 3707719

SUBMITTER (NAME ONLY): Joanne Thomas

TITLE: Optical coherence tomography (OCT) findings in a pediatric uveitis cohort

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Thomas, Augusta University, Augusta, Georgia, UNITED STATES|S. Yeh, University of Nebraska Stanley M Truhlsen Eye Institute, Omaha, Nebraska, UNITED STATES|J. Shantha, Francis I Proctor Foundation for Research in Ophthalmology, San Francisco, California, UNITED STATES|L. Phung, L. Ward, M. Regueiro, G. O'Keefe, Emory Eye Center, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe OCT findings in pediatric uveitis patients and analyze visual acuity changes over time.

Methods: A retrospective chart review of pediatric patients (0 to 18 years old) seen at the Emory Eye Center between 2008 and June 2020 with a diagnosis of uveitis and OCT imaging available was conducted. Data collected included demographic data, uveitis etiology, anatomical uveitis location, best-corrected visual acuity (BCVA), findings on OCT, and treatment.

Results: There were 204 patients and 327 eyes with a diagnosis of pediatric uveitis and at least one OCT on record. The average age was 11.5 years with 57% females (116), 43% Black (87) and 33% Caucasian (68). 137 (67%) patients had bilateral uveitis with the majority, 194 (95%), with a non-infectious etiology. Anatomical location of uveitis was anterior, intermediate, anterior/intermediate, posterior, or panuveitis in 42%, 24%, 9%, 10%, and 15% respectively. At baseline on OCT, there were 222 normal eyes, 19 eyes with an epiretinal membrane (ERM), 53 eyes with macular edema, 14 eyes with both macular edema and ERM, and 19 eyes with subretinal fibrosis. On mixed model analysis controlling for the correlation that exists between eyes of the same subject, the worst initial BCVA was seen in eyes with epiretinal membrane and macular edema, followed by macular edema eyes, subretinal fibrosis, and eyes with an ERM with a logMAR BCVA of 0.95, 0.75, 0.73, and 0.50 respectively ($p<0.0001$). Notably, with most abnormal OCT findings, BCVA improved over 24 months except for ERM eyes, which showed a logMAR BCVA change of 0.50 to 0.60 ($p<0.0001$). In a sub-analysis of patients with macular edema with or without subretinal fluid (SRF), there was no difference between baseline clinical characteristics or BCVA in patients who had SRF.

Conclusions: OCT imaging in pediatric uveitis is important for diagnosis and monitoring progression of sight-threatening complications. Pediatric uveitis cases show a high proportion of bilateral involvement and prevalence of complications leading to worse BCVA, which demonstrates that prompt treatment and continued monitoring via OCT imaging can prevent ocular sequelae leading to blindness.

CONTROL ID: 3707721

SUBMITTER (NAME ONLY): Rohun Gupta

TITLE: Reductions in Retinal Vessel Diameter are associated with Retinal Ganglion Cell Dysfunction and with decreased Ganglion Cell Layer-Inner Plexiform Layer Thickness Measurements in Glaucoma Suspects.

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gupta, A. Tirsi, C.R. Lacher, J. Tsai, V. Gliagias, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|A. Tirsi, C. Tello, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|S. Tello, Rye High School, Rye, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Decrease in retinal vessel diameters (VD) has been well established in glaucoma, but no such relationships were reported in glaucoma suspects (GS) yet. This study hypothesized that decreased VD had a significant relationship with changes in steady-state pattern electroretinography (ss-PERG) and in the ganglion cell layer - inner plexiform layer (GCL-IPL) in GS.

Methods: Thirty-one eyes (20 patients) were enrolled in the study at Manhattan Eye Ear and Throat Hospital, based on normal Humphrey 24-2 visual field test, suspicious optic nerve head, and glaucoma stage 0. Each subject underwent full ophthalmologic examination, optical coherence tomography (OCT), OCT-angiography (OCTA), and ss-PERG. The OCTA images were analyzed in ImageJ. A linear regression analysis was used.

Results: In the linear regression model controlling for age, race, spherical equivalent (SE), and central corneal thickness (CCT), VD explained a 4.7% variance in Magnitude (Mag) ($p = 0.169$), 9.2% variance in MagnitudeD (MagD) ($p = 0.021$), and 16.9% variance in MagD/Mag ratio ($p = 0.009$).

After controlling for age, signal strength, and CCT, the linear regression model with GCL-IPL as the dependent variable found VD significantly associated with the average GCL-IPL (AvGCL-IPL) ($p = 0.006$), minimum GCL-IPL (MinGCL-IPL) ($p = 0.002$), superior sector (S) ($p = 0.007$), superonasal sector (SN) ($p = 0.014$), inferior sector ($p = 0.023$), and inferonasal (IN) sector ($p = 0.014$). In an identical linear regression model, Mag was significantly associated with S ($p = 0.005$), SN ($p = 0.047$), superotemporal (ST) sector ($p = 0.01$), and IN sector ($p = 0.02$). MagD had a significant relationship with AvGCL-IPL ($p = 0.015$), MinGCL-IPL ($p = 0.006$), superior sector ($p = 0.003$), ST ($p = 0.009$), and IN ($p = 0.05$). MagD/Mag ratio was significantly associated with the AvGCL-IPL ($p=0.003$), MinGCL-IPL ($p < 0.001$), and S ($p = 0.046$).

Conclusions: Retinal VD reductions were significantly associated with a decrease in MagD and MagD/Mag ratio as well as with specific GCL-IPL parameters in GS. These findings add evidence to the vascular theory of glaucoma indicating the possible presence of a breakdown of neurovascular coupling in GS, where high demands of retinal ganglion cells in energy are not met by adequate blood supply.

CONTROL ID: 3707727

SUBMITTER (NAME ONLY): Hye Jun Joo

TITLE: Correlation between corneal endothelial cell parameters and complete blood cell count

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Joo, Y. Shin, Kangnam Sacred Heart Hospital, Yeongdeungpo-gu, KOREA (THE REPUBLIC OF)|Y. Shin, Hallym BioEyeTech Research Center, Hallym University College of Medicine, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Hye Jun Joo: Commercial Relationship: Code N (No Commercial Relationship) | Young Joo Shin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the association between the neutrophil-to-lymphocyte ratio (NLR) and human corneal endothelial cells (CEnCs).

Methods: A total of 307 eyes from 307 subjects who underwent specular microscopy were included. Corneal endothelial cell density (CECD), hexagonality (HEX), central corneal thickness (CCT), coefficient of variation (CV), and cell area were measured using specular microscopy. Whole blood samples were obtained to measure the complete blood cell count. The NLR was calculated, and its relationship with CEnCs was evaluated.

Results: CV was positively correlated with the percentage (%) of neutrophils ($r = 0.120$, $p = 0.037$) and absolute neutrophil count ($r = 0.131$, $p = 0.022$) and negatively correlated with the % of lymphocyte ($r = -0.131$, $p = 0.022$). HEX was correlated with the % of neutrophil ($r = -0.156$, $p = 0.006$), % of lymphocyte ($r = 0.141$, $p = 0.014$), % of basophil ($r = 0.142$, $p = 0.013$), NLR ($r = -0.129$, $p = 0.024$), and the mean corpuscular volume ($r = 0.121$, $p = 0.035$). The prevalence of diabetes did not show a statistically significant correlation with various indicators of corneal endothelial cells.

Conclusions: CV and HEX, which indicate the stability of CEnCs, are associated with NLR in the peripheral blood, suggesting that systemic inflammation and immunity may implicate the pathology of CEnCs. In addition, glycemic control may affect the corneal endothelial cells rather than the presence of diabetes.

CONTROL ID: 3707730

SUBMITTER (NAME ONLY): Mamoru Ogawa

TITLE: Intensive outdoor activity for 1 week increased choroidal thickness

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The increasing myopia prevalence globally is a relatively recent social health problem. Outdoor activity is an evidence-based environmental factor that protects against myopia progression. The purpose of the current study was to study the positive ocular effects of intensive outdoor activity for only 1 week.

Methods: Children aged 10 to 13 years participated in an intensive outdoor activity program, i.e., more than 2hours on the first day, 3 hours on the second day, and 6 hours daily on subsequent days for a total of 6 days during the 2021 summer vacation at the National Akagi Youth Friendship Center. Eye examinations included measurement of the refractive error using the HOYA iTrace Surgical Workstation (Tracey Technologies) and axial length and corneal thickness using swept-source optical coherence tomography (SS-OCT) biometry (IOLMaster700, Carl Zeiss Meditec AG), choroidal thickness using SS-OCT (Xephilio OCT-S1, Canon), tear fluid volume (Schirmer test and strip meniscometry test), and a questionnaire. These parameters were analyzed at the start and end of the program using the paired-t test. Data from the left eyes were analyzed.

Results: Seventeen children (mean±standard deviation age, 12.0±1.0 years; 47.1% female) were included. The baseline and final choroidal thicknesses were, respectively, 359.5±121.7 and 397.4±122.1 μm ($p < 0.001$). The respective central corneal thicknesses also differed significantly, i.e., 579.0±45.6 and 584±44.6 μm ($p < 0.002$). The refractive errors and axial lengths did not differ significantly, -1.69±1.48 diopters (D) vs -1.83±1.87 D ($p = 0.201$) and 24.15±0.97 mm vs 24.15±0.96 mm ($p = 0.463$). The tear fluid volume did not differ significantly between the start and end of the program.

Conclusions: Our results suggested that intensive outdoor activity even for 1 week increased the choroidal thickness in Japanese schoolchildren. Further studies are needed to assess the effects in more subjects and thelong term.

CONTROL ID: 3707731

SUBMITTER (NAME ONLY): Ella Berry

TITLE: Greater physical activity is associated with neuroretinal thinning in glaucomatous and normative cohorts

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.C. Berry, H. Marshall, S. Mullany, J. Schmidt, D. Thomson, M. Hassall, S.R. Lake, R.A. Mills, J. Landers, O. Siggs, J.E. Craig, Ophthalmology, Flinders University College of Medicine and Public Health, Bedford Park, South Australia, AUSTRALIA|S. Diaz Torres, S. MacGregor, QIMR Berghofer Medical Research Institute, Herston, Queensland, AUSTRALIA|R. Casson, The University of Adelaide Discipline of Ophthalmology and Visual Sciences, Adelaide, South Australia, AUSTRALIA|O. Siggs, Garvan Institute of Medical Research, Darlinghurst, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: A multicohort investigation of the association between physical activity and longitudinal structural thinning in a cohort of early manifest primary open-angle glaucoma and between self-reported physical activity and total macular thickness in a population-based cohort.

Methods: In the discovery phase, 402 participants from the Progression Risk of Glaucoma: RElevant SNPs with Significant Association study wore a tri-axis accelerometer for a continuous seven-day period. Participants were split into tertiles based on the mean number of daily steps. The retrospective rate of Spectral-Domain Optical Coherence Tomography (SD-OCT) macular ganglion cell-inner plexiform layer (mGCIPL) was compared between tertiles. For the replication phase, self-reported exercise data from 29,708 individuals from the UK Biobank were cross-sectionally correlated with total macular thickness using SD-OCT imaging.

Results: Following adjustment for ocular and demographic covariates, the most active tertile was associated with a thicker cross-sectional mGCIPL (multivariate P=0.013) and demonstrated a 0.23µm/year slower rate of mGCIPL thinning (beta: 0.07µm/year/SD 95% CI 0.02-0.12 P=0.004). The most active tertile also exhibited a 2-fold lower risk of Guided Progression Analysis detected event based mGCIPL progression compared to the least active tertile (hazard ratio: 2.01 95% CI: 1.06-3.34; P=0.027). The magnitude of this association strengthened after adjusting for relevant cardiovascular and systemic comorbidities (0.08µm/year/SD 95% CI 0.03-0.13 P=0.003). A secondary analysis of cross-sectional visual fields demonstrated a higher daily step count was also associated with a higher mean deviation (less visual field damage) at time of accelerometer acquisition (beta: 0.24dB/SD 95% CI: 0.05-0.43 P=0.013). Assessment of the UK Biobank cohort revealed a positive correlation between self-reported days per week of exercise and total macular thickness (0.01SD/day 95% CI: 0.005-0.13 P<0.001).

Conclusions: Greater physical activity was associated with both a thicker cross-sectional mGCIPL and slower rate of mGCIPL thinning in primary open-angle glaucoma. Furthermore, greater physical exercise was associated with a thicker total macular thickness in the UK Biobank. These results implicate physical activity as a relevant covariate for neuroretinal degeneration, which may be relevant to glaucoma disease progression.

CONTROL ID: 3707736

SUBMITTER (NAME ONLY): Meleeka Akbarpour

TITLE: Relationship between pseudoisochromatic plates and cone contrast thresholding to evaluate red and green color vision

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: One commonly utilized color vision deficiency test is the Hardy-Rand-Rittler (HRR) Pseudoisochromatic plates; however, its scoring is categorical and has limitations in detecting subtle deficiencies and disease progression. Cone Contrast Threshold (CCT) has demonstrated sensitivity and specificity in identifying color vision deficit with a numerical score. We sought to correlate the categorical results of the HRR test with quantitative CCT test results.

Methods: Patients initially underwent HRR pseudoisochromatic plate and then CCT testing (ColorDx CCT, Konan Medical, Irvine, CA). They were grouped by their HRR score as either “Normal” (n=44) or “Unclassified” red/green deficit (n= 26). Subjects were first tested with 10 screening plates, and if they incorrectly read any HRR screening plate, they were directed to read specific plates to determine severity of deficit. Subjects with “Unclassified” red/green deficits read all severity plates correctly but scored a 9 out of 10 or lower on the screening plates. CCT scoring between “Normal” and “Unclassified” HRR groups were compared using an independent samples t-test. Subjects that were diagnosed with glaucoma, glaucoma suspect, or any retinal pathologies were excluded from analysis.

Results: Normal subjects had significantly higher CCT scores in red (96.25) and green (91.34) testing than Unclassified subjects, who scored 69.11 and 63.11 respectively (Table 1). Lower CCT scores were related to greater deficits in color vision. Subjects with Unclassified HRR test results showed larger standard deviations in red (SD= 45.82) and green (SD= 42.08) sensitivity scores on CCT, compared to subjects with Normal HRR test results in red (SD= 18.00) and green (SD= 19.40) sensitivity scores on CCT.

Conclusions: Subjects with normal HRR scores had significantly different CCT scores than subjects with unclassified HRR scores. Granular numerical scoring with CCT may enable clinicians to monitor subtle changes in patients’ color vision. Further delineation and analysis of “mild, medium, and strong” HRR categories could be made to allow for improved correlation between HRR and CCT scoring.

CONTROL ID: 3707745

SUBMITTER (NAME ONLY): Quyen Luong

TITLE: Engineering an affibody to modulate angiogenesis via Ang2/Tie2 signaling pathway

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Luong, K. Trempy, A. Galindo, H. Uehara, B.K. Ambati, University of Oregon, University of Oregon, Eugene, OR, US, academic, Eugene, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiopoietin-2 (Ang2) along with VEGF signaling have been implicated in abnormal angiogenesis of ocular diseases, including wet age-related macular degeneration (AMD). Ang2 antagonizes Angiopoietin-1 (Ang1) stabilizing effects while promoting vascular destabilization. Antibody therapies targeting both Ang2 and VEGF lead to reduced vascular permeability with noninferior outcomes compared to anti-VEGF therapy alone. Here, we engineered affibodies, high-affinity proteins that are 10-fold smaller than antibodies, to test the hypothesis that inhibiting the binding of Ang2 to its receptor, Tie2, modulates their interaction and signaling.

Methods: Using yeast surface display, we sorted through a library with 10^8 unique affibody-bearing S. cerevisiae via streptavidin magnetic and fluorescence activated cell sorting (FACS), and identified 20 candidate colonies. Colonies were sequenced, inserted into expressing vector pET-28b+, expressed in BL21(DE)3 E. coli, and purified using Cobalt resin/His-Tag affinity chromatography. The identity of the affibodies were confirmed on protein immunoblot. Binding and inhibitory kinetics of affibodies on the yeast surface and purified affibodies were assessed with FACS and ELISA, respectively. Structure binding were computationally predicted and validated.

Results: DNA sequencing showed distinct sequences for all 20 colonies. Western blot confirmed the successful expression of affibody proteins in E. coli. Out of the 20 candidates, 2 colonies showed high affinity to Ang2 proteins on yeast-surface and ELISA. Colony 2 had high affinity (Kd: 8.2 nM) to Ang2 and partial affinity to Ang1 (Kd: 4.4 nM), with IC50 values equal to 65 and 87 nM in inhibiting Ang1/Tie2 and Ang2/Tie2 interactions, respectively. Colony 4 can bind only to Ang2 (Kd: 12.4 nM), with IC50 value equals to 124 nM. Top docking poses from each program showed points of contact with the active site of Ang2.

Conclusions: We demonstrated the binding and inhibitory effects of affibodies that modulates Ang2/Tie2 interactions on yeast-surface, in ELISA, and in silico, which potentially eliminates the Ang2-antagonism on Ang1 signaling and enhances Ang1 stabilizing effects. These findings will be confirmed on cell cultures and animals. With the ability to prevent Ang2-induced permeability and angiogenesis of AMD, affibody is a potential small therapeutic agent for future treatment of AMD.

CONTROL ID: 3707751

SUBMITTER (NAME ONLY): lucas quagliato

TITLE: EFFECTIVENESS OF TREATMENT OF ABDUCENT NERVE PALSY/PARESIS WITH BOTULINUM TOXIN TYPE A (BTA) INJECTION: ANALYSIS OF 10 CASES

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.B. quagliato, Neuro-Ophthalmology, Instituto Penido Burnier, Campinas, São Paulo, BRAZIL|P.D. Fraiha, D.M. Müller, T.V. Batistel, E.B. Quagliato, E.B. Abreu, Instituto Penido Burnier, Campinas, São Paulo, BRAZIL|S.M. Leite, Faculdade Sao Leopoldo Mandic, Campinas, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Objectively evaluate the efficacy of BTA in the treatment of abducens nerve palsy/paresis in 10 patients, analyzing ectoscopy, decrease in diplopia and patient's satisfaction.

Methods: The method consists of applying BTA to the medial rectus muscle, 10 mm away from the limbus, measured with a surgical compass, without opening the conjunctiva, with an insulin syringe and needle.

In eyes with palsy 7 units were applied and in eyes with paresis 5 units were applied.

The medication used was Botox (Allergan,100 U bottle diluted in 2 ml of 0.9% saline solution).

Thirty days after application, results were objectively evaluated and patients were asked about their satisfaction.

Results: Seven had lateral rerctus muscle paresis and three had palsy.

The age of patients ranged from 35 to 70 years (mean 55 years) and 60% were male.

Three patients were diabetic and hypertensive, two were only hypertensive, two had hypercholesterolemia and three had no comorbidities.

At the time of treatment, 4 patients reported having the diagnosis for more than a year, 6 patients sought care within the first 15 days of the disease and were treated with BTA one month after the onset of the condition.

Seven patients had objective improvement of diplopia, five of which had paresis and two had palsy of the medial rectum. After a year of follow-up, only one patient among the seven required a new application of BTA, 6 months after the first, obtaining again a good result. The others continued without diplopia.

Among the 4 patients who performed the BTA application after 1 year of diagnosis, 2 (50%) had improved diplopia and 2 had not. Only 1 patient (25%) was satisfied with the result.

Among the 6 patients with less than three months of evolution, five (83.4%) were satisfied and showed improvement in diplopia and one was dissatisfied (16.6%) and did not show improvement in diplopia.

As for satisfaction with the procedure, the 6 patients who presented paresis said they were satisfied and 4 said they were dissatisfied (one with paresis and three with palsy).

Conclusions: Our results show that the application of TBA was more effective in cases of paresis with 15 days to three months of evolution.

Paresias had a much stronger improvement in diplopia and satisfaction with the treatment, compared to palsies.

The method of injecting BTA without a microscope use or opening the conjunctiva, was simple, safe and effective.

CONTROL ID: 3707753

SUBMITTER (NAME ONLY): Sung Jin Lee

TITLE: A Nonrandomized Phase 2 Trial of EG-Mirotin, a Novel, First-in-class, Subcutaneously Delivered Peptide Drug for Non-Proliferative Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lee, Soonchunhyang University Hospital, Yongsan-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: EG-Mirotin, which includes an active ingredient; EGT022, targeting Non-Proliferative Diabetic Retinopathy (NPDR), the early stage of retinopathy. EG-Mirotin is a drug that is used before capillary damage progresses to an irreversible stage. Safety and efficacy of EG-Mirotin were investigated in subjects with Type 1 or 2 diabetes and NPDR with the degree from moderate to severe.

Methods: Subjects (n=10, 20 eyes) satisfying the selection criteria through the screening test were administered EG-Mirotin once a day (3 mg in 1.5 ml of sterile saline) for 5 days, 5 times in total, and were evaluated of the Ischemic index changes and safety. End-of-study (EOS) is performed approximately 8 weeks ± 1 (57 days ± 7) from the first dose.

Results: A total of 4 Treatment Emergent Adverse Events (TEAE) were observed in 2 subjects out of 10 (20.00%) who received the investigational drug. Among them, no subjects were reported experiencing a TEAE related to the investigational drug. All injections were well tolerated (3 mg in 1.5 ml of sterile saline) with no dose-limiting adverse events, deaths, serious adverse events. The overall average percent change in ischemic index at each evaluation point compared to baseline was statistically significant (Greenhouse-Geisser $F=9.456$, $p=0.004$ for the main effect of time), and a larger change was observed when the baseline ischemic index value was high (Greenhouse-Geisser $F=10.946$, $p=0.002$ for the time*group interaction).

Conclusions: EG-Mirotin was well tolerated and found to reverse the ischemia and leakage of capillaries in the retina caused by diabetes.

CONTROL ID: 3707754

SUBMITTER (NAME ONLY): Joshua Ong

TITLE: Optical Coherence Tomography Characteristics in Neovascular Age-Related Macular Degeneration with 20/40 or Better Visual Acuity

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure: Joshua Ong: Commercial Relationship: Code N (No Commercial Relationship) | Baraa Nawash: Commercial Relationship: Code N (No Commercial Relationship) | Jay Chhablani: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Abbvie;Code C (Consultant/Contractor):Salutaris

ABSTRACT BODY:

Purpose: Most clinical studies have described imaging characteristics of neovascular age-related macular degeneration (nAMD) with 20/40 or worse visual acuity (VA). Considering the lack of literature on nAMD eyes with 20/40 or better, we aim to describe the OCT characteristics in eyes with this unique presentation at baseline and through 1 year follow-up during anti–vascular endothelial growth factor (anti-VEGF) monotherapy.

Methods: Retrospective study involving nAMD patients with 20/40 or better VA from 2011 to 2021 from a single hospital system. Eyes that had anti-VEGF injections from an outside hospital; previous history of associated ocular disease; or did not have 1 year of follow-up were excluded. Monthly OCTs were analyzed for imaging characteristics such as subretinal fluid (SRF), intraretinal fluid (IRF), subretinal hyperreflective material (SHRM), pigment epithelial detachment (PED), choroidal neovascularization (CNV), central macular thickness (CMT), and subfoveal choroidal thickness. Statistical analysis was conducted for differences through 1 year follow-up.

Results: Forty-nine eyes from 45 patients were included and a total of 331 OCT visits were analyzed. Mean age was 75.4±8.2 years. At baseline, 39 eyes (79.6%) had SRF, 24 eyes (49.0%) had IRF, and 20 eyes (40.8%) had both. CNV location was 33 subfoveal (67.4%), 11 juxtafoveal (22.5%), and 5 extrafoveal (10.2%). A total of 29 eyes (59.1%) had findings of SHRM. PED classification was 32 drusenoid (65.3%), 11 fibrovascular (22.4%), 5 flat irregular (10.2%), 1 serous (2%), and no eyes had hemorrhagic PED. CNV type was 32 mixed (34.7%) and 17 type 1 (65.3%). During the first year of follow-up, mean anti-VEGF injection/year was 6.1±2.7. Mean CNV length at baseline was 1112.0±451.4μm, and at 1 year follow-up was 1132.3 ± 506.9μm (p=0.705). Mean subfoveal choroidal thickness was 156.9±32.9μm at baseline, and at 1 year follow-up was 153.9 ± 32.9μm (p=0.606). Mean CMT was 288.8±54.8μm at baseline, and at 1 year follow-up was 274.32±45.4μm (p=0.199).

Conclusions: Among the eyes with nAMD with 20/40 or better, 1/3rd of the eyes presented with non-subfoveal location of CNV with majority being type 1. There was minimal change in CMT and CNV length during the first year of anti-VEGF monotherapy. Further analysis of the area under the curve for various imaging parameters and correlation with visual outcome is underway.

CONTROL ID: 3707756

SUBMITTER (NAME ONLY): Jihee Choi

TITLE: Retinal Horizontal Cell TDP-43 Pathology in Chronic Traumatic Encephalopathy Patients' Retinas

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Choi, C. De Lillo, J. Lin, Department of Pathology and Ophthalmology, Stanford University, Palo Alto, California, UNITED STATES|V.S. Goodwill, D.G. Coughlin, C.J. Sigurdson, A. Hiniker, Department of Pathology, University of California San Diego, La Jolla, California, UNITED STATES|V.E. Alvarez, A.C. Mckee, Boston University Alzheimer's Disease and CTE Center, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Brain pathology in chronic traumatic encephalopathy (CTE) includes the accumulation of hyperphosphorylated tau (p-tau), as well as TAR DNA binding protein 43 kDa (TDP-43) in late stages. Visual abnormalities including photophobia, visuospatial perception defects, and hallucinations have been described in CTE; however, retinal pathology and its contribution to visual defects in CTE are unknown. In this retrospective study, we examined the retinal histopathology from patients with autopsy-confirmed stage IV CTE.

Methods: Enucleation specimens from 8 control patients (6 males and 2 females; ages 61-81; mean: 69.6; SD: 6.9) and 8 patients with stage IV CTE (8 males; ages 62-93, mean: 77.5, SD: 9.9) were collected. Control patients had no known history of traumatic brain injury and no evidence of CTE at autopsy. CTE patients were former contact sport athletes (football, rugby, or boxing). Pupil-optic nerve cross sections were prepared and stained with hematoxylin and eosin (H&E). Immunohistochemistry was performed using anti-p-tau (AT8, Thermo Fisher; 1:1000), anti-pTDP-43 (Cosmo Bio; 1:1000), and anti-TDP-43 antibodies (Proteintech; 1:6000).

Results: Retinal anatomy including retinal lamina thickness was comparable between CTE and control by H&E. No p-tau pathology was observed in either CTE or normal retinas. pTDP-43 staining was commonly found in CTE retinas (7/8) but rarely seen in controls (1/8). Staining was limited to a small subset of inner nuclear layer (INL) interneurons at the junction between INL and outer plexiform layer. TDP-43 staining also revealed a small subset of INL interneurons with cytoplasmic TDP-43+ inclusions and loss of nuclear TDP-43 expression. The location of these cells in INL is most consistent with retinal horizontal cells. TDP-43 pathology was not identified elsewhere in the retina.

Conclusions: This study identified that stage IV CTE is associated with novel retinal TDP-43 and pTDP-43 neuropathology in a discrete subset of retinal INL interneurons consistent with horizontal cells. Additional studies in larger cohorts are needed to define the role of TDP-43 in normal and diseased horizontal cells. Our findings suggest that abnormalities in horizontal cell functions (e.g., light/dark adaptation, contrast sensitivity) secondary to pTDP-43 accumulation may be possible clinical symptoms in CTE patients.

CONTROL ID: 3707757
SUBMITTER (NAME ONLY): Lingxi Hu
TITLE: Quantification of Quasi-IPE Structure in PS-OCT Images
SESSION TITLE: New improvements in imaging and development of biomarkers
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Hu, B. Yang, R. Higashita, J. Liu, Southern University of Science and Technology, Shenzhen, Guangdong, CHINA|X. Li, J. Liu, School of Biomedical Engineering, Wenzhou Medical University Eye Hospital, Wenzhou, Zhejiang, CHINA|M. Yamanari, L. Liu, K. Okamoto, R. Higashita, Tomey Corporation, JAPAN|
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ABSTRACT BODY:

Purpose: Although the depolarization of iris pigment epithelium (IPE) is one characteristic property in polarization-sensitive optical coherence tomography (PS-OCT) images of the anterior eye segment, it received limited attention and has not been investigated to date. This study aims at exploring quantification standards to assess potential properties of the quasi-IPE region in PS-OCT images.

Methods: This cross-sectional, observational study is based on PS-OCT images from 101 healthy eyes observed under identical environment and machine setting. For the quantitative analysis of depolarization in IPE, we use depolarization metric polarimetric entropy that is known to be associated with density of melanin granules. Three PS-OCT images (intensity, grey-scale entropy, and false-colored entropy) at horizontal cross-section of each eye are shown in Fig. 1.

Scleral Spur (SS) is identified using custom-developed model on the intensity image. The highlighted area under iris is manually segmented from grey-scale entropy images as quasi-IPE region. Thickness of the quasi-IPE is measured at a distance of 2000μm from the SS and defined as T2000. The area of the quasi-IPE is defined as IPE-Area. Melanin concentration rate 0.5(MCR0.5) is defined as a ratio of the entropy over 0.5 compared to the total area in IPE-Area. For each variable, differences in gender and age groups were analyzed through student t-test or one-way ANOVA at its temporal or nasal regions separately.

Results: The 101 participants included 79 male and 22 female with mean age of 39.0±11.3yrs, ranging from 18-64yrs. Among the three quantification values, IPE-Area (averages at temporal or nasal (T/N): 1.52±0.25 or 1.34±0.24 mm2) showed significant difference between gender groups. (T/N: p=0.010 or 0.016). While T2000(T/N: 0.27±0.03mm or 0.27±0.04 mm) and MCR0.5 (T/N: 0.79±0.065 or 0.81±0.04.9) were not significant in both age and gender groups.

Conclusions: Quantitative results suggest a stable structural region under the iris. The quasi-IPE structure that has high depolarization might be a combination of melanin concentrated IPE layer and fuzzy area caused by scattering of light by melanin granules.

To the best of our knowledge, this is the first attempt made on quantification of the quasi-IPE region in PS-OCT images. Future work may involve laboratorial examinations on diseased eyes or anatomy-based research.

CONTROL ID: 3707762

SUBMITTER (NAME ONLY): Yi-Zhong Wang

TITLE: Deep Learning Facilitated Study of the Relationship between Visual Field Sensitivity (VFS) and Photoreceptor Outer Segment (OS) Metrics in Retinitis Pigmentosa (RP)

SESSION TITLE: Retinal Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Wang, K. Juroch, T. Luu, D.G. Birch, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|Y. Wang, D.G. Birch, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is known that VFS correlates with ellipsoid zone (EZ) width or area in RP. However, fewer studies reported the relationship between VFS and OS volume. Here we examined the association between VFS and 3D OS metrics with the assistance of a deep learning model (DLM) for automatic segmentation of retinal layers in OCT images.

Methods: Twenty-five patients with RP participated the study. Octopus spot size III VFS were obtained from both eyes of each patient (10-2 for EZ limited in the macula and 30-2 for EZ extended beyond macula). Spectralis high-resolution 9mm 121-line macular volume scans were obtained for all eyes. EZ and apex RPE were automatically segmented by a DLM (Wang et al., TVST 2021). Two graders performed manual correction of DLM segmentation to serve as a reference. The 3D OS map from a volume scan was reconstructed by interpolating the discrete 2D B-scan OS layers defined by EZ and apex RPE over the scan area. OS metrics, including mean OS length, EZ area and OS volume, were computed from the 3D OS maps generated from both DLM (fully automatic) and the reference (manual grading). A regression analysis was conducted to examine the relationship between the mean VFS in dB over the scan area and log OS metrics. Bland-Altman and correlation analyses were employed to compare OS metrics determined by DLM to the reference.

Results: Mean VFS, average OS length, EZ area, and OS volume ranged from 3.1 to 30.2 dB, 7.4 to 31.4 mm, 0.26 to 66.7 mm^2, and 0.0019 to 1.98 mm^3, respectively. Mean VFS was significantly correlated with log average OS length (r = 0.45), EZ area (r = 0.84) and OS volume (r = 0.84) determined by DLM. The model performed similarly to the reference as shown in the Table. Bland-Altman analysis showed a close agreement between the OS metrics determined by DLM and the reference. EZ area and OS volume measured by the model was highly correlated with the reference (r=0.992 and r=0.996, respectively).

Conclusions: Resembling to EZ area, OS volume significantly correlates with retinal sensitivity. The large dynamic range of OS volume may render it being an effective biomarker to assess RP progression. The close agreement between OS metrics determined by DLM and the reference suggests that deep learning may provide efficient tools to facilitate the study on the structure and function relationship in RP.

CONTROL ID: 3707764

SUBMITTER (NAME ONLY): Somaye Jafari

TITLE: Finite Element Model (FEM) of Orbital Suspensory Tissues During Adduction With Unconstrained Globe Translation

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Jafari, J. Park, Ophthalmology, UCLA, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|J.L. Demer, Ophthalmology, UCLA, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|J.L. Demer, UCLA, Department of neurology ucla, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior models of extraocular mechanics have artificially constrained globe translation either by rigidly fixation eye center, or suspending it with unphysiological virtual springs. In order to clarify the role connective tissues on globe rotation & translation, we developed an FEM of incremental adduction induced by active contractility of extraocular muscles (EOMs), including the suspensory tissues & optic nerve (ON).

Methods: The model implemented hemisymmetric geometries of bilaminar EOMs, ON, orbital wall, & orbital fat were obtained from MRI of 5 healthy adults, and measured constitutive tissue properties. Active & passive strain energies of EOMs were defined using ABAQUS (Dassault Systemes) software. The eye was rotated by EOM deformations caused by twitch activation. Ocular center was not fixed, but the globe was instead suspended by Tenon's fascia and an anatomically realistic pulley system, including orbital layer insertions. Starting from 26° adduction, the medial rectus was commanded to incrementally contract, and the lateral rectus to relax. We alternatively modeled absence of orbital fat, versus fat with Young's modulus ranging up to 7 KPa.

Results: During incremental adduction from 26 to 32°, EOM, ON & connective tissue tensions were physiologically plausible, and stress & strain were concentrated at the optic disc. Maximum principal strain was 6% in peripapillary sclera, lamina cribrosa, & ON sheath, while minimum principal strain was -6% in peripapillary sclera, lamina cribrosa, & disc. Von mises stress averaged 30MPa in lamina cribrosa. Without orbital fat, the globe translated 0.1mm nasally but 1.2mm posteriorly, which is non-physiological. With 7KPa stiffness orbital fat, translation was 0.17mm nasally but only 0.33mm posteriorly, which is physiologically realistic.

Conclusions: This physiologically plausible method of simulating EOM activation along with an anatomically realistic suspension system can provide realistic input to model biomechanical behavior of active and passive tissues in the orbit to clarify biomechanical consequences of ON traction during adduction.

CONTROL ID: 3707765

SUBMITTER (NAME ONLY): Mark Seraly

TITLE: A novel homozygous nonsense mutation in the PDE6C gene discovered in a patient with achromatopsia

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Seraly, J.M. Sullivan, Ophthalmology (Ross Eye Institute), University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|J.M. Sullivan, Research Service, VA Western NY Healthcare System, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report a case of autosomal recessive achromatopsia in a child with a novel homozygous nonsense mutation in PDE6C.

Methods: A retrospective chart review was performed with over 4 years of clinical follow up. Investigators reviewed the patient's visual acuity, optical coherence tomography (OCT), full field electroretinography (ffERG), and serial comprehensive ophthalmologic exam results to ascertain patient's clinical phenotype. The patient underwent genetic testing with an Inherited Retinal Disorders panel (NGS, 248 genes) by Invitae-Spark Therapeutics. Genetic results and counseling were disclosed to the patient's parents in person during a subsequent clinic visit by an inherited retinal disease specialist.

Results: A six-year-old male presented with severe photophobia and pendular nystagmus. The patient was born at full term from a consanguineous marriage of two first cousins. Patient's cycloplegic refraction showed high myopic astigmatism with best corrected visual acuity of 20/150 in both eyes (OU). Dilated fundoscopic examination revealed a mild blunting of the foveal light reflex with subtle subfoveal granular pigmentary changes OU. OCT revealed severe attenuation of the subfoveal outer nuclear layer and punctate disruptions in the ellipsoid zone, both consistent with cone photoreceptor loss. Paucity of panretinal cone photoreceptor function was corroborated by ffERG (sedated), which revealed nonrecordable response to the 30Hz flicker photopic stimuli and severe attenuation of photopic amplitudes; scotopic and maximum combined responses were within normal limits. Due to age, color vision could not yet be performed. Genotyping (NGS) revealed a novel pathogenic nonsense mutation (homozygous) in the PDE6C gene [exon 13, c.1669C>T; p.Arg557*]. The patient has remained clinically stable with serial examination every 4-6 months with no evidence of progression of retinal degeneration by serial OCT imaging.

Conclusions: The novel homozygous nonsense (null) mutation in PDE6C (p.Arg557*) is consistent with an achromatopsia phenotype. Marked loss of PDE6C protein solely in cone photoreceptors is expected to severely attenuate cone phototransduction and perhaps challenge cone vitality. Replacement gene therapy (prior to cone loss) would be a reasonable approach for null PDE6C-induced achromatopsia phenotype in future clinical trials.

CONTROL ID: 3707768

SUBMITTER (NAME ONLY): Harshini Chakravarthy

TITLE: Molecular mechanisms mediating diabetic retinal neurodegeneration: Role of Cell Adhesion Molecules

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Chakravarthy, S. Sharma, S. Shree, V. Devanathan, Biology, Indian Institute of Science Education and Research Tirupati, Tirupati, Andhra Pradesh, INDIA|

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ABSTRACT BODY:

Purpose: Recent studies suggest that diabetes affects retinal neurons before onset of more noticeable vascular anomalies. Using cultured neurons and adult retinal explants, we tested the hypothesis that Cell Adhesion Molecules (CAMs) regulate growth of neuronal processes or neurites. We also investigated glucose-sensitive transcriptional regulation of neuronal CAMs and CAM interactions within retinal layers.

Methods: Caspr1 KO was created using CRISPR-Cas9 in Neuro2a and 661W cell lines. Cells were labelled with F-actin and microtubule probes (n=4). Live imaging was done up to 12 hours, and neurite length measured from randomly chosen fields. To check transcriptional regulation of Caspr1, cells were treated with Actinomycin D for 4-6 hours (10µg/ml, n=6). Luciferase reporter assay was performed in cells transfected with Caspr1 promoter reporter construct (n=6). Retinal explants from 10-week old male chicken were cultured in 5mM or 25 mM glucose up to 6 days, cryosectioned 10µm and stained using CAM-specific antibodies for IHC (n=4).

Results: Caspr1 KO cells show significantly increased neurite lengths (23.4±1.5, 22.2±2.6, 25.6±1.3µm) compared to WT (6±1, 11.2±1.1, 12.8±1µm, $p<0.01$) at 1, 2 and 3 hours respectively. Neurite lengths converged in WT (22.8±4.1µm) and KO (26.2±1.4µm, $p=0.47$) after 4 hours up to 10 hours (26.2±4.3µm WT Vs. 27±1.2µm KO, $p=0.87$). Transcriptional regulation of Caspr1 was confirmed by treating cells with Actinomycin D, which effectively blocked Caspr1 mRNA expression ($p=0.002$). Luciferase assay shows that hyperglycemia significantly reduces Caspr1 promoter activity ($p=0.0004$). Retinal explants show partial colocalization of Caspr1 and Contactin1 (Pearson's coefficient>0.7). Hyperglycemia visibly alters intensity and distribution of CAMs across retinal layers.

Conclusions: Previously we showed that hyperglycemia affects neurite growth and CAM expression in primary adult retinal neurons. We now show that Caspr1 negatively regulates initiation of neurite outgrowth, and hyperglycemia leads to transcriptional downregulation of Caspr1 and altered distribution of CAMs in the retina. Neuronal CAM interactions and their regulation will be explored further using studies in an animal model of diabetic retinopathy.

CONTROL ID: 3707769

SUBMITTER (NAME ONLY): Luis Haro-Morlett

TITLE: Stability study of Amniotic-membrane-derived lumican at different storage temperatures, as a potential eye drops treatment

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Haro-Morlett, B. Buentello-Volante, E. Iturriaga-Goyon, P. Sanchez-Cisneros, J. Aguayo-Flores, I. de la Fuente-Bata, F. Magana-Guerrero, Y. Garfias, Biologia Celular y Tisular, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|C.A. Müller-Morales, A. Navas, E.O. Graue-Hernandez, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: Lumican is a small leucine rich proteoglycan present in the human amniotic membrane (AM) that promotes corneal epithelialization. The aim of the present study was determining whether lumican can be extracted from AM and evaluating its stability as AM extract (AME) stored at different temperatures, which could help design epitheliazing-eye drops.

Methods: One-hundred mg of AM were incubated with dispase II at 37°C for 30 min and mechanically de-epithelialized. The de-epithelialized AM was washed and immersed in liquid nitrogen for 40 min, then crushed until a fine powder was obtained, which was solubilized with 2.5 ml of saline buffer with protease inhibitors and centrifuged. Supernatant was collected and stored at -20°C, 4°C and room temperature (RT) for 6, 12, 20 and 32 days until lumican quantitation. Lumican was calculated in each sample according with: [ng/ml lumican / mg of AM tissue].

Results: We obtained similar protein concentrations among all the AME at basal protein quantification. There was no significant difference between protein concentration and time of storage; however, we found significant differences ($p<0.05$) between the AME of 32- and 20-days with respect their basal protein concentration. After that, we analyzed protein concentration with storage temperature, and found significant differences ($p<0.05$) in the AME of 32 days at 4°C and -20°C respect the RT condition, similarly the AME of 20 days had significant results at -20°C respect other temperature conditions. The quantification of lumican in AME showed that the concentration was affected by time of storage and temperature conditions. Lumican in the AME of 12 days was significantly higher ($p<0.05$) in comparison with the AME of 32, 20 and 6 days. There was no differences between lumican in the AME of 32 and 20 days with respect the temperature conditions of storage. Interestingly, when we analyzed the AME of 12 days we significantly ($p<0.05$) observed a high proportion of lumican in temperature conditions of -20°C and 4°C with respect of RT and -70°C. Similarly, we found a significant difference of lumican in the AME of 6 days stored at -20°C, respect other temperatures.

Conclusions: Lumican can be extracted from AM and stored for 12 days as AME, at both temperature conditions of -20°C and 4°C. Further studies are needed to determine AME lumican's function on corneal epithelial cells.

CONTROL ID: 3707770

SUBMITTER (NAME ONLY): Sahak Hovsepian

TITLE: 1-year outcomes of cataract surgery with history of vancomycin use

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Hovsepian, H. Pakhchanian, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|M. Asahi, D. Belyea, The George Washington University Department of Ophthalmology, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare 1-year post-operative outcomes after cataract surgery in patients with and without a 1-year history of Vancomycin use.

Methods: A retrospective cohort study was done using TriNetX (Cambridge, MA, USA), a federal electronic medical database including 69 million records from multiple large health organizations in the United States. Patients who underwent cataract surgery were identified by CPT code and stratified into two cohorts: those with and without a 1-year history of vancomycin use. Cohorts were controlled for age, gender, and medical comorbidities (essential hypertension, diabetes mellitus, chronic lower respiratory diseases, heart failure, nicotine dependence, and body mass index) using a 1:1 matched propensity score analysis. The 1-year outcomes measured were: vitreous hemorrhage (VH), choroidal hemorrhage (CH), retinal detachment (RD) or break, iridocyclitis, retinal edema (RE), corneal edema (CE), cystoid macular edema (CME), epiretinal membrane (ERM), toxic maculopathy (TM), ischemic optic neuropathy (ION), glaucoma, strabismus, dry eye, central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), vitreous opacities, ptosis, endophthalmitis, and retinal vascular occlusions (RVO).

Results: A total of 32,716 cataract surgery patients were included in analysis with 16,358 in each cohort with and without a 1-year history of vancomycin use. The cohort with history of vancomycin use had a significant greater risk of RE (RR, 1.24; 95% CI, 1.04-1.49), CME (RR, 1.23; 95% CI, 1.08-1.4), ERM (RR, 1.28; 95% CI, 1.1-1.48), ION (RR, 2.17; 95% CI, 1.1-4.3), glaucoma (RR, 1.23; 95% CI, 1.09-1.3), dry eye (RR, 1.26; 95% CI, 1.14-1.39), ptosis (RR, 1.27; 95% CI, 1.06-1.53), and endophthalmitis (RR, 2.02; 95% CI, 1.47-2.76), whereas the cohort with no history of vancomycin use had a significant greater risk of vitreous opacities (RR 0.77; 95% CI, 0.64-0.93). No significant difference was seen in the rate of development of VH, CH, CE, RD or break, iridocyclitis, TM, strabismus, CRVO, CRAO, or RVO between the two cohorts.

Conclusions: Medication history, specifically vancomycin antibiotic use, is an important factor to consider when evaluating postoperative complications of cataract surgery. A 1-year history of vancomycin use increased the risk of developing potentially sight-threatening ocular disorders such as endophthalmitis, glaucoma, and ION, but decreased the risk of vitreous opacities.

CONTROL ID: 3707775

SUBMITTER (NAME ONLY): Subeen Park

TITLE: Real-time in-vivo imaging of marmoset photoreceptors based on adaptive optics incorporated differential interference contrast microscopy system

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Park, J. Kim, Sensor system research center, Korea Institute of Science and Technology (KIST), Seoul, KOREA (THE REPUBLIC OF)|H. Jo, D. Kim, College of Engineering, Center for Sensor Systems, KOREA (THE REPUBLIC OF)|H. Jo, D. Kim, Electrical and Computer Engineering, Measurement Engineering Laboratory, KOREA (THE REPUBLIC OF)|K. Lee, D. Song, S. Kim, Ophthalmology, Seoul Metropolitan Government Seoul National University Boramae Medical Center, KOREA (THE REPUBLIC OF)|R.J. Zawadzki, UC Davis Eyepod Imaging Laboratory, Dept. of Cell Biology and Human Anatomy, University of California Davis, California, UNITED STATES|R.J. Zawadzki, Ophthalmology & Vision Science, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Since the retina cells are non-regenerating neuronal cells, detection at the early stage of cell degeneration is important. We developed an in-vivo optical imaging system incorporated with adaptive optics to obtain photoreceptor images in real time.

Methods: To image photoreceptors, we adopted differential interference contrast (DIC) microscopy composed of a polarizer, DIC prism, and analyzer. Also, to reduce the optical aberration from the eye, adaptive optics (AO) was combined with DIC microscopy. Light sources with the wavelengths of 623nm for cell detection and 840nm for AO were used. We performed in-vivo retina imaging in female adult marmosets (5y and 2y). The pupil in marmoset' eye was dilated to obtain the stable optical path in in-vivo imaging. As imaging the retina cell layers, the marmosets were kept under anesthesia via 1-5% isoflurane inhalation. The photoreceptors in marmoset eye were imaged by charge-coupled device (CCD) detector [2752 x 2192 pixels]. Through a real-time AO feedback loop, the improved image was obtained every 0.5 to 1 second.

Results: The figure 1 is the image of the in-vivo photoreceptor layer of retina in the marmoset eye. The photoreceptor layer with circle shape photoreceptors in a mosaic pattern as reported in a previous study[1] was clearly observed by our system. From the size and pattern of photoreceptor, we could expect that the bright parts are cone cells. The curvature of eyes made the blurred area in the image around the outside. The field of view in the image was calculated about 14,000 μm^2. We observed that photoreceptors were densely and uniformly distributed in photoreceptor layer for the normal marmosets.

Conclusions: Conclusions: We imaged marmoset photoreceptors in-vivo with the DIC imaging system incorporated with AO. Retina layers were imaged in real-time in the feedback of AO correction.

1. Troilo, et al. Vision research. 1993; 33(10): 1301-1310

CONTROL ID: 3707779

SUBMITTER (NAME ONLY): LI RONG

TITLE: TPM1 mediates inflammation by regulating PKA/CREB signaling pathway

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. RONG, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|L. RONG, C. Meng, W. Jiangmei, W. Qiong, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|Z. Jing, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Microglia modulate inflammation and neurodegeneration in common neurodegenerative diseases. However, the signalling systems that induce dysregulation of microglial homeostasis are incompletely understood. We have recently identified that tropomyosin 1 (TPM1), an actin binding protein, regulates inflammation and neuronal remodelling in the aging retina. Here, we further investigated the role of TPM1 in regulating microglia activity in BV2 cells, a murine microglia cell line.

Methods: To study the role of TPM1 in inflammation, we first transfected BV2 cells with TPM1 overexpressed plasmids for two days, and then the molecular and morphological alterations of cells were evaluated by qRT-PCR, Western blotting and immunohistochemistry. To study if inhibition of TPM1 could reverse LPS-induced inflammation, we treated cells with TPM1 specific siRNA for one days followed by LPS treatment, and then the inflammatory cytokines were detected. To further study the PKA/CREB signaling pathway, we treated cells with dbCAMP (an activator of PKA) in TPM1 plasmids treated cells, or H89 (an inhibitor of PKA) in siTPM1 treated cells following LPS treatment.

Results: TPM1 overexpression in BV2 cells significantly activated microglia and promoted the release of pro-inflammatory cytokines TNF-α, IL-1β and IL-6 and chemokines COX-2 and iNOS, and downregulated phosphorylated PKA and CREB. TPM1 overexpression failed to regulated p-CREB after treatment with dbCAMP in BV2 cells. When transfecting with TPM1 siRNA in BV2 cells following LPS treatment, we found that TPM1 knockdown remarkably inhibited microglia activation and inflammatory cytokines release, and reversed the decrease of PKA/CREB signaling pathway which was induced by LPS treatment. By applying H89 in BV2 cells, we found that TPM1 knockdown failed to upregulate p-CREB in LPS-treated cells.

Conclusions: Our data demonstrated that TPM1 mediated microglia activation and inflammation by regulating PKA/CREB signaling pathway. The therapeutic approaches targeting the inhibition of TPM1 could be a potential strategy to study microglia homeostasis and inflammation-related diseases.

CONTROL ID: 3707780

SUBMITTER (NAME ONLY): Elena Pacella

TITLE: Effect of COVID-19 lockdown on refractive errors in children aged 5 – 12 years: a retrospective study

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pacella, E. Trovato Battagliola, M. D'Andrea, P. Mangiantini, M. Malvasi, A. Comberiati, R. Migliorini, Sense Organs, Universita degli Studi di Roma La Sapienza Facolta di Medicina e Odontoiatria, Roma, Lazio, ITALY|

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ABSTRACT BODY:

Purpose: To explore whether the COVID-19 lockdown increased the incidence of myopia among age-school children.

Methods: Retrospective study recruiting children aged 5 – 12. Selection: random. Inclusion criteria: healthy children presenting for an eye exam since 2016. Exclusion criteria: presence of ocular comorbidities other than refractive error, spherical equivalent (SE) less than -4D or greater than +4D, BCVA less than 20/20, blepharoptosis, media opacities, corneal or retinal dystrophies, strabismus, amblyopia, nystagmus, or concurrent therapy with atropine 0.01%. Outcome measure: age measured in months, SE of the right eye (RE) measured in diopters (D) under cycloplegia (cyclopentolate 1%). Statistical analysis: ANOVA, Chi-square, Tukey's test. Significance: $p < .05$.

Results: A total of 803 children. In the years prior to COVID-19, the mean SE ± SD diopters in the RE: 0.54 ± 1.49 D in 2016 (n = 160), 0.43 ± 1.84 D in 2017 (n = 145), 0.34 ± 1.41 D in 2018 (n = 152), 0.35 ± 1.75 D in 2019 (n = 166) (ANOVA, p = .659) (Fig. 1). In 2021 (n = 180), the mean SE was -0.08 ± 1.44 D (ANOVA, p = .005). Using the Tukey's test, the mean SE of 2021 changed by -0.619 D 95% CI [-1.091, -0.147] and -0.501 D 95% CI [-0.986, -0.016] as compared to the SE of 2016 and 2017, respectively (Fig. 2). Mean age was comparable in all groups (ANOVA, p = .307). The decrease of the mean SE of the 2021 group corresponds to an increase in the percentage of myopes (≤-0.5D) and a decrease in the percentage of hyperopes (≥ 2D). Myopes represent the 24.10% of children aged 60 – 96 months, and 63.86% of children aged 97 – 144 months. Hyperopes represent 9.64% of children aged 60 – 96 months, and 6.02% of children aged 97 – 144 months. This represents a statistically-significant increase in the number of myopes (Chi-square, p = .016) and decrease in the number of hyperopes (Chi-square, p = .001), as compared to the previous years (2016-2019).

Conclusions: This retrospective study shows a statistically-significant decrease in the mean SE in children aged 5-12 in the year following the COVID-19 lockdown (2021). The percentage of myopes has increased significantly, while the percentage of hyperopes has decreased. Children aged 8 - 12 years showed the greatest refractive change. The lifestyle changes imposed by the lockdown were likely responsible for the increased prevalence of myopia observed in 2021.

CONTROL ID: 3707782

SUBMITTER (NAME ONLY): Sandra Fiorentini

TITLE: Ocular Surface Dysfunction in Patients Presenting for Refractive Surgery Evaluation in the United Arab Emirates.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.F. Fiorentini, Ophthalmology, Mediclinic Parkview Hospital, Dubai, Dubai, UNITED ARAB EMIRATES|R.R. Sayegh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R.R. Sayegh, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|S. Shore, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|S. Shore, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|M. Almheiri, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|

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ABSTRACT BODY:

Purpose: To report the prevalence of Ocular Surface Dysfunction in Patients Presenting for Refractive Surgery Evaluation in The United Arab Emirates.

Methods: Consecutive patients presenting for refractive surgery evaluation were included. Patient information including demographics and current eye drop use were collected. The Dry Eye Questionnaire 5 (DEQ-5) was administered. Slit-lamp findings, Oxford grading of the corneal and conjunctival staining, tear-break-up time (TBUT), Schirmer test, and tear matrix metalloproteinase-9 (InflammaDry) positivity were recorded.

Results: 38 Emirati patients were included. The mean age was 26±8 years (range 17-45) and 22 (57.9%) were female. Ten (27%) patients were using artificial tears, none used other eye drops such as cyclosporine. The mean DEQ-5 score was 5.05±3.90, with 14 (36.8%) scoring more than 6. 13 (36.1%) right and 18 (50%) left eyes had a score>0 on the Oxford scale. There were no other pathologic findings on slit-lamp examination. Mean TBUT was 4.2±3.4 for the right and 4.1±3.3sec for the left eyes, and mean Schirmer score was 17.5±5.4 and 17.7±5.6mm for the right and left eyes, respectively. 11 (29.7%) right and left eyes tested positive for MMP-9.

Conclusions: Subjective and objective findings of ocular surface dysfunction were common among Emirati patients presenting for refractive surgery. Screening for dry eye in this population is important as it may impact the outcome of refractive surgery.

CONTROL ID: 3707783

SUBMITTER (NAME ONLY): LOURDES VIDAL OLIVER

TITLE: Astigmatism effect and its correction on quantitative metrics using optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. VIDAL OLIVER, Ophthalmology, Hospital Clinico Universitario, Valencia, Valenciana, SPAIN|R. Gallego Pinazo, R. Dolz-Marco, Macula Unit, Oftalvist Clinic, Valencia, Valencia, SPAIN|

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ABSTRACT BODY:

Purpose: Refractive errors produce image defocus and may alter quantitative metrics extracted from en face optical coherence tomography angiography (OCTA) images. Up to date it is possible to correct the sphere in commercialized devices using manual or auto-focus, but astigmatism remains uncorrected. This cross-sectional study assessed the qualitative effect of astigmatism on OCTA images and its quantitative analysis.

Methods: Patients undergoing comprehensive ophthalmic examination, including OCTA, were included. We recruited subjects with a measured astigmatism of 0.5 diopters (D) or more. OCTA scans were acquired with and without astigmatism correction on a single visit using SPECTRALIS HRA-OCT2 (Heidelberg Engineering, Heidelberg, Germany) with follow-up mode activated. Astigmatism correction was applied to either the first or second OCTA image in random order using cylindrical lenses adapted to the OCTA device, with values from -1 to -5. The primary outcome measure was vessel density index (VD) in the nasal macular area of the superficial vascular plexus before and after astigmatism correction. A paired t-test was used for total analysis and a two-way ANOVA test for grouped analysis including astigmatism diopters (0.5-1.25, 1.5-2.25, 2.5-3.25 and >3.5) and axis intervals (with the rule, against the rule or oblique).

Results: Ninety-one eyes of 91 subjects were included in our cohort, showing a mean astigmatism of 1.25D (95% CI 1.09-1.41) with a mean age of 63.6 years. Mean VD was significantly higher with astigmatic correction (mean 0.308 (95% CI 0.294-0.322) vs. 0.274 (95% CI 0.259-0.288) $p<0.0001$). Subgroup analysis suggested consistent effects of astigmatism correction depending on the amount of diopters ($p=0.047$) and regardless of the axis ($p=0.119$).

Conclusions: Our data suggest that astigmatic correction increases VD values in OCTA images. Astigmatism correction should therefore be considered in studies that include analyzing quantitative parameters obtained by OCTA. However, further studies will be needed in order to assess the clinical significance of these changes.

CONTROL ID: 3707784

SUBMITTER (NAME ONLY): Gwendoline PIQUIN

TITLE: Early-onset X-linked Retinoschisis: Clinical Presentation and Outcomes

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. PIQUIN, Y. Abdelmassih, G. Martin, C. Edelson, F. Metge, G. Caputo, T. Chapron, La Fondation Adolphe de Rothschild, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To describe clinical characteristics and outcomes of children with early onset X-linked retinoschisis (XLRS).

Methods: In this retrospective consecutive case series we included children diagnosed with XLRS before the age of 2. Presenting signs, clinical characteristics, treatments and outcomes were recorded.

Results: Eight patients (16 eyes) with a mean age of 17.25+/-5.82 months were included. Strabismus was the most common presenting symptom (6 patients, 75%). Clinical signs at first diagnosis included peripheral retinoschisis in 14 eyes (88%, 8 patients) of which 6 (43%) were bullous, vitreous haemorrhage in 3 eyes (19%) and retinal detachment in 3 eyes (19%). The macula was involved in all the eyes. Six eyes (38%) received surgery. At last follow-up, visual acuity, when available, ranged from no light perception to 20/32, no children had persistent retinal detachment.

Conclusions: Children with early-onset X-linked retinoschisis have severe forms. All children had macular involvement and peripheral retinoschisis. Peripheral retinoschisis can be bullous and often extends to the macula. Diagnosis can be often clinical but handheld OCT can be helpful in atypical forms. Complications requiring surgical management are frequent.

CONTROL ID: 3707785

SUBMITTER (NAME ONLY): Lee Mcilreavy

TITLE: Two-dimensional eye velocity distributions of foveal fixation at different gaze angles

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mcilreavy, V.V. Nedelchev, F.A. Ennis, Optometry and Vision Sciences, Cardiff University, Cardiff, Wales, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Small eye movements (drifts, microsaccades and tremors) keep the eye in continuous motion, even as observers attempt to fixate a target. In this study we examine eye velocity distributions from typical observers as they fixate targets presented at different gaze angle. We hypothesise that the mechanics of the oculomotor plant will bias eye velocity towards primary position.

Methods: Twelve typical observers with normal vision were asked to fixate a target (0.4° green dot) presented for 12s at either 0° (primary position) or at eccentricity of ±16° horizontal or ±16° vertical. The targets were presented in a random order against a black background in an otherwise dark room. Observers viewed the targets binocularly and eye movements were recorded at 1000Hz from the eye with better visual acuity. Saccades and blinks were excluded from eye movement data and a bivariate probability density function of target-relative eye velocity was calculated after filtering eye position data. The centroid of the isocontour that encompassed the highest 68% of data was examined to determine any directional bias.

Results: Preliminary results show the mean x coordinate of the centroid has a leftward bias (-0.030 ± 0.092°/s) during right-gaze (+16°), and a rightward bias (+0.039 ± 0.120°/s) during left-gaze (-16°). This difference (0.072°/s) was statistically significant [$t(11) = 2.697$, $p = 0.010$, $d = 0.779$]. In contrast, the mean y coordinate of the centroid had a downward bias during up-gaze (-0.217 ± 0.310°/s) and down-gaze (-0.230 ± 0.281°/s). This difference (0.012°/s) was not statistically significant [$t(11) = 0.101$, $p = 0.461$, $d = 0.029$]. There were no significant differences between any of the eccentric gaze positions and primary position (i.e. 0°).

Conclusions: We have demonstrated that eye velocity during foveal fixation is dependent on gaze angle. Eye velocity is biased towards primary position during horizontal gaze, and downward during vertical gaze. These findings may relate to differences underlying horizontal and vertical oculomotor control. We speculate that the magnitude of the horizontal differences observed will increase with larger gaze angles (i.e. beyond 16°). Our results may have implications for aspects of foveal vision that are critically dependent on eye velocity, e.g., visual acuity, with thresholds potentially varying as a function of horizontal gaze angle.

CONTROL ID: 3707787

SUBMITTER (NAME ONLY): Mukharram Bikbov

TITLE: Safety and Tolerability of Intraocular Cetuximab in Young and Adult Rabbits

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bikbov, S. Panda-Jonas, G. Kazakbaeva, J. Jonas, Ufa Eye Research Institute, Ufa, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: To assess safety and tolerability of intraocularly applied cetuximab as an epidermal growth factor receptor antibody.

Methods: The experimental study included a group of adult rabbits (body weight: 2.4kg) and a group of young rabbits (body weight: 1.6 kg). All rabbits received three intravitreal injections of 0.5 mg cetuximab (Erbitux®) (0.10 mL) (in a concentration of 5mg cetuximab / mL) into their right eyes in 4-week intervals, while the contralateral eyes received intravitreal injections of Ringer's solution in the same volume at the same time points. After each injection, the intraocular pressure was measured in both eyes. All animals underwent regular ophthalmological examinations at baseline and at two-week intervals, including inspection of the external eye, ophthalmoscopy, tonometry, fundus photography and ocular biometry.

Results: The study included 10 adult rabbits with a mean age of 12 months (range: 10 - 14 months) and 8 young rabbits with a mean age of 6 months (range: 5 to 7 months). Neither in the young animal group nor the adult rabbit group did the biometric measurements of axial length, anterior chamber depth and lens thickness and the IOP readings differ significantly between the right (study) eyes and the left (control) eyes (Table 1). None of the eyes showed an intraocular inflammation during the study period or peculiarities of the fundus such as retinal inflammatory infiltration or retinal hemorrhages. Comparing photographs of the anterior segment and of the fundus taken at the study end and at baseline in a masked manner did not reveal any detected difference.

Conclusions: The repeated intravitreal application of cetuximab did not result in any detected intraocular toxic or destructive effect. The results do not contradict the assumption of intraocular tolerability of cetuximab.

CONTROL ID: 3707789

SUBMITTER (NAME ONLY): Swati Singh

TITLE: Cytokeratin Profile and Keratinocyte Gene Expression in Keratinized Lid Margins of patients with Chronic Stevens-Johnson Syndrome

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Singh, M. Koduri, J. Jaffet, S. Shanbhag, S. Basu, V. Singh, Centre for Ocular Regeneration (CORE), Prof. Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|M. Koduri, J. Jaffet, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|S. Shanbhag, S. Basu, The Cornea Institute, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: To study the cytokeratin profile and keratinization-related genes expression in keratinized lid margins of chronic Stevens-Johnson syndrome (SJS) patients.

Methods: Posterior eyelid margins from 24 chronic SJS patients undergoing mucous membrane grafting, and six healthy margins retrieved from orbital exenteration specimens were studied using immunofluorescence staining (CK10, CK1, filaggrin, transglutaminase 1 (TGM1), CK19, MUC5AC) and quantitative PCR (differential mRNA expression of keratinization-related genes- PTEN, HBEGF, KGF, EGF, TGFA, TGFB and TNFA). The staining as well as gene expression was studied separately in the lid margin epidermis (LME, from eyelash root to meibomian glands opening), and lid margin conjunctiva (LMC) segments of eyelid margins.

Results: The expression of CK 1/10, filaggrin, TGM1 in the LMC was similar to the LME in SJS patients. Expression of CK19 was confined to the basal epithelial layer of the LMC in SJS compared to full-thickness expression in normals. MUC5AC expression was absent in LMC of SJS patients. Increased expression of PTEN ($p \leq 0.0001$), KGF ($p \leq 0.056$), TNFA ($p \leq 0.02$), TGFA ($p \leq 0.01$) was observed in the LME of SJS patients compared to normal LME. LMC of SJS patients showed an increased expression of PTEN ($p \leq 0.002$), HBEGF ($p \leq 0.002$), EGF ($p \leq 0.002$), KGF ($p \leq 0.02$), TNFA ($p \leq 0.04$), TGFA ($p \leq 0.003$), and TGFB($p \leq 0.001$) compared to normal LMC. No significant differences were observed in the expression of these genes between LME and LMC of SJS patients. These genes were also validated using String analysis which also revealed the positive regulation of keratinization.

Conclusions: In lid margins of SJS, there is an increased expression of keratinization-related genes compared to normal lid margin. Keratinized LMC shares similar cytokeratin profile and keratinization genes expression as seen in cutaneous epithelium of SJS patients, indicating the possibility of the cutaneous epithelium as a source for keratinized LMC.

CONTROL ID: 3707790

SUBMITTER (NAME ONLY): Yiu Lun Wong

TITLE: Deep-learning measurement of retinal vessel caliber predicts incident myocardial infarction

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wong, C.Y. Cheung, The Chinese University of Hong Kong Faculty of Medicine, Hong Kong, HONG KONG|M. Yu, C. Chong, T. Wong, C. Cheng, C.Y. Cheung, Singapore Eye Research Institute, Singapore, SINGAPORE|T. Wong, C. Cheng, Ophthalmology and Visual Sciences Academic Clinical Programme, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Retinal arteriolar and venular calibers have been proposed to be surrogate measures of systemic microvascular health. We evaluated the associations of deep-learning based retinal vessel caliber measurements with incidence of fatal and non-fatal myocardial infarction (MI) using data from the UK Biobank.

Methods: Prevalent and incident MI was defined with an algorithm developed by UK Biobank, combining information from self-reported medical conditions, operations and medications, hospital admissions and death registries before and after the code date of baseline assessment respectively. Fully automated measurements of central retinal artery and vein equivalents (CRAE/CRVE) from retinal fundus photographs in the area 0.5-2.0 disc diameters away from the optic disc were estimated with a recently validated deep-learning system (SIVA-DLS). Hazard ratios (HR) and area-under-the-curve (AUC) were calculated for evaluating the association and improvement in discriminative performance between CRAE/CRVE with incident MI.

Results: After excluding individuals with prevalent MI and ungradable retinal photographs, 34,841 subjects at risk of incident MI were included in the final analysis. Baseline assessment was conducted from 2009 to 2013, with subjects at risk of MI followed up to March 2020. A total of 375 subjects developed incident MI. Persons with narrower CRAE were more likely to have incident MI (HR 1.67 [95% CI: 1.19-2.36], comparing 1st to 4th quartile, and HR 0.86 [95% CI: 0.75-0.98], per SD increase in CRAE), adjusting for age and gender. When further adjusted for total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, and other risk factors, the association between CRAE and incident MI persisted (HR 1.64 [95% CI: 1.16-2.32], 1st vs. 4th quartile). CRVE was associated when adjusted for age and gender (HR 1.51 [95% CI: 1.06-2.13]) but not in multivariable models. AUC increased significantly from 0.718 to 0.724 (adjusted for age and gender, $p = 0.030$) when CRAE/CRVE is included in the models.

Conclusions: Narrowed retinal arteriolar caliber, reflecting systemic microvascular damage, was associated with incident MI. Deep-learning based retinal vessel caliber measurements from retinal photographs may be a useful biomarker of cardiovascular disease in clinical and epidemiological studies.

CONTROL ID: 3707791

SUBMITTER (NAME ONLY): Fatma AKKAN AYDOGMUS

TITLE: Real-world outcomes for fellow eyes in neovascular age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.S. AKKAN AYDOGMUS, Ankara Sehir Hastanesi, Cankaya, Ankara, TURKEY|F.S. AKKAN AYDOGMUS, O. Onwuka, C. Lasalle, D.J. Ramsey, Ophthalmology, Lahey Hospital and Medical Center, Burlington, Massachusetts, UNITED STATES|O. Onwuka, C. Lasalle, D.J. Ramsey, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|J. Saddemi, Rowan University Cooper Medical School, Camden, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the outcomes at one year between the first and second eyes in patients who develop sequential age-related neovascular macular degeneration (nAMD).

Methods: Treatment-naive patients who sequentially developed nAMD between March 2015 and March 2020 were identified. Outcomes at one-year were compared between the first and second eyes to develop nAMD. All patients were treated with an initial series of 3 monthly loading doses of anti-VEGF agents, followed by further intravitreal injections (IVI) as required. Outcomes included visual acuity (VA), central macular thickness (CMT), as well as evidence for geographic atrophy (GA) and/or pigment epithelial detachment (PED) on optical coherence tomography (OCT) imaging.

Results: Fifty-six patients who sequentially developed nAMD were identified. The mean age was 81.5 ± 7.9 (range 60-94) and 66% were female. The average time to diagnosis of nAMD in the second eye was 474 ± 369 days. The mean number of IVI for the first eye before second eye conversion was 7.8 ± 6.2 (range 1-33). There was no difference in the number of IVI in the first compared with the second eye at one year (8.4 ± 2.6 injections versus 9.0 ± 2.0, P=0.269). VA at diagnosis and after 12 months were better for the second eye compared with the first eye to develop nAMD (0.72 ± 0.53 logMAR vs. 0.41 ± 033 logMAR, P<0.001, and 0.67 ± 0.63 logMAR vs. 0.42 ± 0.36 logMAR, P=0.008). CMT at diagnosis was thicker for the first eye compared with the second eye to develop nAMD (381 ± 120 µm vs. 335 ± 94 µm, P=0.017), but was similar at one year (296 ± 100 µm vs. 278 ± 82 µm P=0.193). At diagnosis, PED height was thicker for the first eye compared with the second eye to develop nAMD (236±208 µm vs. 154±155 µm, P=0.009), but was similar at one year (195±170 µm vs. 141±139 µm, P=0.053). Finally, 3 eyes (5.4%) had GA at the time of nAMD diagnosis in the first eye, whereas 8 eyes (14%) had GA at the time that the second eye developed nAMD (χ^2=2.520, P=0.112). There was a correlation between presence of GA in the first eye and the development of GA in the second eye by the time of its diagnosis (r=0.356, P=0.007).

Conclusions: At diagnosis the second eye to develop nAMD tends to have better vision and thinner CMT. Although these eyes had better anatomical outcomes at one year, this did not translate into better vision nor a lower disease burden requiring less treatment

CONTROL ID: 3707793

SUBMITTER (NAME ONLY): Stefan Ploner

TITLE: Ultrahigh resolution OCT, volume merging, and advanced signal reconstruction improve visualization of the RPE-Bruch's complex

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.B. Ploner, L. Husvogt, J. Schottenhamml, A. Maier, Pattern Recognition Lab, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|S.B. Ploner, S. Chen, E. Moult, J.G. Fujimoto, Department of Electrical Engineering and Computer Science and Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|N.K. Waheed, Ophthalmology, New England Eye Center, Boston, Massachusetts, UNITED STATES|J. Schottenhamml, Department of Ophthalmology and Eye Hospital, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Subtle structural changes in the outer retina may be associated with physiological aging and age-related macular degeneration (AMD) pathology. We previously reported that basal laminar deposit (BLamD), an established histological marker for AMD, can be visualized clinically in early AMD eyes using ultrahigh resolution OCT (UHR OCT).

However, OCT images are degraded by speckle noise and sharpness is reduced by the acquisition process, making fine features including outer retinal layers and BLamD difficult to visualize directly. Merging multiple volumes can reduce noise and improve contrast, but requires motion correction accuracy below the scanner resolution, which is challenging due to fixational eye motion.

Using our scanner-independent framework for advanced computational motion correction and signal reconstruction (MoReOCT), we correct for involuntary saccadic motion and blinks, and improve signal-to-noise ratio and sharpness to enhance the visualization of thin outer retinal features.

Methods: Retrospective image processing was performed on OCT scans of a prospectively enrolled cohort of AMD patients (53 eyes / 39 subjects), as well as a cohort of healthy adult subjects (63 eyes / 39 s.) using a prototype UHR OCT instrument (2.7 μm axial resolution). For each eye, we acquired 6 volumetric scans over a 6 x 6 mm field centered at the fovea, with alternating horizontal and vertical B-scan direction. The eye motion trajectory of each scan was estimated from the data in a joint optimization such that the consistency of orthogonally scanned volumes was maximized.

To compensate image blur inherent in the acquisition process, we applied deconvolution at the scale of the measured PSF in the axial direction. While deconvolution increases speckle noise when applied to individual OCT acquisitions, this effect can be mitigated by jointly using all volume data in a 3-D iterative reconstruction with total variation denoising. The visualization setup uses moderate denoising, whereas the processing setup, intended for algorithmic analysis, uses more.

Results: The figures compare unprocessed B-scans to virtual B-scans resampled at identical A-scan locations from the MoReOCT volumes.

Conclusions: Volume merging and signal reconstruction can improve visibility of fine retinal structures and could aid in understanding AMD pathogenesis.

CONTROL ID: 3707794

SUBMITTER (NAME ONLY): Ryan Zubricky

TITLE: Injection intervals in real-world neovascular age-related macular degeneration (nAMD) switch brolucizumab (BROL) patients with at least 12 months of follow-up

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zubricky, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|J. McCoy, R. Donkor, C. McCrossin, D.G. Miller, H. Pham, J. Schartman, L. Rao, L.J. Singerman, M. Novak, S. Pendergast, J.M. Coney, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|S. Buxy Sinha, N. Sonbolian, H. Karcher, Novartis AG, Basel, Basel-Stadt, SWITZERLAND|L. Zhou, KMK Consulting, Morristown, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study if nAMD patients switching from one anti-Vascular Endothelial Growth Factor (VEGF) to BROL prolonged injection intervals.

Methods: A retrospective cohort study at Retina Associates of Cleveland, Inc. (extracted December 1, 2021) analyzed nAMD patients who switched from one anti-VEGF to BROL, had at least 3 BROL injections, 12 months follow-up or more and no other anti-VEGF in first 12 months post switch.

Injection intervals, visual acuity (VA), and central macular thickness (CMT) were analyzed at baseline (first BROL injection) and last follow-up, along with follow-up distribution post first BROL injection. Inflammatory events were reported.

Subgroup analyses were based on last interval at baseline,< 56 days and ≥ 56 days, to study previous anti-VEGF and BROL intervals; and on highest to lowest quartile of baseline VA, to study initial VA at switch effects on BROL intervals.

Results: Study identified 172 eyes from 152 patients (53.3% females), with baseline age of 80.7±7.8 years, VA of 1.14±0.87 logMAR and CMT of 300.7±118.1 µm. Quantities reported as mean±standard deviation (SD).

Last interval pre-switch was 48.8±25.8 days. Last post-switch interval follow-up period extended 32.7±61.1 days. First BROL injection follow-up period was 552.5±104.4 days. VA and CMT change from baseline to last follow-up was 0.13±0.75 logMAR (vision gain) and 39.6±112.1 (thickness reduction) respectively (Table 1). Post switch, 1.7% of eyes developed inflammatory events.

For subgroup of intervals < 56 days pre-switch, intervals extended 40.2±50.8 days post-switch and higher VA gain than in main group. Lower interval extension and VA gain for ≥ 56 days subgroup compared to < 56 days subgroup and main group (Table 1). All groups saw similar CMT reduction.

Lowest quartile baseline VA interval extension was much larger compared to other quartile and main groups. Highest quartile VA at baseline saw largest CMT reduction. Vision gain was seen post BROL switch in all quartile subgroups (Table 2).

Conclusions: Treated for a year or more, 172 nAMD BROL switch eyes extended intervals, maintained vision and saw CMT reduction, strengthening real-world BROL use literature findings.

CONTROL ID: 3707796

SUBMITTER (NAME ONLY): Victor Augustin

TITLE: Scheimpflug Tomography versus Optical Coherence Tomography to detect subclinical corneal edema in Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.A. Augustin, M. Köppe, H. Son, T. Yildirim, R. Khoramnia, G. Auffarth, Department of Ophthalmology, University of Heidelberg, David J. Apple International Laboratory for Ocular Pathology and International Vision Correction Research Centre (IVCRC), Heidelberg, GERMANY|J. Meis, Institute of Medical Biometry and Informatics, University of Heidelberg, Heidelberg, GERMANY|

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ABSTRACT BODY:

Purpose: The purpose of this study was to compare the ability of Scheimpflug tomography and anterior segment optical coherence tomography (OCT) in detecting subclinical corneal edema in patients with Fuchs endothelial corneal dystrophy (FECD) without clinical corneal edema.

Methods: In this single-center, consecutive case series, 47 eyes of 29 patients with FECD were analyzed. The main outcome measures were anterior/posterior keratometry and central/thinnest corneal thickness. The criteria for subclinical corneal edema were loss of regular isopachs, displacement of the thinnest point of the cornea, and presence of posterior surface depression. Tomographic analyses were performed using Scheimpflug imaging (Pentacam HR) and OCT (anterior segment swept-source optical coherence tomography).

Results: The measurement of the continuous variables revealed a significant difference between the 2 devices. The anterior curvature was steeper and the posterior curvature was flatter when measured with OCT (P = 0.001). The OCT showed a lower central corneal thickness and thinnest corneal thickness (P = 0.001). The agreement between both devices to detect subclinical corneal edema was high. The interdevice reliability for loss of parallel isopachs as measured by Cohen kappa coefficient was 0.84; for the displacement of the thinnest point of the cornea, it was 0.6, and for the focal posterior corneal surface depression, it was 0.62. Subclinical corneal edema was detected in 72.3% of the patients with both devices. In only 2 cases (4.3%), subclinical corneal edema was detected by one of the devices.

Conclusions: Scheimpflug and OCT imaging were both able to detect tomographic patterns of subclinical corneal edema. Therefore, both devices can help decision-making, favoring early endothelial keratoplasty in symptomatic patients with FECD without clinical corneal edema.

CONTROL ID: 3707798

SUBMITTER (NAME ONLY): Yuta Saito

TITLE: Effect of IGF-1 Administration on Retinopathy in a Low-Birth-Weight Rat Model of Oxygen-Induced Retinopathy

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Saito, K. Yokoyama, H. Onda, Ophthalmology, Showa University, Tokyo, JAPAN|

Commercial Relationships Disclosure: Yuta Saito: Commercial Relationship: Code N (No Commercial Relationship) | Kota Yokoyama: Commercial Relationship: Code N (No Commercial Relationship) | Hidetoshi Onda: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Long-term low levels of serum Insulin-like growth factor-1 (IGF-1) in premature infants have been reported to increase the risk of retinopathy of prematurity and maintaining high serum IGF-1 levels early in life in premature infants may be a way to prevent postnatal complications.

We previously reported a small for gestational age model (SGA-rat) in which pregnant rats were fed a protein-restricted diet to induce intrauterine growth failure of the fetuses and were born with low birth weight (Saito et al. 2014 ARVO). Serum IGF-1 in SGA-rats at day 8 (P8) was significantly lower than that in rats born to pregnant rats fed a normal diet. In this study, we investigated the effect of IGF-1 administration on SGA-rats of Oxygen-Induced Retinopathy (OIR).

Methods: Pregnant Sprague-Dawley rats were purchased and fed a normal diet (20% protein) (control group: Cnt-rat) or a low-protein diet (10% protein) (SGA-rat) with equivalent calories from day 13 of gestation. For OIR, OxyCycler was used for oxygen loading for 7 cycles (from birth to P14) with 50% O_2/24h and then 10% O_2/24h as one cycle, and the rats were kept in ambient air until P18.

Experiment 1: After weighing the pups at P18, the blood was collected from the heart, and the removed right eye was fixed to prepare retinal flatmounts. From these retinal flatmounts, we assessed the severity of retinopathy (Clock Hours: CH) and measured the percentage of avascular area to total retinal area (%AVA). In the left eye, the retina was homogenized and measured the intraretinal vascular endothelial growth factor (VEGF) and IGF-1 concentrations by ELISA. Serum IGF-1 concentration was also measured by ELISA, and the endpoints were compared between SGA-rat and Cnt-rat.

Experiment 2: To exogenously supplement IGF-1 to SGA-rat, IGF-1 (2ug/g body weight) was subcutaneously administered once daily from P4 to P14 (SGA-IGF1-rat), and the same endpoints as in Experiment 1 at P14 and P18 were compared with the control group (SGA-PBS-rat) that received PBS.

The results obtained are presented as mean ± standard deviation, and statistical analysis was performed using Wilcoxon test with p-value < 0.05 as significant difference.

Results: The results are shown in Table 1.

Conclusions: In SGA-rat, low IGF-1 levels immediately after birth did not contribute to the worsening of retinopathy, but rather IGF-1 administration worsened retinopathy.

CONTROL ID: 3707801

SUBMITTER (NAME ONLY): Rebecca Zeng

TITLE: Structure-Function Associations between Contrast Sensitivity Function and Central Foveal Thickness in Patients with Idiopathic Epiretinal Membrane

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zeng, F. Vingopoulos, A. Bannerman, H. Wescott, G. Baldwin, R. Katz, M. Kasetty, T. Koch, I. Garg, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|R. Zeng, F. Vingopoulos, A. Bannerman, H. Wescott, G. Baldwin, T. Koch, I. Garg, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Rebecca Zeng: Commercial Relationship: Code N (No Commercial Relationship) | Filippos Vingopoulos: Commercial Relationship: Code N (No Commercial Relationship) | Augustine Bannerman: Commercial Relationship: Code N (No Commercial Relationship) | Hannah Wescott: Commercial Relationship: Code N (No Commercial Relationship) | Grace Baldwin: Commercial Relationship: Code N (No Commercial Relationship) | Raviv Katz: Commercial Relationship: Code N (No Commercial Relationship) | Megan Kasetty: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Koch: Commercial Relationship: Code N (No Commercial Relationship) | Itika Garg: Commercial Relationship: Code N (No Commercial Relationship) | John Miller: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon;Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Sunovion;Code C (Consultant/Contractor):Carl Zeiss;Code C (Consultant/Contractor):Genentech

ABSTRACT BODY:

Purpose: Contrast sensitivity function (CSF) is a visual function metric that might be of clinical value when evaluating intraretinal changes in patients with epiretinal membrane (ERM). Inherent limitations of existing contrast sensitivity tests have prevented its adoption into practice thus far. Employing a novel active learning quantitative CSF (qCSF) device, we aim to investigate structure-function associations between central foveal thickness (CFT) visual acuity (VA) and contrast sensitivity.

Methods: This prospective cross-sectional study included 115 eyes of 88 patients with idiopathic ERM. Patients underwent complete ophthalmic examination and spectral-domain OCT imaging (SD-OCT, SPECTRALIS® Heidelberg). CFT values were obtained from SD-OCT images. Contrast sensitivity (CS) was measured using the Manifold Contrast Vision Meter (Adaptive Sensory Technology, San Diego, CA). Outcomes included Area under the Log CSF (AULCSF), contrast acuity (CA) and CS thresholds at 1, 1.5, 3, 6, 12, and 18 cycles per degree (cpd). Pearson's correlations and mixed-effects multiple linear regression models were performed to evaluate structure-function associations between CFT, LogMAR VA and CSF outcome measures.

Results: Median LogMAR VA was 0.21 (0.19) and median AULCSF was 0.86 (0.21). Median CFT was 345 (106.2) μm. CFT was moderately correlated with VA (R=0.435, p<0.001), AULCSF (R= -0.489, p<0.001), CA (R=-0.492, p<0.001), and CS thresholds at cpd3 (R=-0.450, p<0.001), cpd6 (R=-0.494, p<0.001), and cpd12 (R=-0.418, p<0.001). CFT showed weak correlation with CS threshold at cpd1.5 (R=-0.291, p=0.002). In the mixed-effects regression models, CFT was positively associated with LogMAR VA (ß=0.0009, p<0.001), and negatively associated with AULCSF (ß=-0.001, p <0.001), CA (ß=-.0009, p<0.001) and CS thresholds at 1cpd (ß=-0.0004, p <0.031), 1.5cpd (ß=-0.0005, p<0.001), 3cpd (ß=-0.001, p<0.001), 6cpd (ß=-0.002, p<0.001), 12cpd (ß=-0.001, p<0.001).

Conclusions: Our results suggest that CFT is more strongly associated with qCSF than VA in patients with ERM. qCSF method may serve as a valuable visual function metric for assessing patients with ERM.

CONTROL ID: 3707804

SUBMITTER (NAME ONLY): Sedona Rosenberg

TITLE: Lifetime Associations Between Patients with Substance Use Disorders and Ocular Disease

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rosenberg, H. Pakhchanian, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|M. Asahi, D. Belyea, Ophthalmology, The George Washington University, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Sedona Rosenberg: Commercial Relationship: Code N (No Commercial Relationship) | Haig Pakhchanian: Commercial Relationship: Code N (No Commercial Relationship) | Rahul Raiker: Commercial Relationship: Code N (No Commercial Relationship) | Masumi Asahi: Commercial Relationship: Code N (No Commercial Relationship) | David Belyea: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the lifetime associations between various ocular conditions in patients with substance use disorders, including alcohol, cannabis, opioid, and nicotine related disorders, from the time of diagnosis.

Methods: We conducted a retrospective cohort study using TriNetX, a national, federated database that provides aggregate electronic health record data from 80 million unique patient files within 56 healthcare organizations. Patients diagnosed with substance use disorders (SUD) were identified using ICD-10 diagnostic codes and followed for subsequent diagnoses of 27 ocular conditions over the span of a patient's lifetime after initial diagnosis of substance use disorder. The primary outcomes were incidence, as listed in Table 1. Patients with pre-existing ocular disease were excluded from this analysis.

Results: A total of 7,546,278 patients were included with 1,460,831 diagnosed with alcohol use disorders (AUD), 775,891 with cannabis use disorders (CUD), 573,583 with opioid use disorders (OUD), and 4,753,973 with nicotine dependence (ND). 37% (10/27) of ocular diagnoses had the same incidence between each SUD cohort. AUD had the most diagnoses with the highest incidence (48%) and CUD had the most diagnoses with the lowest incidence (63%). AUD had the highest incidence of disorders of refraction and accommodation (3.1%), glaucoma (1.4%), and cataract (1.4%). CUD had the lowest incidence of cystoid macular degeneration (0%), puckering of macula (0.1%), and retinal vascular occlusion (0.1%). OUD had the highest incidence of strabismus (0.3%) and dry eye syndrome (1.5%) and lowest incidence of retinal vascular occlusion (0.1%). ND had the highest incidence of conjunctivitis (2.1%), glaucoma (1.4%), and cataract (1.4%). The incidence of glaucoma, cataracts, macular degeneration, blindness, and disorders of refraction and accommodation were higher among patients with alcohol and nicotine use disorders than cannabis and opioid use disorders. The incidence of dry eye syndrome was highest among patients with opioid use disorders while the incidence of conjunctivitis was highest among those with nicotine use disorders.

Conclusions: This the first national-scale study that sheds light on the associations between substance use disorder and the most common ocular diseases. These findings can be useful when examining a patient with a history of SUD.

CONTROL ID: 3707805

SUBMITTER (NAME ONLY): Jason Dossantos

TITLE: Assessment of eye pain symptoms among pediatric students during the COVID-19 pandemic

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Dossantos, J. Thomasian, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|M.M. Manrique, I. Dortonne, R. Birdsong, Ophthalmology, Children's National Hospital, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Computer Vision Syndrome (CVS) is a form of asthenopia that manifests with symptoms such as eye pain/discomfort, headache, and blurred vision, among others. Early identification of CVS is especially relevant during the COVID-19 pandemic, which has led to an increase in virtual schooling and digital screen time among children worldwide. This study seeks to evaluate differences in etiologies of eye pain, treatment recommendations, and the relationship between refractive errors and eye pain in the pediatric population before and during the COVID-19 pandemic.

Methods: After IRB approval, we retrospectively reviewed the records of patients who visited our tertiary care institution between 2018 and 2021 with a chief complaint of eye pain, determined by the encounter's primary ICD-10 code. Patients who visited before 03/11/2020, when the WHO declared COVID-19 a pandemic, were classified as the pre-pandemic group (PPG), while patients who consulted after this date were classified as the during-pandemic group (DPG). Demographics, symptoms, refractive error, treatment, and schooling method were recorded as covariates and analyzed using a Chi-square and Fisher's exact test.

Results: 38 patients were included in the study (21 PPG; 17 DPG). The mean age was 10.1 ± 3.2 years, and the majority were African American (44.7%). Virtual school attendance for the PPG and DPG was 4.8% and 58.8%, respectively ($P<0.05$) (Table 1). There was a higher prevalence of reported blurry vision, headaches, eye redness, eye swelling, and rubbing among DPG patients (Table 1). Counseling on screen time minimization was more likely to be documented in the DPG (Table 2). A greater proportion of patients were prescribed new glasses in the DPG though there was no significant relationship between eye pain and refractive error or anisometropia in either group ($P>0.05$).

Conclusions: The increased prevalence of CVS symptoms in the DPG suggests an association between virtual schooling and CVS in children. There is a role for ophthalmologists to improve rates of counseling for the prevention of eye pain-related symptomatology with digital device usage. Further studies will survey parents to assess their awareness of conservative treatments for eye pain such as artificial tears and decreased screen time.

CONTROL ID: 3707807

SUBMITTER (NAME ONLY): Cameron Czerpak

TITLE: The Strain Response of the Lamina Cribrosa of Glaucoma Patients to Intraocular Pressure Decrease

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Czerpak, T.D. Nguyen, Mechanical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|B.K. Zimmerman, H.A. Quigley, T.D. Nguyen, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M.S. Kashaf, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure: Cameron Czerpak: Commercial Relationship: Code N (No Commercial Relationship) | Michael Kashaf: Commercial Relationship: Code N (No Commercial Relationship) | Brandon Zimmerman: Commercial Relationship: Code N (No Commercial Relationship) | Harry Quigley: Commercial Relationship(s);Code C (Consultant/Contractor):Heidelberg Engineering | Thao Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To measure the strain response to intraocular pressure (IOP) decrease produced in the lamina cribrosa (LC) after suture lysis surgery and analyze for the effects of glaucoma damage.

Methods: Twenty-nine suture lysis procedures after trabeculectomy were performed on 27 eyes from 26 glaucoma patients, average age = 68 years, IOP decrease = 12mmHg, and mean deviation (MD) range = -0.17 to -29.2dB. iCare IOP and radial scans by optical coherence tomography (OCT) of the optic nerve head were captured before and 20 minutes after suture lysis (Midgett et al. 2019). Images were enhanced (Fig. 1) and the anterior LC border manually marked. Digital volume correlation (DVC) was applied to the OCT images to calculate the strain response. Compliance of the strain response (strain/ΔIOP) and retinal nerve fiber layer (RNFL) were averaged overall and in four LC quadrants (inferior, superior, nasal, temporal). Linear regression was used to analyze relationships between strain, compliance, IOP, RNFL, MD, and visual field index (VFI).

Results: A larger IOP decrease produced larger tensile anterior-posterior strain (E_{zz}), maximum principal strain (E_{max}), and maximum shear strain (Γ_{max}) ($p<0.01$). Anterior lamina depth (ALD) did not consistently increase or decrease with IOP decrease; 24% of eyes had posterior ALD change. Eyes with thinner RNFL had a more compliant E_{max}, Γ_{max}, and torsional shear strain ($E_{\theta z}$) response to IOP change ($p<0.04$) (Fig. 2). A more compliant E_{max}, $E_{\theta z}$, and E_{rz} response was found for eyes with worse MD ($p<0.05$), and a more compliant $E_{\theta z}$ and E_{rz} for lower VFI ($p<0.05$). Analyzing quadrant averages showed that the association between thinner RNFL and more compliant E_{max} and Γ_{max} response occurred in the nasal quadrant and also in the inferior quadrant for Γ_{max} ($p<0.05$).

Conclusions: IOP decrease predicted tensile strain, but not ALD change direction. The LC of eyes with greater glaucoma damage (thinner RNFL, worse MD, and lower VFI), had a more compliant strain response. These findings may result from progressive LC remodeling with glaucoma damage into a more curved structure or may represent baseline LC biomechanics prone to damage.

CONTROL ID: 3707808

SUBMITTER (NAME ONLY): David Ramsey

TITLE: Underdiagnosis of Risk of Glaucoma in Patients with Retinal Vein Occlusions

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Ramsey, D.S. Kelly, T. Ganti, Ophthalmology, Lahey Hospital and Medical Center, Burlington, Massachusetts, UNITED STATES|D.J. Ramsey, D.S. Kelly, T. Ganti, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: David Ramsey: Commercial Relationship: Code N (No Commercial Relationship) | Donel Kelly: Commercial Relationship: Code N (No Commercial Relationship) | Tej Ganti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the rate of glaucoma-related diagnoses in patients with branch retinal vein occlusions (BRVOs) or central retinal vein occlusions (CRVOs) with the rate in patients without retinal vein occlusions (RVOs).

Methods: Patients with RVOs were identified from billing records from 2016 to 2020. These were compared to a reference group of patients with bilateral dry eye syndrome, age- and gender-matched 2:1 to the patients with RVOs. Patients were further classified by subtype of glaucoma. Records of patients without known glaucoma-related diagnoses were evaluated for potential underdiagnosis, utilizing criteria of intraocular pressure (IOP) ≥22mmHg and/or cup-to-disc ratio (CDR) ≥0.6 and/or CDR difference between eyes ≥0.2.

Results: 643 patients were identified with RVOs, including 376 patients with BRVOs and 278 patients with CRVOs. Glaucoma-related diagnoses were significantly more common in patients with RVOs compared with a reference group (9.8% versus 5.4%, $p<0.001$). The rate of diagnosed, open-angle glaucoma was significantly greater in patients with BRVOs (4.0%) and CRVOs (4.7%) compared with a reference group (1.7%, $p<0.001$). By contrast, suspicion for open-angle glaucoma was similar between patients with RVOs compared with the reference group (3.9% versus 2.9%, $p=0.235$). However, patients with BRVOs (28.6%) and CRVOs (33.3%) were more likely to have clinical findings associated with glaucoma risk compared with the reference group (18.2%, $p<0.001$).

Conclusions: Patients with RVOs have higher rates of diagnosed glaucoma when compared with a reference group. By contrast, RVO patients with clinical findings associated with glaucoma risk are often not coded as glaucoma suspects.

CONTROL ID: 3707809

SUBMITTER (NAME ONLY): Luca Rosignoli

TITLE: Visual outcomes of central retinal artery occlusion treated with hyperbaric oxygen therapy

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Rosignoli, E. Chu, J. Carter, D. Johnson, J. Sohn, S. Bahadorani, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the difference in visual outcome and incidence of neovascular glaucoma (NVG) among patients with CRAO undergoing hyperbaric oxygen therapy or conservative management.

Methods: We conducted a retrospective chart review of 48 patients presenting with CRAO at University Health System from 2011 to 2020. 15 underwent HBOT based on US Navy Treatment Table 6; 33 patients did not undergo hyperbaric therapy. HBOT parameters and total treatment time were documented. Student's T-test and Chi-square test were used to compare the change in best-corrected visual acuity (BCVA) and incidence of neovascular glaucoma (NVG) in the two groups

Results: In the HBOT group, mean elapsed time between symptom onset and HBOT initiation was 18.27 ± 10.4 hours. In the control group, mean elapsed time between symptom onset and diagnosis was 41.47 ± 55.59 hours. Hyperbaric treatment was stopped for three patients due to anxiety, asymptomatic bradycardia, and one tonic-clonic seizure, respectively. There was no difference in logMAR BCVA improvement among the patients who underwent hyperbaric oxygen therapy and those who did not (0.10 ± 0.14, 0.29 ± 0.30, respectively; p=0.22). Incidence of NVG did not differ significantly between the two groups (HBOT: 20.0%; no-HBOT: 15.2%; p=0.676).

Conclusions: HBOT does not appear to improve final visual outcome or incidence of NVG in cases of CRAO. The efficacy of HBOT in management of CRAO may depend on the implemented treatment algorithm.

CONTROL ID: 3707811

SUBMITTER (NAME ONLY): Kyle Cotten

TITLE: Evaluating the Effect of Lens Status on Corneal and Ocular Biomechanical Parameters in Open Angle Glaucoma

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.G. Cotten, C.J. Roberts, A. Mahmoud, M. Slabaugh, Department of Ophthalmology and Visual Sciences, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|C.J. Roberts, A. Mahmoud, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Kyle Cotten: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Roberts: Commercial Relationship(s);Code C (Consultant/Contractor):Ziemer Ophthalmic Systems AG, Oculus Optikgeräte GmbH;Code R (Recipient):Heidelberg Engineering, Inc | Ashraf Mahmoud: Commercial Relationship: Code N (No Commercial Relationship) | Mark Slabaugh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare corneal and ocular biomechanical parameters in phakic, pseudophakic and aphakic subjects with open angle glaucoma.

Methods: The present study includes 83 eyes of 43 phakic patients with primary open angle glaucoma (POAG), 16 eyes of 10 pseudophakic patients with POAG, and 4 eyes of 2 subjects with aphakic glaucoma, all prospectively enrolled. Biomechanical data were acquired using the Corvis ST and Ocular Response Analyzer (ORA). Additionally, central corneal thickness (CCT) was obtained from the Corvis ST and intraocular pressure (IOP) was recorded by dynamic contour tonometry (DCT). Parameters compared include corneal hysteresis (CH), stiffness parameter at first applanation (SP-A1) and highest concavity (SP-HC) and integrated inverse radius. ANCOVA was used to compare ORA data between groups using corneal compensated IOP (IOP_{CC}) as a covariate, and to compare Corvis ST data between groups using DCT as a covariate. The statistical analysis was performed with SAS and significance threshold was set at $P<0.05$. Due to a low n, the aphakic cohort was excluded from statistical analysis.

Results: T-tests revealed no significant between-group differences in IOP_{CC} (17.37 ± 4.41 vs 15.74 ± 2.81; p=0.1607), DCT (18.65 ± 3.78 vs 17.07 ± 2.46; p=0.1114), or CCT (545.74 ± 34.28 vs 538.63 ± 39.32; p=0.4595). CH was significantly greater in the phakic group (9.55 ± 1.9 vs 9.11 ± 1.82; p<0.0001) after controlling for IOP_{CC}. Integrated inverse radius was greater in the pseudophakic group (8.47 ± 0.99 vs 7.79 ± 0.92; p<0.0001) after controlling for DCT. There were no significant differences in corneal (SP-A1) or scleral (SP-HC) stiffness, although the n in the pseudophakic group was too low to be conclusive. Qualitatively, aphakic eyes had a greater unadjusted mean IOP_{CC}, DCT, CCT, SP-A1, SP-HC and CH than both the phakic and pseudophakic cohorts.

Conclusions: Pseudophakic eyes with POAG demonstrated lower stiffness (resistance to deformation) and lower damping (ability to dissipate energy) than phakic eyes. We propose that the contents of the eye affect its response to air-puff-induced deformation, and that the presence of a crystalline lens aids in energy dissipation and limits fluid displacement in the concave corneal phase leading to a stiffer response when compared to pseudophakic eyes. More data are needed to compare the biomechanics of eyes with aphakic glaucoma.

CONTROL ID: 3707813

SUBMITTER (NAME ONLY): Stephen Kaufman

TITLE: ALTERATIONS IN MEASURED INTRAOCULAR PRESSURE FOLLOWING CORNEAL COLLAGEN CROSS LINKING

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.C. Kaufman, C. Liaboe, Ophthalmology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|S.C. Kaufman, Ophthalmology, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|A. Meduri, Ophthalmology, Universita degli Studi di Messina, Messina, Sicilia, ITALY|

Commercial Relationships Disclosure: Stephen Kaufman: Commercial Relationship: Code N (No Commercial Relationship) | Chase Liaboe: Commercial Relationship: Code N (No Commercial Relationship) | Allesando Meduri: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intraocular pressure (IOP) measurements, which can be affected by changes in corneal morphology, are used to screen and follow glaucoma. Riboflavin with ultraviolet-A-induced corneal collagen crosslinking (CXL) is used to treat keratoconus and also changes corneal morphology. The purpose of this study is to evaluate the effect of CXL on measured intraocular pressure.

Methods: A retrospective chart review of 60 keratoconic human eyes, which underwent CXL, were included. Indentation (Tono-Pen: Reichert. Depew, NY USA) tonometry was used to evaluate IOP preoperatively and at one, three, and six-month post-CXL follow-up visits.

Results: The average preoperative IOP was 14.1 +/- 2.1. The average IOP at the 1-month, 3-month, and 6-month follow-up were 17.1 +/- 2.7, 15.8 +/- 2.3, and 16.8 +/- 1.8 respectively. Relative to the preoperative IOP, the IOP at the 1-month, 3-month, and 6-month follow-up were statistically significantly higher.

Conclusions: A statistically significant increase was noted in measured IOP by Tono-Pen after CXL for keratoconus, which is likely due to an increase in corneal rigidity after CXL.

CONTROL ID: 3707815

SUBMITTER (NAME ONLY): Ankur Nahar

TITLE: Female Authorship Trends in Retina: A 25-Year Analysis

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nahar, M. Rama, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|R. Mahmoudzadeh, R.R. Soares, J.A. Haller, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Authorship is a critical component of career advancement in medicine. While there has been a promising trend towards gender equality in academia, men disproportionately outnumber women in first and last author positions even when factoring in comparable publication counts. We performed a cross-sectional study to examine trends in first and last authorship within the field of retina over the last 25 years.

Methods: Original retina articles published between 1995 and 2020 were selected from four journals with the highest h5-index in ophthalmology. Publications by single authors and collaborative study groups as well as those classified as comments, letters, and editorials were excluded. First and last author names were retrieved, and GenderAPI was used to assign sex. Regression analysis was performed to determine whether the changes over time were significant. Chi-square analyses were used to compare distributions of categorical variables in various samples.

Results: A total of 4142 papers were included. The percentage of women in first and last authorship positions significantly increased from 23% to 37.7%, and 14.2% to 24.6% over 25 years, respectively ($P<0.001$, $P<0.001$, respectively; Figure 1A, 1B). When the last authors were women, 32.5% of the first authors were women, and when the last authors were men, only 27.1% of the first authors were women ($P=0.002$). Based on the ASRS 2020 database, only 17% of retina specialists in the United States are female. From our data, 28.2% of first authors and 22.3% of last authors of retina publications from the United States are female authors in 2020 ($P<0.001$, $P<0.001$, respectively).

Conclusions: While a disparity in authorship persists in ophthalmology's subspecialties, our study suggests that retina is a field where the gap is closing. Significantly, a woman as the senior author is associated with a higher likelihood of female first authorship.

CONTROL ID: 3707816

SUBMITTER (NAME ONLY): Jennifer Radke

TITLE: Ocular Cicatricial Pemphigoid: Characteristics of Patients Treated at a Tertiary Care Center

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Radke, J.M. Samson, B. Glick, C.M. Samson, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|J. Radke, Elon University, Elon, North Carolina, UNITED STATES|J.M. Samson, University of California at San Diego, California, UNITED STATES|

Commercial Relationships Disclosure: Jennifer Radke: Commercial Relationship: Code N (No Commercial Relationship) | James Samson: Commercial Relationship: Code N (No Commercial Relationship) | Briana Glick: Commercial Relationship: Code N (No Commercial Relationship) | C Samson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the characteristics of patients affected by ocular cicatricial pemphigoid, a rare and potentially blinding disorder.

Methods: A retrospective review of the medical records of patients with biopsy-proven ocular cicatricial pemphigoid (OCP) at Manhattan Eye Ear, Throat Hospital was performed. This review includes patients at different stages of OCP seen from January 2017 to July 2021. Age of onset, presenting symptoms and signs, presence or absence of limbal stem cell deficiency, need for immunosuppressive therapy, disease course, and visual outcome were among the data collected.

Results: A total of 29 patient charts were analyzed. 72% of patients were female. Symblepharon and trichiasis were present at the initial visit to the tertiary care center in 82.8% and 82.8% respectively. Significant conjunctival inflammation was a presenting sign in 48.3% of patients, while 44.8% of patients presented with either symblepharon or trichiasis (or both) in an otherwise quiet non-inflamed eye. 20.7% had extraocular involvement, of which oral lesions were the most common. 72.4% of patients required immunomodulatory therapy, and almost one fourth (23.8%) still went completely blind. 82.8% of the cohort had functional vision measured at a single time point, while 48.3% at the same time point had blindness in at least one eye.

Conclusions: Ocular cicatricial pemphigoid is a severe ocular inflammatory condition in which patients have a high predilection of blindness even in the face of aggressive treatment.

CONTROL ID: 3707817

SUBMITTER (NAME ONLY): Jay Pepose

TITLE: The Efficacy of Phentolamine Ophthalmic Solution and Low-Dose Pilocarpine to Improve Distance-Corrected Intermediate Visual Acuity in Patients with Presbyopia

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

The objective of this study is to evaluate the efficacy of a combination of 0.75% phentolamine ophthalmic solution (POS) and 0.4% low-dose pilocarpine (LDP) to improve distance-corrected intermediate visual acuity (DCIVA) in patients with presbyopia.

Methods: The VEGA-1 study is a Phase 2, multi-center, randomized, placebo-controlled, double-masked clinical trial. Subjects with distance-corrected near visual acuity (DCNVA) of 20/50 or worse were randomized to receive either 0.75% POS or placebo vehicle in the evening, followed with and without a morning dose of 0.4% LDP. DCIVA was assessed at multiple time points after a single combination treatment. Logistic regression models comparing POS+LDP to each treatment, with treatment and light/dark irides as factors and baseline DCIVA as a covariate was used to compare the proportion of patients with 5-letter and 10-letter improvements in DCIVA. Mean improvements in DCIVA were also assessed.

Results: Of the 150 participants included in this clinical trial (mean age 53.1 years, 72% female, 89% White), 43 were randomized to placebo alone, 30 to POS alone, 43 to POS+LDP, and 30 to LDP alone. Subjects treated with POS+LDP had a mean (SD) 9.6 (5.7) letter improvement in DCIVA from baseline at 1 hour vs 4.5 (6.7) letters with placebo ($p<0.0001$). This improvement was seen in those with both irides: light 10.4 (5.7) letters; dark 8.4 (5.6) letters. At 6 hours, POS+LDP conferred a 7.1 (6.0) letter improvement from baseline, significantly more than placebo (4.0 [6.3], $p<0.0001$). LDP+POS yielded a greater proportion of patients with a ≥ 10-letter improvement in DCIVA than placebo at 1 hour (49% vs 27%, $p=0.027$). A greater proportion of patients treated with POS+LDP had ≥ 5 letter improvement in DCIVA at 1 hour compared to placebo (86% vs 58%, OR: 5.2, $p=0.004$) and at 6 hours (72% vs 49%, OR: 3.0, $p=0.027$).

Conclusions: In this Phase 2 clinical trial, 0.75% POS and 0.4% LDP significantly improved DCIVA in subjects with presbyopia at 1 hour, with durable results through 6 hours. Phase 3 studies are planned to advance POS+LDP for a potential treatment for presbyopia.

CONTROL ID: 3707818

SUBMITTER (NAME ONLY): Antonio Bergua

TITLE: APSified Bruch's membrane opening (BMO)-based peripapillary OCT-A in glaucoma

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bergua, B. Hohberger, M. Moritz, J. Schottenhamml, C.Y. Mardin, Ophthalmology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Glaucoma is known as neurodegenerative disease with a vascular component. Retinal microcirculation was observed to be impaired even in early glaucoma stages, visualized and quantified by OCT-angiography (OCT-A). Peripapillary OCT-A scans are challenging for analysis as vessel density (VD) is dependent on demarcation of the optic disc. Thus, it was the aim of the present study to investigate APSified Bruch's membrane opening (BMO)-based peripapillary VD of glaucoma with and without visual field loss compared to controls.

Methods: Peripapillary OCT-A scans of 115 participants were acquired using Heidelberg Spectralis II: ocular hypertension (OHT; n=20), pre-perimetric open-angle glaucoma (pre-OAG; n=9), OAG (n=35), and controls (n=51). Mean vessel density (VD) was computed for each of the four sectors (superior, inferior, nasal, temporal) and for the whole scan using the Erlangen AngioTool, enabling an APSified and BMO-based analysis. For the statistical analysis of mean and sectorial VD, an ANCOVA and a linear mixed model were used respectively. The diagnosis was set as a fixed effect and gender and age as covariates. For sectorial VD the sectors were embedded as repeated measures and a random intercept was added additionally to the model.

Results: Mean VD correlated significantly with diagnosis ($p=0.00018$) and age ($p=0.00013$), but not with gender ($p>0.05$). Moreover, the pairwise comparison showed, that there were significant differences between mean VD of OAG and controls ($p<0.0001$) and OHT and pre-OAG ($p=0.016$), yet not for the other groupings ($p>0.05$). For sectorial VD, diagnosis ($p=0.00018$), age ($p=0.00013$) and sector ($p<E-11$) correlated significantly, while gender did not ($p>0.05$). Looking at the pairwise comparisons of the diagnosis per sector revealed, that in each sector again the difference between sectorial VD of OAG and controls ($p<0.0003$) or pre-OAG and OHT ($p=0.016$) correlated significantly, respectively. No significant differences were observed between primary and secondary OAG ($p>0.05$).

Conclusions: Peripapillary microcirculation was observed to be impaired in perimetric glaucoma eyes and even in early glaucoma stages, yet not in OHT. As previous analysis of macular VD yielded a significantly reduced VD in OHT eyes, we assume that either analysis of peripapillary VD as to be enhanced further on, or the involvement of vascular alterations in glaucoma pathogenesis has a more peripheral origin.

CONTROL ID: 3707819

SUBMITTER (NAME ONLY): Neha Chittaluru

TITLE: Patient Perspective of Telehealth for Retinal Disease during the COVID-19 Pandemic

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Chittaluru, University of Central Florida, Orlando, Florida, UNITED STATES|P. Patel, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|D. Bhagat, V. Sheth, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Amidst the COVID-19 pandemic, telemedicine has emerged as a safe and cost-effective alternative to traditional, in-person ophthalmology clinic visits. To better understand the implications of this technology on the patient-physician relationship, this study assessed patient perspectives about telemedicine to identify areas for improvement.

Methods: A cross-sectional survey was distributed to patients at University Retina during July 2021. Responses regarding telehealth's ability to ease anxiety of contracting COVID-19, efficiency, patient education, quality of examination, and convenience were collected on a 5-point Likert scale. A positive attitude was defined as ≥ 4 average Likert rating for all questions. Frequencies of positive attitudes were compared across demographic factors by the Pearson chi-square test. Multivariate analysis was used to evaluate factors influencing patient preference for telehealth over traditional visits.

Results: Of 103 respondents, most were female (53.8%), aged 65-74 (34.6%), and high school educated (46.2%). 38% of patients did not know their diagnosis and 62.1% had no prior history of telehealth usage. Overall, patients had a neutral attitude towards telehealth (mean Likert rating (SD) = 3.11/5 ± 0.82). Nearly one-third (31%) preferred telehealth over face-to-face visits. Questions regarding "patient education" had the greatest proportion of positive attitude, whereas "efficiency" had a largely negative attitude (both 63.1%). "Convenience" of telehealth yielded the highest number of responses in strong agreement or disagreement (38.9%). Patients with no history of telehealth usage more frequently reported negative attitudes compared to those with prior experience (87.5% vs. 71.8%, $p = 0.046$). Patients tended to respond more positively as education level increased, but this trend was not statistically significant ($p = 0.18$). On multivariate analysis, patients younger than 75 were more likely to prefer telehealth over in-person visits compared to patients 75 or older (odds ratio [OR] = 2.25, $p = .007$). Patient gender, knowledge of diagnosis, and history of past telehealth usage did not predict preference for telemedicine.

Conclusions: Patients responded with a net neutral outlook on telehealth, indicating room for improvement. Efforts should focus on addressing technological inefficiencies and age-related barriers to patient satisfaction.

CONTROL ID: 3707822

SUBMITTER (NAME ONLY): Lillian To

TITLE: Defining The Role of Ab Externo Xen Gel Stent in Glaucomatous Eyes with Prior Failed Surgical Intervention

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.K. To, A. Chuang, S. Karimaghaei, R.D. Shah, R. Feldman, Ophthalmology, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|R. Dhoot, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the safety and efficacy of Xen 45 Gel stent (Xen, Allergan, Dublin, Ireland) in eyes that have failed prior surgical intervention, compared to traditional glaucoma drainage device (GDD) or cyclophotocoagulation (CPC). Since this population has low expected success rates with any additional surgery, it is vital to compare to standard of care surgical options.

Methods: This is a retrospective, single-site, case-control study of ab externo transconjunctival Xen in eyes that have previously undergone trabeculectomy and/or GDD surgery. Postoperative data was collected for 18 months. Failure was defined as: 1) no light perception, 2) additional glaucoma surgery required, or 3) intraocular pressure (IOP) of < 6 mmHg after 6 weeks postoperatively.

Results: Eighteen (18) Xen eyes and 36 control eyes matched on both glaucoma type and previous glaucoma surgeries were included. 72% had primary open angle glaucoma, 11% uveitic glaucoma, 6% primary angle closure, 6% pseudoexfoliation and 6% pigmentary glaucoma. 56% of eyes in each group had prior trabeculectomy, 28% of Xen and 31% of control eyes had prior GDD, and 17% of Xen and 14% of control eyes had both. Baseline medicated IOP was lower in the Xen group (21.8 ± 7.2) compared to controls (27.5 ± 9.4, P=0.027). The cumulative failure rate at 1 year was 17% and 20% for Xen and control respectively (P=0.32). All eyes failed by requiring additional surgery, except a control eye which failed due to loss of light perception. The mean survival time was 13.7 (±1.6) months and 11.4 (±0.6) months for Xen and control, respectively. Most Xen failures occurred within the first 6 months. There was no difference in complication rates between groups (P=0.21). When censored for additional glaucoma procedures, there were no differences at post-op month 6 and year 1 in IOP, change of IOP from baseline, number of IOP lowering medications, or number of medications reduced from baseline.

Conclusions: Xen provides a reasonable alternative to traditional surgery in patients that have previously undergone filtering surgery or GDD. But care must be taken to monitor patients closely in the perioperative period as failures occur early. Those devices that were successful beyond 6 months had noninferior IOP reduction compared to GDD and CPC.

CONTROL ID: 3707825

SUBMITTER (NAME ONLY): Richard Rosen

TITLE: Assessing vitreous cortex hyalocyte morphology and dynamics in the living human eye

SESSION TITLE: AMD Translational Research

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.B. Rosen, O. Otero-Marquez, J.V. Migacz, S. Ahsanuddin, K. Rickford, B. Murillo, R. Zhou, L. Spellman, R. Weitz, T.Y. Chui, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|R.B. Rosen, J.V. Migacz, S. Ahsanuddin, R. Zhou, T.Y. Chui, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|A. Dubra, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|K. Rickford, L. Spellman, New York Medical College, Valhalla, New York, UNITED STATES|B. Murillo, Touro College, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hyalocytes are the resident macrophages of the vitreous. They have been implicated in the maintainence of vitreous transparency, response to injury, and involvement in extra-retinal proliferations (PMIDs: 14160361; 32574351; 33168747). Little, however, is known about the behavior of these transparent cells within their native environment, due to the lack of adequate methods of visualization. In this study, we employed a novel imaging system and image processing technique to reliably observe and characterize these cells in living human eyes over time.

Methods: Five healthy subjects were imaged using a non-confocal quadrant-detection adaptive optics scanning light ophthalmoscope (AOSLO) (PMID: 33680539). A 1x1° region of interest (ROI) at the temporal retina was imaged every 5 minutes over 1 hour for a total of 13 time points. To study hyalocyte morphology and movement over time, image registration and cell tracking were performed on all acquired images using ImageJ. Cell velocities were calculated from distances traveled divided by the time elapsed between time points. Hyalocyte morphology and movements over a longer timespan were also evaluated by imaging the same ROI 4 months after the first visit in 2 subjects.

Results: A total of 50 hyalocytes were imaged. Cells demonstrated variability in morphology and movement over time (Fig). Five categories of morphology, described in microglia, were observed, specifically: ramified (74%), hyper-ramified (6%), rod (4%), activated (14%), and amoeboid (2%). Mean±stdev velocities of ramified, hyper-ramified, rod, activated, and amoeboid cells were 0.43±0.22, 0.59±0.30, 1.29±0.40, 1.35±1.21, and 0.26 (one cell only) μm/min, respectively. In the 2 subjects imaged over 4 months, similar numbers of cells were visualized within the same ROI. However, cell tracking between visits could not be confirmed due to substantial variation in cell morphology and location, as well as absence of definitive cell labels.

Conclusions: We have demonstrated the ability to visualize hyalocytes in the living human eye without exogenous labeling using a quadrant-detection adaptive optics scanning light ophthalmoscope. The non-invasive characterization of hyalocyte morphology and movement dynamics may provide better understanding of the roles these cells play in disease progression and response to pharmacologic treatment.

CONTROL ID: 3707829

SUBMITTER (NAME ONLY): Chiara De Lillo

TITLE: Prion Deposits Preferentially Accumulate in the Retinal Outer Plexiform Layer in Patients with Sporadic Creutzfeldt-Jakob Disease (sCJD)

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. De Lillo, J. Choi, I. Dryden, A. Arcia Franchini, J. Lin, Department of Pathology and Ophthalmology, Stanford University, Stanford, California, UNITED STATES|V.S. Goodwill, C.J. Sigurdson, Department of Pathology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Transmissible 'scrapie-type' prion (PrP^{Sc}) deposits have been detected in the retina of patients with sporadic Creutzfeldt-Jakob disease (sCJD); however, the histopathology of retinal PrP^{Sc} deposits is poorly characterized, whereas that in the brain is well established. We performed a retrospective, observational study to characterize the morphometric features of PrP^{Sc} deposits and the histological changes in the retinas of patients with sCJD.

Methods: From July 2015 to July 2017, 14 eyes and 1 brain were collected from 14 neuropathologically-confirmed sCJD autopsy cases (4 males and 10 females; age range: 51-80, mean: 63, SD: 9.0; disease duration: 1.5-27 mo, mean: 10.5, SD: 8.4) and eyes and brains from 6 controls (5 males and 1 female; age range: 51-90, mean: 70.3, SD: 13.8). Immunohistochemistry was performed with Mab12F10 (Cayman Chemical; 1:200) against PrP^{Sc}. The greatest dimension of PrP^{Sc} staining was microscopically measured and statistical significance was evaluated with Mann-Whitney U test, Welch's unpaired t-test, and Brown-Forsythe test.

Results: PrP^{Sc} expression was found in the outer (OPL) and inner plexiform layers (IPL) of the retinas with the strongest deposition as discrete, regularly spaced ovoid deposits in a "beads-on-a-string" pattern along the horizontal axis of the OPL. PrP^{Sc} deposits were not observed in controls nor other ocular structures of the patient group. The average size of retinal PrP^{Sc} deposits in the OPL was 4.94μm, which was significantly smaller than coarse PrP^{Sc} deposits in the brain (32.45μm, $p<0.001$) with a significantly lower SD (0.47μm vs. 23.55μm, $p<0.001$). Retinal lamination and laminar thickness were comparable between sCJD retinas and controls. Spongiotic changes and overt gliosis were not observed in the retinas with PrP^{Sc} deposition.

Conclusions: Our findings show that PrP^{Sc} deposits in the retina have significantly different histologic and morphometric characteristics than those in the brain. Retinal PrP^{Sc} deposits are consistently present in ovoid aggregates in the OPL with a relatively uniform size of 5 μm. In contrast to the spongiform neurodegeneration associated with PrP^{Sc}deposition in the brain, retinal anatomy and organization appear well-preserved despite PrP^{Sc} deposition in OPL. Additional studies are required to determine the cellular location and function of PrP^{Sc} deposits in OPL.

CONTROL ID: 3707830

SUBMITTER (NAME ONLY): Joseph Colcombe

TITLE: Preoperative OCT signal quality as a metric for measuring cataract visual burden

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Colcombe, A. Udeh, S. Choi, G. Wollstein, J.S. Schuman, S.E. Brodie, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Objectively determining the effect of a cataract on visual performance has long been a problem for ophthalmologists. Many candidates for cataract extraction now routinely undergo optical coherence tomography (OCT) prior to surgery. We performed a single center, retrospective, observational study to evaluate the utility of using OCT image quality as an objective measure of the impact of a cataract on visual functioning.

Methods: A database was created of 1645 eyes that underwent cataract extraction and OCT prior to surgery. 1404 eyes met the inclusion criteria of a Best Corrected Visual Acuity (BCVA) of 20/25 or better within 60 days of surgery. This cutoff was chosen to reduce the likelihood of capturing concurrent non-lens pathologies. Pre- and postoperative BCVAs, cataract type and grade, preoperative OCT signal quality, and OCT model were recorded for each eye, and Snellen BCVAs were converted to Logarithm of the Minimal Angle of Resolution (LogMAR) values. The Q value, a standardized measure of signal quality, was created by scaling the proprietary image quality values from all machines to that of the most frequently used model (Zeiss). The data were stratified by postoperative BCVA, OCT model, and cataract type and grade. Simple linear regression was performed for each stratification.

Results: Linear regression of preoperative acuity among all included eyes versus Q returned an R-squared value of 0.1725. The same regression performed with eyes having a postoperative BCVA of 20/20 or better (n=1168) returned an R-squared of 0.2207. Regressing Q on preoperative acuity when stratifying by cataract type returned similar R-squared values for cortical, nuclear sclerotic, and posterior subcapsular cataracts (0.2098, 0.2219, and 0.2520 respectively). Likewise, regressing Q on preoperative acuity when stratifying by machine type returned similar R-squared values for Optovue, Topcon, and Zeiss models (0.2326, 0.2055, and 0.2641 respectively) and a lower value for Heidelberg (0.1502). The R-squared value was low when regressing either Q or preoperative acuity on summed cataract grade (0.0728 and 0.0912 respectively). P-values for all correlations were <0.0001.

Conclusions: These analyses suggest that preoperative acuity correlates better with OCT image quality than clinical cataract grade. Overall, there may be a modest correlation between vision loss caused by cataracts and OCT signal quality.

CONTROL ID: 3707835

SUBMITTER (NAME ONLY): Nathan Fischer

TITLE: Quantitative autofluorescence (qAF) is not associated with early and intermediate age-related macular degeneration (AMD) in pseudophakic eyes of the ALSTAR2 baseline cohort

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Fischer, A. Berlin, M. Clark, T.A. Swain, G. McGwin, K.R. Sloan, J. Crosson, C. Owsley, C.A. Curcio, Ophthalmology & Visual Science, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium lipofuscin and melanolipofuscin (L/ML) gives rise to fundus autofluorescence, which normally increases throughout life and decreases markedly in advanced AMD. Age-related lens opacification reduces light transmission and introduces intrinsic autofluorescence into the light path, thus impacting signal strength. We utilized qAF to investigate L/ML-attributed autofluorescence in eyes with and without early or intermediate AMD, stratified by lens status, in a large cohort of older adults.

Methods: Participants in the ALSTAR2 baseline cohort (NCT04112667) were assessed by the AREDS grading system for color fundus photography. As described (PMID 32855849), qAF images captured using a scanning laser ophthalmoscope and internal fluorescent reference underwent a quality review. Mean qAF intensity values in an 8-segment annulus (inner-outer radii, 9°-11°) centered on the fovea (qAF8) were analyzed with custom FIJI plugins. Pseudophakic eyes were assigned an age of 20 years. Generalized estimating equations were used to evaluate differences in qAF8 by disease status and severity and lens status.

Results: Out of 460 individuals (mean age 72.0 ± 5.9 years, 60% female and 40% male, mean best corrected visual acuity 0.031 LogMAR), 836 eyes were classified as normal (410, 49%), early AMD (eAMD, 250, 29%), and intermediate (iAMD, 176, 21%). Among all eyes, qAF8 differed by lens status (qAF8, median (IQR): phakic 241.0 (198.6-291.1); pseudophakic 208.6 (170.9-257.6); p=0.0009). Additionally, qAF8 differed significantly by AMD presence and severity (mean qAF8: normal 244.1, eAMD 229.8, iAMD 211.4; p=0.0015). When stratified by lens status, this difference remained in phakic eyes (mean qAF8 normal 256.7, eAMD 247.9, iAMD 221.2; p=0.0013) but not in pseudophakic eyes (mean qAF8 normal 228.5, eAMD 211.6, iAMD 205.3; p=0.0974).

Conclusions: In a large cohort, qAF8 was associated with AMD presence and severity in phakic but not pseudophakic eyes, being higher on average in phakic eyes. Unaccounted variation in individual lens density and autofluorescence may explain the association of qAF8 with AMD in phakic eyes. Future studies using qAF in older patients should enroll pseudophakic eyes for best results. Loss of histologic L/ML signal before atrophy in AMD tissues may be undetectable by current qAF.

CONTROL ID: 3707837

SUBMITTER (NAME ONLY): Vasiliki Gliagias

TITLE: Combined Effects of Vessel Density and Intraocular Pressure on Retinal Ganglion Cell Function and Structure in Normal Tension Glaucoma Suspects with Obstructive Sleep Apnea

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Gliagias, A. Tirsi, C.R. Lacher, J. Tsai, R. Gupta, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|H. Sheha, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Tirsi, H. Sheha, S.A. Obstbaum, C. Tello, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vascular factors have been shown to be responsible in the pathogenesis of Normal Tension Glaucoma (NTG). This cross-sectional study examined the ability of vessel density (VD) to predict variance across pattern electroretinogram (PERG) parameters, average retinal nerve fiber layer thickness (avRNFLT) and average ganglion cell-inner plexiform layer thickness (avGCL + IPLT) in NTG suspects with Obstructive Sleep Apnea (OSA).

Methods: Four pre-perimetric glaucoma subjects (7 eyes) with normal Humphrey 24-2 visual field tests, normal intraocular pressure (IOP) levels and suspicious optic nerve head were consecutively recruited at Manhattan Eye, Ear and Throat Hospital. Participants underwent Diopsys NOVA PERG and Cirrus Optical Coherence Tomography tests. Patients with documented OSA diagnosis were included. After controlling for Age (Step 1), hierarchical multiple linear regression analysis was used to determine the ability of IOP (Step 2) and VD (Step 3) to predict variance in dependent variables (Magnitude [Mag], MagnitudeD [MagD], MagnitudeD/Magnitude ratio [MagD/Mag ratio], avRNFLT and avGCL+IPLT).

Results: In prediction of Mag and MagD, after controlling for Age, VD explained 70.1% and 72.8% of variance (B= 0.149 [95% CI: 0.037, 0.262], p=0.024) (B= 0.134 [95% CI: 0.031, 0.237], p=0.026), respectively. IOP was not significant. In the prediction of MagD/Mag ratio, Age and IOP explained 62.3% and 29.3% of variance (B= 0.003 [95% CI: 0.000, 0.006], p=0.035) (B= 0.008 [95% CI: 0.002, 0.014], p=0.020), respectively. VD was not significant.
In prediction of avRNFLT, after controlling for Age, IOP and VD explained 76.9% and 11.0% of variance (B= -2.730 [95% CI: -4.316, -1.143], p=0.009) (B= 0.652 [95% CI: 0.079, 1.225], p=0.036), respectively.
In prediction of avGCL+IPLT, after controlling for Age, IOP and VD explained 69.3% and 6.00% of variance (B= -1.466 [95% CI: -2.115, -0.816], p=0.003) (B=-0.274 [95% CI:-0.480, -0.068], p=0.024), respectively.

Conclusions: In NTG suspects with OSA, VD was a significant predictor for Mag and MagD, demonstrating the importance of healthy microvasculature for normal retinal ganglion cell function. We report combined effects of VD and IOP on avRNFLT and avGCL+IPLT, emphasizing the need to further investigate this relationship, IOP diurnal fluctuations and IOP nocturnal elevations in OSA.

CONTROL ID: 3707838

SUBMITTER (NAME ONLY): ROHAN BAJAJ

TITLE: Guarded Hope: Clinical Presentation, Outcomes, and Practice Patterns of Endogenous Fungal Endophthalmitis

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. BAJAJ, M. Tieger, Y. Lu, S. Hoyek, N.A. Patel, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endogenous fungal endophthalmitis is a rare entity without a consensus approach to management. The aim of the study is to provide data on the presentation and practice patterns to guide future clinical decision making.

Methods: A retrospective chart review was performed on a cohort with established endogenous fungal endophthalmitis between 2009-2021 at Massachusetts Eye and Ear. Linear regression was performed to analyze the correlation between days to pars plana vitrectomy (PPV) and improvement in visual acuity. Wilcoxon Signed-Rank tests were used to compare VA improvement between initial presentation vs. final visit, early (within 3 days) vs. late (after 3 days) PPV, IV vs. topical antifungals, and intravitreal voriconazole vs. amphotericin.

Results: Fourteen eyes from 13 patients (92.8% male) with a median age of 43.5 years (IQR: 23-79) were included. The initial median VA was 1.676 LogMAR (IQR: 0.301-2.477). Initial slit lamp exam most often revealed vitritis (93.0%), AC flare (86.0%), hypopyon (50.0%), and keratic precipitates (50.0%). It took an average of 1.54 days (Median 0; IQR 0-7) to establish a diagnosis of endogenous fungal endophthalmitis. Cultures were obtained via vitreous (78.6%) or anterior chamber (21.4%) aspirates. Within an average of 7.38 days (IQR: 1-38 days), most cultures (85.7%) grew candida species (albicans, dubliniensis, tropicalis, and glabrata). Most patients received intravitreal (85.7%) and IV (73.3%) antifungals. Two patients (14.3%) received PPV within 1 day of presentation as their initial intervention. 78.5% of the cohort received a PPV within an average of 11.3 days (Median 10, IQR: 1-38). There was a statistically significant improvement in the final median VA, 0.544 LogMAR (IQR: 0-2.477) ($Z=2.8241$, $p<0.005$). No eyes had to be enucleated or eviscerated. There were no statistically significant differences ($p>0.05$) in VA outcomes with early vs. late PPV, IV vs. topical antifungals, or between intravitreal voriconazole vs. amphotericin. There was no statistically significant correlation ($p>0.05$) between the days to PPV and final VA improvement.

Conclusions: The most common causative species to cause endogenous fungal endophthalmitis was Candida. Surgical intervention with PPV was often required to achieve an improvement in visual acuity and outcomes were generally favorable.

CONTROL ID: 3707840

SUBMITTER (NAME ONLY): Seungpil Bang

TITLE: Positional Correlation Between Visual Axis and Stile-Crawford Effect Peak in Normal Eyes

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bang, Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|S. Bang, J. Lyu, C.J. Ng, G. Yoon, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|J. Lyu, The Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: One of the major challenges in cataract/refractive surgery is to determine the optimal center position for the optical correction. The entrance pupil center (EPC) and the 1st Purkinje image are common centration references. The visual (foveal achromatic) axis along which no transverse chromatic aberration may be another candidate. The purpose of this study was to locate the visual axis with respect to EPC and evaluate the extent of its correlation to the peak of the Stiles-Crawford effect (SCE).

Methods: Six young typical subjects (12 eyes) were enrolled in the study. An optical system was developed to locate the visual axis and measure SCE. A translatable pinhole (diameter: 600 μm) was placed in the pupil conjugate and its location was imaged with a pupil camera. To find the visual axis, two small laser spots at 450 and 680 nm were co-aligned and delivered to the retina. Subjects were asked to move the translatable pinhole until these spots are perceived to be overlapped each other, i.e. zero transverse chromatic aberration. With the same system, the SCE was assessed by a conventional two-channel (reference and test) Maxwellian view system. Three repeated measurements at 19 pupil entrance points distributed within the central 4 mm pupil diameter were conducted. The peak positions were estimated by a two-dimensional Gaussian fitting function and correlated with the visual axis positions.

Results: The visual axis was, on average, located inferonasal to the EPC [x: 0.22 ± 0.40 mm, y: -0.18 ± 0.42 mm]. The SCE peak was also located inferonasal to the EPC [x: 0.26 ± 0.39 mm, y: -0.16 ± 0.38 mm]. The SCE peak positions were highly correlated in both horizontal and vertical meridians to the visual axes (R^2 = 0.97 for x, 0.96 for y coordinates). Five of the six subjects demonstrated mirror-symmetry in the coordinates of the visual axis and the SCE peak of both eyes (R^2 = 0.92 for the visual axis, 0.90 for the SCE peak).

Conclusions: The visual axis and the SCE peak locations were found to be variable between the subjects but highly correlated with each other within each individual. These findings may suggest a potential feedback mechanism between the ocular optics and the cone photoreceptor alignment.

CONTROL ID: 3707841

SUBMITTER (NAME ONLY): Paula Subirada Caldarone

TITLE: Studies about the cooperative signaling between $p75^{NTR}$ and Trk receptors in the modulation of choroidal neovascularization.

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.V. Subirada Caldarone, A. Anastasía, Instituto de Investigacion Medica Mercedes y Martin Ferreyra, Cordoba, Córdoba, ARGENTINA|P.V. Subirada Caldarone, A. Tovo, M.V. Vaglienti, M.C. Sanchez, Centro de Investigaciones en Bioquimica Clinica e Inmunologia, Cordoba, Córdoba, ARGENTINA|D. Vicentin, N. Ribotta, J.D. Luna Pinto, Clínica Privada de ojos Romagosa, Fundación VER., Córdoba, Córdoba, ARGENTINA|H.U. Saragovi, Lady Davis Institute for Medical Research, Montreal, Quebec, CANADA|P.F. Barcelona, Centro de Investigaciones en Bioquimica Clinica e Inmunologia, Cordoba, Córdoba, ARGENTINA|

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ABSTRACT BODY:

Purpose: Neovascular age-related macular degeneration (AMD) commonly causes vision loss from aberrant angiogenesis, termed choroidal neovascularization (CNV). To unravel the mechanisms underlying CNV, we focused on the p75 neurotrophin receptor ($p75^{NTR}$), a transmembrane protein known to mediate neuronal survival and death, and also vascular changes. $P75^{NTR}$ can couple to different co-receptors to transduce intracellular signals. Our previous results showed that $p75^{NTR}$ increases 7 days post-laser in retinal glia (GS+ or GFAP+) and RPE (retinal pigment epithelium)-choroid infiltrate (F4/80+) cells of mice with CNV. The deletion of the receptor reduced CNV area and prevented photoreceptor dysfunction. It has been reported that $p75^{NTR}$ can potentiate Trk signalling in some scenarios. Thus, we aim to determine if $p75^{NTR}$ modulates Trk activation to modify neovessel formation in a mouse model of laser-induced CNV.

Methods: 2- months old mice were anesthetized and their pupils were dilated; then, 4 injuries were performed in the retina using a photocoagulation laser with a 532nm wavelength slit lamp. 7 days after laser the mice were sacrificed. Samples include RPE-Choroid flatmounts, retina cryosections for immunostaining, and retinal and RPE-Choroid extracts processed separately for Western blot. WT (n=15) and $p75^{NTR}$ KO (n=21) mice were included in the experimental design and animals without CNV (n=10) were used as control.

Results: We estimated Trk activation through the activation of its downstream signaling molecule ERK. We detected decreased expression of phosphor-ERK in retina from CNV mice respect to control (p=0,014) and similar phospho-ERK levels in RPE-choroid 7 days post laser (p=0,227) by Western Blot. Immunostaining did not show localization of pan-Trk nor phospho-ERK in retinal glia. Similarly, no overlapping was detected between pan-Trk and RPE-Choroid infiltrate assessed in RPE-Choroid flatmounts. Consistently, $p75^{NTR}$KO mice showed equal phospho-ERK levels 7 days after laser in retina (p=0,322) and RPE-Choroid (p=0,353).

Conclusions: In sum, our results suggest that the formation of vascular tufts that are produced during the CNV is not mediated by the cooperative signalling between $p75^{NTR}$ and Trk receptors.

CONTROL ID: 3707843

SUBMITTER (NAME ONLY): Fangfang Qiu

TITLE: Adoptive Transfer of Plasmacytoid Dendritic Cells Promotes Allograft Survival in a Murine Allogeneic Corneal Transplantation

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Qiu, B. Kenyon, C. Chao, D.L. Harris, O. esteireiro, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|B. Kenyon, Program in Neuroscience, Tufts University School of Graduate Biomedical Sciences, Boston, Massachusetts, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center; Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Graft rejection remains the leading cause of allograft failure in corneal transplantation. Plasmacytoid dendritic cells (pDCs) are implicated in the maintenance of immune tolerance in other models. Herein, we tested the hypothesis that adoptive transfer of pDCs can promote allograft survival via inducing immune tolerance, using an experimental allogenic corneal transplantation model

Methods: Allogenic corneal transplantation was established using BALB/c recipients and C57BL/6 donors. Adoptive transfer of sorted splenic allo-pDCs or saline were performed using fibrin sealant at d1 post-surgery. Anergic T cells, regulatory T cells (Tregs), Th1, and Th17 cells in draining lymph nodes (dLNs), and infiltrating leukocytes and T cells in corneas, were detected via flow cytometry at d14 post-transfer. Grafts was assessed twice weekly for 70 days with slit-lamp to score graft neovascularization (NV, 0-8^{+} scale), opacity (0-5^{+} scale), and rejection (graft opacity≥ score 3). Rejection-free graft survival was evaluated by Kaplan-Meier survival curves followed by log-rank test; unpaired t-test was used for comparisons.

Results: pDCs induced anergic $CD4^{+}$T cells (CTLA-4^{+}: 1.6-fold, PD-1^{+}: 1.8-fold, LAG-3^{+}: 4.6-fold, compared to the saline group; n=3, all $p<0.05$), and expanded the $Foxp3^{+}CD4^{+}$Tregs compartment (2.5-fold; n=3, $p<0.001$), while they had no effect on $IFN\gamma^{+}CD4^{+}$ Th1 and $IL17^{+}CD4^{+}$ Th17 (1.2-fold and 1.1-fold respectively; n=3, both $p>0.05$) in dLNs. In addition, pDCs ameliorated infiltration of $CD45^{+}$ leukocytes and $CD3^{+}$ T cells in corneal beds ($CD45^{+}$: 87.5%, $CD3^{+}$: 79.0% decrease compared to saline group; n=3, both $p<0.05$) and grafts ($CD45^{+}$: 75.8%, $CD3^{+}$: 71.9% decrease; n=3, both $p<0.01$). Moreover, pDCs suppressed corneal NV from d7 until d70 (score 2.8±0.34 SEM to 5.4±0.36, n=12 for pDCs transfer group vs 4.0±0.23 to 6.4±0.22, n=11 for saline control group; $p<0.05$ for all timepoints). Further, pDCs alleviated graft opacity from d14 until d70 (score 0.4±0.15 to 1.5±0.33, n=12 vs 1.1±0.21 to 3.5±0.45, n=11; all $p<0.05$), and improved survival rate of grafts (83.3%, n=12 vs 36.4%, n=11; $p<0.01$) through the end of 70 days.

Conclusions: Adoptive transfer of pDC promote survival of corneal allograft, which is associated with T cell tolerance, suggesting the translational potential of cell-based pDC therapy use in corneal transplantation

CONTROL ID: 3707844

SUBMITTER (NAME ONLY): Stephen BUMA

TITLE: Comparing Bruch's Membrane Opening, Intraocular pressure, and Pulsatile Ocular Blood Volume when in sitting and supine positions in Glaucomatous and Non-Glaucomatous eyes

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. BUMA, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|N.S. Madhan, Y. Ma, A. Mahmoud, G. Fleming, C.J. Roberts, Ophthalmology and Visual Sciences, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|A. Mahmoud, G. Fleming, C.J. Roberts, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate Bruch's Membrane Opening-Minimum Rim Width (BMO-MRW), Intraocular pressure (IOP) and Pulsatile Ocular Blood Volume (POBV) between glaucomatous and non-glaucomatous eyes in supine and sitting positions.

Methods: Cross-sectional, prospectively acquired data was used to evaluate 323 eyes of 181 healthy controls (NRL) and 66 eyes of 42 subjects diagnosed with primary open-angle glaucoma (GLA). BMO-MRW was measured using Flex-Arm Spectralis Optical Coherence Tomography (OCT) in both sitting and supine positions, as well as pneumatonometry to measure IOP and ocular pulse amplitude (OPA). A surrogate of POBV was calculated by dividing OPA by diastolic IOP. BMO-MRW in GLA and NRL were compared using ANCOVA with IOP as a co-variate. Univariate regression analyses were performed between BMO-MRW and IOP. Paired t-tests were included between sitting and supine positions. SAS statistical analysis software was used with $p<0.05$ as the significance threshold.

Results: BMO-MRW was significantly smaller in GLA eyes compared to NRL in the supine position (211 ± 60 µm vs 357 ± 61 µm; p<.001). IOP is negatively correlated to BMO-MRW in both sitting (R^2=.08; p<.001) and supine (R^2 =.05; p<.001) positions only in NRL eyes. IOP increases significantly in supine position relative to sitting in both GLA (19±4mmHg vs 23±4mmHg; p<.001) and NRL groups (16±3mmHg vs 21±3mmHg; p<.001). POBV surrogate is significantly lower in the supine position compared to sitting in both GLA (.10±.03 vs .12±.05; p<.001) and NRL (.10±.04 vs .14±.06; p<.001) cohorts.

Conclusions: It is known that BMO-MRW is smaller in glaucoma than normal in the sitting position, and the current study confirms this relationship also exists in the supine position with higher IOP. In addition, this study shows higher IOP is associated with smaller BMO-MRW only in NRL. It is also known that IOP increases with extended time in the supine position during sleep. Although there is no immediate change in BMO-MRW between sitting and supine positions, further studies are warranted to determine if BMO-MRW is affected by extended periods of time in the supine position as IOP increases. Additionally, POBV decreases relative to sitting in both groups indicating less perfusion, which may represent additional risk to the glaucomatous eye during extended periods in the supine position.

CONTROL ID: 3707848

SUBMITTER (NAME ONLY): Lucy Cobbs

TITLE: Geographic Distribution and Trends of Self-Reported Visual Impairment in 2010-2019

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Cobbs, R. Mahmoudzadeh, M. Salabati, J. Hamati, R.R. Soares, Y. Yonekawa, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R. Mahmoudzadeh, M. Salabati, R.R. Soares, Y. Yonekawa, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: In our study, we aim to describe changes in the geographic distribution of visual disability over the last decade (2010-2019) in the United States and evaluate these trends in the context of age, gender, and income level.

Methods: Our study used publicly available data from the Census Bureau American Community Survey from 2010-2019. Data gathered from all United States counties (3,220 counties) included age, gender, rate of self-reported vision difficulty (binary responses identifying persons who are “blind or having serious difficulty seeing, even when wearing glasses”), and county-average ratio of income to poverty.

Results: The mean overall prevalence of self-reported visual impairment (VI) from 2010-2019 was 2.31% in the United States, and there was a significant increase in VI over the past decade from 2.25% in 2010-2014 to 2.37% in 2015-2019 ($p<0.001$).VI was significantly higher in rural counties (3.58%), compared to urban (3.10%) or metropolitan counties (2.18%) ($p<0.001$). In terms of geographic region, the South had the highest rate of VI (2.63%), and the Northeast had the lowest rate of VI (2.00%) ($p<0.001$). For age groups >17-years-old in the 2010-2019 data, females had higher rates of VI compared to males. In terms of socioeconomic status, the highest rate of VI occurred in the second lowest income quintile, and the lowest rate of VI occurred in the first, wealthiest quintile. Over the 2010-2019 decade, VI increased by the greatest percentages in the bottom two quintiles.

Conclusions: Prevalence of visual impairment has risen and disproportionately affects certain communities. This includes individuals living in the South, in rural counties, women, and those living in poverty. Patterns of visual impairment over the past decade may inform future trends and guide interventions for populations at highest risk of blindness.

CONTROL ID: 3707853

SUBMITTER (NAME ONLY): Daniel Milad

TITLE: Accuracy of automated machine learning in classifying trachoma from field-collected conjunctival images

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Milad, F. Antaki, R. Duval, Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Trachoma is the leading infectious cause of blindness worldwide and is an important public health problem. Determining the community prevalence of trachoma in endemic countries by conjunctival examination is fundamental to guide public health interventions. While machine learning (ML) models have been proposed to automate trachoma detection from conjunctival images, their development is reserved to artificial intelligence (AI) experts. In this study, clinicians with no coding experience developed automated ML (AutoML) models to detect trachoma using a graphical user interface.

Methods: Ophthalmologists with no coding experience carried out AutoML model design using a public data set of field-collected conjunctival images from clinical trial participants in Niger and Ethiopia. The dataset was previously labelled by experts using the WHO Simplified Grading System. Google Cloud AutoML Vision was used for training and testing. We designed two binary models to detect trachomatous inflammation-intense (TI) and trachomatous inflammation-follicular (TF). We then compared them to bespoke TI and TF detection models designed using the same dataset by AI experts (Kim et al., Plos One, 2019). The AutoML model performance is reported using the area under the precision-recall curve (AuPRC), sensitivity, specificity and accuracy.

Results: A total of 1,656 field-collected conjunctival images were included (1,019 normal, 365 TF, 110 TI and 162 TF and TI). The two AutoML models showed high diagnostic properties that were comparable to bespoke deep-learning models. The AutoML TI model had an AuPRC of 0.980, sensitivity of 85%, specificity of 98% and accuracy of 95% (vs. 96%, 74% and 85% for the bespoke models). The AutoML TF model had an AuPRC of 0.907, sensitivity of 81%, specificity of 93% and accuracy of 89% (vs. 86%, 58% and 72% for the bespoke models).

Conclusions: Our study highlights the value of AutoML in the democratization of AI. We demonstrate the feasibility of using AutoML by ophthalmologists with no coding experience to create deep-learning models to detect trachoma from conjunctival images. The model can detect TF and TI with excellent performance results, with metrics similar or better than those designed by AI experts. Our results also demonstrate the potential value of open-access data and big data in improving public health issues worldwide.

CONTROL ID: 3707856

SUBMITTER (NAME ONLY): Frans Vinberg

TITLE: Upregulation of Rod Ribbon Synapse Components Coincides with Well-preserved Scotopic Vision in the P23H Model of Retinitis Pigmentosa

SESSION TITLE: Photoreceptors and the OPL

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Vinberg, F. Abbas, Ophthalmology, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|M. Tabaka, International Centre for Translational Eye Research, Instytut Chemii Fizycznej Polskiej Akademii Nauk, Warsaw, POLAND|E.H. Choi, K. Palczewski, Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|K. Palczewski, Physiology & Biophysics, and Chemistry, University of California Irvine, Irvine, California, UNITED STATES|F. Vinberg, Biomedical Engineering, The University of Utah, Salt Lake City, Utah, UNITED STATES|U. Seemab, H.O. Leinonen, School of Pharmacy, Ita-Suomen yliopisto, Kuopio, Pohjois-Savo, FINLAND|

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ABSTRACT BODY:

Purpose: Retinal remodeling, triggered by photoreceptor death, could either slow down, or exacerbate vision loss. We hypothesize that in typical less aggressive forms of retinitis pigmentosa, where a fraction of rods remains light responsive, the retina initially compensates for reduced receptor input by increasing signal transmission to bipolar cells. This hypothesis was tested, using a mouse model for the most common autosomal-dominant retinitis pigmentosa-associated mutation of rhodopsin, the P23H mutation ($Rho^{P23H/WT}$ = P23H mouse).

Methods: All comparisons were made between P23H mice and their age-matched wildtype control littermates (n=4-8 per group). Both sexes were represented equally in each group. Statistical significance was determined using two-way ANOVA or two-tailed t-test, with correction for multiple comparisons where needed. For behavior and electrophysiology experiments, mice were bred onto the $Gnat2^{-/-}$ background to eliminate cone-mediated light signals. Sensitivity of vision was assessed by optomotor response in ambient light, ranging from scotopic to mesopic levels. Light signal transmission from rods to rod bipolar cells (RBCs) was assessed by ex vivo ERG, isolating the rod component using DL-AP4 and the RBC component by subtracting rod responses from mixed rod/RBC responses. ScRNA-Seq was used to measure differences in gene expression in the rods and RBCs of P23H mouse retinas versus controls. In addition, expression of selected proteins in whole retinas from P23H and control mice were compared, using Western blotting and immunohistochemistry.

Results: Based on scRNA-Seq analysis we found a significant upregulation of several major rod ribbon synapse genes in P23H rod photoreceptors ($p<0.00001$). Ca^{2+} sensor protein synaptotagmin-1 (Syt1) was overexpressed at P30 ($p=0.02$) in whole P23H retinas, as compared to controls. Scotopic contrast threshold changed only at the dimmest background intensity ($5*10^{-4}$ Cd/m^2) in P60 P23H/$Gnat2^{-/-}$ mice, from 60±6% to 76±4% ($p< 0.001$); and the RBC/rod response ratio increased in 1- 6 mo P23H mice ($p<0.005$).

Conclusions: We discovered increased mRNA expression of rod ribbon synapse proteins in P23H mice. These results suggest that presynaptic scaling, potentially via upregulation of Syt1, mediates a compensatory mechanism that promotes night vision during the slow progression of rod photoreceptor degeneration.

CONTROL ID: 3707858

SUBMITTER (NAME ONLY): Edward Xie

TITLE: Drug-Gene Association Analysis to Identify Novel PVR Therapeutics

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.F. Xie, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|U. Nadeem, Department of Pathology, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|B. Xie, M. D'Souza, D. Sulakhe, Center for Research Informatics, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|L.T. Shaw, D. Dao, D. Skondra, Department of Ophthalmology and Visual Science, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is the dreaded cause of failure following retinal detachment repair; however, to this date, no cures or preventative therapies exists. The purpose of this study is to use advanced bioinformatics tools to study drug-gene associations in order to identify drugs/compounds that interact with genes affected in PVR and that could be candidates for further testing as novel management strategies of PVR.

Methods: We queried PubMed Gene to assemble a list of genes associated with PVR to date. Gene enrichment analysis for the compiled PVR gene list was executed via ToppGene against the drug databases. This analysis identifies overepresented compounds and predicts their statistical significance from multiple drug-gene interaction databases to formulate a Pharmacome. Compounds with adjusted p-value <0.05 were chosen. Compounds with no clinical indications (e.g., ozone, ethanol) were filtered out from the resulting drug lists.

Results: Our query identified 34 unique genes associated with PVR. Out of 77,146 candidate drugs/compounds in the drug databases, our analysis revealed multiple drugs/compounds with significant interactions with genes involved in PVR. The drugs predicted amongst the top 100 most significant compounds include anti-proliferatives, corticosteroids, anti-diabetics, antioxidants, statins, and flavonoids. Prednisone ($P=2.08x10^{-7}$), a corticosteroid that affects 4 of the 34 identified PVR genes, and methotrexate ($P=1.70x10^{-4}$), an anti-neoplastic agent that also affects 4 of the 34 genes, have shown promising results in animal studies and ongoing clinical trials for PVR. Other predicted top compounds including metformin ($P=8.30x10^{-12}$), statins ($P=9.76x10^{-19}$), and curcumin ($P=2.03x10^{-17}$), which affect 11, 17, and 18 of the 34 PVR genes, respectively, have well-established safety profiles and could be readily repurposed for PVR.

Conclusions: This bioinformatics approach of studying drug-gene interactions can speculate drugs which may affect genes and pathways implicated in PVR. We use our growing understanding of systems biology to introduce a computational network medicine process for finding novel therapeutic targets for PVR. While further validation from preclinical/clinical studies is required for bioinformatic predictions, this unbiased approach could identify possible candidates out of existing drugs/compounds that may be repurposed for PVR and guide future investigations.

CONTROL ID: 3707859

SUBMITTER (NAME ONLY): André Ferreira

TITLE: Application of optical coherence tomography angiography for hydroxychloroquine-induced microvascular changes: a systematic review and meta-analysis

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ferreira, M. Afonso, A. Abreu, S. Monteiro, M. Macedo, M. Furtado, M. Lume, Centro Hospitalar Universitario do Porto EPE, Porto, PORTUGAL|R. Anjos, Centro Hospitalar de Lisboa Central EPE, Lisboa, Lisboa, PORTUGAL|R. Anjos, Universidade Nova de Lisboa Comprehensive Health Research Centre, Lisboa, Lisboa, PORTUGAL|M. Furtado, Universidade do Porto Instituto de Ciencias Biomedicas Abel Salazar, Porto, Porto, PORTUGAL|A. Ferreira, R. Vieira, J. Andrade, Universidade do Porto Faculdade de Medicina, Porto, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: Hydroxychloroquine (HCQ) is an antimalarial drug widely used by many specialties for the management of autoimmune diseases. Retinal toxicity with long term HCQ treatment is a major concern and risk factors have been established. Several recent studies detected microvascular changes in patients using HCQ without evident microangiopathy or retinopathy on ophthalmoscopy. In addition, Optical coherence tomography angiography (OCTA) may help to further elucidate the mechanisms of HCQ-induced retinal toxicity. We sought to conduct a systematic review and meta-analysis of the OCTA application to detect HCQ-induced microvascular alterations and further characterize them.

Methods: PubMed, Scopus, Web of Science and Cochrane were systematically searched to November 1st, 2021, along with a manual search. Studies that used OCTA as a primary diagnostic method to evaluate the macular microvasculature of HCQ users were included. Meta-analyses of continuous outcomes were conducted using an inverse variance in the model. Primary outcomes were macular vessel density (VD) and foveal avascular zone (FAZ) at the superficial (SCP) and deep capillary plexus (DCP).

Results: Of 159 screened articles, 8 were found eligible for qualitative and for quantitative analysis. Patients with high risk of HCQ-induced retinopathy due to the longer duration of treatment (> 5 years) presented lower VD in the retinal microvasculature than those with low risk in SCP (SMD -0.53 [-0.93, -0.12], P = 0.01 in fovea; SMD -0.44 [-0.73, -0.16], P = 0.002 in parafovea) and in DCP (SMD -0.53 [-1.01, -0.06], P = 0.03 in fovea) and a trend for wider FAZ in DCP (P = 0.06). When compared with healthy controls, HCQ users had lower VD in SCP (SMD -0.67 [-1.19, -0.15], P = 0.01 in fovea; SMD -0.74 [-1.40, -0.08], P = 0.03 in parafovea) and in DCP (SMD -0.85 [-1.59, -0.10], P = 0.03 in fovea) and presented a wider FAZ only in SCP (SMD 0.61 [0.03, 1.20], P = 0.05).

Conclusions: Microvascular retinal changes were found in patients under HCQ treatment without any kind of retinopathy. These findings seem to precede structural and electrophysiologic changes, placing OCTA as a potential instrument for early detection of reversible retinopathy. In addition, these results support the idea of vasculopathy in the pathogenesis of HCQ-induced retinal toxicity.

CONTROL ID: 3707866

SUBMITTER (NAME ONLY): Minsoo Kim

TITLE: Characterizing and quantifying image artifacts in optical coherence tomography angiograms of normal retinal vasculature

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kim, S.N. Wuppukondur, A.H. Kashani, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|X. Zhou, R.K. Wang, University of Washington Department of Bioengineering, Seattle, Washington, UNITED STATES|X. Jiang, University of Southern California Department of Ophthalmology, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) is highly prone to image artifacts which can hinder the interpretation of OCTA images for clinical and research applications. The aim of this study is to develop a feasible method of characterizing and quantifying OCTA artifacts for objective analysis of image quality.

Methods: This was a retrospective study of 3×3 mm^2 OCTA scans (CIRRUS HD-OCT 5000) from healthy adult subjects without any major eye diseases. The en face angiogram and structural OCT image from each scan at the superficial retinal layer (SRL) was segmented for analysis. Four types of artifact were defined (decentration, motion artifact, defocus, and shadowing) and manually graded on a scale of 0 (not present), 1 (mild), and 2 (severe) as shown in Table 1 and Figure 1. A previously described and validated semiautomated algorithm was used to calculate vessel diameter index (VDI), vessel area density (VAD), vessel skeleton density (VSD), vessel complexity index (VCI), and flux. A linear mixed-effects model was used to analyze the effect of artifact severity on OCTA parameters.

Results: 152 scans from 35 eyes of 19 participants (age 69.4±6.7 yrs, 43.4% male) were included. Severe defocus ($Ps<0.001$), severe shadowing ($Ps<0.001$), and mild defocus ($Ps<0.01$) were negatively correlated with VDI, VAD, VSD, and flux, (range $r=[-3.9\times10^{-3}]$-$[-1.6\times10^{-1}]$). Severe decentration ($Ps<0.05$) was also negatively correlated with VDI, VAD, and VSD, but not flux, with similar magnitudes. Severe motion artifact was positively correlated with VCI ($Ps<0.05$, $r=1.8\times10^{7}$). VCI was not correlated with any other artifacts. Decentration, motion artifact, and shadowing of mild severity were not correlated with any of the vessel parameters.

Conclusions: The presence of severe decentration, defocus, and shadowing on OCTA scans was found to be quantitatively reflected in the vessel parameters of VDI, VAD, VSD, and flux, while motion artifact was uniquely correlated with VCI. Mild artifacts may not significantly impact most OCTA parameters.

CONTROL ID: 3707869

SUBMITTER (NAME ONLY): Muhammad Chauhan

TITLE: Association between systematic use of bio-occlusive dressing to reduce general anesthesia-associated corneal injury

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.Z. Chauhan, R.N. Sanders, A. Elhusseiny, A. Sallam, Department of Ophthalmology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Exposure keratopathy (EK) is the most common potential ocular complication following general anesthesia (GA), presenting with postoperative pain, tearing, photophobia, and blurred vision. The current study aims to evaluate the incidence of post-anesthesia exposure keratopathy before and after implementation of a bio-occlusive dressing eye protection protocol (Fig. 1).

Methods: We conducted a single-center nonrandomized quality improvement study on 15,585 patients from March 2018 to June 2018 (before protocol) and from August 2018 to February 2019 (after protocol). The primary study outcome was the development of anesthesia-related exposure keratopathy in patients. Odds ratios (ORs) were generated using multivariate logistic regression models. Potential confounders in the model included patient demographics, duration of GA, smoking status, diabetic status, American society of anesthesiologists (ASA) wellness score, anesthesiologist type (i.e., CRNA, resident, faculty) and dependent surgical positioning. Inverse probability of treatment weighting (IPTW) was implemented to create a balanced comparison between periods on the baseline variables. Power analysis found that post-weighted samples sizes were large enough to ensure a power of 98.14% with a type I error of 0.05 to detect a 10% difference (RR=1.1) for outcomes. Two-tailed tests were evaluated with an alpha = 0.05.

Results: There was no significant monthly trend in the number of GA cases during the 11-month period (Fig. 2). Prior to introduction of protection protocol, 25/6506 (0.38%) patients undergoing GA developed EK. After protocol implementation, the number of EK was reduced to 3/9352 (0.03%) ($p<0.001$). After IPTW adjustment, the relative risk reduction was 90.0% (CI: 67.3%, 96.9%) and the number needed to treat was 291.52 (CI: 206.7, 501.5). IPTW binary logistic regression analysis controlling for confounding found that there was a significantly decreased odds of developing EK after protocol implementation when compared to before (OR [95% CI], 0.083 [-0.016–0.182], $P < .001$) (Table 1).

Conclusions: The lack of a standardized eye protection protocol results in higher EK incidence, suggesting that lagophthalmos is the most important factor in the development of anesthesia-related EK. The systematic use of a bio-occlusive dressing represents an effective method for reducing the post-GA keratopathy risk.

CONTROL ID: 3707870

SUBMITTER (NAME ONLY): Michelle Antonucci

TITLE: Improving Meridional Acuity Deficits in Astigmatism-Related Amblyopia by Grating Acuity Training

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Antonucci, B.Z. Li, D.M. Levi, University of California Berkeley School of Optometry, Berkeley, California, UNITED STATES|T. Leung, C. Kee, The Hong Kong Polytechnic University, Hung Hom, HONG KONG|R. Li, Nova Southeastern University College of Optometry, Fort Lauderdale, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate whether practicing a full-contrast grating acuity task modifies resolution acuity in adults with astigmatism-related amblyopia.

Methods: We developed a psychophysical test to measure grating acuity. In each trial, a full- contrast sinusoidal grating target (diameter=0.7 deg) was displayed randomly at one of four locations on the monitor screen. The visual task was to indicate the location of the target grating. The spatial frequency of the grating stimuli was controlled using an adaptive staircase technique (3-down 1-up, converged to 79% correct). The mean of the last 12 reversal points was taken as grating acuity. The mean luminance of the grating targets was 70 cd/m2. In the training phase, the participants were required to repeatedly practice the grating acuity task for 10 sessions with the amblyopic eye. The grating orientation was set to the axis of the negative cylindrical correction for myopic astigmatism. Audio feedback was provided for each response. Each participant had given roughly ten thousand responses at the end of the experiment.

Results: Ten adults with astigmatism-related amblyopia participated. Over the course of the grating acuity training, our participants showed rapid recovery from meridional acuity deficits. The meridional anisotropy of grating acuity became significantly normalized from 1.28 to 1.06 after the intervention (paired $t=4.757$, $p=0.001$). All participants showed a significant improvement in grating acuity of the amblyopic eye for the trained grating orientation (mean improvement, 19%; one sample $t=8.228$, $p<0.001$), and the learning effects did not transfer to the untrained orthogonal grating orientation (one sample $t=4.194$, $p=0.683$).

Conclusions: Practicing grating detection near cut-off spatial frequency can improve meridional acuity deficits in astigmatism-related amblyopia. Our findings characterized the learning profile and orientational specificity of grating acuity training. We are currently working towards standardizing this new technique for treatment of meridional amblyopia.

CONTROL ID: 3707872

SUBMITTER (NAME ONLY): Henry Skrehot

TITLE: Epidemiology of Retinopathy of Prematurity in the United States from 2003 to 2016

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Skrehot, A. Bhatnagar, A. Bhatt, H. Herce, C.Y. Weng, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is an eye disorder primarily affecting premature and low birth weight infants that can lead to lifelong vision impairment and blindness. We used a nationwide pediatric inpatient care database to investigate the variability of incidence of ROP across populations, locations, and time in the US.

Methods: The National Healthcare Cost and Utilization Project Kids' Inpatient Databases from 2003 to 2016 were analyzed to find the incidence of ROP across sexes, racial groups, income groups, and geographic regions. Infants with ICD-9 codes (ICD-10 for 2016) for premature birth week or low birth weight (<1500 g) were considered premature. Chi-square tests of independence were used to determine whether incidences changed by year or varied across subpopulations.

Results: The proportion of premature infants diagnosed with ROP has increased from 4.61% in 2003 to 8.54% in 2016. Compared with those born in higher median household income quartiles, premature infants from the lowest quartile had the greatest proportional increase of ROP diagnoses from 5.07% to 9.50% during the same time period ($p < 0.001$). ROP incidence increased between 2003 and 2016 in all considered racial/ethnic groups, but premature Black infants experienced the largest relative increase from 5.98% to 12.12% ($p < 0.01$). The Southern US has seen the greatest growth in the proportion of ROP diagnoses increasing from 3.82% to 9.11% ($p < 0.001$). ROP diagnoses have proportionally increased in urban areas and decreased in rural areas. Premature male and female infants experienced similar relative increases in ROP diagnoses (4.47% to 8.27% vs 4.76% to 8.86%, respectively).

Conclusions: Overall incidence of ROP among premature infants increased from 2003 to 2016. Infants in the poorest areas have the highest proportional incidence of ROP, and this disparity is persistent over time. Black infants appear to be at the highest risk. All regions have experienced a significant increase in ROP incidence, with the most drastic changes occurring in the South and Midwest. Regardless of region, the burden of ROP seems to have partially shifted from rural hospitals to urban ones. These trends indicate ROP is a growing problem in the United States and one that may be disproportionately affecting certain subpopulations.

CONTROL ID: 3707873

SUBMITTER (NAME ONLY): Naomi Hasegawa

TITLE: Comparison of Tumor Size at Presentation and Genomics in Uveal Melanoma Patients Before and After the COVID-19 Pandemic

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Hasegawa, Ophthalmology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|A. Rusakevich, A.C. Schefler, Retina Consultants of Texas, Houston, Texas, UNITED STATES|E. Bernicker, Houston Methodist Hospital, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: One major effect of the COVID-19 pandemic has been a delay in presentation and interruptions in delivery of care to patients with many different cancer types. The purpose of our study is to compare the clinical and genomic variables of uveal melanoma patients presenting before and after the start of the pandemic to assess the effect of the pandemic on a delay in care.

Methods: This study is a retrospective chart review of uveal melanoma patients presenting during two time periods: May 2019 to February 2020 (Group 1: Before the COVID-19 pandemic declaration by the WHO in March 2020) and May 2020 to March 2021 (Group 2: After the start of the COVID-19 pandemic). Disease stages at presentation were analyzed by clinical and genomic variables including: thickness and largest base diameter of tumor, COMS size class, AJCC stage, GEP class, and Prame status.

Results: A total of 80 patients with uveal melanoma were studied [Group 1: 40 (50%) and Group 2: 40 (50%); mean age: 62.5 years (range 25-84) and 64 years (range 30-91)]. There was no statistically significant difference between the tumor thickness, largest base dimension, and COMS size class between Group 1 (Pre-COVID) and Group 2 (During COVID). The majority of patients were found to be in AJCC class I/IIA in both groups [Group 1: 26 (65%) and Group 2: 27 (67.5%)] with no statistically significant difference in staging between the groups. Analyzed genomic data of GEP class and Prame expression also failed to show a difference between Group 1 and Group 2, with majority of patients found to be GEP Class IA [Group 1: 27 (69.2%) and Group 2: 25 (62.5%)] and Prame negative [Group 1: 28 (71.8%) and Group 2: 28 (70%)] for both groups.

Conclusions: The study showed that the COVID-19 pandemic had no effect on the presentation of uveal melanoma patients at our center across various tumor characteristics that can be used as a surrogate marker for delayed presentation, including size, staging, and genomic data. A large-scale, long-term study is necessary to analyze the long-term consequences of the pandemic on uveal melanoma patients.

CONTROL ID: 3707874

SUBMITTER (NAME ONLY): Muhammad Abdulrazik

TITLE: Biopharmaceuticals: are you into designing your own one? then here's the most decorated build recipe – based on architectures with most wins in 2015-2021 FDA's Novel Drug Approvals

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Abdulrazik, Innovative Therapeutic Algorithms, East Jerusalem Eye Research Initiative, East Jerusalem, PALESTINE, STATE OF|

Commercial Relationships Disclosure: Muhammad Abdulrazik: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To provide build insights for future tasks of designing new ocular biopharmaceuticals based on optimal balance of affinity vs. avidity and efficacy vs. potency.

Methods: List of approved biopharmaceuticals was obtained from FDA records and structure/function data was mined from regulatory evaluations, publications and patents.

Results: Of 87 approved 67 were monoclonal-antibodies (mAb) – 63/67 full-mAb (145.5±1.5 kDa): 3/63 chimeric, 30/63 humanized, 30/63 human; 8/63 IgG2, 11/63 IgG4, 2/63 hybrid, 42/63 IgG1; 3 bispecific; 6 Fc-modified; 8 mAb-drug conjugates (5 enzyme-, 2 acid- and 1 non-cleavable – drug/mAb ratio of 4.9±1.9). 4/67 non-full: 1 fragment antigen binding (Fab), 1 single-chain variable fragment (scFv), 1 single-domain antibody (sdAb) and 1 Fv-fusion.

Conclusions: Full-mAb hegemony has yet to be truly contested (typically human/-ized IgG1k). Novelties included bispecific-mAb and Fc-altered amino-acid or fucose to boost avidity. Fab, scFv, sdAb and fusions are emerging – no one a racehorse yet. Eye approvals were cenegermin (nerve GF /Neurotrophic Keratitis), teprotumumab for TED (148 kDa human IgG1k) and brolucizumab for wAMD (26 kDa humanized scFv). With prior approvals, aflibercept (115 kDa Fc-fusion receptor) and ranibizumab (48 kDa humanized Fab), the average MW of ocular anti-VEGFs is 63 kDa, well under all-mAb MW mean and contrast to bevacizumab MW (149 kDa humanized IgG1k). As per the standard IVT doses, 1.2 molecules of ranibizumab, 2.1 of aflibercept and 27.2 of brolucizumab, each has an anti-VEGF potency comparable to just 1 bevacizumab molecule. With molecular-radius roughly twice higher, 1 bevacizumab molecule can still cross the retina and perform an anti-VEGF "work" comparable to that of 27.2 molecules of the smaller brolucizumab – practically setting aside the argument of size-related obstacles to mAb penetration across the retina. A no surprise, since bevacizumab has 2 Fab per 1 molecule and Fc region for FcRn assisted passage across retina barriers. Higher mAb concentrations catalyze a growing risk of unleashing a generic tendency to aggregate (en syringe) that could lead to immune-mediated adverse effects. Thus, despite emerging innovative mAb designs, full-mAb based design (e.g. bevacizumab) is still the molecular design to beat in terms of ocular anti-VEGF potency per 1 molecule.

CONTROL ID: 3707882

SUBMITTER (NAME ONLY): Angelica Garcia

TITLE: Practice Compliance in Documenting and Billing Gonioscopy and Pachymetry in a Resident Ophthalmology Clinic

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Garcia, K.L. Anderson, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure: Angelica Garcia: Commercial Relationship: Code N (No Commercial Relationship) | Kent Anderson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Gonioscopy and pachymetry are billable procedures for those patients with diagnoses that meet medical necessity as indicated. Residents excel in performing these procedures and documenting them where indicated. However, it was noted that residents may often not bill properly for these procedures and often leave the billing to the attending teaching physician. We retrospectively reviewed our documentation and billing practices for these procedures in a resident ophthalmology clinic.

Methods: All patient encounters performed by ophthalmology residents over a 5-month period (January thru May 2021) were retrospectively reviewed for appropriate documentation and billing of gonioscopy and pachymetry. All patient encounters were supervised by teaching physicians in an outpatient ambulatory ophthalmology clinic at the Texas Diabetic Institute, San Antonio, TX. Each electronic medical record (EMR) was reviewed for appropriate documentation and billing. The data was analyzed using R software.

Results: A total of 1,500 patient encounters were reviewed. Gonioscopy was documented in 37 records, but only 14 (38%) of these records were properly billed for. Gonioscopy was billed for in 3 records where the gonioscopy was not properly documented. Pachymetry was documented in 31 records, but only 20 (65%) were properly billed for. No records showed billing of pachymetry without proper documentation. The exclusion of these billing codes was statistically significant ($P_{gonioscopy} = 0.0$, $P_{pachymetry} = 0.0$). All those records were gonioscopy and pachymetry was documented and/or billed had a diagnosis to support medical necessity for the procedure.

Conclusions: Billing for both gonioscopy and pachymetry were preferentially excluded from recording. This result is likely due to inadequate resident understanding of billing for these procedures. It is ultimately up to the attending physician to review the documentation, attest and cosign the note, and verify the final billing diagnosis and procedure codes. Good practices aim for 100% compliance in both documentation and billing. However, these data emphasize the importance of teaching proper coding and billing practices to residents in training as they prepare to enter independent practice.

CONTROL ID: 3707889

SUBMITTER (NAME ONLY): Christopher Wu

TITLE: Spatial Summation of Chromatic Contrast in the Parvocellular Pathway

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.S. Wu, N.B. Patel, D.R. Coates, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Christopher Wu: Commercial Relationship: Code N (No Commercial Relationship) | Nimesh Patel: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Coates: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Perimetry is a widely used tool for assessing visual function. Conventional tests measure locational sensitivity to luminance contrast. While the spatial summation characteristics of luminance are well documented, the summation of color is poorly understood. As the visual mechanisms responsible for achromatic and chromatic contrasts are thought to differ, stimuli in chromatic spaces may offer diagnostic benefits. The aim of this study was to determine the spatial summation characteristics of chromatic contrast mechanisms.

Methods: Contrast detection thresholds were measured as a function of size and eccentricity in four color normal subjects. Stimuli were solid circular patches of either luminance or chromatic contrast increments presented for 300 ms on a background averaging 10 cd/m2. Cone contrasts were calculated in DKL color space by modulating along the achromatic magnocellular (L+M) or chromatic parvocellular (L-M) cardinal axes. Stimuli varied between 0.25° to 4.0° in diameter, and were presented in four principal oblique meridians at 5° intervals within the central 40° of visual field. In the chromatic paradigms, luminance noise was added to non-test positions. Thresholds were obtained using interleaved staircases, with subjects responding with the perceived meridian of presentation.

Results: Achromatic thresholds plotted on a log-log scale were fit with a two-line model. The average slope for smaller stimuli sizes was -1.02 (complete summation) which became shallower, averaging -0.32 (partial summation) beyond a critical area (Ricco's Area). This critical area increased with retinal eccentricity and was similar for locations at a given eccentricity. In the chromatic paradigms, a single linear regression model was used, as a bilinear fit poorly represented the data. In the +(L-M) direction, the average slope was -0.67, with an average r^2 of 0.92. In the -(L-M) direction, the average slope was -0.76, with an average r^2 of 0.86.

Conclusions: While achromatic curves followed the expected two-line model, the distinct linearity of chromatic summation suggests different underlying detection mechanisms. Complete spatial summation was absent for tasks that isolated the chromatic parvocellular mechanism for the range of stimulus sizes tested. The linearity of chromatic spatial summation and lack of critical area may provide improved consistency over achromatic tests, as relative sensitivity is unaffected by stimulus area.

CONTROL ID: 3707897

SUBMITTER (NAME ONLY): Po-Yu Lee

TITLE: Endoscopic dacryocystorhinostomy in patients with functional epiphora after canalicular laceration repair

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Lee, Department of ophthalmology, Chi Mei Medical Center, Tainan, TAIWAN|

Commercial Relationships Disclosure: Po-Yu Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Canalicular laceration usually accompanies eyelid laceration. The orbicularis and medial canthal ligament may be injured at the same time, which leads to defective lacrimal pump function. After canalicular anastomosis and eyelid tightening, most patients can achieve a patent lacrimal system and symptom relief, while few patients may still suffer from functional epiphora. Endoscopic dacryocystorhinostomy (DCR) was considered to reduce the lacrimal drainage resistance and meanwhile preserve lacrimal pump function. We investigate the outcome of endoscopic DCR in patients with functional epiphora after canalicular and eyelid laceration repair.

Methods: Retrospective chart review. All injured patients received primary re-approximation of the canalicus and orbicularis/medial canthal tendon repair. After at least one month, if the patient still complained of tearing, endoscopic DCR with bicanalicular silicone intubation were performed. Patients with re-stenosis of canaliculus or ocular surface disease were excluded. A combination of Munk score and Lac-Q social impact score were used to assess the outcome.

Results: From January 2019 to December 2021, there were 34 patients who received canalicular and eyelid laceration repair. 6 patients received secondary endoscopic DCR due to persistent epiphora after the repair. One had both and the others had lower canalicular laceration. All patients achieved symptom relief immediately after operation. At the last follow-up, all patients were satisfied with the results. Munk score improved from grade 4 to 2 in 2 patients, from grade 4 to 1 in 4 patients). Lac-Q social impact score improved from 5 points to 0 in 3 patients, From 5 to 1 in 1 patient, from 5 to 2 in 2 patients). No recurrence or postoperative complication was found during the follow-up period (Range: 6-17 months, mean: 9.8 months).

Conclusions: Functional epiphora in patients with canalicular laceration can be managed with endoscopic DCR. After successful repair and patent on lacrimal irrigation, there may still be slightly increased outflow resistance. Combining the slightly reduced pump function due to lid laceration, this can lead to postoperative epiphora. Endoscopic DCR decreases lacrimal drainage resistance and affect the lacrimal pump function minimally. There was no significant complication in this study. More case studies are needed to evaluate the outcome.

CONTROL ID: 3707899

SUBMITTER (NAME ONLY): David Tran

TITLE: Efficacy of Kahook Dual Blade Goniotomy with and without Phacemulsification in an Urban Population: A Retrospective Study

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the efficacy of Kahook Dual Blade (KDB) goniotomy with and without phacoemulsification (PE) in an urban population, we performed a retrospective, observational clinical study and examined longitudinal changes to intraocular pressure (IOP) and number of IOP-lowering medications (ILMs).

Methods: This retrospective study includes 61 eyes of 61 patients with glaucoma, 77% with primary open angle glaucoma (POAG), treated by KDB goniotomy with and without PE. IOP and ILMs were assessed at baseline and follow-up visits for up to 42 months. Patients were categorized into lower (Group A) and higher (Group B) IOP groups. IOP goals for Group A, with baseline IOP ≤ the study population median baseline IOP of 15 mm Hg, were defined as ≤ their baseline IOP. Group B, with baseline IOP >15 mmHg, were designated IOP reduction goals of ≥20% or reaching ≤18 mm Hg if baseline IOP is ≤22 or >22, respectively. Assessing Group A primarily by lowering post-operative ILMs was reasoned to be an appropriate endpoint. Complete-success was defined by the following three principles: (1) reaching post-operative IOP goal, (2) achieving 0 ILMs, and (3) lacking additional IOP-lowering intervention or hypotony during follow-up. We also defined qualified-success with the following criteria: (1) reaching post-operative IOP goal, (2) for Group B, maintaining or improving baseline ILMs, and for Group A, if baseline ILMs is ≤3 or >3, then improving ILMs by at least 1 or 2, respectively, and (3) lacking additional IOP-lowering intervention or hypotony during follow-up. If the patient had two or more consecutive visits failing to meet the success criteria above, the patient would fail at the first of the two visits. Survival analysis was performed using Kaplan-Meier curves.

Results: Reduction in IOP from baseline was statistically significant at day 1, week 1, and months 3, 12, 24, and 30. Reduction in ILM burden from baseline was statistically significant at 1 day through 24 months of follow-up. Survival analysis based on complete- and qualified-success criteria demonstrated approximately 50% survival for both criteria at 3 months and 25% survival by 6 months and 18 months, respectively.

Conclusions: KDB with and without PE is effective at reducing IOP up to 30 months and ILM burden up to 24 months in an urban setting. Limitations of our study include attrition due to the length of follow-up.

CONTROL ID: 3707900

SUBMITTER (NAME ONLY): Osama Hirayama

TITLE: Dry eye disease and high myopia in teenagers; a reciprocal relationship

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.I. Hirayama, M. Ayaki, E. Yotsukura, H. Torii, K. Negishi, Department of Ophthalmology, Keio University School of Medicine, JAPAN|M. Ayaki, Otake Clinic Moon View Eye Center, Kanagawa, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the relation between dry eye disease (DED) and high myopia (HM) in Japanese teenagers.

Methods: The Institutional Review Board and Ethics Committee of Tsukuba Central Hospital and Kanagawa Medical Association approved this study. This study was a retrospective, descriptive, consecutive case series. We compared the dry eye condition in 106 HM patients (mean age, 16.4 ± 2.2y), 494 mild myopic (MM) patients (15.0 ± 2.6y), and 82 non-myopic (NM) subjects (13.8 ± 2.6y) aged between 10 and 19 years old at Japanese eye clinics. Myopia, astigmatic error, and anisometropia were assessed. Dry eye-related symptoms questionnaire including; dryness, irritation, pain, fatigue, blurring and photophobia were evaluated. Intraocular pressure, tear film break-up time (BUT) and fluorescein staining were investigated. The need for consent was waived by the Institutional Review Board. Regression analysis of myopic error and other variables was conducted.

Results: Anisometropia and astigmatic error were greatest in the HM group compared with other groups ($P < 0.001$). HM group reported more dryness ($P = 0.034$), less photophobia ($P < 0.001$), and less pain ($P = 0.039$) compared with NM group. Most of the symptoms except for fatigue were apparently associated with myopic error. Regression analysis revealed that astigmatic error ($\beta = -0.231$, $P < 0.001$), anisometropia ($\beta = -0.191$, $P < 0.001$), short BUT ($\beta = -0.086$, $P = 0.028$), and presence of diagnosed DED ($\beta = -0.112$, $P = 0.003$) were correlated with myopic error. Regarding symptoms, dryness ($\beta = -0.127$ $P = 0.004$), photophobia ($\beta = 0.117$, $P = 0.002$), and pain ($\beta = 0.084$, $P = 0.034$) were correlated with myopic error as well.

Conclusions: Our study showed significant clinical findings of DED in HM patients. The present results indicated DED might be associated with HM in teenagers.

CONTROL ID: 3707905

SUBMITTER (NAME ONLY): Nasim Salimiagdam

TITLE: Effects of Quercetin in AMD Cybrid Cell Lines: Implications for a Therapeutic Role in AMD

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Salimiagdam, M. Chwa, A. Nesburn, M. Kenney, UCI, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We evaluated the possible beneficial outcomes of quercetin on human AMD cybrid cell lines.

Introduction

In developed countries, age related macular degeneration (AMD) is the leading cause of progressive central vision loss in aged populations. Previous studies have demonstrated the advantageous impacts of antioxidants such as vitamin E and zinc in lowering the incidence and progression of AMD. Quercetin, a plant flavanol from the flavonoid group of polyphenols, is found in many fruits, vegetables and seeds. Previous in vitro studies have demonstrated the antioxidant and anti-inflammatory properties of quercetin, suggesting it may have therapeutic benefit for human diseases. Its main antioxidant activity is associated with inhibition of the signal transduction pathway and activity of cytosolic glutathione, leading to reduction of reactive oxygen species (ROS) production.

Methods: Cybrids were created by fusion of the mitochondria-deficient (Rho0) ARPE-19 cells with the platelets derived from AMD patients and age-matched non-AMD individuals. The resultant cybrid cell lines have mitochondria originating from different individuals but identical nuclei. Cells were cultured in 96-well plates (10,000 cells/well) and treated with quercetin 20 μM for 24 hours. DMSO was used as vehicle-control. ROS levels and cellular metabolism were measured in control and treated cultures. For ROS assay, after adding 100 μl H2DCFDA solution/well, plates were read via the fluorescent plate reader with the excitation (EX, 492nm) and emission (EM, 520nm) wavelengths. Performing MTT assay, 10 μl of MTT assay reagent was added/well and plates incubated in 37°C for 3 hours. After adding 200 μl/well of DMSO, plates were analyzed (signal at 570 nm and reference at 630 nm) with the absorbance plate reader. Statistical analyses were performed via student t-test.

Results: ROS levels of quercetin treated non-AMD cybrids and AMD cybrids declined to 84.25% (P= 0.0002, n=4) and 86.75% (P= 0.011, n=4), respectively, compared to vehicle-control groups (100%, n=4). Moreover, quercetin increased cellular metabolism of non-AMD cybrids and AMD cybrids to 132.8% (P= 0.002, n=4) and 128.0% (P= 0.001, n=4), in order, versus vehicle-control cells (100%, n=4).

Conclusions: Administration of quercetin 20 μM has positive impacts on treated AMD cybrid cell lines.

CONTROL ID: 3707907

SUBMITTER (NAME ONLY): Philipp Anders

TITLE: Investigation of intermediate AMD with MAIA microperimetry metrics by the PINNACLE Consortium

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Microperimetry (MP) is an important technique to evaluate visual performance in patients with age-related macular degeneration (AMD). In this study we examine a large cohort of patients with intermediate AMD (iAMD) with multiple MP retinal sensitivity and fixation stability metrics.

Methods: This is a cross-sectional analysis of baseline data from 247 patient eyes of the longitudinal, prospective, multicenter and non-interventional PINNACLE study. Best Corrected Visual Acuity (BCVA) and Low Luminance Visual Acuity (LLVA) were measured with ETDRS charts. The MAIA (Centervue, Italy) MP metrics of mean sensitivity (MS), Bivariate Contour Ellipse Area (BCEA) fixation indices (63% and 95%) and percentage of fixation points within 1° and 2° of the foveal center (P1 and P2) were recorded. R code by Josan et al., was applied to obtain 3-D hill of vision surface plots and the total volume (V_{TOT}) beneath the plots in dB-deg^2. We report non-normally distributed data with Spearman's R, medians and interquartile ranges (IQRs).

Results: The following baseline medians and IQRs were measured: BVCA LogMAR 0.02 (-0.06-0.1), LLVA LogMAR 0.32 (0.2-0.45), V_{TOT} 1656 dB-deg^2 (1541-1761), MS 24.2 dB (22.8-25.7), P1 93% (82-98), P2 99% (94-100), BCEA63 1 deg^2 (0.4-2.7), BCEA95 2.9 deg^2 (1.2-8.1). There was a significant positive correlation for V_{TOT} and MS ($r = 0.98$; $p < 0.0001$). V_{TOT} exhibited a significant correlation to all MAIA metrics of fixation stability ($p < 0.05$). All metrics of fixation stability were significantly correlated with each other ($p < 0.0001$). All MAIA metrics were significantly correlated to BCVA and LLVA ($p < 0.01$). The performances in most sensitivity and fixation metrics were significantly inversely correlated to age (BCVA: $r = 0.33$, $p < 0.0001$; LLVA: $r = 0.33$, $p < 0.0001$; V_{TOT}: $r = -0.28$, $p < 0.0001$; MS: $r = -0.29$, $p < 0.0001$; P1: $r = -0.16$, $p = 0.01$; BCEA63: $r = 0.19$, $p = 0.003$; BCEA95: $r = 0.19$, $p = 0.03$).

Conclusions: We report reference data for multiple retinal sensitivity and fixation stability metrics in a large cohort of patients with iAMD. Our analysis provides a strong positive correlation between MS, an established metric, and V_{TOT}, a novel volumetric description of retinal sensitivity. The latter might be more precise, since it eliminates the inaccuracy of averaging. Finally, our data provide evidence for the inverse correlation of retinal functional capacities and age in iAMD.

CONTROL ID: 3707908

SUBMITTER (NAME ONLY): Christopher Yang

TITLE: Toxicity of a stable phospholipid mixture on human retinal pigment epithelium cells

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.D. Yang, J. Jessen, M. Kenney, K.Y. Lin, Gavin Herbert Eye Institute, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|M. Ataei, A.P. Lee, Department of Mechanical and Aerospace Engineering, University of California Irvine, Irvine, California, UNITED STATES|A.P. Lee, K.Y. Lin, Department of Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Microbubble-enhanced ultrasound has been proposed as a method to achieve targeted ocular drug delivery. We designed an in vitro experiment to identify the optimal concentration of a stable phospholipid mixture that biochemically recapitulates a monodisperse microbubble suspension and is nontoxic to human retinal epithelium cells (ARPE-19). We hypothesize that phospholipid mixture exposure reduces ARPE-19 cell viability in a dose-dependent fashion.

Methods: ARPE-19 cells were plated in 96-well plates and treated with 880 µL of solution containing 0.0125, 0.025, 0.05, 0.1, or 0.5 mg/mL of phospholipid mixture. Phospholipid was dissolved in chloroform at a 80:10:10 molar ratio of DPPC:DPPA:DPPE-PEG5000 (Avanti Polar Lipids) and dried by nitrogen stream and vacuum evaporation before resuspension in PBS. Control wells received media only. MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyltetrazolium bromide) assay was performed at 24 and 48 hours post-treatment to quantify intracellular metabolism as a proxy for cell viability. All groups were run as 4 technical replicates and two-tailed Mann-Whitney U tests were used for statistical analysis.

Results: At 24 hours post-treatment, ARPE-19 cells treated with phospholipid mixture at concentrations at or above 0.05 mg/mL exhibited statistically significant ($p<0.05$) decreases in viability while cells treated with phospholipid mixture at concentrations below 0.05 mg/mL exhibited non-significant decreases in viability (Figure 1). This trend appeared to be dose-dependent. Only phospholipid mixture concentrations between 0.0125 mg/mL and 0.05 mg/mL were assessed in the 48-hour experiment; there were no statistically significant changes in cell viability between control and treatment groups in the 48-hour experiment (Figure 2).

Conclusions: This study demonstrates that short-term phospholipid exposure in ARPE-19 cells is cytotoxic in a dose-dependent fashion. This observation suggests that microbubble formulations should be fabricated below a certain phospholipid concentration to avoid cytotoxicity in target tissues. Future experiments evaluating phospholipid and microbubble toxicity in different ocular cell types are underway to more clearly characterize their physiological effects and explore the viability of microbubbles as an ocular drug delivery modality.

CONTROL ID: 3707910

SUBMITTER (NAME ONLY): FEI LIAO

TITLE: Horizontal cells modulate the visual signaling in the retinal first synapse by controlling the flux of HCO3- in the triadic synaptic cleft

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Regarding the functional role of horizontal cells (HCs) in the retina, three mechanisms have been extensively studied at the cone pedicle, including GABA mediated feedback, hemichannel dependent current modulation, and pH effect on calcium current. But, it is yet unclear the functional contribution of HCs in the rod visual pathway. This study tested the hypothesis that HCs may modulate the output signals at the rod synaptic terminal by combining at least two of the three previously mentioned mechanisms.

Methods: Adult, healthy, mouse strain of wild-type C57BL/6J was used for electroretinogram (ERG) and immunohistochemical (IHC) labeling. The physiological study was carried out on dark-adapted (> 12 hours) animals in vivo by recording binocular responses of the rod-mediated ERG signals in response to low intensity full-field light stimuli (≤ 0.01 $cd \cdot s/m^2$) after the right eye of each animal was intravitreally injected with 1 µL of a solution containing GABA (100 mM), Glutamate (100 mM), Bicuculline (10 mM), DNQX (30 mM), APB (25 mM), HEPES (25 mM), TPMPA (5 mM) or the combination of those compounds. Meanwhile, the left eye was injected with 1 µL of PBS solution. We also performed a study about the localization and colocalization of molecular proteins in the retina, including calbindin, GABA, and anion exchanger 3 (AE3).

Results: The rod response was abolished by APB and relevantly diminished by TPMPA. Experimental stimulation of HCs membrane receptors by GABA and glutamate produced a significant increase in the rod response ($p < 0.05$), the injection of its antagonists (Bicuculline and DNQX) produced a significant decrease in the rod response ($p < 0.01$). The rod response showed a statistically significant roll-off decrease since the acid-base condition of the triadic synaptic cleft is justified by intraocular injection of HEPES, whose pH was adjusted to 7.2, 7.4, and 7.6. In the IHC study, it was found that calbindin was localized in the outer plexiform layer, and both GABA and AE3 colocalized with calbindin.

Conclusions: HCs modulate the transmission of light signaling received in the rod visual pathway in the first synapse by strictly sticking to the pH regulation in the synaptic cleft, whose pH condition is determined by the flux of HCO3-, which is controlled by GABAergic HCs′ membrane receptors.

CONTROL ID: 3707912

SUBMITTER (NAME ONLY): Daniel Adeyoju

TITLE: Scotopic Microperimetry: A Volumetric Analysis of Healthy Controls

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Adeyoju, L.J. Taylor, A.S. Josan, R.E. MacLaren, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|D.A. Adeyoju, L.J. Taylor, A.S. Josan, R.E. MacLaren, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|J.K. Jolly, Anglia Ruskin University Vision and Eye Research Institute, Cambridge, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Scotopic microperimetry involves fundus-controlled perimetry performed in dark conditions, enabling spatial assessment of scotopic macular sensitivity. Volumetric analyses have been shown to reflect central retinal sensitivity more accurately but are yet to be applied to scotopic microperimetry. We investigate normative volumetric sensitivity values and their repeatability in two-colour scotopic microperimetry in healthy participants.

Methods: Macular sensitivity in 23 healthy participants was assessed using S-MAIA Microperimeter (Centervue SpA, Padua, Italy) displaying a 37-point radial grid, following 20 minutes dark adaptation (light level <1 lux). Both eyes in each participant were assessed with cyan (505nm) stimuli followed by red (627nm) stimuli, with sensitivity measured in decibels. A sub-cohort underwent further testing in the right eye only within 5 weeks to assess repeatability. Comparative non-parametric statistics using SPSS (IBM Version 25.0.0.1) were applied. Hill of Vision volumetric analysis of results was performed using an open-source program.

Results: Mean retinal sensitivity and volumetric sensitivity in the right eye and left eye were obtained (Table 1, 45 eyes, mean age: 34.3 years range: 20-73). Fixation losses >20% as measured by blind spot losses were used to exclude exams from the final analysis. Median volumetric sensitivity in the right eye and the left eye with cyan and red stimuli were significantly correlated (Spearman's Correlation, cyan ρ=0.871, p=0.001, red ρ=0.621, p=0.01, cyan-red ρ=0.468 p=0.068). There was no significant correlation between age and volumetric sensitivity (Spearman's correlation, cyan ρ=-0.414 p=0.099, red ρ=-0.333 p=0.192). Coefficients of repeatability for volumes were calculated (cyan n=10 ±207.1dB-degrees^2, red n=12 ±367.5dB-degrees^2, cyan-red n=8 ±164.9dB-degrees^2).

Conclusions: For the first time, we describe an application of volumetric analysis and correspond repeatability measures in scotopic microperimetry data. The strong inter eye symmetry suggests no significant learning or fatigue effects on test performance. In diseased patients, volumetric measures offer more detailed indication of function than simple mean sensitivity, so here we display a normative dataset from healthy participants.

CONTROL ID: 3707913

SUBMITTER (NAME ONLY): Rupert Bourne

TITLE: A global and regional analysis of Risk Factors for Blindness and Vision impairment in 2020 and their contribution to the change in prevalence of vision loss over 3 decades.

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.R. Bourne, I. Tapply, Ophthalmology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, Cambridgeshire, UNITED KINGDOM|R.R. Bourne, Vision & Eye Research Institute, Anglia Ruskin University Faculty of Health Education Medicine & Social Care, Cambridge, Cambridgeshire, UNITED KINGDOM|M. Bottone, S. Flaxman, Imperial College London, London, London, UNITED KINGDOM|J. Steinmetz, P. Briant, T. Vos, Institute for Health Metrics and Evaluation, University of Washington, Seattle, Washington, UNITED STATES|R. Casson, Discipline of Ophthalmology and Visual Science, Adelaide University, Adelaide, South Australia, AUSTRALIA|N. Wang, Beijing Tongren Hospital, Capital Medical University; Beijing Institute of Ophthalmology, Beijing, CHINA|J. Jonas, Medical Faculty Mannheim-Heidelberg, Heidelberg, GERMANY|S. Resnikoff, University of New South Wales, Sydney, New South Wales, AUSTRALIA|T. Braithwaite, Ophthalmology, Guy's and St Thomas' Hospital and KCL, London, UNITED KINGDOM|M. Cicinelli, San Raffaele Scientific Institute, Milan, ITALY|H.R. Taylor, Melbourne School of Population Health, University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The Vision Loss Expert Group (VLEG) and Global Burden of Disease Study (GBD) collaboratively updated crude and age-standardised prevalence estimates of blindness and vision impairment and investigated inter-regional and age-specific changes over the 1990 to 2020 timeframe. Here we expand the focus to account for global and regional risk factors and address vision loss severities pertaining to all geographical locations.

Methods: (1) Selection of 24 covariates with a potential link to vision-related disease from a database used across GBD modelling. (2) Analysis of the association of risk factors with crude and age-standardised prevalence estimates of blindness and vision impairment in 2020 separately for each severity: blindness, moderate and severe vision impairment, mild vision impairment, near vision impairment due to uncorrected presbyopia. (3) Analysis of the trend contribution of the percentage rates of change in risk factors to the rates of change in prevalence 1990-2020.

Results: For adults (50+ yrs), for crude and age-standardised prevalence estimates for year 2020, we found a significant negative association of smoking prevalence, for all persons and for each sex. Maternal care and immunisation, sanitation proportion, health access & quality index and socio-demographic index were other significant age-standardised negative associations. Ophthalmologists/million population had a weak but significant protective effect, and we found positive associations for pollution (outdoor and indoor), stronger for greater vision impairment severities. Years in education per capita was weakly, negatively associated with vision loss prevalence yet zero education proportion has a stronger but positive association for both sexes. Multiple variable analysis led to generally lower effect sizes and reductions in significance of single variable findings.

Conclusions: This study has confirmed associations at population level globally which appear to be stable over decades. In addition, the study has quantified the contribution of epidemiologically-based risk factors to vision loss at a macroregional level which is novel. This opens useful avenues for targeted intervention by policymakers. For example, reduction in sex inequity in blindness rates over 30 years has been positively associated with reducing overall blindness prevalence.

CONTROL ID: 3707916

SUBMITTER (NAME ONLY): Andreas Berlin

TITLE: Optical coherence tomography angiography of type 3 macular neovascularization, a clinicopathologic correlation

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Berlin, L. Chen, J.D. Messinger, C.A. Curcio, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|A. Berlin, Ophthalmology, Universitatsklinikum Wurzburg, Wurzburg, Bayern, GERMANY|L. Chen, Chongqing Key Laboratory of Ophthalmology, and Chongqing Eye Institute, The First Affiliated Hospital of Chongqing Medical University, Chongqing, Sichuan, CHINA|D. Cabral, Ophthalmology, CEDOC - NOVA Medical School, Universidade NOVA de Lisboa, Lisbon, PORTUGAL|D. Cabral, K. Freund, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|K. Freund, Ophthalmology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|C. Balaratnasingam, Ophthalmology and Visual Science, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|C. Balaratnasingam, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|R. Mendis, Canberra Retina Center, Canberra, Western Australia, AUSTRIA|

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ABSTRACT BODY:

Purpose: Correlation of in vivo optical coherence tomography angiography (OCTA) of type 3 macular neovascularization (t3 MNV) secondary to AMD with corresponding ex vivo histology.

Exploring the overall value of clinical OCTA for disease observation, diagnosis, and staging by validating OCTA in the analysis of type 3 macular neovascularization secondary to AMD.

Methods: A white woman receiving anti-VEGF (OD, n=37; OS, n=6; last visits 3 and 2 months, respectively, before death at age 97 years) was monitored by optical coherence tomography (OCT) and angiography (OCT and dye-based). Eyes were recovered 4:05 hours after death, processed for macula-wide epoxy-resin histology, and scanned under an oil objective for high-resolution microscopy. Infrared reflectance and eye-tracked spectral-domain OCT(A) clinical imaging were correlated with ex vivo and high-resolution histologic images. Projection artifact removal based on three-dimensional vessel-shape estimation (VSE-PAR) and a Gaussian blur filter for preservation of neovascular flow signal was used.

Results: Clinical OCT(A) imaging showed several neovascular lesions within the central macula of both eyes. Two index lesions of different phenotypes in the right eye displayed a drusenoid pigment epithelium detachment (PED), characteristic of t3 MNV. Projection artifact removal based on VSE-PAR and a Gaussian blur filter demonstrated robust preservation of neovascular flow signal. OCTA decorrelation signal in lesion # 1 corresponded in histology to a vertically oriented collagen-ensheathed vascular complex originating from the intermediate capillary plexus. Lesion # 2 corresponded to a horizontally oriented vascular loop originating from the deep capillary plexus. Both lesions contacted basal laminar deposits that remained after the retinal pigment epithelium (RPE) disappeared due to death in situ or anterior migration. The sub-RPE-basal laminar space (between RPE-basal lamina and inner collagenous layer of Bruch’s membrane) underlying these vascular abnormalities contained calcific nodules and glial processes. No connection between the choriocapillaris and this space was observed for either lesion.

Conclusions: OCTA decorrelation signal of type 3 neovascularization corresponded to two intraretinal neo-vessel phenotypes on histology.
VSE-PAR and Gaussian blur filter demonstrated their value for further use in OCTA decorrelation signal processing.

CONTROL ID: 3707918

SUBMITTER (NAME ONLY): Marlene Sassmannshausen

TITLE: Hyperreflective foci (HRF) in intermediate age-related macular degeneration (iAMD): spatial abundance and impact on retinal morphology

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To analyze the topographic distribution of HRF as well as localized retinal layer thicknesses (RLT) in presence or absence of HRF in eyes with large drusen associated with iAMD.

Methods: Sixty-five eyes (59 iAMD patients, (mean age ± SD) 70.9 ± 8.6 years) with large drusen (>125 µm) and 28 control eyes (27 patients; 64.21 ± 9.04 years; unremarkable macula) underwent spectral-domain optical coherence tomography, SD-OCT (volume scan: 30°x25°, 61 B-Scans, spacing 120µm). Within each SD-OCT scan, retinal layers were semi-automatically segmented by a medical reader, HRF manually annotated (at 300% magnification), RLT at each HRF location extracted (using a custom-written ImageJ plugin) and compared to RLT in areas without HRF (HRF area mirrored horizontally at the foveal level) from the same eyes. RLT between positions were compared using the Wilcoxon test, univariate mixed linear models to investigate associations between RLT, HRF presence and HRF size.

Results: In iAMD eyes, 12.8 ± 12.7 HRF per eye were detected with a peak abundance at 0.5 to 1.5 mm eccentricity of the fovea (6.43 ± 8.16 HRF per eye). When HRF are present, outer nuclear layer (ONL) (p=0.0004, average difference -10.06 µm) and retinal pigment epithelium drusen complex (RPEDC) thicknesses (p = 0.0003, average difference +29.54 µm) differed significantly compared to areas with no HRF. In the presence of HRF, ONL thinning was significantly different (p=0.002) even while accounting for RPEDC thickening. Inner and outer photoreceptor segments (IS, OS) and the outer plexiform layer (OPL) thicknesses did not differ significantly. Mixed linear models further revealed a significant association between increasing HRF size and decreasing ONL (association score -0.19, p < 0.0001; 95%CI: -0.24, -0.13) and IS layer thicknesses (-0.09, p = 0.0072: -0.14, -0.04).

Conclusions: In iAMD migrating HRF leave a trail of remodeling that impacts multiple retinal layers. Thickening of the RPEDC with subsequent reduced oxygen and nutrient supply from the underlying choriocapillaris might trigger RPE migration, while the ONL thickness decrease at areas of HRF could result from cell displacement or degradation. Longitudinal studies on the functional impact as well as long-term retinal changes at a cellular and subcellular level are underway to further characterize the importance of HRF as a biomarker for AMD progression.

CONTROL ID: 3707920

SUBMITTER (NAME ONLY): Margarita Labkovich

TITLE: Virtual Reality Enables Rapid, Multi-Faceted Retinal Function Screenings

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Labkovich, A. Warburton, O. Okome, C. Cheng, R. Serafini, M.S. Hovstadius, J. Chelnis, Medical Education, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies approximate that nearly 900,000 individuals suffer from vision-threatening retinopathy in the United States alone. Early detection of retinal disease matters for timely interventions, however, access to vision screening continues to be a limiting factor. Advancements in virtual reality (VR) technologies allow for the digitalization of several tests used in vision screening. In the present clinical study, our group assessed the viability of VR in administering perimetry, color vision, and Amsler grid exams.

Methods: We performed a non-inferiority trial at the Mount Sinai 102nd street Ophthalmology Practice, in which patients received a 24-2 Humphrey Visual Field Analyzer (HVFA) exam, Ishihara Tile test, and an Amsler Grid along with the VR (VIVE Pro and PICO headset) analogues in a randomized fashion. The perimetry analogue is a 24-2 vision field exam with 25 Apostilibs. The Ishihara analogue consisted of a standard 9-plate screen for red-green color deficiencies. The Amsler analogue is a virtual grid to free-draw visually distorted areas. The primary outcome measure (POM) for perimetry was percent agreement of each stimulus point across all patients. The POM for Ishihara Tiles is number of correct tiles. The POM for Amsler grid is the percent agreement area of grid squares. Secondary outcomes are time to complete the test and the patient experience survey.

Results: Form 69 patients recruited, 57 patients underwent color blindness testing for VR and non-VR and demonstrated no significant difference between the two ($p = 0.9692$ in Wilcoxon rank-sum test with VR tests reporting sensitivity = 100% & specificity = 76%. 50 patients took the Amsler grid, demonstrating no significant difference for the right eye ($p = 0.3092$) sensitivity = 100% & sensitivity = 95% and for the left eye ($p = 0.6546$) and sensitivity = 100% & sensitivity = 98%. 24-2 perimetry analog had a 78% overall agreement in the left eye and 76% overall agreement in the right eye with 46 and 42 eyes respectively. The time required to complete the HVFA was significantly longer compared to the VR, $p < 0.0001$.

Conclusions: Our preliminary data suggest that VR can serve as a platform to deliver rapid vision screening exams, particularly perimetry, color blindness, and Amsler tests. The low cost of VR technologies, increased testing speeds with comparable results, user-friendliness for both operators and the patients presents a high-impact solution.

CONTROL ID: 3707921

SUBMITTER (NAME ONLY): Dror Sharon

TITLE: Identification of autosomal recessive novel genes and retinal phenotypes in members of the solute carrier (SLC) superfamily

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Sharon, T. Millo, J.A. Rivera, A. Obolensky, D. Marks-Ohana, E. Wilhelm, P. Gopalakrish, B. Rosin, M. Hanany, E. Banin, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|M. Gross, Otolaryngology-Head and Neck Surgery, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|A. Tracewska, Lukasiewicz Research Network, Siec Badawcza Lukasiewicz - PORT Polski Osrodek Rozwoju Technologii, Wroclaw, Dolnośląskie, POLAND|O. Schueler-Furman, Microbiology and Molecular Genetics, IMRIC, Hebrew University Institute for Medical Research Israel-Canada, Jerusalem, Jerusalem, IL, academic/medres, Jerusalem, Jerusalem, ISRAEL|S. Roosing, Human Genetics; Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Center for Infectious Diseases, Radboudumc Centrum voor Infectieziekten, Nijmegen, Gelderland, NL, academic/hospital, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To study clinical and genetic aspects of solute carrier (SLC) genes in inherited retinal diseases (IRDs).

Methods: Ethical approval was obtained from the Hadassah Medical Center Institutional Review Board following the tenets of the Declaration of Helsinki. Ocular evaluation included a full ophthalmological examination, Goldmann perimetry, full field electroretinography, color vision testing, and various retinal imaging. Exome sequencing (ES) data were filtered to identify pathogenic variants in SLC genes. Analysis of transcript and protein expression was performed on fibroblast cell- lines and retinal sections.

Results: Comprehensive analysis of 433 SLC genes in ~900 ES IRD samples revealed homozygous pathogenic variants in six SLC genes including two novel ones: Two variants in SLC66A1 causing autosomal recessive retinitis pigmentosa (ARRP) and a variant in SLC39A12 causing AR mild widespread retinal degeneration with marked macular involvement. In addition, a splicing variant in SLC37A3, suggested previously to cause RP, was found in two ARRP patients resulting in enhanced exon skipping and reduced protein expression. Next generation sequenving analysis revealed a complex splicing pattern in which exon 6 is skipped in the vast majority of transcripts leading to no protein expression as verified by Western blotting. The recently reported SLC4A7 - c.2007dup variant was found in two ARRP patients resulting in the absence of protein. Finally, variants in SLC24A1 were found in four individuals with either ARRP or congenital stationary night blindness (CSNB). Immunohistochemical analysis of the human and mouse retinas using antibodoes for four of the studeis SLC proteins revealed expression in the outer nuclear layer.

Conclusions: We report on SLC66A1 and SLC39A12 as novel IRD genes, establish SLC37A3 pathogenicity, and provide further evidence of SLC4A7 as IRD genes. We extend the phenotypic spectrum of SLC24A1 and suggest that its ARRP phenotype may be more common than previously reported.

CONTROL ID: 3707922

SUBMITTER (NAME ONLY): Kyoung Min Lee

TITLE: Posterior Eyeball Topography based on Three-dimensional Magnetic Resonance Imaging and Optic Nerve Head Morphology

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the three-dimensional eyeball protrusion from the best-fitted ellipsoid and its association with the offset between the Bruch's membrane opening (BMO) and lamina cribrosa (LC).

Methods: Three-dimensional magnetic resonance imaging (MRI) scans were taken from 76 subjects (152 eyes) with a diagnosis of glaucoma or glaucoma suspect. To quantify the three-dimensional shape, an ellipsoid was fitted along the posterior 2/3 contour of every eyeball by customized MATLAB codes, and the outermost protruded part (OPP) was determined from the best-fitted ellipsoid. The eyeball was classified into group A (ellipsoid type) when ellipsoid fitting left no significant protrusion, group B (focal bulging type) when a dominant protrusion could be identified: an adjacent pair of outward protrusion and reciprocal inward depression, and group C (complex type) when a singular dominant protrusion cannot be identified. In case with a dominant protrusion (group B), the angular deviation of the OPP was measured from the nasal side of the foveo-BMO axis and the superior location as a positive value. The LC/BMO offset was evaluated by measuring the central retinal vascular trunk (CRVT) location from the BMO center: 1) the angular deviation in the same manner of OPP deviation measurement, and 2) the offset index as the ratio between the CRVT-BMO center distance and the BMO radius on the same direction.

Results: After excluding 15 eyes due to poor MRI image quality, 45 eyes (33%) were classified as group A, 67 eyes (49%) as group B, and 25 eyes (18%) as group C. The average axial length was in the order of group C (26.15±2.04), group B (25.73±1.62), and group A (24.80±1.99). In group B, the angular deviation of the OPP showed a significant correlation with that of the CRVT/BMO offset ($r=-0.620$, $P<0.001$). A generalized estimating equation analysis revealed that the angular deviation of the CRVT/BMO offset was associated with age ($P=0.045$) and the angular deviation of the OPP ($P<0.001$).

Conclusions: In the eyes having a dominant protrusion, the OPP location was closely associated with the LC/BMO offset direction. This indicates that the focal asymmetry during scleral expansion might be associated with the diverse direction of the LC/BMO offset and accompanied anatomical changes in the optic nerve head canal.

CONTROL ID: 3707924

SUBMITTER (NAME ONLY): David Rosen

TITLE: Evaluation of Relationship Between Anterior and Posterior Corneal Astigmatism Using a Swept-Source OCT Biometer

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Rosen, E.V. Karakoleva, N. Devireddy, N. Cannon, S. Pantanelli, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Posterior corneal astigmatism (PCA) is an important contributor to total corneal astigmatism. Its magnitude and direction has been previously elucidated using Scheimpflug imaging. However, its relationship to anterior corneal astigmatism (ACA) and other biometric variables like axial length has not been well described. The purpose of this study is to investigate the relationship between ACA and PCA using a swept-source OCT biometer.

Methods: Biometric measurements obtained between February 2020 and May 2021 were exported from a SS-OCT device (IOLMaster 700, Carl Zeiss Meditec AG). Chart review was preformed to associate the exported data with clinical variables and determine any comorbidities at the time of scan. Inclusion criteria were male or female, age 18 or older at the time of measurement. Exclusion criteria included any significant corneal or intraocular media opacity other than cataract, abnormal corneal findings, any anterior segment pathology that could significantly impact astigmatism, history of intraocular or corneal surgery, and failed or poor quality measurements as determined by the device's internal image quality metrics.

Results: Of 385 eyes, 283 eyes from 170 patients met the criteria for inclusion in the analysis. Of all eyes, 106 eyes had with-the-rule (WTR) ACA, 57 had oblique ACA, and 120 had against-the-rule (ATR) ACA. The average ACA magnitude was 1.12±0.86, 0.67±0.50, and 0.94±0.63 D in eyes with WTR, oblique, and ATR ACA, respectively ($p = 0.0002$). The average PCA magnitude was 0.30±0.16, 0.20±0.08, and 0.16±0.08 D in eyes with WTR, oblique, and ATR ACA, respectively ($p < 0.0001$). The proportion of eyes that had the PCA steep axis oriented vertically was 96%%, 91%, and 70% in eyes with WTR, oblique, and ATR astigmatism, respectively. In eyes with WTR and oblique ACA, there was a significant positive linear correlation between the magnitude of ACA and PCA (R^2=0.58 and 0.36 respectively). There was no significant linear relationship between ACA and PCA in eyes with ATR ACA.

Conclusions: The correlation between ACA and PCA magnitude is strongest in eyes with WTR ACA, weaker in those with obliquely oriented ACA, and weakest in those with ATR ACA. Increasing the number of eyes in the analysis will allow us to further elucidate how ACA and PCA relate in vector space, change with age, and correlate with other variables like axial length.

CONTROL ID: 3707927

SUBMITTER (NAME ONLY): Antonia Howaldt

TITLE: Corneal Myofibromatosis caused by novel activating variants in PDGFRB responsive to Imatinib.

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Two benign-appearing corneal tumors were characterized by histologic, genetic and functional examinations as corneal myofibromas. Disease-causing mutations and susceptibility to targeted treatment were analyzed.

Methods: Two unrelated males, aged 18 and 13 years, born to non-consanguineous parents presented with white corneal opacifications, photophobia, glare sensitivity and reduced vision. In infancy, both patients had nodular skin lesions consistent with infantile myofibromatosis, which was confirmed by histology in Patient 1. There was no evidence of Kosaki overgrowth or Penttinen syndrome. Slit lamp biomicroscopy, anterior segment OCT and surgical tumor excision by lamellar keratectomy with Mitomycin C (MMC) were performed. Histopathologic evaluation using conventional and immunohistochemical stains followed. Genetic testing was carried out on peripheral blood after written informed consent. In Patient 1, Sanger Sequencing of the platelet-derived growth factor receptor-beta (PDGFRB) exon 12 was performed to test for a variant previously found in an affected cousin. In Patient 2, exome-based sequencing of PDGFRB and the neurogenic locus notch homolog protein 3 (NOTCH3) gene was performed. For functional analyses, the PDGFRB variants were transfected into cells, tested for expression, activation and sensitivity to the tyrosine kinase inhibitor imatinib.

Results: Histology was consistent with corneal manifestations of myofibromatosis. Immunohistochemical stainings demonstrated positivity for alpha-smooth muscle actin and b-catenin, a low proliferation rate in Ki-67 (<5%), marginal positivity in Desmin, negative staining for Caldesmon and CD34. In both patients the corneal myofibroma recurred within 4 months requiring re-lamellar keratectomy with MMC. The genetic analysis detected the novel heterozygous mutations PDGFRB c.1766A>G (p.Y589C) in Patient 1 and c.1949C>G (p.S650W) in Patient 2. When transfected in cultured cells, the PDGFRB variants conferred a constitutive activity to the receptor in the absence of its ligand and were sensitive to the tyrosine kinase inhibitor Imatinib. The variants can be classified as ACMG Class 5 (pathogenic).

Conclusions: We describe two cases of corneal myofibromatosis caused by the novel mutations PDGFRB c.1766A>G (p.Y589C) and c.1949C>G (p.S650W). Imatinib sensitivity under laboratory conditions suggests perspectives for targeted therapy preventing recurrences.

CONTROL ID: 3707928

SUBMITTER (NAME ONLY): Javier Tato

TITLE: Pseudodominant inheritance of Retinitis Pigmentosa due to mutations in the PDE6B gene: a case report

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tato, N. Izquierdo, Ponce Health Sciences University, Ponce, PUERTO RICO|L. Molina Thurin, Universidad de Puerto Rico Recinto de Rio Piedras, San Juan, San Juan, PUERTO RICO|N. Izquierdo, A. Oliver, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|

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ABSTRACT BODY:

Purpose: Mutations in the PDE6B gene are a rare cause of autosomal recessive Retinitis Pigmentosa (arRP). We report on a non-consanguinous family with pseudodominant inheritance of RP due to PDE6B mutations.

Methods: We conducted a chart review of four members of a Puerto Rican family who underwent a comprehensive ophthalmic evaluation by at least one of the authors. The mutational screening was done using a genotyping microarray provided by Invitae Corporation, using next-generation sequencing (NGS) technology. Genomic DNA obtained from saliva samples was enriched for targeted regions using a hybridization-based protocol and sequenced using Illumina technology. Descriptive analysis was done.

Results: Patient 1 had a normal ophthalmic examination and a heterozygous pathogenic variant in the PDE6B gene c.1540del PLeu514Trpfs*61. Patients 2, 3, 4 had mid-peripheral retinitis pigmentosa, concentric visual field ring scotomas OU, extinguished ERG, and homozygous pathogenic variants in the PDE6B gene c.1540del PLeu514Trpfs*61.

Conclusions: Even though mutations in the PDE6B gene usually lead to arRP, it may be inherited in a pseudodominant pattern in geographically isolated populations. Genotyping studies in patients with RP are warranted to correctly classify inheritance mode.

CONTROL ID: 3707929

SUBMITTER (NAME ONLY): Manuel Paez

TITLE: OCT inner to outer retina reflectivity ratio-independent predictor of retinal function in retinitis pigmentosa

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Paez, M. Alabek, J.A. Sahel, B. Rosin, Ophthalmology, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop objective measures of retinal function for patient selection in gene therapy of hereditary retinal dystrophies(HRDs).We hypothesize that inner to total mean retinal reflectivity is an independent measure of retinal function

Methods: We have performed a retrospective analysis of a genetically diagnosed RP patient cohort in a tertiary ophthalmological center with a dedicated HRDs service.Data analyzed included visual acuity(VA, ETDRS scale),intraocular pressure(IOP, mmHg),Optical Coherence Tomography imaging(OCT).A custom algorithm was implemented that measured the ratio of the mean reflectance of two areas of an OCT image in MATLAB.We have employed this algorithm to quantify the relative reflectance of the Retinal Nerve Fiber Layer(RNFL) to the retina.Correlation analysis was performed to estimate the interrelations between the different clinical and imaging parameters,Bonferonni corrected for multiple comparisons.All the statistical analyses were performed in MATLAB

Results: We included 115 genetically diagnosed RP patients,with USH2A presenting as the most common genetic defect(23/115,20%).A preliminary analsysis of 60/115 patients is included.Our analysis has revealed a strong positive correlation between the OCT reflectivity ratio and VA in both eyes(OD:r=0.6269,p<0.0001,OS:r=0.5295,p=0.0001.Age was negatively correlated with VA in both eyes (OD:r=-0.3178,p=0.0245,OS:r =-0.4518,p=0.001).There was a weak trend towards negative correlation between age and the OCT reflectivity ratio for both eye(OD:r =-0.2840,OS:r=0.1857).Multiple regression analysis revealed both age and the OCT reflectivity ratio as independent predictors of visual acuity(p=0.0084)

Conclusions: Preliminary results suggest the OCT reflectivity ratio between the RNFL and the retina serves as a predictor of retinal function in genetically diagnosed RP patients.The OCT reflectivity ratio value as computed here can be increased by either or a combination of higher mean reflectance of RNFL and/or lower mean reflectance of the retina.To the best of our knowledge,this is the first work correlating OCT reflectivity and visual function in RP patients.Such approaches can prove to be useful in RP and other HRDs when selecting candidates for gene therapy.Further analysis is needed to elucidate any possible correlation of the OCT reflectivity ratio and the standard analysis of retinal layers thickness by OCT

CONTROL ID: 3707930

SUBMITTER (NAME ONLY): Karissa Wang

TITLE: The association between micro-invasive glaucoma surgery and cystoid macular edema

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Wang, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|V.L. Tseng, F. Yu, A.L. Coleman, Department of Ophthalmology, Stein and Doheny Eye Institutes, David Geffen School of Medicine, Los Angeles, California, UNITED STATES|F. Yu, A.L. Coleman, Department of Epidemiology, Fielding School of Public Health, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Karissa Wang: Commercial Relationship: Code N (No Commercial Relationship) | Victoria Tseng: Commercial Relationship: Code N (No Commercial Relationship) | Fei Yu: Commercial Relationship: Code N (No Commercial Relationship) | Anne Coleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Cystoid macular edema (CME) is a known complication of cataract surgery, which may lead to decreased visual acuity. This cross-sectional study examines the potential association between micro-invasive glaucoma surgery (MIGS) and CME in glaucoma patients undergoing cataract surgery in the California (CA) Medicare population.

Methods: The 2019 CA Master Beneficiary Summary File and 2019 Standard Analytic Files of Part B Carrier Claim data files from the Centers for Medicare and Medicaid Services were used to identify beneficiaries ≥65 years old with open-angle glaucoma (OAG) and cataract surgery. The outcome of interest was CME. Patients with MIGS were defined as those with procedure codes for trabecular microbypass iStent, goniotomy/canaloplasty, XEN subconjunctival gel stent, or cyclophotocoagulation. Chi-squared tests were performed to evaluate univariable associations between MIGS and CME in the study population. Logistic regression was used to assess multivariable associations between MIGS and CME, adjusting for age, sex, race/ethnicity, Charlson comorbidity index, diabetic retinopathy, and retinal vein occlusion.

Results: In 2019, 12,755 CA Medicare beneficiaries with OAG underwent cataract surgery, of whom 6,157 (48.3%) received MIGS. The largest proportion were female (7,118, 55.8%) and White (7,221, 56.6%). Of the 6,157 patients with cataract surgery and MIGS, there were 4,013 (65.2%) with trabecular microbypass iStent, 2,158 (35.0%) with goniotomy/canaloplasty, 94 (1.5%) with XEN subconjunctival gel stent, and 476 (7.7%) with cyclophotocoagulation. CME was not statistically significantly associated with any MIGS in the total study population (odds ratio [OR]=0.92, 95% CI 0.80-1.06) or in diabetic patients (OR=0.89, 95% CI 0.71-1.11). Compared to OAG patients with cataract surgery alone, those with goniotomy/canaloplasty had increased odds of CME in the adjusted analyses (unadjusted OR=1.15, 95% CI 0.96-1.39, adjusted OR=1.25, 95% CI 1.03-1.51), while those with trabecular microbypass iStent had lower odds of CME in unadjusted but not adjusted analyses (unadjusted OR=0.80, 95% CI 0.68-0.95, adjusted OR=0.86, 95% CI 0.72-1.02).

Conclusions: Amongst 2019 CA Medicare beneficiaries with OAG receiving cataract surgery, use of MIGS overall was not associated with increased risk of CME. However, goniotomy/canaloplasty may be associated with increased likelihood of CME, which requires further evaluation.

CONTROL ID: 3707934

SUBMITTER (NAME ONLY): Jay Maturi

TITLE: Race and Insurance based differences in the outcome of anti-vascular endothelial growth factor treatment of diabetic retinopathy - an analysis of 43,274 patient eyes using the IRIS® Registry (Intelligent Research in Sight)

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rates of diabetic retinopathy (DR) and diabetic macular edema (DME) are increasing worldwide, with Black and Hispanic patients displaying worse baseline VA at clinical presentation than White patients (Maholtra, 2021). This study used real-world data to quantify disparities in visual acuity (VA) outcomes at one and two years after initiation of DR/DME treatment in patients based on race/ethnicity (Black, Hispanic, and White) as well as on insurance status (Medicare, Medicaid, or Private).

Methods: We examined the IRIS registry, which includes de-identified data on over 70 million unique patients, including subjects that met strict criteria for presence of a full data-set of information (VA over two years, insurance status, race, treatment provided) and excluding subjects with other comorbidities that might necessitate treatment with anti-VEGF agents. The modified DRSS severity scale was used to classify DR and DME.

Results: With 43,273 eyes, mean VA at baseline were 67.3, 66.3, and 65.2 in White, Black, and Hispanic patients, respectively. After one year, White patients saw a 1.7 letter improvement, relative to a 1.3 and 1.1 letter improvement in Black and Hispanic patients, respectively. Differences persisted after controlling for insurance. A significantly lower proportion of White patients demonstrated 15-letter loss in VA after 1 year than both Hispanic and Black patients and a significantly lower proportion of 15-letter loss in VA after 2 years than Black patients.

Mean modified-DRSS scores at baseline were 56.0, 57.3, 60.7 in White, Black and Hispanic patients. Hispanic patients had a higher proportion of treatment with bevacizumab than White and Black patients across all disease severities, while White patients had a higher proportion of treatment with aflibercept than Black and Hispanic patients across most disease severities.

Conclusions: Race and insurance-based differences in one and two year outcomes following anti-VEGF treatment for DR and differential administration of anti-VEGF therapies by both race and insurance necessitate ongoing examination to ensure earlier and more effective treatment of DR patients nationally.

CONTROL ID: 3707937

SUBMITTER (NAME ONLY): Yasser Althnayan

TITLE: Myopia Progression Among School-Aged Children in the Coronavirus (COVID-19) Distance Learning Era

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.I. Althnayan, Ophthalmology, King Faisal Specialist Hospital and Research Center, Riyadh, Riyadh, SAUDI ARABIA|H.B. Alamer, H.B. AlQahtani, S. Alfreihi, Pediatric Ophthalmology, Ministry of National Guard Health Affairs, Riyadh, Riyadh, SAUDI ARABIA|N.M. Almotairy, M.M. Alharbi, Ophthalmology, King Saud University, Riyadh, Riyadh Province, SAUDI ARABIA|

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ABSTRACT BODY:

Purpose: To investigate the effect of online learning and other environmental factors on myopia progression during the COVID-19 pandemic.

Methods: A retrospective, cohort study on children aged from 6 to 14 years with myopia. Data were gathered from 3 visits; pre-COVID 19, at the beginning of the pandemic, and during the pandemic. Patients' demographics (number of hours spent on screens for educational and recreational purposes, type of screen used, and number of hours spent outdoors), best corrected visual acuity (BCVA), uncorrected visual acuity (UCVA), and cycloplegic refraction to quantify spherical equivalent (SE) were measured for all participants. Progression of myopia was calculated based on difference between the three visits.

Results: One hundred and fifty patients met our inclusion criteria. Mean age was 11±2.4 years. There were 70 males (47%). They mainly used mobile phones (62%) and had insufficient outdoor play (88%). Out of 300 eyes, 221 (74%) had progression in myopia. A significant difference was found in SE between pre-COVID-19 (-0.29 ±0.23) and post-COVID-19 (-0.40 ±0.11) with a p-value of 0.023. Additionally, UCVA showed difference between the initial Vs. 1st follow-up visit (0.57±0.37 vs 0.64±0.36, p-value =0.001), and first follow-up visit Vs. 2nd follow-up visit (0.64±0.36 vs 0.70±0.36, p-value =0.001). Survival analysis showed significant hazard ratio on change in SE for high age group (>9 years), (HR [95% CI], 0.71 [0.51 – 0.84]), recreational screen usage (HR [95% CI], 1.26 [1.15 – 1.66]) and insufficient outdoor time (HR [95% CI], 1.45 [1.35 – 1.67]).

Conclusions: Myopia progression was accelerated compared to pre-COVID-19 times in terms of spherical equivalent. Younger age group, prolonged screen users and insufficient outdoor time contributed to the further increase in myopia. However, the type of device had no effect statistically on the progression of myopia.

CONTROL ID: 3707939

SUBMITTER (NAME ONLY): Christina Kiel

TITLE: Global methylation status of induced pluripotent stem cells, their origins and final differentiations

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kiel, P. Berber, K. Plössl, B.H. Weber, Institute of Human Genetics, Universitat Regensburg, Regensburg, Bayern, GERMANY|B.H. Weber, Institute of Clinical Human Genetics, Universitatsklinikum Regensburg, Regensburg, Bayern, GERMANY|T. Langmann, Laboratory for Experimental Immunology of the Eye, Department of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|T. Langmann, University of Cologne Center for Molecular Medicine Cologne, Cologne, Nordrhein-Westfalen, GERMANY|A. Wolf, Department of Ophthalmology, Universitatsklinikum Ulm, Ulm, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Epigenetic modifications such as DNA methylation are a crucial part of the regulatory repertoire to tailor cell type-specific gene expression. Still, little is known about methylation profiles of induced pluripotent stem cells (iPSCs) and derived cell differentiations. The aim of this project is to assess global methylation in cells of various origin and developmental stages, including primary tissues such as human retina, fibroblasts or peripheral blood mononuclear cells (PBMCs), iPSCs, and iPSC-derived cell lines including retinal pigment epithelium (RPE), endothelial cells (ECs) and 3D retinal organoids (ROs).

Methods: Methylation data were obtained applying the Infinium MethylationEPIC BeadChip (Illumina), which addresses 850k defined methylation sites. After stringent quality control, 127 samples were included in our analysis (retinae N = 12, fibroblast cells N = 4, PBMCs N = 2, iPSCs N = 25 from 22 donors, ECs N = 8, RPE N = 50 from 19 donors, ROs N = 26 from 3 donors). Quantile normalization was performed and clustering of samples was analyzed by principle component analysis. Differences in the methylation status of CpG sites were investigated by a linear regression model adjusting for the donor. Enrichment analysis was performed by gene ontology testing and correction for multiple testing was performed by false discovery rate (FDR < 0.001).

Results: Data showed methylation profiles specific for each cell type/tissue with the highest similarity between ROs and human retinae (24,259 differentially methylated positions, DMPs). Cell type-specific DMPs ranged between 2,762 (ROs) and 47,926 (fibroblast cells). Considering various stages of maturation of iPSC-derived RPE cells and ROs revealed 118,642 and 21,074 DMPs, respectively. Enrichment analysis attributes these changes to developmental processes and structural morphogenesis, as well as cell type-specific pathways for RPEs (cell junction) and ROs (neurogenesis).

Conclusions: Distinct methylation profiles were observed for each primary tissue and cultivated cell line. In the course of maturation of iPSC-derived cell lines general developmental processes are involved besides cell type-specific biological pathways. Of note, iPSC-derived ROs show a strong similarity to human retinae, even more than to their originating iPSC lines, supporting their value as research models for hereditary and complex retinal diseases.

CONTROL ID: 3707941

SUBMITTER (NAME ONLY): Vishal Jhanji

TITLE: Comparative stromal cell therapy for corneal scarring with corneal stromal stem cells versus keratocytes

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Jhanji, M. Santra, G. Yam, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Preclinical studies have shown success using cultivated human corneal stromal keratocytes (CSK) and their progenitors (corneal stromal stem cells [CSSC]) to prevent corneal scarring and regenerate transparent corneal stroma. However, there is no study comparing the treatment efficacy of CSK versus CSSC. This work investigated if both cell types have comparable corneal regenerative effects in a mouse corneal injury model.

Methods: Human CSSC and CSK were isolated from same donor corneas (n=3) and cultured following reported protocols. Cell phenotypes were characterized by marker expression, doubling time and collagen deposition. In a mouse model of anterior stromal injury created by Algerbrush burring, CSSC were topically applied in fibrin gel immediately after injury whereas CSK were intrastromally injected after epithelial healing. Corneas were examined weekly with anterior segment optical coherent tomography and harvested at 14 days post-treatment for scar analysis, fibrosis gene expression (Col3a1, aSMA, fibronectin [FN], and tenascin C [TNC])by qPCR and immunostaining.

Results: Cultivated human CSSC were proliferative and expressed stem cell markers (Pax6, ABCG2, nestin and CXCR4), and lumican but negative for keratocan and ALDH3A1. Growth-arrested CSK became quiescence and expressed ALDH3A1, keratocan, and lumican. Using ELISA, CSSC produced significantly less pro-collagen I than quiescent CSK, and both had minimal collagen III expression when compared to stromal fibroblasts. When applied on mouse corneal wounds, both cell types reduced corneal scarring in a dosage-dependent manner and downregulated inflammatory (iNOS, MCP1) and fibrosis markers (Col3a1, aSMA, FN, and TNC), when compared to wound controls. Comparing between CSSC and CSK, fibrosis gene expression was generally lower in CSK group than those treated with CSSC, particularly significant for MCP1, FN and TNC ($P<0.05$, Mann-Whitney U test). The lowest effective dosage for CSSC was $50x10^3$ cells and CSK was $20x10^3$ cells on mouse corneas.

Conclusions: Treatments with CSSC and CSK were effective to reduce corneal fibrosis and scarring. CSK injection showed a greater scar inhibition than topical CSSC. This could be due to a better retention of functional CSK inside stroma whereas CSSC could be partly removed by blinking. In addtion, batch-to-batch variability and differentiation of CSSC could affect the treatment outcomes.

CONTROL ID: 3707942

SUBMITTER (NAME ONLY): Carolyn Drews-Botsch

TITLE: Prevalence of Obesity in Adolescents with Amblyopia

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Drews-Botsch, K. Machicado, A. Weinstein, Global and Community Health, George Mason University, Fairfax, Virginia, UNITED STATES|S.R. Lambert, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Children with amblyopia, and the resultant loss of stereopsis, may have fine and gross motor deficits which have been associated with a higher risk of obesity. However, the risk of obesity in individuals with amblyopia is unknown.

Methods: These analyses use data from the 1999–2008 National Health and Nutrition Examination Survey (NHANES). We focus on the 8295 children between the ages of 12 and 18 who participated in the visual examination component of NHANES and had a best corrected visual acuity in the better eye of at least 20/40. Amblyopia was defined as at least a two-line intraocular difference in acuity. Obesity was defined as a body mass index (BMI) or a body fat percentage (BFP) greater or equal to the 95^{th} percentile for age and gender. BFP was measured using a dual-energy X-ray absorptiometry (DEXA). Cardiovascular fitness level (CFL) was assessed using a submaximal exercise test. We calculated Mantel-Haenszel odds ratios to examine the relative prevalence odds of obesity in children with and without amblyopia.

Results: The prevalence of amblyopia was 4.3%. Children with amblyopia had a higher prevalence of high BMI than those without (30.3% versus 21.4%; OR =1.56; 95% CI 1.24-1.98). Children with amblyopia were also somewhat more likely to have a high BFP (15.3% versus 13.2%; OR = 1.15 95% CI 0.77,1.70) and have low CFL (OR = 1.15; 95% CI 0.83,1.57) but these measures were available for only about half of the population.

Conclusions: Our findings suggest that adolescents with amblyopia may be more likely to be obese and sedentary. Given the range of morbidities associated with childhood obesity, targeted interventions promoting physical activity among children with amblyopia could be a viable option for preventing and addressing weight-related health issues.

CONTROL ID: 3707943

SUBMITTER (NAME ONLY): Samuel Lee

TITLE: Associations between Statin Use and Glaucoma in the National Health and Nutrition Examination Survey

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lee, K. Kitayama, V. Tseng, D. Pan, F. Yu, A.L. Coleman, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine associations between statin use and glaucoma in the National Health and Nutrition Examination Survey (NHANES) population.

Methods: The study population included adult participants of the 2005-2008 NHANES. Statin use was analyzed as a binary variable, with participants classified as either taking or not taking statins at the time of the survey. Glaucoma was defined according to the Wilmer criteria, where a positive glaucoma diagnosis was marked by the “definite” presence of glaucoma in at least one eye according to disc photos graded by ophthalmologists. Covariates included age, sex, ethnicity, level of education, income, body mass index, smoking status, alcohol intake, steroid intake, and history of diabetes mellitus, cataract extraction, macular degeneration, and myocardial infarction. Logistic regression modeling was used to examine the associations between statin use and glaucoma in the study population. Models were unadjusted, partially adjusted for age, sex, and ethnicity, and fully adjusted for all study covariates. Analyses were weighted using NHANES multistage sampling design.

Results: The study population included 5489 participants, representing a weighted US population of 111,882,981, of whom 620,169 (0.6%) had glaucoma. In the unadjusted model, statin use showed a statistically significant association with increased odds of glaucoma (unadjusted odds ratio [OR] = 2.60, 95% confidence interval [CI] = 1.52, 4.45), but this was no longer statistically significant in the partially (partially adjusted OR = 1.23, 95% CI= 0.67, 2.26) and fully adjusted (fully adjusted OR = 1.01, 95% CI = 0.40, 2.53) models.

Conclusions: In the 2005-2008 NHANES population, statin use was associated with an increased odds of glaucoma in unadjusted but not in adjusted models. Further investigation is needed into potential associations between hyperlipidemia, its treatment, and risk of glaucoma in the general population.

CONTROL ID: 3707948

SUBMITTER (NAME ONLY): Hisham Hamze

TITLE: Phacoemulsification cataract surgery with and without iStent in primary angle closure glaucoma - a retrospective comparative study

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Hamze, H. Selvan, A. Saravanan, P. Pandey, I. Masood, V. Sung, Birmingham and Midland Eye Centre, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Phacoemulsification cataract surgery (PCS) is an important surgical treatment for primary angle closure glaucoma (PACG). Since the introduction of iStent, PCS combined with iStent has been advocated in previous studies, however, there is a paucity of comparative data in this area. We conducted a retrospective observational clinical study to evaluate the efficacy, safety and complication rates of PCS only versus combined PCS with iStent in PACG.

Methods: This retrospective study compared the outcomes of 44 patients who underwent combined PCS and iStent with 45 patients who underwent PCS only. Only patients with a diagnoses of PACG were enrolled. The primary success endpoint was defined as intraocular pressure (IOP)<21 mmHg and ≥20% reduction in IOP at 1 year regardless of the number of glaucoma medications (NGM). Secondary endpoints included IOP, NGM, visual acuity (VA) and complications. All patients had at least 1 year of follow-up.

Results: The mean age, pre-operative IOP and NGM in the PCS-iStent and PCS-only groups were 71.2 ± 13 years and 65.3 ± 13.2 years (P>0.05), 21.1 ± 9.3 mmHg and 17.8 ± 7.1 mmHg (P>0.05), and 3.2 ± 1.2 and 2.2 ± 1.7(P<0.01), respectively. In both groups, there was a significant increase in VA and reduction in the IOP and NGM observed post-surgery (P<0.05). At one year, there was no significant difference in IOP and NGM reduction between both groups (P=0.48, P=0.17), 22.3% (5.7 ± 6.4 mmHg) reduction in IOP and 1.7 ± 1.5 reduction in NGM in the PCS-iStent group compared to 20.7% (5 ± 6.9 mmHg) reduction in IOP and 1.3± 1.7 reduction in NGM in the PCS-only group. Four patients (9%) in the PCS-iStent group required further glaucoma surgery to reduce the IOP compared to none in the PCS-only group. At 1 year, 50% in the PCS-iStent group met the success criteria compared to 51.3% in the PCS-only group.

Conclusions: iStent provides no additional IOP reduction when combined with cataract surgery in PACG. There was no increase in complication rate and no significant difference in NGM reduction. Therefore, there is no additional benefits in the use of iStent at the time of PCS for patients with PACG.

CONTROL ID: 3707949

SUBMITTER (NAME ONLY): Maria Georgiou

TITLE: Activation of autophagy reverses progressive and deleterious protein aggregation in PRPF31 patient induced pluripotent stem cells (iPSCs)-derived retinal pigment epithelium (RPE) cells.

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Georgiou, C. Yang, R. Atkinson, A. Buskin, M. Moya Molina, J. Collin, L. Armstrong, V. Korolchuk, M. Lako, Biosciences Institute, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|K. Pan, S. Ludwig, H. Urlaub, S. Mozaffari-Jovin, Max-Planck Institute of Biophysical Chemistry, Göttingen, Germany, Göttingen,, GERMANY|S. Nagaraja-Grellscheid, University of Bergen, Norway, Department of Biological Sciences, NORWAY|C. Johnson, Leeds Institute of Molecular Medicine, University of Leeds, UK, UNITED KINGDOM|R. Ali, King's College, London, UK, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mutations in pre-mRNA processing factor 31 (PRPF31) result in autosomal-dominant retinitis pigmentosa (adRP) known as RP11, characterised by global dysregulation of spliceosome in retinal cells and the adjacent RPE cells. This study aims to investigate the disease pathomechanisms in Retinitis Pigmentosa caused by mutations in the PRPF31 gene.

Methods: Human iPSCs from three patients with severe and very severe PRPF31-adRP, unaffected individuals and a CRISPR/Cas9-corrected isogenic control were used to generate RPE monolayers. To fully assess the impacts of PRPF31 mutations, quantitative proteomics analyses of control and RP11-RPE cells and biochemical assays were performed.

Results: Quantitative proteomic analysis of control and patient RPE cells showed RNA splicing, retinoid metabolism and visual perception, and protein folding (UPR) pathways to be affected in RP11-RPE cells. The patient-derived RPE cells were characterised by reduced amounts of tri-snRNPs, spliceosome activity, and the presence of insoluble aggregates containing the mutant PRPF31 and misfolded, ubiquitin conjugated proteins, which accumulated progressively with time. The waste disposal mechanisms via autophagy and proteasome-mediated degradation were impaired, further exacerbating aggregate formation, which was closely linked with activation of cell death. Targeting the waste disposal mechanisms by activating the autophagy pathway using rapamycin resulted in the reduction of these cytoplasmic aggregates in RP11-RPE cells and improved cell survival.

Conclusions: Together these data indicate a vicious circle initiated by mutations in PRPF31, which lead to spliceosome dysregulation and accumulation of misfolded proteins in the form of insoluble cytoplasmic aggregates that affect RPE cell viability. Relieving the RPE cells from accumulation of these insoluble cytoplasmic aggregates presents a novel therapeutic strategy for RP11-patients.

CONTROL ID: 3707950

SUBMITTER (NAME ONLY): Maximilian Pfau

TITLE: Prospective, Longitudinal, Multifaceted Evaluation of Visual Function Loss in Stargardt Disease

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pfau, L. Huryn, M.P. Boyle, C.A. Cukras, W.M. Zein, R.B. Hufnagel, B.P. Brooks, B. Jeffrey, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify the long-term progression of macular and retina-wide photoreceptor degeneration in Stargardt disease (STGD1) using an array of performance outcome (PerfO) assessments and to assess their responsiveness.

Methods: In a prospective, natural-history study (NCT01736293), patients with a Stargardt disease (STGD1) phenotype and at least one pathogenic ABCA4-mutation underwent extensive visual function testing, including best-corrected visual acuity (BCVA), ISCEV ganzfeld electroretinography (ERG), mesopic microperimetry (MP, OD only, 10-2 grid), and the low-vision Cambridge Color Test (lvCCT) for five years (baseline, month 6, then annually). MP data were summarized in terms of the perilesional sensitivity of responding points (PLS, distance of 2 deg from scotomatous points) and mean responding points sensitivity (RPS). Responsiveness was analyzed using mixed models with the PerfO as the dependent variable, follow-up time as the independent variable, and eyes nested in patients as a random-effects term. To compare responsiveness across different parameters, we computed the effect sizes (i.e., estimates from standardized [std.] data) and the Eta-squared (η^2) defined as the ratio of variability-explained-by-time to overall-variability.

Results: A total of 134 eyes from 67 patients with a median [IQR] follow-up of 4.5 years [3.1, 4.1] were included. There was a statistically significant loss of function across all PerfOs ($P<0.05$) with exception of the light-adapted cone a-wave latency and lvCCT achromatic area.

Among the MP derived PerfOs (available for N=46 patients), the mean PLS was most sensitive to change over time (estimate [95% CI]: -1.24 dB/y [-1.56, -0.91], std. effect of -0.54 [-0.67, -0.4], η2=0.62). Among the full-field ERG parameters (N=67 patients) the scotopic 3.0 cd*s/m^2 b-wave amplitude (-0.02 log10(μV)/y [-0.03, -0.02], std. eff. -0.22 [-0.3, -0.15], η2=0.36) was most responsive. BCVA (0.01 LogMAR/y [0.01, 0.02], std. eff. 0.06 [0.03, 0.09], η2=0.25) showed only minor change over time.

Conclusions: The ability-to-detect-change was best for MP-derived PerfOs. However, MP data could not be acquired for all patients. Full-field ERG did reveal significant changes over time, but the standardized effect sizes indicate that these are suboptimal as a clinical trial endpoint. In STGD1, responsive measures of function enabling inclusive trial designs still constitute an unmet need.

CONTROL ID: 3707953

SUBMITTER (NAME ONLY): Daniel Vail

TITLE: Ophthalmic evaluations among patients receiving systemic therapies associated with uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Vail, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|A. Al Moujahed, Q.D. Nguyen, Ophthalmology, Stanford Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Daniel Vail: Commercial Relationship: Code N (No Commercial Relationship) | Ahmad Al Moujahed: Commercial Relationship: Code N (No Commercial Relationship) | Quan Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent studies have raised concerns that several classes of systemic medications may increase patients' risk of developing uveitis. Currently, there are no guidelines for ophthalmic screening when initiating therapy. We examine current practice patterns for ophthalmic screening among patients who receive systemic medications associated with increased risk of uveitis.

Methods: We use insurance claims to identify patients with exposure to checkpoint inhibitors, MEK or BRAF inhibitors, TNF- inhibitors, bisphosphonates, cidofovir, and rifabutin. We calculate the percentage of patients who receive baseline visual testing prior to receiving therapy, and the percentage that receive periodic exams after initiating therapy. We calculate the incidence of new diagnoses of uveitis, blurry vision, and exudative retinal detachments in patients after starting therapy. We compare these results to patients receiving hydroxychloroquine, a medication for which ophthalmic screening guidelines have been established for many years.

Results: Of 383,851 patients who met inclusion criteria, 532 developed a new diagnosis of uveitis within 365 days of initiating therapy (0.16%). Approximately 1.4% of patients (N=4,429) developed a new diagnosis of blurry vision within 365 days of initiating therapy. One third of patients (N=108,411, 33%) received an eye exam in the 365 days preceding their first dose; 23,980 (6.2%) had an eye exam within the 30 days preceding the initiation of therapy. One third (N=122,717, 37%) of patients had an eye exam within 365 days after their first dose of medication. One fifth of patients (N=71,909, 21.9%) had both a baseline exam during the 365 days preceding their first dose of medication and a follow-up exam within the 365 days following their first dose.

Conclusions: Patients on medications that may cause uveitis receive irregular and infrequent ophthalmic evaluations. We found no evidence that patients on any of the drugs included in this analysis are routinely being referred for ophthalmic evaluation in the pre-treatment or the immediate post-treatment window. Future recommendations for the ophthalmic management of patients on these medications must account for both the risk that the medications pose to patients' vision as well as the current practice patterns for ophthalmic care that these patients receive.

CONTROL ID: 3707955

SUBMITTER (NAME ONLY): Tatyana Appelbaum

TITLE: Detection and characterization of circular RNAs hosted by RPGR exon ORF15.

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Appelbaum, L. Murgiano, G.D. Aguirre, W.A. Beltran, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in RPGR exon ORF15 cause X-linked retinitis pigmentosa characterized by severe visual impairment early in life. The underlying disease mechanism and variability in the disease severity remains to be fully elucidated. The present study examines structural features of the ORF15 exonic region to provide new insights into the disease pathogenesis.

Methods: RNA samples from canine and human retinas and cultured cells (canine fibroblasts and human cell lines Y79 and ARPE19) were used to examine RPGR transcript heterogeneity, the presence of internal introns (exitrons) in ORF15 exonic region and RPGR circular RNAs (circRNAs). Treatment with RNase R was performed for circRNAs enrichment and validation of circularization. Polysomes from a crude cell homogenate were obtained by ultracentrifugation, using a sucrose cushion.

Results: We found a subset of novel RPGR ORF15-like transcripts in canine and human retina and in cultured cells. Annotation of these transcripts showed that portions of the ORF15 sequence were removed in a variable manner through utilization of noncanonical splicing sites. Notably, the presence of the $RPGR^{orf15}$ transcript was detected only in the retina. Furthermore, using outward-facing primers designed inside exitrons in ORF15 exonic region we discovered a previously unidentified RPGR circRNAs formed via back-splicing events. The RPGR circRNAs were found in all studied cells and tissues and were present in total RNA pool, in cytoplasmic and polysomal RNA fractions.

Conclusions: The obtained data on novel RPGR circRNAs further underline the complexity of RPGR gene organization and provide potential molecular basis of disease phenotypic heterogeneity.

CONTROL ID: 3707957

SUBMITTER (NAME ONLY): Eirini Chatziralli

TITLE: Optical coherence angiography changes in macular area in patients with proliferative diabetic retinopathy treated with panretinal photocoagulation

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Chatziralli, E. Dimitriou, A. Chatzirallis, D. Kazantzis, P. Kapsis, G. Theodossiadis, P. Theodossiadis, 2nd Department of Ophthalmology, Ethniko kai Kapodistriako Panepistemio Athenon, Athens, Attica, GREECE|

Commercial Relationships Disclosure: Eirini Chatziralli: Commercial Relationship(s);Code F (Financial Support):Thea Laboratories;Code C (Consultant/Contractor):Bayer;Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Allergan/AbbVie | Eleni Dimitriou: Commercial Relationship: Code N (No Commercial Relationship) | Alexandros Chatzirallis: Commercial Relationship: Code N (No Commercial Relationship) | Dimitrios Kazantzis: Commercial Relationship: Code N (No Commercial Relationship) | Petros Kapsis: Commercial Relationship: Code N (No Commercial Relationship) | George Theodossiadis: Commercial Relationship: Code N (No Commercial Relationship) | Panagiotis Theodossiadis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Controversy exists regarding the impact of panretinal photocoagulation (PRP) in retinal perfusion in patients with proliferative diabetic retinopathy (PDR). The purpose of this prospective study was to evaluate the changes of foveal avascular zone (FAZ) area and vessel density (VD) in superficial (SCP) and deep capillary plexus (DCP) in association with functional changes in patients with PDR treated with PRP.

Methods: Participants in this study were 21 patients with PDR and no macular edema, who were eligible for PRP. All participants underwent best-corrected visual acuity (BCVA) measurement, optical coherence tomography (OCT) and OCT angiography (OCTA) at baseline (before treatment) and at months 1, 6 and 12 after completion of PRP treatment. Comparison of OCTA parameters and BCVA between baseline and months 1, 6 and 12 after PRP was performed. Correlation of OCTA parameters and BCVA was also done.

Results: 25 eyes of 21 patients with PDR were included in the study. There was a statistically significant decrease in FAZ area at months 6 and 12 of the follow-up period compared to baseline ($p<0.001$ in both comparisons), while no difference was noted at month 1 of the follow-up period ($p>0.05$). Of note, FAZ became significantly more circular 6 months after PRP ($p=0.019$). There was no statistically significant difference in VD in both SCP and DCP at month 1 and 6 of the follow-up period ($p>0.05$ in both comparisons), while VD was significantly higher at month 12 compared to baseline ($p<0.001$). The FAZ area was associated with BCVA during the whole follow-up period ($p<0.001$, $p=0.014$, $p<0.001$ and $p<0.001$ for baseline and months 1, 6 and 12 respectively).

Conclusions: At month 12 after PRP, VD significantly increased compared to baseline, while the FAZ area became significantly circular and decreased significantly, suggesting that re-distribution of blood flow may occur in hypo-perfused foveal capillary plexus after PRP in patients with PDR.

CONTROL ID: 3707959

SUBMITTER (NAME ONLY): Sarah Weber

TITLE: Vitreous Biopsy Device and Potential Change in Practice Patterns in Patients with Infectious and Non-Infectious Uveitis

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Weber, J. Sundstrom, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|S. Weber, T.W. Gardner, J. Sundstrom, Kellogg Eye Center, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|T. Marten, J. Plott, Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|L.V. Ojeda, Mechanical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|D.F. Harris, Insight and Measurement LLC, Raleigh-Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Posterior uveitis, both infectious and non-infectious, is a potentially vision-threatening condition caused by systemic inflammatory states. This survey was conducted to 1) better understand the current practice patterns in this patient population and 2) evaluate the interest and likelihood of use of a novel vitreous biopsy device (VBD) for use in an office-based setting. The VBD is designed to safely aspirate 0.25 - 0.4mL of vitreous within 30 seconds in an office-based setting.

Methods: A questionnaire was designed to survey retina and uveitis specialists who treat endophthalmitis and posterior uveitis and gather information on their diagnostic and treatment protocols. The questionnaire consisted of a 12-minute internet survey with 24 questions. The questionnaire focused on practice patterns relating to acquisition of ocular fluid, diagnostic tests used, culture outcomes, and potential interest in using a novel VBD.

Results: We received 77 completed surveys from 34 retinal specialists, 16 uveitis specialists, and 27 retinal and uveitis specialists. On average, each specialist saw 174 patients annually with suspected endophthalmitis or uveitis. Currently, vitreous samples are acquired 32% of the time with a needle and syringe in the office and 15% of the time in the OR. With availability of the VBD, physicians stated they would use the VBD in 30% of endophthalmitis/uveitis cases, they would acquire vitreous more often (5% increase), and for obtaining vitreous samples they would decrease the use of needle and syringe in the office by 39% and frequency of going to the OR by 57%.

Overall, the participants appreciated the ease of use of the VBD, that the device fits within current clinical workflow, the sterile single-use package, and increased efficacy of acquiring vitreous. Concerns raised by the participants included verification of safety, cost, and reimbursement.

Conclusions: Overall, access to a novel vitreous biopsy device (VBD) for use in an office-based setting will improve clinical efficiency and reduce cost by facilitating acquisition of vitreous in an office-based setting. In conclusion, VBD may lead to more rapid and definitive diagnosis as well as improved visual outcomes in patients with uveitis.

CONTROL ID: 3707960

SUBMITTER (NAME ONLY): Leah O'Neill

TITLE: The expression of NFkB pathway components upregulates in lens epithelial cells post injury

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. O'Neill, A. Faranda, S.G. Novo, Y. Wang, M.K. Duncan, Biological Sciences, University of Delaware College of Arts and Sciences, Newark, Delaware, UNITED STATES|

Commercial Relationships Disclosure: Leah O'Neill: Commercial Relationship: Code N (No Commercial Relationship) | Adam Faranda: Commercial Relationship: Code N (No Commercial Relationship) | Samuel Novo: Commercial Relationship: Code N (No Commercial Relationship) | Yan Wang: Commercial Relationship: Code N (No Commercial Relationship) | Melinda Duncan: Commercial Relationship(s);Code P (Patent):US Patent application 62/944,151

ABSTRACT BODY:

Purpose: While surgical treatment of cataract is highly effective, it also results in ocular inflammation which has the potential to exacerbate other ocular diseases while also contributing to posterior capsular opacification (PCO). Though the pathogenesis of post surgical inflammation is unclear, we discovered that the lens epithelial cells (LECs) remaining behind post cataract surgery (PCS) rapidly upregulate inflammatory cytokine expression. While the mechanisms underlying this upregulation are unknown, NFkB signaling pathways regulate cytokine expression in other systems. Further, Alexander et al. 2003 showed that the lens rapidly elicited NFkB signaling when treated with known inducer, lipopolysaccharide (LPS). The objective of this study is to investigate the dynamics of NFkB pathway activation post lens injury and to elucidate its potential role in inflammation and PCO.

Methods: The Lens Injury Response Time Course (LIRTS), a database of mouse LEC transcriptome profiles generated from multiple time points post lens fiber cell removal, was used to reveal expression dynamics of NFkB signaling components in naive and injured mouse lenses. NFkB signaling was studied by subjecting a dual GFP-luciferase NFkB reporter mouse [FVB.Cg-Tg(HIV-EGFP, luc)8Tsb/J] to lens fiber cell removal surgery.

Results: LIRTS analyses revealed that several components of the NFkB signaling pathway, RelA, RelB, NFkBia, and Map3k8 upregulate their mRNA levels in LECs at 6 hours post injury, trend down at 24 hours and reach baseline by post 5 days. In contrast, the NFkB target gene, Il1b, first upregulates at 24 hours PCS. Little to no NFkB reporter activity was observed in naive adult mouse lenses; however, LECs remaining behind following fiber cell removal exhibited significant reporter gene activity at 6, 24 and 48 hours PCS, with maximal activity at 48 hours PCS which trended down by 72 hours.

Conclusions: The observation that components of the NFkB signaling pathway are expressed at the mRNA level in naive LECs is consistent with prior reports finding that the lens is responsive to LPS induction of the NFkB pathway. The further upregulation of the mRNA levels of NFkB pathway components PCS and the induction of NFkB reporter activity PCS suggests that this pathway may play important roles in post surgical inflammation and PCO pathogenesis. Future work will test the function of the NFkB pathway in the lens injury response.

CONTROL ID: 3707963

SUBMITTER (NAME ONLY): Jia Xu

TITLE: The impact of race on surgical outcomes for rhegmatogenous retinal detachments

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Xu, S. Davoudi, S. Ness, M.L. Subramanian, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|J. Yoon, S. Ness, M.L. Subramanian, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Jia Xu: Commercial Relationship: Code N (No Commercial Relationship) | Jamie Yoon: Commercial Relationship: Code N (No Commercial Relationship) | Samaneh Davoudi: Commercial Relationship: Code N (No Commercial Relationship) | Steven Ness: Commercial Relationship: Code N (No Commercial Relationship) | Manju Subramanian: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine whether race is an independent risk factor for successful surgical repair of rhegmatogenous retinal detachments (RRDs).

Methods: A retrospective cohort study was conducted for patients who underwent surgical repair of RRDs at Boston Medical Center between October 2013 to September 2021. Surgical repairs included any combination of the following: laser retinopexy, pneumatic retinopexy, cryotherapy, scleral buckle, and pars plana vitrectomy. Patients were excluded if they had previous RRD repair. Main outcome was the single surgery success rate for primary RRD repair, defined as anatomical reattachment without the presence of tamponade agents, between black and non-black patients. Secondary outcomes include whether preoperative anatomical or socioeconomic factors differ between black patients and non-black patients.

Results: A total of 231 patients were identified. Patients were characterized as black (n=85) and non-black (n=146) based on self-reported race. Black race was not associated with worse single surgery success after primary RRD repair (p=0.437) compared to non-black race, and overall had the same final surgery success rate after re-operation (p=0.749). Both groups had similar mean age, distribution amongst sexes, and mean household income. Black patients had no difference in their preoperative visual acuity, intraocular pressure, history of myopia, history of prior cataract surgery, and history of trauma as non-black patients. There was no difference in the location of retinal breaks, number of breaks, number of quadrants detached, the rate of macula-off detachments, nor the presence of proliferative vitreoretinopathy, posterior vitreous detachments, vitreous hemorrhage, choroidal detachments, retinoschisis, or lattice degeneration.

Conclusions: Black race was not associated with primary surgical failure after rhegmatogenous retinal detachment repair. Black patients had similar preoperative baseline characteristics as non-black patients. In contrast to prior studies, our study showed that black race is not an independent risk factor for poor surgical outcomes of RRD repairs if baseline demographic and socioeconomic factors are similar.

CONTROL ID: 3707964

SUBMITTER (NAME ONLY): Justin Liu

TITLE: Eye-Net: A Novel Transparent Machine Learning Ensemble for the Efficient Diagnosis and Localization of Lesions in Diabetic Retinopathy

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Liu, Palos Verdes Peninsula High School, Rolling Hills Estates, California, UNITED STATES|J. Cuadros, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|J. Cuadros, EyePACS, Inc., California, UNITED STATES|

Commercial Relationships Disclosure: Justin Liu: Commercial Relationship: Code N (No Commercial Relationship) | Jorge Cuadros: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is an ocular disease that can progress asymptomatically to an advanced vision-threatening stage. DR is particularly pervasive in developing countries, where there exists a severe deficiency of ophthalmologists, and thus alternate diagnosis methods are pressing.

Methods: Exploratory data analysis by way of dimensionality reduction was leveraged to interpret similarities between color fundus images derived from the Asia Pacific Tele-Ophthalmology Society. Subsequently, 16 image enhancement filters were systematically investigated for feature engineering purposes. 24 convolutional neural network architectures, including the previously untested EfficientNet and MobileNet families, were then designed, trained, and compared by their efficacy in the binary classification of DR. Ensemble stacking was leveraged to fuse the top four models through a meta-learner whose weights were optimized by a Dirichlet distribution-based randomized search. Finally, this project developed three small-object detectors (YOLO), serving as the first to localize microaneurysms, hemorrhages, cotton-wool spots, and hard exudates.

Results: Upon evaluation, the ensemble model (286 KB) surpassed all individual models across all metrics considered, attaining an F1-score of 0.978. Coupled with contrast-limited adaptive histogram equalization, the YCbCr color space augmentation was found to be the best feature engineering filter. Further, Shapley value analysis and four novel gradient-based visualizations successfully identified imaging biomarkers characteristic of DR. The YOLOv5x algorithm, with an inference time of 48.4 ms, achieved a mean average precision score of 0.504 at an Intersection over Union threshold of 0.5, a significant improvement over prior lesion localization studies.

Conclusions: Eye-Net is a highly performant machine learning tool for DR diagnosis and lesion localization; it may benefit clinicians or offer an alternate form of DR screening. Additionally, Eye-Net's lightweight frameworks postulate deployment onto mobile applications as promising avenues. Future work will focus on patient risk stratification and prognosis, which could further facilitate the early detection of DR.

CONTROL ID: 3707965

SUBMITTER (NAME ONLY): Francesca Kahale

TITLE: Cyto-protective effect of neuropeptide alpha-Melanocyte-Stimulating Hormone on UV-A irradiation-induced Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Kahale, T.H. Dohlman, J. Yin, U.V. Jurkunas, R. Dana, Ophthalmology, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|F. Kahale, N. Deshpande, H. Alemi, S. Wang, T. Blanco, T.H. Dohlman, J. Yin, U.V. Jurkunas, R. Dana, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T. Blanco, Harvard University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Francesca Kahale: Commercial Relationship: Code N (No Commercial Relationship) | Neha Deshpande: Commercial Relationship: Code N (No Commercial Relationship) | Hamid Alemi: Commercial Relationship: Code N (No Commercial Relationship) | Shudan Wang: Commercial Relationship: Code N (No Commercial Relationship) | Tomas Blanco: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Dohlman: Commercial Relationship: Code N (No Commercial Relationship) | Jia Yin: Commercial Relationship(s);Code O (Owner):Kera therapeutics | Ula Jurkunas: Commercial Relationship: Code N (No Commercial Relationship) | Reza Dana: Commercial Relationship(s);Code O (Owner):Kera therapeutics

ABSTRACT BODY:

Purpose: Fuchs Endothelial Corneal Dystrophy (FECD) is characterized by a progressive loss of corneal endothelial cells (CEnC) from accumulated exposure to oxidative stress. It is one of the leading causes of corneal transplantation worldwide, and no definitive pharmacologic treatment is available. We have previously demonstrated the cytoprotective function of the neuropeptide alpha-Melanocyte-Stimulating Hormone (α-MSH) against oxidative stress in CEnC ex vivo. This study aims to investigate the in vivo protective effect of α-MSH in a mouse model of FECD induced by UV-A irradiation.

Methods: 8-week-old female BALB/c mice (n=6/group) were irradiated with UV-A at 500J/cm^2 for 16 minutes. Mice received an intraperitoneal injection of 0.01mL/g of α-MSH (10^{-4} M) immediately following irradiation and thrice weekly for 8 weeks. The control group received no treatment. CEnC density, hexagonality, and cell size variability (CV) were evaluated by in vivo confocal microscopy pre-irradiation and at 1, 2, and 4 weeks post-irradiation. ZO-1 staining was performed at 8 weeks. Corneal edema was evaluated by measuring central corneal thickness on OCT.

Results: At 4 weeks post-irradiation in the control treatment group, there was a 50.5% decrease in CEnC density (1373±199 cell/mm^2 vs baseline 2773±66, p=0.002), a 29% decrease in hexagonality (41±2.5 vs baseline 57.8±1.7, P=0.032) and a 61% increase in polymegathism (CV: 58±1.22 vs baseline 36±1.3, P=0.001). Compared to controls, the α-MSH treatment group demonstrated significant improvements in these parameters: the decrease in CEnC density was 18.7% (2255±116 vs control 1373±199, P=0.012), the decrease in hexagonality was 6.7% (53.9±2 vs control 41±2.5, P=0.014) and the increase in polymegathism was 8.6% (39±1.8 vs control 58±1.22, P=0.007). Corneal thickness was assessed in N=4 mice at 4 weeks where edema subsided in the α-MSH treatment group but remained elevated in the control group (107.8 ±14.6μm vs 166.3±39.4μm, p<0.05).

Conclusions: Intraperitoneal treatment with α-MSH leads to decreases in UV-A-induced CEnC cell loss, polymegathism and pleomorphism, along with resolution of corneal edema.

CONTROL ID: 3707970

SUBMITTER (NAME ONLY): Sophie Lee

TITLE: Utilization and insurance coverage of tele-retinal imaging during the COVID-19 pandemic

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.C. Lee, M.K. Lieng, P. Emami-Naeini, G. Yiu, Department of Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|S. Alber, Department of Public Health Sciences / Biostatistics, Clinical and Translational Science Center, University of California Davis, Sacramento, California, UNITED STATES|M.K. Lieng, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|G. Yiu, OptumLabs Visiting Fellow, Eden Prairie, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Greater utilization and insurance coverage for tele-retinal screening during the COVID-19 pandemic in 2020 may enhance awareness and expand remote retinal imaging services. In this study, we performed a retrospective, cross-sectional analysis of utilization and insurance payments of tele-retinal imaging services in the United States in 2020.

Methods: We examined remote retinal imaging utilization and insurance payments from January 1, 2020, to December 31, 2020, using the OptumLabs® Data Warehouse (OLDW), a comprehensive database of de-identified administrative claims for commercial and Medicare Advantage enrollees in the U.S.. We evaluated frequency of claims and insurance payment for services using Current Procedural Terminology codes 92227 and 92228 for remote eye imaging by any provider, and 92250 for fundus photography by non-eye care providers.

Results: Use of remote retinal imaging declined rapidly from 3627 claims in February 2020 to 1414 claims in April 2020, but returned to 3133 claims by December 2020, similar to pre-pandemic levels in 2019 (2841 ± 174.8 claims). Proportion of insurance payments for remote imaging increased temporarily from 47.4% in February to 56.7% in April, then returned to 45.9% in December.

Conclusions: Utilization of tele-retinal imaging declined steeply while insurance coverage increased during the initial COVID-19 lockdown in 2020, but returned to pre-pandemic levels by end-of-year. Changes in utilization and relaxed restrictions on insurance reimbursements for remote retinal imaging during the COVID-19 pandemic were not sustained.

CONTROL ID: 3707971

SUBMITTER (NAME ONLY): Su Mae Ang

TITLE: Analysis of Reoperation Rates in Strabismus Surgery from Health Databases

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ang, A.E. Pogrebniak, Department of Ophthalmology, Prisma Health Midlands, Columbia, South Carolina, UNITED STATES|M. Durkin, Department of Neurology, Prisma Health Midlands, Columbia, South Carolina, UNITED STATES|

Commercial Relationships Disclosure: Su Mae Ang: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Pogrebniak: Commercial Relationship: Code N (No Commercial Relationship) | Martin Durkin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Limited information has been published describing reoperation rates for various strabismus surgeries in relation to age at first surgery. We performed a retrospective, observational clinical study to analyze reoperation rates compared to type of strabismus, age at first surgery, and geographic location within South Carolina and to determine factors associated with repeat strabismus surgery.

Methods: We analyzed 25 years of longitudinal data from the South Carolina Revenue and Fiscal Affairs Office (RFAO). The inclusion criteria for the study were: (1) any admission for procedure with CPT codes 67311, 67312, 67314 or 67316 between January 1, 1996 and December 31, 2016, and (2) patient age <18 years during the time of admission for first surgery. If a second surgery was done, surgery data up to December 31, 2020 was obtained and included in analysis. Patients were categorized into 5 age groups: <2, 2 to <4, 4 to <6, 6 to <10, or 10 to <18 years old. Strabismus types were grouped as pure esotropia, esotropia plus vertical misalignment, pure exotropia, exotropia plus vertical misalignment, vertical misalignment alone, superior oblique palsy, restrictive, paretic, or other. A logistic regression model was constructed using repeat surgery as the outcome and using age and strabismus type as predictors.

Results: A total of 9237 unique patients were identified; 1833 (19.8%) had repeat surgeries captured within the RFAO database, with follow-up time ranging from 4 to 25 years depending on the date of initial surgery. Increasing age was correlated with a decreasing reoperation rate.

For all types of strabismus, reoperation was higher in the <2 years age group compared to ages 2 to <4 years (OR 0.66), ages 4 to <6 years (OR 0.48), 6 to <10 years (OR 0.34), 10 to <18 years (OR 0.24, all P <0.001). The strabismus type with the greatest number of index cases was other (n=3901, 42.2%), followed by pure exotropia (n=2496, 27.0%) and pure esotropia (n=1760, 19.0%).

Conclusions: Across all types of strabismic surgeries, patients operated on at a younger age require a higher rate of reoperation.

CONTROL ID: 3707972

SUBMITTER (NAME ONLY): Qian Wang

TITLE: The lens-corneal separation requires precision control of Hippo-Yap signaling

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Wang, H. Wu, X. Zhang, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Qian Wang: Commercial Relationship: Code N (No Commercial Relationship) | Hao Wu: Commercial Relationship: Code N (No Commercial Relationship) | Xin Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The Hippo-Yap signaling pathway is implicated in tissue development and homeostasis. In the lens, Yap is required for the maintenance of the lens progenitor pool, but it is not clear whether this is due to Yap's function as a transcriptional activator or as part of the cell junction complex. In this study, we aim to investigate the role of Hippo-Yap signaling network and its mechanism in regulating murine lens development.

Methods: We generated both conditional knockout and conditional transgenic mouse models using Le-cre, which is specifically expressed in the lens progenitors. Immunofluorescence was performed to characterize the lens phenotype.

Results: Consistent with a previous study, genetic ablation of Yap resulted in substantial loss of the lens epithelium (LE) compartment at embryonic day 13 (E13). This LE defect could be rescued by expression of nuclear Yap (Yap^{5SA}), which is resistant to serine phosphorylation induced by Hippo signaling. In addition, expression of nuclear Yap led to ectopic expression of LE markers in the lens fiber compartment in a cell autonomous manner, suggesting that the nuclear but not the membrane function of Yap is responsible for maintenance of the lens progenitor property. Interestingly, the Yap^{5SA}-expressing lens remained connected to the surface ectoderm (which later develops into the cornea) and formed persistent lens stalk, indicating that Yap signaling is involved in the lens vesicle separation. Moreover, genetic ablation of Hippo signaling kinases mammalian STE20-like kinase (MST) and large tumor suppressor (LATS) recapitulated Yap gain of function (Yap^{5SA}) lens stalk phenotype.

Conclusions: Our study demonstrated that the nuclear function of Yap is both necessary and sufficient to maintain the lens progenitor pool. However, the level of active nuclear Yap must be tightly controlled by Hippo Signaling to ensure separation of the lens vesicle from the surface ectoderm. Suppression of Hippo signaling leads to the lens-corneal separation defect, which mimics Peters Anomaly in humans, suggesting that the Hippo-Yap signaling may underlie congenital lens disease.

CONTROL ID: 3707973

SUBMITTER (NAME ONLY): Mauranda Men

TITLE: Evaluation of public interest using internet search queries for uveitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Men, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|E. Tsui, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Mauranda Men: Commercial Relationship: Code N (No Commercial Relationship) | Edmund Tsui: Commercial Relationship(s);Code C (Consultant/Contractor):Kowa Company Ltd;Code F (Financial Support):Cylite Pty Ltd

ABSTRACT BODY:

Purpose: The rarity of uveitis makes it difficult to gauge overall trends in patient behavior; however, the internet is a popular resource for medical self-education. This study used search engine data to characterize search patterns around uveitis, to better understand what people look for online.

Methods: Google Trends data were analyzed from 2004-21 to find the top related search queries with "uveitis" and "iritis" in the United States (USA), United Kingdom (UK), Canada, Australia, and India. This was further divided into top search terms for three 6-year periods: 2004-09, 2010-15, and 2016-21. Queries were categorized as relating to disease information, disease treatment, other eye conditions, related systemic conditions, or other. The relative search frequency of each term, and the sum of them for each term in a category, measure how many people search for information in those categories after first searching "uveitis" or "iritis."

Results: Within searches for "uveitis," the term "anterior uveitis" was the top or second top related search term in every country in every time period studied. Only the USA had "iritis" or "iritis uveitis" as common terms, with 42 people searching for them out of every 100 people searching for "uveitis." Also in the USA, in 2016-21, 13 of every 100 people searched for "uveitis vs iritis" or "iritis or uveitis" when searching for "iritis." In every country, the majority of related "uveitis" search terms concerned disease information. In the UK, Canada, Australia, and India, the next most common search categories were disease treatment, systemic conditions, followed by other eye conditions. In the USA, the next most common search categories were other eye conditions, disease treatment, then systemic conditions. In each country except India, where it was "psoriasis," the top searched systemic condition was "ankylosing spondylitis," with 10/100 searches in the USA and UK and 22/100 searches in Canada and Australia.

Conclusions: Query categories have been stable over time in several countries, indicating persistent knowledge gaps for the average searcher regarding uveitis causes and presentations. "Anterior uveitis" as a top related search term is logical given the high prevalence of anterior uveitis compared to other subtypes, suggesting demand for more knowledge about it. These data may help caregivers anticipate topics of interest for patients and improve counseling accordingly.

CONTROL ID: 3707974

SUBMITTER (NAME ONLY): Lucia Brunel

TITLE: Collagen hydrogels covalently crosslinked by bioorthogonal click chemistry resist cell-induced contraction while preserving encapsulated corneal stromal cell phenotype

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.G. Brunel, S.M. Hull, Chemical Engineering, Stanford University, Stanford, California, UNITED STATES|D. Myung, Ophthalmology, Stanford Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|P.K. Johansson, S.C. Heilshorn, Materials Science and Engineering, Stanford University, Stanford, California, UNITED STATES|D. Myung, Ophthalmology, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure: Lucia Brunel: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Hull: Commercial Relationship(s);Code P (Patent):US20210244659A1 | Patrik Johansson: Commercial Relationship: Code N (No Commercial Relationship) | David Myung: Commercial Relationship(s);Code P (Patent):US20210244659A1 | Sarah Heilshorn: Commercial Relationship(s);Code P (Patent):US20210244659A1

ABSTRACT BODY:

Purpose: Due to the dearth of graft tissue available globally for patients with corneal blindness, improved corneal regeneration will require bioengineered strategies. Collagen hydrogels have demonstrated potential as matrices for corneal mesenchymal stromal cells (cMSCs) but commonly suffer from opacity and cell-induced contraction, affecting the optical properties of the material. We have developed a transparent, bioorthogonally-crosslinked collagen hydrogel with enhanced stability against cMSC-induced contraction while maintaining cell phenotype for improved regenerative potential.

Methods: Covalently-crosslinked collagen hydrogels were formed by strain-promoted azide-alkyne cycloaddition (SPAAC), a bioorthogonal click chemistry. The hydrogel fibrillar microstructure and corresponding transparency were characterized with second harmonic generation microscopy and UV/Vis spectroscopy, respectively. Human cMSCs were encapsulated within SPAAC-crosslinked or non-chemically crosslinked control collagen hydrogels, and the contraction was monitored over time. In addition, cMSC viability, differentiation markers, and secretome within the hydrogels were analyzed using a Live/Dead assay, immunocytochemistry, and a Luminex immunoassay, respectively.

Results: We demonstrated the improved transparency of the SPAAC-crosslinked collagen across the visible light range compared to non-chemically crosslinked collagen (e.g., 98% vs. 52% transmittance at 500 nm), which resulted from the disruption of collagen fibril formation. The SPAAC-crosslinked collagen resisted deformation from encapsulated human cMSCs over 72 h: the non-chemically crosslinked collagen hydrogels contracted to 20% of their initial diameters, while SPAAC-crosslinked collagen did not detectably contract. In addition, the cMSCs in the SPAAC-crosslinked collagen maintained their characteristic phenotype, with high viability (> 90%), expression of the keratocyte differentiation marker aldehyde dehydrogenase 3A1, and secretion of cytokines similar to cMSCs within the non-chemically crosslinked collagen.

Conclusions: Our results indicate that human cMSCs may be successfully encapsulated within SPAAC-crosslinked collagen to create transparent, bioengineered hydrogels that resist cell-induced contraction while simultaneously preserving the corneal cell phenotype.

CONTROL ID: 3707976

SUBMITTER (NAME ONLY): Lilla Simon

TITLE: Eye911: Interim analysis of pilot teleophthalmology protocol for ER and urgent care settings

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Simon, Morehouse School of Medicine, Atlanta, Georgia, UNITED STATES|H. O'Malley, K. Patterson, Memphis Veterans Affairs Healthcare Center, Memphis, Tennessee, UNITED STATES|J. Damonte, A. Maa, VISN 7, Clinical Resource Hub, Regional Telehealth Services, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: 1) Explore the feasibility of the Eye911 protocol for the ER and urgent care setting. 2) Assess diagnostic accuracy of protocol and impact of slit lamp (SL) video for diagnosis of ocular pathologies.

Methods: Thirteen patients presenting to the Memphis Veterans Affairs (VA) ER with ocular complaints were recruited. Following informed consent, the Eye911 protocol was carried out. Eye911 protocol includes initial eye workup (history, vision, IOP) and 2D external photos of the eyes. Then, SL video was captured for both eyes (JedMed). A single undilated fundus photo (Canon) was obtained for each eye. The patient was then seen by the on-call ophthalmologist in the traditional face to face (F2F) eye exam. The study data, images, and videos were uploaded into REDCap and sent to four reading ophthalmologists for interpretation. They were blinded to patient identity, F2F exam, and each other's interpretations. The readers first reviewed clinical information and external and fundus photos to make an initial diagnosis (pre-SL). They then accessed the SL video and made a subsequent diagnosis (post-SL). Using percent agreement and Cohen's kappa (κ) statistics, concordance pre and post-SL video between each of the readers and the F2F "gold standard" diagnosis was calculated.

Results: For reader 1, 2, 3, and 4 respectively, the percent agreement pre-SL between reader and F2F diagnosis was 46.2%, 33.3%, 30.8%, and 46.2%. There was no change in percent agreement post-SL (Table 1 and Table 2). In both the pre-SL and post-SL video period, there was no agreement between reader 1 vs 2 ($\kappa = -0.36$) or reader 2 vs 3 ($\kappa = -0.20$). There was slight agreement between reader 2 vs 4 ($\kappa = 0.00$). There was fair agreement between reader 1 vs 3 ($\kappa = 0.37$), reader 1 vs 4 ($\kappa = 0.38$), and reader 3 vs 4 ($\kappa = 0.37$) (Table 1 and Table 2).

Conclusions: Overall, percent agreement between readers and F2F exam ranged from ~30-46%, suggesting that the Eye911 protocol is feasible with moderate diagnostic accuracy. Surprisingly, the SL video did not increase percent agreement. There was also a wide range of agreement between the readers during the pre and post-SL video period ranging from none ($\kappa < 0$) to fair ($\kappa = 0.21$-0.40). These findings suggest that the protocol requires further study. Results may improve as more participants are recruited.

CONTROL ID: 3707978

SUBMITTER (NAME ONLY): Shreya Sirivolu

TITLE: Chromosome 6p amplification detected in blood cell-free DNA in advanced retinoblastoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sirivolu, L. Xu, J.L. Berry, The Vision Center, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|S. Sirivolu, L. Xu, J.L. Berry, Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|P. Kuhn, J. Hicks, Department of Biological Sciences, Dornsife College of Letters, Arts, and Sciences, University of Southern California, Los Angeles, California, UNITED STATES|P. Kuhn, J. Hicks, Norris Comprehensive Cancer Center, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Shreya Sirivolu: Commercial Relationship: Code N (No Commercial Relationship) | Liya Xu: Commercial Relationship(s);Code P (Patent):Aqueous Humor Cell Free DNA for Diagnostic and Prognostic Evaluation of Ophthalmic Disease | Peter Kuhn: Commercial Relationship: Code N (No Commercial Relationship) | James Hicks: Commercial Relationship(s);Code P (Patent):Aqueous Humor Cell Free DNA for Diagnostic and Prognostic Evaluation of Ophthalmic Disease | Jesse Berry: Commercial Relationship(s);Code P (Patent):Aqueous Humor Cell Free DNA for Diagnostic and Prognostic Evaluation of Ophthalmic Disease

ABSTRACT BODY:

Purpose: Both aqueous humor (AH) and blood-based liquid biopsies can carry tumor-derived cell-free DNA (cfDNA) in retinoblastoma (RB) patients. Detection of somatic copy number alterations (SCNAs) requires approximately 5% tumor fraction, as such have only previously been detected in AH, which is an enriched source of tumor DNA. We analyzed AH and blood cfDNA taken at the time of primary enucleation to compare SCNA profiles and somatic RB1 mutation detection between both biospecimens.

Methods: One patient diagnosed with advanced unilateral RB (Group D/AJCC Stage cT2B) was included. After isolating cfDNA from AH and blood, constructed whole genome libraries were sequenced on an Illumina platform to assess genome-wide SCNAs, which were considered positive at 20% deflection from the baseline. Correlation between SCNA profiles was calculated using Pearson correlation coefficient. The libraries were also used to identify somatic RB1 pathogenic variants using a comprehensive cancer panel that includes all RB1 exons.

Results: In the peripheral blood, a germline RB1 mutation was not detected, however a heterozygous mutation (c.3920T>A) in the APC gene was reported from clinical testing. Genomic analysis of the tumor revealed two somatic RB1 mutations that were not present in germline, c.1589_1590del with a variant allele frequency (VAF) of 84.0% and c.2330dupC with VAF of 40.0%. These mutations were similarly detected in the AH, with VAFs of 78.9% and 45.27% respectively, but were not detected in the blood. Genomic analysis of both tumor and AH demonstrated highly recurrent RB SCNAs such as gains on 1q, 2p, and 6p, in addition to other alterations. The AH SCNA profile was highly concordant with the tumor profile ($r=0.987$; $p<0.0001$). 6p gain was detected in the blood and comparison of the 6p amplitude between AH and blood suggests approximately 12% tumor fraction in the blood.

Conclusions: To our knowledge, this is the first time an SCNA has been detected in the blood of an RB patient, suggesting a high enough tumor fraction. No metastasis has been identified, however monitoring is ongoing. The results illustrate the benefits and limitations of both AH and blood-based liquid biopsies. While AH is composed of more highly enriched eye-specific tumor information, only blood can provide information regarding systemic disease and metastasis.

CONTROL ID: 3707983
SUBMITTER (NAME ONLY): Anne Dersch
TITLE: Retinal Mitochondrial Function in Amblyopia
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Dersch, J.K. Kulwin, R.M. Bhakta, J.M. Smith, J.M. Holmes, The University of Arizona Department of Ophthalmology and Vision Science, Tucson, Arizona, UNITED STATES|J. SanGiovanni, The University of Arizona BIO5 Institute, Tucson, Arizona, UNITED STATES|
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ABSTRACT BODY:
Purpose: Functional and structural deficits have been reported in the retina of amblyopic eyes compared with fellow eyes. Non-invasive in vivo flavoprotein fluorescence (FPF) imaging provides clinic-based quantitative physiological biomarkers of retinal metabolic function. Based on previous studies in eyes with diabetic retinopathy and glaucoma exhibiting mitochondrial dysfunction, we hypothesized that amblyopic eyes would have higher levels of oxidized mitochondrial flavoproteins (FPF intensity and curve width) than those of fellow non-amblyopic eyes.
Methods: 14 children (aged 5y to 11y) with unilateral anisometropic, strabismic, or combined amblyopia underwent retinal metabolic imaging with the OcuMet Beacon (Ann Arbor, MI). The FPF sampling space was a 13° diameter target centered on the fovea identified with an IR alignment after pupil dilation. Retinal mitochondrial flavoprotein enzymes were activated for 30ms with an excitation wavelength of 467nm; emission filters were tuned to 535nm. Images were reviewed by an investigator masked to the clinical and FPF parameters and excluded if poor quality or decentered. We compared mean FPF intensity values and curve width between amblyopic and fellow eyes using paired t-tests, calculating mean difference with 95% confidence intervals (CI). We hypothesized that if there was a difference between amblyopic and fellow eyes, the mean difference of FPF intensity would be at least 5 units higher in affected eyes (based on studies in diabetic retinopathy).
Results: 9 pairs of images were graded by the masked grader as sufficient quality for analysis. Included children ranged from age 5 to 11 years and amblyopic eye acuity from 20/80 to 20/30. There was no statistically significant difference in FPF intensity between amblyopic and fellow eyes (mean difference -1.6 units, p=0.27) and the 95% CI (-4.59 to 1.47) excluded the hypothesized +5 unit mean difference. There was no difference in FPF curve width between amblyopic and fellow eyes (-1.33 units, 95% CI -2.72 to 0.05, p=0.06).
Conclusions: In contrast to previous reports of functional and structural deficits in the retinas of eyes with amblyopia, we found no evidence of retinal mitochondrial dysfunction by flavoprotein fluorescence (assuming an expected effect size of 5 intensity units greater in amblyopia). Retinal changes in amblyopia do not appear to manifest as abnormalities in retinal mitochondrial function.

CONTROL ID: 3707986

SUBMITTER (NAME ONLY): Rishabh Singh

TITLE: Do Normative Percentiles of Retinal Nerve Fiber Layer Thickness (RNFLT) Improve Prediction of Glaucomatous Visual Field Loss?

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Zebardast, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|R. Singh, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|R. Singh, Y. Li, M. Eslami, S. Kazeminasab, M. Wang, T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) manufacturers add color-coded normative information to circumpapillary RNFLT printouts, to aid in the clinical diagnosis of glaucoma (Fig 1A). In this retrospective study, we investigate whether normative percentiles of RNFLT (pRNFLT) from the Spectralis OCT platform (2009 European-descent norms) enable better prediction of glaucomatous visual field (VF) loss than absolute RNFLT.

Methods: A longitudinal database of Mass Eye & Ear Infirmary patients seen in glaucoma clinic from 2009-2020 was extracted. From a source of 158,484 Humphrey 24-2 VFs and 30,452 OCT scans, reliable OCT-VF pairs acquired within 30 days of each other were selected (Fig 1B). Spectralis normative distributions were extracted from color-coded machine printouts (Fig 1A). Supervised machine learning models predicting mean deviation (MD) and respective glaucoma staging were applied (Fig 1B). Regional structure-function associations were explored with univariate regression, correlating RNFLT or pRNFLT by scan sector with MD. Then, multivariate classification methods were applied to predict VF loss using age, scan radius, and 32-sector RNFLT or pRNFLT. R^2, ROC-AUC, and accuracy scores of models were estimated using cross-validation (CV) techniques.

Results: 3021 OCT-VF pairs from 1427 patients met our reliability criteria. Extracted Spectralis norms were found to be normally distributed across the 768-point scan circle and independent of patient-specific parameters. Regional analysis showed significant decrease in R^2 from pRNFLT input compared to RNFLT in inferotemporal sectors, across all tested regressors (T-tests, p=0.00-0.02). Other regions showed no significant differences (Example in Fig 2A). In multivariate classification, there were also no statistically significant differences in CV accuracy of any model between RNFLT and pRNFLT inputs (T-tests, p>0.05). This is confirmed by the ROC-AUC analysis on the testing set for each model (Fig 2B), with mean score change 0.00±0.02.

Conclusions: Our results challenge the assumption that normative percentiles from OCT machines improve prediction of VF loss. RNFLT alone shows strong prediction of glaucomatous VF loss, with no models showing significant improvement from the manufacturer norms. Greater patient stratification based on demographic factors may produce more predictive norms.

CONTROL ID: 3707988
SUBMITTER (NAME ONLY): Christa Prentiss
TITLE: Attitudes Toward and Difficulties with Childhood Amblyopia Patching Treatment
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C.J. Prentiss, M. Hribar, K.N. Bellsmith, T. Zaback, E. Kim, A. Lucero, L.G. Reznick, Oregon Health & Science University, Portland, Oregon, UNITED STATES|
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ABSTRACT BODY:

Purpose: Amblyopia is the leading cause of visual loss in children and young adults, affecting up to 5% of people of all ages. Patching and atropine eyedrops successfully treat this condition. However, adherence to treatment is often poor. Current literature has identified factors impacting compliance, but less is known about successful interventions to improve adherence. This study's purpose is to identify parent attitudes towards amblyopia treatment and barriers to treatment compliance in order to inform future provider and multidisciplinary approaches to improve adherence.
Methods: Parents of amblyopic patients ages 0 - 9 years old were recruited from 1 pediatric ophthalmology clinic at the Oregon Health & Science University from May – December 2021. Participants were given surveys to complete in the waiting room before their child's clinic visit. The survey assessed attitudes toward and difficulties with amblyopia treatments, specifically patching and atropine.
Results: A total of 37 participants completed the survey; 34 of these were parents of patients currently patching for amblyopia. Boys accounted for 18 (53%) of children and the average child's age was 5 years old (range 1 - 8). Subjective patching ease and compliance were assessed (Tables 1 and 2). Twenty-four (71%) said that their child had difficulty with how the patch feels. Twenty-six (76%) indicated that their child easily wears the patch. Nineteen (56%) reported that their experience had gotten easier over time.

Write-in responses were collected. The most commonly reported (n = 32) hardest parts of patching were keeping the patch on (9; 28%) and remembering the treatment (7; 22%). Parents (n = 34) indicated that they thought better patch designs and quality (9; 26%) and rewards (6; 18%) could help. Respondents (n = 34) used rewards (21; 62%) and flexibility with patching time (15; 44%) to help encourage their child to wear the patch.
Conclusions: This study suggests that while most parents at our clinic found patching manageable, many had significant difficulties such as logistical issues and discomfort, which is consistent with literature. Suggestions for improvement included improved comfort in patch design and positive reinforcement. Goals for further study include linking difficulties with treatment and its duration, evaluating parent suggestions, and determining whether adjustments based on survey data improve adherence.

CONTROL ID: 3707990

SUBMITTER (NAME ONLY): Stephanie Watson

TITLE: The Save Sight Dry Eye Registry: One year capture of real-world data for dry eye

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Watson, M.P. Cabrera Aguas, Ophthalmology, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|L.E. Downie, Optometry, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|F. Stapleton, Optometry, University of New South Wales, Sydney, New South Wales, AUSTRALIA|D. Mingo Botin, F. Arnalich, Ophthalmology, Hospital Universitario Ramon y Cajal, Madrid, Madrid, SPAIN|S. Rauz, Ophthalmology, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|J.P. Craig, Optometry, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|G. Geerling, Ophthalmology, University of Duesseldorf, GERMANY|V. Daien, F. Babeau, Ophthalmology, University Hospital of Montpellier, FRANCE|

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ABSTRACT BODY:

Purpose: The Save Sight Dry Eye Registry (SSDER) is the first international web-based multinational, interdisciplinary registry able to collect high-quality outcome data from dry eye patients in clinical settings. We report the characteristics of patients with dry eye disease (DED) at their baseline visit from routine clinical practice from 1 November 2020 to 30 November 2021.

Methods: The SSDER collected data from routine clinical practice in Australia, Spain, Germany, and the United Kingdom. Patient demographics, medical history and index visit characteristics including visual acuity, tear break up time (TBUT), ocular surface staining (none, minimal, mild, moderate, severe) and Oxford ocular surface staining score (OSS, 0-15) were recorded in the prospectively designed electronic database. The Ocular Surface Disease Index (OSDI) symptom questionnaire was also completed. Primary outcomes were the baseline demographic data and dry eye diagnosis, and secondary outcomes, logMAR visual acuity, TBUT, and OSS and OSDI scores.

Results: 31 clinicians from 26 sites were registered to use the registry. Data from 122 patients (222 eyes) were curated. Patient age ranged from 18-85 years (mean 58 ± 15 (SD) years) and 98 (87.5%) were female. Mixed DED and evaporative DED comprised the largest groups 107 (48.2%) eyes versus 99 (44.6%) eyes, respectively. The remainder had aqueous deficient DED 14 (6.3%) eyes or neuropathic corneal pain (NCP) 2 (0.9%) eyes. Four (3.5%) patients (8 eyes) wore a contact lens within the month prior to their visit. Most of the patients (90; 177/222 (88%) eyes) had meibomian gland disease.

The median visual acuity and TBUT were 84 (IQR 76-85) logMAR letters and 4 (IQR 2-8) seconds, respectively. The majority of eyes had minimal or moderate ocular surface staining (none 83(37%); minimal 65(29%); mild 46(21%); moderate 21(9%); severe 7(3%)) that was scored using the OSS as < 3 in 78%(174 eyes), 4-8 in 19%(42), and > 9 in 3%(6). Ninety-six percent of patients completed the OSDI, the median score was 31 (IQR 17-46). The two NCP eyes (one patient) had an OSS of 3 (each eye) and OSDI of 79.

Conclusions: The SSDER allows the efficient capture of dry eye patient data from everyday clinical practice. Meibomian gland disease was present in most patients with dry eye from this real-world setting.

CONTROL ID: 3707992
SUBMITTER (NAME ONLY): Kazuo Tsubota
TITLE: Relationship between Dry Eye and Myopia in Children
SESSION TITLE: Myopia epidemiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Tsubota, Tsubota Laboratory, Inc., Shinjuku-ku, Tokyo, JAPAN|K. Tsubota, D. Hazra, E. Yotsukura, K. Mori, T. Maruyama, M. Ogawa, A. Hanyuda, K. Negishi, H. Torii, T. Kurihara, Opthalmology, Keio University School of Medicine, Shinjuku-ku, Tokyo, JAPAN|D. Hazra, E. Yotsukura, K. Mori, M. Ogawa, A. Hanyuda, H. Torii, T. Kurihara, Laboratory of Photobiology, Keio University School of Medicine, Shinjuku-ku, Tokyo, JAPAN|
Commercial Relationships Disclosure: Kazuo Tsubota: Commercial Relationship(s);Code E (Employment):Tsubota Laboratory, Inc.;Code I (Personal Financial Interest):TissueTech, Inc., Tear Solutions, Cellusion, Inc., Tsubota Laboratory, Inc., RestoreVision | Debabrata Hazra: Commercial Relationship: Code N (No Commercial Relationship) | Erisa Yotsukura: Commercial Relationship: Code N (No Commercial Relationship) | Kiwako Mori: Commercial Relationship: Code N (No Commercial Relationship) | Tomoki Maruyama: Commercial Relationship: Code N (No Commercial Relationship) | Mamoru Ogawa: Commercial Relationship: Code N (No Commercial Relationship) | Akiko Hanyuda: Commercial Relationship: Code N (No Commercial Relationship) | Kazuno Negishi: Commercial Relationship: Code N (No Commercial Relationship) | Hidemasa Torii: Commercial Relationship: Code N (No Commercial Relationship) | Toshihide Kurihara: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the association between dry eye disease (DED) and myopia by evaluating higher order aberrations (HOAs) and choroidal thickness (CT) among myopic children with DED symptoms. The incidence of dry eye and myopia have increased dramatically in modern society. Is it a coincidence or related to the lifestyle in modern society?

Methods: In this cross-sectional study, we recruited 72 myopic (spherical equivalent of ≤ -0.5 diopter) children with DED symptoms (age, 12.8 ± 2.7 [mean ± standard deviation] years) who presented to Keio University Hospital Myopia Clinic. They were measured for the tear film breakup time (BUT), HOAs, CT, axial length (AL) and refraction. Lifestyle questionnaires were administered, and the correlations between the BUT and HOAs were evaluated. Multiple regression analyses were performed to identify relationships among myopia and BUT/lifestyle factors, myopia and corneal/intraocular/total ocular HOAs (spherical aberration [SA], 3rd-order [S3], 4th-order [S4] and the sum of the 3rd- to 6th-order aberrations [THOA] evaluated with a natural pupillary diameter [average value, φ = 6.1 mm]), CT and BUT/AL.

Results: The BUT, CT, AL, and cycloplegic refraction were 5.7 ± 3.1 seconds, 285.3 ± 38.4 μm, 25.52 ± 1.14 mm, and -4.61 ± 2.38 diopters, respectively. The BUT was correlated significantly with the corneal HOAs (SA, β = -0.323, P = 0.02; S4, β = -0.497, P < 0.001; THOA, β = -0.362, P = 0.009) and intraocular HOAs (S3, β = -0.299, P = 0.04; S4, β = -0.369, P = 0.008; THOA, β = -0.368, P = 0.009) but not with total ocular HOAs. Multiple regression analyses showed that the AL was associated significantly with the BUT (β = -0.067, P = 0.004) and the intraocular S3, intraocular THOA, total ocular S3, and total ocular THOA (β = -21.8, 21.2, -41.7, and 43.6, respectively; P = 0.02, 0.048, 0.045, and 0.049, respectively) but not with the corneal HOAs. The CT was associated significantly with the BUT and AL (β = 9.15 and -7.85, respectively; P < 0.001 and = 0.01, respectively).

Conclusions: We showed that the BUT was associated significantly with the CT that is related to the AL. As the parasympathetic nervous system affects the lacrimal glands and CT, the parasympathetic nervous system might be a common upstream factor in the association between DED and myopia.

CONTROL ID: 3707997

SUBMITTER (NAME ONLY): Hsu-Hang Yeh

TITLE: PhacoTrainer: Deep Learning for Cataract Surgical Videos to Track Surgical Tools

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yeh, K. Sebov, Biomedical Data Science, Stanford University, Stanford, California, UNITED STATES|A.M. Jain, S.Y. Wang, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|M. Jallow, Georgetown University School of Medicine, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Hsu-Hang Yeh: Commercial Relationship: Code N (No Commercial Relationship) | Anjal Jain: Commercial Relationship: Code N (No Commercial Relationship) | Mariama Jallow: Commercial Relationship: Code N (No Commercial Relationship) | Kostya Sebov: Commercial Relationship: Code N (No Commercial Relationship) | Sophia Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Deep learning provides a powerful approach to analyze surgical videos and assess surgical skills objectively. We aim to build a model that automatically identifies the locations of cataract surgical tools and eye landmarks, which can be used to grade surgical performance.

Methods: We sampled 1156 frames from 9 core steps of 268 cataract surgical videos, and annotated the regions of 8 different surgical tools, and the pupil border and limbus. We pretrained a real-time object detection and segmentation model called YOLACT on the CaDIS dataset, a public dataset for semantic segmentation of cataract surgical videos. The pretrained model was fine-tuned on our dataset. Object detection was evaluated by average precision score (AP), calculated by averaging the precision of the bounding boxes along the precision-recall curve, and segmentation was evaluated by intersection-over-union (IoU), calculated as the intersection of the predicted mask and the true mask over their union. Tooltip positions were estimated by identifying the edge point of the predicted mask closest to the screen center. Pupil centers were estimated by fitting an ellipse to the outer edges of the pupil mask and localizing the ellipse center. For further validation, the tip position estimation was compared with the ground truth positions of the tips from 46620 frames of 4 phacoemulsification video clips.

Results: The mean AP and IoU across different classes of objects were 0.78 and 0.82, respectively. The segmentation performed the best for the blade, weck sponge, and phaco instruments, whereas performance in the needle or cannula class of instruments was the worst (Table). The average deviation of estimated phaco tip positions from ground-truth positions was 6.13 pixels. Examples are shown in Figure. When considering predictions within 10 pixels from the true position as true positives, the average sensitivities and precisions were 81% and 100%, respectively.

Conclusions: We trained a deep learning model to perform real-time surgical instrument and tooltip detection with good accuracy. The model could be used to develop an automated feedback system that rates surgical performance using cataract surgical videos.

CONTROL ID: 3707999

SUBMITTER (NAME ONLY): Juan Arias

TITLE: Investigating the genetic and clinical features associated with cystoid macular edema in retinitis pigmentosa patients

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Arias, F. Kalaw, V. Alex, S. Yassin, H. Ferreyra, E. Walker, S. Borooah, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cystoid macular edema (CME) is a known endophenotype of retinitis pigmentosa (RP). Currently, factors associated with CME in RP are unclear. This study aims to identify associations between clinical-genetic findings in RP with CME.

Methods: This was a retrospective cross-sectional study. Patients with RP were identified from a database of inherited retinal disease patients seen at the Shiley Eye Institute, UCSD. Patient clinical, demographic, spectral domain-optical coherence tomography (SD-OCT) and genetic testing data was recorded. PCR amplified genetic tests. A masked retinal fellow assessed SD-OCT images for presence of CME, Epiretinal Membrane (ERM), Posterior Vitreous Detachment (PVD) and Vitreo-macular Traction (VMT).

Two-sample t-tests and $\chi 2$ measured clinical differences between CME patients and Fisher Test was used for multifactorial and two-factor variables which were disproportionate. A generalized linear mixed effect model was created to fit the binomial nature of CME with an array of independent variables. Odds ratio analysis also targeted demographics. Analysis used R statistical software.

Results: The database contained 571 patients. A total of 113 patients (225 eyes) had confirmed RP and were included in the analysis.The mean age of the cohort was 47 years (SD+-19), with 62 (54.91%) females (Table 1). 36% (81 eyes) presented with CME (OD = 38.9%, OS = 32.7%). A correlation was found between ERM (CI= 95%, p = 0.023) and VMT (CI = 95%, <0.001) and CME (Table 2).

An odds ratio of 2.92 (CI = 95%, <.254) was found for CME in males, although gender failed to meet significance during modeling. Black (n= 4, μ = 3.5%) and Asian (n = 11, μ = 9.7%) ethnicities presented with the highest odds of CME presence when compared to Caucasian subjects with CME (n = 33, μ = 40.7%).

Cases with X-linked, AD and AR mutations did not have any significantly increased odds of having CME. Additionally, no significant relationship was found between CME and genetic cause of RP.

Conclusions: CME was commonly seen in RP patients and was associated with vitreoretinal interface changes including ERM and VMT. However, no relationship was found between genetic causes of RP and CME in our cohort despite some genes nearing significance.

Interestingly, males had a higher risk of CME in our cohort. Further study in larger cohorts is warranted to confirm the findings from this study.

CONTROL ID: 3708001

SUBMITTER (NAME ONLY): Preston Thomas

TITLE: Gene expression in cone photoreceptors of adult zebrafish is plastic to exogenous hormone treatment

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Thomas, J. Huang, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|A.A. Farre, A. Duncan, R. Poulsen, D.L. Stenkamp, University of Idaho, Moscow, Idaho, UNITED STATES|

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ABSTRACT BODY:

Purpose: Color vision in vertebrates requires differential expression of multiple specific cone opsins in different cone populations. One model for the regulation of the human long and medium wavelength sensitive (LWS/MWS) opsin tandem array suggests an upstream regulatory region randomly interacts with replicated opsin genes, resulting in the mutually exclusive expression of a specific opsin. However, our prior investigations into the long wavelength sensitive (lws1/lws2) array in zebrafish (sharing a common ancestral LWS gene with the human array) demonstrates that thyroid hormone (TH) and retinoic acid serve as trans regulators of this gene array in larvae/juveniles (Mitchell et al., 2015, PLOS Genetics; Mackin et al., 2019, PNAS). This project utilizes opsin mRNA expression to explore if cone opsin plasticity to TH treatment is retained in adult zebrafish, where the cone distribution has otherwise been considered stable.

Methods: Adult zebrafish (6-18 months old; both sexes) were treated with NaOH (0.01%, control) or TH (386 nM) for 1 or 5 days. After the treatment period, eyes were harvested and homogenized for mRNA quantification through qRT-PCR. In addition, whole retinas of treated fish underwent hybridization chain reaction (HCR) in situ and then were analyzed by confocal imaging for endogenous expression of lws1 vs lws2 mRNA.

Results: Exogenous TH treatment in adult zebrafish significantly increased lws1 expression in both 1 and 5 day-treated groups ($p<1e-7$, 0.01, respectively) while decreasing lws2 expression ($p<0.001$, 0.001). Other phototransduction-related transcripts (gngt2b, rh2-1) also demonstrated expression changes following TH treatment. Whole retinas showed a substantial expansion of the lws1 domain and restriction of lws2, complementing the qRT-PCR results.

Conclusions: Consistent with our previous studies of larvae and juveniles, exogenous TH induced a drastic shift from lws2 to lws1 in adult zebrafish. The change in gene expression was observed within as little as 1 day of treatment of TH. Visualization through HCR of lws1/lws2 mRNA revealed a switch from lws2 to lws1 in much of the retina. This rapid shift demonstrates a high degree of plasticity retained in adult zebrafish.

CONTROL ID: 3708003

SUBMITTER (NAME ONLY): Kwanchanok Chanthowong

TITLE: Comparison of ziv-aflibercept and bevacizumab for treatment of naïve central retinal vein occlusion with macular edema: interim analysis of a randomized non-inferiority trial

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chanthowong, S. Sinawat, Y. Yoipaiboon, S. Hemanak, Ophthalmology, Khon Kaen University Faculty of Medicine, Khon Kaen, Khon Kaen, THAILAND|

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ABSTRACT BODY:

Purpose: Macular edema (ME) is the most common visual threatening complication of central retinal vein occlusion (CRVO) due to an increased level of vascular endothelial growth factors (VEGF). Considering the high cost of other anti-VEGF, bevacizumab is the most used anti-VEGF for ME in real-world practice. Ziv-aflibercept, an anti-VEGF with similar molecules with aflibercept, is now available for off-label ophthalmic use. This study hypothesized that intravitreal ziv-aflibercept (IVZ) is non-inferior to intravitreal bevacizumab (IVB) as the treatment of ME in CRVO.

Methods: The participants who were diagnosed with ME from CRVO were randomly assigned 1:1 to receive IVZ (1.25 mg/0.05ml) or IVB (1.25 mg/0.05ml) at baseline, 1, and 2 months. Later the participants were followed once every month until 6 months. Additional intravitreal injection of allocated drug was given as a pro-re-nata protocol for recurrent or persistent ME. The primary outcome was the best-corrected visual acuity (BCVA) change from baseline. Mean change in central subfield thickness (CST), the number of injections and adverse events were considered as secondary outcomes.

Results: 22 of 26 participants had completed 6 months follow-up, 11 in each group. The initial mean BCVA was 1.13±0.57 logMAR in IVZ cohort and 1.17±0.59 log MAR in IVB cohort. The initial mean CST was 738.42±264.97 μm and 756.93±262.51 μm in IVZ and IVB, respectively. Baseline characteristics were well balanced between each treatment group. At the endpoint, no statistically significant difference was observed in both visual (mean difference in BCVA change 0.21 log MAR, 95% CI -0.29-0.7, p=0.389) and anatomical outcome (mean difference in CST change 64.53 μm, 95% CI -97.78-171.42, p=0.573) between 2 groups. Although the mean number of injections was less in IVZ group (4.5+1.3) than IVB group (4.8+1.3), there was no statistically significant (p=0.68). No sign of intraocular inflammation, increase lens opacity and IOP elevation and serious systemic adverse events were observed.

Conclusions: Interim results demonstrated that ziv-aflibercept had comparable visual and anatomical outcomes with bevacizumab for treatment of CRVO with ME at 6-months of follow-up. Ziv-aflibercept was safe and efficacious; therefore enrollment to 42 patients should be continued.

CONTROL ID: 3708004

SUBMITTER (NAME ONLY): Sarah Tan

TITLE: Novel Artificial Intelligence (AI) Choroidal Segmentation of Optical Coherence Tomography (OCT) Scans in Eyes with Pathologic Myopia

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.Y. Tan, D.A. Cahyo, D. Wong, C. Wong, L. Schmetterer, L. Foo, Singapore Eye Research Institute, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|C. Wong, Asia Pacific Eye Centre, Gleneagles Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To evaluate the performance of a novel AI algorithm for precise segmentation of the choroidal thickness in Optical Coherence Tomography (OCT) macular scans in eyes with pathologic myopia.

Methods: 91 pathological myopia eyes were acquired using a commercial swept-source OCT (SS-OCT) system, (PLEX Elite 9000, Carl Zeiss Meditec Inc., Dublin, CA, USA) at a 1050 nm wavelength, scanning speed of 100,000 A-scans/sec and 3 mm × 3 mm scanning protocol, centred at the macula. Manual segmentation of the retina and choroid on OCT images were used as the ground truth. We implemented a novel multi-task deep convolutional neural network architecture, Spatial Aggregated Networks (SA-Net), that reconstructs and segments a target B-scan with the incorporation of spatial context from neighbouring B-scans. Intersection over Union (IoU) of the volumetric segmentation, Dice coefficient and Structural Similarity Index Measure (SSIM) were used to assess performance.

Results: A total of 91 eyes with pathologic myopia were analysed with spherical equivalent of -7.00 ± 3.96 and axial length of 27.54 ± 1.30. Subjects were aged 51.07 ±13.02 with 64 (70.32%) females. 94.51% were Chinese, 4.40% were Malay and the remaining were Others. SA-Net was able to replicate segmentation of the anatomical layers of the retina and choroid on OCT images that was comparable to that of the manually segmented ground truths, with an IoU of 0.87 ± 0.09, Dice coefficient of 0.93 ± 0.05 and SSIM of 0.60 ± 0.18.

Conclusions: Our study demonstrated that the novel SA-Net approach showed a high accuracy in segmentation and delineation of choroid from volumetric OCT cube scans in eyes with pathologic myopia. The results are promising for the automated detection of the choroid and could be beneficial in further studies pertaining to the choroid in eyes with pathologic myopia.

CONTROL ID: 3708005

SUBMITTER (NAME ONLY): Huy Tran

TITLE: Myopia control efficacy of topical Caffeine alone and in combination with Atropine – Results from a prospective, longitudinal clinical trial- Part I

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.D. Tran, Y.H. Tran, T. Ha, Hai Yen Vision Institute, Ho Chi Minh City, VIET NAM|H.D. Tran, T.D. Tran, University of Medicine and Pharmacy Ho Chi Minh City, Ho Chi Minh City, VIET NAM|M. Coroneo, University of New South Wales, Sydney, New South Wales, AUSTRALIA|T.J. Naduvilath, P. Sankaridurg, University of New South Wales School of Optometry and Vision Science, Sydney, New South Wales, AUSTRALIA|T.J. Naduvilath, K. Philip, R. Weng, M. Jong, P. Sankaridurg, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine the role of topical Caffeine, a Xanthine derivative in slowing myopia either alone or in combination with Atropine.

Methods: In a prospective, randomized, dispensing clinical trial, 96 Vietnamese children with myopia (mean age 10.4 ± 2.0 years, -4.1±1.3D) were randomized to nightly use of either 2% Caffeine, 0.02% Atropine with 2% Caffeine, or 0.02% Atropine (Customcare Compounding Pharmacy, NSW, Australia). Additionally, 86 children with myopia (mean age 10.1 ± 2.1 years, -3.3±1.4D) were enrolled concurrently in a parallel group to wear single vision spectacles only. Cycloplegic autorefraction was conducted six monthly in addition to baseline using a Shin-Nippon NK5001 autorefractor. Axial length was assessed 3-monthly in addition to baseline using a Lenstar LS900. Comparison for change in cycloplegic spherical equivalent and axial length between groups was performed using a linear mixed model. Post-hoc multiple comparisons were conducted using Bonferroni corrections. Level of significance was set at 0.05%.

Results: All groups progressed in myopia. At twelve months, there was a significant difference in progression between the groups. Unadjusted change in spherical equivalent and axial length in the single vision spectacle lens group was -0.76D±0.51D/0.37±0.20mm. In comparison, change in spherical equivalent/axial length with 2% Caffeine, 0.02% Atropine with 2% Caffeine, or 0.02% Atropine was -0.70±0.55D/0.35 ±0.23mm, -0.47±0.38D/0.23 ±0.18mm and -0.46±0.50D/0.24 ±0.19mm, respectively. After adjusting for confounders, change in axial length was found to be significantly less with 0.02% Atropine ($p < 0.001$), and 0.02% Atropine with 2% Caffeine ($p=0.047$) in comparison to single vision spectacles and change in spherical equivalent was significantly less with 0.02% Atropine compared to spectacle lens wearers ($p=0.004$). The 12-month progression was similar between those randomized to 2% Caffeine and single vision spectacle wearers ($p=1.000$). The change in progression between 0.02% Atropine versus 2% Caffeine with 0.02% Atropine was similar ($p=1.000$).

Conclusions: When used in isolation, topical caffeine did not have an impact on progression of myopia. When combined with Atropine, it had no impact on the efficacy of Atropine in slowing myopia.

CONTROL ID: 3708006

SUBMITTER (NAME ONLY): Matteo Airaldi

TITLE: Automated segmentation of retinal nerve fiber layer excluding retinal blood vessels: integrating OCT and OCT Angiography.

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Airaldi, S. Bochicchio, A. Dipinto, G. Staurenghi, Eye Clinic, Department of Biomedical and Clinical Science "Luigi Sacco", Universita degli Studi di Milano, Milano, Lombardia, ITALY|J.D. Oakley, Voxeleron LLC, San Franscico, CA, USA, San Francisco, California, UNITED STATES|S. Prandoni, G. Triolo, Ophthalmic Hospital, ASST Fatebenefratelli-Sacco, Universita degli Studi di Milano, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: Peripapillary retinal blood vessels (RBVs) are currently segmented within the retinal nerve fiber layer (RNFL) in commercially available OCT segmentation software, contributing to automated calculation of RNFL thickness (std-RNFLT). In this cross-sectional clinical study we developed a fully automated segmentation algorithm capable of subtracting RBVs from RNFLT using OCT Angiography (OCT-A) scans of the optic nerve head (ONH), and we compared vessel-free RNFLT (vf-RNFLT) to std-RNFLT in order to evaluate the impact of RBVs on RNFLT.

Methods: ONH scans of 22 healthy eyes and 4 explicative glaucomatous eyes were analysed. After convolutional neural network-based RNFL and disc margin segmentation, an en face OCT-A image of the RNFL plexus was generated, enhanced and thresholded. Assuming vessels' tubularity, the RBV thickness in the axial direction was extrapolated from vessel pixels distance to the nearest non-vessel pixel. The contribution of RBV thickness was then subtracted from the std-RNFLT map to obtain vf-RNFLT. Std- and vf-RNFLT of healthy eyes were compared with t-test. The influence of covariates was analysed by a linear mixed-effects model (GLMM).

Results: In healthy subjects, average (Avg), superior (S), nasal (N), inferior (I), temporal (T) std-RNFLT and vf-RNFLT (all values in microns, mean±SD) were 111.6±25.1 vs. 104.1±21.7 ($p = .035$), 134.7±14.2 vs. 124.2±13.6 ($p = .016$), 82.9±11.3 vs. 78.2±10.5 ($p = .16$), 130±14.1 vs. 117±12.3 ($p = .002$), 98.7±11.7 vs. 96.9±12 ($p = .633$). The clock hour thickness analysis showed that clock hours 5, 7, 12 were significantly different (all $p < .05$). Peripapillary RBVs accounted for 6.3%, 7.8%, 5.6%, 10%, and 1.8%, of the Avg, S, N, I, T std-RNFLT in healthy eyes, and 9,8%, 15%, 9.4%, 12.7%, and 2.1% in glaucomatous eyes. GLMM showed no association of age, axial length and keratometry values with the difference in clock hour std- and vf-RNFLT.

Conclusions: Peripapillary RBVs account for a significant percentage of the RNFLT, if measured by commercially available OCT segmentation software. Our fully automated deep learning-based segmentation software excluding the RBVs, which are spared by glaucomatous damage, provides more accurate estimates of RNFLT, possibly improving OCT ability to detect early neural damage due to glaucoma.

CONTROL ID: 3708007

SUBMITTER (NAME ONLY): Alaa Fayed

TITLE: Retrospective analysis of the management outcomes of uveal melanomas at the new Cairo University ocular oncology service

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Fayed, A.M. Khattab, T.A. Macky, D.H. Hassanein, A.M. Abdullatif, S.H. Salah, A.M. Noureldine, Y.A. Helmy, M.R. Fadel, A.G. Elnahry, I.Y. Swaify, H. Hamza, Ophthalmology, Cairo University Kasr Alainy Faculty of Medicine, Cairo, EGYPT|

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ABSTRACT BODY:

Purpose: To investigate the demographic data & interventional clinical outcomes of patients presenting to the new Cairo University ocular oncology service with uveal melanomas.

Methods: This was a retrospective analysis of the medical records of patients managed for choroidal & ciliochoroidal melanomas. We reviewed the demographic data & different management modalities, compared the ultrasound measurements of the tumors before and after intervention and analyzed the complications & failure rates.

Results: 41 eyes of 41 patients were included. 30 eyes were managed with episcleral Ruthenium-106 plaque radiotherapy, or brachytherapy, of which four eyes were considered failures. One of the four eyes developed a rhegmatogenous retinal detachment & endophthalmitis necessitating pars plana vitrectomy that ended in exenteration due to extrascleral extension, while the remaining three eyes were enucleated due to progression in the tumor dimensions, demonstrating a failure rate of 13.3%. 10 of the remaining 11 eyes were enucleated based on the large baseline tumor size, while the eleventh eye showed extrasceleral extension necessitating exenteration. The mean age of the brachytherapy group was 56.4 +/- 12.1 years, while the enucleation & exenteration group was 50.2 +/-11.5 years ($p = 0.18$). Mean baseline dimensions for the brachytherapy group was 5.52 +/-2.1 mm height & 9.42 +/-3.2 mm diameter, while the enucleation group was 10.52 +/-3.49 mm height & 13.79 +/- 3.18 mm diameter. ($p < 0.001$ & < 0.01, respectively). For the brachytherapy group, the mean duration of plaque application was 7.02 +/- 4.06 days & the mean delivered radiation dose was 113.34 +/-5.3 Grey. Mean final sonographic follow up periods for the brachytherapy group was 26.4 +/- 16.16 weeks, with the mean height at 4.83 +/- 2.4 mm & base diameter at 8.12 +/- 3.36 mm. ($p = 0.24$ & 0.182, respectively). None of the patients demonstrated metastatic spread on serial Pan or PET/CT.

Conclusions: Timely referral & accurate clinical & investigative assessment of cases with uveal melanomas are invaluable for achieving higher success rates of tumor regression, as well as ocular and/or visual preservation in eyes managed with brachytherapy. Patients with more advanced tumors should be counseled on the importance of more invasive techniques, such as enucleation & exenteration for achieving lower malignancy dissemination & mortality rates.

CONTROL ID: 3708008

SUBMITTER (NAME ONLY): James Tribble

TITLE: Valproic acid reduces resident neuroinflammation and provides neuroprotection following retinal ganglion cell axotomy

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.R. Tribble, E. Kastanaki, A. Uslular, C. Rutigliani, T.J. Enz, P.A. Williams, Clinical Neuroscience, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: Neuroinflammation is an early and persistent feature of retinal pathophysiology. Understanding the interaction of retinal neurons and resident glia cells (microglia, astrocytes, and Müller glia) is important for identifying disease mechanisms and drug targets. Attributing neuroinflammatory events to resident or infiltrating immune cells is non-trivial since simple tools and models to separate these do not exist. Using a retinal explant model, where axotomy and maintenance of the retina ex vivo drives rapid retinal ganglion cell neurodegeneration, we assessed resident neuroinflammation

Methods: Retina from C57BL/6J mice were dissected and maintained as retinal explants for 0 (control) or 24 hrs. LPS (100 ng / mL) or Valproic acid (1 mM) were dissolved in the culture media. Retinal neuroinflammation was quantified by morphological and protein analysis. Fixed retinas were immunofluorescently labeled for RBPMS (retinal ganglion cells), IBA1 (microglia), and GFAP (astrocytes), imaged on a confocal microscope, and 3D morphology reconstructed using Imaris. Dissociated retinas were assessed for cytokine and chemokine expression by protein array (109 proteins)

Results: Twenty-four hours after axotomy, retinas displayed significantly altered microglia and astrocyte morphologies. The morphology of microglia processes was, on average, more contracted and voluminous, consistent with a shift towards inflammatory phenotypes. Astrocyte networks increased in filament density and connectivity. Key inflammatory cytokines were significantly upregulated (Ccl5, Cxcl10, Ccl2, Il-1α, Cxcl1, Icam-1). This is consistent with in vivo retinal ganglion cell injury. As a putative positive control, LPS (a known inflammatory activator), further retracted microglial morphology and further increased Ccl5, Cxcl10, and Il-12, but did not affect astrocyte morphology. Valproic acid provided neuroprotection, significantly reduced morphological changes of both microglia and astrocytes, and maintained Ccl5, Cxcl10, Ccl22, Il-12, Ccl2, and Cxcl1 at uninjured control levels

Conclusions: We demonstrate that the retinal explant model allows for the isolated study of resident glial neuroinflammation without the influence of the circulatory system. This model allows for rapid testing of compounds which may modify neuroinflammation and identifies Valproic acid as a drug which limits retinal neuroinflammation

CONTROL ID: 3708009

SUBMITTER (NAME ONLY): Francine Behar-Cohen

TITLE: Decorin for choroidal neovascularization fibrosis and epithelial-mesenchymal transition of retinal pigment epithelium

SESSION TITLE: Subretinal fibrosis – clinical challenges, mechanism, and diagnostic tools

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.F. Behar-Cohen, L. Benichou, M. Zhao, physiopathology of ocular diseases : therpaueitc innovations, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|F.F. Behar-Cohen, L. Debillon, OPhthalmopole, Assistance publique-hôpitaux de Paris, Paris, FRANCE|K. Bigot, T. Bordet, Eyevensys, Paris, FRANCE|

Commercial Relationships Disclosure: Francine Behar-Cohen: Commercial Relationship(s);Code P (Patent):Inserm-université de Paris | laura Benichou: Commercial Relationship: Code N (No Commercial Relationship) | Louis Debillon: Commercial Relationship: Code N (No Commercial Relationship) | Karine Bigot: Commercial Relationship(s);Code E (Employment):Eyevensys | Thierry Bordet: Commercial Relationship(s);Code E (Employment):Eyevensys | Min Zhao: Commercial Relationship(s);Code P (Patent):Inserm, Université de Paris

ABSTRACT BODY:

Purpose: Despite anti-VEGF, subretinal fibrosis and scar cause vision loss in wet AMD patients. Epithelial-mesenchymal transition (EMT) of retinal pigment epithelial (RPE) cells contributes to subretinal fibrosis. Decorin (DCN) is a proteoglycan with anti-fibrotic and anti-angiogenic properties. The aim of this study was to evaluate the effect of DCN on CNV fibrosis and EMT in a rat model of choroidal neovascularization (CNV)

Methods: Long-Evans rats with to laser-induced CNV were followed by fluorescein angiography (FA) on day 14 and 30. DCN (10µg/eye) or vehicle was injected in the vitreous, either at the time of laser burn, or at day 14, when CNV had developed. At day 30, rats were injected with intravenous FITC-dextran before sacrifice and RPE/ choroid flat-mounts were stained with collagen 1 and phalloidin. CNV volumes were quantified, morphometrics of RPE surrounding laser burns were quantified (size, shape, number of neighbors). In a separate experiment, rats with CNV were injected with DCN at 13 and they were sacrificed at day 16 for RNA seq analysis of RPE-choroid using Illumina HiSeq2000. Differential expression was analyzed using EASYGO threshold-free gene ontology.

Results: On FA, although leakge regressed similarly in both groups at day 30 (71% vs 65% of grade 0 lesions), the CNV volume was significantly reduced in rats treated with DCN at day 14 ($p<0.0001$). In addition to perivascular collagen 1 staining, a dense plug at the center of the impact could be seen. Day 14 DCN treatment significantly reduced perivascular collagen 1 ($p<0.001$) and limited the formation of collagen 1-positive scar at the center of the laser burns (31% of the lesions with central scar vs 62% in controls).

In control rats, at day 30, the RPE that surround the laser burn undergo EMT, with significant increase in RPE mean area and elongation. While no effect of DCN at day 14 was seen on EMT at day 30, normalization of RPE morphometrics was observed with DCN administration at the time of laser. RNA seq analysis showed that DCN significantly regulated pathway involved in angiogenesis, fibrosis, EMT, oxidative stress, inflammation and nerve maturation

Conclusions: DCN reduces the volume of established CNV and its fibrotic scaring. Early DCN treatment prevents EMT.

DCN is a promising candidate for wet AMD patients on top of anti-VEGFs therapies

CONTROL ID: 3708011

SUBMITTER (NAME ONLY): Amine Maamri

TITLE: Impact of relative graft size and decentration on the frequency of immune reactions after penetrating keratoplasty in 2160 eyes

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Maamri, N. Tischer, B. Seitz, E. Zemova, Ophthalmology, Universitatsklinikum des Saarlandes und Medizinische Fakultat der Universitat des Saarlandes, Homburg, Saarland, GERMANY|

Commercial Relationships Disclosure: Amine Maamri: Commercial Relationship: Code N (No Commercial Relationship) | Nicola Tischer: Commercial Relationship: Code N (No Commercial Relationship) | Berthold Seitz: Commercial Relationship: Code N (No Commercial Relationship) | Elena Zemova: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To analyze the impact of ratio of graft size to recipient corneal size and graft decentration on the frequency of endothelial immune reactions (IR) after penetrating keratoplasty (PKP).

Methods: We analyzed eleven years of our longitudinal PKP database at the Department of Ophthalmology in Homburg/Saar (2009-2019). This retrospective study included 2160 patients. Two types of IR were observed: acute diffuse or chronic focal endothelial reaction. The patient age ranged from 1 to 95 years. Microsoft Access and SPSS version 25 were used for statistical analysis and the corneal measurements were performed with ImageJ. With this software we measured the area of the graft and the host cornea as well as the distances between the interface and the limbus at four points (12, 3, 6 and 9 o'clock).

Results: A total of 203 (9.4%) patients presented with an IR (158 (7.1 %) acute diffuse and 50 (2.3 %) chronic focal). The IRs happened on average 14.9 months after PKP for acute diffuse IR and 15.3 months after PKP for chronic focal IR. There were no discernible differences between males and females. There was no significant correlation between donor age and frequency of IR. The smaller the size of the graft, the lower the likelihood of an IR ($p < 0.0001$). A significant correlation between centration from the graft and an IR was found: the smaller the distance between the graft and the limbus (at 12, 3, 6, and 9 o'clock), the higher the likelihood of an immune reaction ($p < 0.01$). Moreover, the strongest correlation appeared at the inferior limbus (6 o'clock) ($p < 0.0001$).

Conclusions: The monitoring in the second postoperative year after PKP should be intensified to detect an IR early. The bigger the size of the graft in relation to the host and the smaller the distance from the limbus, especially at 6 o'clock, the higher the likelihood of an immune reaction. Therefore, the graft size should be adjusted individually to the size of the host cornea. Further advanced methods (possibly intraoperative) for the limbal centration of the graft will be needed, in order to minimize future risk factors of immune response and to improve the postoperative outcome.

CONTROL ID: 3708021

SUBMITTER (NAME ONLY): Alessandro Arrigo

TITLE: Inner retinal involvement in retinitis pigmentosa: a quantitative integrated multimodal imaging approach.

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Arrigo, E. Aragona, M. Battaglia Parodi, F. Bandello, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: To investigate the involvement of the inner retina in retinitis pigmentosa (RP) and to assess the influence of each retinal structure on retinal sensitivity status through a quantitative multimodal imaging approach.

Methods: The study was designed as observational, prospective, involving a cohort of RP patients and healthy controls. Multimodal imaging protocol included fundus autofluorescence (FAF), optical coherence tomography (OCT), OCT angiography (OCTA) and microperimetry (MP). The follow-up was 12-months. We performed the overall quantitative analysis of each imaging modality, considering the most used metrics. We also performed a detailed investigation based on the ETDRS-9 sectors grid centered to the fovea. Quantitative parameters included the thickness of each retinal and choroidal layer, vessel density (VD), choriocapillaris porosity (CCP), FAF intensity and MP retinal sensitivity. The main outcome measure was the assessment of those retinal structures ruling the status of retinal sensitivity in RP.

Results: We included 40 eyes (40 patients) affected by RP and 40 healthy eyes (40 controls). Baseline BCVA was 0.14±0.18 LogMAR, resulting 0.18±0.24 LogMAR after 1-year of follow-up ($p>0.05$). RP eyes showed significnatly impaired retinal and choroidal layers on ETDRS-9 sectors grid, together with significant reduction of VD values and significantly higher CCP, with respect to controls (all $p<0.05$). MP retinal sensitivity and FAF intensity resulted significantly decreased in RP than controls. Inner retinal layers were found significantly related with the functional integrity of the posterior pole. In addition, the status of the outer retina, both considering vascular and non-vascular layers, less correlated with MP retinal sensitivity. FAF intensity showed no correlation with MP, whereas it was significantly associated with structural OCT and BCVA alterations. Our ROC analysis provided quantitative cutoffs significantly associated with partial sparing of MP retinal sensitivity.

Conclusions: Inner retina is strongly involved in RP and is more associated with the functional integrity of the posterior pole than the outer retina. Vascular involvement contributes to the morpho-functional deterioration of the macular region in RP. FAF intensity reduction may be interpreted as pigments loss associated with increased phototoxic distress for retinal structures.

CONTROL ID: 3708022

SUBMITTER (NAME ONLY): Nina Stallwitz

TITLE: A novel approach to analyze white noise ERGs in mice

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Stallwitz, A. Joachimsthaler, J.J. Kremers, Department of Ophthalmology, Section for Retinal Physiology, University Hospital Erlangen, Erlangen, Bayern, GERMANY|N. Stallwitz, A. Joachimsthaler, Biology, Section for Animal Physiology, Friedrich-Alexander-Universitat Erlangen-Nurnberg Naturwissenschaftliche Fakultat, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: To analyse the correlation between ERG response to temporal white noise (TWN) stimuli while modulating luminance or single photoreceptor types.

Methods: Mice, with human L-opsin instead of the murine M-opsin were dark adapted overnight, all further handling was done under dim red light. Recordings of the anesthetized animals were performed with the Celeris Ganzfeld stimulator. Measurements were performed at different mean luminances (MLs). The animals adapted to a new mean luminance for 1 min prior to recordings.

ERGs to TWN stimuli (containing all frequencies up to 20 Hz with equal amplitudes and random phases) were recorded. The stimuli were luminance modulation (100% contrast white light) at MLs ranging from −0.7 to 1.1 log cd/m^2. In addition, photoreceptor isolating stimuli using the silent substitution method (52% rod-contrast, 48% L-Cone contrast, 77% S-Cone contrast) were employed with MLs between −0.8 and 1.0 log cd/m^2.

Each recording was performed twice. To study the reproducibility of the recordings, ERG potentials in the two recordings at identical instances during stimulation were plotted against each other. The square of the correlation coefficient (r^2_{repr}) of the linear regression through the data quantified the correlation between the two.

To see how well preserved the distinct peaks of the wnERG were at different MLs, the ERG potentials at all MLs were plotted against those to the highest ML (for the cones) and at the lowest ML (for the rods) at identical instant during recording. The linear regressions and the r^2 (r^2_{ML}) were used to quantify the correlations between them.

Results: For luminance stimuli r^2_{repr} values decreased with increasing ML to −0.1 log cd/m^2 ML above which r_{2repr} increased. For rod isolating stimuli r^2_{repr} values decreased with increasing MLs; for cone isolating stimuli they were similar at all MLs.

R^2_{ML} values for luminance and L- and S-opsin stimuli increased with increasing ML, whereas they decreased for rods.

Conclusions: The differences between the characteristics of the r^2 values between rods and cones point at fundamental differences of the dynamics of the ERG origins. Origins of luminance ERGs are a mixture and depend on ML.

CONTROL ID: 3708025

SUBMITTER (NAME ONLY): Brian Gilger

TITLE: Topical peptide inhibitors of MARCKS reduce signs of dry eye in the alacrimal rat model

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.C. Gilger, J.H. Salmon, Clinical Sciences, NC State University, Raleigh, North Carolina, UNITED STATES|B.C. Gilger, Ophthalmology, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|K.B. Adler, Molecular Biological Sciences, NC State University, Raleigh, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Brian Gilger: Commercial Relationship(s);Code F (Financial Support):Biomarck, Inc | Jacklyn Salmon: Commercial Relationship: Code N (No Commercial Relationship) | Kenneth Adler: Commercial Relationship(s);Code I (Personal Financial Interest):BioMarck, Inc.;Code P (Patent):BioMarck, Inc.

ABSTRACT BODY:

Purpose: To determine if inhibition of Myristoylated Alanine Rich C Kinase Substrate (MARCKS) protein, using novel topical MARCKS inhibitor peptides, will reduce the severity of dry eye.

Methods: Dry eye was induced in the left eye of Sprague-Dawley rats by removal of the extraorbital lacrimal gland. One group of rats had a skin incision, but no lacrimal gland removal (sham group). Topical administration of test compounds was initiated 2 weeks after surgery, given 4 times a day and continued for 24 days. Sham rats (n=6) were untreated. Alacrimal rats (n=6 each) were dosed bilaterally with 10uL of phosphate buffered saline (PBS), or 100 uM of either of two MARCKS inhibitors: BIO-11006 [high molecular weight] or BIO-91201{lower molecular weight]. The efficacy of these MARCKS inhibitor peptides was assessed via clinical examination using biomicroscopy and phenol red test (PRT) tear volume with the observers masked to the treatments. Examinations were at baseline, 2 weeks after surgery, and on days 1, 3, 7, 14, 21, and 24 after initiating dosing. Clinical scores for corneal opacity, vascularization, and corneal fluorescein (FL) retention were recorded at each examination.

Results: Clinical signs of dry eye were observed 2 weeks after surgery in groups with lacrimal gland removal, but not in rats in the sham group. No clinical abnormalities were observed in the right eyes (non-surgical) of the rats throughout the study. Left eyes of rats in the sham group had significantly lower clinical scores and higher PRT values than the PBS-dosed group at each examination day after surgery. Corneal scores were significantly elevated in the PBS and BIO-11006 dosed groups compared to sham ($p<0.002$; pairwise Wilcoxon), but no difference between sham and BIO-91201 was observed. Similarly, BIO-91201 dosed groups had significantly lower FL retention than PBS or BIO-11006 dosed eyes ($p<0.02$) and through day 14, BIO-91201 FL retention scores were not significantly different than sham eyes. PRT was higher in MARCKs inhibitor-dosed groups compared to PBS groups on days 14, 21, and 24 after surgery ($p<0.02$; t test).

Conclusions: Topical MARCKS inhibitor peptides appear well tolerated and may reduce inflammation, corneal opacity, corneal FL retention, and improve tear production in dry eye. Further development of topical MARCKs inhibitors, especially the smaller peptide, BIO-91201, for treatment of dry eye appears warranted.

CONTROL ID: 3708027

SUBMITTER (NAME ONLY): Kristina Hess

TITLE: The functional impact of Low dose Vitamin A supplementation in AMD with and without reticular pseudodrusen

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hess, C.A. Cukras, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|K. Hess, Department of Ophthalmology, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|B. Jeffrey, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Kristina Hess: Commercial Relationship(s);Code R (Recipient):Novartis | Brett Jeffrey: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Cukras: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the functional impact of systemic Vitamin A supplementation in patients with intermediate age-related macular degeneration (iAMD) with and without reticular pseudodrusen (RPD) demonstrating dysfunction in dark adaptation (DA).

Methods: In this prospective non-randomized study, patients with iAMD were separated into a group without RPD (AMD group) and with RPD (RPD group). Assessments included DA, best-corrected visual acuity (BCVA), low luminance visual acuity (LLVA) and the low-luminance quality of life questionnaire (QoL). After a 30% bleach, DA testing was performed on 8 locations (4°,6°,8°, 12° in the sup. and inf. meridian). Rod-intercept time (RIT), steepness of the S2 slope, cone plateau, R-slope and pre-bleach thresholds of red and blue stimuli were analyzed.
After baseline examination, patients were supplemented with 15,000 IU of Vitamin A palmitate for 8 weeks. Follow-up examinations were at 4 and 8 weeks with a final follow-up 12 weeks, 4 weeks after cessation of Vitamin A supplementation.

Results: Five patients were enrolled in the AMD group (age 78.0±4.7 years) and seven in the RPD group (age 74.1±11.2 years). Baseline RIT was significantly lower in the AMD group (17.7 ± 6.5 min) compared to the RPD group (23.4 ± 10.9 min).
In the linear mixed model, RIT improved significantly in the AMD group (mean [IQR] -1.1 min [-1.8; -0.5] after 4 weeks and -2.2 min [-2.9; 1.6] after 8 weeks of Vitamin A supplementation, both $p<0.001$). 4 weeks after cessation, the RIT value was decreasing but a residual treatment effect was measurable (-0.99 min [-1.63; -0.35], $p=0.002$).
For the RPD group, no significant RIT improvement with supplementation was identified.
BCVA, LLVA and QoL were not significantly changed after 4 and 8 weeks of treatment.

Conclusions: Supplementation with 15,000 IU Vitamin A, a lower dose than used in previous studies, appears to improve this function in eyes with AMD but without RPD. This result supports a mechanism where a diseased Bruch's membrane serves as a barrier between the systemic circulation and the photoreceptors. Increases the systemic Vitamin A availability partially overcomes the barrier in less severely affected eyes, as evidenced by changes towards improved the DA.
This study was a pilot study, and it is not yet clear what the long-term effects of supplementation would be and if functional improvement could leads to a preservation of structure.

CONTROL ID: 3708028

SUBMITTER (NAME ONLY): Alfredo Dubra

TITLE: Automated correction of jitter, interleaving and non-uniform image sampling in scanning ophthalmoscopes

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Dubra, V. Akondi, A. Hargrave, B. Kowalski, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Alfredo Dubra: Commercial Relationship: Code N (No Commercial Relationship) | Vyas Akondi: Commercial Relationship: Code N (No Commercial Relationship) | Aubrey Hargrave: Commercial Relationship: Code N (No Commercial Relationship) | Bartlomiej Kowalski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Sampling jitter and non-uniform scanning angular velocity limit the accuracy and precision of scanning ophthalmoscopes. Here we explore the mitigation of these problems through the recording of the optical scanners' orientation in synchrony with the light detection, followed by resampling of retinal image.

Methods: Distortion grid and photoreceptor mosaic images were captured using a custom scanning light ophthalmoscope modified to record scanner orientation for each image pixel. The horizontal (resonant) scanner orientation samples were fitted to a cosine model for each image line to correct image warping and sampling jitter through image data resampling, as well as to interleave images collected during the clockwise and counterclockwise portions of the scanner rotation. This was followed by image warp correction due to non-uniform angular speed of the vertical scanner through a second image resampling. Jitter correction was evaluated using normalized cross-correlation within each line of images from a Ronchi ruling, and as the norm of standard deviation maps from a stack of co-registered retinal images.

Results: The fitting of the cosine models showed ~0.36 pix jitter (STD) which reduced jitter by more than a factor of 6 after resampling and allowed interleaving image lines captured during the counter-rotating portions of the horizontal scan cycle with sub-pixel precision. The norm of the standard deviation maps, a registration error metric, decreased by ~10-15% with jitter correction and ~16-20% with jitter and vertical warping correction in the distortion grid images. More modest ~1 and ~7% respective reductions were observed in a small set of photoreceptor images affected by eye rotation (not corrected by the registration).

Conclusions: The proposed jitter and warp correction in retinal images from scanning ophthalmoscopes can improve the sensitivity of retinal imaging biomarkers by producing more anatomically truthful images. In adaptive optics scanning ophthalmoscopes, these corrections can also help to reduce the number of images that is captured at each retinal location for subsequent averaging, necessary to increase signal to noise ratio (SNR), and a most important barrier to the translation of this technology to the clinic. This approach could also increase SNR in angiograms from optical coherence tomography.

CONTROL ID: 3708030

SUBMITTER (NAME ONLY): Chunxiao Sun

TITLE: Comparison of the surgical outcomes of ab interno trabeculotomy using Tanito microhook, suture, and Trabectome

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Sun, H.O. Ikeda, T. Hasegawa, S. Numa, K. Suda, M. Miyake, T. Kameda, A. Tsujikawa, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: This study compared the clinical outcomes between ab interno trabeculotomy using Tanito microhook (TMH), suture (sLOT), and Trabectome (TOM) and explored the most beneficial trabecular meshwork (TM) incision range.

Methods: A retrospective analysis of pre- and postoperative (up to 60 months) intraocular pressure (IOP), glaucoma medications, and complications was performed for patients with primary open angle glaucoma who underwent cataract extraction combined with ab interno trabeculotomy using TMH, sLOT, or TOM at Kyoto University Hospital between January 2016 and June 2021.

Results: The mean preoperative IOP was 18.8±4.4, 18.8±6.7 and 17.1±6.1 mmHg in TMH (58 eyes), sLOT (69 eyes), and TOM (29 eyes) groups, respectively (P=0.37). The mean IOP value and IOP reduction% were similar at all the study time points. The mean IOP was 13.6±2.3, 14.1±3.5, and 12.9±2.8 mmHg (P=0.19), and IOP reduction% was 24.7±18.6, 18.8±23.8, and 21.0±18.0 % (P=0.31) in TMH, sLOT, and TOM groups at postoperative 3-moth follow-up. IOP spike and hyphema occurred most often in the sLOT group (27.5%, 26.1%), followed by the TOM group (13.8%, 17.2%), and the least in TMH group (6.9%, 6.9%). In all three groups, patients with spike or hyphema did not undergo wider degrees of incision but achieved similar IOP reduction when compared with those without spike or hyphema. The use of anticoagulant and antiplatelet did not increase the risk of hyphema in each group. A correlation between TM incision degrees and IOP reduction was only found in the TMH group (P=0.0014) and not in the sLOT (P=0.31) and TOM (P=0.41) groups. After mixing all the data and reclassifying them by incision degrees into 1- to 4-quadrant groups, we found that the 2-quadrant group had the least incidence of hyphema (P=0.26) and spike (P=0.02), while the 3-quadrant group had the greatest IOP reduction% (P=0.02). Consistently, TM incision degree was a predicator of postoperative IOP reduction% in multiple linear regression analysis of patients within 270 degrees' incision (P=0.0002).

Conclusions: TMH, sLOT, and TOM trabeculotomy provided comparable IOP reduction efficacies, while hyphema and IOP spike were more frequent in the sLOT group. Hyphema and IOP spike did not result from wider TM incision degrees. Incision of 90–180° had the least incidence of complications, while a 180–270° incision conferred the greatest IOP reduction.

CONTROL ID: 3708031

SUBMITTER (NAME ONLY): Shruti Nishanth

TITLE: Accurate measurement of outdoor activities in children with myopia: Development of an affordable wearable device

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Nishanth, Department of Paediatric Ophthalmology, MN Eye Hospital Private Ltd, Chennai, Tamil Nadu, INDIA|K. Manoharan, Nissi Engineering solutions, INDIA|M. Srinivasan, V. S, Department of Optometry, MN Eye Hospital Private Ltd, Chennai, Tamil Nadu, INDIA|K. Govindasamy, The GenVams Trust, Chennai, INDIA|N. Bauer, T. Berendschot, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Sunlight exposure has been found to play an important role in myopia as a lifestyle modification factor. The purpose of this study was to evaluate the performance of an affordable wearable device for measurement of sunlight exposure in children and provide metrics through a dedicated mobile phone algorithm.

Methods: A wearable device LUMINO-SD (India Patent Application no:202141040647) was built that can measure sunlight in terms of light intensity (LI), ultraviolet (UV) and infrared (IR) through an ambient light sensor, and the captured data was synchronised to a mobile phone algorithm. The light data were programmed to be captured once every minute between 7 am to 7 pm and stored. Validation of the measurements was done by placing the device in sunlight alongside a standard luxometer (Lutron LX-101A, USA). Eight protomodel devices were lab tested by placing in the following locations for 1 week each: outdoor sunlight, outdoor shade, indoor near window, indoor with artificial illumination. Hourly readings from 8 devices were averaged, analysed and plotted on a 12 hour graph. Real time data captured over 1 month were incorporated into Python software to define the thresholds of outdoor sunlight exposure duration (60% training, 40% testing). No human beings were used in the study at this point.

Results: Hourly mean LI was found to range between 136 - 5344 lux indoors & 976 – 30,112 lux outdoors. There was statistically significant difference (p=0.046) between outdoor sunlight/outdoor shade and between indoor window/indoor artificial illumination(p=0.001). Hourly mean UV index ranged between 0-15 indoors and 2.5 - 64 in sunlight outdoors. Hourly mean IR was between 0-16 for indoors and 122-3764 for outdoors. The validation between luxometer and device was R^2= 0.786. Machine learning using Python was reliable to define outdoor time based on testing accuracy of 67%.

Conclusions: This prototype – LUMINO-SD provides reliable measurements on sunlight spectrum exposure of the wearer, based on real time data as thresholds. It could be a useful tool to study the correlation between sunlight, UV, IR and outdoor/indoor activities. It would be an effective tool for promoting outdoor time in kids and parental monitoring to manage the myopia epidemic in children worldwide. Because of the low cost manufacturing in India, the device would serve as an affordable one.

CONTROL ID: 3708033

SUBMITTER (NAME ONLY): Si Chen

TITLE: Toward blood flow quantification using spectrally extended line field optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chen, K. Lin, L. Liu, Nanyang Technological University, Singapore, Singapore, SINGAPORE|S. Lou, Tianjin University, Tianjin, Tianjin, CHINA|

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ABSTRACT BODY:

Purpose: Blood flow quantification with optical coherence tomography angiography (OCTA) is hindered by the limited dynamic range, which is determined by the B-scan interval time. Multiple interscan time is currently achieved by increasing the number of repeated B-scans at the same sample position. The purpose of this study is to evaluate the feasibility of a novel imaging platform, spectrally extended line field OCTA (SELF-OCTA), in realizing OCTA high dynamic range without increasing the number of B-scan repetitions or sacrificing field of view.

Methods: A 1060-nm spectral domain OCT system with a customized sample arm, SELF-OCTA, is developed for retinal angiographic imaging in vivo. OCTA images were acquired from the macular region in healthy subjects with two B-scan repetitions at each sample position.

Results: SELF-OCTA generated four sets of flow images with the interscan time of 0.54 ms, 1.35 ms, 2.70 ms, and 5.40 ms from one volume scan. These interscan times spanning the range of one order of magnitude enable blood flow quantification over a significantly extended dynamic range: slow flows in small vessels could be visualized with higher contrast, and also, fast flows in large vessels can be differentiated by their different OCTA signals.

Conclusions: SELF-OCTA has the capability to realize flow imaging with high dynamic range but without compromising the imaging speed or field of view, making it a promising tool for blood flow quantification. This technique may help with the understanding and the early detection of retinal disorders associated with blood flow impairment.

CONTROL ID: 3708034

SUBMITTER (NAME ONLY): Xue Bai

TITLE: The Neuroprotection Role of Sirtuin 1 Activator SRT2104 in Retinal Injury Induced by Acute Ocular Hypertention

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Bai, D. Ye, Y. Shi, Y. Feng, C. Hu, Y. Xu, J. Huang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Sirtuin 1 (Sirt1) is a histone deacetylase belonging to the sirtuin family which plays a key role in stress response pathways, apoptosis, and inflammation. It has been reported that Sirt1 expresses in normal ocular structures and plays neuroprotective role in various diseases including retinal degeneration. In this study, we intended to investigate the role of intravitreal administration of Sirt1 activator SRT2104 in retinal injury induced by acute ocular hypertention (AOH) and its underlying mechanisms.

Methods: Intraocular pressure (IOP) was elevated manometrically to 80 mmHg by instilling saline solution into the anterior chamber for 1 h in adult C57BL/6J mice. Intravitreal injection of SRT2104 (200 pmol, 2 μL) was administered immediately after the AOH model was constructed. Immunofluorescence was applied to detect retinal ganglion cells (RGCs) survival and apoptosis, leukocyte infiltration, glial cells activation and inflammation. The protein expression level of related inflammatory factors was observed by western blot. Optical coherence tomography (OCT) and Hematoxylin-eosin (HE) staining were performed to analyse retinal structure. Electroretinogram (ERG) was used to evaluate retinal function.

Results: The expression of SIRT1 significantly increased after SRT2104 treatment. SRT2104 treatment effectively recovered the inner retinal thickness loss indicated by OCT and HE staining ($p < 0.05$). Retinal function partly improved on average amplitude and latency of a-wave, b-wave, and oscillatory potentials in ERG analysis ($p < 0.05$). Furthermore, intravitreal administration of SRT2104 reduced the expression of cleaved-caspase 3, acetyl-p53 and acetyl-NF-κB, declined the levels of inflammatory factors (IL-1β, TNF-α, IL-8, CCL2), and decreased the number of $CD45^+$ leukocyte, activated $Iba1^+/CD68^+$ microglia and $GFAP^+/Vimentin^+$ astrocytes caused by AOH (all $p < 0.05$).

Conclusions: Our data suggested that intravitreal injection of SRT2104 effectively reduced retinal inflammation and protected RGCs from caspase 3 dependent apoptosis via inhibiting deacetylation dependent p53 and NF-κB pathway after AOH injury, and it is expected to be a potential therapeutic method for acute glaucoma.

CONTROL ID: 3708035

SUBMITTER (NAME ONLY): Andrew Carkeet

TITLE: Different pictogram vision charts give different slopes for psychometric functions, in preschool children.

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Carkeet, A. Johnson, S. Hopkins, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|A. Carkeet, A. Johnson, S. Hopkins, Centre for Vision and Eye Research, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Knowledge about the shape of the psychometric function for visual acuity charts allows for better modelling of vision testing and more efficient estimation of acuity thresholds. We assessed whether 4 commonly used monitor based chart systems gave different shaped psychometric functions for child participants.

Methods: Data were obtained from 22 children, aged between 38 and 71 months (mean 54), with acuity better than 0.32 logMAR on LEA or EVA testing. For each child acuity measurements were attempted twice on right and left eyes for each of 4 commercially produced pictogram charts, presented on LED monitors: VistaVision Visual Acuity Tester; Thomson Test Chart; Rodenstock Phoromat 2000; and Optos Smart Chart (optotype sets for each, Figure 1). Measurements were analyzed if the maximum correct on one line was 80% or more and the minimum correct on one line was 40% or less. Probit analysis was performed on each measurement's data set (logMAR units), with the upper asymptote set for a 1 % lapse rate and the lower asymptote based on the number of alternatives for each optotype set (Vista 25%, Thomson 12.5%,Rodenstock 16.7%,Optos 11.1%). For each measurement a threshold acuity was obtained and a Probit size (an indication of the flatness of the psychometric function). For each participant the acuity and Probit size were averaged across eyes and sessions (i.e.based on up to four measurements).

Results: Different charts yielded different shaped psychometric functions. Probit sizes differed for different charts, ($F_{3,39}=8.198$, $p<0.001$) averages being (from steepest to flattest): Thomson 0.05logMAR, SD0.024; Optos 0.10logMAR, SD0.04; Vista 0.13logMAR, SD0.05; Rodenstock 0.15logMAR, SD0.11. Acuity values also differed between chart types ($F_{3,39}=51$, $p<0.001$): averages Thomson-0.04 logMAR, SD0.12; Optos 0.08logMAR, SD0.12; Vista 0.13logMAR, SD0.08; Rodenstock 0.24logMAR, SD0.13.

Conclusions: The chart design with the smallest Probit values (Thomson) gives a similar shaped psychometric function to that obtained previously with letter charts in adults. Other charts give much flatter functions, indicating unreliable and inefficient acuity measurements. Optotype selection matters for pediatric acuity measurement.

CONTROL ID: 3708036

SUBMITTER (NAME ONLY): Ariel Gore

TITLE: Use of transgenic mice for in-vivo monitoring of corneal pathologies following chemical insult

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gore, R. Efrati, S. Atanelov, P. Glick, M. Cohen, H. Gutman, R. Gez, S. Dachir, V. Horwitz, Pharmacology, Israel Institute for Biological Research, Ness Ziona, Israel, ISRAEL|

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ABSTRACT BODY:

Purpose: The dynamic course of sulfur mustard (SM) induced ocular insult is characterized by an acute phase, which may be continued to a chronic phase or a quiescent period followed by a late pathology. Visually observing corneal morphological changes in living animals could greatly enhance our understanding of additional aspects of the insult and assist in developing treatments.

Methods: Chemical SM burn was induced in the right eyes of three transgenic mice strains: K15-GFP, VE-Cad-RFP and Thy1-YFP, by vapor exposure. General evaluation, cell infiltration, neovascularization (NV), innervation loss and stem cells (SC) depletion in the cornea were monitored in-vivo by stereomicroscopy up-to 8 weeks. Corneal whole-mount preparations were used to identify 360° structures, infiltrating cells and the decrease in the sub-basal nerve plexus (SNP). Histological evaluation was determined by using H&E, Masson-Trichrome and Periodic acid-Schiff staining.

Results: A 35 seconds exposure induced a mild ocular surface insult with minor mid stromal nerve fiber (MSNF) insult, moderate SNP changes presenting cell infiltration and reversible SC loss, mostly resolving at 4w post exposure. A 120 seconds exposure induced a moderate-severe ocular surface insult involving NV, with extensive MSNF and SNP loss, a wide $CD45^{+}$, $Iba1^{+}$ cell infiltration and irreversible SC depletion. NV, stromal inflammation and edema, epithelial structural changes and conjunctival goblet cells were identified in corneal histological sections, in correlation with the fluorescent stereoscope findings.

Conclusions: The results in this study demonstrate the potential use of transgenic mice as a powerful animal model for studying the SM induced insult and developing new therapies.

CONTROL ID: 3708037

SUBMITTER (NAME ONLY): LAN ZHANG

TITLE: Extracellular Matrix Protein Periostin Regulates Epithelial Mesenchymal Transition of Lens Epithelial Cells

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. ZHANG, D.W. Li, Zhongshan Ophthalmic Center, Sun Yat-sen University, CHINA|

Commercial Relationships Disclosure: LAN ZHANG: Commercial Relationship: Code N (No Commercial Relationship) | David Li: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Epithelial mesenchymal transition (EMT) of lens epithelial cells (LECs) is one of the most important pathogenic mechanisms in lens fibrotic disorders such as anterior subcapsular cataract (ASC) and posterior capsule opacification (PCO). We recently showed that AKT-EZH2-H3K27me3 axis regulates the activation of mesenchymal genes during lens fibrosis. In the present study, we demonstrated that an important extracellular matrix (ECM) gene POSTN plays an essential role in lens EMT.

Methods: All experiments were based on injury induced ASC mouse model and TGF β-induced EMT of human lens epithelial cells. Quantitative real-time PCR, Digital Droplet PCR, Western Blot, and whole-mount immunofluoresce were used to examine the differential EMT gene expression.

Results: The ECM protein coding gene POSTN was upregulated in TGFβ-induced EMT of human lens epithelial cells, and in the lens capsule of injury-induced ASC mouse model as well as human ASC patients. POSTN gene silencing led to attenuated expression of EMT marker genes in TGFβ-induced EMT of human lens epithelial cells, which can be partially rescued by AKT1 overexpression. Moreover, POSTN knockout using CRIPSR-Cas9 technology in mouse led to suppressed expression of EMT marker genes and ASC plaque formation after injury-induced ASC procedure.

Conclusions: The present study demonstrated that the ECM gene POSTN plays an important role in regulating lens fibrosis. Mechanistically, the TGFβ-AKT–EZH2-H3K27me3 signaling axis activates POSTN expression, and in turn, though the activation of Integrin-AKT signaling, Periostin, encoded by POSTN, controls the activation of mesenchymal genes in lens epithelial cells. Thereby, Periostin participates in a feed-forward EMT signaling cascade, contributing to lens fibrosis. Intervention of important activated ECM genes such as POSTN may present a novel strategy for the prevention of lens fibrosis diseases. Supported by NSFC#81970787, #82000876, #81770910, NSF-Guangdong Province and Guangzhou City Joint Program#20191515120014, ZOC-SKLO#3030901010110.

CONTROL ID: 3708042

SUBMITTER (NAME ONLY): Timur Gilmanshin

TITLE: Prevalence and Associations of Dry Eye Disease and Meibomian Gland Dysfunction in Russia. The Ural Eye and Medical Study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Gilmanshin, M. Bikbov, S. Panda-Jonas, G. Kazakbaeva, R. Zainullin, J. Jonas, Ufa Eye Research Institute, Ufa, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: To assess the prevalence of dry eye disease (DED) and Meibomian gland dysfunction (MGD) in a population in Russia.

Methods: The population-based Ural Eye and Medical Study was conducted in an urban and rural region in Bashkortostan/Russia and included 5,899 (80.5%) out of 7328 eligible persons, aged 40+ years. DED and MGD were assessed by Schirmer's test, slit-lamp based examination of the Meibomian glands, and an interview with DED-related questions.

Results: The study included 5153 (87.4%) individuals with DED and MGD assessments (mean age:58.5±10.5 years). Schirmer's test in the worse eye (mean:10.7±6.3mm) was ≤5 mm in 1098 participants (21.3%;95% confidence intervals (CI):20.2,22.4), and the mean subjective dry eye symptoms score was 1.37±1.82. MGD grade 1 (telangiectasia at the lid margin), grade 2 (plugged Meibomian gland orifices with translucent serous secretion when the lid margin was compressed), grade 3 (plugged Meibomian gland orifices with viscous or waxy white secretion when the lid margin was compressed), grade 4 (plugged Meibomian gland orifices and no secretion when the lid margin was compressed), or any grade in the worse eye was diagnosed in 901 (21.1%), 1161 (27.1%), 158 (3.7%), 32 (0.7%), and 2252 (52.6%;95%CI:51.1,54.1) eyes respectively. The prevalence of DED diagnosis #1, #2 and #3 (Schirmer's test ≤5 mm, and dry eye score ≥1, ≥2, and ≥3, respectively), #4 (dry eye score ≥1, Schirmer test ≤5 mm, MGD grade 1+), and #5 (dry eye score ≥1, Schirmer test ≤5 mm, MGD grade 2+) were 598/5142 (11.6%), 426/5153 (8.3%), 273/5142 (5.3%), 335/5142 (6.5%), and 186/5142 (3.6%), respectively. Higher DED prevalence (definition #4) was associated (multivariable analysis) with female sex (odds ratio (OR):1.71;95%CI:1.31,2.22; P<0.001), higher depression score (OR:1.04;95%CI:101,1.07; P=0.009), and higher prevalence of thyroid disease history (OR:1.63; 95%CI: 1.19, 2.24; P=0.006).

Conclusions: DED and MGD were common in this rural and urban population, and their prevalence was associated with female sex, thyroid disease, and depression.

CONTROL ID: 3708043

SUBMITTER (NAME ONLY): Ansu Ann John

TITLE: CORNEAL GRAFT REJECTIONS DUE TO COVID 19 INFECTION OR VACCINATIONS : A CASE SERIES

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ann John, H. Matalia, N. C, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: To report 4 cases of corneal graft rejections which occurred due to COVID19 infection or vaccination.

Methods: Case 1

A 24-year old woman presented with corneal scar in her right eye (due to a resolved microbial keratitis) for which she underwent optical penetrating keratoplasty (PK). The patient presented with hyperacute endothelial rejection 5 weeks later. She had epithelial and endothelial corneal graft rejection (Figure 1) for which she was treated with intravenous methylprednisolone, along with topical steroids prescribed hourly and systemic steroids. 3 days later, she was diagnosed with COVID 19 infection. In spite of adequate treatment, her corneal graft could not be salvaged.

Case 2

A 31-year old male who had history of chemical injury in the right eye in 2017, underwent second PK in 2020, and had graft rejection 4 weeks after 1st dose of COVID vaccine (COVISHIELD). He was successfully treated with hourly topical steroids along with systemic steroids and the corneal graft cleared up.

Case 3

Another 29-year old male diagnosed with Macular corneal dystrophy underwent corneal transplantation in 2016 had graft rejection following 1st dose of COVID vaccine (COVISHIELD) 3 weeks later. The patient was treated with topical and systemic steroids. Though most part of the graft cleared up but inferior graft edema was found to persist (Figure 2).

Case 4

A 17-year old girl, underwent PK for Congenital Hereditary Endothelial Dystrophy and had corneal graft rejection 1 month after the 2nd dose of COVID vaccine (COVISHIELD). With adequate treatment of topical and systemic steroids, the patient’s corneal graft improved and cleared up, and the patient reports an improvement in visual acuity as well.

Results: -

Conclusions: COVID 19 infection and vaccination can induce graft rejection. Hyperacute endothelial rejection is possible with COVID 19 infection. COVID vaccine related corneal graft rejections may be less severe and may be reversed with adequate treatment.

CONTROL ID: 3708044

SUBMITTER (NAME ONLY): Mohit Uppal

TITLE: A 10-Year Retrospective Analysis of the Specialties and Methods Involved in the Treatment of Eyelid Laceration

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Uppal, T. Murphy, Rush Medical College, Rush University, Chicago, Illinois, UNITED STATES|K. Williams, Department of Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Eyelid lacerations commonly present to academic institution emergency departments as a result of trauma or injury. While eyelid lacerations are often repaired by different medical specialties--despite varying levels of training requirements dictated by the Accreditation Council for Graduate Medical Education (ACGME)--no literature currently exists regarding the incidence of such repairs. We performed a retrospective chart analysis to determine the frequency of eyelid lacerations and respective treatment methods performed by different specialties.

Methods: The electronic health record was queried using International Classification of Disease codes to identify cases of eyelid laceration occurring between 2011 and 2020, determine the specialty involved in treatment, and the respective method of treatment at Rush University Medical Center, a Level II trauma center. The treatment method was classified into two categories: suture or non-suture repair.

Results: Of 468 total cases of eyelid laceration identified, 303 (64.74%) were treated by emergency medicine, 98 (20.94%) by ophthalmology, 27 (5.77%) by plastic surgery, 20 (4.27%) by primary care, 11 (2.35%) by pediatrics, and 9 (1.92%) by otolaryngology. Of these cases, 310 (66.24%) were treated using sutures. Suture-treatment occurred during 181 (59.74%) of emergency medicine's total cases, 86 (87.76%) of ophthalmology's total cases, 26 (96.30%) of plastic surgery's cases, 6 (30%) of primary care's cases, 3 (27.27%) of pediatrics' cases, and 8 (88.89%) of otolaryngology's cases. Year of presentation significantly affected the number of cases that ophthalmology treated, with cases increasing over time ($p=0.032$).

Conclusions: All specialties besides primary care and pediatrics utilized sutures during treatment in most cases. Although ophthalmology-involvement has increased throughout the years, ophthalmology was only involved in a minority of total eyelid laceration cases while emergency medicine was involved in most cases. According to the ACGME, only ophthalmology residents, opposed to residents of other specialties, are required to gain experience treating eyelid lacerations during their training. Despite this uniquely specialized training, ophthalmologist-involvement in eyelid laceration cases is relatively low compared to other specialties, warranting further studies to determine if differences in outcomes exist between specialties.

CONTROL ID: 3708045

SUBMITTER (NAME ONLY): Rohit Sharma

TITLE: 24 hour IOP diurnal variation analysis with contact lens sensor (triggerfish)-potential benefits, limitations & future challenges.

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sharma, Ophthalmology, university hospitals derby & burton NHS trust, UNITED KINGDOM|

Commercial Relationships Disclosure: Rohit Sharma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diurnal IOP variation is well-known. The exact pattern of circadian IOP fluctuation in glaucomatous patients remains debatable. This prospective observational study is to evaluate the 24-hour pattern of IOP changes in patients with glaucoma measured with a contact lens sensor (CLS) and to compare the variation between CLS and tonometry.

Methods:

The eyes of 24 glaucomatous patients (9 females, 15 males) were examined for diurnal IOP fluctuations for 24 hours with Sensimed Triggerfish® CLS while they carry out their normal activities. The 24-hour period was divided into eight 3-hour time slots (0000-0259, 0300-0559, 0600-0859, 0900-1159, 1200-1459, 1500-1759, 1800-2059, 2100-2359) and the peak and trough values of IOP with their corresponding time slots were recorded. The coefficient variation of mean average of peak and trough value of CLS data and mean average of IOP measured using Goldmann applanation tonometry (GAT) in clinics were compared.

Results:

All patients successfully completed the 24-hour measurement of IOP with CLS safely with no adverse reactions.
The mean patient age was 69.83 (SD: 7.8) years. 15 (62.5%) were left eyes.
13 subjects (54.1%) showed early morning peak.
12 (50%) subjects have their peak IOP at 0600-0859 period, mean peak value was 319.6 mVeq (SD: 174.6). 18 (75%) subjects have their trough IOP at 2100-2359 period, mean trough value was -113.3 mVeq (SD: 123.1). The mean peak and trough average of CLS data was 216.4 mVeq (SD: 77.6) whilst the mean average of IOP value was 16.6 mmHg (SD: 3.02). The coefficient of variation of CLS value was 35.9%. The coefficient of variation of IOP measured by GAT was 18.2%.

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Conclusions:

The most common circadian IOP pattern was early morning acrophase. Most glaucomatous patients had highest IOP in the morning which coincides with the circadian cortisol peak. These peaks can be missed by the contemporary practice of IOP measurement during daytime clinic hours. The coefficient variation of CLS value was higher than the IOP in daytime IOP clinic measurements. The impact of dimensional corneal curvature change and the standardisation of units of measurement by GAT & CLS needs evaluation. CLS has the potential of supplementing or replacing phasing, better study the therapeutic 24 hour response to medications, laser, surgery & analyse "low" or "normal" pressure glaucoma cases.

CONTROL ID: 3708048

SUBMITTER (NAME ONLY): Aarya Ramprasad

TITLE: The Risk of Thermal Dermal Damage in Cataract Phacoemulsification

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ramprasad, F. Qureshi, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|W. White, Ophthalmology, The University of Kansas Hospital, Prairie Village, Kansas, UNITED STATES|

Commercial Relationships Disclosure: Aarya Ramprasad: Commercial Relationship: Code N (No Commercial Relationship) | Fahad Qureshi: Commercial Relationship: Code N (No Commercial Relationship) | William White: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Modern cataract surgery relies on a phacoemulsification handpiece to disassemble cataracts. The handpiece can generate excessive heat leading to corneal burns which are prevented by using irrigation. The occurrence of burns outside of the eye is not well documented. This study aimed to determine whether the handpiece could cause thermal injury to patients outside the eye and if the device is able to ignite drapes.

Methods: Porcine skin was used due to its physiological similarity to human skin. 3 trials were completed to assess the possibility and speed of char occurring with the handpiece tip being in contact with different materials including the tip directly on a pig foot with no drape, a Henry Schein standard drape, and a 3M plastic Steri-Drape. Trials were performed with the silicone cover on the tip and without. Each trial was repeated 3 times with no statistically significant difference between trials of the same material ($P<0.05$). The Infiniti Vision System by Alcon Labs was used.

Results: With no drape, the tip without sleeve caused char within 3.0 seconds while with sleeve caused char at 10.0 seconds or above(Figure 1). Trials with the standard drape did not cause char but did burn a hole through the drape regardless of the sleeve. The tip with the sleeve burnt through the plastic drape, charring in 2.7 seconds, while no sleeve led to the same result in less than 1.0 seconds(Figure 2). In all trials, charring was quicker without the silicone sleeve. No trials resulted in drape ignition.

Conclusions: Charred skin is considered to be a 3rd-degree full-thickness burn with less severe burns possibly not being visible. One trial showed the body of the handpiece at 53.6°C degrees with immediate destruction of the epidermis known to occur above 44°C. The silicone tip proved to be protective but not effective in preventing burns. The trials were not completed in an oxygen-enriched environment. Increased risk of burn is present in true operating conditions due to the risk of ignition of the oxygen provided beneath the drape or via nasal cannula leading to the possibility of facial, airway, or nasal burns. While beneficial to consider in future studies, it did not prevent us from concluding that focused efforts on using the silicon tip, irrigation, and placing the phacoemulsification handpiece on a surface other than the patient could prevent burns from occurring.

CONTROL ID: 3708050

SUBMITTER (NAME ONLY): Gustavo Ortiz

TITLE: IL-6 drives Treg dysfunction in desiccating stress-induced dry eye disease

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ortiz, F. Kahale, T. Blanco, A. Naderi, Y. Chen, R. Dana, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have demonstrated that T regulatory cells (Tregs) become dysfunctional during dry eye disease (DED) being less able to control pathogenic Th17 cells. Th17-associated cytokines (IL-6, IL-17, IL-23) are implicated in altering Treg function; however, the precise functions of these cytokines on Treg in DED have remained unclear.

Methods: Using a controlled environmental chamber, female C57BL/6 mice were exposed to desiccating stress (relative humidity 10% vs. ~40% normal environment) to induce DED. Western blot of IL-6R, IL-17RA, IL-23R was performed on isolated Tregs (using magnetic activated sorting) from naïve and DED animals. Mean Fluorescent Intensity (MFI) of FoxP3, CD25, CTLA-4 and GITR of naïve and DED Tregs was measured using flow cytometry. Isolated naïve Tregs were in vitro stimulated with 20 ng/ml of IL-6, IL-17A and 30 ng/ml of IL-23 separately for 24 and 72hs. MFIs of IL-6R, IL-17RA, IL-23R, FoxP3, CD25, CTLA-4 and GITR were analysed. The cytokine-stimulated Tregs were then co-cultured with in vitro differentiated Th17 cells for 72hs. Treg suppression assay was calculated as % of inhibition of Th17 cells by flow cytometry. IL-10 and TGFβ1 supernatant levels (in Treg-Th17 co-culture) were quantified by ELISA.

Results: DED Tregs expressed higher levels of cytokine receptors IL-6R ($p=0.004$), IL-17RA ($p<0.001$), IL-23R ($p=0.002$) and lower levels of FoxP3 ($p<0.001$), CD25 ($p=0.013$) and CTLA-4 ($p=0.022$) as compared to naïve Tregs. Culturing Tregs with each of the three Th17-associated cytokines all led to a significant decrease in FoxP3 ($p<0.01$), CD25 ($p<0.05$) and CTLA-4 ($p<0.05$) expression. Conversely, IL-6 and IL-17 enhanced expression of IL-6R ($p<0.001$ for both), IL-17RA ($p<0.05$ for both), IL-23R ($p<0.001$ for IL-6; $p<0.05$ for IL-17). The suppressive function on Th17 by cytokine-stimulated Tregs was reduced with IL-6 being the most potent at rendering Tregs dysfunctional (31.2 ± 4.2% vs. 63.4 ± 2.3% naïve; $p=0.043$). IL-6-stimulated Tregs produced significantly less IL-10 (79.6 ± 6.5 pg/ml) as compared to unstimulated Tregs (198.6 ± 19.4; $p<0.001$).

Conclusions: These results suggest that IL-6 is the most potent cytokine that drives Treg dysfunction in DED, and thus can be a promising therapeutic target for restoring Treg function and reducing disease severity.

CONTROL ID: 3708051

SUBMITTER (NAME ONLY): Juana Gallar

TITLE: Thalamic and somatosensory cortex neurons innervating the ocular surface are multimodal

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gallar, E. Velasco, M. Acosta, Instituto de Neurociencias, Universidad Miguel Hernandez-CSIC, San Juan de Alicante, Alicante, SPAIN|J. Gallar, Grupo 1. Neurociencias, Instituto de Investigacion Sanitaria y Biomedica de Alicante, Alicante, Comunidad Valenciana, SPAIN|M. Zaforas, J. Aguilar, Laboratorio de Neurofisiología Experimental y Circuitos Neuronales, Fundacion del Hospital Nacional de Paraplejicos para la Investigacion y la Integracion, Toledo, Castilla-La Mancha, SPAIN|

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ABSTRACT BODY:

Purpose: Activation of sensory nerves innervating the ocular surface (OS) by mechanical and thermal stimuli does not generates tactile and pure thermal sensations but rather evokes sensations referred as dryness, freshness, gritty eyes, discomfort or pain. Central circuits involved in OS sensitivity are still largely unknown. Here we describe the activity of thalamic and somatosensory cortex neurons responding to OS stimulation, analyzing the processing of OS sensory input at higher levels of the CNS.

Methods: In the anesthetized rat, the spontaneous and stimulus-evoked activity of 49 trigeminal ganglion (TG) neurons, 69 somatosensory thalamus (Th) neurons and 101 primary somatosensory cortex (S1) neurons conveying OS information was recorded extracellularly using tungsten electrodes. Stimulation was performed by topical application of saline drops at different temperatures, producing five types of thermal stimulus: intense cooling, mild cooling, neutral, warming, and noxious heating. Neurons were classified into various functional types depending on their response to one or more of the different types of applied stimuli.

Results: Neurons responding to OS stimulation were found in precise locations of Th and S1, spatially grouped depending on their functional type. They encoded the type and intensity of the applied stimulus as the magnitude and temporal components of the firing response. Neurons responding to only one or to two types of stimulus (modality-specific neurons) were found in the TG while Th and S1 neurons responded to multiple types of stimulus (multimodal neurons). Furthermore, in Th and S1 there were more functional types of neurons than in TG. In S1 and Th neurons, noxious and innocuous stimulation evoked responses with different time course, the noxious ones being long lasting.

Conclusions: Thalamic and cortical representation of the OS is functionally reported. While ocular trigeminal neurons are quite selective, being activated most of them by 1-2 types of stimulus, Th and S1 OS neurons process information originated by multiple types of stimulus, suggesting divergence and convergence of ocular sensory information along the somatosensory pathway. This central convergence of information on different types of stimulus does not occur in other territories innervated by the trigeminal nerve, and would explain the diverse and unique sensations evoked at the ocular surface.

CONTROL ID: 3708052

SUBMITTER (NAME ONLY): Muhammad Ali

TITLE: The association of social determinants of health with cataracts in the U.S.

SESSION TITLE: Refractive Error and Social Determinants of Vision Function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Ali, A. Awidi, J. Wang, V. Varadaraj, C. Cai, D. Srikumaran, P.Y. Ramulu, A. Sommer, F. Woreta, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Social determinants of health (SDOH) are factors defining an individual's social environment that impact eye care and vision outcomes. We used nationally representative data from the National Health Interview Survey (NHIS) to investigate the association of person-level SDOH, including gender, race/ethnicity, level of education, economic stability, employment, and access to healthcare with cataracts in the U.S.

Methods: Sociodemographic and health data for adults aged ≥18 years was extracted from NHIS cycles 2008, 2016, and 2017. Participants were asked if they had ever been diagnosed with cataracts and whether they had undergone cataract surgery. Multivariable logistic regression analysis, adjusted for age, was used to assess the association between SDOH variables and self-reported cataract diagnosis and surgery.

Results: Of the total 81,551 participants, 44,950 (55.12%) were females. 13,453 (16.50%) reported a diagnosis of cataracts, of which 8,012 (59.56%) had undergone cataract surgery. Americans who were unemployed or retired were more likely to report cataracts than working individuals (OR, 1.63; 95% CI, 1.50-1.77). They were also more likely to undergo cataract surgery (OR, 1.39; 95% CI, 1.22-1.58). Individuals who delayed any type of medical care because they could not get an appointment soon enough were more likely to report cataracts than those who had no issues obtaining appointments on time (OR, 1.29; 95% CI, 1.14-1.46). They were also less likely to have undergone cataract surgery (OR, 0.81; CI, 0.68-0.98). Individuals who reported their health status as excellent, very good, or good were less likely to report cataracts than those who reported fair or poor health (OR, 0.76; 95% CI, 0.70-0.82) with no significant difference in odds of undergoing cataract surgery. Compared with Whites, Blacks (OR, 0.68; 95% CI, 0.61-0.77), and Hispanics (OR, 0.63; 95% CI, 0.54-0.72) were less likely to self-report a diagnosis of cataract. Blacks were also less likely to have undergone cataract surgery (OR, 0.76; 95% CI, 0.63-0.91).

Conclusions: Unemployed or retired status, difficulty accessing care, and fair or poor health status were significantly associated with higher odds of reporting cataracts. Future research regarding the impact of SDOH and vision loss from cataracts in terms of its severity, bilaterality, and access to surgery are warranted to address avoidable health disparities.

CONTROL ID: 3708053

SUBMITTER (NAME ONLY): Leo Hahn

TITLE: The evolution and spectrum of structural changes in X-linked retinoschisis on retinal imaging

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Thorough knowledge of structural changes in inherited retinal dystrophies and their correlation with visual function is crucial for optimal insight into clinical disease course, prognosis, and the selection of suitable candidates as well as endpoints for the therapeutic interventions. This study aims to investigate the evolution of pathological changes on imaging in X-linked retinoschisis (XLRS) patients, and assesses potential correlations with visual acuity and genotype.

Methods: This multicenter, retrospective study collected fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (SD-OCT) images from medical records of XLRS patients. The location of cystoid spaces, foveal volume, foveal thickness was evaluated on SD-OCT. The foveal cystoid space area was measured by adding up the areas of foveal cystoid spaces in the central b-scan on SD-OCT using a novel semi-automated algorithm developed in MeVisLab.

Results: In total, 75 affected males from 43 presumably unrelated families were included. Longitudinal imaging was available in 52 patients, with a mean follow-up time of 4.1±2.2 years, and a mean number of 3.2±1.5 visits. The mean age at last visit was 28.5±9.3 years. The mean foveal cystoid space area, foveal thickness and foveal volume had a significant correlation with age ($R=-0.33$, $R=-0.28$, $R=-0.42$, respectively; all $P<0.001$), but no correlation with visual acuity ($P=0.524$, $P=0.496$ and $P=0.613$, respectively). These parameters also did not differ significantly between patients with truncating and non-truncating variants in the RS1 gene ($P=0.867$, $P=0.672$ and $P=0.785$, respectively). In 65/75 (86.6%) of the patients, the cystoid spaces were located in the inner nuclear layer, in 34/75 (45.3%) in the outer nuclear layer and in 19/75 (25.3%) in the ganglion cell layer. On FAF, 10/75 (13.3%) patients had a normal-appearing macula, 31/75(41.3%) showed spoke wheel pattern, 14/75 (18.6%) showed central hyperautofluorescence, and 20/75 (26.6%) showed central hypo-autofluorescence.

Conclusions: The foveal cystoid space area as well as the foveal volume and foveal thickness, decreased slowly with increasing age in XLRS, but did not correlate with visual acuity or genotype. Phenotypes remained relatively stable during follow-up. The developed method of measuring foveal cystoid space area may be useful in future studies of retinal dystrophies with central cystoid fluid collections.

CONTROL ID: 3708054

SUBMITTER (NAME ONLY): Jose-Carlos Pastor

TITLE: Safety of intravitreal allogeneic mesenchymal stem cells for Acute Non-Arteritic Optic Neuropathy. Pilot study

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To comunicate the results after 6 months of follow-up of a pilot clinical trial (CT), carried out in five patients, with Non-Arteritic Optic Neuropathy, in its acute phase, who received an intravitreal injection of allogeneic bone-marrow derived mesenchymal stem cells (MSV®-allo) during the first 15 days after acute event.

Methods: Prospective, non-randomized, phase I-IIa CT. (Eudra number 2016-003029-40 and Clinical Trial Registry NCT03173638). After verifying the inclusion criteria (patients ≧ 50 years old, with a vissual acuity less than 0,4 and at least two of the following characteristics: sudden and painless loss of monocular vision; optic nerve head edema; clear relative afferent pupillary defect and without evidence of giant cell arteritis through medical history, erythrocyte sedimentation rate, C-reactive protein)and exclusion criteria, and having signed the informed consent, patients received an intravitreal injection of 0.05 ml containing 150 µl of isotonic medium composed of Ringer-lactate + 0.5% human albumin + 5 mM glucose with a cell concentration of $1.5x10^{6}$ cells / ml with a 25G needle via pars plana after topical anesthesia. Patients were followed at days 1, 7, 30, 90 and 180 after injection. Best corrected visual acuity, anterior and posterior pole examination searching for inflammatory signs. Pattern Reversal Visual Evoked Potential (PRVEP) and Flash Visual Evoked Potential (FVEP) and retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness was assessed using a Spectral domain optical coherence tomograph (OCT).

Results: One patient developed an epiretinal membrane. Another one showed a retrolental aggregate that was not complicated with cataract progression. No signs of intraocular inflammation were detected in any patient. Most of them showed a clear visual improvement and all patients presented increase in the P2 amplitude on the FVEP. OCT results (RNFL and GCL thickness) showed a significant decrease in agreement with the visible papillary atrophy developed during the follow up.

Conclusions: Despite the appearance of an epiretinal membrane in one patient and a possible cellular deposit in retrolental space, the functional results are encouraging for further studies.

CONTROL ID: 3708055

SUBMITTER (NAME ONLY): Sanjay Patel

TITLE: Ten-Year Changes in Vision, Refractive Error, and Corneal Thickness after Descemet stripping endothelial keratoplasty for Fuchs Endothelial Corneal Dystrophy.

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.V. Patel, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine changes in best-corrected visual acuity (BCVA), refractive error, and central corneal thickness (CCT) during the first decade after Descemet stripping endothelial keratoplasty (DSEK).

Methods: Medical records of all consecutive eyes (including the learning curve) undergoing DSEK for Fuchs endothelial corneal dystrophy (FECD) by one surgeon were reviewed and eyes with comorbidities prior to DSEK, except for cataract, were excluded. DSEK was performed through a 4.5-6 mm temporal scleral tunnel and all eyes were pseudophakic postoperatively. Postoperative changes in BCVA, spherical equivalent refractive error, refractive cylinder (vector analysis), and CCT, were assessed by using generalized estimating equation models (paired analyses). Postoperative data were excluded if new comorbidities affected vision or CCT.

Results: Of 130 eyes (81 subjects) undergoing DSEK for FECD, 34 eyes were excluded because of preoperative comorbidities. BCVA improved between 6 months (0.18 ± 0.12 logMAR; Snellen equivalent, 20/30) and 5 years (0.10 ± 0.10 logMAR; 20/25; n=74, p<0.001) and then remained stable at 10 years (0.09 ± 0.10 logMAR, n=48, p=0.22 vs. 5 years). There was a myopic shift of -0.20 ± 0.51 D between 6 months and 5 years (n=60, p=0.002) that remained stable at 10 years (-0.09 ± 0.44 D; 20/25; n=33, p=0.33 vs. 5 years). Refractive cylinder drifted with-the-rule between 6 months and 5 years (0.76 D axis 075; n=65, p<0.001) and between 5 and 10 years (0.75 D axis 082; n=34, p<0.001). CCT was stable between 6 months (672 ± 57 µm) and 5 years (677 ± 55 µm, n=63, p=0.47), but increased at 10 years (702 ± 60 µm, n=39, p=0.001). The change in BCVA was not correlated with the change in CCT during either interval (p≥0.74).

Conclusions: After DSEK for FECD, BCVA improves through 5 years and remains stable thereafter in functioning grafts. Changes in BCVA are not associated with changes in CCT. Increasing with-the-rule astigmatism after DSEK might be related to late changes in the temporal incision.

CONTROL ID: 3708057

SUBMITTER (NAME ONLY): Veshesh Patel

TITLE: Intraocular Lens Exchange: Indications and Outcomes at a Tertiary Referral Center

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Patel, J. Lai, A. Watane, D. Mehra, T. Eatz, N. Patel, N. Yannuzzi, J. Sridhar, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|N. Patel, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Currently, the method of intraocular lens (IOL) exchange and choice of lens currently largely rests on surgeon preferences. The purpose of the current study was to analyze the indications, outcomes, and complications of IOL exchanges among a variety of techniques and IOL models at a tertiary ophthalmic referral center.

Methods: Patients at Bascom Palmer Eye Institute that underwent IOL exchange recorded between May 1, 2014 to August 31, 2020 were included. Demographic, clinical, and surgical data were collected, as well as information regarding the IOLs employed.

Results: IOL exchange was identified in 513 eyes of 490 patients. The mean best corrected visual acuity (BCVA) in logarithm of the minimum angle of resolution (logMAR) prior to IOL exchange was 0.695 ± 0.685 (Snellen: 20/99). The most common precipitating reasons for exchange were IOL dislocation (n=285, 46.6%), subluxation (n=52, 8.5%), uveitis-glaucoma-hyphema (UGH) (n=35, 5.7%), broken haptic (n=22, 3.6%), refraction error (n=20, 3.3%), and corneal edema (n=18, 3.0%). The most common lenses used for IOL exchange were Alcon MA60AC (n=116, 22.6%), Alcon MTA3/4/5UO (n=113, 22.0%), Akreos AO60 (n=88, 17.2%), ABBOTT Tecnis PCB00 (n=37, 7.2%), and Alcon MA50BM (n=37, 7.2%). The most frequent complications following IOL exchange were cystoid macular edema (n=38, 11.2%), corneal edema (n=36, 10.1%), elevated intraocular pressure (n=27, 7.9%), and epiretinal membrane (n=22, 6.5%). 14 out of the 21 reoperations following IOL exchange were indicated for a repeat exchange, most commonly due to dislocation (n=9, 64.3%), vitreous hemorrhage (n=3, 21.4%), UGH (n=1, 7.1%), subluxation (n=1, 7.1%), corneal edema (n=1, 7.1%), ruptured globe (n=1, 7.1%), dysphotopsia (n=1, 7.1%), and Weill-Marchesani syndrome (n=1, 7.1%).

Conclusions: In conclusion, lens dislocations were the most common indications for IOL exchange. Certain lens models were also associated with complications, including Akreos AO60 with corneal edema, Alcon MTA3/4/5UO and Akreos AO60 with cystoid macular edema, and ABBOTT Tecnis PCB00 with posterior chamber opacification. While the these complications may also be explained by a patient's ocular history, surgeons may use these findings to guide IOL selection in the setting of IOL exchange.

CONTROL ID: 3708059

SUBMITTER (NAME ONLY): Jingyuan Yang

TITLE: Diagnostic performance of deep learning for multiple retinal diseases based on wide-field fundus photographs of true color

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep learning (DL) technology in recent studies has shown that automated screening, assisted diagnosis, and grading of retinal diseases using conventional fundus photographs (FPs) of about 50° view angle are efficient in saving workforce and time. Compared to conventional FPs, wide-field (WF) images of true color can provide wider view with sufficient resolution, which might further improve the efficiency of screening and DL models, but have not been investigated. Therefore, we investigated the diagnostic performance of DL models for 8 common retinal conditions using fundus photographs captured using Zeiss Clarus 500, by adapting conventional FP models into WF images.

Methods: We retrospectively analyzed 474 WF images from 197 consecutive volunteers with retinal conditions, including healthy condition, pathologic myopia, macular abnormalities, retinal vein occlusion, retinal detachment, diabetic retinopathy, after laser photocoagulation treatment, and other abnormalities, which were diagnosed by a panel of retinal specialists. An image could be diagnosed with multiple conditions simultaneously. 258 images without any annotations were used to adjust DL models, and the other 216 images with annotations were used to test the models (Table 1).

Considering that WF images show similar appearance in lesions and structures with conventional FPs, we have tried 3 different methods. A model pre-trained on conventional FPs was used to classify whole WF images, and splitted images from WF images, respectively. We also develop a novel method, Global-Local Consistency (GLC), to reach similar diagnostic result between whole and splitted WF images (Figure).

Results: The GLC method was identified as the best diagnostic method for WF images with the highest mean AUC (area under the curve value, 0.8735 vs 0.8541-0.8613). This method was superior to previous models in all conditions except health conditions and retinal vein occlusion (Table 2).

Conclusions: GLC method showed better diagnostic performance for common retinal conditions in this pilot study, even training with a relatively small sample size. Benefit from the similarity between the intrinsic feature of true color of Clarus images and CFPs, model pre-trained on CFPs can be directly used to predict WF images. Our GLC method combining with Clarus facilities might help improve the process of screening retinal diseases.

CONTROL ID: 3708060

SUBMITTER (NAME ONLY): Lejin Wang

TITLE: An artificial intelligence platform for the surgical planning of intermittent exotropia

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Intermittent exotropia (IXT) is the most common type of exotropia, and can lead to abnormal visual function. The success rate of surgical interventions for IXT varies from 42%–63% . The factors involved in the surgical strategy in cases of strabismus are complex, demanding both theoretical knowledge and experience from the surgeon. This study aims to develop a artificial intelligence (AI) strabismus surgery design platform to provide proper surgical advice.

Methods: An AI platform with deep learning (DL) system for operation planning was trained and retrospectively validated using a retrospective development data set. We collected 1076 IXT patients who achieved successful surgical outcomes from September,2015 to November,2020 in Peking University People's Hospital. The following information was recorded including: age; IXT type; Visual Acuity (VA); refraction result; measurement of the deviation in the primary gaze at near and distance; eye dominance; the measurement of versions and ductions. We also collected the surgical parameter including the millimeters of resection of medial rectus and recession of lateral rectus. Wasserstein Generative Adversarial Network with gradient penalty (WGAN-GP) model with was used to enlarge the training dataset, and we conducted Light Gradient Boosting Machine (LightGBM) to test the accuracy rate.

Results: We random selected 80% of the original data as the training set, and 10% of the data are as the test set, and the other 10% as the validation set. Through the step of data enhancement using WAGN-GP model, there were 0.3 million medical records could be automatically generated. DL advice system was trained by these enhancement records. Tested by LightGBM, the accuracy of the AI platform, comparing to the real design, could reach to 84.52%.

Conclusions: Our AI platform can provide reliable references for strabismus surgical planning.

CONTROL ID: 3708061

SUBMITTER (NAME ONLY): Sanil Joseph

TITLE: A Delivery Model for Telemedicine-based Eye Care in Rural Southern India

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Telemedicine-enabled primary eye-care centres (Vision Centre) may be an important component of achieving universal eye care. Thus, we sought to evaluate the use of telemedicine-enabled Vision Centres (VCs) compared with the gold-standard, in-person examinations (IPEs) by an ophthalmologist.

Methods: This prospective, diagnostic accuracy validation study was conducted at a VC belonging to Aravind Eye Hospital (AEH) in south India. We included consecutive new patients, aged ≥16 years, visiting the VC. All participants underwent the tele-ophthalmic examination (TOE), followed by IPE on the same visit. The in-person ophthalmologist was masked to the TOE diagnosis and treatment advice. The primary outcomes were percent agreement, kappa (k), sensitivity, and specificity of TOE versus gold standard, IPE.

Results: The TOE had high percent agreement for all eye conditions ranging from 91.3% (allergic conjunctivitis) to 98.8% (injury, and pterygium). There was substantial agreement between the TOE and IPE for cataracts (k = 0.72; 95% CI: 0.63-0.82) and moderate to substantial agreement for injury (k = 0.55; 95% CI: 0.27 to 0.83), allergic conjunctivitis (k = 0.51; 95% CI: 0.41 to 0.62), infective conjunctivitis (k = 0.61; 95% CI: 0.43 to 0.78), and pterygium (k = 0.55; 95% CI: 0.27 to 0.83) and fair agreement for diabetic retinopathy (k = 0.34; 95% CI: 0.09 to 0.59), and slight agreement for glaucoma (k = 0.16; 95% CI: -0.13 to 0.45). Overall, the sensitivity of TOE ranged from 12.5% (glaucoma) to 91.7% (cataracts) and the specificity ranged from 93.5% (normal eyes) to 99.8% (injury). With respect to treatment advice (cataract surgery, spectacles and medications), there was substantial agreement (k≥0.67) with a sensitivity ranging from 58.1% to 77.2% and specificity ranging from 96.9% to 100%.

Conclusions: The TOE in rural VCs has comparable accuracy to an IPE by an ophthalmologist for correctly identifying and treating major eye ailments. Through providing universal eye care to rural populations, this model may contribute to work toward achieving the U.N. Sustainable Development Goals.

CONTROL ID: 3708062

SUBMITTER (NAME ONLY): TingFang Lee

TITLE: The estimation of breakpoints in piecewise-linear association models for longitudinal studies

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The commonly used approach in ophthalmology to determine the breakpoints in brokenstick analysis in either longitudinal or cross-sectional studies is by using the data as if it was acquired cross-sectionally which does not consider repeated measurements per eye. The purpose of this study is to introduce and evaluate alternative approaches of brokenstick analysis in longitudinal studies.

Methods: Four methods for estimating the breakpoints in longitudinal studies were evaluated: 1) segmented mixed model (SEG) using an iterative procedure, 2) backfitting algorithm of the mixed-effect segmented model (MLE), 3) robust backfitting that incorporates the least trimmed squares (LTS) to accommodate outliers, and 4) bootstrap method that uses segmented linear model by resampling longitudinal data cross-sectionally. These methods were compared with the conventional approach where cross-sectional analysis is used by aggregating repeated measurements. A simulation study was conducted to evaluate the performance of each method by comparing bias and mean square error (MSE) in which two breakpoints were simulated. We further apply these methods to a clinical longitudinal study with 216 eyes (145 subjects) of which 164 had open angle glaucoma, 45 glaucoma suspects, and 7 healthy eyes, followed for an average of 3.7±1.3 years, and evaluate the temporal association between visual field mean deviation (MD) and retinal nerve fiber layer (RNFL) thickness.

Results: The simulation study showed all methods performed well in prediction accuracy while the cross-sectional method fail to capture the breakpoints (Table). Among the 4 proposed methods, the average bias and MSE of SEG and MLE are smaller than LTS and bootstrap. In the clinical longitudinal study, the results from SEG indicated that 2 breakpoints at MD = -15.5 and -4.56 dB exist with a significant difference between the rate of change before and after each breakpoint ($p<0.001$) (Figure). Using the cross-sectional approach, a single breakpoint was detected at -6.67 dB.

Conclusions: SEG is recommended in studies with complex dependencies such as repeated measurements and correlations between two eyes because of the accuracy and computational stability. As illustrated, the cross-sectional approach in this setting is not recommended due to the marked differences in the analysis outcome noted in the simulation and clinical data.

CONTROL ID: 3708063

SUBMITTER (NAME ONLY): Paul Micevych

TITLE: Cone structure and function in RPGR- and USH2A-associated retinal degenerations

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Variants in genes whose products are expressed at the photoreceptor connecting cilium, including RPGR and USH2A, are common causes of rod-cone degeneration. We compared cone structure and function between RPGR- and USH2A-associated retinal degenerations.

Methods: This single-center, cross-sectional study included 13 eyes (9 subjects) with RPGR-related X-linked retinitis pigmentosa (RPGR), 16 eyes (9 subjects) with USH2A-related autosomal recessive retinitis pigmentosa (ARRP), 15 eyes (10 subjects) with USH2A-related Usher syndrome type 2 (USH2), and 5 healthy eyes (4 subjects). Structural measures included cone density from adaptive optics scanning laser ophthalmoscopy (AOSLO) and photoreceptor inner segment (IS), outer segment (OS) and outer nuclear layer (ONL) thickness from optical coherence tomography (OCT) images. Cone function was assessed by macular integrity assessment (MAIA) microperimetry. OCT angiography (OCTA) images were used to study choriocapillaris flow deficit percent (CCFD%), using the area ratio of flow deficits greater than one mean standard deviation from a normal database. Measures were compared at designated regions (Figure 1) through ANOVA with pairwise comparisons among disease groups, adjusted for disease duration and region eccentricity.

Results: Comparisons to healthy eyes revealed lower cone density in RPGR and USH2 (p=0.02, p=0.04), shorter OS in RPGR and USH2 (p=0.0001, p=0.047), shorter IS in RPGR (p=0.004), thinner ONL in RPGR (p=0.008), and reduced macular sensitivity in RPGR, USH2, and ARRP (p=0.008, p=0.0498, p=0.04). OS were shorter in RPGR than either USH2 (-16.8 μm, p=0.01) or ARRP (-21.2 μm, p=0.001; Figure 2). IS were shorter in RPGR than USH2 (p=0.03). ONL was thinner in RPGR than either USH2 (p=0.03) or ARRP (p=0.03). Mean CCFD% was greater in RPGR than USH2 (p=0.02).

Conclusions: Differences in outer retinal thickness and CCFD% reveal more advanced structural and vascular alteration in RPGR than USH2A-related retinal degenerations. Similarities in macular sensitivity suggest comparable levels of cone dysfunction in these retinal degenerations.

CONTROL ID: 3708069

SUBMITTER (NAME ONLY): Lauren Major

TITLE: A novel mouse model of Usher Syndrome Type II designed for testing of base editing therapeutics

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Major, L. Fry, R.E. MacLaren, M.E. McClements, A. Salman, A. King, L. McDermott, NDCN, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|J. Yang, University of Utah Hospital, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Usher Syndrome is an autosomal recessive retinal degeneration associated with deafness. Usher type IIA is caused by mutations in the USH2A gene which encodes the protein usherin, which normally localises to the photoreceptor cilium and cochlear hair cells. CRISPR-mediated base editing is a potential treatment approach for 37.3% of USH2A mutations caused by single base transitions. USH2A c.11864G>A (p.W3955X) accounts for 3-5% of pathogenic alleles worldwide, and is potentially correctable with base editing. We developed an Ush2a knockout mouse model containing a premature termination codon in the homologous location of the murine Ush2a transcript (c.11840G>A; p.W3947X). We investigate the phenotype of this mouse as a model for testing of base editing therapeutics for Usher Syndrome.

Methods: Ush2a-W3947X mice were generated using a homology directed repair knock-in strategy, with a single-stranded DNA template, gRNA and SpCas9 mRNA delivered to zygotes via pro-nuclear injection. Mice were bred on a C57BL/6J background with a repaired Cdh23 age-related hearing loss allele. Homozygous mice were evaluated at 3-, 6-, 9- and 12-months with OCT and ERG. Auditory brainstem response (ABR) threshold testing was performed at 9 weeks. Immunostaining of retinal and cochlear sections and western blot of retinal protein lysates were performed.

Results: Heterozygous Ush2a-W3947X mice were successfully generated with successful insertion of a single copy of the donor confirmed by Sanger sequencing and a ddPCR copy counting assay. Usherin was not detected in immunostaining of retinal or cochlear sections of homozygous W3947X animals, or by western blot of retinal lysates. ABR thresholds were significantly elevated at higher frequencies (8-24kHz). No significant differences were seen in photoreceptor or total retinal thickness on OCT imaging relative to wildtype mice. No differences between dark-adapted, light adapted or flicker responses were seen with ERG testing between mutant and wildtype mice.

Conclusions: The Ush2a-W3947X mouse lacks usherin expression in the retina and cochlea, and displays an early hearing loss phenotype. Ongoing analysis with age will determine if a slow retinal degenerative phenotype is present similar to other Ush2a$^{-/-}$ models. This model is useful for testing of base editing strategies for Usher syndrome.

CONTROL ID: 3708071

SUBMITTER (NAME ONLY): Judith Goldstein

TITLE: Developing a care delivery framework for older adults with visual impairment: A mixed methods study on ophthalmologist perspectives

SESSION TITLE: Health Economics and Health Care Delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.E. Goldstein, F. Naufal, X. Guo, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|C. Kerr-Niermann, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the ophthalmologists' perspective on providing care to older adults with visual impairment (VI), aiming to better understand and improve healthcare delivery to this unique group of patients.

Methods: Ophthalmologists from glaucoma, retina and neuro-ophthalmology subspecialities from Johns Hopkins Wilmer Eye Institute participated in an observational mixed-methods study. Interviews and surveys covered major themes including identification of and methods used to screen for vision-related functional deficits, counselling practices, and low vision rehabilitation (LVR) provision to enhance function.

Results: Participating ophthalmologists (N=20, 65% male) were mostly over the age of 40 (60%) and had 9 years of experience (median) in their respective subspeciality. Most (55%) reported spending 5-10 minutes face-to-face with the patient per encounter and estimated that 36% (5%-67%) of older patients on average have difficulty with visual function. Most (70%) did not systematically screen for visual function difficulty, but when initiated relied on the following parameters: asking the patient directly (90%), visual acuity (70%), visual field (60%), and diagnosis criteria (25%). Time available to screen and counsel patients on visual function and LVR was reported as inadequate (70%), and only one-fifth noted that use of ophthalmic technicians or trainees was a viable option to identify and refer patients to LVR. Use of a reminder within the electronic health record (EHR) to prompt identification and referral to LVR was of interest in over half (55%) surveyed. Most ophthalmologists (70%) referred to LVR when patients expressed difficulty with visual function; over half of ophthalmologists (55%) reported that most patients were interested in pursuing LVR and found LVR beneficial.

Conclusions: Most ophthalmologists recognized the importance of querying about patients' visual function and referring to LVR, however screening approaches were not routine and time constraints often preclude adequate counselling. Relinquishing this responsibility to trainees or technicians was not considered viable given the effect on clinic workflow. An EHR reminder triggered by patient-reported vision concerns and visual acuity offers an initial framework where ophthalmology practices can be standardized to enhance healthcare delivery to older adults with VI.

CONTROL ID: 3708072

SUBMITTER (NAME ONLY): Ellen Rhodes

TITLE: Allele-specific targeting of AMD-related SNPs in ARPE19 cells using a CRISPR Cas9 dual plasmid targeting approach

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Rhodes, A. Salman, W. Song, M.E. McClements, R.E. MacLaren, NDCN, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|W. Song, R.E. MacLaren, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Age-Related Macular Degeneration (AMD) is a leading cause of blindness in the developed world. Despite extensive research, there remains incomplete understanding of disease development and progression. Single nucleotide polymorphisms (SNPs) are one of several mechanisms that have been associated with a predisposition to develop AMD. SNPs have previously been shown to be editable with CRISPR machinery, causing endonuclease mediated double-strand DNA breaks specified by guide RNA (gRNA) targeting. In this instance, CRISPR gene editing can target SNPs in an allele-specific manner. To investigate CRISPR editing of AMD-related SNPs, a retinal pigment epithelium (RPE) cell line, ARPE19, which possesses several AMD-related SNPs, was used. ARPE19 is a spontaneously arising RPE cell line derived from the healthy eye of a 19-year-old male. These cells grow in a stable monolayer, express RPE-specific markers CRALBP and RPE-65 and exhibit a typical RPE morphology including tight junction formation, representing a suitable model to validate CRISPR targeting of AMD-related SNPs.

Methods: SNPs in the ARPE19 cell line were identified via genotyping. U6 promoter driven gRNAs targeting AMD-related SNPs and VEGF were cloned into a gRNA cloning plasmid using BbsI cut sites. gRNAs were transfected into ARPE19 and HEK293T cells in combination with a CMV promoter driven SpCas9 plasmid to achieve a dual transfection system. To assess editing efficiency via tracking of indels by decomposition (TIDE) analysis, target SNPs were PCR amplified using primers designed to flank the target SNP with ~200bp on the 5’ end and ~500bp on the 3’ end.

Results: TIDE analysis of PCR products from ARPE19 cells with dual plasmid transfection of SpCas9 and gRNAs against the following AMD-related SNPs [rs1410996, rs380390, rs2230199, rs147859257, rs641153 CFB SNP, rs4541862] and VEGF targeting gRNA, showed 4-5% targeting efficiency, compared to 30% in HEK293T cells.

Conclusions: The dual plasmid targeting approach using SpCas9 and U6-driven gRNA plasmids efficiently delivers the CRISPR system to HEK293T cells. Low editing efficiency in ARPE19 cells may be due to inadequate time for CRISPR mechanisms to elucidate effect, as ARPE19 cells begin to degrade after 24 hours, or due to the more stable differentiation of these cells which may involve epigenetic changes to targeted genes.

CONTROL ID: 3708074
SUBMITTER (NAME ONLY): Sara Patterson
TITLE: Receptive field diversity in the primate foveal retina
SESSION TITLE: Retinal ganglion cells and central processing
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: S.S. Patterson, Q. Yang, W. Merigan, D.R. Williams, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|T. Godat, D.R. Williams, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|W. Merigan, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|
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ABSTRACT BODY:
Purpose: While the fovea is best known for its specialized role in spatial acuity mediated by a high density of midget retinal ganglion cells (RGCs), anatomy and transcriptomics indicate that ~15 rarer RGC types are present. However, our understanding of the visual information these RGC types convey to the brain is limited because both the fovea and rarer RGC types are difficult to address with standard physiology approaches. Here, we address these gaps in knowledge by utilizing in vivo calcium imaging to explore the diversity of foveal RGC types in the living primate eye.
Methods: Experiments were conducted in two macaque monkeys expressing GCaMP6s in the foveal ganglion cell layer. We used a fluorescence adaptive optics scanning light ophthalmoscope to measure the calcium responses of a population of GCaMP6s-expressing foveal cells to light stimuli presented directly to the photoreceptors. With this approach, we could simultaneously survey the response properties of 171 and 177 distinct cells in each macaque. Receptive fields were characterized by their responses to achromatic and cone-isolating spatially-uniform stimuli varying in contrast. In addition, we coarsely mapped spatial extent with 4.5 μm wide bars presented in different locations in one macaque.
Results: The vast majority of the 348 cells imaged were consistent with the well-studied L vs. M midget RGCs that dominate in the foveal output, in that they showed either ON or OFF responses, did not respond to S-cone isolating stimuli and had small receptive fields. However, 7% (26/348) had ON-OFF responses and 6% (22/348) had strong S-cone responses. We also mapped the spatial receptive fields in one macaque and found that 13% (23/177) had large receptive fields. Of those 23 cells, 11 had ON-OFF responses and 2 had S-cone responses.
Conclusions: Here we demonstrate an underappreciated functional diversity in the visual information the fovea sends the brain. While the dominance of midget RGCs is consistent with the fovea's specialization for spatial acuity, our results indicate that this is an incomplete picture of visual processing in the fovea. An advantage of our in vivo approach is that we can return to the same cells in subsequent experiments. As a result, the ability to functionally identify the rarest foveal RGCs established here lays the foundation for future experiments directly targeting these elusive RGC types.

CONTROL ID: 3708079

SUBMITTER (NAME ONLY): Tanvi Chokshi

TITLE: Association of Aqueous Retinol Binding Protein 3 (RBP3) and Diabetic Retinopathy Severity

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Chokshi, W. Fickweiler, M. Mitzner, I. Wu, T. Boumenna, D. Robinson, H. Park, K. Park, Research Division, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|T. Chokshi, W. Fickweiler, M. Mitzner, D. Robinson, L.P. Aiello, J.K. Sun, Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|L.P. Aiello, J.K. Sun, G. King, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G. King, Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although laser photocoagulation and anti-VEGF treatment are effective for advanced diabetic retinopathy (DR), there remains an important need to identify markers and therapeutic targets for DR worsening at earlier stages. Retinol-binding protein 3 (RBP3) is a potential protective factor against DR in the vitreous and retina of individuals with type 1 diabetes for 50 years or longer (Joslin Medalist Study). This study aims to evaluate the association between RBP3 in the aqueous fluid and DR severity in patients with type 1 and type 2 diabetes.

Methods: Aqueous samples were obtained from diabetic patients during cataract surgery at the Joslin Beetham Eye Institute (N=30) and from post-mortem eyes (N=101) of Medalists. RBP3 concentration was measured in all samples using a specific ELISA assay. Individual retinal layer thicknesses in the foveal 1x1mm area were measured by optical coherence tomography (Spectralis) with automated layer segmentation (Heidelberg v6.0c, Germany, N=45).

Results: 131 participants had a mean age of 73 ± 8 years, A1c 7.4 ± 1%, 84% type 1 diabetes, and 72% female. RBP3 levels in aqueous samples decreased with increasing DR severity from mild DR (median 0.7nM ± 0.2) to proliferative DR (PDR, 0.5nM ± 0.2, P=0.001). Aqueous RBP3 concentrations in Beetham Eye Institute and Medalists samples were similar for eyes with PDR (P=0.11). Aqueous RBP3 concentration was inversely associated with the presence of pan-retinal laser photocoagulation scars (β estimate -22.0, 95% CI -31.9;-12.0, P<0.0001), but not with A1c (P=0.60). RBP3 concentrations in aqueous were well correlated between fellow eyes (r=0.65, P<0.0001). RBP3 concentrations in aqueous and vitreous samples were correlated within the same individual (r=0.32, P=0.003, N=89). On average, RBP3 concentration in aqueous was 12-fold lower compared to vitreous samples. Higher aqueous concentrations were associated with increased thickness of the ganglion cell layer (β estimate 0.002, 95% CI 0.0019;0.0023, P<0.0001) and inner nuclear layer (0.0026, 0.0025;0.0028, P<0.0001), and decreased thickness of the retinal pigment epithelium (-0.001, -0.0017;0.0003, P=0.004).

Conclusions: These findings suggest that RBP3 concentrations in aqueous and vitreous fluids are correlated and reduced in people with advanced DR, supporting its potential use as a biomarker and therapeutic agent in people with type 1 and type 2 diabetes.

CONTROL ID: 3708080

SUBMITTER (NAME ONLY): Karina Esquenazi

TITLE: A Decade of Transition from Fundus Photography to OCT in the Care of Glaucoma Patients

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Esquenazi, A.C. Brown, L.R. Pasquale, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to better understand imaging modality utilization for diagnosis of glaucoma over the past decade through analysis of trends among glaucoma specialists. Understanding these trends may contribute to proper planning and development of the healthcare apparatus and newer machine learning models.

Methods: This was a retrospective study of Medicare Provider Utilization and Payment Data from 2012-2019, which is a publicly available aggregate of nationwide information on services and procedures provided to Medicare beneficiaries on a fee-for-service basis. 556 glaucoma providers were identified throughout the Unites States. Procedure count for 92250 (fundus photography with interpretation and report), 92133/92134 (scanning computerized ophthalmic diagnostic imaging with interpretation and report), 92083 (visual field examination with interpretation and report), and 92020 (gonioscopy) were obtained. Trends were analyzed using Mann-Kendall trend test.

Results: Each testing modality increased over the eight year period studied, with the greatest percent increase in optical coherence tomography (OCT) (89.2%). Color fundus photography represented the lowest average year over year increase (Figure 1). A direct ratio of fundus photographs to OCTs showed a downward trend, where in 2012 one fundus photograph was taken for every 3.3 OCTs and in 2019 one fundus photograph was taken for every 4 OCTs (p-value 0.004).

Reimbursements did not decrease significantly for gonioscopy throughout the study period (p-value 0.53619) and decreased for the remaining three modalities. Fundus photography reimbursement decreased by 30% (p-value 0.173), OCT decreased by 20% (p-value 0.009) and visual field testing decreased by 31% (p-value =0.035) (Figure 2).

Conclusions: While visual field testing and color fundus photography did increase in the period analyzed, the change in OCT use increased by almost double. At the current rate, vanishingly few fundus photographs will be captured as part of the management of glaucoma patients. This paradigm shift represents an important change in the field.

CONTROL ID: 3708082

SUBMITTER (NAME ONLY): Matthias Hamdorf

TITLE: Aflibercept (Eylea) inhibits dendritic cell migration

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hamdorf, J. Weindler, A. Salabaria, F. Bock, Cornea Lab Experimental Ophthalmology, University Hospital of Cologne, Cologne, GERMANY|M. Hamdorf, Terasaki Institute for Biomedical Innovation (TIBI), Los Angeles, California, UNITED STATES|C. Cursiefen, Zentrum für Augenheilkunde - Department of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: The potential to control vascular endothelial growth factor (VEGF) induced intracellular signaling by targeting this cytokine offers promising therapeutic potential for vascular diseases and cancer. VEGF-A regulates angiogenesis but modulates the immune microenvironment. Dendritic cells are one of the responsible cell types that orchestrate the immune response in a transplant setting. Modulation of DCs by VEGF-A -trap (Aflibercept) might benefit in reduced inflammation and subsequent transplant survival. In this study, we analyzed the effect of Aflibercept and combinations of VEGF-A bound to Aflibercept on dendritic cells and possible positive effects on the immune system and graft survival.

Methods: Human monocytes were treated with Aflibercept during differentiation, and the expression of surface and activation markers were analyzed. Biological differences of treated cells were determined in a transwell migration assay. To verify the findings in human cell culture, we confirmed them in a murine model of suture-induced neovascularization and subsequent high-risk corneal transplantation. Mice were treated with VEGFR1/R2 trap before transplantation. We analyzed transplant integrity, CD11c+ dendritic cells, and tolerance marker 2 and 8 weeks later.

Results: The treatment of monocytes, with a combination of VEGF-A and Aflibercept during differentiation to DCs leads to an down regulation of MHC II and costimulatory markers on dendritic cells. Furthermore, the frequency of VEGFR1-positive cells increased significantly. As a functional outcome we found that in the presence of VEGF-A and Aflibercept the migration of mature DC was inhibited by aproximatly 50 %. To characterize this results more in details we went into the mouse model and local VEGFR1/R2 trap treatment significantly inhibits the infiltration of CD11c+ dendritic cells into the cornea. Subsequent increased corneal transplantation success was accompanied by a local upregulation of Foxp3 gene expression.

Conclusions: This study demonstrates that the application of Aflibercept modulates the differentiation and migration ability of dendritic cells and contributes to increased transplantation success and less inflammation mediated by DCs in a mouse cornea transplantation model.

CONTROL ID: 3708083

SUBMITTER (NAME ONLY): Elizabeth Roll

TITLE: The Efficacy of Rhopressa in Lowering Intraocular Pressure in Patients with Secondary Glaucoma

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Roll, M. Oydanich, Y. Shah, A. Khouri, Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the efficacy of Rhopressa (Netarsudil, 0.02%) in lowering intraocular pressure (IOP) in patients with secondary forms of glaucoma.

Methods: A total of 68 patients (87 eyes) with either primary open angle glaucoma (POAG) or a secondary form of glaucoma were reviewed retrospectively over the course of one year after starting Rhopressa. The secondary glaucoma group was composed of patients with uveitic, neovascular, traumatic, congenital, and pseudoexfoliative glaucoma. Patient IOP measurements were collected at baseline, 1 month, 3 month, 6 month, and 12 month intervals. Patients that underwent surgical intervention during the study period were not included in the final data analysis. IOP levels and discontinuation rates, due to intolerance or inefficacy, were tracked and monitored at each patient visit. A two sample T-test was used to determine differences in the IOP lowering effect of Rhopressa in the POAG and secondary glaucoma groups.

Results: All patients with either POAG or secondary glaucomas were matched for age (Mean ± SD; 69.7 ± 16.5 vs. 67.3 ± 21.5; $p>0.05$). Both the POAG and secondary glaucoma patients exhibited significant decreases in IOP at each time point (1, 3, 6, and 12 months) when compared to each group's baseline ($p<0.05$). No significant differences were observed in IOP between the POAG and secondary glaucoma groups at most time points, with the exception of the 12 month interval ($p<0.05$). However, both groups showed similar overall decreases in IOP from baseline after 1 year of treatment (5.8 ± 4.5 vs. 5.3 ± 7.3; $p>0.05$). Discontinuation rates of Rhopressa due to intolerance or inefficacy were similar in both groups and less than 10% (Table).

Conclusions: Rhopressa is similarly effective in lowering IOP in patients with secondary glaucomas compared to those with POAG. Discontinuation rates were similar in both groups, supporting Rhopressa's utility in treating secondary forms of glaucoma.

CONTROL ID: 3708084

SUBMITTER (NAME ONLY): Alfredo Desiato

TITLE: Optimisation and evaluation of a soluble ocular insert for sustained release of levofloxacin.

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Desiato, P. Bhogal-Bhamra, S. Naroo, R. Gil-Cazorla, Optometry, Aston University, Birmingham, West Midlands, UNITED KINGDOM|A. Desiato, A. Iyire, Pharmacy, Aston University, Birmingham, West Midlands, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Antibiotic-loaded ocular inserts can address challenges in drug delivery and overcome limitations of eye drops use. The aim of this in vitro study was to optimise a sustained ocular drug delivery system for levofloxacin (LFX), a broad-spectrum antibiotic commonly used for external ocular infections.

Methods: Inserts were prepared by a refined quality by design solvent casting procedure, using 0.2%, 0.5% and 1.0% concentrations of LFX solutions with hypromellose, sodium alginate, gelatin and PEG400. Formulations were characterised for physicochemical properties: uniformity of mass and thickness, loss on dryness, moisture absorption, and surface pH. Mechanical properties were assessed and compared against a marketed buccal film, as no ocular formulation was available. Inserts' uniformity of drug content and release profile were assessed by validated analytical method. The effect of LFX fractions released over time on growth dynamics of Staphylococcus Aureus and Pseudomonas Aeruginosa was studied to evaluate extended antimicrobial efficacy.

Results: The optimised formulation including hypromellose (5%), sodium alginate (3%), gelatin (1%), PEG 400 (10%), and prepared with 0.5% LFX solution, resulted in inserts holding good physicochemical properties, in line with eye characteristics. Inserts mass (11.1 ± 0.3 mg), thickness (160 ± 10 µm) and LFX content (232.8 ± 4.4 µg) were found consistent and complying with International Pharmacopoeia guidelines. Inserts withstood unilinar (elongation at max load 25.5 ± 1.9%) and repeated (foldability > 300 times) mechanical stresses, suggesting suitability to manipulation linked to eye administration. The release pattern of 0.5% LFX showed that half of drug content was released within the first 30 minutes, indicating immediate effectiveness of inserts against bacteria, with the remaining LFX released in 24 hours. Kinetic growth assays indicated that the fractions of LFX released within the 24 hours testing period were adequate to prevent Staph. Aureus and P. Aeruginosa growth.

Conclusions: The new LFX-loaded inserts exhibited good physicochemical and mechanical properties, indicating compatibility with ocular anatomophysiology and administration procedure. LFX content and release pattern showed immediate and sustained antimicrobial efficacy of inserts on bacterial growth.

Current research is focusing on formulation cytotoxicity and transepithelial drug permeability.

CONTROL ID: 3708088

SUBMITTER (NAME ONLY): Aaron Loewen

TITLE: Localization of sector RP-associated mutated RHODOPSIN suggests multiple pathogenic mechanisms in transgenic Xenopus laevis

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Loewen, B.M. Tam, R.T. Scharbach, C.N. Chiu, O.L. Moritz, Ophthalmology & Visual Sciences, The University of British Columbia, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: 15% of non-syndromic retinitis pigmentosa (RP) cases belong to a subclass called sector RP. Sector RP is defined by the diseased phenotype being restricted to one or two quadrants of the retina. The most common causes of sector RP are mutations in RHODOPSIN (RHO), where over a dozen mutations have been associated with sector RP including T4K and P23H. Previously, we have shown that altered lighting conditions can modulate retinal degeneration (RD) in transgenic Xenopus laevis models of sector RP. Here, we investigated sector RP-associated RHO mutations for changes in RHO localization in rod cells and RD under different lighting regimes.

Methods: X. laevis expressing human RP-associated RHO mutants under control of the X. laevis rod opsin promoter were generated by restriction enzyme-mediated integration. Transgenes were based on the human RHO cDNA. Tadpoles were raised for 14 days in either constant light, cyclic light, or complete darkness. Eyes were enucleated and used for histology or for protein level analyses through western and dot blots using mammalian rod opsin antibodies.

Results: We found variable degrees of inner segment (IS) RHO retention associated with RP-associated mutations. Most sector RP-associated RHO mutations did not affect RHO trafficking to the outer segment (OS); however, a third of the mutations studied caused significant IS retention of RHO. RD in animals with OS-localizing RHO mutants (including L31Q and T58R) was mitigated when the animals were dark reared. RD in animals with intermediate RHO localization patterns (significantly different than wildtype but with some OS localization, including S22R and D190G) was not prevented by dark rearing.

Conclusions: Localization of mutant RHO in the IS suggests an ER stress-related cell death mechanism while RHO mutants with localization indistinguishable from wildtype is likely indicative of a photoactivation-induced mechanism. The majority of mutations that we examined did not mislocalize to the IS and therefore likely act via a mechanism originating in the OS; however, mutants that localize to both the IS and OS could have multiple cell death mechanisms occurring simultaneously. Classification of RHO mutations using this system may identify mutations that are most likely to benefit from ER stress-alleviating therapies.

CONTROL ID: 3708089

SUBMITTER (NAME ONLY): Jason Greenfield

TITLE: The Use of High-Resolution Optical Coherence Tomography in the Diagnosis of Ocular Surface Masqueraders

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Greenfield, D. Theotoka, S.C. Wall, A. Galor, R.A. Abou Khzam, V. Tang, S.R. Dubovy, C.L. Karp, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Greenfield, University of Miami School of Medicine, Miami, Florida, UNITED STATES|A. Galor, Ophthalmology, Miami Veterans Medical Administration Medical Center, Miami, Florida, UNITED STATES|R.A. Abou Khzam, V. Tang, S.R. Dubovy, Florida Lions Eye Bank Ocular Pathology Laboratory, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the utility of anterior segment high-resolution optical coherence tomography (HR-OCT) in guiding the diagnosis and management of clinically ambiguous ocular surface lesions.

Methods: Individuals with a clinically ambiguous ocular surface lesion with slit-lamp photographs (SLP), HR-OCT images, and histopathological examination were included in the study. The presumptive clinical diagnosis based on SLP was compared to the diagnosis suggested by HR-OCT findings and ultimately to the definitive diagnosis by histopathology. The main outcome of this study was the frequency in which HR-OCT findings guided the clinician to the correct diagnosis.

Results: Twenty-two individuals were included in this study with a mean age of 53 ± 20 years, of whom, 59% were male, 86% identified as white and 21% as Hispanic. Seven lesions were epithelial, 3 had an epithelial and a subepithelial component, and 12 were subepithelial. HR-OCT was most effective in discerning lesion location (epithelial, subepithelial, or both), successfully identifying the location in 100% of cases. In terms of the final diagnosis, classic HR-OCT findings were detected in 68.18% of cases while suggestive features were detected in 31.8% of cases. Figure 1A-E.

Conclusions: HR-OCT can be a valuable diagnostic tool, assisting in the differentiation of ambiguous ocular surface lesions. It provides morphological patterns of the lesion aiding in the localization and diagnosis of the mass.

CONTROL ID: 3708090

SUBMITTER (NAME ONLY): Kayla Knoll

TITLE: Comparison of Stress Distribution Patterns in Keratoconus and Healthy Eyes

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Knoll, C.J. Roberts, A. Mahmoud, A. Hendershot, Department of Ophthalmology and Visual Sciences, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|C.J. Roberts, A. Mahmoud, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|P.T. Yuhas, The Ohio State University College of Optometry, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare stress distribution patterns in keratoconus (KCN) and normal (NRL) corneas and the relationships between areas of greatest curvature, thinnest pachymetry and high vs low stress.

Methods: Geometric Corneal Stress Factor (GCSF) was defined according to the hoop stress formula without intraocular pressure (IOP), R/2t, where R is radius of curvature and t is thickness. GCSF was calculated on 66 KCN eyes of 40 subjects and 310 NRL eyes of 155 subjects who were prospectively enrolled and received Pentacam Tomography (Oculus, Wetzlar, Germany). Custom software was developed and used to identify the 2mm diameter zone of greatest curvature ($AvgK_{Max}$), 2mm diameter zone of thinnest pachymetry ($Pach_{Min}$), 2mm zone of greatest GCSF ($Stress_{Max}$), 2mm zone of lowest GCSF($Stress_{Min}$). Average maps were created for KCN and NRL cohorts with central $AvgK_{Max}$ (center located within 3.0 mm diameter central zone), Inferior-Nasal $AvgK_{Max}$ and Inferior-Temporal $AvgK_{Max}$. Paired T-tests were performed between locations of $AvgK_{Max}$ and $Stress_{Max}$ and locations of $AvgK_{Max}$ and $Stress_{Min}$ as well as between locations of $Pach_{Min}$ and $Stress_{Max}$ and $Pach_{Min}$ and $Stress_{Min}$. Univariate linear regressions were performed with significance threshold of $p < 0.05$ for all analyses.

Results: In NRL, greatest stress is significantly associated with both thinnest pachymetry and greatest curvature, while in KCN, lowest stress is significantly associated with greatest curvature. The range of greatest stress in KCN is 6.50 – 15.27 with a mean of 8.82 +/-1.70 and the range of greatest stress in NRL is 5.85 – 8.45 with a mean of 7.07 +/-0.44. The range of lowest stress in KCN is 4.97 – 7.42 with a mean of 6.40 +/-0.54 and the range of lowest stress in NRL is 5.07 – 7.42 with a mean of 6.14+/-0.44. There is a significant difference in greatest stress between KCN and NRL, with KCN being higher than NRL. There is also a significant difference in lowest stress between KCN and NRL, with KCN being higher than NRL.

Conclusions: The hoop stress formula shows greater stress with either lower thickness or flatter curvature (greater R). In NRL, corneal stress distribution is driven by thickness, with greatest stress at lowest pachymetry and greatest curvature. However, in KCN, corneal stress distribution shifts such that it is driven by curvature with lowest stress at greatest curvature.

CONTROL ID: 3708091

SUBMITTER (NAME ONLY): Zafar Gill

TITLE: RO-634 half-life as compared to published data on Aflibercept, Faricimab, Ranibizumab, and Bevacizumab.

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Gill, J.L. Olson, J. Morgenstern, A. Jones, A. Strong, S. Droho, S. Bevers, N. Mueller, N. Mehta, M. Huvard, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus in Aurora, Colorado, Aurora, Colorado, UNITED STATES|P.K. Kaiser, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R. Bhandari, Eye Institute, Springfield Clinic LLP, Springfield, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: RO-634 is a novel intravitreal bispecific protein (surrobody) with dual inhibition of both Vascular Endothelial Growth Factor-A (VEGF-A) and Angiopoietin-2 (ANG-2). We aim to investigate the half-life of this protein as compared to published data on Aflibercept, Faricimab, Ranibizumab, and Bevacizumab. These findings may have important clinical implications for treatment of retinal disease including diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), and exudative age-related macular degeneration (AMD).

Methods: All experiments were performed in accordance with the ARVO statement for Use of Animals in Ophthalmic and Vision Research. The half -life of RO-634 was determined by measuring vitreous VEGF levels in 6 New Zealand White Cross rabbits with an ocular fluorophotometer (Ocumetrics, Mountain View, CA). These measurements were taken before an injection of fluorescein labeled VEGF (concentration 0.3 ug/mL) and post-injection at hours 1, 12, 24, 48, 72, 96, and 120. Determination of the vitreous fluorescence was made by averaging the values around the vitreous plateau as described by Gray et al.

Results: In vivo intraocular half-life measurements of RO-634 in New Zealand White Cross rabbits were longer than previously published data on aflibercept (3.92 days), ranibizumab (2.88 days), and similar to bevacizumab (6.51 days). Measurements taken from peak averages, demonstrated RO-634 half-life was an average of 6.75 days ± 2.13 days.

Conclusions: Our study demonstrates that RO-634 has a similar half-life when compared to bevacizumab and a longer half-life when compared to aflibercept and ranibizumab. Given RO-634's excellent half-life and novel dual-inhibitory mechanism of action, we propose that this protein is a possible therapeutic candidate for exudative AMD, DME, and PDR. We are hopeful that future studies will continue to shed light on RO-634s safety and efficacy in both animal and human models.

CONTROL ID: 3708092

SUBMITTER (NAME ONLY): Pablo Zoroquiain

TITLE: Low expression of the vitamin D receptor in patients with dry eye disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zoroquiain, Pathology and Ophthalmology, Pontificia Universidad Catolica de Chile, Santiago, CHILE|J. Meza, Pathology, Pontificia Universidad Catolica de Chile, Santiago, CHILE|A. Vieira, A. Grau, Ophthalmology, Pontificia Universidad Catolica de Chile, Santiago, CHILE|

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ABSTRACT BODY:

Purpose: Vitamin D (vitD) has been associated not only with bone metabolism but also with inflammatory and degenerative processes. The vitamin D receptor (VDR) is a transcription factor that, linked to vitD, regulates the expression of numerous genes. Dry eye disease (DED) is a frequent multifactorial disease that leads to a serious deterioration in the quality of life. Studies have shown an association of DED with vitD deficiency, however, there are no studies that have analyzed the metabolism of this pathway at the cellular level. It is our objective to study the expression of the VDR in patients with DED.

Methods: Nineteen patients with DED without previous treatment and 10 age matched healthy subjects were studied. The Ocular Surface Disease Index (OSDI) and a cytobrush ocular surface cytology were performed on all patients. Squamous metaplasia was morphologically evaluated by liquid phase cytology with PAP-PAS staining using the Nelson's score (scale 0 to 3, higher score to higher metaplastic change). The immunohistochemical expression of VDR by fully automated immunohistochemistry was also evaluated by multiplying the percentage of cells with nuclear positivity (0-100) by their intensity (0-3) generating a score ranging from 0 to 300 (VDR-SCORE).

Results: Squamous metaplasia was observed in 74% of the individuals with DED in contrast to 0% in the control group. In patients with DED, there was lower expression of VDR compared to the control group (VDR-SCORE: 11.2 ± 13.9 versus 80.9 ± 56; P = 0.0001). Furthermore, an inverse correlation was observed between the Nelson score and VDR-SCORE (P = 0.0001, Sp = -0.71), No correlation was observed between OSDI and VDR-SCORE.

Conclusions: To the best of our knowledge, this is the first study to evaluate VDR in patients with DED. Patients with DED present a lower expression of VDR and this decrease was associated with a greater degree of squamous metaplasia, indicating a greater alteration of the ocular surface. However, the expression of VDR would not be related to the symptoms. The findings described support that VitD could be a therapeutic target in patients with DED.

CONTROL ID: 3708093
SUBMITTER (NAME ONLY): Abtin Shahlaee
TITLE: Outcomes of Rhegmatogenous Retinal Detachment Repair in Patients with Nystagmus
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Shahlaee, M. Salabati, R. Mahmoudzadeh, M. Klufas, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|
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ABSTRACT BODY:

Purpose: To report the anatomic and functional outcomes of rhegmatogenous retinal detachment (RRD) repair in patients with congenital or acquired nystagmus.
Methods: A retrospective review was conducted of the clinical and operative records of eyes with nystagmus and RRD underdoing surgical repair from January 1st, 2015 to April 1st, 2021. The primary outcome was the final attachment rate and single surgery anatomic success (SSAS) three months after initial repair. Secondary outcomes included final visual acuity, and mean number of subsequent operations required for complete retinal reattachment.
Results: A total of eight eyes with nystagmus including seven male (87.5%) and one female (12.5%) patient were included in this study. The mean age was 52.1 years (range, 14 to 77 years) and the mean follow-up time was 18.6 months (range, 2.8 to 32.9 months).

Four patients underwent primary pars plana vitrectomy (PPV), three underwent primary scleral buckle (SB), and one underwent PPV-SB. Three eyes required a second PPV which were due to new breaks. Two (25.0%) required a third PPV, one of which was for proliferative vitreoretinopathy (PVR). Mean time to first re-detachment was 29 days. Complete final retinal reattachment was achieved in all patients. SSAS was achieved in five patients (62.5%). This consisted of all three patients undergoing a primary SB and half of those undergoing PPV. The final visual acuity improved or stabilized in seven (87.5%) eyes. Two eyes had silicone eye tamponade, one 1000 centistokes and the other 5000 centistokes, on their final visit and there was no evidence of emulsification 253 and 201 days after surgery respectively.
Conclusions: Repair of RRD in nystagmus is an uncommon but challenging clinical scenario. Single surgery anatomic success in this series was 62.5%. Eyes with nystagmus and long-term silicone oil tamponade did not display silicone oil emulsification with moderate-term follow-up.

CONTROL ID: 3708096

SUBMITTER (NAME ONLY): Elizabeth Martin

TITLE: Schlemm's Canal Outflow Resistance System (SCORS) visualized by Clarification and Immunohistochemistry (IHC)

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Schlemm's canal (SC) inner wall forms funnel-shaped regions that enter SC, narrow to form a tubular conduit with an endothelial-lined lumen and cross SC lumen to attach to the external wall in humans and NH primates. These SC inner wall valve-like (SIV) conduits attach to mobile leaflets forming a second SC outer wall valve-like arrangement (SOV) at collector channels (CC). The TM adheres to SOV-hinged flaps through SIV. Real-time OCT imaging demonstrates that the linkage permits pressure-induced TM motion to modulate CC entrance size. The purpose of our study is 1) To describe a novel combination of techniques permitting IHC to image a distal resistance system. 2) To further characterize the walls, lumen, and connections of the SIV.

Methods: Anterior segments of 16 M. Nemestrina primates underwent IHC labeling; 14 perfused with fluorescent microspheres (MS). Limbal tissues divided into quadrants, viscoelastic introduced into SC, and tissues fixed. Radial segments were cut, tissues clarified, confocal microscopy performed, imageJ 3D projections encompassing the TM, SC, and distal pathways obtained.

Results: 3D relationships between SIV, SOV, and CC were obtained with IHC confocal imaging. Imaging demonstrated CD 31, Collagen Type 1 & 4 in the walls surrounding the SIV lumen and distal pathways. In four eyes, 231 segments were examined, and 293 SIV were identified; 9.2% of the SIV contained microspheres.

Conclusions: Increased imaging depth with clarification and IHC permits the identification of SIV linkage between the TM and SOV. The SIV walls are continuous with SC inner wall endothelium; CD 31 vascular endothelial labeling is identical. Perfused MS demonstrated TM and lumen continuity. The attachments of the SIV to hinged flaps at SC external wall create the SOV. The relationships thus provide a mechanism to control CC entrance dimensions and regulation of distal resistance. The SIV-SOV relationships may provide a SC outflow resistance system.

CONTROL ID: 3708098

SUBMITTER (NAME ONLY): Migle Lindziute

TITLE: Correlation of Macular Vessel Density and Foveal Avascular Zone Metrics in Optical Coherence Tomography Angiography with laboratory and ocular findings in Fabry Patients

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lindziute, K. Hufendiek, I. Volkmann, D. Brockmann, C. Framme, J. Tode, K. Hufendiek, University Eye Hospital, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|J. Kaufeld, Division of Nephrology, Center for Internal Medicine, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|S. Hosari, B. Hohberger, C.Y. Mardin, Department of Ophthalmology, Friedrich-Alexander-Universitat Erlangen-Nurnberg Medizinische Fakultat, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: To evaluate macular microvascular changes in patients with Fabry disease (FD) using OCT-A and to correlate with laboratory and ocular findings.

Methods: A total of 76 eyes (38 patients) and 40 eyes of 20 healthy controls were enrolled in this retrospective-prospective study. Macular Vessel Density (MVD) and Foveal Avascular Zone (FAZ) were calculated in 2.9 x 2.9 mm OCT-A images (Heidelberg Spectralis II, Heidelberg, Germany). MVD was measured in three layers: Superficial Vascular Plexus (SVP), Intermediate Capillary Plexus (ICP), and Deep Capillary Plexus (DCP) in circular sectors (c1, c2, and c3). All scans were analyzed using the EA-Tool (Version 1.0), which was coded in MATLAB (The MathWorks Inc, R2017b). FAZ area (mm^2), horizontal and vertical diameters were manually measured in full-thickness scan, SVP, ICP and DCP.

Results: In FD group FAZ was increased in horizontal, vertical SVP and all DCP measurements vs. controls ($p<0.05$). MVD was higher in all sectors except DCP c1 in FD group vs. controls ($p<0.05$). MVD of the SVP, ICP and DCP in c1 and SVP and DCP in c2 showed moderate to strong negative correlation with FAZ. MVD in patients with reduced GLA Enzyme activity was decreased in DCP c1 vs. patients with normal enzyme activity. MVD in patients with elevated lysoGb3 activity was increased in DCP full-thickness, c2 and c3, ICP full-thickness and c3 vs. normal lysoGb3 activity. LysoGb3 activity was increased in patients with cornea verticillata (CV) compared with patients without CV ($p<0.05$). MVD in patients with CV was increased in all ICP and DCP sectors ($p<0.02$). There was no difference in MVD in patients with and without tortuositas vasorum. Extended results are presented in Fig. 1 and Fig. 2.

Conclusions: FAZ and MVD are increased at first examination in FD patients. Enlargement of FAZ could be a result of an underlying microvascular dysfunction in FD. Increased MVD in FD could be a result of vasodilation caused by an increased endothelium-mediated vascular reactivity due to accumulation of the glycosphingolipids in the vascular endothelium. Cornea verticillata and increased lysoGB3 activity seem to be associated with impaired microvasculature in FD.

CONTROL ID: 3708099

SUBMITTER (NAME ONLY): Hazem Mousa

TITLE: The P-DUKE calculator: a novel tool for predicting outcomes after penetrating keratoplasty

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.M. Mousa, M. Soifer, N. Azar, A.J. Snyder, V.L. Perez, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|J. Feghali, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|A. Song, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify pre-operative characteristics in penetrating keratoplasty (PK) predictive of graft survival in order to develop a standardized web-based outcome risk calculator.

Methods: A retrospective chart review was carried out at the Duke Eye Center using procedure code 65730. Inclusion criteria were adults that underwent full-thickness PK from January 1, 2013, till December 31, 2017, that had at least a 4-year follow-up or failed within. Lack of success was concluded if the patient underwent rejection (acute or chronic) despite anti-inflammatory therapy, graft failure, graft dehiscence, visually significant edema, or complications requiring repeat transplantation. Univariable analysis of pre-operative characteristics was performed followed by a stepwise multivariable logistic regression to obtain a predictive model with a $p<0.05$ cutoff. Discrimination and calibration were assessed using the area under the curve (AUC) and Hosmer-Lemeshow (HL) test, respectively.

Results: 178 transplants were included of which 62 (34.8%) were unsuccessful. History of anterior segment surgery (same eye) ($p<0.001$), diabetes ($p=0.008$), smoking ($p<0.001$), corneal neovascularization ($p<0.001$), conjunctival injection ($p<0.001$), synechiae presence ($p=0.002$), and indication other than keratoconus ($p<0.001$) were associated with non-success in the univariable analysis. Multivariable analysis produced a model consisting of: (1) previous ocular surface surgery in the same eye (OR: 2.09, $p=0.06$), (2) diabetes mellitus (OR: 3.48, $p=0.013$), (3) use of tobacco (OR: 3.77, $p=0.007$), (4) KNV (i.e. corneal neovascularization) (OR: 2.42, $p= 0.042$), and (5) erythematous conjunctiva (i.e. conjunctival injection) (OR: 4.36, $p=0.001$). The predictive model was summarized by the acronym P-DUKE. The AUC achieved was 0.82 and the HL test indicated adequate calibration ($p>0.05$). The calculator was then deployed under the URL: https://pduke.shinyapps.io/PDUKE/

Conclusions: The P-DUKE calculator is a readily accessible tool allowing for a standardized assessment of risk in patients planned for PKs and can supplement clinical judgment regarding follow-up and patient expectations irrespective of physician expertise.

CONTROL ID: 3708106

SUBMITTER (NAME ONLY): Jennifer Nadelmann

TITLE: SGLT2 inhibitors and diabetic retinopathy progression

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. McGeehan, Y. Yu, Center for Preventive Ophthalmology and Biostatistics, Penn Medicine, Philadelphia, Pennsylvania, UNITED STATES|J.B. Nadelmann, C.G. Miller, B.L. VanderBeek, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sodium-glucose co-transporter 2 (SGLT2) inhibitors are widely used for the management of diabetes mellitus (DM). SGLT2 is expressed by retinal pericytes, thus SGLT2 inhibition may prevent retinal pericyte loss and have a protective effect in diabetic retinopathy. By decreasing glucose in the retinal microcirculation, SGLT2 inhibitors may reduce glucose-induced endothelial dysfunction. This study aims to evaluate whether SGLT2 inhibitors affect progression of non-proliferative diabetic retinopathy (NPDR) compared to standard of care.

Methods: A retrospective cohort study was conducted to compare subjects enrolled in a commercial and Medicare advantage medical claims database who filled a prescription for a SGLT2 inhibitor between the years 2013 to 2020 to unexposed controls, matched in a 1:3 ratio, who initiated an alternative diabetic anti-hyperglycemic agent. Patients were excluded if they were enrolled for less than two years in the plan, had no prior ophthalmologic exam, had no diagnosis of NPDR on or prior to the index date, had a diagnosis of diabetic macular edema (DME) or proliferative diabetic retinopathy (PDR), had received treatment for vision threatening diabetic retinopathy (VTDR), or were younger than 18 years. To balance covariates of interest between the exposed and unexposed cohorts, an inverse probability treatment weighting (IPTW) propensity score for SGLT2 inhibitor exposure was used. Multivariate Cox proportional hazard regression modeling was employed to assess the hazard ratio (HR) for VTDR, PDR or DME relative to SGLT2 exposure.

Results: A total of 6065 patients initiated a SGLT2 inhibitor were matched to 12890 controls. There were 734 (12%), 657 (10.8%) and 72 (1.18%) cases of VTDR, DME and PDR, respectively in the SGLT2 inhibitor cohort. Conversely, there were 1479 (11.4%), 1331 (10.3%), 128 (0.99%) cases of VTDR, DME and PDR, respectively in the control cohort. After IPTW, Cox regression analysis showed no difference in hazard for VTDR, PDR or DME in the SGLT2 inhibitor-exposed cohort relative to the unexposed group [HR=1.04, 95% CI 0.94 to 1.15 for VTDR; HR=1.03; 95% CI 0.93 to 1.14 for DME; HR=1.22; 95% CI 0.89 to 1.67 for PDR].

Conclusions: Exposure to SGLT2 inhibitor therapy was not associated with progression of NPDR compared to patients receiving other diabetic therapies.

CONTROL ID: 3708108

SUBMITTER (NAME ONLY): Mohammad Eslami

TITLE: Evaluation of Deep Learning Visual Field Prediction Models for Clinical Relevance

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep learning methods have recently been used for predicting future visual fields (VFs) using baseline or longitudinal VFs. In clinical practice, glaucomatous VF loss progression is a comparatively rare event. It is of particular clinical relevance if these prediction models can accurately identify patients with disease progression to aid clinicians in avoiding vision loss. Here, we evaluate two previously described models for potential biases in over- or underestimating VF changes over time.

Methods: We consider two recent studies, namely Wen et al. (MWen) to predict VF sensitivity and Park et al. (MPark) to predict total deviations (Fig. 1). All reliable (false negatives/positives≤30%, fixation losses≤30%) Humphrey 24-2 VFs from Mass. Eye and Ear glaucoma service from 1999 to 2020 were included. We re-implemented the methods and made them available to other investigators. As in the original studies, pointwise mean absolute error (PMAE) was used to measure model prediction accuracy. A 5-fold cross-validation scheme was utilized, and the models are additionally compared against a no-change model, i.e. the baseline VF for MWen and the last-observed VF for MPark were used as the predicted VF.

Results: The evaluation dataset included 54,373 samples from 7,472 people for MWen and 24,430 samples from 1,809 people for MPark, depending on the method's needs. The PMAEs obtained by each method are shown in Fig. 1, and the results (%95 CI, MWen:2.21-2.24, MPark:2.56-2.61) are close to the original papers. Fig. 2 depicts 4 scatterplots w.r.t. mean of sensitivity for MWen and mean of deviation for MPark where A and B show predicted vs. truth, C and D show the prediction’s errors concerning actual changes. While both approaches produce satisfactory outcomes in Figs 2A and 2B, both methods exhibit a large error in projecting worsening cases, as seen in Figs 2C and 2D (the green dashed line shows a hypothetical unbiased model). It may also be deduced that the MPark that uses longitudinal VFs is superior to MWen that uses only baseline VFs.

Conclusions: Our evaluation of the two VF prediction models confirms the low PMAEs reported in the original studies. However, both models underpredicted worsening of VF loss over time. As detecting the progression of VF loss is a major motivation to obtain clinical VFs, we suggest explicitly considering this aspect in future model evaluations as well as the data characteristics.

CONTROL ID: 3708110

SUBMITTER (NAME ONLY): Cord Huchzermeyer

TITLE: Comparing functional defects measured by mfERG and standard automated perimetry in patients under (hydroxy-)chloroquine therapy

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.R. Huchzermeyer, J.J. Kremers, Ophthalmology, Universitatsklinikum Erlangen, Erlangen, Bayern, GERMANY|

Commercial Relationships Disclosure: Cord Huchzermeyer: Commercial Relationship: Code N (No Commercial Relationship) | Jan Kremers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We characterized the relationship between multifocal electroretinograms (mfERG) and standard automated perimetry (SAP) in patients receiving therapy with (hydroxy-)chloroquine.

Methods: In this retrospecitve observational study, data from patients who were screened for toxic maculopathy in our outpatient clinic were included. Perimetry was performed with the Octopus 900 perimeter (Haag-Streit, Switzerland) using the M-pattern (81 locations in the central 10°) and a full-threshold algorithm. MfERGs were measured in 61 hexagons in the central 30° of the visual field with the RetiPortSystem (RolandConsult). MfERGs with an amplitude ratio between rings 2 and 5 smaller or equal to 2 were defined as having Bull's-Eye-Maculopathy (BEM).

Results: The right eyes of 49 patients (age at baseline: 52.7 ± 13.4 yrs, 40 female, 35 hydroxychloroquine) were included. Follow-up was between 0.5 and 8.0 years. Clinically, no patient showed clear progression or developed new BEM during follow-up. Therefore, we averaged measurements over several visits for this first analysis. The spatial distribution of functional losses in mfERG and SAP in patients with BEM (n = 9) is shown in Figure 1.

Both mfERGs and visual fields demonstrate that locations/segments that correspond to the second ring were not equally affected - in our patients, regions inferior to the foveola retained better function. Patients with definite BEM in the ERG also had visual field defects. In a first exploratory analysis, a quadratic linear model seemed adequate to describe the relationship between mfERG amplitude and perimetric defect (see inset of Figure 1, $p < 0.001$).

Conclusions: Improved screening for functional consequences of toxic maculapathy might be achieved by techniques that 1) analyze individual loci instead of rings (possibly using artificial intelligence) and 2) combine mfERG and perimetry measurements.

CONTROL ID: 3708111

SUBMITTER (NAME ONLY): Luis Martinez-Velazquez

TITLE: Predicting Visual Outcomes in Central Retinal Vein Occlusion (CRVO) with Vascular Metrics and Non-Perfusion Area (NPA) Measured by Wide-Field Swept-Source OCT-Angiography (WF SS-OCTA)

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Martinez-Velazquez, G. Baldwin, I. Garg, R. Zeng, M. Duich, J.Y. Moon, F. Vingopoulos, H. Wescott, T. Koch, N.A. Patel, D.M. Wu, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.A. Martinez-Velazquez, G. Baldwin, I. Garg, Y. Cui, R. Katz, R. Zeng, M. Duich, J.Y. Moon, F. Vingopoulos, H. Wescott, T. Koch, N.A. Patel, D.M. Wu, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Cui, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Previous studies have used optical coherence tomography angiography (OCTA) to evaluate CRVOs using smaller sized angiograms, namely 3x3 mm and 6x6 mm. We used WF SS-OCTA to quantify macular vascular metrics following CRVO and used these to model the observed visual acuity (VA).

Methods: 109 eyes of 59 patients, (59 eyes with CRVO- 9 ischemic, and 50 fellow eyes) were imaged using WF SS-OCTA (PLEX® Elite 9000, Carl Zeiss Meditec) between March 2019 and October 2021. We analyzed 12x12mm angiograms centered on the fovea using ARI Network (Zeiss Portal) Macular Density Algorithm (v0.7.3) for vessel density (VD), vessel skeleton density (VSD), foveal avascular zone (FAZ) area, circularity, and perimeter. The NPA of each macula was calculated using ImageJ. We performed mixed effects multivariate regression analyses.

Results: Our study population consisted of 33 Male (55.93%) patients with a median age of 63 years (21-86). The median logMAR visual acuity for CRVO eyes was 0.24 (20/35) vs. 0.03 (20/21) in the fellow eye ($p<0.0001$). CRVO eyes had larger NPAs than fellow eyes (median (m) 27.5, 7.16; Interquartile Range (IQR) 23.98, 8.47; $P<0.0001$), and greater irregularity of the FAZ (m 0.53, 0.79; IQR 0.25, 0.15; $P=0.005$). We did not detect a statistical difference in FAZ area (m 0.90, 0.27; IQR 0.29, 0.25, $P=0.66$) or perimeter (m 4.35, 1.23; IQR 1.88, 1.23; $P=0.2$).

Our regression analyses suggest that after controlling for age, ischemic CRVOs (ß= 0.35, $p=0.006$), larger NPAs (ß=0.007, $p<0.0001$), and larger FAZ area (ß= 0.048, $p=0.008$) were associated with worse VA. On receiver operating curve (ROC) analysis, wide-field NPA was the best OCTA metric in predicting VA worse than 20/50, area under the curve (AUC) 0.91.

Conclusions: In patients with CRVO, the WF SS-OCTA allows for quantification of NPAs in a larger region of the macula, while still providing useful information pertaining to the perifoveal vascularity. Our study reinforces prior reports that larger NPAs and larger FAZ area are associated with worse VA. WF SS-OCTA could therefore contribute to the evaluation, management, and counseling of a patient with CRVO, by identifying factors associated with worse visual outcomes following the diagnosis.

CONTROL ID: 3708113

SUBMITTER (NAME ONLY): Ethan Cohen

TITLE: Cobalt causes a rapid long lasting swelling of neurons in the mouse retina using confocal and optical coherence microscopy.

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.D. Cohen, S.C. Wood, OSEL/CDRH, US Food and Drug Administration, Silver Spring, Maryland, UNITED STATES|J. Hanig, CDER/OPQ/OTR, US Food and Drug Administration, Silver Spring, Maryland, UNITED STATES|H. Qian, National Eye Institute, Bethesda, Maryland, UNITED STATES|R. Brehl, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cobalt-containing hip implants can in rare cases cause retinopathy in patients. We have examined cobalt's effects in real time on the retinal structure and glia in the mouse eye.

Methods: We examined the effects of cobalt using either an isolated retina or a mouse retinal eyecup preparation. The retina was perfused with an oxygenated Ames Ringer and time lapse imaged using either confocal or optical coherence microscopy on a modified Leica MP microscope. Cobalt (0.2-1mM), cadmium 0.2mM, nickel 0.2mM, and ATP (0.1-1mM) solutions were held in gassed wells and applied by bath application at 35^{O}C. Test agents were applied for 10 minutes followed by a >30min wash out period. To track the microglia, an CX3CR1 GFP (green fluorescent protein) transgenic mouse was used and Z-stack confocal images were taken.

Results: Application of cobalt (1mM) for 10min. caused a rapid increase in the subretinal space (SRS) width in the OCT B-scan which averaged 22±10% at wash out (mean ±s.d., n=6 retinas), and the SRS width continued to swell even after returning to normal Ringer. After cobalt, the width of the outer nuclear layer (photoreceptor cells) also began to slowly increase. A hyperreflective line developed at the border of the inner nuclear and inner plexiform layer. After application of 1mM cobalt, there was a 47±11% increase in the average number of microglia filopodia in the inner retina (n=4 retinas, mean ±s.d. $p < 0.05$), while the outer retinal microglia were less affected. Application of cadmium increased the number of inner microglia filopodia similar to that seen with cobalt, while nickel had little effect. Application of 100uM ATP also increased the number of filopodia of inner microglia, while the outer microglia were less affected (n=5,6 retinas).

Conclusions: Our results indicate cobalt application has rapid and persistent effects on the retina even after prolonged washout. Cobalt was particularly toxic causing photoreceptor swelling. After cobalt application, the number of inner retinal microglia filopodia increased in a manner similar to that seen with ATP. Although cobalt is known for inducing hypoxia dependent transcription mechanisms, our results imply there is a more rapid direct effect of cobalt ions on the photoreceptors and other retinal neurons possibly due to oxidative stress. Which ion channels allow influx of cobalt into the retinal cells is currently unknown.

CONTROL ID: 3708114

SUBMITTER (NAME ONLY): Marko Oydanich

TITLE: Tolerability and Persistence with Netasurdil Containing Regimens in Patients with Primary and Secondary Glaucomas

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Oydanich, E. Roll, Y. Shah, A. Khouri, Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Registration clinical trials have reported adverse effects of Netasurdil 0.02% and Netasurdil/Latanoprost 0.02%/0.05% (Rhopressa and Rocklatan, Aerie Pharmaceuticals, NJ, USA) with hyperemia occurring in a significant proportion of glaucoma patients. However, less is known about Netasurdil's tolerability in "real-life" clinical practice and in multi-drug regimens. The purpose of this study was to examine the adverse effects and discontinuation rates in primary and secondary glaucoma patients taking Rhopressa or Rocklatan as part of a multi-drug regimen.

Methods: A total of 105 patients (138 eyes) with either primary open angle glaucoma (POAG) or a secondary form of glaucoma were reviewed retrospectively over the course of one year after starting either Rhopressa or Rocklatan. Discontinuation rates due to intolerance or inefficacy, and patient reported side effects were followed over the course of one year after starting the medication. Chi-squared analysis was used to examine differences in rate of side effects between patient groups.

Results: Reported side effects of Netasurdil regimens included tearing, itching, redness, pain, blurred vision, and headaches. All patients with either POAG or secondary glaucomas were on multi-drug regimens (Mean ± SD; 3.3 ± 1.2 vs. 3.6 ± 1.2; $p = 0.08$). POAG patients reported higher rates of tearing, itching, redness, and headaches compared to secondary glaucoma patients. However, this difference was not statistically significant between groups ($p>0.05$). Patients with secondary glaucoma had a higher discontinuation rate than POAG patients (8.8% vs 4.9%). Further analysis of the discontinuation rate revealed that 4.9% and 5.3% of POAG and secondary glaucoma patients respectively, discontinued their Netasurdil regimens due to intolerance. In 3.5% of secondary glaucoma patients discontinuations were due to inefficacy (none in the POAG group).

Conclusions: Patient reported side effects of Netasurdil regimens ranged from 0-22% in patients on multiple medications. Patient reported hyperemia occurred less frequently than in clinical trials. Discontinuations rates were 4.9-8.8% and were more likely in secondary glaucomas. Many of the side effects overlapped with ocular surface disease signs and symptoms. This information can be useful in guiding physicians using Netasurdil regimens in patients with glaucoma on multiple pharmacotherapies.

CONTROL ID: 3708115
SUBMITTER (NAME ONLY): Jennifer Pham
TITLE: Neuroprotection of human and rodent retinal ganglion cells by a hybrid small molecule, SA-2
SESSION TITLE: Neuroprotection, blood flow and ischemia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J.H. Pham, G.A. Johnson, S. Acharya, D.L. Stankowska, Department of Pharmacology and Neuroscience, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|
Commercial Relationships Disclosure: Jennifer Pham: Commercial Relationship: Code N (No Commercial Relationship) | Gretchen Johnson: Commercial Relationship: Code N (No Commercial Relationship) | Suchismita Acharya: Commercial Relationship: Code N (No Commercial Relationship) | Dorota Stankowska: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Current treatments of glaucoma are aimed at lowering intraocular pressure (IOP), which is a key driver of retinal ganglion cell (RGC) death. Another contributing factor to RGC death is exposure to reactive oxygen species (ROS). At present, there is no FDA-approved neuroprotective treatment to prevent glaucomatous optic neuropathy and loss of RGCs. Our novel hybrid molecule, SA-2, contains both a nitric oxide (NO) donating group to lower IOP and a ROS scavenging group to protect RGCs. We hypothesize that SA-2 will inhibit the death of RGCs in an in vitro and an ex vivo neurotrophic factor deprivation model.

Methods: Retinal punches from human explants (n=4 donors/experiments) were isolated and treated with either SA-2 [1 mM] or vehicle and maintained without neurotrophic factors for 7 days ex vivo. In each experiment, 4 baseline retinal explants were collected on day 0. At the end of the experiment, explants were immunostained with RBPMS and Brn-3a (RGC-specific markers) and cell survival was analyzed.

In three biological replicates, primary RGCs were isolated from rat pups and treated with either SA-2 (1 mM, 500 µM, 100 µM) or vehicle with or without neurotrophic factors for 48 h. Active caspase 3 and 7 assay was performed and cell counts were analyzed.

In another set of experiments, rat retinal explants were isolated and incubated with tert-Butyl hydroperoxide (TBHP) along with either SA-2 [1 mM] or vehicle for 2 h (n=2-4 explants/group). Production of superoxide by mitochondria was assessed using MitoSOX reagent.

All cell counts were performed in a masked manner using ImageJ. One-way ANOVA or nonparametric Kruskal-Wallis was used for statistical analysis.

Results: In ex vivo human retinal explants, there was a significant increase in RGC survival by 39% in the SA-2 treated group compared to the vehicle group at day 7 ($p<0.0001$). In rodent primary RGCs, SA-2 mediated a significant decrease in apoptotic cells by 30% ($p<0.01$) and a 67% ($p<0.05$) decrease in dead cell count. In rodent retinal explants, there was a significant decrease (by 59%, $p<0.0001$) in the production of superoxide by mitochondria in the TBHP and SA-2 treated group, compared to the TBHP vehicle group.

Conclusions: SA-2 was shown to be effective at preserving retinal ganglion cell survival in human retinal explants, rat retinal explants and primary rat RGCs by preventing apoptosis and protecting the cells from oxidative stress.

CONTROL ID: 3708117

SUBMITTER (NAME ONLY): T Michael Nork

TITLE: Effect of intraocular pressure (IOP), volume and location on the distribution of aqueous solutions injected into the suprachoroidal (SC) space

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Nork, A.W. Katz, C.B. Kim, C.A. Rasmussen, J.N. Ver Hoeve, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|T. Nork, H.D. Wabers, E. Bentley, Ocular Services On Demand (OSOD), Madison, Wisconsin, UNITED STATES|C.B. Struble, Labcorp Drug Development, Madison, Wisconsin, UNITED STATES|A. Savinainen, Aura Biosciences, Cambridge, Massachusetts, UNITED STATES|E. Bentley, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported variable distribution of endothelin-1 effects on choroidal blood flow when injected suprachoroidally (ARVO 2019, #1637). We wanted to determine if this was due differences in IOP at the time of injection. We also wanted to know if a larger volume or splitting the same volume in opposite quadrant injections provided more complete distribution.

Methods: For the SC injections, 34-gauge needles with a stop exposing 700 µm of the needle tip were used. New Zealand White rabbits were injected with 0.0074% indocyanine green (ICG) in balanced salt solution. A single injection of 50 µL was given 5 mm posterior to the corneal limbus in the superotemporal quadrant. The fundus was imaged with a Heidelberg scanning laser ophthalmoscope. The IOP was adjusted to 10 mmHg in one eye and either 35 mmHg or 55 mmHg in the fellow eye manometrically. Six rabbits with a crossover design were used for the 35 mmHg study and three rabbits for the 55 mmHg study. The distribution of ICG in the inferonasal quadrant was measured. In a separate study, two 50 µl injections with ICG and 0.1% fluorescein in opposing quadrants assessed coverage. Single injections of 100 µL were also done. To confirm that the observed fluorescence was not immediately transient, another set of rabbits were injected SC with 50 µL of a virus like particle (VLP) derived from HPV16 conjugated with Alexa Fluor 488 and imaged at 30 minutes and 24 hours post-dose.

Results: IOP did not significantly affect the distribution of ICG given as a single superotemporal SC injection. A single injection of 100 µL had better but still incomplete coverage than 50 µL. Two injections of 50 µL each (one of ICG and one of fluorescein) in opposite quadrants provided nearly complete SC coverage although some overlap and small gaps were present. Labeling with VLP*Alexa Fluor 488 was also incomplete following 50 µL injections and there was no change in the labeling pattern after 24 hours.

Conclusions: Distribution of aqueous solution SC injection is not dependent on IOP but on injection parameters including volume, number, and location of injections. A 100 µL single injection provides improved coverage compared to 50 µL and there is further improvement when two injections are administered in opposite quadrants of 50 µL each.

CONTROL ID: 3708118

SUBMITTER (NAME ONLY): Amisha Dave

TITLE: Correlations between Renal Function and Age-Related Macular Degeneration (AMD) Phenotypes

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Dave, K. Hess, K. Chen, H. Wiley, T.D. Keenan, E. Agron, E.Y. Chew, C.A. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a leading cause of blindness in the elderly. Chronic kidney disease (CKD) is also commonly associated with age. These two diseases share risk factors such as age, smoking, and hypertension as well as pathophysiologic similarities affecting the glomerular capillaries and the retinal choroid. This study investigates potential correlations between renal function and AMD features as assessed with multimodal retinal imaging.

Methods: Participants were part of a study that investigated dark adaptation (DA) function in those ≥ 50 years of age with varying AMD severities (NCT01352975) who also had eGFR (ml/min/1.73m^2) values obtained from renal function laboratory testing of serum creatinine and cystatin C. Multimodal imaging included color fundus photography and optical coherence tomography volumes from visit dates associated with serum samples and were graded by the Wisconsin Reading Center for the presence of AMD features. Associations of eGFR with AMD features and severity grades, age, smoker status, and DA function represented by rod-intercept time (RIT) were investigated. Simple univariate analyses, age-corrected multivariate analyses, and a feature-selecting LASSO regression were performed for eGFR as a continuous dependent variable.

Results: A total of 110 patients (mean age ± SD 75.1 ± 9.4 years [range 53–95]; mean eGFR ± SD 70.7 ± 18.2 ml/min/1.73m^2 [range 19.3–109.8]) were included. 95 patients had eGFRs < 90 and 36 patients had eGFRs < 60. In univariate analyses age (estimate -1.16 units/year, [CI -1.46 – -0.87], p<0.0001), RIT (estimate -0.54 units/minute, [CI -0.81 – -0.27], p<0.001) and reticular pseudodrusen (RPD) (-11.12 units for RPD presence in either eye, [CI -20.23 – -2.01], p=0.017) were associated with decreased renal function. However, in age-corrected multivariate models, age was the only significant variable associated with renal function, confirmed by LASSO regression.

Conclusions: Age was found to be strongly correlated with decreased renal function in both univariate and age-corrected multivariate analyses. While one of the strengths of this study is the well-phenotyped AMD cohort with serum values estimating renal function, it was a relatively small study. Further studies investigating the relationship between CKD and AMD phenotypes will need larger populations to better understand possible correlations between these diseases.

CONTROL ID: 3708119

SUBMITTER (NAME ONLY): Harrison Sciulli

TITLE: Real World Ophthalmic Ambulatory Surgery Center Endophthalmitis and Toxic Anterior Segment Syndrome Rates

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Sciulli, A. Miller, D.G. Miller, Ophthalmology, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|H. Sciulli, Ophthalmology, University of Kansas School of Medicine, Kansas City, Kansas, UNITED STATES|A. Miller, Ophthalmology, University of Missouri System, Columbia, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Harrison Sciulli: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Miller: Commercial Relationship: Code N (No Commercial Relationship) | David Miller: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Published rates of endophthalmitis and toxic anterior segment syndrome (TASS) vary in the literature. Due to rarity and hesitation to report, there is a gap in understanding of occurrences of these conditions. We performed a retrospective data analysis of endophthalmitis and TASS rates at a high volume ophthalmic only ambulatory surgery center (ASC).

Methods: We gathered data from the ASC from 2016 to September 2021 for endophthalmitis and from 2009 to September of 2021 for TASS. Surgeries were organized into anterior segment (referring to cataract surgery, glaucoma surgery, and cornea surgery) as well as posterior segment surgery (referring to retina surgery only) relative to case volume. Only intraocular surgeries were counted. Laser surgeries as well as oculoplastic surgeries were excluded. Additionally, we analyzed the responsible organisms by type and gram stain.

Results: The overall rate of endophthalmitis was 0.12% (36 out of 32,051 intraocular surgeries). For anterior segment surgeries, the rate of endophthalmitis was 0.10% (21 out of 21,138). For posterior segment surgeries, the rate of endophthalmitis was 0.14% (16 out of 11,513). The p value using a student's t-test between anterior and posterior segment total cases of endophthalmitis was not statistically significant (P=0.517) nor was the case rate statistically significant (P=0.380). The most common gram positive organism was staphylococcus epidermidis, and the most common gram negative organism was serratia marcescens. The p value using a student's t-test between gram positive and gram negative organisms was significant for both surgery types favoring gram positive (P=0.045 for anterior segment and 0.042 for posterior segment). The rate of TASS from the years recorded per total number of cases was 0.073%.

Conclusions: The rate of endophthalmitis between anterior and posterior segment surgeries was not statistically significant. This information is clinically significant for several reasons. When discussing risks during the pre-operative visit, one can more accurately describe the risk. Additionally, this has led to introspection and changed practices regarding sanitation at the surgery center. The rate of TASS was low without a single case most years.

CONTROL ID: 3708120

SUBMITTER (NAME ONLY): Samuel Cohen

TITLE: Importance of 23 Selection Criteria Considered When Offering Interview Invitations to Ophthalmology Residency Applicants: A Survey of Program Directors

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Cohen, S. Pershing, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Samuel Cohen: Commercial Relationship: Code N (No Commercial Relationship) | Suzann Pershing: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Competition for ophthalmology residency positions continues to grow. The purpose of our study was to identify the factors that ophthalmology residency program directors consider most important when determining whether to extend an interview invitation to residency applicants.

Methods: We developed a six-question web-based questionnaire to be distributed to all ophthalmology residency program directors. The first three questions inquired about program demographics while the remaining three questions elicited information regarding the importance (Likert scale 1-5, with one being “not important” and five being “very important”) of 23 different selection criteria used by ophthalmology residency program directors when evaluating applicants for residency interviews. Program directors were also asked to identify the one selection criteria they felt was most important in evaluating residency applicants.

Results: The overall response rate was 56.5% (70/124). The selection criteria with the highest average importance score were core clinical clerkship grades (4.26/5) followed by letters of recommendation (4.06/5), and USMLE Step 1 score (4.03/5) (Table 1). When asked for the single most important selection criteria used when deciding to offer an applicant an interview invitation, the most frequent answer provided was “core clinical clerkship grades” (19/70, 27.1%), with “USMLE Step 1 score” (9/70, 12.9%) and “rotations at your department” (6/70, 8.6%) also common responses (Figure 1).

Conclusions: Our results reveal that core clinical clerkship grades, letters of recommendation, and USMLE step 1 score were the selection criteria deemed most important by ophthalmology residency program directors. With fundamental changes to both USMLE step 1 scoring and the clerkship grading system for many medical schools rapidly approaching, the relative importance of other selection criteria evaluated in this study will likely increase. The results of our study may be useful to medical students navigating the ophthalmology residency application process as well as to residency programs and program directors.

CONTROL ID: 3708121

SUBMITTER (NAME ONLY): Lukas Mees

TITLE: Ophthalmic surgical procedures in patients with inherited retinal dystrophy

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mees, A. Liu, A. Wu, X. Kong, M.S. Singh, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M. Li, X. Kong, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited retinal dystrophies (IRDs) affect over two million people worldwide, and commonly have ocular comorbidities requiring surgery. Ocular surgery in IRDs may pose unique risks. There is a lack of information on those risks, partly because the distribution of surgery types in IRDs in poorly understood. The current study aims to describe the associations of IRD phenotype and genotype, age, and sex with surgical prevalence.

Methods: A retrospective chart review was performed on 1472 eyes from 736 individuals seen at the inherited retinal dystrophy clinic at Johns Hopkins. Phenotypes were categorized as belonging to the macular, cone, and cone-rod (MCCRD) spectrum or retinitis pigmentosa (RP) spectrum conditions. Surgeries were grouped into major categories. Descriptive statistics, prevalence odds ratios for surgical categories, age at cataract surgery based on phenotype, sex, and eye were analyzed using R.

Results: Cataract extraction and intraocular lens insertion (CEIOL) made up the majority of surgeries (53.6%). Among all patients, the RP:MCCRD prevalence odds ratio for CEIOL was 2.59 ($p = 0.002$), 0.4 ($p = 0.04$) for refractive surgery, and 0.47 ($p = 0.04$) for retinal surgery. Neither genetic testing status nor sex were significantly associated with surgery prevalence. The age to the first CEIOL surgery in each patient was lower in RP-spectrum compared to MCCRD-spectrum patients (hazard ratio = 2.11, $p < 0.001$), but was not associated with sex, eye, or genetic testing status.

Conclusions: CEIOL was the most common procedure in this cohort of IRD patients, and may generally occur earlier in RP patients than in MCCRD patients. IRD phenotype category may be associated with the prevalence of the different types of ophthalmic surgical procedures in IRD patients. Further studies are needed to further understand the influence of genotypes and phenotypes on ocular surgery prevalence and outcomes in IRD patients.

CONTROL ID: 3708125

SUBMITTER (NAME ONLY): Himeesh Kumar

TITLE: Exploring Reticular Pseudodrusen Extent and Impact on Cone-Mediated Visual Sensitivity in Intermediate Age-Related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Kumar, R.H. Guymer, L.A. Hodgson, X. Hadoux, Z. Wu, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|H. Kumar, R.H. Guymer, Z. Wu, Surgery (Ophthalmology), The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To explore the impact of the extent of reticular pseudodrusen (RPD) on cone-mediated visual sensitivity in individuals with intermediate age-related macular degeneration (AMD).

Methods: 570 eyes from 285 participants with bilateral large drusen underwent microperimetry testing under mesopic conditions to assess the visual sensitivity of the central 3.6-mm region and multimodal imaging to determine the extent of RPD in the central 20^{o}x20^{o} region (at the eye level). Mean visual sensitivity within five sectors in the central 3.6-mm region sampled on microperimetry and the extent of RPD in these sectors, were derived. Linear mixed models were used to examine the association between the extent of RPD on (i) overall mean visual sensitivity, and (ii) sector-based mean sensitivity.

Results: An increasing extent of RPD at the eye level and within sectors were associated with a significant reduction in overall and sector-based mean sensitivity respectively ($P<0.001$ for both). However, when both RPD parameters were considered together in a multivariable model, only an increasing extent of RPD at the eye level ($P<0.001$), and not within each sector ($P=0.178$), was independently associated with reduced sector-based mean sensitivity.

Conclusions: Cone-mediated visual sensitivity is generally reduced in non-late AMD eyes with RPD compared to AMD eyes without RPD, with greater reductions with an increasing extent of RPD. However, reduced sector-based visual sensitivities are explained by the overall extent of RPD present, rather than their extent within the sector itself. These findings suggest that there are generalized pathogenic changes in eyes with RPD accounting for the observed cone-mediated visual dysfunction.

CONTROL ID: 3708128
SUBMITTER (NAME ONLY): Tarushi Tanaya
TITLE: Impact of Cataract Surgery on Rod-Mediated Dark Adaptation in Older Adults
SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: T. Tanaya, A. Berlin, T.A. Swain, G. McGwin, M. Clark, M.A. Callahan, V. Lolley, J. Swanner, C.A. Curcio, C. Owsley, Department of Ophthalmology & Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|
Commercial Relationships Disclosure: Tarushi Tanaya: Commercial Relationship: Code N (No Commercial Relationship) | Andreas Berlin: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Swain: Commercial Relationship: Code N (No Commercial Relationship) | Gerald McGwin: Commercial Relationship: Code N (No Commercial Relationship) | Mark Clark: Commercial Relationship: Code N (No Commercial Relationship) | Michael Callahan: Commercial Relationship: Code N (No Commercial Relationship) | Virginia Lolley: Commercial Relationship: Code N (No Commercial Relationship) | Jason Swanner: Commercial Relationship: Code N (No Commercial Relationship) | Christine Curcio: Commercial Relationship(s);Code I (Personal Financial Interest):MacRegen;Code C (Consultant/Contractor):Genetech, Hoffman LaRoche;Code C (Consultant/Contractor):Regeneron | Cynthia Owsley: Commercial Relationship(s);Code P (Patent):MacuLogix

ABSTRACT BODY:

Purpose: There is little to no information available on the impact of phakia versus pseudophakia on the rate of rod-mediated dark adaptation (RMDA) in older adults. RMDA is increasingly used to understand the pathogenesis of AMD and considered as a potential endpoint measure in trials. There is some concern as to whether phakic and pseudophakic participants should be considered separately in studies evaluating rod intercept time (RIT), a measure of the rate of RMDA. Cataract reduces intensity and increases intraocular light scatter reaching the retina. The current analysis compares RIT in a sample of older adults before versus after cataract surgery.
Methods: Sixteen adults, ages ≥ 60 years old with nuclear sclerotic and/or cortical cataract were recruited from three cataract surgeons at UAB. One eye, scheduled for cataract surgery, was studied in each participant. Prior to surgery, RMDA was measured with the AdaptDx, and a slit-lamp photo of the cataractous lens was taken. The Lens Opacity Classification II system (LOCS II) was used by a trained, masked grader to assess the type and severity of the cataract. Approximately 2-3 weeks following surgery, RMDA was again measured. Fundus photography was performed. A trained, masked grader evaluated macular health using the AREDS 9-step classification system.
Results: Eyes had normal macular health (13), early (2) or intermediate AMD (1). Mean visual acuity improved after cataract surgery from 20/25 to 20/20, p=0.02. Mean RIT before cataract surgery was 13.2 minutes (SD 7.3), and mean RIT after cataract surgery was 14.8 minutes (SD 7.3), p=0.03. This difference is within test-retest limits of agreement for RIT. Eyes with more severe cataract (≥ 4 in LOCS II grades in nuclear opacity, nuclear color and/or cortical cataract) had greater increase in RIT post-surgery compared to those with less severe cataract (p=0.0057).
Conclusions: Considering the sample regardless of cataract severity, measuring RIT in pseudophakia provides values similar to RIT measured before cataract surgery, taking test-retest repeatability into account. However, those with more advanced cataract yielded slower RMDA (higher RIT) post-surgery as compared to eyes with mild cataract, perhaps stemming from the bleaching light being more intense after cataract removal. Results can facilitate decisions in AMD clinical trial design where RMDA is used as an outcome measure.

CONTROL ID: 3708132

SUBMITTER (NAME ONLY): Christopher Fortenbach

TITLE: The economic burden of vision loss falls disproportionately on inhabitants of low-income nations

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.R. Fortenbach, M.D. Abramoff, Ophthalmology and Visual Sciences, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|M.D. Abramoff, Digital Diagnostics Inc, Coralville, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Over 200 million people worldwide suffer from moderate-to-severe vision impairment (MSVI) with an estimated global cost of hundreds of billions of US dollars per year in treatment, rehabilitation, and lost income. In absolute terms, most of the cost occurs in high income countries. However, this absolute cost does not fully convey the real-world impact of lost income, for example whether an individual's MSVI implies poverty, as poverty levels differ dramatically across countries. As no suitable measures exist to compare such normalized cost and impact, we propose a new metric by which to estimate and compare the impact of lost income due to MSVI globally.

Methods: Gross national income data per capita (adjusted to purchasing power parity in current international $, GNI-PPP) for 2020 as well as national poverty thresholds (in GNI PPP) were obtained from the World Bank for all available countries (https://data.worldbank.org/indicator/NY.GNP.PCAP.PP.CD). Variance data were not available. MSVI was assumed to carry a 30% average loss of income at the national level (Eckert et al., 2015; Marques et al., 2021). The poverty threshold for the nation was then expressed as a percentage of the adjusted income (Blindness Poverty Risk or BPR).

Results: Among the Global Burden of Disease super regions, high-income countries are home to approximately ten percent of the world's MSVI population but account for thirty percent of the lost income. When evaluating the proportion of income required to exceed the poverty threshold however, lower-income nations bore much of the global burden. The BPR was low in many of the countries with the greatest absolute losses in GNI-PPP due to MSVI (e.g., 19% in the United States), meaning that these countries had a lower proportion of income required to meet the poverty threshold. Central (51%) and East (58%) Sub-Saharan Africa, and Oceania (49%) had the most with Burundi (135%), the Central African Republic (102%), and the Democratic Republic of Congo (94%) requiring the greatest proportion of income to meet the poverty threshold.

Conclusions: Despite higher-income countries having the greatest absolute amount of lost earnings, the risk of poverty due to MSVI is greatest in lower-income countries. These first estimates provide a quantitative measure of the impact of lost income due to MSVI across countries where income and cost of living can vary dramatically.

CONTROL ID: 3708133

SUBMITTER (NAME ONLY): Mark Barakat

TITLE: Anti-VEGF Injections Prior to Cataract Surgery in Eyes with Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Barakat, Retinal Consultants of Arizona, Phoenix, Arizona, UNITED STATES|N. Boucher, R. Fernando, Vestrum Health, Naperville, Illinois, UNITED STATES|M. Barakat, The University of Arizona College of Medicine Phoenix, Phoenix, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: The incidence of macular edema after cataract surgery in patients with diabetes mellitus is higher than in the non-diabetic population, with both diabetic macular edema (DME) and pseudophakic cystoid macular edema (CME) correlating with the severity of pre-operative diabetic retinopathy. Treatment with intravitreal anti-vascular endothelial growth factor (VEGF) has shown improvement in the severity of diabetic retinopathy, as well as reduced the incidence of center-involving DME. The purpose of this study is to explore whether pre-operative anti-VEGF treatment has a positive impact on post-operative development or exacerbation of CME/DME in a large clinical database.

Methods: A retrospective study was performed on the Vestrum Health Database (EMR) looking at the incidence rate of macular edema (ME) seen in DR patients following cataract surgery, stratified by anti-VEGF use prior to surgery. Incidence of ME, VA and FT were tracked at 3 and 6 months post-surgery. Patient specific factors such as age, sex, DR severity were also assessed in modeling.

Results: Of 5,383 eyes matching inclusion/exclusion criteria, 4,565 (84%) were diagnosed with DME prior to cataract surgery. The rate of new onset, post-operative ME was 26% at month 3 (M3) and 33% at month 6 (M6) in eyes with no baseline ME. Of the 548 eyes that reported foveal thickness (FT) at baseline, M3, and M6, the FT remained relatively stable with pre-op anti-VEGF (n=347), with mean changes of +11 and +1 μm at M3 and M6. Eyes without pre-op anti-VEGF (n=201) experienced a lasting increase in FT: +25 and +23 μm at M3 and M6. The largest, independent driver of post-operative FT was baseline FT. However, in multiple linear regression modeling, pre-op anti-VEGF had a stabilizing effect on FT on those < 55 years old ($p = .006$). Multiple linear regression modeling of the 1531 eyes reporting visual acuity (VA) at all time points also demonstrated a beneficial correlation of pre-op anti-VEGF on VA at M3 ($p = .0004$) and M6 ($p = .0008$), independent of patient age.

Conclusions: In a systematic, retrospective review of over 5,000 eyes, anti-VEGF treatment prior to cataract surgery may have positive anatomic and functional effects on eyes with diabetic retinopathy and/or DME. Further study is warranted.

CONTROL ID: 3708136

SUBMITTER (NAME ONLY): Derek Orshan

TITLE: New Combined Structure-Function Models for Estimating Retinal Ganglion Cell Count in Glaucoma Subjects using Steady-State Pattern Electroretinography.

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Orshan, New York Institute of Technology, Old Westbury, New York, UNITED STATES|A. Tirsi, V. Gliagias, J. Tsai, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|S. Tello, Rye High School, Rye, New York, UNITED STATES|P. Derr, Diopsys Inc., New Jersey, UNITED STATES|A. Tirsi, S.A. Obstbaum, C. Tello, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To estimate retinal ganglion cell (RGC) count in preperimetric and early glaucoma eyes using optical coherence tomography (OCT) and steady-state pattern electroretinography (ssPERG) parameters.

Methods: In this prospective cross-sectional study, 25 subjects (50 eyes) were recruited at the Manhattan Eye, Ear, and Throat Hospital. Subjects underwent complete eye examinations, OCT, standard automated perimetry (SAP), and ssPERG testing. Eyes were divided into three groups based on clinical data: control (N= 30), preperimetric (N = 14), and early glaucoma (N = 6) eyes. The combined structure-function index (CSFI), which estimates retinal ganglion cell count from SAP and OCT parameters, was calculated in each study subject. Two prediction models were then derived using a step-wise linear regression to predict the CSFI from ssPERG parameters, age, and ARNFLT in 30 eyes selected at random (training sample). The prediction models were then validated using cross-validation with the remaining 20 eyes in our cohort (validation sample).

Results: Average retinal nerve fiber layer thickness (ARNFLT) and all ssPERG parameters were significantly different among groups (ANOVA $p < 0.001$). In each study group, ARNFLT and ssPERG parameters correlated with the CSFI ($r^2 \geq 0.31$, $p < 0.001$). In our training sample (N = 30), two step-wise linear regression models using ssPERG parameters magnitude (Mag) and magnitudeD (MagD), ARNFLT, and age resulted in significant equations ($F(3,26) \geq 63.00$, $R^2 \geq 0.88$, $p < 0.001$). The standard error of the estimate (SE) (SE ≤ 69,771.65) for each model corresponded to a small relative standard error (RSE) ≤ 7.20%. Applying the equations of each model to the validation sample (N = 20) resulted in similar metrics ($R^2 \geq 0.91$, SE ≤ 60,917.46, RSE ≤ 6.29%). ANOVA Games-Howell Post-Hoc analysis demonstrated that study groups exhibited more significant differences in RGC estimates than individual ssPERG and OCT measurements.

Conclusions: ssPERG parameters can be combined with OCT measurements to estimate RGC count in preperimetric and early glaucoma eyes, accounting for > 88% of variance from RGC counts estimated with the CSFI. These new combined structure-function models can distinguish preperimetric eyes from early glaucoma eyes.

CONTROL ID: 3708139

SUBMITTER (NAME ONLY): Megan Quinn

TITLE: A Retrospective Audit of Large Macular Hole Repair Techniques: ILM Peel vs ILM Flap.

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.C. Quinn, University Hospital Wishaw, North Lanarkshire, UNITED KINGDOM|D. Yorston, Gartnavel General Hospital, Glasgow, Glasgow, UNITED KINGDOM|

Commercial Relationships Disclosure: Megan Quinn: Commercial Relationship: Code N (No Commercial Relationship) | David Yorston: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Historically, macular holes > 400um have been classified as “large”. However, there is growing evidence that closure rates are not reduced until macular hole diameter exceeds 500um. A previous audit of macular hole closure in Glasgow confirmed that holes with a diameter >500um have a worse prognosis. From 1/10/19, we adapted our technique to use an inverted ILM flap in large holes >500um diameter. This study compares large macular hole outcomes in ‘ILM peel’ vs ‘ILM flap’ repair techniques in a tertiary NHS Ophthalmology Unit.

Methods: Electronic participant data was collected from 2015 – 2021, and separated into two groups guided by the macular hole repair technique used. The pre-operative MLD, and the participant’s BCVA, were recorded at first clinic presentation. Post-operative outcomes, including anatomical hole closure and post-operative BCVA were recorded at follow-up. Only macular holes with a MLD >500um were included in this study.

Results: 115 participants were included. After exclusion for insufficient follow-up BCVA data, 110 participants: 13 males and 97 females were studied. In the ILM peel cohort, 78 participants were studied: 8 males and 70 females; 33 left eyes and 45 right eyes. The mean age was 69 years old. In the ILM flap cohort, 32 participants: 5 males and 27 females; 15 left eyes and 17 right eyes were reviewed. The mean age was 71 years old. The average MLD was 606 +/- 78 um vs 612 +/- 131 um, in the ILM peel vs ILM flap groups respectively. Pre-operative BCVA was 1.1 +/- 0.34 logMAR in the ILM peel group vs. 1.3 +/- 0.37 logMAR in the ILM flap group. Failed closure rates were 12/78 (15.4%) in the ILM peel group vs. 1/32 (3.1%) (p=0.11, Fisher’s exact test) in the ILM flap group. In the ILM peel group, BCVA improved by 0.5 logMAR vs. approximately 0.6 logMAR in the ILM flap group.

Conclusions: This audit has shown how the use of clinical data collected contemporaneously in an electronic record can be used to improve patient outcomes. In our practice the ‘ILM flap’ technique leads to higher macular hole closure rates in macular holes >500um compared to ILM peel. The average improvement in BCVA post-operatively was also slightly greater in the ILM flap group. A larger randomised clinical trial is required to confirm that the improved outcomes are the result of the inverted ILM flap technique.

CONTROL ID: 3708142
SUBMITTER (NAME ONLY): Zachary Heinzman
TITLE: Validation of visual field results of a new open-source virtual reality headset
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Z. Heinzman, K. Alawa, M. Wall, Ophthalmology and Visual Sciences, University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|I. Marín-Franch, Computational Optometry, Atarfe, SPAIN|A. Turpin, The University of Melbourne Department of Computing and Information Systems, Melbourne, Victoria, AUSTRALIA|
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ABSTRACT BODY:
Purpose: Open-source virtual reality (VR) visual field testing offers a substantially more cost-effective and accessible alternative to visual field testing for underserved patients. In this comparative analysis, our aim was to assess the validity of visual field results from a novel open-source VR headset perimeter and test the hypotheses that visual field defect patterns and test-retest repeatability would be similar between the VR headset and Octopus 900 perimeter.
Methods: We tested 19 ocular healthy and 2 subjects with primary open-angle glaucoma five times on the VR headset and twice on the Octopus 900 perimeters using the Open Perimetry Interface perimetry platform with size V stimuli, P-Central 26 grid pattern, and Zippy Estimation by Sequential Testing (ZEST) algorithm. Previous data was also obtained from past studies using the Humphrey Field Analyzer. Additionally, test point locations were divided into three concentric zones for analysis based on distance from center fixation target, and test-retest repeatability for all results was analyzed with the repeatability coefficient (RC). Finally, visual field defect detection was qualitatively assessed through side-by-side comparisons of all fields.
Results: The RC—the expected absolute difference between 2 repeated tests with 95% probability—for the VR headset was 1.03 dB and was 1.16 dB for the Octopus 900. The RC for the HFA, using a different dataset but matched testing parameters was 1.25 dB. Within the central 10° of fixation, the VR headset and Octopus 900 perimeters had an RC of 0.86 dB and 1.31 dB, respectively. Peripherally, between 21.4°-28.2° from center fixation, the VR headset and Octopus 900 perimeter had an RC of 1.71 dB and 1.37 dB, respectively. Visual field defects were qualitatively similar between the VR headset and Octopus 900 perimeter for all glaucoma subjects tested.
Conclusions: It was demonstrated that the open-source VR headset is statistically as repeatable as the Octopus 900 perimeter, and it is capable of accurately mapping glaucomatous visual field defects for both large arcuate defects and smaller peripheral defects. The open-source VR headset is a substantially more cost-effective alternative than traditional perimeters with the potential to improve the accessibility of visual field testing in third-world countries and low-income communities.

CONTROL ID: 3708143

SUBMITTER (NAME ONLY): Mustafa Ozgul

TITLE: Analysis of 1-month-old Humanin-G in H2O and PBS Using High Resolution Mass Spectrometry

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ozgul, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|B. Katz, Chemistry, University of California Irvine, Irvine, California, UNITED STATES|E. Taylan, Department of Obstetrics and Gynecology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Mustafa Ozgul: Commercial Relationship: Code N (No Commercial Relationship) | Ben Katz: Commercial Relationship: Code N (No Commercial Relationship) | Enes Taylan: Commercial Relationship: Code N (No Commercial Relationship) | M.Cristina Kenney: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Humanin is the first identified mitochondrial derived peptide. Humanin-G (HNG) is a variant of Humanin that has significantly higher cytoprotective properties. Here, we describe the stability features of HNG peptide in different conditions and characterize HNG degradation and oxidation patterns. State-of-the-art techniques can be used to develop to identify Humanin-G fragments and dimers for possible use in future therapeutic investigation in age-related disease such as Alzheimer's, cancer and AMD.

Methods: For 1-month stability analyses, HNG solutions were stored in H_2O and phosphate buffer saline (PBS) for 28 days at 37°C. For High-Resolution Mass Spectrometry (HRMS) studies, samples with a concentration of 25 µg/ml HNG in HPLC water or PBS were used to analyze 28-day-old HNG products.

Mass spectrometric analysis was performed using Xevo G2-XS Quadrupole Time-of-Flight mass spectrometer (HRMS) coupled to UPLC. The UPLC method used at 0.3 mL/min from 97% A to 97% B where A is 0.1% Formic Acid in water and B is 100% Acetonitrile. For HRMS analysis, positive electrospray ionization mode was utilized. A capillary transfer temperature of 300°C and a spray voltage of 3.0 kV were used to accomplish ionization. A resolution of 30,000 Full Width at Half Maximum was used for a full scan experiment within a range of m/z 100–2000. Leucine Enkephalin was used as a lock mass for nominal mass correction, and a CsNaI ladder was used for detector calibration.

Results: HNG peptide (molecular mass 2655.46), the main ions were +5, +4, +3 charged states at m/z 532.09, 664.88, and 886.19 (Fig. 1). In Humanin-G, oxidations of cysteine and methionine amino acids were determined using HRMS. Disulfide dimerization in HNG fragments were observed upon incubation of Humanin-G in HPLC water for 28 days at $37^{O}C$ constant. HRMS spectrum of other HNG degradation and their oxidation products are presented in Figures 2, 3 and Table Peptide Sequences.

Conclusions: For the first time, oxidation and degradation patterns of HNG peptide have been analyzed in detail using advanced HRMS technologies. We have identified various HNG fragments that may possess different cellular functionalities and/or receptor activities. Our results may help researchers design better in vitro and in vivo experimental parameters to further understand the critical role of HNG in physiological conditions and human diseases.

CONTROL ID: 3708144

SUBMITTER (NAME ONLY): David Miller

TITLE: Visible-Light Optical Coherence Tomography Fibergraphy of the Tree Shrew Retina

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Miller, H. Zhang, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|M. Grannonico, M. Liu, K. McHaney, E. Savier, X. Liu, Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|A. Erisir, X. Liu, Psychology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tree shrew eyes share many similar features to human eyes, including a structured lamina cribrosa, making them a preferred model for glaucoma than rodents. However, as an emerging animal model, a technique for quantifying and visualizing the retinal ganglion cell (RGC) axon bundle structure for tracking optic neuropathies has yet to be developed. We demonstrate visible-light optical coherence tomography fibergraphy (vis-OCTF) in the tree shrew retina to visualize individual RGC axon bundles and their surrounding vasculature.

Methods: We acquired vis-OCTF images from healthy 5-36-month-old tree shrews. Before imaging, tree shrews were anesthetized using 3% isoflurane with supplemental oxygen and given tropicamide and phenylephrine drops to dilate the pupils. During imaging, tree shrews were kept warm with an infrared heat lamp and given artificial tears to prevent corneal dehydration. We positioned the retina to maximize RGC axon bundle reflectance throughout the field-of-view. We acquired 5 repeated OCTA volumes consisting of 512 A-lines × 512 B-scans with each B-scan repeated twice. With an A-line rate of 75 kHz, each acquisition was completed in ~35 seconds. We registered the repeated volumes in the axial and lateral dimensions and then averaged to reduce speckle noise. Fibergram images were generated by segmenting the retinal nerve fiber layer and taking the mean intensity projection along the axial dimension.

Results: Vis-OCT images are shown in Fig. 1. The mean intensity projection fundus image in Fig. 1a and angiogram in Fig. 1b highlight the tree shrew's unique retinal vasculature. The fibergram in Fig. 1c and resampled B-scan in Fig. 1d depict the densely packed RGC axon bundles around the optic nerve head (ONH). We observed ~16 bundles/mm at 1.2 mm from the ONH with an axial bundle thickness of 59.4±19.8 μm (n=54) and a lateral bundle width of 25.0±8.7 μm (n=96).

Conclusions: Vis-OCTF enables a more wholistic evaluation of RGC axon bundle health and provides new parameters for tracking the progression of optic neuropathies in tree shrews.

CONTROL ID: 3708145

SUBMITTER (NAME ONLY): Samantha Paul

TITLE: Automatic Identification of Ancillary Features of Diabetic Macular Edema in Optical Coherence Tomography Using Deep Learning

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Paul, E. Zhou, A. Mehra, W. Sobol, Department of Ophthalmology, University Hospitals, Cleveland, Ohio, UNITED STATES|I. Pan, Department of Radiology, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|W. Sobol, Department of Ophthalmology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Samantha Paul: Commercial Relationship: Code N (No Commercial Relationship) | Ellie Zhou: Commercial Relationship: Code N (No Commercial Relationship) | Ankur Mehra: Commercial Relationship: Code N (No Commercial Relationship) | Ian Pan: Commercial Relationship(s);Code C (Consultant/Contractor):MD.ai;Code C (Consultant/Contractor):Centaur Labs;Code C (Consultant/Contractor):Diagnosticos da America (Dasa) | Warren Sobol: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is a leading cause of vision loss in patients with diabetes. DME is frequently accompanied by other retinal abnormalities on two-dimensional optical coherence tomography (2D OCT). We trained and tested a CNN to identify various retinal features on 2D OCT images from patients with DME.

Methods: 1,896 2D OCT images through the fovea from 93 patients with DME were randomly sampled from a publicly available dataset of 108,316 2D OCT images. Each image was labeled with the following 5 features: hyperreflective foci, ellipzoid zone disruption, subretinal fluid, vitreoretinal interface abnormalities, and distortion of the foveal contour. An EfficientNet-B3 CNN was trained to identify these features. The training process was repeated 3 times with separate random seeds, resulting in an ensemble of 3 CNNs. Inference was subsequently performed on an independent test set of 250 B-scans from 167 patients with DME by taking the average prediction scores across the 3 CNNs. The area under the receiver operating characteristic curve (AUC) was calculated for each feature. The 95% confidence interval (95% CI) was calculated using the bootstrap method.

Results: The distribution of the 5 features in the training set was: hyperreflective foci (37.1%), ellipsoid zone disruption (23.8%), subretinal fluid (5.2%), vitreoretinal inferface abnormalities (62.3%), and distortion of the foveal contour (50.9%). Among the 5 features, performance (AUC, 95% CI) was highest for subretinal fluid, 0.947 (0.914, 0.974); hyperreflective foci, 0.918 (0.877, 0.954); and distortion of the foveal contour 0.887, (0.802, 0.957). AUCs for ellipzoid zone disruption and vitreoretinal inferface abnormalities were 0.757 (0.693, 0.819) and 0.738 (0.643, 0.824), respectively. Figures 1 and 2 depict class activation maps illustrating which areas of the image contributed most to the predicted features.

Conclusions: CNNs were effective in identifying ancillary DME features in 2D OCT images, particularly hyperreflective foci, subretinal fluid, and distortion of the foveal contour. This can allow for more nuanced assessment of DME severity and prognosis in settings where retina subspecialists are not readily available.

CONTROL ID: 3708146

SUBMITTER (NAME ONLY): Giovanni Campagna

TITLE: Effect of Eye Drop Reminder Software on Medication Counseling Time

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Campagna, V.L. Tseng, K. Shah, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Giovanni Campagna: Commercial Relationship: Code N (No Commercial Relationship) | Victoria Tseng: Commercial Relationship: Code N (No Commercial Relationship) | Kayur Shah: Commercial Relationship(s);Code O (Owner):EyeDropAlarm

ABSTRACT BODY:

Purpose: To examine the effect of patient use of a medication reminder software application on counseling time in an office setting.

Methods: The study population included patients who were being counseled on their prescribed eye drops for after surgery or active uveitis. All patients were provided information about how to install a software application (EyeDropAlarm). Patients were randomly assigned to either use the application or to not use the application. The length of counseling time was compared between patients who used the software application and those who did not. Counseling was given for the name(s) of the medication(s) and the schedule.

Results: Twenty-five patients were in the study. Thirteeen patients (52%) used the mobile application, and twelve did not. Of the thirteen patients who installed and used the application, eleven patients had underwent cataract surgery, and two had a history of uveitis. Of the twelve patients who did not use the application, ten patients had underwent cataract surgery, and two had a history of uveitis. The mean counseling time for the patients who did not use the application was 2.9 minutes. The mean counseling time for the patients who did use the application was 1.1 minutes. This difference was statistically significant ($P < 0.0001$, Student's t-test).

Conclusions: In this office setting, patient use of a medication reminder application, EyeDropAlarm, was associated with reduced counseling time.

CONTROL ID: 3708147

SUBMITTER (NAME ONLY): Manuel Colon

TITLE: Patient Satisfaction with an Ocular Telehealth Platform: A Local Experience after 1 Year.

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Colon, J.D. Henderer, S. Weiss, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|J.D. Henderer, S. Weiss, VA Medical Center Wilmington, Wilmington, Delaware, UNITED STATES|

Commercial Relationships Disclosure: Manuel Colon: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Henderer: Commercial Relationship: Code N (No Commercial Relationship) | Stephanie Weiss: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: As telemedicine in eye care has become increasingly widespread, the clinical accuracy and reliability of these platforms has been well established; but there is limited data regarding patient satisfaction. Since 2015, the national Technology-based Eye Care Services (TECS) program in the Veterans Health Administration has provided ocular telehealth services to veterans with the goal of increasing accessibility to care in underserved and rural communities. After 1 year with a local TECS site, we performed a retrospective review of feedback surveys to evaluate patient satisfaction with the telemedicine experience.

Methods: 145 surveys were distributed to veterans who participated in a visit at the local TECS site from October 1, 2020 to September 30, 2021. Nationally, 3,062 surveys were distributed. The 5-point, Likert-type survey was comprised of 7 statements used to gauge participant experience. Survey response data was analyzed and summarized as proportions of respondents who strongly agreed or agreed, neither agreed or disagreed, and strongly disagreed or disagreed with the statements.

Results: Of 3,062 surveys distributed nationally, 375 were completed and analyzed. Locally, 26 of 145 surveys were completed and analyzed. 84.9% of local respondents felt satisfied overall with care received (75.6% nationally). When asked about increased confidence in this healthcare system as a result of care received, 89.7% strongly agreed/agreed (79.2% nationally). 87.2% strongly agreed/agreed care provided was efficient (85.6% nationally). 100% strongly agreed/agreed they were treated fairly (88.2% nationally). 89.3% strongly agreed/agreed high quality care was provided and their needs were addressed (86.1% nationally). 88.1% strongly agreed/agreed the provider had been helpful (84.7% nationally). Regarding ease in meeting patient needs, 92.5% strongly agreed/agreed (82.5% nationally). 0% to 5.9% of local respondents strongly disagreed/disagreed with the survey statements (3.0% to 8.1% nationally).

Conclusions: The majority of survey respondents demonstrated high levels of satisfaction in all aspects of TECS. This suggests ocular telehealth platforms may represent an alternative means of providing care that is not only high quality but also leaves patients feeling satisfied with their care.

CONTROL ID: 3708148

SUBMITTER (NAME ONLY): Nicole Lifson

TITLE: A Novel 3D Printed Silicone Simulation Model for Effective Instruction of Marginal Eyelid Laceration Repair

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Lifson, D. Booy, Y. Vaishnav, M.E. Migliori, J. Schaefer, Ophthalmology, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|J. Crozier, A.S. Woo, Plastic Surgery, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|J. Nguyen, B. Thuro, Ophthalmology, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmology residents are often called upon to repair complex eyelid lacerations, particularly marginal eyelid lacerations, with limited prior experience. Using 3D printing technology we created a novel silicone model of the eyelid to allow residents to easily and affordably practice their surgical skills. We performed a prospective study to determine the efficacy of these models as a training tool for marginal eyelid laceration repair.

Methods: 3D design software was used to create a model of the face and eyelids which served as the scaffold for a silicone eyelid mold. A total of 18 ophthalmology residents participated in a training session on marginal eyelid laceration repair, practicing on these models. Prior to and following the session, residents anonymously responded to a survey assessing their degree of confidence in repairing marginal and non-marginal eyelid lacerations, as well as their overall opinion of the workshop. Questions related to their confidence and ability utilized a 5-point Likert Scale: 1. Poor 2. Fair 3. Good 4. Very Good. 5. Excellent. The responses were compared using the Wilcoxon Signed-Rank test.

Results: Following the training session, residents showed a significant improvement in confidence and knowledge of marginal eyelid laceration repair. Amongst all residents, the average confidence level for repairing marginal eyelid lacerations increased from 2.33 to 3.22 ($p=0.005$) following training with the silicone models. The residents with no prior marginal eyelid repair experience reported a larger increase in the degree of confidence with scores rising from 1.14 pre-session to 2.29 post-session ($p=0.01$). Overall, attitudes regarding the training session were positive. Residents found the simulation to be beneficial with a mean score of 4.47 (SD 0.62). When asked to compare this model to other eyelid simulations for eyelid laceration repair, the silicone model was found to be superior with a mean score of 4.50 (SD 0.53).

Conclusions: 3D printed silicone eyelid models provide an effective and realistic simulation of marginal eyelid laceration repair.

CONTROL ID: 3708149

SUBMITTER (NAME ONLY): Selwyn Prea

TITLE: Visual field home-monitoring with a tablet perimeter by glaucoma patients.

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. Prea, A.J. Vingrys, Department of Optometry & Vision Sciences, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|S.M. Prea, G.Y. Kong, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|G.Y. Kong, A.J. Vingrys, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Selwyn Prea: Commercial Relationship: Code N (No Commercial Relationship) | George Kong: Commercial Relationship(s);Code P (Patent):Glance Optical Pty. Ltd. | Algis Vingrys: Commercial Relationship(s);Code P (Patent):Glance Optical Pty. Ltd.

ABSTRACT BODY:

Purpose: The primary aim is to determine long-term retention of glaucoma patients to the request for weekly home-monitoring (HM) of visual field. A secondary aim considers test reliability and concordance to in-clinic outcomes.

Methods: Participants with stable glaucoma in one eye performed HM over a 12-month period using the Melbourne Rapid Fields-glaucoma iPad application (MRFg). Loan iPads with broadband connection were provided for a weekly test schedule with text message reminders. Participants attended 6-monthly clinical reviews. Monthly retention (28+1 days), test reliability (false positives and fixation loss <33%), and concordance to Humphrey Field Analyzer (HFA) outcomes were determined. Diagnoses based on linear trends (MRFg mean deviation vs HFA Guided Progression Analysis (GPA)) were compared to the clinical diagnosis of an ophthalmologist (chi-square analysis).

Results: Eighty-five eyes of 47 participants with a mean age±SD of 64±17 years were enrolled. Forty subjects (85%) had successful uptake (≥1 test) with 58% active after 12-months. Retention to HM was 97% after weekly reminders with 77% of results reliable. Progression (≥1.25dB/yr) was identified by HFA-GPA in 3 eyes after 30 months and MRFg linear trend in 4 eyes by 3 months. Two of these eyes from both devices were classified as changed by the ophthalmologist (agreement =96%, χ^2 (3,37)=13.5, p<0.01).

Conclusions: HM over 12-months was sustained in 58% of volunteers with excellent monthly retention (97%). The high volume of tests returned by HM provides good concordance with in-clinic assays identifying 2 cases of progression early. HM should be considered for all high-risk cases of glaucoma.

CONTROL ID: 3708150

SUBMITTER (NAME ONLY): Hassaam Choudhry

TITLE: Racial trends and disparities persist in ocular injuries reported to the emergency room

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Choudhry, O.M. Aftab, A. Patel, H. Choudhry, M. Lemdani, M. Jaffry, M. Dastjerdi, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous research suggests racial minorities may experience disparities in the emergency room (ER) such as longer wait times compared to White Americans. We performed retrospective data analysis to further explore trends by race in epidemiology and disposition of ocular injuries reported to the ER.

Methods: The National Electronic Injury Surveillance System (NEISS) was queried for eye injuries reported from 2010 to 2020, and weights were assigned in accordance with NEISS guidelines. Analysis was performed with IBM SPSS 24 and stratified by race (White, Black, non-White Hispanic, and Asian). Incidence of ocular injuries reported over time was recorded, alongside codes corresponding to most common diagnoses, consumer products involved, and dispositions. Logistic regression analysis adjusting for variables such as age, gender, and diagnosis was performed for further analysis of racial implications on dispositions.

Results: Cases of 1,113,325 White, 212,176 Black, 21,942 Asian, and 115,548 non-White Hispanics reporting to the ER with ocular injuries from 2010 to 2020 were included. While incidence of Whites, Asians, and Hispanics reporting to the ER with ocular-related complaints decreased over time, little change was observed in Black populations. Contusions/abrasions were the most common coded ocular diagnosis in all groups (>40%), however in Whites and Hispanics foreign bodies were the second leading cause followed by dermatitis/conjunctivitis, while in Blacks and Asians this was reversed. Sources of ocular injury varied by race, for example workshop buffers were responsible for over 10% of ocular injuries in Whites, twice as much for any other race. Finally, while the majority of both racial groups were treated/examined and released (>94%), a significantly increased probability of leaving the ER without being seen was associated with being a racial minority versus White ($p<.001$), with the greatest risk in Hispanics (OR 1.962, 95% CI 1.881 to 2.046, $p<.001$).

Conclusions: These findings suggest racial variation but also shared trends in epidemiology of ocular injuries. These results also suggest a harmful outcome of racial minorities waiting longer in the ER than Whites may be an increased likelihood of patients leaving without being seen.

CONTROL ID: 3708152

SUBMITTER (NAME ONLY): Chen Yu

TITLE: Augmentation of Protective Microglia Restricts Outer Retinal Degeneration and Preserves Vision

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Yu, E.M. Lad, A. Proia, D.R. Saban, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|A. Proia, Pathology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|D.R. Saban, Immunology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Immune processes in many forms of retinal degeneration, including age-related macular degeneration (AMD), involves migration and ectopic accumulation of macrophages in the subretinal space. Recently, we described a unique subtype of bona fide microglia that are dominant in the subretinal space in mouse models of retinal degeneration. These subretinal microglia are transcriptionally reprogrammed and contribute to protecting the retina pigment epithelium (RPE) from damage caused by degeneration. These findings now prompt new investigations aimed at identifying the molecular players underlying this protective response.

Methods: We utilized single cell RNA-seq and compared subretinal microglia in four distinct disease mouse models that represent key pathobiological aspects of outer retinal degenerative diseases. These individual models included the light damage model, the sodium iodate induced RPE injury model, rhodopsin-P23H knockin mice, and an advanced aging model of 2-year-old mice. Global and microglial-conditional knockout mice were generated to assess the contributions of microglia in mediating this protective response.

Results: We found that the transcriptional signature of subretinal microglia is consistent among all mouse models studied. Confocal microscopy revealed that subretinal Iba1^{+} cells dominantly expressed markers of this signature in all mouse models. Likewise, these markers were also observed in human postmortem retinas with intermediate to advanced AMD, whereas few positive cells were found in either healthy or early AMD subjects. Moreover, we showed that genetic inhibition of this protection exacerbated death of photoreceptors, loss of RPE integrity and impairment of visual function in multiple models. Importantly, the protective activity by microglia was compromised during retinal degeneration, whereas pharmacological bolstering of subretinal microglia protected the retina from degeneration and better-preserved the RPE integrity and vision in mice.

Conclusions: Our findings demonstrate a general signature of subretinal microglia in mice and the possible relevance of this microglial population in forms of human AMD. These results provide a novel focal point for therapeutic strategies in vision preservation with retinal degenerative diseases.

CONTROL ID: 3708153

SUBMITTER (NAME ONLY): Masaki Tanito

TITLE: “SU-PAP” - A Simple Grading System Integrating Cosmetic and Tonometric Aspects of Prostaglandin-Associated Periorbitopathy

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tanito, A. Ishida, S. Ichioka, Y. Takayanagi, A. Tsutsui, K. Manabe, T. Shirakami, K. Sugihara, M. Matsuo, Department of Ophthalmology, Shimane University Faculty of Medicine, JAPAN|

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ABSTRACT BODY:

Purpose: To report a possible usefulness of a novel grading for prostaglandin-associated periorbitopathy (PAP) which we referred to the Shimane University PAP Grading System (SU-PAP), distribution of PAP severity among subjects using a topical FP or EP2 receptor agonist was assessed.

Methods: Consecutive 460 Japanese subjects (211 men; mean age ± SD, 69.9±14.5 years) who had used either a FP agonist (latanoprost, tafluprost, travoprost, bimatoprost, or fixed combinations of these) or EP2-agonist (omidenepag) for >3 months in at least one eye were retrospectively included. Age, sex, prostaglandin, intraocular pressure (IOP) measured by Goldmann applanation tonometry (IOP_{GAT}) and iCare rebound tonometry (IOP_{RBT}), difference between IOP_{GAT} and IOP_{RBT} ($IOP_{GAT-RBT}$), and PAP grade were were collected. Clinical parameters were compared among groups stratified by SU-PAP grades; SU-PAP grades were descried and compared among groups stratified by prostaglandins.

Results: Of the study subjects, 114 (25%) had grade 0 (no PAP), 174 (38%) grade 1 (superficial cosmetic PAP), 141 (31%) grade 2 (deep cosmetic PAP), and 31 (7%) grade 3 (tonometric PAP). The IOP_{GAT} was significantly higher in grade 3 (17.5±5.4 mmHg) than grades 0 (15.0±5.1 mmHg, P=0.0324) and 1 (14.5±4.2 mmHg, P=0.0076), and the $IOP_{GAT-RBT}$ was significantly higher in grade 3 (5.8±3.2 mmHg) than the other three grades (1.3-1.9 mmHg, P<0.0001 for all comparisons); the IOP_{RBT} was equivalent among the four grades. The PAP grade was significantly higher associated with travoprost (2.0±0.8) and bimatoprost (2.0±0.7) than latanoprost (1.0±0.8, P<0.0001 for both comparisons) and tafluprost (1.0±0.7, P<0.0001 for both comparisons), but significantly lower associated with omidenepag (0.0±0.0, P<0.0001 for all comparisons) than the other four prostaglandins. Multivariate analyses showed older age (standard β=0.11), travoprost (0.53, referenced by latanoprost) and bimatoprost (0.65) were associated with higher PAP grades, while tafluprost (-0.18) and omidenepag (-0.73) were associated with lower PAP grades.

Conclusions: The PAP graded using SU-PAP reflects the degree of overestimation of the IOP_{GAT} and different severities of PAP among the different prostaglandins. SU-PAP, the grade system constructed based on the underlining mechanisms of PAP, is a simple grading system for PAP that is feasible for use in a real-world clinical situation.

CONTROL ID: 3708155

SUBMITTER (NAME ONLY): Priyanka Ramulu

TITLE: Identifying the Greatest Barriers and Challenges in Performing Successful Corneal Transplantation in India

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Mathews, G. Li, D. Cui, E.K. Akpek, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|P. Ramulu, River Hill High School, Clarksville, Maryland, UNITED STATES|P. Mathews, Florida Eye Specialists and Cataract Institute, Florida, UNITED STATES|R. Fogla, Apollo Specialty Hospitals Pvt Ltd, Hyderabad, INDIA|

Commercial Relationships Disclosure: Priyanka Ramulu: Commercial Relationship: Code N (No Commercial Relationship) | Priya Mathews: Commercial Relationship(s);Code C (Consultant/Contractor):Dompe;Code C (Consultant/Contractor):SUN Pharmaceutical;Code C (Consultant/Contractor):W.L. Gore, Inc. | Gavin Li: Commercial Relationship: Code N (No Commercial Relationship) | David Cui: Commercial Relationship: Code N (No Commercial Relationship) | Rajesh Fogla: Commercial Relationship: Code N (No Commercial Relationship) | Esen Akpek: Commercial Relationship(s);Code F (Financial Support):Novartis, Ocular Therapeutics, W.L. Gore, Inc, Regeneron Healthcare Solutions Inc., National Eye Institute;Code C (Consultant/Contractor):Dompe, Epitech, FirstString Medical Research, Novalique, Shire, Sinqi, HanAll, Adelphi Values, Regeneron Healthcare Solutions Inc., Sjogren's Foundation;Code P (Patent):Up-To-date

ABSTRACT BODY:

Purpose: Currently, an estimated 1 in 70 individuals worldwide in need of a corneal transplant will actually undergo corneal transplantation. There is a lack of objective data explaining the underlying reasons for why this discrepancy exists. The purpose of this study was to use a newly developed questionnaire to identify the barriers for successfully performing corneal transplantation in India.

Methods: An online survey was sent to approximately 700 currently-practicing corneal specialists who were members of the Cornea Society of India. Members were invited to complete an online survey between January 1 and July 1, 2021. The survey asked the participants to rate the difficulty or ease of 11 steps of corneal transplantation using a Likert scale. Categories included factors related to donors, organ procurement, tissue harvesting/storage, logistical, physician/staff/facility related, and recipient related.

Results: A total of 148 individuals participated in the online survey (~21% response rate). Of the 11 evaluated steps, the greatest barrier to transplantation was the difficulty in finding donors who fulfilled the screening criteria (55% of respondents reported difficulty). The second greatest barrier was donor willingness to donate (32% of respondents reported difficulty). Lastly, the third most reported barrier was the ability to store tissue after it was prepared by the eye bank (20% of respondents reported difficulty). The two steps with the least reported difficulty were availability of operating room (OR) time and staff, as well as using prepared corneal tissue before the expiration date.

Conclusions: There is a significant shortage of corneal transplants performed around the world, however there has never been a standardized way of identifying forces driving this shortage. Our online survey evaluated each step needed to successfully perform corneal transplantation. In India, it appears that the donor-related factors (both fulfilling donor criteria and patient/family willingness to donate) and ability to store prepared tissue were the greatest barriers in performing corneal transplantation. Therefore, both government and private institutions should focus their resources and efforts on addressing these issues to ultimately reduce the burden of corneal blindness.

CONTROL ID: 3708156

SUBMITTER (NAME ONLY): Clara Castillejo Becerra

TITLE: Ocular, periocular, and facial injuries from cat bites

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Castillejo Becerra, E. Bradley, Department of Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|D.O. Hodge, Department of Health Sciences Research, Mayo Clinic in Florida, Jacksonville, Florida, UNITED STATES|

Commercial Relationships Disclosure: Clara Castillejo Becerra: Commercial Relationship: Code N (No Commercial Relationship) | David Hodge: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Bradley: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There are scarce data regarding the rates of ocular and periocular injuries from animal bites with minimal emphasis on cats as the perpetrators. In this population-based study, we described the incidence and characteristics of ocular, periocular, and facial injuries from cat bites over a 17-year period.

Methods: The Rochester Epidemiology Project (REP), a medical records-linkage system, was used to identify all potential cases of facial injuries from cat bites in Olmsted County, Minnesota from January 1, 1999 and December 31, 2015. The ophthalmic cohort included patients with ocular and periocular injuries with or without facial injuries while the non-ophthalmic cohort included patients with facial injuries not involving the ocular or periocular regions.

Results: There were 19 patients with facial injuries from cat bites in the study period, 6 ophthalmic and 13 non-ophthalmic. Mean age was 8.4 years (0.4-26.1) and 10 (53%) were male. The overall age- and sex-adjusted incidence of facial injuries from animal bites was 0.7 per 100, 000 per year (95% CI: 0.4-1.0) adjusted to the 2010 US white population, 0.2 per 100, 000 per year (95%: 0.0-0.4) ophthalmic and 0.5 per 100, 000 per year (95%: 0.2-0.7) non-ophthalmic. Most cat bites were provoked (n=10, 76.9%) and caused by animals known to the victim (n=14, 88%). All patients with ophthalmic injuries had eyelid lacerations, and none sustained ocular trauma. Patients with ophthalmic injuries had similar rates of cheek laceration (33% vs. 39%), antibiotic prophylaxis (83% vs. 77%), tetanus prophylaxis (17% vs. 39%), and wound closure (33% vs. 15%) as patients with non-ophthalmic injuries. There was a trend toward more cellulitis complicating ophthalmic injuries (17% vs 0%), this difference was not statistically significant.

Conclusions: Periocular and facial injuries from cat bites are rare, with little if any risk of ocular trauma. Children and young adults are at most risk.

CONTROL ID: 3708158

SUBMITTER (NAME ONLY): Ema Karakoleva

TITLE: Association of age and HgbA1C with lens thickness and central corneal thickness

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.V. Karakoleva, N. Devireddy, D. Rosen, N. Cannon, S. Pantanelli, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Ema Karakoleva: Commercial Relationship: Code N (No Commercial Relationship) | Nitya Devireddy: Commercial Relationship: Code N (No Commercial Relationship) | David Rosen: Commercial Relationship: Code N (No Commercial Relationship) | Nathan Cannon: Commercial Relationship: Code N (No Commercial Relationship) | Seth Pantanelli: Commercial Relationship(s);Code F (Financial Support):Alcon, Carl Zeiss Meditec, Ocular Therapeutix, Ziemer;Code R (Recipient):Alcon, Carl Zeiss Meditec;Code C (Consultant/Contractor):Bausch and Lomb, Carl Zeiss Meditec

ABSTRACT BODY:

Purpose: The aim of this study was to investigate the relationship between age, HgbA1C, lens thickness (LT), and central corneal thickness (CCT) in eyes of patients with diabetes mellitus (DM) using a swept-source optical coherence tomography (SS-OCT) based optical biometer.

Methods: This was a single-center, retrospective consecutive case series including patients with optical biometry (IOLMaster 700, Carl Zeiss Meditec AG) obtained between 02/2020 and 05/2021 in anticipation of cataract surgery. Charts were retrospectively reviewed to associate the biometric data with clinical variables including diabetic status and HbgA1C. Inclusion criteria included male or female, age 18 or older. To be included in the diabetic group, patients must have had a known history of DM (type I or type II) with a documented HbgA1C within 4 months of biometry. Eyes of patients presenting with any clinically significant corneal or intraocular media opacity other than cataract, abnormal corneal findings, any anterior segment pathology, or history of intraocular or corneal surgery (other than panretinal photocoagulation, laser peripheral iridotomy, selective laser trabeculoplasty, or argon laser trabeculoplasty), or failed or poor-quality measurements as determined by the device's quality metrics were excluded.

Results: In total, 256 eyes from 151 patients were identified as eligible for analysis. This included 182 eyes from 107 non-diabetic and 74 eyes from 44 diabetic patients. There was a positive linear correlation between age and LT in both the control and diabetic groups with R-squared values of 0.188 and 0.129, respectively. Despite non-diabetics and diabetics having similar age distributions ($p = 0.57$), diabetics (4.696 ± 0.49 mm) had significantly larger LTs than their non-diabetic (4.47 ± 0.43 mm) counterparts ($p = 0.0007$). Mean CCT values were 0.56 ± 0.03 mm in non-diabetic and 0.55 ± 0.03 mm in diabetic patients ($p = 0.42$). No age-related differences were observed. There was no relationship between HbgA1C and LT in controlled DM (HgbA1C ≤ 7; R-squared = 0.000) but LT decreased with HgbA1C in uncontrolled DM (HgbA1C > 7; R-squared = 0.148).

Conclusions: There is a correlation between age and LT but not CCT in patients without and with DM. Diabetics have increased LT compared with non-diabetics. More sophisticated analysis is needed to evaluate whether HgbA1C is an independent predictor of LT or CCT once the effect of age is removed.

CONTROL ID: 3708160

SUBMITTER (NAME ONLY): Isuru De Silva

TITLE: A review of concentric macular rings seen on scanning laser ophthalmoscopy ultra-widefield pseudocolour reflectance images

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.G. De Silva, Medical Retina, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Isuru De Silva: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the relationship between foveal morphology and the presence of concentric macular rings (CMR) on ultra-widefield scanning laser ophthalmoscopy (SLO) pseudocolour images

Methods: Retrospective analysis of ultra-widefield (SLO) pseudocolour images (Optos California, Optos plc, Dunfermline, UK) performed on patients in a single tertiary care clinic, in the first half of 2021 were reviewed. Patients were included if they had spectral-domain optical coherence tomography (SD-OCT) scans (Spectralis [Heidelberg Engineering GmbH, Heidelberg, Germany) of the macula performed at the same visit. Foveal morphology, visual acuity and diagnosis were recorded.

Results: Fourteen (14) subjects met the inclusion criteria, with a mean age of 8.9 years (standard deviation 3.59, range 3 - 17 years) of whom 8 were female. Of all these patients with concentric macular rings, only 9 demonstrated some degree of foveal hypoplasia on SD-OCT. This included 6 patients with oculocutaneous albinism and one each with a diagnosis of Hermansky-Pudlak syndrome, Microphthalmia and atypical epiretinal membranes. Amongst the 5 subjects demonstrating normal foveal development despite the presence of CMRs, a molecular diagnosis was obtained in 4 which included NR2E3 (2), CHM (1), and RPGP(1). Visual acuity was better in the group with normal foveal development (avg Logmar 0.16) compared to those with foveal hypoplasia (0.47).

Conclusions: Concentric macular rings on SLO ultra-widefield pseudocolour images are infrequently reported findings, previously reported to occur in presence of foveal hypoplasia. Although these findings were more common with foveal hypoplasia, we report that they may be noted in its absence.

CONTROL ID: 3708162

SUBMITTER (NAME ONLY): Victoria Tseng

TITLE: Prevalence of Glaucoma by Race/Ethnicity in the California Medicare Population

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Tseng, K. Kitayama, F. Yu, A.L. Coleman, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|K. Kitayama, A.L. Coleman, Epidemiology, University of California Los Angeles, Los Angeles, California, UNITED STATES|F. Yu, Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the prevalence of glaucoma by race/ethnicity in the 2019 California (CA) Medicare population.

Methods: The study population included all 2019 CA Medicare beneficiaries ≥65 years old who had both Part A and Part B coverage. Race/ethnicity was obtained from the Medicare enhanced race/ethnicity code and was categorized into White, Black, Asian, Hispanic, and Other/Unknown. Glaucoma was defined by diagnosis codes and included any glaucoma, primary open angle glaucoma (POAG), secondary open angle glaucoma (SOAG), and angle closure glaucoma (ACG). Covariates included age, sex, Charlson Comorbidity Index, pseudophakia, and macular degeneration. Univariable comparisons of glaucoma prevalence by race/ethnicity was performed using chi-squared tests. Multivariable analyses were performed using logistic regression, while adjusting for all covariates.

Results: The study population included 5,856,492 CA Medicare beneficiaries, of whom 3,340,658 (57.0%) were White, 317,631 (5.4%) were Black, 760,673 (13.0%) were Asian, 1,203,503 (20.6%) were Hispanic, and 234,027 (4.0%) were Other/Unknown. There were 220,662 (3.8%) beneficiaries with any glaucoma, 171,988 (2.9%) with POAG, 8,827 (0.2%) with SOAG, and 12,978 (0.2%) with ACG. Compared to White beneficiaries, Black, Asian, Hispanic, and Other/Unknown beneficiaries had increased adjusted odds of any glaucoma (Black odds ratio [OR]=1.70, 95% confidence interval [CI]=1.67, 1.73; Asian OR=1.60, 95% CI=1.58, 1.62; Hispanic OR=1.05, 95% CI=1.04, 1.07; Other/Unknown OR=1.30, 95% CI=1.27, 1.33), POAG (Black OR=1.79, 95% CI=1.75, 1.83; Asian OR=1.40, 95% CI=1.38, 1.42; Hispanic OR=1.07, 95% CI=1.06, 1.09; Other/Unknown OR=1.26, 95% CI=1.23, 1.30), and ACG (Black OR=2.18, 95% CI=2.02, 2.37; Asian OR=5.09, 95% CI=4.89, 5.30; Hispanic OR=1.69, 95% CI=1.60, 1.78; Other/Unknown OR=2.05, 95% CI=1.88, 2.24) but lower adjusted odds of SOAG for most race/ethnicities (Black OR=0.30, 95% CI=0.25, 0.35; Asian OR=0.47, 95% CI=0.44, 0.51; Hispanic OR=0.47, 95% CI=0.44, 0.51; Other/Unknown OR=1.17, 95% CI=1.06, 1.29).

Conclusions: In the 2019 CA Medicare population, there were racial/ethnic differences in the prevalence of glaucoma with higher odds in Black and Asian relative to Hispanic and White populations, which is different from prior population-based studies. Further investigation is required to determine the etiology of these differences.

CONTROL ID: 3708163

SUBMITTER (NAME ONLY): Diana Kim

TITLE: Demographic variables and systemic comorbidities associated with diagnosis of chalazion and chalazion incision/excision from a US claims database

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Kim, B. McGeehan, C.A. Briceno, B.L. VanderBeek, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify risk factors associated with chalazion and chalazion surgery.

Methods: Patients with an incident chalazion diagnosis from 2002-2019 were compared 1:5 with matched controls. Multivariate logistic regression identified variables associated with diagnosis and surgical excision, separately.

Results: Chalazion patients (n=134,959) and controls (6,878,160) were analyzed. Risk factors for diagnosis included female sex, non-white race, Northeast location, conditions affecting periocular skin and tear film (blepharitis, meibomian gland dysfunction, rosacea, pterygium), several non-ocular inflammatory conditions (gastritis, inflammatory bowel disease, sarcoidosis, seborrheic dermatitis, Grave's disease) and smoking ($p<0.001$). Diabetes and systemic sclerosis decreased odds of diagnosis ($p<0.001$). Male sex and rosacea increased odds of surgery ($p<0.001$). Anxiety, diabetes, gastritis, seborrheic dermatitis, Sjogren's, and smoking decreased odds of surgery ($p<0.001$).

Conclusions: Female sex, non-white race, conditions affecting periocular skin and the tear film, several non-ocular inflammatory conditions, and smoking were risk factors for chalazion diagnosis. Male sex and rosacea were risk factors for surgical intervention for chalazion. Our results prompt further study of these variables and their relationship to chalazion diagnosis to understand physiology and improve clinical outcomes.

CONTROL ID: 3708166

SUBMITTER (NAME ONLY): Siegfried Wagner

TITLE: Association of retinal fractal dimension with incident cardiovascular events in a hospital-attending population in London, United Kingdom

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Wagner, R. Struyven, N. PONTIKOS, K. Balaskas, A. Petzold, P.A. Keane, NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, UNITED KINGDOM|M. Cortina-Borja, J. Rahi, University College London Institute of Child Health, London, London, UNITED KINGDOM|A.K. Denniston, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|E. Trucco, M. Rama Krishnan Mookiah, University of Dundee, Dundee, Dundee, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Changes in retinal vascular morphology are related to cardiovascular morbidity. Here, we assessed the association between retinal fractal dimension (FD) and incident cardiovascular (CV) events in an ophthalmic hospital-attending population in London, United Kingdom.

Methods: A retrospective cohort study, the AlzEye project, linking retinal imaging of patients aged ≥ 40 years with systemic disease data from hospital admissions between January 1st 2008 and March 31st 2018. Cardiovascular event diagnoses were myocardial infarction and ischaemic stroke, as defined by the International Classification of Diseases, 10^{th} revision codes. Retinal FD was calculated from macular-centered color photographs using the Vascular Assessment and Measurement Platform for Images of the Retina. Odds ratios (OR) from multivariable logistic regression examined the association between incident CV events and retinal FD adjusting for known confounders.

Results: Among a cohort of 62,143 patients, 674 had a CV event at one year, 1731 at three years, and 2330 at five years. Those, who had a CV event, were older (72.2 +/- 11.9 vs 68.8 +/- 12.4, p<0.001) and more likely to be men (53.1% vs 47.9%, p<0.001), diabetic (60.4% vs 46.6%, p<0.001) and hypertensive (90.5% vs 80.5%, p<0.001). Retinal FD was reduced in patients with an incident CV event (1.50 versus 1.51, p<0.001). After adjustment by age, sex, hypertension and diabetes mellitus, retinal FD was inversely associated with incident CV events with similar ORs for one-year, three-year and five-year incidence (one-year, 0.91, 0.85-0.97, three-year 0.91, 0.87-0.95, five-year 0.90, 0.87-0.93 per standard deviation increase). Effect modification by sex was apparent. Stratification by sex showed significant association of retinal FD with female sex only (five-year incident events, Female: 0.86, 0.81-0.92, Male 0.96, 0.90-1.02 per standard deviation increase).

Conclusions: An inverse relationship was found between retinal FD and incident CV events but only among those of female sex. Subsequent research will assess other retinal vascular indices, the contribution of longitudinal oculomic biomarkers and prediction rather than etiological objectives.

CONTROL ID: 3708167

SUBMITTER (NAME ONLY): Amy Lo

TITLE: α-Melanocyte-stimulating hormone reduces severity of retinal damage after retinal ischemia/reperfusion injury in type I diabetes

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Lo, R.K. Goit, W. Lam, Department of Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|A.W. Taylor, Department of Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Amy Lo: Commercial Relationship: Code N (No Commercial Relationship) | Rajesh Goit: Commercial Relationship: Code N (No Commercial Relationship) | Wai-Ching Lam: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Taylor: Commercial Relationship(s);Code C (Consultant/Contractor):Palatin Technologies;Code F (Financial Support):Palatin Technologies

ABSTRACT BODY:

Purpose: Retinal ischemia is a major cause of vision loss and a common feature of diabetic retinopathy (DR). This study hypothesized that α-Melanocyte-stimulating hormone (α-MSH) decreased severity of retinal damage after retinal ischemia/reperfusion (I/R) injury by downregulating oxidative stress and excitotoxicity while upregulating anti-inflammatory factor expression under hyperglycemia condition.

Methods: I/R injury was induced in type 1 diabetic C57BL/6J $Ins2^{Akita/+}$ mice by blocking the middle cerebral artery (MCA) for 2 h with reperfusion for either 2 h or 22 h using the intraluminal method. Since ophthalmic artery originates proximal to the origin of the MCA, the filament also occluded blood flow to the retina. Animals were treated intraperitoneally with either vehicle or various doses of α-MSH at 1 h after ischemia and 1 h after reperfusion. Electroretinogram was recorded after dark adaptation. Paraformaldehyde-fixed eye sections were used to count ganglion cells, measure thickness of retinal layers and oxidative stress. Western blot was performed to measure anti-inflammatory factor expression and qPCR was performed to reflect excitotoxicity.

Results: α-MSH significantly increased amplitudes of b-wave and oscillatory potentials (OPs). α-MSH also prevented the I/R-induced histological changes and the development of retinal swelling. Loss of retinal ganglion cells as well as poly-ADP-ribose immunoreactivity were significantly decreased in the α-MSH-treated group. Level of interleukin-10 was significantly increased after α-MSH treatment. In addition, gene expression of glutamate aspartate transporter 1, monocarboxylate transporter (MCT) 1 and MCT-2 were significantly higher in animals treated with α-MSH.

Conclusions: α-MSH was associated with reduced severity of I/R induced retinal damage under hyperglycemic condition. In addition, increased amplitudes of b-wave and OPs were observed in animals treated with α-MSH. These beneficial effects of α-MSH may have important therapeutic implications against retinal I/R injury under hyperglycemic condition.

CONTROL ID: 3708170

SUBMITTER (NAME ONLY): Marina Peskina

TITLE:

Geographic distribution of astigmatism in pediatric patients of Latin American descent

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Peskina, R. Weiss, Ophthalmology, Jamaica Hospital Medical Center, Jamaica, New York, UNITED STATES|

Commercial Relationships Disclosure: Marina Peskina: Commercial Relationship: Code N (No Commercial Relationship) | Rebecca Weiss: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

Previous research has shown that there is a higher prevalence of astigmatism in Hispanic children compared to Asians, African Americans and Caucasians, but there is no data available evaluating unique characteristics within the pediatric Hispanic population. We performed a retrospective chart review to determine if there is an association among familial country of origin, astigmatism and refractive amblyopia in pediatric patients of Hispanic heritage.

Methods:

The electronic medical records from 10/1/2020 to 9/30/2021 of pediatric Hispanic patients, aged 2-18 years, with regular astigmatism of 1.5 Diopters or more detected by cycloplegic autorefractometry and/or cycloplegic retinoscopy were reviewed. Cycloplegic refraction was obtained with autorefractometry and retinoscopy at least 30 minutes after instillation of tropicamide 1% and cyclopentolate 1% with or without phenylephrine 2.5%. Only the eye with a higher degree of astigmatism that met inclusion criteria was analyzed in the study. Patients were divided into 13 groups based on familial country of origin. Country of origin, visual acuity, degree of astigmatism and presence of amblyopia were analyzed. One-way ANOVA and Chi-square tests were used for statistical analysis.

Results:

A total of 81 patients meeting inclusion criteria were identified. Three patients were excluded due to comorbidities affecting degree of astigmatism or best corrected visual acuity (such as: ptosis, keratoconus, congenital CMV retinitis), and 1 was excluded due to mixed Hispanic heritage. The study group consisted of 42 females and 35 males. Age distribution was positively skewed with a mean of 7.8 years. Majority of patients were from Ecuador, Guatemala, Mexico, and El Salvador. Descriptive statistical analysis showed a tendency towards higher astigmatism in children with parents from Ecuador and El Salvador, but no statistical significance was reached. Statistical analysis showed higher prevalence of amblyopia in children with families from Ecuador, Guatemala, Honduras and El Salvador ($P>0.05$).

Conclusions:

In our study group, pediatric patients with astigmatism from Ecuador, Guatemala, Honduras and El Salvador had a higher prevalence of refractive amblyopia than patients from other Latin American countries.

CONTROL ID: 3708176

SUBMITTER (NAME ONLY): Ailin Song

TITLE: Assessment of deep learning-based triage for robotically acquired retinal optical coherence tomography (OCT) images in an emergency department population

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Song, J. Lusk, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|K. Roh, N. Valikodath, E.M. Lad, R.P. McNabb, A.N. Kuo, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|A.T. Limkakeng, Division of Emergency Medicine, Department of Surgery, Duke University, Durham, North Carolina, UNITED STATES|J.A. Izatt, A.N. Kuo, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is difficult for emergency department (ED) providers to evaluate the posterior segment of the eye with their current standard of care tools. We have previously described the use of robotically aligned OCT (RAOCT) to semi-autonomously acquire high-resolution retinal images. As a next step, we utilize deep learning to triage retinal RAOCT images in a general ED population.

Methods: A deep learning model was developed to classify retinal OCT images as referable vs. non-referable for ophthalmology consultation. Using TensorFlow, the model was trained and internally validated on two publicly available datasets (Kermany DS, et al. Cell 2018; Srinivasan PP, et al. BOEx 2014) and images previously captured with our system. For external testing, adult Duke ED patients presenting with suspected posterior eye conditions were consented and enrolled under an IRB-approved protocol and imaged with the RAOCT. For model evaluation, a reference standard was established using a combination of ophthalmology consult diagnosis and OCT image interpretation by two retina specialists. For interpretability, the integrated gradients method was used to generate heatmaps showing areas contributing most to the model classification.

Results: The training and internal validation datasets included 91739 images, of which 60928 were abnormal. The model had a training accuracy of 96% and a validation accuracy of 98%. For external testing, our ED population (RAOCT volumes for 72 eyes of 38 patients; 51% with referable pathology) included a broad range of posterior eye pathologies such as retinal artery occlusion, papilledema, retinal detachment, macular degeneration, and acute retinal necrosis. In this set, the model had an AUC for the detection of referable posterior eye pathology of 0.88, an accuracy of 82%, a sensitivity of 95%, and a specificity of 69% (Fig 1). Areas contributing most to the model classification matched pathologic regions (Fig 2).

Conclusions: An automated OCT-based approach combining robotic OCT imaging and deep learning triage of the images shows promise to help ED providers evaluate patients with potential posterior eye disease.

CONTROL ID: 3708177

SUBMITTER (NAME ONLY): Xi Zhu

TITLE: Evaluation of Objective Dry Eye Parameters and Sjögren's Syndrome Status in a Longitudinal Cohort of Patients Evaluated with Novel, Tissue-Specific Autoantibodies

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhu, A. Dhungana, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|X. Dai, E.K. Akpek, S. Karakus, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|D. Cui, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the long-term clinical outcomes of dry eye patients suspected of Sjögren's syndrome (SS) who received serologic testing for three tissue-specific autoantibodies: anti-carbonic anhydrase 6 (CA6), anti-salivary gland protein 1 (SP1), and anti-parotid secretory protein (PSP).

Methods: Medical records between 2014-2019 were reviewed for 316 dry eye patients who presented at a tertiary academic medical center and received serologic testing for tissue-specific antibodies for suspicion of underlying SS. Patients with a minimum of 3 years follow-up included. Conjunctival lissamine green staining, corneal fluorescein staining, Schirmer's test without anesthesia, and tear osmolarity were recorded for the worst eye at baseline and final clinic visits.

Results: A total of 103 patients with a mean follow-up of 54.7 months were included. Forty-four patients (42.7%) tested positive for tissue-specific antibodies at baseline visit (24 positive for anti-CA6, 10 for anti-SP1, and 17 for anti-PSP) and were included in the antibody-positive group. The remaining 59 were included in the antibody-negative group. At baseline, 3 in the antibody-positive group (1 positive for anti-CA6 and 2 positive for anti-PSP) and 7 in the antibody-negative group were diagnosed with SS based on positive anti-SSA and/or positive minor salivary gland biopsy. Prevalence of SS was not different between the tissue-specific antibody-positive versus negative groups at baseline (%7 vs. %12, P>.05). Two additional patients in the antibody-positive group (1 positive for anti-CA6 and anti-PSP and 1 positive for anti-CA6) and 1 in the antibody-negative group were diagnosed with SS during the follow-up (4% vs. 2%, P>.05). Mean values for objective dry eye parameters at baseline and final visit did not show a statistically significant difference between groups regardless of tissue-specific antibody status.

Conclusions: Tissue-specific autoantibodies did not indicate severe dry eye disease in this longitudinal cohort. However, two patients with tissue-specific antibodies developed SS during the follow-up, albeit the sample size was not large enough. Perhaps the follow-up duration was not long enough to suggest that tissue-specific antibodies are early markers for SS. A larger prospective study with a longer follow-up and repeat serological testing is warranted.

CONTROL ID: 3708183

SUBMITTER (NAME ONLY): Ksenia Denisova

TITLE: Corneal toxicity associated with belantamab mafodotin: a case series

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Denisova, J. Kang, Ophthalmology, Montefiore Health System, Bronx, New York, UNITED STATES|R.A. Sica, Oncology, Montefiore Health System, Bronx, New York, UNITED STATES|

Commercial Relationships Disclosure: Ksenia Denisova: Commercial Relationship: Code N (No Commercial Relationship) | Roberto Sica: Commercial Relationship: Code N (No Commercial Relationship) | Joann Kang: Commercial Relationship(s);Code F (Financial Support):Clinical Care Options

ABSTRACT BODY:

Purpose: Belantamab mafodotin is a new treatment for adults with relapsing or remitting multiple myeloma (RRMM). There are few studies characterizing belantamab-induced corneal toxicity. Our goal is to characterize the ocular adverse effects and toxicities in an underserved minority patient population.

Methods: This is a retrospective case series of 6 patients who were treated with belantamab for RRMM from August 2020 to November 2021. Eye examination findings and visual acuity were graded based on the Keratopathy Visual Acuity (KVA) scale by a single examiner at baseline and every 3 weeks for the duration of treatment.

Results: The average age of patients was 58 years. Three were female, 3 identified as Hispanic, and 3 as African-American. No patients had evidence of preexisting keratopathy on baseline exam. All were started on artificial tear drops prior to belantamab therapy. Three patients reported ocular symptoms after starting belantamab, including blurry vision, photopsias, and ocular irritation. Five patients developed Grade 1 keratopathy at 38.6 days and after 2 doses on average. Of those, 3 progressed to Grade 2 keratopathy after 78 days and 3.7 doses. One patient progressed to Grade 3 keratopathy after 73 days and 3 doses. The most common finding on slit lamp exam after treatment was diffuse superficial punctate epitheliopathy (83%), bilateral in all cases except for one. Three patients developed bilateral peripheral microcystic keratopathy and one patient progressed to central involvement (Figure 1). Mean change from baseline logarithm of the minimum angle of resolution UCVA was -0.05 in those with Grade 1 keratopathy, -0.24 for Grade 2 keratopathy, and -0.32 for Grade 3 keratopathy. Four of the 6 patients required dose interruption due to ocular toxicity, after an average of 3.5 treatments. Response to withholding of treatment was not fully evaluated as patients were lost to follow up due to worsening of their disease.

Conclusions: Ocular toxicity occurred in all but 1 patient after starting belantamab, and 4 patients required dose interruption due to ocular toxicity. Worsening keratopathy correlated with decrease in visual acuity. Corneal changes were not always accompanied by symptoms or changes in visual acuity. Given the high frequency and often asymptomatic nature of keratopathy, close monitoring of the cornea and changes in visual acuity is prudent.

CONTROL ID: 3708188

SUBMITTER (NAME ONLY): Andrew Tirsi

TITLE: Relationships Between Retinal Ganglion Cell Dysfunction and Structural Thickness Measurements Are Mediated by the decrease in the Estimated Retinal Ganglion Cell Count in Glaucoma Suspects

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tirsi, S.A. Obstbaum, C. Tello, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|A. Tirsi, B. Wong, J. Tsai, V. Gliagias, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|J. moehringer, sandford H Calhoun high school, Merrick, New York, UNITED STATES|

Commercial Relationships Disclosure: Andrew Tirsi: Commercial Relationship(s);Code C (Consultant/Contractor):Diopsys, Inc | Derek Orshan: Commercial Relationship: Code N (No Commercial Relationship) | Benny Wong: Commercial Relationship: Code N (No Commercial Relationship) | Joby Tsai: Commercial Relationship: Code N (No Commercial Relationship) | Vasiliki Gliagias: Commercial Relationship: Code N (No Commercial Relationship) | julie moehringer: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Obstbaum: Commercial Relationship: Code N (No Commercial Relationship) | Celso Tello: Commercial Relationship(s);Code C (Consultant/Contractor):Diopsys, Inc

ABSTRACT BODY:

Purpose: Substantial loss of retinal ganglion cells (RGC) has been shown in perimetric glaucoma and empirical estimates of RGC count combining structural and functional test results were found to significantly correlate with the histological reports.in early glaucoma. The purpose was to determine whether estimated RGC count mediated the relationships among steady-state pattern electroretinography (ssPERG) and optical coherence tomography (OCT) thickness measures in glaucoma suspects (GS).

Methods: In this prospective cross-sectional study, 10 GS subjects (20 eyes) were recruited at the Manhattan Eye, Ear, and Throat Hospital, with normal Humphrey visual field tests with 24-2 MD better than -2dB, and suspicious optic nerves. Subjects underwent complete eye examinations, OCT, standard automated perimetry (SAP), and ssPERG testing. Two groups of 10 eyes in each, were created based upon clinical data: healthy subjects and GS. RGC counts were estimated using the combined structure-function index (CSFI). We performed mediation analyses with each ssPERG parameter (Magnitude, MagnitudeD and Mag/MagD ratio) as independent variables (X), estimated RGC count as the mediator (M), and average retinal nerve fiber layer thickness (AvRNFLT), mean deviation (24-2 MD), and average ganglion cell layer and inner plexiform layer thickness (AvGCIPLT) as the dependent variables (Y), for a total of nine analyses. For each analysis, the significance of the indirect and direct effects of X on Y were determined using 5,000 bootstrapped samples with a 95% confidence interval (CI).

Results: Estimated RGC count, AvRNFLT, 24-2 MD, and AvGCIPLT were reduced in GS ($p < 0.015$ for all parameters). Pearson and partial (age-adjusted) correlations revealed that all ssPERG parameters correlated with ARNFLT ($r > 0.51$, $p < 0.027$). MagnitudeD/Magnitude (MagD/Mag) ratio correlated with average GCIPLT ($r = 0.47$, $p = 0.042$). Nine mediation analyses revealed that estimated RGC count mediated the relationships among ssPERG parameters, ARNFLT, and average GCIPLT.

Conclusions: Estimated RGC count mediates the relationships between ssPERG parameters and OCT thickness measures in GS, underlying the importance of addressing the RGC dysfunction as early as possible to prevent future structural damage and RGC apoptosis.

CONTROL ID: 3708192

SUBMITTER (NAME ONLY): Xinxin Zhang

TITLE: The characterization of RPGR mutations and the investigation of their pathogenic mechanism

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhang, C. Liu, H. Li, Z. Bing, H. Liu, M. Wang, S. Lei, J. Kong, Department of Ophthalmology, China medical university, Shenyang, Shenyang, CHINA|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is a group of clinically and genetically heterogeneous diseases characterized by progressive photoreceptor degeneration. RP can be inherited as many traits, of which X-linked RP (XLRP) is one of the most severe forms of retinal degeneration and mainly caused by the mutations of the retinitis pigmentosa GTPase regulator (RPGR) gene. We reported RPGR mutations encountered in clinic and investigated the potential role of RPGR and the pathogenesis of mutant RPGR via Rpgr knockout mice and cellular experiments.

Methods: Rpgr knockout mice were efficiently established via CRISPR-Cas9 gene editing technique. The phenotype of Rpgr knockout mice was evaluated by fundus photography, optical coherence tomography (OCT) scans, HE staining, Electron microscope (EM), and electroretinogram (ERG). The potential role of RPGR was investigated by RNA-seq,qRT-PCR, immunofluorescence and western blot.

Results: Rpgr knockout mice were generated successfully. Fundus revealed multiple wide-spread yellowish spots which got larger as the increase of mice age in Rpgr knockout mice. OCT scans of Rpgr knockout mice showed thinner outer retina with uniform hyperreflexia as young as 1 mos of age. The ONL thickness of Rpgr knockout mice reduced from 3 mos onward while the total retina thickness reduced from 5 mos onward. HE staining suggested the abnormal hyperreflexia shown in OCT may well be the disorganized outer segment, which was supported by the findings of EM. Scotopic a wave of Rpgr knockout mice was significantly reduced as young as 3 mos of age. However, photopic b wave was still conserved at even the age of 12 months. Compared with male mice, the retina of Rpgr knockout female mice was impaired both structurally and functionally.

Conclusions: We established the model of Rpgr knockout mice with the characterization of progressive photoreceptor degeneration, including disorganized outer segment, thinned ONL and impaired visual function. We also revealed a series of pathophysiological alterations in Rpgr knockout mice, including chronic inflammatory response, endoplasmic reticulum stress (ERS), changes of vascular regulatory factors, etc. Meanwhile, we revealed abnormalities after Rpgr knockdown: including chronic inflammatory response, ERS, dysregulation of vascular regulatory factors, and even retinal degeneration in XLRP.

CONTROL ID: 3708193

SUBMITTER (NAME ONLY): Kenneth Mitton

TITLE: Frequency of Multigenic Variants Among Genes Regulating Retinal Vascular Development in FEVR Patients.

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.P. Mitton, W.A. Dailey, M. Sun, A. Petrelli Cicerone, A. Santos, D. Jeong, M. Drekh, L. Jones, K. Koustas, K. Schmitz, E.A. Guzman, M.T. Trese, K.A. Drenser, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|K.P. Mitton, M. Sun, A. Santos, D. Jeong, M. Drekh, L. Jones, K. Koustas, K. Schmitz, OUWB School of Medicine, Oakland University, Rochester, Michigan, UNITED STATES|M.T. Trese, A. Capone, K.A. Drenser, Associated Retinal Consultants, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The potential contribution of multigenic variants in persons with Familial Exudative Vitreo Retinopathy (FEVR) remains as one possible factor contributing to the variable phenotypic severity seen even within a family. Understanding the frequency of combinations of protein-altering variants in different FEVR-related genes is an important first step to establishing if multigenic contributions require attention or can be disregarded. To determine the abundance of multigenic protein-altering variants, we employed a novel custom sequencing panel to analyze seven FEVR-related genes in FEVR patient samples.

Methods: Research genetic sequencing of samples from the Associated Retinal Consultants DNA Eye-Bank was approved by the Oakland University IRB. An Ampliseq panel was designed using the Illumina Design Studio. A three-pool PCR option was designed for a final 180 amplicons, 8 genes, 83 exons with 25 bp adjacent intron sequence. Seven FEVR genes and the Retinoschisis gene were included.: NDP (ChrX), CTNNB1 (Chr3); TSPAN12 (Chr7); KIF11 (Chr10), FZD4 (Chr11), LRP5 (Chr11), ZNF408 (Chr11), RS1(ChrX). A cohort of 76 samples comprised FEVR patients and some unaffected relatives. Ampliseq libraries from up to 50 samples were pooled per sequencing run using the Illumin iSeq-100 platform. Variant impacts and allele frequency data were determined from ClinVar and The Genome Aggregation Databases (gnomAD).

Results: 33 protein-altering variants were found with the following distribution: LRP5 13/33 (40%), FZD4 9/33 (27%), ZNF408 6/33 (18%), (KIF11 3/33 (9%), NDP 1/33 (3%), CTNNB1 1/33 (3%). 37% of persons sequenced had di-genic or tri-genic variants that alter protein sequences. The average number of genes with protein-altering variants was greater in samples from confirmed FEVR (1.46, N=30) compared to unaffected persons (0.95, N=20), (p=0.009).

Conclusions: Multigenic protein-altering variants were present in a substantial fraction of FEVR subjects, 37%. While the contributions to disease are unknown for most of the variants in a multigenic context, their greater multigenic frequency in FEVR subjects suggests that potential multiple endothelial gene contributions to variable phenotypes are a possibility that clinics should consider for patients with FEVR / Norrie Disease.

CONTROL ID: 3708195

SUBMITTER (NAME ONLY): Nikhil Bommakanti

TITLE: Classification and growth rate of retinal atrophy after voretigene neparvovec-rzyl for RPE65-mediated retinal dystrophy

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Bommakanti, B. Young, C.G. Besirli, University of Michigan, Ann Arbor, Michigan, UNITED STATES|A.M. Berrocal, University of Miami, Florida, UNITED STATES|J.L. Duncan, University of California San Francisco, San Francisco, California, UNITED STATES|B. Bakall, Associated Retina Consultants, Phoenix, Arizona, UNITED STATES|M. Mathias, University of Colorado, Denver, Colorado, UNITED STATES|R. Sisk, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|A. Nagiel, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|A. Nagiel, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Classify the appearance of retinal atrophy and quantify the growth rate in patients who received voretigene neparvovec-rzyl (VN) for RPE65-mediated retinal dystrophy

Methods: Atrophy was qualitatively classified into different subtypes by expert consensus then manually segmented in ImageJ by two graders. Area of atrophy was calculated and fit to linear models of atrophy and square root of atrophy using Python. Main outcome measures were number of eyes, and slopes and coefficients of determination of linear regression models for each subtype of atrophy. Values are reported as mean ± standard deviation.

Results: 20 eyes from 10 patients across 4 centers developed progressive chorioretinal atrophy after subretinal administration of VN. A mean of 4.9 ± 3.0 images per eye obtained over 1.7 ± 0.7 years were reviewed, and atrophy was categorized into touchdown site (8 eyes), perifoveal (13 eyes), and nummular (11 eyes) subtypes (Fig. 1). 10 eyes demonstrated more than one type of atrophy (mixed). All eyes demonstrated atrophy involving the macula.

The growth rate of all atrophy by area and by square root of area was 18.0 ± 11.0 mm^2/year (R^2 0.9 ± 0.1) and 2.6 ± 1.2 mm/year (R^2 0.8 ± 0.2). Growth rates of the atrophy subtypes were 2.0 ± 1.7 mm^2/year (R^2 0.9 ± 0.2) and 0.8 ± 0.4 mm/year (R^2 0.9 ± 0.2) for touchdown atrophy, 17.2 ± 12.5 mm^2/year (R^2 0.9 ± 0.1) and 2.7 ± 1.4 mm/year (R^2 0.8 ± 0.2) for perifoveal atrophy, and 3.8 ± 2.7 mm^2/year (R^2 0.9 ± 0.0) and 1.5 ± 0.4 mm/year (R^2 0.9 ± 0.1) for nummular atrophy (Fig. 2)

Conclusions: Chorioretinal atrophy following subretinal administration of VN for RPE65-mediated retinal dystrophy developed according to a touchdown site, perifoveal, and/or nummular pattern. Perifoveal atrophy trended toward growing the most rapidly whereas touchdown site atrophy trended toward growing the least rapidly. Atrophy growth was more strongly correlated with atrophy area rather than square root of area, in contrast to other causes of macular atrophy such as dry AMD. These findings suggest distinct mechanisms of atrophy development and demonstrate the need for close observation in studies involving other gene therapies using similar vectors.

CONTROL ID: 3708200

SUBMITTER (NAME ONLY): Fahd Naufal

TITLE: Developing a care delivery framework for older adults with chronic eye disease and vision impairment: A mixed methods study on patient perspectives

SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Naufal, X. Guo, J.E. Goldstein, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|C. Kerr-Niermann, University of Missouri-St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To understand the perspective of older adult patients with visual impairment (VI) and develop a framework that integrates eye and supportive health care services.

Methods: Adults ≥60 years recruited between 11/2019-10/2020 with a diagnosis of glaucoma, retina, and/or neuro-ophthalmologic-related disorders participated in an observational mixed-methods study. Eligible participants were identified through an electronic health record-based query using age and ICD-10 diagnostic code criteria for chronic eye diseases; criteria for participation included self-reported difficulty performing everyday activities due to vision loss (functional deficits). All participants completed a questionnaire and a one-on-one interview. We analyzed perspectives on major themes including changes in vision and condition; loss of functional ability; emotional health and healthcare delivery.

Results: Participants (N=65; mean age 73 years; 70% female) had a median visual acuity (VA) of 20/30 in the better eye. Most participants were diagnosed (41.5%) and experienced functional deficits (53.8%), such as reading, driving, or recognizing faces, within the last 1-5 years. Participants reporting VI in both eyes (60%) were more likely to report a longer duration of functional deficits (p_{trend}=0.03). Worse VA nor VI in both eyes were not associated with emotional health concerns or reliance on others for support. Half (53.8%) reported anxiety or depression related to VI; 70.8% required additional support with function. Despite levels of anxiety and depression, few participants (16%) self-identified a need for additional education, or support groups. Half (50.8%) reported that their eyecare provider adequately inquired about emotional status and one-third (33.8%) tended to normalize chronic eye disease, VI and functional loss as an expected outcome of ageing or family history.

Conclusions: A framework for older adults with chronic eye disease and on average mild VI should include identifying and discussing functional and emotional health concerns to determine individual need. Despite high levels of anxiety, depression, and visual function deficits there was limited interest in pursuing supportive services. However, inquiry regarding emotional health by eyecare providers was important to patients.

CONTROL ID: 3708201

SUBMITTER (NAME ONLY): Remi Shittu

TITLE: Two photon subtractive biofabrication of the human lamina cribrosa

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.J. Shittu, H.G. Kollech, J.P. Vande Geest, Bioengineering, University of Pittsburgh Swanson School of Engineering, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Remi Shittu: Commercial Relationship: Code N (No Commercial Relationship) | Hirut Kollech: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Vande Geest: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent advances in multiphoton fabrication have made the production of complex structures possible and may allow the production of unique ocular models useful in mechanobiological studies. The purpose of this study is to optimize two photon (2P) subtractive fabrication techniques for patient-specific lamina cribrosas (LC) from segmented images.

Methods: For this study, we used multiphoton images of the human LC from a previous study. The segmented second harmonic signal of these images were used to generate the 2P input binary images. 2P subtractive fabrication was executed on a quarter of the LC image using an Olympus BX51 upright laser-scanning microscope (Insight DS+, Spectra Physics, Santa Clara, CA). The laser was centered at 780 nm and electro-spun polycaprolactone (PCL) sheet was used to laser-cut the LC.

Results: Preliminary results show that the human LC can be produced using 2P subtractive fabrication. An image of the fabricated LC is shown in Figure1. Figure 1A shows the LC segmented input image and Figure 1B shows the fabricated LC.

Conclusions: While we are able to produce a portion of a human LC using 2P subtractive fabrication, there are limitations to this technique. While it may be possible to use this technique to generate LC structural alterations in the Z dimension, our current approach is limited as it is currently only able to produce excellent details of the LC in the X-Y plane. Further work is needed to optimize our technique to improve the fabrication of 3D LC structures.

Research reported in this abstract was supported by the National Eye Institute under award number R01EY020890 to JPVG and grant number R01FD006582 (JV Co-I, PI: Feinberg and Badylak).

CONTROL ID: 3708208

SUBMITTER (NAME ONLY): Aileen Arevalo

TITLE: The Association between Obstructive Sleep Apnea and Diabetic Retinopathy in the Elderly US California Medicare Population

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Arevalo, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|F. Yu, A.L. Coleman, Ophthalmology, UCLA, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|A. Arevalo, Charles Drew University of Medicine and Science, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: While sleep apnea has been linked as a potential risk factor for several eye diseases, the relationship between obstructive sleep apnea and diabetic retinopathy has been inconsistent. We performed a cross-sectional study to explore the association between obstructive sleep apnea and diabetic retinopathy in the elderly US California (CA) Medicare population.

Methods: This study was conducted among US CA Medicare beneficiaries using the 2019 part B carriers claims databases attained from the Centers for Medicare and Medicaid Services (CMS). The inclusion criteria were patients who were residing in CA during 2019, were 65 years of age or older, had both Medicare Part A and Part B coverages, and had at least one Part B claim in 2019. The exposure was obstructive sleep apnea (OSA) and the outcome of interest was diabetic retinopathy (DR), both of which were defined by the corresponding ICD-10-CM diagnosis codes in any claims. Potential confounders included age, sex, race/ethnicity, and Charlson Comorbidity Index (CCI) scores. Unadjusted associations were performed using chi-squared tests. Multivariable logistic regression models were utilized to assess the adjusted association by controlling for all aforementioned potential confounders.

Results: Among 2,717,346 CA Medicare beneficiaries who met inclusion criteria, 27.9% (759,062) were 65-69 years of age, 56.8% (1,544,479) were female, 62.8% (1,706,807) were white, 4.3% (117,856) were black, 12.8 (346,723) were Asian, 15.9% (430,597) were Hispanic, and 65.6% had a CCI score of 1 or more. The overall prevalence of OSA was 5.9% (161,350), and the overall prevalence of DR was 3.3% (89,693). Those with OSA had an increased odds of DR (adjusted OR=1.54; 95% CI:1.51, 1.58; $p<0.001$) compared to those without OSA.

Conclusions: Our study identified a statistically significant association between obstructive sleep apnea and diabetic retinopathy in the senior CA Medicare population. This finding indicates the need for further studies to analyze the impacts of OSA on DR, such as the severity and development of DR subtypes.

CONTROL ID: 3708209

SUBMITTER (NAME ONLY): Michael Wong

TITLE: Outcomes of Bimatoprost sustained-release intracameral implant in patients with glaucoma

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Wong, M.E. Bowers, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|R. Niknam, M.R. Moster, M.J. Pro, E. Dale, N.N. Kolomeyer, D. Lee, C.X. Zheng, Glaucoma, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Ventimiglia, University of Maryland at College Park, College Park, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bimatoprost sustained-release intracameral implant (Bimatoprost SR, Durysta, Allergan) was approved by the U.S. Food and Drug Administration for one-time use in patients with ocular hypertension or open angle glaucoma (OAG) in March 2020. The purpose of the present study is to determine real-world outcomes of Bimatoprost SR on intraocular pressure (IOP) and number of IOP lowering medications in patients with glaucoma. A secondary objective is to determine the efficacy of Bimatoprost SR in patients with a prior history of selective laser trabeculoplasty (SLT).

Methods: 122 eyes that received Bimatoprost SR by six glaucoma specialists at Wills Eye Hospital from March 2020 until September 2021 were examined using a retrospective chart review. A paired sample t-test for IOP and a binomial change test for number of medications was used. Multilevel models were then used to determine if statistical significance remained when controlling for demographic variables and prior history of SLT utilizing the lme4 package in R.

Results: Of the 122 eyes, there were 113 OAG, 4 chronic-angle closure, 3 ocular hypertension, and 2 others. 46 (54%) patients were female, and the median age was 78 years old. Mean follow-up time was 26.9 ± 18.9 weeks. 82 (67%) eyes were on a topical prostaglandin medication prior to intracameral Bimatoprost SR injection. 68 (83%) of these eyes stopped topical prostaglandin medication after injection. Mean post-treatment IOP of 16.6 ± 5.3 mmHg was significantly lower than mean pre-treatment IOP of 18.5 ± 5.8 mmHg ($t=-3.50$, $p<0.01$). The average number of medications following Bimatoprost SR was 1.3 ± 1.3, which was significantly lower than the average number of pre-treatment medications of 2.1 ± 1.4 ($p<0.01$). Analysis of multilevel models demonstrated that there was a statistically significant reduction in IOP and number of medications post-treatment even when demographic variables were controlled for ($p<0.01$ for both). A prior history of SLT ($n=54$) had no impact on treatment outcomes for IOP or number of medications, when controlling for demographics ($p>0.1$ for both).

Conclusions: Intracameral Bimatoprost SR reduced IOP and decreased the number of medications. Prior history of SLT did not impact Bimatoprost SR treatment outcomes.

CONTROL ID: 3708210

SUBMITTER (NAME ONLY): Alexander Miller

TITLE: Incidence Rates of Endophthalmitis after Various Pharmaceutical Intravitreal Injections

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Miller, C. Miller, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|H. Sciulli, M.W. Carbone, C. McCrossin, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze the incidence rates of endophthalmitis after intravitreal injection of the following medications: bevacizumab (BEVA), brolucizumab (BROL), aflibercept (AFL), ranibizumab (RAN), dexamethasone implant (DEXA), and triamcinolone acetonide (TRIA).

Methods: A retrospective cohort study was performed at a private retinal practice in Ohio. The Institutional Review Board (Sterling) determined this study consisted of non-human subjects. All data was collected through the practice management of Retina Associates of Cleveland, Inc. Data was collected from patients who received injections over a 2 year period of AFL, BEVA, BROL, DEXA, TRIA and RAN from January 2020 through November 2021 and includes: patient number, injection service dates, intravitreal drug injected, procedure codes, and primary diagnoses. The rates of endophthalmitis were then compared amongst the different injections. The total percentage of endophthalmitis cases was tabulated as well.

Results: From January 2020 through November 2021, 109,202 injections were administered. The breakdown of the 109,202 injections was as follows: 66,095 AFL, 28,762 BEVA, 8,650 RAN, 3,010 BRON, 1,958 DEXA and 727 TRIA. Of the 109,202 injections, 39 (0.036%) cases of endophthalmitis occurred. Of the 39 endophthalmitis cases, 22 (0.033% of total AFL injections) after AFL injection, 5 (0.688% of total TRIA injections) after TRIA injection, 5 (0.03% of total BEVA injections) after BEVA injection, 3 (0.153% of total DEXA injections) after DEXA injection, 2 (0.066% of total BROL injections) after BROL injection, and 2 (0.023% of total RAN injections) after RAN injection. Using a student’s t-test, the rate of endophthalmitis for TRIA versus all other medications was statistically significant with a p-value of 0.00152.

Conclusions: The results of the study show a total incidence rate of 0.036% of endophthalmitis after intravitreal injection. This review suggests that TRIA yielded a significantly higher incidence rate of endophthalmitis as compared to the other medications.

CONTROL ID: 3708213

SUBMITTER (NAME ONLY): Fengting Ji

TITLE: Corneo-sclera collagen fibers exhibit substantial transverse inclination

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Ji, M. Quinn, M. Bansal, Y. Hua, I.A. Sigal, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies of cornea transverse architecture have shown that collagen fibers that are inclined relative to the cornea surface play a crucial mechanical role, increasing stiffness and controlling shape. However, although the sclera spans most of the globe, the extent that its fibers are also transversely inclined remains unknown. Our goal was to quantify collagen fibers transverse inclination over the whole globe.

Methods: Whole-globe sagittal sections from 7 sheep eyes were imaged using previously described polarized light microscopy (PLM) tools to obtain local collagen fiber orientation and density (1.49 μm/pixel). The measured orientations were post-processed to compensate for local tissue orientation introduced by eye shell curvature. Fiber orientation and inclination angle distributions weighted by fiber density were quantified for 15 regions (Fig 1). Each regional inclination angle distribution was then fitted by a gaussian curve, and the inclination angle range was determined from the full width at half maximum (FWHM) (Fig 2).

Results: Posterior pole (PPS, posterior sclera) had less aligned fibers and a wider range of inclination angles than anterior pole (limbus, peripheral/central cornea) and equator ($p<0.001$). Fiber inclinations were substantial in all regions, whereby even the most aligned regions had inclination angle spread by 15 degrees. Results were consistent across eyes.

Conclusions: Fiber inclinations occur across the globe, not just the cornea. Transverse inclinations may represent interweaving or other features of collagen architecture. It seems likely that they play a role in stiffness, strength and shape in the rest of the globe as they do in the cornea.

CONTROL ID: 3708219

SUBMITTER (NAME ONLY): Donald Tran

TITLE: Measure of efficacy and tolerability of immunosuppressive agents using drug retention time in Behçet's uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Tran, S. Rogers, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|L.L. Lim, Centre for Eye Research Australia, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|L.L. Lim, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Behçet's disease (BD) is a recurrent multisystem vasculitis associated with a blinding uveitis. The advent of TNF-α inhibitors have significantly improved treatment, however comparative studies between conventional disease-modifying antirheumatic drugs (DMARDs) and biologic DMARDs in BD are limited. As retention time is a measure of drug effectiveness and tolerability, we compared this in patients with BD uveitis.

Methods: Retrospective case review of patients who met the revised International Criteria for Behçet's Disease (ICBD) treated at the Royal Victorian Eye and Ear Hospital, Australia, between 1985–2021. Demographic, ophthalmic and systemic features, DMARD use and reasons for discontinuation were recorded. Retention time was calculated as total days on drug and number of days per person within each DMARD group.

Results: Forty-eight patients (37 males) with a median age of 28.6 years (IQR 25.4–35.0) were followed-up for a median of 7.8 years (IQR 2.6–13.9). At initial presentation, exactly half had bilateral disease (N=24), and of the 62 eyes with uveitis (16 anterior uveitis, 11 intermediate, 2 posterior and 33 panuveitis) the median logMAR visual acuity was 0.176. During the first visit, 33 patients met ICBD criteria, and the systemic manifestations were oral ulcers (N=33), genital ulcers (N=11), skin (N=7), joint (N=6), and vascular (N=1). Corticosteroid sparing agents used were Cyclosporin (CSA, N=24), Mycophenolate (N=22), Azathioprine (N=21), Methotrexate (N=15), Adalimumab (ADA, N=15), Infliximab (IFX, N=2), and Rituximab (RTX, N=1). Total median drug retention time was 1064, 704, 231, 623, and 917 days, respectively, and 44.3, 32.0, 11.0, 41.5, and 61.1 days per person after adjusting for number of patients per drug (not calculated for IFX and RTX due to low use). DMARDs were discontinued 119 times and the reasons for cessation were adverse reaction (N=34), failure of treatment (N=28), poor adherence (N=25), sustained quiescence (N=15), loss to follow-up (N=14), and unclear documentation (N=3).

Conclusions: Our data suggests that the tolerability and efficacy, as measured with retention time, of ADA is at least comparable to, and possibly better than cDMARDs in young males with BD, who often suffer from vision threatening disease at first presentation. Median drug retention time for CSA was longer than ADA but not after adjusting for patients in each DMARD group.

CONTROL ID: 3708222

SUBMITTER (NAME ONLY): AYA KAMIMURA

TITLE: Clinical outcome of central serous chorioretinopathy with or without choroidal neovascularization

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. KAMIMURA, A. Miki, M. Kishimoto, W. Matsumiya, H. Imai, S. Kusuhara, M. Nakamura, Ophthalmology, Kobe University Graduate School of Medicine, Kobe, JAPAN|

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ABSTRACT BODY:

Purpose: To compare the 2- year outcome of half-time photodynamic therapy (htPDT) in chronic central serous chorioretinopathy (cCSC) with or without choroidal neovascularization (CNV)

Methods: This was a retrospective study of 88 eyes from 88 patients with cCSC who underwent htPDT and were followed up for more than 24 months. Patients were divided into two groups with (21 eyes) or without (67 eyes) CNV before htPDT treatment. Best-corrected visual acuity (BCVA), central retinal thickness (CRT), subfoveal choroidal thickness (SCT), and resolution and recurrence of subretinal fluid (SRF) were evaluated at baseline and 1, 3, 6, 12, and 24 months after PDT.

Results: There was a significant difference in age between the two groups ($P < 0.01$). A significant improvement in the BCVA was found at all time points in eyes without CNV but only at 24 months after htPDT in eyes with CNV. There were significant differences in BCVA between groups at any time points. CRT was significantly reduced in both groups at all time points with no significant intergroup differences. A significant reduction in the SCT was found at all time points in the eyes without CNV, but only at 1 and 24 months after htPDT in the eyes with CNV. There were significant differences between groups in the rate of recurrent and persistent SRF ($P=0.013$ and $P=0.017$, respectively). Multivariate analysis revealed that the presence of CNV was significantly associated with recurrence and persistence of SRF after initial PDT ($P=0.012$ and $P=0.023$, respectively). Logistic regression analysis showed that baseline BCVA, not the presence of CNV, was significantly associated with BCVA at 24 months after initial PDT ($P<0.01$).

Conclusions: A htPDT for cCSC was less effective in eyes with CNV than without CNV regarding the recurrence and the persistence of SRF. Additional treatment might be required in eyes with CNV during 24-months follow-up periods.

CONTROL ID: 3708223

SUBMITTER (NAME ONLY): Madeleine Puig

TITLE: Comparison of Outcomes of Trifocal and Extended-depth-of-focus Intraocular Lenses

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Puig, Y. Salem, M. Morrow, C. Waldman, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate and compare distance and near visual acuity, spectacle independence, and visual disturbances of the trifocal intraocular lens Acrysof Panoptix and the extended-depth-of-focus lenses Acrysof Vivity, Tecnis Eyhance, and Tecnis Symfony.

Methods: One hundred and twenty-seven eyes of 68 patients who underwent bilateral or unilateral cataract surgery with implantation of the non-toric or toric Acrysof Panoptix, Acrysof Vivity, Tecnis Eyhance, and Tecnis Symfony IOL between 2019 and 2021 were included in this retrospective study. Eyes with pre-existing ocular comorbidities were included in this study and 23 eyes undergoing concurrent glaucoma surgery. Pre- and postoperative corrected visual acuities, spectacle independence and visual disturbances were collected and analyzed. Descriptive statistics (mean and standard deviation) were calculated for all visual acuities. Comparison of more than two groups was performed using the Kruskal-Wallis test, non-parametric type of the one-way analysis of variance, and Chi-squared test. P values of 0.05 or less were considered to be statistically significant in all cases.

Results: No statistically significant differences were noted in the best corrected distance visual acuity (BCDVA) after surgery between the cohorts (p-value = 0.3302, Kruskal-Wallis test $p<0.05$). However, there was a significant difference between the best corrected near visual acuity (BCNVA) after surgery between the four cohorts ($p=0.00497$, Kruskal-Wallis test, $p<0.05$). The Symfony lens had the best average BCNVA. There was no statistical difference for spectacle independence at distance between the cohorts ($p = 0.247$; Chi-squared test $p<0.05$). However, the rate of spectacle independence at near between the four cohorts was significantly different (the p-value is < 0.00001, Chi-squared test) and Panoptix has the greatest proportion of spectacle independence. There wasn't a significant difference between the cohorts in regards to visual disturbances (p-value =.06127, Chi-squared test $p<0.05$)

Conclusions: All lenses were similarly effective in visual acuity and spectacle independence with minimal visual disturbances at distance. However, at near, each lens has its own advantages and disadvantages and the preference of each patient should be considered when selecting a trifocal or extended-depth-of-focus lens.

CONTROL ID: 3708224

SUBMITTER (NAME ONLY): Nina Cherian

TITLE: Comparison of a novel hyper-parallel optical coherence tomography biometer with a swept source OCT biometer in patients with cataracts

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Cherian, S. Al-Hashimi, S. Fung, O. Leyva, E. Tsui, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The hyper-parallel optical coherence tomography (HP-OCT^{TM}; Cylite, Melbourne, Australia) is a novel platform that uses a light source-splitting micro-lens array to allow for the rapid capture of whole-eye volumetric scans and resulting biometry measurements, with minimal artifact from patient movement. In this pilot study we compared the HP-OCT with the Argos (Santec Corporation, Komaki, Japan) swept-source OCT biometer to compare biometry measurements in patients with mature cataracts.

Methods: Patients with mature cataracts underwent 3 repeat measurements on both the HP-OCT and the Argos biometer. Axial length (AL), anterior chamber depth (ACD), central corneal thickness (CCT), lens thickness (LT), white-to-white distance (WTW), and mean keratometry (K) measurements were compared between the two biometers. Statistical analysis was performed using paired t-tests and Pearson's correlation coefficient.

Results: 21 eyes of 17 patients were measured. Mean AL measured by HP-OCT was 24.61±1.54 mm and by Argos 24.59±1.49 mm ($p=0.34$), with $r= 0.99$ ($p< 0.001$). Mean keratometry values were also similar ($p=0.21$), measuring 43.20±1.94 diopters and 43.31±2.08 diopters for the HP-OCT and Argos, respectively ($r=0.98$, $p<0.001$). ACD was 3.21±0.43 mm (HP-OCT) and 3.33±0.37 mm (Argos), $p < 0.002$, with $r=0.93$ ($p<0.0001$). CCT was 514.22±48.71 µm (HP-OCT), and 511.31±47.80 µm (Argos), $p=0.19$, with $r=0.98$ ($p<0.0001$). LT was 4.65±0.42 mm (HP-OCT) and 4.75±0.40 mm (Argos), $p <0.017$, with $r=0.91$ ($p<0.0001$). WTW was 11.24±0.73 mm (HP-OCT) and 12.43±0.69 mm (Argos), $p<0.0001$, with $r=0.44$ ($p=0.046$).

Conclusions: The HP-OCT and Argos biometers showed excellent correlation and similar measurements for axial length, mean keratometry, and CCT values. Statistically significant differences were seen in ACD, LT, and WTW measurements between the two biometers. Larger studies are necessary to further evaluate the agreement between the HP-OCT and Argos biometers.

CONTROL ID: 3708226

SUBMITTER (NAME ONLY): YIHAO LI

TITLE: Multimodal information fusion for the diagnosis of diabetic retinopathy

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. LI, H. Al Hajj, M. Lamard, Universite de Bretagne Occidentale, Brest, Bretagne, FRANCE|Y. LI, H. Al Hajj, P. Conze, M. Lamard, G. Quellec, INSERM, LaTIM, UMR 1101, FRANCE|R. Tadayoni, Hopital Lariboisiere, Paris, Île-de-France, FRANCE|S. Bonnin, Hopital Rothschild, Paris, Île-de-France, FRANCE|H. Ren, N. Manivannan, S. Magazzeni, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|P. Conze, IMT Atlantique Bretagne-Pays de la Loire - Campus de Brest, Brest, Bretagne, FRANCE|

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ABSTRACT BODY:

Purpose: The EviRed project aims to improve the management of diabetic retinopathy (DR), by taking advantage of new imaging modalities and artificial intelligence. In this study, we investigate the fusion of different modalities acquired simultaneously with a PLEX® Elite 9000 (Carl Zeiss Meditec Inc. Dublin, California, USA), namely 3-D structural optical coherence tomography (OCT), 3-D OCT angiography (OCTA) and 2-D Line Scanning Ophthalmoscope (LSO), for the automatic detection of proliferative DR.

Methods: 151 OCT volumes from 64 diabetic patients were collected for the study. This collection was divided as follows: 88 acquisitions (from 31 patients) for training, 28 acquisitions (from 14 patients) for validation and 35 acquisitions (from 19 patients) for testing. DR severity level, according to the ICDR scale, was graded by a retina specialist using fundus photographs: 30 acquisitions (including 16 in the train set, 5 in the validation set and 9 in the test set) had proliferative DR. Three fusion methods were evaluated: Early Fusion, Intermediate Fusion and Hierarchical Fusion. For each method, the following backbones were investigated: Resnet50, Resnet101, Densenet121, and Densenet169. We used the Area under the ROC Curve (AUC) to assess classification performance. These fusion methods were compared to the classification of a single modality separately.

Results: Using a single modality, the structure data achieved the best performance: AUC reaches 0.859 using Resnet101; this is our baseline. The Flow data reached an AUC of 0.816, using Densenet169. The LSO data reached an AUC of 0.662, using Densenet121. Hierarchical fusion achieves the best results, AUC reaches 0.911 using Densenet121, with an increase in AUC of over 0.052 compared to baseline. While the AUC increase for Early Fusion, on Densenet121, was around 0.006. Intermediate Fusion on Densenet121 performed worse than baseline.

Conclusions: The results show the effectiveness of our multimodal fusion method for proliferative DR detection. Hierarchical fusion method is currently showing good results: in particular, it outperforms the detection in a single modality. However, these experiments will have to be replicated in a larger dataset to achieve clinically useful detection performance.

CONTROL ID: 3708236

SUBMITTER (NAME ONLY): wei liu

TITLE: Heterochromatin suppresses oxidative stress-induced cGAS and STING expression in mouse RPE and retina

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. liu, Z. Ming, R. Qi, Q. Ke, X. zhu, D.W. Li, L. Gong, ZhongShan Ophthalmic Center,Sun Yat-sen University, Sun Yat-Sen University, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: wei liu: Commercial Relationship(s);Code F (Financial Support):National Natural Science Foundation of China (Grants 82070969, 81970787) ;Code F (Financial Support): Natural Science Foundation of Guangdong Province of China (2021A1515011793) | Zou Ming: Commercial Relationship: Code N (No Commercial Relationship) | Ruili Qi: Commercial Relationship: Code N (No Commercial Relationship) | Qin Ke: Commercial Relationship: Code N (No Commercial Relationship) | xingfei zhu: Commercial Relationship: Code N (No Commercial Relationship) | David Li: Commercial Relationship: Code N (No Commercial Relationship) | Lili Gong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Heterochromatin is a highly compact, transcription inert chromatin status. cGAS and STING are two key components mediating innate immune response, and are recently shown contributes to geographic atrophy (GA) . After analyzing the published transposase-accessible chromatin sequencing (ATAC-Seq) datasets , we found that STING gene loci exhibited decreased chromatin compaction in RPE of the GA patient. Therefore, we are aimed to investigate whether heterochromatin may regulate cGAS and STING expression upon oxidative stress

Methods: The in vivo oxidative stress was induce by intraperitoneal injection of sodium iodate (SI, 10-70 mg/kg). cGAS and STING expression were determined by qRT-PCR and western blot (WB) analysis in control (PBS-injected) or SI-injected mouse retina and RPE. Retina and RPE structure were asses by immunofluorescence and HE staining. cGAS and STING chromatin accessibility was assessed by the micrococcal nuclease (MNase) digestion assay. The in vivo effects of heterochromatin on cGAS and STING expression were determined in CBX5 knockout mice, in which the heterochromatin structure protein HP1α was depleted.

Results: Both cGAS and STING RNA and protein were upregulated in a dose-dependent manner in mouse retina and RPE. Decreased chromatin compaction were detected in both cGAS and STING gene loci upon SI injury. Increased cGAS, STING and the downstream IL6 and IL1β expression were detected in CBX5 knockout mice retina after SI injection. Depletion of this heterochromatin structure protein led to more severe retina destruction and IBA1-positive immune cell infiltration upon SI injury.

Conclusions: Heterochromatin represses cGAS and STING expression during oxidative injury. Our results suggest a potential role for targeting heterochromatin in the treatment of age-related macular degeneration (AMD).

CONTROL ID: 3708239

SUBMITTER (NAME ONLY): Charles Huang

TITLE: Changes in visual acuity using standardized ETDRS protocol refractions versus non-standardized Snellen testing in patients enrolled in prospective clinical trials.

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Huang, M. Salabati, R. Mahmoudzadeh, J. Hsu, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|C. Shah, OCB, Boston, Massachusetts, UNITED STATES|H. Yu, E. Chen, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|K. Jeng-Miller, Ophthalmology and Visual Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare standardized Early Treatment Diabetic Retinopathy Study (ETDRS) best corrected visual acuity (BCVA) and nonstandardized Snellen visual acuity (VA) among subjects enrolled in clinical trials.

Methods: Retrospective multi-center study of subjects enrolled in prospective clinical trials. Best available Snellen VA at the last visit before entering the study and the first visit after exiting the study was compared with the ETDRS BCVA at trial initiation and conclusion. The correlation and discrepancies between Snellen VA and ETDRS methods were evaluated.

Results: A total of 273 eyes were included. Mean Snellen VA was 20/71 (median 20/50, range 20/2000-20/20) at the visit before study entry while mean ETDRS BCVA was 20/49 (med. 20/42, ran. 20/914-20/13) at study entry (mean difference, 8.5 ETDRS letters,$p<0.001$). Mean ETDRS BCVA was 20/39 (med. 20/32, ran. 20/693-20/11) at study exit while mean Snellen VA was 20/62 (med. 20/50, ran. 20/6324-20/15) at the next visit after study exit (mean diff, 10 ETDRS letters,$p<0.001$). The worse the baseline VA, the greater the discrepancy between ETDRS and Snellen ($p<0.001$).

No significant difference in VA change from study entry to exit was found when comparing ETDRS (5 letter gain) and Snellen (3.3 letter gain) methods ($p=0.063$). In 184 (67.4%) eyes, ETDRS and Snellen changed concordantly while in 89 (32.6%) eyes, ETDRS and Snellen changed discordantly. In eyes changing discordantly, 70 (78.7%) improved with ETDRS but worsened with Snellen, while 19 (21.3%) worsened with ETDRS and improved with Snellen. In eyes with concordant vision gain, mean VA change was 12.6 letter gain for ETDRS and 16.8 letter gain for Snellen ($p=0.01$,$n=120$). In eyes with concordant vision loss, mean VA change was 10.4 letter loss with ETDRS and 15.1 letter loss with Snellen ($p=0.04$,$n=64$). In eyes with discordant visual change, mean VA change was 5.8 letter gain for ETDRS and 1.7 letter loss for Snellen ($p<0.001$).

Conclusions: ETDRS BCVA methods produce higher VA scores compared to Snellen VA, especially in patients with worse vision. Snellen may be underestimating VA change when there is a discrepancy in direction of VA change. When Snellen and ETDRS change in the same direction, Snellen may be overestimating VA change. This may have implications for interpreting real world VA outcomes compared to clinical trials.

CONTROL ID: 3708240

SUBMITTER (NAME ONLY): Dhanwini Rudraprasad

TITLE: Characterization and proteome profiling of extracellular vesicles in a murine model of Pseudomonas aeruginosa endophthalmitis

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Rudraprasad, J. Joseph Ruben, Jhaveri Microbiology Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|D. Rudraprasad, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|A.K. Rengan, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|M.N. Naik, Ophthalmic Plastic Surgery & Facial Aesthetics, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Extracellular vesicles (EVs) are representators of the cellular microenvironment and mediate intercellular communication and pathogenesis. Here, we investigate the protein topology of EVs derived from C57BL/6 murine model of P. aeruginosa endophthalmitis with an aim to understand the pathobiology of the disease.

Methods: Endophthalmitis was induced by intravitreal injection of Pseudomonas aeruginosa in C57BL/6 mice followed by enucleation at 24 hours. EVs were extracted by ultracentrifugation, characterized by DLS and western blotting with tetraspannin markers, CD9 and CD81, and quantified by ExoCet quantification kit. EVs were trypsin digested and subjected to LC-MS/MS. The proteins were analysed for its biological process and protein class by Gene Ontology (GO) and identification of enriched pathways by Kyoto Encyclopedia of Genes and Genomes (KEGG). Statistical analysis was performed by Unpaired t-test and all values represent mean ± SD for 3 biological replicates per time point.

Results: DLS and western blot confirmed the presence of EVs having a mean diameter of 332.2±93nm in infected eyes, while the EVs from the control set was 362±40 nm. Total number of EVs in infected eyes was $1.5X10^{10}$ ($\pm 2.6X10^{9}$), compared to $6.8X10^{9}$ ($\pm 3.6X10^{9}$) in control eyes. Proteome analysis of these EVs identified 2010 proteins (FDR ≤0.01) in infected eyes, of which 131 were differentially expressed (DEPs) (P-value ≤0.05). A total of 101 proteins were upregulated and 36 were downregulated while 55 proteins were found to be unique to the infected set. KEGG and GO analysis revealed presence of Cav1, Cav2, Coronin 1A, Integrin β, Protein kinase C, Tubulin-α, Tubulin-β, Complement C8, G-protein signalling 9 and IL-17 in EV from infected eyes. While Cav1 and Cav2 are reported to regulate inflammatory response of the host, Calnexin, prolactin induced protein and thioredoxin-related transmembrane protein-1 were present significantly in the infection set, suggesting a major role in host immunity and protection against microbial infections.

Conclusions: This study is the first attempt to comprehensively investigate the global proteome of EVs derived from mice model of P. aeruginosa endophthalmitis. The EV proteins Cav1, Cav2, Coronin 1A, Integrin β, type I keratin are known mediators of pathogenesis and are most suitable to study them as potential prognostic markers for endophthalmitis.

CONTROL ID: 3708247

SUBMITTER (NAME ONLY): Ala Moshiri

TITLE: Gene therapy rescues cone function in rhesus macaques with PDE6C cone disorder

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Moshiri, A. Lopez, S.M. Thomasy, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|S. Park, S.M. Thomasy, Surgical & Radiological Sciences, University of California Davis, Davis, California, UNITED STATES|J. Rogers, Human Genome Sequencing Center, Baylor College of Medicine, Houston, Texas, UNITED STATES|J. Rogers, R. Chen, Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|R. Chen, Biochemistry & Molecular Biology, Baylor College of Medicine, Houston, Texas, UNITED STATES|T. Issa, T. Stout, Cullen Eye Institute, Baylor College of Medicine, Houston, Texas, UNITED STATES|E. Bliss-Moreau, Psychology, California National Primate Research Center, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the age of disease onset and the degree to which viral mediated gene therapy can rescue cone function in a nonhuman primate model of an inherited cone disorder.

Methods: Infant rhesus macaques homozygous for the PDE6C R565Q mutation were generated through a selective breeding program at the California National Primate Research Center (CNPRC). Their genotypes were confirmed by genetic sequencing in the first few months of life. At age 9 months, two of the homozygous animals were treated in the right eye with either a high (1.5×10^{11} vg/eye) or low (1.5×10^{10} vg/eye) dose of adeno-associated virus (AAV5) carrying the rhesus macaque PDE6C gene under the control of the PR1.7 cone-specific promoter. The left eye was used as a control. Animals were tested in each eye by full-field and multifocal electroretinography (ERG) before and after injection. Behavioral testing was performed to assess visual acuity and color perception.

Results: All offspring homozygous for the PDE6C R565Q mutation had an absent cone signal and foveal autofluorescence abnormalities from early infancy. Subretinal injection in infant macaques was successfully accomplished. The virus was given along with systemic corticosteroids and was found to be safe without significant inflammation or toxicity. There were no obvious alterations in retinal lamination or cell loss in treated eyes. The therapeutic virus transduced retinal cells very efficiently and was expressed specifically in cone photoreceptors. Eyes treated with the high dose of the virus exhibited mild inflammation that was controlled with corticosteroids. The high dose restored cone responses on ERG within one month of injection. The responses were sustained and durable for at least 6 months without evidence of decline. Chromatic ERG testing showed restoration of amplitudes in all three cone subtypes. Behavioral testing to assess visual acuity and color perception is in progress.

Conclusions: AAV-mediated gene therapy for PDE6C was safe in the nonhuman primate model. It effectively restored cone function in all cone subtypes. Treated animals had durable restoration of the cone signal on ERG. These results suggest similar approaches in human patients may warrant investigation.

CONTROL ID: 3708248

SUBMITTER (NAME ONLY): SungWho Park

TITLE: Effect of Topical Bromfenac on Macular Thickness Changes after Vitrectomy or Phacovitrectomy for Epiretinal Membrane

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Park, M. Zaidi, J. Regenold, G. Uludag, A. Akhavanrezayat, A. Mobasserian, C. Or, C. Yasar, H. Ghoraba, N. Than, Q.D. Nguyen, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|S. Park, I. Byon, Ophthalmology, Pusan National University School of Medicine, Busan, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To evaluate the effect of topical bromfenac on macular thickness after vitrectomy or phacovitrectomy for epiretinal membrane (ERM).

Methods: Medical records of consecutive patients aged ≥50 who had undergone vitrectomy or phacovitrectomy for ERM removal by a single surgeon from January 2015 to December 2018 were retrospectively reviewed. Phacovitrectomy was performed in all phakic eyes and vitrectomy alone was performed in all pseudophakic eyes. Each group (phacovitrectomy or vitrectomy) was further subdivided into two subgroups according to use topical bromfenac (bromfenac versus none), resulting in a total of four subgroups: Phacovitrectomy-Bromfenac, Phacovitrectomy-None, Vitrectomy-Brofenac, and Vitrectomy-None. Cystoid macular edema (CME) was defined as an increase in macular thickness of 30 μm or greater at the one-month postoperative visit compared to that at baseline. Changes of macular thickness and visual acuity were analyzed for 3 months after the ERM removal.

Results: The four subgroups, Phacovitrectomy-Bromfenac, Phacovitrectomy-None, Vitrectomy-Bromfenac, and Vitrectomy-None included 56, 158, 11, and 42 patients, respectively. CME occurred in 13.6% of the Phacovitrectomy group, which was higher than 1.9% of the Vitrectomy group ($p<0.001$). Comparing among various subgroups, CME occurred in 17.7% of the Phacovitrectomy-None subgroup, which was higher than 1.8% of the Phacovitrectomy-Bromfenac subgroup ($p=0.001$). Macular thickness significantly decreased at 1 month after the ERM removal in all subgroups except the Phacovitrectomy-None subgroup.

Conclusions: CME rarely (1.9%) occurred after the vitrectomy for ERM removal in pseudophakic patients. While not uncommon after phacovitrectomy (13.6%), incidence of CME may be reduced by topical bromfenac. A trigger of Irvine-Gass syndrome may be crystalline lens removal itself rather than inflammation due to intraocular surgery or surgical trauma.

CONTROL ID: 3708256

SUBMITTER (NAME ONLY): Randolph Glickman

TITLE: Specialized Pro-Resolving Lipid Mediators, Maresin 1 (MaR1) and Neuroprotectin D1 (NPD1), Preserve Retinal Rod Function After Ocular Blast Trauma

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate specialized pro-resolving lipid mediator (SPMs) as neuroprotective interventions to ameliorate neuroinflammation, mitigate tissue damage, and preserve visual function after blast exposure. We hypothesized that early administration of the SPMs, NPD1 or MaR1, will preserve visual function in a blast-induced eye injury model by mitigating injurious processes.

Methods: A compressed-air driven shock tube was used to expose anesthetized adult male Long-Evans rats to shock waves simulating an open-field blast exposure. Blast waves of peak overpressure of 133 ± 4 kPa and a positive phase duration of 3.34 ± 0.05 ms were used. The overpressure specific impulse was 163.5 ± 10.4 kPa-ms. Anesthetized rats were exposed to a blast wave. Approximately 30 minutes after blast exposure, rats were treated with either 1.0 µg/kg MaR-1, 0.1 µg/kg NPD1 or vehicle (0.9% saline) delivered via tail vein injection and treated daily thereafter until day 7. Unexposed rats were included as controls. Visual function was assessed using a UTAS BigShot workstation (LKC Technologies) at pre-blast and 8-, 22-, and 32-days post-blast timepoints. This initial analysis is based on the scotopic ERG response, using the Vmax and Km parameters obtained by fitting the Naka-Rushton equation to the scotopic V-LogI curve. Pre- and post-blast statistical analysis was done with ANOVA and Bonferroni multiple comparisons.

Results: The Naka-Rushton function yields an objective measure of Vmax (the maximum response of the ERG rod branch) and the Km (the stimulus intensity at half-maximal response). In rats exposed to the blast wave only, Vmax was reduced up to 25% by day 30 post-blast, compared to the pre-blast average ($p \approx 0.003$). In the blast-exposed and vehicle treated rats, Vmax was depressed up to 50% (p=0-.001) and Km was elevated (p=0.003), indicating reduced visual sensitivity. In the animals exposed to blast and treated with either MaR1 or NPD1, there was no significant change ($p > .0.05$) in the Vmax or Km, indicating maintained visual sensitivity.

Conclusions: Blast wave exposure resulting in retinal damage, manifested by loss of rod sensitivity, was mitigated by either MaR-1 and/or NPD1 intervention. Thus, the treatments of MaR1 or NPD1 suggest an effective strategy to preserve visual function due to retinal and optic nerve injuries following ocular blast trauma.

CONTROL ID: 3708261

SUBMITTER (NAME ONLY): Gregor Reiter

TITLE: Comparison between a deep learning algorithm and human expertise predicting the progression of geographic atrophy (GA) secondary to age-related macular degeneration

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Geographic atrophy (GA) secondary to age-related macular degeneration is a progressive disease with irreversible loss of visual function. Artificial intelligence (AI)-algorithms are able to monitor disease progression on an individual level. The aim of this study was to investigate the predictive power of AI for GA progression in comparison to retinal expert judgement.

Methods: The set-up of the study consisted of three rounds with two weeks of breaks to prevent memorization, each round entailing two tasks: 1) Experts had to sort GA progression into three subgroups based on anticipated growth rates: slow, intermediate and fast, with a square root growth of <0.2mm, 0.2-0.4mm and >0.4mm, respectively. 2) Experts selected the faster growing case out of two cases. The first round comprises baseline fundus autofluorescence (FAF), the second infrared (IR) and optical coherence tomography (OCT) and the third FAF, IR and OCT images. To compare AI prediction with human experts, FAF annotations of GA performed by a centralized reading center were employed as the reference. For the first task, accuracy and Kappa index between predictions and ground truth were evaluated. For the second task, the concordance index was calculated.

Results: A total of 134 eyes from 134 patients from a phase II clinical trial (FILLY, Apellis) were included, among those 53 were from sham arm and 81 from fellow eyes. Four retinal experts evaluated 120 eyes and 120 eye pairs for respective tasks in each round, resulting in 2880 human gradings. The experts on average reached accuracy of 0.37, 0.43, 0.41 and a Kappa index of 0.05, 0.14, 0.12 on FAF, IR+OCT and FAF+IR+OCT, respectively. On the second task experts achieved a concordance index of 0.62, 0.59 and 0.60. The AI was able to reach an accuracy of 0.48 and Kappa index of 0.21 on the first task, and concordance index of 0.69 on the second task solely utilizing OCT imaging.

Conclusions: Prediction of lesion growth will become an important task for future patient counselling, most importantly after treatments become available. Human gradings improved when the estimation was based on OCT features. However, AI performs this task in a superior manner compared to human experts. AI-supported decisions will guide future management and improve patient care in one of the leading causes for irreversible loss of vision.

CONTROL ID: 3708264

SUBMITTER (NAME ONLY): shiva ram Male

TITLE: Impact of color vision deficiency on quality of life in a sample of Indian population.

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: According to the Colorblind awareness organization, color vision deficiency (CVD) affects 1 in 12 men (8.3%) and 1 in 200 women (0.5%) globally. In India (Kundu et al., 2020), the overall prevalence of CVD is 3.89% in males, followed by 0.18% in females. However, most cases are undiagnosed and only detected in screening programmes or during work empowerment. Besides this, CVD patients experience multiple difficulties in day-to-day life. The current study aimed to investigate the quality of life in a sample of CVD patients in India and how color vision impairment affects them psychologically, economically, and work-productivity wise.

Methods: This descriptive and cross-sectional questionnaire study was conducted on N=44 diagnosed CVD patients (male=36 and female=8) who visited two eye hospitals in the Hyderabad region between 2020 to 2021. The comparison group included a age matched control group of normal color vision (normal CV) participants (N=12). In the current study, we validated and used a Telugu version of a questionnaire (CVD-QOL) which was developed and validated by Barry et al. in 2017 for CVD patients. In this study, Color vision was assessed by Ishihara color vision test. The questionnaire consists of twenty-three questions on Likert scale with variables (Lifestyle, Emotions and Work). Six-point Likert scale was used, with lower scores indicating worse quality of life (1=severe problem to 6=no problem).

Results: Data analysis included 66 participants (CVD= 44 and normal CV= 12). Shapiro Wilk normality test resulted in normal data distribution. The mean age of participants did not show ($p=0.064$) a significant difference between the groups. There was a significant difference between CVD and normal CV participants for Color vision score ($p<0.001$). There was also a significant difference between the groups for the CVD-QoL variables, Lifestyle ($p<0.001$), Emotions ($p<0.001$) and Work ($p=0.027$) The results are shown in Table-1. The group differences among gender revealed that men tend to be more psychologically weaker in facing CVD than women.

Conclusions: This study results revealed that color vision deficiency has a significant impact on the quality of life in this sample of Indian population. The mean scores on the questionnaire for Lifestyle, Emotions and Work was much lower than the UK sample (Barry et al. 2017) indicating that there was a higher impact of CVD on these domains in this population.

CONTROL ID: 3708265

SUBMITTER (NAME ONLY): Suh-Hang Juo

TITLE: The clinical applications of anti-microRNA-328 therapy in myopia control and dry eye disease

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.H. Juo, China Medical University, Taichung, TAIWAN|C. Liang, Bright Eyes Clinic, TAIWAN|J. Chen, W. lai, Kaohsiung Veterans General Hospital Department of Ophthalmology, Kaohsiung, TAIWAN|

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ABSTRACT BODY:

Purpose: We previously reported that over-expression of miR-328 in the retina and sclera as a novel risk factor for myopia. Our recent study showed that corneal miR-328 also leads to dry eye disease. The present report is to show the first-in-human clinical trial of anti-miR-328 oligonucleotide in healthy subjects.

Methods: Several anti-miR-328 oligonucleotides were synthesized and tested in both in vitro and in vivo models. The candidate oligonucleotide, called SHJ002, was selected based on its anti-sense effect and safety data. SHJ002 was formulated as an ophthalmic solution for topical instillation. SHJ002 was used for good-laboratory-practice (GLP) toxicity studies via ocular instillation and systemic IV injection. With sufficient pre-clinical results and satisfactory safety data, we filed the investigational new drug (IND) application to both US and Taiwan FDA for a first-in-human clinical trial. The clinical trial recruited pediatric subjects with mild to moderate myopia. For each study subject, one eye was randomly selected to receive one eye drop, and the fellow eye was not treated. The initial 3 subjects were assigned to the dose-escalating study, where 3 different doses were sequentially tested for tolerability. The highest tolerable dose was used for 28 days in another 9 subjects to test the safety of SHJ002 ophthalmic solution.

Results: The SHJ002 ophthalmic solution was produced by a good manufacture practice (GMP) manufacturer, and it has very good stability under 4^{o}C and 25 ^{o}C. The toxicity studies did not observe any adverse effects via systemic or ocular topical administration. Both US and Taiwan FDA approved the IND application for a phase-I trial in pediatric subjects. In the clinical trial, all 3 different doses were well tolerated, and accordingly the highest dose was selected for a 28-day treatment. The results show that SHJ002 was well tolerated and no adverse effect was reported in the treated eyes. Although punctate keratitis was reported in one non-treated eye during the study period, this event was judged not-drug related and it was transient and spontaneously resolved before the end of this study.

Conclusions: This is a first-in-class ophthalmic drug for myopia control and dry eye disease. The phase-I data demonstrate its safety and high tolerance. The phase-II trials will be conducted to test its efficacy in controlling pediatric myopia and treating dry eye disease in adults.

CONTROL ID: 3708268

SUBMITTER (NAME ONLY): Noriko Kubota

TITLE: Fluorescence lifetime of ex-vivo retinal pigment epithelium in the state of enhanced mitochondrial uncoupling

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mitochondrial uncoupling is one of the intrinsic cellular functions that directly modifies the energy metabolism of the cell. It induces hyperactivation of mitochondrial respiration by interfering with the proton gradient. Recent studies have shown that mitochondrial uncoupling is also closely associated with the maintenance of various cellular functions, such as antioxidative stress. In this study, the influence of mitochondrial uncoupling on fluorescence lifetime (FLT), the possible indicator of metabolic change, of ex-vivo retinal pigment epithelial (RPE) cells was investigated.

Methods: RPE/choroid-explants from freshly enucleated porcine eyes were maintained in static culture conditions and incubated with or without mitochondrial uncoupler, carbonyl cyanide 4-(trifluoromethoxy) phenylhydrazone (FCCP), for; (1) 24 hours under 5% CO_2 at 37°C, and then FLT was measured once, or (2) 70 minutes in a custom-made chamber for FLT measurement at room temperature, during which FLT measurements were repeated several times. The sublethal FCCP concentration was determined in advance by calcein-AM assay, and the experiments were conducted with 0.6 µM FCCP. The respiratory function of ex-vivo RPE exposed to FCCP was confirmed with Seahorse metabolic analyzer. FLT was measured with Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO, excitation at 473 nm, Emission: short spectral channel (SSC) for 498-560 nm, long spectral channel (LSC) for 560-720 nm).

Results: Calcein-AM assay showed that FCCP less than 10 µM did not significantly increase the death of RPE cells after 24h of incubation. FLIO results indicated that the RPE explants incubated with FCCP for 24 hours had significantly shorter mean FLT (τ_m) than those of explants without FCCP in SSC (252.7 ± 5.5 ps vs. 279.6 ± 6.7 ps, $p<0.05$). In the time course measurement of the FLT, larger decrease in τ_m was observed in FCCP-treated RPE than non-treated ones. Mitochondrial assay indicated the rapid increase of oxygen consumption rate of ex-vivo RPE by treatment of 0.6 µM FCCP.

Conclusions: Results suggest that the enhanced mitochondrial uncoupling may shorten FLT of the RPE and this could be detected by FLIO. We assume that this is due to the increased activity of fluorescent co-factors associated with the respiratory function. For treatments that may activate endogenous uncoupler, FLIO might be a useful tool to evaluate their efficacy.

CONTROL ID: 3708269

SUBMITTER (NAME ONLY): Nathan Breuillard

TITLE: Comparison of long-term gene expression and protein secretion of non-virally transfected Retinal Pigment Epithelial (RPE) cells from human, pig and rabbit for preclinical efficiency analyses.

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Breuillard, T. Bascuas, N. Harmening, G. Sealy, M. Mohit, G. Thumann, M. Kropp, Experimental Ophthalmology, University of Geneva, Geneva, SWITZERLAND|N. Breuillard, T. Bascuas, N. Harmening, G. Sealy, M. Mohit, G. Thumann, M. Kropp, Department of Ophthalmology, University Hospitals of Geneva, Geneva, SWITZERLAND|

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ABSTRACT BODY:

Purpose: We are developing a gene therapy approach, in which autologous pigment epithelial cells will be genetically modified to overexpress the anti-angiogenic Pigment Epithelium-Derived Factor (PEDF) using the Sleeping Beauty (SB100X) transposon system to treat neovascular Age-Related Macular Degeneration (nvAMD). We compared the long term hPEDF expression and secretion from primary RPE cells transfected directly after isolation (“freshly isolated”) or after ≥3 weeks of culture (“pre-cultured”) from different species and their usability in preclinical efficiency studies.

Methods: Human (h), porcine (p) and rabbit (r) RPE cells were transfected using the Neon Transfection System with 0.03 and 0.47µg of the SB100X transposase and the pFAR4-ITRs CMV PEDF BGH miniplasmid, seeded (n=5) with 10k (pre-cultured) or 50k (freshly isolated, pre-cultured) cells; and cultured in DMEM/Ham’s 12 with 10% (pre-cultured) or 20% FBS (freshly isolated) until confluence (reduction to 1% FBS). PEDF expression and secretion were monitored with RT-PCR and ELISA. Cultures were maintained and analyses performed every 3 weeks until cells detached.

Results: pRPE and hRPE cells grew normal for up to 252d, while rRPE start to detach around 90d. We saw significant differences in PEDF gene expression at 82d with low expression in pre-cultured rRPE cells (10k=5.9k; 50k=12.0k fold change) compared to freshly isolated rRPE (50k=467.2k fold change) and pre-cultured pRPE (10k=67.7k; 50k=431.3k fold change); hRPE RT-PCR is ongoing. PEDF secretion differed significantly between species (p=0.037) with following amounts of PEDF for 10k pre-cultured cells: rRPE=1.2±2.5; pRPE=4.6±6.5; hRPE=32.5±93.5ng/h/10^4cells; 50k pre-cultured cells: rRPE=3.9±3.7; pRPE=4.9±5.0; hRPE=8.7±15.2 and 1.2±1.6ng/h/10^4cells for freshly isolated hRPE cells. Gene expression did not differ significantly between species and did not correlate well to protein expression and though hRPE were the most fragile cells, their PEDF secretion was highest.

Conclusions: Summarized, pRPE cells can be transfected similarly efficient as hRPE and are a suitable long-term efficiency model, differentially to rRPE that are not viable in long-term culture. Differences between 10 and 50k cells seeded are not significant and a high gene expression does not necessarily mean high protein secretion.

CONTROL ID: 3708277

SUBMITTER (NAME ONLY): Maya Eiger-Moscovich

TITLE: BAP1 immunohistochemistry in post-brachytherapy uveal melanoma

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Eiger-Moscovich, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|C.L. Shields, Ocular Oncology Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R.C. Eagle Jr., T. Milman, Pathology, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: BAP1 immunohistochemical (IHC) stain has emerged as a powerful and inexpensive prognostic tool in uveal melanoma (UM), correlating with UM molecular genetics and patient outcome. We aim to assess BAP1 IHC in irradiated UM eyes that ultimately underwent enucleation and to compare performance of BAP1 IHC with non-irradiated UM.

Methods: The medical records of all UM patients who underwent enucleation at the Oncology Service of Wills Eye Hospital from December 1st, 2007 to December 31st, 2014 with available paraffin-embedded tissue and either chromosome 3 (ch3) status or sufficient follow-up (>5 years or development of metastasis) were reviewed. Nuclear BAP1 (nBAP1) IHC was interpreted as intact (positive in >90% of nuclei), lost (positive in <5% of nuclei), or heterogeneous (positive in 5-90% of nuclei). Retina, intratumoral inflammatory cells, and blood vessels served as internal positive controls. Eyes without sufficient internal positive controls or with <5% viable tumor were labeled “non-interpretable”.

Results: There were 34 irradiated UM enucleated eyes compared to 47 non-irradiated UM eyes (controls). BAP1 IHC was non-interpretable in 7/81 (9%) eyes (4 irradiated and 3 non-irradiated). There was no significant difference between irradiated and non-irradiated UM with respect to nBAP1 IHC (lost in 41% vs 51%, p=0.19), ch3 status (monosomy 3 in 59% vs 60%, p=0.48), and outcome (metastatic disease in 44% vs 47%, p=0.8). Correlation of BAP1 IHC with disomy 3 (ch3D), monosomy 3 (ch3M), and outcome [intact BAP1:ch3D and/or no metastasis AND lost BAP1:ch3M and/or metastasis] in irradiated tumors was significantly lower when compared with non-irradiated tumors [21/30 (70%) vs 41/44 (93%), p=0.004*, Bonferroni correction 0.04*]. On re-evaluation of discordant cases, decreased or absent retinal staining overlying the tumor and weak intratumoral control were seen in six irradiated UM, pointing to a false-negative nBAP1 stain. With those cases excluded, the correlation of nBAP1 IHC with ch3 status and outcome was not significantly different in irradiated and non-irradiated UM [18/24 (75%) vs 41/44 (93%), p=0.017*, Bonferroni correction 0.15].

Conclusions: There are pitfalls in the interpretation of BAP1 immunostain in irradiated UM. This test should be used judiciously in tumors with prior plaque brachytherapy.

CONTROL ID: 3708279

SUBMITTER (NAME ONLY): Vered Horwitz

TITLE: Predicting clinical outcome of sulfur mustard induced ocular injury in the rabbit model using machine learning

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The sight threatening sulfur mustard (SM) induced ocular injury presents specific symptoms for each clinical stage. The acute injury develops in all of the exposed eyes and may heal or deteriorate into chronic pathology. Early detection of eyes at risk to develop the chronic pathology may assist in providing unique monitoring and treatments only to relevant cases. In this study, we used machine-learning model for predicting the development of chronic pathology in rabbits.

Methods: Clinical data from 166 rabbit eyes that were exposed to SM vapor was collected retrospectively. The data included a comprehensive clinical evaluation of the cornea, eyelids and conjunctiva using a semi-quantitative clinical score. A machine-learning model, based on random forest classifier, was trained to predict the development of corneal neovascularization at 4 weeks using clinical data collected three weeks earlier.

Results: The overall accuracy in predicting the clinical outcome of SM-induced ocular injury was 73%. The accuracy in identifying eyes at risk to develop corneal neovascularization and future healed eyes was 75% and 59%, respectively. The most important parameters for accurate prediction were conjunctival secretion and corneal opacity at 1week and corneal erosions at 72 h post exposure.

Conclusions: Predicting clinical outcome of SM-induced ocular injury based on the acute injury parameters using machine-learning model is demonstrated for the first time. Although the prediction accuracy was limited, probably due to small dataset, it pointed out towards various parameters during the acute injury that are important for the prediction of SM-induced chronic pathology.

CONTROL ID: 3708284

SUBMITTER (NAME ONLY): Shikha Gupta

TITLE: intra-Corneal channels as drainage aqueducts in Axenfeld Rieger subjects with glaucoma

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gupta, V. Gupta, V. Nathiya, K. Mahalingam, RPC, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Glaucoma associated with Axenfeld Rieger Syndrome (ARS) is often refractory, presents in advanced stage and requires surgical intervention. An in-vivo study of the angle using high definition ASOCT showed some prominent alternate routes of aqueous drainage in these children. Hence this study was conducted to look at routes of aqueous drainage in children with ARS.

Methods: A cross-sectional single center observational study comparing ARS children with Primary congenital glaucoma (PCG) was conducted. Study population for clinical arm consisted of 32 treated patients of ARS and 28 children with PCG old enough (≥8 years) to cooperate for ASOCT (Spectralis, Heidelberg Inc.). Children (20) formed the control arm. High resolution in vivo ASOCT of ARS subjects was used to assess the angle and the cornea and compared with the PCG arm and the control arm. For histopathology, ARS corneal tissues (5) harvested for keratoplasty were compared with those of PCG (5) and bullous keratopathy corneae (5).

Results: On ASOCT, ARS eyes displayed severe angle dysgenesis in form of iris adhesions over the TM visible as PAS, membrane over TM (46%) and absent Schlemm's canal (83%) as causes of angle dysgenesis (90%); this was comparable to PCG eyes. Besides this, they showed well-defined intra-corneal dilated cisterns forming discrete communications either with supraciliary aqueous drainage pathway (5/32, 15.6%; figure 1a) or conventional pathway of aqueous drainage (4/32, 12.5%;figure 1b) or both (figure 1c). No such finding was perceived in eyes with PCG or healthy controls. ($p<0.001$; chi square test) Histo-pathologically, presence of large intracorneal cisterns lined by basement membrane were confirmed in ARS eyes (Figure 2a), which was significantly greater in dimensions compared to those seen in PCG (Figure 2b), PBK (Figure 2c) or controls ($p<0.01$; Wilcoxon rank sum test).

Conclusions: Despite the presence of severely distorted angle drainage in ARS, these intracorneal communications with both conventional and unconventional pathways of aqueous drainage could be considered the alternative aqueous drainage pathways in the affected eyes. This could explain why many ARS patients present with glaucoma later in life.

CONTROL ID: 3708288

SUBMITTER (NAME ONLY): Miriam Stolwijk

TITLE: Barriers and facilitators in the referral pathway to low vision services: a qualitative study

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Stolwijk, R.M. van Nispen, E. Veenman, G.H. van Rens, Amsterdam UMC, Vrije Universiteit, Department of Ophthalmology, Amsterdam Public Health research institute, Amsterdam, NETHERLANDS|A.J. van der Ham, Amsterdam UMC, Vrije Universiteit, Department of Ethics, Law and Medical Humanities, Amsterdam Public Health research institute, Amsterdam, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Despite the benefits of low vision services (LVS), a discrepancy in the need and the uptake of these services has been reported internationally. Only a few studies examined the professional's perspective regarding barriers and facilitators in accessing LVS. This study aims to explore these parameters from both the perspective of visually impaired people and professionals from different eye care providers in the Netherlands.

Methods: A sample of older adults with macular degeneration, diabetic retinopathy and glaucoma (n=14) and a sample of healthcare professionals including ophthalmologists, low vision optometrists and LVS professionals (n=17) participated in this study. Semi structured interviews with patients and professionals were conducted and were analyzed with framework analysis using Atlas.ti software.

Results: Both patients and professionals consider having self-advocacy, motivation, social support, acceptance of the impairment, high participation needs and experienced negative impact of the impairment to facilitate access to LVS. Having good communication skills, paying attention to patient's LVS needs and informing them about LVS as a provider, as well as having a long patient-provider relationship were also identified as facilitators. In addition, professionals perceived communication between providers regarding LVS, the presence of low vision consultation hours in the ophthalmic practice and national service provision of LVS to facilitate referral to LVS. Barriers in accessing LVS that have been identified in both samples are being less assertive, and having low motivation, low acceptance of the impairment and lack of awareness about LVS as a patient. Besides that, lack of time and absence of communication about LVS by eye care providers to patients were mentioned as barriers. According to professionals, low participation needs of patients, short disease duration, short patient-provider relationship and unavailable care coordination hinder referral to LVS as well.

Conclusions: Findings imply that provider's lack of information provision about LVS, especially to patients who are less assertive, hamper referral to LVS. Providers should have attention for patient's LVS needs and actively inform them and their social network about LVS to facilitate access to LVS. Educating and training providers about how and when to address LVS may help to reduce barriers in the referral pathway to LVS.

CONTROL ID: 3708289

SUBMITTER (NAME ONLY): CHANGZOO KIM

TITLE: An Improved Strabismus Screening Method with Combination of Meta-Learning and Image Processing under Data Scarcity

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. KIM, S. Lee, Ophthalmology, Kosin University Gospel Hospital, Busan, Busan, KOREA (THE REPUBLIC OF)|S. Choi, Pukyong National University, Busan, Busan, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Meta-learning provides a promising pathway to train convolutional neural networks (CNNs) under data scarcity, yet its accuracy is restricted in screening strabismus due to the inability to make full use of eye information of data. To alleviate this issue, this study proposed a method by combining a meta-learning approach with image processing methods to fully extract the information that helps determine strabismus, thereby improving the classification accuracy for screening strabismus

Methods: The meta-learning approach was initially pretrained on a public dataset to obtain a well-generalized embedding network for extracting relevant pixel features while image processing methods were used to extract the position features of eye regions (e.g., iris position, corneal light reflex) as supplementary features. The dimensionality of pixel features was reduced to integrate with the low-dimensional supplementary features via principal component analysis, and the integrated features were used to train a support vector machine classifier for performing strabismus screening. A total of 60 images (30 normal and 30 strabismus) were used to verify the effectiveness of the proposed method, and its classification performance was assessed by computing the accuracy, specificity, and sensitivity through 5000 experiments.

Results: The classification accuracy using only the meta-learning approach achieved 0.709 with a sensitivity (i.e., correctly classify strabismus) of 0.740 and a specificity (i.e., correctly classify normal) of 0.678 while the proposed method achieved 0.805 classification accuracy with a sensitivity of 0.768 and a specificity of 0.842 in strabismus screening.

Conclusions: The proposed strabismus screening method achieved promising classification accuracy and improved the classification performance by about 10% than using the meta-learning approach alone under data scarcity. We expect that this combination approach can be an effective solution in medical fields where data scarcity is common.

CONTROL ID: 3708290

SUBMITTER (NAME ONLY): Gwenole Quellec

TITLE: 3-D style transfer between structure and flow channels in OCT angiography

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Quellec, Y. Li, H. Al Hajj, P. Conze, M. Lamard, LaTIM, UMR 1101, INSERM, FRANCE|Y. Li, H. Al Hajj, M. Lamard, Universite de Bretagne Occidentale, Brest, Bretagne, FRANCE|S. Bonnin, Hopital Rothschild, Paris, Île-de-France, FRANCE|H. Ren, N. Manivannan, S. Magazzeni, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|R. Tadayoni, Hopital Lariboisiere, Paris, Île-de-France, FRANCE|P. Conze, IMT Atlantique Bretagne-Pays de la Loire - Campus de Brest, Brest, Bretagne, FRANCE|

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ABSTRACT BODY:

Purpose: OCT angiography (OCTA) is a promising imaging modality for improving the management of diabetic retinopathy (DR). The EviRed project aims to develop artificial intelligence tools to automate DR diagnosis and prognosis evaluation using this imaging among others. Given the large amount of data to process, we investigate the potential redundancy of the two 3-D channels in OCTA scans, namely structure and flow. In particular, can any of these two channels be predicted by the other?

Methods: High-definition OCTA scans (6x6mm) from 112 eyes of 61 diabetic patients (one scan per eye) were acquired with a PLEX® Elite 9000 (Carl Zeiss Meditec Inc., Dublin, CA, USA). DR severity level in each eye was graded by a retina specialist using fundus photographs. Scans were randomly distributed between three subsets with equal distributions of DR severity: 84 scans (45 patients) to train, 12 scans (6 patients) to validate and 16 scans (10 patients) to test. Next, various 3-D U-Nets were trained to predict the flow channel from the structure channel. A similar set of 3-D U-Nets was trained to predict the structure channel from the flow channel.

Results: Using the ICDR scale, 29 eyes had no DR, 28 had mild NPDR, 26 had moderate NPDR and 29 had more advanced DR; the test set contained 4 scans from each severity category. Based on the validation set, the best neural architecture was 3-D U-Net with a ResNet-152 backbone. In the test set, the mean absolute error (MAE), in 3-D, between the true and predicted flow was 4.19% and the MAE between the true and predicted structure was 4.11%. The Pearson correlation coefficient (PCC) between the true and predicted flow was 0.684 and the PCC between the true and predicted structure was 0.961. No significant Spearman correlation was found between the PCC and DR severity (p-value = 0.721 for both transfer tasks).

Conclusions: Flow and structure channels in 6x6mm PLEX® Elite OCTA scans can be predicted from one another, which indicates potential redundancy between these channels. Prediction performance does not depend on DR severity. Visually, we observe that pathological features (e.g., exudates in the structure channel, avascular zones in the flow channel) can be also predicted. Further investigations are needed to quantify the prediction accuracy, at voxel level, and evaluate the possibility of using one single OCTA 3D channel for DR management in the future.

CONTROL ID: 3708292

SUBMITTER (NAME ONLY): Rogerio Garcia Nespolo

TITLE: Real-Time Framewise Semantic Understanding of Instruments and Tissues Via Deep Learning in Vitreoretinal Surgery

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Garcia Nespolo, D. Yi, Y. Leiderman, Department of Ophthalmology and Visual Sciences - Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|R. Garcia Nespolo, D. Yi, Y. Leiderman, Richard and Loan Hill Department of Biomedical Engineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Real-time imaging in vitreoretinal surgery directly impacts the handling of surgical instrumentation and the decision-making process of the surgeon. This experimental study tested the hypothesis that deep learning neural networks can concurrently track and segment instruments and target tissue landmarks within the retina when attached to a surgical microscope.

Methods: A hundred and one (101) vitreoretinal procedures consisting of core vitrectomy, membranectomy, and endolaser application were employed to train and validate an instance segmentation convolutional neural network. Three vitreoretinal surgeons manually annotated the following features from six-hundred and six (606) fundus frames: vitrector, forceps and endolaser tooltips, optic disc, fovea, retinal tear and detachment, fibrovascular proliferation, endolaser spot, the area where endolaser was applied, and macular hole. Five-fold cross-validation was employed to assess the performance of the model.

Results: The model detected and classified the vitrector tooltip with a mean area under the precision-recall curve (AUPR) of 0.972±0.009. Segmentation of target tissues such as optic disc, fovea, and macular hole reached mean AUPR values of 0.928±0.013, 0.844±0.039, and 0.916±0.021 respectively (Table 1 and Figure 1). The post-processed image was rendered at a resolution of 1920x1080 pixels at 38.77±1.52 frames per second when attached to an intraoperative visualization system.

Conclusions: Deep learning neural networks can detect, classify, and segment tissues and instruments during different phases of vitrectomy surgery in real time. We propose a model that creates a framework to develop surgical guidance tools that may guide surgical decision-making in real time. Potential applications include (1) warning of unintended instrument-tissue interactions and potential intraoperative complications, (2) data extraction for the control of equipment parameters such as the vitrector cutting rate, and (3) retroactive data acquisition of instrument maneuvers for surgeon’s skills analysis.

CONTROL ID: 3708295

SUBMITTER (NAME ONLY): Anqi Lyu

TITLE: Visual cortex anodal tDCS does not alter reading performance for Chinese characters presented in left lateral peripheral vision

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lyu, A.M. Cheong, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|A.E. Silva, B. Thompson, Optometry & Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|B. Thompson, A.M. Cheong, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|L.A. Abel, School of Medicine, Deakin University, Burwood, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Anqi Lyu: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Silva: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Larry Abel: Commercial Relationship: Code N (No Commercial Relationship) | Allen Cheong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: When applied to primary visual cortex, anodal transcranial direct current stimulation (a-tDCS) has been reported to reduce crowding in peripheral vision indicating a potential therapeutic use for patients with central vision loss. To further assess the potential of a-tDCS as a vision rehabilitation tool, we tested the hypothesis that visual cortex a-tDCS, but not sham a-tDCS, would improve reading of Chinese characters presented to left lateral peripheral vision in normally sighted adults.

Methods: Sentences of Chinese characters were presented one character at a time 10^{o} to the left of fixation at various speeds and print sizes. Participants (n = 10, 60 to 73 yrs. of age) read the sentences out loud and character recognition accuracy was recorded. Accuracy data were fitted with a continuous linear piecewise function that rises and then flattens to estimate all combinations of print sizes and speeds that elicit 55% accuracy. The point where both linear functions meet denotes the critical print size (CPS), defined as the smallest print size eliciting the participant's fastest reading speed. Using a double-blind, within-subject design, participants were then tested with sentences of print size and reading speed corresponding to 0.2 logMAR below the CPS on 2 stimulation days on which 20 mins of active or sham a-tDCS was applied to the visual cortex. Each test consisted of 15 sentences, and one test was administered before, during, 5 mins post, and 30 mins post stimulation. Reading accuracies were compared across time-points.

Results: A within subjects ANOVA revealed no significant interaction between Stimulation Type (anodal vs. sham) and Time (pre, during, 5 min post and 30 min post stimulation) ($F(3,27)=0.59$, $p=0.63$).

Conclusions: A-tDCS did not improve reading of Chinese characters in left lateral peripheral vision in normally sighted individuals. The effect of a-tDCS on reading of Chinese characters or other writing systems presented to other regions of the visual field, including inferior peripheral vision, is yet to be determined.

CONTROL ID: 3708299

SUBMITTER (NAME ONLY): Krunalkumar Ramanbhai Patel

TITLE: Anti-VEGF response prediction towards change in OCT central subfield thickness (CST) for diabetic macular edema (DME) patients

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Patel, Translational Research Lab, Carl Zeiss Meditec AG, München, Germany, Munich, Bavaria, GERMANY|R. Raman, C. Deviahamani, Shri Bhagwan Mahavir Department of Vitreo Retinal Services, Sankara Nethralaya Medical Research Foundation, Chennai, Chennai, Tamil Nadu, INDIA|A. Vankayala, M. Gupta, G. TUMKUR CHANDRA, . Center of Application and Research in India, Carl Zeiss India (Bangalore) Pvt. Ltd., Bangalore, INDIA|

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ABSTRACT BODY:

Purpose: Among the treatment options available for DME, intravitreal injections of anti-VEGFs have been the most practiced option. However, response to the anti-VEGF injection varies from patient to patient. In order to assist clinicians in optimizing treatment, we developed an automatic algorithm that predicts the potential change in CST for a given DME patient before administrating the anti-VEGF injection.

Methods: For the development and verification of the machine learning (ML) models, we collected data from a total of 906 DME patients who received anti-VEGF treatment. Each patient's multiple visit data points were collected where both pre- and post-injection OCT scans were acquired using CIRRUS™ HD-OCT 4000/5000 (ZEISS, Dublin, CA) with signal strength ≥ 0.4. The patients' data were divided into train and test sets containing 775 and 131 patients' data respectively.

Four benchmark models including Linear Regression, Support Vector Regression (SVR) with Radial Basis Function (RBF) kernel, SVR with linear kernel and Random Forest (RF) were trained using clinical parameters such as patient's age, gender, near BCVA value, distance vision (DV) BCVA value, pre-injection CST value, the other eight ETDRS grid values, number of previous anti-VEGF injections, and number of days after injection. Fig 1 shows the schematic diagram of the ML model development.

Using the test set, the performance of the CST change prediction algorithms was evaluated in terms of correlation coefficient (CC). The performance of all 4 models was further evaluated for four different scenarios - number of injections administered: ≥ 1, ≥ 2, ≥ 3 and > 3.

Results: SVR with linear kernel model achieved best performance in terms of CC with 0.65, 0.73, 0.75 and 0.85 for four scenarios respectively. Fig 2 shows the performance of all four ML models for the four scenarios. Linear regression, RF and SVR with RBF kernel model perform in the descending order of correlation coefficient.

Conclusions: In this study, we demonstrated how various ML regression models perform, with best CC of 0.85 with linear SVR for > 3 injections, in predicting the change in CST value for DME patients undergoing anti-VEGF treatment. This may help specialists to better plan the treatment of DME patients.

CONTROL ID: 3708301

SUBMITTER (NAME ONLY): Doreen Schmidl

TITLE: The effect of azithromycin eye drops or oral doxycycline on tear film thickness in patients with Meibomian gland dysfunction

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Schmidl, A. Schlatter, N. Hommer, M. Kallab, K. Zeller, L. Schmetterer, G. Garhofer, Department of Clinical Pharmacology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|A. Schlatter, K. Zeller, S. Palkovits, O. Findl, Vienna Institute for Research in Ocular Surgery (VIROS) - Karl Landsteiner Institute, Hanusch-Krankenhaus, Wien, Wien, AUSTRIA|H. Stegmann, R.M. Werkmeister, Center for Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|H. Stegmann, R.M. Werkmeister, Christian Doppler Laboratory for Ocular and Dermal Effects of Thiomers, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) is a common condition of the eyelids leading to tear film instability and resulting in dry eye disease or ocular surface disease (OSD). Oral doxycycline has been used for a long time for the treatment of MGD but is associated with systemic side effects. Topical azithromycin has therefore been proposed as a valuable alternative to systemic antibiotic treatment. The present study set out to compare the effect of topical azithromycin with oral doxycycline on tear film thickness (TFT) in patients with MGD.

Methods: Twenty patients with MGD were included in this observer-masked, parallel-group study and were randomized to either receive topical azithromycin for 4 weeks or oral doxycycline for 6 weeks. Main outcome of the study was the change in TFT as measured with ultra-high resolution optical coherence tomography before and 6 weeks after treatment start.

Results: Six weeks after treatment initiation, TFT increased from 5.0 ± 1.0 to 5.5 ± 1.1 µm (11.5 ± 30%) in the azithromycin group and from 4.7 ± 0.9 to 5.6 ± 1.1 µm (21.0 ± 28.6%) in the doxycycline group ($p = 0.028$ over time) with no difference between the two groups ($p = 0.267$). Systemic Adverse Events (AEs) occurred more frequently in the doxycycline group, while eye-related AEs were more common in the azithromycin group.

Conclusions: The present study found that topical azithromycin as well as systemic doxycycline improves TFT in patients with MGD with no difference between the two treatments. Due to the higher occurrence of systemic side effects when taking doxycycline, azithromycin eye drops seem to be an alternative with comparable efficacy.

CONTROL ID: 3708303

SUBMITTER (NAME ONLY): Anne Thykjær

TITLE: Inter grader agreement in the Danish screening program for diabetic retinopathy

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Thykjær, J. Grauslund, Ophthalmology, Odense Universitetshospital, Odense, Southern Denmark, DENMARK|A.S. Thykjær, K. Højlund, J. Grauslund, Clinical institute, Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Odense, Southern Denmark, DENMARK|L. Stokholm, K.H. Rubin, OPEN, Open Patient Data Explorative Network, Odense, Southern Denmark, DENMARK|R. Kawasaki, Osaka Daigaku Daigakuin Igakukei Kenkyuka Igakubu, Suita, Osaka, JAPAN|K. Højlund, Endocrinology, Odense Universitetshospital, Odense, Southern Denmark, DENMARK|J. Andresen, Association of Danish ophthalmologists, DENMARK|N. Andersen, The Danish registry of diabetic retinopathy and maculopathy, DENMARK|S. Heegaard, Ophthalmology, Rigshospitalet, Kobenhavn, DENMARK|K. Schielke, Ophthalmology, Aalborg Universitetshospital, Aalborg, North Denmark Region, DENMARK|C. Laugesen, Ophthalmology, Sjaellands Universitetshospital Roskilde, Roskilde, Sjaelland, DENMARK|

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ABSTRACT BODY:

Purpose: The Danish Registry of Diabetic Retinopathy (DiaBase) includes screening information from approximately 200,000 patients attending diabetic retinopathy (DR) screening in Denmark between 2013-2018. We performed a national, clinical validation study of the DR-gradings in the database to explore the inter grader agreement between the primary, screening ophthalmologist and a secondary certified grader.

Methods: Invitations to participate in the study were sent to all screening hospital departments as well as every practicing ophthalmologist nationwide. Fundus images and information on DR level, region of screening, image style and screening facility was uploaded by the primary grader to a secure database. These data were all blinded to the secondary grader during the grading process.

All grading of DR in a clinical setting in Denmark is standardized and performed using the International Clinical Diabetic Retinopathy (ICDR) scale, which was also the system applied in this study.

Fundus photographs from 230 patients (457 eyes) were included in the analysis.

Results: Images were received from all five Danish regions, from both practices (52.6%) and hospital based (47.4%) screening facilities.

Overall the reported levels of DR was 67.4%, 12.4%, 13.5%, 1.3% and 6.2% for no, mild, moderate, severe and proliferative DR. A significant difference ($P<0.001$) in the reported levels of DR between the screening facilities was observed; images from practicing ophthalmologists showed a distribution of 92%, 5%, 2%, 0% and 1% whereas images from hospital based ophthalmologists showed a distribution of 41%, 21%, 26%, 3%, and 11% for no, mild, moderate, severe and proliferative DR.

A weighted prevalence-adjusted, bias-adjusted kappa (PABAK) analysis was performed. The overall agreement between the primary and secondary graders was 93% ($\kappa = 0.83$). When sub-analyzed for screening facility the results were 96% ($\kappa = 0.89$) for practices and 90% ($\kappa = 0.76$) for hospitals.

Exact agreement between graders was observed in 78% of images.

Conclusions: In this nationwide study, we observed a high inter grader agreement of the gradings of DR performed by primary screening ophthalmologist and secondary certified grader in this nationwide study. From these results, it is reasonable to assume that the DR grades available in DiaBase, used for several large register-based studies, are primarily correct and eligible for continued use.

CONTROL ID: 3708304

SUBMITTER (NAME ONLY): Katerina Prokopiou

TITLE: A prospective, multicentre, randomised, double-blind study designed to assess the potential effects of omega-3 fatty acids supplementation in dry age-related macular degeneration or Stargardt disease

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Prokopiou, P. Kolovos, T. Georgiou, Ophthalmos Research and Educational Institute, CYPRUS|K. Prokopiou, Basic and Clinical Sciences, University of Nicosia Medical School, Nicosia, CYPRUS|H. Tsangari, University of Nicosia School of Business, Nicosia, CYPRUS|F. Bandello, Department of Ophthalmology, University Vita Salute scientific Institute of San Raffael Via Olgettina, Milan, ITALY|L.M. Rossetti, Centre for Clinical Trials at San Paolo Hospital, University of Milan, Milan, ITALY|L. Mastropasqua, Excellence Eye Research Centre, University G. d'Annunzio of Chieti-Pesara, Ospedale Clinicizzato Via dei Vestini, ITALY|S. Mohand-Said, Centre d'Investigation Clinique Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: The need for an effective therapeutic intervention in patients with vision loss due to retinal degeneration still remains high. We performed a multicentre, prospective, randomised, double-blind, placebo-controlled study to investigate the effects of omega-3 fatty acids in patients with dry age-related macular degeneration (AMD) or Stargardt disease (SD).

Methods: The main inclusion criterion was the best-corrected visual acuity (BCVA) to be between 21 and 55 (ETDRS letters) at screening visit. The final number of patients was 21; of those, 9 females and 12 males, with mean age 60.0 ± 2.3 years. Treatment consisted of daily oral administration of either placebo (sunflower oil; 7 patients) or active product (Eyetas®, 3.7g of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA); EPA:DHA=5:1; 14 patients), for 24 weeks. The number of letters gained from BCVA measurements and the ratio of arachidonic acid (AA)/EPA (using gas chromatography) was determined at screening, 12 weeks and 24 weeks. The total score of a questionnaire on perceived vision and subjective mood was obtained at 12 weeks and 24 weeks. The SPSS software (version 25.0) was used for the statistical analyses.

Results: Within the active group, the mean BCVA increased from 40.93 ± 9.18 at screening to 46.93 ± 9.18 at 24 weeks (p=0.003; Wilcoxon signed-rank test), whereas within the placebo group there was no significant increase. A comparison of the mean letters gained at 24 weeks showed a significant difference between the active and placebo groups (p=0.002; independent samples t-test). Similar findings were obtained for the letters gained at 12 weeks. For the active group, the mean level of AA/EPA had a significant decrease from screening (5.84 ± 1.05) to 12 weeks (1.50 ± 0.23, p=0.002, Wilcoxon signed ranks tests) and 24 weeks (1.47 ± 0.16, p=0.002), whereas for the placebo group, the AA/EPA had no significant differences. Finally, the mean score of the questionnaire was similar in the two groups at 12 weeks (9.23 ± 3.14 in active, 9.33 ± 2.42 in placebo), but it was higher for the active group compared to the placebo group at 24 weeks (9.38 ± 3.35 vs. 7.28 ± 2.36).

Conclusions: Oral supplementation of omega-3 fatty acids (3.7g; EPA:DHA=5:1) can improve objective and subjective vision in patients with dry AMD and SD.

CONTROL ID: 3708310

SUBMITTER (NAME ONLY): Katrine Frederiksen

TITLE: Navigated laser and aflibercept in treatment of branch retinal vein occlusion and macular edema: a 12 months randomized clinical trial

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In branch retinal vein occlusion (BRVO), central retinal laser has to some extend been replaced by angiostatic agents as first line treatment. While these efficiently reduce macular edema and increase visual acuity, the treatment is often inconvenient and expensive. In order to investigate a novel treatment strategy, we aimed to evaluate if combined treatment of aflibercept and navigated central retinal laser could lower injection burden in patients with BRVO and macular edema.

Methods: Forty treatment-naïve patients with BRVO and macular edema were included and randomized 1:1 to three monthly intravitreal injections of 2.0 mg aflibercept with (Group A) or without (Group B) navigated central retinal laser at month three. Patients were followed monthly from month four through 12, and re-treated with aflibercept according to re-treatment criteria: increase in central retinal thickness (CRT) ≥ 20% compared with lowest measurement, or decrease in best corrected visual acuity (BCVA) > 5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters as compared to baseline.

Results: Median age was 69.6 years, 45% were male, median BCVA was 66.6 letters, and median CRT was 541.4 µm, with no difference between groups. Seventy-five percent of patients needed retreatment after month three, and median number of retreatments was one with no difference between groups A and B (71.4% vs 79.0%, p=0.72, and one vs. two, p=0.38). Between baseline and month 12, median BCVA increased 13.0 ETDRS letters and median CRT was reduced by 192 µm with no difference between groups (+12.0 vs. +14.0 ETDRS letters, p=0.30, and -195µm vs. -185µm, p=0.96). Change in central retinal sensitivity, measured by microperimetry, did not differ according to treatment regimen (+2.87dB vs. +3.93 dB, p=0.40).

Conclusions: In a randomized trial of patients with treatment-naïve BRVO and macular edema, we found no difference in efficacy, side effects or treatment-burden when comparing combinational treatment of aflibercept and navigated central laser with aflibercept monotherapy. This may to some extend be explained by a lower than expected need for re-treatment of the intravitreal monotherapy group.

CONTROL ID: 3708311

SUBMITTER (NAME ONLY): Jose Hurst

TITLE: The expression of SARS-CoV 2 co-receptors and glia reaction in eyes of normal and COVID-19 diseased patients

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hurst, D. Suesskind, T. Bayyoud, S. Thaler, S. Schnichels, University Eye Hospital Tübingen, GERMANY|F. Ziemssen, Universitatsklinikum Leipzig, Leipzig, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: With this research project we wanted to approach the question of whether SARS-CoV 2 can infect the eye. In order to infect ocular tissues, virus-specific receptors; coreceptors or proteases must be present in the eye tissue. SARS-CoV 2 uses the human angiotensin converting enzyme 2 (ACE2) receptor to enter cells. In addition, the mammalian serine protease TMPRSS2, the protease furin and the glycoprotein neuropilin are identified as relevant proteases for the interaction of the virus with ACE2. Last year, we were able to show that ACE2 is significantly more expressed in ocular tissue of covid patients. Here the expression level of the co-receptor and glia markers, as well as the present of virus was confirmed in this study.

Methods: Seven eyes from donors without covid disease (COVID-) as well as ten fixed eyes from COVID-19 patients (COVID+) were analysed for their expression profile of ACE2, TMPRSS2, neuropilin and furin in the retina and cornea. The ocular tissues were examined for protein expression by immunohistochemical staining or for RNA expression by quantitative real-time PCR. In addition, viral spike protein was detected histologically in eyes, and expression profiles of GFAP and Iba-1 were assessed.

Results: Similar to ACE2 and TMPRSS2, the two proteases neuropilin and furin were detected in the retina and cornea. Interestingly, the expression profile differed in terms of strength and localization, especially in the retina. The presence of the virus in both cornea and retina was also demonstrated by the detection of viral spike protein. In all COVID+ retinas, strong GFAP staining was observed as well as some Iba-1 positive cells, suggesting activation of macro- and microglia.

Conclusions: Expression of ACE2, TMPRSS2, furin and neuropilin was demonstrated in COVID+ ocular tissues. In addition to the virus detection in retina and cornea, a glial reaction could also be observed. One can therefore assume an infection of the eye in these cases. However, in summary it can be said that an infection of the eye tissue is possible since all demanded receptors are present.

CONTROL ID: 3708312

SUBMITTER (NAME ONLY): Chun Yap

TITLE: Age-related Macular Degeneration Lesion Prediction with a Machine Learning and Multimodal Imaging Approach

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Yap, T. Tan, D. Wong, L. Schmetterer, A. Tan, Singapore Eye Research Institute, Singapore National Eye Centre, SINGAPORE|D. Wong, L. Schmetterer, SERI-NTU Advanced Ocular Engineering (STANCE), Nanyang Technological University, SINGAPORE|A. Tan, Ophthalmology and Visual Sciences Academic Clinical Program, Duke-NUS Medical School, SINGAPORE|

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ABSTRACT BODY:

Purpose: Microperimetry (MP) process requires an uncomfortable amount of time to assess elderly age-related macular degeneration (AMD) patients. This study aims to develop a machine learning model that predicts terminal AMD end-stage lesions (ESLs) of the retina using information provided by multi-modal imaging, shortening the MP process by only analysing the ameliorable early-stage retinal lesions.

Methods: Optical coherence tomography (OCT), infra-red (IR) and colour fundus images were taken from 130 AMD-afflicted eyes. OCT B-scans were graded for AMD lesions by 2 markers where discrepancies were resolved by a senior retina specialist. The OCT markings were translated onto the IR fundus to form lesion boundaries that acts as ground truth. A data framework (Fig. 1) was established using template matching of retinal vasculature in each imaging type, resulting in the superimposition of the different imaging modalities. The dataset used to train a XGBoost classification model was generated by running circular beams throughout and across the framework where each beam will encapsulate information of all framework layers. Physical properties of each layer were condensed into the mean and standard deviation of the pixels captured within the beam.

Results: The dataset was split into testing, training, and validation sets (10/85/5%). The models were evaluated by lesion prediction rate (LPR) and overall prediction rate (OPR). LPR and OPR is defined by the proportion of the lesion and overall beams being classified correctly respectively. The modelling process was performed twice with 2 different validation datasets where each set was taken from only early or late AMD eyes. LPR and OPR of both types of beams in the test set is 98-99%. Beams in the validation set have an LPR of 69-72% while the OPR of early AMD eyes is at 90% and late AMD eyes at 77%. A visualisation of the model's prediction on an eye in the validation dataset is in Fig. 2.

Conclusions: There is strong evidence that the classification model can pick up information provided by multiple imaging modalities to identify areas affected by ESLs. Model output visualisation shows that the central areas of ESLs were well established, though model performance deteriorated at the boundaries. Inclusion of more imaging modalities into the framework may improve future models.

CONTROL ID: 3708316

SUBMITTER (NAME ONLY): Qingge Guo

TITLE: Phenotype heterogeneity and the association between visual acuity and outer retinal structure in a cohort of Chinese X-linked juvenile retinoschisis patients

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Guo, Henan Eye Institute, Henan Provincial People's Hospital, Zhengzhou, Henan, CHINA|

Commercial Relationships Disclosure: Qingge Guo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: X-linked juvenile retinoschisis (XLRS), caused by mutations in the RS1 gene, is an X-linked recessive inherited disease that typically involves both eyes in the first two decades of life. Recently, phenotype heterogeneity of this condition has drawn increasing attention. We reported various phenotypes caused by RS1 gene mutations in eleven patients from ten Chinese families.

Methods: Data on the medical history of the patients from ten Han families of central China were collected. Ophthalmic examinations including the BCVA, fundus photography, ultra-wide angel sweep source optical coherence tomography, electroretinography were performed. Adaptive optics (AO) images were acquired to evaluate the cone photoreceptor mosaic when applicable. Venous blood of the probands and their family members was collected, and DNA was subjected to sequencing based on next-generation sequencing with a custom designed targeted gene panel PS400 for inherited retinal diseases. Validation was performed by Sanger sequencing and cosegregation. Pathogenicity was determined in accordance with the American College of Medical Genetics and Genomics (ACMG) guidelines.

Results: Ten RS1 mutations including 8 missense mutations and 2 terminator mutations were identified in 10 XLRS families. These patients showed a variety of clinical phenotypes including fovea schisis, bullous retinoschisis, macular or peripheral atrophy. Fifteen eyes of eight patients exhibited macular retinoschisis, and twelve eyes of seven patients exhibited peripheral retinoschisis. In addition, three patients showed asymmetrical fundus manifestations.Of importance, three patients without macular retinoschisis were misdiagnosed until genetic testing results were obtained. AO showed decrease of cone density and loss of regularity in the cystic schisis macular of XLRS. Furthermore, the BCVA was associated with the photoreceptor inner segment and outer segment (IS/OS) thickness.

Conclusions: With complicated clinical manifestations, a considerable portion of XLRS patients may present various phenotypes. It should be noticed that asymmetry fundus appearance in both eyes could lead to misdiagnosis easily. Thus, genetic testing is crucial for making a final diagnosis in those patients. In addition, residual cone photoreceptor structure was critical for the maintenance of useful vision.

CONTROL ID: 3708317

SUBMITTER (NAME ONLY): Arisara Kaeowichian

TITLE: Complete traumatic optic nerve head avulsion after blunt ocular trauma: two case reports and literature review.

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kaeowichian, Ophthalmology, Srinagarind Hospital, Khon Kaen, THAILAND|

Commercial Relationships Disclosure: Arisara Kaeowichian: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic nerve head (ONH) avulsion is the traumatic separation of the optic nerve fibers at the lamina cribosa with intact the nerve sheath and adjacent sclera. It is a rare and usually visually devastating form of anterior traumatic optic neuropathy. We report cases of complete ONH avulsion following blunt ocular trauma.

Methods: Medical charts, ocular imagings and radiological investigations were reviewed.

Results: Two patients had sudden visual loss after motorcycle accident and slingshot rebounding attack. Their initial and final visual acuity (VA) was no light perception (LP). Microscopic hyphema, mild mydriasis and relative afferent pupillary defect were found in the first teenager. Fundus examination showed dense preretinal hemorrhage overlying the ONH area with surrounding retinal edema and vitreous hemorrhage. Although there were multiple displaced orbital fractures, normal eye globe and optic nerve contour were demonstrated on the computerized tomography. The intravenous methylprednisolone was prescribed. The second boy presented with partial corneal laceration and total hyphema. Ocular ultrasound showed normal globe contour, dense vitreous opacity and posterior lens dislocation. Due to questionable no light perception, pars plana vitrectomy was performed. Total ONH excavation and central retinal artery occlusion were found intraoperatively. The total retinal detachment and epimacular membrane developed one week later, however, the ONH was clearly seen and the optical coherence tomography revealed bottomless cup. A probable small gap of nerve at the entry point of globe was detected after reviewing the magnetic resonance imaging.

Conclusions: Complete ONH avulsion is a rare manifestation of blunt ocular trauma. Radiological imaging usually could not detect the ONH avulsion which was support and obscured by the orbital tissue and optic nerve sheath. In case of media opacity, we suggest the visual evoked potential test for evaluation optic nerve function.

CONTROL ID: 3708319

SUBMITTER (NAME ONLY): Gwen Musial

TITLE: Dynamic contrast microscopic optical coherence tomography as a novel method for assessing corneal epithelium during exposure to benzalkonium chloride

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kohlfaerber, Medizinisches Laserzentrum Lübeck GmbH, Universitat zu Lubeck, Lubeck, Schleswig-Holstein, GERMANY|G. Musial, P. Steven, Ophthalmology-Medical Faculty UniKlinik Cologne, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|H. Schulz-Hildebrandt, G. Hüttmann, Institut fur Biomedizinische Optik, Universitat zu Lubeck, Lubeck, Schleswig-Holstein, GERMANY|

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ABSTRACT BODY:

Purpose: Microscopic optical coherence tomography (mOCT) has an imaging resolution of 1 μm in all voxel dimensions but individual epithelial cells are difficult to resolve due to lack of scattering contrast. Adding dynamic contrast processing to mOCT (dmOCT) scans enables visualization of individual cells and quantification of subcellular motion to evaluate cell function. We propose this technique as a novel method of evaluating the ocular surface after exposure to a toxic chemical, benzalkonium chloride (BAK).

Methods: Ex-vivo cross-section images were acquired with a custom-built frequency domain mOCT system. A dynamic contrast (dmOCT) scan consists of 150 B-scans with 512 A-scans. Five sets of dmOCT scans were consecutively taken at each imaging time point per eye. Eyes were explanted from healthy adult (21 weeks) C57BL/6 mice (n = 6; 6 control group, 6 BAK group), glued to cell culture dishes, and immersed in cell culture media. After baseline images were acquired in all eyes, BAK group media was replaced with 0.005% BAK media. Eyes were imaged every 30 min and were incubated at 37C between imaging sessions. Total epithelium and stroma thickness were measured from a single mOCT B-Scan while measures of cell motility and hue were acquired from dmOCT scans. Cellular motility was calculated by the normalized intensity standard deviation over time. Hue was created from the frequency spectra of the dmOCT signal with the blue channel for slow (0-0.5 Hz), green for medium (0.5-5 Hz), and red fast motion (5-25 Hz).

Results: After 30min exposure to 0.005% BAK, epithelium thickness increased and cell motility decreased compared to controls (Fig 1). Basal cell motility decreased after 60min exposure and the hue shifted red after 90min. Stroma thickness did not significantly swell until 120min exposure to BAK.

Conclusions: dmOCT allows us to view the behavior of the cornea epithelium under toxic stress due to BAK, showing changes to subcellular motion and swelling of the extracellular matrix.

CONTROL ID: 3708321

SUBMITTER (NAME ONLY): Luís Mendes

TITLE: Automatic detection of drusen-like deposits on OCT using EfficientNet models

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Drusen-like deposits are hallmarks of age-related macular degeneration (AMD) that can be found between the retinal pigment epithelium and Bruch’s membrane. On OCT they can present different sizes, shapes, and localizations. We evaluate the performance of models based on EfficientNet B0 architectures to automatically detect B-scans with drusen-like deposits (DLD).

Methods: OCT(A) data acquired in the scope of a DR screening program that is running in Coimbra, Portugal were used for training the models. The imaging data were acquired by the ZEISS AngioPlex OCT Angiography (ZEISS, Dublin. CA) using the Angio 6x6 mm protocol. The dataset includes 960 B-scans collected from 67 healthy eyes (71±4.8 years) and 842 Bscans collected from eyes having drusen-like deposits (DLD) from 123 eyes (68±3.5 years). The DLD were identified by an ophthalmologist that classified the pathological scans into two categories: with the presence of DLD with a size equal or superior to 63 µm (28%), and with the presence of DLD of size less 63 µm (72%). Deep learning models based on EfficientNets B0 architectures were trained and evaluated using a 5-fold cross-validation approach to detect B-scans having DLS. The specificity and the sensitivity metrics were used to evaluate the performance of the models.

Results: An overall sensibility equals to 84.4±10.5 % and a specificity equals to 80±11.9 % were measured on the testing folders. When were only considered DLD equals or largers than 63 µm the value of the sensibility was equal to 92±7% and the and specificity to 80.0±11.6%.

Conclusions: Our results show that EfficientNet B0 architectures can detect DLD even when trained with a small dataset. Is expected that the addition of more data will improve the performance of the models. Automatic detection of DLD is especially important in the scope of screening programs.

CONTROL ID: 3708322

SUBMITTER (NAME ONLY): Lin Yang

TITLE: A novel mutation located in the intermembrane space domain of AFG3L2 causes dominant optic atrophy through decreasing the stability of the encoded protein by ubiquitin-proteasome pathway

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Yang, B. Lei, Zhengzhou University, Zhengzhou, Henan, CHINA|L. Yang, J. xiuxiu, B. Lei, Henan Provincial People's Hospital, Zhengzhou, Henan, CHINA|

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ABSTRACT BODY:

Purpose: To verify the mutation of AFG3L2 intermembrane spaces can cause mitochondria disfunction dominant optic atrophy (DOA) and investigate the potential pathologic mechanisms.

Methods: The AFG3L2 gene variant was detected by whole-exome sequencing (WES), and then Sanger sequencing and co-segregation were conducted in the family members. We established fibroblast cell lines from this DOA family harboring AFG3L2 mutation and normal controls. Pathogenicity and molecular mechanisms of the identified variant was studied in patient-derived fibroblasts and HEK293T cell lines.

Results: We showed a large DOA family with 11 patients. WES revealed a novel pathogenic mutation (c.524T>C, p.F175S) in the AFG3L2 gene intermembrane space domain (IMSD), rather than in the ATPase domain which is the hot mutation region associated with most of the DOA reported previously. Functional studies in the skin fibroblasts generated from the patient donors and HEK293T cells showed that the mutation impaired mitochondrial function and decreased the ability of AFG3L2 protein entering the mitochondrial inner membrane. In addition, the novel mutation leaded to protein degradation and reduced the stability of AFG3L2 protein, which appeared associated with the proteasome-ubiquitin pathway.

Conclusions: A AFG3L2 mutation (c.524T>C, p.F175S) located between two transmembrane domainsIn caused isolated DOA. This may be related to the decreased stability of mutated protein mediated by the ubiquitin-proteasome pathway.

CONTROL ID: 3708324

SUBMITTER (NAME ONLY): Daniel de Bruyn

TITLE: Metabolic expression patterns from peripheral blood distinguish between low and high risk of metastasizing in uveal melanoma

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. de Bruyn, D. Paridaens, N. Naus, E. Kilic, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|D. de Bruyn, M. Bongaerts, A. de Klein, E. Brosens, Clinical Genetics, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|M. Bongaerts, Center for Metabolic and Lysosomal diseases, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|D. Paridaens, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|A. de Klein, E. Kilic, E. Brosens, Erasmus MC Kanker Instituut, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is the most common intraocular primary malignancy. Patients with UM are predominantly treated by irradiation. This eye-sparing treatment results in absence of tumor tissue for mutation-analyses. Mutations in BAP1-mutated tumors metastasize regularly within 5 years, SF3B1-mutated tumors pose an intermediate risk and metastasize in 5-15 years and EIF1AX mutations rarely metastasize. Without tumor tissue, the gene mutation related prognosis is unobtainable.

We aimed to elucidate prognostic information non-invasively by deriving serum metabolic expression patterns from patients harboring either a BAP1, SF3B1 or EIF1AX mutated tumor.

Methods: We have performed untargeted liquid chromatography tandem mass spectrometry (LC-MS/MS) using an Orbitrap system on plasma isolated from peripheral blood from 58 UM-patients in our discovery cohort. Additionally, plasma samples from a replication cohort and non-UM controls were used. Blood was drawn prior to treatment between 1998 and 2021 and gene-mutation was used for group stratification. Afterwards, the obtained metabolite expression was analyzed using MetaboAnalyst 5.0 and supervised clustering for metabolic patterns was performed using R.

Results: We have obtained patterns in differentially expressed metabolites between patients harboring an EIF1AX (low metastatic risk) and BAP1 (high metastatic risk) mutated tumors (Figure 1). In the metabolite expression we have identified two clusters, each with two subclusters. These subclusters are correlated with a gradual worsening of survival from patients harboring an EIF1AX to SF3B1 and BAP1-mutated tumor ($p < 0.0001$) (Figure 2).

Conclusions: Our preliminary data show that metabolomics performed on plasma of peripheral blood can distinguish between low and high risk of metastasizing and these promising results can be combined with other modalities for an integrative noninvasive prognosticator.

CONTROL ID: 3708325

SUBMITTER (NAME ONLY): Boris Stanzel

TITLE: Large-Area RPE Removal by Microsecond Laser followed by hiPS-RPE transplantation

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.V. Stanzel, S. Al-Nawaiseh, P. Wakili, G. Farese, P. Szurman, A. Schulz, Klaus Heimann Eye Research Institute, Sulzbach, Saarland, GERMANY|B.V. Stanzel, P. Wakili, G. Farese, P. Szurman, A. Schulz, Eye Clinic Sulzbach, Sulzbach, Saarland, GERMANY|S. Al-Nawaiseh, Ophthalmology, University of Muenster, Muenster, North-Rhine Westfalia, GERMANY|C. Kroetz, Fraunhofer IBMT, GERMANY|B. Greber, Catalent Pharma Solutions, GERMANY|C. Burri, C. Meier, Institute for Human Centered Engineering - optoLab, Berner Fachhochschule, Bern, Bern, SWITZERLAND|C. Burri, M. Frenz, Institute of Applied Physics, Universitat Bern, Bern, Bern, SWITZERLAND|S.J. Gasparini, M. Ader, Center for Regenerative Therapies Dresden, Technische Universitat Dresden, Dresden, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Cell therapeutics for AMD were often implanted regardless of RPE status in the target zone. This may result in RPE multilayering. Here we study a novel laser to remove RPE without collateral damage prior to RPE implantation to encourage better subretinal integration.

Methods: Pigment rabbits (n=24) were immunosuppressed with Sirolimus, Doxycyclin and Minocyclin. Using a SLO/ OCT (Heidelberg Engineering) extended with a prototype laser (Meridian Medical; wavelength: 532 nm; pulse duration, 8 µs), a large area of RPE was selectively removed in 19 rabbits. Animals without laser lesions served as controls (n=5). A 25 gauge vitrectomy (Geuder) with removal of posterior hyaloid membrane was performed thereafter. Human iPS-RPE (1000 cells/ µl) were manually injected using a 100 µl syringe (Hamilton) connected to a 38G cannula (MedOne) into the RPE laser lesion, or over healthy RPE in controls, monitored by intraoperative OCT imaging (RESCAN 700, Zeiss). In vivo follow up/ retinal imaging was up to 12 weeks including fluorescein and indocyanine angiography, as well as SD-OCT (Spectralis ®, Heidelberg Engineering).

Results: Representative RPE laser wounds exhibited mild late phase FA& ICGA leakage, without abnormal outer retinal or choroidal hyperreflectivity on OCT. By contrast, lesions with earlier leakage on FA/ ICGA showed beam-sized outer retinal hyperreflectivity on OCT, suggesting coagulation. The size of the RPE wounds was typically 10-12mm^2.

iOCT demonstrated in an immediate and directed spread of the bleb retinal detachment (bRD) within the lasered zone. By contrast, bRDs performed over non-lasered RPE raised slower with a circular spread. Subretinal injection ranged from 5-70µl, with lesser volumes/ larger bRDs areas over lasered regions.

At 6 and 12 weeks, none of implanted regions showed FA/ICGA leakage, some lesions had blockage due to hyperpigmentation; on OCT, representative areas showed preserved ellipsoid bands, with some RPE undulations. Lasered/implanted areas with a peripheral hyperpigmentation showed central outer retinal atrophy along with irregular RPE. Control implantation sites showed retinal atrophy and a variably thickened RPE band.

Conclusions: Large-area RPE removal with laser disruption is feasible in healthy rabbits and appears to facilitate superior integration of RPE suspension grafts, compared to subretinal injection alone. Future work aims to correlate histology with in vivo imaging.

CONTROL ID: 3708326

SUBMITTER (NAME ONLY): Wenting You

TITLE: Reversible Mitochondrial Injury in Dying Retinal Ganglion Cells

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. You, T. Berendschot, C.A. Webers, T.G. Gorgels, Ophthamology, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|W. You, C. Reutelingsperger, Biochemistry, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Glaucoma is a neurodegenerative disease in which various triggers induce cascades of secondary events, which ultimately lead to retinal ganglion cell (RGC) death. Once started, the cell death program is generally considered to be irreversible. However, recent studies reveal that recovery of dying cells is possible, even after reaching critical events in the cell death program. This phenomenon is termed anastasis. Harnessing mechanisms of anastasis may represent a previously unrecognized therapeutic strategy to rescue dying differentiated cells that are difficult to replace. We study neuronal cell death with the aim of rescuing dying RGCs in glaucoma.

Methods: Primary rat RGCs and differentiated PC12 cells were treated with ethanol to induce cell death. Live cell imaging with fluorescent probes (Mito-Tracker, TMRM, DCFDA, Fluo-8AM) were used to visualize the progression of the cell death program in individual RGCs and differentiated PC12 cells with high-resolution live-cell spinning disk confocal microscopy. Electron microscopy (EM) was used to observe the ultrastructure of mitochondria. Immunostaining was used to detect cytochrome c translocation.

Results: Exposure to 5% ethanol for 24 h induced 80.7% ($p<0.001$) and 69.1% ($p<0.001$) cell death in RGCs and PC12 cells, respectively. In both cell lines, live cell imaging showed significant mitochondrial fragmentation and membrane potential loss after ethanol treatment for 3 h. The average length of mitochondria decreased from 7.2 ± 6.2 μm to 1.3 ± 0.3 μm in RGCs ($p<0.0001$), and 6.1 ± 4.5 μm to 1.1 ± 0.12 μm in PC12 cells ($p<0.0001$). Moreover, removal of ethanol and further culturing in fresh cell culture medium for 20 h restored normal mitochondrial structure (RGC, 6.1 ± 4.5 μm; PC12, 4.7 ± 3.7 μm) and membrane potential. EM results confirmed the ethanol induced mitochondrial fragmentation and its reversibility. In addition, during the mitochondrial fragmentation cells showed higher levels of reactive oxygen species ($p<0.001$) and intracellular Ca^{2+} ($p<0.001$), which levels returned to normal after removal of ethanol stimulus. However, immunostaining showed that no cytochrome c release from mitochondria had occurred at this stage of reversible mitochondrial injury.

Conclusions: The results indicated that targeting and harnessing mitochondria may hold promise as therapeutic strategy to rescue dying RGCs in glaucoma and reduce its vision loss.

CONTROL ID: 3708327

SUBMITTER (NAME ONLY): Sophie Riedl

TITLE: Automated detection of morphologic changes on SD-OCT leading toward outer retinal atrophy in intermediate age-related macular degeneration in the prospective PINNACLE trial

SESSION TITLE: AMD Imaging

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To report preliminary data on the automated detection of focal morphologic changes - Focal Events - on spectral domain-optical coherence tomography (SD-OCT) in the ongoing PINNACLE trial, a prospective observational study in intermediate age-related macular degeneration (NCT04269304).

Methods: Four automated algorithms, segmenting drusen, photoreceptors, hypertransmission, as well as intra- and subretinal fluid are applied. Pre-specified post-processing criteria define four types of Focal Events, as shown in Figure 1, for which eyes are screened at every 4-monthly visit in the prospective PINNACLE trial. We herein report interim descriptive data on the frequency and sequence of Focal Event occurrence.

Results: Volume OCT data of 855 follow-up visits of 334 eyes of 259 patients have so far been screened for the occurrence of Focal Events. Drusen regression (DR) was detected in 3%, photoreceptor loss + hypertransmission (PLH) in 11%, subretinal fluid in 1% and intraretinal fluid in less than 1% of visits. In 44 eyes Focal Events occurred at more than one follow-up visit. The majority (52%) of such sequential events consisted of sole recurrence of PLH, followed by 11% of cases in which PLH was followed by a combination of PLH and DR. A representative example case is shown in Figure 2.

Conclusions: The established processing pipeline has shown reliable detection of predefined morphologic changes. The occurrence of sequential non-fluid related Focal Events, showing aggravation of outer retinal atrophy, as well as atrophic signs preceding drusen regression and vice versa, demonstrate these subtle changes to present meaningful events along progressive outer retinal degeneration. Once prospective data collection is completed, evaluation of the predictive value of Focal Events for the progression toward late non-neovascular as well as neovascular AMD will be performed.

CONTROL ID: 3708328

SUBMITTER (NAME ONLY): Sotiris Plainis

TITLE: Effectiveness of presbyopia correction with multifocal contact lenses: an evaluation of reading performance with the use of eye fixation analysis

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Plainis, E. Ktistakis, M.K. Tsilimbaris, Laboratory of Optics and Vision (LOV), Panepistemio Kretes Iatrike Schole, Heraklion, Crete, GREECE|

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ABSTRACT BODY:

Purpose: Many activities of daily living rely on reading, thus is not surprising that complaints from presbyopes originate in reading difficulties rather in visual acuity. Here the effectiveness of presbyopia correction with multifocal contact lenses (CLs) is evaluated using a new method of sustained reading performance, based on eye fixation analysis.

Methods: Visual performance of thirty presbyopic volunteers (age: 50±5 yrs) was assessed monocularly and binocularly using monthly disposable CLs (Air Optix Plus Hydraglyde, Alcon Laboratories) with: (a) single vision (SV) lenses – uncorrected for near (b) aspheric multifocal (MF) CLs. LogMAR acuity was measured with ETDRS charts. Reading performance was evaluated using standard IReST paragraphs displayed on a screen (0.4 logMAR print size at 40cm distance). Eye movements were monitored with an infrared eyetracker (Eye-Link II, SR Research Ltd). Data analysis included computation of reading speed, fixation duration, fixations per word and percentage of regressions. Frequency distributions of fixations durations were analysed with an ex-Gaussian fitting, a convolution of a normal (with μ as the mean) and exponential (with τ as the mean) distribution, that can characterize its location and shape.

Results: Average reading speed was 250±68 and 235±70 wpm, binocularly and monocularly, with SV CLs, improving statistically significantly to 280±67 and 260±59 wpm, respectively, with MF CLs ($p<0.001$ in both conditions).Moreover, fixation duration, fixations per word and ex-Gaussian parameter of fixation duration, μ, showed a statistically significant improvement when reading with MF CLs, with fixation duration exhibiting the stronger correlation ($r=0.79$) with improvement in reading speed. The correlation between improvement in VA and reading speed was low ($r=-0.36$), as was also the case between VA and any eye fixation parameter.

Conclusions: Reading speed in a presbyopic population was found improved with MF compared to SV CL correction and was faster with binocular compared to monocular viewing: this was mainly due to the faster average fixation duration. The enhancement in reading performance could not be predicted by the observed improvement in VA. Evaluating reading performance using eye fixation analysis could offer a reliable outcome of functional vision in presbyopia correction.

CONTROL ID: 3708330

SUBMITTER (NAME ONLY): Frederik Pedersen

TITLE: Bidirectional associations between diabetic retinopathy and major depression: results from a Danish nationwide registry-based cohort study

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Earlier studies have indicated that the associations between depression and diabetic microvascular complications may be bidirectional, but evidence from population-based studies is still scarce. We aim to test whether the associations between diabetic retinopathy (DR) and major depression are bidirectional in a 5-year prospective cohort study.

Methods: In Denmark, DR screening has been nationally implemented and results have mandatorily been registered in the Danish Registry of Diabetic Retinopathy (DiaBase) database since 2013. We performed a register-based national cohort study including persons with type 2 diabetes who had attended DR screening with data collected between January 2, 2013 and December 28, 2018. Major depression was defined according International Classification of Disease 10 codes: F32 (unipolar depression), F33 (recurrent depression) or F34.1 (dysthymia) from the Danish National Patient Register. Multivariable adjusted Cox proportional hazard models were used to evaluate the risk of incident major depression among persons with DR along the reverse association.

Results: In 164,452 patients with type 2 diabetes followed for 508,133 persons-years, 1.2% developed at least one episode of major depression. In a model adjusted for age and gender, hazard ratio (HR) of incident major depression was 1.39 (95% CI 1.24-1.56) for patients with DR at baseline compared to those without. However, this was no longer statistically significant after adjusting for insulin use (HR 1.07 95% CI 0.95-1.21). Conversely, major depression did not predict 5-year incident of DR (adjusted HR 0.97 95% CI 0.88-1.06).

Conclusions: Although DR and major depression were not longitudinally linked, the use of insulin was a strong predictor of incident major depression in a nationwide cohort of persons with type 2 diabetes. Insulin use may be a proxy of dysregulated blood glucose or more advanced disease, which may cause the increased risk. Psychological problems due to insulin injections should also be suspected.

CONTROL ID: 3708331

SUBMITTER (NAME ONLY): Claudia Farinha

TITLE: Rare variants in CFH and phenotype in Age-related Macular Degeneration in the Coimbra Eye Study.

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Farinha, P. Barreto, R. Coimbra, M. Cachulo, J.G. Cunha-Vaz, R. Silva, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|C. Farinha, M. Cachulo, R. Silva, Department of Ophthalmology, Centro Hospitalar e Universitário de Coimbra, Coimbra, PORTUGAL|A. Lutis, Department of Mathematics, Universidade de Aveiro, Aveiro, Aveiro, PORTUGAL|Y.T. Lechanteur, C.C. Hoyng, Department of Ophthalmology, Radboud University Medical Center, Donders Institute for Brain Cognition and Behaviour, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To determine the associations between rare genetic variants in the complement factor H(CFH) and the phenotypic characteristics of age-related macular degeneration(AMD) patients from the Coimbra Eye Study(CES).

Methods: AMD patients from the Incidence Study(NCT02748824) underwent multimodal imaging: color fundus photography(CFP), spectral-domain optical coherence tomography(SD-OCT), fundus autofluorescence(FAF), near-infrared imaging(NIR). Phenotypic characterization of both eyes was performed in a centralized reading center. The coding and splice-site regions of the CFH gene were sequenced in collaboration with the EYERISK consortium. Variants with MAF<0.05 resulting in splice-site or protein change(nonsynonymous) were selected. Differences in phenotypic features between carriers and noncarriers were analyzed using generalized estimated equations logistic regression models, considering inter-eye correlations and controlling for age, sex and AMD stage.

Results: We included 39 eyes of 23 carriers and 284 eyes of 188 noncarriers. Carrying rare CFH variants was associated with larger drusen areas in the inner ETDRS circle (OR,3.29[95%CI,1.16–8.98];p=0.025); and having a total area occupied by drusen of 10-50% in: inner ETDRS circle (OR,5.53[95%CI,1.63–18.82;p=0.006), outer ETDRS circle (OR,4.39[95%CI,1.10–17.49];p=0.036), and full ETDRS grid (OR,4.89[95%CI,1.17–20.37];p=0.024). In SD-OCT a lower total macular volume (OR,0.456[95%CI,0.254–0.946];p=0.034) and of the inner retinal layers (OR,0.490[95%CI,1.25–22.59];p=0.024) was more common in carriers. Despite not reaching statistical significance, hard drusen were more common in non-carriers, and intermediate/large drusen were more common in carriers. Plus, carriers had thinner choroids (208.7±83.8µm vs 228.3±87.7µm), larger pseudodrusen areas (7.89±16.8mm^2 vs 4.64±10.10mm^2), and a trend of more pigment epithelial detachments (12.82% vs 3.17%, p=0.062) and hyperreflective foci (28.21% vs 15.85%, p=0.073).

Conclusions: We identified phenotypic differences between carriers and non-carriers of CFH variants in AMD patients. Carriers seem to present with more severe disease, including superior drusen burden and thinner retinas, independently of AMD stage. These patients are probably at increased risk for progression, and identification of such features could direct towards further genetic investigation if complement targeted therapies are to be pursued.

CONTROL ID: 3708336

SUBMITTER (NAME ONLY): Cristina Rovira-Gay

TITLE: Validation of objective methods to measure fusional vergence ranges

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Rovira-Gay, M. Argiles, J. Pujol, Centre for Sensors, Instruments, and Systems Development, Universitat Politecnica de Catalunya, Barcelona, Catalunya, SPAIN|C. Mestre, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fusional vergence ranges are typically measured subjectively using Risley prisms or a prism bar. In this study, new methods to measure fusional vergence ranges at near objectively were validated against the two conventional tests used in clinics.

Methods: A total of 46 typical adults (23.3±3.0 years) participated in the study. Participants' BO (base out) and BI (base in) near fusional vergence ranges were measured objectively in an haploscopic set-up and recording eye movements with an Eyelink 1000 Plus (SR Research) at 500Hz. Firstly, stimulus disparity changed smoothly at 1PD/s up to 45PD for both divergence (BI) and convergence (BO), mimicking a Risley prism. Secondly, disparity was changed in steps of 2PD every 2 seconds mimicking a prism bar. Break and recovery points were determined offline using a custom Matlab code for the analysis of eye movements. Fusional vergence ranges were also measured with the conventional tests using a Risley prism and a prism bar, and the results were compared.

Results: When stimulus disparity changed smoothly, narrower BI ranges were obtained with the objective method (mean±SD break of 13.7±4.7PD and 10.6±5.1PD recovery) than with the Risley prism (break of 17.5±3.8PD and 12.8±4.2PD recovery) with a mean±SD difference between methods of -3.8±3.5PD (break) and -2.2±4.7PD (recovery). BO ranges were wider with the objective method (35.4±10.9PD break and 24.4±10.7PD recovery) than with the Risley prism (25.8±7.5PD break and 14.6±5.8PD recovery) with a mean difference of 9.2±10.7PD for the break, and 9.6±10.1PD for the recovery. When disparity changed in steps, fusional ranges measured with the objective method (15.7±5.1PD BI break, 12.8±4.7PD BI recovery, 36.3±11.4PD BO break, 23.9±10.6PD BO recovery) were not significantly different than with the prism bar (14.5±3.8PD BI break, 10.7±3.4PD BI recovery, 34.0±7.8PD BO break, 23.0 ±5.7PD BO recovery). Mean differences between these two methods were 1.2±5.2PD (BI break), 2.1±4.7PD (BI recovery), 2.3±13.0PD (BO break), and 0.9±11.3PD (BO recovery).

Conclusions: This study showed the possibility to measure fusional vergence ranges objectively. The agreement between the objective method with smooth-changed disparity and the conventional test using the Risley prism was considerably poorer than between the two methods where disparity changed in steps. However, a wide variability across subjects was still found, especially for the BO fusional ranges.

CONTROL ID: 3708339

SUBMITTER (NAME ONLY): Reena Durai

TITLE: Effect of interocular difference in retinal illuminance on monocular and binocular flicker perception

SESSION TITLE: Vision assessment and Clinical applications

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Detection of luminance-modulated flicker under monocular and binocular viewing conditions worsen with a reduction in retinal illuminance.The impact of interocular difference in retinal illuminance on these thresholds however remain unknown.This study investigated the impact of purposely-induced variations in retinal illuminance of one or both eyes on monocular and binocular flicker modulation thresholds (FMTs) and on the binocular summation ratios (BSRs) of flicker.

Methods: Monocular and binocular FMTs were measured using the Flicker-Plus test for 30' target at fovea and four parafoveal (5^{O}) locations in 10 healthy adults at a baseline retinal illuminance of 930Td (7mm pupil diameter) and with 10 to 80% (827 to 186Td) induced interocular difference in retinal illuminance using neutral density filters over one eye,all in random order. The measurements were repeated in 5 subjects with bilateral change in retinal illuminance from 388 to 1553Td. BSRs were calculated by dividing the monocular threshold of the non-attenuated eye (for interocular difference condition) or the better eye (for bilateral condition) to the binocular threshold.

Results: The mean (±1SE) non-attenuated monocular foveal and parafoveal FMT was 2.98±0.28% and 5.3±0.63% respectively. These FMTs increased with reduction in monocular retinal illuminance (3.71±0.73% to 6.2±0.9%) and with increasing interocular difference in retinal illuminance(1.99±0.35% to 3.19±0.76%)($p<0.05$, for both).The resultant BSRs were thus larger for interocular differences <50% (1.56±0.12) than for those ≥60% (1.27±0.13) ($p\leq0.01$).This trend remained the same in the parafoveal region. Monocular(3.83±0.1% to 3.0±0.12%) and binocular(1.84±0.1% to 1.82±0.09%) FMTs and BSRs (1.68±0.1) remained largely stable with bilateral reduction in retinal illuminance.

Conclusions: The worsening of binocular flicker detection capability is proportional to its monocular value up to 50% of interocular difference in retinal illuminance. Beyond this range, the binocular loss is proportionally greater than the monocular loss, leading to a reduction in binocular summation of flicker. These results are in agreement with the negative impact of naturally-occurring interocular differences in monocular FMTs on binocular summation of flicker, observed in our earlier study.

CONTROL ID: 3708343

SUBMITTER (NAME ONLY): Lorenzo Ferro Desideri

TITLE: The role of antiseptic prophylaxis before intravitreal injections: a novel ocular spray containing Biosecur citrus extract for the reduction of preoperative microbial load

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Ferro Desideri, C. Del Noce, C. Traverso, A. Vagge, IRCCS Ospedale Policlinico San Martino, Genova, Universita degli Studi di Genova, Genova, Liguria, ITALY|G. Giannaccare, V. Scorcia, Department of Ophthalmology, Universita degli Studi Magna Graecia di Catanzaro Dipartimento di Medicina Sperimentale e Clinica, Catanzaro, Calabria , ITALY|L. Ferro Desideri, C. Del Noce, C. Traverso, A. Vagge, University of Genoa (DINOGMI), Universita degli Studi di Genova, Genova, Liguria, ITALY|D. Camposampiero, D. Ponzin, Fondazione Banca degli Occhi del Veneto, Mestre, Veneto, ITALY|M. Pellegrini, Istituto Internazionale per la Ricerca e Formazione in Oftalmologia (IRFO),, Forlì, ITALY|M. Pellegrini, Ospedali Privati Forlì "Villa Igea", Department of Ophthalmology, Forlì, Italy, Forlì, ITALY|

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ABSTRACT BODY:

Purpose: The adoption of antiseptic prophylactic strategies is important for patients receiving IVTs to prevent endophthalmitis onset, by avoiding the administration of antibiotics and their associated risk of antimicrobial resistance. The aim of this study was to evaluate the antimicrobial activity of a novel ocular spray containing Biosecur citrus extract (Oftasecur®, Off Health, Florence, Italy).

Methods: This study had a prospective and cross-sectional design. Patients undergoing IVTs were included and trained to administer Oftasecur spray into the treatment eye 4 times a day starting 4 days before the IVT procedure. The sound eye not undergoing IVT procedure was adopted as control. At baseline, a conjunctival swab for microbiological analysis was done in both eyes before the 4-day Oftasecur treatment regimen and at the time of IVT. All the patients were administered a Brief Ocular Discomfort Inventory (BODI) questionnaire, based on a 11-point scale (0 for no discomfort and 10 for maximum discomfort).

Results: In this study 30 patients were enrolled, including 15 males and 15 females (average age 64.7 ± 11.6 [standard deviation, SD] years). At baseline, 53.3% of the total eyes resulted positive after the microbiological analysis of the conjunctival swabs. After the completation of the treatment cycle, only 20% of the eyes were positive at the time of the IVT, referring a significant decrease in the microbial load ($p < 0.01$). In the treatment group, there was a significant reduction in the positive swabs' percentages between baseline and the completation of the Oftasecur ocular spray treatment cycle (decreasing from 70.4% to 29.6%; $p = 0.003$, McNemar's test). Overall, Oftasecur ocular spray resulted safe and well tolerated, showing a mean BODI score of 1.2 (± 0.70 SD).

Conclusions: Prophylactic treatment with Oftasecur ocular spray is associated with a significant reduction in the microbial load in those patients undergoing IVTs. Thus, Oftasecur ocular spray may display a role in the reduction of the risk of IVTs-related endophthalmitis without the need of using antibiotics.

CONTROL ID: 3708345

SUBMITTER (NAME ONLY): Yoshiaki Nishio

TITLE: Experimental autoimmune uveoretinitis inhibited by regulatory T cells augmented in type 1 diabetic mice.

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Several studies have indicated that inflammatory process is involved in the pathogenesis of diabetes, however little is known for an effect of immune responses impaired in diabetic condition on development of autoimmune diseases. Experimental autoimmune uveitis (EAU) is widely accepted as a model of endogenous uveitis of suspected autoimmune etiology in humans. In this study, we investigated effects of hyperglycemia on development of EAU using type 1 diabetic mice.

Methods: In this study, we used $Ins2^{Akita}$ (Akita) mice, which spontaneously develop Type 1 Diabetes Mellitus by a mutation in the insulin 2 gene. C57BL/6 (B6) mice and Akita mice were subcutaneously immunized with 200 μL total CFA supplemented with M. tuberculosis strain H37RA to 2.5 mg/mL emulsion containing 2 mg/mL human IRBP 1-20 (1:1 wt/vol) and administration of 0.5 μg pertussis toxin (i.p.). Clinical scores of EAU were performed by funduscopic examinations on day 0, 7, 14, 21 after immunization and histological scoring was evaluated on day 21. Splenocytes were also obtained on day 21 and were stimulated with 0, 5, 10 μg/mL human IRBP 1-20 for 72 hr. Supernatants were collected and contained cytokines (IL-2, IL-4, IL-6, IL-17A, and IFN-γ) were measured by Bio-Plex Multiplex Immunoassay System. In addition, cell-surface expression of CD4 and Foxp3, and production of cytokines were analyzed by flow cytometory.

Results: Clinical scores of EAU in Akita mice (0.23±0.53) were significantly lower than those in B6 mice (1.75±0.91). There was also statistically difference in histological scores between Akita mice (0.11±0.52) and B6 mice (1.1±0.22). IFN-γ production by splenocytes was apparently reduced in Akita mice compared with B6 mice (935±514 pg/ml vs. 2031±1237 pg/ml), although IL-17A production was higher in Akita mice (1084±35 pg/ml) than in B6 mice (739±140 pg/ml). There were no differences in IL-2, IL-4, and IL6 production between Akita mice (323±75, 62±25, and 126±18 pg/ml) and B6 mice (396±8.4, 107±4.0, and 212±0.8 pg/ml). Similar results were obtained by flow cytometory for splenic $CD4^+$ cells. On the other hand, population of $CD4^+$ $Foxp3^+$ T cells in the spleen was significantly augmented in Akita mice (9.03±0.91%) compared with B6 mice (4.80±1.04%).

Conclusions: It is indicated that EAU in Akita mice was downregulated by impaired Th1 cell activation rather than Th17 cells via augmentation of Treg cells.

CONTROL ID: 3708346

SUBMITTER (NAME ONLY): Takefumi Yamaguchi

TITLE: Transcriptomic and metabolomic analyses of Fuchs endothelial corneal dystrophy and bullous keratopathy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Yamaguchi, Y. Yagi-Yaguchi, T. Suzuki, K. Higa, J. Shimazaki, Ophthalmology, Tokyo Shika Daigaku Ichikawa Sogo Byoin, Ichikawa, Chiba, JAPAN|M. Sugimoto, 2.Health Promotion and Pre-Emptive Medicine,, Tokyo Ika Daigaku Igakuka Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|H. Kasamatsu, Cornea Center Eye Bank, Tokyo Shika Daigaku Ichikawa Sogo Byoin, Ichikawa, Chiba, JAPAN|H. Noma, Data Science, The Institute of Statistical Mathematics, Tachikawa, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is a leading cause of endothelial keratoplasty worldwide. To elucidate the pathophysiology of FECD, we conducted multi-omic analyses of FECD in Japan.

Methods: A total of 104 eyes of 104 Japanese participants were included in our analyses, comprising a mix of cases (FECD: 13 eyes, bullous keratopathy [BK]: 46 eyes, healthy control: 45 eyes). Transcriptomic analysis of corneal endothelial cells (CEnC) was conducted in 27 eyes (FECD: 7 eyes, BK 12 eyes, healthy controls: 8 eyes). Metabolomic analysis of aqueous humor (AqH) was conducted in 77 eyes (FECD: 6 eyes, BK: 34 eyes, healthy controls: 37 eyes).

Results: Among the 57,955 genes in the transcriptomic analysis of CEnCs, 1241 up-regulated and 242 down-regulated genes were identified in FECD, while 730 up-regulated and 1270 down-regulated genes were identified in BK. Compared to healthy controls, these findings were statistically significant with non-FDR P values < 0.05. Functional gene ontology enrichment showed several cellular components: genes with significantly higher expression in FECD exhibited T cell receptor signaling, reactive oxygen production, and cytokine signaling, while genes with lower expression in FECD exhibited RNA synthesis, regulation of cell death and ER stress. However, no statistically differences were observed between FECD and BK in transcriptomic analysis. Metabolomic analysis of AqH identified 82 out of 147 metabolites, measured by mass spectrometry. Among the 82 metabolites in AqH, only lactate was significantly lower in FECD compared to healthy controls ($P<0.05$ after Bonferroni correction). Furthermore, in BK, 10 up-regulated and 9 down-regulated metabolites were identified, compared to healthy controls ($P<0.05$). No differences were detected in metabolite levels between FECD and BK.

Conclusions: The multi-omic analyses of CEnCs and AqH suggested that the mRNA and metabolites in the Japanese population affected by FECD may be similar to those with BK, although specific alterations were detected both in both.

CONTROL ID: 3708348

SUBMITTER (NAME ONLY): Shiri Zayit-Soudry

TITLE: The retinal toxicity of the pro-inflammatory and amyloidogenic S100A9 proteins

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Zayit-Soudry, M. Harel, A. Qarawani, R. Ben Zvi Elimelech, C. Itzkovich, R. Khoury, S. Safuri, E. Naaman, Clinical Research Institute, Rambam Health Care Campus Department of Ophthalmology, Haifa, Haifa, ISRAEL|S. Zayit-Soudry, M. Harel, A. Qarawani, R. Ben Zvi Elimelech, R. Khoury, S. Safuri, Technion Israel Institute of Technology The Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Haifa, ISRAEL|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a complex multifactorial disease in which inflammation is considered a key factor, but the exact molecular mechanisms are unclear. The pro-inflammatory S100A9 proteins were amply found in drusen. These calcium-binding proteins have diverse signaling roles and can contribute to chronic inflammation, but their pathological and possibly physiological role in the retina is unknown. S100A9 were shown to be intrinsically amyloidogenic, possessing the capacity to self-assemble into amyloid structures in vitro and in vivo. Here, we hypothesized that the retinal effects exerted by S100A9 are related to their amyloid conformation.

Methods: ARPE-19 cells were treated with monomeric or fibrillary S100A9 (0.1 nM- 0.1 μM) for 12 h. Cell viability was determined by the XTT assay.

Wild type rats were treated with intravitreal injection (10μl) of monomeric or fibrillary S100A9 (0.1 μM) to right eye and vehicle in the left eye. Retinal function was assessed at baseline and through 28 days post injection. At each time point, electroretinography (ERG) measures were compared between eyes.

Results: Cell viability assays and ERG in rats delineated distinct retinal effects of S100A9. The number of living ARPE-19 cells was increased by exposure to 0.1- 1nM fibrillar S100A9 but was decreased by treatment with 0.01- 0.1 μM of the S100A9 fibrils. Monomeric S100A9 had no significant impact on the cellular counts.

Similarly, while retinal function remained normal in the eyes treated with monomeric S100A9, amplified ERG responses constituting increased amplitudes mostly of the b-wave were noted in the experimental eyes compared with their fellow (control) eyes through 14 days following injection of fibrillar S100A9 in rats. Thereafter, the retinal function became impaired, showing decreased ERG amplitudes in the treated eyes compared with controls.

Conclusions: Fibrillar S100A9 exerted pronounced effects on the retina, which included cell proliferation in vitro and increased amplitudes of the ERG responses in rats. In contrast, exposure to higher doses of S100A9 fibrils induced cell death in vitro and prolonged exposure to these assemblies resulted in decreased retinal function in vivo. This complex behavior supports the importance of the amyloid conformation of S100A9 to its retinal implications, and suggests a clue both to the pathological and possibly physiological role of S100A9 in the human retina.

CONTROL ID: 3708350

SUBMITTER (NAME ONLY): Reiko Arita

TITLE: Layer by layer measurement of tear film and its association with clinical signs and symptoms in patients with dry eye and meibomian gland dysfunction

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this study was to assess the quantified parameters by Tear Film Imager (TFI), a new technology that enables quantification of the lipid and muco-aqueous layer thicknesses of the tear film on the cornea with a nanometer resolution developed by AdOM (Israel) and compare the clinical parameters from conventional ophthalmic examinations and other commercially available interferometry devices.

Methods: Patients with dry eye (DE), meibomian gland dysfunction (MGD), and non-DE/MGD were enrolled at Itoh Clinic (Saitama, Japan) from February 2020 to January 2021. Quantified outputs from TIF were as follows: Lipid Layer Thickness (LLT), Muco-Aqueous Layer Thickness (MALT), MALT Rate of change (MALTR), and Lipid Break Up Time (LBUT). Two other interferometry devices, LipiView2 (Johnson & Johnson Vision, CA, USA) and DR-1α (Kowa, Nagoya, Japan), were used for comparison. Correlation analysis was conducted with these TFI values and the following clinical signs: lid margin abnormalities, fluorescein staining score, meiboscore, fluorescein tear breakup time (BUT), Schirmer's test, the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire score, Dry Eye related Quality of life Score (DEQS), LLT measured by LipiView2, and interferometric patterns and noninvasive BUT measured by DR-1α. Each patient had one or several study visits. Baseline and changes from baseline values were analyzed.

Results: Twenty-eight patients (8 DE, 13 MGD, and 7 non-DE/MGD) participated in this study. The baseline values of TFI, LipiView2, and DR-1α were correlated with different clinical parameters. The LLT of TFI and LipiView2 showed correlation with lid margin abnormalities: Plugging and Vascularity scores (R=-0.42, -0.43). LBUT and MALTR correlated with Schirmer (R=0.47, -0.46). In correlation with changes, many TFI values showed higher correlation than those of LipiView2 and DR-1α, especially with the questionnaire scores. The correlation coefficients of MALTR and LBUT with SPEED score were 0.59 and -0.50.

Conclusions: TFI can measure the time variation of the thickness of the lipid and aqueous layers separately, and shows good correlation with key DE and MGD parameters. These results suggest that TFI might be useful for objective quantification of the signs and symptoms of DE or MGD, and for treatment monitoring.

CONTROL ID: 3708354

SUBMITTER (NAME ONLY): Chung Shen Chean

TITLE: Bilateral persistent placoid maculopathy following COVID-19 Vaccines: real or co-incidence?

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: COVID-19 vaccination has been accompanied by reports of inflammatory events. We aim to report the first case of bilateral persistent placoid maculopathy (PPM) following COVID-19 vaccination.

Methods: Case report

Results: A 58-year-old man presented with bilateral sudden painless decrease in vision approximately two weeks after the second dose of AstraZenaca® COVID-19 vaccine. Visual acuity (VA) at presentation was 1.00 LogMAR in the right eye (RE) and hand movement in the left eye (LE). He had no known medical or ophthalmic history, up until after his first AstraZenaca® COVID-19 vaccine dose, he was diagnosed with palmoplantar pustular psoriasis and was started on 60mg of oral Prednisolone. Fundus examination revealed bilateral well-delineated whitish plaque-like macular lesions involving the fovea, sparing the peripapillary region in the RE (Figure 1a & e). Multimodal imaging including fluorescein angiography, indocyanine-green angiography, fundus autofluorescence and optical coherence tomography were consistent with PPM (Figure 1 & 2). Infective and auto-immune screen were all negative apart from a positive MPO-ANCA, prompting a rheumatology review which subsequently excluded any systemic vasculitis. Patient was monitored closely and his VA improved and stabilised with tapering regime of oral Prednisolone. To prevent relapse of PPM, patient was commenced on Mycophenolate Mofetil as a long-term steroid sparing immunosuppression.

Conclusions: Our case demonstrated a likely inflammatory or autoimmune response affecting choriocapillaris driven by the COVID-19 vaccine and there may be a correlation between the two. The patient in our case portrayed features classical of PPM, which is a selective autoimmune vasculitis causing microinfarcts on choriocapillaris, resulting in focal choroidal hypoperfusion after the COVID-19 vaccine.

CONTROL ID: 3708355

SUBMITTER (NAME ONLY): Torcato Santos

TITLE: Characterization of two-year occurrence of subclinical macular edema in different risk phenotypes of diabetic retinopathy

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To characterize the two-year occurrence of macular edema of different diabetic retinopathy phenotypes in type 2 diabetes (T2D) focusing in changes in central retinal thickness (CRT).

Methods: A prospective longitudinal cohort study (CORDIS, NCT03696810) was conducted with 3 visits (baseline, 6-months and two-year). Demographic and systemic data included age, sex, diabetes duration, lipidic profile and hemoglobin A1c (HbA1c). Ophthalmological examinations included visual acuity, color fundus photography (CFP) and optical coherence tomography (OCT and OCTA), identified the presence of nonproliferative diabetic retinopathy. Phenotype classification was performed, at 6-month visit, based on microaneurysm turnover (MAT, on CFP) and CRT (on OCT). Only risk phenotypes B (MAT<6 and increased CRT) and Phenotype C (MAT≥6 with or without increased CRT) were included. ETDRS grading was performed at the baseline and last visits based on 7-fields CFP. OCT data was analyzed with OCT-Leakage, a novel technique for noninvasive assessment of abnormal accumulation of fluids in the retina through low optical reflectivity ratios (LOR).

Results: Of the 133 T2D individuals included in the study, 81 eyes (60%) were classified as phenotype B and 52 (40%) eyes as phenotype C. Of these 127 completed the two-year follow-up, with 24 (19%) developing central-involved macular edema (CIME) and 2 (1.6%) clinically significant macular edema.

Patients that developed CIME showed an increase in CRT with time when compared to patients that did not (ß=10.318, p<0.001). This difference remains statistically significant when controlling for age, sex, diabetes duration and HbA1c.

Changes in time for CRT, over the two-year period of follow-up, are positively associated with longitudinal changes in LOR ratios (ß=53.113, p<0.001) and with longitudinal changes in vessel density (increase) in the deep capillary plexus (ß=0.811, p<0.001) and superficial capillary plexus (ß=1.516, p<0.002). Patients with different ETDRS levels have similar alterations across visits for CRT, as well as for both phenotypes, B and C.

Conclusions: In the two-year period of follow-up CRT changes followed similar response patterns for both phenotypes and different ETDRS levels. CRT changes showed a clear association with the development of CIME.

CONTROL ID: 3708356

SUBMITTER (NAME ONLY): Kenichiro Asahara

TITLE: Recent clinical features of uveitis in southwest region of Japan

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Asahara, N. Yawata, E. Hasegawa, S. Yamana, M. Shirane, A. Hayashida, K. Yoshitomi, T. Fukui, N. Himeno, T. Ito, A. Takeda, K. Sonoda, Dept. of Ophthalmology, Kyushu University, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the recent trends of uveitis in Kyushu University Hospital, the regional center for uveitis care in southwestern Japan.

Methods: We retrospectively investigated the medical records of patients with uveitis who first visited Kyushu University Hospital between April 2015 and March 2020. Clinical data obtained included age, gender, diagnosis, anatomical location of ocular inflammation (anterior, intermediate, posterior, pan). We compared them with the previous studies of our facility and the national survey (Jpn J Ophthalmol. 2021).

Results: The total number of new patients with uveitis who visited Kyushu University Hospital was 790 (327 males, 463 females) accounting for 4.8% of all the new cases in our eye clinic. Mean age was 52.9 ± 19.8 years (men 52.0 years, women 53.5 years). The frequency of anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis were 23.0%, 3.0%, 9.9%, and 64.1%, respectively. Definite diagnoses were made in 506 cases (64.1%). In contrast to the national survey, Vogt-Koyanagi-Harada disease was the most frequent (11.4%), followed by sarcoidosis (9.4%), scleritis (5.8%), acute anterior uveitis (5.1%), herpetic iridocyclitis (4.9%), Behçet's disease (4.7%), malignant diseases (3.2%), acute retinal necrosis (3.2%), cytomegalovirus (CMV) retinitis (2.2%), and human T lymphotropic virus type 1 (HTLV-1)-associated uveitis (1.8%). Four of the top 10 most frequent uveitis were infectious in our study, whereas only 2 in the national survey. When compared with our previous reports, the present study showed increasing trends in Vogt-Koyanagi-Harada disease, scleritis, herpetic iridocyclitis, acute retinal necrosis, CMV retinitis, and malignant diseases. Among the herpetic iridocyclitis, CMV was found to be the most frequent agent. Behçet's disease and HTLV-1-associated uveitis were decreasing. Among the patients over 70 years old, intraocular lymphoma was the second most frequent disorder after sarcoidosis.

Conclusions: Although southwestern Japan has been an endemic area of HTLV-1, frequency of HTLV-1-associated uveitis is decreasing, reflecting on improvements in public health. Increases of CMV-associated diseases and malignant diseases, commonly observed in this study and the national survey, seem to be associated with the development of the diagnostics.

CONTROL ID: 3708360

SUBMITTER (NAME ONLY): Caroline Manicam

TITLE: Acute Dietary Supplementation with Omega-3 Fatty Acid Confers Novel Mechanistic Changes in Retinal Proteome in Mice with Targeted Gene Deletion of Cytochrome P450

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Manicam, A. Herfurth, F. Grus, N. Pfeiffer, N. Perumal, Department of Ophthalmology, Universitatsmedizin der Johannes Gutenberg-Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|

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ABSTRACT BODY:

Purpose: Cytochrome P450 (CYP) gene mutations are a common predisposition associated with glaucoma. Although the molecular mechanisms are largely unknown, omega-3 polyunsaturated fatty acids (ω3) and their CYP-derived bioactive mediators play significant roles in proper maintenance of neurovascular functions and homeostasis in the retina. We tested the hypothesis that acute dietary supplementation with ω3 confers neuro-vasculoprotective effects attributed to inherent lack of the main murine CYP gene (Cyp2c44) in the retina in vivo.

Methods: Male mice with targeted deletion of the Cyp2c44 gene (KO) and their wild type floxed littermates (WT) were subjected to daily oral gavaging for 7 days with 0.01 ml/g ω3 composed of menhaden fish oil. Another group in respective strains served as vehicle-treated controls. Retina was isolated at day 8 post-treatment (n=9/group) and subjected to mass spectrometry (MS)-based proteomics and in-silico bioinformatics analyses.

Results: Proteomics analysis identified a total of 1402 retinal proteins (FDR<1%) and ω3 administration elicited significant ($p < 0.05$) differential expressions of 56 and 61 proteins in KO and WT mice, respectively. Noteworthy, ω-3 had a profound influence on the regulation of proteins involved in neuronal and mitochondrial activities in WT mice, while significantly improving the retinal metabolic status in the KO mice. The key molecular mechanistic changes conferred by ω3 in the WT retina were implicated in neurotransmission (p=4.22E-3), mitochondrial organization (p=1.62E-2), inhibition of neuronal cell death (p=2.33E-2) and activation of nitric oxide signalling (p=1.39E-2). Remarkably, ω3 supplementation in KO mice resulted in significant changes in the proteins involved in vision functions (p=3.69E-2), heightened metabolic activity via glycolysis (p=2.11E-2) and AMPK signalling pathway (p=2.33E-2), and inhibited apoptosis (p=7.78E-3).

Conclusions: Our findings provide the first in-depth experimental data that support our hypothesis that short-term dietary supplementation with ω3 can provide physiologically relevant beneficial effects in the retina via specific neuro-vasculoprotective signalling mechanisms, particularly by ameliorating retinal bioenergetics in the absence of Cyp2c44. The potential adjunct use of ω3 for glaucoma therapy needs further investigation.

CONTROL ID: 3708367

SUBMITTER (NAME ONLY): Dong Hyun Jo

TITLE: Demographic and clinical characteristics of patients with retinoblastoma in Seoul National University Children's Hospital in recent 30 years

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Jo, Department of Anatomy and Cell Biology, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|J. Kim, Department of Ophthalmology, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: This study aims to demonstrate the demographic and clinical characteristics of patients with retinoblastoma who visited Seoul National University Children's Hospital, Seoul, the Republic of Korea from 1991 to 2020.

Methods: Medical records of patients with retinoblastoma who visited Seoul National University Children's Hospital from 1991 to 2020 were reviewed. Age at diagnosis, sex, laterality, and tumor grading were recorded. During the study period, gross national incomes per capita were obtained from Statics Korea.

Results: In total, there were 464 patients with retinoblastoma during the study period. Among them, 209 (45%) were female. The mean age of diagnosis was 21 months. In recent ten years, it was 19 months, which showed a significant decrease. During the study period, gross national incomes per capita were increased from 7,634 USD (the year 1991) to 31,634 USD (the year 2020).

Conclusions: Seoul National University Children's Hospital is a representative tertiary center in the Republic of Korea. From 1991 to 2020, 464 patients with retinoblastoma visited the center. There was a dramatic increase in gross national incomes per capita during the study period, which reflected economic progress. This case series might be an excellent example for studying the effects of economic status and technical development on treatment patterns and outcomes in patients with retinoblastoma.

CONTROL ID: 3708370

SUBMITTER (NAME ONLY): Mirella Barboni

TITLE: Unbalanced binocular interactions in amblyopic color vision revealed by dichoptic color test

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To measure monocular and dichoptic color vision thresholds in amblyopic patients, controls, and congenital color deficient subjects.

Methods: Ten patients with amblyopia (mean age = 31.4 ± 9.2 years; 6 males) and without congenital color vision deficiency were included in the study. The control group (mean age = 27.8 ± 6.3 years) comprised 17 color normal (10 males) and 10 color deficient (8 males) subjects. Visual stimulation was based on pseudoisochromatic tests: the target was a mosaic made of small chromatic dots on a borderless background with random varying luminance (mean luminance = 11.9 ± 0.2 cd/m^2) presented dynamically (10Hz). Color vision thresholds were measured from the reference stimulus (background mean chromaticity: u'=0.1894, v'=0.4415, CIE1976) towards u'=0.3187, v'=0.4583, approximating protan and towards u'=0.1821, v'=0.2354, approximating tritan confusion lines with a 3D calibrated (LG) display using interleaved polarization via 3D goggles. Measurements were performed monocularly and dichoptically (non-tested eye viewing background noise). Color deficient subjects also performed the Cambridge Colour Test (CCT) to characterize their color deficiency and to validate the new test.

Results: There was high correlation between our monocular condition and CCT thresholds, especially for the protan vector (Spearman $rho_{(N=9)}$=0.82, p=0.007, $rho_{(N=9)}$=0.70, p=0.036 for protan and tritan, respectively). In the monocular condition, interocular differences were comparable for both protan and tritan thresholds (group main effect: $F_{(2,34)}$=2.04, p =0.14, group*vector $F_{(2,34)}$=0.70, p =0.50) among the groups, both eyes having similar thresholds (single mean t-test against zero mean: all t≤1.92, p≥0.09). On the other hand, protan and tritan interocular thresholds were significantly elevated in amblyopic subjects under dichoptic condition compared to both color normal and color deficient subjects (main effect of group: $F_{(2,34)}$=7.70, p=0.0017, group*vector $F_{(2,34)}$=0.40, p=0.67). Most likely, this increase is the result of unbalanced binocular interactions preventing the background noise presented to the amblyopic eye to influence color perception of the dominant eye in amblyopic subjects.

Conclusions: The results emphasize potential use of dichoptic stimulation to measure color thresholds when evaluating amblyopic status as well as to test the effects of amblyopic treatment for visual improvement.

CONTROL ID: 3708381

SUBMITTER (NAME ONLY): Ellen Ingolfsland

TITLE: Iron Status and Retinopathy of Prematurity Outcomes among Infants in the Preterm Erythropoietin Neuroprotection Trial (PENUT Trial)

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.C. Ingolfsland, R.B. Rao, Pediatrics, University of Minnesota Academic Health Center, Minneapolis, Minnesota, UNITED STATES|N. Rubin, Clinical & Translational Science Institute, University of Minnesota Academic Health Center, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Ellen Ingolfsland: Commercial Relationship: Code N (No Commercial Relationship) | Nathan Rubin: Commercial Relationship: Code N (No Commercial Relationship) | Raghavendra Rao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the impact of iron status on short- and long-term ROP outcomes among extremely preterm infants (<28 wk gestation) enrolled in the randomized trial of erythropoietin (EPO) or placebo (PENUT Trial). We hypothesized that infants with evidence of low or high iron status would have more severe ROP compared with those with normal iron status.

Methods: A post-hoc analysis of archived NINDS data from the PENUT trial was conducted. Baseline characteristics, iron status (defined as low when serum ferritin (SF, ng/mL) was ≤ 75 or zinc protoporphyrin to heme ratio (ZnPP/H) > 184, normal when SF 75-400 or ZnPP/H 30-183, or high when SF > 400) at 14, 28 and 42 days and 36 wk corrected gestational age (CGA), ROP outcomes (any ROP, ROP stage ≥ 2, ROP requiring treatment, retinal detachment, glasses and strabismus), growth rates, infection rates, hematocrit (hct) and inflammatory biomarker data were reviewed. Association with ROP was analyzed with Chi-squared tests (iron status) and analysis of variance (continuous variables) (significance set at $p < 0.05$).

Results: 940 infants (mean gestation 25.9 wk; mean birth weight 799 g) were included in the analysis. 51% received EPO. Any stage ROP occurred in in 398 infants (59%), ROP stage ≥ 2 in 229 (34%), and ROP requiring treatment occurred in 47 (7.1%). In unadjusted analysis, there was an association between higher iron status at 14, 28 and 42 days, but not at 36 wk CGA, with any ROP, ROP stage ≥ 2, and ROP requiring treatment. Table 1 summarizes associations between iron status and ROP requiring treatment. Higher IL-6, IL-8, IL-10 and EPO levels on day 14 were associated with ROP requiring treatment. Iron status at 14, 28, and 42 days was associated with EPO administration, delayed cord clamping, rate of weight gain, number of infections from day 0-14 and 14-42 and mean hct wk 1 and wk 2.

Conclusions: Severe ROP may be impacted by systemic iron status. Association with higher iron status on univariate analysis may be explained by pending analyses of timing and dosing of iron supplementation, RBC transfusions and hematocrits. As management of iron status through these means is highly controlled by the clinician, determining this association may have important clinical implications to reduce severe ROP.

CONTROL ID: 3708382

SUBMITTER (NAME ONLY): Mei ZHAO

TITLE: Cone morphometrics and contrast sensitivity in high myopia

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Excessive eyeball elongation leads to various changes in retinal structures and visual functions, as characterized by the chorioretinal thinning, enlarged photoreceptors spacing, and declined contrast sensitivity. This study compared the cone morphometrics and contrast sensitivity at central and mid-peripheral retina between highly myopic and emmetropic eyes, and investigated the relationships between structural and functional changes.

Methods: Thirty-six healthy adults aged 19 to 41 years were recruited, including 17 high myopes (HM, ≤ -8.00D) and 19 emmetropes (EM, -0.50 to +0.50D). Monocular contrast detection thresholds of vertical sinusoidal gratings (spatial frequency at 0°: 1, 2, 4, 8, and 16 c/deg; 10°: 0.5, 1, 2, 4 and 8 c/deg) were measured at central and 10° temporal retina, by 3-down-1-up staircases using 2-interval-forced-choice paradigms. After log transformation, the contrast sensitivity (i.e., a reciprocal of contrast detection threshold) was fitted with symmetric parabolic function to calculate the area under the curve (AUC). Cone morphometrics (i.e., density, cell spacing, regularity, dispersion) at fovea (1.5° to 2°) and 10° temporal retina were determined from the retinal images captured by the adaptive optics retinal camera using customized Matlab software with ocular magnification corrected.

Results: The contrast sensitivity at central vision was comparable in HM and EM, as suggested by comparable AUC in two groups (2.16 vs. 2.27 log unit, p=0.248). In contrast, HM exhibited a general reduction of contrast sensitivity at 10° peripheral vision, with smaller AUC than EM (1.72 vs. 1.89 log unit, p=0.037). For the cone morphometrics, HM had lower cone density (2011.80 vs. 2396.09 cells/deg^2, p=0.002) and regularity (91.10% vs. 93.15%, p=0.019), but increased cell spacing (1.50 vs. 1.38 arcmin, p=0.019) and dispersion (13.97% vs. 11.83%, p<0.001) than EM at fovea. However, the cone density (1311.08 vs. 1163.83 cells/deg^2, p=0.008) was increased while the cell spacing was decreased (1.84 vs. 1.94 arcmin, p=0.017) at the temporal retina of HM. There were no significant correlations between contrast sensitivity and cone morphometrics at 10° temporal retina.

Conclusions: Eyeball elongation affected the cone morphometrics at both foveal and mid-peripheral retina diversely. However, retinal function in terms of contrast sensitivity was preserved at central vision but was less resistant to high myopia at mid-periphery.

CONTROL ID: 3708385

SUBMITTER (NAME ONLY): Petra Rausch - Koster

TITLE: Post-hoc simulation study to optimize performance of the computer adaptive EyeQ

SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Rausch - Koster, F. Verbraak, G.V. Rens, R.M. van Nispen, Ophthalmology, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|P. Rausch - Koster, Ophthalmology, Bergman Clinics BV, Naarden, Noord-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: In previous research the EyeQ item bank which measures vision-related quality of life (Vr-QoL) was developed and calibrated for future use as a computer adaptive test (CAT). In theory, the CAT-algorithm uses only a few items for a reliable Vr-QoL estimation ('ability'), reducing patient burden. But before using a CAT in clinical practice it is essential to conduct preliminary analyses to evaluate the appropriateness of patient ability estimations (θ) against full test length and actual test length reduction. The aim of the current study was to optimize performance of the CAT-EyeQ by customizing stopping rules.

Methods: Post-hoc CAT simulations were performed using real responses. Patients (N=704, mean age 76.2), having macular edema due to several exudative retinal diseases completed the EyeQ (46 items). θ's were estimated after fitting Samejima's graded response model. Subsequently, plausible responses were imputed and again θ`s based on complete data were obtained. Pearson`s correlation was calculated between EyeQ θ_{incom} (incomplete data) and EyeQ θ_{imput} (plausible imputed data). Four CAT simulations were performed which varied in combinations of stopping rules: for $CAT_{DefaultPROMIS}$, a minimum and maximum length of 4 and 12 items, and an accuracy level of 0.32 (4|12|0.32) was set; for CAT_{Alt1} 2|15|0.32 and for CAT_{Alt2} 4|12|0.25. $CAT_{Besthealth}$ was defined as CAT $_{DefaultPROMIS}$ plus abort if the first four responses were rated as 'best possible health'. Mean test length, percentage unreliably estimated CAT θ`s and mean standard error was evaluated. The conditional standard error across different levels of ability was examined graphically.

Results: Pearson`s correlation between EyeQ θ_{incom} and EyeQ θ_{imput} was 0.99. $CAT_{DefaultPROMIS}$ showed the lowest mean number of items needed to administer (6.9), where CAT_{Alt1} showed the lowest amount of unreliably estimated CAT scores (11.5%). CAT_{Alt2} performed worst; mean number of items needed (9.7) and 37% unreliable estimations. Outcomes of $CAT_{BestHealth}$ were similar to $CAT_{DefaultPROMIS,}$ but further reduced the mean test length to 6 items. In all applied conditions, the conditional standard error was found to be highest at lower levels of ability.

Conclusions: This study shows that measuring Vr-QoL in clinical practice using the CAT-EyeQ with optimized stopping rules is useful as it leads to a higher measurement efficiency where reliable test outcomes can still be achieved.

CONTROL ID: 3708386
SUBMITTER (NAME ONLY): Edine van Munster
TITLE: Improving detection of depression in adults with vision impairment
SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: E. van Munster, R.M. van Nispen, H.P. van der Aa, Ophthalmology, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|E. van Munster, H.P. van der Aa, Expertise, Innovation and Knowledge, Robert Coppes Foundation, Vught, NETHERLANDS|C. Nollett, Cardiff University, Cardiff, Cardiff, UNITED KINGDOM|M. Heymans, Epidemiology and Data Science, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|E. Holloway, The Australian Centre for Behavioural Research in Diabetes, Victoria, AUSTRALIA|O. Maarsingh, Department of General Practice & Elderly Care Medicine, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|
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ABSTRACT BODY:

Purpose: One in three adults with vision impairment (VI) experience symptoms of depression. However, healthcare providers often experience difficulties in recognizing and discussing depression in this population. Detection of depression, and subsequently providing mental health support, can be improved by determining predictors to detect depression in adults with VI from the perspective of healthcare providers.

Methods: Cross-sectional data on demographics, work, confidence, experienced barriers, intention to identify depression and taking initiative to discuss depression was analyzed in Welsh (n=122), Australian (n=94) and Dutch (n=100) healthcare providers. Multivariable logistic regression analysis was performed in the Welsh sample. The derived model was internally validated by using a bootstrap method, followed by external validation of the recalibrated model in the Australian and Dutch samples.

Results: Work experience (β -0.05; 95% confidence interval (CI) 0.92 to 0.99) and experienced barriers (β -0.05; 95% CI 0.92 to 0.98), such as lack of time, knowledge and standard procedures, were found to predict healthcare providers' initiative to discuss depression. Internal validation of the model provided an area under the curve (AUC) of 0.73, reflecting good discrimination. The recalibrated model showed a good fit in the Australian sample (AUC = 0.77) and a poor fit in the Dutch sample (AUC = 0.63).

Conclusions: Predictors for discussing depression by healthcare providers lacked generalizability. Dutch healthcare providers experienced less barriers in depression management than their Welsh and Australian colleagues, which could be a result of the increased attention for mental health in their education and work, and the difference in healthcare systems. Furthermore, a previous study showed intention to discuss depression, self-efficacy and social support predict healthcare providers' initiative to discuss depression. To improve the detection of depression in adults with VI, the found predictors for each country should be addressed, for instance by means of tailored training programs and effective referral pathways.

CONTROL ID: 3708387

SUBMITTER (NAME ONLY): Chang-Jun Zhang

TITLE: Fluorescent protein tdTomato is deleterious to the retina

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Zhang, H. Mou, Z. Jin, Beijing Institute of Ophthalmology, Beijing Tongren Eye Center, Beijing Tongren Hospital, Beijing, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: Fluorescent proteins (FPs) are widely used in imaging techniques to investigate cellular molecular interactions and trace biological events. However, some FPs have been demonstrated to cause undesirable cellular damage. So far, the effects of red fluorescent protein (RFP) tandem dimer Tomato (tdTomato) on retina remains unknown. Here we study the effects of tdTomato expression on mice retina.

Methods: Electroretinography (ERG) was carried out to investigate the changes of retinal function comparing tdTomato mice with C57BL/6J wild-type control mice. Optokinetic Response (OKR) was measured to detect visual contrast sensitivity. Color fundus camera and high-resolution spectral-domain optical coherence tomo-graphy (SD-OCT) were taken to compare the retinal structural alteration. Immunofluorescence staining was used to label proteins in retina. Transmission Electron Microscope (TEM) was used to observe the retinal ultrastructure. Expression levels of mitochondrial specific genes were quantified via quantitative real-time PCR (qPCR).

Results: The tdTomato mice showed progressively attenuated electroretinogram (ERG) responses in scotopic a-wave and photopic b-wave, and reduction of visual contrast sensitivity was detected via OKR. Mitochondrial vacuolation and broken mitochondrial crest were found by TEM. And down-regulated mitochondrial DNA (mtDNA) expression were found in tdTomato mice. The apparent changes in retina of color fundus camera, SD-OCT and immunofluorescence staining measurements were not found.

Conclusions: tdTomato expression cause functional and ultrastructural defects in the retinas of tdTomato mice, indicates potential toxicity of tdTomato to mouse retina. Mitochondria should be a potential target of the fluorescent protein tdTomato that hazard to the mouse retina. Our findings provide valuable insights into using the tdTomato mice more efficiently and reasonably.

CONTROL ID: 3708390

SUBMITTER (NAME ONLY): Felix Reichel

TITLE: Removal of an idiopathic epiretinal membrane and recurrence - an OCT study

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.F. Reichel, E.A. Labbé Münzenmayer, F. Gelisken, Center for Ophthalmology, Universitatsklinikum Tubingen, Tubingen, Baden-Württemberg, GERMANY|E.A. Labbé Münzenmayer, Departamento de Oftalmología, Hospital Militar de Santiago, Providencia, Santiago, CHILE|F.F. Reichel, Universitatsklinikum Tubingen Forschungsinstitut fur Augenheilkunde, Tubingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To assess the rate of epiretinal membrane (ERM) recurrence after the surgical removal and to describe the morphological features of recurrent ERM as well as their clinical course over time. Finally, clinical and optical coherence tomography (OCT) findings were correlated to identify associated risk factors.

Methods: 640 patients who underwent pars plana vitrectomy (PPV) for an ERM at University Eye hospital, Tübingen, Germany between 02/2007 and 05/2017 were included into a retrospective observational study. ERM recurrence was identified by OCT imaging at a first visit within 3 months after surgery and at the last follow-up examination available. ERM extension was classified as “dot-like” (small dot or deposit-like circumscribed ERM), “focal-ERM” (measuring 50 µm or less) and “large ERM” (measuring more than 50 µm). Morphology analysis included if an ERM remnant edge was within the 1.5mm radius of the foveal center, if the membrane was extrafoveal or involved the fovea and if intraretinal cysts were visible at any postoperative visit. OCT endpoints were correlated with patient related clinical parameters and surgery related factors.

Results: Out of 506 eyes 38% showed OCT signs of an epiretinal membrane at the last available follow up visit (mean follow up period 28.3 months). Large foveal ERM however was only visible in 10% and only 4% of all eyes were reoperated a second time for an epiretinal membrane. An ERM remnant edge, hyperreflective epiretinal dots, small focal ERM and intraretinal cystic spaces were found to be possible risk factors for large foveal ERM recurrence at later timepoints with an odds ratio of 5.66 (95% confidence interval: 2.0-15.99; p=0.003), 3.63 (95% confidence interval: 1.34-9.84; p=0.02), 2.89 (95% confidence interval: 1.21-6.89; p=0.02) and 1.95 (95% confidence interval: 1.06-3.58; p=0.03).

Conclusions: The recurrence rate depends significantly upon the definition of ERM recurrence. Foveal ERM recurrence is much less frequent than ERM recurrence outside of the fovea. Insufficient peeling with neighboring remnant membrane is an important predisposing factor for clinically relevant foveal ERM recurrence.

CONTROL ID: 3708393

SUBMITTER (NAME ONLY): Yingna Liu

TITLE: Prospective, longitudinal feasibility study: daily self-imaging with home OCT in neovascular age-related macular degeneration

SESSION TITLE: AMD Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Liu, Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|N.M. Holekamp, Retina Services, Pepose Vision Institute, Chesterfield, Missouri, UNITED STATES| Y. Liu, J.S. Heier, Retina Service, OCB, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Yingna Liu: Commercial Relationship: Code N (No Commercial Relationship) | Nancy Holekamp: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan, Annexon, Apellis, Bayer, Cardinal, Clearside Biosciences, EyePoint Pharmaceuticals, Gemini, Genentech, Gyroscope, Katalyst Surgical, Nacuity, NGM, Notal Vision, Novartis, Ocuphire, Outlook Therapeutics, Regeneron, Thea Laboratoires, Stealth Biosciences | Jeffrey Heier: Commercial Relationship(s);Code C (Consultant/Contractor):Notal Vision

ABSTRACT BODY:

Purpose: To validate the feasibility and performance of the Notal Vision Home OCT (NVHO) system for daily self-imaging at home, and to characterize retinal fluid dynamics in neovascular AMD (nAMD).

Methods: In this prospective observational study, 15 participants who have at least one eye with nAMD undergoing anti- VEGF treatments performed daily self-imaging at home with NVHO for 3 months. Scans were uploaded to the cloud, analyzed by the Notal OCT Analyzer (NOA), evaluated by human experts for fluid presence and compared with in-office OCT scans. Weekly self-scan rate, image quality, scan duration were obtained; agreement between NOA and human expert grading for fluid presence and agreement between NVHO and in-office OCT scans for fluid presence, central subfield retinal thickness (CST) and retinal fluid volume, characteristics of fluid dynamic during the study and in response to treatments were analyzed.

Results: The mean weekly scan frequency was 5.7±0.9 scans per week, and 93% of scans were eligible for NOA analyses. Mean scan time was 42 seconds. NOA and human experts agreed on the fluid status in 83% of scans and discrepancies were limited to trace amounts of fluid. NVHO scans analyzed by NOA and in-office OCT scans graded by human experts agreed on the fluid status in 96% of cases. CST and retinal fluid volume measurements from home OCT and in-office OCT scans demonstrated Pearson correlation coefficients of $r = 0.90$ and $r = 0.92$, respectively. Novel parameters such as retinal fluid volume, area under the retinal fluid volume curve (AUC) demonstrated wide variations in fluid exudation and fluid load over time among patients. Parameters, such as the rate of reduction in fluid volume in the first week after treatments and AUC between treatments captured the speed and duration of response to anti-VEGF agents.

Conclusions: Daily home OCT imaging is feasible among patients with nAMD. It demonstrated good agreement with human expert grading for retinal fluid identification, and excellent agreement with in-clinic OCT scans. Home OCT allows for detailed graphical and mathematical analyses of retinal fluid volume trajectories, including novel parameters to inform clinical decision making.

CONTROL ID: 3708394

SUBMITTER (NAME ONLY): Catherina Li

TITLE: Disease progression in STGD1 patients with c.768G>T mutation

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.H. Li, P.P. Dhooge, J. Pas, C.C. Hoyng, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|R.W. Collin, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|C.H. Li, P.P. Dhooge, J. Pas, C.C. Hoyng, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

Commercial Relationships Disclosure: Catherina Li: Commercial Relationship: Code N (No Commercial Relationship) | Patty Dhooge: Commercial Relationship: Code N (No Commercial Relationship) | Jeroen Pas: Commercial Relationship: Code N (No Commercial Relationship) | Rob Collin: Commercial Relationship(s);Code O (Owner):ASTHERNA;Code P (Patent):6078940 | Carel Hoyng: Commercial Relationship(s);Code O (Owner):ASTHERNA

ABSTRACT BODY:

Purpose: In the Netherlands, c.768G>T (p.Leu257Valfs*17), a severe mutation in ABCA4, is one of the most frequently found variants underlying Stargardt disease (STGD1). In light of potential upcoming mutation-specific intervention trials, we performed a retrospective study on the disease progression in a large cohort of STGD1 patients homozygous or compound heterozygous for the c.768G>T mutation.

Methods: We included patients with genetically confirmed STGD1 and that were homozygous or compound heterozygous for the c.768G>T mutation in ABCA4, from the STGD1 database of Radboud university Medical center, Nijmegen, The Netherlands. Clinical data were extracted from medical files, including age of onset and best-corrected visual acuity (BCVA). Atrophy was quantitatively assessed with area of definitely decreased autofluorescence (DDAF) and questionably decreased autofluorescence (QDAF) on fundus autofluorescence (FAF). Total decreased autofluorescence (DAF) was calculated as the sum of DDAF and QDAF. External limiting membrane (ELM) and ellipsoid zone (EZ) loss was measured at the foveal OCT-scan. Mean progression rates per year were calculated and data was compared between ages of onset and genotype.

Results: We included 72 patients. Median age of onset was 16.5 years (IQR 9.0-31.5). A larger part consisted of early onset patients (age of onset ≤10 years) compared to our general STGD1 population (32.4% vs. 23.4%). Median DDAF and QDAF progression per year was 0.30 mm^2 (IQR 0,00-1.26) and 0,00 mm^2 (IQR 0.00-0.16). ELM and EZ decreased by 160 µm per year (ELM IQR 68.7-324.7; EZ IQR 68.7-310.8) . BCVA detoriated by 0.10/year (Snellen decimals (IQR -0.06-0.00)). Rate of ELM and EZ loss was significantly higher in late onset (≥45 years) compared to intermediate onset (11-44 years) (p=0,04 and p=0.02). DAF progression rate was also significantly higher in patients with another severe mutation next to c.768G>T, compared to patients with a second mild/moderate mutation (DAF 2.33mm^2 (IQR 1.56-2.99) in severe vs 0.33mm^2 (IQR 0.00-1.42) in mild/moderate, p=0.02).

Conclusions: The c.768G>T variant is one of the most occurring mutation in STGD1 and is of high interest due to possible mutation-specific intervention. The disease progression rate of STGD1 patients with c.768G>T seems to be dependent on age of onset and severity of the second mutation and can be monitored using DDAF/QDAF and ELM/EZ loss measurements.

CONTROL ID: 3708395

SUBMITTER (NAME ONLY): Chang Ki Yoon

TITLE: Detection and Localization of Retinal Breaks in Ultra-Widefield Fundus Photography using a YOLO v3 Architecture-Based Deep Learning Model

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Yoon, R. Oh, H. Yu, Opthalmology, Seoul National University Hospital, Jongno-gu, Seoul, KOREA (THE REPUBLIC OF)|H. Yu, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Chang Ki Yoon: Commercial Relationship: Code N (No Commercial Relationship) | Richul Oh: Commercial Relationship: Code N (No Commercial Relationship) | Hyeong Gon Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We aimed to develop a deep-learning model for detecting and localizing retinal breaks in ultra-wide-field fundus (UWF) images

Methods: We retrospectively enrolled treatment-naive patients diagnosed with retinal break or rhegmatogenous retinal detachment and who had UWF images. The YOLO v3 architecture backbone was used to develop the model, using transfer learning. The performance of the model was evaluated using per-image classification and per-object detection.

Results: A total of 4,505 UWF images from 940 patients were used in the current study. In the per-image classification, the model showed an area under the receiver operating characteristic curve (AUROC) of 0.957 within the test set. With the best threshold from the validation set, the accuracy, sensitivity, and specificity were 0.9118, 0.9474, and 0.8535, respectively. With respect to per-object detection , the average precision for the object detection model considering every retinal break was 0.840. (Figure)

Conclusions: The UWF image-based deep-learning model evaluated in the current study performed well in diagnosing and locating retinal breaks. Owing to its fast detection speed, we conclude that this model can be generalized for the real-time detection of retinal breaks.

CONTROL ID: 3708396

SUBMITTER (NAME ONLY): Mark Chia

TITLE: Validation of a deep learning system for the detection of diabetic retinopathy in Indigenous Australians

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chia, P. Keane, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Chia, P. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A. Turner, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|A. Turner, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|F. Hersh, R. Sayres, P. Bavishi, Google Inc, Mountain View, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The increasing demand for diabetic retinopathy (DR) screening represents a significant burden for eye care services. Deep learning systems (DLS) for DR detection have shown promise in bridging the gap between demand and availability of health resources. However, an important limitation is a tendency for poor generalisability. External validation within populations intended for use is therefore critical. Indigenous Australians are an understudied ethnic group who suffer disproportionately from diabetic-related blindness. This study evaluates the performance of a DLS for DR detection in an Indigenous Australian population.

Methods: We performed a retrospective external validation study comparing the performance of a DLS against a retinal specialist for the detection of more-than-mild (mtmDR) and vision-threatening diabetic retinopathy (vtDR). The validation set consisted of 1682 consecutive, single-field, macula-centered retinal photographs from diabetic patients at an urban Indigenous primary health service in Perth, Australia. Adjudication by a panel of three retinal specialists and trained graders served as the reference standard.

Results: The validation set comprised 1682 eyes of 866 patients (mean age 54.9 years, 52.4% female). For mtmDR detection, sensitivity of the DLS was superior to the retinal specialist (98.0% [95% CI:96.2-99.1%] vs 88.0% [95% CI:84.5-91.2]) with a small reduction in specificity (95.0% [95%CI:93.5-96.5%] vs 97.9% [97.0-98.8%]; both significant by two-sided permutation test, $p < 0.001$). For vtDR, the DLS's sensitivity was again superior to the human grader (96.2% [95% CI:93.9-96.3%] vs 84.5% [95% CI:79.3-89.7%], $p<0.001$) with a slight drop in specificity (95.5% [95%CI:94.3-96.7%] vs 98.3% [95%CI:97.6-99.0%], $p<0.001$). These results are comparable to reported performance in other populations, including Indian and Thai diabetic screening populations.

Conclusions: In this retrospective sample, the DLS showed improved sensitivity and similar specificity compared to a retinal specialist for the detection of mtmDR and vtDR. This demonstrates the potential of the system to support DR screening amongst Indigenous Australians, an underserved population with a high burden of diabetic eye disease. Further prospective validation in real-world clinical settings is required.

CONTROL ID: 3708400

SUBMITTER (NAME ONLY): Daren Hanumunthadu

TITLE: Biomarkers of macular neovascularisation activity using optical coherence tomography angiography in treated stable neovascular age related macular degeneration

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hanumunthadu, Royal Free London NHS Foundation Trust, London, London, UNITED KINGDOM|D. Hanumunthadu, K. Balaskas, D. Florea, P.A. Keane, A.M. Dubis, P. Patel, NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|T. Aslam, School of Pharmacy and Optometry, Faculty of Biology, Medicine and Health, Manchester Metropolitan University, Manchester, Greater Manchester, UNITED KINGDOM|T. Aslam, Manchester Royal Eye Hospital, Manchester, Manchester, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Biomarkers of activity of macula neovascularisation (MNV) in those deemed stable with conventional structural optical coherence tomography (OCT) could help to determine the requirement for further treatment and their associated monitoring interval for further visits. The aim of this study was to describe features of disease activity of treated stable MNV due to neovascular age related macular degeneration (nAMD) using optical coherence tomography angiography (OCTA).

Methods: 32 eyes of 32 patients with nAMD were included in this prospective, observational study. These patients were undergoing treatment with aflibercept on a treat-and-extend regimen. They were identified as attending a 16-week interval treatment visit and had been assessed as clinically stable based on clinical evaluation (visual acuity assessment, clinical examination and structural OCT assessment). All patients then underwent macular OCT imaging and OCT angiography on the same day (Spectralis, Heidelberg Engineering, Heidelberg, Germany). These images were analysed by the Moorfields Eye Hospital Reading Centre, London, United Kingdom.

Results: Evaluation of structural OCT confirmed no evidence of subretinal or intraretinal edema, but presence of subretinal hyperreflective material (13, 40.6%), pigment epithelial detachment (31, 96.9%), outer retinal tubulation (10, 31.3%) and macula atrophy (19, 59.4%). 31/32 OCTA images were gradeable (1 had significant signal attenuation); 28/32 (87.5%) OCTA images were noted to have signal artefacts. The mean MNV size was 3.6 ± 4.6mm and 29 (93.5%) and 27 (87.1%) had detectable MNV blood flow. 29 (93.5.%) subjects had MNV maturity including 10 non-specific, 10 tangle, 3 deadtree and no medusa or seafan phenotypes. MNV halo and MNV central feeder vessel were noted in 18 (58.1%) and 19 (61.3%) of subjects respectively; only 1 (3.2%) subject was noted to have a MNV capillary fringe.

Conclusions: CNV blood flow is still detectable using OCTA in the majority of subjects in this study. The majority of MNV were of mature phenotype. OCTA features associated with this clinically stable MNV activity included MNV maturity, feeder vessel, halo and absence of capillary fringe. These features could be helpful as possible OCTA biomarkers of disease activity and help inform treatment decisions with anti-vascular endothelial growth factor agents.

CONTROL ID: 3708404

SUBMITTER (NAME ONLY): Aysenur Musaogullari

TITLE: Non-invasive assessment of pulsatile ocular blood volume demonstrates a decrease in the supine position in healthy subjects

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Musaogullari, C.J. Roberts, C.B. Toris, J. Gilbert, D. Reed, S.E. Moroi, Department of Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|C.J. Roberts, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|C.B. Toris, V. Gulati, Department of Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|A.J. Sit, Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Aysenur Musaogullari: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Roberts: Commercial Relationship(s);Code C (Consultant/Contractor):Ziemer Ophthalmic Systems AG;Code C (Consultant/Contractor):Oculus Optikgeräte GmbH;Code R (Recipient):Heidelberg Engineering, Inc | Carol Toris: Commercial Relationship: Code N (No Commercial Relationship) | Jesse Gilbert: Commercial Relationship: Code N (No Commercial Relationship) | David Reed: Commercial Relationship: Code N (No Commercial Relationship) | Vikas Gulati: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Sit: Commercial Relationship: Code N (No Commercial Relationship) | Sayoko Moroi: Commercial Relationship(s);Code F (Financial Support):NIH;Code R (Recipient):Wolters Kluwer Health

ABSTRACT BODY:

Purpose: Ocular blood flow is important for eye health and for understanding the pathogenesis of ocular diseases, such as diabetic retinopathy and glaucoma. The purpose of this study was to a test a simple, noninvasive method to assess pulsatile ocular blood volume (POBV) in healthy subjects and to determine effects of posture changes and glaucoma medications.

Methods: A subset of data was evaluated from a prospective, randomized crossover-design of glaucoma medications (ClinicalTrials.gov NCT04412096) in healthy subjects. Aqueous humor dynamic measurements were made at baseline, after 1 week of timolol 0.5% dosed twice daily, and after 1 week of latanoprost 0.005% dosed nightly. The treatments were separated by a 6-week washout period. Study criteria for this subset analysis included high quality recordings of intraocular pressure (IOP) by pneumatonometry with two or more pulses measured at each visit in sitting and then supine positions. Thirty-two eyes from 16 subjects, ages 44 to 72 years, met study criteria. Ocular pulse amplitude (OPA) was defined as the IOP difference between diastolic (IOPdia) and systolic (IOPsys) values. POBV was calculated as OPA/IOPdia, as previously described. Student t-test with Bonferroni correction for multiple comparisons was used with significance threshold at $p<0.017$ to compare the effects of posture and under medication treatment conditions.

Results: At baseline, there was a significant increase in supine versus sitting position in IOPsys (16.7 ± 2.3 mmHg to 21.4 ± 2.4 mmHg, $p<0.0001$), IOPdia (14.4 ± 2.2 mmHg to 19.5 ± 2.2 mmHg, $p<0.0001$), and mean IOP (15.5 ± 2.2 mmHg to 20.5 ± 2.2 mmHg, $p<0.0001$). Calculated POBV was significantly decreased in supine versus sitting positions (0.17 ± 0.06 vs. 0.10 ± 0.04, $p<0.001$). These effects were similar at baseline and after treatments with timolol or latanoprost. The position-related POBV change was not affected by treatment or order of treatment.

Conclusions: In the supine position of healthy adults, IOP increased and POBV calculated by OPA/IOPdia decreased relative to the sitting position. Our future studies will compare POBV in patients with glaucoma where the autoregulation of retinal blood flow may be affected, to investigate whether changes in pulsatile blood volume in the supine position may play a role in glaucoma pathogenesis. Changes from glaucoma treatments also will be investigated.

CONTROL ID: 3708405

SUBMITTER (NAME ONLY): Silke Becker

TITLE: Susceptibility of photoreceptor and ON-bipolar cell function to hypoxia in retinal disease models

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Becker, F. Vinberg, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Silke Becker: Commercial Relationship: Code N (No Commercial Relationship) | Frans Vinberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To ensure adequate oxygenation of the retina, one of the most metabolically demanding tissues in the body, photoreceptors are mainly supplied by the choroid and inner retinal neurons by the retinal vasculature. Vascular damage in retinal degenerative diseases, e.g. diabetic retinopathy, or attenuated retinal blood vessel development in retinopathy of prematurity (ROP) result in retinal hypoxia. We tested whether hypoxia underlies compromised phototransduction and light signal transmission, and whether changes are reversible, by measuring photoreceptor (PR) and ON-bipolar cell (ON-BC) light responses in mouse models of these conditions.

Methods: Diabetic (db/db) and non-diabetic (db/+) mice were used as a diabetes model. For oxygen-induced retinopathy (OIR, a model of ROP), we exposed C57BL/6J pups to high (75%) O_2 from postnatal day (P)7 to P12, before returning them to room air. We recorded scotopic in vivo electroretinograms (ERGs) or ex vivo ERGs in isolated retinas. To modulate O_2 concentrations we provided hypoxic gas (8% O_2) through a nose cone in vivo or perfused with hypoxic superfusate (containing 2.5% O_2) ex vivo.

Results: ON-BCs lose function within 8 minutes of ex vivo hypoxia, whereas PRs retain >50% response amplitudes after 30 min (n=2-3). In vivo PR and ON-BC amplitudes in diabetic mice progressively decrease at 4.5 and 6, but not at 3 months. Diabetes reduces the b/a-wave ratio at 6 months (2.20±0.23 in db/db compared to 2.65±0.27 in db/+, p= P<0.001, n=9-10), indicating that ON-BCs or light signal transmission are more susceptible to diabetes than phototransduction. During ex vivo ERG (with 95% O_2) PR and ON-BC responses were not different between 6 month old db/db and db/+ mice (n=11). Ex vivo PR and ON-BC function were reduced in OIR mice on P12 (n=7-10, P<0.001) and on P24 (n=8-10, P<0.001).

Conclusions: Although retinal neurons critically depend on sufficient O_2 supply, PRs maintain better function during hypoxia compared to ON-BCs, possibly by adapting to low O_2 conditions they are exposed to daily during the normal light-dark cycle. Deficits in retinal function in diabetic mice in vivo are reversed ex vivo with high O_2. Irreversible PR damage in OIR likely occurs during the hyperoxic phase, before hypoxic damage. Investigating these discrepancies will allow us to better understand importance and therapeutic potential of adequate O_2 supply in different retinal diseases.

CONTROL ID: 3708412

SUBMITTER (NAME ONLY): Jose Rico-Jimenez

TITLE: Deep-learning-based volumetric quantification of retinal lesions in murine model of focal laser injury

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Rico-Jimenez, Y. Tao, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|D. Hu, I. Oguz, Electrical Engineering and Computer Science, Vanderbilt University, Nashville, Tennessee, UNITED STATES|E.M. Levine, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Jose Rico-Jimenez: Commercial Relationship: Code N (No Commercial Relationship) | Dewei Hu: Commercial Relationship: Code N (No Commercial Relationship) | Edward Levine: Commercial Relationship: Code N (No Commercial Relationship) | Ipek Oguz: Commercial Relationship: Code N (No Commercial Relationship) | Yuankai Tao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Focal laser retinal injury models are a robust platform for in vivo testing of retinal regeneration strategies. However, quantitative assessment of the retinal structural changes resulting from laser photodamage is prohibitively labor-intensive, requiring manual segmentation of longitudinal volumetric datasets. Here, we present a deep-learning based approach for automated qualitative assessment of lesion volumes using OCT images to enable real-time assessment of injury severity and longitudinal tracking of tissue response to photodamage.

Methods: In vivo OCT retinal imaging was performed longitudinally to track retinal injury response and analyze the reproducibility of retinal photodamage in murine models. Lesions with different severity were induced by varying the laser pulse duration, pulse power, and number of pulses. OCT images were denoised using self-fusion and fed into a convolutional neural network to segment lesion cross-sections. The network was trained to quantify photodamage between the outer plexiform layer (OPL) and retinal pigmented epithelium (RPE) accurately without the need for extensive image pre- and post-processing. The consensus of manually labeled OCT cross-sections from two independent image annotators were used as ground-truth.

Results: The automated method was compared against the manual segmentation using the Dice coefficient achieving a score of 0.91 for training and 0.87 for testing. Figure 1 shows high degree of spatial co-registration between the manual (B) and automated lesion segmentation (C). Likewise, projections of lesion height of manually (E) and automatically (F) segmented lesions overlaid on the OCT en face projections demonstrate that both methods are well-correlated.

Conclusions: Automated volumetric OCT segmentation enables efficient and robust quantification of lesion severity after laser delivery and during longitudinal follow-up. The proposed approach will allow for large-scale quantitative injury studies by eliminating the need of burdensome manual lesion segmentation. While promising, this initial proof-of-concept study will need to be validated on larger comparative studies with multi-grader segmentations that evaluate benefits in segmentation sensitivity and specificity.

CONTROL ID: 3708414

SUBMITTER (NAME ONLY): Alex Bowers

TITLE: Pilot testing of a pedestrian collision detection test for field expansion devices

SESSION TITLE: Vision Impairment: Impact on Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.R. Bowers, A.D. Hwang, J. Jung, S. Manda, S. Shekar, E. Peli, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A.R. Bowers, A.D. Hwang, J. Jung, E. Peli, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Peripheral prism glasses expand the field of view for patients with homonymous hemianopia (HH), but perimetry fails to evaluate effectiveness for real world mobility. We report pilot testing of a new pedestrian collision detection test, including the challenge of developing a method to keep gaze and attention toward the forward path, as would be the case in everyday walking.

Methods: The test, presented on a large screen (104°H × 63°V), simulated walking through a busy shopping mall with multiple pedestrians moving in various directions. For each trial, there were three possibilities: pedestrian on a collision course (constant eccentricity with looming) from the left, from the right, or neither side. Iterative rounds of development and pilot testing were conducted with HH subjects. We report results from 3 phases: free gaze; following a lead child through the mall; and addition of a secondary task (ST). Collison detection rates and response times (RT) were recorded for pedestrians at eccentricities of 20° or 25°. Misses were assigned the maximum response time, 5 s (maximum time to collision).

Results: With free gaze, HH subjects quickly learned to “beat the test” by keeping their gaze well over to the blind side in a manner impossible when walking in the real world. A lead child and walking path were added, but even with instructions to “not lose sight of the child”, blind side detection rates were still very high. A ST was then added to keep gaze and attention mostly toward the forward path, but still allow scanning. Subjects called out numbers appearing within a string of letters moving randomly (±1.25°H × ±2.5°V) behind the lead child’s head. In ST-1, each character subtended 1.5° and was presented for 1 s. Blind-side median detection (N = 6) was 50% without prisms. In ST-2, the characters were smaller (1°) and presented for a random variable duration (0.5 to 1.5 s, mean 1 s). Blind-side median detection was 0% without prisms (N = 7), suggesting ST-2 better kept gaze in the walking direction. With ST-2 and 57Δ oblique peripheral prisms, blind-side detection improved significantly to 90% ($p = 0.03$) and median response times improved significantly from 5.0 s without to 3.4 s with prisms ($p = 0.03$).

Conclusions: Our test measures the impact of field loss and the effectiveness of field expansion aids in a task relevant to real-world walking.

CONTROL ID: 3708418
SUBMITTER (NAME ONLY): Guillermo Requejo
TITLE: Infectious Scleritis: A 30 years Retrospective Study
SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G.A. Requejo, A. Santiago, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|E. Vázquez Valencia, E. Báez Rivera, L. Rivera Román, A. Oliver, C. Santos, Ophthalmology, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|

ABSTRACT BODY:

Purpose: Infectious scleritis is a rare disease with few large series reports in the literature and an etiology that varies based on geographic region and different climates. In addition, knowledge of disease epidemiology and predisposing factors is scarce. Since there is no previous study describing this ocular infection in Puerto Rico, we decided to determine the etiology of infectious scleritis, predisposing factors, complications, treatment strategies, and final disease outcomes in a cohort of patients living in Puerto Rico.

Methods: A retrospective chart review of infectious scleritis cases, dating from 1988 to 2018, of three cornea specialist practices in Puerto Rico. Both culture-proven, as well as cultures-negative cases, were included in the study. Demographic characteristics were recorded. In addition, the following information was gathered from each patient chart: inciting event, time from predisposing event to disease development, time of infection onset to cornea specialist evaluation, cultures results, involved organism (for positive culture cases), presenting signs and symptoms, visual acuity upon presentation, final visual acuity outcome, photographic documentation, treatment strategy, complications, and final disease outcome.

Results: Forty-five patients who met the research criteria for a diagnosis of infectious scleritis were identified and included in the analysis. The most common ocular sign was hyperemia (87%) and the most frequent symptom was pain (87%). Visual acuity at presentation was worse than 20/200 in 36% of eyes. The median duration of therapy was 112 days. Surgical intervention was performed on 17% of eyes which consisted of debridement (4%), tenoplasty and amniotic membrane graft (4%), corneal/scleral patch graft (2%), removal of a hardware device (6.7%, 3 scleral buckles), and pars plana vitrectomy (2%). Final visual acuity was 20/200 or better in 69% of eyes. 100% of the patients were able to save their eye from infection and 69% maintained useful vision.

Conclusions: Our findings are consistent with previous reports. Pterygium surgery was the most common surgical intervention associated with the subsequent development of infectious scleritis, followed by glaucoma surgery. Pseudomonas aeruginosa is the most common bacteria involved in the widespread use of adjunctive therapies, like mitomycin C, in these two ophthalmic procedures, which may explain the high incidence of infectious scleritis after these surgeries.

CONTROL ID: 3708419

SUBMITTER (NAME ONLY): Rachel Daley

TITLE: Akt2 signaling in diabetes-induced dysfunction of the outer blood retina barrier

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Daley, S. Ghosh, P. SHANG, N.A. Stepicheva, A. Strizhakova, O. Chowdhury, V. Koontz, S.L. Hose, D. Sinha, H. Liu, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, The Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) is a significant complication of diabetes that causes blindness in adults. DR is also associated with the disintegration of the blood-retina barrier (BRB). The altered inner BRB formed by endothelial cells in the plexiform layers has been investigated broadly in DR pathogenesis; however, in DR the malfunction of the outer BRB consisting of retinal pigment epithelium (RPE) and choroid has rarely been studied. This study investigates the potential role of Akt2 in the diabetes-induced breakdown of the outer BRB in RPE cells.

Methods: Best1-Cre generated RPE-specific Akt2 conditional knockout (cKO) mice were used. Rodent body weights and blood glucose levels were monitored while diabetes was induced in $Akt2^{fl/fl}$ and Akt2 cKO mice by intraperitoneal injection of Streptozotocin for 5 consecutive days. The mice were sacrificed after an 8 month duration of diabetes (10 months of age), and HbA1c, tight junction proteins, and epithelial-mesenchymal transition (EMT) markers were examined.

Results: Blood glucose and HbA1c were elevated in diabetic $Akt2^{fl/fl}$ and Akt2 cKO mice. $Akt2^{fl/fl}$ and Akt2 cKO diabetic mice exhibited significantly lower body weights than appropriate non-diabetic controls. After 8 months of diabetes, the $Akt2^{fl/fl}$ mice showed a diabetes-induced reduction of the RPE tight junction protein ZO-1 and adherence junction proteins occludin and E-cadherin; Both RNA and protein levels of the EMT markers SNAIL/SLUG and TWIST were elevated in the RPE cells of $Akt2^{fl/fl}$ diabetic mice compared to $Akt2^{fl/fl}$ non-diabetic mice, while such alterations were inhibited in Akt2 cKO diabetic mice. Vimentin was elevated in the RPE of $Akt2^{fl/fl}$ diabetic mice and was decreased in Akt2 cKO diabetic mice. The junction proteins and EMT markers in the non-diabetic control groups showed no significant changes.

Conclusions: Deletion of Akt2 in the RPE prevents diabetes-induced alterations in outer BRB and inhibits diabetes-induced elevation of EMT markers.

CONTROL ID: 3708421

SUBMITTER (NAME ONLY): Alice Chandra Verticchio Vercellin

TITLE: Differences in the relationship between intraocular pressure and optic nerve head oxygenation in open angle glaucoma patients of African and European Descent

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Verticchio Vercellin, A. Harris, L. Pasquale, B.A. Siesky, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|G. Eckert, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|J. Beach, University of Minnesota Center for Drug Design, Minneapolis, Minnesota, UNITED STATES|R.B. Rosen, O. Otero, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|J. Arciero, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Alice Chandra Verticchio Vercellin: Commercial Relationship: Code N (No Commercial Relationship) | Alon Harris: Commercial Relationship(s);Code C (Consultant/Contractor):AdOM, Qlaris, Luseed, Cipla;Code S (non-remunerative):AdOM, Qlaris, Phileas Pharma;Code I (Personal Financial Interest):AdOM, Luseed, Oxymap, Qlaris, Phileas Pharma, SlitLed, QuLent | James Beach: Commercial Relationship: Code N (No Commercial Relationship) | Richard Rosen: Commercial Relationship(s);Code C (Consultant/Contractor):OptoVue;Code F (Financial Support):OptoVue;Code P (Patent):OptoVue;Code C (Consultant/Contractor):Boehringer-Ingelheim;Code I (Personal Financial Interest):Opticology;Code I (Personal Financial Interest):Guardion;Code F (Financial Support):Ocusciences;Code F (Financial Support):Topcon | George Eckert: Commercial Relationship: Code N (No Commercial Relationship) | Oscar Otero: Commercial Relationship: Code N (No Commercial Relationship) | Julia Arciero: Commercial Relationship: Code N (No Commercial Relationship) | Louis Pasquale: Commercial Relationship(s);Code C (Consultant/Contractor):Eyenovia, Twenty Twenty, and Skye Bioscience | Brent Siesky: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine the relationship between intraocular pressure (IOP) and retinal oxygen saturation in open angle glaucoma (OAG) patients of African (AD) and European descent (ED).

Methods: 31 patients with OAG (13 AD, 18 ED) were assessed in a cross-sectional analysis for IOP via Goldmann applanation tonometry and retinal oxygenation via retinal photographic oximetry (Oxymap Retinal Oximeter; Oxymap ehf, Reykjavik, Iceland). Age-adjusted two-sample t-tests and Spearman correlations were used to test for differences and associations between measurements, with $p<0.05$ considered statistically significant.

Results: OAG patients of AD and ED demonstrated significantly different relationships between IOP and retinal venous oxygen biomarkers, despite statistically similar IOP ($p=0.418$) and visual field outcomes (mean deviation, pattern standard deviation, and visual field index, all $p>0.05$). Strong negative correlations were found between IOP and oxygenation biomarkers in OAG patients of ED, while these correlations were weaker and/or positive in AD patients ($p=0.008$-0.038; e.g., IOP vs. oxygen saturation ($SatO_2$) in the inferior nasal vein ED $r=-0.99$, AD $r=-0.19$, $p=0.008$). IOP was also strongly and positively correlated with the infero-nasal arterio-venous difference in OAG patients of ED, while the correlation was weak and negative in AD patients (ED $r=0.97$, AD $r=-0.13$, $p=0.021$). Although OAG patients of AD had higher ocular perfusion pressures (OPP), compared to those of ED ($p=0.021$); OPP was not found to be significantly different in its relationships with ONH oxygen biomarkers ($p<0.05$) between groups.

Conclusions: In this cohort of patients, the relationship between IOP and retinal oxygen saturation were significantly different between OAG patients of AD and ED. Our results suggest that despite statistically similar IOP, the impact of IOP on retinal metabolism may be different in persons of AD, especially within the venous circulation.

CONTROL ID: 3708426

SUBMITTER (NAME ONLY): SRIKANTH DUMPATI

TITLE: Antimicrobial efficacy of novel Ultraviolet- C device against microorganisms related to Contact lens keratitis.

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. DUMPATI, S. Shah, S. Naroo, D. Dutta, School of Optometry, Aston University, Birmingham, Birmingham, UNITED KINGDOM|

Commercial Relationships Disclosure: SRIKANTH DUMPATI: Commercial Relationship: Code N (No Commercial Relationship) | Sunil Shah: Commercial Relationship: Code N (No Commercial Relationship) | Shehzad Naroo: Commercial Relationship: Code N (No Commercial Relationship) | Debarun Dutta: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the antimicrobial activity of a novel ultraviolet-C device against microorganisms implicated in contact lens related adverse events.

Methods: The Ultraviolet-C device with 265nm emitting LED was used. Delfilicon-A (Dailies Total-1), Senofilicon-A (Acuvue OASYS), Comfilicon-A (Biofinity), Balafilicon-A (Purevison 2), Samfilicon- A(Ultra) silicone hydrogels, Omafilicon-A (Proclear) hydrogel contact lens materials and Lens cases (B&L) were exposed to Staphylococcus aureus 38, Pseudomonas aeruginosa 6294, Candida albicans ATCC 76615 and Fusarium Solani 10696 with overnight incubation at 37°C followed by 30 seconds exposure to UVC from 8 mm distance. After this, lenses were gently washed with phosphate buffer saline and were plated on nutrient agar plates for determination of viable count. Viable bacteria were enumerated as CFU/lens and CFU/lens case.

Results: Exposure to ultraviolet rays by a novel UVC device statistically significantly ($P<0.05$) reduced mirobial contamination of contact lens and lens cases. Exposure to UVC device induced 2.15±1.52, 3.15±0.92, 3.27±0.19, 2.80±0.64, 3.54±0.82, 3.15±0.28 and 4.69±0.04 log reduction against S. aureus 38, 0.90±1.28, 3.01±0.85, 1.72±0.43, 2.56±0.56, 3.54±0.35, 2.28±1.06 and 4.79±0.54 log reduction against P. aeruginosa 6294 ,1.55±1.07, 2.09±0.30, 0.72±0.25, 1.66±1.47, 1.66±0.13, 1.32±0.16, and 3.76±0.13 log reduction against C.albicans ATCC 76615, 4.18±0.07, 2.16±0.32, 4.03±0.50, 3.34±0.77, 2.16±0.32, 2.16±0.32 and 3.60±0.35 log reduction against F.Solani 10696 on Delfilicon-A, Senofilcon-A, Comfilicon-A, Omafilicon- A, Balafilicon-A, Samfilicon-A lenses and lens cases respectively.

Conclusions: Ultraviolet-C has high antimicrobial efficacy against most of the predominant microorganisms implicated in contact lens related keratitis and it could be readily used as a broad-spectrum antimicrobial treatment.

CONTROL ID: 3708427

SUBMITTER (NAME ONLY): Seitaro Komai

TITLE: Gene Regulation Differences Between TLR3 and IPS-1 in Poly(I:C) Stimulated Murine Corneal Epithelial Cells

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Purpose: Toll-like receptor 3 (TLR3) and interferon-beta promoter stimulator-1 (IPS-1) are associated with antiviral responses to double-stranded (ds) RNA viruses, and contribute to innate immunity. We previously reported that TLR3 is expressed on the surface of corneal epithelial cells (CECs), and confirmed that MDA5 and RIG-I, dsRNA receptors that bind to IPS-1, are also expressed in CECs (Ueta M, et al. Prog Retin Eye Res. 2012). We also reported that TLR3 and IPS-1 signaling regulates the distribution and migration of $CD11c^{+}$ cells in murine corneas (Ueta M, et al. Immunol Lett. 2019). However, the functions of TLR3 and IPS-1 in CECs and the differences in their respective roles for their common ligands remain unclear. The purpose of this present study was to elucidate the function of TLR3 and IPS-1 in CECs via comprehensive analysis of gene expression in response to polyinosinic:polycytidylic [poly(I:C)] stimulation using cultured primary murine CECs (PMCECs) derived from TLR3 and IPS-1 knock-out (KO) mice.

Methods: Methods: PMCECs were obtained from the corneas of 4- to 6-week-old BALB/c background wild-type (WT), TLR3KO, and IPS-1KO mice, and then stimulated with or without poly(I:C) (10 μg/ml) for 6 hours. Total RNA was then extracted from the PMCECs, and comprehensive gene expression analysis was performed using the GeneChip™ (Thermo Fisher Scientific) microarray scanner system. Gene expression was further evaluated via quantitative polymerase chain reaction analysis.

Results: Results: The expression of 121 genes was upregulated more than 2-fold in the WT PMCECs after poly(I:C) stimulation compared with those without stimulation. Gene ontology analysis showed that the upregulated genes included those associated with viral responses. Compared to the WT PMCECs, genes downregulated in the TLR3KO or IPS-1KO PMCECs also included those associated with viral responses. The genes Neurl3, Irg1, and Lipg were specifically downregulated in the TLR3KO PMCECs, while the genes Oas2, Slfn4, Trim30a, and Gbp9 were downregulated in the IPS-1KO PMCECs.

Conclusions: Conclusions: Our findings show that murine CECs contribute to the antiviral response through TLR3 and IPS-1 signaling, thus suggesting that both immune cells and CECs play an important role in innate immunity, and that TLR3 and IPS-1 may possibly regulate genes involved in different viral response pathways.

CONTROL ID: 3708428

SUBMITTER (NAME ONLY): Elena Solfato

TITLE: Nanostructured microemulsion systems (NaMESys) for Sorafenib delivery to the posterior segment of the eye

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Solfato, I. Abbate, D. Spina, A. Pricoco, F. Giuliano, M.G. MAZZONE, Research, Preclinical Development and Patents, SIFI SpA, Lavinaio, Sicilia, ITALY|

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ABSTRACT BODY:

Purpose: Overcoming the burden of intravitreal injections represents an unmet need in retinal pharmacotherapy. NaMESys is a novel drug delivery systems composed of monophasic, optically isotropic, thermodynamically stable, clear and self-assembling dispersions formulated by oil, water, surfactants and cosurfactant. Aiming to delivery sorafenib to the posterior segment of the eye, NaMESys formulations were developed and characterized by stability and ocular biodistribution studies after single dose administration.

Methods: NaMESys containing sorafenib were prepared by self-assembling method (phase titration method). The performance of preparations by means of stability and pharmacokinetic profile was evaluated. Long term (36 month 25±2°C/60±5%RH) and accelerated condition (6 month 40±2°C/75±5%RH) stability studies were conducted, chemical-physical parameters were evaluated at different time points. Bioavailability study in NZW rabbits (n=6 per time point) after single dose administration (50µL topical administration in the right eye) was conducted and sorafenib ocular distribution at t= 5, 15, 30, 60, 90, 120 min was quantified by LC-MS.

Results: Long-term and accelerated stability data showed a stable profile of all chemical-physical parameters under study. The droplet size of the dispersed phase is equal or less than 30 nm with a very low polydispersity and the recovery percentage of sorafenib is within specification limits (95-105%) for all formulations. Biodistribution study showed that sorafenib was detected in cornea, vitreous, conjunctivae and sclera but not in the aqueous humor of the treated eye neither in tissues of the contralateral eye. In retina of treated eyes, sorafenib maximum content (170 ±80 ng/g) was observed 5 min after treatment and decreased rapidly 2h post dose and was not quantified in left untreated eye. Sorafenib was not detected in plasma between 5 min to 30 min post dose, maximum content was observed 2h after treatment.

Conclusions: NaMESys was shown to allow topical delivery of poorly water-soluble drugs, such as sorafenib, increasing their penetration and bioavailability to the ocular posterior segment otherwise possible only by intravitreal injection. Data highlight a strong stability profile endowed with a low droplet size distribution guaranteeing a 36-month shelf life. NaMESys promises to be a tool to improve delivery strategies in retinal pharmacotherapy.

CONTROL ID: 3708429

SUBMITTER (NAME ONLY): Sjoerd Driessen

TITLE: Risk factors for compliance to medication in African glaucoma patients

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Nelson-Ayifah, A. Ampong, Ophthalmology, Komfo Anokye Teaching Hospital, Kumasi, Ashanti, GHANA|D. Nelson-Ayifah, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|P.W. Bonnemaijer, Ophthalmology, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|S. Driessen, C.C. Klaver, Opthalmology/Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|A.A. Thiadens, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Ghana has the highest rate of glaucoma in the world, often resulting in blindness. We aimed to investigate therapy compliance and identify associated risk factors in Ghanaian glaucoma patients to define targets for functional improvement.

Methods: A total of 468 patients visiting the eye clinic of the Komfo Anokye Teaching Hospital who were treated with at least one type of glaucoma medication were included in this study. Therapy compliance was determined using the Simplified Medication Adherence Questionnaire (SMAQ); potential risk factors for compliance such as socio-economic and treatment-related characteristics were assessed with structured questionnaires and analyzed using multivariate logistic regression.

Results: 195 (41.7%) patients were labeled as non-compliant to their glaucoma treatment regimen. Compliance was significantly associated with higher age (OR, 1.03; 95% CI, 1.01-1.04; $P<0.01$) and monthly prescription costs (OR/USD increase, 1.02; 95% CI, 1.00-1.03; $P<0.05$). Patients were less compliant when they were treated for more than 2 years (OR, 0.54; 95% CI, 0.33-0.91; $P<0.05$) or when they had difficulty with applying eye drops (OR, 0.45; 95% CI, 0.23-0.87; $P<0.05$). Awareness of glaucoma was poor in this population; 211 (45.1%) patients were not convinced that ceasing medication could lead to blindness.

Conclusions: Therapy compliance in this African population of glaucoma patients was poor. Here, the most important risk factors for non-compliance were young age, low prescription costs, long duration of treatment, and difficulty with application of eye-drops.

CONTROL ID: 3708430

SUBMITTER (NAME ONLY): Christian Grefkes

TITLE: Brain responsivity in visual cortex is linked to visual field deficits in acute stroke patients

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Grefkes, C. Tscherpel, Department of Neurology, University Hospital Cologne, Cologne, GERMANY|C. Grefkes, Institute of Neuroscience and Medicine, Jülich Research Center, Juelich, GERMANY|M.M. Hermann, Department of Ophthalmology, University Hospital Cologne, Cologne, GERMANY|

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ABSTRACT BODY:

Purpose: Neural reorganization following lesions of the central visual system and the mechanisms enabling recovery of visual function are still poorly understood. We here combined transcranial magnetic stimulation (TMS) and electroencephalography (EEG) to directly assess visual cortex function in stroke patients in order to non-invasively capture lesion-induced alterations in neural signal processing as well as their associations to visual field deficits.

Methods: We employed neuronavigated TMS-EEG over primary visual cortex (V1) of the lesioned and the intact hemisphere (120 single TMS pulses per hemisphere at 80% maximal stimulator output) in 10 patients with hemi- or quadrantanopia due to ischemic stroke in occipital cortex. TMS-evoked EEG potentials were recorded using a TMS-compatible 64-channel EEG system. Preprocessing and data analyses, i.e., global mean field power, time-frequency analysis, and phase locking value, were performed using in-house MATLAB scripts based on functions of the open-source toolbox EEGLAB.

Visual field deficits were quantified using an Octopus 900 perimeter and PeriData. Mean defects (MD) were computed for each visual hemifield averaged across both eyes to quantify the homonymic deficit, and subsequently correlated with TMS-EEG parameters.

Results: TMS-EEG revealed signal alterations in the time and time-frequency-domain of ipsilesional as well as contralesional V1 in the acute phase after stroke. This indicates not only changes of neuronal processing in the ischemic area but also in contralateral brain regions that are functionally connected, yet structurally intact. Interestingly, when analyzing the local spreading of induced activity, we found a shorter time course of significant coupling in the contralesional hemisphere ($p=0.029$), which was directly linked to visual field deficit ($r=-0.771$ $p=0.036$). Moreover, stronger alterations of the TMS-evoked oscillatory activity in both hemispheres were associated with more pronounced visual field deficits (ipsilesional: $r=0.78$, $p=0.033$; contralesional: $r=0.829$ $p=0.021$).

Conclusions: Brain responsivity parameters as assessed by TMS-EEG are linked to visual field deficits in stroke patients. Hence, TMS-EEG does not only present a novel tool to assess central visual system integrity, but may also help to uncover brain mechanisms driving functional compensation following lesions to the visual system.

CONTROL ID: 3708431

SUBMITTER (NAME ONLY): Ebenezer Daniel

TITLE: Prevalence and Factors Associated with Optic Disc Gray Crescent in the Primary Open-Angle African American Glaucoma Genetics (POAAGG) Study

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Daniel, J. Gao, Y. Chen, R. Salowe, V. Addis, Q.N. Cui, H.V. Gudiseva, P. Sankar, G. Ying, J. O'Brien, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the prevalence and factors associated with optic disc Gray Crescent (GC) in African Americans with primary open-angle glaucoma.

Methods: Two experienced readers independently graded quantitative features of the optic disc in stereo color images, including GC (Figure 1), cup shape and depth, tilt, sloping of the retina to the outer rim border, beta peri-papillary atrophy, baring of lamina cribrosa and circumlinear vessels, bayoneting, , Cilio-retinal vessels, notching, and pallor of the disc rim. Differences were adjudicated by an ophthalmologist. Univariable and multivariable logistic regression modelling through backward variable selection were performed to identify risk factors of GC. Generalized estimating equation was used to account for the inter-eye correlation.

Results: The multivariable results are shown in the Table. Among 1437 glaucoma subjects, 272 (18.9%) had GC, including 11.7% % unilateral and 7.2% bilateral. Among 2759 eyes, 376 (14%) had GC. Adjusted Odds Ratio (aOR) with 95% CI was 0.77 (0.68, 0.87) for every age decade ($p<0.001$) and 1.62 (1.23,2.12) for subjects with diabetes. Among 2759 glaucoma eyes, 376 (14%) had GC. The aOR with 95% CI was 1.86 (1.41, 2.47) for stereoscopically identified disc tilt ($p<0.001$), 1.81 (1.41, 2.32) for sloping of the retina towards the disc outer rim ($p<0.001$), and 1.30 (1.01, 1.68) for vessel bayoneting ($p=0.04$) (Table).

Conclusions: Unilateral gray crescent is not uncommon in African Americans with open-angle glaucoma. Diabetes and several ocular features are associated with GC.

CONTROL ID: 3708433
SUBMITTER (NAME ONLY): Jem Martin
TITLE: Application of Rasch analysis to the TeachCVI survey tool in a spectrum of CVI patients
SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: J. Martin, S. Yee, N. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|C. Bradley, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|
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ABSTRACT BODY:
Purpose: Cerebral visual impairment (CVI) is the leading cause of visual impairment in children. Given the diversity of clinical presentations of CVI, we are interested in whether questionnaires appropriately target the spectrum CVI cases, specifically the TeachCVI Screening Tool. Rasch analysis is a common psychometric technique for assessing the targeting of questionnaire items, however to date, this analysis technique has not yet been applied to this questionnaire.
Methods: We performed a retrospective review of clinical CVI cases from the NECO Center for Eye Care and Perkins School for the Blind from January 1, 2016 to December 31, 2021. Electronic medical records were reviewed to identify patients with an ICD-9 or ICD-10 code of CVI or other neurological visual impairment. Age, gender, diagnoses, visual acuity, contrast sensitivity, visual fields, ocular alignment, and TeachCVI survey responses were collected.
We applied the method of successive dichotomizations, a polytomous Rasch model, to estimate item measures and person measures from the three levels of the TeachCVI survey. Targeting of questionnaire items to the sample population was explored by comparing estimated item measures to person measures. Multiple linear regression was used to determine which factors influence patient functional ability (i.e., person measure).
Results: 102 patients fit our inclusion criteria; 51% were female. The mean (SD) age was 9.49 (5.7) years, with a range of 0 to 33. 8.8% of patients had no impairment, 5.9% only had CVI, 38% had CVI and an ocular impairment, 8.8% had CVI and a physical disability, and 38% were multiply impaired (CVI, ocular, and physical). Mean (SD) visual acuity was 0.40 (0.40) logMAR, mean (SD) contrast sensitivity was 1.58 (0.47) logCS, and 33% had a visual field deficit.
Estimated item measures were well-targeted to the persons: the mean item measure was 0 by convention with an SD = 0.92 logits, and the mean (SD) person measure was 0.27 (1.19) logits. The only statistically significant factor in influencing patient functional ability was the level of impairment, i.e., the presence of multiple comorbidities. Visual acuity, age, gender, contrast sensitivity and visual field loss were not statistically significant.
Conclusions: This study shows that TeachCVI surveys are well targeted and are appropriate screening tools for CVI.

CONTROL ID: 3708434

SUBMITTER (NAME ONLY): Paras Vora

TITLE: Novel Camera Device for Enhanced Stereoscopic Ophthalmology Exams and Teaching

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Vora, J. Bader, E. Higgins, A. Bastos de Carvalho, Ophthalmology and Visual Sciences, University of Kentucky, Lexington, Kentucky, UNITED STATES|A. Bastos de Carvalho, Ophthalmology, Hôpital de l'Université d'État d'Haiti, Port-au-Prince, HAITI|

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ABSTRACT BODY:

Purpose: Stereo vision is a vital aspect of ophthalmic exams and diagnosis of ocular disease. Limited options exist to extend stereo viewing for use in real-time ophthalmic education and remote consultation. We aimed to develop a novel stereoscopic device prototype using virtual reality (VR) headsets to allow for 3D live streaming of ophthalmic exams, with intention for low-cost, adaptable use in education, outreach, and consultation

Methods: Color cameras (See3CAM-CU135 by e-consystems),13.0 MP, 60 fps, were mounted to slit-lamp oculars in an ophthalmic exam room, using custom mounting hardware. The slit-lamp operator and an in-room observer each wore customized VR headsets of varying resolution (Operator: 4k, observer: Smartphone),. while a slit lamp exam of the anterior segment and external anatomy was performed in multiple test iterations. Live video of the slit lamp exam was fed via USB-C cables to a laptop. Using Open Broadcasting Software, the side-by-side 3D live video feed from each slit-lamp camera was optimized and securely streamed to the VR headsets worn by the slit lamp operator (streamed via HDMI) and the in-room observer (streamed via the VR's smartphone WiFi).

Results: A stereoscopic Prototype A Teleophthalmology Device was developed and provided high-quality, real-time, dynamic, and replicable 3D visualization of the anterior segment and external anatomy to the slit-lamp operator and in-room observer. Advantages of the device included ease of set-up, reliable stereopsis, low cost of development, and wide availability of device components. Limitations of the prototype included wired connections to computer and operator VR headset, intermittent feed latency, exposure variability, and intermittent user disorientation before adaptation.

Conclusions: The Prototype A Teleophthalmology Device is a visual communication system developed to capture and distribute 3D exam imaging among providers and trainees to enable diagnosis, consultation, and educational goals. Widespread availability of device components allow for low-cost, adaptable use, including for teaching and consultation in low-resource environments. Additional optimization and study of the prototype in the clinical environment is needed to further establish its utility and to assess performance parameters.

CONTROL ID: 3708436

SUBMITTER (NAME ONLY): Noémie Bonneau

TITLE: Effects of CX3CR1 deficiency on trigeminal cell death in an in vitro Toxicity-Induced Dry Eye model

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Bonneau, C. Guerin, Horus Pharma, Saint-Laurent-du-Var, FRANCE|N. Bonneau, F. Brignole-Baudouin, S. Melik-Parsadaniantz, C. Baudouin, A. Réaux-Le Goazigo, Sorbonne Universite, Paris, Île-de-France, FRANCE|F. Brignole-Baudouin, C. Baudouin, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Tear levels of CX3CL1/fractalkine, a chemokine implicated in inflammation, were found increased in dry eye patients. Benzalkonium chloride (BAC) is a well-known preservative used at low doses in eyedrops for which toxic effects on ocular surface were described, mainly based on oxidative stress, apoptosis and chronic inflammation mechanisms. BAC not only alters the ocular surface epithelia but also corneal innervation, emerging from the trigeminal ganglion (TG).

Our aim is to investigate the role of CX3CL1/CX3CR1 axis in an in vitro BAC Toxicity-Induced Dry Eye (TIDE) model on a TG cell culture, in relation with the cell death mechanisms induced, apoptosis, ferroptosis, and pyroptosis.

Methods: We established a reproducible method for primary cultures of TG from wild type (WT) or CX3CR1-KO mice. We investigated the modulation of oxidative stress (CellRox assay, HO1), apoptosis (CASP3), ferroptosis (GPX4) and pyroptosis (NLRP3, GSDM) after exposure to a low concentration (5.10^{-4}%) of BAC. A RT-PCR gene expression kinetic study (1h, 2h, 4h, 6h, 8h and 24h of BAC exposure) and western blot analysis were conducted.

Results: We found that BAC-induced oxidative stress was reduced at 4h, correlated to a major increase (from 2h to 24h) of HO-1 gene expression in CX3CR1-KO compared to WT. Moreover, GPX4 protein, known to protect against ferroptosis, was depleted at 2h, its gene expression being only upregulated at 1h and 2h in presence of CX3CR1. The increase of CASP3 gene expression was delayed in CX3CR1-KO mice (6h instead of 2h in WT). As for inflammatory cell death processes, NLRP3 inflammasome and GSDM pyroptosis modulator regulations occurred at later time points and were more important in presence of CX3CR1. Indeed, NLRP3 gene expression was upregulated at 24h only in WT whereas GSDM gene expression and protein level were increased at 6h only in WT. Nevertheless, GSDM gene expression at 24h was increased in both WT and CX3CR1-KO mice.

Conclusions: We confirm that BAC induces not only apoptosis but also other emerging cell death mechanisms with key events occurring in a kinetic manner as follows: 1. oxidative stress, 2. apoptosis, 3. inflammasome activation and pyroptosis. In absence of CX3CR1, oxidative stress is reduced and this effect impacts the subsequent cell death mechanisms. Further studies are needed to deepen the exact role of CX3CR1 axis on cell death mechanisms involved in TIDE.

CONTROL ID: 3708439
SUBMITTER (NAME ONLY): Julian Perrin
TITLE: Functional analysis of a zebrafish knockdown of the optic atrophy-associated gene ssbp1
SESSION TITLE: Retinal ganglion cells
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Perrin, V. Gisbert, M. Pequignot, C. Delettre, INSERM U1298, Institut des Neurosciences de Montpellier, Montpellier, Occitanie, FRANCE|N. Cubedo, M. Rossel, INSERM U1198, Mecanismes moleculaires dans les demences neurodegeneratives, Montpellier, Occitanie, FRANCE|
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ABSTRACT BODY:

Purpose: Dominant Optic Atrophy (DOA) is characterized by degeneration of the retinal ganglion cells (RGC) that can lead to vision loss for which there is no treatment. The optic atrophy (OA) can be isolated or syndromic: OA associated with sensorineural deafness, myopathy, etc. DOA is caused by mutations in genes with a mitochondrial function. The underlying pathophysiology remains to be understood.

The single strand DNA-binding protein 1, SSBP1 gene was recently identified for causing DOA. SSBP1 tetramers bind mitochondrial DNA (mtDNA) and is essential for mtDNA replication. Our purpose is to shed light on the pathophysiological consequences of ssbp1 alteration in a zebrafish model.

Methods: A knockdown (KD) of ssbp1 in zebrafish was generated by microinjection of translation blocking morpholino (MO-ssbp1) in Zebrafish embryo. Fish injected with Standard-MO designed to have no impact in zebrafish and non-injected zebrafish were used as controls. KD was validated by Western Blot analysis of Ssbp1.

The transgenic zebrafish line tg(Brn3c:mGFP) labeling RGC and ON was used throughout this study. Confocal microscopy and the IMARIS software were used to generate 3D reconstruction of the optic nerve GFP labeling. Sensorimotor responses were investigated using either Visual Motor Response assay (VMR) to measure the locomotor response to a visual stimulus (traveled distance measurement) or Auditory Startle Response (ASR) to measure motility after acoustic and vibration stimuli.

Results: ON morphology analysis revealed an atrophy of the ON in 2dpf ssbp1 KD zebrafish, with a significant reduction of its volume.

A significant decrease of the traveled distanced by 5dpf MO-ssbp1 fish was found in both light and dark stimuli conditions using VMR assay. However, the ability to perceive differences in bright light stimulation did not seem impaired in MO-ssbp1.

A diminution of motility of 5dpf MO-ssbp1 was also found using the ASR assay and preliminary result show a decrease of startle response induced by sound and vibration stimuli.

Conclusions: ssbp1 KD in zebrafish revealed an optic nerve atrophy at 2 dpf which could indicate that ssbp1 is important for ON development. This result did not translate to bright light perception defect in 5dpf ssbp1 KD fish. Moreover, the KD caused an overall diminution of the traveled distance that could reflect locomotion defect as well as a likely alteration of sound and vibration perception.

CONTROL ID: 3708448
SUBMITTER (NAME ONLY): Julia Schottenhamml
TITLE: Unsupervised OCT Denoising using speckle split
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Schottenhamml, T. Würfl, S.B. Ploner, L. Husvogt, A. Maier, Pattern Recognition Lab, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|J. Schottenhamml, B. Hohberger, Department of Ophthalmology and Eye Hospital, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|L. Husvogt, J.G. Fujimoto, Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: Julia Schottenhamml: Commercial Relationship: Code N (No Commercial Relationship) | Tobias Würfl: Commercial Relationship: Code N (No Commercial Relationship) | Stefan Ploner: Commercial Relationship(s);Code P (Patent):IP related to VISTA-OCTA | Lennart Husvogt: Commercial Relationship: Code N (No Commercial Relationship) | Bettina Hohberger: Commercial Relationship: Code N (No Commercial Relationship) | James Fujimoto: Commercial Relationship(s);Code I (Personal Financial Interest):Optovue;Code P (Patent):Optovue;Code P (Patent):Carl Zeiss Meditec;Code P (Patent):IP related to VISTAOCTA;Code C (Consultant/Contractor):Optovue;Code F (Financial Support):Topcon | Andreas Maier: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:
Purpose: Optical coherence tomography (OCT) scans are often degraded by noise, which complicates further analysis. We demonstrate an unsupervised denoising method that uses OCT angiography (OCTA) information to keep the informative speckle used for OCTA computation and removes flow-unrelated speckle noise. Qualitative and user-study analyses demonstrate noise removal and improved sharpness compared to other unsupervised denoising methods.
Methods: In a first step, a U-Net is trained via unsupervised Noise2Void (N2V) to denoise OCTA B-scans. In a second step, a second U-Net is trained via N2V on OCT B-scans. A constraint in the loss function ensures that the OCTA image computed from two denoised OCT B-scans is similar to the denoised OCTA B-scans from the first step. The workflow of this algorithm is depicted in Figure 1. The training/test set consisted of 90/18 measurements (with 500 B-scans per volume and 2 volumes per patient) from 30/9 patients. Field sizes included 3x3 mm and 6x6 mm areas around the fovea and included various pathologies (choroidal neovascularization, diabetes mellitus without diabetic retinopathy (DR), non-proliferative DR, proliferative DR, early age-related macular degeneration, geographic atrophy, non-arteritic anterior ischemic optic neuropathy and healthy controls). We compared our method (speckle split N2V (SSN2V)) to other unsupervised denoising algorithms (N2V (without the constraint), BM3D, TV, WNNM). A user study was performed on the test set. One expert ophthalmologist graded 35 randomly selected B-scans and the results of the denoising algorithms from 0 (does not like the image) to 5 (likes the image).
Results: The user study shows that the clinical expert preferred the results produced by our proposed algorithm (input: 1.11±0.622; BM3D: 2.2±0.92; TV: 2.74±0.73; WNMM: 3.37±0.93; N2V: 1.51±0.77; SSN2V: 4.09±0.87). Qualitative results of the results of the different denoising algorithms are shown in Figure 2.
Conclusions: Using the additional constraint for the unsupervised OCT denoising improves the denoising capability and performs superior to the compared methods in an expert user study.

CONTROL ID: 3708452

SUBMITTER (NAME ONLY): Tiarnan Keenan

TITLE: Adherence to the Mediterranean Diet and Geographic Atrophy Enlargement Rate in the Age-Related Eye Disease Study 2

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.D. Keenan, E. Agron, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|J.A. Mares, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Tiarnan Keenan: Commercial Relationship: Code N (No Commercial Relationship) | Elvira Agron: Commercial Relationship: Code N (No Commercial Relationship) | Julie Mares: Commercial Relationship: Code N (No Commercial Relationship) | Emily Chew: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: No approved treatments exist to slow geographic atrophy (GA) enlargement. The aim was to determine whether closer adherence to a Mediterranean diet (and its individual components) was associated with altered speed of GA enlargement.

Methods: The design was a cohort study within the AREDS2 clinical trial. The study population comprised 1155 eyes (of 850 participants, mean age 74.9 years) with GA at two or more consecutive visits. GA area was measured by planimetry from color fundus photographs collected at annual study visits. A modified Alternative Mediterranean Diet Index (aMedi) score was calculated for each participant by food frequency questionnaire at baseline. Mixed-model regression analyses of square root GA area were performed according to aMedi. The outcome measure was change in square root of GA area over time.

Results: Over mean follow-up of 3.1 years from first appearance of GA, the mean GA enlargement rate was 0.282 mm/year (95% confidence interval 0.270-0.293). GA enlargement was significantly slower in those with higher aMedi, at 0.256 mm/year (0.236-0.276), 0.290 (0.268-0.311), and 0.298 (0.280-0.317; P=0.008), for aMedi tertiles 3, 2, and 1, respectively. Of the nine aMedi components considered separately, significant differences in GA enlargement rate were observed for four: whole fruit (P = 0.0004), red meat (P = 0.0002), alcohol (P = 0.006), and monounsaturated: saturated fatty acid (MUFA: SFA; P = 0.040). GA enlargement was slower in those with higher whole fruit, lower red meat, moderate alcohol, and higher MUFA: SFA intake (Table).

Conclusions: A Mediterranean-type diet was associated with slower GA enlargement. Such diet patterns may therefore lead to clinically meaningful delays in vision loss, particularly for individuals without foveal involvement. Several components contributed most to this protective association, in a pattern that differed from those most associated with decreased progression to GA. Hence, the Mediterranean diet is associated with protection against both faster progression to GA and faster enlargement of GA, but for partially distinct reasons. Understanding the mechanisms responsible may provide insights into the underlying biology and lead to the development of dietary recommendations and nutritional supplements.

CONTROL ID: 3708453

SUBMITTER (NAME ONLY): Ziming Luo

TITLE: Understanding RGC differentiation and development in retinal organoids by scRNA-seq

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Luo, K. Chang, B. Tanasa, J.L. Goldberg, Spencer Center for Vision Research, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) replacement therapy could provide an approach to vision restoration in glaucoma and other optic neuropathies. RGCs generated from retinal organoids are promising donor cells. The present research aims to understand how organoid RGCs (oRGCs) differ from human fetal RGCs.

Methods: We generated retinal organoids from Brn3b-tdTomato-H9 hESC line. Then, we utilized single cell-RNA sequencing (scRNA-seq) to delineate the oRGC differentiation and compare their transcriptomic profiles to human fetal RGCs. EdU incorporation assays were used to visualize the newly born oRGCs in retinal organoids of different developmental stages. All experiments were conducted at least three times independently. Data were analyzed by ANOVA and post-hoc t-test with Tukey correction, with a P-value of <0.05 considered statistically significant.

Results: At early developmental stages, oRGCs had similar expression patterns to fetal RGCs in corresponding timepoints. By UMAP plotting and pseudotime analyses, we found oRGCs overlapped with fetal RGCs at earlier time points. However, with ongoing development, RGC numbers decreased rapidly in retinal organoids, and their transcriptomes diverged from fetal developmental patterns. Transcripts from neurofilament genes were relatively low and did not increase along developmental time in oRGCs, but were highly expressed in adult RGCs. Moreover, POU4F2 (Brn3b) expression in oRGCs was maintained at a high expression level for a longer time, while in fetal RGCs, Brn3b was significantly downregulated with maturation. Interestingly, RBPMS, an RGC-specific marker, was barely expressed in organoid RGCs. EdU incorporation assays revealed that oRGC generation slowed down around the 10^{th} week of differentiation, coming nearly to a complete halt by the 15^{th} week in retinal organoids.

Conclusions: In the present study, we describe the transcriptomic differences between oRGCs and fetal RGCs, providing substantial insight into towards stem cell-derived RGC development, towards enhancing our understanding of stem cell differentiation and in the future, stem cell-based therapeutic interventions towards restoring vision in human disease.

CONTROL ID: 3708456

SUBMITTER (NAME ONLY): ines hernanz

TITLE: Sulfasalazine on the course of recurrent anterior uveitis: three-year effectiveness

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. hernanz, M. Fernandez Gurria, F. vicente abreu, O. Olivas, C. arconada, O. Sánchez-Pernaute, E. Carreno, Hospital Universitario Fundacion Jimenez Diaz, Madrid, Madrid, SPAIN|I. Robles Barrena, Universidad Rey Juan Carlos, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the efficacy of sulfasalazine (SSZ) for recurrent acute anterior uveitis (AAU) in a cohort of Spanish patients.

Methods: Retrospective chart review of patients diagnosed with recurrent AAU treated with SSZ from January 2008 to December 2021. The grading of uveitis activity was defined as per SUN working group. The major outcome was the reduction in the number of uveitis flare-ups over a one-year and three year-period, compared to pretreatment year. The response criteria of SSZ were defined as normal ophthalmologic examination. Mann-Whitney Paired samples Wilconxon test U testand Kaplan-Meier survival curve were calculated using SPSS statistical software ($p < 0,05$).

Results: Thirty-three patients were included, (males =17; 51,5%). The mean age at the beginning of SSZ was 42 years old (range 22-73, SD= 11.3) and at uveitis onset was 37 years old (range 18-54, SD= 10.1). Mean time of follow up was 48.3 months (range 2-270, SD= 58.75). In 60.6 % of cases (n=20) uveitis was bilateral. Two patients (6.1%) presented with associated macular edema. One patient developed hypertransaminasemia (3%) and two patients showed leukopenia (6.1%). Three patients (9%) had to interrupt SSZ due to clinical inefficacy. Ankylosing spondylitis was the most frequent association (n=18, 54.5%), followed by idiopathic juvenile arthritis (n=2, 6.1%). 8 patients (24.2%) were not related to immune-mediated disease. HLA-B27 was positive in 66.7% (n=22). Indication for SSZ was based on ocular activity in 36.4 % (n=12), joint activity in 36.4% (n=12) or both in 24.2 % (n=8). At the time of SSZ onset, 97% of patients (n=32/33) were on systemic steroids and 48% (n=16/33) on topical steroids; and 3% (n= 1/30) and 20% (n= 6/29), respectively at one year. Four patients (12%) had started SSZ associated with other immunomodulators. The mean number of flare-ups in the pretreatment year was 1.9 (SD 1.4), at one year 0.7 (SD=0.95) with statistical significance (p=0.02), and at third year 1.0 (SD 1.0) with no significance (p=0.10). The mean time to flare-up of AAU after SSZ was 53.5 moths (IC 95%, Range: 23.3-83.8).

Conclusions: We suggest sulfasalazine as an effective treatment to reduce flare-ups in patients with recurrent non-infectious AAU of different etiologies. Its low cost and high safety profile make it an interesting therapeutic alternative, especially in women of childbearing age

CONTROL ID: 3708457

SUBMITTER (NAME ONLY): Anthony Marte

TITLE: Gender Trends in Visiting Lectures at Ophthalmology Programs in the United States

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Marte, J. Rosenberg, W. Yao, Department of Ophthalmology and Visual Sciences, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|A. Adebayo, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The current rate of female ophthalmologists in the United States is 26.7%. Gaps in female representation still exist in ophthalmology with regards to appointment of senior faculty positions and chairpersons. Invited lectures are an important factor in career advancement. This report examines the gender differences in faculty invited to give visiting lectures at top ophthalmology programs in the United States.

Methods: This retrospective observational study analyzed the invited lectures at 20 ophthalmology programs from January 2019 - June 2022. The top 20 institutions on the Doximity Residency Navigator reputation ranking were selected for inclusion in this study. Institution websites were queried for ophthalmology lecture events. Examples include grand rounds lectures, eponymous visiting professor lectures, and featured presentations at institutional conferences. The names, years since completion of training, and genders of visiting faculty were recorded. Chi-square test and student t-test were used for data analysis. Primary analysis focused on the proportion of female invited lectures.

Results: Of the 20 institutions selected, 13 had publicly-available information on their websites about their lectures, which yielded a sample size of 200 invited lectures. Of those 200 lectures, 29.5% were given by female faculty members, which was similar to the ratio of female ophthalmologists ($p=0.8750$). When examining only the eponymous lectureships, there was a trend toward fewer women, with only 2 of the 20 listed given by women, although the comparison with overall rates of women in ophthalmology was not statistically significantly different ($p=0.4075$). Female lecturers were found to have completed their training more recently than non-female lecturers on average, 2002 compared to 1995 ($p < 0.001$).

Conclusions: Overall, female representation in the invited lectures of our sample matches overall female representation in ophthalmology. The more prestigious eponymous lectureships did show a trend toward fewer women, although it was not statistically significant. It is possible that a larger sample size would show a statistically significant difference in this type of lecture. Future research should focus on both identifying gender ratios and in determining best practices for rectifying any discrepancies.

CONTROL ID: 3708459

SUBMITTER (NAME ONLY): Manisha Parikh

TITLE: Risk Factors for Meibomian Gland Morphology Changes in Children Aged 4 to <18 years

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Parikh, Y. Pang, L. Sicks, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the meibomian gland (MG) morphology (atrophy and tortuosity) in children aged 4 to <18 years. In addition, risk factors were identified for MG atrophy and tortuosity.

Methods: A total of 160 children (4 to 18 years) presenting at the Illinois Eye Institute from Sep 2020 to July 2021 were recruited into the study. All children had a comprehensive eye exam as well as height/weight was measured for BMI. Tear film parameters was collected with the Keratograph 5M (Oculus), including non-invasive tear film break-up time and tear meniscus. The upper and lower eyelids were everted and the meibomian glands imaged with the Keratograph 5M (Oculus). MG dropout scores were assessed by two masked graders using a validated 4-point JENVIS scoring system. Tortuosity of MG were evaluated by two masked graders using a 5-point HALLERAN scoring system. Both children and their parents were surveyed on electronic screen time, diet, and outdoor activities. To determine relationships between MG morphology and potential risk factors (including age, gender, race/ethnicity, refractive error, screen time, diet, outdoor activities, and BMI), linear multiple regression analyses were performed.

Results: Among 160 children recruited into the study, 76 were males and 84 were females (mean age = 10.9 years, ranged from 5.7 to 17.8). Mean tear meniscus were 0.23mm and 0.36mm, OD and OS respectively. Mean NI-TBUT were 15.60 sec and 15.96 sec, OD and OS, respectively. Severe MG atrophy (MG score of 2 or greater) presented in children: 6.8% of upper eyelid OD, 19.7% of lower eyelid OD, 5.6% of upper eyelid OS, and 19.7% of lower eyelid OS. Severe MG tortuosity (Score of 2 or higher) presented in children: 72.7% of upper eyelid OD, 3% of lower eyelid OD, 65.6% of upper eyelid OS, and 4.4% of lower eyelid OS. Significant risk factors for MG atrophy and/or tortuosity were identified including BMI (OD MG atrophy: $\beta=0.36$, $p < 0.001$, OS MG atrophy $\beta=0.25$, $p=0.007$), diet (lower eyelid tortuosity: $\beta=0.23$, $p = 0.011$), and outdoor activity (OD MG atrophy: $\beta= -0.21$, $p = 0.022$). No association was found between MG morphology and screen time.

Conclusions: High BMI, decreased outdoor activities, and unhealthy diet are the significant risk factors for the MG morphology change in children aged 4 to 18 years. Eye care practitioners should consider evaluating MG morphology routinely in children during eye exam.

CONTROL ID: 3708460

SUBMITTER (NAME ONLY): Grace Baldwin

TITLE: Structure-Function Associations between Novel Contrast Sensitivity Function (CSF) Testing and Widefield Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA) in Diabetic Macular Edema (DME)

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Baldwin, F. Vingopoulos, I. Garg, J.Y. Moon, R. Zeng, Y. Cui, R. Katz, R. Le, E.S. Lu, D.N. Sayah, Z. Hassan, J.B. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|G. Baldwin, F. Vingopoulos, I. Garg, J.Y. Moon, R. Zeng, E.S. Lu, D. Husain, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Cui, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|R. Le, Wenzhou Medical University Affiliated Eye Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|

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ABSTRACT BODY:

Purpose: To elucidate the relationship between CSF and WF SS-OCTA metrics in patients with DME.

Methods: This cross-sectional prospectively recruited observational study included 53 eyes of 37 patients with DME imaged with WF SS-OCTA (PLEX® Elite 9000, Carl Zeiss Meditec) and tested for CSF with the Active Learning Quantitative CSF (qCSF) Manifold Contrast Vision Meter (Adaptive Sensory Technology) from November 2018 to March 2021. Functional outcomes included Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity (VA), and the following qCSF metrics: Area under the Log CSF (AULCSF), contrast acuity (CA), and contrast sensitivity thresholds at 1 to 18 cycles per degree (cpd). The ARI Network (Zeiss Portal v5.4) was used to quantify vessel density (VD) and vessel skeleton density (VSD) in the superficial (SCP) and deep (DCP) capillary plexus and whole retina, as well as foveal avascular zone (FAZ) area, circularity, and perimeter on 3x3 mm, 6x6 mm, and 12x12 mm OCTA images. Mixed effects multivariate regression analyses were performed.

Results: In our DME cohort, VA and contrast sensitivity (CS) outcomes were strongest associated with vascular metrics measured on 3x3 mm OCTA images compared to 6x6 mm and 12x12 mm images. While controlling for age and lens status, regression analyses revealed worse LogMAR VA was significantly associated with decreased SCP VD ($\beta = -0.049$, $p = 0.026$) and VSD ($\beta = -2.562$, $p = 0.026$) on 3x3 mm images. Among the CS outcomes, decreased AULCSF, CA, and CS thresholds at 1.5, 3, and 6 cpd were significantly associated with decreased SCP VSD ($\beta = 3.533$, $p = 0.020$; $\beta = 2.826$, $p = 0.029$; $\beta = 2.629$, $p = 0.035$; $\beta = 3.590$, $p = 0.033$; $\beta = 4.672$, $p = 0.023$, respectively). Decreased CS thresholds at 6 cpd was also significantly associated with SCP VD ($\beta = 0.080$, $p = 0.043$). While VA was not significantly associated with FAZ circularity, decreased CS thresholds at 1 and 1.5 cpd were significantly associated with decreased FAZ circularity ($\beta = 0.567$, $p = 0.028$; $\beta = 0.669$, $p = 0.026$, respectively).

Conclusions: We demonstrate novel structure-function associations in patients with DME leveraging a novel CSF device and WF SS-OCTA. Our results suggest that decreases in VD and VSD in the SCP of DME patients may be associated with larger changes in contrast sensitivity than in VA.

CONTROL ID: 3708461

SUBMITTER (NAME ONLY): Meredith Weksler

TITLE: Model development of VEGF challenge in miniature swine

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Weksler, A. McDougal, T. Pegoraro, S. Williams, M.A. deLong, C. Kopczynski, D. Hollander, J.C. White, Aerie Pharmaceuticals Research and Development, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Meredith Weksler: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | Alan McDougal: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | Tyler Pegoraro: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | Stuart Williams: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | Mitchell deLong: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | Casey Kopczynski: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | David Hollander: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals | Jeffrey White: Commercial Relationship(s);Code E (Employment):Aerie Pharmaceuticals

ABSTRACT BODY:

Purpose: The Vascular Endothelial Growth Factor (VEGF) challenge model first developed by Edelman et. al.[1], is routinely used in the rabbit to evaluate the potential of therapies for ocular diseases such as neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), and retinal vein occlusion (RVO). Compared to the rabbit, the minipig is a useful species for evaluating intravitreal ocular therapies due to the size, fluid dynamics, and vasculature of the minipig eye. We have developed an experimental VEGF challenge model for use in the Yucatan minipig to evaluate the effect of anti neovascularization therapies on the retina/choroid.

Methods: Yucatan minipigs were injected IVT with a dose range of $VEGF_{165}$. Fluorescein angiography (FA) was used to image the retinal vasculature, and a clinical scoring system was developed to quantify retinal vasculopathy at several timepoints post VEGF challenge. Placebo polymer implants and an Avastin positive control were utilized to assess viability of the model.

Results: An optimal amount of $VEGF_{165}$ was determined that induces significant leakage in the miniature swine, with the ability to induce leakage for up to 5 days post VEGF challenge. The positive control Avastin was able to inhibit the $VEGF_{165}$ induced leakage, while the negative control placebo polymeric implants did not protect against retinal vasculature leakage.

Conclusions: The VEGF challenge model commonly utilized in rabbits can be adapted for use in the Yucatan minipig, a species with more relevant ocular anatomy to humans.

1. Edelman, J.L. Lutz, D., Castro, M.R. Corticosteroids inhibit VEGF-induced vascular leakage in a rabbit model of blood-retinal and blood-aqueous barrier breakdown. Experimental Eye Research, 2005, (80) 249-258.

CONTROL ID: 3708463

SUBMITTER (NAME ONLY): Heonuk Jeong

TITLE: Bunazosin inhibited axial elongation with an increase of the choroidal blood perfusion in a murine model of myopia

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Jeong, T. Kurihara, X. Jiang, K. Negishi, K. Tsubota, Department of Ophthalmology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|H. Jeong, T. Kurihara, X. Jiang, Laboratory of Photobiology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|K. Tsubota, Tsubota Laboratory, Inc, JAPAN|

Commercial Relationships Disclosure: Heonuk Jeong: Commercial Relationship(s);Code P (Patent):Tsubota Laboratory, Inc. | Toshihide Kurihara: Commercial Relationship(s);Code I (Personal Financial Interest):Tsubota Laboratory, Inc., Restore Vision Co., Ltd.;Code P (Patent):Tsubota Laboratory, Inc. | Xiaoyan Jiang: Commercial Relationship(s);Code P (Patent):Tsubota Laboratory | Kazuno Negishi: Commercial Relationship(s);Code F (Financial Support):SEED Co., Ltd.;Code P (Patent):Keio University School of Medicine | Kazuo Tsubota: Commercial Relationship(s);Code F (Financial Support):Tsubota Laboratory, Inc.;Code I (Personal Financial Interest):TissueTech, Inc., Restore Vision Co., Ltd., Tsubota Laboratory, Inc., Cellusion Inc.;Code E (Employment):Tsubota Laboratory, Inc.;Code R (Recipient):Tsubota Laboratory, Inc.;Code P (Patent):Tsubota Laboratory, Inc.

ABSTRACT BODY:

Purpose: The prevalence of myopia is accelerating worldwide possibly because of the decrease in outdoor activity including COVID-19 home confinement. We have reported the effective treatments of suppressing myopia progression, including oral administration of crocetin (Mori K et al. Sci Rep. 2019) and violet light exposure (Jiang X et al. Proc Natl Acad Sci USA. 2021). In this study, we examined the therapeutic effects of bunazosin, known as one of the α1-adrenergic receptor antagonists, in a lens-induced myopia mouse model.

Methods: C57BL/6J mice were induced myopia at 3-week-old by a method established in our research group (Jiang X et al. Sci Rep. 2018). For 3 weeks, mice were equipped with lenses in both eyes, a left for 0 D lens as internal control and a right for -30 D lens as myopia induction. During this period, we administered 0.01% bunazosin hydrochloride solution by intraperitoneal injection (IP group) and eye drop (E group) once a day, and PBS as control. Ocular components including refraction error, axial length, and choroidal thickness before and after myopia induction were measured by an infrared photorefractor and an SD-OCT. The choroidal blood flow was evaluated by an SS-OCT angiography.

Results: In the eye with -30D lens of control group, significant changes in a myopic shift of refraction ($p < 0.01$), axial elongation ($p < 0.05$), and choroidal thinning ($p < 0.01$) compared to 0D lens were observed. In contrast, IP or E groups showed no significant difference between both eyes, suggesting myopia progression was suppressed by bunazosin treatment. The choroidal blood flow of the eye with -30D in E group (58.9±8.9%) was higher than that of the control group -30D (44.0±6.4%)($p < 0.05$).

Conclusions: Bunazosin has a preventive effect on myopia progression by suppressing axial elongation and choroidal thinning together with an increase of choroidal blood flow.

CONTROL ID: 3708464

SUBMITTER (NAME ONLY): Chieko Koike

TITLE: Loss of Trpm1, the gene for the ON bipolar cell transduction channel, in 15q13.3 microdeletion syndrome contributes to central behavioral deficits

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Hori, Graduate School of Pharmacy, Ritsumeikan Daigaku - Biwako Kusatsu Campus, Kusatsu, Shiga, JAPAN|C. Koike, Center for Systems Vision Science, Ritsumeikan Daigaku - Biwako Kusatsu Campus, Kusatsu, Shiga, JAPAN|S. Ikuta, Graduate School of Life Sciences, Ritsumeikan Daigaku - Biwako Kusatsu Campus, Kusatsu, Shiga, JAPAN|S. Hattori, T. Miyakawa, Institute for Comprehensive Medical Science, Fujita Ika Daigaku, Toyoake, Aichi, JAPAN|K. Takao, Department of Behavioral Physiology, Faculty of Medicine, Toyama Daigaku, Toyama, Toyama, JAPAN|K. Takao, Research Center for Idling Brain Science, Toyama Daigaku, Toyama, Toyama, JAPAN|C. Koike, K. Iwao, College of Pharmaceutical Sciences, Ritsumeikan Daigaku - Biwako Kusatsu Campus, Kusatsu, Shiga, JAPAN|

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ABSTRACT BODY:

Purpose: 15q13.3 microdeletion syndrome is characterized by a broad spectrum of psychiatric disorders. Seven genes are located in the target region of chromosome 15 (MTMR10, FAN1, TRPM1, MIR211, KLF13, OTUD7A, and CHRNA7). While the contributions of several of the genes to the disorder have been studied using mutant mouse models, no single mouse model has been able to recapitulate the whole behavioral spectrum of human 15q13.3 microdeletion syndrome. Trpm1, one of the genes located in the target region of 15q13.3 microdeletion syndrome, has been implicated as a retinal ON bipolar cell visual signal transduction channel. Trpm1 has not been investigated concerning this syndrome because the visual impairment in $Trpm1^{-/-}$ mice may confound the results of behavioral tests involving vision. Emphasizing non-visual behaviors, we performed a comprehensive behavioral test battery using Trpm1 null mutant mice to examine the relationship between TRPM1 and 15q13.3 microdeletion syndrome.

Methods: $Trpm1^{-/-}$ mice were generated as described previously [Koike, et al, PNAS 2009]. Mice used for behavioral test battery were housed as pairs of $Trpm1^{-/-}$ and WT mice. Brain weight measurement and monoamine quantification in brain tissues were performed with 129 Sv/Ev males at 4 months or 1 month. Gene expression analysis was performed with 129 Sv/Ev male mice at 1 month. Mice used for monoamine quantification were housed in pairs of $Trpm1^{-/-}$ mice and WT mice, and tissue dissection was performed at the same time-point.

Results: $Trpm1^{-/-}$ mice exhibit abnormal behaviors that may explain some phenotypes of 15q13.3 microdeletion syndrome: including reduced anxiety-like behavior, abnormal social interaction, attenuated fear memory, and, most prominently, hyper locomotor activity. While the ON visual transduction pathway is impaired in $Trpm1^{-/-}$ mice, we did not detect compensatory higher sensitivities for other sensory modalities. The pathway for visual impairment is the same between $Trpm1^{-/-}$ mice and $mGluR6^{-/-}$ mice, but hyper locomotor activity has not been reported in $mGluR6^{-/-}$ mice. Unexpectedly, the data suggest that the phenotype of $Trpm1^{-/-}$ mice extends beyond that predicted from visual impairment alone.

Conclusions: We present the first evidence associating TRPM1 with impairment of cognitive function similar to that observed in phenotypes of 15q13.3 microdeletion syndrome.

CONTROL ID: 3708465

SUBMITTER (NAME ONLY): Marita Feldkaemper

TITLE: Dynamic ON/OFF stimulation changes choroidal thickness in chickens: effects of temporal and spatial frequency

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.P. Feldkaemper, S. Bernhard-Kurz, H. Liu, F. Schaeffel, Centre for Ophthalmology, Institute for Opthalmic Research, Tuebingen, GERMANY|

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ABSTRACT BODY:

Purpose: Imposing defocus on the retina triggers short-term changes in choroidal thickness that are assumed to predict future refractive changes, both in humans and animal models. Artificial visual stimuli, on the other hand, can uncouple choroidal thickness changes from changes in axial eye growth. It is therefore necessary to verify under which conditions thicker choroids can predict less myopia development.

Methods: Seven day old chicks were kept in large plastic boxes (60x60x30 cm) with walls covered with 27” screens. Dynamic stimuli were presented on the screens and were also projected on the floor from above by two video projectors as described by Wang et al. (doi: 10.1167/iovs.18-26471). Checkerboard patterns with squares with repeated sawtooth-shaped temporal luminance profiles, either with a rapid ON or rapid OFF, were presented. Stimuli were applied at 3 different square sizes (68x39, 40x22, 28x16 squares/monitor) in combination with different cycle frequencies (0 Hz, 0.8 Hz, 1.2 Hz, 2 Hz, 3 Hz, 5 Hz, 8 Hz). SD-OCT (HRA+OCT Spectralis) was used to measure choroidal thickness in alert animals at baseline and 3 hours after treatment. A multi-factor ANOVA was used to determine the influence of size, frequency and character (ON/OFF) on choroidal thickness (ChT) changes.

Results: The size of the stimuli had a significant main effect (delta ChT: smallest size: -26.4±1.6 µm, medium size: -6.9±2.14 µm, largest size: -15.1±2.3 µm). Changes in ChT were also significantly influenced by the stimulus frequency with the strongest effect at 3 Hz (-30.2±4.6 µm) and smallest at 2 Hz (-12.1±3.3 µm). The interaction between frequency and size was also significant. Comparing all treatment groups, only one of the stimuli (1.2 Hz ON, medium size) caused an increase in choroidal thickness (+4.75±6.5 µm) while OFF stimuli at this field size and frequency caused the thinnest choroids (-41.6±6.2 µm).

Conclusions: Dynamic artificial stimuli of different frequency, size and ON/OFF characteristic influence choroidal thickness in a complex way. Except for one stimulus (1.2 Hz ON medium size), all others caused choroidal thinning which was partially explained by diurnal choroidal thickness changes during the examination period. Further experiments, using longer stimulation periods, are needed to fully describe the predictive power of choroidal thickness changes on axial eye growth.

CONTROL ID: 3708466

SUBMITTER (NAME ONLY): Megan Haghnegahdar

TITLE: Long-term Outcomes of Alpha Cor Keratoprosthesis For Management Of High-Risk Keratoplasty Patients: Device Retention, Complications, and Snellen Vision

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Haghnegahdar, J.E. Sutphin, K. Goins, Ophthalmology, The University of Kansas Medical Center, Kansas City, Kansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the long-term clinical outcomes of AlphaCor keratoprosthesis implantation through analysis of complications, device retention, and visual outcomes in eight patients.

Methods: This is retrospective chart review of eight patients who received AlphaCor keratoprosthesis between 2004 and 2008. Primary data points collected included presence of ocular surface disease (OSD), post-operative complications, time from device implantation to removal, and best corrected visual acuity (BCVA). OSD was defined as aniridia, chemical or thermal injury, herpetic or microbial keratitis, ocular rosacea, stem cell deficiency, and cicatricial conjunctival disorders. Comparisons between both groups were made using the 2-tailed student's t-Test. P value less than 0.05 was considered statistically significant.

Results: Device retention rate at 1, 5, and 10 years was 87.5%, 50%, and 12.5% respectively. Device retention was decreased in OSD eyes at 67.8 months compared to 92 months in those without OSD ($p = 0.20$). Eyes that were able to achieve surface protection with bandage contact lens wear had a longer mean retention time of 128.5 months compared to those that could not at 55.67 months ($p = 0.16$). Complications included retroprosthetic membrane formation (50%), corneal melt (62.5%), infection (25%), and optic deposits (62.5%). Of the five patients that developed corneal melt around the device, four had OSD. Patients with OSD demonstrated stromal loss sooner postoperatively (51.4 months) compared to the patient without OSD (85 months). Five of the eight patients had the device removed (62.5%). Reasons for removal were stromal melt without associated infection in three patients, melt associated with infection in one patient, and discoloration with poor visual acuity in one patient. Preoperative BCVA ranged from hand motion to 20/100. Four eyes had little change in postoperative BCVA, however Snellen BCVA in the four remaining eyes improved an average of 8.5 lines, with a BCVA range of 20/70 to 20/20 using various contact lenses.

Conclusions: Patients with OSD who have undergone AlphaCor keratoprosthesis implantation are more likely to develop negative outcomes. Modern treatment options, such as serum tears, recombinant human nerve growth factor, and scleral contact lenses may offer a contemporary solution for these patients.

CONTROL ID: 3708467

SUBMITTER (NAME ONLY): Steffen Schmitz-Valckenberg

TITLE: Quantification of lesion progression of incomplete and complete retinal pigment epithelium and outer retinal atrophy in age-related macular degeneration

SESSION TITLE: AMD Imaging

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To quantify changes of individual early atrophic features over time that are part of the recently introduced definitions of incomplete and complete retinal pigment epithelium and outer retinal atrophy (iRORA and cRORA) in age-related macular degeneration (AMD)

Methods: Optical coherence tomography (OCT) data from fellow eyes with intermediate AMD at baseline, that were obtained from a prospective natural history study of disease progression in patients with unilateral geographic atrophy (GA, NCT02399072), were assessed for presence of iRORA and cRORA lesions at the final study visit. Two independent readers, followed by mixed arbitration review involving up to two senior readers, assessed qualitative AMD characteristics and annotated – on the most representative B-scan – seven individual features of each iRORA and cRORA lesion at the final and each preceding study visit. Kappa statistics and Bland-Altman agreements between readers were determined and linear regression analysis applied to estimate changes over time.

Results: In 24 out of 32 fellow eyes with iRORA and cRORA but no conversion to exudative AMD or GA (minimum lesion size 0.15 mm^2) during the study, a total of 49 individual lesions (193 time points) were included. Moderate agreement was found for presence of choroidal hypertransmission (kappa 0.54), followed by subsidence of outer plexiform (0.46) and inner nuclear layers (0.43). For quantification of lateral dimensions of features, choroidal hypertransmission (mean difference 7.1 µm [-302.2;316.4]) was again the feature with the highest agreement, while lowest was found for RPE attenuation/disruption (-238.1 µm [-1101.2;624.9]). The mean dimensions of choroidal hypertransmission and external limiting membrane disruptions at first manifestation were 319.7 µm (95% confidence interval [231.3;408.1]) and 609.1 µm [382.6;835.6], showing an enlargement of 141.2 µm/year [75.58;206.8] and 108.6 µm/year [63.2;154.0], respectively.

Conclusions: Early progression of iRORA and cRORA lesions can be reliably quantified, which may be helpful to assess new therapeutic interventions aiming to slow down the early growth of atrophy. Further, these results suggest

that the enlargement rate of these early atrophic lesions is slower compared to previously published data on the lateral spread of larger GA lesions.

CONTROL ID: 3708469

SUBMITTER (NAME ONLY): Alan McDougal

TITLE: Ocular PK/PD of a Novel Non-Steroidal Anti-Inflammatory Compound in a Murine Model of Meibomian Gland Dysfunction

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. McDougal, R. Brown, M. Weksler, S. Miller, C. Kelly, M. Ina, H. Gordhan, S. Williams, D. Ellis, J.C. White, Aerie Pharmaceuticals Research and Development, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The long-term use of an efficacious and safe topical anti-inflammatory compound with a rapid onset of action for dry eye and other chronic ophthalmic inflammation mediated diseases presents an unmet medical need in ophthalmology. In this study, a murine allergic eye disease (AED) model of dry eye disease (DED) was used to evaluate mitigating effects of a class of anti-inflammatory compounds on DED progression. We hypothesize that compounds that engage and down-regulate disease-relevant pro-inflammatory pathways in our AED model have potential to treat ocular signs and symptoms of DED in human patients.

Methods: Female C57Bl/6 mice immunized against ovalbumin (OVA) were challenged with a topical OVA solution to induce inflammation and DED progression prior to treatment. A representative compound (compound A) from a novel class of Aerie anti-inflammatory compounds was evaluated in the AED model of DED. An ophthalmic solution of compound A, vehicle control, and a dexamethasone phosphate (positive control) solution was applied topically TID. Subjective masked and randomized clinical scoring of observable ocular inflammation was taken over the course of 4 days. Post-mortem tissue measurements of inflammation include flow cytometry of immune infiltrate, qPCR analysis of inflammatory biomarkers within Meibomian Gland (MG), and ELISA assays for inflammatory biomarkers.

Results: Topical administration of Compound A and the positive control dexamethasone phosphate significantly reduced clinical signs of inflammation including lid edema, conjunctival hyperemia, and MG plugging compared to vehicle. Quantitative analysis by qPCR demonstrates that both Compound A and dexamethasone reduced IL-17a, INFg, IL-6, IL-1b, and MPO infiltrates relative to vehicle in the mouse eyelid, the target site for MGD associated DED.

Conclusions: By targeting and engaging inflammatory pathways in a murine AED model of DED we show a significant reduction in inflammation and clinical signs of disease. Compound A represents a novel class of Aerie anti-inflammatory compounds that have the potential to be fast-acting, safe and efficacious treatment for ocular inflammatory diseases.

CONTROL ID: 3708470

SUBMITTER (NAME ONLY): Divya Jagadeesh

TITLE: Effect of Glare on Contrast Sensitivity for Myopia Control Spectacles

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Jagadeesh, A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|A. Ho, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Divya Jagadeesh: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Ho: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Lenslet-type optics utilized in myopia-control spectacle lenses (MCSL) has been shown to cause minimal impact on visual performance under conventional clinical light conditions (Li et al, 2021). Whether lenslet features introduce visual artefacts under more severe conditions such as glare has not been tested. This study explored the feasibility of a glare tester (GT) to detect and discriminate between MC lenses.

Methods: A GT based on that of Buhren et al (2006) was constructed to measure Glare Effect (GE) on contrast sensitivity (CS), consisting of a ring of 8 equally-spaced 6400 mcd LEDs, positioned on a dark base board. A square aperture at the centre of the LED ring enabled viewing of test charts displayed on an electronic vision chart (EVC) monitor (Sony LMD-DM20) 6 metres from the participant. The ring of LEDs subtended an angle of 6.4° at the participant's eye. The participant viewed Pelli Robson CS letters displayed on the EVC. Letter sizes tested were 6/38, 6/24, 6/15 and 6/9.5. CS for each letter size was measured monocularly under mesopic (<8 lux) and photopic (380–400 lux) conditions with and without LED-induced glare for two commercially-available MCSL (Hoya MiYOSMART and Essilor Stellest) and habitual correction for 4 participants and were instructed to view through the lenslet region of the lenses. A glare effect quotient (GE, Figure 1 equation) was calculated as a measure of device-induced glare relative to habitual correction. General linear model was used to account for the effect of lens type, light and letter size on GE. 95% CI was used to determine the difference from habitual correction.

Results: Participants age range was 25 to 39 years. The 95% CI showed that MiYOSMART lens had a similar or better contrast sensitivity when compared to habitual correction for all letter sizes under both illumination conditions (Table 1). Although not statistically significant, reduction in CS by 0.02 $\log_{10}$ units was observed at 6/38 for the Stellest lens under both light conditions and in photopic condition a minimal reduction in CS was noted at 6/9.5. At 6/15, the MC devices had similar CS increase of around 0.05 $\log_{10}$ units.

Conclusions: This small-sample exploratory study suggests that a GT can identify differences in participant performance of MCSL under glare conditions. With further refinements, a GT may be useful in determining the vision acceptability of MCSL.

CONTROL ID: 3708475

SUBMITTER (NAME ONLY): Niamh Wynne

TITLE: Presence of a scotopic scotoma in individuals with fragmented foveal avascular zones

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Individuals with macular-foveal capillaries (i.e., a fragmented foveal avascular zone, FAZ) have been proposed to have an anomalous distribution of macular photoreceptors, based on an absence of the typical foveal scotoma on scotopic microperimetry.[1] Here we sought to replicate these findings in individuals objectively classified as having a fragmented FAZ.

Methods: 14 individuals participated, 7 with fragmented FAZs and 7 with normal FAZ morphometry. Each subject had testing performed on their right eye. Five 3 × 3-mm (nominal area) angiograms were acquired with the AngioVue OCT-A system (Optovue, Inc., Fremont, CA). Two scans (1 horizontal, 1 vertical) each consisting of 304 B-scans with 304 A-scans/B-scan were acquired and co-registered to create an angiogram for analysis (AngioVue software version:2018.1.0.43). From each volume, a custom slab from inner limiting membrane to 9mm above the outer plexiform layer was extracted. Slabs from five volumes were registered and averaged using bUnwarpJ in FIJI. The presence of a fragmented FAZ was objectively determined using a previously described method.[2] Scotopic microperimetry testing was performed using a MP-1S microperimeter (Nidek Technologies, Gamagori, Japan). A customized microperimetry pattern of 45 points within the central 8 degrees centered near the fovea was used, and interpolated maps of foveal sensitivity were generated from scotopic microperimetry responses. Where possible, scotoma area in deg^2 was estimated using a 1db threshold.

Results: For all participants (10 female, 4 male; aged 12-55 years) there was a central area of reduced sensitivity, though the scotoma area could only be estimated in 12 participants. The mean scotoma area in those with fragmented FAZs was 1.86 deg^2 (range: 0.310-4.15 deg^2), while the mean scotoma area in the normal FAZ group was 1.53 deg^2 (range: 0.293-3.62 deg^2). These values are consistent with histological estimates of the rod-free zone. There was no significant difference in scotoma area between individuals with normal and fragmented FAZs (p=0.42, unpaired t-test).

Conclusions: In contrast to previous reports, we do not observe an absence of a foveal scotoma using scotopic microperimetry in individuals with a fragmented FAZ.

References:

1. PMID: 31274711

2. PMID: 31956075

CONTROL ID: 3708478

SUBMITTER (NAME ONLY): Danielle Swinkels

TITLE: Systemic supply of DHA is essential for retinal DHA levels and retinal integrity in mice

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Swinkels, Y. Das, S. Kocherlakota, M. Baes, Pharmaceutical and Pharmacological sciences, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|B.K. jun, N.G. Bazan, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|F. Vaz, UMC Amsterdam, NETHERLANDS|P. van Veldhoven, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|

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ABSTRACT BODY:

Purpose: Patients deficient in peroxisomal β-oxidation, which is essential for the synthesis of DHA (C22:6n-3) and the breakdown of VLC-PUFAs, present with retinopathy and reduced plasma DHA. A mouse model lacking peroxisomal multifunctional protein 2 ($Mfp2^{-/-}$ mice) also develops an early onset retinal decay, accompanied by reduced plasma and retinal DHA. We hypothesized that a reduced supply of DHA causes the $Mfp2^{-/-}$ retinal phenotype.

Methods: To define the contribution of local versus systemic supply of DHA for the neural retina, we investigated the retina of photoreceptor-specific $Mfp2^{-/-}$ ($Crx\text{-}Mfp2^{-/-}$) and of liver specific $Pex5^{-/-}$ mice, which lack all peroxisomal functions in hepatocytes. Next, a 0.1% DHA or control diet was fed to $Mfp2^{+/-}$ pregnant female mice and their offspring until sacrifice at 4w, 8w or 16w. $Mfp2^{-/-}$ mice and controls were analyzed for retinal function via full-field ERG, for lipid composition of NR and plasma with LC-MS/MS and GC, and histologically using retinal sections and RPE flatmounts.

Results: $Alb\text{-}Pex5^{-/-}$ mice displayed reduced plasma and retinal DHA levels, impaired ERG responses and shortened POS at 8w. In contrast, DHA levels and retinal morphology were normal in $Crx\text{-}Mfp2^{-/-}$ mice. DHA supplementation to $Mfp2^{-/-}$ mice increased plasma DHA even above levels in WT mice on control diet. Lipidome analysis showed normalization of DHA-containing phospholipids in the NR, such as LPC(22:6) and PC(44:12). Phospholipid species containing ultra-long-chain-PUFAs (>C36) still accumulated. Remarkably, until the age of 8w, the retinal morphology considerably improved with regard to: POS length, photoreceptor cell death and maintenance of the RPE honeycomb pattern, and inflammation was dampened. However, visual function improved only at the age of 4 weeks and deteriorated subsequently. Despite the initial rescue of retinal integrity, DHA supplementation could not prevent a complete retinal degeneration at 16w.

Conclusions: Our data prove that systemic supply of DHA is essential for the DHA pool in the NR. DHA supplementation rescues the retinal morphology of $Mfp2^{-/-}$ mice at an early age, but cannot prevent the retinal demise at later age. We hypothesize that the supplied DHA is converted into the protective lipid mediator Neuroprotectin D1 but that accumulating ultra-long-chain-PUFAs are toxic.

CONTROL ID: 3708479

SUBMITTER (NAME ONLY): Nancy Aguilera

TITLE: Visualization of the Photoreceptor / RPE / Choriocapillaris Complex in Choroideremia Using Adaptive Optics Enhanced Indocyanine Green Imaging

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Aguilera, T. Liu, J. Li, A.J. Bower, R. Lu, J. Giannini, B.P. Brooks, W.M. Zein, L. Huryn, J. Tam, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics enhanced indocyanine green (AO-ICG) imaging can be used to image the photoreceptor (PR) - retinal pigment epithelium (RPE) - choriocapillaris (CC) complex in the living human eye (PMID 30456310). In this study, we applied this technique to evaluate the PR-RPE-CC complex in choroideremia, an X-linked retinal degeneration.

Methods: AO-ICG imaging was performed at the fovea in 6 female carriers and 3 affected male patients (n=16 eyes) with confirmed mutations in the CHM gene. A subset of patients (3 carriers, 1 affected male, n=7 eyes) were imaged a second time, approximately 1-2 years after the initial visit. The transit phase immediately after ICG dye injection was used to obtain an image of the CC, and the late phase (at least 30 minutes afterward) was used to image the RPE. Images of the cone PRs were simultaneously obtained. Images were co-registered and quantified for cell-to-cell spacing (PR, RPE) or average flow void diameter (CC) were quantified using custom software.

Results: The PR-RPE-CC complex was intact in all patients imaged. Quantitative analysis of the initial visit of each eye revealed that the RPE was the most disrupted layer (average cone spacing increase compared to the expected normal value, 7%; RPE spacing increase, 156%; CC flow void diameter increase, 14%). Longitudinal follow-up imaging further corroborated this result, with the largest visit-to-visit changes occurring in the RPE when compared to the cone PR and CC layers (average increase from visit 1 to visit 2: cone PR, 1%; RPE, 24%; CC, 4%). Together, these results suggest that the PR, RPE and CC degenerate at different rates, with the largest changes occurring in the RPE.

Conclusions: We demonstrate, for the first time, longitudinal assessment of the PR-RPE-CC complex using AO-ICG. In choroideremia, the RPE appears to be affected to a greater degree than the surrounding cone PR and CC layers and shows the largest change over time.

CONTROL ID: 3708480
SUBMITTER (NAME ONLY): Ari Leshno
TITLE: Assessment of Alternative Tests for the ICD-10 Glaucoma Severity Score
SESSION TITLE: Structure-Function Relationship
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: A. Leshno, N. Harizman, Q. Wang, C.G. DeMoraes, G.A. Cioffi, J.M. Liebmann, Ophthalmology, Columbia University, New York, New York, UNITED STATES|E. Tsamis, S. La Bruna, A. Rai, D.C. Hood, Department of Psychology, Columbia University, New York, New York, UNITED STATES|A. Rai, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: The ICD-10 glaucoma severity classification is based on 24-2 visual field (VF) test.[1] Given that 24-2 can miss central or early damage,[2] we hypothesized that using the same principles, the optical coherence tomography (OCT) would provide a better estimation of severity.

Methods: Severity was determined for 55 eyes with glaucoma, according to the ICD-10 guidelines, which include assessing the presence of regional abnormalities in each hemifield, as well as the central 5 degrees of fixation (Fig. 1a). Grading was performed for each eye using either 24-2 VF or OCT macular and RNFL images by two independent groups of masked graders. Agreement between the two grading methods was evaluated. In addition, the accuracy of each method was determined by comparing the results to a reference standard (RS) based upon an automated structure-function topographic agreement method for the evaluation of regional abnormalities.[3]

Results: Based on the VF, glaucomatous eyes were classified as mild, moderate and advanced in 13, 17 and 25 cases respectively. Based on the OCT alone, glaucomatous eyes were classified as mild, moderate and advanced in 7, 4 and 44 cases respectively. The OCT classification was more severe than the VF in 22 (40%) of the 55 cases. In 26 (47%) cases, central involvement was detected by OCT, but not by the 24-2. In only 5 (9%) of the 55 cases, the OCT classification was less severe than the VF. The Kappa value showed weak agreement between VF and OCT (0.16±0.08, P=0.041). According to the RS, eyes were classified as mild, moderate and advanced in 3, 14 and 38 cases, respectively. The 24-2 gradings showed fair agreement with the RS (Kappa value 0.30±0.1, P=0.001), while the OCT gradings had good agreement with the RS (Kappa value 0.40±0.1, P<0.001). Compared to 24-2, the OCT also had better agreement with the RS in all 3 regions (Fig. 1b). A combination of using 24-2 to determine hemifield involvement and OCT for central involvement did not improve agreement compared to OCT alone (Kappa 0.36±0.1, P=0.001).

Conclusions: The current ICD-10 system relies on a functional (24-2 VF) test alone, which can underestimate the severity of glaucoma in a significant portion of eyes. OCT revealed advantages over 24-2 for accurate classification. Adding 24-2 to OCT data did not improve classification accuracy. 1. ICD-10 Glaucoma Reference Guide, 2019, aao.org; 2. Hood et al., PRER, 2013; 3. Tsamis et al., TVST, 2020.

CONTROL ID: 3708483

SUBMITTER (NAME ONLY): Monichan Phay

TITLE: Masking the “eat me” signal drastically increases the short-term survival of donor human retinal ganglion cells after xenotransplantation

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.H. Phay, S.G. Bauer, P.Y. Baranov, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M.H. Phay, P.Y. Baranov, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S.G. Bauer, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: A key challenge in retinal ganglion cell (RGC) replacement therapy is low donor cell survival. Phosphatidylserine (PS) is a ubiquitous “eat me” signal that is externalized and permanently displayed on the surface of apoptotic cells to facilitate their engulfment and clearance by tissue macrophages. Under stress, viable neurons also expose PS to the outer membrane in a reversible fashion. Since donor RGCs experience a significant stress during the isolation and transplantation process, we hypothesize that PS-mediated neurophagy by the host microglia/macrophages is a major contributor to donor cell death.

Methods: Donor human RGCs were derived from Brn3b-Tdtomato-Thy1.2 embryonic stem cells through retinal organoid approach with gentle dissociation and sorting for Thy1.2. To mask the externalized PS from macrophage/microglia recognition, donor cells were pretreated with annexin V (5mg/mL) for at least 20 minutes. We transplanted 20,000 viable donor RGCs subretinally into wild-type mice and processed whole mount retinas at day 1 and day 4 for immunostaining and confocal imaging to carry out subsequent analysis.

Results: Annexin V pretreatment led to the increase in transplant success: 92% (11 out of 12 recipients) had >1% (200) donor cells at day 4, compared to only 55% (6 out of 11) in the control group. We also observed ~2.5 fold-change in number of donor RGCs per eye: 1,280 cells in pretreated vs. 520 cells in control. In both groups, grafted donor RGCs displayed extensive neurite outgrowth (>150mm) and axon projections (>1000mm). Furthermore, donor cells axon fasciculation and entry into the optic nerve head were observed in the successful grafts: 33% vs. 9% in the Annexin V group vs. control. The recruitment of $Iba1^+$ and $CD45^+$ cells to the delivery site and their co-localization with donor RGCs was lower in the annexin V pretreated group at day 1 (19% vs. 40%) and was not different between groups at day 4.

Conclusions: Blocking externalized PS “eat me” signal with annexin V resulted in a drastic improvement in donor RGC survival and transplant success. However, persistent recruitment of $Iba1^+$ and $CD45^+$ to the delivery site and their co-localization with donor RGCs indicates that annexin V pretreatment only offers temporary protection. Our findings suggest that neurophagy by host microglia plays a significant role in eliminating viable donor RGCs.

CONTROL ID: 3708485
SUBMITTER (NAME ONLY): Elana Meer
TITLE:
Symptom Based Triage Tool in Ophthalmology
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Meer, M.S. Ramakrishnan, G. Whitehead, B.L. VanderBeek, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|
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ABSTRACT BODY:
Purpose: Acute care ophthalmic clinics can suffer from call overload and inefficient triage, leading to suboptimal patient access. An automated symptom checker and triage tool may offload the call volume while creating a more efficient and effective system for matching patients with their appropriate level of care. Here we describe the development and preliminary results from a novel automated ophthalmology triage tool.
Methods:
A symptom based triage algorithm was developed using the Wills Eye Manual and literature searches of acute ophthalmic diagnoses.[1] This patient facing automated algorithm (Figure 1) used a series of questions and answers to triage patients into 3 different acuity levels based on duration and characterization of symptoms (i.e. eye pain, blurry vision, flashes/floaters, eyelid lesions, etc): 1. Urgent: Same day appointment 2. Semi-Urgent: Appointment in less than 4 weeks 3. Non-Urgent: Appointment in 4 - 9 weeks.

The automated triage tool was built into an academic eye institution's website, available to both patients and non-clinical personnel for triaging eye-related symptoms. Upon completion of the tool, results were sent via an automatically generated email along with the patient information for review by an ophthalmic technician who would schedule the patient based on triage output.

Basic descriptive statistics were used to present demographic data, tool usage data, and time from symptom presentation to care access across the call center and patient-facing website.
Results:
Via the call center and the clinical website, the automated triage tool was used 1370 and 95 times, respectively. 66.7% of patients utilizing the tool were female, 50.7% identified as African-American, 28.7% Caucasian, 4.4% Asian, and 9.8% Hispanic/Latino. Among call center triage tool users, 33.5% were triaged to non-urgent, 60.4% were triaged to semi-urgent, and 6.1% were triaged to urgent same-day appointments. Among patient-facing website triage tool users, 15.5% were triaged to non-urgent, 39.7% were triaged to semi-urgent, and 44.8% were triaged to urgent same-day appointments.
Conclusions:
Automated Triage algorithms may be beneficial by offloading non-acute phone calls and clinical volume. Similarly, it can be used by non-clinically oriented staff members to guide clinical judgements. Additional work should focus on validation and electronic implementation into EHR systems.

CONTROL ID: 3708486

SUBMITTER (NAME ONLY): Haitao Liu

TITLE: The Role of the STING/Type I IFN Signaling Pathway in Diabetic Retinopathy

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Liu, A. Strizhakova, S.L. Hose, D. Sinha, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|C. Huang, P. Strassburger, G. Widmer, P. Westenskow, N. Mitrousis, D. Feenstra, Roche Pharma Research and Early Development, Ophthalmology Discovery, F Hoffmann-La Roche AG Research and Development Division, Basel, Basel-Stadt, SWITZERLAND|A.D. Proia, Pathology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|E. Lad, Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|D. Sinha, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is one of the leading causes of blindness in the modern world. Recent studies show an association between cell senescence and DR, but the underlying mechanism is not clear. The cyclic GMP–AMP synthase(cGAS)/stimulator of interferon genes (STING) pathway has been implicated in type I interferon (IFN)-induced cell senescence, inflammation, and oxidative stress, which are known contribute to the development of DR, indicating that this pathway might be a novel target for DR. This study investigates the potential role of STING in the pathogenesis of DR.

Methods: Immuno-blot and immunohistochemistry were used to characterize the activated state of retinal cGAS/STING in proliferative DR (PDR) patients and diabetic mice. β-galactosidase-based cell senescence assays and flow cytometry were used to determine whether IFN-β and STING activator 2′,3′-cyclic GMP-AMP (cGAMP), induced cell senescence in human retinal microvascular endothelial cells (hRMEC) and mouse retinal microvascular endothelial cells (mRMEC) in vitro. To evaluate the role of STING in diabetes-induced retinal alterations, diabetes was induced by IP injection of streptozotocin in STING mutant ($STING^{GT}$), $STING^{-/-}$ and wild type mice. Retinal blood vessels, expression of inflammatory proteins, production of superoxide, acellular capillary formation, and pericyte loss were measured.

Results: The retinal protein level of cGAS and STING increased in PDR patients and diabetic mice compared to non-diabetic controls. PDR patients show positive STING staining in retinal blood vessels. cGAMP-mediated STING activation increased IFN-β secretion in mRMEC. The percentage of senescent hRMEC and mRMEC increased when cells were treated with IFN-β relative to untreated cells. Diabetes-induced increase in retinal vascular senescence, leukostasis, inflammatory proteins ICAM-1 and iNOS, and production of superoxide were inhibited in $STING^{-/-}$ and $STING^{GT}$ mice after 2 months of diabetes in mice. $STING^{-/-}$ and $STING^{GT}$ also inhibited acellular capillary formation and pericyte loss in diabetic mice at 8 months.

Conclusions: Retinal cGAS/STING is activated in PDR patients and diabetic mice. Activation of STING increases IFN-β secretion in hRMEC and mRMEC in vitro, thereby leading to cell senescence. Loss of STING function inhibits retinal vascular senescence, inflammation, oxidative stress, capillary degeneration and pericyte loss caused by diabetes.

CONTROL ID: 3708489

SUBMITTER (NAME ONLY): Francesco Romano

TITLE: Microperimetry in Extensive Macular Atrophy with Pseudodrusen-like appearance

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Romano, M. Cozzi, A. Invernizzi, E. Riva, A. Bertoni, G. Staurenghi, A. Salvetti, Ospedale Luigi Sacco-Polo Universitario, Milano, Lombardia, ITALY|F. Bosello, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Veneto, ITALY|

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ABSTRACT BODY:

Purpose: To assess retinal sensitivity (RS) in extensive macular atrophy with pseudodrusen-like appearance (EMAP) using microperimetry (MP)

Methods: Cross-sectional, observational study. 22 EMAP patients without pathogenic mutations for dystrophies and without macular neovascularization (44 eyes) and 12 healthy controls (24 eyes) underwent best-corrected visual acuity (BCVA), MP, fundus photography, optical coherence tomography (OCT) and blue autofluorescence (BAF).
A customized 20-stimuli grid was used to test mesopic (mRS) and dark-adapted scotopic (sRS) sensitivity in macular and paramacular areas. Fibrosis was evaluated on fundus photographs, while BAF images were analyzed for background autofluorescence of the posterior pole (iso- or hyper-autofluorescent) and to measure the size of macular atrophy. Foveal atrophy, vitreo-macular interface abnormalities, outer retinal tubulations, central sub-field thickness (CST) and sub-foveal choroidal thickness (SCT) were also investigated on OCT.

Results: Mean age was similar for patients and controls (57.6±3.2 vs 57.3±2.1 years, p=0.77). BCVA was significantly lower in the EMAP group (60.1±21.0) compared with controls (85.0±0.0) (p<0.001).
RS turned out to be significantly reduced in EMAP patients both in macular and paramacular regions (all p<0.001). Lower mRS was significantly associated with foveal atrophy, fibrosis, hyper-autofluorescent background, larger atrophic areas and with lower BCVA, CST and SCT. Reduced sRS was instead associated with hyper-autofluorescent background, lower BCVA and with smaller CST and SCT.
On multivariate analysis, only fibrosis (p=0.04) and more extensive macular atrophy (p=0.02) were associated with reduced RS under mesopic conditions while no independent factor meaningfully affected scotopic RS in EMAP patients.

Conclusions: Impaired dark adaptation and night blindness are frequent, burdensome symptoms arising in the early stages of EMAP.
Our study is the first functional assessment in EMAP using MP and provides evidence on the reduced macular function particularly under dark conditions. Our findings indicate that macular sensitivity significantly drops when signs of end-stage disease (e.g., fibrosis and extensive macular atrophy) appear. The absence of independent factors associated with sRS might be related to the presence of diffuse pseudodrusen-like deposits. This explains the significant visual impairment referred by this group of patients.

CONTROL ID: 3708498

SUBMITTER (NAME ONLY): Angela Garriz

TITLE: Effects of proinflammatory cytokines on lacrimal gland myoepithelial cells contraction

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Garriz, J. Morokuma, M. Bowman, D.Z. Zoukhri, Comprehensive Care, Tufts University School of Dental Medicine, Boston, Massachusetts, UNITED STATES|D.Z. Zoukhri, Ophtalmology, Tufts University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Due to the important role that myoepithelial cells (MEC) play in lacrimal gland contraction helping to expel lacrimal fluid, the purpose of the current study was to investigate if the proinflammatory cytokines, interleukin-1β (IL-1β), tumor necrosis factor alpha (TNFα) and interferon gamma (IFNγ), are implicated in the reported impaired MEC contraction in chronically inflamed lacrimal glands.

Methods: MEC were isolated from lacrimal gland explants of α-Smooth Muscle Actin (SMA) - GFP mice (C57BL6) / $SMA^{CreErt2}$ strain strain. Cultured lacrimal gland MEC were treated with IL-1β alone (10 ng/ml) or a combination of IL-1β, TNFα and IFNγ (10 ng/ml) for a total of 7 days. Cells were maintained in complete RPMI-1640 medium (Roswell Park Memorial Institute) supplemented with 5% fetal bovine serum, and media was changed every other day with fresh addition of cytokines. At day 2, 4 and 7, GFP intensity, cell area, amounts of contractile proteins SMA and calponin, and MEC contraction were assessed. Analyzing GFP intensity is an indicator of SMA protein levels since GFP expression is under the control of the SMA promoter.

Results: At day 0, control and treated cells showed no differences in GFP intensity and cell size. GFP intensity started to decrease in treated MEC at day 2 (20% ± 0.32; $p=0.02$), continuing at day 4 (25% ± 0.51; $p=0.007$) and day 7 (30% ± 0.48; $p=0.0001$). Mean cell area was also reduced at day 2 (34% ± 0.0001; $p=0.0005$), day 4 (51% ± 0.0003; $p<0.0001$) and day 7 (30% ± 0.001; $p=0.0015$). The contraction assay at day 2 showed a 70% ± 0.032 decrease of contraction in treated MEC compared with control ($p<0.0001$), 73% ± 0.008 ($p<0.0001$) at day 4 and a significant drop of 82% ± 0.006 ($p=0.0015$) at day 7. Also, at the last time point, levels of contractile proteins were measured by western blotting showing a decrease in the amount of SMA and calponin protein in treated MEC compared with the control group (30% ± 0.001; $p=0.0016$ and $p=0.0206$; respectively). Similar results were observed when tumor necrosis factor alpha (TNFα) or interferon gamma (IFNγ) were added along with IL-1β.

Conclusions: Our results demonstrated that MEC contractile ability is impaired in the presence of pro-inflammatory cytokines IL-1β, TNFα, IFNγ making them potential therapeutic targets to restore MEC contractile ability and tear secretion in Sjogren syndrome dry eye disease.

CONTROL ID: 3708500

SUBMITTER (NAME ONLY): Krishna Sargur

TITLE: Functional Vision Assessment in People with Ultra-Low Vision using Virtual Reality: A Reduced Version

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sargur, Whiting School of Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|A. Kartha, R. Sadeghi, C. Bradley, G. Dagnelie, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultra-Low Vision (ULV) is a profound visual impairment limiting individuals to only detecting lights, silhouettes, and high contrast objects. Previous studies (Adeyemo et al 2017, Dagnelie et al 2017) have shown that visual information gathering under variable lighting conditions is one of the most common functional domains affected by ULV. In this study, we tested a reduced version of the functional assessment (Kartha et al. 2018) that can be useful for clinical evaluations.

Methods: Participants were tasked with completing a series of spatial localization and detection activities in a virtual reality environment. They were scored on the number of correct responses (m-alternative forced choice; m-AFC), for each of the 22 scenes presented. Data was processed into d prime (d') values that assessed participant performance compared to average (Person Measure), and scene difficulty based on chance performance (Item Measure; 0 for chance performance, more negative for easier tasks). Data collected from two centres (n=59 for C1; n=45 for C2) were compared using item and person measures.

Results: The results from C1 and C2 lie within the expected range, and all scenes except one have a better than chance performance. An expected trend is that scenes with lower contrast had less negative d' values as they were more difficult tasks.

There was significant correlation between the item measures from both centres ($r_{(21)} = 0.70$, $p<0.05$). Item measures from C2 were consistently higher than those from C1 for all items. On examining person measures, it became evident that person measures from C2 were significantly higher than those from C1 ($p<0.001$) which shows a higher functional ability and therefore, less item difficulty for C2 than C1.

Conclusions: Our data suggests that item measures and person measures can be compared across centres but may be shifted, depending on the functional ability of participants in each centre. They also suggest that this reduced set is an effective functional measure of ULV. The use of a VR headset enables this test to be performed easily both at homes and hospitals, making this a novel tool with a potential for widespread impact due to its portability, and ease of administration.

CONTROL ID: 3708501

SUBMITTER (NAME ONLY): Raúl Ramos-Sánchez

TITLE: Characteristics upon Presentation of Herpes Simplex Virus Associated Uveitis Patients in the Hispanic Population

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ramos-Sánchez, G.A. Requejo, N. González, A. Jiménez, M. Crespo, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|A. Cotto, M. Pappaterra- Rodriguez, Ponce Health Sciences University, Ponce, PUERTO RICO|A. Oliver, C. Santos, Ophthalmology, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|E. Rivera, Recinto Universitario de Mayaguez Universidad de Puerto Rico, Mayaguez, PUERTO RICO|

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ABSTRACT BODY:

Purpose: Herpes family viruses represent a well-established etiology for infectious uveitis, specifically anterior uveitis. Information regarding such patients' demographic and presentation characteristics in Hispanic populations is scarce. We aim to describe the demographic and clinical characteristics in a cohort of Hispanic patients with Herpes Simplex Virus (HSV) associated uveitis who live in Puerto Rico.

Methods: We performed a retrospective medical chart review of patients with a clinical diagnosis of Herpetic Uveitis at two private uveitis practices in Puerto Rico. All patients underwent an appropriate medical workup; those whose uveitis diagnosis could be explained by any etiology other than HSV were excluded from the study. The demographic characteristics and ocular findings were recorded and moved to an external database, and a descriptive statistical analysis was performed.

Results: The analysis included 145 patients who met the criteria for HSV-associated uveitis. The median age at presentation was 65 years (range 24 – 93 years); 62.86% of the patients were female, and 100% were Hispanic. Prior diagnosis of glaucoma was present in 61.43% of patients. From those patients whose serological data were available, 93.67% of patients were positive for HSV1 IgG (N=79), 26.92% were positive for HSV1 IgM (N=52), 44.16% were positive for HSV2 IgG (N=77), and 28.57% were positive for HSV2 IgM (N=49). Seventy-three percent of patients presented with unilateral uveitis. Visual acuity was equal or better than 20/50 in 78.93% of the involved eyes. Active anterior uveitis was present in 91.43% of eyes, while 41.41% were pseudophakic, 32.86% had keratic precipitates, 16.43% had cells in the anterior vitreous, and 12.86% had iris atrophy with transillumination defects.

Conclusions: As was expected, our study suggests that HSV-associated uveitis most commonly affects females and occurs unilaterally. Interestingly, over half of the patients with HSV-associated uveitis had a past ocular history of glaucoma, suggesting a possible association between both conditions. In general, we found the clinical and demographic characteristics of patients with HSV-associated uveitis to be similar to those of Caucasian cohorts.

CONTROL ID: 3708503

SUBMITTER (NAME ONLY): Peng Shang

TITLE: HDAC11 is a crucial regulator for visual cycle genes and retinal function

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Shang, R. Daley, E.R. Mahally, N.A. Stepicheva, S. Ghosh, H. Liu, A. Strizhakova, O. Chowdhury, V. Koontz, S.L. Hose, D. Sinha, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, J. Qian, D. Sinha, The Wilmer Eye Institute, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been reported that RPE cells isolated from age-related macular degeneration (AMD) patients present decreased chromatin accessibility and reduced expression of RPE signature genes, likely due to the upregulation of histone deacetylase 11 (HDAC11), an enzyme that deacetylates the histones and results in a more closed chromatin structure. In this study, we aim to dissect the role of HDAC11 in regulating RPE genes and RPE function.

Methods: Best1-Hdac11 constitutive knock-in (KI) mice were generated for this study. Hematoxylin-eosin (HE) and periodic acid-Schiff (PAS) staining were performed on retina sections from 12-month-old WT and Hdac11 KI mice. Electroretinography (ERG) was performed on Hdac11 KI and age-matched WT mice to measure retina function. RPE flatmount cultures and Hdac11 adenoviral constructs were used for Hdac11 gain of function studies in vitro. Quantitative PCR analyses were performed to evaluate mRNA levels of genes involved in multiple biological processes in RPE cells from WT and Hdac11 KI mice or RPE flatmounts.

Results: Histological results revealed decreased pigmentation of RPE cells, increased thickness of Bruch's membrane (BM), BM breaks, and abnormal photoreceptor outer segments in 12-month-old Hdac11 KI mice. ERGs showed decreased a, b and c wave amplitudes in 12-month-old Hdac11 KI mice indicating impaired retina function compared to WT mice. Immunofluorescence experiments showed reduced opsin and PNAL (peanut agglutinin lectin) staining in 12-month-old Hdac11 KI mice. Decreased expression of visual cycle genes such as Rpe65 and Lrat were found in Hdac 11 KI mice relative to WT mice at both 5 and 12 months of age. RPE flatmounts overexpressing Hdac11 also showed significantly decreased expression of visual cycle genes (Rpe65, Lrat, Rdh5, Rbp1, Rgr), but not lysosomal genes (Atp6v0, Lamp1), or genes involved in other processes such as Il1b, Bcl-2, and Sox9. No significant changes in the expression of Hdac1, Hdac2, Hdac6, Hdac7, Hdac8 were found in RPE flatmounts overexpressing Hdac11.

Conclusions: Our results suggest that HDAC11 may control the chromatin accessibility for RPE-specific genes, such as visual cycle genes, and thereby normalize physiological functions of the RPE/retina. The current study provides mechanistic insight as to the upregulation of HDAC11 reported in patients with dry AMD and thereby provides a novel therapeutic avenue for delaying the progression of the disease.

CONTROL ID: 3708505

SUBMITTER (NAME ONLY): Samuel Berchuck

TITLE: A framework for automating psychosocial distress screening in ophthalmology clinics using an EHR-derived AI algorithm

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Berchuck, A.A. Jammal, K. Weinfurt, D. Page, T. Somers, F.A. Medeiros, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: In patients with ophthalmic disorders, psychosocial risk factors play an important role in morbidity, mortality, and overall disease outcomes. Proper and early screening of psychosocial distress (i.e., anxiety and depression) can result in prompt intervention, and mitigate many of the factors listed above. Since screening is resource intensive, we developed a framework for automating distress screening using an electronic health record (EHR) derived artificial intelligence (AI) algorithm.

Methods: We performed a retrospective longitudinal study using the Duke Ophthalmic Registry (DOR). DOR consists of EHR data of over 100,000 patients seen at the Duke Eye Center (DEC) from 2009 to 2018. Our cohort included encounters for patients with at least two DEC encounters and a year of follow-up. At each encounter, distress was defined using a validated computable phenotype that relied on diagnostic and procedure codes, and medical history. Risk factors included available EHR history, including diagnostic and procedure codes, medical and encounter history, demographics (age, race, sex, ethnicity, marital status, income, education, and alcohol, smoking and illicit drug use), and problem list items. At each encounter, risk factors were used to discriminate patient distress status using the elastic-net classifier. Performance of the model was evaluated using the area under the receiver operating characteristic curve (AUC). Odds ratios (OR) for the top-25 predictors are presented, along with all non-zero demographic variables.

Results: Our cohort consisted of 358,135 encounters from 40,326 patients with an average of 9 encounters per patient over 4 years. The AUC was 0.91, with sensitivity of 0.97, and 0.90 at specificity levels of 0.75, and 0.9, respectively. Top predictors are listed in Figure and contained mostly predictors associated with psychiatric conditions. Also, present are conditions associated with high levels of distress, including suffocation, esophageal disorders, and headaches.

Conclusions: Using EHR data, we automatically identified psychosocial distress in ophthalmology patients upon encounter to a tertiary eye clinic. Our screening framework will be most effective on improving ophthalmic outcomes when paired with an effective referral and treatment program.

CONTROL ID: 3708507

SUBMITTER (NAME ONLY): Pinaz Nasim

TITLE: Test-retest variability of Zippy Adaptive Threshold Algorithms (ZATA) compared with Swedish Interactive Thresholding Algorithms (SITA) in persons with glaucoma and healthy controls.

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Nasim, R. S Ve, P. Naik, P.H. Artes, S. Ballae Ganeshrao, Department of Optometry, Manipal College of Health Professions, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|N.I. Kuzhuppilly, Department of Ophthalmology, Kasturba Medical College Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|P.H. Artes, Faculty of Health, University of Plymouth, Plymouth, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Test-retest variability (TRV) is an important characteristic of perimetric algorithms. We evaluated the TRV of Zippy Adaptive Threshold Algorithm (ZATA) Standard and ZATA Fast and compared it with the Swedish Interactive Thresholding Algorithm (SITA) Standard and SITA Fast, in a prospective cross-sectional study.

Methods: We recruited 22 healthy participants and 53 patients with glaucoma, mean (±SD) age 54.7 (±11.0) and 64.0 (± 9.4) years, respectively, from the ophthalmology clinics at Kasturba Hospital, Manipal, India. Participants had no additional ocular condition other than cataract or uncomplicated operated cataract. Those who could complete a session of approximately 1.5 hours, with four visual field tests, were included. Glaucoma patients with uncontrolled intraocular pressure (IOP) or known to be inconsistent with medication or follow-up visits were not included. Participants performed ZATA tests on a Henson 9000 perimeter (Topcon Healthcare, UK) and SITA tests on Humphrey Field Analyser (720i, Carl Zeiss Meditec, USA). Tests were repeated within one to ninety days.

Results: The Mean Deviation (MD) values of the ZATA strategies were closely related to those estimated with the SITA strategies (Figure 1). Differences between test and retest appeared similar between the four strategies (Bland Altman plots in Figure 2). ZATA Standard was approximately 30% faster than SITA Standard and ZATA Fast was approximately 6% faster than SITA-Fast.

Conclusions: In terms of MD, the ZATA strategies agreed closely with SITA. Compared with SITA, the retest variability of the ZATA strategies appeared similar or lower, but with a shorter test duration.

CONTROL ID: 3708510

SUBMITTER (NAME ONLY): Sai Kocherlakota

TITLE: Peroxisomal β-oxidation deficiency in RPE leads to progressive RPE dedifferentiation and retinal degeneration

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Kocherlakota, Y. Das, D. Swinkels, M. Baes, Department of Pharmaceutical and Pharmacological Sciences, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|D. Sinha, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|D. Sinha, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|F. Vaz, Department of Clinical Chemistry, Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Noord-Holland, NETHERLANDS|F. Vaz, Core Facility Metabolomics, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|M. Fransen, Department of Cellular and Molecular Medicine, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|

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ABSTRACT BODY:

Purpose: A mouse model with a knockout of multifunctional protein 2 (MFP2), the central peroxisomal β-oxidation enzyme, shows retinal degeneration mimicking the pathology in MFP2 deficient patients. To understand the origins and mechanisms of this degeneration, specifically in the RPE, we used global and RPE-specific Mfp2 knockout mice.

Methods: Eyes were collected either in the morning (2-3h post light onset) or in the afternoon (7h post light onset) at ages between 3 weeks and 12 months. They were used for immunostaining, immunoblotting, LC-MS lipidomic analysis and TEM imaging.

Results: The first pathological signs in $Mfp2^{-/-}$ RPE were lipid accumulations at 3w visualized by Perilipin-2 staining, which were not present at 2w, suggesting that peroxisomal β-oxidation is important for digestion of lipids coming from ingested POS, rich in VLC-PUFAs. The accumulation of neutral lipids and lipid species containing VLC-PUFAs was confirmed using lipidomics. TEM analysis at 3w showed accumulation of POS phagosomes, suggesting lysosomal dysfunction, confirmed with rhodopsin staining on RPE flat mounts. In addition, mitochondria were increased in number and were more circular in appearance. Immunostaining on flat mounts showed loss of the honeycomb structure and mislocalization of mitochondrial and peroxisomal markers. $Mfp2^{-/-}$ RPE progressively dedifferentiated with mislocalization of ezrin, a reduction in visual cycle genes and increases in dedifferentiation markers PCNA and SMA. mTOR, previously shown to induce RPE dedifferentiation, was already activated at 3w. The distribution and expression of the principle lactate transporters MCT1 and 3 was altered, suggesting impairment of lactate transport in the retina of these mice. The RPE-specific MFP2 knockouts show similar RPE degeneration. Interestingly, this caused pathology in the neural retina, as evidenced by increased inflammation, loss of photoreceptor nuclei and visual function towards 10-12 months of age.

Conclusions: Our results strongly indicate a crucial role for peroxisomal β-oxidation in the digestion of POS, with defects leading to lysosomal and mitochondrial abnormalities in RPE cells and their dedifferentiation. The RPE-specific MFP2 knockouts showed that the RPE degeneration was cell autonomous, but had negative consequences for the underlying neural retina.

CONTROL ID: 3708514
SUBMITTER (NAME ONLY): Maryna Ivanchenko
TITLE: Development of Dual-PCDH15 AAV Gene Therapy for Usher Syndrome Type 1F Blindness and Deafness
SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: M. Ivanchenko, D. Hathaway, E. Mulhall, A. Klein, Y. Li, D. Corey, Neurobiology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. Wang, B. György, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|
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ABSTRACT BODY:

Purpose: Usher 1F is caused by mutations in the PCDH15 gene, which encodes the tip-link protein PCDH15 in the inner ear. In the eye it has been shown to localize to the calyceal processes of the photoreceptor. Usher 1F is characterized by profound congenital deafness, and by progressive blindness beginning in the second decade. Gene addition therapy could be an attractive treatment, however, the PCDH15 coding sequence of ~5.8 kb is too large to fit into a single AAV capsid. We used a dual-AAV strategy to circumvent the size limitation.
Methods: We engineered two vectors that each encode part of the full-length protein. In cells, AAV genomes can recombine to creat a full-length coding sequence. To evaluate function in cochlea in vivo, Pcdh15 cKO mice were treated with dual AAVs. Hearing tests and histological analyses were performed at P30. To assess the potential of dual-AAV gene expression in human retina in vitro, we transduced retinal organoids from human iPSCs with dual AAVs and five weeks later evaluated HA-tagged PCDH15 expression and localization with immunofluorescence and immunogold SEM imaging.
Results: In HEK cells, full length PCDH15 was successfully produced using dual-AAV delivery. Proper recombination and splicing were confirmed with RT-PCR and Sanger sequencing. We found that Pcdh15 cKO mice, injected into inner ear with dual AAVs, displayed tip links four weeks after injection. They also showed robust rescue of hair bundle morphology, and rescue of mechanotransduction. While uninjected Pcdh15 cKO mice were deaf and had degenerated hair bundles, mice treated with dual AAVs encoding PCDH15 demonstrated good hearing rescue.

We also characterized the ultrastructure of photoreceptors in retinal organoids. SEM showed that a majority of photoreceptors developed inner segments, while some formed outer segments and connecting cilia. We observed nascent calycal processes at the apical ends of inner segments. Retinal organoids from human iPSCs transduced with dual AAVs encoding HA-tagged PCDH15 showed antibody labeling of HA-tag in photoreceptors, which was localized on the surface of the inner segments and at the inner/outer-segment junction where calyceal processes develop.
Conclusions: Dual-AAV delivery of PCDH15 mostly restores hearing in a mouse model of Usher 1F, and mediates expression and normal localization of PCDH15 in human photoreceptors in vitro. It holds promise for treatment of Usher 1F.

CONTROL ID: 3708524

SUBMITTER (NAME ONLY): Priyamvada Pitale

TITLE: Selective Vulnerability of the Intermediate Retinal Capillary Plexus Precedes RGC Loss in Experimental Glaucoma.

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.M. Pitale, G. Shen, R. Sigireddi, M. Polo Prieto, Y.H. Park, B.J. Frankfort, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|P. Westenskow, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|R. Channa, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The impact of glaucoma on the retinal capillary plexi (RCP) and its relationship to retinal ganglion cell (RGC) injury is not well understood. In this project, we studied microvascular injury in mice exposed to elevated IOP with the microbead model.

Methods: We used microbead injection in one eye of seven 12-week-old wild-type mice to induce IOP elevation. IOP was measured prior to injection and then 3 times per week. After 2 weeks, we immunostained retinas with CD31 (endothelium), Collagen IV (vascular basement membrane), and RBPMS (RGCs) and performed z-stack confocal microscopy. We performed Sholl analysis to quantify the number of intersections in the retinal capillary network. Using ImageJ we quantified RGC density and processed the confocal images to separate the three RCP into distinct images. We then established a novel, optimized image workflow to semi-automatically quantify the vascular anatomy using Angiotool (NIH, open-source). This provided topographical vascular features as well as spatial dimensions for the vascular network.

Results: IOP elevation of 1-4 mmHg above baseline was achieved throughout the study. IOP elevation to this level and duration did not cause RGC loss. Sholl analysis showed a 15% ± 3.50% reduction ($p \leq 0.01$) in the total number of capillary intersections at a distance of 1500µm from the optic nerve head. We also identified a plexus-selective phenotype. There was a significant reduction in the number of capillary junctions/mm^2 for both CD31 (26% ± 5.91%, $p \leq 0.01$) and Collagen IV (26% ± 5.77%, $p \leq 0.01$) in the intermediate retinal capillary plexus (IRCP). Furthermore, the total capillary vessel length/mm^2 was reduced for both CD31 (12% ± 2.04%, $p \leq 0.01$) and Collagen IV (12% ± 2.55%, $p \leq 0.001$) in the IRCP. There was also a decrease in the IRCP vessel area for CD31 (19% ± 2.09%, $p \leq 0.01$). No differences between control and bead injected eyes were detected for the superficial or deep RCP.

Conclusions: We have discovered a novel vascular phenotype in which the IRCP is rapidly sensitive to the effects of IOP elevation. This vascular phenotype is not detected in other retinal plexi and precedes RGC loss. This study advances our knowledge of microvascular deficits during glaucomatous pathology.

CONTROL ID: 3708525

SUBMITTER (NAME ONLY): Ambar Lugo

TITLE: Risk Factors Leading to Evisceration or Enucleation in Patients with Endophthalmitis

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lugo, G.A. Requejo, A. Meléndez, S. Álvarez, A. López, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|L. Montalvo, R. Ríos, V. Villegas, A. Oliver, Ophthalmology, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|

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ABSTRACT BODY:

Purpose: The treatment of endophthalmitis consists of intravitreal antibiotics injections and, in selected circumstances, pars plana vitrectomy. However, severe or refractory cases may require an enucleation or evisceration (ENEV) to control the infectious process. Our study seeks to identify risk factors leading to enucleation or evisceration in patients with infectious endophthalmitis.

Methods: Medical records covering from August 2015 to August 2020 in a tertiary referral hospital in Puerto Rico were reviewed. Charts of patients with a clinical diagnosis of infectious endophthalmitis were selected for analysis. Affected eyes were stratified into two groups; those undergoing ENEV and those in which the globe was preserved (EP). Accordingly, the frequencies of clinical characteristics in each of the two groups were compared and statistically analyzed using Pearson's Chi-square test, Fisher's exact test, and Welch Two Sample t-test.

Results: A total of 69 patients diagnosed with endophthalmitis were identified and included in our study, of which 32 underwent ENEV. The median age was 70, and 40.6% were female. There was a higher frequency of exogenous endophthalmitis in the ENEV group versus the EP group (56.2% and 13.5%, p=0.0002). However, there was a lower post-surgical endophthalmitis frequency in the ENEV versus the EP groups (21.9% vs. 51.4%, p=0.014). A visual acuity of no light perception was most common in the ENEV vs. the EP group (46.9% vs. 5.4%, p= 0.00003). While a visual acuity of finger counting or better was less common in the ENEV group vs. the EP group (9.4% vs. 32.4%, p= 0.04). Orbital involvement (panophthalmitis) was more frequent in the ENEV versus the EP group (37.5% vs. 5.4%, p= 0.002).

Conclusions: Our study suggests that eyes with endophthalmitis that present with a visual acuity of no light perception, panophthalmitis, or exogenous etiology have a higher risk of ENEV. Conversely, patients with a post-surgical etiology or a visual acuity of finger counting or better may be at a lower risk of ENEV.

CONTROL ID: 3708527

SUBMITTER (NAME ONLY): Kaylin Dong

TITLE: Evaluation of factors affecting visit adherence in patients receiving intravitreal injections for neovascular age-related macular degeneration during the COVID-19 Pandemic

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Dong, A. Bains, S. Davoudi, A.H. Nguyen, X. Chen, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 Pandemic has disrupted the care of patients receiving intravitreal injections for neovascular age-related macular degeneration (nAMD). This study looks at the factors that affected visit adherence for this population of patients during the height of the first pandemic surge.

Methods: In this retrospective, observational, case-control study, we included nAMD patients receiving anti-VEGF injections with an appointment scheduled during the target periods of March 11, 2020 – May 26, 2020 at either an urban hospital-based or suburban eye clinic. Patients who did not present for their appointment (cases) were compared to patients who did present to their appointment (controls). Medical records were reviewed to collect age, sex, race, presence of appointment attendance, language, marital status, distance from clinic, and area of deprivation index (ADI), which is a measure of socioeconomic health. Multivariate regression models were created with Stata (College Station, Texas) to determine the differences of these factors between no-show and show groups.

Results: 115 no-show patients (21% male, mean age 81 years) and 129 controls (26 % male, mean age 80.9 years) were enrolled. The odds of no-show were higher in non-White patients compared to White [(odds ratio (OR) = 2.7, 95% Confidence Interval (CI) = 1.22-6.17, P = 0.01)], the urban site compared to suburban site (OR = 3.1, 95% CI = 1.70-5.76, P = 0.0001) and single patients compared to married (OR = 2.3, 95% CI = 1.09-4.89, P = 0.02) in univariate analysis. The associations remained significant in multivariate analysis for non-White patients (OR = 3.1, 95% CI = 1.30-6.88, P = 0.01) and urban site (OR = 4.3, 95% CI = 1.78-10.3, P = 0.001) after adjusting for age, gender, language, distance from clinic and ADI. Age, distance from clinic, gender, ADI, and language were not statistically different between the two groups.

Conclusions: Visit adherence was lower for non-White patients during the first surge of the COVID-19 pandemic underlying the disparities which can be seen during the pandemic. Patients treated at an urban hospital were less likely to present for their anti-VEGF treatments than those receiving care in a suburban clinic. Further research is needed to determine whether differences in visit adherence effected long-term vision outcomes.

CONTROL ID: 3708528

SUBMITTER (NAME ONLY): Carly Feldman

TITLE: Generating and characterizing iPSC-RPE cells for studying disease mechanisms in peroxisomal biogenesis disorders

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Feldman, T. Fufa, R.B. Hufnagel, M. Benson, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Peroxisomal biogenesis disorders (PBDs) represent a group of rare diseases that can cause retinal degeneration, sensorineural hearing loss, and other systemic abnormalities, due to defects in peroxisome structure and function. Over two-thirds of all PBDs are caused by biallelic pathogenic variants in PEX1 or PEX6. Despite retinal degeneration manifesting in many PBDs, precisely how peroxisomal dysfunction causes retinal pathology is not well understood. To this effect, we differentiated PEX1 and PEX6 wild-type and knock-out induced pluripotent stem cells (iPSCs) into retinal pigment epithelial (RPE) cells to evaluate the effect of peroxisome dysfunction on this disease-relevant cell type.

Methods: CRISPR/Cas9-mediated genome-editing was used to generate PEX1 and PEX6 gene knockouts in the Gibco Human Episomal iPSC Line (Thermo Fisher Scientific, Inc.). We differentiated RPE from knock-out iPSC lines, normal parental lines, and a positive control line (3D1.8). We characterized and validated the iPSCs with flow cytometry using the pluripotency markers SOX2, NANOG and TRA-1-60 antibodies. At day 40 of RPE differentiation, we purified the cells by cell sorting and characterized the iPSC-derived RPE by morphology, pigmentation, and analysis of proteins associated with differentiated RPE using immunostaining followed by flow cytometry. Lastly, we evaluated peroxisome function by assessing very long-chain fatty acid and phytanic acid content in our iPSC-derived RPE cells.

Results: We successfully characterized and validated PEX1 and PEX6 knock-out iPSCs, parental control iPSCs, and a positive control iPSC line. The iPSCs expressed the appropriate stem cell markers as determined by flow cytometry. In addition, we successfully differentiated each iPSC line into RPE cells. The differentiated RPE cells expressed the appropriate markers indicating maturation. Detailed biochemical and peroxisomal function studies are underway.

Conclusions: We have demonstrated the successful differentiation, characterization, and validation of human-derived iPSC into RPE cells to model the effect of PBDs on a retinal cell type. Future studies will evaluate the requirements of PEX1 or PEX6 in RPE maturation and how abnormalities in peroxisome structure and metabolism influence RPE function.

CONTROL ID: 3708529

SUBMITTER (NAME ONLY): Hamid Alemi

TITLE: Efficacy of Neuropeptide Alpha-Melanocyte Stimulating Hormone (α-MSH) on Corneal Endothelial Cell Regeneration following Injury

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Alemi, S. Wang, N. Deshpande, T. Blanco, F. Kahale, G. Ortiz, T.H. Dohlman, U.V. Jurkunas, J. Yin, R. Dana, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal Endothelial Cells (CEnC) maintain normal corneal hydration. Damage to the corneal endothelium can lead to persistent corneal edema due to limited CEnC proliferative capacity. Studies have shown a concomitant decrease in density and/or function of both corneal nerves and CEnC following ocular injuries, suggesting nerves exert trophic effects on CEnC. Here we investigate the efficacy of neuropeptide α-MSH on CEnC proliferation and function following injury.

Methods: Wound healing was evaluated using CEnC derived from a healthy 21-year-old male donor cultured in Chen's medium supplemented with/without α-MSH (10-5M, 10-7M, or 10-9M) for 48hrs. Corneal injury was induced by transcorneal freezing in BALB/c mice (n=8/group) by placing a -72^{O}C 2 mm-diameter steel rod on the center of the cornea. Mice received 10μL subconjunctival injections of α-MSH (10-4M) or PBS (control) twice weekly for two weeks. Mice were injected with 5-ethynyl-2'-deoxyuridine (EdU) every 6 hours for 48hrs, and CEnC proliferation was evaluated by frequency of EdU+ cells. CEnC functional differentiation was assessed by comparing mRNA and protein expression of Na+/K+-ATPase by RT-PCR and Western blot, and by measuring central corneal thickness (CCT) via optical coherence tomography (OCT).

Results: Supplementing culture media with 10-5M α-MSH resulted in the fastest wound healing compared to the culture medium alone (P=0.03). In vivo, α-MSH treatment following injury increased the frequency of EdU+-CEnC within the wound area (61.6%±8.3% vs. control: 33.7%±5.0%; P=0.02) after 48hrs. CEnC Na+/K+-ATPase expression decreased 0.35-fold (P=0.01) at the mRNA level and dropped 0.63-fold (P=0.002) at the protein level in the control group 2 wks after the injury relative to values before injury; there was also a significant edema at 28 days post-injury (CCT:78.1±28.5mm; P=0.04). α-MSH administration restored CEnC Na+/K+-ATPase expression to baseline control values by causing a 2.3-fold increase in mRNA (P=0.04) and a 1.85-fold increase in protein expression (P<0.001) vs. control. α-MSH treatment led to a 54.9±15.0mm decrease in CCT (P=0.03) compared to the control group by 42d post-injury.

Conclusions: Our results demonstrate that following corneal endothelial injury, treatment with α-MSH prevents corneal edema by promoting proliferation of CEnC and maintaining function of mobilized/newly-generated CEnC.

CONTROL ID: 3708530

SUBMITTER (NAME ONLY): Milagros Mateos

TITLE: Hair cortisol level as molecular biomarker in retinitis pigmentosa patients

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mateos, S. Pastor-Idoate, Ophthalmology, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|M. Mateos, K.L. Puertas-Neyra, C. García-Vazquez, R. Coco, J. Pastor, E.M. Sobas Abad, S. Pastor-Idoate, R. Usategui-Martín, Instituto de Oftalmobiologia Aplicada, Valladolid, Castilla y León, SPAIN|M. Peralta-Ramírez, Mind, Brain and Behavior Research Center (CIMCYC), Faculty of Psychology, University of Granada, Granada, Granada, SPAIN|R. Gonzalez-Pérez, Pharmacology, CIBERehd, School of Pharmacy, Instituto de Investigación Biosanitaria ibs.GRANADA, University of Granada, Granada, SPAIN|J. Martín-Vallejo, Statistics, Universidad de Salamanca, Salamanca, Castilla y León, SPAIN|R. Coco, J. Pastor, R. Usategui-Martín, Cooperative Health Network for Research in Ophthalmology (Oftared), National Institute of Health Carlos III, ISCIII, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) patients commonly experience negative psychological states due to their progressive and unpredictable loss of vision and visual variations related to stress. The aim of this study was to examine hair cortisol concentrations (HCCs), which is usually associated with chronic stress, pretending to unveil possible associations between underlying psychological factors and disease severity in RP patients.

Methods: Seventy-eight RP patients and 148 healthy controls were included in this A complete ophthalmological exam was performed in all patients to grade into severity disease groups. Perceived stress and trait-anxiety were measured by the State-Trait Anxiety Inventory (STAI) questionnaire.

Results: Fifty-two (67%) patients had severe RP and 26 (33%) mild-moderate RP. Fifty-eight (58,9%) patients reported severely levels of stress and 18 (23.,1%) highly levels assessed by STAI questionnaire. RP patients exhibited higher HCCs (500.04±120.99 pg/mg) than in controls (136.17±60.51 pg/mg; $p<0.001$). Severe RP patients had significant higher HCCs than mild-moderate patients differing in 274.27pg/mg ($p<0.001$). There were no differences between RP severity grade and perceived anxiety levels in the questionaries. Group differences were not affected by relevant covariates (age, grade of severity, stress status, and gender).

Conclusions: HCC seems an effective biomarker associated with chronic stress in RP patients. This study shows that HCC in patients with RP are elevated compared to population-based controls, and association between HCC and RP severity was found. Future research is needed to characterize the effect of untreated negative psychological states on increased variability of vision and progression of the disease if any.

CONTROL ID: 3708532

SUBMITTER (NAME ONLY): Mark Solinski

TITLE: Health Related Quality of Life in Patients with Uveitis and Sarcoidosis

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Solinski, E. Wong, S. Shing, S. Swamy, Department of Ophthalmology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|V.R. Raiji, Department of Ophtalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|V.R. Raiji, Department of Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many activities that define independence and productivity in our society rely on good vision. As a result, one of the most devastating consequences of advancing visual impairment in any type of uveitis is loss of independence which would then affect the patient's quality of life. In this study, we will examine Quality of Life (QOL) data between patients with non-ocular vs ocular sarcoidosis and determine if the treatments (ex. systemic vs ocular implant) they receive have a significant impact on visual QOL or general QOL outcomes.

Methods: This is a prospective cross-sectional study of patients recruited from Loyola University Medical Center. Each participant was asked to complete a scientifically validated vision-related quality of life questionnaire, the National Eye Institute Visual Function Questionnaire (NEI-VFQ), and a scientifically validated HRQOL questionnaire, the Sarcoidosis Health Questionnaire (SHQ). Clinical data collected included a complete ophthalmic examination and systemic evaluations as indicated.

Results: In our sample, there was not a correlation between Best corrected visual acuity (BCVA) and NEI VFQ or SHQ scores. Patients on systemic therapy had lower NEI VFQ and SHQ scores regardless of their diagnosis. No correlation was found between the NEI VFQ and the SHQ.

Conclusions: As treatments in sarcoidosis and uveitis advance, it is important to see how patients' quality of life is affected to determine where further advancements should be focused and what types of accommodations or services may be most beneficial to them. Currently, there is little data in the literature studying QOL in patients with uveitis and systemic diseases. We would like to add to this area of research because increasing clinicians' understanding of which patients have low QOL and why will allow them to be better able to holistically care for their patients. Ophthalmologists get a unique view into how patients are able to go about their daily lives, and because of the necessity of good vision to function independently in our society, the front line for directing patients to social and mental health resources.

CONTROL ID: 3708534

SUBMITTER (NAME ONLY): Elise Ma

TITLE: Aging is associated with increased reactive gliosis and accelerated retinal ganglion cell loss after optic nerve injury.

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.L. Ma, J. Kwong, J. Caprioli, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|J.C. Lee, University of California Los Angeles College of Letters and Science, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is a risk factor in the development of glaucoma, an optic neuropathy characterized by progressive degeneration of retinal ganglion cells (RGCs). Astrocytes interact closely with RGCs and have been demonstrated to be maladaptive to injury in aged humans; however, the mechanisms related to aging or to astrocyte reactivity in optic neuropathies are poorly understood. In this study, we utilized an optic nerve crush (ONC) injury model to test the hypothesis that aging increases susceptibility to nerve injury by altering glial responses.

Methods: Young adult (3-months old) and aged (16-months old) C57/Bl6 wild-type mice underwent ONC in the left eye by implementation of self-closing forceps 1mm posterior to the globe for 1 second. Injured and fellow uninjured eyes were collected on post-injury day (PID)-3 and PID-7. Retinal whole mounts were prepared and stained for RGC-specific marker Rbpms and glial-specific markers S100β and GFAP. To further investigate candidate pathways and mechanisms for differentiated injury response in aged animals, whole retina transcriptomics was performed on PID-3.

Results: Cell counts revealed a significant decrease in RGC density at PID-3 among aged (-18.7±0.94%, n=6, p=0.01) but not young mice. By PID-7, young and aged animals demonstrated 64.1% and 51.2% loss of Rbpms cells, without significant difference between age groups. Aged animals demonstrated a significant decrease in S100β cell density (265.7 vs 224.5 cells/mm^2, n=6, p=0.002) and GFAP reactivity (1.5×10^6 vs 1.1×10^6 integrated density per field, n=6, p=0.0003) compared to young animals at uninjured baseline. Significant increases were seen in S100β cell density on PID-7 in both young and aged animals, but GFAP reactivity was significantly increased on PID-7 in aged animals alone. Whole retina transcriptomics on PID-3 is underway, and may reveal early differential molecular changes that occur in aged animals in response to injury.

Conclusions: Age-related acceleration of neurodegenerative RGC loss after optic nerve injury is associated with increased reactive gliosis. Elucidating RGC and glial cell responses after optic nerve injury in young and aged animals could clarify mechanisms of progressive vision loss in age-related optic neuropathies (e.g., glaucoma) and assist development of novel neuroprotective strategies.

CONTROL ID: 3708537

SUBMITTER (NAME ONLY): Mariella Pappaterra- Rodriguez

TITLE: Choroidal and Optic Nerve Manifestations in Patients with Asymptomatic West Nile Virus Infection

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.A. Requejo, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, PUERTO RICO|M. Pappaterra- Rodriguez, Ponce Health Sciences University, Ponce, PUERTO RICO|S. Muns, E. Rivera Grana, A. Oliver, Ophthalmology, Universidad de Puerto Rico Escuela de Medicina, San Juan, PUERTO RICO|G. Sanz, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmic manifestations of West Nile virus (WNV) infection include optic neuritis, retinal vasculitis, and chorioretinitis. In general, most reports of ophthalmic WNV involve patients with a history of symptomatic systemic disease. However, the vast majority of human WNV infections occur without systemic symptoms. Our study aims to describe a cohort of patients with serologic evidence of WNV infection, no history of systemic symptoms, yet with characteristic features of ophthalmic WNV involvement.

Methods: We performed a retrospective medical records review of all patients with a history of optic neuritis, retinal vasculitis, and chorioretinitis with positive WNV serology. Patients with a history suggestive of symptomatic WNV infection, or any other systemic condition that may have explained the ocular findings, were excluded from the study. The University of Puerto Rico, Medical Sciences Campus Internal Review Board reviewed and approved this protocol.

Results: Six patients met the study criteria and were included in the analysis. The median age at presentation was 61 years; all the patients were female and Hispanic. All patients were positive for WNV IgG antibodies. Eighty-three percent of patients had bilateral disease—eleven eyes were affected. Eighty-one percent of eyes had a visual acuity of 20/30 or better upon presentation, 67% had chorioretinal lesions, and 50% had vitritis. Optic neuritis and retinal vasculitis were present in 33% of eyes each.

Conclusions: Our study suggests that patients with asymptomatic WNV infection may develop ocular manifestations, which are similar to those with symptomatic disease. Physicians should beware of the possibility of ophthalmic WNV without systemic manifestations and consider adding WNV to the work-up of patients with the characteristic choroidal lesions or optic neuritis.

CONTROL ID: 3708538

SUBMITTER (NAME ONLY): Christopher Mugnaini

TITLE: Evaluation of Baseline Quantitative Ultra-widefield Leakage Patterns with Angiographic Features, Diabetic Retinopathy Severity and Treatment Response in the PRIME Study

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Mugnaini, G. Kalra, K. Talcott, S.K. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the relationship between leakage patterns, quantitative ultra-wide field fluorescein angiography (qUWFA) parameters, diabetic retinopathy severity score (DRSS) and measures of treatment response using baseline images in the PRIME study.

Methods: The PRIME study is a prospective randomized trial. Baseline angiograms were analyzed using an automated machine learning platform to acquire qUWFA parameters including perivascular leakage index (PLI), general leakage index (GLI), microaneurysm (MA) count, and ischemic index for both panretinal and macular regions. Perivascular leakage was identified as leakage within 5 pixels of the segmented blood vessel wall. General leakage was classified exclusively as leakage which exceeded the 5 pixel distance from the segmented blood vessel wall. PLI and GLI were correlated with other qUWFA metrics and measures of treatment response including the time required for 2-step DRSS improvement. The baseline DRSS score was used to sort eyes into severe non-proliferative (NPDR) and proliferative (PDR) DR groups. Time until 2-step improvement was used to sort eyes into ≤16 weeks and >16 weeks groups. Mean LIs were compared between NPDR, PDR, ≤16 weeks and >16 weeks groups using Student's t-test.

Results: Thirty-eight eyes were included for this analysis. Panretinal PLI correlated positively with total MA count (r=0.32, p=0.04) and panretinal ischemic index (r=0.39, p=.01). Panretinal GLI positively correlated with macular MA count (r=0.40, p=0.009) and panretinal ischemic index (r=0.39, 0.01). Severe NPDR eyes had a greater macular PLI compared to PDR eyes (4.5% vs 2.8%, p=0.035), however there was no significant difference between groups for other leakage parameters. Eyes requiring >16 weeks of monthly therapy for achieving 2 step DRSS improvement had a greater baseline panretinal GLI than eyes in ≤16 weeks group (2.8% vs 1.9%, p=0.026).

Conclusions: Perivascular and general leakage patterns appeared to be uniquely linked to different angiographic and DR-related variables. The ability to quantify and discriminate between these leakage types may provide important information regarding additional DR features and should be further explored for prognostic significance.

CONTROL ID: 3708543

SUBMITTER (NAME ONLY): Ingryd Lorenzana FCOVD FAAO

TITLE: Relationships Among Clinical Factors and Patient-Reported Outcome Measures of Symptoms and Quality of Life in Adults with Convergence Insufficiency

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Lorenzana FCOVD FAAO, Advanced Vision Center, Schaumburg, Illinois, UNITED STATES|D.A. Leske, S.R. Hatt, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|T.W. Dean, Z. Li, Jaeb Center for Health Research, Tampa, Florida, UNITED STATES|E.C. Jenewein, Salus University, Philadelphia, Pennsylvania, UNITED STATES|L.R. Dagi, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|C.J. Beal, University of Florida, Gainesville, Florida, UNITED STATES|Y. Pang, Ticho Eye Associates, Chicago Ridge, Illinois, UNITED STATES|D.V. Retnasothie, S.A. Cotter, Southern California College of Optometry, Fullerton, California, UNITED STATES|C.A. Esposito, Midwestern University Eye Institute, Glendale, Arizona, UNITED STATES|S.A. Erzurum, Eye Care Associates, Inc., Poland, Ohio, UNITED STATES|A.E. Aldrich, Snowy Range Vision Center, Laramie, Wyoming, UNITED STATES|E.R. Crouch, Virginia Pediatric Eye Center, Virginia Beach, Virginia, UNITED STATES|J.M. Holmes, Ophthalmology and Vision Science, University of Arizona, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Convergence insufficiency is associated with a variety of symptoms, but the relationship between symptoms and quality of life has not been studied. We explored associations among clinical measures, symptoms, and quality of life before and after treatment in adults with symptomatic convergence insufficiency.

Methods: In a prospective observational study we evaluated 57 adults with symptomatic convergence insufficiency (near exodeviation ≥4Δ and at least 4Δ larger than distance, reduced near point of convergence, reduced near positive fusional vergence, and Convergence Insufficiency Symptom Survey [CISS] score ≥ 21 points). 35 participants were treated with vision therapy/exercises and 22 with base-in prism. Spearman correlation coefficients (R) and 95% confidence intervals (CI) were used to assess associations among near clinical measures (exodeviation magnitude, near point of convergence, positive fusional vergence) and patient-reported outcome measures (CISS, Diplopia Questionnaire, and the Adult Strabismus (AS)-20 quality-of-life (QOL) questionnaire [general function, reading function, interactions, and self-perception domains]) prior to treatment (baseline), and 10 weeks and 1 year after treatment initiation. To account for multiplicity, associations were interpreted as present only when the lower limit of the 95% CI indicated a moderate to strong association [R ≥ 0.4].

Results: At baseline, the only moderate to strong correlation was between the CISS and AS-20 reading function scores (R = 0.62; 95% CI: 0.43 − 0.76). For change from baseline, the only moderate to strong correlations were between change in CISS score and change in AS-20 reading function score at 1 year in the vision therapy group (R = 0.78; 95% CI: 0.57 − 0.89), and at 10 weeks (R = 0.78; 95% CI, 0.52 − 0.91) and 1 year (R = 0.85; 95% CI, 0.65 − 0.94) in the prism group.

Conclusions: In adults with symptomatic convergence insufficiency, baseline symptoms correlated with reading function QOL, and improvements in symptoms following treatment with vision therapy/exercises or prism correlated

with improvements in reading function QOL. There were no correlations between clinical measures and symptoms or QOL. Patient-reported outcome measures appear useful in the assessment and management of convergence insufficiency in adults.

CONTROL ID: 3708547

SUBMITTER (NAME ONLY): Dominik Lewandowski

TITLE: Pharmacological Lowering Of Ceramide Buildup In AdipoR1$^{-/-}$ Mice Increases Photoreceptor Survival And Improves Vision

SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Lewandowski, R. Smidak, E.H. Choi, J. Zhang, A. Tworak, S. Suh, Z. Dong, E. Tom, D. Skowronska-Krawczyk, K. Palczewski, Ophthalmology; Gavin Herbert Eye Institute, University of California Irvine, Irvine, California, UNITED STATES|E.H. Choi, S. Suh, Medical Scientist Training Program, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|T. Hoang, S. Blackshaw, Neuroscience, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|D. Lyon, Anatomy and Neurobiology, University of California Irvine, Irvine, California, UNITED STATES|D. Skowronska-Krawczyk, Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|K. Palczewski, Physiology and Biophysics; Chemistry; Molecular Biology and Biochemistry, University of California Irvine, Irvine, California, UNITED STATES|A.F. Pinto, 7Clayton Foundation Laboratories for Peptide Biology, Salk Institute for Biological Studies, La Jolla, California, UNITED STATES|A. Foik, M. Tabaka, ICTER, Instytut Chemii Fizycznej Polskiej Akademii Nauk, Warsaw, POLAND|

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ABSTRACT BODY:

Purpose: Adiponectin receptor 1 (ADIPOR1) is a regulator of lipid and glucose metabolism that possesses ceramidase activity. ADIPOR1 mutations are associated with retinitis pigmentosa. Ablation of ADIPOR1 in mice leads to photoreceptor death; however, the underlying mechanisms remain unclear. We hypothesize that (1) lack of ADIPOR1 ceramidase activity in AdipoR1$^{-/-}$ mice leads to ceramide accumulation in the retina; (2) pharmacological inhibition of ceramide generation can prevent photoreceptor death and improve retinal function.

Methods: We analyzed ceramide levels in the retina and retinal pigmented epithelium (RPE) by liquid chromatography-mass spectrometry (LC-MS). To reduce ceramide levels, two groups of AdipoR1$^{-/-}$ mice (n=6) were i.p.-injected with desipramine and L-cycloserine (DC) or saline; and examined with optical coherence tomography (OCT), electroretinography (ERG), measurements of visually evoked potential (VEP), and V1 cortex neuron responses. Then, the eyes were used for histology, TUNEL assay, and ceramide quantification by LC-MS.

Results: We found an accumulation of ceramides in the retina (up to 7.4-fold increase; p=0.011) and RPE (up to 3.1-fold increase; p=0.0008) of 4-week-old AdipoR1$^{-/-}$ mice, and confirmed its localization with ceramide antibody staining.

DC-treatment for ~4 months resulted in:

(1) Increased number of photoreceptors in the DC- vs. saline-treated AdipoR1$^{-/-}$ mice, as shown by OCT (33.8±3.9%, p<0.0001) and histology (37.3±4.8%, p<0.0001); (2) 16-28% decrease in ceramide levels (p<0.028); (3) fewer apoptotic photoreceptors (56.8±11.8%, p=0.023); (4) improved ERGs (p=0.013); (5) enhanced electrical responses of the primary visual cortex to visual stimuli (p=0.003); (6) improved V1 cortex neuron responses to drifting-grating stimuli (p<0.001).

Conclusions: Our results support the hypotheses that (1) mice with ablated ADIPOR1 have pathologic build-up of ceramides in the retina and RPE; (2) DC-treatment lowers ceramide levels, resulting in increased photoreceptor survival.

We found that DC-treatment of AdipoR1$^{-/-}$ mice improved photopic ERGs and the electrical responses of the primary visual cortex to visual stimuli, approaching near-normal levels for some parameters. These studies suggest that a similar approach with retinitis pigmentosa patients could effectively attenuate the photoreceptor degeneration resulting from elevated ceramide levels.

CONTROL ID: 3708549

SUBMITTER (NAME ONLY): Emmanouil (Manos) Tsamis

TITLE: An automated, structure-function method for detecting progression of glaucoma

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Leshno, G.A. Cioffi, J.M. Liebmann, C.G. DeMoraes, D.C. Hood, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|E. Tsamis, S. La Bruna, A. Rai, D.C. Hood, Psychology, Columbia University, New York, New York, UNITED STATES|A. Rai, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop and test an automated method for detecting progression based upon topographical agreement of changes in the optical coherence tomography (OCT) maps and 24-2 and 10-2 visual fields (VF) in eyes with early glaucoma.

Methods: Widefield OCT (12x9mm) scans and 24-2 and 10-2 VFs were acquired from 55 eyes with early or suspected glaucoma (baseline 24-2 mean deviation >-6dB) and 25 healthy controls (HC) as part of a longitudinal, prospective study. Baseline (V1) OCT maps and VFs were compared to those from the last follow-up visit (V2), which was obtained at least 1 year later. Continuous probability change (pc-) maps were determined for both the retinal nerve fiber layer (RNFL) and retinal ganglion cell plus inner plexiform layer (GCL+) (Fig. 1) by comparing the difference of the thickness between V1 and V2 to an estimation of short-term variability for scans within 4 months. Red (p<1%) and yellow (p<5%) in Figs. 1 & 2 indicate significant change. The same approach was applied for the VFs. A custom R program [1] superimposed VF locations on RNFL and GCL+ pc-maps and determined the number of locations with both progressive structural (pS, p<10%) and functional (pF, p<5%) change (diamonds in Figs. 1&2). The criterion number of pS-pF locations for a 95% specificity was estimated based upon sampling the HC group with replacement. A reference standard based upon experts' evaluation of V1 and V2 OCT data (b-scans, and RNFL and GCL thickness and change maps) and VF tests identified 12 progressing (P) eyes.

Results: For the HC eyes, a threshold of 10 total pS-pF locations on the RNFL and GCL+ pc-maps achieved a specificity of 95% (1 HC false positive). The same threshold identified 8 eyes as 'progressors', 7 of which were true positives (sensitivity from 12 P eyes: 58%). A post-hoc analysis of the other 5 P eyes revealed that 4 of the 5 showed a very narrow progressive region on the OCT with pS-pF agreement within the same arcuate region, but no overlap (Fig. 2). The commercial GPA correctly identified only 4 of the 12 P eyes (sensitivity: 33%).

Conclusions: An automated method for detecting progression based upon topographical OCT and VF agreement showed good specificity and identified more P eyes than the commercial GPA. Eyes with narrow arcuate progression can still be missed, mainly due to the spatial resolution of the 24-2 and the limited extend of the OCT scan size. 1. Tsamis et al, TVST, 2020.

CONTROL ID: 3708550

SUBMITTER (NAME ONLY): Tylor Lewis

TITLE: IFT20 is critical for outer segment maintenance and photoreceptor survival

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lewis, C. Castillo, V.Y. Arshavsky, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|G. Pazour, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The intraflagellar transport (IFT) complexes have a well-established role in the assembly and maintenance of primary cilia, including photoreceptor outer segments. The focus of our study was IFT20, a non-conventional subunit of the IFT-B particle that associates with the rest of IFT-B reversibly and is thought to play a role in recruiting IFT cargo from the Golgi to the cilium. We sought to explore the role of IFT20 in photoreceptor cells by analyzing the phenotype of the conditional IFT20 knockout.

Methods: A rod-specific knockout of IFT20 in mice was generated by crossing a floxed IFT20 line with the iCre75 line that expresses Cre under control of the rhodopsin promoter. While Cre expression in this line begins as early as postnatal day 7, the depletion of IFT20 protein does not complete until after photoreceptor outer segments are fully developed. This allowed us to study the function of IFT20 in outer segment maintenance independent of its role in the outer segment development.

Results: We found that the depletion of IFT20 protein from rods was followed by a complete degeneration of these cells within a period of several weeks. During this period of time, outer segment structure rapidly disintegrates followed by cell death. Yet, our analysis of outer segment resident proteins during the short window when outer segments are still present revealed only a minor mislocalization of rhodopsin and no mislocalization of peripherin-2. Interestingly, mislocalized rhodopsin was not found in the inner segment biosynthetic membranes but rather in extracellular vesicles accumulating around photoreceptor cell bodies.

Conclusions: Taken together, this data suggest that the primary function of IFT20 in photoreceptors is in ciliary maintenance rather than in post-Golgi protein transport.

CONTROL ID: 3708552

SUBMITTER (NAME ONLY): Francisco Valentín Bravo

TITLE: CHARACTERIZATION OF VITREORETINAL TAMPONADE-RELATED COMPLICATIONS: IT`S TIME TO MOVE FORWARD

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.J. Valentín Bravo, J. Pastor, S. Pastor-Idoate, Opthalmology, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|R. Usategui-Martín, C. Andrés-Iglesias, J. Pastor, S. Pastor-Idoate, Opthalmology, Instituto de Oftalmobiologia Aplicada, Valladolid, Castilla y León, SPAIN|

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ABSTRACT BODY:

Purpose: The aim of the present study is to evaluate the different clinical complications associated with vitreous substitutes, especially silicone oil (SO).

Methods: This is a retrospective, observational and single-center study of consecutive patients operated by pars plana vitrectomy (PPV) between 2015 and 2020 at the Clinical University Hospital of Valladolid due to different vitreoretinal pathologies, such as retinal detachment (RD), epiretinal membrane (ERM), macular hole (MH) or vitreous hemorrhage (VH). The characteristics of the patients and their complications were recorded in an Microsoft Excel database. The statistical analysis was performed with the SPSS program (version 21.0).

The mean (± standard deviation) or median was used to describe all continuous variables, and frequencies to explain nominal or categorical variables. Normality was analyzed using the Kolmogorov-Smirnov statistic for data greater than 50 and the Shapiro-Wilk statistic when less. The analysis of the study data was performed with the Chi-square test, establishing significance $p<0.05$.

Results: We included 669 surgeries performed on 472 eyes of 424 patients. Their mean age was 60 years (range 8-87) and their follow-up was 25.24±1.02 months. The main cause of primary surgery was retinal detachment or re-detachment in 406 cases (60.8%), followed by epiretinal membrane (14.5%), hemovitreous (12.8%) and macular hole (10.3%).

In 140 surgeries, SO was used as a tamponading agent and in the rest; air, balanced saline or gas. The median time of AS permanence was 7 months (range 1-107). Long-term complications in both groups included acute ocular hypertension in 254 eyes (28.6% vs 20%) and chronic ocular hypertension in 105 interventions (15.7%). Other undesirable events were ERM formation (29.04%), vitreoretinal proliferation (21.41%), retinal re-detachment (10.8%), cystic macular edema (25.4%), corneal decompensation (8.98%), cystic macular edema (25.4%) and posterior synechiae (SPs), all occurring with a higher frequency and statistical significance in the AS group ($p<0.01$).

Conclusions: Vitreous substitutes agents used in PPV generate complications that should be recognized early. Among them, SO is the one that causes the most severe complications and adverse events. Hence, future directions in the development of vitreous substitutes are needed.

CONTROL ID: 3708553

SUBMITTER (NAME ONLY): Milda Reith

TITLE: Multimodal retina examination of patients with CNGA1 retinitis pigmentosa

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mutations in CNGA1 result in autosomal recessive retinitis pigmentosa (arRP), a rare progressive degenerative disease, leading to blindness.
A detailed clinical observation of the phenotype correlated with the genotype is necessary for the future development of potential treatments.

Methods: Six patients with arRP and mutations in CNGA1 were examined at the University Eye Hospital in Tübingen. This included BCVA, visual field, photopic and scotopic pupil campimetry (CPC), dark adapted chromatic perimetry (DAC), full-field stimulus threshold test (FST) as well as imaging with funduscopy, optical coherence tomography (OCT) and fundus autofluorescence (FA). All six patients were examined at baseline and five patients at follow-up one year later.

Results: The median age of the patients was 46 years (range 38-67 years). The BCVA varied between 20/80 and 20/20 with stable findings at follow up. The kinetic perimetry showed concentric restriction of the visual field in all patients. Scotopic and photopic CPC showed loss of rod function in all patients with good cone function in the morphologically preserved central retinal area. The FST measurements showed increased thresholds for blue and red color, indicating loss of rod function, whereas dark-adapted cone thresholds were unaffected. DAC with blue and red stimuli showed a small central island with preserved rod function in three patients. OCT and widefield FA underlined peripheral degeneration and preserved central retina. OCT findings showed perifoveal loss of outer retinal cells. One patient had macular edema.

Conclusions: CNGA1-linked arRP presents with late-onset, slowly progressive rod-cone degeneration with pronounced loss of rods but well-preserved cone-function into late adulthood. Clinical examination showed stable results within an expected range of variation during a one-year follow up period. Carefully chosen multimodal diagnostics can detect residual rod function in small, morphologically preserved retinal areas of CNGA1-RP patients.

CONTROL ID: 3708558

SUBMITTER (NAME ONLY): Kosha Dholakia

TITLE: Kinetics of rolling and crawling immune cells in retinal venules during inflammation imaged with label-free adaptive optics ophthalmoscopy

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Dholakia, Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|C.J. Chu, Translational Health Sciences, University of Bristol, Bristol, Bristol, UNITED KINGDOM|C.J. Chu, UCL Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|J. Schallek, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|J. Schallek, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early vascular changes in response to tissue inflammation includes the selective rolling and crawling of circulating immune cells along the venular endothelium. Recently, we have imaged single immune cells in vivo using label-free adaptive optics scanning light ophthalmoscopy (AOSLO) with phase contrast. Here, we image and measure the rolling/crawling speeds of immune cells that precede cell transmigration into the retina.

Methods: A custom AOSLO with phase contrast capabilities (796 nm, 200-500 μW, 800 μm pinhole, 30 airy disc diameter offset) was used. Image locations were within 10° of the optic disc, focusing on arterioles and venules adjacent to the ganglion cell layer. C57BL/6J male mice were anesthetized using ketamine (100 mg/kg)-xylazine (10 mg/kg) and isoflurane (1% v/v). Baseline videos were captured before mice were injected intravitreally with 0.5 ng of lipopolysaccharide in 1 μL PBS. The same mice were reimaged within five epochs: 0.5, 4, 6, 24 and 72 hours post injection. Rolling cell speed was quantified at 6 hours (n=4 venules in 3 mice, 53 cells tracked) by manually tracking cell position over time using ImageJ Manual Tracking plugin (Fig 1).

Results: By morphology, we observed two types of adherent cells; those with a circular appearance rolling along the endothelium and a more adherent class of cells showing tank-treading behaviors (Fig 2). Rolling and crawling immune cells were found in venules; arterioles showed few endothelial interactions. Rolling and crawling was predominantly observed at the 4-6 hour time epoch; few rolling cells were observed in 24 and 72 hours epochs. Average rolling speed was 10.9±9.9 μm/s. Speeds were variable across the same cells (0-103.9 μm/s) indicating patches of greater adhesion. Two cells were nearly stationary (0.2±0.9μm/s), indicating firmly adherent cells that may later extravasate. We observed one cell actively moving against the direction of blood flow in a venule shown as negative velocity -0.3±0.5 μm/s (Fig.2).

Conclusions: Here we reveal some of the earliest features of inflammation at the single cell level in vivo. Phase contrast AOSLO enables label-free noninvasive measurements, allowing an unperturbed assessment of retinal inflammatory response. This work provides a foundation for detailed study of immune cell adhesion in vivo, a key target for new drugs that seek to modulate such behavior.

CONTROL ID: 3708560

SUBMITTER (NAME ONLY): Shandiz Tehrani

TITLE: Pilot study of novel gene delivery technique to specifically target retinal ganglion cells

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tehrani, K. Delf, K. Cook, B. Sivyer, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: While intravitreal injection of viral vectors is the mainstay for gene delivery to retinal ganglion cells (RGCs), the delivery technique results in non-specific targeting of other retinal cells including amacrine cells. Here, we developed a novel strategy to more specifically target RGCs for gene delivery using optic nerve injection of viral vector in rodents.

Methods: Five 8-9 month old Brown Norway rats underwent unilateral delivery of 2.5mL of AAV-PhP-eb expressing GFP (1×10^{13} vg/mL), either intravitreally (n=3) or directly into the optic nerve via a retro-orbital approach (n=2). Animals were euthanized 21 days post-injection. Retinal whole mounts were fixed and underwent immunofluorescent labeling with anti-GFP antibodies, Lycopersicon esculentum to label vasculature and glia, and DAPI, followed by confocal microscopy. Contralateral eyes served as negative controls. Random sampling of the retinas by a blinded observer were analyzed and quantified for total DAPI-labeled and GFP-labeled nuclei in the ganglion cell layer (GCL) and the inner nuclear layer (INL). Student's t-test was used for statistical analysis.

Results: Direct optic nerve injection of viral vector resulted in GFP expression specifically in the retina, without expression in other cells within the optic nerve (including astrocytes and blood vessels) or the contralateral eye. GFP expression rate within the retina was highest in the GCL after optic nerve injection of viral vector (26.0 ± 21.9%) and was statistically comparable to post-intravitreal injection GFP expression rates within the GCL (45.3 ± 5.6%; p=0.28). However, GFP expression in the INL appeared much less after optic nerve injection of viral vector (0.012 ± 0.008%) compared to intravitreal injection GFP expression rates within the INL (0.11 ± 0.042%; p = 0.07). Among all GFP-expressing cells within the retina, optic nerve injection of viral vector appeared to more specifically target GCL neurons relative to intravitreal injection (86.9 ± 5.6% vs. 72.7 ± 6.0%; p = 0.09). Neurons within the INL following optic nerve injection appeared to be displaced RGCs. Further studies are underway with larger animal groups.

Conclusions: Optic nerve injection of viral vector AAV-PhP-eb for gene delivery to the retina specifically targets the retina, with comparable expression efficiency to intravitreal injection and a potential advantage of higher specificity for RGCs.

CONTROL ID: 3708563

SUBMITTER (NAME ONLY): Jessica Lee

TITLE: Risk Factors Associated with Surgical Failure After Primary Scleral Buckling for Rhegmatogenous Retinal Detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, J. Hamburger, M. Rama, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|M. Salabati, S.N. Patel, R. Mahmoudzadeh, M.A. Khan, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|A. Gupta, Ophthalmology, Geisinger Medical Center, Danville, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the single surgery anatomic success (SSAS) rate after scleral buckling (SB) procedure for primary rhegmatogenous retinal detachment (RRD), and to identify clinical factors associated with increased risk of surgical failure. Surgical failure was defined as any additional intervention required for retinal re-attachment. Interventions included pneumatic retinopexy, SB revision, or pars plana vitrectomy (PPV) at any time after SB placement.

Methods: Single-center, retrospective cohort study. Demographic, clinical, and surgical characteristics were extracted from patient charts and compared between eyes with SSAS and eyes experiencing surgical failure. A multivariable logistic regression model was completed to assess the effect of demographic, clinical, or surgical characteristics on SSAS.

Results: A total of 499 patients with primary RRD who underwent primary SB were included, with a SSAS of 86% (n=430/499). On multivariate analysis, eyes with surgical failure after primary SB placement were more likely to be male (adjusted odds ratio [aOR]: 2.98, 95% CI: 1.58-5.62, p = 0.0007), have a macula-off status on preoperative examination (adjusted OR: 2.15, 95% CI: 1.10-4.20, p = 0.03), and have presence of preoperative PVR (adjusted OR: 4.26, 95% CI: 1.10, 16.5, p = 0.04).

Conclusions: SSAS after primary SB for primary RRD was 86%. Male sex, macula-off status at presentation, and presence of PVR were factors with increased odds of surgical failure.

CONTROL ID: 3708564
SUBMITTER (NAME ONLY): Taylor Flaherty
TITLE: Foveal Morphology in Williams-Beuren Syndrome
SESSION TITLE: OCT Clinical Applications
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Williams-Beuren Syndrome (WBS) is a complex genetic disorder caused by a microdeletion on chromosome 7q11.23. This work aims to provide a detailed description of foveal features in WBS through quantitative metrics and qualitative classification.

Methods: Individuals with WBS who were examined at the National Institutes of Health as part of the Impact of Elastin Mediated Vascular Stiffness on End Organs study and had Optical Coherence Tomography (OCT) were included in this analysis. The inner limiting membrane and retinal pigment epithelium were manually segmented on foveal OCT scans and processed for pit diameter (PD), foveal slope (FS) and central foveal thickness (CFT). Scans were qualitatively classified as broad if they had a widened area of extrusion of the inner retinal layers or widened PD. Mann-Whitney, Fisher's Exact test and Spearman correlations were used for analyses.

Results: Forty-four WBS patients were included in this study; 21 males and 23 females, 77.3% identifying as non-Hispanic White, with a median age of 22 years (range 5-60 years). Mean best-corrected visual acuity (BCVA) was 20/30 (range 20/20-20/100) OU. Imaging of the right eye of one patient and the left eye of two patients was excluded for poor quality. Mean PD was 1832 μm (range 1195-2345 μm) OD and 1836 μm (range 1278-2304 μm) OS, strongly correlated between eyes ($R=0.84$, $p<0.001$). CFT had a moderate inter-eye correlation ($R=0.56$, $p<0.001$), mean 186 μm (range 157-250 μm) OD and 187 μm (range 166-234 μm) OS, which is thinner than reported healthy population means. FS was also correlated between eyes (Nasal $R=0.78$, $p<0.001$; Temporal $R=0.62$, $p<0.001$). Subgroup analyses were performed on those qualitatively classified as broad fovea (N=36, 81.8%) and normal; there was no significant difference in BCVA, refractive error, age, or sex between groups. PD was significantly wider ($p\leq0.003$) and CFT was thinner ($p=0.002$) in the broad fovea group, while FS did not differ between groups. Thinner CFT was not correlated with BCVA.

Conclusions: This study provides foveal metrics in a cohort of WBS patients, showing a thinned CFT and quantitatively widened PD in eyes with a qualitatively broad fovea, despite a largely White racial identity and balanced sex representation in the cohort. We postulate this foveal morphology is associated with the WBS microdeletion region, supporting the need for future studies of WBS to help understand the molecular basis of foveal development.

CONTROL ID: 3708571

SUBMITTER (NAME ONLY): Christine Sanfilippo

TITLE: Preliminary Antibiotic Resistance Data Among Ocular Bacterial Pathogens in the ARMOR 2021 Study

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Asbell, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|C.M. Sanfilippo, H. DeCory, Medical Affairs, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: Christine Sanfilippo: Commercial Relationship(s);Code E (Employment):Bausch Health US, LLC | Heleen DeCory: Commercial Relationship(s);Code E (Employment):Bausch Health US, LLC | Penny Asbell: Commercial Relationship(s);Code C (Consultant/Contractor):Glia, Senju, Blephex;Code F (Financial Support):Regeneron, Mitotech, Sylentis, Tear Science, MC2, RPB, NIH/NEI

ABSTRACT BODY:

Purpose: Antibiotic resistance among pathogenic bacteria can hinder treatment of infections. Data from antibiotic resistance surveillance studies can provide clinicians with information to guide empiric therapy. The annual Antibiotic Resistance Monitoring in Ocular micRoorganisms (ARMOR) study is the only ongoing nationwide surveillance initiative focused exclusively on antibiotic resistance among common ocular pathogens. Here, we report on interim findings for bacterial isolates collected in 2021.

Methods: As in prior years of the ARMOR study, participating clinical sites across the US submitted isolates of Staphylococcus aureus, coagulase-negative staphylococci (CoNS), Streptococcus pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae cultured from ocular infections to a central laboratory for species confirmation and in vitro antibiotic susceptibility testing. Minimum inhibitory concentrations (MICs) for up to 16 antibiotics (10 drug classes) were determined using broth microdilution methodology and interpreted as per Clinical and Laboratory Standards Institute (CSLI) guidelines and breakpoints.

Results: A total of 446 isolates were included in this interim analysis. Among staphylococci (167 S. aureus/178 CoNS), in vitro resistance was 53%/60% to azithromycin, 37%/37% to oxacillin/methicillin, and 31%/20% to ciprofloxacin; as well, 29% of CoNS exhibited trimethoprim resistance. Multidrug resistance (MDR; ≥3 antibiotic classes) was found among 32% of S. aureus (32%) and 40% of CoNS isolates (40%), with the rate of MDR more than doubled among methicillin-resistant (MR) isolates (81% and 84% among MR S. aureus [MRSA] and MRCoNS, respectively). All 84 P. aeruginosa isolates were resistant to polymyxin B, with <10% resistance to other drug classes. Among the 7 S. pneumoniae isolates, resistance to azithromycin and oral penicillin (both 43%) as well as tetracycline (29%) was detected. The 10 H. influenzae isolates exhibited no resistance to tested drugs.

Conclusions: High rates of in vitro antibiotic resistance were observed among ocular staphylococci collected in 2021, with MR isolates demonstrating considerable MDR. Overall, these resistance profiles should be considered in combination with known ocular pharmacokinetic attributes of antibiotics. These preliminary findings appear consistent with 2020 ARMOR data.

CONTROL ID: 3708572

SUBMITTER (NAME ONLY): Caroline Tipton

TITLE: Analyzing Uveitis Demographics in an Indigent Population to Identify Prescribing Practices to Limit Treatment Cost

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Tipton, G. Reilly, J.M. Ackert, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|E. Chang, Massachusetts Eye and Ear, Massachusetts, UNITED STATES|P. Liberman, Pontificia Universidad Catolica de Chile, Santiago, CHILE|M. Berkenstock, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study the types of uveitis examined in a hospital serving indigent populations in need of low-cost care and to assess prescribing patterns required to limit treatment cost.

Methods: A retrospective chart review examined the electronic medical records of all patients with uveitis-related ICD-9 codes from September 1, 2011 through September 30, 2014 at Drexel Eye Physicians. Data collected included sex, race, anatomic location of the uveitis, systemic disease associations, treatment modalities and insurance carrier. Statistical analysis was performed using χ^2 or Fischer exact tests.

Results: 270 patients (366 eyes) were included for analysis, 67% of patients identified as African American. Most eyes (95.3%, N=349) were treated with topical corticosteroid drops, and only 6 (1.6%) received an intravitreal dexamethasone implant. Nearly 80% depended to some extent on Medicare or Medicaid Assistance for treatment coverage and patients had a median copay of $4 (range $0-80) per eye drop bottle.

Conclusions: Oral prednisone and intravitreal triamcinolone injections were more financially feasible treatments as bridge therapy until the start of antimetabolites as first line agents. Biologic agents may have a higher up-front cost and patients were only switched to that class if it was required for treatment of an associated systemic disease or if the patient was intolerant of antimetabolite side effects.

CONTROL ID: 3708573

SUBMITTER (NAME ONLY): Farzan Abdolahi

TITLE: Retinal vascular perfusion is positively associated with cognitive measures of new learning, information processing, and executive function in African Americans

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: An estimated 55 million people live with dementia worldwide mainly due to Alzheimer's disease and vascular dementias (e.g. cerebral small vessel disease). There is increasing interest in identifying novel tools for early detection of cognitive impairment. We investigated optical coherence tomography angiography (OCTA) based metrics of retinal capillary density and perfusion as a biomarker of cognitive function in asymptomatic, community-dwelling African Americans, who are at high risk of vascular dementia.

Methods: African American participants over the age of 40 without any history of cognitive impairment were recruited. In-clinic neurocognitive assessment was conducted using NIH Toolbox Cognitive Function Battery tests, including Fluid Cognition Composite (episodic memory, executive function, and information processing abilities), Oral Symbol Digit (simple processing speed), and Crystallized Cognition Composite (past learning) tests. 3x3 mm swept source OCTA images centered on the fovea were captured from both eyes. Quantitative measures of retinal vascular density (Vessel Area Density (VAD)) and perfusion (Vessel Area Flux (VAF)), were computed for both eyes and averaged. The relationship between the OCTA measures and cognitive function tests was evaluated using multiple linear regression analysis controlling for age, gender, and level of education.

Results: Ninety six participants were recruited (mean age, 66.4 ± 9.6 years; 31 male, 32.3%, Table 1). VAD and VAF were positively correlated with Fluid Cognition Composite ($p = 0.02$ and 0.005, respectively) and Oral Symbol Digit test scores ($p = 0.0007$ and 0.005, respectively; Fig 1) in the multivariable analyses. OCTA measures were not significantly correlated with Crystallized Cognition Composite score. Results were similar if analyses were limited to data from one eye per person.

Conclusions: OCTA-derived measures of retinal perfusion were correlated with cognitive measures of new learning, information processing, and executive function, but not with measures of past learning. Our results suggest that OCTA might be a useful additional tool for screening and early diagnosis of cognitive impairment.

CONTROL ID: 3708575

SUBMITTER (NAME ONLY): Shelby Hetzer

TITLE: Different functional and histological outcomes in blunt head vs single or repeat blast injury

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hetzer, N. Evanson, Neuroscience, University of Cincinnati College of Medicine, Cincinnati, Ohio, UNITED STATES|C. O'Connell, M. Robson, Pharmacy, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|N. Evanson, Pediatric Medicine and Rehabilitation, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Traumatic brain injury (TBI) research is undergoing an overhaul via the creation of “common data elements” with the goal of improving comparability of work between laboratories. There is also a growing push to understand differences in outcomes between injury models. For example, what are benefits to precise, focal injury models like controlled cortical impact vs diffuse models like weight-drop? While a blunt head injury results in bilateral damage to the optic nerve, is visual system injury also present after diffuse blast injury to the left cranium? Characterization of visual/optic system disruption after a diffuse blast injury of this type has not been characterized in comparison to other TBI models, and little is known about visual system injury outside the optic tract after blast TBI. Our labs hypothesized that there would be differences in functional and histologic outcomes after blast vs blunt head trauma-induced optic nerve injury.

Methods: Male C57BL6/J mice underwent a mild closed-head weight drop (blunt) TBI, one or two mild closed-head blast injuries, or sham injury. Within 7 days, mice underwent behavioral testing for the optokinetic response (OKR). Seven days after injury, eyes were enucleated and flash frozen for western blotting against retinal ganglion cell (RBPMS) and apoptosis (Caspase 3) markers. Mice were then perfused with 4% paraformaldehyde and brains taken for immunohistochemical analysis for neurodegeneration (FluoroJade-B) with planned regions of interest including: optic tract, lateral geniculate nucleus, superior colliculi, and accessory optic system nuclei.

Results: Blunt injury reproducibly resulted in bilateral injury with a significantly blunted OKR, reduced RBPMS, and increased degeneration and gliosis in all regions. Although blast injury also resulted in OKR deficits, we found no reduction in RBPMS. More interestingly, degeneration was limited to the contralateral optic tract and superior colliculi with no degeneration in other visual regions.

Conclusions: Injury modality influences behavioral and histological outcomes to the visual system with a blunt injury producing more severe damage in retina, optic tract, and optic nerve projection targets. Additionally, we appear to be the first to note unilateral injury after blast TBI.

CONTROL ID: 3708577

SUBMITTER (NAME ONLY): Giovanni Montesano

TITLE: Five-year visual field outcomes of the HORIZON trial

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Montesano, G. Ometto, G. Gazzard, NIHR Biomedical Research Centre and UCL Institute of Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|G. Montesano, G. Ometto, D.P. Crabb, Optometry and Visual Sciences, City, University of London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To compare the rate of progression (RoP) of visual field (VF) damage between the two arms of the HORIZON prospective randomized multicentre trial

Methods: A total of 556 participants (one eye per participant) were randomised 1:2 to receive cataract surgery alone (CS, n = 187) or in combination with a Hydrus Microstent (Ivantis, Inc. Irvine, CA; CS-HMS, n = 369). Patients followed for 5 years had planned VF tests at baseline and 6, 12, 24, 36, 48 and 60 months after surgery using a Humphrey Field Analyzer (HFA, Zeiss Meditec, Dublin, CA, USA), 24-2 pattern, SITA-Standard strategy. Additional tests were performed if a worsening in mean deviation of 2.5 dB or more was observed. A total of 3701 VF from 554 (99.6%) patients were available for analysis. Of these, 121 VFs were excluded due to poor reliability (false positive rate > 15%). To eliminate any effects of cataract on VF, pre-surgery baseline tests were excluded from the analysis (561 reliable VFs). We analysed eyes with at least 3 VFs available over at least one year (165 CS and 352 CS-HMS, 2966 VFs). A secondary more inclusive analysis was conducted on all eyes with at least 2 VFs (177 CS and 361 CS-HMS, 3008 VFs). The difference in RoP between the two groups was estimated using a hierarchical mixed effect Bayesian model, modelling point-wise sensitivity values grouped by location, Garway-Heath clusters, eye (all random effects) and arm of the trial (fixed effect). A statistically significant difference in RoP was tested via an interaction term between the effect of the arm assignment and the time from surgery. Significance was reported using a Bayesian p-value. Estimates of the effect are reported, along with 95% Bayesian Credible Intervals.

Results: There was no significant difference in the estimated baseline (intercept of the model) between the two arms, either with the main or secondary analysis. The RoP was -0.26 [-0.36, -0.16] dB/year (47%) slower in the CS-HMS arm (p = 0.0138) in the main analysis and -0.23 [-0.40, -0.05] dB/year (43%, p = 0.0284) in the secondary analysis. Numerical results are reported in Table 1 and Figure 1.

Conclusions: CS-HMS significantly reduced the speed of VF loss compared to CS alone in glaucoma patients by a clinically significant amount.

CONTROL ID: 3708578

SUBMITTER (NAME ONLY): Viktor Gill

TITLE: Presence of Micrometastases of Uveal Melanoma at Autopsy After Non-Melanoma-Related Death

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine the presence of micrometastases (MM) in the liver and other organs in patients diagnosed with primary uveal melanoma who underwent autopsy without previously known metastatic disease. The study was a retrospective, observational study.

Methods: Data from a total of 4282 patients who had been diagnosed with primary uveal melanoma at St. Erik Eye Hospital between 1960 and 2020 was cross-referenced against autopsy and pathology registers. Formalin-fixed paraffin-embedded (FFPE) tissue was collected from patients who had undergone autopsy without known macrometastases. MM was defined as clusters of tumor cells that had not been detected in radiological examinations and had a diameter of ≤ 5 mm. The density of MM per mm^2 was calculated for each organ with digital image analysis (DIA). FFPE tissue was then stained with BAP1, MIB1, CD3, CD20 and CD56.

Results: Eleven patients who had no metastases during routine radiological screening were identified and included. Out of these, three (27 %) had been diagnosed with metastatic disease while hospitalized shortly before death, whereas no macrometastases had been detected in radiological screening of the remaining eight (73 %). In eight of 11 patients (73 %), MM were detected. In turn, four of eight patients with MM (50 %) did not have macrometastases (>5 mm). MM were most common in the liver and lung and their highest density was in the liver. There were no differences in the presence of MM (Fisher's exact p=0.24) or in the density of MM in organs from patients with and without macrometastases (p>0.16). MM showed a low proliferative activity with MIB1, ranging from 0 to 3 % positivity, indicating possible dormancy. There was a 100 % proclivity for CD3 infiltration in all MM, whilst 79 % of MM in the lung and liver was positive for CD20 and 70 % were positive for CD56.

Conclusions: MM could be identified in most patients with primary uveal melanoma, regardless of concurrent macrometastases. This seems to confirm that uveal melanoma can seed MM early.

CONTROL ID: 3708580

SUBMITTER (NAME ONLY): Mark Christopher

TITLE: Comparison of Deep Learning Glaucoma Detection Using Optic Nerve Head Fundus Photos and Optical Coherence Tomography

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Christopher, C. Bowd, E. Walker, A. Belghith, M.H. Goldbaum, J. Rezapour, R.N. Weinreb, L. Zangwill, Hamilton Glaucoma Center, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|M.A. Fazio, C.A. Girkin, Callahan Eye Hospital, Heersink School of Medicine, University of Alabama - Birmingham, Birmingham, Alabama, UNITED STATES|G. De Moraes, J.M. Liebmann, Bernard and Shirlee Brown Glaucoma Research Laboratory, Edward S. Harkness Eye Institute, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|A. Grzybowski, Department of Ophthalmology, Uniwersytet Warminsko-Mazurski w Olsztynie, Olsztyn, POLAND|A. Grzybowski, Institute for Research in Ophthalmology, Poznan, POLAND|

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ABSTRACT BODY:

Purpose: To compare the accuracy of deep learning (DL) in detecting glaucoma using optic nerve head (ONH) fundus photos versus optical coherence tomography (OCT) across different patient populations, disease severity, and axial lengths.

Methods: Longitudinal imaging and 24-2 visual field (VF) testing was collected on a Diagnostic Innovations in Glaucoma Study (DIGS) and African Descent and Glaucoma Study (ADAGES) cohort of 546 glaucoma (935 eyes) and 346 healthy (626 eyes) patients. The dataset included 20,828 ONH fundus photos and 25,751 unsegmented Spectralis circle scans. Eyes in the glaucoma group had repeatable glaucomatous VF damage or glaucomatous ONH damage based on clinical ONH examination or expert review of photos. Healthy eyes were required to have normal appearing ONHs and VF results. Participants were randomly divided into independent training (85%), validation (5%), and test (10%) sets. Accuracy was evaluated using area under the receiver operating characteristic curve (AUC) and evaluated as a function of participant ancestry (African vs. European), glaucoma severity (24-2 MD > -4.0 dB vs. 24-2 MD <= -4.0 dB), and axial length (AL <= 25 mm vs. AL > 25 mm).

Results: Fundus DL models achieved an AUC of 0.91 (95% CI: 0.89 – 0.92), significantly higher ($p=1.3x10^{-5}$) than OCT DL models, AUC = 0.86 (95% CI: 0.84 – 0.87). Fundus DL accuracy was significantly higher ($p<1x10^{-6}$) in

African (AUC = 0.97) vs. European (AUC = 0.85) descent participants, significantly higher (p $p<1x10^{-6}$) in eyes with 24-2 MD <= -4.0 dB (AUC = 0.99) vs. 24-2 MD > -4.0 dB (AUC = 0.88), and significantly higher (p=0.03) in eyes with AL > 25 mm (AUC = 0.94) vs. AL <= 25 mm (AUC = 0.90). ONH OCT DL accuracy was significantly higher (p=0.001) in European (AUC = 0.87) vs. African (AUC = 0.81) descent participants, significantly higher ($p<1x10^{-6}$) in eyes with 24-2 MD <= -4.0 dB (AUC = 0.95) vs. 24-2 MD > -4.0 dB (AUC = 0.81), and comparable (p=0.82) in eyes with AL > 25 mm (AUC = 0.84) vs. AL <= 25 mm (AUC = 0.85).

Conclusions: Photo-based DL glaucoma detection significantly outperformed OCT-based detection. In both cases, ancestry and disease severity had a significant impact on DL model accuracy. These findings underscore the importance of understanding how patient characteristics, disease severity, and reference standard definitions influence the performance of DL models in glaucoma.

CONTROL ID: 3708584

SUBMITTER (NAME ONLY): Kristen Segars

TITLE: Conductor cells drive cell-cell communication in corneal and corneal-limbal regions

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: When a cornea is injured, the release of ATP from damaged cells activates the ionotrophic purinergic receptor P2X7, which localizes to the wound edge within two hours of injury. This correlates with the presence of prominent calcium signaling events that have a high probability of communication between clusters of adjacent cells. Our goal is to determine if calcium signaling differs between the corneal epithelium and the corneal-limbal interface, and analyze whether calcium signaling correlates with cellular motility after injury.

Methods: A 3-D printed holder was used to stabilize the intact globe for imaging cell-cell communication and motility after injury. Globes were incubated in Fluo-4AM and CellMask DeepRed, and imaging performed over time using the Zeiss 880 Confocal Microscope. Images were collected after injury on the corneal epithelium and corneal-limbal regions of male C57Bl6 mice. Image J and MATLAB were used for analysis of clustering between cells, the probability of communication between adjacent cells, and to identify the presence and abundance of conductor cells

Results: Calcium signaling was detected at both the central corneal epithelium and at the corneal-limbal interface. Mobilization was detected between layers of basal and wing cells in the central cornea and was absent in apical cells. In the corneal-limbal region, we again did not detect communication in the apical cells and detected a strong correlation between sensory nerves and basal cells. Only the basal cells migrated into the wound bed to close the wound. Using a unique machine learning approach we identified a subpopulation of cells that signal at a significantly greater frequency and duration than others. We hypothesize that the presence of this functionally distinct cellular population is decreased with age.

Conclusions: Injury induces P2X7-driven calcium signaling events in both the corneal and the corneal-limbal regions. The calcium signaling events propagate between different layers of epithelial cells in both central and peripheral corneal regions, and between epithelial cells and nerves in peripheral regions. High-signaling conductor cells were found throughout the cornea after injury, with the greatest number of conductor cells found adjacent to the wound. These results demonstrate that cell-cell communication driven by a functional subpopulation of conductor cells occurs throughout the corneal region.

CONTROL ID: 3708586

SUBMITTER (NAME ONLY): Nathan Grove

TITLE: Cataract phacoemulsification in people with dementia: Characterization and outcomes.

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Grove, B.D. Wagner, University of Colorado School of Public Health Department of Biostatistics & Informatics, Aurora, Colorado, UNITED STATES|N.C. Grove, V.S. Pelak, K.L. Christopher, A.M. Lynch, J.L. Patnaik, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cataract surgery in people with dementia (PWD) has been evaluated in the context of claims-based retrospective studies. However, due to limitations of these studies, detailed clinical and surgical information is lacking for this population. This retrospective cohort study characterizes pre-, intra-, and post-operative information from PWD in a cataract surgery outcomes database.

Methods: Demographics, medical and ocular history, surgical characteristics, and postoperative measures were analyzed for differences between PWD and non-PWD cohorts. Patient-level data were analyzed with Fisher's Exact Test, and eye-level data were analyzed with logistic regression using generalized estimating equations to account for correlation of eyes from the same individual.

Results: 507 eyes from 296 PWD were identified using appropriate ICD codes and cross referenced to a cataract surgery outcomes database containing 12,949 eyes from 7,853 patients who underwent cataract phacoemulsification at a single center between January 2014 and October 2019. PWD were older by almost 5 years (73.4 (SD=11.5) vs. 68.5 (SD=11.1), $p<0.001$) and all subsequent analyses were adjusted for age. PWD had shorter duration cataract surgeries (18.2 (SD=11.0) min. vs. 20.4 (SD=14.8) min., $p=0.010$), were more likely to have mature cataract (3.9% vs. 2.4%, $p=0.013$), and were more likely to have complex surgeries (capsular staining, mechanical pupillary expansion, CTR) (19.9% vs. 15.6%, $p=0.028$). The rate of general anesthesia was higher in PWD (1.6% vs. 0.7%, $p=0.003$). There were no differences in complication rates between PWD and non-PWD cohorts. Both preoperative best corrected LogMAR visual acuity (BCVA) (0.454 (SD=0.586) vs. 0.378 (SD=0.519), $p<0.001$) and postoperative BCVA (0.153 (SD=0.387) vs. 0.096 (SD=0.305) $p<0.001$) were worse in PWD. BCVA significantly improved in both groups ($p<0.001$), however, the average magnitude of improvement in BCVA was better in PWD (-0.308 (SD=0.439), vs. -0.286 (SD=0.423), $p=0.030$).

Conclusions: In this single center analysis, PWD present for cataract surgery at a later age, and were more likely to have mature cataracts, complex surgery, and general anesthesia, but did not have higher rates of complication, and showed significant improvement in BCVA following surgery. These findings should be encouraging to PWD undergoing counseling for cataract surgery, and for the potential for improved function in PWD.

CONTROL ID: 3708590

SUBMITTER (NAME ONLY): Ken Kitayama

TITLE: The impact of COVID-19 on adults with vision and/or hearing impairment in California

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kitayama, V. Tseng, D. Pan, F. Yu, A.L. Coleman, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|K. Kitayama, A.L. Coleman, Epidemiology, University of California Los Angeles, Los Angeles, California, UNITED STATES|D. Pan, F. Yu, Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore associations between sensory impairment (vision and/or hearing) and Coronavirus disease 2019 (COVID-19) in the adult 2020 California Health Interview Survey (CHIS) population.

Methods: A cross-sectional study was conducted using the 2020 CHIS, the nation's largest state health survey with a sample representative of the population of California. The exposure of interest was having sensory impairment, defined as answering "Yes" to the question, "Are you blind or deaf, or do you have a severe vision or hearing problem?" The outcome of interest was whether a health professional suspected the respondent had COVID-19, assessed among those adults who had or thought they had COVID-19 and contacted a health professional. Logistic regression models were constructed to determine the odds of suspected COVID-19 by sensory impairment status, controlling for the following covariates: age, sex, race/ethnicity, self-reported general health status, current smoking habits, overweight/obese body mass index, and current health insurance status. All analyses were weighted according to the CHIS sampling design.

Results: A total of 21,949 sampled participants were included, representing a weighted estimate of 29,684,882 individuals. The weighted prevalence of sensory impairment was 5.9% (95% confidence interval [CI] 5.4-6.4%). Approximately 10.9% (95% CI: 10.3-11.6%) of all participants had or thought they had COVID-19, 4.9% (95% CI: 4.5-5.3%) contacted a health professional about COVID-19 concerns, and 1.7% (95% CI: 1.4-2.0%) were suspected of having COVID-19 by a health professional. Regression analyses were performed in a subgroup of 988 participants representing 1,431,690 individuals who had or thought they had COVID-19 and contacted a health professional. Those with sensory impairment had 2.12 times the unadjusted odds of suspected COVID-19 compared to those without sensory impairment (odds ratio [OR]: 2.12, 95% CI: 0.98-4.63). Those with sensory impairment had 2.51 times the adjusted odds of suspected COVID-19 compared to those without sensory impairment (adjusted OR: 2.51, 95% CI: 1.03-6.10).

Conclusions: In the 2020 CHIS adult population, individuals with vision and/or hearing impairment had greater odds of having COVID-19 suspected by a health professional. Additional studies are necessary to triangulate these findings and further explore this possible increased risk for COVID-19 in this vulnerable population.

CONTROL ID: 3708594

SUBMITTER (NAME ONLY): Janice Maliakkal

TITLE: Characteristics of Patients with Highest Severity of Illness in Hospitalizations for Eye Conditions

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Maliakkal, W. Foos, B. Bernstein, H. Pakhchanian, S. Shin, Ophthalmology, The George Washington University, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify income levels and demographics among patients admitted to the hospital with a primary diagnosis of an eye disease and severe illness during hospitalization.

Methods: Inpatients with a principal diagnosis of an eye disease were identified from the National Inpatient Sample (NIS), a nationally representative de-identified database of US hospitalizations for years 2014, 2016, and 2018. The healthcare cost and utilization project (HCUP) uses MDCs (Major Diagnostic Categories) to provide insight into what conditions are being treated in hospitals. Only patients with a principal diagnosis (MDC) of Diseases and Disorders of the Eye during admission were included. Cases with the highest severity of illness were identified based discharges with a score of 3 or 4 on the all patient refined diagnostic related group (APR-DRG) severity of illness scale (4 indicating extreme severity of illness). Age, insurance type and status (Medicare, Medicaid, private insurance, or uninsured), median income of patient zip-code, sex, and geography of patient residence were recorded. Descriptive statistics were analyzed among these patients.

Results: 24,829 inpatients with a principal diagnosis of eye disorder or disease and highest severity of illness were identified during the three-year period. 51.8% were male and most patients resided in large central metropolitan areas. Medicare insurance (50.1%) was the most prominent payer, and the average age of adult patients was 60.7. Most patients resided in large central metropolitan areas. Patients from low-income codes comprised a minority of patients with highest severity of illness (30%) and represented a decreasing percentage of these patients over time.

Conclusions: Between 2014-2018, an increasing number of patients were hospitalized with a primary diagnosis of an eye condition and categorized with highest severity of illness during their hospital stay. Patients from low-income zip codes comprised a minority of these patients with decreasing prevalence over time. This study shows that low-income status may not be associated with increased severity of illness during hospitalization for eye diseases. Further studies involving specific eye conditions and complications are necessary to explore this conclusion.

CONTROL ID: 3708595

SUBMITTER (NAME ONLY): Yuzuru Sasamoto

TITLE: Transit-amplifying cell genes CAV1 and CAV2 are required to maintain corneal epithelial phenotype.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Caveolin (CAV) 1 and 2 are integral membrane proteins that constitute the major components of small membrane pouches termed caveolae. Despite the recognized pleiotropic functions in diverse tissues, their roles in the ocular surface compartments are not fully understood. In the cornea, CAV1 expression was previously found to increase with aging and was negatively associated with wound healing. However, the exact molecular roles of CAV1 and CAV2 in corneal epithelium remain to be elucidated. In the current study, we investigated the contribution of CAV1 and CAV2 to the maintenance of the corneal epithelial phenotype.

Methods: Human donor corneas were obtained from the Saving Sight eye bank, Kansas City, MO and CorneaGen, Seattle, WA. Immunostaining was performed to determine the distribution of CAV1 and CAV2 expression in the cornea. Limbal epithelial cell cultures were transfected with CAV1- and CAV2-targeting siRNAs designated as CAV1 KD #1, CAV1 KD #2, CAV2 KD #1 and CAV2 KD #2. Western blotting, colony-forming assays and RNA-seq were performed using CAV1 and CAV2 knockdown cells and their controls.

Results: Immunohistochemical analyses revealed high CAV1 and CAV2 expression by the transit-amplifying cells (TACs) located in the basal epithelial layer of the limbus and to a lesser degree of the central cornea. siRNA-induced CAV1 and CAV2 KD in cultured limbal TACs resulted in significant reduction of their self-renewal potential as evidenced by attenuated

colony-forming efficiency (66.6 +/- 16.8% decrease by CAV1 KD #1 and 36.8 +/- 21.4% decrease by CAV1 KD #2; 72.4 +/- 13.2% decrease by CAV2 KD #1 and 34.8 +/-14.7% decrease by CAV2 KD #2; all compared to controls, Ps = 0.0002, 0.0118, <0.0001 and 0.0024, respectively). RNA-seq analyses showed that loss of CAV1 and CAV2 led to significant downregulation of genes involved in corneal epithelial formation (e.g., IVL, MUC21, and KRT78) and induction of genes involved in stromal development (e.g., FBN1 and SMPD1).

Conclusions: Our study reveals novel functional roles of CAV1 and CAV2 expressed by TACs in the human cornea. Specifically, CAV1 and CAV2 are essential for TAC self-renewal and the maintenance of the corneal epithelial phenotype.

CONTROL ID: 3708597
SUBMITTER (NAME ONLY): Muriel Schornack
TITLE: Tear Exchange in Established Scleral Lens Wearers
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Tear exchange beneath rigid contact lenses helps to supply the cornea with the oxygen required for normal corneal metabolism. Studies of short-term wear of scleral lenses (SLs) in healthy volunteers have suggested that minimal tear exchange occurs during SL wear. The purpose of the present study was to document tear exchange in established SL wearers.

Methods: Established SL wearers (≥ 6 months of wear) were recruited for this study during routine follow-up evaluations. All participants had worn their SLs for at least 2 hours prior to their study visits. Demographic data and landing zone (LZ) design for each lens was recorded. Sodium fluorescein (NaFl) was instilled over the lens in each eye. Presence or absence of NaFl in the post-lens fluid reservoir (FR) was recorded 10 seconds, 1 minute, 2.5 minutes, and 5 minutes after instillation. Differences between NaFl uptake into the FR between different lens designs and diameters were compared using Chi-squared tests.

Results: 30 established SL patients (53 eyes) with a were recruited (mean age of 46 ± 14.6 years (range 24-76)). Mean duration of lens wear prior to study visit was 4.8 ± 2.1 hours (range: 2.1-10 hours). Twenty-seven lenses (50%) had quadrant-specific LZ, 18 (34%) had toric LZ, and 8 had spherical LZ. Overall, NaFl was observed in the FR in 9 eyes (17%) at 10 seconds, 14 eyes (26.4%) at 1 minute, 25 eyes (47.2%) at 2.5 minutes, and 33 eyes (62.3%) at 5 minutes. With quadrant-specific LZ (n=25), NaFl was observed in the FR in 4 eyes (14.8%) at 10 seconds, 5 eyes (18.5%) at 1 minute, 11 eyes (40.7%) at 2.5 minutes, and 14 eyes (51.9%) at 5 minutes. With toric LZ (n=18), NaFl was observed in the FR in 3 eyes (16.7%) at 10 seconds, 7 eyes (38.9%) at 1 minute, 12 eyes (66.7%) at 2.5 minutes, and 15 eyes (83.3%) at 5 minutes. With spherical LZ (n=8), NaFl was observed in the FR in 2 eyes (25%) at 10 seconds, 1 minute, and 2.5 minutes and in 4 eyes (50%) at 5 minutes. No significant differences were noted between any LZ design at any time point (p=0.8, 10 seconds; p=0.3, 1 minute; p=0.08, 2.5 minutes; p= 0.09, 5 minutes).

Conclusions: Tear exchange occurs beneath SLs in a majority of established wearers. Neither lens diameter nor LZ design were associated with an increased likelihood of tear exchange in this sample.

CONTROL ID: 3708600

SUBMITTER (NAME ONLY): Alexander Alfonso

TITLE: Toxicologic Profiles of Alpha-Hemolytic Streptococci Recovered from Endophthalmitis

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Alpha-hemolytic streptococci, especially viridans group streptococci (VGS), have been increasingly associated with endophthalmitis. The prevalence and diversity of toxins secreted by alpha-hemolytic streptococci are largely uncharacterized. The purpose of this study was to identify and characterize the toxicological profiles of recent alpha-hemolytic streptococci recovered from endophthalmitis.

Methods: Twenty ocular streptococcal isolates recovered from endophthalmitis between January 10, 2019 and October 29, 2021 were included in this study. PCR and DNA sequencing were conducted to confirm genotype identification and screen for 3 toxins: autolysin, hyaluronidase, and pneumolysin. Isolates' genotypes were compared to phenotypes generated using Vitek2 and/or API kits. E tests were used to confirm antibiotic susceptibility profiles for cefuroxime, vancomycin, levofloxacin, benzylpenicillin, and moxifloxacin.

Results: Nineteen (95%) isolates were identified as members of the alpha-hemolytic group. Thirteen (68.4%) isolates of this group included members of the VGS group. S. mitis/oralis (n=8, 57.1%) was the most common isolate among VGS species. Other members included S. sanguinis (n=3), and 1 each of S. mutans, S. pseudopneumoniae, and S. thermophilus. S. pneumoniae (n=5) was the most common isolate among non-VGS group isolates. Streptococcus dysgalactiae was the sole non-alpha-hemolytic strain. Phenotype-genotype identification agreement was present among 15 (75%) of the 20 isolates.

At least one toxin was found among 9 (45%) isolates, with 5 (55.5%) identified as members of VGS. Hyaluronidase was identified in 5 (25%) samples, pneumolysin in 4 (20%) samples, and autolysin in 2 (10%) samples. Dual toxins (hyaluronidase, pneumolysin) were identified in a S. pneumoniae and S. mitis/oralis strain. No isolate was positive for all three toxins. In vitro susceptibility profiles included: vancomycin (100%, MIC90-1 mcg/mL), moxifloxacin (90%, MIC90-0.642 mcg/mL), levofloxacin (90%, MIC90-5 mcg/mL), cefuroxime (80%, MIC90-3.3 mcg/mL), and benzylpenicillin (75%, MIC90-0.492 mcg/mL).

Conclusions: Definitive laboratory identification of alpha-hemolytic streptococci may be challenging. The high level of toxin production among endophthalmitis VGS isolates could contribute to their aggressive clinical course and poor patient outcomes.

CONTROL ID: 3708602

SUBMITTER (NAME ONLY): Michael Shi

TITLE: Association among basement membrane diseases of the eye: Fuchs endothelial corneal dystrophy (FECD), anterior basement membrane dystrophy (ABMD) and age-related macular degeneration (AMD)

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shi, H. Greyner-Almeida, A. Sima, T. Ruster, P. Gianfagna, B. Plotke, J.M. Sullivan, S.P. Patel, Ophthalmology, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|A.E. Millen, Epidemiology and Environmental Health, University at Buffalo School of Public Health and Health Professions, Buffalo, New York, UNITED STATES|J.M. Sullivan, S.P. Patel, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The pathophysiologic processes in FECD, ABMD, and AMD all involve basement membrane dysfunction. We tested the hypothesis that FECD is independently associated with presence of ABMD and AMD.

Methods: This is a single-center cross-sectional study, approved by the University at Buffalo IRB. A single ophthalmologist for this study systematically examined consecutive patients for FECD, ABMD and AMD. We enrolled individuals >18 years old with documented exam findings for all three ocular diseases, and excluded those with bilateral corneal scarring (preventing full exam) and penetrating keratoplasty. FECD was graded (modified Krachmer scale) based on findings of central corneal guttae (0=absent to 6=confluent with corneal edema). Patients that had undergone endothelial keratoplasty were assigned FECD grade 7. Patients with characteristic map-dot fingerprint changes of the epithelium were considered ABMD positive. Patients with macular drusen, pigmentary changes, or atrophy of the retinal pigment epithelium were considered AMD positive. Those with sparse small drusen or absence of pigment abnormalities were considered AMD negative. Poisson regression with robust estimation was used to estimate crude and age-adjusted prevalence ratios and 95% confidence intervals of ABMD, AMD or both among participants with different severity levels of FECD compared to individuals with absent FECD (grade 0 used as reference group). Significance was set at $p<0.05$.

Results: Among 435 participants (ages 18-96, mean 61 years; 262 female, Table 1), the prevalence of having ABMD, AMD, or both, was greater in those with FECD grades of 3-5, 7, and ≥ 1 vs. 0 (Table 2). After age adjustment, we continued to find a statistically significant increased prevalence of ABMD, AMD or both among those with FECD grade 7 vs. 0 (Table 2).

Conclusions: Advanced FECD may be significantly associated with ABMD and AMD. However, these findings seem to be driven by associations in those who have undergone corneal transplantation, suggesting a role for corneal transplantation in the progression of ABMD and AMD.

CONTROL ID: 3708603

SUBMITTER (NAME ONLY): Matthew Wilson

TITLE: Targeting Bromodomain of Brg-1 in Uveal Melanoma Cells with Small Molecule PFI-3: A Possible Novel Therapy

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.W. Wilson, E. Louie, The University of Tennessee Health Science Center Department of Ophthalmology Hamilton Eye Institute, Memphis, Tennessee, UNITED STATES|C. Yang, Y. Wang, L.M. Pfeffer, Pathology, University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Brg-1 is a catalytic subunit of the SWI/SNF chromatin-remodeling complex, which contains a bromodomain and helicase/ATPase activity. Although mutated in some cancers, Brg-1 is not mutated in uveal melanoma. Targeting Brg-1 in uveal melanoma (UM) could promote chromatin instability and sensitize it to alkylating agents. Herein, we examined the effects of the small molecule inhibitor PFI-3 which binds the bromodomain of Brg-1 in non-metastatic MEL270 and metastatic OMM2.5 UM cell lines. We previously showed that the STAT3 transcription factor was highly activated in metastatic UM cells versus non-metastatic UM cells. We also examined BRG1 and STAT3 expression in UM tissue in situ.

Methods: Brg-1 protein expression was verified using immunoblot analysis. UM cells were plated into 96 well plates and exposed to varying concentrations and combinations of PF-I3 and temozolomide (10-100 mM), and cell death assays were performed by ELISA. RNA in-situ hybridization was performed on 5-µm FFPE sections of archived enucleated eyes.

Results: Immunoblot analysis shows the Brg-1 protein is present in both UM cell lines. PFI3 alone had minimal effect on either UM cell line at 72 hours but increased sensitivity to TMZ-induced apoptosis. RNA-ISH showed co-localization of Brg-1 and STAT3 in vivo.

Conclusions: Our study shows Brg-1 is present in UM cell lines. PFI3 sensitizes UM cell lines to temozolomide leading to increased cell death. Targeting the bromodomain in Brg-1 presents a possible novel therapeutic treatment for metastatic UM. Furthermore, BRG1 and STAT3 RNA is co-expressed in specific niches in UM tissue in situ.

CONTROL ID: 3708605

SUBMITTER (NAME ONLY): Rebecca Schur

TITLE: Suppression of electromagnetic interference in electroretinography from a patient with an implanted left ventricular assist device (LVAD)

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Schur, A. Yuan, Ophthalmic Research, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|B. Eck, Imaging Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: A left ventricular assist device (LVAD) is an implantable cardiac pump that uses a magnetically-levitating rotor to pump blood into circulation in patients with congestive heart failure. In a patient with an implanted LVAD, the high-frequency pump rotation introduces significant interference in electroretinography (ERG) recordings. We evaluate filtering methods to improve ERG quality in the presence of LVAD interference.

Methods: A patient with an implanted LVAD was referred for ERG testing on suspicion of a retinal dystrophy. Full-field ERG (ffERG) and pattern ERG (pERG) were performed according to ISCEV standards. Recordings were acquired in full-bandwidth mode and again in low-bandwidth mode. Digital low-pass and band-stop filtering were performed to mitigate ERG interference. Post-processing was also evaluated in a control subject with no implanted device.

Results: High-frequency interference corresponding to the speed of the pump was present in all recordings (Fig. 1). When applied in post-processing, both low-pass and band-stop filters suppressed the interference and presented readable ERGs without affecting peak times or amplitudes (Fig. 2). By contrast, when recording in low-BW mode, the filter drop-off was not steep enough to remove the interference and peak delays were introduced that could not be readily corrected.

Conclusions: LVAD interference in ERGs can be successfully removed using simple digital filters. If post-hoc data processing capabilities are unavailable, a large amount of interference can be suppressed with a lower acquisition bandwidth and additional recordings of each stimulus response.

CONTROL ID: 3708607

SUBMITTER (NAME ONLY): Homayoun Bagherinia

TITLE: A novel deep learning method for choroidal-scleral junction segmentation

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Bagherinia, L. De Sisternes, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|L. Omlor, Corporate Research and Technology, Carl Zeiss Inc., Pleasanton, California, UNITED STATES|Y. Shi, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|H. Zhou, J. Lu, R.K. Wang, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reliable choroidal layer analysis has become an important diagnostic tool for retinal diseases. We propose a choroidal-scleral junction (CSJ) segmentation method for swept-source optical coherence tomography (SS-OCT) volumes. Our method is independent of scan field of view (FOV) and designed based on a novel deep learning (DL) algorithm.

Methods: Manually graded multi-retinal layer segmentation (MLS) was used to generate the ground truth which is defined as the region between RPE and CSJ. The inputs consist of 3 mm OCT patches extracted from five neighboring B-scans along with the attenuation corrected patches. A total of 17,722 training and 10,596 validation data from 603 3x3 mm, 6x6 mm, 9x9 mm, 12x12 mm scans acquired using PLEX® Elite 9000 (ZEISS, Dublin, CA), with eye diseases such as age-related macular degeneration (AMD), were used to train a model. A network was designed with the first half of an autoencoder (encoder) followed by a discrete cosine transform (decoder). In prediction, an uncertainty algorithm detects the low segmentation confidence regions that are replaced by interpolation to generate the complete CSJ surface. 61 6x6 mm and 61 12x12 mm scans from the same eyes with eye diseases such as AMD were used to generate choroidal thickness maps using manual and automated segmentation which are defined as the distance between the MLS Bruch's membrane (BM) and the CSJ. The performance of the algorithm was reported using correlation between manual and automated methods for each sector of the ETDRS grid (Fig 2). Regression and Bland-Altman plots were used for 3 mm, 6 mm and 11 mm zones.

Results: Fig 1 shows five neighboring 3 mm OCT input and ground truth patches, and examples for CSJ segmentation results overlaid on OCT images for different scan FOV. Fig 2 shows the ETDRS and correlation between the manual and automated segmentation in each sector including the regression and Bland-Altman plots for the central 3 mm, 6 mm and 11 mm zones. Most ETDRS sectors show significant correlation (>0.85) between manual and automated measurements. Lower correlation within the ONH vicinity was explained by increased difficulties in the BM segmentation.

Conclusions: We proposed a novel deep learning based CSJ segmentation. The choroidal thickness maps generated by automated and manual segmentation have a strong correlation and good agreement. Automated segmentation may be a valuable diagnostic tool for retinal diseases.

CONTROL ID: 3708608

SUBMITTER (NAME ONLY): Jean Jiang

TITLE: Mechano-activated Connexin Hemichannels and Glutathione Transport Protect Lens Fiber Cells against Oxidative Insults

SESSION TITLE: Lens Physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Jiang, Y. Tong, M. Riquelme, Y. Du, Y. Quan, S. Gu, University of Texas Health Science Center, SAN ANTONIO, Texas, UNITED STATES|Y. Tong, Second Xiangya Hospital, Central South University, CHINA|

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ABSTRACT BODY:

Purpose: Long-lived lens fiber cells require strong cellular protective function against oxidative insults for maintaining their hemostasis and viability; however, the underlying molecular mechanism remainly large elusive. We hypothesize that mechano-activated connexin (Cx) hemichannels (HCs) and glutathione (GSH) transport protect lens fiber cells against oxidative insults.

Methods: Site-directed mutagenesis was used to prepare recombinant RCAS(A) DNA constructs containing different Cx50 site mutations. High-titer recombinant RCAS(A) retrovirus was prepared and used to infect chick embryonic fibroblast cells and lens primary cells to express exogenous Cxs. Western blot was performed to determine expressions of Cxs. Fluid flow shear stress was used to apply mechanical stimulation. Cx HC activity was determined by Lucifer yellow/rhodamine dextran uptake assay. Hydrogen peroxide and ultraviolet B radiation were used to induce oxidative stress. Intracellular GSH and reactive oxygen species were determined by using commercial fluorescence-based kits. Cell apoptosis and necrosis were measured by Annexin V and PI staining. Single lens fiber cells were isolated by enzymatic digestion and cell dissociation.

Results: We found that mechano-activated Cx HCs mediated the transport of GSH into lens fiber cells, leading to the decrease of the accumulation of intracellular reactive oxygen species induced by both hydrogen peroxide and ultraviolet B radiation, and protection of lens fiber cells against cell apoptosis and necrosis. In addition, HCs formed by both homomeric Cx50, Cx46 and heteromeric Cx50/Cx46 were mechanosensitive and facilitated the transport GSH into the cell. Among them, mechano-activated Cx50 HCs showed higher Km than Cx46 HCs (Km: Cx50: 0.72 ± 0.12 mM; Cx46: 0.43 ± 0.14 mM) and Vmax (Cx50: 44.50 ± 2.00 AU/20 min; Cx46: 17.18 ± 1.34 AU/20 min) in transporting GSH. Consistently, deficiency of Cx50 in single lens fiber cells exhibited a higher level of oxidative stress. Moreover, outer cortical short lens fiber cells expressing full length Cxs were more resistant to oxidative injury than central core long lens fibers

Conclusions: Activation of Cx HCs by interstitial fluid flow in lens fiber cells is essential in cellular uptake of reductants and protection of lens fiber cells against oxidative stress-induced cell death.

CONTROL ID: 3708610
SUBMITTER (NAME ONLY): Basma Baccouche
TITLE: Activin A limits VEGF-induced permeability
SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: B. Baccouche, L. Lietuvninkas, Y. Li, A. Kazlauskas, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|A. Kazlauskas, Department of Physiology and Biophysics, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|
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ABSTRACT BODY:
Purpose: Elucidating principles of vascular permeability will enable development of novel approaches to diagnose and treat retinopathy, which eventually develops in the majority of patients with diabetes. Transforming growth factor b (TGF-β) plays an important role in regulating endothelial (EC) function. We examined the effect of activin A (activin), a member of the TGF-β superfamily, on vascular endothelial growth factor (VEGF) and cytokine-induced permeability.
Methods: High glucose-treated (30 mM D-glucose for at least 10 days) primary human retinal endothelial cells (HG-HRECs) were used for all experiments. Permeability was quantified by electric cell-substrate impedance sensing. VEGF-dependent signaling, and VEGF receptor 2 (VEGFR) half-life was investigated by Western blot analysis.
Results: We discovered that activin A and its biding partner follistatin (FST) influenced the response of HG-HRECs to VEGF. Pretreating HG-HRECs with activin A attenuated VEGF-induced barrier relaxation whereas FST counteracted the effect of activin on VEGF-dependent permeability. We also investigated the mechanism by which activin restrained VEGF-induced permeability. Activin reduced the half-life of activated VEGFR and suppressed VEGF-dependent activation of signaling enzymes. Taken together, these observations suggest that activin accelerates degradation of activated VEGFR and thereby attenuates signaling events and permeability. Finally, activin had no effect on barrier relaxation in response to TNF-α (transforming necrosis factor a) and IL1-β (interleukin 1 b).
Conclusions: Members of the TGF β family such as activin A are capable of contributing to vascular homeostasis by attenuating responsiveness to VEGF, but not to cytokines. The underlying mechanism appears to include accelerated degradation of activated VEGFR2.

CONTROL ID: 3708611

SUBMITTER (NAME ONLY): Elmira Jalilian

TITLE: Exosomes from 3D cultures of Bone Marrow Mesenchymal Stem Cell (BM-MSCs) have higher neuro-regenerative potential than those generated from 2D conditions

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Jalilian, B. Bigit, S. Amin, H. Massoumi, E. Katz, V.H. Guaiquil, M. Rosenblatt, A.R. Djalilian, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|E. Jalilian, Department of Bioengineering, University of Illinois at Chicago, University of Illinois at Chicago, Chicago, IL, US, academic, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal nerves and innervation are susceptible to several diseases including diabetes. Despite the clinical need to promote corneal nerve regeneration, few specific therapeutic interventions are available. MSCs and their paracrine effect mediated by exosomes presents an attractive treatment for enhancing nerve regeneration. In this study, we assessed the neuro regenerative potential of exosomes from BM-MSCs cultured in 2D and 3D systems.

Methods: Human BM-MSCs were cultured in 2D monolayer and 3D bioreactor systems. Exosomes were isolated using ultracentrifugation followed by size and concentration measurements utilizing NanoSight and Exoview. Mouse trigeminal ganglia (TG) neurons were isolated from Thy1-YFP mice possessing fluorescent corneal nerves. The neurons were plated in the presence and absence of exosomes derived from 2D or 3D culture systems. Neuronal growth and morphology were monitored over 5 days. Thereafter, the neurons were fixed and immune-stained with β3 tubulin followed by confocal microscopy. Images were analyzed by Neurolucida software to obtain the density and length of the neurites.

Results: The Nanosight tracking analysis revealed significant increase in concentration of exosomes obtained from 3D vs. 2D culture condition (24X fold-change). Exoview analysis showed significantly higher concentration of CD63, CD81 and CD91 exosomal markers in 3D vs. 2D condition. Furthermore, a notable shift towards a more heterogeneous exosome phenotype was observed in the 3D compared to 2D culture systems. Exosomes derived from both 2D and 3D condition significantly induced neurite growth after 5 days in culture compared to untreated control. Neurolucida analysis of the Immunostaining images (β3 tubulin) showed a significant increase in density and complexity of the neuronal growth of TG neurons in 3D vs. 2D condition. Additionally, a significant increase in neuron branching was observed in 3D versus 2D.

Conclusions: Our results demonstrate the distinct effect of BM-MSCs-derived exosomes in neurites growth and elongation. Exosomes obtained from 3D culture system enhanced the neurite complexity and branching compared to the effect of vesicles from 2D culture. This specific property could potentially enhance the therapeutic effect of EVs in vivo and provide new therapeutic interventions for the restoration of damaged corneal nerves.

CONTROL ID: 3708612
SUBMITTER (NAME ONLY): Noah Heilenbach
TITLE: Neighborhood-Level Social Determinants of Health and Follow Up
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Heilenbach, T. Ogunsola, C. Elgin, Y. Abazah, A. Aboseria, R. Alshamah, J. Alshamah, V. Patel, M. Iskander, L.A. Al-Aswad, Ophthalmology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|N. Heilenbach, L.A. Al-Aswad, Population Health, New York University Grossman School of Medicine, New York, New York, UNITED STATES|D. Fry, G. Lovasi, Drexel University, Philadelphia, Pennsylvania, UNITED STATES|A. Aboseria, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|S. Mooney, University of Washington, Seattle, Washington, UNITED STATES|G. Maestre, The University of Texas Rio Grande Valley, Brownsville, Texas, UNITED STATES|T. Ogunsola, M. Iskander, New York Medical College, Valhalla, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: To investigate whether our screening program targeted low socioeconomic neighborhoods in New York City and whether physical disorder and social vulnerability correlate with follow up after ophthalmic screening.

Methods: The TeleOphthalmology Mobile Unit screened 957 participants for cardiovascular risk factors and common causes of blindness. The participants' demographic information and residential addresses were collected at the time of screening. Physical disorder scores were generated using the CANVAS virtual audit system. Google street view was used to evaluate building conditions, building vacancy, graffiti, and litter. Physical disorder ratings were interpolated using ordinary kriging and each participant was assigned a score based on a 500-meter radius around their address. Social vulnerability scores were generated using data from the Centers for Disease Control 2018 Social Vulnerability Index (SVI) database. Each participant was assigned the SVI score of their residential census tract. Multinomial logistic regression was performed to identify predictors of successful follow up (N=156) as compared with lack of follow up (N=160) or inability to contact (N=228).

Results: The mean summary SVI score of the study population recommended for follow up was 0.81 (SD=0.21), with 0 indicating low vulnerability and 1 indicating high vulnerability. Age of participants was inversely correlated with failing to follow up with an ophthalmologist after screening (coefficient=-0.28; p=0.008). Population density of the Census tract was inversely correlated with being unreachable by the researchers (coefficient=-4.77e-06; p=0.042). Per capita income, percentage uninsured, and physical disorder were not significantly different between those who did follow up and those who did not follow up or could not be reached.

Conclusions: Our study participants disproportionately live in Census tracts that are more socially vulnerable than the national average. Older patients were more likely to follow up and may have had more symptomatic disease or more serious diagnoses. Population density was positively associated with follow up, possibly because denser tracts in New York City have more affluent residents and greater access to medical care. Our study demonstrates that the SVI can identify populations in need of eye care and that older patients are more likely to follow up than younger patients.

CONTROL ID: 3708613

SUBMITTER (NAME ONLY): Aileen Rowland

TITLE: Limited betadine preparation prior to nonhuman primate intravitreal dosing decreases adverse reactions in control animals

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rowland, J. Schroud, T. Streit, P. Sonnentag, Covance Inc, Madison, Wisconsin, UNITED STATES|A. Rowland, E. Bentley, Department of Surgical Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nonhuman primates are routinely utilized in ocular preclinical research because of their homology to human ocular anatomy. Intravitreal dosing is one the most investigated dose administration routes, and is performed on more than 150 nonhuman primates annually at Labcorp Drug Development, in Madison, WI. In 2018, our preparation method for intravitreal dosing was changed from swabbing the conjunctiva and eyelids with dilute betadine-soaked cotton-tipped applicators (full preparation), to soaking the globe and conjunctiva with dilute betadine for 2 minutes (limited preparation). Both methods are followed by rinsing with saline. It was hypothesized that a limited preparation may reduce adverse events after dosing compared to a full preparation as betadine has a known potential to cause hypersensitivity reactions.

Methods: Control animal data from January 2014-June 2021 for all preclinical toxicology studies with intravitreal dosing was retrospectively analyzed. Data recorded included preparation method, control article composition, number of control animals, number of intravitreal injections, post-injection medications and additional procedures performed. Recorded adverse events included squinting, rubbing, face pressing and periorbital swelling.

Results: Full preparation was used for 96 control animals that were dosed 394 times in total, and limited preparation was used for 107 control animals that were dosed 465 times in total. No differences were noted in control article composition, number of intravitreal injections per study or post-injection medications. However, the number of animals with adverse reactions (Figure 1) and total number of adverse reactions (Figure 2) were reduced using the limited preparation compared to full preparation. Most notably, after changing to a limited preparation method, there was a 68% reduction in the number of animals noted to squint post-dosing, and an 82% reduction in the number of squinting observations.

Conclusions: The change in preparation from full to limited has decreased the number of adverse events. This reduction in adverse events both improves animal welfare and also allows for a more accurate interpretation of post-injection adverse events in test article-treated animals.

CONTROL ID: 3708614
SUBMITTER (NAME ONLY): IMANE TARIB
TITLE: Digital Media Effect on Diabetic Eye Care During COVID-19 pandemic
SESSION TITLE: Telehealth
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: I. TARIB, B. Parekh, V. Tabor, D. Patel, A. Deb, P. P. Patel, J.G. Parekh, EyeCare consultants of New Jersey, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|S. J. Parekh, St. Joseph's Health Hospital, New York Medical College, Valhalla, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: To gauge the impact of healthcare technology in the management of diabetic retinopathy during the COVID-19 pandemic.

Methods: The study was conducted at EyeCare Consultants of New Jersey's in their two locations in NJ, Woodland Park and Edison. Eye care professionals (ECPs–two ophthalmologists, one optometrist) surveyed 400 diabetic patients during the first year of the pandemic (March 2020- February 2021).

The patients all received previous instructions with CheckedUp, a patient education digital platform utilizing audiovisual and touchscreen to further educate patients, during in-office visits.

The 400 diabetic patients were divided equally into two groups. To ensure the adherence of dietary and behavioral modifications related to diabetes mellitus, Group 1 received traditional phone calls while Group 2 received video calls and supplementary education with CheckedUp.

Both groups had a follow-up in person in September 2021. Surveys elicited responses to gauge consistency of HbA1C management.

Results: Adherence was defined as HbA1C values which remained within a target value lower than or equal to their baseline and/or <7.0% as well as compliance with medications, dietary restrictions, regular physical activity and follow-up visits. The results found a significant difference between educating the patient with a phone call versus a video call and CheckedUp.

At the next follow-up visit in person: Group 1 had an adherence of 48% (96 patients) and had several patients with HbA1C values exceeding the targeted value. Group 2 had an adherence of 69% (138 patients) and were more compliant with a healthier lifestyle. They also stated that their telehealth appointment with CheckedUp helped reinforce the importance of maintaining a normal HbA1C value.

Conclusions: This study illustrates the ability of digital medicine platforms to supplement virtual and in-person consultations to manage diabetic retinopathy, especially during the pandemic. Compliance is an important matter in the management and preventing progression of diabetic retinopathy. Digital tools like CheckedUp assist with optimizing patient care in these unprecedented times.

CONTROL ID: 3708615

SUBMITTER (NAME ONLY): Benjamin Chaon

TITLE: Using the Electronic Medical Record to Increase Laboratory Test Monitoring in Ocular Inflammation Patients: A Quality Improvement Study

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Treatment of chronic, non-infectious ocular inflammation includes corticosteroids, disease modifying anti-rheumatic medications (DMARDs), and biologics. To mitigate adverse effects associated with the use of these medications, routine laboratory test monitoring is recommended throughout treatment. We evaluated the effectiveness of an alert added to the electronic medical record (EMR) to aid in laboratory test monitoring for patients prescribed these high-risk medications.

Methods: A prospective, interventional study assessed the effect of an alert within the EMR on laboratory test ordering at the Division of Ocular Immunology at the Wilmer Eye Institute. The primary outcome measure was the change in number of ordered lab tests at 3, 6, and 12-months after the alert activation compared to pre-interventional levels and overall throughout the study period. The laboratory tests that were monitored included complete blood count (CBC), comprehensive metabolic panel (CMP), dual-energy x-ray absorptiometry (DEXA) scans, fasting lipid panel, hemoglobin A1c, and interferon gamma release assays (IGRA).

Results: The laboratory test orders for 162 patients on high-risk medications were analyzed. Only the frequency of ordering the DEXA and IGRA increased significantly, compared to baseline, throughout the study. Conversely, there was a significant decrease in the frequency of ordering of fasting lipid profiles and hemoglobin A1c at each time point and for CBC and CMP at the 6-month time point.

Conclusions: An EMR alert results in increased laboratory test ordering initially for tests drawn on a yearly basis, but the effect on more frequently ordered tests wanes with time if the alert can be silenced by the provider. Nonetheless, it provides a novel mechanism to increase laboratory ordering in patients on high-risk medications that can be adapted for use in other EMR software. Future studies are needed to assess if physician laboratory test ordering behavior is altered throughout the study period with the use of a non-silenceable alert.

CONTROL ID: 3708616

SUBMITTER (NAME ONLY): Kira Lin

TITLE: Comparison of Near and Distance Visual Acuity Measured via ETDRS Charts in neovascular Age-related Macular Degeneration and Diabetic Macular Edema Study Participants Managed with Anti-VEGF Therapy

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To minimize the number and reliance on in-person clinical care and trial visits, many mobile apps for visual acuity (VA) self-assessment have been introduced recently. However, few publications, to our knowledge, have compared near VA with distance VA, routinely tested in clinical practice, using standardized charts. The purpose of this paper is to evaluate the level of agreement between near and distance VA obtained with Early Treatment Diabetic Retinopathy Study (ETDRS) charts in the clinic.

Methods: This study is a multi-site study for 90 participants with neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME). Patients with nAMD or DME in one eye, aged ≥18 years, VA better than 20/200 were eligible. Each participant had the study eye assessed two times with each chart at both the Baseline (V2) and end of study (V3) visits, using habitual correction for distance VA at 4 m and near VA at 40 cm. Bland-Altman plots with repeated measurements per participant were produced. The 95% limits of agreement (LoA) for the difference between near and distance VA assessment methods are presented, along with 95% confidence intervals (CIs) around the LoAs calculated using the method of variance estimates recovery.

Results: From the preliminary results, 39 participants had completed the V2 visit, of which 34 (87%) had nAMD, mean (±SD) distance VA in the study eye was 0.27 logMAR (0.214), mean (±SD) age was 73.0 (8.4) years and 20 (51%) were female. A total of 35 participants with data at both V2 and V3 visits from the Johns Hopkins University clinical site were included in this analysis. Agreement between BCNVA obtained with the near ETDRS chart in the clinic and BCDVA obtained with the distance ETDRS chart in the clinic observed a mean difference of 0.04 with an upper LoA of -0.22 logMAR (95% CI: -0.29, -0.18) and a lower LoA 0.29 logMAR (95% CI: 0.25, 0.36).

Conclusions: Our results suggest that the LoAs CIs when comparing the VA obtained with the near and distance charts were close to being within a 0.3 logMAR threshold, beyond which typically is considered a clinically relevant change for these diseases. Differences might come from some participants being less optimally corrected with their habitual near correction.

CONTROL ID: 3708618

SUBMITTER (NAME ONLY): Doina Gherghel

TITLE: Variable contrast flicker in patients with non-advanced age-related macular degeneration: results from the 3rd year follow-up

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Gherghel, E. Besinger, K. Dieter, J.D. Rodriguez, G. Wallstrom, M.B. Abelson, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of effective therapies for non-advanced age-related macular degeneration (AMD) has been hindered by a lack of sensitive, reversible endpoints to be used in clinical trials. Our group has previously reported (1) on the Ora Variable Contrast Flicker (Ora-VCF™) test which has successfully identified differential contrast sensitivity (CS) thresholds for non-advanced AMD patients as compared to matched controls. The present study reports follow-up results from the third longitudinal visit for a cohort of non-advanced AMD patients originally tested in 2017.

Methods: Nine non-advanced AMD patients with visual acuity of 20/25 (at the entry point) and 16 age matched controls were included in this follow-up visit. On a single study visit, all participants completed a battery of visual function assessments, including Ora-VCF™ tests. During the Ora-VCF™ test, patients viewed flickering targets presented via a customized software. Stimuli were presented at three temporal frequencies (low, mid, and high) and two background luminance levels (low- and high-mesopic) as previously reported (1).

Results: Patients with non-advanced AMD had significantly higher contrast thresholds for the intermediate flicker rate (between 10-20 Hz) at both background luminance levels (both $p < 0.03$), as well as a trend for the high flicker rate (> 20 Hz) when presented on the low luminance background ($p = 0.0714$), as compared to matched controls. These results are consistent with patterns observed during prior visits across the duration of the longitudinal study.

Conclusions: The Ora-VCF™ test indicates that, compared to matched healthy subjects, non-advanced AMD patients with good BCVA have higher contrast sensitivity thresholds for flickering images presented at mid- and high-flicker rates – particularly when presented in the low-mesopic luminance range. The general pattern of differentiation between non-advanced AMD patients and matched controls on this test has remained relatively consistent over a 3-year longitudinal period. This suggests a repeatable test over time that can effectively serve as a reliable, reversible functional endpoint for future clinical trials for therapies aimed at treating non-advanced AMD. It also suggests relative stability in visual function for patients with non-advanced AMD over a period of 3 years.

CONTROL ID: 3708619

SUBMITTER (NAME ONLY): Mary-Grace Reeves

TITLE: State-level differences in duties permitted to be performed by medical assistants in the delivery of eye care

SESSION TITLE: Health Economics and Health Care Delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Reeves, John F. Hardesty, MD, Department of Ophthalmology and Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|M. Reeves, J. Xue, A. Milstein, G. Tabin, J.L. Goldberg, K. Schulman, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: High quality, high volume international surgical sites implement a strategy of deskilling, or assigning well-circumscribed care tasks to personnel trained for this limited role, as a means of achieving cost savings. Our previous work has demonstrated personnel costs account for the largest categorical difference in cost of cataract surgery between international and US sites. This paper examines the extent to which deskilling strategies are available to US ophthalmic surgical practices by evaluating state differences in care tasks allowed to be performed by medical assistants. Engaging medical assistants to the full extent of their scope of practice could reduce personnel costs by optimizing care teams for skill mix and efficiency.

Methods: We defined seven central tasks in cataract surgery care, most of which are performed by mid-level ophthalmic providers at international eye hospitals. These tasks include taking a patient's vital signs, administering eye drops, collecting point of care glucose levels, inserting IVs, counseling patients on their surgery, and performing post-op monitoring. Using the American Association of Medical Assistants State Scope of Practice Laws, we determined which of these tasks are allowed, not allowed, and not addressed in regulations governing medical assistants' practice in each state.

Results: States varied in the extent to which each task is allowed to be carried out by lower level providers. New York and Washington have the greatest number of tasks allowed to be performed by medical assistants. The most commonly permitted tasks included IV insertion (48%) and taking vital signs (36%). 6% of states prohibit MAs from administering eye drops, while 28% either explicitly or possibly allow this. A few states remain silent on these issues in the official regulations, which begs the question of whether the services are permitted or excluded in MA scope of practice there.

Conclusions: Significant variation exists in state-by-state regulations of medical assistant activities. Understanding scope of practice of medical assistants in the United States will permit better integration of MAs into delivery of eye care and optimize cost and efficiency of cataract surgery.

CONTROL ID: 3708620

SUBMITTER (NAME ONLY): Trisha Miglani

TITLE: Age-stratified quantitative ultrasound biomicroscopy image analysis of iris thickness using multivariable analysis to optimize reliability

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Miglani, M. Chang, T. Kolosky, M.R. Levin, J. Alexander, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|C. Martinez, M. Bazemore, M. Jaafar, W. Madigan, Children's National Hospital, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Normative data for human iris parameters is not well established, resulting in a lack of understanding of the association between quantitative iris features and presence of intraocular disease. The purpose of this study was to quantify iris thickness of pediatric subjects in ultrasound biomicroscopy (UBM) images using an optimized image processing protocol with high repeatability and reliability of measurements.

Methods: Eligible participants' parents were offered consent and subjects were enrolled prior to imaging. 86 images from 26 eyes in 14 healthy pediatric subjects (mean age 2.0+/-1.1yrs, median 1.8yrs, range 0.2-4.1yrs) were analyzed according to a prospective protocol. Two trained observers measured iris thickness on two axial and two longitudinal UBM images per eye in raw format and with image processing using edge detection. Image quality was graded by a trained ultrasonographer. Logistic regression was used to determine association between image features and consistency of measurements. Intraclass correlation coefficient (ICC) between observers was the outcome of interest. Covariates of interest were orientation (axial vs longitudinal), quality (good vs excellent), and processing (raw vs edge detection). Covariates contributing to improved ICC were used in UBM analysis to determine iris thickness stratified by age. Mean values were determined for ages <1yrs, 1-2yrs, and >2yrs. ANOVA was performed to see if there were statistically significant differences in thickness measurements based on age.

Results: Normative data for iris parameters were found to differ significantly by age strata (0-1yrs, 1-2yrs and 2-5yrs). Maximal iris thickness increased with age ($p<0.001$) while minimal and central iris thickness did not vary by age. ICC for these parameters ranged from 0.70-0.97. Preliminary results of multiple linear regression suggest that orientation and image processing were associated with improved ICC. Image quality was not significantly associated with ICC.

Conclusions: Iris measurement consistency is improved by use of longitudinal image orientation and edge detection in image processing. Normative data based on the optimized image analysis protocol suggests that iris thickness varies significantly with age.

CONTROL ID: 3708622

SUBMITTER (NAME ONLY): Lien Vu

TITLE: Contrast Sensitivity with Take-Home SpotChecks Test in Healthy Adults

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Vu, H. Cheng, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Lien Vu: Commercial Relationship: Code N (No Commercial Relationship) | Han Cheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: SpotChecks is a newly designed disposable contrast sensitivity (CS) test that has a fine step change of 0.01 logCS and multiple versions. This study evaluated the repeatability of CS with take-home Spot-Checks, in-office Spot-Checks and near Pelli-Robson (PR) charts in healthy adults.

Methods: Thirty-nine healthy adults (age 22-84, mean 43±17, M:F = 21:18) participated in two office visits (7-66 days apart, mean 11±10 days) and an at-home component. Each visit included monocular high-contrast acuity and 12 different CS tests (6 SpotChecks and 6 PR charts in random orders) under the same lighting (luminance 110 cd/m2) all at near in the same eye with habitual correction. SpotChecks consists of 24 rows by 5 columns of 9 mm grey round spots on a white paper with contrast decreasing by 0.01 log units per spot (logCS ranges 0.90 to 2.09). At-home testing was self-administered SpotChecks once a day on six different days using the same eye. Subjects held the SpotChecks at a comfortable reading distance while marking spot positions with guessing encouraged. The third incorrectly marked spot determined threshold. PR charts were read at 40 cm and scored counting 0.05 for each letter read correctly then subtracting 0.15. Repeatability limit for two measurements was calculated as $\sqrt{2}*1.96*Sw$, Sw was within-subject standard deviation determined with one way analysis of variance. Limits of agreement (LOA) between single measurements of SpotChecks and PR were evaluated with Bland-Altman plots considering multiple observations per subject.

Results: Mean high contrast logMAR near acuity was -0.04±0.07, -0.03±0.08 for visit 1 and 2, respectively. Mean logCS from SpotChecks (1.90±0.08 visit 1, 1.92±0.09 visit 2, 1.93±0.09 home) was about 0.10 higher than that of PR (1.80±0.07 visit 1, 1.83±0.07 visit 2). Intravisit repeatability limit of logCS was similar between SpotChecks (0.13 visit 1, 0.14 visit 2) and PR (0.16 visit 1, 0.14 visit 2). Interday repeatability limit for take-home SpotChecks was 0.14, similar to that of intervisit SpotChecks (0.15) and PR (0.19). LOA between SpotChecks and PR was 0.10±0.19 for visit 1 and 0.09±0.20 for visit 2.

Conclusions: Take-home SpotChecks showed similar repeatability as in-office SpotChecks and PR charts. SpotChecks therefore has the potential to be used for self-monitoring of vision between office visits.

CONTROL ID: 3708628

SUBMITTER (NAME ONLY): Jo-Hsuan Wu

TITLE: Association Between Macular OCT/OCTA Parameters and Visual Acuity in Glaucoma

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Wu, S. Moghimi, T. Nishida, V. Mohammadzadeh, A. Kamalipour, L.M. Zangwill, R.N. Weinreb, Shiley Eye Institute and Viterbi Family Department of Ophthalmology, University of California, San Diego, Hamilton Glaucoma Center, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate if macular optical coherence tomography (OCT)/OCT angiography (OCTA) parameters demonstrate correlation with visual acuity (VA) in glaucoma eyes.

Methods: Pseudophakic primary open angle glaucoma eyes were included in this cross-sectional study. Foveal VD (fVD), parafoveal VD (pfVD), perifoveal VD (perifVD), and whole-image VD (wiVD) of both superficial and deep layers, and their corresponding GCC thicknesses were calculated from OCTA 6x6 mm^2 macular scans. The area and circumferences of foveal avascular zone (FAZ) and foveal density 300 (FD300) were also measured. Univariable and multivariable linear mixed model were performed to characterize the correlation between OCT/OCTA parameters and logMAR VA in different glaucoma severities.

Results: 144 eyes (mean age=80.0 years) were included. VA differed significantly between early (80 eyes, mean logMAR VA=0.05) and moderate-severe (64 eyes, mean logMAR VA=0.11) glaucoma groups (P=0.003). In the multivariable analysis of early glaucoma eyes, none of the OCT/OCTA parameters correlated with VA (P>0.05 for all). In the multivariable analysis of moderate-advanced glaucoma, greater FAZ area (β=0.228, P=0.035) and circumference (β=0.063, P=0.032) were associated with worse logMAR VA (R^2=0.11), but FD300 was not. Lower measurements of almost all GCC thicknesses, including superior hemifield thicknesses, were significantly associated with worse VA (β=0.002-0.003, P<0.05, R^2=0.11-0.33), except for the inferior hemifields of perifGCC and wiGCC. For superficial VD, lower superior hemifield perifVD (β=0.007, P=0.045) and lower superior hemifield wiVD (β=0.008, P=0.042) correlated with worse logMAR VA (R^2=0.11-0.12). For deep VD, only fVD was associated with worse logMAR VA (β=0.004, P=0.049, R^2=0.11).

Conclusions: Some macular OCT/OCTA parameters, particularly GCC thickness, FAZ area and circumference were associated with VA in moderate-advanced glaucoma, but not early-stage glaucoma. Superficial and deep VD showed region-dependent association with VA, indicating the potentially differential involvement of local vasculatures in VA performance.

CONTROL ID: 3708629

SUBMITTER (NAME ONLY): Or Shmueli

TITLE: Geographic atrophy area measurement: comparison between fundus autofluorescence and OCT

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Shmueli, Y. Shwartz, J. Levy, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|I. Benhamou, L. Joskowicz, School of Computer Science and Engineering, Hebrew University of Jerusalem, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: To compare geographic atrophy (GA) area and shape descriptors using fundus autofluorescence (FAF) annotation versus optical coherence tomography (OCT) annotation with complete retinal pigment epithelium and outer retinal atrophy (cRORA) criteria in cases of dry age-related macular degeneration (AMD).

Methods: Retrospective annotation of GA in FAF and OCT in a single timepoint. Primary outcomes: GA area, focality, perimeter, circularity and minimal distance from the center. The primary outcomes were compared between both modalities. Correlations of the primary outcomes on OCT with the difference in GA area between both modalities were analyzed using multivariate regression analysis.

Results: 30 pairs of FAF and OCT scans from 30 eyes of 18 patients with dry AMD were included. The mean total GA area measured 8.77±4.38 mm^2 with FAF and 2.78±3.39 mm^2 with OCT ($P<0.0001$). The mean FAF-OCT area difference was 5.99±4.22 mm^2. Multivariate regression analysis revealed a significant correlation between the FAF-OCT area difference and GA focality and minimal distance from the center on OCT (adjusted $r^2 = 0.66$).

Conclusions: This study quantitatively measured and compared GA area using fundus autofluorescence as compared to OCT. The mean GA area measured on OCT was 3.15 times smaller than that on FAF. FAF-OCT area difference correlated with GA focality and minimal distance from the center on OCT. Further research is needed to establish the clinical application of these findings.

CONTROL ID: 3708630
SUBMITTER (NAME ONLY): Eitan Shemuelian
TITLE: Can the Inner Nuclear Layer Thickness Help Detect Progression in Advanced Glaucoma?
SESSION TITLE: Imaging in glaucoma
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: E. Shemuelian, G. Wollstein, M. Ramos Cadena, Z. Ghassabi, T. Lee, H. Ishikawa, J.S. Schuman, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|G. Wollstein, J.S. Schuman, Department of Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|T. Lee, J. Hu, Department of Population Health, NYU Langone Health, New York, New York, UNITED STATES|J. Hu, Department of Environmental Science, NYU Langone Health, New York, New York, UNITED STATES|H. Ishikawa, Departments of Ophthalmology, Medical Informatics, and Clinical Epidemiology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|F. Lavinsky, School of Medicine, Universidade do Vale do Rio dos Sinos, Sao Leopoldo, RS, BRAZIL|
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ABSTRACT BODY:

Purpose: The ability to detect progression in eyes with advanced glaucoma is challenging because of known limitations of commonly used structural and functional parameters reaching their minimal measurable limit (floor effect) or increased measurement variability. We examined the ability of inner nuclear layer (INL) thickness measurements to demonstrate change longitudinally in eyes with early and advanced severity glaucoma.

Methods: Subjects with glaucoma and ≥4 visits were included in the study. Subjects in the “Early/Moderate” group (EG) had average circumpapillary retinal nerve fiber layer (cRNFL) thicknesses ≥60µm and subjects in the “Advanced” group (AG) had average cRNFL thicknesses ≤60µm. All subjects had comprehensive ophthalmic examination, Humphrey visual field (Zeiss, Dublin, CA) testing, and spectral-domain OCT (Cirrus HD-OCT; Zeiss) optic nerve head (ONH) and macula scans. Segmentation of the INL was performed using the Iowa Reference Algorithms (Retinal Image Analysis Lab, Iowa Institute for Biomedical Imaging, Iowa City, IA) and segmentation errors were manually corrected by a trained grader. Overall INL thickness along with the superior and inferior hemifields were used for analysis. Rates of progression were estimated from longitudinal OCT and visual field (VF) data using mixed effects models adjusting for baseline age, follow-up duration, and signal strength at each visit.

Results: 23 eyes (23 subjects), 12 with EG and 11 with AG, were included in the study. At baseline, a statistically significant difference between groups was detected in MD, cRNFL, and GCIPL thicknesses (Table 1). In EG eyes, the rate of change was significantly different than a zero slope for cRNFL thickness, C:D ratio, and GCIPL thickness (Table 2). Inferior INL thickness was the only INL parameter showing significant rate of change. However, in the advanced group, all parameters (including both global and sectoral INL thicknesses) showed significant rate of change except for the cRNFL.

Conclusions: Longitudinal measurements of INL thickness may be useful for following disease progression in subjects with advanced-stage glaucoma where cRNFL thickness is no longer useful.

CONTROL ID: 3708633

SUBMITTER (NAME ONLY): Xu Cheng

TITLE: Evaluating accommodative response of eyes wearing soft contact lenses for myopia control

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Accommodation of the eye in response to multifocality of a lens may impact the myopia control efficacy of the lens. A soft contact lens (SCL) with the RingBoost^{TM} technology (RB) was designed to maximize myopia control effect without affecting normal accommodation of the eye. The study evaluated accommodative response (AR) of the RB lens by comparing with other SCL and spherical spectacle (SL) corrections.

Methods: The study was double-masked with a cross-over design. AR of 10 adults (18-24 yrs) was assessed with bilateral wear of SL at baseline and four SCLs of different designs in random order: single-vision (SV), dual-focus (DF), center-distance multifocal (MF), and RB. Refractive states (RS) of the subject's right eye under four levels of target vergences (TV) between 0.25 and 4.59 D were determined based on spherical equivalent power measured by an open-field auto-refractor (GS) and Shack-Hartmann wavefront aberrometry (under natural pupils) with three analytical methods: minimum wavefront RMS (minRMS), best-sphere fit to the wavefront (MTR), and paraxial focus (PF). Slopes of accommodative responses (SAR) were obtained from linear fit of RS to TV and compared among lens types.

Results: AR of RB, DF, MF, SV, and SL by four refractive methods are provided in Figure 1. Results varied by method of RS determination and lens type. SARs (D/D) of RB were not significantly different from SV with all four refractive metrics ($p>0.05$) and was statistically larger than SL with minRMS by 0.13 (95%CI: 0.05, 0.21). SARs of DF were statistically smaller than SV with MTR and minRMS but larger than SV and SL with GS ($p<0.05$). SARs of MF were statistically smaller than SV and SL with all four metrics ($p<0.05$) except for PF when compared to SV ($p>0.05$). Compared to DF, SARs of RB were statistically larger by 0.13 (0.05, 0.22) and 0.11 (0.03, 0.19) with minRMS and MTR, respectively, but smaller with GS by 0.09 (0.03, 0.15).

Conclusions: This exploratory study demonstrated interpretation of accommodative response differed by method of RS determination. However, across all metrics, RB lens had similar or better AR than single-vision corrections. AR measured with the open-field auto-refractor provided largely consistent results with those of wavefront-based methods except with DF. Optimal method to quantify RS in myopia control lenses requires further investigation.

CONTROL ID: 3708636

SUBMITTER (NAME ONLY): Christopher Rosenberg

TITLE: Locality is the strongest predictor of performance in image-based differentiation of bacterial and fungal corneal ulcers from India

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.R. Rosenberg, T.K. Redd, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Christopher Rosenberg: Commercial Relationship: Code N (No Commercial Relationship) | Travis Redd: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Infectious keratitis (IK) is a major cause of blindness. Clinical recognition of the underlying cause of infection is necessary to guide empiric treatment but is often difficult even for cornea specialists. Our prior work showed India-based experts were significantly better than an international cohort at differentiating Indian cases of bacterial and fungal keratitis (BK/FK) on an image-based test. FK is much more common in tropical regions like India compared to more temperate environments like much of the US and Europe. In this secondary analysis, we explored whether this difference in performance could be explained by regional variability in FK burden.

Methods: We used a test set of 100 culture-proven photos of IK, 50 each of FK and BK. 66 cornea specialists from 16 countries (Table 1) graded each image, providing a predicted probability of FK or BK. Area under the curve (AUC) was calculated as the primary performance metric for each respondent. Because FK prevalence data are not available in most regions, the following known risk factors were used as surrogates of FK burden: tropical climate (based on latitude, average annual temperature, and dew point) and agricultural work (based on percent of gross domestic product). These predictors were incorporated into a multivariate linear regression model along with local (Indian) vs. external (non-Indian) practice location to predict respondent AUC.

Results: Bivariate analyses showed significant associations between AUC and Indian practice location ($P<0.01$), latitude ($P<0.01$), agricultural economy ($P<0.01$), dew point ($P=0.01$), and average temperature ($P<0.01$). However, multivariate regression revealed that only Indian practice location was statistically significant after controlling for all other predictors ($P=0.01$).

Conclusions: Local experts remained significantly better at differentiating Indian cases of FK and BK compared to their international counterparts, regardless of regional variability in FK burden. Future work should determine whether similar regional effects occur elsewhere, or if India-based cornea specialists are simply better at this task due to the extraordinarily high volume of IK in their patient population. The results may inform educational efforts to enable earlier initiation of appropriate antimicrobial therapy and improved visual outcomes.

CONTROL ID: 3708637

SUBMITTER (NAME ONLY): Martin Zinkernagel

TITLE: Compositional features of the gut microbiome in patients with uveitis

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Zinkernagel, M.R. Munk, E. Herzog, S. Wolf, D.C. Zysset-Burri, Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland., Bern, SWITZERLAND|

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ABSTRACT BODY:

Purpose: The human gut microbiome is a complex ecosystem and refers to the combined genetic material of microorganisms in the gut. The gut microbiome has many important physiological functions, such as promoting digestion and absorption of nutrients, regulating the function of the immune system or synthesizing vitamins and amino acids. Dysbiotic conditions can favor invasion and growth of pathogenic species and can disrupt immune homeostasis, thus potentially induce diseases. In this study we investigated compositional alterations of the gut microbiome in patients with recent onset acute anterior uveitis (AAU).

Methods: Twenty three patients with recent onset AAU without therapeutic intervention were included. Twenty three individuals with no history of uveitis were included. The metagenomic DNA was analyzed in stool samples using the TruSeq DNA PCR-Free Library Preparation kit for library preparation and the Illumina NovaSeq 6000 platform for sequencing. HLA-B*27 genotypes were confirmed by allele-specific PCR.

Results: Mean age of both groups was 46 years with a matched female to male ratio. The taxonomical features and compositional difference between both groups will be presented. To identify taxonomic and functional features with significantly different relative abundances between both groups and to identify associations with clinical metadata, the multivariate association between by linear models (MaAsLin) R package was applied using default settings. A difference was considered to be statistically significant if $q < 0.20$ after adjusting for false discovery rate (Benjamini-Hochberg)

Conclusions: The development of noninfectious anterior uveitis may be influenced by compositional alterations of the intestinal microbiome. Possible mechanisms include antigenic mimicry, destruction of the intestinal barrier and priming of immune cells.

CONTROL ID: 3708639

SUBMITTER (NAME ONLY): Sara Emami

TITLE: The Association Between Glaucoma and Cardiovascular Disease in the Elderly California Medicare Population

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Emami, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|F. Yu, A.L. Coleman, Ophthalmology, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma and cardiovascular disease (CVD) are common in the elderly population. Although a few studies have proposed both conditions to share pathophysiologic mechanisms, inconsistent findings on their relationship exist in the literature. Thus, we performed a cross-sectional study to investigate the association between glaucoma and CVD in the 2019 California (CA) Medicare population.

Methods: Using the 2019 CA Master Beneficiary Summary File and Standard Analytic Files of Part B Carrier Claim data files from the Centers for Medicare and Medicaid Services, patients with International Classification of Diseases, Tenth Revision (ICD-10) diagnosis codes for glaucoma were identified. Inclusion criteria were 65 years or older, CA residence, coverage with both Medicare Part A and B, and at least one Part B claim in 2019. The comparison group included all CA Medicare beneficiaries without glaucoma diagnosis. Demographic characteristics including age, sex, and race/ethnicity were extracted, along with Charlson Comorbidity Index (CCI) that served as an indicator for systemic comorbidities. The main outcome was CVD, which was defined by having at least one ICD-10 diagnosis code for the following: ischemic heart disease, congestive heart failure, valvular disease, angina, arrhythmias, myocardial infarction, stroke, cardiac arrest, or tamponade. Logistic regression models were performed to assess the association between glaucoma and CVD after adjusting for potential confounders mentioned above.

Results: Among 2,717,346 patients who met the inclusion criteria, 411,099 (15%) had a glaucoma diagnosis. Glaucoma beneficiaries were more likely to be between the ages of 70 to 74 (24%), female (60%), white (58%), and had a CCI score of 1 to 2 (36%). Moreover, 188,458 (46%) glaucoma beneficiaries had a CVD diagnosis. On univariate analysis, glaucoma beneficiaries had a statistically significant increased odds of having CVD (odds ratio [OR]=1.38, $P<0.001$) compared to their non-glaucoma counterparts. After adjusting for confounders in the multivariable analysis, the association remained statistically significant (aOR=1.12, $P<0.001$).

Conclusions: This study found glaucoma to be associated with CVD in the 2019 CA Medicare population. Further studies are needed to elucidate the mechanism that links the two diseases, and determine if glaucoma patients may benefit from early interventions for prevention of CVD.

CONTROL ID: 3708640

SUBMITTER (NAME ONLY): Emma Mahally

TITLE: PITPβ/βA3/A1-crystallin complex is critical for PIP metabolism in retinal pigment epithelium (RPE)

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.R. Mahally, R. Daley, N.A. Stepicheva, S. Ghosh, H. Liu, O. Chowdhury, A. Strizhakova, V. Koontz, S.L. Hose, D. Sinha, P. SHANG, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|K. Teel, A. McCauley, R.V. Rajala, Dean McGee Eye Institute, University of Oklahoma Health Science Center, Oklahoma City, Oklahoma, UNITED STATES|J.S. Zigler, D. Sinha, Wilmer Eye Institute, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Phosphatidylinositol phosphates (or PIPs) have emerged as key regulators of diverse cellular processes including membrane trafficking, receptor tyrosine kinase signaling, and cytoskeleton dynamics. However, the regulation of PIP metabolism in RPE cells has been rarely investigated. We have reported that βA3/A1-crystallin, an ocular moonlighting protein with diverse functions interacts with a phosphatidylinositol transfer protein-PITPβ. In this study, we examined their effect on PIP-metabolism in RPE cells.

Methods: Cryba1 (encoding βA3/A1-crystallin) RPE conditional KO (cKO) mice and Cryba1$^{fl/fl}$ control mice were used in this study. RPE explant cultures isolated from either wildtype C57BL/6J mice or transgenic mice were utilized for in vitro RPE studies. RNA-seq was performed to examine the changes in transcriptome profile in RPE cells overexpressing βA3/A1-crystallin. Immunoprecipitation studies were utilized for detecting the interaction between βA3/A1-crystallin and PITPβ. The expression of proteins involved in EGFR (epidermal growth factor receptor) activation and PLCγ1 (phospholipases C gamma 1) signaling were detected by western blotting. The PIP fraction was isolated from RPE tissue and PIP levels were determined by ELISA.

Results: RPE cells overexpressing Cryba1 have decreased expression of genes involved in inositol phosphate metabolism, such as phosphatidylinositol phosphatases and kinases, and phospholipases. βA3/A1-crystallin interacts with PITPβ in polarized RPE cells, and the binding was more significant when cells were stimulated with EGF. Both PI(4,5)P2 and PI(3,4,5)P3 were significantly reduced, and the EGFR activation was compromised in RPE cells lacking βA3/A1-crystallin. In Cryba1 cKO RPE cells overexpressing βA3/A1-crystallin, EGFR activation was rescued and the PI(3,4,5)P3 level was upregulated, although the PI (4,5)P2 was not increased. PLCγ1 activity was found to be negatively correlated with βA3/A1-crystallin in RPE cells. Moreover, PITPβ overexpression stimulates PLCγ1/PKC activity and inhibits EGFR activation, but RPE flatmounts overexpressing both βA3/A1-crystallin and PITPβ showed no significant changes of PLCγ1/PKC activity or EGFR activation.

Conclusions: The data suggest an important role for βA3/A1-crystallin and PITPβ in the regulation of PIP metabolism, particularly in regulating PLCγ1 activity in the turnover of PI(4,5)P2 in RPE cells.

CONTROL ID: 3708647

SUBMITTER (NAME ONLY): Ashten Stambersky

TITLE: Functional optimization of electric cell-substrate impedance sensing (ECIS)® using human corneal epithelial cells

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Stambersky, T. Ebrahim, H. Kani, T. Carion, A. Ibrahim, E. Abdul Shukkur, E.A. Berger, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: An intact epithelium is key to maintaining corneal integrity and barrier function. Bacterial keratitis and diabetes are among the conditions that can compromise the corneal epithelium leading to impaired wound healing and sight-threatening opacity. Electrical cell-substrate impedance sensing or ECIS® is a non-invasive method to measure real-time cellular behaviors such as barrier function and cell migration. The current study optimizes human corneal epithelial cells as assessed by ECIS® to generate quantifiable measurements that more accurately reflect changes in cell behavior and prove as a more advanced assay to monitor cells in vitro.

Methods: Human telomerase-immortalized corneal epithelial cells (HUCLs) were used to optimize the ECIS® system. Cells were placed in either K-SFM or DMEM+F12 media (37 degrees Celsius, 5% CO_2). Five cell densities (30,000 – 500,000 cells/well of a 96-well plate) were used to determine the optimal seeding density for ECIS® monitoring of cellular behavior over time. Parameters of assessment included: overall impedance (Z), barrier resistance (R), and cell capacitance (C). Mathematical modeling of the R data further generated R_b, α, and C_m values. ARPE-19 cells were used as a control.

Results: Impedance, resistance, and cell capacitance measurements revealed DMEM+F12 at 60,000 cells as the optimal condition for ECIS® assessment. This was further supported by logarithmic curves that reached a cell migration plateau (time to confluency) at 8h with DMEM+F12 compared to 14h with K-SFM; and resistance and capacitance ratios with optimal cell migration slope and plateau achieved with DMEM+F12 at 60,000 cells compared to all other groups. Additionally, ECIS® modeling analysis indicated the contribution of α (basolateral adhesion), R_b (paracellular junctional space), and C_m (membrane capacitance) to overall barrier function were significantly improved for DMEM+F12 compared to K-SFM.

Conclusions: Our results consistently demonstrated that 60,000 cells are an optimal seeding density for ECIS® analysis of HUCLs. Further, DMEM+F12 media provided better growing conditions, allowing for enhanced barrier function compared to widely used K-SFM. This work highlights the sensitivity of the ECIS® biosensor technology and the importance of optimizing not only cell density but media used for in vitro culturing.

CONTROL ID: 3708650

SUBMITTER (NAME ONLY): Penny Asbell

TITLE: Antibiotic Resistance among Ocular Staphylococcal Pathogens: Longitudinal Trends in the ARMOR Study

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Asbell, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|C.M. Sanfilippo, H. DeCory, Medical Affairs, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Staphylococci are among the most frequently reported causative bacteria in ocular infections, and antibiotic resistance in these pathogens can complicate treatment. The Antibiotic Resistance Monitoring in Ocular micRoorganisms (ARMOR) study is a nationwide surveillance study on in vitro antibacterial resistance levels among ocular pathogens now in its 13th year. Here, we examined resistance trends over time among staphylococcal isolates collected from 2009 through 2021 to date in ARMOR.

Methods: Each year as part of ARMOR, Staphylococcus aureus and coagulase-negative staphylococci (CoNS) from ocular infections were collected and sent to a central laboratory for species confirmation. Minimum inhibitory concentrations (MICs) were determined for up to 16 different antibiotics and interpreted as susceptible/resistant based on Clinical and Laboratory Standards Institute methods and breakpoints. Longitudinal trends in resistance were evaluated using Cochran-Armitage tests for linear trends in a proportion.

Results: A total of 2847 S. aureus and 2416 CoNS were included in this analysis. Over the 13-year collection period, methicillin/oxacillin resistance decreased among both S. aureus (39 to 37%; P<0.001) and CoNS (53 to 37% P=0.003). Decreases in resistance were also observed for azithromycin (62% to 53%), ciprofloxacin (39% to 31%), and tobramycin (24% to 12%) among S. aureus, and for ciprofloxacin (46% to 20%) among CoNS (P<0.001 for all). In contrast, increases in resistance were noted for chloramphenicol among S. aureus (6% to 34%; P<0.001) and for trimethoprim among CoNS (26% to 29%; P=0.044). Of staphylococci collected in 2021 specifically, >80% of methicillin-resistant isolates exhibited multidrug resistance (≥3 antibiotic classes). Cumulative besifloxacin MIC_{90}s (1 µg/mL for S. aureus and 2 µg/mL for CoNS) were 4- to 128-fold lower than other fluoroquinolones and comparable to vancomycin.

Conclusions: Analyses of antibiotic resistance among staphylococci collected over 13 years in ARMOR indicate that in vitro resistance has decreased only slightly over this timeframe for several antibiotics and is still prevalent in 2021. Although the clinical relevance of in vitro data is unclear without consideration of the ocular pharmacokinetics of tested antibiotics, these findings warrant attention when choosing empiric therapy for the management of ocular staphylococcal infections.

CONTROL ID: 3708651

SUBMITTER (NAME ONLY): Angela Chen

TITLE: Three-Year Change in Refractive Error Associated with Overminus Lens Treatment for Children with Intermittent Exotropia

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chen, S. Han, S.A. Cotter, Southern California College of Optometry, Fullerton, California, UNITED STATES|P.S. McDowell, Michigan College of Optometry at Ferris State University, Big Rapids, Michigan, UNITED STATES|J.M. Holmes, Ophthalmology and Vision Science, University of Arizona, Tucson, Arizona, UNITED STATES|D.L. Chandler, A. Hercinovic, Z. Li, R.T. Kraker, Jaeb Center for Health Research, Tampa, Florida, UNITED STATES|S.A. Erzurum, Eye Care Associates, Inc., Poland, Ohio, UNITED STATES|J.W. Erickson, Nemours Children's Clinic, Jacksonville, Florida, UNITED STATES|M. Vricella, SUNY College of Optometry, New York, New York, UNITED STATES|B.H. Ticho, Ticho Eye Associates, Chicago Ridge, Illinois, UNITED STATES|A.L. Waters, Children's Mercy Hospitals and Clinics, Kansas City, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: In a randomized trial comparing overminus versus non-overminus spectacles in children with intermittent exotropia (IXT), we found that overminus spectacles improved distance IXT control but also increased myopic shift at 1 year (-0.42D in 189 overminus vs -0.04D in 169 non-overminus participants, respectively; adjusted difference = -0.37D; 95% CI = -0.49 to -0.26). (Chen et al, JAMA Ophthalmol 2021;139(4):464-476) We now report refractive error change over 3 years in a post-RCT subcohort.

Methods: 386 children 3 to 10 years old with IXT and spherical equivalent (SE) refractive error between -6.00 diopters (D) and +1.00D were randomly assigned to overminus spectacles (-2.50D over cycloplegic refraction for 12 months, -1.25D for 3 months, then non-overminus for 3 months) or non-overminus spectacles for 18 months. 221 participants (124 of 196 [63%] in overminus; 97 of 190 [51%] in non-overminus) re-enrolled for 2- and 3-year follow-up, with IXT treatment at investigator discretion. Refractive error was determined by cycloplegic retinoscopy.

Results: The 3-year visit was completed by 83% (103 of 124) of participants in the overminus group and 88% (85 of 97) in the non-overminus group. Between 1 to 3 years, mean myopic shift was -0.37D in both groups (SD = 0.68 in overminus; SD = 0.67 in non-overminus). The mean overall change in refractive error from baseline to 3 years was greater in the overminus group (-0.82D) vs the non-overminus group (-0.46D; adjusted difference = -0.43D; 95% CI = -0.68 to -0.19), with 30% (30 of 101) in the overminus group vs 16% (13 of 83) of the non-overminus group having >1D of myopic shift over 3 years (risk ratio = 1.9; 95% CI = 1.0 to 3.6). Risk ratios for developing >1D of myopic shift over 3 years between overminus and non-overminus groups were 2.7 (95% CI= 1.4 to 6.0; 78% vs 29%) in 46 participants with baseline myopia (SE -0.50D to -6.00D), 2.6 (95% CI = 0.9 to 20.3; 36% vs 14%) in 58 emmetropes (SE -0.375D to +0.375D), and 1.1 (95% CI = 0.2 to 10.9; 7% vs 6%) in 78 with low hyperopia (SE +0.50D to 1.00D) at baseline.

Conclusions: While the greater myopic shift that occurred during 1 year of overminus lens treatment was still present at 3 years, the myopic shift during the 2 years after treatment cessation was similar in both groups. The risk of prolonged myopic shift should be discussed with parents when considering overminus lens treatment.

CONTROL ID: 3708660

SUBMITTER (NAME ONLY): Marc-André Dubois

TITLE: Significant sex difference on ERG responses using non-invasive dermal electrodes

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Dubois, Psychologie, Universite Laval Faculte des sciences sociales, Quebec, Quebec, CANADA|M. Dubois, C. Pelletier, M. Hébert, Axe Neurosciences cliniques et cognitives, Centre de recherche CERVO, Quebec, Quebec, CANADA|M. Hébert, ophtalmologie et ORL-chirurgie cervico-faciale, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|C. Pelletier, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|

Commercial Relationships Disclosure: Marc-André Dubois: Commercial Relationship: Code N (No Commercial Relationship) | Charles-Antoine Pelletier: Commercial Relationship: Code N (No Commercial Relationship) | Marc Hébert: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this project is to replicate the study of Brûlé et al., 2007, which shows a decreased amplitude of electroretinogram in men of about 30%, but this time using much less invasive dermal electrodes than the traditionally used DTL electrodes.

Methods: Full-field photopic and scotopic ERGs were performed with an Espion E3 system (Diagnosys LLC, Lowell, MA). Recordings were obtained in nondilated eyes using self-adhesive skin electrodes (LKC Technologies, Gaithersburg, MD) applied 2 mm below the eyes. ERGs were performed in 25 subjects (16 women [27.1 +/- 4.7 years]; 9 men [28.1 +/- 4.8 years]). The photopic ERG was performed with a background light set at 80 cd/m2 and using 7 white flashes (luminance ranging from 1.33 to 50 cd.s/m2). The scotopic condition was performed after 20 minutes of dark adaptation using 12 green flashes (peak: 509 nm) (luminance ranging from 0. 001778 to 1 cd.s/m2). Each flash intensity was repeated twice (20 flashes per trial) and averaged for both eyes.

Results: In photopic conditions, and at the intensity allowing maximum amplitude (7.5 cd.s/m2), men (M) demonstrated when compared to women (W), an 18% lower cone a-wave amplitude (p=0.017 [M mean=-7.9; s.d.=1,3 mV] [W mean=-9,9 mV; s.d.=2,4 mV]) and a 23% lower cone b-wave amplitude (p=0.002 [M mean=36,6 mV; s.d.=7,2 mV] [W mean=47,6 mV; s.d.=8,8 mV]). In scotopic conditions and at the intensity allowing maximum pure rod response (0.1 cd.s/m2), men demonstrated a 24% lower b-wave amplitude (p=0.001 [M mean=60,8 mV; s.d.=8,4 mV] [W mean=80,2 mV; s.d.=15 mV]. At the maximum intensity used (1 cd.s/m2), men exhibited a 25.5% lower mixed cone and rod b-wave amplitude (p<0.001 [M mean=69,9 mV; s.d.=10 mV] [W mean=93,8 mV; s.d.=14,8 mV]).

Conclusions: The data obtained replicate those shown by Brûlé et al., 2007. More and more researchers are interested in using the ERG to detect biomarkers in mental health. The present project demonstrates the importance of considering biological sex in this field. The difference in ERG amplitudes between men and women increases the variability within groups when not accounted for, reducing the overall statistical power of the projects. The data also validates the use of the less invasive dermal electrodes, as they replicate the results obtained with traditional DTL electrodes, albeit smaller amplitudes are achieved which is not a concern when investigating a normal eye.

CONTROL ID: 3708662

SUBMITTER (NAME ONLY): Cayla Ontko

TITLE: IL-1β initiates and sustains inflammation between hMC and hRMEC

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ontko, Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|D. Padovani-Claudio, J. Penn, Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inflammatory cytokines are elevated in the retina/vitreous in DR pathogenesis and levels correlate with retinopathy severity and progression. Human Müller cells (hMC) and human retinal microvascular endothelial cells (hRMEC) are proposed to be sources of inflammatory cytokines, such as TNFα and IL-1β, in DR. Evidence indicates that IL-1β is a multifunctional inflammatory cytokine and a primary trigger of the neuro-inflammatory cascade in DR, and IL-1RA, an IL-1 receptor antagonist, may dampen its effects. This study tests the hypothesis that (1) reactive glia serve as an important source of inflammation in DR and (2) IL-1β, among other inflammatory mediators, acts to both initiate and sustain tissue inflammation in DR.

Methods: Primary hMC were treated in serum-depleted media with 1ng/mL IL-1β or 1ng/mL TNFα for 2h to simulate DR inflammation (n=4). Media were replaced with FBS-containing EBM for 6h to generate conditioned media (CM). hRMEC were pretreated +/- IL-1RA for 2h. hMC derived-CM was transferred onto HRMEC +/- 10ng/mL IL-1RA for 4h. Relative expression of inflammatory mediators was analyzed via qRT-PCR, and ANOVA with Tukey's multiple comparisons test was used to evaluate significant differences among treatment groups.

Results: CM generated by hMC + IL-1β, not hMC + TNFα, caused hRMEC to increase gene expression of inflammatory cytokines TNFα, IL-1β, IL-6 and IL-8, and adhesion molecules ICAM-1, VCAM-1, and E-selectin significantly ($p<0.0001$). IL-1RA significantly reduced expression of TNFα (49%, $p=0.0006$), IL-1β (37%, $p=0.005$), IL-6 (24%, $p=0<0.001$), IL-8 (26%, $p=0.0013$), ICAM (19%, $p=0.0028$) and VCAM (42%, $p=0<0.0001$) in hRMEC treated with IL-1β-stimulated CM, but did not significantly alter their levels in hRMEC treated with TNFα-stimulated CM.

Conclusions: CM from IL-1β-stimulated hMC causes hRMEC to react in a proinflammatory manner, confirming our hypothesis that reactive glia elicit inflammatory responses from retinal endothelium. This was not the case for CM from TNFα-treated hMC, indicating an essential role for IL-1β in initiating inflammatory amplification in hMC and subsequent vascular inflammation. Moreover, IL-1RA significantly decreased the effects of hMC-CM on hRMEC, suggesting that IL-1β contributes a dominant share of the inflammatory capacity of hMC CM. These findings indicate that IL-1β both initiates and sustains retinal inflammation, underscoring its potential as a therapeutic target in DR.

CONTROL ID: 3708664

SUBMITTER (NAME ONLY): Claire Malley

TITLE: High HDL or low LDL, total cholesterol confer greater risk of advanced age-related macular degeneration in mendelian randomization

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Malley, K. Yu, J. Advani, T.D. Keenan, E. Agron, A. Swaroop, E.Y. Chew, DECA, National Eye Institute, Bethesda, Maryland, UNITED STATES|K. Yu, National Cancer Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The complement system is a well-known modulator of risk for age-related macular degeneration (AMD), a progressive, blinding disease. But few treatments are available because the causal regulatory pathways connecting systemic inflammation, lipids, and AMD are poorly understood. In Mendelian Randomization (MR), reports from independent genome-wide association studies (GWAS) are jointly analyzed to discover exposures that have direct effects on an outcome, and which may not yet be known. Genetic proxies for cholesterol can be statistically tested at a large scale to pinpoint the causal effects of exposures on AMD.

Methods: The MRC IEU OpenGWAS Database was mined for associations between exposure phenotypes containing cholesterol keywords and outcome of advanced AMD from the 2016 International Age-related Macular Degeneration Consortium GWAS. The consortium encompassed 12,711 cases, including the Age-Related Eye Disease Studies (AREDS and AREDS2), and 14,590 controls of European descent. Two studies were used for three exposures (HDL and total cholesterol: 297,626 controls; LDL: 283,251 controls).

Results: All cholesterol phenotypes were found to have strong effects on advanced AMD by MR Egger tests: 47 SNPs were reported for HDL association, 55 for LDL, and 43 for total cholesterol. Overall effect size for HDL was 1.83 (s.e. = 0.37, p = 1.21E-05). Each + mg/dL HDL in blood plasma approximately doubled risk of developing advanced AMD. LDL and total cholesterol were significant but moderated: -0.43 (s.e. = 0.19, p = 3.11E-02), -0.96 (s.e. = 0.35, p = 8.34E-03). One SNP was shared between HDL and LDL: rs429358 in APOE (Apolipoprotein E), an essential metabolizer of triglyceride-rich lipoprotein. In single-SNP MR (LDL, Wald test) this had an effect size of -1.78 (s.e. = 0.13, p = 1.35E-41).

Conclusions: As reported from independent GWASes, genetic instrumental variables for high HDL conferred significant risk to develop advanced AMD, while lowering of LDL or total cholesterol reduced risk. Elevated HDL or too-low LDL may trigger a local inflammatory response causing irreparable macular damage over time. All three types are metabolically interrelated, and it is advisable to consider patient cholesterol levels when evaluating disease risk. MR can decipher the etiology of complex eye diseases by pointing to the most effective targets to lower risk of progression.

CONTROL ID: 3708669

SUBMITTER (NAME ONLY): Christian Akotoye

TITLE: “Thaw-wash-inject” approach for cryopreservation and transplantation of human organoid-derived retinal ganglion cells

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Phay, S.G. Bauer, P.Y. Baranov, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M.H. Phay, S.G. Bauer, P.Y. Baranov, Harvard Medical School, Boston, Massachusetts, UNITED STATES|C. Akotoye, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously we have shown that human retinal ganglion cells (hRGC) can be derived from human embryonic stem cells using organoid approach. These neurons survive and grow neurites following subretinal transplantation in mice. The translation of cell therapy relies on the opportunity to cryopreserve large numbers of cells to make them accessible for pre-clinical/clinical studies and further application. There are no gentle protocols available for banking of organoid-derived RGCs.

Methods: Here we selected 7 commercially available DMSO-free cryopreservation agents (CPAs) [Bambanker(BB), ReproCryo, FREEZEstem, Stem-cellbanker(SC), CryoSoFree, CryoScarless, and pZerve) and tested if they can maintain the viability of human stem-cell-derived RGCs and astroglia cells after freeze-thaw. Two DMSO-free (SC and BB) and one DMSO-based [Cellbanker-1(CB)] formulations were used for further investigation. Cell viability, cell recovery, proportion of cells with neurites and neurite length after re-plating in vitro was recorded 48 hours post-thaw. Immediate transplantation of RGCs after thawing was conducted with histological assessment at 3 days for cell quantification and neurite analysis. Non-frozen hRGCs (RGC media) were used as a positive control in all experiments.

Results: Relative to RGC media, the cell count per well was higher in DMSO-based CPA compared to DMSO-free CPA: 147% (CB), 73% (SC), and 65% (BB). Post-thaw RGC viability, however, was comparable across all three CPAs: 54% (BB), 41% (CB), 39% (SC) and 70% (RGC media). Furthermore, a comparable proportion of RGCs recovered their ability to grow neurites when cryopreserved using DMSO-free CPAs or DMSO-based CPA: 80% (SC), 66% (BB), 73% (CB) and 62% (RGC media). Neurite length at 48 hours post-thaw was comparable among all groups:161 µm (SC), 134 µm (BB), 181 µm (CB), and 146 µm (RGC media). Lastly, the xenotransplantation studies highlighted that cryopreserved RGCs survive and grow neurites: RGC media (100% engraftment rate; 64% neurite growth rate), both CB and BB (67% engraftment rate; 33% neurite growth rate), and SC (33% engraftment rate; 0% neurite growth rate).

Conclusions: Early results signify that DMSO-based and DMSO-free CPAs could be an acceptable alternative for RGC cryopreservation as these protocols maintain high cell viability upon recovery and engrafted RGC extend neurites following transplantation.

CONTROL ID: 3708670

SUBMITTER (NAME ONLY): Timothy Janetos

TITLE: Clinical Outcomes in Exudative Macular Degeneration: A Prospective Study of Patients with Care Delay Due to the COVID-19 Pandemic

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Janetos, R. Zandi, D. Younessi, G. Johnson, A. Randolph, M. Gill, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: During the emergeing COVID-19 pandemic, patient care was delayed due to clinic closures and patient hesitancy in seeking necessary care. We aimed to characterize clinical outcomes of exudative macular degeneration (AMD) patients who had delay in their care. As the uncertainly of the pandemic unfolds, this study aims to inform clinical decision making on future care delay decisions.

Methods: Patients with a chart diagnosis of exudative AMD who had an appointment canceled from 3/16/20 through 5/4/20 were selected. This timeframe encompassed the official clinic closure and a time during which many patients self-delayed care. Patients with concurrent macular disease were excluded. Data from each ophthalmology encounter was collected from 3/1/2019 through 7/1/2021. A linear longitudinal multilevel model was used to model best-corrected visual acuity (BCVA) over time. Time varying covariates included injection at visit, presence of subretinal fluid, intraretinal fluid, geographic atrophy, and macular hemorrhage. Baseline covariates included age, race, sex, treatment interval, treatment vs. observation, delay interval, anti-VEGF agent, baseline subretinal fluid, intraretinal fluid, and geographic atrophy, prior PDT, and smoking status.

Results: 161 eyes encompassing 2,555 ophthalmology encounters were selected. An initial model without addition of time varying or baseline predictors show a daily change in BCVA of 0.00151 logMAR ($p = 0.05$) over the study period. The pre-closure BCVA daily change was lower than the post-closure suggesting vision dropped at a faster rate after care delay, however this was not statistically significant (Figure 1). With time varying and baseline covariates added, intraretinal fluid status at baseline was the only statistically significant factor that predicted a larger BCVA slope ($p=0.05$).

Conclusions: Initial data suggests that BCVA fell during the time period, but there was no significant difference between the pre-closure and post-closure data. Patients with intraretinal fluid at baseline may potentially have worse long-term visual outcomes if care is delayed. Further model refinement needs to be undertaken prior to any definite conclusions.

CONTROL ID: 3708672

SUBMITTER (NAME ONLY): Brendan Fry

TITLE: Predicted impact of flow regulation mechanisms and intraocular pressure on retinal tissue oxygenation

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Fry, Metropolitan State University of Denver, Denver, Colorado, UNITED STATES|J. Arciero, A. Albright, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|A. Verticchio, B.A. Siesky, A. Harris, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: This work employs a theoretical model of the human retina to predict blood flow and tissue oxygenation in retinal vessels and tissue for varied levels of intraocular pressure (IOP) and in the presence or absence of blood flow regulation.

Methods: A previously established hybrid model of the human retina, which includes a heterogeneous representation of retinal arterioles and a compartmental representation of capillaries, small venules, and large venules, is adapted here to include blood flow regulation mechanisms in response to changes in mean arterial pressure, shear stress, and metabolism. One of the four main branches of the retinal arterioles is simulated here to reduce computational expense; behavior in the remaining branches is similar. A Green's function method is used to model oxygen transport in the arterioles, and a Krogh cylinder model is used in the capillaries and venules. The model is simulated for a healthy or elevated level of IOP (15 and 25 mmHg, respectively). Additionally, the model is used to simulate retinal tissue oxygenation when all regulation mechanisms are present or absent.

Results: The impact of IOP is depicted in the first and second rows of Figure 1. The model predicts a 6% decrease in tissue oxygenation as IOP is increased from 15 to 25 mmHg. A greater decrease of 11% is predicted in tissue oxygenation when the flow regulation response mechanisms to pressure, shear stress, and metabolism are inhibited, as shown in the first and second columns of Figure 1.

Conclusions: This study demonstrates the utility of a mathematical model of the human retinal vasculature to identify factors that impact the oxygenation and health of the human retina. Specifically, this model demonstrates that both increased IOP and impaired flow regulation mechanisms can cause decreased retinal tissue oxygenation. Importantly, the heterogeneity of the vascular network demonstrates that average values of tissue partial pressure of oxygen (PO_2) levels hide significant localized defects in tissue oxygenation that may be involved in retinal health and ocular disease.

CONTROL ID: 3708673

SUBMITTER (NAME ONLY): Ygal Rotenstreich

TITLE: Machine learning for comprehensive prediction of high risk for Alzheimer's Disease based on chromatic pupilloperimetry

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Rotenstreich, Y. Lustig, Y. Feldman, I. Sher-Rosenthal, Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|Y. Rotenstreich, Y. Lustig, Y. Feldman, R. Ravona-Springer, I. Sher-Rosenthal, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, ISRAEL|I. Sharvit-Ginon, M. Schnaider Beeri, R. Ravona-Springer, The Joseph Sagol Neuroscience Center, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|I. Sharvit-Ginon, A. Weller, Department of Psychology, Bar-Ilan University, Ramat Gan, Tel Aviv, ISRAEL|M. Mrejen, Condensed Matter Physics Department, Tel Aviv University, Tel Aviv, ISRAEL|M. Schnaider Beeri, Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|A. Weller, Gonda Brain Research Center, Bar-Ilan University, Ramat Gan, Tel Aviv (Gosh Dan), ISRAEL|

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ABSTRACT BODY:

Purpose: To characterize the pupil light reflex (PLR) for small focal chromatic light stimuli in 125 cognitively normal middle-aged subjects at high risk for Alzheimer's disease (AD), due to family history and 61 controls.

Methods: 186 subjects were enrolled, 125 offspring of AD patients (FH+) and 61 age-matched controls (FH-), ages 44-71. Ophthalmic assessments included a Chromatic Pupilloperimetry test and a complete ophthalmologic examination to exclude ocular pathologies. Cognitive assessment, to verify subjects were asymptomatic, included executive function and episodic memory tests. 35 pupilloperimetry features were measured in 54 spots in a 24-2 visual field. Machine learning classification models were trained such that each model was introduced to a single feature type (measured in 54 spots) in the training data, and the same hyperparameters and training protocol were used in all models. Each model was then tested to quantify how well it can discriminate between FH+/FH-. The accuracy of a model was used as an indication of the correlation of a feature type to AD family history, using a standard confidence interval (CI) of 95%.

Results: Chromatic pupilloperimetry-based learning models were highly discriminative in differentiating subjects with and without AD family history, using short focal red (primarily cone-mediated), and dim blue (primarily rod-mediated) light stimuli. Features associated with transient PLR latency achieved Area under the Receiver Operating Characteristic Curve (ROC AUC) of 0.90 ± 0.051 (left-eye) and 0.87 ± 0.048 (right-eye). Parameters associated with the contraction arm of the transient PLR were more discriminative compared to parameters associated with the relaxation arm.

Conclusions: Chromatic pupilloperimetry differentiated between individuals at high risk for AD due to a parental family history from those without AD family history, with high sensitivity and specificity. Subtle changes in pupil contraction latency may be detected decades before the onset of AD clinical symptoms using a simple, non-invasive test.

CONTROL ID: 3708675

SUBMITTER (NAME ONLY): Spencer Fuller

TITLE: A Cross-Sectional Study on the Effect of the COVID-19 Pandemic on Ocular Health at a Tertiary Care Department of Ophthalmology

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Fuller, J. Anderson, P. Rao, John F Hardesty Department of Ophthalmology and Visual Sciences, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic caused disruptions in ophthalmic care, and may have negatively impacted some patients more than others. We performed a retrospective, cross-sectional study at our large, tertiary care ophthalmology referral center in the Midwest region of the United States in an attempt to identify patients at risk for worsening ocular health during the COVID-19 shutdowns.

Methods: We completed retrospective Electronic Health Record data extraction of demographic and clinical outpatient encounter-level data for all patients examined in our department from March-May 2019, August-October 2019, March-May 2020 (peak COVID), and August-October 2020 (COVID recovery). Changes in mean logMAR visual acuity (logMAR VA), mean intraocular pressure (IOP), and mean number of procedures per encounter were tested and stratified by age (<18, 18-64, and 65+ years-old), and compared based on associated billing codes.

Results: During peak COVID, there was a 73% decrease in the number of outpatient clinical encounters compared to the control time period in 2019 (6,976 vs. 26,068), and mean patient age was significantly lower during peak COVID (mean age 53.4, 95% CI 52.8-54.0) compared with the other time periods. Documented best-corrected logMAR VA of the right and left eyes worsened for pediatric, adult, and elderly patient age groups; IOP of the right and left eyes worsened when evaluating all patients together; and the mean number of procedures performed per encounter increased by 74% comparing early 2019 to peak COVID months. The billing diagnoses associated with the worst ocular health outcomes during the COVID-related shutdowns include patients with anophthalmia of the fellow eye; infectious keratitis; open, chronic angle closure, and secondary causes of glaucoma; ocular inflammatory disorders; optic neuritis and ischemic optic neuropathies; and vitreoretinal disorders related to diabetes, macular degeneration, and vitreous or retinal hemorrhages.

Conclusions: Patients seen during the COVID-19 pandemic were younger, had worsened logMAR VA, increased IOP, and underwent more procedures compared to the COVID-recovery and 2019 control months. Numerous billing diagnoses were associated with worse measures ocular health. Patients with these ocular disorders may need prioritization during future periods of reduced access ophthalmic care.

CONTROL ID: 3708676

SUBMITTER (NAME ONLY): Justin Huynh

TITLE: Use of Generative Adversarial Network to Improve Glaucoma Gradability of Fundus Images

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huynh, B.G. Chuter, M. Christopher, C. Bowd, R. Fan, M.H. Goldbaum, A. Belghith, M.A. Fazio, R.N. Weinreb, L. Zangwill, Hamilton Glaucoma Center, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|J. Huynh, Department of Computer Science and Engineering,, University of California San Diego, La Jolla, California, UNITED STATES|R. Fan, College of Electronics and Information Engineering, Tongji University, Shanghai, Shanghai, CHINA|C.A. Girkin, M.A. Fazio, Department of Ophthalmology, School of Medicine, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|C.G. DeMoraes, J.M. Liebmann, Bernard and Shirlee Brown Glaucoma Research Laboratory, Edward S. Harkness Eye Institute, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low-quality retinal images may impair a clinician’s ability to detect glaucoma and preclude use of deep learning (DL) models for glaucoma identification. The study’s purpose is to assess whether ungradable images can be improved by use of a paired Generative Adversarial Network (GAN) DL model, to yield gradable images.

Methods: 3217 fundus photographs from the Diagnostic Innovations in Glaucoma Study (DIGS) and African Descent and Glaucoma Evaluation Study (ADAGES) datasets were organized into 10,000 image pairs, of one inherently low quality source image and one high quality target image from the same eye. Image quality was calculated by a previously developed quality assessment DL model trained by ground truth of expert graders. The image pairs were used to train a Pix2Pix based GAN to perform image to image translation from low to high quality. The GAN was trained for 30 cycles (epochs) using adam optimizer with learning rate 2e-4, with L1 and adversarial binary cross entropy loss functions.

Results: Generated images from the model had a mean L1 distance of 0.275 and cross entropy of 4.034 from the target high quality images. Generated images had an average brightness increase of 18.30% and contrast increase of 34.31% from the source low quality images, indicating that the GAN tends to increase the brightness and contrast of input images. Qualitatively, the GAN learns quickly, requiring one epoch to improve its output from random noise (fig 1a) to a blurry rendition of the optic nerve head (figure 1b). After 30 epochs, the GAN learns to produce images with

clear retinal vasculature and detail that resembles the target images (fig 1c). The GAN seems to increase brightness and improve contrast of the optic nerve head and vasculature. In some examples, the GAN may insert vasculature into the image (fig 2b). Also, the GAN may insert cropping into the generated image, mimicking the cropping in the ground truth images (fig 2c).

Conclusions: GAN shows promise to improve human gradability of fundoscopic images in the detection of glaucoma. Further investigation must be done to explain unexpected output and assess glaucoma gradability of generated images.

CONTROL ID: 3708678

SUBMITTER (NAME ONLY): Xikun Han

TITLE: Integrating genetics and metabolomics data reveals putative mechanisms for age-related macular degeneration

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Han, J. Li, F. Hu, W. Willett, L. Liang, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|I. Lains, J.W. Miller, D. Husain, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Q. Qi, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|J. Lasky-Su, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S. MacGregor, QIMR Berghofer Medical Research Institute, Herston, Queensland, AUSTRALIA|B. Yu, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a leading cause of vision loss among the elderly. Understanding the shared genetic components between metabolites and AMD can provide better insights into the pathogenesis of AMD.

Methods: Leveraging large-scale genetic and metabolomic data, we performed genome-wide association studies for 346 plasma metabolites with a median sample size of 6,610 participants in the Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow Up Study (NHS, NHSII, and HPFS). AMD GWAS summary statistics from the International AMD Genomics Consortium with 16,144 advanced AMD cases and 17,832 controls were used to investigate the putative causal associations between metabolites and risk of AMD in a bi-directional two-sample Mendelian randomization (MR) framework and Bayesian genetic colocalization analysis. Finally, we develop a metabolome-wide association study (MWAS) pipeline to identify metabolite-AMD associations.

Results: In the NHS, NHSII, and HPFS, we prioritized 41 putative causal associations between metabolites and AMD. Bayesian colocalization analysis revealed 249 shared common causal variants for metabolites and AMD. In the MWAS, we identified 119 metabolites, of which 39 were further prioritized in MR analysis. Pathway analysis revealed that the identified metabolites were mapped to the glycerophospholipid metabolism pathway.

Conclusions: Our results provide genetic evidence that highlights the contribution of metabolites to AMD risk. The shared causal variants and prioritized causal metabolites provide new insights into the pathogenesis of AMD.

CONTROL ID: 3708680

SUBMITTER (NAME ONLY): Takashi Nishida

TITLE: Association Between Ganglion Cell Complex Thinning and Vision-Related Quality of Life in Glaucoma

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the association between the rate of ganglion cell complex (GCC) thinning and the vision function questionnaire (VFQ) in glaucoma.

Methods: In this longitudinal study, 236 eyes of 118 patients with diagnosed or suspected glaucoma followed up for an average of 4.1 years were enrolled from the Diagnostic Innovations in Glaucoma Study and the African Descent and Glaucoma Evaluation Study. The VFQ was evaluated using the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ) at the last follow-up visit. GCC thickness was derived from macular optical coherence tomography scans and averaged within 3 circle areas (3.4-degree, 5.6-degree, and 6.8-degree from the fovea) and superior and inferior hemiregions. Linear mixed-effects models were used to investigate the association between the rate of GCC thinning and Rasch-calibrated VFQ score.

Results: Faster rate of global GCC thinning was significantly associated with higher disability of Rasch-calibrated NEI-VFQ score (-0.31 (95% CI) (-0.57, -0.04) um/year per 100 score; P=.02). When stratified by degrees from the fovea, the 3.4-degree area had the highest association with the composite NEI-VFQ Rasch-calibrated score (-0.52 (-0.91, -0.13) um/year per 100 score: P=.009) followed by the 5.6-degree (-0.34 (-0.62, -0.06) um/year per 100 score: P=.02) and 6.8-degree (-0.16 (-0.32, 0.00) um/year per 100 score: P=.05).

Conclusions: The faster and more central locations of GCC thinning are associated with vision-related quality of life in glaucoma patients. Monitoring macular structure provide useful information in determining the risk of functional impairment in glaucoma.

CONTROL ID: 3708681

SUBMITTER (NAME ONLY): Ting Wang

TITLE: Cholesterol regulates actin polymerization in trabecular meshwork

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Wang, P.P. Pattabiraman, Medical Neuroscience, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|T. Wang, P.P. Pattabiraman, Ophthalmology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Ting Wang: Commercial Relationship: Code N (No Commercial Relationship) | Padmanabhan Pattabiraman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The trabecular meshwork (TM) actin cytoskeleton plays a key role in regulating intraocular pressure (IOP). This study aims at understanding the role of cholesterol in the regulation of actin polymerization in TM.

Methods: Human TM (HTM) cells were treated with SiR-Actin in serum-free media overnight and F-actin changes were recorded using live-cell time-lapse (every 5min) confocal imaging before and during exposure to A) 10mM methyl-β-cyclodextrin (MβCD) (1h) for acute cellular cholesterol removal, B) 100μM cholesterol-saturated MβCD (MβCD-CHOL) (1h) to enrich cholesterol. F-actin changes were calculated, and an unpaired t-test was used for statistical analyses and results were significant if $p<0.05$ with n= 3-4. HTM cells plated on coverslips were treated as mentioned above, C) with 100μM (24h) atorvastatin -cholesterol synthesis inhibitor, D) 10μM cytochalasin D (CYTD) (1h) -actin polymerization disruptor, E) 10μM CYTD (1h) followed by 100μM MβCD-CHOL (1h). Untreated cells acted as the control. After treatments, cells were fixed and immunofluorescence (IF) was performed for cholesterol using filipin, F-actin by phalloidin, focal adhesion (FA) -vinculin and paxillin-localization. Further F/G-actin in vitro assay was performed to quantify the actin polymerization changes under the conditions A–E compared to control.

Results: Imaging analysis showed cholesterol removal significantly decreased F-actin from 20min sustaining up to 1h ($p<0.05$, n=3) and decreased FA distribution. Cholesterol enrichment significantly increased F-actin from 10min sustaining up to 1h ($p<0.05$, n=4) and reorganized FA. IF results showed that atorvastatin decreased F-actin and FA distribution. CYTD disrupted F-actin networks leaving remnant filament ends and decreased FA but cholesterol enrichment increased F-actin branches formed at ~70° angle indicating Arp2/3 activation. These results were confirmed by quantitative F/G-actin ratio decrease and increase upon cholesterol removal/synthesis inhibition and enrichment, respectively. Interestingly, F/G-actin ratio increased under CYTD treatment indicating that CYTD disrupted longer actin filaments but helped polymerization of newly formed actin filaments.

Conclusions: This systematic evaluation of cholesterol modulation on TM actin polymerization identifies the significance of maintaining membrane and cellular cholesterol levels for achieving IOP homeostasis.

CONTROL ID: 3708684

SUBMITTER (NAME ONLY): Ehud Isacoff

TITLE:

Restoration of high-sensitivity patterned vision in motion with an engineered light-gated G protein-coupled receptor

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Isacoff, A. Holt, M. Berry, J.G. Flannery, Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, California, UNITED STATES|J. Broichhagen, Chemistry, Leibniz-Forschungsinstitut für Molekulare Pharmakologie, Berlin, GERMANY|

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ABSTRACT BODY:

Purpose: Inherited retinal degenerations (IRDs) result in blindness due to apoptotic cell death of rods and cones, but spare other retinal neurons, providing a potential that delivery of a light-activated signaling protein to surviving neurons may restore vision. Aspects of vision are restored when mGluR2 is engineered to respond to light by tethering of a photoswitchable agonist. However, as with channelrhodopsins, the system has such low sensitivity that it would require intensifying goggles to work in roomlight. We increasd sensitivity to obtain high acuity vision in dim light.

Methods: Using AAV, we delivered to retinal ganglion cells (RGCs) the gene encoding the GCPR, mGluR2, engineered to contain an N-terminal SNAP domain, to which we could tether a photoswitchable agonist. We increased the sensitivity with a branched photoswitch containing four light-activatable glutamates for each glutamate binding site. Light sensitivity was tested in a Light/Dark box; object recognition in open field under dim light; acuity and abilility to recognize line patterns in motion using standard 500 nit LCD computer screens displaying pairs of lines at different spacings.

Results: 4-branched BGAG SNAP-mGluR2 in all RGCs restores the ability to perform visual tasks in dim room light and using standard LCD computer screens. The system restores line pattern differentiation to approximately the acuity of normal mouse vision and supports pattern recognition at 48^{O}/s of motion.

Conclusions: We achieve high-sensitivity and high-acuity vision that works at high speed of motion and which supports object exploration in dim incidental light. While photopharmacology adds an additional layer of treatment to gene therapy, it provides the dual advantage of upgrade as new photoswitches are developed and the ability to be discontinued at will.

CONTROL ID: 3708685

SUBMITTER (NAME ONLY): michel desjarlais

TITLE: Unprecedented efficacy of rytvela in reversing vasculogenic dysfunction of endothelial progenitor cells in oxygen-induced retinopathy by restoring FOXF1 / CXCR4 expression through inhibition of miR-875

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. desjarlais, A. Nazzari, pharmacology, Universite de Montreal, Montreal, Quebec, CANADA|M. desjarlais, P. hardy, S. Chemtob, pediatric, Sainte Justine Research Center, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Retinal vaso-obliteration is associated with an inability of Endothelial Progenitor Cells (EPCs) to promotes vasculogenesis in oxygen-induced retinopathy (OIR). Because interleukine-1b (IL-1b) is convincingly reported as an important pro-inflammatory factor contributing to vascular degeneration during OIR, we investigated the potential beneficial effects of rytvela (a new non-competitive allosteric (IL)-1 receptor inhibitor) on the post-transcriptional mechanism involved EPC dysfunction during OIR.

Methods: The effect of rytvela on the bioactivity of EPCs subjected to hyperoxia (80% O2) or IL-1b stimulation (100ng/mL), has been examined by senescence, migration and vasculogenic assay. We next profiled micro-RNAs (miRs) expression using next generation sequencing (NGS), in the same condition to identify the post-transcriptional mechanisms associated with EPC dysfunction.

Results: First, we found that EPCs subjected to hyperoxia or IL-1b exhibit a phenotype of early senescence, associated with a significant decrease of their migratory and vasculogenic properties. Interestingly, rytvela inhibits hyperoxia/IL-1b-induced EPC-senescence and rescued their migration and tubulogenic function. At post-transcriptional level, NGS analysis reveal that 26 miRs are significantly modulated by both IL-1b and hyperoxia, and the expression of 9 of these miRs are recovered by rytvela. Interestingly we found that miR-875 - predicted to negatively regulate the expression of FOXF1, a key transcriptional factor for multiple pro-angiogenic genes including CXCR4 – to be upregulated. We next performed a gain-and-loss of function to study the precise role of miR-875 on EPC bioactivity. The result confirms that overexpression of miR-875 in native EPCs leads to downregulation of FOXF1/CXCR4 signaling, that in turn decreases the migratory and vasculogenic properties of native EPCs. Conversely, inhibition of miR-875 protects EPCs functions against OIR conditions by restoring FOXF1/CXCR4 expression.

Conclusions: Altogether, our results suggest that rytvela can protect vasculogenic properties of EPCs in OIR conditions. Bioengineering EPCs with rytvela or antagomiR-875 based-therapy could provide a new potential strategy to preserve vessel integrity in ischemic retinopathies.

CONTROL ID: 3708686

SUBMITTER (NAME ONLY): Wenlin Zhang

TITLE: Sex Difference in Congenital Hereditary Endothelial Dystrophy and a $Slc4a11^{-/-}$ mouse model

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Zhang, D. Williams, O. Onyia, A.J. Aldave, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|M. Morselli, M. Pellegrini, Department of Molecular, Cell & Developmental Biology, University of California Los Angeles, Los Angeles, California, UNITED STATES|A. Arnold, Department of Integrative Biology and Physiology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We investigated the role of sex in the pathogenesis of Congenital Hereditary Endothelial Dystrophy (CHED) in published cases and in a $Slc4a11^{-/-}$ mouse model of CHED.

Methods: Data of age, sex and pre-operative central corneal thickness (CCT) in published cases of individuals with CHED (49 male, 29 female eyes) were collected. CCT of $Slc4a11^{-/-}$ (KO, 100 eyes) and $Slc4a11^{+/+}$ (WT, 88) mice was monitored using AS-OCT. RNAseq analysis of in vivo corneal endothelium (CEn) from 10-week KO and WT mice (3 male and 3 female each) was carried in a 2-genotype by 2-sex matrix. Mitochondrial superoxide (Mito-$O_2^{\bullet -}$) was quantified in ex vivo CEn from KO and WT mice at 10, 24 and 40 weeks (w) by oxidized MitoSOX in LC-MS.

Results: Individuals with CHED and KO mice demonstrated a progressive increase in CCT with age ($p=0.026$ and <0.001). Male individuals with CHED and male KO mice showed greater rate of increase in CCT than females ($p=0.011$ and 0.046), with no difference of CCT between male and female WT mice ($p=0.945$). RNAseq revealed 502 upregulated and 364 downregulated genes in CEn from KO mice compared to WT, controlling for sex. The most upregulated gene, Echdc2, encodes a mitochondrial enzyme in lipid β-oxidation. The two most downregulated genes, Cyp1b1 and Myoc, both have roles in anterior segment dysgenesis. The expression of androgen receptor (Ar) was decreased 6-fold in CEn from KO mice, but the expression of estrogen receptors (Esr1, Esr2) was unchanged. Testing genotype*sex interaction identified 86 genes influenced by Slc4a11 KO in a sexually dimorphic pattern, including an overrepresentation of genes with androgen response elements (ARE) compared to genes with ARE in the mouse genome (42% vs 22%, $p=0.005$). In the 86 genes, there were several regulating factors of lipid metabolism with roles in inducing sex differences: Srebf1, Insig1, Scd1, Scd4, Slc22a14, and Mir22hg. Glucose dependent Mito-$O_2^{\bullet -}$ was significantly increased in CEn from male but not female KO mice at 24w and 40w compared to WT ($p =0.029$ and <0.001). Glutamine dependent Mito-$O_2^{\bullet -}$ was significantly increased in CEn from 40w male but not in female KO compared to 40w WT ($p=0.043$), and not in 10w and 24w mice.

Conclusions: Male sex is associated with more severe phenotype in individuals with CHED and in $Slc4a11^{-/-}$ mice. Sexually dimorphic response to Slc4a11 loss was observed at transcriptomic and functional levels in CEn of $Slc4a11^{-/-}$ mice.

CONTROL ID: 3708690

SUBMITTER (NAME ONLY): Leana Rohman

TITLE: Quantification of lens thickness microfluctuations in young and pre-presbyopic eyes using dynamic OCT biometry

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Rohman, M. Ruggeri, A. Ho, J. Parel, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|L. Rohman, M. Ruggeri, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|A. Ho, J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: According to earlier studies utilizing ultrasound, analysis of the dynamics of the lens can provide insights into the lens' mechanical properties and their changes over time, causing presbyopia. This study aims to determine if they are differences in the mechanical microfluctuations of the lens between young and pre-presbyopic subjects.

Methods: Using a custom-built extended depth OCT system (Ruggeri et al., BOE, 2012) and following an IRB-approved protocol, we imaged the lens of the left eye of 3 young subjects (age range: 21 to 25 years; MSE: -0.38 to -3.38 D) and 3 pre-presbyopic subjects (age range: 38 to 45 years; MSE: -0.75 to -4.38 D). We recorded 500 OCT images of the central 2 mm zone of the lens at 50 frames/s (10 s recording session) for each participant at different accommodative demands (young subjects: 0D, 2D, 4D, 7D; pre-presbyopic subjects: 0D, 4D). Each image consisted of 170 A-lines. For each frame, the lens thickness was quantified using a custom-made, semi-automatic MATLAB application. The power spectrum of the lens microfluctuations is calculated by using the Fourier Transform in MATLAB. Then, the microfluctuations are assessed by calculating the area under the power spectrum curve between 0 and 4 Hz.

Results: The amplitude of lens microfluctuations was higher in the accommodated state than in the relaxed state in both age groups. Compared to the relaxed state, the average amplitude of microfluctuations for young subjects is 2.3 times greater at 4D, while for pre-presbyopic subjects it is 1.8 times greater (Fig.1). For young subjects, the microfluctuations of the lens do not increase with increasing accommodation demand once it has reached an accommodative state (Fig. 2).

Conclusions: The results demonstrate the feasibility of quantifying lens thickness microfluctuations using dynamic OCT. Also, the study suggests that the magnitude of lens microfluctuations is larger in the accommodated state and in young compared to pre-presbyopic eyes. Moreover, the amplitude of microfluctuations in the accommodated state is independent of the accommodative response.

CONTROL ID: 3708692

SUBMITTER (NAME ONLY): Nagaraj Kerur

TITLE: Innate Immune Mechanisms in Oxidative Retinal Damage

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Kerur, A. Kumar, D.H. Biddle, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|D. Banerjee, Aravind Medical Research Foundation, Madurai, INDIA|

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ABSTRACT BODY:

Purpose: Clinical and experimental evidence implicate oxidative stress in the pathogenesis of multiple vision threatening diseases such as age-related macular degeneration (AMD), diabetic retinopathy (DR), and glaucoma. Oxidative stress damages biological macromolecules such as proteins, lipids, and DNA. The pathological consequences of oxidative damage to lipids and proteins in the retina have been well studied. However, whether oxidative damage to DNA – which is elevated in AMD, DR, and glaucoma eye specimens, as well as in experimental animal models – contributes to retinal pathology remains a major gap in the knowledge. The goal of this study is to examine the hypothesis cGAS which is activated by damages self-DNA, plays crucial roles in mediating oxidative retinal damage.

Methods: Human primary RPE and THP1 cells were exposed to oxidative stress by incubating with sodium iodate and cigarette smoke extract. cGAS pathway was blocking by either lentivirus delivered shRNA or CRISPR/Cas9. Activation of cGAS pathway was assessed by examining signaling activity downstream of cGAS by immunoblotting for phospho-STAT2 (pSTAT2), phosphor-ATM (pATM) and phospho-CHK2 (pCHK2).

Results: Exposure to oxidative stress via incubation with sodium iodate and cigarette smoke extract activated type I interferons and DNA damage signaling as demonstrated by induction of pSTAT2, pATM and pCHK2. These signaling activities were dampened in cGAS knockdown and knockout cells.

Conclusions: Our results suggest that cGAS pathway is activated by oxidative stress providing rationale for detailed analysis of role of cGAS in oxidative retinal damage.

CONTROL ID: 3708693

SUBMITTER (NAME ONLY): Odalys Torne

TITLE: Effect of acute intraocular pressure (IOP) elevation in normal and feline congenital glaucoma (FGC) eyes due to LTBP2 mutation

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Torne, K. Oikawa, G.J. McLellan, Surgical Sciences - School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|K. Oikawa, J. Kiland, G.J. McLellan, Department of Ophthalmology and Visual Sciences - School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate effects of acute IOP elevation on structural abnormalities in the post-trabecular aqueous outflow tract of normal cats and cats homozygous for LTBP2 mutation, causal for FCG, prior to spontaneous, sustained IOP elevation.

Methods: 0.4% indocyanine green aqueous angiography (AA) and anterior segment optical coherence tomography (OCT) was performed ex vivo at physiological pressure (15 mmHg) in 14 cannulated eyes from 14 cats at 10-12 wks of age (7 FCG and 7 age-matched control) <2hrs postmortem, imaged by Spectralis HRA+OCT (Heidelberg Engineering). Additionally, 4 eyes per group were imaged 30 mins after IOP elevation (45 mmHg). Images were then exported, and scleral vessel shape was analyzed in 4 different images/quadrant/eye using ImageJ (v1.53n). Eyes were perfusion fixed with 4% PFA for 30 minutes following AA, and were routinely paraffin embedded, sectioned and stained. Morphometric analysis and quantitative assessment of collagen orientation surrounding scleral vessels was performed in each eye in H&E and Picrosirius Red stained sections by polarized light microscopy. Statistical comparisons were performed in GraphPad Prism (v.9.3.1).

Results: All but one cat (an LTBP2 mutant) exhibited homogenous, circumferential AA outflow signal <10mins after tracer perfusion. Scleral lumen minor axis was smaller in LTBP2-mutant FCG eyes relative to controls ($P=0.0004$), and in all feline eyes lumens appeared partially collapsed after acute IOP elevation ($P<0.001$). Scleral vessel lumens in FCG cats appeared significantly collapsed and posteriorly displaced when compared to age matched controls. Scleral collagen orientation differed between FCG and normal cats, especially in anterior perivascular regions.

Conclusions: Differences in perivascular scleral collagen organization, scleral vessel profile and their response to increased IOP were identified in this congenital glaucoma model prior to sustained, spontaneous IOP elevation.

CONTROL ID: 3708698

SUBMITTER (NAME ONLY): George Lin

TITLE: Resident operative time is an independent predictor of cataract surgery early outcomes

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Lin, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|H. Andrews, A. Chomsky, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|A. Chomsky, VA Tennessee Valley Healthcare System, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: George Lin: Commercial Relationship: Code N (No Commercial Relationship) | Hans Andrews: Commercial Relationship: Code N (No Commercial Relationship) | Amy Chomsky: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Resident surgeons are quoted to take an average of 12 minutes longer when compared to an attending physician. Studies have shown that operative time may impact complications and outcomes in cataract surgery, but this observation is up for debate. This study aims to show the impact of operative time on early postoperative outcomes in resident cataract surgery.

Methods: This retrospective case series includes 100 randomly selected eyes from 100 patients from all PGY-4 resident cataract surgeries performed at a single Veterans Affairs Hospital between March 1, 2018 and March 31, 2020. Eyes with attending as primary surgeon or laser-assisted cataract surgery were excluded. Electronic medical records were reviewed to extract age, nuclear sclerotic cataract grade, and operative factors (use of epinephrine, use of trypan blue, iris expansion device (IED), cumulative dissipated energy (CDE), and operative time). Post-operative outcomes were reviewed, including visual acuity (VA) and intraocular pressure (IOP). Multiple ordinal logistic regression was performed to assess impact of risk factors on post-operative visual acuity.

Results: Operative time (OR=0.95, CI=0.92-0.99, p=0.01) and use of IED (OR= 0.07, CI= 0.01-0.03, p=0.001) are inversely associated with post-operative day one (POD1) pinhole visual acuity when controlling for co-variates as listed above. Other factors including CDE (OR=0.96, CI=0.90-1.03, p=0.29) are not significantly associated. No risk factors are significantly associated with decreased postop week one or month one best corrected visual acuity.

Conclusions: The results suggest that increased resident operative time is a significant risk factor for decreased POD1 pinhole VA, independent of CDE and other operative factors. At the one week and one month, however, resident operative time is not significantly associated with VA, suggesting that resident operative time has minimal effect on long-term VA outcomes. Interestingly, CDE is not significantly associated with decreased VA at any stage in our sample of 100 patients. Understanding effects of resident operative time on early VA outcomes improves understanding of trainee surgery and improves patient counseling when trainees are involved. Safely minimizing intraoperative delays shows promise as a method of improving early post-operative visual outcomes.

CONTROL ID: 3708709

SUBMITTER (NAME ONLY): Parisa Emami-Naeini

TITLE: Effectiveness of Teleophthalmology for Diabetic Eye Screening for Improving Eye Care Access in Patients with Diabetes

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Emami-Naeini, S.C. Lee, N.S. Mehta, G. Yiu, Ophthalmology, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|M.K. Lieng, S. Alber, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a common cause of vision loss among patients with diabetes mellitus, and early diagnosis can reduce the risk of vision loss. In this study, we investigate if remote retinal imaging enables earlier eye care access in patients with newly diagnosed diabetes mellitus in the United States over the past decade.

Methods: We identified patients with newly-diagnosed type II diabetes and at least 1 year and up to 5 years of continuous enrollment between 2011-2020 using the OptumLabs® Data Warehouse (OLDW) – a longitudinal, real-world dataset with de-identified administrative claims and electronic health record data for commercial insurance and Medicare Advantage enrollees in the U.S.. We compared the time from initial diagnosis to the first eye exam by 1) teleretinal screening, defined by Current Procedural Terminology codes for remote retinal imaging (92227 or 92228) or fundus photography (92250) by non-eye care providers, or by 2) in-person eye exam, defined as any encounter with an eye care provider.

Results: We identified 968 846 patients with newly diagnosed type II diabetes who were continuously enrolled for at least 1 year. At year 1, 5 459 (0.6%) patients underwent remote eye imaging and 208 023 (27%) underwent an in-person DR screening. The median time (95% confidence interval) to screening was 2.0 (0-10.9) months for remote imaging and 3.4 (0-11.0) months for in-person visits. Interestingly, 27.5% of remote screenings were performed on the same day of diabetes diagnosis. Excluding same-day screenings, median time to screening was 4.1 months (0.2-11.3) for remote eye imaging and 4.3 months (0.3-11.1) for in-person exams. After year 1, the proportion of eyes that underwent remote imaging remained stable at 0.75% in year 2 and 0.7% in year 5, while the proportion that underwent in-person eye care visits increased slowly to 32.1% and 43.5% at years 2 and 5, respectively.

Conclusions: Teleophthalmology using remote retinal imaging enabled earlier access to eye care among patients newly diagnosed with diabetes, primarily by enabling same-day ophthalmic screening at the time of initial diagnosis. More widespread use of teleretinal screening may enable earlier diagnosis of diabetic retinopathy and prevent vision loss.

CONTROL ID: 3708710

SUBMITTER (NAME ONLY): Japnit Dham

TITLE: Partially closed angle glaucoma model exhibits altered conventional pathway with a preserved uveoscleral pathway

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Anterior segment dysgenesis involves abnormal development of one or more anterior segment structures, including the trabecular meshwork (TM) and Schlemm's canal (SC); this increases risk of developing glaucoma due to elevated intraocular pressure (IOP). We have generated a unique mouse model by deleting activating protein-2β (AP-2β) transcription factor from the developing periocular mesenchyme and its derivatives. The resultant mutant shows a partial angle closure and increased IOP. We hypothesize that the uveoscleral pathway remains functional in this model and thus IOP can be reduced through treatment with prostaglandin analogs such as latanaprost (LTP).

Methods: $MgpCre^{+/-}$ mice were bred with $tfap2b^{+/-}$ mice. Male $MgpCre^{+/-};tfap2b^{+/-}$ offspring were then crossed with female $tfap2b^{lox/lox}$ mice to obtain the final offspring, the $MgpCre^{+/-};tfap2b^{-/lox}$ or AP-2β trabecular meshwork region knockout (TMR-KO) mice, as well as littermate controls. A 40 kDA FITC-conjugated dextran tracer was injected into the anterior segment of mutant and control mice. 0.005% LTP eye drops were used for topical treatment of the eye. The mice were euthanized 10 minutes after injection and eyes were enucleated, fixed, and cryosectioned. RNAscope Hiplex Assay was performed to determine changes in key genes in the mutants that are critical for proper functioning of TM and SC.

Results: In control mice, dextran clumps were observed in the TM region, both with and without LTP treatment (n=6 eyes). This was absent in the mutant mice, likely due to a blocked conventional pathway as demonstrated by previous histological staining. In comparison, dextran was observed along the uveoscleral pathway in the mutants after 5 and 10 minutes of LTP treatment (n=6 eyes). The RNAscope Assay performed in control and mutant mice revealed decreased levels of important SC markers, including Prox1 and Klf4, in the mutant.

Conclusions: Our findings show that while the conventional pathway is blocked in the TMR-KO mutants, the uveoscleral pathway remains functional. Reduction in both Prox1 and Klf4 levels further supports that development of the conventional pathway is altered in the TMR-KO mutants. Since these genes encode pressure-induced transcription factors, it is surmised that lack of aqueous flow through the SC region during development contributed to the phenotype.

CONTROL ID: 3708711

SUBMITTER (NAME ONLY): Haig Pakhchanian

TITLE: Evaluating the Risk of Retinal Vascular Occlusion among COVID-19 patients

SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: SARS-CoV-2, the viral infection that causes COVID-19, is known to induce a hypercoagulable state in patients. While there have been isolated reports of retinal vascular occlusion among patients with a pre-existing COVID-19 infection, research into this topic remains scant. Therefore, the purpose of this study is to investigate the short-term prevalence and risk for retinal vascular occlusion between COVID-19 and influenza A patients.

Methods: TrinetX is a national, federated database that was utilized in this retrospective cohort analysis. At the time of the study, electronic medical records from over 80 million patients across 57 healthcare organizations were analyzed to create two cohorts of patients. At the time of the analysis, 1,224,770 patients with a previous history for COVID-19 were compared to 61,555 patients with a previous history for influenza A. Then, 1:1 propensity score matching (PSM) was utilized to balance each cohort by demographics and comorbidities (age, sex, BMI, history of hypertension, chronic lower respiratory disease, diabetes mellitus, nicotine dependence, heart failure, and alcohol related disorders). Adjusted risk ratios (aRR) using 95% confidence intervals (CI) were used to assess risk of retinal vascular occlusion 120 days after initial diagnosis for COVID-19 or influenza A.

Results: Before PSM, COVID-19 patients were at significantly lesser risk for retinal vascular occlusion within 120 days of initial diagnosis than influenza A patients (aRR [95% CI] = 0.58 [0.42,0.8]; $p<0.001$). However, the incidence for influenza patients to develop retinal vascular occlusion was very small (0.1%). After PSM, two balanced cohorts of 61,555 patients were compared to one another and revealed that there is no significant difference in developing a retinal vascular occlusion after a previous diagnosis of COVID-19 or influenza A (0.92 [0.58,1.46]; $p=0.725$). Likewise, the incidence for retinal vascular occlusion remained very small (0.1% between both cohorts) (Table 1).

Conclusions: This is the first large-scale study investigating the risk of retinal vascular occlusion among COVID-19 and influenza A patients. We found that each cohort was at similar risk for developing retinal vascular occlusion within 120 days. Likewise, the incidence for retinal vascular occlusion was miniscule among patients in this study.

CONTROL ID: 3708712

SUBMITTER (NAME ONLY): Tomas Blanco

TITLE: An Acquired Immunostimulatory Function by Type-1 CD103^{+} Dendritic Cells Promotes Alloimmunity in High-risk Corneal Transplantation

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Blanco, H. Nakagawa, A. Musayeva, H. Alemi, T.H. Dohlman, Y. Chen, S. Chauhan, J. Yin, R. Dana, Ophthalmology, Harvard University, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have shown that allograft survival in recipients at low-risk (LR) of rejection is sustained by type-1 dendritic cells (DC1) that exhibit potent immunoregulatory function defined by high IL-10 and low IL-12 expression. Herein, we examined the environment-mediated immunostimulatory reprogramming of CD103^{+} DC1 in recipients at high-risk (HR) of rejection

Methods: HR or LR allogeneic corneal transplantation was performed using C57BL/6 mice as donors and BALB/c as hosts. M290-SAP antibody was used to deplete CD103^{+} DC1. Post-transplant, kinetics of CD103^{+} DC1 were assessed. Bone-marrow-derived (BMD) CD11b and naïve CD4 T cells were co-cultured with either FACS-sorted CD103^{+} DC1 from HR recipients, or with BMD induced DC1 (iDC1) pulsed with exogenous IFN-y. Either CD103^{+} DC1 from LR recipients or iDC1 were cultured in a transwell with Th1 cells. Adoptive transfer of iDC1 pulsed with or without IFN-y was performed in HR and LR recipient mice. Readouts include flow cytometry, ELISA, RT-PCR and clinical follow-up

Results: CD103^{+} DC1 numbers were significantly higher in HR compared to LR recipients ($p<0.001$), and these cells expressed lower IL-10 ($p<0.001$), and higher IL-12 ($p<0.001$). While depletion of CD103^{+} DC1 led to 100% graft rejection in LR ($p<0.0001$), it resulted in 40% survival in HR ($p<0.001$). Maturation of BMD CD11b^{+} APC (measured by MHC-II and IL-12) expression and their immunogenic function (assessed by IFN-g production by sensitized Th1 cells) were significantly increased when co-cultured with either HR CD103^{+} DC1 ($p<0.0001$), or IFN-y-pulsed iDC1 ($p<0.0001$). In the presence of IFN-y producing Th1 cells, both LR CD103^{+} DC1 or BMD-iDC1 expressed low IL-10 ($p<0.0001$) and high IL-12 ($p<0.0001$). Finally, adoptive transfer of immunosuppressive iDC1 to HR recipient mice led to 90% allograft survival ($p<0.0001$); while adoptive transfer of IFN-y-sensing iDC1 led to 100% graft rejection in LR recipient mice ($p<0.0001$)

Conclusions: These results demonstrate that the transplant environment alters the function of IFN-y-sensing migratory CD103^{+} DC1. This acquired immunostimulatory function negatively impacts alloimmunity and allograft survival

CONTROL ID: 3708713

SUBMITTER (NAME ONLY): Andrea Leonardi

TITLE: Onset of Improvement in Signs and Symptoms of Vernal Keratoconjunctivitis (VKC) in Patients Treated with Cyclosporine A Cationic Emulsion (CsA CE) in the NOVATIVE Study

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Leonardi, Department of Neuroscience, Ophthalmology Unit, Universita degli Studi di Padova, Padova, Veneto, ITALY|S. Doan, Bichat Hospital and Foundation A. de Rothschild, FRANCE|P. Pisella, Universite de Tours, Tours, Centre-Val de Loire, FRANCE|M. Amrane, D. Ismail, Santen SAS, FRANCE|D. Bremond-Gignac, Hopital universitaire Necker-Enfants malades, Paris, Île-de-France, FRANCE|D. Bremond-Gignac, INSERM Unit 1138 T17 Paris University, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: NOVATIVE (NCT00328653) was a randomized phase II/lll trial that evaluated the efficacy and safety of CsA CE in children and adolescents with moderate-to-severe VKC. This analysis examined the time to onset of improvements in signs and symptoms of VKC in CsA CE treated patients.

Methods: 118 patients (mean age, 8.8± 3 y; 81.4% male) were randomized to 4x daily treatment with CsA CE 0.05%, 0.1%, or vehicle eye drops. Rescue treatment (corticosteroids, mast cell stabilizers, or antihistamines) was not allowed. The primary efficacy endpoint was overall rating of subjective symptoms at Day 28. Efficacy was evaluated based on change from Baseline in ratings of subjective symptoms (BenEzra's 5-point scale) and in keratitis as identified by corneal fluorescein staining (CFS) and graded using the Oxford scheme.

Results: All NOVATIVE treatment groups showed improvement in overall subjective VKC symptoms at Day 28; however no statistically significant differences were noted between either CsA CE arm and the vehicle group. Although the primary end-point was not met, patients treated with CsA CE 0.05% and 0.1% showed improvement in subjective itching after 1 week and continued to improve through Month 1. Change from Baseline to Week 1 in the 0.1% treatment group was statistically significant (P=0.049). At Month 1, severe itching was reported by just 5.6% of patients in the 0.1% arm and none in the 0.05% arm vs 11.1% in the vehicle arm. All treatment groups showed improvement in CFS at Week 1; at Month 1 both CsA CE arms showed significantly greater improvements when compared to vehicle (P<0.05). Corresponding decreases in grade severity were also seen over time.

Conclusions: CsA CE 0.1% treatment led to a reduction in signs and symptoms in patients with moderate-to-severe VKC, with efficacy evident 1 week after initiating therapy. These data, along with data from the VEKTIS study, suggest that CsA CE 0.1% may be an effective corticosteroid-sparing VKC treatment.

CONTROL ID: 3708716

SUBMITTER (NAME ONLY): Osmel Alvarez

TITLE: Incidence of punctal and canalicular stenosis following topical 5-fluorouracil eye drop therapy for ocular surface squamous neoplasia

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Alvarez, M. Zein, A. Serrano, A. Galor, C.L. Karp, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|O. Alvarez, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To present cases of punctal and canalicular stenosis following treatment of ocular surface squamous neoplasia with topical 5-fluorouracil 1% eye drops.

Methods: A retrospective chart review of patients with ocular surface squamous neoplasia (OSSN) treated with topical 5FU as primary or adjuvant treatment between 2013 and 2021 was performed. Patients diagnosed with punctal or canalicular stenosis during or after use of topical 5FU were included in the study. Four patients were identified who met these criteria. We report the clinical findings and treatment for each patient.

Results: Five eyes of four patients were included in this study out of a total of 303 charts reviewed for an incidence of 1.3%. For this subset, the mean age at initiation of 5FU was 61 (range 53-69). Most patients were male (75%), white (75%), and non-Hispanic (100%). Five eyes were treated with topical 5FU for a mean of 4.87 cycles (standard deviation, SD 2.0). The most common presenting symptom was epiphora, which presented at a mean of 4.6 months after initiating topical 5FU. Two patients who developed epiphora at 4.3 and 10.3 months after initiating 5FU eye drop therapy underwent surgical intervention (external dacryocystorhinostomy and punctoplasty, respectively) after evaluation by an oculoplastic specialist confirmed punctal and canalicular stenosis, respectively. A third patient developed epiphora of the left eye after two cycles of 5FU. Clinical examination showed mild punctal stenosis and the puncta were dilated in the office with resolution of symptoms. The fourth patient received 5FU in both eyes and reported epiphora at 3.2 months in the left eye and 3.9 months in the right. Fortunately, left eye epiphora resolved after stopping therapy but the right eye epiphora persisted. An oculoplastic evaluation revealed right punctal stenosis. The patient’s symptoms resolved following punctal dilation.

Conclusions: Punctal or canalicular stenosis is a rare adverse effect of topical 5FU eye drops that may require surgical treatment.

CONTROL ID: 3708721

SUBMITTER (NAME ONLY): Maëlle Wirth

TITLE: micro-RNA-125 attenuates retinal inflammation to preserve vascular integrity in a rat model of oxygen-induced retinopathy

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Retinal inflammation is associated with vascular degeneration in oxygen-induced-retinopathy (OIR). micro-RNAs (miRs) have been identified as key regulators of genes expression. miR-125 is reported as strongly expressed in the retina, implicated in retinal development and in inflammatory processes. This study aimed to investigate the potential anti-inflammatory properties of miR-125 in a rat model of OIR.

Methods: qRT-PCR and western blot were performed to evaluate the expression of miR-125 and inflammatory cytokines. In vitro: miR-125 function was investigated using a miR-125 mimic on activated microglial cells (SIM-A9) by hyperoxia or LPS. The angiogenic effects were analyzed by Matrigel assay and qRT-PCR. In vivo: OIR rat pups were intravitreally injected with miR-125 mimic (10 nmol/kg) or a control-miR at P5 during the cycling OIR model. Retinal tissues were collected at P10 and P14 and the vascular density was analysed by retinal lectin-immunostaining. Apoptosis was analyzed in vitro and in vivo.

Results: miR-125 expression is significantly reduced in the retina of OIR rats compared to control rats, and in SIM-A9 subjected to hyperoxia or LPS. This is correlated with an upregulation of key proinflammatory cytokines including TNF-a, IL-6 and IL-16. Interestingly, we found a significant decrease of TNF-a, IL-6 and IL-16 expression, associated with decreased apoptosis in SIM-A9 transfected with miR-125 before hyperoxic or LPS treatment. Retinal endothelial cells (HRMEC) exposed with the culture medium of SIM-A9 pre-subjected to hyperoxia display a decrease in their angiogenic capacity associated with an increase of apoptosis. Interestingly, overexpression of miR-125 in SIM-A9 reverses the deleterious effects of hyperoxia on their secretome to rescue vasculogenic function of HRMEC. In vivo, OIR rat pups intravitreally supplemented with miR-125 mimic display a significantly decrease of TNF-a, IL-6, IL-16 and activated Caspase-3, associated with lower vasoobliteration area compared to the miR-control group at P10 and P14.

Conclusions: This study suggests that miR-125 acts as an inflammatory and apoptotic suppressor of activated-microglial cells protecting microvascular density during OIR. miR-125-based therapy could potentially constitute a novel anti-inflammatory therapeutic strategy to limit vascular degeneration in the initial step of ischemic retinopathies.

CONTROL ID: 3708725

SUBMITTER (NAME ONLY): Chase Hellmer

TITLE: Multiple glycinergic subunits mediate inhibitory inputs to mouse ON-OFF Direction Selective Ganglion Cells

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.B. Hellmer, I. Pyle, C. White, M.A. McCall, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|C. Zhang, University of Washington Department of Biological Structure, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal amacrine cells provide one of two sources of inhibition (GABA or glycine) to ganglion cells (GCs). Various roles for GABAergic inhibition have been discovered. For example, in ON-OFF Direction Selective GCs (ON-OFF-DSGCs), asymmetric GABAergic input restricts sensitivity to objects moving in only one direction. While ON-OFF DSGCs also receive glycinergic input, its function has not been examined. Here we examined GlyRα mediated synaptic inputs and their light evoked currents in WT and GlyRα knockout ON-OFF-DSGCs.

Methods: We pharmacologically isolated glycinergic inputs by eliminating $GABA_A$/$GABA_C$ inputs (PTX and TPMPA) and verified the remaining currents were glycinergic using strychnine. Whole-cell patch clamp recording assessed spontaneous glycinergic currents (sIPSCs) from GFP labeled ON-OFF DSGCs in TRHR mice. GlyRα subunit composition was predicted from known sIPSC decay τ's and tested in mice lacking specific GlyRα subunits (KO mice). Glycinergic light-evoked inhibitory postsynaptic currents (L-IPSCs) were compared between WT and GlyRα KO TRHR cells to evaluate the contribution of GlyRα 2, 3 or 4 inputs at light onset and offset.

Results: Isolating glycinergic inputs reduced the L-IPSC amplitude by ~45% in TRHR ON-OFF DSGCs, indicating that glycine mediates a significant inhibitory input. In WT TRHR GCs, the median sIPSC decay τ was 11.3 ms and this shifted to a slower decay τ of 13.9ms in TRHR/GlyRα3-KO mice. This indicates that the remaining currents should be mediated by GlyRα2 or GlyRα4. The median decay τ was similar in TRHR/GlyRα2-KO and TRHR/GlyRα4-KO GCs, which is inconsistent with their predicted decay τ's (~20 vs 40 msec, respectively). Ongoing studies of glycinergic sIPSCs and L-IPSCs in TRHR double KOs: GlyRα2/GlyRα3 and GlyRα3/GlyRα4 will determine if one or both provide synaptic input.

Conclusions: Our results clearly show that glycinergic currents represent a significant source of inhibition to TRHR ON-OFF-DSGCs. These GCs receive predominant synaptic input via GlyRα3 and an additional input from GlyRα's with slower decay τ's. The different decay kinetics between GlyRα3 (fast τ decays) and GlyRα2 and GlyRα4 (slow τ decays) could lead to subunit specific inhibition in ON-OFF DSGCs on different time scales. Ongoing analyses of light evoked responses will evaluate the functional contributions GlyRα mediated input in ON-OFF DSGCs.

CONTROL ID: 3708726

SUBMITTER (NAME ONLY): Nuria Suárez-Herrera

TITLE: Combined AON-U7snRNA therapy decreases aberrant splicing caused by multiple deep-intronic ABCA4 variants in vitro

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Suárez-Herrera, I.B. Riswick, I. Vázquez-Domínguez, L. Duijkers, A. Garanto, R.W. Collin, Department of Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|N. Suárez-Herrera, I.B. Riswick, I. Vázquez-Domínguez, R.W. Collin, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|D. Piccolo, M.E. Cheetham, UCL Institute of Ophthalmology, London, London, UNITED KINGDOM|A. Garanto, Department of Pediatrics, Radboudumc Radboud Institute for Molecular Life Sciences, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Stargardt disease is a progressive inherited retinal disease caused by ABCA4 mutations. Over the years, an increasing number of pathogenic intronic ABCA4 variants has been reported, usually causing splicing alteration at the pre-mRNA level. Antisense oligonucleotides (AONs) are an attractive therapeutic strategy to rescue these splicing defects, yet they are designed to target individual variants. In this study, we experimentally analyze the potential of combined AON-U7snRNA splicing modulation therapy to target multiple intronic ABCA4 variants using midigene-based splice assays in vitro.

Methods: HEK293T cells were transfected with wild-type or mutant ABCA4 midigenes harboring the genomic region where selected intronic variants are located. Twenty-four hours post-transfection, cells were left non-treated (NT) or transfected with single or multiple AON-U7snRNA cassette vectors, including the respective positive (naked AON, 0.5 μM) or negative (single/multiple empty U7snRNA cassette vectors) controls. RNA was isolated after 48 hours and transcripts were detected through RT-PCR (n=2). Levels of correct/aberrant splicing were measured by transcript band semi-quantification of each condition, using one-way ANOVA as statistical analysis.

Results: For an intron 30 variant, aberrant splicing was decreased from 97.95% (SD: 2.9) in NT to 26.17% (SD: 17.44) when transfected with the multiple-cassette vector ($p<0.0001$), whereas its respective single-cassette vector reduced aberrant levels to 17.17% (SD: 10.71 , $p<0.0001$) and naked AON achieved full rescue (0%, SD: 0, $p<0.0001$). In case of an intron 36 variant, aberrant splicing decrease was observed when delivering the naked AON (0%, SD: 0, $p=0.0106$), single (0.51%, SD: 0.72, $p=0.0131$) or multiple-cassette vector (0.87%, SD: 1.23, $p=0.0152$) compared to NT (16.61%, SD: 2.05). No relevant effect was observed after delivering empty controls or single-cassette vectors targeting a different region.

Conclusions: These splice assays showed significant reduction of aberrant ABCA4 transcripts through multiple AON-U7snRNA cassette delivery in vitro, illustrating the therapeutic potential of the system to correct different splicing defects caused by several intronic variants simultaneously. To corroborate the observed results, delivery of the U7snRNA system through AAV in patient-derived photoreceptor cells and retinal organoids is currently ongoing.

CONTROL ID: 3708727

SUBMITTER (NAME ONLY): Oscar Otero-Marquez

TITLE: Retinal Blood Flow Biomarkers in Healthy Human Subjects Measured with Clinical Doppler Optical Coherence Tomography

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Otero-Marquez, S. Ahsanuddin, J.V. Migacz, A. Harris, T.Y. Chui, R.B. Rosen, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|S. Ahsanuddin, A. Harris, T.Y. Chui, R.B. Rosen, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|K. Minamide, M. Akiba, Kabushiki Kaisha Topcon, Itabashi-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Doppler optical coherence tomography (DOCT) holds the promise of measuring retinal blood flow (RBF) biomarkers such as average blood velocity, vessel diameter, and flow volume within a single cardiac cycle. Using a recently developed DOCT, we investigated whether there is a difference in RBF biomarkers between the superotemporal and inferotemporal retinal vessels of healthy human eyes.

Methods: Eighteen eyes of 18 healthy subjects, 24 to 61 years old (mean 39 ± 12 years) were included in a cross-sectional study. Vessel diameter (D), average velocity (V) and retinal blood flow (RBF) measurements were assessed at the primary artery (TA) and vein (TV) of the superotemporal (ST) and inferotemporal (IT) arcades using a prototype DOCT flowmeter (3D OCT-1 (Maestro2); Topcon Corp., Tokyo, Japan). Median parameter values from 3 measurements acquired at the same location and similar Doppler angle, were used to ensure reliability and accuracy. RBF biomarkers from the superotemporal and inferotemporal arcades were compared using non-parametric independent t-tests. The association between RBF and D in both arteries and veins was assessed using Spearman rank correlation coefficient. A p-value <0.05 was considered statistically significant.

Results: Comparison of retinal blood flow biomarkers between the ST and IT vessels showed no significant differences. The V (mm/seg), RBF (μL/min), and D (μm) at the ST and IT arteries and veins are shown in Table 1. RBF and D were slightly higher in the inferotemporal region of the retina. Positive correlations were found between RBF and D in arteries (Figure 1A, $r= 0.38$; $p= 0.014$) and veins (Figure 1B, $r= 0.46$; $p= 0.002$).

Conclusions: DOCT is capable of consistent measurement of retinal blood flow biomarkers in healthy subjects, supporting its potential as a clinical tool for the evaluation of retinal blood flow. Establishing normative RBF values with this technology, as provided in this study, will be important for confirming its clinical utility for pathological assessment of conditions such as glaucoma, diabetes, and other retinal vasculopathies.

CONTROL ID: 3708734

SUBMITTER (NAME ONLY): Billie Beckwith-Cohen

TITLE: Gene augmentation therapy restores vision in a CaBP4-mutant canine model of cone-rod synaptic disorder

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Beckwith-Cohen, P.A. Winkler, L.M. Occelli, K. Sun, L. Marinho, M. Parys, V. Yuzbasiyan-Gurkan, S. Petersen-Jones, Michigan State University, East Lansing, Michigan, UNITED STATES|F. Montiani-Ferreira, L. Marinho, Department of Veterinary Medicine, Universidade Federal do Parana, Curitiba, PR, BRAZIL|A. Lee, Department of Neuroscience, The University of Texas at Austin, Austin, Texas, UNITED STATES|W.W. Hauswirth, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited retinal degenerations (IRDs) are a leading cause of blindness. While a variety of treatments are being developed to address specific IRDs, we currently have a poor understanding of the degenerate retina's ability to reshape, and restore visual function after treatment. Calcium binding protein-4 (CaBP4) is necessary for the normal development of photoreceptor synaptic morphology and visual function. We identified a mutation in CaBP4 in a pedigree of dogs with a progressive IRD. We used the CaBP4-mutant canine model to examine functional and structural recovery following gene therapy.

Methods: Exome sequencing was performed. Visual function and retinal structure of treated and untreated mutant-dogs were assessed in vivo with ERG, visual behavior and SD-OCT. Gene therapy (AAV8(733)-GRK1-CaBP4) was delivered subretinally to 4 eyes (n=3 dogs) at different stages of the disease. Enucleated globes from affected (n=3) and unaffected animals (n=4) were evaluated for structural changes in treated and untreated eyes with histology, IHC and TEM. Antibodies included CaBP4, CtBP2, GPR179, S and M/L opsin, SNAP-25, hCAR, calbindin, RetP1 and PNA. Western blot for CaBP4 was performed on retinal samples.

Results: A missense mutation in CaBP4 was identified. Affected animals exhibited reduced and mislocalized CaBP4 (IHC, Western blot). Photoreceptor synaptic organization was severely disrupted with a thin outer plexiform layer, and synaptic ribbons appearing immature in affected animals. Impaired photoreceptor synaptic transmission in affected animals was shown by a lack of scotopic and photopic ERG b-wave. Gene therapy restored synaptic transmission as shown by the presence of relatively normal ERG b-waves. SD-OCT and histology supported retinal layer preservation. Rescue was maintained for over two years in one dog (both eyes treated). Two dogs with established photoreceptor layer loss also showed vision and ERG rescue. Visual performance assessed with a 4-choice task was improved in scotopic conditions, showing a 4-fold reduction in time to complete the task, and 50% increase in success for treated eyes (n=3 dogs).

Conclusions: CaBP4-mutant dogs have profound photoreceptor synaptic dysfunction and develop a progressive IRD. Gene augmentation therapy is successful in restoring visual function in treated dogs showing photoreceptor synaptic plasticity.

CONTROL ID: 3708736

SUBMITTER (NAME ONLY): Jaclyn Hwang

TITLE: Multifocal electroretinographic findings in eyes with posterior uveitis and angiographic macular leakage

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Hwang, I. Karaca, S. Lajevardi, C. Or, M. Zaidi, J. Regenold, M. Halim, G. Uludag, C. Yasar, V. Bazojoo, N. Than, A. Mobasserian, Y.J. Sepah, H. khojasteh, Q.D. Nguyen, H. Ghoraba, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|M. Halim, OIRRC, Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this retrospective study, we used multifocal electroretinogram (mfERG) to evaluate the functional implications of angiographic macular leakage without presence of intraretinal fluid on optical coherence tomography (OCT) in eyes with posterior uveitis.

Methods: The STAnford Research Repository (STARR) database was used to identify subjects with posterior uveitis. Subjects who had fluorescein angiography (FA), OCT and mfERG were included, provided that FA and OCT were done at the same visit and mfERG was done within 1 month of the other two imaging modalities. Macular edema (ME) was defined as evidence of intraretinal fluid on OCT. Macular leakage on FA was referred to as angiographic macular leakage. The study cohort was then divided into two groups based on the presence of angiographic macular leakage and ME: Group 1 (no ME and no angiographic macular leakage) and group 2 (presence of angiographic macular leakage without ME). Baseline data, clinical criteria, and mfERG values were analyzed across both groups.

Results: Twenty-three patients (33 eyes) were included. Mean age was 35.9 (± 21.2) and 73% were female. There were 15 eyes in group 1 and 18 eyes in group 2. Groups 1 and 2 had an average age of 34.9 (± 21.0) and 36.7 (± 21.9), respectively ($p>0.8$). Underlying ocular conditions included retinal vasculitis (70%), panuveitis (26%) and intermediate uveitis (4%).

Mean central macular thickness and logMAR BCVA values were 266.6 (± 26.50) μm and 0.12 (± 0.14), respectively; differences were not statistically significantly between groups 1 and 2 ($p>0.1$ and $p>0.7$, respectively). mfERG ring 2 N1 implicit times were significantly delayed in group 2 as compared with group 1 ($p<0.02$). Other mfERG values did not show statistically significant differences between the two groups. Table 1 shows mfERG values of rings 1 (0^{O}) and 2 (3.5^{O}) for the two groups.

Conclusions: Angiographic macular leakage in posterior uveitis without intraretinal fluid on OCT can be associated with photoreceptor dysfunction detectable in the form of delayed implicit timings of ring 2 N1 waves in mfERG. Angiographic macular leakage can be a marker of disease activity and possibly an indication for treatment even in the absence of ME on OCT.

CONTROL ID: 3708739

SUBMITTER (NAME ONLY): HOURI Esmaeil Khanian

TITLE: Relationship between a Categorical Diabetic Retinopathy Severity Score and Quantitative Assessments of Diabetic Lesions

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The qualitative, categorical Diabetic Retinopathy (DR) Severity Scale (DRSS) derived from the Early Treatment Diabetic Retinopathy Study (ETDRS) is commonly used to grade the severity of DR in clinical trials. In this study, we correlate this subjective DRSS score with precise quantifications of numbers and surface area of DR lesions on fundus images.

Methods: In this retrospective study, we collected ultra-widefield (UWF) pseudocolor images from adult diabetic patients. Eyes with evidence of retinal diseases aside from DR, history of ocular treatment for DR, or poor-quality images which precluded assessment of DR severity were excluded. A mask corresponding to the area circumscribed by the 7 standard ETDRS fields was applied to the UWF images, and the DRSS grade (no DR, mild, moderate (mod), or severe non-proliferative DR [NPDR], proliferative DR [PDR]) was assessed according to the ICDR protocol by two masked graders. Within the same ETDRS seven-fields, intra-retinal hemorrhages (H), microaneurysms (Ma), intra-retinal microvascular abnormalities (IRMA), and venous beadings (VB) were manually segmented. The numbers and surface area of these lesions were computed and correlated against the DRSS score using ANOVA with posthoc Bonferroni.

Results: Among 258 diabetic eyes (163 patients), 176 eyes (83 right eyes) of 113 patients (68 females) with a mean age of 59.18 ± 15.57 years were included. 4% were graded as no DR, 12.5% as mild NPDR, 69.3% as mod NPDR, 6.3% as severe NPDR, and 8% as PDR. There was strong intergrader agreement for the DRSS (Cohen’s Kappa = 0.95, $p < 0.05$). H/Ma area, H count, Ma count, and IRMA count were generally significantly different ($p < 0.05$) between DRSS levels (Figure 1). Specifically, these DR lesions' counts/area increased with DRSS level up to severe NPDR, but the lesions counts/area then decreased in PDR eyes. There was no significant difference in VB count between the DRSS levels ($p = 0.42$).

Conclusions: While DR lesions counts/area generally show a positive correlation with the DRSS level, lesion counts seem to decrease from severe NPDR to PDR. This seemingly paradoxical reduction in lesions may reflect the impact of progressive capillary nonperfusion.

CONTROL ID: 3708741

SUBMITTER (NAME ONLY): Gunay Uludag

TITLE: Posterior manifestations and longitudinal outcomes in TINU syndrome

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Uludag, M. Hassan, J. Regenold, A. Akhavanrezayat, A. Mobasserian, C. Yasar, C. Or, H. khojasteh, H. Ghoraba, I. Karaca, M. Zaidi, N. Yavari, N. Than, S. Park, V. Bazojoo, Q.D. Nguyen, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this retrospective study, we aim to describe the ocular clinical features and long-term visual outcomes of Tubulointerstitial Nephritis and Uveitis Syndrome (TINU).

Methods: Medical records (January 2005 to August 2021) from a tertiary eye care hospital were reviewed. All patients who met the diagnostic Criteria for TINU Syndrome were included. Demographic and clinical data were collected.

Results: Twelve patients (24 eyes) with TINU were included. Median age at onset of uveitis was 13.5 years (9-45). 66.6% (n=8/12) of patients were female. Median follow-up period was 29.5 months (6-89 months). All patients had bilateral anterior uveitis. 41.6% (n=5/12) of patients had biopsy-proven acute interstitial nephritis (AIN); urinary beta-2 microglobulin (Ub2M) measurements were elevated in all tested patients (n=9/9). Posterior segment findings were seen in 66.6% of eyes (n=16/24). Posterior segment findings were including papillitis 58.3% (n=14/24), retinal vasculitis 45.8% (n=11/24), vitritis 33.3%(n=8/24), macular edema 25% (n=6/24), presence of snowballs 16.6% (n=4/24), and chorioretinal lesions 8,3% (n=2/24). 14 eyes had available fluorescein angiography (FA) imaging and of those, 78.5% (n=11/14) revealed retinal capillary leakage, and 71.4% (n=10/14) revealed optic disc staining/leakage. Visual outcomes were favorable in most eyes (n=17/20) except for 3 (one had persistent ME, one with macular scar formation, and one developed amblyopia). 91.6% (n=11/12) patients received systemic treatment. Of those, 75% (n=9/12) received systemic corticosteroid treatment and/or immunomodulatory therapy (IMT), with 41.6% (n=5/12) patients requiring biologics to control intraocular inflammation (IOI). 66.6% (n=8/12) of patients achieved IOI quiescence and of those, 2 achieved drug-free remission during follow-up period. However, one patient in remission developed a recurrence 10 months after discontinuation of IMT. Figure 1 demonstrates fundus and FA findings in a representative patient.

Conclusions: Ub2M is a useful biomarker for the diagnosis of TINU syndrome. Posterior segment manifestations are not uncommon in TINU patients. Therefore, FA is critical for the management of patients with TINU. The majority of patients required systemic treatment in order to control IOI and prevent relapses.

CONTROL ID: 3708742

SUBMITTER (NAME ONLY): Yuntian Xue

TITLE: Retinal Organoids Cultured by Microfluidic Bioreactor Demonstrated Functionality Measured by a High-Density Microelectrode Array System

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Human stem cell-derived retinal organoids (RtOgs) are able to develop matured photoreceptor cells and outer segment structures. Fully functional RtOgs should obtain complete and intact neural pathways between retinal cell layers. The purpose of this study was to apply an advanced electrophysiology testing system for verifying the functionality of matured RtOgs cultured by a customized microfluidic bioreactor platform.

Methods: RtOgs were derived from CRX-GFP genetically modified human embryonic stem cell (hESC) line (Collin et al. 2016, Stem Cells), and cultured on a customized microfluidic bioreactor system (Xue et al. 2021, Lab Chip) from day 103 to 170. On day 170, two RtOgs with outer segment structures were cut into half, with the inner layer retinal cells faced down and seeded on two high-density microelectrode arrays (HD-MEA) wells, respectively. Spontaneous discharge of RGCs and light stimulation on photoreceptor cells were measured using the full scan and network recording modes provided by the MaxOne recording system. The light stimulation experiment used natural light generated from a multi-spectral light source with controlled illuminance (ranging from 20.57 to 883.92 lux). RtOgs were cultured on the HD-MEA system from day 170 to 204 and dark-adapted before the light stimulation experiment.

Results: Spontaneous discharge of retinal cells was observed initially on day 184, the total firing rate, burst frequency, and the number of spikes per burst increased over time. RtOgs' light responsiveness was confirmed by the denser raster scanning plot, increased firing rate, and the number of spikes per burst.

Conclusions: RtOgs cultured by the microfluidic bioreactor system developed functional inner retinal cell and photoreceptor layers, as well as the neural pathway in between. The HD-MEA recording system used in this study achieved in vitro longitudinal live recording of the RtOgs' electrophysiological properties.

CONTROL ID: 3708746

SUBMITTER (NAME ONLY): Sean Donahue

TITLE: Bilateral Lateral Rectus Muscle Recessions Versus Recess-Resect for Childhood Intermittent Exotropia (IXT): 8-year Outcomes

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: In a randomized clinical trial comparing bilateral lateral rectus muscle recessions (BLR) with unilateral recess-resect (R&R) for childhood intermittent exotropia (IXT), we previously found no significant difference in cumulative probability of suboptimal surgical outcome by 3 years (46% in BLR and 34% in R&R; difference = 9%; 95% confidence interval (CI): -6% to 23%). (PEDIG, Ophthalmology 2019;126(2): 305-317) We now report outcomes after 8 years of follow-up.

Methods: After a 3-year randomized trial, 123 (64 in BLR and 59 in R&R) of the 197 original cohort (age 3 to <11 years with basic-type IXT 15 to 40 prism diopters (Δ), stereoacuity of 400 arc sec or better and no prior surgery), consented to participate in an additional 5 years of follow up, with treatment at investigator discretion. The primary outcome measure was “suboptimal surgical outcome” by 8 years, defined as any of the following at any visit: exotropia ≥10Δ by simultaneous prism cover test (SPCT) at distance or near; constant esotropia ≥6Δ by SPCT at distance or near; loss of near stereoacuity by ≥2 octaves from baseline; re-operation without meeting any of aforementioned criteria. "Complete or near complete resolution" at 8 years was defined as: any exodeviation <10Δ by SPCT and prism alternate cover test (PACT) at distance and near AND ≥10Δ reduction in baseline angle by PACT at distance and at near (if ≥10Δ at baseline); any ET <6 Δ at distance and near; no decrease in stereoacuity by ≥2 octaves; and no additional treatment for IXT.

Results: The cumulative probability of suboptimal surgical outcome by 8 years was 66% for BLR and 53% for R&R (difference = 13%, 95% CI: -4% to 30%). Complete or near complete resolution at 8 years occurred in 14% (6 of 42) for BLR and 39% (16 of 41) for R&R (difference = -25%, 95% CI: -44% to -5%). The cumulative probability of reoperation by 8 years was 32% for BLR versus 10% for RR (difference = 22%, 95% CI = 7% to 37%).

Conclusions: There was no significant difference in the study-defined suboptimal surgical outcome by 8 years between BLR and R&R for childhood IXT. However, the R&R group had a higher resolution rate and lower rate of reoperation by 8 years. Taken together, our findings suggest that a unilateral recess-resect procedure may provide superior long-term outcomes to bilateral lateral rectus recession for basic-type childhood IXT.

CONTROL ID: 3708748

SUBMITTER (NAME ONLY): Christin Hanke-Gogokhia

TITLE: Dynamin-1 and -3 are essential for the structure and function of mouse rod photoreceptor synaptic terminals

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hanke-Gogokhia, T. Zapadka, J.B. Demb, Ophthalmology and Visual Science, Yale University, New Haven, Connecticut, UNITED STATES|S. Finkelstein, M. Klingeborn, C. Bowes Rickman, V.Y. Arshavsky, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptors are highly polarized retinal neurons that absorb light and generate an electrical signal through the process of phototransduction. Light-dependent changes in the membrane potential drive glutamate release from the synaptic terminal onto the second order neurons, bipolar cells (BCs) and horizontal cells (HCs). The photoreceptor's synaptic ribbon facilitates a high rate of exocytosis (vesicle fusion), which is complemented by endocytosis (vesicle retrieval). Endocytosis commonly requires the GTPase dynamin, whose two isoforms, Dnm1 and Dnm3, are expressed specifically in neurons. Here, we evaluated the impact of deleting Dnm1 and 3 on rod photoreceptor structure and function.

Methods: Dnm1- and Dnm3-floxed mice were bred with transgenic iCre75 mice to generate rod-specific single ($^{rod}Dnm1^{-/-}$ and $^{rod}Dnm3^{-/-}$) and double knockouts ($^{rod}Dnm1^{-/-}/3^{-/-}$). ERG recordings were used to test photoreceptor function and signal transmission to BCs. Photoreceptor structure was evaluated by immunohistochemistry, confocal microscopy and electron microscopy.

Results: Immunostaining confirmed the conditional deletion of Dnm1 and 3 from rods. In $^{rod}Dnm1^{-/-}/3^{-/-}$ mice, scotopic ERG a-waves were normal at P90, consistent with normal outer nuclear layer thickness and rod outer segment length; whereas scotopic b-waves were significantly impaired, consistent with a thinning of the outer plexiform layer. Immunostaining of photoreceptor synaptic terminals with ribbon synapse-related proteins (RIBEYE and bassoon) and synaptic vesicle-related proteins (VGLUT1 and complexin-3) showed degeneration of rod terminals. Consistent results were obtained by electron microscopy. In contrast, cone pedicles and the cone-driven ERG in $^{rod}Dnm1^{-/-}/3^{-/-}$ mice remained intact. At P90, $^{rod}Dnm1^{-/-}/3^{-/-}$ retinas showed a reduced number of HCs (anti-calbindin) and an increase in neurite sprouting from rod BCs (anti- PKCα). No abnormalities of any sort were observed in single knockouts of either Dnm1 or 3, suggesting that their function in rods is redundant.

Conclusions: Deletion of Dnm1 and 3 from rods causes functional impairment and degeneration of the synaptic terminal. This degeneration is accompanied by structural defects in postsynaptic neurons and loss of light-driven signals in rod BCs. Normal function of rod synapses requires dynamin-dependent endocytosis.

CONTROL ID: 3708750

SUBMITTER (NAME ONLY): Emiliano Teran

TITLE:

Refractive Errors of Teenager Students from Sinaloa, Mexico

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We assessed the prevalence of refractive error in a sample of children of Northwest Mexico using the Refractive Error Study in Children protocol of the World Health Organization, which allows the comparison with other global studies.

Methods: A total of 783 students (384 female and 399 male) in Sinaloa's basic school system participated in the study from 2020 to early 2021. Optometrists and student clinicians from the Optometry Program of the Autonomous University of Sinaloa conducted the testing. Tests included visual acuities and static retinoscopy. We did use a cycloplegic agent when the far visual acuity of the students was equal to or worse than 20/40.

Results: The results showed a high prevalence of uncorrected refractive errors. Myopia, defined as a refractive error ≤ -0.50 D, had a prevalence of 24.64% (95% CI: 21.45— 27.58) hyperopia, defined as a refractive error ≥ +2.00 D had a prevalence of 2.04% (95% CI: 1.14— 3.19) and astigmatism, defined as a refractive error with a cylinder ≥ 0.75 D had a prevalence of 19.79% (95% CI: 16.85—22.47). We did not find a significant effect of sex on myopia (Chi square = 0.27, p = 0.60), hyperopia (Chi square = 0.17, p = 0.18) or astigmatism (Chi square = 0.82, p = 0.36).

Conclusions: The prevalence of myopia found in children (24%) is similar with a high prevalence of myopia reported in adolescents worldwide and in Mexico's northern regions (40%). The results suggest that students attending basic school and entering high school should be required to have an optometric eye examination.

CONTROL ID: 3708752

SUBMITTER (NAME ONLY): Padmaja Sankaridurg

TITLE: Pupillary diameter and accommodative amplitude with Atropine alone and combined with Caffeine- Results from a prospective, longitudinal clinical trial- Part II

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Use of Atropine to slow myopia is associated with undesirable side effects, particularly, pupil dilation and a decrease in accommodative amplitude. We report changes in pupil diameter (PD) and accommodative amplitude (AA) with Atropine (Atr) used alone and in combination with Caffeine (Caf).

Methods: In a prospective, clinical trial, 96 Vietnamese children with myopia (mean age 10.4±2.0 yrs, -4.1±1.3D) were randomized to nightly use of either 2% Caf, 0.02% Atr with 2% Caf, or 0.02% Atr (Customcare Compounding Pharmacy, Australia) and single vision spectacles during day. Additionally, 86 children with myopia (mean age 10.1 ± 2.1 yrs, -3.3±1.4D) were enrolled in a parallel group to serve as controls with single vision spectacles only (SVL). At baseline, 2 wk, 3, 6, 9 and 12 months, PD (photopic: 300 lux at eye; mesopic: 30 lux; Oculus Park 1, OCULUS GmBH, Wetzlar, Germany) and AA (Royal Near Pt Ruler, push up method with best corrected SVL, -4.0D) was measured. An average of 3 measurements were considered for PD and AA. Change in PD and AA from baseline was averaged over follow-up visits and differences between groups analysed using linear mixed model and logistic regression. Level of significance was 5%.

Results: Compared to baseline and to SVL, Atr and Atr+Caf increased PD and reduced AA (Table). Caf was similar to SVL. Importantly, change in photopic PD with Atr+Caf was significantly lower compared to Atr alone (0.8mm vs 1.2mm, p=0.006) but not different for change in mesopic PD (0.4mm vs 0.6mm, p=0.678) and AA(-2.8D vs -3.5D, p=1.000).Risk of an increase in mesopic PD over time was 1.5X greater with Atr than Atr+Caf (p=0.033). A photopic PD increase of ≥1mm and ≥2mm was 3.3X and 7.0X greater with Atr compared to Atr+Caff (p=0.001 & 0.008 respectively). The probability of having a photopic PD of ≥1.2mm was reduced by ≥45% with Atr+Caff for all ages and visits.

Conclusions: When Caffeine was combined with Atropine, the observed PD change was smaller compared to the PD change with Atropine alone. Caffeine did not affect the slowing of myopia observed with Atropine (seeTran HDM, ARVO abstract 2022). Caffeine has potential in reducing risk of side effects associated with Atropine without affecting its efficacy.

CONTROL ID: 3708753

SUBMITTER (NAME ONLY): J. Heur

TITLE: Deletion of Zeb1 blocks injury-induced endothelial mesenchymal transition in the mouse corneal endothelium in vivo

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.M. Heur, J. Lee, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: FGF2-induced mesenchymal transition (MT) in human and mouse corneal endothelium ex vivo leads to Zeb1 activation and subsequent retrocorneal membrane (RCM) formation. We investigated whether Zeb1 deletion can block RCM formation in FGF2-induced MT in the mouse corneal endothelium in vivo following surgical injury.

Methods: Hemizygous UBC-CreERT2 mice were crossed with homozygous mice harboring loxP-flanked Zeb1 alleles ($Zeb1^{flox/flox}$) to generate $Zeb1^{flox/flox}$:UBC-CreERT2 mice. Intracameral injection of 4-hydroxytamoxifen (4-OHT) renders the Zeb1 allele into a loss of function mutant in the corneal endothelium. Corneal endothelium in anesthetized mice was surgically injured in vivo under direct visualization 7 days after intracameral injection of 4-OHT. Gene expression was analyzed by semi-quantitative RT-PCR and by immunoblotting in the mouse corneal endothelium in vivo.

Results: Conditional deletion of Zeb1 by 4-OHT in $Zeb1^{flox/flox}$ mice inhibited FGF2-induced expression of Zeb1 mRNA and protein. FGF2- and surgical injury-induced expression of EnMT-related genes, including fibronectin, vimentin and type I collagen, and suppression of E-cadherin were inhibited by Zeb1 deletion mouse corneal endothelium in vivo. Surgical injury led to corneal edema, 189.0 ± 14.6um (injury) vs 92.3 ± 2.8um (control), and injury-induced edema was significantly reduced by Zeb1 targeting, 182.2 ± 15.5um (injury) vs 106.8 ± 11.1um (injury + 4-OHT), $F = 120.9$, $p < 0.00001$. Moreover, conditional knock-out of Zeb1 also inhibited injury-dependent RCM formation in mouse corneal endothelium in vivo.

Conclusions: Our data show that Zeb1 is key mediator of FGF2- and surgical injury-dependent endothelial mesenchymal transition in mouse corneal endothelium, with Zeb1 regulating type I collagen, fibronectin, and vimentin expression. These results suggest that Zeb1 signaling could be a therapeutic target for inhibiting anterior segment fibrosis.

CONTROL ID: 3708754

SUBMITTER (NAME ONLY): Cheryl Fonteh

TITLE: Mental Health and Visual Acuity in Patients with Age-related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Fonteh, A.M. Lynch, R. Navo, N. Mandava, M. Mathias, J.L. Patnaik, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is an established association between visual acuity (VA) loss and depression in patients with AMD. However, there is a paucity of research linking VA with mental health amongst the different subgroups of AMD. The goal of this study was to describe the relationship between VA and mental health questions on the NEI-VFQ-25 questionnaire in patients with different classifications of AMD, and to identify predictors of mental health subscale scores.

Methods: Patients with AMD defined by multi-modal imaging were recruited into a Colorado AMD registry. Habitual VA was obtained by a trained certified ophthalmic technician using the Snellen VA as distance viewing. At enrollments, patients completed the 25-item NEI-VFQ-25, a visual questionnaire that includes 25 questions regarding the patient's visual functionality with regular daily activities. Mean scores on the mental health subscale of the VFQ were calculated by AMD classification and VA groups. Univariate and multivariable general linear models were used to estimate associations between mental health scores and variables of interest.

Results: A total of 875 patients were included in the study. Patients with bilateral both (geographic atrophy and neovascular) scored lowest on the mental health subscales with a mean ± SD of 59.6 ± 29.3. Patients with a habitual VA of 20/200 or worse scored the lowest on mental health subscales scores in both the better and worse seeing eye of 44.8 ± 25.9 and 63.9 ± 28.4 respectively. Patients with a VA of 20/20 or better had the highest scores on the mental health subscales in both the better and worse seeing eye of 85.3 ± 17.7 and 89.1 ± 13.0 respectively (Fig 1). VA of the better and worse seeing eye and AMD classification were significant predictors of mental health subscale scores (all $p<0.0001$ except the worse-seeing eye in multivariable model where $p=0.012$). Patients enrolled during the COVID pandemic had mental health scores that were 2.7 points lower than prior to the pandemic, but this difference was not significant ($p=0.22$).

Conclusions: There is a significant association between mental health questionnaire scores and AMD classification, as well as VA in both the better-seeing and worse-seeing eyes in patients with AMD. It is important for clinicians to recognize feelings of worry/ frustration in these patients, so they can be appropriately diagnosed, referred, and treated for depression and/or anxiety.

CONTROL ID: 3708755

SUBMITTER (NAME ONLY): Atika Safitri

TITLE: Health-related quality of life in glaucoma and ocular hypertension: utility values and disease severity

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Safitri, G. Gazzard, K. Hu, Institute of Ophthalmology, University College London, London, UNITED KINGDOM|A. Safitri, E. Konstantakopoulou, G. Gazzard, K. Hu, NIHR Moorfields Biomedical Research Centre, London, Greater London, UNITED KINGDOM|E. Konstantakopoulou, Division of Optics and Optometry, University of West Attica, London, GREECE|

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ABSTRACT BODY:

Purpose: Glaucoma is the commonest cause of irreversible blindness globally, affecting patients' quality of life. There have been several attempts to evaluate health-related quality of life using different instruments. Here, we assess utility values (UVs) in a cross-section of patients with ocular hypertension and glaucoma at all stages of severity.

Methods: Patients (n=341) requiring treatment for ocular hypertension and open-angle glaucoma (primary open-angle glaucoma, pseudo exfoliative, and normotension glaucoma) were recruited from two clinical sites in London, United Kingdom. UVs were evaluated for patients' health states using the standard gamble for death and standard gamble for blindness. The Mean Deviation from Humphrey visual field analyser of each patient's worse eye was used to classify participants into mild, moderate, and severe visual field loss groups according to Hodapp-Parrish-Anderson Criteria.

Results: Mean UV for the whole patient cohort was 0.77 (standard deviation (SD) 0.27; 95% confidence interval (CI) 0.74 to 0.80) with the standard gamble for blindness; and 0.87 (SD 0.22; 95% CI 0.85 to 0.90) for a gamble of death. Only 43% of patients were willing to risk blindness in return for perfect vision; whereas 60% were willing to risk dying in return for perfect vision.

Mean UV in patients with severe visual field loss was 0.73 (SD 0.27) with standard gamble for blindness and 0.83 (SD 0.25) with standard gamble for death. With each method, mean UV was lower in those with severe visual field loss compared to those with mild visual field loss (0.80 (SD 0.26), and 0.92 (SD 0.18), respectively). The mean difference in UV between mild and severe groups was 0.076 (95% CI 0.010 to 0.142; P = 0.0071) with standard gamble for blindness. In standard gamble for death, the mean difference between mild and severe groups was 0.085 (95% CI 0.031 to 0.140 P = 0.0001).

Conclusions: Most patients requiring treatment for glaucoma and ocular hypertension are willing to risk their lives in return for the hypothetical offer of normal vision. Severity of visual field loss is inversely correlated with quality of life assessed using utility values. This information is useful for cost-utility analysis in clinical trials.

CONTROL ID: 3708756

SUBMITTER (NAME ONLY): Sydney Roston

TITLE: Identification of clinical factors associated with delayed or prolonged ROP regression

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Roston, J. Schoephoerster, J. Anderson, E.C. Ingolfsland, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|S. Lunos, University of Minnesota Clinical and Translational Science Institute, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to identify factors that influence the timing and duration of retinopathy of prematurity (ROP) regression, a variable process in preterm infants. We hypothesize that more inflammatory exposures and slower growth before a corrected gestational age (CGA) of 36 weeks delay and prolong ROP regression.

Methods: This retrospective chart review included infants born ≤ 30 weeks CGA and < 1500 grams previously included in three prospective cohort studies. Baseline characteristics, growth rates, and inflammatory events were collected for 76 infants who developed ROP not requiring treatment. The outcomes of interest were gestational age (GA) at the most severe stage of ROP (GA MSROP), GA at which ROP regression began, GA at the time of complete vascularization (GA CV), and duration of ROP regression. Continuous variables were analyzed with Pearson's correlation coefficients and categorical variables were analyzed with t-tests or analysis of variance ($P<0.05$).

Results: Mean GA was 35.3 weeks at MSROP, 40.0 weeks at time that ROP regression began, and 49.8 weeks at time of CV. Mean duration of ROP regression was 9.5 weeks. As summarized in Tables 1 and 2, later GA MSROP was associated with slower head growth, increased number of positive cultures, increased platelet transfusion volume in the first week of life, increased red blood cell transfusion volume, greater severity of ROP, and iron deficiency (ferritin<40). Later GA CV and prolonged duration of ROP regression were associated with slower length gain, increased number of positive cultures, higher mean total insulin dose in the first week of life, higher total number of inflammatory events, greater severity of ROP, maternal chorioamnionitis, and chronic lung disease (CLD). Increased IL-6 on day of life 5 was associated with prolonged duration of ROP.

Conclusions: This study confirms prior findings that increased severity of ROP is associated with later GA at MSROP and CV and prolonged duration of regression. New associations were found between slower neonatal growth and inflammatory comorbidities and prolonged or delayed ROP regression. These findings suggest that infants with these comorbidities may require longer surveillance for resolution of ROP.

CONTROL ID: 3708759

SUBMITTER (NAME ONLY): Cynthia Roberts

TITLE: Comparison of elastic and viscoelastic biomechanical metrics in primary open angle glaucoma and normal controls

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Roberts, G. Fleming, A. Mahmoud, Ophthalmology & Visual Sciences, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|C.J. Roberts, G. Fleming, A. Mahmoud, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low corneal hysteresis (CH) is a risk factor for glaucoma progression, as well as a combination of thin, stiff corneas. This study investigates viscoelastic and elastic metrics from air puff deformation in Normal (NL) and Primary Open Angle Glaucoma (POAG).

Methods: A prospective study of 107 subjects was done with 110 eyes of 55 NL subjects, age>50 years, 104 eyes of 52 POAG subjects. Viscoelastic response was evaluated with CH from the Ocular Response Analyzer; elastic response was evaluated with Corvis ST corneal metrics: Stress Strain Index (SSI) and stiffness parameter at first applanation (SP-A1). Scleral stiffness at highest concavity (SP-HC) and central corneal thickness (CCT) were included. Ganglion Cell Complex (GCC) from Optovue OCT was acquired. ANOVA was performed for age, CCT and IOPcc, while ANCOVA was used with IOPcc and CCT as co-variates for GCC, CH, SP-A1, and SP-HC. Regressions were performed between viscoelastic and elastic metrics, as well as between GCC and biomechanical metrics. Stepwise regressions with 0.15 entry/exit criteria were performed to predict GCC as a function of biomechanical metrics, and to predict CH as a function of elastic metrics. Statistical analysis was performed using SAS with significance threshold at $p<0.05$.

Results: No difference in age was found. CCT was thinner and IOPcc higher in POAG. GCC was thinner in POAG ($p < 0.0001$), with CH, SP-A1 and SP-HC not different when controlling for CCT and IOPcc. CH was significantly associated with CCT, SP-A1, SP-HC, and IOPcc in both groups. GCC was significantly positively associated with CH and CCT, only in POAG, but not with SP-A1, SP-HC or IOPcc in either group. GCC was predicted in POAG inversely by SSI, and directly by CH and SP-HC. In NL, GCC was predicted by SSI, CCT and IOPcc. CH was predicted in POAG directly by SP-HC, and inversely by corneal stiffness metrics and IOPcc. CH was predicted in NL by SP-HC, corneal stiffness metrics, IOPcc and CCT.

Conclusions: In POAG, thinner GCC was associated with lower CH and greater corneal stiffness, consistent with the literature on risk factors, as well as low scleral stiffness. Although greater cornea or sclera stiffness were associated independently with greater CH in POAG, when all elastic parameters were included in a predictive model, low CH was predicted by a combination of greater corneal stiffness, higher IOP, and lower scleral stiffness.

CONTROL ID: 3708762

SUBMITTER (NAME ONLY): Fatima Abbas

TITLE: Speed of the human phototransduction

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Abbas, F. Vinberg, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|A.M. Hanneken, Scripps Research Institute Department of Molecular and Experimental Medicine, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure: Fatima Abbas: Commercial Relationship: Code N (No Commercial Relationship) | Anne Hanneken: Commercial Relationship: Code N (No Commercial Relationship) | Frans Vinberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The speed of human vision is expected to be rate-limited by the slowest deactivation reaction of phototransduction. Our high-acuity color vision is mediated mainly by the cones in the central foveal/macular retina. However, the speed of the rate-limiting deactivation reaction of human phototransduction in the macula is not known. To address this gap in knowledge, we analyzed photoreceptor light responses in different geographical regions of the human retina from posterior eyes procured during organ donations.

Methods: Using ex vivo Electroretinogram (ERG) we measured light-evoked photoreceptor responses from Ø0.5mm areas of peripheral and macular punches from eyes recovered < 20 min postmortem from two organ donors. Retinas were maintained in the dark in Ames' media oxygenated with 95% O_2 5% CO_2 and perfused in Ames' containing $BaCl_2$ and DL-AP4 to isolate photoreceptor responses during recordings. Cone responses were isolated by a double-flash stimulus protocol. We plotted the times taken for photoreceptor responses to return 50% (cones) or 30% (rods) from saturation against natural logarithm of the flash intensities, and applied a linear fit to determine the slope (τ_D), i.e. dominant time constant of the phototransduction termination, as described by Pepperberg et al (1992).

Results: We found the average τ_D of macular human cones was 25 ms (±4 ms S.D., n= 6 punches) and macular rods was 313 ms (±54 ms S.D., n =5 punches). In peripheral retina the τ_D of cones was 27 (± 8ms S.D., n = 6 punches) and rods 367 (± 100ms S.D., n = 6 punches). While macular rods had a τ_D >10 fold longer than that of macular cones, we found no significant difference between macular and peripheral cone dominant time constants, nor of the peripheral and macular rods.

Conclusions: These results indicate that the rate limiting step of human macular cone photoreceptors is significantly shorter than the lifetime of activated phosphodiesterase or rhodopsin determined previously in mouse rod photoreceptors. This is expected to contribute significantly to the high temporal resolution of the human high-acuity color vision. Our results demonstrate the potential of using human donor retinas to understanding the physiology of the human macula in health, aging and disease.

CONTROL ID: 3708767

SUBMITTER (NAME ONLY): Parameswaran Sreekumar

TITLE: Regulation of LDLR in hRPE and loss of retinal function in Ldlr -/- mice exposed to NaIO3

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.G. Sreekumar, C. Spee, R. Kannan, Doheny Eye Institute, Pasadena, California, UNITED STATES|F. Su, S.T. Reddy, Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, California, UNITED STATES|E. Araujo, S. Nusinowitz, R. Kannan, Jules Stein Eye Institute, University of California at Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lipid peroxidation induces oxidative stress (OS) which is one of the major underlying causes of age-related diseases including AMD. In early AMD, extracellular deposits, cholesterol, lipids, and proteins accumulate between the RPE and the Bruch membrane. Cholesterol content is abundant in the retina and circulating low density lipoprotein (LDL) is taken up by low density lipoprotein receptor (LDLR) in the RPE and Müller cells. Lldr-/- mice develop thickened Bruch membrane and show increased VEGF with high fat diet; however, the role of LDLR in dry AMD has not been systematically investigated. The aim of this study is to determine the role of LDLR in an OS-induced model of dry AMD.

Methods: Confluent RPE cells were treated with150 µM tBH and expression of LDLR was studied using immunofluorescence. Kinetic activation of caspase-3/7 in Ldlr silenced RPE cells co-treated with 300 µM tBH and 10 or 40 µg/ml of an HDL- mimetic HM 10/10 peptide was quantified by live-cell imaging using the Incucyte system. In vivo studies were conducted with male C57BL6/J (7-8 weeks old) and Ldlr $^{-/-}$ mice. OS was imposed in mice with intravenous NaIO3 (20mg/kg BW). On day 7, fundus imaging, OCT and ERG were performed, and retinal thickness was measured from OCT images. Posterior eye cups were processed for histology, TUNEL staining and immunostaining for cleaved caspase 3.

Results: In primary human RPE cells, LDLR is predominantly found in the cytosol and tBH-induced OS altered its expression pattern. tBH markedly increased caspase activation in a time-dependent manner for 24 h in Ldlr silenced RPE cells. Co-treatment with HM-10/10 (10 µg/ml) significantly blocked caspase activation. Severe pathophysiological changes and functional impairment were observed in the retinas of NaIO3-treated Ldlr$^{-/-}$ mice. LDLR deficiency resulted in significant thinning of retina and compromised rod and cone functions with a total abolition of the rod function. Furthermore, RPE/BM was discontinuous with patchy RPE loss and irregular degenerated cell aggregates were more prominent in the NaIO3-treated retina of Ldlr$^{-/-}$ mice. Moreover, the percentage of apoptotic cells and cleaved caspase 3 was significantly elevated in stressed Ldlr$^{-/-}$ mice vs WT mice.

Conclusions: Our data suggest that loss of LDLR impairs retinal function which could play a significant role in the development of AMD.

CONTROL ID: 3708769

SUBMITTER (NAME ONLY): Kevin Eade

TITLE: Deoxysphingolipids mediate toxicity though the Unfolded Protein Response (UPR)

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.T. Eade, S. Giles, S. Harkins-Perry, M. Friedlander, Lowy Medical Research Institute, Lowy Medical Research Institute, La Jolla, CA, US, other/medres, California, UNITED STATES|K.T. Eade, J. Rosarda, S. Giles, S. Harkins-Perry, R. Wiseman, M. Friedlander, The Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal degenerative disease Macular Telangiectasia (MacTel) is a complex genetic disease with a common metabolic signature, decreased systemic serine and increased deoxysphingolipids (dSLs). Elevated dSLs are toxic to the retina and correlate with disease severity. However, the mechanism of dSL-mediated toxicity is not understood.

Methods: We model dSL toxicity in the retina by adding deoxysphinganine to mature retinal organoids. Toxicity is quantified by assaying cell death in photoreceptors using TUNEL staining. To characterize the retina's cell stress response to dSL toxicity we perform bulk RNAseq and single-cell RNAseq along with targeted and untargeted pathway analyses. We then utilize selective pharmacological inhibitors and activators of cell stress pathways to assay their functional relevance in the dSL toxicity response.

Results: Through bulk RNAseq we identify the Unfolded Protein Response (UPR) as one of the major stress pathways activated in dSL toxicity, with two of the UPR sub-branches, ATF6 and PERK, comprising the majority of the response. Using single-cell RNAseq we then characterize cell-specific dSL toxicity responses, identifying unique cell-type dSL susceptibility. We next determined the functional role of the UPR pathway sub-branches in dSL toxicity. Inhibition of the UPR PERK pathway prevents cell death indicating that apoptosis from dSL toxicity is mediated through PERK. Conversely, inhibition of the UPR ATF6 pathway exacerbates dSL induced cell death, indicating its role in homeostasis. Next, we screen ATF6 activating drugs to identify multiple compounds that alleviate dSL toxicity through the activation of ATF6.

Conclusions: We provide the first characterization of cell stress responses to dSL toxicity in the retina, identifying the UPR as a major cell stress pathway activated by dSL toxicity. Subsequent single cell RNAseq is used to characterize its unique effect in each cell type providing insight to its pathological mechanism in MacTel. We subsequently identify multiple classes of drugs that can prevent cell death as well as promote compensatory signaling pathways to promote cell health and survival through modification of the UPR.

CONTROL ID: 3708770

SUBMITTER (NAME ONLY): Huy Nguyen

TITLE: SZN-413, a monospecific Fzd4 Agonist as a Potential Novel Therapeutic for the Treatment of Diabetic Retinopathy

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Nguyen, S. Lee, E. Whisler, K. Logas, H. Chen, P. Sampathkumar, J. Ye, N. Suen, Y. Li, W. Yeh, Surrozen, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Norrin/Fzd4 signaling is indispensable for retinal vascular development and vessel function in humans and rodent models. These studies examined whether a novel Norrin mimetic could promote the regeneration of damaged blood vessels and their functions in diabetic retinopathy animal models.

Methods: We generated an antibody-based bi-specific Norrin mimetic (SZN-413) that targets Fzd4 and low-density lipoprotein receptor-related proteins and evaluated its effects on damaged retinal vessels in mice and rabbit models. In an oxygen-induced retinopathy (OIR) mouse model, SZN-413 was delivered intravitreally (IVT) and the avascular (AV) area and neovascularization (NV) area were measured 5 days later. Furthermore, the impact on vascular leakage by SZN-413 was examined in a VEGF-induced retinal vascular leakage rabbit model, in which the level of fluorescein leakage was measured 3 days after IVT delivery of VEGF together with SZN-413 or vehicle. ANOVA was used for statistical analysis.

Results: Results: In the OIR mouse model, nanogram quantities of SZN-413 significantly reduced the NV area size ($p<0.001$) to a level comparable to the group treated with 60 ug aflibercept. SZN-413 also showed a dramatic reduction in AV area size compared to vehicle ($p<0.001$) and compared to aflibercept ($p<0.01$). In the VEGF-induced retinal vascular leakage rabbit model, SZN-413 significantly reduced retinal vascular leakage by 78%, compared to the vehicle-treated group ($p<0.01$). No observable abnormalities were detected in ocular exams in these studies.

Conclusions: The novel Norrin mimetic, SZN-413, demonstrated anti-NV properties and reduced the avascular area in OIR mice, and reduced VEGF-driven retinal vascular leakage in rabbits. The results strongly suggests that the pathological cellular responses can be modulated by SZN-413, with possible therapeutic implications for diabetic retinopathy.

CONTROL ID: 3708773

SUBMITTER (NAME ONLY): sruti tekumalla

TITLE: Diagnostic Yield of Vitreous Biopsy for Primary Vitreoretinal Lymphoma

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Primary vitreoretinal lymphoma (PVRL) is the most common intraocular lymphoproliferative disorder. The disease is often difficult to diagnose, having an insidious onset that can masquerade as chronic uveitis. Histologic identification remains important for diagnosis, and vitreous biopsy is frequently obtained. Degradation of fragile lymphoma cells after pars plana vitrectomy (PPV) occurs in many cases, and may be impacted by the transition to smaller gauge and very high cut rate vitrectomy. We evaluated the diagnostic yield of PPV, specifically using modern high-cut rate dual-cycle cutters, on in vitro cell viability and diagnostic yield.

Methods: Human Burkitt lymphoma cell line Namalwa was processed by 25-G dual blade guillotine-type vitrectomy at five different cut rates (500, 1000, 4000, 7500, or 15000 cuts per minute [cpm]) at 2x10^5 cells/mL suspended in BSS. The cell viability and diagnostic yield in each subtype group was determined using hemocytometry with trypan blue staining, viable cell count using Cell Counting Kit-8 (CCK-8), and ocular pathologist-guided manual count. Yield was analyzed by regression analysis and ANOVA test.

Results: Linear regression and ANOVA were performed using viable cell concentration as measured by CCK-8 and cut rate (Figure 1). Linear regression analysis of CCK-8 samples demonstrated no significant variation of cellular yield by cut rate (R^2= 0.188, P=0.47). ANOVA found no statistically significant differences (P=0.61). The same were performed for histological cell count as a function of cut rate (Figure 2). Linear regression was not statistically significant (R^2= 0.531, P = 0.16) as well as ANOVA (P = 0.096).

Conclusions: Using a dual blade, high cut rate vitrector system, there was no statistical significance correlating number of viable cells with increasing cut speed. These results suggest that in contrast to prior findings using 20G or 23G vitrectomy for diagnostic vitrectomy, modern vitrectomy systems may be employed at their maximum cut rate without compromising the viability of lymphoma cells and potential PVRL diagnoses.

CONTROL ID: 3708782

SUBMITTER (NAME ONLY): Yue Wu

TITLE: Generalizing 7 layer OCT segmentation from Heidelberg to Topcon devices without labels

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep learning (DL) models have transformed medical image analysis, including OCT image analysis. However, these models require copious labeled data for each device of interest, as they do not generalize across devices from different manufacturers. We sought to use Generative Adversarial Networks (GAN) to generalize a DL model trained on Heidelberg OCTs to segment Topcon OCTs.

Methods: We developed an unsupervised GAN model, GANSeg, to segment Topcon 1000 OCTs (domain B) from the UK Biobank while training on 110 labeled 7-layer segmentations from the Duke Heidelberg dataset (domain A). Traditional supervised DL models learn a mapping from A to A_{label} (Figure 1a), and do not generalize to B images. In contrast, GANSeg uses a GAN to apply B style to the contents of A images, while simultaneously making the U-Net segmenter robust to images in both styles (Figure 1b). To validate GANSeg segmentations, three graders manually segmented the 7 layers on 30 OCTs from UK Biobank, and the Intersection over Union (IOU) between the graders, a U-Net trained only on Heidelberg ($U\text{-}Net_{Heidelberg}$) and $U\text{-}Net_{GANSeg}$ are compared on the 30 OCTs.

Results: $U\text{-}Net_{GANSeg}$ significantly outperforms a $U\text{-}Net_{Heidelberg}$ in segmenting Topcon 1000 in all layers (Figure 2). It achieves comparable IOUs, between 60% to 70%, to human graders, all while having no labeled Topcon 1000 data. Moreover, GANSeg retained the ability to segment Heidelberg OCTs after learning to segment Topcon OCTs.

Conclusions: GANSeg achieved comparable IOUs to human graders, and the GANSeg framework enables us to transfer supervised DL algorithms across devices without labeled data, thereby greatly expanding the applicability of DL algorithms.

CONTROL ID: 3708783

SUBMITTER (NAME ONLY): Luna Krstić

TITLE: Topical Ophthalmic Delivery of Quercetin and Resveratrol using Elastin-like Recombinamer Nanoparticles

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Quercetin (QUE) and resveratrol (RSV), natural occurring polyphenols, have been proven to be a potential new line of treatments for the ocular surface diseases related to oxidative stress. To use these molecules as a topical treatment, a formulation strategy is required due to their low bioavailability.Our aim was to encapsulate QUE and RSV into Elastin-like recombinamer nanoparticles (NPs) and test their biocompatibility and antioxidant activity in vitro on a Human Corneal Epithelial (HCE) cell line and assess their penetration of corneal tissues ex vivo on excised porcine eyes.

Methods: The biocompatibility of the NPs containing QUE, RSV or both with the HCE cells was assessed by the XTT cell viability assay after a 24-hour exposure.To induce oxidative stress, HCE cells were subjected to UV-B light. The antioxidant activity of NPs was evaluated using H_2DCFDA, a fluorescent indicator of reactive oxygen species (ROS). For QUE and QUE/RSV containing NPs the concentration range employed was 5-50 μM, while for RSV NPs this was 25-300 μM.To ex vivo evaluate the permeation through porcine corneal tissues, NPs were loaded with Nile Red, a fluorescent dye used as hydrophobic model drug.All experiments were performed in triplicate (n=3). The statistical analysis of data was performed via ANOVA followed by Games-Howell or Tukey's post-hoc tests.

Results: None of the formulations reduced the viability of HCE cells. At the highest concentration of QUE in the NPs, 79 % ($p<0.01$) of total intracellular ROS was scavenged, while the NPs containing RSV were able to neutralize 70.6 % of ROS ($p<0.05$). NPs encapsulating QUE/RSV showed to be able to decrease the total ROS by 81.16 % ($p<0.05$). Images taken by Fluorescence Microscopy revealed that encapsulated Nile Red was more efficient in permeating ex vivo porcine corneas than the free compound.After 5 minutes of contact the encapsulated Nile Red was observed in the corneal epithelium, while at longer contact times, 30 and 60 minutes, it was observed in the corneal stroma.

Conclusions: Our results show that the ELR NPs containing QUE, RSV or both are biocompatible with HCE cells and possess excellent antioxidant properties in vitro.Improved permeation in ex vivo corneal tissues were noticed when the fluorescent drug model was encapsulated into the ELR NPs.This formulation strategy seems a promising method for topical delivery of QUE/RSV to the ocular surface.

CONTROL ID: 3708784

SUBMITTER (NAME ONLY): Bhavatharini Ramakrishnan

TITLE: Effect of Rapid Alternating and in phase flicker occlusion on Stereopsis

SESSION TITLE: Vision assessment and Clinical applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Ramakrishnan, S.B. Stevenson, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rapid alternating occlusion of the eyes is a relatively new treatment for amblyopia that has shown promise for improving both stereoacuity and visual acuity in some amblyopic subjects. Previously we looked at the effect of alternate and in-phase occlusion on vergence eye movements and found that vergence responses were disrupted by out-of-phase flicker more than in-phase flicker, particularly at lower frequencies. In this current study compared the effect of alternate vs. in phase occlusion of different frequency on stereopsis for normal subjects, to dissociate the effect of flicker per se from the effect of alternate occlusion.

Methods: Disparity thresholds were measured using a 30 trial, 1 up 2 down staircase beginning at 10 arc minutes disparity. Five staircases were obtained from five healthy adult subjects for all combinations of contrast (100%, 50%, 25%) and flicker (2, 4, 8, 16 and 32 Hz, In-phase and out of phase binocular flicker, and no flicker). The stimulus was a filtered noise pattern (1 cpd, 1 octave bandwidth), presented for one second. Horizontal disparity was added to one half of the image, and subjects indicated which half appeared closer. Left and right eye images were displayed side by side on a gamma corrected monitor and viewed through a mirror haploscope while wearing Eyetronix shutter glasses. With shutter glasses open the luminance was 71cd/m^2 ' closed it was 0.53cd/m^2. Testing distance was 97cm.

Results: Flicker elevated stereoscopic thresholds in most subjects. The flicker did not abolish stereopsis, however: subjects were able to detect a few arc minutes of disparity at all but the lowest frequencies of out-of-phase flicker. Two subjects showed almost no effect of flicker on stereo thresholds except at the lowest frequencies of out-of-phase flicker.

Conclusions: The results of this study show that stereopsis thresholds are elevated by both alternate and in phase flicker but are severely impacted only at the lowest temporal frequencies of 2 and 4 Hz. Flicker overall had an impact on three of five subjects. Taken together with our findings on vergence, it appears that the alternating occlusion provides some of the effects of patching, while still allowing binocular function during treatment, but the dramatic flickering may be disruptive for many subjects.

CONTROL ID: 3708786

SUBMITTER (NAME ONLY): Koji Kitazawa

TITLE: Elimination of senescent cells protects against angiogenesis and corneal opacity at the ocular surface of old mice

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The aging population is rapidly increasing in the world and various pathological conditions are associated with aging, for example, the ocular surface becomes more vulnerable to external stimuli, potentially leading to corneal opacity and angiogenesis, resulting in blindness. Dry eye disease (DED) is a common age-related ocular surface pathology. It is unknown whether cellular senescence (a state of permanent cell cycle arrest) influences the ocular surface microenvironment during DED. We, therefore, investigated the presence of senescent cells in young versus old mice before and after exposure to desiccating stress due to lacrimal gland excision (LGE), and we determined the potential role of senescent cells.

Methods: We used our p16-3MR transgenic mice model, which allows the visualization and elimination of senescent cells that express the cell cycle inhibitor and tumor suppressor $p16^{Ink4a}$. Ocular surface, including cornea and conjunctiva, was analyzed using imaging and quantitative reverse transcription in young (4 months) and old mice (24 months). LGE, which triggers dry eye conditions at the ocular surface, was performed, and ocular surface changes were assessed by measuring the expression of $p16^{Ink4a}$, matrix metalloproteinase 9 (Mmp9), and vascular endothelial growth factor (Vegf). To eliminate senescent cells, topical ganciclovir treatment, which enables the elimination of p16-expressing senescent cells through the herpes simplex virus thymidine kinase, was applied to p16-3MR transgenic mice.

Results: Old mice displayed more punctate epithelial damage in the cornea and a significant decrease in goblet cell density in the conjunctiva compared to young mice. In addition, $p16^{Ink4a}$ mRNA levels showed an age-related increase in both the cornea and the conjunctiva. LGE caused punctate corneal damage, accompanied by lower tear secretion. Even though the cornea remained clear in young mice, LGE in old mice caused corneal opacity with severe angiogenesis and an increase in $p16^{Ink4a}$, Mmp9, and Vegf expression. Topical ganciclovir applied to LGE-treated eyes of old mice reduced angiogenesis and corneal epithelial hyperproliferation and downregulated $p16^{Ink4a}$, Mmp9, and Vegf.

Conclusions: We conclude that selective elimination of senescent cells is a potential approach for the treatment of ocular diseases, such as DED, that are associated with aging.

CONTROL ID: 3708787

SUBMITTER (NAME ONLY): Pujan Patel

TITLE: Quantitative Assessment of Optic Disc Development in Preterm Infants

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The optic nerve head is incompletely developed at birth and continues to grow postnatally. Recent advancements in noncontact handheld optical coherence tomography (OCT) enable us to directly image the optic nerve head at the bedside. Our goal is to quantify optic disc development in preterm infants using OCT-generated disc diameter (DD), disc-fovea distance (DF), and DD:DF (same parameters used to evaluate for the presence of optic nerve hypoplasia).

Methods: In this retrospective cohort study, we analyzed bedside OCT scans of the left eye that were captured during the prospective BabySTEPS study. We included imaging sessions that occurred between 30 and 50 weeks postmenstrual age (PMA), occurred prior to retinopathy of prematurity (ROP) treatment, and captured the fovea and both edges of the Bruch's Membrane Opening (BMO) on a single OCT volume. Graders marked the BMO and fovea using custom infant-specific software. We performed cross-sectional analysis on 36 eyes with OCT scans acquired at 36±1 weeks PMA and longitudinal analysis on 29 eyes with at least three scans between 30 and 50 weeks PMA. We evaluated the change in DD, DF, and DD:DF ratio over time and their associations with the following demographic and ROP characteristics: gestational age, birthweight, sex, maternal race, maternal parity, and ROP stage at imaging.

Results: Mean gestational age (GA) was 27.3±2.6 weeks for the cross-sectional cohort and 26.5±2.3 weeks for the longitudinal cohort. In the cross-sectional analysis, GA was significantly correlated with DF (r=-0.39 [-0.64, -0.07], p=0.02) and DD:DF (r=0.49, 95% [0.20, 0.71], p=0.002). Infants with ROP stage 0-1 had significantly smaller DF (4169±337 vs. 4394±279 μm, p=0.04) and significantly larger DD:DF (0.25±0.03 vs. 0.23±0.02, p=0.02) than those with ROP stage 2-3. In the longitudinal analysis, DD increased by 20.5±0.9 μm/week (p<0.001), DD:DF increased by 0.0044±0.0003 per week (p<0.001), and DD:DF correlated with GA (0.0047±0.0019 per gestational week, p=0.02).

Conclusions: In premature children in the early few weeks of life, DD:DF is frequently less than 0.35 which meets the current definition of optic nerve hypoplasia. However, it slowly increases and normalizes with growth. Future larger studies are necessary to verify these conclusions.

CONTROL ID: 3708789

SUBMITTER (NAME ONLY): Katarzyna Chwiejczak

TITLE: Short-term endotamponade with perfluoro-N-octane as a safe and effective treatment option in vitreoretinal surgery

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Short term endotamponade with perfluprocarbon liquids (PFCL) is used as a surgical technique in treatment of certain vitreoretinal conditions. Controversy exists around its safety, as cases of retinal toxicity and inflammation were described. We present indications for use and results of short term endotamponade with a PFCL, perfluoro-N-octane (PFO) in treating surgical retinal pathology at Sydney and Sydney Eye Hospital (SSEH)

Methods: A retrospective case series of 42 eyes of 42 patients (31 male, 11 female, 10- 87 yr, mean:55.4 yr) who underwent vitrectomy with short term PFO endotamponade at SSEH between September 2019 and June 2021. Patients consented to data use, and their medical records were reviewed retrospectively. We recorded presenting diagnosis, pre-operative best-corrected visual acuity (BCVA), duration of PFO endotamponade, type of subsequent endotamponade used, additional surgeries, complications and final BCVA. Statistical analysis was carried out using R: A Language and Environment for Statistical Computing, version 4.0.5, R Core Team, R Foundation for Statistical Computing, Vienna, Austria.

Results: Preoperative BCVA was available in 37cases (mean:1.42logMAR). Indications included: giant retinal tear (GRT) (n=18); recurrent retinal detachment (RD)(n=7), RD with large or multiple breaks(n=5); penetrating eye injury (n=3). PFO was removed after 3-21days (mean:8.9days) and exchanged to long-acting gas in 58%(100%GRTs). Mean follow-up:177,3 days. Complications included: recurrent RD: n=3, cataract: n=7, significant epiretinal membrane: n=8 (5/8 in recurrent RD), macular oedema: n=7 (5/7 in recurrent RD), PFO in the anterior chamber: n=5, intraocular inflammation: n=2. We did not observe retinal toxicity. Mean final BCVA was 0.85logMAR overall and 0.40logMAR in the GRT group. Where preoperative data was available mean BCVA improved by 0.54logMAR. Visual improvement: 70.3%, deterioration:18.9%. Final BCVA was positively correlated with initial BCVA ($p < 0.001$). Diagnosis was significantly differentiating final BCVA ($p=0.001$).There was no significant correlation between final BCVA and duration of tamponade ($p=0.637$).

Conclusions: Short-term tamponade with PFO provides good anatomical and functional outcomes and can be safely used in selected cases. The final result depends on the complexity of the underlying pathology and initial BCVA, not length of the tamponade.

CONTROL ID: 3708790

SUBMITTER (NAME ONLY): Ruchi Shah

TITLE: Dual epigenetic regulation of WNT5A in diabetic corneal epithelial wound healing

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Shah, T.M. Spektor, S. Turjman, C. Amador, M. Saghizadeh, A.A. Kramerov, A.V. Ljubimov, Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|R. Shah, S. Turjman, S. Ghiam, S.T. Chun, C. Amador, Y.S. Rabinowitz, A.A. Kramerov, Cedars-Sinai Medical Center Board of Governors Regenerative Medicine Institute, Los Angeles, California, UNITED STATES|M. Saghizadeh, A.V. Ljubimov, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|S.T. Chun, University of California Los Angeles, Los Angeles, California, UNITED STATES|H. Ding, R. Patil, Cedars-Sinai Medical Center Department of Neurosurgery, Los Angeles, California, UNITED STATES|S. Ghiam, Tel Aviv University, Tel Aviv, ISRAEL|T.M. Spektor, MEI Pharma Inc, San Diego, California, UNITED STATES|V. Punj, D.J. Weisenberger, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|Y.S. Rabinowitz, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|E. Maguen, American Eye Institute, California, UNITED STATES|J.Y. Ljubimova, Terasaki Institute for Biomedical Innovation, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes mellitus (DM) is a leading cause of blindness in working-age adults. It involves various epigenetic modifications such as altered DNA methylation and miRNA changes. In the cornea, DM causes persistent epithelial alterations including impaired wound healing, which may occur due to the dysfunction of limbal epithelial stem cells (LESC). Previously, we reported hypermethylation of WNT5A at the promoter region and up-regulation of Wnt5a regulating miR-203a in diabetic limbal epithelial cells (LEC) enriched in LESC, resulting in decreased Wnt5a expression. Our purpose was to use DNA demethylation and gene therapy approaches to normalize diabetic corneal epithelial wound healing and limbal stem cell expression by increasing Wnt5a expression.

Methods: Diabetic organ-cultured corneas obtained from postmortem human donor eyes were pre-treated with (A) DMSO control or DNA methylation inhibitor, zebularine (20 μM) for 48 hours or (B) biodegradable nanobioconjugates based on polymalic acid (PMLA) scaffold containing a control scrambled antisense oligonucleotide (AON) or AON to miR-203a (supposed to increase Wnt5a) for 4 days. Corneal epithelial 5-mm wounds were created with 1-heptanol, and wound healing was monitored over time. The healed corneas were embedded in OCT and sectioned (5 μm) for immunostaining to determine the limbal stem cell and diabetic marker expression.

Results: In diabetic organ-cultured corneas treated with 20 μM of zebularine, DNMT1 was significantly inhibited and Wnt5a expression was increased, resulting in the acceleration of corneal epithelial wound healing as compared to DMSO controls. Moreover, this treatment also increased the expression of putative stem cell markers, keratins 15 and 17, as well as diabetic markers, integrin α3β1 and nidogen-1, and activated the wound healing mediator, p-Akt at Ser 473. Similarly, treatment with the nanodrug PMLA-AON miR-203a also increased Wnt5a expression and stimulated epithelial wound healing vs. scrambled AON control. It also increased putative LESC (keratins 15 and 17) and diabetic (integrin α3β1 and nidogen-1) marker expression.

Conclusions: Our study documented for the first time the dual regulation of WNT5A in the diabetic cornea through DNA hypermethylation and miRNA action. Inhibition of DNA hypermethylation and miR-203a action can normalize corneal epithelial wound healing and limbal stem cell expression through the upregulation of Wnt5a.

CONTROL ID: 3708792

SUBMITTER (NAME ONLY): Jee Myung Yang

TITLE: Multimodal Evaluation of Immune-Vascular Interaction of Experimental Autoimmune Uveitis

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To characterize the vascular phenotypes of an experimental autoimmune retinal uveitis (EAU) model induced by interphotoreceptor retinoid-binding protein (IRBP) using multimodal imaging techniques.

Methods: We systemically administered IRBP or vehicle to adult C57BL/6 mice. Fundus photography, optical coherence tomography (OCT), in vivo live confocal imaging using different tracers, blood flow analysis by OCT angiography (OCTA), and electroretinogram (ERG) were performed after IRBP immunization. Hematoxylin and eosin and immunofluorescent staining were performed to characterize the immune reaction and vascular permeability. Cx3cr1-GFP mice (microglia-reporter mouse) and LysM-GFP mice (neutrophil-reporter mouse) were used for immune cell phenotyping.

Results: EAU mice exhibited perivascular inflammation, vitritis, and superficial retinal inflammation on fundus photography and OCT. H&E revealed immune cell infiltration in the perivascular area of the retina and choroid accompanied by a significant degree of peri-vasculitis that subsequently damaged the photoreceptors 3 weeks post-immunization. Immunofluorescent staining showed subsequent transcytosis induction after local microglial activation followed by neutrophil recruitment at the perivascular area. Transcytosis in the superficial and deep vascular areas was improved by suppressing immune cells (anti-Ly6C- induced neutrophil inhibition and minocycline-induced microglial inhibition). Intravital in vivo confocal imaging showed signs of neutrophil infiltration and obstructive vasculitis with perivascular leakage 3 weeks post-immunization. OCTA revealed a significant decrease in vascular flow in the deep capillary layer of the retina. Function analysis showed that scotopic responses were intact in 2 weeks; however, normal photopic and scotopic responses were hardly detected in EAU mice 3 weeks post-immunization.

Conclusions: Our data suggest that inflammatory cell activation and subsequent transcytosis induction in endothelial cells might be a major pathogenic factor for vascular leakage in uveitis, bring new insights into the pathophysiology of retinal vasculitis in non-infectious uveitis.

CONTROL ID: 3708794

SUBMITTER (NAME ONLY): Qiurong Zhu

TITLE: Hypoxia-driven transcriptional programming in uveitogenic memory $CD4^+$ T cells

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We have recently demonstrated the pathogenicity of memory $CD4^+$ T cells in a well-characterized murine model of chronic autoimmune uveitis (CAU). Herein, we aim to determine whether chronic inflammation in CAU is associated with tissue and cellular hypoxia and if so, whether hypoxia regulates transcriptional programming of the uveitogenic memory T cells.

Methods: CAU was induced in wild-type C57BL/6 mice by immunization with interphotoreceptor retinoid-binding protein (IRBP) peptides emulsified in complete Freund's adjuvant (CFA), along with Bordetella pertussis toxin injection. Establishment of CAU was confirmed by digital fundus imaging at week 12. CAU mice were then intraperitoneally injected with pimonidazole (Hypoxyprobe^{TM}). After 24 hours, mice were sacrificed, and eyeballs, draining lymph nodes (dLN) and spleen were collected. Tissue cross sections were stained with Red549-anti-pimonidazole, AlexaFluor488-anti-CD3, and DAPI to detect tissue and cellular hypoxia. In addition, $CD44^{hi}CD4^+$ (memory T cells) and $CD44^{-/low}CD4^+$ (control T cells) were isolated using CD4 negative MACS sorting combined with FITC-CD44 FACS sorting. The sorted cells were subjected to qPCR analysis of mRNA genes. Flow cytometric analysis was also performed by staining BV421-CD4, PerCP/Cy5.5-CD44 and PE-hypoxia-inducible factor-1α (HIF-1α).

Results: Local hypoxia was demonstrated in the inflamed retina in CAU, most prominent in the destructed photoreceptor layer (PRL). In addition, significantly more T cells showing hypoxic state were present in the dLN (18.3 ± 0.9 vs 4.3 ± 0.5 per section) and spleen (29.3 ± 2.2 vs 3.5 ± 0.3 per section) in CAU as compared to normal controls. The sorted memory T cells showed ~ 2-fold up-regulation of HIF-1α mRNA expression (no difference in HIF-2α). Consistently, expression of HIF-1α protein in CAU-memory T cells was significantly increased (mean fluorescent intensity: 1496 ± 44 vs 964 ± 34). Finally, genes of HIF-1-associated transcriptional pathways including glycolysis (Hk2, Ldha, Slc2a1, and Slc16a3) and canonical Wnt/β-catenin activity (Ctnnbl1, Axin2, and GSK3b) were up-regulated in memory T cells.

Conclusions: Our data demonstrate that the uveitogenic memory $CD4^+$ T cells in CAU are in hypoxic state and exhibit hypoxia-driven transcriptional activity that is potentially essential for their long-term survival and function.

CONTROL ID: 3708798

SUBMITTER (NAME ONLY): Onnisa Nanegrungsunk

TITLE: Prevalence of Hypertransmission Defects in Eyes with Intermediate Age-related Macular Degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Hypertransmission defects (HTD), one feature of retinal pigment epithelial and outer retinal atrophy (RORA), visible on en face optical coherence tomography (OCT) images, have been suggested as a risk factor for progression to geographic atrophy (GA). We aimed to determine the prevalence of these HTDs in eyes with intermediate age-related macular degeneration (iAMD).

Methods: Choroidal (64-200 µm below Bruch's membrane) en face spectral domain OCT images (Cirrus OCT, Carl Zeiss Meditec, Dublin, CA) of consecutive iAMD patients examined in an ophthalmology clinic setting were evaluated by trained graders for the presence of HTDs. HTD's were defined by the presence of a well-demarcated region of hyperreflectivity on the en face image of at least 80 µm in diameter, with evidence of at least some retinal pigment epithelial alteration on the corresponding B-scan as the explanation for the hypertransmission. By definition, as these were eyes with iAMD (i.e., no late AMD), none of these lesions met criteria for complete RORA or GA. Graders counted the number of HTD in each eye and also measured their greatest linear dimension (GLD).

Results: A total of 137 eyes with iAMD from 121 subjects were identified and included in this analysis. Among this cohort, 22 eyes (16.1%) of 20 participants (16.5%) demonstrated evidence of HTD(s) on the baseline (first available) en face OCT. For this subgroup of patients with HTD, mean (±SD) age was 77.2 (10.9) years, 12 (60.0%) were female and 18 (90.0%) had unilateral HTD. Of the 22 HTD eyes, 19 (86.4%) had a single HTD lesion (mean [range] number of lesions per eye, 1.2 [1-3]). Among the 22 HTD eyes, 13 (59.1%) had a GLD ≥ 250 µm, 5 (22.7%) had a GLD ≥ 125 µm but < 250 µm, and 4 (18.2%) had a GLD ≥ 80 µm but < 125 µm. Only 14 (63.6%) of the HTD eyes fulfilled all criteria of iRORA, of which 11 had a GLD ≥ 250 µm or more.

Conclusions: HTD are present in a significant proportion (~16%) of eyes with iAMD and they overlap partially with iRORA. If longitudinal studies confirm that HTD confer an increased risk for progression to GA, HTD may provide an efficient biomarker for identifying high-risk iAMD patients for enrollment into early intervention therapeutic trials.

CONTROL ID: 3708799

SUBMITTER (NAME ONLY): Mariano González-Pérez

TITLE: From linear questionnaires to computer-adaptive tests: Content development and calibration of the Digital Eye Strain Computer Adaptive Test (DESCAT)

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. González-Pérez, A. Barrio de Santos, B. Antona-Peñalba, Facultad de Optometría y Visión, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|M. González-Pérez, Departamento de formación, Alain Afflelou Optico, Madrid, Madrid, SPAIN|R. Susi-García, Facultad de Estudios Estadísticos, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: We published in 2015 a linear Rasch-based scale (Computer Vision Symptom Scale, aka CVSS17) for measuring the computer-related visual and ocular symptoms in workers using video-display terminals. Because Computer adaptive testing (CAT) is currently considered a more efficient and less time-consuming (for test-takers) method than traditional linear questionnaires, we decided to create a new CAT for assessing these symptoms in general population. Therefore, the aim of our study is to identify content for this new CAT and to calibrate the items included in it.

Methods: For content identification, we used three different sources: (1) items from existing instruments, including a review of the item bank developed for the CVSS17; (2) open questionnaires and semi-structured interviews with digital devices users; and (3) review of social media comments. Items emerged from this phase were reviewed and revised by a group of experts before including them in the new item bank. After that, students and staff of the Faculty of Optics and optometry along with workers from a technological company (DXC Technology) were invited to answer the 76 item bank's items. Subjects aged over 18 and using digital devices at least four hours a day were included in the study while those unable to understand the item descriptors were excluded. Responses were analyzed using Partial Credit Model (PCM) with Winsteps 4.5.1, to assess the item bank's reliability, DIF according to sex and age group (presbyopes or non-presbyopes), item point bi-serial correlation and person/item measure Infit and outfit characteristics.

Results: 76 unique items exploring 19 different symptoms were included in the item bank and the responses of 377 participants (70.82% women, median age: 23.00 years, range interquartile of age: 21.00 –47.00). PCM and differential item functioning (DIF) analyses supported the retention of 38 items in the final item bank. The 38 items fitted the Rasch model (mean square Infit and outfit 0.77–1.26) and there was no DIF. Item point bi-serial correlation was (0.41, 0.67) and item difficulty –in logits- ranged from -2.14 to 1.77.

Conclusions: A new item bank for the Digital Eye Strain Computer Adaptive Test (DESCAT) was developed using a systematic approach and all the items included in the DESCAT showed adequate psychometric properties.

CONTROL ID: 3708803

SUBMITTER (NAME ONLY): Shibandri Das

TITLE: The Efficacy of Vyzulta as Replacement Therapy for Latanoprost in an Urban Population of Primary Open Angle Glaucoma Patients of a Tertiary Health Care System.

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ketkar, K. Tur, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|S. Das, C. Kim, F. Ridha Al-Timimi, M. Juzych, B.A. Hughes, Department of Ophthalmology, Kresge Eye Institute, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaluating the efficacy of Vyzulta as replacement therapy for latanoprost in primary open angle glaucoma (POAG) patients within a large tertiary care center.

Methods: A retrospective review of patients with POAG, who were treated with Vyzulta as replacement therapy (RT) for latanoprost, was performed from January 1st, 2018 to June 30th, 2021. Noted demographic and clinical data include age, race, gender, systemic diabetes mellitus (DM) or hypertension (HTN), intraocular pressure (IOP), and medical/surgical management. Data was collected prior to the addition of Vyzulta to patients' drop regimen (treated baseline) as well as at 1, 3, 6, and 12 months follow-up from initial Vyzulta start date. Criteria for success of Vyzulta as RT for latanoprost was defined as a percentage reduction of IOP from treated baseline, resulting in IOP between 5 - 21 mmHg at two consecutive follow-up visits, without additional medical or surgical intervention needed within 12 months. Percentages analyzed included 10%, 15%, 20%, and 30% IOP drop from treated baseline, and were defined as loose (LCr), qualified (QCr), moderate (MCr) and stringent (SCr) success criteria, respectively. QCr was chosen as 15% reduction of IOP from treated baseline as 80% of patients had IOP < 24 mmHg; thus success by QCr statistically would best correlate with a clinically meaningful decrease of IOP to within a normal range.

Results: 2611 patient charts reviewed; 65 patients (65 eyes) met inclusion criteria and were analyzed. Mean age (SD) was 72.28 (11.84) years. Demographics included 50.8% male, 84.6% African American, 33.8% with DM, and 75.4% with HTN. Mean baseline IOP (SD) was 22.2 (6.07) mmHg. Success rate of Vyzulta as RT for latanoprost was 40%, 29.2%, 18.5%, and 10.8% based on LCr, QCr, MCr, and SCr, respectively. There is no significant difference in success with any criteria, among patients with or without DM or HTN ($p>0.05$).

Conclusions: In an urban patient population with POAG, Vyzulta as RT for latanoprost is successful in 29% of patients in which goal IOP for treatment is IOP at 15% reduction from treated baseline, resulting in IOP between 5 - 21 mmHg at two consecutive follow-up visits, without additional medical or surgical intervention needed within 12 months.

CONTROL ID: 3708808

SUBMITTER (NAME ONLY): Caroline Simon

TITLE: Peripapillary Retinal Vessel Density as an Ocular Biomarker for Schizophrenia

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Simon, E. Gunnarsson, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|V. Chen, O. Saeedi, Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|H. O'Neill, E. Hong, Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|K. Zhang, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pathology has been linked to neurodegenerative diseases. Schizophrenia is a neurodegenerative disease with major research gaps and significant burden to society. Discovery of ocular biomarkers could lead to earlier diagnosis and improved outcomes for patients with schizophrenia. Additionally, identifying ocular manifestations of schizophrenia can lead to an improved understanding of the disease pathophysiology. In this study, we sought to examine the link between schizophrenia spectrum disorders (SSD) and vessel density in participant's optic nerve head (ONH) regions of the retina using Optical Coherence Tomography Angiography (OCTA).

Methods: The study included 73 SSD patients and 57 age-matched healthy controls. Schizophrenia diagnosis was confirmed through structured diagnostic interviews. OCTA was used to noninvasively image retinal vessels in the whole retinal thickness (WR) and superficial capillary plexus (SCP) of the ONH region. OCTA images were binarized using the Phansalkar threshold method and subsequently skeletonized in ImageJ (image 1).

Results: The mean binarized vessel densities for the controls and SSD in the WR were 64.1±4.0 and 65.1±3.0, respectively (p=0.12). Skeletonized vessel densities in the WR were 15.5±0.8 in the controls and 15.7±0.6 in SSD (p=0.30). In the SCP, the binarized vessel densities were 61.5±2.8 in the controls and 62.0±3.3 in SSD (p=0.39). The mean skeletonized densities in the SCP were 15.0±0.6 in the controls and 15.0±0.7 in SSD (p=0.74).

Conclusions: Phansalkar binarization and skeletonization of retinal OCTA images did not find significant differences in vessel density in the ONH regions between schizophrenia patients and healthy controls. Vessel density in the ONH region of the retina of patients with schizophrenia may provide an important tool in the diagnosis and further understanding of the disease.

CONTROL ID: 3708810

SUBMITTER (NAME ONLY): Troy Teeples

TITLE: Outcomes and timing of surgical intervention in eyes with microbial keratitis treated with therapeutic penetrating keratoplasty

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Teeples, K.L. Christopher, S.G. Hauswirth, J.L. Patnaik, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the rates of persistent infection, secondary glaucoma and visual acuity outcomes for patients who underwent penetrating keratoplasty (PKP) for an infectious corneal ulcer, as well as determine how timing of therapeutic PKP affects surgical outcomes.

Methods: A retrospective review was conducted of patients who underwent PKP between the years 2014 and 2020 at an academic medical center in Aurora, Colorado. Demographic information, insurance coverage, pre-operative exam findings, infectious organism, and size of transplant were compared for the outcomes of recurrent infection, transplant failure or rejection, secondary glaucoma and visual acuity before and after transplant. Chi-square testing was used for categorical comparisons and the Wilcoxon rank sum test for continuous variables.

Results: 56 patients (56 eyes) underwent PKP for an infectious corneal ulcer during the study period. There were 27 females (48.2%) and 29 males (51.2%) with a mean age of 58.3 (standard deviation 18). The most common infectious organism was bacterial (55.4%) followed by fungal (10.7%), viral (7.1%) and acanthamoeba (7.1%). For patients that had at least 30 days of clinic follow up after PKP (n = 46), 17 (37.0%) had recurrent infection, 16 (34.8%) had transplant failure or rejection, 16 (34.8%) developed secondary glaucoma, 15 (32.6%) required repeat PKP and 16 (35.6%) had post-op vision better than 20/200. Neither the infectious organism nor the size of the ulcer or donor transplant had any impact on post-operative outcomes. Those who developed recurrent infection following PKP had a greater duration of time between ulcer onset and PKP than those who did not (median 60 days from ulcer onset to PKP vs 17.5 days, p= 0.02). Those who developed secondary glaucoma had a greater duration of time between ulcer onset to date of PKP compared to those who did not develop secondary glaucoma (median 60 vs 14 days, p= 0.04).

Conclusions: Neither the infectious organism (bacterial, viral, fungal, acanthamoeba) nor the size of the ulcer or donor transplant had any impact on post-operative outcomes (recurrent infection, transplant failure, secondary glaucoma, visual acuity) following PKP. On average, patients who had recurrent infection and patients who developed secondary glaucoma underwent PKP later following ulcer onset compared to those who did not.

CONTROL ID: 3708812

SUBMITTER (NAME ONLY): Marianna Bacellar-Galdino

TITLE: Novel rabbit model for particulate matter-induced allergic conjunctivitis

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Iqbal, Integrated PhD Program in Biomedical Sciences, Loyola University Chicago, Maywood, Illinois, UNITED STATES|M. Bacellar-Galdino, A.K. Ghosh, N. Pappenhagen, S. Kaja, R&D Division, Experimentica Ltd, Forest Park, Illinois, UNITED STATES|S. Kaja, Department of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|A.K. Ghosh, Graduate Program in Molecular Biology and Biochemistry, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Particulate matter (PM) is a primary trigger for the development of acute and chronic ocular surface disease, including allergic conjunctivitis. The purpose of the present study was to develop a novel rabbit model for PM-induced allergic conjunctivitis to facilitate future targeted drug discovery and development.

Methods: Standardized Reference Material (SRM® 2786) consisting of fine atmospheric particulate of < 4 µm diameter was obtained from the NIST. Male and female New Zealand White rabbits (1.5 -2 kg) were exposed to PM by topical instillation (5 mg/ml, TID, 35 µl) for a period of up to 10 days. Ophthalmic lifitegrast solution (5%, formulated as Xiidra®) was administered for a period of 10 days following discontinuation of PM instillations. Ophthalmic examinations were performed by a veterinary ophthalmologist in awake animals and scored using the SPOTS system. Schirmer Tear Test (STT)
was collected using sterile diagnostic test strips. Corneal fluorescein staining was performed under isoflurane anesthesia using fluorescein ophthalmic strips. Images were recorded with a Spectralis HRT system in fluorescein angiography mode. Images were scored using the Oxford scoring system (0 - 5 scale) and the NEI scoring system (0 - 4 scale per quadrant with a maximum score of 16).

Results: Exposure to PM for 7 days caused severe hyperemia; tear volumes showed a small but significant reduction (10 ± 1 mm vs. 7.7 ± 0.8 mm, n = 16 eyes, $P < 0.05$). PM treatment significantly increased median corneal fluorescein staining (+ 2 scores in Oxford grading; n = 15 - 16 eyes, $P < 0.001$ and + 9 scores in NEI grading; n = 15 - 16 eyes, $P < 0.001$). Changes to the tear film and cornea were detectable by anterior segment SD-OCT imaging. Discontinuation of PM treatment did not improve hyperemia or corneal fluorescein staining in untreated eyes after 10 days. In contrast, topical instillation of lifitegrast resolved hyperemia (n = 4 eyes, $P < 0.05$) and significantly reduced corneal fluorescein staining (n = 4, $P < 0.001$). Lifitegrast treatments had no effect on STT.

Conclusions: PM exposure induces ocular surface disease that is responsive to immunosuppressant therapy. To our knowledge this is the first report of a large animal model to study PM-induced ocular surface disease. Our new rabbit model offers a standardized experimental paradigm for the in vivo testing of novel therapeutic approaches targeting PM-induced allergic conjunctivitis.

CONTROL ID: 3708816

SUBMITTER (NAME ONLY): Monica Diaz-Aguilar

TITLE: Achromatopsia Retinal Organoid Transcriptomes Reveal Increased Gliosis and Dysregulation of Unfolded Protein Response

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Variants of Activating Transcription Factor 6 (ATF6), a key regulator of the Unfolded Protein Response (UPR), cause severe morphologic and molecular defects in cone photoreceptors leading to achromatopsia (ACHM). ATF6 is expressed in all retinal cell types, and it is unclear how ATF6 disease variants affect retinal cells other than cones. Here, we analyzed the transcriptomes of major retinal cell types in retinal organoids created from induced pluripotent stem cells (iPSC) of ACHM patients carrying biallelic ATF6 disease variants.

Methods: Retinal organoids were generated using iPSCs from ACHM patients with biallelic ATF6[Y567N] variant and from asymptomatic heterozygous family members as controls. Bulk RNAseq was performed on individual organoids at day 290 (n=3 each for patients and controls). Transcriptomic gene sets specifically associated with cones, rods, horizontal cells, bipolar cells, amacrine cells, retinal ganglion cells, and Müller cells (MC) were extracted from 3 RNAseq analyses of non-diseased human retina and retinal organoids (2019 Liang PMID: 31848347; 2019 Menon PMID: 31653841, 2020 Cowan PMID: 32946783). Using these normal human retinal cell type transcriptome profiles, we evaluated expression levels of these retinal cell specific gene-sets in ATF6 mutant ACHM retinal organoids.

Results: Cone photoreceptor-specific genes were significantly down-regulated in ATF6-ACHM retinal organoids (RO) compared to controls (Wilcoxon, $P < 0.001$). In contrast, Muller cell gene expression was increased in ATF6-RO versus controls (Wilcoxon, $P < 0.01$). No significant changes in gene expression were observed in all other retinal cell types in ATF6-ACHM retinal organoids. Last, we identified dysregulation of UPR specifically a significant increase of IRE1-XBP1-regulated genes (Wilcoxon, $P=0.02$) in the ATF6-RO.

Conclusions: Consistent with prior study (2021 Kroeger PMID: 34561305), ATF6-RO showed severely impaired cone photoreceptor-specific gene expression when compared with the 3 new wild-type human retina/retinal organoid transcriptome datasets. Interestingly, Muller cell-specific gene expression was increased in ATF6-RO. The IRE1-XBP1 signaling pathway of the UPR was also upregulated in the ATF6-RO. Our data suggest 2 new potential retinal pathomechanisms that may contribute to ATF6-associated ACHM – Muller gliosis and abnormal activation of the IRE1-XBP1 branch of the UPR.

CONTROL ID: 3708818

SUBMITTER (NAME ONLY): Jordan Comstock

TITLE: Long-term Outcomes of Inflammatory Glaucoma/Ocular Hypertension in Children

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Comstock, S. Gangaputra, K.M. Joos, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|Q. Chen, Biostatistics, Biomedical Informatics, and Ophthalmology & Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|K.M. Joos, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pediatric uveitic glaucoma is a complex interplay between structural change from the disease process as well as the treatment options. We hypothesize that early treatment and regular monitoring with therapeutic adjustments by a glaucoma and uveitis specialist team will lead to long-term visual acuity, inflammatory, and intraocular pressure stability.

Methods: Records of pediatric uveitic glaucoma patients with at least 5 years of surveillance beginning in 2000 at a single-site center were retrospectively analyzed following Vanderbilt IRB approval (211820). Outcomes including vision, inflammatory presence, and IOP, along with required medical and surgical therapies, were assessed at 5 years and 7 years of follow-up.

Results: 19 children (33 involved eyes) met criteria for inclusion with 14 patients (23 eyes) having data at 7 years. 12.9% and 17.4% eyes had a ≥ 2-line visual acuity decline at 5 and 7 years, respectively. One patient returned legally blind OU after a 7-year hiatus. 77.4% and 91.3% eyes had no observable inflammation at 5 and 7 years, respectively. 83.3% and 78.6% patients were on immunomodulatory therapy, 5.6% and 7.1% patients were on oral steroids, 32.3% and 52.2% eyes were on topical steroids, and 26.3% and 57.1% eyes were on glaucoma meds at 5 and 7 years, respectively. IOP (6-21 mmHg) occurred in 96.8% and 78.3% eyes at 5 and 7 years, respectively. 16 eyes (51.6%) required glaucoma shunt surgery by 5 years. 4 eyes (25%) required repeat surgery.

Conclusions: Historically, patients with uveitic glaucoma had poor outcomes with limited therapies. However, our study indicated that children with inflammatory glaucoma have good long-term outcomes with uveitis and glaucoma team care. Maintaining IOP in our cohort required adjusting glaucoma medication needs and/or surgical intervention. Regular monitoring with therapeutic adjustments for inflammatory and IOP control in pediatric uveitic glaucoma can maintain vision.

CONTROL ID: 3708820

SUBMITTER (NAME ONLY): Anne Strong Caldwell

TITLE: Combined Cataract Surgery and Kahook Dual Blade Goniotomy in Patients with Limited English Proficiency

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Strong Caldwell, Z. Gill, J.L. Patnaik, N.C. Grove, L. Mudie, C. Ifantides, M.K. Ertel, C.E. Capitena Young, J.R. SooHoo, M.B. Pantcheva, M.Y. Kahook, L. Seibold, Sue Anschutz-Rodgers Eye Center University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Few studies have examined the effects of language barriers in ophthalmology. This retrospective observational study explores differences in outcomes between limited English proficiency (LEP) patients and English proficient (EP) patients undergoing combined cataract surgery and Kahook Dual Blade (KDB) goniotomy.

Methods: Patients who underwent cataract surgery between 2014 and 2019 in the University of Colorado Cataract Surgery Outcomes Database were analyzed. We defined LEP as need or preference for an interpreter during medical encounters. Demographic and pre-operative characteristics analyzed included gender, race/ethnicity, intraocular pressure (IOP), logMAR best corrected visual acuity (BCVA), presence of mature cataract, and type of glaucoma. The main outcomes of this study included the complexity of surgery, intraoperative complications, change in BCVA, post-operative IOP, and number of IOP-lowering medications. Comparisons between groups were made using logistic regression analysis with general estimating equations to account for some patients having two eyes included in the study.

Results: A total of 43 LEP and 666 EP patients who underwent combined cataract surgery and KDB goniotomy were analyzed. LEP patients had a significantly higher rate of mature cataracts (4.6%) and complex surgery (46.5%) compared to EP patients (0.3% and 13.8%, respectively; $p < 0.01$ for both). Post-operative change in BCVA was significantly greater in LEP patients compared to EP patients (mean improvement of 0.260 versus 0.157, $p = 0.01$). No differences were observed between groups for pre- or post-operative IOP, number of IOP-lowering medications, or intraoperative complications.

Conclusions: This study highlights healthcare disparities associated with language barriers and suggests delayed access to specialty eye care. Encouragingly, it confirms the benefit of combined cataract surgery and KDB goniotomy in the LEP population. These findings demonstrate the need for outreach to LEP patients to ensure regular ophthalmologic care.

CONTROL ID: 3708822

SUBMITTER (NAME ONLY): Pedro Tetelbom

TITLE:

Assessment of systemic and ocular risk factors for the progression of diabetic retinopathy following cataract surgery

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.S. Tetelbom, J. Shin, S. Mahesh, Ophthalmology, New York Medical College, Valhalla, New York, UNITED STATES|P.S. Tetelbom, S. Mahesh, Ophthalmology, Westchester Medical Center, Valhalla, New York, UNITED STATES|

Commercial Relationships Disclosure: Pedro Tetelbom: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Shin: Commercial Relationship: Code N (No Commercial Relationship) | Sankara Mahesh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Cataract surgery has been known to worsen the progression of diabetic retinopathy (DR), including development of Proliferative diabetic retinopathy (PDR) and its complications. Previous reports explored this relationship and associated systemic risk factors, but studies on ocular factors associated with such progression have been limited. We performed a retrospective study to assess baseline clinic characteristics associated with progression of DR in patients following cataract surgery.

Methods: We conducted a retrospective cohort study consisting of 175 consecutive eyes of 130 diabetic patients undergoing cataract surgery at Westchester Medical Center, Valhalla, NY, between January 2016 and August 2021 with a follow-up period of at least 3 months. Patients had to be at least 18 years old at the time of surgery and were excluded if they had other retinal pathology or uveitis. Patients were assessed for progression as defined by onset or advancement in non-proliferative DR (NPDR) stage, onset of PDR, or development of new neovascular complications on the first 6 months of postoperative follow up. Baseline ocular and systemic factors were compared between patients with documented progression and no progression using chi-square test for categorical variables and non-paired Student's t-test for continuous variables.

Results: Seventeen out of 175 eyes presented with progression. All the eyes that progressed had DR at baseline. We found that younger age, insulin use, history of anti-VEGF use, history of diabetic macular edema (DME), previous pars plana vitrectomy and panretinal photocoagulation were associated with DR progression. Intraoperative posterior capsule rupture or iris manipulation were not associated with DR progression. Within the group of patients with DR at baseline, the stage of DR (mild, moderate or severe NPDR or PDR) was not associated with progression, and history of DME was the only ocular factor that remained statistically significant as a risk factor (P=0.048).

Conclusions: Progression only happened in patients with DR at baseline, and among those, having a history of DME was associated with increased risk. Our findings may assist in identifying patients who require more intensive pre and postoperative surveillance and treatment, as well as in better directing the focus of prospective studies on this subject.

CONTROL ID: 3708824

SUBMITTER (NAME ONLY): Robert Thomson

TITLE: Age-related macular degeneration (AMD), cardiovascular disease and stroke

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Thomson, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|J. Chazaro, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|O. Otero-Marquez, G. Ledesma-Gil, Y. Tong, K. Tai, H. Lloyd, R.B. Rosen, R. Smith, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|G. Ledesma-Gil, K. Freund, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|A. Coughlin, R.B. Rosen, R. Smith, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|Z.R. Teibel, Hackensack University Medical Center, Hackensack, New Jersey, UNITED STATES|L. Yannuzzi, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The relationship between age-related macular degeneration (AMD), cardiovascular disease (CVD) and stroke has been long sought, with decades of inconsistent results. We demonstrate new, specific strong associations by first separating AMD into its two major intermediate phenotypes, soft drusen (SD) and subretinal drusenoid deposits (SDD), and comparing their associations with certain common high risk vascular diseases.

Methods: Two hundred AMD patients, ages 51 to 100, 121 females were recruited. Retinal imaging, health history questionnaires, and lipid profiles were obtained. Patients were assigned by volume spectral-domain optical coherence tomography (SD-OCT) into two groups, SDD (with or without SD) and SD (SD only). Fundus autofluorescence (AF) and near-infrared reflectance (NIR) imaging were used to confirm the presence of SDD. Self-reported health history questionnaires further classified patients into those with and without these high risk vascular disorders (HRV): 1) cardiac valve defect; 2) cardiac pump defect (myocardial infarction, congestive heart failure, etc); 3) carotid stroke or transient ischemic attack (TIA) with carotid stenosis. Chi-square testing was used for categorical variables. ‘Waikato 222 Environment for Knowledge Analysis (WEKA) Version 3.8.5’ was used to build a multivariate risk model for presence of HRV as a function of SDD status and other covariates.

Results: The prevalence of HRV was 41.24% (40/97) and 6.80% (7/103) in the SDD and SD groups respectively ($p = 0.000000009$). Differences in the prevalence of HRV sub-types in these groups were also significant: valve defects 14/97 in SDD vs. 3/103 in SD ($p = 0.0035$), pump defects 16/97 vs. 3/103 ($p = 0.0011$), stroke/TIA 10/97 vs.1/103 ($p = 0.0038$). A serum HDL < 62 mg/dL was a strong predictor in our total AMD cohort of HRV ($p = 0.0046$). Data modeling showed that the joint presence of SDD and an HDL<62 predicted the presence of HRV with an accuracy of 85%, 95% CI, 77.5 %-90.7 %.

Conclusions: HRV were significantly more prevalent in subjects with SDD than those with SD only. This suggests that SDD specifically are a biomarker of these life-threatening systemic vasculopathies, all of which are likely to compromise ocular perfusion. This in turn suggests a direct vascular mechanism for SDD that merits investigation. Risk modeling shows a potential for saving lives by detecting occult HRV with non-invasive SD-OCT imaging and serum risk factors.

CONTROL ID: 3708830

SUBMITTER (NAME ONLY): Jimin Park

TITLE: Comparison of long-term efficacy between intravitreal anti-VEGF and photodynamic therapy for the treatment of central serous chorioretinopathy with flat irregular pigment epithelium detachment

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Park, Y. Kim, J. Lee, J. Lee, J. Kim, Y. Yoon, Asan Medical Center, Songpa-gu, Seoul , KOREA (THE REPUBLIC OF)|J. Yeo, Chung-Ang University, Seoul, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To compare the anatomic and functional efficacy of intravitreal anti-vascular endothelial growth factor (VEGF) versus half-dose photodynamic therapy (PDT) treatment in central serous chorioretinopathy (CSC) with flat irregular pigment epithelium detachment (fiPED).

Methods: This retrospective, interventional, comparative study included 72 treatment naive patients with CSC who exhibited fiPED. Among 75 eyes from 72 patients, 42 eyes from 41 patients received anti-VEGF treatment and 33 eyes from 31 patients received half-dose PDT. Treatment outcomes, including the visual acuity, central retinal thickness (CRT), and presence of subretinal fluid (SRF) were evaluated at baseline and 1, 6, 12 and 24 months after treatment and compared between two groups.

Results: There were no differences in baseline characteristics between the two groups. In both groups, a significant improvement of CRT was observed at 1 month after treatment and was maintained throughout the 24-month follow-up period ($P < 0.01$). Whereas 10 out of 42 eyes (23.8%) with anti-VEGF treatment (mean 6.1 injections/ 2 years) required the alternative treatments (6 with PDT and 4 with focal laser), 1 out of 33 eyes (6.0%) with PDT treatment (mean 1.0 treatment/ 2 years) received focal laser treatment. In addition, PDT group showed significantly higher percentage of SRF resolution than anti-VEGF group ($P < 0.05$, PDT : 93.75%, anti-VEGF : 45.24% at 12-month follow-up), with lower recurrence rate of SRF ($P < 0.05$, PDT : 13.8%, anti-VEGF : 68.75% at 24-month follow-up). Likewise, the visual outcome had the similar trend with the anatomic outcomes.

Conclusions: While treatment responses to anti-VEGF and PDT were favorable in CSC with fiPED, PDT treatment showed faster recovery of functional and anatomic outcomes with the lower recurrence, compared with anti-VEGF.

CONTROL ID: 3708832

SUBMITTER (NAME ONLY): John Lin

TITLE: Characteristics of large publicly available databases used in big data research in ophthalmology

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Lin, M. Lee, S. Ghauri, P.B. Greenberg, Brown University, Providence, Rhode Island, UNITED STATES|I.U. Scott, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To comprehensively describe large publicly available health databases used in published big data research in ophthalmology.

Methods: To identify studies using large publicly available health databases for ophthalmic research, a literature search was formulated by a health sciences librarian and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using the PubMed and Embase digital literature databases from inception (1809 and 1947, respectively) through August 1, 2021. Databases were identified from full-text articles. Study selection and data extraction were performed independently by two investigators, and a third investigator arbitrated any disagreements.

Results: In total, 204 databases were identified in the included studies; most (52%; 107/204) were available online. Most were provided by government agencies (52%; 55/106) or academic institutions (30%; 32/106) and were from high-income (87%; 92/106) or English-speaking (68%; 72/106) countries; no publicly available databases were identified from Latin America and the Caribbean, the Middle East and North Africa, or Sub-Saharan Africa. Half were comprised of administrative data (50%; 53/106). Few published details about their sampling methods (23%; 24/106) or study populations (41%; 43/106). Some common requirements to access data included an application requirement (29%; 31/106), training requirement (10%; 11/106), purchase requirement (8%; 9/106), or other requirements such as citizenship or employment (8%; 8/106). One-third were freely available (33%; 35/106).

Conclusions: Big data research in ophthalmology was concentrated on databases based in high-income countries. Access to many publicly available databases was restricted by application, training, purchase, and other requirements. Infrequent disclosure of sampling methods and study populations may impact the quality, transparency, and generalizability of big data research in ophhtalmology.

CONTROL ID: 3708834
SUBMITTER (NAME ONLY): Rebecca Weng
TITLE: Progression of myopia with novel myopia control spectacle lenses
SESSION TITLE: Myopia epidemiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Weng, H.D. Tran, T.J. Naduvilath, P. Sankaridurg, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|H.D. Tran, Haiyen Eye Care, Ho Chi Minh City, VIET NAM|D.P. Spiegel, B. Drobe, R&D Vision Sciences AMERA, Essilor International SAS, Singapore, Singapore, SINGAPORE|P. Sankaridurg, University of New South Wales, Sydney, New South Wales, AUSTRALIA|
Commercial Relationships Disclosure: Rebecca Weng: Commercial Relationship(s);Code F (Financial Support):Essilor R&D Centre, Singapore | Huy Tran: Commercial Relationship(s);Code F (Financial Support):Essilor R&D Centre, Singapore | Daniel Spiegel: Commercial Relationship(s);Code E (Employment):Essilor R&D Centre, Singapore | Bjorn Drobe: Commercial Relationship(s);Code E (Employment):Essilor R&D Centre, Singapore;Code P (Patent):Essilor R&D Centre, Singapore | Thomas Naduvilath: Commercial Relationship(s);Code F (Financial Support):Essilor R&D Centre, Singapore | Padmaja Sankaridurg: Commercial Relationship(s);Code F (Financial Support):Essilor R&D Centre, Singapore

ABSTRACT BODY:

Purpose: To evaluate the progression of myopia in children wearing novel spectacles with highly aspherical lenslets (HAL) versus conventional single-vision spectacles (SV) in a randomized, double-masked, and cross-over trial.
Methods: 119 Vietnamese children, aged 7 to 13 years with baseline (BL) refractive error ranging from -0.75 to -4.75D, cylinder ≤ 1.50D were assigned to 2 groups to wear either HAL or SV, and after 6 months (Stage 1) crossed over to wear the other lens type for another 6 months (Stage 2). At the end of stage 2, all children (n=105) wore HAL for a further 6 months. Based on the order in which they wore the lenses at each stage, Group I was designated HSH (HAL - SV – HAL) and Group 2 SHH (SV-HAL-HAL). Cycloplegic autorefraction was performed at BL and then every 6 months and axial length (AL) measurements were collected at BL and 3 monthly thereafter. Myopia progression (change in spherical equivalent refractive error (SE) and AL) was compared between groups. A linear mixed model with subject random intercept (adjusted for confounders -age, gender, parental myopia) was used for analysis. Post hoc multiple comparisons were Bonferroni corrected. The level of significance was set at 5%.
Results: During stages 1 and 2, myopia progressed slower with HAL than SV (significant for AL for both stages and SE for Stage 2). In the HSH group, myopia progression with SV during Stage 2 was not different to SV progression observed at Stage 1 SHH group ($p=0.208$ and 0.092 for SE and AL respectively) and indicates no rebound of myopia. In the SHH group, Stage 3 change in SE with HAL was greater compared to stage 2 ($p<0.001$) but not for AL. Children reported long hours of wearing (>13 hrs/day) and there were no subjective issues with lens wear.
Conclusions: HAL spectacles slow myopia. This is evidenced by a) inter-group comparisons at Stages 1 and 2, and b) intragroup comparison when children switched between HAL and SV between stages. Children were compliant with lens wear and in this short-term, cross-over study there was no rebound when children were switched from HAL to SV. The reduced SE change with prolonged wear of HAL (Stage 2 to Stage 3 in the SHH group) needs further exploration.

CONTROL ID: 3708835
SUBMITTER (NAME ONLY): Stuart Gardiner
TITLE: Using Moving instead of Static Stimuli to Extend the Dynamic Range of Perimetry
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: S.K. Gardiner, S.L. Mansberger, Discoveries In Sight, Devers Eye Institute, Portland, Oregon, UNITED STATES|
Commercial Relationships Disclosure: Stuart Gardiner: Commercial Relationship: Code N (No Commercial Relationship) | Steven Mansberger: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Pointwise perimetric sensitivities below ~20dB are unreliable due to excessive variability. Dynamically increasing stimulus size to increase detectability extends this dynamic range, allowing testing in more severe glaucoma. However, larger stimuli overlap multiple nerve fiber bundles so may miss smaller defects; and the bundles being stimulated differ even with perfect fixation. We propose instead using moving stimuli to increase detectability and hence increase the dynamic range of perimetry in glaucoma.
Methods: A Size V moving stimulus was designed that travels parallel to the average nerve fiber bundle orientation at each location, with speed proportional to local magnocellular ganglion cell spacing (Fig 1). 34 locations across the visual field were tested with moving and static stimuli, using an otherwise identical Zippy Estimation by Sequential Thresholding (ZEST) seen / not seen algorithm on a clinical perimeter. 152 subjects with glaucoma / suspects were tested, of whom 52 were retested 6 months later. Resultant pointwise sensitivity estimates were compared using generalized estimating equation (GEE) regression. Test-retest variability for each stimulus was assessed by Bland-Altman plots, with limits of agreement adjusted for within-eye clustering.
Results: The 152 subjects tested had average Mean Deviation -3.1dB from standard perimetry (interquartile range -3.7 to -0.3dB). Sensitivities using moving stimuli were 1.8dB higher; this difference increased with damage and eccentricity (both $p<0.001$, Fig 2A). Test-retest limits of agreement among 52 eyes were narrower for moving stimuli (-6.3 to +6.7dB, Fig 2B) than static stimuli (-12.7 to +7.9dB, Fig 2C), and test-retest variance was significantly smaller ($p<0.001$, F-test). 53% of subjects stated preferring the moving stimulus, vs. 24% who preferred the static stimulus.
Conclusions: Using a moving stimulus for perimetry increases sensitivities, and hence locations stay within the dynamic range longer, allowing reliable testing at locations with more severe damage without the problems caused by increasing stimulus size. Results are more repeatable, and the test is preferred by most subjects. Work is underway to assess the normative range. Since stimulus speed is a continuous variable, a clinical test could either use moving stimuli at all sensitivities, or could increase speed proportional to loss ensuring that early detection would be unaltered.

CONTROL ID: 3708841

SUBMITTER (NAME ONLY): Samir Touma

TITLE: Development of a Code-Free Machine Learning Model for the Classification of Cataract Surgery Phases

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Touma, F. Antaki, R. Duval, Ophthalmology, Universite de Montreal Faculte de Medecine, Montreal, Quebec, CANADA|

Commercial Relationships Disclosure: Samir Touma: Commercial Relationship(s);Code F (Financial Support):Bayer | Fares Antaki: Commercial Relationship(s);Code F (Financial Support):Bayer | Renaud Duval: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon, Novartis, Bayer, Roche;Code F (Financial Support):Alcon, Novartis, Bayer, Roche

ABSTRACT BODY:

Purpose: Automated machine learning (AutoML) is a novel tool machine learning research that does not require coding. This study assessed the performance of AutoML in classifying cataract surgery phases from surgical videos.

Methods: Two ophthalmology trainees without coding experience designed a deep learning model in Google Cloud AutoML Video Classification for the classification of 10 different cataract surgery phases. We used two open-access publicly available datasets (total of 122 surgeries) for model training, validation and testing. Overall, 1,280 video segments were used for training and 144 segments for testing. External validation was performed on 10 surgeries issued from another dataset.

Results: The AutoML model demonstrated excellent discriminating performance, even outperforming bespoke deep learning models handcrafter by experts. The area under the precision-recall curve was 0.855. At the 0.5 confidence threshold cut-off, the overall performance metrics were as follows: sensitivity (81.0%), recall (77.1%), accuracy (96.0%) and F1 score (0.79). The per-segment metrics varied across the surgical phases (precision 66.7–100%), recall 46.2–100% and specificity 94.1–100%. Hydrodissection and phacoemulsification were the most accurately predicted phases (100 and 92.31% correct predictions, respectively). During external validation, the average precision was 54.2% (0.00–90.0%), the recall was 61.1% (0.00-100%) and specificity was 96.2% (91.0-99.0%).

Conclusions: A code-free AutoML model created by two ophthalmology trainees can accurately classify cataract surgery phases from surgical videos with an accuracy comparable or better than bespoke deep learning models developed by experts.

CONTROL ID: 3708842

SUBMITTER (NAME ONLY): Yasha Modi

TITLE: Angiopoietin-2 (Ang-2) signaling and vascular stability with faricimab in diabetic macular edema (DME)

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Modi, NYU Langone Health, New York University, New York, New York, UNITED STATES|K. Csaky, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|V. Sheth, University of Illinois, Chicago, Illinois, UNITED STATES|J. Willis, Z. Haskova, Genentech, Inc., South San Francisco, California, UNITED STATES|P. Westenskow, Roche Pharma Research and Early Development, Roche Innovation Center, F. Hoffman-La Roche AG, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Ang-2 and vascular endothelial growth factor (VEGF)-A are key drivers of vascular instability in DME. We explored the effect of dual Ang-2/VEGF-A pathway inhibition on vascular stability using preclinical and phase 2/3 clinical data.

Methods: JR5558 mice (spontaneous model of choroidal neovascularization [CNV]) received anti−Ang-2, anti−VEGF-A, dual anti–Ang-2/anti–VEGF-A (VA2), or none/immunoglobulin G (IgG) as controls. Vascular stability was evaluated by analyzing neovascular leakage and subretinal inflammatory cell infiltration (Iba1+, CD11b+, CD45+) at baseline and at 1 week (1W), 3W, and 5W posttreatment. In the phase 2 BOULEVARD trial (NCT02699450), the effect of faricimab, a bispecific Ang-2/VEGF-A neutralizing antibody, on sustained retinal stability (SRS; defined as the achievement and maintenance [< 10% worsening] of central subfield thickness [CST] ≤ 325 µm to week 24) was assessed. Vascular stability with faricimab was also evaluated in the phase 3 YOSEMITE/RHINE trials (NCT03622580/NCT03622593) over 2 years.

Results: In JR5558 mice, CNV lesion leakage was reduced at 1W with anti−Ang-2, anti−VEGF-A, and VA2 versus controls ($P < 0.05$ to $P < 0.001$); at 3W and 5W, this was maintained with anti−Ang-2 and VA2 only ($P < 0.05$ to $P < 0.0001$). Compared with IgG, VA2 treatment reduced Iba1+, CD11b+, and CD45+ cell infiltration at 1W ($P < 0.05$); at 5W, only anti−Ang-2 and VA2 reduced Iba1+ cell infiltration ($P < 0.0001$). In BOULEVARD, SRS was achieved by > 50% of patients receiving faricimab 6.0 mg and 1.5 mg at weeks 8 and 16, respectively, compared with week 20 for patients receiving ranibizumab. During year 1 of YOSEMITE/RHINE, change in CST from baseline consistently favored faricimab over aflibercept, and absence of DME and intraretinal fluid were achieved by a higher proportion of patients treated with faricimab versus aflibercept. Year 2 vascular stability data from YOSEMITE/RHINE will be presented at the meeting.

Conclusions: Preclinical data suggest that Ang-2 inhibition may contribute to reduced inflammation and increased vascular stability. Furthermore, dual Ang-2/VEGF-A blockade with faricimab promoted SRS in BOULEVARD and improved DME disease control in YOSEMITE/RHINE. These data support the role of Ang-2 in vascular stability and the potential for dual Ang-2/VEGF-A inhibition with faricimab to improve outcomes in patients with DME over anti-VEGF alone.

CONTROL ID: 3708843
SUBMITTER (NAME ONLY): Wentao Liang
TITLE: Wnt Signaling Regulates Cornea Wound Healing
SESSION TITLE: Corneal epithelial biology and repair mechanisms
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: W. Liang, J. Ma, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|
Commercial Relationships Disclosure: Wentao Liang: Commercial Relationship: Code N (No Commercial Relationship) | Jian-Xing Ma: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: The regulation of corneal wound healing remains elusive. Wnt signaling is known to mediate cell proliferation, differentiation, and migration. We hypothesize that Wnt signaling may regulate cornea wound healing.
Methods: i) The very low-density lipoprotein receptor (VLDLR) and kallistatin (KS) are negative regulator of the Wnt signaling pathway. VLDLR knock out (VKO) mice and kallistatin-transgenic (KS-Tg) mice were used for experiments. The corneal epithelial layer was removed in anesthetized mice using Algerbrus II Ocular Burr. The abraded region was measured daily after topical application of 0.1% fluorescein solution. The corneal healing rates were also determined in mice following subconjunctival injection of different Wnt signaling inhibitors or activators.
ii) Primary human corneal epithelial cells (HCEC) were treated with Wnt conditioned medium (WCM) and purified KS after 100% confluence. The acellular area was measured after a straight-line scratch across the monolayer.
iii) After being treated with WCM with/without KS, HCEC numbers were evaluated by Trypan blue dye exclusion method.
Results: VKO mice showed higher Wnt/β-catenin signaling activities while KS-Tg mice had lower Wnt signaling in the cornea compared with WT mice. Corneal with wound healing showed increased Wnt signaling activities. Cornea wound healing rate was significantly increased in VKO mice and decreased in KS-Tg mice compared with WT mice. Wnt signaling inhibitors such as adenovirus expressing the soluble VLDLR ectodomain, an LRP6-blocking antibody, and KS protein delayed corneal wound healing in mice. Activation of Wnt signaling in the cornea by adenovirus expressing a constitutively active mutant of β-catenin (Ad-S37A) in which the phosphorylation site Ser37 in β-catenin was substituted by Ala (S37A), and lithium chloride accelerated wound healing. In vitro, WCM enhanced HCEC migration and proliferation, while KS reversed this effect in a dose-dependent manner.
Conclusions: Wnt/β-catenin signaling is activated during corneal wound healing. Wnt signal enhances cornea epithelial cell migration and proliferation and subsequently promotes corneal wound healing.

CONTROL ID: 3708844

SUBMITTER (NAME ONLY): Rohit Balaji

TITLE: Implementation of a Large-Scale Retinal Image Curation Workflow Using Deep Learning Framework

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Balaji, J. Heathcote, R. Slater, N. Barrett, R. Voland, V. Tomic, J. McDonald, B.A. Blodi, A. Domalpally, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of artificial intelligence (AI) algorithms for analyzing retinal pathologies requires training based on well-organized, labeled images. The goals of this project are to develop an AI model to curate 7-field retinal photographs and to explore ways to implement the AI model at the Wisconsin Reading Center (WRC) with high-volume image submissions.

Methods: Stereoscopic 7 modified field images of the retina are used for the evaluation of diabetic retinopathy via the Early Treatment Diabetic Retinopathy Study (ETDRS) Severity Scale as an outcome in clinical trials. The imaging protocol includes 7 pairs of images of the optic disc, macula, and surrounding retinal quadrants along with an image of the anterior part of the eye (red reflex). Each field of the retina is identified by a field designation number (Figure 1). Clinical images submitted to the WRC are often inefficiently organized for the training of AI algorithms. We trained a neural network to differentiate red reflex images from retinal images and to provide the appropriate retinal field designation. Model outputs included classification of the retinal images into 8 classes (7 fields and red reflex) and a probability score (0 – 1) for each class to predict potential classification errors. The AI model was trained and internally validated on 17,529 images from multiple sites and tested on 3004 independent images. The ground truth was generated by 2 WRC graders.

Results: Exact agreement on field designations between graders and the AI model was found for 2651/3004 images (88%, kappa 0.87) (Figure 2). AI probability scores were 0.95-0.99 for labels that matched the human assessment and 0.39-0.84 for labels that did not match. Fields with non-matched labels included images with poor image quality/focus and improper localization of retinal landmarks.

Conclusions: The deep learning model provides an accurate, automated method for curating retinal images. The probability score provides a tool to flag potential errors in AI labels that can be routed for human oversight. Large-scale AI implementation systems need a tiered approach to augment workflow, increase trust in AI models, and to provide a means for continuous model development.

CONTROL ID: 3708848

SUBMITTER (NAME ONLY): Shijun Sung

TITLE: Characterization of superficial periocular tissue using Spatial Frequency Domain Imaging

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The ability to measure markers of inflammation and tissue remodeling in periocular tissue would help better understand disease processes and improve clinical decision making. However, quantitative methods to measure these activities are not well established. We hypothesize that spatial frequency domain imaging (SFDI), a noninvasive, quantitative, multispectral imaging technology, can provide periocular tissue's absorption and scattering characteristics to inform about the tissue composition, hemodynamics, edema, and inflammation.

Methods: SFDI of periorbital regions were obtained in nine healthy volunteers in compliance with an IRB approved protocol. Imaging is performed at eight center wavelengths (471,526,591,621,659,731,851 nm) and 5 spatial frequencies (0-0.2 mm^{-1}, evenly spaced) over 20cm x 15cm field of view, with typical exposure times of 5-60 ms per image. For each pixel, absorption and reduced scattering coefficients (μ_a and μ'_s, respectively) were determined. Regions of interest (ROI) along the superior/ inferior temporal quadrant, and inferior nasal quadrant are selected for analysis, and compared with adjacent maxillary skin (Figure 1). Tissue optical properties are locoregionally correlated. Paired student's t-test was used for statistical analysis.

Results: The periocular region shows several distinct optical property trends. Notably, there is a local increase in the absorption along the inferior temporal quadrant compared to surrounding facial skin (Mean $\mu_{a\ ITQ}/\ \mu_{a\ face}$ at 659nm is 1.38, [CI: 1.23, 0.53], $p < 0.001$). Reduced optical scattering is observed in all three ROIs (19% to 25% reduction in the amplitude of μ'_s across the spectra) Deoxyhemoglobin concentration as well as oxygen saturation can be inferred from multispectral data and skin melanin content.

Conclusions: SFDI provides wide-field assessment of chromophore concentrations of periocular tissue, showing increased absorption by tissue chromophores and decreased scattering. The cutaneous tissue of the periocular region has a thinner epithelium and is devoid of subcutaneous fat, which presents distinct optical properties that optimize SFDI interrogation of inflammatory disease sub-types. Further studies will involve subjects with various etiologies of inflammatory processes in this region using this methodology.

CONTROL ID: 3708850

SUBMITTER (NAME ONLY): Sathishkumar Chandrakumar

TITLE: Retinal vascular stiffening contributes to leukocyte-mediated endothelial apoptosis in diabetes

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Upregulation of retinal endothelial ICAM-1 and subsequent leukostasis promote vascular degeneration in early diabetic retinopathy (DR). Our previous in vitro studies identified lysyl oxidase (LOX)-mediated subendothelial matrix stiffening as a potent regulator of ICAM-1 upregulation in diabetic conditions. Here we determined the extent to which LOX-mediated retinal vascular stiffening promotes ICAM-1-dependent leukostasis and vascular degeneration in a mouse model of early DR.

Methods: Male (8-10 wk old) C57BL/6 mice were divided into three groups (n=8/group) viz. nondiabetic (ND), streptozotocin-induced diabetic (D), and diabetic + LOX inhibitor BAPN (3mg/kg drinking water) (D+BAPN). After 20 weeks of BAPN treatment, fresh retinal vessels (isolated using isotonic method) was used for qPCR analysis while fixed retinal vessels (isolated using trypsin digestion) were used for stiffness measurements with an atomic force microscope (AFM). Leukocyte adhesion to retinal vessels was determined using fluorescein-coupled concanavalin A. Finally, retinal capillary degeneration was assessed at 8 months' duration of diabetes using Periodic acid-Schiff staining.

Results: When compared with ND group, D group exhibited a 2.2-fold increase ($P<0.001$) in retinal vascular LOX mRNA levels that was accompanied with a 2.0-fold increase ($P<0.01$) in retinal capillary stiffness. Importantly, LOX inhibition (D+BAPN) significantly prevented the diabetes-induced retinal capillary stiffening (47% decrease; $P<0.01$ vs D), which was associated with a concomitant inhibition of ICAM-1 mRNA (53% decrease; $P<0.0001$ vs D) and leukostasis (37% decrease; $P<0.05$ vs D). Further, LOX inhibition in long-term diabetic mice (D+BAPN) significantly reduced (16% decrease; $P<0.05$ vs D) retinal capillary degeneration. Since adherent leukocytes exert cytotoxicity toward retinal endothelial cells, we are currently investigating whether and how cell and subendothelial matrix stiffening regulates retinal endothelial apoptosis by adherent neutrophils.

Conclusions: These findings reveal a new and potentially crucial role of LOX-dependent retinal vascular stiffening in inflammation-mediated vascular degeneration in early DR. Importantly, these findings provide the basis to examine LOX-dependent retinal vascular stiffening and its downstream mechanotransduction pathways as new anti-inflammatory targets for effective DR management.

CONTROL ID: 3708858

SUBMITTER (NAME ONLY): Qi Wei

TITLE: Biomechanical Simulation of Compartmental Superior Oblique (SO) Palsy

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Wei, Bioengineering, George Mason University, Fairfax, Virginia, UNITED STATES|J.L. Demer, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|J.L. Demer, Neurology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Histology and quantitative analysis in the past decade revealed that compartmentalization is a general feature of extraocular muscles (EOMs). Such discovery motivates consideration of strabismus potentially associated with compartmental pathology. We developed a biomechanical model and simulated the strabismus caused by compartmental SO palsy.

Methods: A new model simulating actively controlled pulley mechanics of the horizontal EOMs was developed recently (Wei and Demer, IOVS, 62: 2606, 2021). The orbital (OL) and global (GL) layers of the horizontal rectus EOMs, as well as the pulley sleeves and their suspensions, were explicitly modeled as coupled via elastic strands. The model was elaborated by adding these pulley modeling primitives to the vertical EOMs to enable realistic pulley simulation in tertiary gazes. Two mechanically-independent neuromuscular SO compartments (Suh et al., IOVS, 57:13:5535-5540, 2016) were explicitly modeled. The medial SO compartment tendon inserts more anteriorly and medially than the lateral compartment, while the two compartments share the same path from origin to trochlea. Independent innervations of the two SO compartments were assumed to model compartmental SO palsy. The neural controller minimized simulated eye velocity error and total innervation level during and after saccades. We simulated 25 fixational eye positions formed by 15^{o} horizontal and vertical increments around central gaze. The controller estimated innervations of 11 actuators comprising 2 layers of each rectus EOM, 2 SO compartments, and one inferior oblique unit. Compartmental SO palsy was simulated by zeroing innervation of one SO compartment.

Results: Predicted innervations for fixations (Fig. 1) and saccades were consistent with previous computational work as well as known functions of EOMs and their compartments. Simulation of lateral compartment SO palsy (Fig. 2) predicted greater hypertropia than medial compartment palsy in infraduction, and less excyclotorsion in infraducted adduction, demonstrating differential mechanical functions of the two SO compartments.

Conclusions: An improved biomechanical model implementing realistic actively controlled pulleys and SO compartments provides a computational tool to examine compartmental functions of the SO muscle. Modeling might assist diagnosis of compartmental palsy, and be used to quantitatively predict the effectiveness of selective strabismus surgeries.

CONTROL ID: 3708859

SUBMITTER (NAME ONLY): Harmin Chima

TITLE: Soft Contact Lens Prescribing Habits for Patients with Astigmatism in the United States

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Chima, West Point Optical Group, LLC, Ohio, UNITED STATES|S. Rosinski, J. Kwan, Coopervision Inc, Fairport, New York, UNITED STATES|

Commercial Relationships Disclosure: Harmin Chima: Commercial Relationship(s);Code C (Consultant/Contractor):Coopervision, Bausch and Lomb, Alcon | Steve Rosinski: Commercial Relationship: Code N (No Commercial Relationship) | Justin Kwan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Approximately 47% of the population has ≥ 0.75 D of astigmatism in at least one eye. While most contact lens manufacturers have a wide range of parameters in frequent replacement and daily disposable soft toric options, that begins to diminish substantially when considering the needs of higher astigmats that have cylinder powers of more than 2.25 D. The purpose of this work was to understand the current soft toric prescribing habits of eye care professionals (ECP) in the United States (US) for the most prescribed monthly replacement soft toric contact lens, Biofinity® toric (comfilcon A, CooperVision, Inc.).

Methods: CooperVision revenue data by volume for Biofinity® toric (BT) and Biofinity® XR toric (BXRT) from November 2020 to July 2021 were reviewed. BXRT includes cylinder powers from 2.75 to 5.75 D in five degree axis steps. Frequency of power parameters ordered were sorted from highest to lowest and by sphere power, cylinder power (DC), and axes for sub-analyses.

Results: BT axes distribution was 65% with the rule (WTR), 29% against the rule (ATR), and 6% oblique. BXRT was 85% WTR, 12% ATR, and 3% oblique. When considering the sphere component of these soft toric orders, the ratio of myopia to hyperopia to plano was 24.1 to 5.5 to 1.0 respectively. For every 9.1 BT orders, there was 1 BXRT order. For spheres -6.50 D or higher, the percentage of -0.75 and -1.25 DC orders was 47.5% to 52.5%. The 56 most ordered powers were in 0.50 D sphere increments with the 57th being the first 0.25 D sphere increment (-3.75 / -0.75x180). In addition, 0.50 D sphere steps were ordered 3.4 times more than 0.25 D sphere steps. The 32 most ordered powers had axes of 180 or 090.

Conclusions: These data for soft toric orders can be used to optimize selection of powers for diagnostic fit sets, minimize waste of expired trials, and improve the practice and patient experience. The need for extended range cylinder powers beyond 2.25 D is not infrequent as nearly 11% of orders are for Biofinity® XR toric. For the ECP, it's important to note the potential room for more accurate prescribing in the sphere component of these soft toric lenses; 0.50 DS steps may be ordered more often reflecting the US fit set configuration.

CONTROL ID: 3708862

SUBMITTER (NAME ONLY): Kevin Chen

TITLE: A performance analysis of diabetic retinopathy screening at a student-run free clinic before and during the COVID-19 pandemic period

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chen, J. Dayao, A. Lieu, B.G. Chuter, J.J. Bu, School of Medicine, University of California San Diego, La Jolla, California, UNITED STATES|S.L. Baxter, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|S.L. Baxter, Health Department of Biomedical Informatics, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of the COVID-19 pandemic on diabetic retinopathy screening (DRS) to uninsured, predominantly Latino patients at the UC San Diego Student-Run Free Clinic Project (SRFCP).

Methods: A retrospective analysis of the electronic medical records of all diabetic patients seen in the years 2019, 2020, and 2021 (N = 196, 183, and 178 respectively) at the SRFCP was performed. Ophthalmology specialty clinic metrics from before, during, and after the COVID-19 pandemic-related lockdowns were compared to assess the impact of the COVID-19 pandemic lockdowns on DRS rates. All statistical analyses were performed in Microsoft Excel.

Results: In patients with available demographic data (N=164), 92.1% were Latino, 69.5% female, with a mean age of 58.7 years (SD=10.6). A chi-squared test for goodness of fit showed that the distribution of patients seen ($p<0.001$), referred ($p=0.012$), or scheduled ($p<0.001$) in 2020 and 2021 differed significantly when compared to 2019. In 2019, 99 (50.5%) of 196 patients requiring DRS were referred, of which 97 (49.5%) were scheduled, and 89 (45.4%) were seen by the ophthalmology clinic (Figure 1). In 2020, a similar percentage of patients were referred (76/183 patients, or 41.5%), but the number of patients scheduled and seen dropped to 37 (20.2%) and 21 (11.4%), respectively. In 2021, clinic performance recovered with 113 (63.5%) of 178 patients eligible for DRS referred, 100 (56.2%) scheduled, and 82 (46.1%) seen. No-shows and cancellations constituted 12 (12.4%) and 6 (6.2%) of the 97 encounters in 2019. Conversely, of the 37 encounters scheduled in 2020, the no-show (10.8%) and cancellation (40.5%) rates were notably higher.

Conclusions: The COVID-19 pandemic significantly diminished the delivery of eye care to patients at the SRFCP. 2020 saw a meaningful decline from 2019 in all clinic performance metrics which was reversed in 2021. These results show the current need for annual DRS surpassed the ability of the ophthalmology specialty clinic to schedule and deliver care to these patients in all years evaluated, especially in 2020 due to COVID-19 restrictions. SRFCP patients may benefit from telemedicine-based DRS programs such as remote imaging during primary care visits to further improve screening capacity.

CONTROL ID: 3708866

SUBMITTER (NAME ONLY): Yaeram Jeong

TITLE: Glaucoma-associated human Optineurin mutations increase transmitophagy in the Xenopus laevis tadpole optic nerve

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Jeong, N. Marsh-Armstrong, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure: Yaeram Jeong: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Marsh-Armstrong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Different mutations in the mitophagy adaptor Optineurin (OPTN) are associated with either glaucoma or Amyotropic Lateral Sclerosis (ALS). The purpose of this research was to investigate whether disease-associated OPTN variants alter the behavior of mitochondria, OPTN or the autophagy receptor LC3b within retina ganglion cell (RGC) axons in the optic nerve (ON).

Methods: Transgenes encoding GFP-LC3b and human mCherry-OPTN variants (Wt, glaucoma-associated mutations E50K, M98K and H486R, ALS-associated mutations E478G, and synthetic mutations F178A and D474N affecting LC3b or ubiquitin binding) were expressed selectively in Xenopus RGCs in a tetracycline inducible manner using the zebrafish Isl2b RGC-specific promoter 3 days prior to imaging. For sparse-labeling studies, small groups of cells were transplanted from transgenic donors to non-transgenic hosts early in eye development. The ONs of 4-6 tadpoles per transgene were live imaged using a spinning disc confocal as 1-minute single plane t-series acquired at 1 Hz, and Z-scan imaging the full thickness of the ON. Imaging data were analyzed using ImageJ, IPLab scripts and Imaris and the movement of mitochondria, OPTN and LC3b measured using kymographs. Vision was assessed in a dot-avoidance assay.

Results: Wt OPTN and LC3b were found to move ortho- and retro-gradely in comparable numbers with very few (~2%) of puncta stalled within the ON, whereas 23-88% of OPTN and LC3b were found stalled after expression of all OPTN mutants. In addition, a greater fraction (~65%) of axonal mitochondria were also found stationary in E50K mutants. In the imaging of sparsely labeled axons, E50K OPTN expression resulted in increased OPTN (5.7% in Wt→21.8% in E50K) and mitochondria (15.2% in Wt→35.8% in E50K) outside of RGC axons. Tadpoles expressing E50K OPTN had normal vision at the time of live imaging but developed vision impairment a week later.

Conclusions: OPTN mutations associated with ALS and glaucoma as well as synthetic mutants perturbing its interaction with damaged mitochondria or autophagosomal machinery all affect the movement of mitophagy machinery (OPTN and LC3). The glaucoma-associated mutations in addition increased the amount of axonal mitochondria and OPTN outside of axons. Visual impairment in the E50K animals subsequent to increased transmitophagy suggests that the increased or dysregulated transmitophagy may be detrimental.

CONTROL ID: 3708870

SUBMITTER (NAME ONLY): Fangyao Tang

TITLE: A Deep Learning System to Predict Response to Anti-Vascular Endothelial Growth Factor (VEGF) Therapy in Eyes with Diabetic Macular Edema for Optical Coherence Tomography Images

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Tang, C. Cheung, Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|X. Wang, P. Pheng-Ann Heng, Computer Science and Engineering, The Chinese University of Hong Kong, Hong Kong, HONG KONG|X. Wang, Radiation Oncology, Stanford University School of Medicine, Stanford, California, UNITED STATES|H. Chen, Computer Science and Engineering, The Hong Kong University of Science and Technology, Hong Kong, HONG KONG|Y. Cai, Electronic and Computer Engineering, The Hong Kong University of Science and Technology, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Although intraocular anti-vascular endothelial growth factor (VEGF) injection is now considered first-line treatment for diabetic macula edema (DME), 30-50% of patients poorly respond to the treatment, resulting in poor compliance and placing heavy finical burden on patients. We developed a deep-learning (DL) system for predicting anti-VEGF treatment response for eyes with DME using optical coherence tomography (OCT) images, aimed to personalize treatment for patients with DME.

Methods: Training dataset from an OCT device (Spectralis, Heidelberg Engineering, Germany) were collected from patients with center involved-DME (CI-DME) who received 3 injections within 6 months from 3 hospitals in Hong Kong. We extracted macular volumetric scans prior to receive anti-VEGF treatment, obtained with high-resolution 6.3mm × 6.3mm (25 B-scans) and high-speed 6.5mm × 4.9mm (19 B-scans) scanning protocol. A volumetric scan with good response was defined according to the DRCR.Net protocol-defined thresholds: ≥1-line gain on the Early Treatment Diabetic Retinopathy Study letter score or Snellen VA chart and >10% reduction in central subfield thickness. Label of a given volumetric scan was applied to its corresponding B-scans. Treatment response-related features were manually segmented in approximately two representative B-scans of each volumetric scan to train the system to predict robust outcome. A convolutional neural network-based B-scan classifier was established and trained with the volumetric labels. By feeding all B-scans of a given volumetric scan sequentially as input, we took the maximum prediction value among all B-scans as the volume-level result (good or poor response, Fig.1).

Results: 949 OCT volumes (23,356 B-scans) from 679 eyes of 531 patients were included for training (60%), validation (20%) and testing (20%). The DL system achieved dice scores of 0.689, 0.880, and 0.856 for segmentation of sub-retinal fluid, outer-retinal defects, and disorganization of the retinal inner layers. The system achieved AUROC of 0.731 for prediction good or poor response at volume-level.

Conclusions: The DL system could predict anti-VEGF treatment response with good performance. It may optimize treatment modality for an individual’s condition of DME for better compliance and less financial burden.

CONTROL ID: 3708872

SUBMITTER (NAME ONLY): Simon Kaja

TITLE: Novel murine model for autoantibody-induced dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Kaja, Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|S. Kaja, M. Bacellar-Galdino, A.K. Ghosh, R&D Division, Experimentica Ltd., Forest Park, Illinois, UNITED STATES|C. Mun, S. Jain, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|A.K. Ghosh, Graduate Program in Biochemistry and Molecular Biology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Simon Kaja: Commercial Relationship(s);Code F (Financial Support):Experimentica Ltd., K&P Scientific LLC;Code I (Personal Financial Interest):Experimentica Ltd., K&P Scientific LLC;Code C (Consultant/Contractor):Experimentica Ltd.;Code P (Patent):eyeNOS, Inc.;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code S (non-remunerative):Experimentica Ltd., K&P Scientific LLC | Marianna Bacellar-Galdino: Commercial Relationship(s);Code E (Employment):Experimentica Ltd.;Code C (Consultant/Contractor):AcuiSee LLC | Christine Mun: Commercial Relationship: Code N (No Commercial Relationship) | Anita Ghosh: Commercial Relationship(s);Code I (Personal Financial Interest):Experimentica Ltd., eyeNOS, Inc.;Code E (Employment):Experimentica Ltd. ;Code C (Consultant/Contractor):Experimentica Ltd., K&P Scientific LLC;Code P (Patent):eyeNOS, Inc.;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code S (non-remunerative):Experimentica Ltd., eyeNOS, Inc. | Sandeep Jain: Commercial Relationship(s);Code C (Consultant/Contractor):Neutrolis Inc, Ocugen Inc, Roche, GlaxoSmithKline;Code O (Owner):Advaite Inc, Selagine Inc;Code P (Patent):PCT/US19/60566

ABSTRACT BODY:

Purpose: Our previous studies have demonstrated the presence of anti-citrullinated protein autoantibodies (ACPA) in ocular surface washes from patients with autoimmune dry eye disease (DED). Moreover, this pathology was responsive to ocular surface immunoglobulin G (OSIG) treatment. The purpose of this study was to develop a murine model of autoantibody-induced DED to support future mechanistic and pharmacological studies.

Methods: Male C57BL/6J mice (8-10 weeks of age) received four daily instillations (5 µl) of either anti-histone 4 (citrulline R3) antibody (H4R3 ACPA; 100 ng/ml) or anti-histone 4 wildtype antibody (H4 WT; 100ng/ml). Corneal pathology was evaluated at baseline, day 5 and day 8 by fluorescein staining using a hand-held slit lamp with built-in cobalt blue light. Fluorescence was captured using a Spectralis HRT with anterior segment module (Heidelberg Engineering) in fluorescein angiography mode. Fluorescein staining was graded using both the Oxford scoring system and National Eye Institute (NEI) grading system. Data were analyzed by Two-Way ANOVA with Holm-Šídák's multiple comparisons test.

Results: Eyes treated topically with H4R3 ACPA showed significant corneal damage on day 5 (median score: 2.5, range 2 – 4, $n = 6$, $P < 0.01$) and on day 8 (median score: 3.5, range 2 – 4, $n = 6$, $P < 0.01$), when compared with baseline. In contrast, eyes treated with H4 WT antibody showed some signs of corneal damage (median score: 1.5, range: 1 – 2, $P < 0.01$), but pathology was significantly lower than in H4R3 ACPA-treated eyes.

Conclusions: Topical instillation of H4R3 ACPA antiserum results in significant corneal damage in mice mimicking autoimmune DED pathology in patients. The novel model for autoantibody-induced dry eye disease offers a validated and standardized experimental paradigm that will allow for the rigorous testing of targeted therapeutics for autoimmune DED.

CONTROL ID: 3708873

SUBMITTER (NAME ONLY): Markus Spurlock

TITLE: Neuroinflammation after transient intraocular pressure fluctuations drives retinal ganglion cell disfunction and death

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Spurlock, W. An, T. Chou, G. Reshetnikova, H. Wang, V. Porciatti, V. Shestopalov, Bascom Palmer Eye Institute, Dept. Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Spurlock, Neurology, University of Miami School of Medicine, University of Miami, Coral Gables, Florida, UNITED STATES|V. Shestopalov, Cell Biology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Transient intraocular pressure spikes (spOHT) are induced by certain activities, including yoga, playing wind instruments, and caffeine intake, and are associated with an increased risk of glaucoma. To understand mechanisms underlying the spOHT-induced retinal ganglion cell (RGC) loss, we examine the role of innate immune response in RGC disfunction in a rodent model of non-ischemic IOP spikes.

Methods: C57BL/6J mice (2-3 month) were challenged by either “spiking” IOP changes (spOHT) or by a steady elevation (stOHT) at 40mm Hg above baseline via cannulation of the anterior eye chamber. For spOHT, the reservoir is elevated 1 minute and then lowered for 1 minute for seven cycles. For steady stress, the column remains raised for 7 minutes. We measured changes in intravitreal IL1-β using ELISA, and monitored activation of GsdmD, NLRP1, caspases-1 in retina by qRT-PCR. Retinal function was measured with pattern electroretinogram (PERG). RGC counts were performed on whole mount retina with RBPMS antibody at 7 days after stress. The role of inflammasome was examined using Caspase 1, NLRP1, and GSDMD null mice. TRPV1 blocker was administered to test the role of mechanical stress signaling. Data were evaluated with ANOVA with multiple comparisons to controls.

Results: Fluorescent label showed caspase 1, caspase 3, and GSDMD activation in RGCs 6 hours after spOHT. IL1β measured in vitreous at 6, 12, and 24 hours post spOHT showed 1, 12, and 13 fold increase. qRT-PCR showed significant transcription increase in retina for casp1, NLRP1, and GSDMD at 24h after spOHT. PERG revealed a decline in amplitude of 31.8% at 1 week following spOHT. RBPMS+ cell counts of retina at 1 week also showed 22.6% reduction in cells per sampled regions. Significant inflammasome markers and functional and structural loss were not observed in the stOHT group. Casp1 knull mice demonstrated reduced loss in PERGamp (1.8%) and RBPMS+ (7.7%) count at 1 week, as did NLRP1 null (10%), (5.9%), and GSDMD null (18%), (4.7%) after spOHT. TRPV4 blocker treatment prior to spOHT ablated singificant deficts in PERGamp (5%) and RBPMS+ (3.1%).

Conclusions: Rapid IOP fluctuations drive innate immune responses in retinal ganglion cells, leading to functional disruption and cell loss. Ablation of inflammation-initiating proteins, as well as blockade of pressure-sensitive TRPV4 channel protected from functional disruption.

CONTROL ID: 3708877

SUBMITTER (NAME ONLY): Paul Yang

TITLE: 18 Month Analysis of Macular Structure using Optical Coherence Tomography (OCT) from a Phase 1/2 Clinical Study of Subretinal Gene Therapy Drug AGTC-501 for X-Linked Retinitis Pigmentosa

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: X-linked retinitis pigmentosa (XLRP) is caused by mutations in the retinitis pigmentosa GTPase regulator gene, RPGR, which leads to progressive night blindness, loss of peripheral vision, and eventually central vision loss. This is a follow-up report of macular structure analysis from an ongoing, phase 1/2, open label, dose escalation clinical trial using a recombinant adeno-associated viral (rAAV) vector to deliver a functioning gene copy of RPGR via subretinal injection.

Methods: Male participants (n=29), age ≥6, were assigned to five dose groups and received subretinal injection of AGTC-501 (rAAV2tYF-GRK1-RPGR) into the central or peripheral region of the study eye. Primary outcome was safety. Among the 21 centrally dosed patients analyzed in this study, the secondary outcome was macular structure (OCT) and function (MAIA microperimetry and best-corrected visual acuity (BCVA) as assessed by ETDRS). Up to 18 months post-treatment data were analyzed.

Results: Subretinal administration of AGTC-501 was well-tolerated across a wide dose range. The majority of adverse events were mild-moderate in severity, consistent with the subretinal injection and vitrectomy procedures, and/or concomitant prophylactic steroid regimen used to mitigate inflammation. Of the 21 patients who received a subretinal injection within the macula of the study eye, 13 had visible foveal ellipsoid zone (EZ) on OCT at baseline. Post-injection, the macular EZ recovered by 3-6 months in 9 eyes (69%). Of these eyes, six (67%) subsequently showed improvement of EZ line area and reflectivity compared to baseline by month 12, which was sustained to month 18. Treated eyes with EZ improvement had improved macular function on MAIA ($p = 0.003$) and stable foveolar thickness on OCT ($p = 0.0003$) compared to eyes without EZ improvement.

Conclusions: Consistent safety and efficacy signals in the study eyes that underwent subretinal administration of AGTC-501 were observed up through month 18. Of the study eyes with visible EZ at baseline, most showed recovery of foveal EZ after macular injection, and nearly half had improved EZ appearance which correlated with improvement in macular sensitivity. Follow-up is ongoing through 5 years to assess long-term safety and durability of response.

CONTROL ID: 3708880

SUBMITTER (NAME ONLY): Ji Hyun Kim

TITLE: Mutation-independent RNA replacement approach based on RHO-targeting ribozyme rescues rod photoreceptor function in mice model of autosomal dominant Retinitis pigmentosa (adRP)

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kim, S. Lee, R&D, Rznomics, Seongnam si, 253, Pangyo-ro / Bundang-gu, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Ji Hyun Kim: Commercial Relationship(s);Code E (Employment):Rznomics | Seong-Wook Lee: Commercial Relationship(s);Code O (Owner):Rznomics

ABSTRACT BODY:

Purpose: Rhodopsin (RHO) mutations account about 25~30% of adRP. Although a single P23H mutation in the RHO gene is known to be the most common cause of adRP in USA, more than 150 mutations have been identified. Group I intron-based trans-spicing ribozyme enables to reprogram target RNA into gene of interest through RNA replacement. Here, we developed a mutation-independent therapeutic strategy based on specific trans-splicing ribozyme that can replace, and thus edit mutant RHO RNA with functional RHO RNA using AAV delivery system.

Methods: Target site of RHO RNA was first identified by in vitro mapping. To improve the trans-splicing specificity and efficacy, we optimized RHO-targeting ribozyme through modification of ribozyme structure. To verify in vivo function, AAV vector encoding the optimal ribozyme was constructed and delivered by subretinal injection into the eye of human P23H knock-in mice. After administration, scotopic ERG was measured on dark-adapted mice and retinas were dissected and processed for H&E staining, RT-PCR, and qPCR.

Results: Sequencing analysis of trans-splicing sites through mapping revealed that the most efficient target site occurred at the 5’ UTR of RHO RNA. We modified and optimized the structure of the ribozyme targeting the most accessible site of target RHO RNA. We observed that various mutant RHO RNAs were successfully targeted and replaced with WT RHO RNA by the optimized ribozyme. When assessed the electrical response function of eye in human P23H knock-in mice model, the b-wave amplitudes significantly increased in eyes injected by AAV encoding the ribozyme as compared to those of control-injected eyes. Molecular and cellular analysis of retina tissue showed that P23H RNA is replaced with WT RHO with high efficacy and fidelity and ONL appears significantly thicker in the ribozyme-treated eyes.

Conclusions: Various mutant RHO RNAs were trans-spliced with high fidelity and restored to WT RHO by RHO-targeting ribozyme in cells. The ribozyme effectively prevents the degeneration of photoreceptor cells and preserve their electrical response function in P23H knock-in mice through specifically targeting and trans-splicing of target RHO RNA. These results suggest that RNA replacement based on RHO-targeting ribozyme could be potent and mutation-independent therapeutic strategy for RHO-adRP.

CONTROL ID: 3708883

SUBMITTER (NAME ONLY): Kanae Fukutsu

TITLE: Neural-network-measured retinal vascular area is associated with pulse wave velocity

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Fukutsu, M. Saito, K. Noda, M. Murata, S. Kase, S. Ishida, Ophthalmology, Hokkaido Daigaku Daigakuin Igaku Kenkyuin, Sapporo, Hokkaido, JAPAN|K. Noda, M. Murata, S. Ishida, Ocular Circulation and Metabolism, Hokkaido Daigaku Daigakuin Igaku Kenkyuin, Sapporo, Hokkaido, JAPAN|R. Shiba, N. Isogai, Kabushiki Kaisha Nidek, Gamagori, Aichi, JAPAN|M. Dohke, Keijinkai Maruyama Clinic, Sapporo, Hokkaido, JAPAN|M. Kase, Teine Keijinkai Byoin, Sapporo, Hokkaido, JAPAN|

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ABSTRACT BODY:

Purpose: Retinal vessels reflect the alteration of physical status related to hypertension and arteriosclerosis. Previously, we reported a deep learning algorithm to detect retinal vessels full-automatically and to measure the total retinal vascular area in fundus images (Fukutsu et al. Ophthalmology Science. 2021). In the present study, we investigated the relationship between the total retinal vascular area and brachial-ankle pulse wave velocity (baPWV), which is known as a gold standard for arterial stiffness assessment in clinical practice.

Methods: Retinal photographs (n=696) obtained from 372 individuals who visited Keijinkai Maruyama Clinic for a regular health checkup were used to analyze the total retinal vascular area. PWV was also measured in each patient. Automatic retinal vessel segmentation was performed using our deep learning algorithm, and the total arteriole area (AA) and the total venule area (VA) were measured. The correlation between PWV and several parameters including AA and VA were assessed.

Results: The baPWV correlated negatively with AA ($R = -0.40$, $n = 696$, $P < 2.2e-16$) and VA ($R = -0.36$, $n = 696$, $P < 2.2e-16$). Each of the independent variables (AA, gender, age, and systolic blood pressure) selected using the stepwise method showed a significant correlation with the value of baPWV. The predicted value of baPWV, calculated from regression equation using the variables including AA, showed a better correlation with the measured baPWV value ($R=0.70$, $n=696$, $P < 2.2e-16$) than the predicted value without AA ($R=0.68$, $n = 696$, $P < 2.2e-16$).

Conclusions: AA and VA showed a significant correlation with baPWV. In addition, the predicted value of baPWV using AA well correlated with the actual baPWV value. The present data indicate that the retinal vascular area serves as an alternative biomarker for evaluating arteriosclerosis.

CONTROL ID: 3708885

SUBMITTER (NAME ONLY): Deniz Oncel

TITLE: Effect of OCT B-scan Density on Sensitivity for Detection of Intraretinal Hyperreflective Foci

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Oncel, N. Manafi, M.G. nittala, S.B. Velga, S.R. Sadda, Doheny Eye Institute, Pasadena, California, UNITED STATES|D. Oncel, N. Manafi, M.G. nittala, S.B. Velga, S.R. Sadda, Department of Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|D. Stambolian, Ophthalmology and Genetics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|M.A. Pericak-Vance, Hussman Institute for Human Genomics, University of Miami, Miami, Florida, UNITED STATES|J.L. Haines, Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|J.L. Haines, Cleveland Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intraretinal hyperreflective foci (IHRF) have been identified as an important optical coherence tomography (OCT) biomarker for progression of age-related macular degeneration (AMD). In this study, we evaluate the impact of reducing B-scan density on the sensitivity for detecting IHRF on spectral domain OCT (SD-OCT) volumes in eyes with intermediate AMD.

Methods: A total of 165 eyes from 106 patients with intermediate AMD and IHRF enrolled in the Amish Eye Study were evaluated in this retrospective analysis. For each case, raw SD-OCT (Cirrus OCT 512x128, 6x6mm, fovea centered) volumes were imported into 3D-OCTOR software. The number of IHRF was assessed on all 128 B-scans (spaced 47 μm apart) using a categorical scale (graded as 1-4, 5-9, 10-14, 15-19, and >20). Additionally, B-scan densities in the volume were lowered to 64 B-scans (spaced 94 μm apart), 43 B-scans (spaced 140 μm apart), and 32 B-scans (spaced 188 μm apart), respectively, by removing intervening B-scans prior to presenting the volume to the grader. The number of eyes with any IHRF and the number category of IHRF were used to compare the sensitivity at each reduced B-scan density against the reference 128 B-scan volume.

Results: In the reference 128 B-scan volume, there was a median IHRF score of 1-4 IHRF/eye. For the primary analysis of qualitative presence or absence of IHRF, the sensitivity decreased with decreasing B-scan density from 98.2% ($p= 0.0819$) at 64 B-scans, 92.7% ($p<0.0001$) at 43 B-scans, and 75.2% ($p<0.0001$) at 32 B-scans. With regards to the number of IHRF/eye, there was no significant difference in the numerical category when the density was reduced to 64 B-scans ($P=0.0753$) but was significantly different (with a lower level on the scale chosen) when the B-scan density was reduced to 43 or 32 B-scans ($p<0.0001$ and $p<0.0001$, respectively).

Conclusions: Increasing the inter B-scan spacing from 47 to 188 microns significantly reduced the ability to accurately determine whether IHRF were present in an eye. For quantification of the severity of IHRF within an eye, even an increase in inter B-scan spacing to 140 microns, was associated with a significant misclassification of the IHRF quantity. These findings may be of relevance in the design of OCT scanning protocols for studies utilizing biomarkers for AMD progression.

CONTROL ID: 3708886
SUBMITTER (NAME ONLY): Anindya Samanta
TITLE: Three dimensional analysis of Haller vessels in healthy eyes
SESSION TITLE: Machine Learning: Segmentation and Classification
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Samanta, Department of Ophthalmology and Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, Texas, UNITED STATES|M.N. Ibrahim, A. Selvam, J.A. Sahel, K.K. Vupparaboina, J. Chhablani, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|S. Singh, Nilima Sinha Medical College & Hospital, INDIA|M. Rasheed, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|
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ABSTRACT BODY:

Purpose: To report quantitative and quantitative analysis of Haller vessel layer using 3-dimensional (3-D) model of choroidal vasculature in healthy subjects.

Methods: A retrospective study of patients (n = 14) of healthy subjects with no history of previous retinal disease underwent swept-source optical coherence tomography. Previously validated algorithm was used to create a 3-D Haller vessel reconstruction was constructed. Two independent personnel evaluated the images of the Haller vessels via a three dimensional representation on MeshLab® and graded them on qualitative criterias including symmetry, hot areas showing thicker vessels, branching, rarefaction, and focal constriction. Quantitative analysis was performed using heat maps which included mean, relative distribution (range) of radius, quadrant analysis and curvature analysis.

Results: The average age of the patient was 38.4 ± 16.2. The average of the minimum (15.0 ± 1.2 μm) and maximum (174.1± 6.6 μm) of the vessels was calculated. Qualitative analysis on Haller vessels based on symmetricity (100% symmetric), branching (42.9% occasional; 57.1% moderate), rarefaction (50.0% absent; 42.9% mild-moderate; 7.1% severe), focal hot area (28.6% absent; 57.1% few; 14.3% absent), course of vessels i.e., parallel to each other (92.9% yes; 7.1% no), and focal vascular constriction (14.3% yes; 85.7% no) was performed. Further analysis on other quantitative parameters is underway.

Conclusions: Healthy subjects largely had symmetric distribution with parallel arrangement of Haller layer blood vessels with mild branching and rarefaction with few focal hot areas and focal constriction. Normative database for different age groups for Haller vessel analysis will be established.

CONTROL ID: 3708887
SUBMITTER (NAME ONLY): Xi Wang
TITLE: The dichoptic flash-lag effect in controls and amblyopes
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: X. Wang, Y. Song, M. Liao, L. Liu, Department of Ophthalmology, West China Hospital, Sichuan University, Chengdu, Sichuan, CHINA|R.F. Hess, A. Reynaud, McGill Vision Research Unit,Department of Ophthalmology & Visual Sciences, McGill University, Montreal, Quebec, CANADA|X. Wang, Y. Song, M. Liao, L. Liu, Laboratory of Optometry and Vision Sciences, West China Hospital, Sichuan University, Chengdu, Sichuan, CHINA|
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ABSTRACT BODY:

Purpose: Neural processing of sensory input in the brain takes time, due to the time taken for neural transmission and sensory integration. This creates a potential challenge for the visual system to accurately localize moving objects. One way the brain might overcome this is through motion extrapolation: using the past trajectory of a moving object to predict its future position. In this study we wanted to investigate (i) whether such extrapolation mechanism operate between the eyes in normally sighted observers; and (ii) whether extrapolation processes could be defective in the amblyopes as these patients exhibit an interocular processing delay.

Methods: To measure interocular extrapolation we used a dichoptic flash-lag effect (FLE) paradigm. Twelve adults amblyopes and 12 control subjects participated in the experiment. We measured the FLE magnitude of the subjects under binocular, monocular and dichoptic conditions.

Results: In controls, the FLE magnitude of binocular viewing was significantly smaller than that of monocular and dichoptic viewings ($P \leq 0.023$), but there was no difference between monocular and dichoptic conditions. Amblyopes exhibited a smaller FLE magnitude in the dichoptic condition when the moving bar was presented to the amblyopic eye and the flash to the dominant eye (DA condition) compared to the opposite way around (DF condition), consistent with a delay in the processing of the amblyopic eye ($P = 0.041$).

Conclusions: Our observations confirm that trajectory extrapolation mechanisms transfer between the eyes of normal observers. However, such transfer may be impaired in amblyopia. The smaller FLE magnitude in DA compared to DF in amblyopes could be due to an interocular delay in the amblyopic visual system. The observation that normal controls present a smaller FLE in binocular conditions raises the question whether a larger FLE is or is not an indicator of better motion processing and extrapolation.

CONTROL ID: 3708890

SUBMITTER (NAME ONLY): Kira Wang

TITLE: Evaluating retinal microvascular changes in COVID-19 using wide-field swept-source optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.L. Wang, J.Y. Moon, N. Baig, R. Katz, I. Garg, R. Zeng, M. Duich, G. Baldwin, D.N. Sayah, F. Vingopoulos, H. Wescott, T. Koch, J.B. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|J.Y. Moon, I. Garg, R. Zeng, G. Baldwin, F. Vingopoulos, H. Wescott, T. Koch, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Kira Wang: Commercial Relationship: Code N (No Commercial Relationship) | Jade Moon: Commercial Relationship: Code N (No Commercial Relationship) | Noor Baig: Commercial Relationship: Code N (No Commercial Relationship) | Raviv Katz: Commercial Relationship: Code N (No Commercial Relationship) | Itika Garg: Commercial Relationship: Code N (No Commercial Relationship) | Rebecca Zeng: Commercial Relationship: Code N (No Commercial Relationship) | Margaret Duich: Commercial Relationship: Code N (No Commercial Relationship) | Grace Baldwin: Commercial Relationship: Code N (No Commercial Relationship) | Diane Sayah: Commercial Relationship: Code N (No Commercial Relationship) | Filippos Vingopoulos: Commercial Relationship: Code N (No Commercial Relationship) | Hannah Wescott: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Koch: Commercial Relationship: Code N (No Commercial Relationship) | John Miller: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon, Allergan, Carl Zeiss, Sunovion, Genentech

ABSTRACT BODY:

Purpose: The effects of COVID-19 on the retina have been debated since the start of the pandemic. This study aims to assess how COVID-19 may alter retinal microvasculature using wide-field swept-source optical coherence tomography angiography (WF SS-OCTA).

Methods: This prospective, cross-sectional, observational study included patients with a positive COVID-19 polymerase chain reaction (PCR) test who underwent WF SS-OCTA imaging from August 2020 to November 2021. The mean days from PCR diagnosis to imaging was 175.6. Age-matched controls included healthy eyes and fellow eyes of retinal detachment, retinal tears, retinal artery occlusion, and retinal vein occlusion. Patients with diabetes, uncontrolled hypertension, retinal disease, prior retinal surgery, and a positive COVID-19 test >365 days before imaging were excluded. Vessel density (VD) and vessel skeletonized density (VSD) were calculated (Macular Density Algorithm v0.7.3.3, ARI Network) for the superficial capillary plexus (SCP), deep capillary plexus (DCP), and whole retina using 3x3, 6x6, and 12x12 mm scans centered on the fovea. A mixed-effect multivariate multilevel linear regression model was used to identify any difference between controls and COVID-19 groups.

Results: 34 eyes of 29 patients with COVID-19 and 54 eyes of 45 controls were included. Generalized reductions in VD and VSD were seen in COVID-19 eyes compared to controls (Fig 1). Controlling for age, COVID-19 was associated with a statistically significant overall reduction in VD in the SCP and whole retina in 3x3 mm and DCP of 6x6 mm scans as well as decreased VSD in the DCP in 6x6 mm scans (Table 1). Looking at changes by region, COVID-19 eyes had significant reductions in superior sectors in VD across all scan sizes and layers except the whole retina in 6x6 mm scans, and in VSD across all scan sizes and layers except the SCP in 3x3 and 6x6 mm scans and whole retina in 6x6 mm scans. Additional region-specific reductions in VD and VSD were seen in the DCP in 6x6 and 12x12 mm scans, whole retina in 12x12 mm scans, and SCP in 12x12 mm scans.

Conclusions: Patients with COVID-19 showed reduced VD and VSD compared to controls. This may indicate that there are some retinal microvasculature changes in patients with prior COVID-19 infection.

CONTROL ID: 3708891

SUBMITTER (NAME ONLY): Simran Mangwani-Mordani

TITLE: Effect of Trigeminal Nerve Stimulation on Chronic Ocular Pain and Corneal Nerve Density in Sub-basal Plexus

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Mangwani-Mordani, A. Ramírez-Miranda, E.O. Graue-Hernandez, A. Navas, Cornea and Refractive Surgery, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|S. Mangwani-Mordani, Cornea and External Diseases, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Individuals with neuropathic ocular pain (NOP) have poor response to conventional topical therapies targeting the ocular surface. Common descriptors of NOP such as chronic pain, burning sensation, photoallodynia, and hyperalgesia to wind elucidate somatosensory dysfunction. We performed a prospective, open, single-arm pilot study without randomization to quantify changes in chronic ocular pain and corneal nerve density in sub-basal plexus after long-term use of trigeminal nerve stimulation (TNS).

Methods: During January-December 2021, seven subjects with NOP were identified as candidates for daily 20-minute TNS sessions at home for six months. Participants gave subjective scores on a 0-10 scale to questions evaluating severity of pain, dryness, burning sensation, sensitivity to light and wind before and after a 20-minute in-clinic TNS trial. The same questions and scale were used to monitor changes in symptom severity monthly. In vivo confocal microscopy (IVCM) was performed prior to initiating TNS therapy and measurements were repeated every two months to quantify changes in corneal nerve density for a total of six months.

Results: Paired t-tests were performed comparing baseline measurements vs. in-clinic TNS trial, response at three and six months. In-clinic TNS trial showed overall decrease in symptom severity. Reduction of ocular pain and sensitivity to wind were statistically significant ($p=0.014$ and $p=0.048$, respectively). Follow up at three months, maintained the same trend with an important decline in wind hyperalgesia ($p = 0.002$). 6 month follow up showed a clinically significant reduction in ocular pain of 24% ($p = 0.025$) and decrease in wind sensitivity by 18% ($p= 0.019$). IVCM did not show changes in corneal nerve density in the subbasal plexus.

Conclusions: Six months of TNS therapy significantly reduces chronic ocular pain and wind hyperalgesia exhibiting its potential use as adjunctive therapy for NOP. TNS does not modify corneal nerve density.

CONTROL ID: 3708893
SUBMITTER (NAME ONLY): Chrysanthi Stevens
TITLE: Use of Advanced Driver Assistance Systems by Bioptic and Normal Vision Drivers
SESSION TITLE: Mobility, Reading and Driving with Vision Impairment
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Stevens, New England College of Optometry, Boston, Massachusetts, UNITED STATES|J. Xu, A.R. Bowers, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Xu, Envision Research Institute, Wichita, Kansas, UNITED STATES|A.R. Bowers, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|
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ABSTRACT BODY:

Purpose: In the majority of states, drivers with reduced visual acuity are permitted to drive with a bioptic telescope which magnifies distant objects. Advanced driver assistance systems (ADAS) have become widely available in new cars and may be helpful for drivers with impaired vision, but little is known about whether bioptic drivers use these systems. We conducted a survey to quantify usage of ADAS by bioptic compared to normal vision (NV) drivers.
Methods: The telephone survey included questions pertaining to subjects' demographics, vision, vehicle, driving habits, experience, and use of 8 ADAS: forward collision warning, forward collision avoidance, blind spot warning, lane departure warning, rearview camera, adaptive cruise control, cruise control, and GPS navigation.
Results: 46 bioptic drivers (25 male; median age 53, range 24-84 years) and 47 NV drivers (25 male; median age 55, range 24-89) completed the survey. Weekly mileage (median 50 miles) and days per week driving (median 5) did not differ between the two groups. Yet, bioptic drivers had overall newer cars (medians 4 vs. 7 years, p =0.041) and used more ADAS (medians 3 vs. 2, p = 0.113) than NV drivers. For bioptic drivers, the most commonly used ADAS were GPS (89% bioptic, 91% NV), rearview camera (61% bioptic, 49% NV) and blind spot warning (50% bioptic, 23% NV). Forward collision warning (p=0.038), blindspot warning (p=0.009), and rearview camera (p = 0.026) were used more by bioptic than NV drivers. The ADAS most commonly believed to improve safety were blind spot warning (89% bioptic, 83% NV) and rearview camera (74% bioptic, 83% NV). The majority (83%) of bioptic drivers reported that GPS compensated for their reduced vision (compared to < 57% for other ADAS) and 50% commented that it replaced the need to read road signs. However, 37% of bioptic drivers reported difficulty using GPS because of their vision.
Conclusions: Bioptic drivers have newer cars and use ADAS more than NV drivers, most notably forward collision warning, blind spot warning, and rearview camera. For bioptic drivers, blind spot warning was reported to be most likely to improve safety and GPS was most likely to compensate for vision impairment, even though they experienced visual difficulties when using GPS and believed other ADAS to have greater potential to improve driving safety.

CONTROL ID: 3708894

SUBMITTER (NAME ONLY): Brent Siesky

TITLE: Retinal and Optic Nerve Head Structure and hemodynamics in Open Angle Glaucoma Patients of African and European Descent

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine optic nerve head (ONH) and retinal nerve fiber layer (RNFL) structure and its relationship to optical coherence tomography angiography (OCTA) biomarkers of hemodynamics in open angle glaucoma (OAG) patients of African (AD) and European descent (ED).

Methods: In a cross-sectional analysis, thirty one patients with OAG (13 AD, 18 ED) were assessed for visual field (VF), intraocular pressure (IOP), ONH and RNFL structure and hemodynamics via OCTA for radial peripapillary capillary vessel density (VD) of all the vessels (ALL) and small blood vessels (SV) (AngioVue Imaging System, RTVue XR Avanti, Optovue Inc., Fremont, CA, USA). Age-adjusted nonparametric tests and Spearman correlations were used to identify differences and associations between measurements, with $p<0.05$ considered statistically significant.

Results: OAG patients of AD and ED demonstrated significant differences between hemodynamics and structure even with statistically similar IOP and VF biomarkers ($p>0.05$). Strong and positive correlations were found between average global RNFL thickness and vascular parameters in OAG patients of ED, while these correlations were weak in AD (correlations between RNFL thickness and peripapillary VD SV: ED r=0.90, AD r=0.34, p=0.019; inferior hemisphere (IH) VD SV: ED r=0.88, AD r=0.29, p=0.025; whole image VD ALL: ED r=0.85, AD r=0.25, p=0.038; peripapillary VD ALL: ED r=0.90, AD r=0.26, p=0.010; IH VD ALL: ED r=0.85, AD r=0.02, p=0.009). Moderate to strong negative correlations were found between ONH structural parameters and hemodynamic biomarkers in OAG patients of AD, with positive associations identified in ED patients (correlation between cup to disc horizontal ratio and inside disc VD ALL: AD r=-0.30, ED r=0.62, p=0.029; between cup volume and whole image VD SV: AD r=-0.63, ED r=0.27, p=0.032; IH VD SV: AD r=-0.78, ED r=0.06, p=0.020; inside disc VD ALL: AD r=-0.65, ED r=0.18, p=0.043; and IH VD ALL: AD r=-0.76, ED r=0.06, p=0.026).

Conclusions: In this cohort, vascular biomarkers in OAG patients of AD were more strongly associated with structural damage at the level of the ONH, while in OAG patients of ED hemodynamic parameters were more strongly associated with RNFL thickness. Large well-designed longitudinal studies are required to investigate how differences in hemodynamic biomarkers may affect the risk for OAG onset and progression.

CONTROL ID: 3708895

SUBMITTER (NAME ONLY): Paul Parker

TITLE: Effect of Lens Status on Visual Acuity and Intraocular Pressure Outcomes after Baerveldt Glaucoma Implant Placement

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The effect of preoperative lens status (phakic, pseudophakic, aphakic) on outcomes in glaucoma drainage implants (GDI) remains unclear. We compared visual acuity (VA), intraocular pressure (IOP), and medication use outcomes in patients undergoing GDI placement by the lens status.

Methods: Patients undergoing Baerveldt GDI surgery were reviewed retrospectively from 2015-2021. Inclusion criteria were primary and secondary glaucomas, and a minimum follow up of six months. We excluded pediatric patients <18 and fellow eyes in patients with previous surgery. Main outcome measures were LogMAR VA, IOP, and number of medications at final visit. Failure was defined as IOP < 6 or > 21 at two consecutive visits after postoperative month three, IOP not < 20% from baseline, need for subsequent glaucoma filtration surgery, or loss of light perception vision. 160 eyes in 160 patients undergoing both 250 and 350 mm2 Baerveldt GDI were eligible up to two years post-operatively. A two-way ANOVA was conducted to investigate the effect of Baerveldt GDI surgery and lens grouping on these measures.

Results: Mean follow-up time was 11.6 months. All patients showed significantly lower mean IOP pre vs. postoperatively (26.4 vs. 14.5, p<0.01) and fewer number of medications (3.7 vs. 2.4, p<0.01), however there was no difference in these outcomes based on lens status. No significant difference was seen between pre and postoperative visual acuity by LogMAR in any groups. Aphakic patients had the greatest decrease in mean pre vs. postoperative medications (3.57 vs. 1.86), followed by pseudophakics (3.48 vs. 2.23), and then phakics (3.78 vs. 2.53). 21 patients met failure criteria of which there was a higher rate in 15 phakic patients (15.6%) vs. 6 pseudophakic patients (10.5%); however, this was not significant (OR=1.57, p=0.39). Four of these 21 patients required repeat filtration surgery, all of whom were phakic preoperatively.

Conclusions: No significant difference was found between pre and postoperative IOP and number of medications in patients undergoing Baerveldt GDI on the basis of lens status. Aphakics showed the fewest number of medications postoperatively. Phakic patients showed a slightly higher, but not significant, rate of Baerveldt GDI failure. Further studies are needed to confirm the characteristics of patients that confer both greater IOP lowering response, and higher risk of failure.

CONTROL ID: 3708896

SUBMITTER (NAME ONLY): Janet Coleman-Belin

TITLE: Age adjusted differences in vascular and metabolic biomarkers between patients with open-glaucoma and healthy controls

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine the age-adjusted differences in biomarkers of ocular blood flow and oxygen metabolism between patients with open angle glaucoma (OAG) and healthy controls.

Methods: 143 patients (102 with OAG; 41 healthy) were assessed in a cross sectional analysis for: intraocular pressure (IOP), blood pressures (BP), ocular perfusion pressure (OPP), visual field (VF mean deviation (MD), pattern standard deviation, (PSD); VF index, (VFI)); retinal photographic oximetry (Oxymap); optic nerve head (ONH) and retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) structure and vascular biomarkers via optical coherence tomography angiography (OCTA, Optovue). Age-adjusted chi-square tests, two-sample t-tests and nonparametric tests were used to test for differences with $p<0.05$ considered statistically significant.

Results: Compared to healthy controls, patients with OAG had lower vascular biomarkers of: peripapillary small vessel density (mean, standard deviation): (46.11, 6.30 vs. 51.67, 4.12; p=0.008), superior hemisphere small vessels density (46.89, 6.36, vs. 51.75, 4.75; p=0.016), whole image all vessels density (50.14, 4.30 vs. 55.28, 3.18; p=0.025), peripapillary all vessels density (51.60, 6.24 vs. 57.60, 4.09; p=0.002), superior hemisphere all vessels density (52.49, 6.25 vs. 58.01, 4.38; p=0.011), and inferior hemisphere all vessels density (50.58, 7.12 vs. 57.21, 4.12; p=0.038). In addition, OAG patients had lower oxygen saturation in the superior nasal vein (57.57, 10.46) compared to controls (60.49, 9.47); (p=0.018) leading to a significant difference in the supero-nasal arterio-venous difference (p=0.045). The lower vascular biomarkers occurred despite higher mean OPP in patients with OAG (89.2, 16.3) compared to controls (79.6, 13.3); (p=0.002).

Conclusions: OAG patients had significantly lower vascular and metabolic biomarkers compared to healthy controls. Importantly, these differences were present despite higher OPP in the OAG group. Our data suggest localized reductions in blood flow may occur despite higher perfusion pressures and/or occur from autoregulation deficits present in patients with glaucoma.

CONTROL ID: 3708897

SUBMITTER (NAME ONLY): Joseph DeSimone

TITLE: Validation of a Virtual Visual Acuity Screening for Teleophthalmology in a Pediatric Population

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Telemedicine allows physicians to provide care virtually, limiting patient exposure during the COVID-19 pandemic. As a follow up to a previous analysis (Gore R, et al. IOVS 2021;68:ARVO E-Abstract 146), we performed a retrospective chart review on a separate patient cohort to test whether virtual visual acuity (VA) tests are a reliable means of screening vision in a pediatric population.

Methods: Families screened were sent instructions and an Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart calibrated for 5 feet. Volunteer screeners instructed children over the phone, and those who failed the screen were referred to Wills Eye Hospital (WEH) for further evaluation. The institutional review board at WEH approved the current study. Demographic characteristics and VA screenings (virtual and in-person) were analyzed and compared using Pearson correlation coefficients. Bland-Altman plots were constructed to visualize this comparison.

Results: A total of 242 eyes of 121 patients were included. The mean ± SD age was 11.7±3.1 years. Using Pearson correlations, the in-person and virtual VA measurements were moderately correlated in both the right eye (OD: $r=0.506$, $p<0.001$) and left eye (OS: $r=0.610$, $p<0.001$). Comparing in-person to virtual settings, the mean ± SD LogMAR of VA of the right eye (OD) was 0.37±0.36 (Snellen 20/46) vs. 0.55±0.30 (Snellen 20/70), respectively ($p<0.001$). The mean ± SD LogMAR of VA of the left eye (OS) was 0.38±0.43 (Snellen 20/47) in-person vs. 0.52±0.30 (Snellen 20/66) in the virtual setting ($p<0.001$). However, when the VA range was classified based on the median of in-person VA (LogMAR 0.3, Snellen 20/40), there was no significant difference between in-person and virtual VA measurements in VA >20/40 OD (0.70±0.30, 20/100 vs. 0.67±0.29, 20/93, $p=0.538$) and OS (0.76±0.45, 20/115 vs. 0.70±0.29, 20/100, $p=0.274$) (Table 1). Compared to in-person VA measurement (gold standard), the Bland-Altman plot shows a mean difference of 0.17 LogMAR with virtual VA measurements OD (Fig 1A) and a mean difference of 0.14 LogMAR with virtual VA measurements OS (Fig 1B).

Conclusions: An ETDRS VA test delivered at home demonstrated good correlation with a standard ophthalmologist-administered VA test in a pediatric population. Virtual screening may underestimate vision in patients with good vision at the in-person visit, but the virtual screening does not fail to detect poor vision.

CONTROL ID: 3708898

SUBMITTER (NAME ONLY): Amber Wolf

TITLE: Using mathematics and experiments to identify regional tissue hypoxia masked by mean global retinal oxygenation

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Local tissue ischemia has been shown to cause retinal ganglion cell death, but the translation of vascular biomarkers into predictors of open angle glaucoma (OAG) has been challenging. Oximetry and hemodynamics data were collected in OAG and healthy subjects to identify correlations between biomarkers of blood flow and visual function. Mathematical modeling of blood flow and oxygen transport was used to reveal differences in localized tissue oxygenation despite similar measured levels of arteriolar and venous saturation.

Methods: Clinical data from a prospective cross-sectional study included matched examples of healthy and OAG individuals with evaluations of: IOP, blood pressure, visual field (VF) mean defect (MD), pattern standard deviation (PSD), visual field index (VFI), and retinal oxygenation via retinal photographic oximetry. Our mathematical model of the human retinal vasculature was used to predict the arteriolar tissue oxygenation in one quadrant of the eye given an assumed pressure drop across the retinal vasculature of 25 mmHg and an intraocular pressure (IOP) of 15 mmHg.

Results: Healthy (VFI: 99%; MD: 0.29 decibel; PSD: 1.62 decibel) and OAG (VFI: 90%; MD: -5.47 decibel; PSD: 4.83 decibel) samples (both male and Hispanic) exhibited similar IOP and arterial saturations yet had very different clinical outcomes. The model predicted similar disparate outcomes; the two red stars in Fig. 1A highlight two tissue positions where PO_2 = 62 mmHg and PO_2 = 45 mmHg despite identical arterial saturation entering that retinal branch. The histogram in Fig. 1B gives the predicted values of all tissue PO_2, ranging from 35 to 70 mmHg.

Conclusions: This analysis demonstrated that average values frequently reported as mean global values obscure the possibility of regional hypoxia and/or ischemia in some individuals. Developing methodology to discriminate localized tissue metabolic disturbances from global averages may improve translational use of vascular biomarkers in glaucoma and identify patients at elevated risk for progression.

CONTROL ID: 3708900

SUBMITTER (NAME ONLY): Wei Chieh Huang

TITLE: Comparison of EZ Loss Evaluation with Low- and High-resolution SD-OCT in Classic CLN2 Disease

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Progressive retinal degeneration has been demonstrated in classic CLN2 disease, particularly loss of central retinal thickness with symmetrical bilateral onset and progression. However, changes in the outer retina, especially the ellipsoid zone (EZ), have not been described in detail. This retrospective, observational clinical study was therefore undertaken to examine whether longitudinal observations are possible between low- and high-resolution SD-OCT scans in children with classic CLN2 disease.

Methods: SD-OCT macular cubes (8.8 x 7.8 mm, 61 B-scans, low resolution) were collected in 23 classic CLN2 patients, ages 24 to 122 months. In a subset of subjects, both low- and high-resolution macular cubes consisting of 241 B-scans were also collected on the same day. The contour of EZ loss was marked manually where the EZ band became indistinguishable from retinal pigment epithelium in cross-sectional B-scans and EZ area loss was measured using Heidelberg Eye Explorer (V1.9.10). In subjects with both low- and high-resolution scans acquired, EZ area loss was measured in both resolutions from the same eye for analysis of agreement. EZ loss from the same scans were assessed again after a 2 day washout period for estimation of repeatability. Bland-Altman analyses were used to determine the cutoffs in agreement and precision. Outer nuclear layer (ONL) thickness was measured using the standard ETDRS grid. Longitudinal data were analyzed when available.

Results: Repeatability between EZ loss measurement by the same reader in the same scan was -0.28 to 0.25 mm^2. EZ area loss measured with both low- and high-resolution scans showed strong correlation (Pearson's correlation coefficient = 0.999, $p < 0.01$, with limits of agreement of -0.43 to 0.22 mm^2). The area of EZ loss increased with disease progression and was associated with the magnitude of ONL reduction.

Conclusions: Strong correlation and agreement in measurement of EZ loss between low- and high-resolution scans indicated the method is reliable, while low test-retest variability suggests it is repeatable. This allows comparison of EZ area loss between scans of different resolutions. Additional longitudinal data are needed to understand the pattern of EZ loss in CLN2 disease and its relationship with degeneration of other photoreceptor layers.

CONTROL ID: 3708901

SUBMITTER (NAME ONLY): Ryan Zukerman

TITLE: Physiology-informed Transfer Learning reveals differences in choroidal thickness categorized by hemodynamic and intraocular pressure dynamics

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Currently, utilization of choroidal thickness (CT) in the management of glaucoma is inhibited by its lack of translation in clinical applications. Here, we use Transfer Learning (TL) applying outcomes from glaucoma progression data to analyze a prospective cross-sectional study in patients with OAG and healthy controls.

Methods: We applied Fuzzy c-Means (FCM) clustering to a prospective cross-sectional dataset (Indianapolis Glaucoma Progression Study (IGPS): n=115) enhanced with hemodynamic variables predicted by a validated mathematical model (Guidoboni et al, IOVS, 2014). The model specifically uses intraocular pressure (IOP-Goldmann), blood pressure (BP-automated) and heart rate (HR-automated) as individualized inputs. The 3 clusters identified via FCM on IGPS are then applied to categorize the cross-sectional dataset (n=45 healthy, 11 OAG) based on the mean arterial pressure (MAP) and IOP measured on each subject. CT measured via optical coherence tomography angiography (OCTA) using enhanced depth imaging (EDI) is analyzed by (i) distinguishing between healthy and OAG subjects, and then (ii) sectioning each group by the 3 established IGPS-based clusters.

Results: Figure 1 displays data categorized via the FCM-based clusters and the CT medians, 25th, and 75th percentiles. Overall, CT in OAG eyes is found to be 29% lower than in healthy eyes ($p<0.01$). When further sub grouped, the difference in CT between OAG and healthy eyes was found to be 58% in Cluster 1 ($p=0.03$) and 35% in Clusters 3 ($p<0.01$) (p values obtained with the 2-sample Wilcoxon signed rank test for medians).

Conclusions: TL reveals significantly lower CT in patients with OAG compared to controls as separated into clusters by a hemodynamic and IOP input-based model. FCM applications of clinical datasets combined with transfer learning have the ability to discriminate patients with OAG into those where CT is lowest and patients may be at highest risk for progression compared to healthy controls. These differences were previously unseen when solely comparing OAG and healthy eyes, without the TL-informed subgrouping.

CONTROL ID: 3708902

SUBMITTER (NAME ONLY): Anna Fabczak-Kubicka

TITLE: Choroidal thickness and its association with age, hemodynamic and structural parameters measured by optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the relationships between choroidal thickness (CT), age, hemodynamic and structural parameters measured by optical coherence tomography angiography (OCTA) in open-angle glaucoma (OAG) patients and healthy controls.

Methods: In a prospective cross-sectional analysis, 48 eyes (13 OAG and 35 healthy) underwent OCTA (Optovue) assessment of: subfoveal CT, retinal nerve fiber layer (RNFL) thickness, cup-to-disc vertical ratio (C/D), average ganglion cell complex (GCC) thickness, and radial peripapillary capillary (RPC) vessel density percentages (VD%). Using enhanced depth imaging (EDI) and a defined anatomical landmark protocol, CT was assessed perpendicularly from the outer edge of the hyper-reflective retinal pigment epithelium to the inner sclera at the fovea. Intra-operator repeatability and inter-operator agreement were evaluated using intraclass correlation coefficients (ICC) and Bland-Altman plots. Associations were calculated across all patients, as well as by presence or absence of OAG, using Pearson’s correlation coefficient and two-tailed, two-sample T-tests assuming unequal variances, repeated before and after adjustment for age.

Results: Mean age was significantly higher in OAG group compared to control group (65.5+/-16.6 years vs. 40.3+/-17.9, $p<0.001$). In all subjects, after adjusting for age, CT was positively correlated with average RNFL thickness ($r=0.39$, $p=0.040$), GCC thickness ($r=0.36$, $p=0.046$), and peripapillary RPC VD% ($r=0.38$, $p=0.0035$), and negatively correlated to vertical C/D ($r=-0.47$, $p=0.013$). CT also had a strong positive correlation with peripapillary RPC VD% ($r=0.90$, $p=0.010$) only in OAG patients. Mean CT was significantly lower in OAG eyes only prior to age adjustment (166.6+/-80.4 µm vs. 266.6+/-85.9 µm, $p=0.001$; after adjustment $p=0.077$). The inter-operator agreement of three independent operators was 0.90.

Conclusions: CT was positively correlated with RNFL thickness, GCC thickness, and peripapillary RPC VD%, and negatively correlated with vertical C/D. CT also had a strong positive correlation with retinal peripapillary capillary density in OAG subjects. After adjusting for differences in age, average mean CT was not statistically significantly different between OAG patients and controls.

CONTROL ID: 3708903

SUBMITTER (NAME ONLY): Lucas Rowe

TITLE: Transfer Learning reveals differences in arterio-venous oxygenation biomarkers in patients with glaucoma and healthy controls

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Lower retinal arterio-venous oxygen saturation (A/V-diff) has been reported in patients with open angle glaucoma (OAG). However, utilization of biomarkers of reducted oxygen extraction in retinal tissues is complex. This analysis applies Transfer Learning (TL) of glaucoma progression data outcomes to analyze a prospective cross-sectional sample of OAG and healthy controls retinal photographic oximetry images.

Methods: Fuzzy c-Means (FCM) clustering is applied to a prospective glaucoma progression dataset (n=115) enhanced with hemodynamic variables predicted by a validated mathematical model (Guidoboni et al, IOVS, 2014). The model specifically uses intraocular pressure (IOP), blood pressure (BP) and heart rate (HR) as individualized model inputs. The 3 FCM-based clusters are then applied to categorize cross-sectional data (n=45 healthy, 11 OAG) based on subjects mean arterial pressure (MAP) and IOP. Optical coherence tomography (OCT) biomarkers of retinal nerve fiber layer thickness (RNFL) and the optic nerve head and oximetry biomarkers were analyzed by (i) distinguishing between healthy and OAG subjects and then (ii) sectioning each group by the 3 FCM-based clusters.

Results: Table 1 displays the FCM TL data for patients with OAG and healthy controls. Structural markers are worse in OAG than healthy eyes in both analyses (i) and (ii). Superior temporal (ST) A/V-diff reveal a 7% increase from healthy to OAG eyes (p=0.12) while inferior temporal (IT) A/V-diff display a 15% increase (p=0.07). When further sectioned, there was an increase in the ST A/V-diff in cluster 1 by 12% (p=0.21), but in cluster 3 there was no change (p=0.63); IT A/V-diff shows a 10% decrease (p=0.46) in cluster 1, but a 9% increase (p=0.09) in cluster 3 (p values via 2-sample Wilcoxon signed rank test for medians).

Conclusions: Specific clustering from TL confirms worse OCT structural markers for OAG eyes in all clusters. It further reveals A/V differences among clusters that were masked when subgrouping was not considered, with no change in cluster 3 for ST A/V-diff, and a decrease in cluster 1 for IT A/V-diff. TL and FCM clustering of clinical inputs may improve specificity of individualized risk assessment.

CONTROL ID: 3708906
SUBMITTER (NAME ONLY): Jennifer Harthan
TITLE: High Contrast Visual Acuity and Fogging in Established Scleral Lens Wearers
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
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ABSTRACT BODY:
Purpose: Patients may be fit with scleral lenses (SLs) for indications such as ocular surface disease or irregular corneal astigmatism. Patients wearing SLs often report improved vision and comfort, but some experience mid-day fogging, which may require removal and reapplication of their SLs due to blurry or hazy vision.

The purpose of the present study was to document high contrast visual acuity pre- and post-scleral lens removal in patients with (foggers) and without (non-foggers) subjective mid-day fogging.
Methods: Scleral lens wearers who had worn SLs for a minimum of six months were recruited from five clinical sites. Subjects who wore SLs for at least 2 hours prior to follow-up examinations were asked to participate. Informed consent was obtained, and the following information was collected: patient demographics, subjective complaint of mid-day fogging, and high contrast Freiburg Visual Acuity and Contrast Test (FrACT) pre- and post- scleral lens removal. Descriptive statistics are reported, and comparisons were made by t-test.
Results: Thirty established scleral lens wearers (53 eyes) participated in this study with a mean age of 46 ± 14.6 years (range 24-76 years). Subjects reported a mean SL wear time of 12.5 + 3.2 hours per day (range: 5-17 hours) and 6.5 + 0.8 days per week (range: 4-7 days). 57% (17/30) of subjects reported mid-day fogging.

Mean FrACT acuity in foggers was 0.23 + 0.3 logMAR (range: -0.09-0.94 logMAR, n=13) for right eyes and 0.08 + 0.2 (range: -0.23-0.32 logMAR, n=12) for left eyes. There was no statistically significant difference in FrACT acuity pre- or post-scleral lens removal in foggers for the right (p=0.5) or left (p=0.3) eyes. There was a barely significant difference in FrACT acuity between foggers and non-foggers in the right eye (p=0.05) but not in the left (p=0.3) eye with over two hours of lens wear.
Conclusions: Over half of the subjects in this study reported mid-day fogging but there was no difference in high contrast visual acuity pre-and post-scleral lens wear and minimal to no difference between foggers and non-foggers. Further analysis may provide more insight into the correlation between the subjective complaint of mid-day fogging and clinician observed findings.

CONTROL ID: 3708907

SUBMITTER (NAME ONLY): Anitha Krishnan

TITLE: Anti-inflammatory role of a glycan-coated nanoparticle in modulating macrophages and complement in non-exudative AMD

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Krishnan, R. Shinde, M. Tolentino, D. Callanan, D. Kunimoto, M. Genead, Aviceda Ophthalmics, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a progressive retinal disease which causes irreversible blindness in elderly. Studies indicate a prominent role of inflammation in the pathogenesis of AMD. Both the cellular and non-cellular components of the innate immune system including cytokine production have been extensively studied to understand the pathophysiology of the disease.

We utilize a novel strategy to address severe chronic “non-resolving” inflammation via the body’s own self recognition system. Our lead asset is a glycan-coated nanoparticle exhibiting dual function in regulating the immune system. It directly modulates the self-pattern recognition receptors on the immune cells, Siglecs (sialic acid binding immunogloblulin like lectins), by dampening the activity of inflammatory cells and enhancing the activity of complement factor H.

Methods: We performed cell-based assays using our proprietary asset in two cell types; THP-1-derived macrophages and PBMC-derived macrophages to characterize the biological activities. Cytokine release as pro-inflammatory markers and complement factor H levels were measured 24 hours post treatment.

Results: Our glycan-coated nanoparticle significantly reduces the production of pro-inflammatory markers (TNF-a) by 2 folds in THP-1-derived macrophages and 2-fold increase in complement factor H levels in PBMC derived M1 macrophages compared to the cells treated with a negative control

Conclusions: Our glycan coated nanoparticle leads to a significant reduction in pro-inflammatory markers and an increase in CFH levels. Our approach for the treatment of non-exudative AMD is to selectively repolarize the macrophage into a resting state. These preclinical studies provide evidence that our molecule targets both cellular and complement mediated aspects of the innate immune system, which are believed to be involved in the pathogenesis of non-exudative AMD and support the advancement of our glycan coated nanoparticle for further development.

CONTROL ID: 3708914

SUBMITTER (NAME ONLY): Rachael Warrington

TITLE: Inhibiting contractility using an in vitro model of proliferative vitreoretinopathy

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.E. Warrington, T.A. A Blenkinsop, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|R.E. Warrington, T.A. A Blenkinsop, Cell Development and Regenerative Biology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Rachael Warrington: Commercial Relationship: Code N (No Commercial Relationship) | Timothy A Blenkinsop: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is an abnormal wound healing response following retinal tears. Cellular membranes form on the subretinal and/or epiretinal surface of the retina resulting in scarring, which can be contractile causing retinal detachments and vision loss. The most aggressive forms of PVR derive from retinal pigment epithelial (RPE) cells. The cytokines TGFβ and TNFα have been shown to play a role in PVR. An in vitro model of PVR combined these cytokines (referred to as TNT), inducing contractile membranes in RPE. A p38 inhibitor (Comms Bio 2019; 2: 1-14) and nicotinamide (Stem Cell Rep 2020; 14: 631-647) prevented these aggressive contractile masses in RPE. Additional tests on patient derived PVR membranes would validate the TNT model, confirming the anti-PVR effects of p38 inhibition and nicotinamide.

Methods: A patient-dissected membrane was divided for immunofluorescence or digestion with collagenase II. The isolated cells were cultured, expanded and assessed for their ability to contract under the TNT conditions of the in vitro PVR model, as well as determine if p38 inhibition and nicotinamide can prevent TNT induced contraction.

Results: The PVR membrane contained RPE and glia, along with markers for epithelial to mesenchymal transition (EMT), motility and extracellular matrix (ECM). Isolated cells from the patient-dissected PVR membrane may have undergone mesenchymal to epithelial transition (MET), as EMT markers were only present in TNT conditions. TNT induced the cells to undergo EMT forming contractile masses. The p38 inhibitor and nicotinamide prevented contraction, however, EMT was not fully reversed as EMT markers (αSMA and SNAI1) positively labelled cells. Motility and ECM markers were present in all conditions, with TNT treatment having the highest expression. Cells treated with the p38 inhibitor or nicotinamide exhibited decreased motility (ACTG2) and ECM (COL1a2 and Laminin) protein production compared to TNT treatment.

Conclusions: Both the p38 inhibitor and nicotinamide prevented membrane contraction showing promise to become a therapeutic treatment for patients at risk of developing PVR and individuals with already formed membranes, both treatments warrant further study in an in vivo model of PVR.

CONTROL ID: 3708921

SUBMITTER (NAME ONLY): Sheila Angeles-Han

TITLE: Alternative therapy in pediatric chronic anterior uveitis refractory to methotrexate, adalimumab and infliximab

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.T. Angeles-Han, N. Mwase, A. Cassedy, T. Hennard, H. Brunner, A. Grom, M. Henrickson, J. Huggins, D. Lovell, T. Ting, Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|S.T. Angeles-Han, V.M. Utz, E. Dosunmu, S. Lopper, R. Sisk, A. Kaufman, Division of Pediatric Ophthalmology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: More than 50% of children with chronic anterior uveitis (CAU) fail standard methotrexate (MTX) and conventional tumor necrosis factor α inhibitors (cTNFi) therapy. Data are lacking on optimal next therapy. Our aim is to compare the characteristics of children treated with MTX, cTNFi, and alternative biologic agents (ABT) for CAU.

Methods: We reviewed records of 52 children. We grouped based on therapy required to control CAU for ≥3 months. CAU control was defined by all: 1) inactive per SUN criteria, 2) no vitreous haze or uveitis activity by dilated exam or imaging, 3) ≤2 drops of prednisolone acetate 1% or equivalent/day, and 4) no oral corticosteroid.

Results: Of 52 children, CAU was controlled by MTX monotherapy in 15/52, cTNFi in 28/52, and ABT in 9/52 (abatacept-1, tocilizumab-3, and/or golimumab-5). All patients requiring ABT were ANA positive compared to MTX (67%) and cTNFi (71%) groups but not significantly different (NS) (Table 1).

Comparing 28 children controlled on adalimumab (ADA) to 9 who escalated to ABT, the ADA dose, non-biologic DMARD use, and treatment duration were similar. Neutralizing anti-ADA antibodies occurred in 1 patient on ADA compared to 4 on ABT ($p<0.005$).

Comparing 36 children controlled on infliximab (IFX) to 3 who escalated to ABT, IFX was given every 4 weeks at 10 mg/kg/dose (IQR 9.6-11.5) in those on cTNFi, and 7.5 mg/kg/dose (IQR 5-10) on ABT (NS). Infusion reactions occurred in 2 of 3 escalating to ABT. Human anti-chimeric antibodies occurred in 2 patients on ABT compared to 0 on cTNFi despite MTX (NS).

Ocular complications at presentation were similar among all groups. Those on MTX were less likely to develop synechiae, cataracts, ocular hypertension and glaucoma compared to those on cTNFi or ABT (Table 2). Total ocular complication rate (3.4 per person) was higher in those on ABT compared to MTX (0.7 per person) ($p<0.001$) and cTNFi (1.5 per person) ($p<0.001$). Patients on ABT were more likely to have used intraocular pressure-reducing agents prior to ABT compared to cTNFi ($p=0.011$).

Conclusions: Abatacept, golimumab, and tocilizumab may be useful in CAU children who fail MTX and cTNFi. Patients that required ABT had more complications, and anti-cTNFi neutralizing antibodies. The higher incidence of complications may reflect prolonged duration of poor CAU control prior to initiation of ABT.

CONTROL ID: 3708923

SUBMITTER (NAME ONLY): Daniel Spiegel

TITLE: The effects of spectacle lenses with aspherical lenslets on the retinal shape

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.P. Spiegel, A. Yang, E. Lim, B. Drobe, R&D Vision Sciences AMERA, Essilor International SAS, SINGAPORE, SINGAPORE, SINGAPORE|D.P. Spiegel, J. Bao, Y. Huang, X. LI, A. Yang, E. Lim, B. Drobe, Wenzhou Medical University–Essilor International Research Center (WEIRC), CHINA|J. Bao, Y. Huang, X. LI, Eye Hospital and School of Ophthalmology and Optometry of Wenzhou Medical University, CHINA|

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ABSTRACT BODY:

Purpose: We have recently shown that spectacle lenses with concentric rings of contiguous highly aspherical lenslets (HAL) and slightly aspherical lenslets (SAL) reduce myopia progression in Chinese children. The purpose of this analysis was to evaluate the two-year effect of these lenses on the retinal shape.

Methods: In this randomized, controlled, double-masked clinical trial, 156 children (age 8 to 13 years, myopia between -0.75 D and -4.75 D) were randomized into three groups wearing either HAL, SAL, or single vision (SVL) lenses for 24 months. The central and peripheral axial length of the right eye (between 30 degrees nasally and temporally in 15 degrees steps) were acquired at the baseline and every six months. Individual peripheral eye length data were fitted with a quadratic function, and the quadratic coefficient served as an indicator of the retinal shape per child per study visit. These values were subjected to a between-group comparison using Fisher's LSD-adjusted paired comparisons. The relationship between two-year myopia progression and retinal shape changes was evaluated using Pearson's correlations.

Results: The quadratic function fit well the data (mean $r^2 = 0.94$). As expected, the eyes in the SVL group have become progressively more prolate indicated by the mean two-year decrease of the quadratic term by $-1.96 \pm 2.25 \times 10^{-4}$ mm/deg^2. This trend was significantly weakened in the SAL group ($-0.96 \pm 1.84 \times 10^{-4}$ mm/deg^2; $p < 0.01$) and completely absent in the HAL group ($0.28 \pm 2.00 \times 10^{-4}$ mm/deg^2; $p < 0.001$). The changes in the quadratic coefficient were negatively correlated with the two-year changes in axial length in all groups (all $r < -0.321$, $p < 0.02$).

Conclusions: Wearing HAL lenses abolished the characteristic retinal shape changes associated with increasing myopia. In the SAL group, this trend was also present but less prominent. From the clinical perspective, these findings are important and indicate that myopia control with lenses with aspherical lenslets may provide an additional benefit besides a "simple" reduction of the axial elongation and refractive error.

CONTROL ID: 3708925

SUBMITTER (NAME ONLY): Christopher Conrady

TITLE: A mouse model of acute retinal necrosis to study innate immunity of the retina

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Conrady, S. Fan, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

Commercial Relationships Disclosure: Christopher Conrady: Commercial Relationship: Code N (No Commercial Relationship) | Shan Fan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The innate immune response activated by acute retinal necrosis, a rapidly progressive herpes virus infection (herpes simplex virus [HSV] -1 or -2, or varicella-zoster virus) of the retina, is poorly understood. We aimed to create an experimental mouse model of acute retinal necrosis in which the retina is directly infected with herpes virus and that mimicks human disease.

Methods: Using both male and female C57Bl/6J mice between 6-8 weeks of age consisting of 2 experiments of 2-3 mice per group. Mice receiving subretinal HSV-1 were compared 1, 3, and 5 days post-infection to subretinal sterile saline controls. Histology, OCT, fundus imaging and viral plaque assays were evaluated. A student's t test was then used to compare the two groups with statistical significance defined as a p value less than 0.05.

Results: Following subretinal injection of herpes simplex virus -1, retinal whitening insues and results in full thickness retinal necrosis with overlying vitreous inflammation on OCT, histology, fundus imaging within 3 days of infection and progressively expands in size (n = 2-5 mice / group consisting of 2 independent experiments) [FIGURE]. Viral load was then compared at 5 days post infection and was significantly elevated when compared to PBS controls (3.94±0.332 versus 0±0; $p < 0.01$) [FIGURE].

Conclusions: We have created a reproducible mouse model of acute retinal necrosis similar to human disease and in which replicating virus can be isolated from the retina. This model will help us better understand the innate immune response to HSV infection of the retina and could be utilized to better understand innate immunity to other bacterial, viral, or viral-vector pathogens.

CONTROL ID: 3708930

SUBMITTER (NAME ONLY): Vivek Srinivasan

TITLE: Investigation of band 2 in the human outer retina with visible light Optical Coherence Tomography (OCT)

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.J. Srinivasan, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|V.J. Srinivasan, P. Chauhan, Tech4Health, NYU Langone Health, New York, New York, UNITED STATES|A. Kho, Biomedical Engineering, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure: Vivek Srinivasan: Commercial Relationship(s);Code P (Patent):Optovue, Inc. | Aaron Kho: Commercial Relationship(s);Code E (Employment):Zeiss Medical Technology | Pooja Chauhan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: With recent technical advances, visible light OCT has revealed previously unseen retinal bands in the living human retina and enabled quantification of other bands for the first time. Here, we investigate outer retinal band 2, referred to as the ellipsoid zone or inner segment / outer segment (IS/OS) junction, with 1 micron axial resolution visible light OCT.

Methods: Spectral/Fourier domain visible light OCT, with 1 micron axial resolution, was performed along the horizontal meridian from the fovea to the periphery in 2 male subjects aged 27 and 40. Data from a single subject (27 year-old Asian male with brown iris) is shown. A noise-corrected transverse cross-correlation matrix of the flattened volumetric OCT intensity data sets, displayed as an image, was employed to examine associations between various axial positions in the outer retina. The logarithm of the p value (not corrected for multiple comparisons) was also examined. All findings were confirmed qualitatively in the second subject (not shown).

Results: Band 2 appeared as a single entity in the fovea, yet was clearly split into nominal bands 2a and 2b in the peripheral retina (Figure 1). The cross-correlation matrix showed that band 2a is associated with band 3 (Figure 2), referred to as the cone outer segment tips (COST) or cone interdigitzation zone (CIZ). On the other hand, band 2b was not associated with band 2a or band 3, though it was weakly associated with the rod IZ or rod OST in band 4 (Figure 2).

Conclusions: Visible light OCT revealed a split band 2 in the human peripheral retina. The topography and transverse intensity variations of the outermost band 2b suggest an association with rods. Band 2b may relate to the rod IS/OS or ellipsoid zone which has been reported in various animal models.

CONTROL ID: 3708931

SUBMITTER (NAME ONLY): tian lu

TITLE: Phenotype-Based Genetic Analysis Reveals Missing Heritability of ABCA4-Related Retinopathy: Deep Intronic Variants and Copy Number Variations

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. lu, C. chen, Y. song, X. zhang, K. xu, Y. Xie, Z. Jin, Y. Li, Beijing Institute of Ophthalmology, Beijing, Beijing, CHINA|T. lu, Capital Medical University, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: To identify the missing heritability of ABCA4-related retinopathy in a Chinese cohort.

Methods: 33 unrelated patients with ABCA4-related retinopathy carrying a monoallelic variant in ABCA4 were recruited. All patients underwent ophthalmic examinations. Next-generation sequencing of the whole ABCA4 sequence, including coding and non-coding regions, was performed to detect deep intronic variants (DIVs) and copy number variations (CNVs).

Results: Eight missing pathogenic ABCA4 variants were identified including five DIVs and three CNVs in 20 patients (60.6%). The five DIVs, including four novel (c.1555-816T>G, c.2919-169T>G, c.2919-884G>T, and c.5461-1321A>G) and one reported (c.4539+1100A>G), accounted for the missing alleles in 51.5% of the patients. Minigene assays showed that four novel DIVs activated cryptic splice sites leading to the insertions of pseudoexons. The three novel CNVs consisted of one gross deletion of 1273 bp (exon 2), and two gross duplications covering 25.2 kb (exons 28–43) and 9.4 kb (exons 38–44). Three microhomology domains were identified at the breakpoints and revealed the potential mechanisms of CNV formation.

Conclusions: DIVs and CNVs explained about two-thirds of the unresolved Chinese cases with ABCA4-related retinopathy. Combining results from phenotypic screening, targeted the whole ABCA4 sequencing, and in silico tools can help to identify the missing heritability and lay the foundation for future drug and gene therapy.

CONTROL ID: 3708939

SUBMITTER (NAME ONLY): Brian Schott

TITLE: Validation of portable slit lamp videos and anterior segment photographs as telemedicine modalities

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Schott, A. Zhu, Medical Student, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|B. Szirth, M. Habiel, Ophthalmology, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Brian Schott: Commercial Relationship: Code N (No Commercial Relationship) | Aretha Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Bernard Szirth: Commercial Relationship: Code N (No Commercial Relationship) | Miriam Habiel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The COVID-19 pandemic has highlighted the need for telemedicine across all specialties. Though its utilization has increased since the start of the pandemic, ophthalmology has been reported to be among the specialties least likely to utilize telemedicine in practice. We evaluated the potential utility of portable slit lamp exam (SLE) videos and anterior segment photos as telemedicine modalities by comparing the findings from these modalities to those identified in-person in the clinic.

Methods: Data was collected from 98 subjects at Rutgers Institute of Ophthalmology and Visual Science by non-ophthalmic trained staff, which included portable SLE videos and anterior segment photos, collected with Microclear digital hand-held slit lamp (Suzhou, China) and Canon non-mydriatic retinal camera CR-2 Plus AF (Tokyo, Japan), respectively. Analysis included anterior segment photos taken from 92 patients (183 eyes) and SLE videos taken from 91 patients (177 eyes), which were interpreted and compared to exam findings identified in-person in the clinic. Sample t-tests were used for statistical analysis.

Results: Nuclear sclerotic cataract (NSC) had the most agreement between telemedicine interpretation and in-person exam (photo 93.8%, video 93.75%). Cortical cataract showed less agreement (photo 65.63%, video 45.16%) and posterior subcapsular cataract (PSC) showed the least agreement (photo 8.33%, video 0%) among cataract findings. Cornea findings were among those least likely to be identified (photo 12.5%, video 14.86%). Findings that showed statistically significant differences between photo and video included pinguecula ($p=0.00032$). PSC ($p=0.044$) and posterior capsule opacification ($p=0.00098$) showed statistically significant differences regarding identifying findings on telemedicine interpretation that were not documented in clinic.

Conclusions: Portable SLE videos and anterior segment photos may have potential for utility as means of telemedicine, particularly for NSC. Portable SLE requires more training to display a full ophthalmic exam whereas photographs can easily be done by non-ophthalmic trained staff, displaying similar findings. Differences in exam findings may be attributed to lack of documentation when patients present to the clinic for more urgent concerns and lack of focus on slit lamp videos by non-ophthalmic trained staff.

CONTROL ID: 3708940

SUBMITTER (NAME ONLY): Arman Mosenia

TITLE: Kidney Injury after Intravitreal Anti-Vascular Endothelial Growth Factor Injection: A Multi-Center Study Using Electronic Health Records

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mosenia, A. Shahlaee, J. Schallhorn, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|A. Shahlaee, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Arman Mosenia: Commercial Relationship: Code N (No Commercial Relationship) | Abtin Shahlaee: Commercial Relationship: Code N (No Commercial Relationship) | Julie Schallhorn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: An increasing number of cases of acute kidney injury (AKI) have been reported after intravitreal anti-Vascular Endothelial Growth Factor (anti-VEGF) injections. The purpose of this study was to evaluate the real-world evidence for AKI in a large cohort of patients receiving anti-VEGF therapy using routinely collected electronic health records.

Methods: De-identified data from over 6 million patients treated across University of California Health system from 2012 to 2021 were queried. All patients with a creatinine measurement within 6 months prior to and 14 days after the intervention were considered, and those with a baseline creatinine ranging from 0.4 to 4.0 were included. Rate of acute kidney injury (a rise of creatinine by 0.3 mg/dl within 48 hours or 150% within two weeks) was calculated after the patients first record of anti-VEGF injection (intervention group) or posterior segment optical coherence tomography scan without anti-VEGF injection (OCT, control group). The χ^2 test was used to assess statistical significance (α = 0.05). Information on a pre-existing diagnosis of diabetes mellitus (DM) was also included.

Results: A total of 191,211 and 9,149 unique patients in the database received OCT and intravitreal anti-VEGF, respectively. Pre- and post-intervention creatinine were available for 7,367 (control) and 347 (intervention). Baseline creatinine was similar between the two cohorts. Rate of AKI in anti-VEGF group was 2.88%, which was not significantly different from the control group (1.87%, p=0.18). Creatinine data availability was significantly higher in the subset of patients with a previous diagnosis of DM ($p < 0.0001$). However, in those with DM, creatinine availability was similar between the two cohorts ($p = 0.06$), and rate of AKI was not significantly different (Anti-VEGF: 4.76% vs OCT: 2.50%, p=0.0503).

Conclusions: The rate of AKI after intravitreal anti-VEGF was low and not statistically different from the control group, even in those with a prior diagnosis of DM. Future analyses will attempt to investigate whether other patient characteristics impact the risk of kidney injury in those receiving this treatment.

CONTROL ID: 3708941

SUBMITTER (NAME ONLY): Paola Oquendo

TITLE: COMPARISON OF THE PHOTORECEPTOR MOSAIC BEFORE AND AFTER MACULAR HOLE SURGERY WITH HIGH RESOLUTION ADAPTIVE OPTICS IMAGING

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Oquendo, H. Hamli, F. Faleel, F. Nagel, R.H. Muni, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|T. Wright, P. Yan, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

Commercial Relationships Disclosure: Paola Oquendo: Commercial Relationship: Code N (No Commercial Relationship) | Hesham Hamli: Commercial Relationship: Code N (No Commercial Relationship) | Fathima Afira Faleel: Commercial Relationship: Code N (No Commercial Relationship) | Tom Wright: Commercial Relationship: Code N (No Commercial Relationship) | Flavia Nagel: Commercial Relationship: Code N (No Commercial Relationship) | Peng Yan: Commercial Relationship: Code N (No Commercial Relationship) | Rajeev Muni: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to assess the photoreceptor mosaic in patients diagnosed with idiopathic macular hole (MH) before and after surgical repair using adaptive optics enhanced retinal imaging (AO).

Methods: This is a REB-approved, prospective case series, performed at Kensington Eye Institute. Subjects presenting with idiopathic MH treated with pars plana vitrectomy (PPV) between May and December 2021 were included. AO imaging was performed preoperatively and at 3 months after successful macular hole repair using the RTX1 camera (Imagine Eyes, Orsay, France). All images were manually assessed for quality and images without a clearly resolvable cone mosaic were excluded from the analysis. Cone density, packing regularity, and dispersion were measured at 2 and 4 degrees of eccentricity in all 4 quadrants (superior, inferior, nasal, and temporal) using the manufacturer's software with manual correction. After correction for axial length, mixed effects modeling with repeated measures were used to identify significant changes.

Results: 8 patients (8 eyes) with idiopathic MH and with a successful surgical closure were analyzed. Mean cone density at 2° was 13407 mm^3 preoperatively and 12154 mm^3 postoperatively (95% CI= [-1227.77, 3734.21]); at 4°, cone density was 13542 mm^3 preoperatively and 11807 mm^3 postoperatively (95% CI= [892.68, 2577.80]). Mean regularity at 2° was 86.2% preoperatively and 83.6% postoperatively (95% CI= [-1.22, 6.57]); at 4°, was 87.7% preoperatively and 84.9% postoperatively (95% CI= [-3.04, 8.59]). Mean dispersion at 2° was 19.8% preoperatively and 22.6% postoperatively (95% CI= [-8.77, 3.22]); at 4°, was 20.09% preoperatively and 21.6% postoperatively (95% CI= [-4.83, 1.71]). There is no significant change to cone density ($F_{(1,29)}$ = 0.02, p =0.87), cone regularity ($F_{(1,24)}$ = 0.29, p =0.60) or cone dispersion ($F_{(1,17)}$ = 0.001, p =0.97) at either 2° or 4° eccentricity.

Conclusions: Adaptive optics imaging allows quantitative assessment of the photoreceptor mosaic before and after successful PPV in patients with idiopathic macular hole. This will enable further investigation of the photoreceptor remodeling process and microstructural changes following surgery.

CONTROL ID: 3708942

SUBMITTER (NAME ONLY): Songhua Li

TITLE: Deletion of FATP4 in Rpe65-null rd12 mice improves cone vision but not rod vision

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Li, M. Jin, Neuroscience Center of Excellence, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|M. Jin, Department of Ophthalmology, LSU School of Medicine, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure: Songhua Li: Commercial Relationship: Code N (No Commercial Relationship) | Minghao Jin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We recently showed that deletion of fatty acid transport protein-4 (FATP4) significantly promotes cone opsin solubility, cone photoreceptor survival, and cone-mediated vision in the RPE65 R91W knock-in mouse model of Leber congenital amaurosis (LCA). The purpose of this study was to test whether FATP4-deficiency can improve cone survival and function in RPE65-null rd12 mice.

Methods: Using rd12 and Fatp4$^{-/-}$;Ivl-Fatp4$^{tg/+}$ (shown as Fatp4$^{-/-}$ hereafter) mice, we generated rd12;Fatp4$^{-/-}$ mice. Key visual cycle enzymes and FATP4 in the retinal pigment epithelium (RPE) of these mice were detected by immunoblot analysis. Synthesis of 11-cis-retinal (11cRAL) in dark adapted mice were analyzed by high-performance liquid chromatography. Retinal degeneration was assessed by immunoblot and immunohistochemical analyses of rod and cone specific proteins. Visual functions of rod and cone photoreceptors were determined by scotopic and photopic electroretinographies (ERG) evoked with various flash intensities of white, 530-nm green or 360-nm UV light. For recording cone ERGs, animals were light adapted for 10 min by exposing to 40 cd/m^2 white light.

Results: RPE65 was undetectable in the both rd12 and rd12;Fatp4$^{-/-}$ RPEs while FATP4 was expressed only in the rd12 RPE. Expression levels of lecithin:retinol acyltransferase in the rd12 RPE were similar to those in age matched rd12;Fatp4$^{-/-}$ RPE. Similar to rd12 mice, dark adapted rd12;Fatp4$^{-/-}$ mice contained undetectable 11cRAL. Both immunoblotting and immunohistochemistry showed that the expression levels of rhodopsin in 2- and 4-month-old rd12 mice were similar to those in age-matched rd12;Fatp4$^{-/-}$ mice whereas the expression levels of M-opsin and cone arrestin in the rd12;Fatp4$^{-/-}$ mouse retina were significantly higher than those in the rd12 retina. Consistent with these results, rd12 and rd12;Fatp4$^{-/-}$ mice exhibited comparable scotopic ERG responses whereas green light-evoked ERG responses of M-cones were clearly greater in rd12;Fatp4$^{-/-}$ mice as compared to rd12 mice.

Conclusions: Our results indicate that 1) cone survival and function are supported by a RPE65-independent mechanism(s) that may be an important therapeutic target for LCA caused by loss of RPE65 function; and 2) FATP4 negatively regulates this RPE65-independent pathway.

CONTROL ID: 3708948

SUBMITTER (NAME ONLY): David Mora-Boellstorff

TITLE: Can Serum Drops Containing Doxycycline Provide Potential Anti-Bacterial Effect in the Treatment of Bacterial Keratitis?

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Mora-Boellstorff, K. Matharu, V. Jhanji, R.P. Kowalski, The Charles T. Campbell Ophthalmic Microbiology Laboratory, Department of Ophthalmology, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: David Mora-Boellstorff: Commercial Relationship: Code N (No Commercial Relationship) | Kanwal Matharu: Commercial Relationship: Code N (No Commercial Relationship) | Vishal Jhanji: Commercial Relationship: Code N (No Commercial Relationship) | Regis Kowalski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Systemic doxycycline has been prescribed to enhance corneal healing in the setting of bacterial keratitis. Topical autologous serum drops containing doxycycline via oral supplementation may additionally confer an anti-bacterial effect. The potential of this treatment supplementation was evaluated by determining the in vitro susceptibility of bacterial keratitis isolates to doxycycline.

Methods: The minimum inhibitory concentrations (MICs) to doxycycline of 100 bacterial keratitis isolates submitted to the Charles T. Campbell Ophthalmic Microbiology Laboratory at the University of Pittsburgh Medical Center were determined using Etests. Twenty-seven (27%) Staphylococcus aureus, 10 (10%) coagulase-negative Staphylococci, 6 (6%) Streptococcus pneumoniae, 7 (7%) Streptococcus viridans group, 7 (7%) other Gram-positive bacteria, 19 (19%) Pseudomonas aeruginosa, 8 (8%) Serratia marcescens, 4 (4%) Moraxella spp., 2 (2%) Haemophilus spp., and 10 (10%) other Gram-negative bacteria isolates were tested. MICs to doxycycline were compared to a serum standard concentration of doxycycline (SD) of 4 µg/ml as well as concentrations of doxycycline in serum drops at 50% SD (2 µg/ml) and 20% SD (0.8 µg/ml) as would be found in clinical preparations of autologous serum 50% and 20% drops, respectively. MICs equal or less than these values were deemed susceptible.

Results: For Gram-positive bacteria, susceptibilities to SD, 50% SD, and 20% SD were respectively, 86%, 65%, and 60%. For Staphylococcus aureus, susceptibilities to SD, 50% SD, and 20% SD were respectively, 92.6%, 85.2%, and 77.8%. For Gram-negative bacteria, susceptibilities to SD, 50% SD, and 20% SD were respectively, 37.2%, 23.3%, and 11.6%. Pseudomonas aeruginosa tested resistant to doxycycline at all concentrations. For the composite dataset of bacterial keratitis isolates, susceptibilities to SD, 50% SD, and 20% SD were respectively, 65%, 47%, and 39%. Chi-squared analyses comparing Gram-positive and Gram-negative susceptibilities showed significantly greater susceptibility of Gram-positive bacteria at all three tested MICs (<.0001, <.0001, <.0001).

Conclusions: Our data suggests that serum drops containing doxycycline may have a select advantage for treating Gram-positive bacterial keratitis, especially Staphylococcus aureus, over Gram-negative bacterial keratitis.

CONTROL ID: 3708949

SUBMITTER (NAME ONLY): Victor Gonzalez

TITLE: Two Randomized, Double-Masked, Placebo-Controlled, Parallel-Group Studies of the Local Anesthetic Effect of Articaine Sterile Topical Ophthalmic Solution 8% (AG-920)

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.H. Gonzalez, Ophthalmology, Valley Retina Institute, McAllen, Texas, UNITED STATES|V.H. Gonzalez, Molecular, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|G.D. Novack, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|D. Wirta, Ophthalmology, Eye Research institute, New Port Beach, California, UNITED STATES|M. Uram, American Genomics, Little Silver, New Jersey, UNITED STATES|A. Schupp, CMC Turnkey solutions, Lone tree, Colorado, UNITED STATES|M.C. Widmann, Cal Clinical Trials solution, Apex, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Victor Gonzalez: Commercial Relationship(s);Code F (Financial Support):Genentech, Regeneron, Allergan, Alimera, Valeant, Bausch and Lomb, Santen, Iconic, Boehringer, insite, Topcon, Beaver-Visitec, Astellas, Opthea, 60 degree pharm, Apellis, RIBOMIC, Iveric, Nanoscope, Occuphire, Unity,;Code C (Consultant/Contractor):Unity, Bausch and Lomb, American Genomics, | Gary Novack: Commercial Relationship(s);Code C (Consultant/Contractor):American Genomics | David Wirta: Commercial Relationship(s);Code C (Consultant/Contractor):American Genomics | Martin Uram: Commercial Relationship(s);Code C (Consultant/Contractor):American Genomics | Audrey Schupp: Commercial Relationship(s);Code C (Consultant/Contractor):American Genomics | Michelle Widmann: Commercial Relationship(s);Code C (Consultant/Contractor):American Genomics

ABSTRACT BODY:

Purpose: We desired to develop a new topical ocular anesthetic with good bioavailability in anterior segment tissues. As well, given concerns about contamination and sterility in multi-dose products, we selected a unit-dose, non-preserved presentation in blow-fill-seal containers (similar to currently marketed pharmacological therapies for dry eye disease). The primary objective of these two Phase 3, randomized, placebo-controlled, double-masked, parallel design studies in healthy subjects was to evaluate anesthetic efficacy of AG-920. The secondary objectives included and the safety and tolerability of AG-920.

Methods: In each study, 120 subjects were randomized to receive a single dose of AG-920 or identical looking placebo into one (study) eye (2 drops 30 seconds apart). Subjects underwent a conjunctival pinch procedure and the pain associated with the pinch assessed. A priori, the primary endpoint was “no pain at 5 minutes”.

Results: AG-920 provide a rapid onset of local anesthesia (less than one minute) with clinically and statistically significantly greater effect in AG-920 (68% and 83%) than placebo (3% and 18%, for Study 1 and Study 2, respectively, $p < 0.0001$). The most frequently adverse event was instillation site pain (27% vs 3%), followed by conjunctival hyperemia (probably related to the pinch, 9% vs 10%) in the AG-920 and placebo groups, respectively.

Conclusions: A single dose of AG-920 (two drops 30 seconds apart) resulted in local ocular anesthesia in a short period of less than half minute and lasting up to approximately 15 minutes or longer. Other than mild conjunctival hyperemia, there were no clinically significant safety findings.

CONTROL ID: 3708951

SUBMITTER (NAME ONLY): Dong Hyun Kim

TITLE: Investigation of the anti-inflammatory effects of RCI001 as therapeutics for ocular surface diseases: insight into the mechanism of action

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kim, Ophthalmology, Gil Medical Center, Gachon University College of Medicine, Incheon, KOREA (THE REPUBLIC OF)|D. Kim, Y. Jang, S. Kim, Y. Shin, Y. Kim, RudaCure Co., Ltd, Incheon, KOREA (THE REPUBLIC OF)|Y. Kim, Gachon Pain Center and Department of Physiology, Gachon University College of Medicine, Incheon, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Dong Hyun Kim: Commercial Relationship(s);Code P (Patent):Rudacure | Ye Won Jang: Commercial Relationship(s);Code E (Employment):Rudacure | Seunghoon Kim: Commercial Relationship(s);Code E (Employment):Rudacure | Yungyeong Shin: Commercial Relationship: Code N (No Commercial Relationship) | Yong Ho Kim: Commercial Relationship(s);Code O (Owner):Rudacure

ABSTRACT BODY:

Purpose: We previously showed that topical application of RCI001 had excellent anti-inflammatory and antioxidant effects in dry eye disease and ocular chemical burn model. In this study, we investigated the inhibiting effects of RCI001 on Rac1 and NLRP3 inflammasome in vitro and in vivo model.

Methods: We confirmed Rac1 activity by RCI001 treat in RAW264.7 cells and Swiss 3T3 cells by GST (glutathione-S-Transferase) pull-down assay and G-protein activation assay kit. And the production and gene expression changes of IL-1β, IL-6 and TNF-α by RCI001 were quantified by ELISA and real-time PCR on RAW264.7 cell stimulated by LPS. In the mouse ocular alkali burn model, RCI001 was administered via eye drop (10mg/ml, twice daily) for 5 days. As a positive control, prednisolone acetate (PDE) ophthalmic suspension 1% was used. Corneal epithelial integrity (on Day 0, 3, 4 and 5) and histological changes were compared between RCI001 and PDE. Gene and Protein levels of Rac1, NLRP3, Caspase-1 and IL-1β were quantified by real-time PCR and western blotting in corneal tissues collected on day 3 and 5.

Results: RCI001 inhibited Rac1 activity and various inflammatory cytokines dose-dependently in LPS-stimulated murine macrophage. Additionally, RCI001 restored corneal epithelial integrity and thickness faster than PDE in chemically injured cornea. Activation of Rac1 and NLRP3 inflammasome/ IL-1β axis was suppressed in RCI001 group compared with saline group especially in early phase of ocular alkali burn model.

Conclusions: Topical RCI001 suppressed expressions of activated Rac1 and inflammatory cytokines in vitro and restored injured cornea quickly by inhibiting the activation of Rac1 and NLRP inflammasome/ IL-1β axis in vivo. We believe that RCI001 could be a promising therapeutic agent for ocular surface disease.

CONTROL ID: 3708960
SUBMITTER (NAME ONLY): Po-Yen Lee
TITLE: Correction of involutional lower lid entropion without retractor reinsertion in Asians
SESSION TITLE: Oculoplastics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: P. Lee, Department of Ophthalmology, Kaohsiung Medical University Chung Ho Memorial Hospital, Kaohsiung, TAIWAN|P. Lee, Department of Ophthalmology, Chi Mei Medical Center, Tainan, TAIWAN|
Commercial Relationships Disclosure: Po-Yen Lee: Commercial Relationship: Code N (No Commercial Relationship) | Po-Yu Lee: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Involutional entropion correction usually involves lower lid retractor plication/reinsertion. In Asian patients, congenital entropion associated with epiblepharon has been corrected with modified Hotz procedure, without reinforcement of retractor. This method avoids the unwanted postoperative lower lid crease from aesthetic aspect. The enhanced adhesion between tarsal plate and subcutaneous tissue may also increase the stiffness of tarsus and help to overcome orbicularis muscle tone. Besides, aging lower retractors in Asians are usually thin, atrophy and not sufficient to rotate the direction of the lashes. Excessive tightening of the retractors can instead cause lid retraction. We investigate the outcome of this single method without combination of retractor reinsertion and lid tightening.
Methods: Retrospective chart review. Modified Hotz procedure was performed soley. Pretarsal skin and orbicularis muscle were partially removed along subciliary incision. Several rotational sutures then anchor the subcutaneous tissue just beneath the lash base onto tarsal plate to evert the lash line.
Results: From January 2019 to December 2021, 43 patients with 57 eyes were included (mean age: 67.89, range: 55-95 years old). The mean follow-up period was 10.56 months. (Range: 6-29months). After operation, immediate improvement of irritation, tearing and discharge were observed in all patients. 5 (8.7%) eyes presented slightly increased scleral show within 2mm. No patient presented ectropion due to overcorrection. Only one patient (one eye) recurred during the period of follow-up (7 months after surgery). This was mainly due to excessive lid laxity and after receiving lateral tarsal strip procedure, she achieved symptom relief. At the final follow-up, all patients were satisfied with the results. While 51 eyes (89.4%) reported complete remission, 6 eyes (10.5%) reported mild and easily tolerated symptoms.
Conclusions: Involutional lower lid entropion can be corrected without retractor plication/reinsertion in certain Asian patients. It prevents from forming lower lid crease and may reduce tendency of overcorrection. The tarsal plate stability may be increased due to scar formation. Lower lid laxity should be evaluated before surgery with consideration of adding a lid tightening procedure. More case studies are needed to assess the outcomes and complications.

CONTROL ID: 3708961

SUBMITTER (NAME ONLY): Devy Deliyanti

TITLE: Neutrophils as regulators of retinal inflammation in ocular neovascular disease

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Deliyanti, V. Suphapimol, J.L. Wilkinson-Berka, Anatomy and Physiology, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|D. Deliyanti, Diabetes, Monash University Faculty of Medicine Nursing and Health Sciences, Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Devy Deliyanti: Commercial Relationship: Code N (No Commercial Relationship) | Varaporn Suphapimol: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Wilkinson-Berka: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Neovascularization is the vision-threatening vascular pathology that develops in diabetic retinopathy (DR) and retinopathy of prematurity (ROP). This pathological process is primarily driven by angiogenic factors such as vascular endothelial growth factor (VEGF), which cause retinal vessels to become proliferative and leaky. Inflammation drives the development of neovascularization and features the activation of retinal microglia, resident immune cells of the retina. However, circulating immune cells, such as leukocytes and lymphocytes, can enter the retina due to breakdown of the blood-retinal barrier, further exacerbating inflammation. Neutrophils are the most abundant type of leukocytes and are found in the vitreous of DR patients, but their role in neovascularization is largely unknown.

Methods: Two robust models of retinal inflammation and vasculopathy were studied: oxygen-induced retinopathy (OIR) and streptozotocin (STZ) type-1 diabetes. OIR was induced by exposing C57BL6/J mice at postnatal day (P) 7 to 75% oxygen for 5 days and then room air (21% oxygen) until P18. Comparisons were made to mice housed in room air. A neutrophil depletion antibody (anti-Ly6G, 100µg) was given via IP injection every 3 days from P7, and controls received an isotype antibody. To induce DR, 6-7 week old C57BL6/J mice were administered STZ and studied for 26 weeks. Comparisons were made to non-diabetic mice administered vehicle. Twelve to 24 animals were studied per group, and data analyzed by unpaired t-tests or one-way ANOVAs. Statistical significance was defined as $p<0.05$.

Results: Neutrophils (flow cytometry, $CD45^{+}CD11b^{+}Ly6G^{+}$) increased in the blood and lymphoid organs of OIR mice from P9 to P18, and in DR mice at 13 and 26 weeks post-STZ, coinciding with the presence of retinal inflammation and vasculopathy. In OIR, the depletion of neutrophils reduced retinal vasculopathy including neovascularization, vascular leakage and VEGF levels compared to controls. In OIR, depletion of neutrophils reduced the recruitment of leukocytes to the retina, suggesting that neutrophils are major contributors to retinal inflammation.

Conclusions: Neutrophils are one of the first responders to retinal injury in OIR, and they contribute to the development of inflammation and vasculopathy including neovascularization. Drugs targeting neutrophils may be beneficial for treating and preventing leading causes of blindness, such as DR and ROP.

CONTROL ID: 3708975

SUBMITTER (NAME ONLY): Arthur Brant

TITLE: Progression and Regression of Diabetic Retinopathy in the IRIS® Registry (Intelligent Research in Sight)

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Brant, K. Mishra, A.T. Perlroth, H. Bair, C. Xu, S. Pershing, D.V. Do, Stanford University, Stanford, California, UNITED STATES|S. Pershing, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) is a leading cause of blindness in the United States. While many studies have assessed incidence and prevalence of DR, understanding of odds of transitions between mild, moderate, severe, and proliferative DR is limited. We generate a Markov Model to quantify DR progression and regression, and highlight disparities in DR course based on patient characteristics.

Methods: We identified patients with a new diagnosis of mild non-proliferative diabetic retinopathy (NPDR), moderate NPDR, severe NPDR, or proliferative diabetic retinopathy (PDR) in 2016 in the IRIS Registry database. Within each category, we analyzed the percentage of eyes whose DR progressed (to more severe disease) or regressed (to milder disease) over a two-year period from disease onset. We stratified analyses by patient characteristics, including age, sex, race, and insurance.

Results: In 2016, 202,777 eyes had a new diagnosis of mild NPDR, 92,319 moderate NPDR, 32,471 severe NPDR, and 125,289 PDR. Within two years, 1.57% of mild NPDR eyes developed PDR, 4.56% of moderate NPDR developed PDR, and 9.64% of severe NPDR developed PDR. 5.43% of eyes with PDR regressed to NPDR within two years. Among eyes with moderate DR, 5.93% regressed to mild NPDR and 7.87% progressed to severe NPDR or PDR. Among eyes with severe NPDR, 10.01% regressed to mild/moderate NPDR and a 9.64% progressed to PDR. Greater progression from NPDR to PDR was observed in patients with Hispanic race (2.48%), age 21 to 40 years (2.27%), and Medicaid insurance (2.12%). Less progression was observed in those of white race (1.37%), age 81-100 years (1.04%), and commercial insurance (1.60%). Regression from PDR to NPDR was most frequent in Asians (7.38%), ages 61-80 (5.78%), and VA insurance (6.20%), and least frequent in black patients (4.77%), ages 21 to 40 (3.91%), and Medicaid (4.76%) insurance.

Conclusions: We identified four key findings: (1) patients with more advanced NPDR more often progress to PDR (6x more often in severe NPDR vs. mild NPDR); (2) The vast majority of eyes neither progressed nor regressed over 2 years; (3) Moderate NPDR progressed 32% more often than it regressed, whereas severe NPDR regressed 4% more often than progressed; (4) Hispanics, ages 21-40, and Medicaid patients most often progressed, while Asians, ages 61-80, and VA insurance patients most often regressed.

CONTROL ID: 3708977

SUBMITTER (NAME ONLY): Jieming Fu

TITLE: Binocular Disparity Selectivity and Orientation Tuning in Mouse V1

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fu, Neuroscience Graduate Program, University of Virginia, Charlottesville, Virginia, UNITED STATES|S. Tanabe, J. Cang, Psychology, University of Virginia, Charlottesville, Virginia, UNITED STATES|J. Cang, Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Jieming Fu: Commercial Relationship: Code N (No Commercial Relationship) | Seiji Tanabe: Commercial Relationship: Code N (No Commercial Relationship) | Jianhua Cang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The brain combines 2-dimensional images collected by the eyes to form a 3-dimensional representation of its surroundings. This process of stereopsis arises from the binocular integration circuitry in the primary visual cortex (V1) that include neurons tuned to certain disparities between visual stimuli viewed by the two eyes. V1 neurons are also known to be tuned to orientations of visual stimuli. We examined whether these two well-known properties of V1 neurons are related in the mouse, expecting cells tuned to vertical orientations to have the strongest disparity selectivity tuning.

Methods: Adult C57BL/6 mice were surgically fitted with a headplate and had a craniotomy performed over the binocular zone of V1 to facilitate in vivo electrophysiological recording in awake animals. A combined projector and polarizing alternator system was used to display dichoptic visual stimuli. The stimulus set consisted of drifting gratings, in which each binocular condition consisted of a specific combination of orientation and phase disparity, and the associated controls were two monocular conditions at the same orientations. Binocular and monocular conditions were displayed in a randomly interleaved order. A high density 64-channel silicon probe was inserted to collect extracellular voltage signals, which were later sorted into single unit spikes for further analysis.

Results: We acquired a total of 338 single units across 15 animals. Of this population, 107 were significantly responsive to our set of drifting gratings (random permutation test $p<0.05$). For each neuron, we measured its tuning in the joint parameter space of orientation and phase disparity, as well as its orientation tuning for monocular stimulation. The strength of tuning along the phase disparity axis was quantified using a selectivity index (gPDSI), and orientation corresponding to highest gPDSI was determined. The distribution of orientations corresponding to highest gPDSI was not equally spread among the 4 orientation conditions in the stimulus set ($\chi^2(3)=8.238$, $p=0.041$). However, there was also no significant correlation between gPDSI and preferred orientation ($R^2=0.001$, $F_{(107,105)}=0.065$, $p=0.8$).

Conclusions: Binocular disparity selectivity in mouse V1 is not significantly stronger in cells tuned to vertical orientations. Studies utilizing only vertical gratings in their stimulus set may be mis-estimating the prevalence of disparity selective cells in binocular V1.

CONTROL ID: 3708987

SUBMITTER (NAME ONLY): Peter Westenskow

TITLE: Use of collagen-hybridizing peptides to assess active fibrosis in 2 mouse models of choroidal neovascularization

SESSION TITLE: Subretinal fibrosis – clinical challenges, mechanism, and diagnostic tools

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Westenskow, R. Foxton, M. Linder, Roche Pharma Research and Early Development, Roche Innovation Center, F. Hoffman-La Roche AG, Basel, SWITZERLAND|L. Bennink, M. Kirkness, 3Helix.com, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Subretinal fibrosis causes irreversible vision loss in patients with neovascular age-related macular degeneration (nAMD). Ophthalmic imaging techniques allow detection of fibrosis with limited efficiency and there is a clinical need for novel tools to monitor fibrosis-related changes. We report in vivo imaging of active fibrosis using collagen-hybridizing peptides (CHPs), small molecules that bind to single α-chain collagen structures, allowing identification of collagen remodeling (a hallmark of active fibrosis) in the subretinal space.

Methods: Using 2 independent mouse models (laser-induced choroidal neovascularization [CNV]; JR5558 spontaneous CNV), we investigated the effectiveness of sCy7.5-labeled CHPs to image active fibrotic lesions in vivo. Validation studies assessed correlation between CHP and epithelial mesenchymal transition (EMT) markers, laser intensity and CHP binding in vivo, and between in vivo and ex vivo CHP quantification of active collagen. The antifibrotic effects of a bispecific angiopoietin-2/vascular endothelial growth factor-A antibody (VA2) were examined in vivo by assessing CHP binding in 42-day-old JR5558 mice after 3 weekly VA2 injections versus IgG control (10 mg/kg body weight; days 21, 28, 35; sCy7.5-CHP injected on day 37).

Results: Integration of retinal pigment epithelium (RPE)/choroid flatmount images of JR5558 eyes showed coexpression of CHPs with fibrosis and EMT-related markers, correspondence between sCy7.5-labeled and sCy3-labeled CHP binding, and increased CHP binding in RPE/choroid with age. After laser-induced scarring, sCy7.5-CHP binding in vivo correlated to the intensity of laser and ex vivo CHP ($r = 0.76$; $P = 0.03$) and fibronectin ($r = 0.69$; $P = 0.058$) binding. In laser-induced CNV, there was decreased CHP binding in vivo and ex vivo at 8 weeks (stabilized scars) versus 1 week after injury. In JR5558 mice treated with VA2, CHP integration detected significantly decreased collagen remodeling (CHP binding in vivo and ex-vivo; $p < 0.01$) versus IgG control.

Conclusions: CHPs bound specifically to active fibrosis and detected increased collagen remodeling in JR5558 mouse eyes in vivo as they aged, in contrast to reduced binding over time in laser-induced scarring. The antifibrotic effects of dual Ang-2/VEGF-A inhibition were clearly demonstrated using this method, which has potential to support clinical development of nAMD treatments.

CONTROL ID: 3708997

SUBMITTER (NAME ONLY): Jaewook Yang

TITLE: The novel peptide inhibits progression of pathological neovascularization in animal models of retinal vascular disease

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yang, Y. Cho, J. Jang, B. Ahn, EYEBIOKOREA, Busan, KOREA (THE REPUBLIC OF)|J. Yang, Inje University Busan Paik Hospital, Busan, Busan, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: This study aimed to confirm the potential of novel peptide with anti-angiogenic effect, as a therapeutic agent for retinal vascular disorders such as wet age-related macular degeneration (w-AMD) and retinopathy of prematurity (ROP) using mouse and monkey models.

Methods: The novel peptide and aflibercept as a positive control were intravitreally injected in laser-induced choroidal neovascularization (CNV) mouse and monkey model of w-AMD and oxygen-induced retinopathy (OIR) mouse model of ROP. The analysis of vascular leakage by fundus fluorescein angiography (FFA) and CNV lesions by Optical coherence tomography (OCT) to evaluate efficacy was conducted in laser-induced CNV mouse and monkey models. Retinal neovascularization in OIR model was evaluated by retinal flat mount stained with isolectin B4 for blood vessels.

Results: In CNV mouse model, the vascular leakage and CNV volume were statistically reduced by 38.1% and by 23.5% in the novel peptide injected eyes compared with that of control of PBS injected. The mean vascular leakage and retinal thickness were reduced 13.9% and 48.5% ($P<0.05$ vs. Control) in CNV monkey model for 28 days after a single injection of novel peptide injection. The vessel tuft area in OIR mouse eye exhibited markedly decreased by 54.3% after novel peptide treatment compared to the control group.

Conclusions: Intravitreally injected novel peptide showed significant efficacy in pathological angiogenesis in three types of animal models of retinal disease. Especially in CNV mouse model, the novel peptide was shown the equivalent reducing CNV compared with aflibercept. These findings suggest that novel peptide has potential as a therapeutic agent for the wet AMD by preventing vascular leakage and increase in the retinal thickness.

CONTROL ID: 3709000
SUBMITTER (NAME ONLY): Jacqueline Chua
TITLE: Assessing the external validity of machine learning-based detection of glaucoma
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Chua, C. Li, L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|A. Popa-Cherecheanu, Universitatea de Medicina si Farmacie Carol Davila, Bucuresti, Bucuresti, ROMANIA|D. Wong, Nanyang Technological University, Singapore, Singapore, SINGAPORE|
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ABSTRACT BODY:

Purpose: To validate a machine learning model from spectral-domain optical coherence tomography (Cirrus, Carl Zeiss Meditec, Dublin, CA) data along with patients' background information for glaucoma detection and assess its external validity.

Methods: In this cross-sectional study, 514 Asians (257 glaucoma and 257 controls) were enrolled to construct a machine learning model for glaucoma detection, which was then tested on an independent dataset of 356 Asians (183 glaucoma and 173 controls) and an external dataset of 138 Caucasians (57 glaucoma and 81 controls). The machine learning model was also compared to the existing multivariate-adjusted retinal nerve fiber layer (RNFL) thickness compensation model and Cirrus-generated (measured) RNFL model. The area under the receiver operating characteristics curve (AUC) for glaucoma detection was calculated.

Results: The machine learning-based model (AUC=0.97) outperformed both the compensation model (AUC=0.93; P<0.001) and the measured RNFL model (AUC=0.93; P<0.001) for glaucoma detection in the Asian dataset. However, in the Caucasian dataset, the compensation model (AUC=0.90 to 0.93) outperformed both machine learning-based (AUC=0.85; P<0.001) and measured RNFL (AUC=0.82; P<0.001) models, and there was no significant difference in the AUC between the machine learning-based model and measured RNFL model (P=0.174) for glaucoma detection.

Conclusions: While the machine learning model detected glaucoma at a higher accuracy as compared to the compensation model or measured RNFL model in the internal dataset, this finding was not fully replicated in the external validation with the Caucasian dataset. Care must be taken when machine learning models are applied to patient cohorts of different ethnicities.

CONTROL ID: 3709004

SUBMITTER (NAME ONLY): Jialing Fu

TITLE: The SP Family Transcription Factors Act As Major Regulators in the Transcription of the Major Heat Shock Protein, HSP90β in lens epithelial cells

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fu, J. Wang, Y. xiao, Y. Wang, S. Zheng, J. Xiang, Y. Gan, X. Liang, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Heat shock protein 90 (HSP90) plays fundamental role in protecting various biological systems from stress condition and also from pathogenesis. Previous studies have shown that HSF1 plays an important role in regulating expression of HSP90. Whether other transcription factors also play essential roles in regulating expression of HSP90 remains largely unknown. In the present study, we have demonstrated that except for HSF1, the SP family transcription factors including SP1/SP3/SP4 also play essential roles in regulating HSP90β transcription in lens epithelial cells.

Methods: Gel mobility shifting assays were used to determine binding of SP family transcription factors to various HSP90β gene promoter and enhancer regions. ChIP assays were used to confirm the binding of different SP factors to the HSP90β gene promoter and enhancer regions. Various reporter gene constructs driven by different promoter and enhancer regions of the HSP90β gene were generated and used to assay the relative strength of different HSP90β gene promoter and enhancer regions. CRISPR/Cas9 technology was used to create various mutants. QRT-PCR and Wes were used to analyze mRNA and protein expression levels.

Results: In the proximal promoter and downstream enhancer regions, numerous SP1/SP3/SP4 binding sites were identified. These cis-elements were able to mediate binding by SP family transcription factors via EMSA and ChIP, and most of these elements also provide positive regulation on the expression of HSP90β. The cis-elements in different promoter and enhancer regions have differential strength in mediating control of HSP90β expression.

Conclusions: The SP family transcription factors play an important role in regulating transcription of the major heat shock protein HSP90β in lens epithelial cells. Among different SP family transcription factors, SP1 is the most important factor in regulating HSP90β expression. Supported by National Natural Science Foundation of China (Grants #81970787, #82000876, #81770910) and Natural Science Foundation of Guangdong Province and Guangdong City Joint Program of China (Grant # 2019B1515120014)，and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center.

CONTROL ID: 3709005

SUBMITTER (NAME ONLY): Kevin Zhang

TITLE: Split-tendon medial transposition of lateral rectus for treatment of pediatric oculomotor palsy

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.X. Zhang, V.S. Shah, Pediatric Ophthalmology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|K.X. Zhang, MSTP, University of Cincinnati College of Medicine, Cincinnati, Ohio, UNITED STATES|H. Varma, Ophthalmology, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|V.S. Shah, Ophthalmology, University of Cincinnati College of Medicine, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Split-tendon medial transposition of lateral rectus (STMTLR) for complete oculomotor palsy can correct large angles of exotropia in adults, but outcomes are variable and complications are frequent. Although outcomes in pediatric cases have been reported, further insight is needed to assess the child’s ability to gain sensory function and/or demonstrate neuroplasticity post-surgically. The purpose of our study is to report the outcomes of this technique in pediatric cases of complete oculomotor palsy.

Methods: A retrospective review of outcomes was conducted on 5 consecutive patients with complete oculomotor palsy treated with STMTLR by a single surgeon between 2012-2019 at a tertiary pediatric referral center. All patients underwent unilateral surgery utilizing the same technique. Primary outcome was postoperative horizontal alignment, and secondary outcome was demonstration of gain-of-function activity in the field of action of the paretic medial rectus muscle.

Results: Patients averaged 5.3 years old (range 10m-16y). Two were female. Etiologies were heterogeneous, with two subjects possessing bilateral disease secondary to miliary tuberculosis with CNS involvement, two with congenital unilateral palsy, and one iatrogenic case resulting from a pineal gland tumor extraction. All presented with oculomotor palsy with a mean preoperative exotropia of 75 ± 33.96 prism diopters (PD, range 35 to >120). Mean surgical decrease in exotropia was 49 ± 15.47 PD (range 37.5 to 75). Both patients with congenital oculomotor palsy regained convergence.

Conclusions: STMTLR was a safe and effective approach for the surgical correction of pediatric oculomotor palsy in our case series. If performed early, pediatric patients may additionally benefit in potential gain-of-function activity in the transposed lateral rectus muscle owing to the adaptive neuroplasticity of childhood.

CONTROL ID: 3709008

SUBMITTER (NAME ONLY): Anita Chan

TITLE: Single cell MYD88^{L265P} mutation and IgH gene rearrangement analysis is more sensitive and specific compared to cytology for vitreoretinal lymphoma diagnosis.

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chan, M. Wang, M. Wu, T. Lim, Singapore National Eye Centre Ocular Inflammation and Immunology Department, Singapore, SINGAPORE|A. Chan, Translational Ophthalmic Pathology Platform, Singapore Eye Research Institute, Singapore, SINGAPORE|T. Lim, Menarini biomarkers Singapore Pte Lted, SINGAPORE|N. Somasundaram, National Cancer Center Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Published diagnostic sensitivity of cytology, the gold standard in vitreoretinal lymphoma (VRL) diagnosis varies greatly from 45-87% and is dependent on the cytologist's experience. This study aims to determine the diagnostic accuracy of single cell MYD88^{L265P} mutation and Immunoglobulin (Ig) H gene rearrangement analysis in comparison to specialised cytology with the purpose of improving VRL diagnosis rates.

Methods: This study was performed with informed consent and institutional review board approval. A total of 12 patients with clinically proven VRL and 7 patients with chronic inflammatory vitritis were recruited. Vitreous cytology was analysed by experienced ophthalmic and lymphoma pathologists. Single cell (sc)-MYD88L265P and sc-IgH rearrangement analysis was performed using DEPArray™ Nxt single cell selection, followed by Whole Genome Amplification (WGA) and specific targeted sc-PCR. Measures of diagnostic accuracy included sensitivity and specificity using receiver operating characteristic (ROC) curve analysis.

Results: In our lab, cytology analysis by experienced ophthalmic pathologists and hematopathologist had a higher diagnostic sensitivity (88.9%) than most published diagnostic rates, however, specificity was only 66.7% for diagnosing VRL. Using a cut-off of >2.3% homozygous MYD88^{L265P} to define the presence of a MYD88^{L265P} mutation, this test was more sensitive (100%) and specific (83.3%) test than cytology. However Sc-IgH gene re-arrangement analysis was the most sensitive (100%) and specific (100%) test for VRL diagnosis when a cut off > 74% was used to define a dominant clone.

Conclusions: Although vitreous cytology remains highly sensitive for VRL diagnosis when analysed by experienced ophthalmic and lymphoma pathologists, the use of sc-MYD88^{L265P} mutation and/ or sc-IgH gene rearrangement analysis can improve the sensitivity and specificity of VRL diagnosis.

CONTROL ID: 3709010

SUBMITTER (NAME ONLY): Hang I Christie Lam

TITLE: Proteomic Profiling of Photoreceptor Cells under simulated hyperglycemia with SWATH mass spectrometry

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Lam, K. Cheung, T. Lam, D.Y. Tse, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|K. Cheung, T. Lam, D.Y. Tse, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is one of the leading causes of blindness and vision impairment in 2020. Apart from vasculopathy, DR has been found to involve retinal neurons including amacrine cells and retinal ganglion cells. Recent literature also suggested that photoreceptors secret proinflammatory molecules and produce reactive oxygen species that contribute to the development of DR. The effect of hyperglycemia on photoreceptors is not well understood. Here, we aimed to investigate the high glucose-induced changes in the proteomic profile of 661w photoreceptor-like cell line with data-independent Sequential Window Acquisition of all Theoretical Mass Spectra (SWATH) based proteomic analysis.

Methods: 661w cells were incubated in normal glucose (5.5mM glucose) and high glucose (55mM glucose) conditions for 48 hours. The sample (n=3 in each group) were then processed with S-Trap™ Micro Spin Column Digestion (S-Trap) protocol according to the manufacturer's guideline. The MS data were acquired using a hybrid quadrupole time-offlight TripleTOF 6600 mass spectrometer (SCIEX) with Analyst TF 1.7 software. Data obtained were exported and analyzed using ProteinPilot 5.0.1, PeakView 2.2, MarkerView 1.3 software, and OneOmics cloud-based platform (SCIEX). Pathway analysis was conducted with Ingenuity® Pathway Analysis (IPA).

Results: A total of 625 proteins out of 3,613 proteins was found to be differentially expressed ($p<0.05$, Fold-change ≥ 1.5 or ≤ 0.667) in the 661w cells under high glucose condition compared to normal glucose condition. Three hundred thirteen proteins were found to be up-regulated, while 312 proteins were found to be down-regulated. The top three enriched pathways revealed by IPA included 1) Protein Ubiquitination Pathway, 2) Mitochondrial Dysfunction, and 3) Oxidative Phosphorylation.

Conclusions: Our data suggested that high glucose condition may trigger changes in these three metabolic pathways in photoreceptor cells. These changes may have led to compromised mitochondrial function and increased cell apoptosis in the 661w cells previously reported by our team. The alternation of these three pathways has also been shown to affect the physiology of other retinal cell types under simulated hyperglycemia. The underlying molecular changes and their role in the pathogenesis of DR warrant further investigation.

CONTROL ID: 3709013

SUBMITTER (NAME ONLY): Judy Weng

TITLE: Ameliorative Effect of Insulin Treatment on Type 1 and Type 2 Diabetes Mellitus Mediated Damage to Ocular Surface

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Weng, C. Ross, K. Shamloo, A. Sharma, Chapman University School of Pharmacy, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Judy Weng: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Ross: Commercial Relationship: Code N (No Commercial Relationship) | Kiumars Shamloo: Commercial Relationship: Code N (No Commercial Relationship) | Ajay Sharma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patients of diabetes mellitus suffer from high incidence of corneal epithelial defects, ocular surface infections and dry eye disease. Ocular surface glycocalyx, mucins and goblet cells play a critical role to keep the ocular surface hydrated and protected from pathogens. We have previously shown that hyperglycemia can compromise ocular surface epithelial barrier function. The goal of the present study was to investigate the effect of diabetes mellitus on tear film, glycocalyx, mucins and goblet cells and to test whether restoration of euglycemia by insulin treatment has ameliorative effects on hyperglycemia-mediated ocular surface damage.

Methods: Streptozotocin-induced and db/db mouse models of type 1 and type 2 diabetes were used. Tears were quantified using phenol red thread and corneal keratopathy was visualized with slit lamp after fluorescein staining. Eyes were harvested at week1, 2 and 4 after diabetes. Glycocalyx was stained with wheat germ agglutinin and whole cornea mounts were imaged using confocal microscope. Tissue sections were used for goblet cell staining with PAS and imaged using brightfield microscope. Mucin gene expression was quantified in corneal tissue using real time PCR. Mice were implanted with subcutaneous insulin pellets. Effect of insulin treatment on diabetes-associated changes in tear film, glycocalyx, goblet cells and mucins were examined.

Results: Our data shows that type 1 and type 2 diabetes caused a 60% and 30% decrease in tear film volume and resulted in corneal keratopathy score of 10 and 8, respectively. A 65% and 45% decrease in glycocalyx area was noted in the corneas of type 1 and type 2 diabetic mice. Goblet cell number was decreased by 40% and 16%. Diabetes mellitus also modulated gene expression of membrane-tethered mucins. Treatment of diabetic mice with insulin pellets restored blood glucose levels to euglycemia. Insulin treatment reduced the severity of diabetes-mediated corneal keratopathy and remarkably prevented diabetes-mediated decrease in tear secretion, glycocalyx area and goblet cell number.

Conclusions: Diabetes mellitus causes damage to ocular surface and more detrimental effect was observed with higher levels of hyperglycemia due to type 1 diabetes as compared to type 2 diabetes mellitus. Restoration of euglycemia by insulin treatment remarkably prevented diabetes-mediated damage to tear film and ocular surface.

CONTROL ID: 3709023

SUBMITTER (NAME ONLY): Yan Wang

TITLE: Differential Expression of the Major Components of the cGAS/STING Pathway in Normal Human Lens and Cataractous patients

SESSION TITLE: Lens Physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Wang, J. Fu, S. Zheng, Y. xiao, J. Wang, J. Xiang, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|L. Wang, Changsha Medical University, Changsha, Hunan, CHINA|

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ABSTRACT BODY:

Purpose: The cGAS-STING pathway plays an important role in innate immunity. Previous studies have shown that activation of cGAS-STING is implicated in AMD pathogenesis. Whether this pathway is implicated in cataractogenesis remains to be studied. In the present study, we have analyzed the expression patterns of the major signal components of the cGAS-STING pathway in normal human lens and cataract patients.

Methods: Normal human lens were collected from Guangdong Province Eye Bank. Cataract capsular epithelia were harvested during surgical operation with consent of cataract patients. Micro-Western blot analysis (Wes) was used to detect the expression levels of cGAS, STING, TBK1 and IRF3.

Results: From normal human lens to cataractous lens, cGAS protein was significantly downregulated. Among different age groups of cataract patients, cGAS was upregulated from 50s to 60s, and then returned to the similar level of 50s in both 70s and 80s. Different from cGAS, the STING protein level in normal human and cataract patients lenses of 60-year old was similar. In different groups of cataract patients, STING became downregulated from 60s to 80s. For TBK1 and IRF3, they were barely detectable in normal human lens. In cataract patients, both TBK1 and IRF3 were easily detected. From 60s to 80s, however, they were downregulated.

Conclusions: The major components of the cGAS/STING pathway were differentially expressed from normal human lens to cataractous lens. The cGAS/STING pathway may play a protective role against cataractogenesis.Supported by National Natural Science Foundation of China (Grants 81970787, 82000876, 81770910) and Natural Science Foundation of Guangdong Province and Guangdong City Joint Program of China (2019B1515120014)，and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center.

CONTROL ID: 3709025

SUBMITTER (NAME ONLY): Jin won Huh

TITLE: In vivo flow cytometry in retina to study rare blood cells

SESSION TITLE: Blood flow and ischemia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Huh, Institute of Optics, University of Rochester Hajim School of Engineering and Applied Sciences, Rochester, New York, UNITED STATES|K. Dholakia, Department of Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|J. Huh, K. Dholakia, D. Power, J. Schallek, Center for Visual Science, Rochester, New York, UNITED STATES|D. Power, J. Schallek, University of Rochester David and Ilene Flaum Eye Institute, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: Jin won Huh: Commercial Relationship(s);Code F (Financial Support):Genentech | Kosha Dholakia: Commercial Relationship(s);Code F (Financial Support):Genentech | Derek Power: Commercial Relationship(s);Code F (Financial Support):Genentech | Jesse Schallek: Commercial Relationship(s);Code P (Patent):University of Rochester;Code F (Financial Support):Genentech

ABSTRACT BODY:

Purpose: Adaptive optics scanning light ophthalmoscopy (AOSLO) can image single blood cells in the retina. AOSLO can serve as a new platform to study the cellular components of whole blood in vivo. Here, we demonstrate an imaging-based method to study two rare blood cell types in the retinal circulation of living mice.

Methods: Two sparse populations of white blood cells (WBCs) were imaged in the living retina: circulating GFP-labeled monocytes (CX3CR1, Jackson Labs stock 005582), and CD8+ T-cells harvested from a GFP donor mouse (stock 006567) and adoptively transferred into a healthy C57BL/6J (stock 00664) mouse via intraperitoneal injection. A single retinal arteriole and a single venule from each mouse were imaged with a custom-built AOSLO with reflectance (796 nm) and fluorescence (488 nm ex/520Δ35 nm em) capabilities. Circulating cells were imaged using a 15kHz point scanned obliquely across a vessel, which simultaneously images the red blood cells and fluorescent WBCs. Cell velocities were quantified using the automated Radon approach previously described (Joseph et al., 2019). Total imaged blood volume was approximated by flow speed x π x radius^2 of the blood vessel. Fluorescent WBC populations were automatically counted and manually validated.

Results: In CX3CR1+ mouse, we observed the passage of labeled monocytes at rates of 27.7 cells/min in the arteriole and 14.0 cells/min in the venule. Based on the estimated blood volume imaged, this represents monocyte density of 244 cells/μL in the arteriole and 95 cells/μL in the venule. These counts in vivo were within an order of magnitude of the expected density of monocytes in circulation (van Furth & Sluiter, 1986). In the T-cell recipient mouse, we detected an average of 328 cells/min in the arteriole and 204 cells/min in the venule. Scaled by the blood volume imaged relative to total blood volume, we estimate 1.01-1.61 million CD8+ T-cells in systemic circulation. The total number of cells injected into the peritoneum was estimated to be 10 million cells, indicating 10 to 16% of the cells entered systemic circulation.

Conclusions: Here we demonstrate the ability to count and measure the speeds of monocytes and T-cells in high flow vessels in the body. Such capability provides the foundation for studying rare immune cells of interest that fight inflammation, infection and even mediate cutting-edge therapies that use adoptively transferred immune cells.

CONTROL ID: 3709026

SUBMITTER (NAME ONLY): Shuyu Zheng

TITLE: Developmental Expression of the cGAs/STING Pathway Signal Components during Development of Mouse Lens

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zheng, Y. Wang, J. Fu, J. Wang, Y. xiao, J. Xiang, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|L. Wang, Changsha Medical University, Changsha, Hunan, CHINA|

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ABSTRACT BODY:

Purpose: The cGAS-STING pathway plays an important role in innate immunity. Previous studies have shown that activation of cGAS-STING is implicated in AMD pathogenesis. Whether this pathway plays a role during lens development remains elusive. In the present study, we have analyzed the developmental expression patterns of the major signal components of the cGAS-STING pathway and revealed its potential role in governing lens development.

Methods: Normal mouse embryos of different stages and adult mice were used for isolation of eye tissues. RT-PCR and in situ hybridization were used to analyze the mRNA expression levels of cGAS, STING, TBK1 and IRF3. Immunohistochemistry was used to detect the protein expression levels of the above components.

Results: At the mRNA level, cGAS and TBK1 mRNAs were detected at ED 14.5, reached the highest expression levels in the newborn lens and then were downregulated to 60-70% in the mature lens, and were further downregulated during aging in 7- to 8-month. In contrast, expression of the STING mRNA was low at the ED14.5, and gradually upregulated in newborn and adult mouse lenses and further upregulated in the aging lens. Different from cGAS, TBK1 and STING, the IRF3 mRNA was low at the ED 14.5, then upregulated in the newborn lens and maintained at this level in the mature and aging lens. At the protein level, the cGAS signal was relatively weak. The STING signal was very strong from ED 11.5 to newborn mice, and the IRF3 signal was intermediate between cGAS and STING.

Conclusions: The signal components of the cGAS/STING pathway are clearly expressed during lens development. Activation of this pathway may be important to protect lens development. Supported by National Natural Science Foundation of China (Grants 81970787, 82000876, 81770910) and Natural Science Foundation of Guangdong Province and Guangdong City Joint Program of China (2019B1515120014)，and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center.

CONTROL ID: 3709027

SUBMITTER (NAME ONLY): Qin Wang

TITLE: Neuronal firing between retinal ganglion cells and coupled amacrine cells in the mouse retina

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q. Wang, C. So, F. Pan, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|Q. Wang, F. Pan, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Qin Wang: Commercial Relationship: Code N (No Commercial Relationship) | Chung Him So: Commercial Relationship: Code N (No Commercial Relationship) | Feng Pan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Gap junctions between retinal ganglion cells (RGCs) and amacrine cells (ACs) are important in visual information transmission. In the mouse retina, ON αRGCs are coupled to displaced ACs, and OFF αRGCs are coupled to conventional ACs and other OFF αRGCs. This study is to investigate the role of gap junctions in synchronization and cell driving activities in the mouse retina.

Methods: Adult C57BL/6J wild-type mice were used. Electrical activities of RGCs or ACs in the retina were recorded by patch-clamp. In the first part, two cells activities were recorded by green (525 nm) light stimuli. SKF38393 (10μM) and SCH23390 (5μM), which are agonist and antagonist for dopamine receptor 1 (D1), were applied to study the effect of ACs coupling to RGCs synchronization. Currents were injected into one cell in whole-cell mode, and the other cell activity was recorded. In the second part, viral vectors carrying a fusion construct of channelrodopsin2 (ChR2) and green fluorescent protein (GFP) were injected into the intravitreal space of both eyes and kept for 5 days before euthanized. A blue (460 nm) light was used as stimulus. The electrical recordings were performed between one ChR2-expressed cell and one non-ChR2-expressed cell.

Results: The synchronous firings in ganglion cells layer: ON αRGCs, OFF αRGCs and ON αRGC-displaced AC were investigated. The synchrony between these couplings could be abolished by gap junction blocker-MFA (50 μM) or 18β (30 μM). D1 agonist decreased the correlations of synchrony, while D1 antagonists increased the correlations. This suggested coupling between ACs decreased the synchronous correlations of RGCs. Injecting currents into one cell could induce spikes in the coupled cell. After virus transduction, the ChR2-expressed cells could fire without chemical input. More importantly, light-evoked spiking activity of a ChR2-expressed AC drove the activity of a non-ChR2 expressed RGC, gap junction blocker MFA diminished this activity.

Conclusions: Coupling of ACs affected synchronization between ON or OFF αRGCs. ACs could drive RGCs firing through gap junctions and vice versa. Gap junctions underlie the arbitrary manipulation of one cell by the other cell or external stimuli.

CONTROL ID: 3709031

SUBMITTER (NAME ONLY): Sebastian Dinesen

TITLE: Progression to proliferative diabetic retinopathy in the Danish Registry of Diabetic Retinopathy (DiaBase)

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dinesen, J. Grauslund, Odense Universitetshospital Ojenafdeling E, Odense, DENMARK|S. Dinesen, Y. Subhi, J. Grauslund, Syddansk Universitet Klinisk Institut, Odense, Syddanmark, DENMARK|L. Stokholm, Open Patient Data Explorative Network, Syddansk Universitet Klinisk Institut, Odense, Syddanmark, DENMARK|Y. Subhi, Department of Ophthalmology, Rigshospitalet, Kobenhavn, DENMARK|T. Peto, Queen's University Belfast Centre for Public Health, Belfast, Belfast, UNITED KINGDOM|T.R. Savarimuthu, The Maersk Mc-Kinney Moller Institute, Syddansk Universitet, Odense, Syddanmark, DENMARK|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is the most common long-term complication to diabetes mellitus and the most common cause of visual loss in the working-aged population. In a national 5-year register-based cohort study, we aimed to identify demographic and clinical characteristics of patients, who later developed proliferative diabetic retinopathy (PDR) compared to patients who did not.

Methods: The study population includes all Danish diabetes patients above 18 years who attended the Danish DR-screening program. We included 147,802 patients from the Danish Registry of Diabetic Retinopathy followed from the 2th of January 2013 to the 30th of December 2018.

We used the first screening episode as index date and included both eyes of patients with and without subsequent development of PDR. We linked data with various national databases in order to investigate relevant clinical and demographic parameters.

A multivariable Cox regression model was performed to measure the hazard ratio (HR) for incident PDR for all relevant demographic and clinical parameters. We used the k-sample test on equality-of-medians and chi-square test for continuous and categorical variables to test for baseline differences between patients with and without incident PDR-progression.

Results: Subsequent progression to PDR was identified in 1.741 (1.2 %) patients. 5-year rates of progression to PDR were 0.2%, 3.4% and 20.8% for eyes with DR-levels 0, 1, 2, and 3, respectively.

The HR for incident PDR were duration of diabetes (HR 4.40 per 10 years; 95% confidence interval (CI) 3.61 to 5.35), type 1 diabetes (HR 13.16; 95% CI 10.84 to 15.97), Charlson Comorbidity Index score >0 (Score 1 = HR 4.93; 95% CI 4.20 to 5.79; score 2 = HR 2.01; 95% CI 1.51 to 2.68; score ≥3 = HR 3.09; 95% CI 2.16 to 2.68), use of insulin (HR 4.84; 95% CI 3.84 to 6.11), use of anti-hypertensiva (HR 2.35; 95% CI 1.88 to 2.94) and compared to DR-level 0, the risk of progression was increased with DR-level 1 (HR 11.15; 95% CI 8.92 to 13.93), DR-level 2 (HR 23.88; 95% CI 18.63 to 30.61) and DR-level 3 (HR 77.72; 95% CI 57.59 to 104.89).

Conclusions: In a 5-year longitudinal DR-screening study of an entire nation, longer duration of diabetes, type 1 diabetes, systemic comorbidity, use of insulin and blood pressure lowering medicine, as well as increasing baseline level of DR, independently predicted progression to PDR.

CONTROL ID: 3709032
SUBMITTER (NAME ONLY): Moosa Zaidi
TITLE: Diopsys Flicker ERG findings in Retinal Vasculitis
SESSION TITLE: Retinal vascular diseases
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Zaidi, H. Ghoraba, J.J. Hwang, C. Or, S. Lajevardi, J. Regenold, A. Mobasserian, A. Akhavanrezayat, S. Park, I. Karaca, Y.H. Khan, C. Yasar, G. Uludag, N. Than, M. Hassan, Q.D. Nguyen, Ophthalmology, Byers Eye Institute, Palo Alto, California, UNITED STATES|
Commercial Relationships Disclosure: Moosa Zaidi: Commercial Relationship: Code N (No Commercial Relationship) | Hashem Ghoraba: Commercial Relationship: Code N (No Commercial Relationship) | Jaclyn Hwang: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Or: Commercial Relationship: Code N (No Commercial Relationship) | Sherin Lajevardi: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Regenold: Commercial Relationship: Code N (No Commercial Relationship) | Azadeh Mobasserian: Commercial Relationship: Code N (No Commercial Relationship) | Amir Akhavanrezayat: Commercial Relationship: Code N (No Commercial Relationship) | SungWho Park: Commercial Relationship: Code N (No Commercial Relationship) | Irmak Karaca: Commercial Relationship: Code N (No Commercial Relationship) | Youan Khan: Commercial Relationship: Code N (No Commercial Relationship) | Cigdem Yasar: Commercial Relationship: Code N (No Commercial Relationship) | Gunay Uludag: Commercial Relationship: Code N (No Commercial Relationship) | Ngoc Than: Commercial Relationship: Code N (No Commercial Relationship) | Muhammad Hassan: Commercial Relationship: Code N (No Commercial Relationship) | Quan Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal vasculitis (RV) is a sight-threatening condition that can be idiopathic or associated with local or systemic inflammation due to infectious, neoplastic, or autoimmune diseases. While the structural changes associated with RV, as seen on ophthalmoscopy, angiography, optical coherence tomography, and other imaging modalities have been well documented, functional changes as may be seen on electrophysiology have not been well characterized. This retrospective study examines the Diopsys® Flicker Electroretinogram (ERG) findings present in cases of RV and tests whether these findings correlate with RV severity.

Methods: All retinal vasculitis cases seen by the uveitis service at a tertiary care center over a 14-month period were retrospectively reviewed and screened for inclusion in the study. Eyes with retinal vasculitis were included if there was at least one pair of Diopsys® flicker ERG recording and corresponding Fluorescein Angiogram (FA) within 2 months of each other for that eye. Eyes with other confounding retinal diagnoses were excluded. Each FA was scored for retinal vasculitis severity by two independent graders using the semi-quantitative Angiography Scoring
for Uveitis Working Group FA scale and the mean RV severity score was compared to the corresponding Diopsys® Flicker ERG findings (phase and magnitude values) across eyes and time points.

Results: A total of 50 eyes from 33 patients (mean age 26.3 years) were included. There was a moderate, highly significant correlation between retinal vasculitis severity and the Diopsys® flicker ERG Phase, both for Fixed-Luminance (FL) (-0.65, $p<0.001$) and for Multi-Luminance (ML) ERG settings (-0.63, $p=<0.001$) (Figure). Similarly, there was a mild correlation between RV severity and ERG Magnitude for both FL (-0.26, $p=0.04$) and ML (-0.33, $p<0.001$).

Conclusions: Increasing retinal vasculitis severity is associated with increasingly abnormal flicker ERG findings suggesting progressive dysfunction of the cone photoreceptor pathway.

CONTROL ID: 3709034

SUBMITTER (NAME ONLY): Romina Lasagni Vitar

TITLE: Safety and efficacy of novel Aprepitant formulations in the treatment of ocular surface pain

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Lasagni Vitar, F. Bonelli, P. Fonteyne, P. Rama, G. Ferrari, Eye Repair Lab, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: To test ocular toxicity and long-term analgesic efficacy of two novel ocular formulations of Substance P receptor antagonist Aprepitant in comparison with Diclofenac and Oxybuprocaine.

Methods: 7/8-week-old male C57BL/6N mice received topical (eye) treatment as follows: formulation A vehicle (n=18), formulation A 0.005% (n=7), 0.05% (n=7), and 0.5% (n=7); formulation B vehicle (n=18), formulation B 0.05% (n=7), and 0.5% (n=7); 0.4% Oxybuprocaine (n=7), 0.1% Diclofenac (n=7), and saline (n=6). Eye-drops were applied 3 times/day for 90 days. The animals were monitored by in vivo slit-lamp microscopy imaging. At days 0, 45, and 90 the eye-wiping test and corneal sensitivity measure were performed immediately after the last treatment to evaluate corneal nociception and sensitivity. At day 90, mice were euthanized and corneas were dissected to assess nerve density and leukocyte infiltration by immunofluorescence and to evaluate inflammation/pain-associated markers (TNF-α, IL-6, IL-1β, and Neurokinin-1 receptor) by RT-PCR.

Results: We found that both formulations A and B did not induce any significant epithelial damage or change in corneal transparency and nerve density. However, the Diclofenac group displayed a significant reduction in corneal nerve density after 90 days of treatment ($p<0.01$). Formulation A groups showed increased CD45+ infiltration ($p<0.01$) and up-regulation of inflammatory markers ($p<0.05$), which was not observed in formulation B groups. Both formulation B groups significantly reduced nociception ($p<0.05$) and corneal sensitivity ($p<0.01$) after 45 and 90 days. Similarly, Diclofenac significantly decreased nociception only after the first administration (day 0) ($p<0.05$) and sensitivity at all time points ($p<0.001$). As expected, the anesthetic medication Oxybuprocaine was the most effective in preventing pain ($p<0.001$) and in reducing corneal sensitivity ($p<0.0001$) at all time points. Finally, formulation A candidates were effective only at day 90 ($p<0.05$).

Conclusions: Both formulations B (0.05% and 0.5%) exhibit analgesic efficacy at day 45 and 90, differently from 0.1% Diclofenac, which is effective only at day 0. Differently from Diclofenac, both formulation B groups are not toxic for corneal nerves even after long-term (90 days) administration.

CONTROL ID: 3709035

SUBMITTER (NAME ONLY): Jingmiao Wang

TITLE: Differential Expression of the SP Family Transcription Factors in Normal Human Lens and Cataract Patients

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, J. Fu, Y. Wang, S. Zheng, Y. xiao, J. Xiang, Y. Gan, X. Liang, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: The SP family transcription factors including SP1/SP3/SP4 play essential role in regulating lens differentiation through control of various crystallin genes [Gong et al., 2014. Proc. Natl. Acad. Sci. USA]. In our most recent studies, we also found that the SP family transcription factors also play an important role in the regulating transcription of the major heat shock protein HSP90β in lens epithelial cells. Whether these transcription factors are implicated in cataractogenesis remains to be further studied. In the present studies, we have analyzed the differential expression patterns of SP1/SP3/SP4 in normal human lens and cataract patients.

Methods: Normal human lens were collected from Guangdong Province Eye Bank. Cataract capsular epithelia were harvested during surgical operation with consent of cataract patients. Micro-Western blot analysis (Wes) was used to detect the expression levels of SP1/SP3/SP4.

Results: From normal human lens to cataractous lens, all SP1 family transcription factors were down-regulated. Among the different age groups of cataract patients, SP1 was upregulated over 50% from 50s to 60s. From 60s to 70s, however, SP1 was down-regulated more than 80%. From 70s to 80s, SP1 was upregulated to the level between 50s and 60s, but down-regulated over 80% again from 80s to 90s. In contrast, SP3 and SP4 remain relatively stable from 50s to 70s.

Conclusions: The SP family transcription factors display clearly differential expression patterns. Such patterns are consistent with the down-regulated expression of the major heat shock protein, HSP90β in lens epithelial cells. These results suggest that down-regulation of the SP family transcription factor level is implicated in cataractogenesis.Supported by National Natural Science Foundation of China (Grants #81970787, #82000876, #81770910) and Natural Science Foundation of Guangdong Province and Guangdong City Joint Program of China (Grant # 2019B1515120014), and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center.

CONTROL ID: 3709039

SUBMITTER (NAME ONLY): Miriam Martínez Santos

TITLE: Regulation of vasculogenic processes by miR-302a-3p encapsulated in small extracellular vesicles

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Martínez Santos, M. Oltra, H. Rowland, J. Sancho-Pelluz, M. Ybarra, J. Barcia, Anatomía y Fisiología, Universidad Catolica de Valencia - San Carlos Borromeo, Valencia, Valenciana, SPAIN|M. Martínez Santos, M. Ybarra, Escuela de Doctorado, Universidad Catolica de Valencia - San Carlos Borromeo, Valencia, Valenciana, SPAIN|M. Oltra, H. Rowland, J. Sancho-Pelluz, J. Barcia, Centro de Investigación Traslacional San Alberto Magno, Universidad Catolica de Valencia - San Carlos Borromeo, Valencia, Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: Environmental cell conditions can promote extracellular vesicles (EVs) release. EVs are nanovesicles produced by most human cells containing numerous products including mRNA, microRNA (miRNAs), proteins and signaling molecules that have a crucial role in cell-to-cell communication. miRNAs are noncoding RNAs about 22 nucleotides long. They are considered post-transcriptional regulators of gene expression that influence the expression of hundreds of genes simultaneously. They are involved with up and downregulation is associated with many pathologies. Diabetic retinopathy (DR), age-related macular disease (AMD) and cancers are characterized by neovascularization processes. Oxidative damage increases the EVs release regulating angiogenesis. It has been proved that miR-302a-3p inhibits vessel formation targeting VEGFA via zinc finger protein 91 (ZFP91) and hypoxia induced factor 1α (HIF-1 α).

Methods: Our objective was to demonstrate that oxidative stress stimulates EVs release, down regulating miR-302a-3p and increasing angiogenesis. We used arising Retinal Pigment Epithelial cell line (ARPE-19) treated with 600 μM H_2O_2 or 4mM N-Acetylcysteine (NAC). Then, Human Vein Endothelial Cells (HUVEC) were grown indifferent conditions with or without EVs from control media, H_2O_2 or NAC media collecting EVs and isolating miRNA in order to confirm the results.

Results: H_2O_2 and H_2O_2-induced EVs exposure increases reactive oxygen levels (ROS) levels and decreases cell viability in ARPE-19 overexpressing VEGFA mRNA levels, those changes were reverted with NAC. miR-302a-3p mimic exposure decreased H_2O_2 induced VEGFA mRNA expression similarly to NAC addition. It is known that miR-302a-3p decreases vascular processes. Control-released EVs significantly downregulated the new vessels formation. More EVs were released after miR-302a-3p mimic addition and it was correlated with a stronger angiogenesis inhibition, showing a relationship between them. The use of miR-302a-3p inhibitor abolishes the effect. On the other hand, the miR-302a-3p mimic inhibitor restored VEGFA mRNA expression to control levels.

Conclusions: Oxidative stress promotes EVs release with proangiogenic properties. Those are inhibited by miR-302a-3p and promoted by ROS. This opens a new strategy against oxidative- induced angiogenesis by promoting miR-302a-3p as VEGFA mRNA repressor.

CONTROL ID: 3709042

SUBMITTER (NAME ONLY): Shuwen JIA

TITLE: Effect of visual task complexity and surface instability on perturbed balance performance among healthy older adults

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. JIA, A.M. Cheong, The Hong Kong Polytechnic University School of Optometry, HONG KONG|U. Bello, A.M. Cheong, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|S. Winser, The Hong Kong Polytechnic University Department of Rehabilitation Sciences, Hong Kong, HONG KONG|W.W. Tsang, T.T. Yam, Hong Kong Metropolitan University School of Nursing and Health Studies, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Balance control is vital for safe ambulation among older adults, especially under challenging environments like dual task paradigm and unstable surfaces. Our study aimed to assess older adults' perturbed balance in simulated real-life scenarios during visual searching and negotiating unstable surfaces. We hypothesized that experimental conditions with more challenging visual tasks and unstable surfaces would result in a decline in postural stability and longer latency among older adults.

Methods: Eighteen participants (age: 65.8±4.0 years; F/M: 15/3) without any systemic or eye diseases were recruited. All participants were instructed to stand on a perturbed force-plate on their bare-feet and complete balance assessments using Bertec Balance Advantage™ system for the following conditions: 1) standing surface (firm/ foam surface) and 2) visual task (fixating on a stationary target/ visual searching [1 target/ 3 targets]). All measurements were repeated 3 times. Reactive balance control in terms of latency reacting to perturbation (randomly moved forward and backward) and root mean square (RMS) sway of Center of Pressure (CoP) for dominant leg in anterior-posterior (AP) and medial-lateral (ML) directions were measured. Independent t-test and one-way analysis of variance (one-way ANOVA) were used to analyze the data.

Results: Contrary to our hypothesis, the effect of visual task showed non-significant influence on latency and RMS sway of the participants ($F<3.682$, $p>0.10$). Latency for the conditions with foam surface was not significantly different from firm surface ($p>0.10$). Instead, the RMS sway on the foam surface in ML direction was significantly lower than firm surface ($p<0.05$), but not in AP direction. The interaction effect of visual task and standing surface showed that RMS sway in ML direction reduced further when standing on the foam surface and conducting visual tasks ($F>3.682$, $p<0.01$).

Conclusions: Opposing to our hypothesis, the effect of visual task and standing surface on latency and RMS sway were weak. Surprisingly, the RMS sway on the foam surface was significantly less than firm surface. The results may be explained by posture priority. Older adults will take posture as the priority, mainly for safety reasons. They may sacrifice their attention on the visual task. Alertness may also alter the performance, therefore standing on foam may create less sway.

CONTROL ID: 3709043
SUBMITTER (NAME ONLY): Grazia Giorgio
TITLE: The role of Tet3 in retinal development and function
SESSION TITLE: Retinal Development
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: G. Giorgio, E. Murenu, S. Michalakis, Department of Ophthalmology, Ludwig-Maximilians-Universitat Munchen, Munchen, Bayern, GERMANY|G. Giorgio, S. Michalakis, Graduate School of Systemic Neurosciences, Ludwig-Maximilians-Universitat Munchen, Planegg, Bayern, GERMANY|S. Haverkamp, Department of Computational Neuroethology, Stiftung caesar, Bonn, Nordrhein-Westfalen, GERMANY|
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ABSTRACT BODY:

Purpose: Tet3 is a member of the ten-eleven translocation enzymes, which include also Tet1 and Tet2. Their canonical function is the oxidation of the 5-methylcytocine (5mC) on the DNA into 5-hydroximethylcytosine (5hmC), and subsequent oxidative states, thereby promoting increased gene expression. Tet3 is expressed in the mouse retina from early postnatal stages, implying its role during the same time window in which retina cells develop and mature. Although Tet3 is the most abundant member in brain and retina, its role in the latter has not been addressed.

Methods: Mutations in the Tet3 catalytic domain has been previously identified and linked to neurological, but also ophthalmological defects. Using a Rax-Cre driver line and a Tet3 floxed mouse, we generated conditional mutant (cMut) mice lacking part of the Tet3 catalytic domain in retinal progenitors and their progeny. Mice have been characterized using a variety of techniques ranging from immunohistochemistry with cell specific markers, ultrastructural analysis of cell morphology by electron microscopy (EM) and electroretinography (ERG) to assess retinal functionality.

Results: Cone photoreceptors, responsible for diurnal and color vision, are of two subtypes in the mouse retina. S-cones, sensitive to blue light, have an increasing dorsal to ventral gradient. M-cones, responsive to green light, are more evenly distributed, although less abundant in the ventral part. Except for the dorsal retina with a prevalence of M-cones, many cones are hybrid and express both S and M photopigments. Preliminary results show that cMut mice have an increased number of cones and altered cone subtype distribution. In fact, S opsin-positive cones are higher in numbers and lack the characteristic dorsal to ventral gradient. As a consequence, all the cones of Tet3 mutant mice appear to be hybrid. The increased cone number is accompanied by a reduction in the total cell number of the inner nuclear layer affecting the functionality of the retina and the propagation of the light stimulus as shown by ERG b-wave measurements. This altered functionality seems not be linked to missing or defective synaptic components as revealed by EM analysis.

Conclusions: These results suggest that Tet3 has a selective role in retinal development and/or lineage specification. Elucidating the mechanisms downstream of Tet3 will improve our understanding of retinal homeostasis under physiological and pathophysiological conditions.

CONTROL ID: 3709044

SUBMITTER (NAME ONLY): Charumathi Sabanayagam

TITLE: Transition probabilities of diabetic retinopathy and death in an Asian population with diabetes

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Sabanayagam, F. He, H. Hamzah, T. Wong, C. Cheng, G. Tan, Singapore Eye Research Institute, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|C. Sabanayagam, T. Wong, C. Cheng, G. Tan, The Ophthalmology & Visual Sciences Academic Clinical Programme (EYE ACP), Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To longitudinally examine the transitions in diabetic retinopathy (DR) severity over time and determine which state deteriorates rapidly in an Asian population with diabetes.

Methods: We analysed 20453 clinic visits by 9481 Chinese, Malay and Indian adults diagnosed with diabetes who attended the annual DR screening visits in primary care clinics as part of the Singapore Integrated Diabetic Retinopathy Screening (SiDRP) programme from 2010-2015 and linked to death data at Ministry of Health. DR was assessed from retinal photographs and graded for severity by professional graders. We applied a multistate Markov model to estimate the annual transition probabilities between states (none, mild, moderate and severe/proliferative DR and the absorbing state, death), and the expected waiting time in each state (sojourn time) adjusted for risk factors including age, sex, systolic blood pressure (SBP), duration of diabetes, HbA1c, and body mass index (BMI).

Results: The median time between assessments was 12 months, and the majority of patients had at least 3 assessments. The annual transition probability from none-to-mild, mild-to-moderate and moderate-to- severe in the adjusted model were 6.1%, 7.0% and 19.1% and of death from each state were 1.2%, 2%, 19.1%, and 29.8%; mean time spent in each state (sojourn time) were 8.2, 0.8, 0.8 and 2.2 years. While 0.1% progressed from none-to-severe DR, 1.9% progressed from mild-to-severe DR; Probability of regression from mild-to-none, moderate-to-mild and severe-to-moderate DR were: 55.4%, 17.1% and 4.3%. While 12.4% regressed from moderate-to-none, 0.4% regressed from severe DR-to-none. Higher levels of HbA1c and SBP were associated with progression of none-mild and mild-moderate DR and duration of diabetes with no-mild and moderate to severe/proliferative DR. Lower levels of HbA1c were associated with regression from mild-to-none and moderate-to-mild; higher BMI with mild-to-none DR.

Conclusions: Our results suggest that the mean time to develop mild DR was long (~8 years), while transitions from mild or moderate states were faster within a year. Moderate/above DR greatly increases the probability of progression and death as compared to mild DR/below. HbA1c was associated with both progression as well as regression.

CONTROL ID: 3709046

SUBMITTER (NAME ONLY): Bjorn Drobe

TITLE: Influence of wearing time on myopia control efficacy of spectacle lenses with aspherical lenslets

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Within the MyCAL (Myopia Control with Aspherical Lenslets) clinical trial, to analyse the impact of wearing time on the myopia control efficacy of two spectacle lenses with aspherical lenslets, compared with single vision lenses (SVL).

Methods: In this prospective, randomized, double masked clinical trial, 170 children were randomized to wear either spectacle lenses with highly aspherical lenslets (HAL), spectacle lenses with slightly aspherical lenslets (SAL) or control SVL. Daily wearing time of glasses was assessed over two years through 6-monthly questionnaires. Average wearing time over the full duration of the clinical trial in hours per day (WT) was used for analysis. Influence of WT on change of spherical equivalent of cycloplegic autorefraction (SER) and axial length (AL) were analysed for two WT categories: full-time wearers (at least 12 hours per day, every day) and part-time wearers (less than 12 hours per day or not every day) and through cumulative minimum WT.

Results: WT was analysed for the 157 children who completed all 6-monthly visits. For SVL, full- (n=34)/part-time (n=16) wearing did not impact change in SER (p=0.76) or AL (p=0.92). Myopia progression and axial elongation decreased with increasing minimum WT for HAL and SAL. For both HAL WT groups, SER and AL progression were significantly slower than for SVL ($p<0.01$). HAL full-time wearers (n=32) experienced significantly higher myopia control efficacy compared with SVL group for both SER (0.99±0.12D) and AL (0.41±0.05mm) than HAL part-time wearers (n=22, 0.54±0.15D, p=0.01; 0.26±0.07mm, p=0.03 respectively). For SAL, myopia control efficacy was comparable for full- (n=30, SER: 0.51±0.13D; AL: 0.23±0.06mm) and part-time wearers (n=23, SER: 0.31±0.15D, p=0.11; AL: 0.12±0.06mm, p=0.10).

Conclusions: Myopia control efficacy increased with wearing time for spectacle lenses with highly aspherical lenslets, reaching 0.99D less myopia progression and 0.41mm less axial elongation over two years for full-time wearers.

CONTROL ID: 3709047

SUBMITTER (NAME ONLY): Frank van der Heide

TITLE: A higher level of glycemia, high alcohol consumption, lower adherence to a healthy diet, and use of antihypertensive medication, an index of history of hypertension, are cross-sectionally associated with lower RNFL thickness in a population-based study – The Maastricht Study

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. van der Heide, S. Mokhtar, R. Henry, A. Kroon, P. Dagnelie, S. Eussen, M. Schram, C. van der Kallen, M. van Greevenbroek, N. Schaper, C. Stehouwer, CARIM, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|F. van der Heide, S. Mokhtar, R. Henry, A. Kroon, P. Dagnelie, C. van der Kallen, M. van Greevenbroek, N. Schaper, C. Stehouwer, Internal Medicine, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|A. Khanna, department of Ophthalmology, Sharp sight eye hospital, New Delhi, INDIA|T. Berendschot, C.A. Webers, Ophthalmology, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|T. Berendschot, M. Schram, C.A. Webers, MHeNS, Universiteit Maastricht Faculty of Health Medicine and Life Sciences, Maastricht, Limburg, NETHERLANDS|J. Schouten, Ophthalmology, Canisius Wilhelmina Ziekenhuis, Nijmegen, Gelderland, NETHERLANDS|H. Savelberg, NUTRIM, Universiteit Maastricht Faculty of Health Medicine and Life Sciences, Maastricht, Limburg, NETHERLANDS|H. Savelberg, Movement sciences, Universiteit Maastricht Faculty of Health Medicine and Life Sciences, Maastricht, Limburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy is preceded by subtle neurodegenerative changes, including retinal nerve fiber layer (RNFL) thinning. Presently it remains unclear whether potentially modifiable risk factors may be determinants of RNFL thinning. We investigated, using prospectively-collected cross-sectional data from an observational cohort study, whether potentially modifiable risk factors were associated with RNFL thickness.

Methods: We used cross-sectional data from The Maastricht Study (up to 5,255 participants,49.0% men,mean±SD age59.5±8.7 years, and 23.3% with type 2 diabetes [T2D; T2D oversampled by design]). We assessed RNFL thickness with optical coherence tomography (i.e. mean peripapillary RNFL thickness of both eyes). We used linear regression analyses with adjustment for potential confounders; and tested for interaction by sex and T2D (yes/no).

Results: After full adjustment, greater HbA1c and lower healthy diet score were significantly associated with lower RNFL thickness (per SD, standardized beta [95% CI], -0.05 [-0.08; -0.02] and -0.03 [-0.06; -0.00], respectively); high (>2 units/ day for men or >1 unit/day for women) versus none alcohol consumption was significantly associated with lower RNFL thickness (-0.09 [-0.18; -0.00]); antihypertensive medication use was significantly associated with lower RNFL thickness (-0.12 [-0.19; -0.05]); and greater 24-hour ambulatory systolic blood pressure and greater total cholesterol were, respectively, significantly associated with lower and greater RNFL thickness in individuals with, but not in individuals without, T2D (in individuals with T2D, -0.06 [-0.13; 0.00]; 0.09 [0.03; 0.16]). Smoking,cardiorespiratory fitness, accelerometer-assessed physical activity, and waist circumference were not associated with RNFL thickness. Sex did not modify associations under study.

Conclusions: This population-based study found that a higher level of glycemia, lower adherence to a healthy diet, high alcohol consumption, and a history of hypertension, estimated from the use of antihypertensive medication, were

associated with a lower RNFL thickness. Hence, early-stage prevention of these adverse factors may contribute to the prevention of RNFL thinning, and, ultimately, diabetic retinopathy.

CONTROL ID: 3709048

SUBMITTER (NAME ONLY): Jan Kremers

TITLE: ERG signals elicited by temporal white noise in macaques

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Kremers, A. Aher, Dept of Ophthalmology, University Hospital Erlangen, Erlangen, GERMANY|N. Parry, Vision Science Centre, Manchester Royal Eye Hospital, Manchester, Manchester, UNITED KINGDOM|N.B. Patel, L.J. Frishman, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study ERGs elicited by temporal white noise (TWN) stimuli that excite only the L- or the M-cones or all photoreceptors in concert.

Methods: ERGs were recorded from the right eyes of five anesthetized macaques (Macaca mulatta ; three males, two females). Stimuli were created with a 4-colour ganzfeld stimulator. The stimuli were luminance (22% contrast), selective L-cone excitation and selective M-cone excitation (both 22% cone contrast). Cone isolating stimuli were generated using triple silent substitution. The stimuli had equal amplitudes at all frequencies between 0 and 512 Hz. Inverse Fourier transform resulted in a TWN stimulus with a Gaussian luminance or cone excitation distribution. All ERG measurements were performed twice to study reproducibility and correlations.

Results: The repeated measurements showed that the measured ERGs were reproducible. The responses to identical stimuli measured in different animals were correlated but less strongly as the responses to the same stimuli in the same animals. A cross-correlation between ERG responses and stimuli resulted in impulse response functions (IRFs) for luminance stimuli that were similar to flash ERGs in having an a-wave-like negativity and a b-wave-like positivity, but lacked oscillatory potentials and showed a late (after 40 ms) positive wave. L-cone driven IRFs were similar to luminance IRFs albeit smaller. The a- and b-wave-like components were absent in the M-cone driven IRFs. The M-cone driven late positivity was of similar amplitude as those obtained for L-cone isolating stimuli.

Conclusions: ERGs elicited with temporal white noise are reproducible. The a-like and b-like waves of the luminance IRF are L-cone dominated as previous seen for ERG responses in humans and macaques to sine wave, square wave and sawtooth stimuli. A late positive wave, present in luminance, L- and M-cone IRFs but not visible in conventional flash ERGs may provide a new measure of retinal function.

CONTROL ID: 3709051

SUBMITTER (NAME ONLY): Mary Labowsky

TITLE: Specific MRI Sequences for Optic Nerve Improve Diagnosis and Reveal Clinical Associations in Acute Optic Neuritis and Chronic Optic Neuropathy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Labowsky, Neuro-Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|C. Sanders, P. Belani, B. Delman, M. Schecht, M.J. Kupersmith, Mount Sinai Health System, New York, New York, UNITED STATES|H. Sharma, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Application of tailored MRI sequences should improve diagnostic accuracy in acute optic neuritis (ON) and chronic optic neuropathy. This retrospective, observational study compares short tau inversion recovery (STIR) and 3D-fluid attenuation inversion recovery (FLAIR) in acute and chronic ON and correlates radiographic metrics to vision function and optical coherence tomography (OCT) structure.

Methods: Orbital MRIs of 57 patients (56% female; mean age 50.8±16.7 years) with acute ON (n=15), chronic ON (n=31), or clinically normal (n=11) were retrospectively analyzed by masked neuroradiologists (2) and neuro-ophthalmologist (1) for presence of lesion, lesion signal normalized to normal frontal white matter, and lesion length. Clinical data included visual acuity (VA), OCT retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness, and automated perimetry mean deviation (MD) at presentation and outcome.

Results: The diagnostic accuracy per reader for acute and chronic ON were 73-100% and 58-71%, respectively, for STIR and 87-100% and 48-71%, respectively for 3D-FLAIR. Diagnostic accuracy for chronic ON was lower than acute ON for one reader on STIR and both readers on 3D-FLAIR ($p=0.02$). Average ROI of acute and chronic ON lesions were higher than clinically normal cases on STIR ($p=0.01$ and $p<0.01$, respectively) and 3D-FLAIR ($p=0.07$ and $p=0.08$, respectively). Presenting LogMar VA for acute ON correlated with mean lesion length ($r=0.55$) and ROI ($r=0.54$) on STIR ($p<0.05$). The mean lesion length on STIR correlated to presenting ($r=-0.67$) and final ($r=-0.92$) GCL in acute ON ($p<0.01$) and to RNFL ($r=-0.44$) and GCL ($r=-0.48$) in chronic ON cases ($p<0.05$). In acute ON, the mean lesion length on FLAIR correlated with the presenting GCL ($r=-0.69$, $p<0.01$); and the outcome GCL with the mean lesion ROI on STIR ($r=-0.67$, $p<0.05$). No MRI features correlated with final VA or MD for acute or chronic ON.

Conclusions: 3D-FLAIR and STIR have similar detection rates for ON lesions, but FLAIR had slightly greater sensitivity for acute ON. Use of a normalized quantitative ROI increased diagnostic accuracy for detecting abnormal signal. In acute ON, longer lesions and increased signal on STIR corresponded to worse presenting VA and greater structural loss reflected by OCT GCL and RNFL thinning, suggesting MRI might help predict outcome neuronal loss in acute ON.

CONTROL ID: 3709055

SUBMITTER (NAME ONLY): Bernhard Baumann

TITLE: Four-Dimensional OCT Imaging of Pulsatile Tissue Deformation Dynamics in the Mouse Retina and Choroid

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal tissue structures are subject to rhythmic movements caused by pulsatile ocular blood flow. Alterations of ocular pulsatility and mechanical tissue properties have been associated with some of the most sight-threatening eye diseases. Currently available methods for the visualization and quantitative assessment of fundus pulsations have been limited to one or two spatial dimensions. Here we present volumetric imaging of pulsatile tissue dynamics in the murine retina and choroid based on 4D optical coherence tomography (OCT).

Methods: A spectral-domain OCT ophthalmoscope optimized for rodent retinal imaging was used to investigate pulsatile motion patterns in the posterior eyes of mice. The system operated in the 840-nm wavelength band and provided an axial resolution of 3.8 µm. Volumetric OCT data sets comprising 2,000 B-scans across a field of view of roughly 1 mm x 1 mm were acquired in the posterior eyes of wildtype mice and a mouse model of retinal neovascularization. An analysis of the complex-valued OCT data was performed in order to detect changes of the signal phase between successive B-scans. Using the photoreceptor layer as a reference, tissue deformation patterns were visualized and quantified with high volumetric resolution.

Results: Pulsatile tissue displacements in the ±20 µm/s range were visualized and charted with a frame rate of 130 Hz. Volume scans enabled sampling motion patterns during the murine pulse cycle with ~15 volumes per cycle. Pronounced pulsatile displacements in the in vivo imaging data were localized in the vicinity of retinal vessels as well as in the choroid (see Figure 1). Increased pulsatility was observed in the outer retina of the mouse model at locations exhibiting high reflectivity associated with neovascular lesions.

Conclusions: The concept of fundus elastography (FUEL) was demonstrated based on high-speed 4D-OCT imaging and proved capable of visualizing subtle tissue deformation dynamics related to ocular pulsation. This high-resolution retinal elastography technique may enable a new paradigm of OCT based measurements and image contrast.

CONTROL ID: 3709056

SUBMITTER (NAME ONLY): Shuya Deng

TITLE: Strain dependent influence of UVA-based corneal crosslinking (CXL) on corneal immune cell populations

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Deng, W. Zhang, A.P. Schönberg, F. Bock, C. Cursiefen, Department of Ophthalmology, Universitat zu Koln, Köln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Corneal collagen crosslinking (CXL) is an established technique to halt the progression of keratectasia and was recently shown to also regress mature pathologic corneal blood and lymphatic vessels in inflamed corneas. However, the effect of UVA-based CXL on corneal immune cells remains unknown. This study investigates the early and strain dependent influence of CXL on corneal immune cell populations.

Methods: After corneal abrasion, BALB/c mice and C57BL6/N mice received a 9 minutes topical application of 0.1% riboflavin in 20% dextran phosphate sodium followed by a 9 minutes UVA irradiation (370 nm, 3 mW/ cm^2) using the CCL- vario CXL system. The corneal limbus was protected by a light-preventing plastic shield. Fresh eyeballs were collected at day 1, 4, 7 (each n=5) after CXL for cryosection. Stainings for F4/80, MHC-II, CD11c were analyzed with a fluorescence microscope.

Results: A significantly reduced amount of $F4/80^+$ cells was observed in BALB/c mice on day 1 ($p=0.012$) and day 4 ($p<0.001$) after treatment compared to C57BL6/N mice. $F4/80^+$ $MHC\text{-}II^+$ cells in BALB/c ($p<0.001$, compared to BALB/c naïve mice) significantly went down at day 1 after CXL, whereas C57BL6/N mice showed a significant decrease ($p=0.014$, compared to C57BL6/N naïve mice) only at 4 days after CXL. $F4/80^+$ $MHC\text{-}II^+$ cells in BALB/c mice reversed to baseline on day 7. Interestingly, $F4/80^+$ $MHC\text{-}II^+$ cells in C57BL6/N mice remained at very low levels on day 7 after CXL.

On day 1 also the percentage of $CD11c^+$ MHC -II^+ mature dendritic decreased significantly in BALB/c group (23.76%, $p=0.006$) compared to naïve mice (57.23%) but not in the C57BL6/N group (43.55%). On day 7 the proportion of mature dendritic cells increased in both the BALB/c group (91.02%) and C57BL6/N group (86%) equally.

Conclusions: Our results show a strain dependent influence of CXL on corneal immune cell populations in BALB/c and C57BL/6N mice. This suggests individually different immune responses of patients after UVA-based CXL treatment and sheds light on the heterogenous outcomes of this treatment strategy.

CONTROL ID: 3709057

SUBMITTER (NAME ONLY): Paolo Silva

TITLE: Automated machine learning (AutoML) model for diabetic retinopathy (DR) image classification from ultrawide field (UWF) retinal images

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.S. Silva, J. Cavallerano, M. Ashraf, C.P. Jacoba, D. Doan, F.S. Wang, J.K. Sun, L.P. Aiello, Beetham Eye Institute, Joslin Diabetes and Endocrinology Research Center, Boston, Massachusetts, UNITED STATES|P.S. Silva, J. Cavallerano, M. Ashraf, J.K. Sun, L.P. Aiello, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|D. Lewis, Estenda Solutions Inc, Conshohocken, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To create and validate automated deep learning models for DR that are trained on UWF images obtained from a DR teleophthalmology program.

Methods: AutoML Vision (Google) models were generated based on nonmydriatic UWF images from the Joslin Vision Network (JVN). Image labeling was based on standardized evaluation by the JVN reading center following the clinical Early Treatment Diabetic Retinopathy Study Severity Scales (ETDRS-SS). Images for the initial model were split 8-1-1 for training, validation and testing to detect referable DR [(refDR), defined as moderate nonproliferative DR (NPDR) or worse]. External testing of the autoML model was performed using a published image set with matching nonmydriatic UWF, clinical exam and standard 7-Field ETDRS photos (N=192 eyes). Sensitivity and specificity (SN/SP) for refDR were calculated. Based on published FDA requirements, prespecified performance thresholds were defined at 0.85/0.825 for SN/SP.

Results: Distribution of ETDRS-SS in training set (N=3,999 images): no DR 33.8%, mild 16.2%, moderate 29.4%, severe NPDR 5.0%, PDR 16.6%, RefDR was present in 50.0% of images. Area under the precision-recall curve (AUPRC) was 0.947 (figure 1). The model's overall accuracy for RefDR was 92.2%. External testing set distribution of ETDRS-SS by UWF/clinical exam/ETDRS photos: no DR 10.9/8.9/12.5%, mild NPDR 22.9/18.7/22.9%, moderate NPDR 33.8/33.8/29.7%, severe NPDR 10.9/12.0/8.3%, PDR 21.3/26.6/26.6% with RefDR was present in 66.1/72.4/64.6%. SN/SP for refDR on the external test set was 0.79/0.83 for UWF, 0.76/0.90 for clinical exam, 0.79/0.81 for ETDRS photos. Table 1 shows a comparison with reported metrics from FDA approved and UWF algorithms.

Conclusions: Despite the increasing adoption, there are no commercially available artificial intelligence DR algorithms for UWF images. This study demonstrates feasibility of using autoML models for the identification of refDR from UWF obtained in a teleophthalmology program. Despite the large image size and complexity of UWF compared to standard retinal images, the performance approaches published diagnostic accuracy metrics of commercial models used for DRSP. This proof of concept use emphasizes the broad future potential by allowing programs with large image datasets to address emerging clinical needs with AI applications

CONTROL ID: 3709058

SUBMITTER (NAME ONLY): Ester Carreno

TITLE: Retinal findings and vessel caliber measurements in admitted patients with COVID-19

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The main purpose of this study is to describe the fundoscopic alterations and retinal vessel caliber measurements in SARS-CoV2 positive patients admitted to a tertiary referral hospital in Madrid (Spain) and to correlate the retinal vessel caliber with the severity of the disease.

Methods: A single-center cross-sectional observational study to document the retinal vascular findings in SARS-CoV2 patients admitted to a tertiary Hospital during the first wave in Madrid, Spain. Fundoscopy was performed in both eyes (when possible) with a manual retinography Zeiss Visuscout 100. All patients signed a consent form to participate in the study. Pharmacological mydriasis prior to retinography was achieved by applying one drop of tropicamide 1% in each eye. Data collected included previous medical and ophthalmic history, prescribed medical and postural treatments, and laboratory findings at the time of admission. All cases were classified according to their outcome as per the WHO clinical progression scale on a scale of 0 to 10, with being 0 the uninfected state and 10 being death. All the retinal images were analysed by two medical retina experts independently. Retinal vessel calibers were measured by a single masked grader using a validated research software with high reproducibility.The relationship between the WHO clinical progression scale and retinal vessel caliber was assessed by Kruskal-Wallis test for independent samples.

Results: In total, 81 patients and 154 eyes were included in the study. The fundus retinal assessment disclosed signs of hypertensive retinopathy in 8 right eyes (OD) (8/77) and 9 left eyes (OS) (9/77); vascular tortuosity was present in 13 OD (13/77) and 13 OS (13/77); age-related macular degeneration was found in 13 OD (13/77) and 12 OS (12/77); myopic retinopathy in 3 OD (3/77) and 3 OS (3/77); finally incidental choroidal nevi were found in 4 OD (4/77) and 2 OS (2/77). The retinal microvascular caliber assessment was performed in a total of 72 eyes from 72 subjects, the right eye was used in 61 cases, left eye in the rest. There was no statistically significant difference according to vessel caliber and WHO outcome score.

Conclusions: COVID-19 has been linked to an increase risk of cardiovascular events. However, we could not find a correlation among retinal vascular findings and clinical outcome in our cohort.

CONTROL ID: 3709060

SUBMITTER (NAME ONLY): SUDIPTA CHAKRABORTY

TITLE: A genome wide copy number variation analysis reveals NLGN1 is overrepresented in primary angle closure glaucoma patients

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. CHAKRABORTY, C. Das, T. Rachel. V, R. Kaur, P. Das, N. Biswas, M. Acharya, National Institute of Biomedical Genomics, Kalyani, West Bengal, INDIA|

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ABSTRACT BODY:

Purpose: Primary angle closure glaucoma (PACG) is one of the leading causes of blindness worldwide with a complex genetic aetiology. For complex genetic disorders, copy number variation (CNV) is anticipated to play an essential role in disease vulnerability. The impact of CNVs on PACG has not been studied yet. In India, ~30% of people show narrow angles but 0.5-1% of people actually develop PACG. To exclude heterogeneity, we compared genome-wide CNVs between older (age ≥60 years) anatomically suspects (PACS) showing narrow angle <15° and PACG individuals having age ≤50 years. In doing so we would therefore be able to identify genes that are involved in the glaucomatous neurodegeneration, which we believe will be separate from genes controlling angle-related parameters.

Methods: Genome-wide genotyping was performed on 148 PACG (40.15 ± 6.62 years) and 92 PACS (68.03 ± 7.56 years), followed by CNV calling using the PennCNV package's Hidden Markov model-based approach. For all deletions and duplications, CNV frequencies were analyzed statistically through the Wilcoxon test between PACG and PACS. The significant genomic regions were subjected to validation by qPCR and subsequently, bioinformatic analyses were carried out to determine the role of PACG pathophysiology.

Results: There is no significant deletion was found between two groups but in amplification, we discovered that NLGN1 genic region (Gr37Chr3; bp:173239453-173246813) was overrepresented in PACG (P = 0.008413). That genic area of NLGN1 was successfully validated in qPCR by SYBR green assay. In PACG, the mean Ct values were significantly lower than in PACS (P= 0.079).NLGN1 is highly expressed retinal ganglion cells (PLIER: 44.3257). Gene network analyses showed that the NLGN1 are associated with many neurodegenerative and eye diseases. Moreover, genotype-phenotype correlation revealed that NLGN1 is linked to the assessment of a greater optic-cup area that is positively correlated with glaucomatous neurodegeneration.

Conclusions: NLGN1 is involved in regulating the activity of NMDA receptors. Amplification of NLGN1 may promote more synaptic clustering of NMDARs in retinal ganglion cells (RGCs). The overexpression of these NMDARs leads to mitochondrial dysfunction of the RGCs. That eventually leads to the death of RGCs and subsequent glaucomatous neurodegeneration.

CONTROL ID: 3709066

SUBMITTER (NAME ONLY): ruili qi

TITLE: Heterochromatin Represses Senescence-associated Secretory Phenotype Gene Expression in Senescent Retinal Pigment Epithelial Cells

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. qi, L. Gong, Q. Ke, X. zhu, W. Liu, D.W. Li, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Heterochromatin alterations is a hallmark of aging process. This study is aimed to investigate structure and distribution of heterochromatin on retinal pigment epithelial (RPE) cell premature senescence induced by oxidative stress exposure or X-ray irradiation, and to explore the effects of heterochromatin in regulating senescence-associated secretory phenotype (SASP) gene expression during RPE senescence.

Methods: Heterochromatin structure was assessed by confocal microscopy and transmission electron microscope. Genome-wide heterochromatin distribution was studied by chromatin immunoprecipitation (ChIP)-seq analysis. ARPE-19 cells were continually exposed to tert-Butyl hydroperoxide (t-BHP) or X-ray irradiation to induce cell senescence, which was confirmed by senescence-associated ß-galactosidase (SA ß-gal) staining, senescent-associated gene expression and RPE barrier function analysis. Chromatin structure on SASP gene locus was assessed by formaldehyde-assisted isolation of regulatory elements (FAIRE), and the occupancy of heterochromatin there was determined by quantitative ChIP (q-ChIP) analysis. Heterochromatin was disrupted by chaetocin treatment. Expression of inflammatory cytokines were examined by qRT-PCR and cytokine protein array.

Results: Heterochromatin mark H3K9me3 was enriched in SASP gene locus. A prominent nuclear peripheral heterochromatin loss was found in senescent RPE cells. Decreased chromatin compaction was detected in proinflammatory genes upregulated during RPE senescence. Disruption of heterochromatin led to robust upregulation of SASP genes.

Conclusions: Heterochromatin represses SASP gene expression during RPE senescence. Our data suggest a potential role for targeting heterochromatin in the treatment of retinal diseases related to RPE senescence, such as age-related macular degeneration (AMD).

CONTROL ID: 3709068

SUBMITTER (NAME ONLY): Rishi Singh

TITLE: Results of a Delphi consensus study of geographic atrophy (GA) diagnosis and current management

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.P. Singh, Cleveland Clinic Cole Eye Institute Beachwood, Beachwood, Ohio, UNITED STATES|W.M. Amoaku, Nottingham University Hospitals NHS Trust, Nottingham, Nottingham, UNITED KINGDOM|F.K. Chen, Centre for Ophthalmology and Visual Science, The University of Western Australia, Perth, Western Australia, AUSTRALIA|F.G. Holz, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|L. Kodjikian, Hopital de La Croix-Rousse Ophtalmologie, Lyon, Rhône-Alpes, FRANCE|C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|P. Joshi, Apellis Pharmaceuticals Inc, Crestwood, Massachusetts, UNITED STATES|F. Bandello, Ospedale San Raffaele Sede di San Raffaele Turro, Milano, Lombardia, ITALY|J.M. Ruiz-Moreno, Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: With emerging therapies for GA, little is known about how GA is evaluated. A Delphi survey was conducted to determine consensus among healthcare professionals (HCPs), specifically retina specialists, on GA diagnosis and management.

Methods: Initial consensus was developed by 8 retina specialists, serving as a steering committee, with an electronic questionnaire (round 1) sent to 175 randomly selected retina specialists globally. In round 2, 125 HCPs (selected from the same respondents) were probed further on question areas that did not achieve consensus in round 1. Questions were open ended, multiple choice, rank order, level of agreement (Likert scale). Consensus (defined as ≥75% agreement for a response) was sought in areas relating to GA diagnosis and current patient management.

Results: Reading difficulties (93% agreement) and impaired ability to recognize faces (84%) are the most elicited symptoms during an initial clinical visit by HCPs. The most often used functional measures for GA are best corrected visual acuity (94%) and the Amsler grid (86%). Optical coherence tomography (OCT) is the most regularly used imaging modality (98%), followed by fundus autofluorescence (81%), and color fundus photography (77%). OCT was ranked as the first or second most important imaging modality (out of 6) for GA diagnosis and monitoring by 85% and 82% of HCPs, respectively. There is consensus among HCPs (76%) that foveal involvement is the most important variable for determining GA prognosis. Impact on daily living (89%) and visual-aid options (75%) are important topics

to discuss with newly diagnosed patients. Most (90%) felt a GA treatment option would have a significant positive effect on patient quality of life. Low vision aids (90%), smoking cessation (86%), and vitamin supplementation (75%) are thought to be beneficial for GA. Active neovascular age-related macular degeneration (in either eye) was selected as the most common circumstance requiring a patient with GA to be followed more closely (76%). Most (82%) of HCPs agreed that patients with choroidal neovascularization controlled by anti-vascular endothelial growth factor therapy can continue to experience vision loss due to atrophic lesions.

Conclusions: There was agreement among HCPs that GA is a significant burden, meriting close management. In lieu of treatment options, HCPs also agreed on general clinical management approaches.

CONTROL ID: 3709071

SUBMITTER (NAME ONLY): Michelle Grunin

TITLE: Spatial modeling of variants in complement genes associated with age-related macular degeneration

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Grunin, E. Palmer, B. Jin, J.L. Haines, W.S. Bush, Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|M. Grunin, Braun School of Public Health and Community Medicine, Hebrew University of Jerusalem, Jerusalem, Jerusalem, ISRAEL|E. Palmer, B. Jin, J.L. Haines, W.S. Bush, Cleveland Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|D. Rinker, J.A. Capra, Department of Biological Sciences, Vanderbilt University, Nashville, Tennessee, UNITED STATES|C. Moth, Center for Structural Biology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|J.A. Capra, Department of Biomedical Informatics, Vanderbilt University, Nashville, Tennessee, UNITED STATES|A.I. Den Hollander, AbbVie Inc, North Chicago, Illinois, UNITED STATES|S. de Jong, Department of Ophthalmology, Donders Institute for Brain, Cognition, and Behavior, Radboud University Medical Center, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Genetic variants in complement genes are associated with age-related macular degeneration (AMD). However, the functional impact of the majority of missense variants is unknown. We evaluated spatial placement on protein structure, using the International AMD Genomics Consortium(IAMDGC) data(16,144 cases/17,832 controls).

Methods: The IAMDGC data was imputed using the HRC, with a 30% improvement over the original. Missense variants were extracted for CFH,CFI,CFB,C9,& C3 genes. We evaluated variants' placement in protein structure space: spatial proximity in the protein, and AMD association. We compared the spatial proximity of known AMD variants(KAV) to unassociated, assessed variants' likelihood of protein destabilization, and performed gene-based testing. Gene-based tests included: all variants; variants near KAV; and variants predicted to destabilize proteins. SKAT testing was used to confirm spatial associations. Logistic regression on KAV in CFI identified variants leading to >50% reduction in protein expression compared to wild type in vitro. These results were compared to functional impact scores, showing if a variant has a functional impact genome wide.

Results: Multiple destabilizing variants were found. Gene-based tests using all variants identified significant associations of the C3,C9,CFB,andCFH genes with AMD risk after controlling for age and sex($P=3.22\times10^{-5}$;7.58×10^{-6};2.1×10^{-3};1.2×10^{-31}). Filtering on protein destabilization and SKAT-O tests found several missense variants in CFI and CFH associated with AMD(P=CFH:0.05,CFI:0.01, threshold<0.05).We identified spatial associations for AMD risk in structures for C3,C9,CFB,CFH,and CFI at P<0.05. Both structural and functional scores were predictive of reduced CFI protein expression, and ROC curve analyses suggest structural scores are a better predictor(AUCs of 0.76 and 0.69).

Conclusions: We demonstrate missense variants in complement genes cluster spatially and are associated with AMD status. Using this method, we can identify CFI and CFH variants previously classified as unknown significance, but are predicted to destabilize proteins. This method can predict in-vitro tested CFI protein expression changes, indicating that it is a useful tool for selecting variants for functional follow-up. Further investigation is needed to validate the models for additional variants in other complement and AMD-associated genes.

CONTROL ID: 3709074

SUBMITTER (NAME ONLY): Alicia Canalejo

TITLE: Separate Attention for Dark and Bright Structures in a Deep Learning Framework for Diabetic Retinopathy

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Canalejo, M. López Gálvez, Ophtalmology, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|

Commercial Relationships Disclosure: Alicia Canalejo: Commercial Relationship: Code N (No Commercial Relationship) | Maria Isabel López Gálvez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Manual analysis of fundus images in diabetic retinopathy screening programme is time consuming due to the large number of patients and limited resources. We propose an end-to-end deep learning framework for automatic Diabetic Retinopathy (DR) grading.

Methods: To perform the experiments, we used the largest public retinal image dataset provided by EyePACS for the Diabetic Retinopathy Detection with 35,126 images meant for training and 53,576 for testing and included a real-world scenario with images affected by noise. We randomly selected 10% of the images and used 18,860 images for training, 2,096 images for validation and 32,017 for testing. Only images with enough quality for analysis underwent the DR grading stage. 35,729 images were discarded and, therefore, 52,973 images were used for subsequent analysis.

The approach done by our group is based on an attention mechanism which performs a separate attention of the dark and the bright structures of the retina. The framework includes an image quality assessment stage and additional deep learning-related techniques such as data augmentation, transfer learning and fine-tuning. The architecture Xception as feature extractor and the focal loss function to deal with data imbalance was used. The Kaggle DR detection dataset was used for method development and validation.

Results: The Quadratic Weighted Kappa (QWK) achieved with the proposed method was 0.78 on the test set, which corresponds to 83.7% accuracy. However, when dealing with class unbalance, QWK is dominated by the most representative classes, which is the class of No DR in our dataset. This is the reason why the confusion matrix is also important to evaluate the results.

First, the class of No DR was detected with high accuracy: only 2.9% (706 out of 23,962) of the R0 images were over-diagnosed. More importantly, only 0.0005% (12 out of 23,962) of them were rated as severe or very severe. Conversely, the class Mild DR was easily misguided with the classes no DR and mild to moderate. Finally, poor detection accuracy for class R4 was obtained.

Conclusions: Our results suggest that our framework could be a diagnostic aid for the early detection and grading of DR. Further validation and comparative studies are needed.

CONTROL ID: 3709075

SUBMITTER (NAME ONLY): Therese Cronin

TITLE: Generation of a compound heterozygous ABCA4 phenotype in a Stargardt rat model for the G1961E mutation

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Cronin, O. Adjali, Nantes University, Nantes, Pays de la loire, FRANCE|T. Cronin, L. Libeau, J. Demilly, O. Adjali, Inserm U1089, Nantes, Pays de la loire, FRANCE|L. Libeau, Centre Hospitalier Universitaire de Nantes, Nantes, Pays de la Loire, FRANCE|S. Remy, I. Anegon, Inserm UMR_S 1064, Nantes, FRANCE|M. Croyal, Inserm UMR_1280, Nantes, Pays de la loire, FRANCE|

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ABSTRACT BODY:

Purpose: We investigated the most common mutation underlying a mild to moderate Stargardts disease (STGD1) phenotype in a rat model carrying the paralogue to the ABCA4 G1961E mutation. By crossing with another rat line that lacks ABCA4 protein we reveal a phenotype in line with that described for STGD1 patients carrying this mutation in compound heterozygosity. The model is used to test the potential of therapies such as the CFTR corrector Lumacaftor.

Methods: Following in silico modelling, the rat Abca4 gene was targeted for disruption by SpCas9 RNP microinjection into the pronucleus of intact Sprague-dawley rat zygotes in complex with a guide RNA targetting the nuclease to exon 42 of Abca4 as well as a 112-nt ssDNA oligo carrying the required G-to-E substitution to generate the knock-in Abca4$^{E/E}$ line. The functional consequences of the mutation on ABCA4 protein purified from ocular extracts was tested by mass spectrometry, ATPase and flippase assay in the presence or absence of lumacaftor. The ocular phenotype was assesed by in vivo imaging and ERG.

Results: Surprisingly, an increase in the protein levels was determined in the retinas of Abca4$^{E/E}$ rats including an increase in a residual mislocalised cytosolic fraction. Bisretinoid analysis shows an increase of 2-fold and 3.5-fold in A2E dimers for the Abca4$^{E/E}$ and Abca4$^{E/-}$ lines respectively. The structure and function of the knockin Abca4$^{E/E}$ rat retina is normal while being moderately impacted in the double transgenic Abca4$^{E/-}$ rat. At the same time ABCA4 purified from Abca4$^{E/E}$ rat eyes and reconstitued onto artificial liposomes shows a drop of ATP hydrolysis and of flippase activity across the membrane in the presence of an excess of retinal. This can potentially be rescued by the small molecule corrector VX-809.

Conclusions: The Abca4$^{E/E}$ and Abca4$^{E/-}$ rats display a disruption in retinoid metabolism that make them suited to testing novel STGD1 therapies that aim at restoring normal ATPase function. One such therapy investigated here using these novel models is the CFTR small molecule corrector VX-809. Changes in ATPase activity of the ABCA4 protein in the Abca4$^{E/E}$ rat retina can be corrected through this approach.

CONTROL ID: 3709077

SUBMITTER (NAME ONLY): Josephine Nguyen

TITLE: Increased sensitivity of SF3B1 mutated uveal melanoma by spliceosome inhibition

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Nguyen, W. Drabarek, A. Leeflang, T. Brands, N. van der Horst, E. Medico-Salsench, D. Paridaens, E. Kilic, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Nguyen, W. Drabarek, A. Leeflang, T. Brands, N. van der Horst, E. Medico-Salsench, A. de Klein, E. Brosens, Clinical Genetics, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|T. van den Bosch, R. Verdijk, Pathology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|R. Verdijk, Pathology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|H. van de Werken, J. van Riet, Cancer Computational Biology Center, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|D. Paridaens, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Effective treatment of uveal melanoma (UM) patients with metastatic disease is unfortunately not yet available. Twenty percent of UM harbors a mutation in splicing factor gene SF3B1, suggesting that an aberrant spliceosome function plays a vital role in tumorigenesis. Inhibiting the spliceosome could prevent formation of aberrant transcripts. Splicing inhibitors (e.g. E7107) have been shown to exploit the preferential sensitivity of spliceosome compromised cells to these compounds. E7107 targets the SF3B subunit 1 and interferes with splicing by binding non-covalently to the SF3B subunit of the U2 snRNP complex. This prevents the U2 snRNP complex to bind to the pre-mRNA branch point. We have studied the effect of E7107 using UM cell lines (Mel202 and 92.1) and SF3B1 and BAP1 mutated primary ex vivo tumor slices.

Methods: Cell lines and ex vivo tumor slices were exposed for 24h to different concentrations of E7107. Tumor slices were stained with H&E, BAP1, MelanA, MIB-1 and caspase-3 antibodies. RNA was isolated for transcriptome and gene expression analysis. The type and number of alternative and aberrant transcripts was evaluated after exposure to E7107 with the MISO and FRASER analysis, respectively.

Results: Of twenty UM slices were included from September 2018-2021. E7107 exposed on UM cell lines showed decreased cell viability and increased apoptosis. This effect was significant in SF3B1 mutated cells compared to SF3B1 wild-type cells ($p = 0.0004$). A similar effect was observed in UM tumor slices. A decrease in MIB-1 (proliferation) positive cells and increase in caspase-3 (apoptosis) positive cells was observed. Furthermore, a decrease in mainly aberrant transcript formation was observed after E7107 exposure, especially at a concentration of 5 nM E7107. Ninety-seven transcripts had a decrease in aberrant transcripts after E7107 exposure, and this effect was mostly in exon skipping/intron retention.

Conclusions: This study demonstrates that SF3B1 mutated UM cells are more sensitive to splicing inhibitor E7107 compared to SF3B1 wild-type UM cells. Splicing inhibitors such as E7107 have therapeutic potential in SF3B1 mutated UM. Further research is recommended to assess and maximize the efficacy of E7107 as well as other potential splicing inhibitors in a therapeutic setting. An optimal dose should be determined with no serious adverse events but high enough for an increased effect in mutated cells.

CONTROL ID: 3709080

SUBMITTER (NAME ONLY): Shiama Balendra

TITLE: Trehalose is neuroprotective in in vitro and not neurotoxic in in vivo models of neurodegenerative disease

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.I. Balendra, L. Guo, V. Luong, S. Choi, D. Hill, E. Shamsher, M. Cordeiro, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|S.I. Balendra, M. Cordeiro, Western Eye Hospital, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Trehalose is a naturally occurring bioprotective disaccharide in non-mammalian species, allowing survival in unfavourable environments. It acts as a signalling molecule by activating autophagy and reducing cell death associated with apoptosis and inflammation. It is currently used clinically in ocular surface disease and is shown in vivo to be neuroprotective in neurodegenerative disease including Parkinson's Disease, Huntington's Disease and Amyotrophic Lateral Sclerosis. Its potential as a neuroprotective agent in glaucoma has also therefore been postulated. We hypothesised that trehalose could be demonstrated in vitro and in vivo to have a neuroprotective effect in neurodegenerative insults.

Methods: Trehalose solution was formed by dissolving trehalose in phosphate buffer solution. Toxicity of trehalose was assessed by investigating the cell viability of increasing concentrations of trehalose co-incubated with retinal cells. Cultured retinal cells were treated with insults of cobalt chloride, glutamate, paraquat and homocysteine. They were then co-incubated with either 70 mM trehalose solution or culture media only for 24 hours. Assessment of trehalose-mediated neuroprotection in vitro was achieved using an alamarBlue cell-viability assay. Direct application of trehalose to the optic nerve was used in an optic nerve crush mouse model of neurodegeneration with primary endpoints after 1 week of DARC (Detection of Apoptosing Retinal Cells) imaging and whole retinal RBPMS histology.

Results: Toxicity studies demonstrated that trehalose was not toxic to retinal cells up to its maximal solubility of 50 mg/mL (146 mM). 70mM trehalose was significantly neuroprotective in vitro in insults of cobalt chloride; IC50 trehalose 520.9μM vs vehicle 390.24μM ($p<0.05$); and in glutamate; IC50 trehalose 4.761mM vs vehicle 3.231mM ($p<0.01$). There was no significant neuroprotective effect in paraquat and homocysteine insults. Trehalose was not neurotoxic after 1 week of in vivo study and displayed no adverse effects systemically or locally.

Conclusions: This work demonstrates that trehalose is safe at high concentrations, is neuroprotective in vitro and not neurotoxic in vivo. Its efficacy in cobalt chloride and glutamate insults suggests a mechanism of action of trehalose which interferes with HIF-1α and calcium excitotoxicity pathways.

CONTROL ID: 3709081

SUBMITTER (NAME ONLY): Jaryi Lippek

TITLE: OCT segmentation of vitreous opacities inside a new silicone eye model for laser vitreolysis

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lippek, P. Dyrøy, M. Zabic, S. Johannsmeier, T. Ripken, Industrial and Biomedical Optics, Laser Zentrum Hannover e V, Hannover, Niedersachsen, GERMANY|M. Zabic, Hannover Centre for Optical Technologies, Leibniz Universitat Hannover, Hannover, Niedersachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Vitreous opacities, also known as floaters, are a common phenomenon in most people’s lives. For those who suffer from a more severe amount of these floaters, laser vitreolysis is one treatment option. But due to the manual handling of the procedure, there is a significant risk to misguide the laser into critical areas near retina or lens. To enhance the safety for the patient and simplify the handling for the physician we introduce a method to visualize and segment vitreous opacities via optical coherence tomography for an improved computer-guided procedure. Moreover, we present an easy method to build eye models for training and testing purposes in ophthalmology.

Methods: We developed a Swept Source OCT setup that is specialized to capture the vitreous volume inside a silicone model eye with a high volume per second rate. Our lens setup allows us to shift the laser focus through the whole eye, thus no change of the patient contact interface is necessary. Our custom-made software segments and visualizes floaters in the two- and three-dimensional space, optimized for the high-speed B-Scan rate of the OCT. To adapt the eye model to reality, we also developed a new procedure to create hollow silicone eyes that are suitable for clinical patient contact interfaces and can be filled with a viscous floater solution.

Results: The combination of a patient contact interface and our silicone eye model enables a clear view inside the eye for camera and OCT view. We are able to segment single B-Scans in under 10 milliseconds. The software highlights the floater material and provides suitable coordinates for the laser treatment. To prevent treatment near critical structures like retina and lens, their distance from the floater material can be measured.

Conclusions: We introduced a simple method to create silicone eyes that could be used for other training purposes in the field of ophthalmology as well. With our OCT setup and software, we present a way to improve the safety for the patient and simplify the procedure for the physician.

IGF- Vorhaben Nr: 21011 N; Feinmechanik, Optik und Medizintechnik; Funded by Federal Ministry for Economic Affairs and Energy based on a resolution of German Bundestag

CONTROL ID: 3709082

SUBMITTER (NAME ONLY): xingfei zhu

TITLE: Cytosolic DNA accumulated in senescent retinal and retinal pigment epithelium cells promotes inflammatory response.

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. zhu, R. Qi, Q. ke, W. Liu, D.W. Li, L. Gong, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: xingfei zhu: Commercial Relationship: Code N (No Commercial Relationship) | Ruili Qi: Commercial Relationship: Code N (No Commercial Relationship) | qin ke: Commercial Relationship: Code N (No Commercial Relationship) | Wei Liu: Commercial Relationship: Code N (No Commercial Relationship) | David Li: Commercial Relationship: Code N (No Commercial Relationship) | Lili Gong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Accumulation of cytosolic DNA has been found during cell senescence, a terminal cell cycle arrest and usually associated with pro-inflammatory responses. Aging is one of the highest risk factors for age-related macular degeneration (AMD) and other degenerative eye diseases. The functional significance of cytosolic DNA during retinal cell senescence is largely unexplored. Here, we are aimed to investigate the distribution, composition and pro-inflammatory effect of cytosolic DNA during RPE and photoreceptor cell senescence.

Methods: Hydrogen peroxide (H_2O_2, 600 μM, 2 h) was used to induce cell senescence in human RPE cell line ARPE-19 and in mouse photoreceptor cell line 661W. β-galactosidase (β-gal) analysis and Western blot (WB) analysis confirmed cell senescence upon oxidative stress. Immunofluorescence determines DNA leakage, DNA damage and enriched chromatin marker in cytoplasm. To determine the potential pro-inflammatory of cytosolic DNA, genomic DNAs were extracted from ARPE-19 cells with or without H_2O_2 exposure. The obtained DNA was then transfected into ARPE-19 cells. Inflammatory factors were determined by qRT-PCR analysis at 16 h post transfection.

Results: Oxidative stress leads to senescence of RPE and 661W cells. Leakage of nuclear DNA into cytosol and formation of micronuclei were evident in those senescent cells. The cytosolic DNA contains unrepaired fragment as evidenced by positive staining of DNA damage marker γH2AX, which is achieved by extrusion of chromatin through lamina/C-coated nuclear envelope. Transfection of genomic DNA derived from senescent cells lead to significant higher expression of IL6, IL1β and INFβ as compared to untreated normal cells.

Conclusions: Together, our results demonstrate RPE and photoreceptor senescence is accompanied by accumulation of cytosolic DNA, which may initiate a pro-inflammatory response in age-related eye diseases.

CONTROL ID: 3709083

SUBMITTER (NAME ONLY): Henar Albertos-Arranz

TITLE: Retinas of human donors with COVID-19 disease show morphological alterations and signs of inflammation including glial activation

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Albertos-Arranz, N. Martínez-Gil, X. Sánchez-Sáez, A. Noailles, M. Ruiz-Pastor, C. Sánchez-Castillo, P. Lax, N. Cuenca, Physiology, Genetics and Microbiology, Universitat d'Alacant Facultad de Ciencies, Alacant, Comunitat Valenciana, SPAIN|C. Monferrer-Adsuara, L. Remolí-Sargues, R. Calvo-Andrés, Ophthalmology, General University Hospital Consortium of Valencia, Valencia, Comunidad Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: Different signs of inflammation have been described in the brains of COVID-19 patients. In the retina, the fundus eye exam of these patients shows cotton wool spots, microhemorrhages, and a decrease in vascular density. However, morphological alterations of retinal cells in these patients are unknown. Thus, the aim was to analyze the morphological changes of the retinal cells from human donors with COVID-19 to establish several stages of response to damage in these cells and to define correlations with clinical parameters.

Methods: The retinas of human donors with COVID-19 (n = 16) and control subjects (n = 12) obtained from the General University Hospital Consortium of Valencia were analyzed. Immunohistochemical stainings were performed on transversal sections or flat-mount retinas to study photoreceptors, microglial cells, Müller cells, astrocytes, and the presence of ACE2. TUNEL assays and confocal microscopy imaging were carried out. Correlations were calculated between retinal and clinical parameters.

Results: Mean age of COVID-19 and control group were 80±10 and 70±8 years respectively. Müller cells, outer segment of cones and retinal pigment epithelium presented ACE2 staining. Larger staining of ACE2 and CRALBP was observed in cell bodies of Müller cells in COVID group. Disorganization of honeycomb-like pattern formed by Müller cells in the outer nuclear layer and disruption of external limiting membrane was found in the 81.3% of COVID patients. The 56.3% of COVID patients showed gliosis compared to controls (40%). COVID-19 retinas also presented epiretinal membranes and astrocytes protruding to vitreous humor. The 93.8% of COVID-19 patients had activated or ameboid-shape microglia. Microglial nodules around vessels and a reduction of the area occupied by microglia in these retinas were observed. COVID-19 group showed a more severe degeneration of cones. Cone degeneration correlated with Müller cell activation. Age of COVID patients correlated inversely with total retinal degeneration.

Conclusions: Morphological alterations in the cone photoreceptors as well as glial activation showing an inflammatory state of the retina were observed in COVID-19 patients.

CONTROL ID: 3709086

SUBMITTER (NAME ONLY): Conceicão Lobo

TITLE: Characterization of two-year progression of neurodegeneration in different risk phenotypes of diabetic retinopathy

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.F. Lobo, M. Ribeiro, I. Marques, S. Ferreira, A. Santos, T. Santos, J.G. Cunha-Vaz, AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|C.F. Lobo, Department of Ophthalmology, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, PORTUGAL|M. Ribeiro, I. Marques, A. Santos, J.G. Cunha-Vaz, Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To characterize the two-year progression of neurodegeneration in different diabetic retinopathy (DR) risk phenotypes in type 2 diabetes.

Methods: A prospective longitudinal cohort study (CORDIS, NCT03696810) was conducted with 3 visits (baseline, 6-months and one-year). Demographic and systemic data included age, sex, diabetes duration, lipidic profile and hemoglobin A1c (HbA1c). Ophthalmological examinations included visual acuity (BCVA), color fundus photography (CFP) and optical coherence tomography (OCT and OCTA). Phenotype classification was performed, at 6-month visit, based on microaneurysm turnover (MAT, on CFP) and central retinal thickness (CRT, on OCT). Only risk phenotypes B (MAT<6 and increased CRT) and C (MAT≥6 with or without increased CRT) were included. ETDRS grading was performed at the baseline and last visit based on 7-fields CFP.

Results: Of the 133 T2D individuals included in the study, 81 (60%) eyes were classified as phenotype B and 52 (40%) eyes as phenotype C. Of these, 127 completed the two-year follow-up, with 24 (19%) developing central involved macular edema (CIME) and 2 (1.6%) clinically significant macular edema (CSME).
Neurodegeneration represented by thinning of the GCL+IPL was present in both phenotypes showing no differences between these phenotypes. Furthermore, GCL+IPL thickness decreased with time (average of -0.605 µm/year; p=0.010). This decrease remained statistically significant (ß=0.624, p=0.006) when controlling for age, sex, diabetes duration and HbA1c. Changes in time for GCL+IPL thickness are also associated with longitudinal changes in FAZ area, FAZ perimeter and deep capillary plexus vessel density particularly in phenotype C. No correlation was found between the presence of increased neurodegeneration and the development of CIME.

Conclusions: In the two-year period of follow-up both phenotypes B and C showed similar progression in retinal neurodegenerative changes. The neurodegeneration is associated with microvascular related variables indicative of capillary closure. There is no association between the progression in neurodegeneration and development of CIME.

CONTROL ID: 3709089

SUBMITTER (NAME ONLY): Monica Del-Rio-Vellosillo

TITLE: Comparisons of different retinal segmentation thicknesses at fovea and parafovea between dyslexic and non-dyslexic patients

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To study thickness of intraretinal segmentations at the fovea and parafovea in dyslexic individuals and controls.

Methods: 22 dyslexic participants and 22 non-dyslexic controls had OCT scans of the macula using the 8x8 posterior pole algorithm. The sixteen most centrally-located superpixels of the grid, corresponding to the fovea and parafovea (4x4 grid), were considered in the these segmentations: complete retina, outer retina, inner retina, outer nuclear layer + outer plexiform layer + inner nuclear layer (ONL+OPL+INL, in other words, middle retinal layers) and ganglion cell complex (GCC). The results of the right and left eyes were compared between groups with unpaired t test.

Results: Significant increases of thickness in the superpixels of the studied 4x4 grid were found in the dyslexic group in right an left eyes, mainly in ONL+OPL+INL (13 thicker cells in the right eye and 16 in the left one in the dyslexic group, with mean superpixel thickening ranging from 4.95 to 11.15 microns) but also in complete retina (4 thicker superpixels in the right eye and 8 in the left one in the dyslexic group, with mean superpixel thickening ranging from 7.80 to 11.30 microns) and inner retina (6 thicker superpixels in the right eye and 10 in the left one in the dyslexic group, with mean superpixel thickening ranging from 6.50 to 12.4 microns). In contrast, GCC only showed one thicker superpixel in the dyslexic group (in the left eye, with mean superpixel thickening of 4.33 microns, but none in the right eye) and outer retina did not show any significant difference in the superpixels of right or left eyes between groups.

Conclusions: Middle retinal layers are thicker at the fovea and parafovea in dyslexia. This fact allows to consider that the fovea and parafovea could play a role in dyslexia.

CONTROL ID: 3709090

SUBMITTER (NAME ONLY): Helena Isla

TITLE: All-trans retinoic acid function in multiocular organoids early development: effects in pigmentation, neuroretina maturation, and corneal transparency

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Isla, M. Zufiaurre, J. García-Arumí, A. Duarri, Ophthalmology, Vall d'Hebron Institut de Recerca, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: All-trans retinoic acid (ATRA) plays an essential role during human eye development, being temporally and spatially adjusted to create gradient concentrations. Perturbations in ATRA signaling can result in severe ocular developmental diseases including microphthalmia, anophthalmia, or coloboma. However, the effects of ATRA in the different ocular tissues during embryonic development of the eye remain unknown. Here we performed a preclinical study to test the effects of high and low ATRA concentrations on early development and maturation of ocular tissues using an in vitro model of human induced pluripotent stem cells (hiPSC) derived multiocular organoids.

Methods: The differentiation protocol started by multizone ocular progenitor cells generation from hiPSC in 2D, and lifted at day 30, to generate 3D ocular organoids consisting of retina, retinal pigment epithelium (RPE) and cornea. Organoids in suspension were cultured in medium containing low or high ATRA concentrations from days 30 to 90. Histology, immunochemistry, PCR and WB were used to study gene and protein differential expression among groups. Unpaired two-tailed Student’s t-test was applied to determine statistical significance between high and low ATRA concentrations groups. For more than two groups, 2-way ANOVA with Bonferroni posttest was used.

Results: Significant differences were observed between tested groups revealing some effects of ATRA during early eye development. The presence of high ATRA concentration promotes transparent corneal organoids and neuroretinal development in retinal organoids while inhibiting the pigmentation of RPE organoids and the maturation of photoreceptors (PR). By contrast, low ATRA concentrations enhanced pigmentation of RPE organoids, the opacity of corneal organoids - due to an increase of collagen type IV in the stroma– and PR maturation in retinal organoids.

Conclusions: ATRA modulates the corneal epithelial integrity and transparency, promotes PR development and maturation of the RPE in a dose-dependent manner. These results demonstrate the relevance of ATRA during ocular tissue development and suggest a potential new strategy to better modulate the development and maturation of ocular organoids by controlling ATRA concentrations temporally and spatially.

CONTROL ID: 3709092

SUBMITTER (NAME ONLY): Ales Neubert

TITLE: Machine learning approach to identify future treatment requirement in pretreated nAMD patients based on OCT images

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop an interpretable machine learning model to predict anti-VEGF treatment requirements for previously treated patients with nAMD.

Methods: 547 patients from the ranibizumab 0.5 and 2.0 mg as-needed arms of HARBOR (NCT00891735) were included. 144 (26%) patients had a high treatment requirement (≥ 6 injections from 9 visits between month [M] 9 and M17). Boundaries of 5 retinal layers and 4 pathological features (intra- and subretinal fluid [IRF, SRF], subretinal hyperreflective material, pigment epithelial detachment [PED]) were automatically segmented from spectral-domain OCT (SD-OCT) scans acquired at M9 and M10. Segmentations were used to extract quantitative features (69 for layers, 36 for the 4 pathologies per visit). Extreme gradient-boosting model was used for binary classification using stratified 5-fold cross-validation repeated 10 times. The experiment was run separately for each feature group (4 pathologies and layers) and on the combined set of all features. Feature importance was analyzed using SHapley Additive exPlanations (SHAP).

Results: The best performance was achieved with retinal layers (area under the receiver operating characteristic curve [AUC], 0.76 ± 0.04 with M9 only and 0.79 ± 0.05 with M9 and M10 data) and was very close to the performance with the combined set of all features. For all experiments, adding M10 data only improved the results marginally. The layer features also contain information about the presence of pathologies such as fluids and cysts (thickness and volume increase), and therefore achieved better performance than individual pathological feature groups (Figure 1). However, good performance was observed for the SRF alone (AUC > 0.70), as well as for the PED features (Figure 1, Table 1). Predictive value of SRF and PED was confirmed by SHAP analysis (Table 1), where they were among the most important features.

Conclusions: This exploratory study showed the feasibility of identifying future high treatment requirements for previously treated patients with nAMD using automatically segmented SD-OCT. Further confirmation of model performance will contribute to future development of personalized health care algorithms.

CONTROL ID: 3709096

SUBMITTER (NAME ONLY): Thomas Volatier

TITLE: UVB activates autophagy in corneal epithelial stem cells

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ultraviolet B (UVB) irradiation may induce DNA lesions in all directly exposed tissues. In the human body, only two tissues are chronically exposed to UV: the skin and the cornea. The cornea lacks some of the phsycical barrier properties that the skin has, this makes the cornea particularly vulnearable damage. The induction of autophagy, a process that removes damaged cytoplasmic components, is of great importance in the cornea and extremely so in the stem cells that maintain the cornea. Here, we aim to characterise autophagy in isolated corneal epithelial stem cells (CESC) exposed to UV.

Methods: Epithelial cells were extracted from the limbus of discarded donor cornea (n=3). The cells were sorted to remove any fibroblasts. Cells were irradiated with 0.05J/cm^2 UVB. Autophagy and stem cells markers were observed using qPCR and immunofluorescent imaging. UVB damage was confirmed using DNA-lesion immunofluorescence assay.

Results: The putative stem cell character was assessed with ABCB5 and p63a. In culture, p63a+ epithelial cells have a high expression of mTOR that decreases by -0.96±0.6 log2 fold with UVB irradiation. Additionally, phosphrylated-mTOR (p-mTOR) position changes in CESC after irradiation, concentrating at the nucleus. Other assayed autophagy controllers had increased expression following UVB irradiation. ATG5 expression increased by 6.9±0.08 log2 fold, ATG7 expression increased by 7.7±2.9 log2 fold, ATG12 expression increased by 2.9±0.4 log2 fold, and LC3B expression increased by 1.05±0.3 log2 fold.

Conclusions: The decrease in expression of mTOR expression as well as the relocalisation of p-mTOR to the nucleus suggests that autophagy in CESC cytolasm is no longer inhibited. Additionally, both higher expression and visible presence of key autophagy controllers ATG5, ATG7, ATG12, and LC3B strongly suggests that short UVB exposure triggers autophagy in CESC.

CONTROL ID: 3709098

SUBMITTER (NAME ONLY): Karina Hadrian

TITLE: The transcription factor NFAT5 is a crucial regulator of corneal edema resolution after injury

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The cornea is physiologically free of blood and lymphatic vessels ([lymph]angiogenic privilege). However, injury or inflammation may lead to an ingrowth of these vessels. Recently, corneal lymphangiogenesis (LA) has been implicated to play a role in the regulation of corneal edema and inflammation resolution. Nuclear factor of activated T-cells 5 (NFAT5/TonEBP) has recently been identified as an important transcription factor that regulates LA and fluid homeostasis in skin. Here, NFAT5 enhances the expression of pro-lymphangiogenic vascular endothelial growth factor C (VEGF-C) in skin macrophages (MΦ), resulting in increased LA. So far, it has not been investigated whether NFAT5 is expressed in the cornea and which role it plays in the inflammatory response after corneal injury.

Methods: The corneal expression pattern of NFAT5 was investigated by immunofluorescence staining (IF) and qPCR in naïve and injured mouse corneas using a perforating corneal injury model to induce inflammation, LA and edema. The role of NFAT5 in corneal inflammation and the resolution of corneal edema was investigated using a tamoxifen-inducible NFAT5 knockout (KO) (Ubc-Cre/NFAT5$^{fl/fl}$) mouse model. Corneal thickness and resolution of corneal edema was measured by optical coherence tomography (OCT). Inflammation and LA were analyzed using IF.

Results: In naive corneas, NFAT5 was mainly expressed in corneal fibroblasts. After injury, NFAT5 expression in fibroblasts was downregulated and mainly expressed by MΦ (Correlation coefficient of TonEBP^{+}/Vimentin^{+}: 0.446±0.111 in naive corneas vs 0.153±0.024 after injury [p<0.0001]); TonEBP^{+}/F480^{+}: 0.113±0.032 in naive cornea vs. 0.446±0.018 after injury [p<0.0001]). In uninjured corneas, NFAT5 KO did not lead to changes in corneal thickness, however, the number of MΦ was significantly increased (24.76±3.54% in KO vs. 16.14±0.36%; p=0.0094 of corneal area covered by F480^{+} cells). After injury, the resolution of corneal edema was enhanced in NFAT5 KO mice (corneal thickness: 97.1±10.0 µm in KO vs. 137.1±28.8 µm [p=0.002]).

Conclusions: Our results demonstrate that NFAT5 is highly expressed in the cornea and its expression shows considerable changes after injury. Furthermore, our data indicate that the loss of NFAT5 leads to a faster resolution of corneal edema. The suppression of NFAT5 might be a promising strategy for the treatment of diseases associated with corneal edema.

CONTROL ID: 3709102
SUBMITTER (NAME ONLY): Gabriel Guardiola
TITLE: Bilateral Acute Iris Transillumination Associated to Moxifloxacin/Antibiotic Use
SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Bilateral acute iris transillumination (BAIT) is characterized by conjunctival injection and photophobia, with clinical findings of bilateral severe iris transillumination, pupils that are fixed and mid-dilated, and anterior chamber pigment dispersion. BAIT has a documented association with antibiotic use, in particular systemic moxifloxacin. The data regarding predisposing factors and demographic characteristics in the Latino population is limited. Our retrospective study aims to report the clinical and demographic characteristics and identify risk factors leading to BAIT in our population.

Methods: A retrospective review of patients diagnosed with BAIT was performed in two private ophthalmology practices in San Juan, Puerto Rico. All the patients were personally examined by either of two uveitis specialists who established the BAIT diagnosis. Prior to the diagnosis, all patients underwent an extensive systemic workup to rule out other possible etiologies such as HSV, syphilis, tuberculosis, and sarcoidosis; no evidence of these or other systemic conditions to explain the diagnosis of BAIT was found.

Results: A total of 72 eyes of 36 patients with BAIT were identified. The total antibiotic use within our BAIT cohort was 83%, of which 66% reported the use of moxifloxacin. The median age at presentation was 53 years; 80% of the patients were female. The most common systemic conditions were hypertension (31%) and chronic obstructive pulmonary disease (17%). Seventy-two percent of eyes had a best-corrected visual acuity greater than or equal to 20/50. At presentation, the median intraocular pressure (IOP) was 18 mmHg (range 8-50); 20 eyes (27%) had IOP greater than 21 mmHg, and 18 had IOP greater than or equal to 30 mm Hg. Anterior uveitis and pigmented cells in the anterior chamber, both observed in 38% of eyes, were the most prevalent associated ocular findings. Transillumination was diffuse in 59% of patients, and 63% also had pupillary sphincter atrophy.

Conclusions: As reported in prior studies, within our cohort, BAIT was more common in women, and the most common antibiotic predisposing to BAIT was moxifloxacin. To our knowledge, this is the first retrospective epidemiologic study of BAIT in the Puerto Rican population.

CONTROL ID: 3709103

SUBMITTER (NAME ONLY): John Lawrenson

TITLE: Development of interventions to facilitate uptake of diabetic retinopathy screening in young adults

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Attendance for diabetic retinopathy screening (DRS) in young adults (YAs) is consistently below recommended levels. We used a behavioural approach to develop intervention strategies to improve uptake that target YAs, healthcare professionals (HCPs) and the healthcare system.

Methods: We identified barriers/enablers to DRS uptake through a process of qualitative interviews and online surveys with YAs (18-34 years) and HCPs. Data were collected and analysed using the Theoretical Domains Framework (TDF) to explore potential individual, sociocultural and environmental influences on attendance. Barriers/enablers were mapped to behaviour change techniques (BCTs) to identify potential intervention components to increase attendance. We then undertook a Knowledge Exchange process with stakeholders to prioritise and discuss the acceptability and feasibility of delivering the proposed interventions.

Results: Barriers to attendance reported by YA in 29 qualitative interviews included: not understanding reasons for attending DRS or available treatments (22/29), lack of support after receiving results (12/29) and lack of appointment flexibility (14/29). Social support of family and the diabetes team was a key enabler (14/29). Reported HCP barriers by 140 survey respondents included poor communication between HCPS involved in diabetes care (62.9%) and 46.1% of DRS providers lacked a dedicated strategy to improve screening uptake in YAs. Strategies perceived by stakeholders to be most likely to improve screening uptake included: tailored health information packages emphasising the positive outcomes of DRS, a more flexible appointment booking system and integration of DRS with other aspects of diabetes care.

Conclusions: Using a method that combines behavioural theory with user involvement, we have identified a number of strategies to support DRS attendance in YAs. Interventions are more likely to be effective if they include components that specifically target the empirically identified modifiable determinants of behaviour and behaviour change. Interventions need to be targeted at both individual and organizational levels and are likely to vary in scope and intensity.

CONTROL ID: 3709104

SUBMITTER (NAME ONLY): Quincy Bosch

TITLE: FOXD1 is involved in uveal melanocyte development and associated with high-risk uveal melanoma

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q.V. Bosch, J. Nguyen, T. Brands, D. Paridaens, N. Naus, E. Kilic, Ophthalmology, Erasmus Universiteit Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS|T. van den Bosch, R. Verdijk, Pathology, Erasmus Universiteit Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS|Q.V. Bosch, T. Brands, A. de Klein, E. Brosens, Clinical Genetics, Erasmus Universiteit Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS|

ABSTRACT BODY:

Purpose: Uveal melanoma (UM) arises from melanocytes located in the uveal tract and is the most common primary intraocular malignancy. Driver mutations are mainly found in GNAQ and GNA11, followed by mutually exclusive mutations in BAP1, SF3B1 and EIF1AX which predicts prognosis. (Fig.1A) BAP1-UM is known to be highly aggressive, although the mechanism remains unclear. Multiple studies used transcriptomics to study BAP1-UM and implicate a more stem-like profile in BAP1-UM with an unique immune-landscape compared to SF3B1- and EIF1AX-UM. We hypothesized that BAP1-UM reactivate genes involved in uveal melanocyte development to increase aggressiveness. To identify transcripts involved in uveal melanocyte development, we used public scRNA-seq datasets of zebrafish and human and validated our finding in RNA-seq datasets of UM

Methods: To gain insights in uveal melanocyte transcriptomes, we utilized embryonic zebrafish scRNA-seq datasets lacking the eyes and used genes found in melanocytes as a filter against whole zebrafish scRNA-seq. Similarly, we used postnatal human skin scRNA-seq dataset as a filter against human eye to identify uveal melanocyte genes. Uniquely found transcripts in ocular melanocytes were then validated in 106 UM samples (Fig.1B)

Results: After filtering the zebrafish dataset, cluster 199 was identified as uveal melanocytes. Expression of melanocyte core genes (Fig.2A) and ocular genes pmelb and otx1 (Fig.2B) were expected, yet interestingly we uniquely found foxd1 to be involved in this cluster. We were unable to detect FOXD1 in healthy human scRNA-seq, suggesting spatial expression during embryonic vertebrate development. This prompted us to study FOXD1 in UM and found near exclusive expression in the BAP1-UM (Fig.2C), which is correlated to poor prognosis (Fig.2D)

Conclusions: Using a multi-species scRNA-seq approach we found genes involved ocular pigmentation and identified foxd1 in embryonic zebrafish melanocytes. Absence of FOXD1 transcripts in healthy human ocular melanocytes suggested spatial expression of FOXD1 as the human dataset consists of postnatal tissue. In UM we found expression of FOXD1 in BAP1-UM, which is correlated to poor prognosis. This study identified FOXD1 as a novel gene involved in high-risk UM

CONTROL ID: 3709105

SUBMITTER (NAME ONLY): Rebecca Chakram

TITLE: Does vision correlate with overall development in children with cerebral visual impairment?

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Chakram, P. Satgunam, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA| R.S. Chakram, A. Subramanian, M. Conway, City University of London, London, London, UNITED KINGDOM|L. Lingappa, P. Errolla, S. Naraganti, U. Hyndavi, Rainbow Children's Hospital Banjara Hills, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: A significant portion of a child's early overall development is accomplished through visual learning. Children with neurological conditions such as cerebral visual impairment (CVI) are likely to have visual concerns as well as developmental delays in areas such as motor, cognition and speech. Through this study, we aim to determine the correlation between vision loss and the overall development of children with CVI.

Methods: A prospective cross-sectional study was conducted on children with CVI visiting a paediatric neurology unit in India. Grating acuity (Teller Acuity Cards), contrast sensitivity (Ohio Contrast Cards), functional vision (Lantzy's CVI range; phase 1=building visual behaviour, phase 2=integrating vision with functions, phase 3=resolution of CVI characteristics) and developmental quotient (DQ) (Denver Developmental Screening Test-II) were assessed.

Results: Forty-seven children (males: 35) with CVI were included with a mean chronological age of 2.9±1.7 years (range= 9 months to 6.8 years). The mean binocular grating acuity was 1.35±0.67 logMAR (range=2.27 to 0.37 logMAR) and mean binocular contrast sensitivity was 0.49±0.56 logCS (range=0.0 to 1.66 logCS). Grating acuity ($r=-0.36$, $p=0.01$), contrast sensitivity ($r=0.41$, $p<0.01$) and functional vision score ($r=0.5$, $p<0.01$) were significantly and moderately correlated with DQ. Using linear mixed model (age adjusted), the outcome parameters of grating acuity, contrast sensitivity and DQ were compared to the CVI phases. Significant difference was noted across the 3 phases of CVI for grating acuity ($p<0.01$). There was no significant difference between phase 1 and 2 for contrast sensitivity and DQ ($p=0.09$), however phase 3 showed significant difference when compared with other two phases ($p<0.01$).

Conclusions: Vision parameters correlate with DQ in children with CVI. Although there is no separate vision domain in most developmental screening tools, psychologists could consider referring children particularly with lower DQs for vision assessment. Eye-care personnel should also ensure providing referrals to therapists for child's overall development particularly during the early years. The results do not establish any causation between the 2 parameters (visual vs. DQ) and can be further explored by studying the DQs of children having ocular visual impairment and no additional developmental delays.

CONTROL ID: 3709110

SUBMITTER (NAME ONLY): Amandeep Josan

TITLE: Assessment of the bivariate contour ellipse area (BCEA) as a marker of microperimetry reliability

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Josan, L. Taylor, R.E. MacLaren, University of Oxford Nuffield Laboratory of Ophthalmology, Oxford, Oxfordshire, UNITED KINGDOM|A.S. Josan, T.M. Buckley, L. Taylor, R.E. MacLaren, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Microperimetry has increased the accuracy in measurement of retinal sensitivity compared with standard perimetry. It is increasingly utilised in assessing the effects of novel therapies. However, errors from loss of fundus tracking has not been quantified resulting in a lack of understanding of the limitations and reliability of any given examination, particularly in those with poor fixation. The currently used measure, fixation losses, only samples the optic nerve approximately once every minute and may lead to erroneous conclusions about reliability. This study quantifies reliability using fixation data gathered in the form of the 63% and 95% fixation bivariate contour ellipse areas (BCEA63 and BCEA95).

Methods: A custom grid of 181 densely arranged points was constructed using the Macular Integrity Assessment System (MAIA; CenterVue, Padova, Italy), (see fig 1). This grid was centred on the optic nerve of 16 healthy participants and the scotoma mapped. The test was repeated with the participant's gaze directed away from the fixation target in an attempt to reduce fixation performance. Number of false positives and BCEA63 and BCEA95 values extracted for each participant.

Results: Of the 16 participants, four were rejected due to small pupils. A linear mixed effects model with BCEA as the fixed effect independent variable and participant ID as the random effect variable demonstrated a significant ($p = 0.006$) linear correlation between the number of false positives and the BCEA. A value of 30 percent false positives corresponds to a BCEA95 of 143 degrees^2 and a BCEA63 of 48 degrees^2.

Conclusions: The MAIA microperimeter gathers a significant amount of fixation information during testing. We have shown for the first time that this fixation data is significantly correlated to the reliability of any given examination with BCEA providing a surrogate marker for test accuracy. Further investigations is warranted to determine what an acceptable false positive value should be as the current value of 30% derives largely from historical static perimetry glaucoma studies. This study suggests any examination with a BCEA63 or BCEA95 of greater than 48 and 143 degrees^2 respectively should be viewed with caution and considered potentially unreliable regardless of the quoted level of fixation losses.

CONTROL ID: 3709113

SUBMITTER (NAME ONLY): Antonio Morilla-Grasa

TITLE: The effect of Citicoline, Vitamin C and Docosahexaenoic acid in the visual function of glaucoma patients. Updated results.

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Morilla-Grasa, V. Garcia, M. Munoz, E. Sanchez, L. Surroca, P. Blanco, L. Araujo, M. Martinez, A. Anton, Institut Catala de Retina SL, Institut Catala de Retina SL, Barcelona, Catalunya, ES, corporate/medprac, SPAIN|J. Moreno-Montanes, Ophthalmology, Universidad de Navarra, Pamplona, Navarra, SPAIN|A. Anton, Ophthalmology, Universidad Internacional de Catalunya, Barcelona, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the effectiveness of citicoline (Cebrolux ®), Vitamin C and docosahexaenoic acid (Brudypio ®) on the visual function of glaucoma patients.

Methods: This ongoing study is a prospective, randomized and controlled study. On December 2021, 67 patients had finalized the study. All participant persons had chronic glaucoma with structural damage as measured by OCT and visual-field damage compatible with glaucoma, mean defect (MD) between – 4 dB and -20 dB at least in one eye, a minimum of 3 reliable fields before baseline and 3 after baseline and, age between 50 and 75 years old. Persons were excluded if they were taken vitamins or nutraceutical treatments, or suffered pathologies that could alter visual fields, or had hypersensitivity to acetylsalicylic acid or fish proteins, or prior glaucoma surgery. Persons were randomly assigned receive vitamin C (VC), docosahexaenoic acid (DHA), Citicoline (C) or C + DHA. MD and Visual Field Index (VFI) slopes were calculated and a minimum positive slope-change ≥ 0,5 dB/month (MD) or ≥1.5 %/month (VFI) were considered clinically significant. Percentage of persons with positive slope-change was calculated and its association with a certain treatment was analyzed with Chi-squared test. Mann Whitney Test and T test were used to compare MD and VFI slopes, pre and post-treatment in every group.

Results: Table 1 shows mean ± sd of slopes by group:

Chi-squared test showed association with slope improvement of 0.5 dB/month in MD (p=0.003) and 1.5 %/month in VFI (p=0.02) for group 4 only. Furthermore, only group 4 showed significant improvement in MD (p=0.001) and VFI slopes (p=0.003) after 3 months of treatment.

Conclusions: C + DHA treatment improved visual field results of persons with glaucoma at short term. A larger, longer and multicenter study would be advisable to confirm these results.

CONTROL ID: 3709114

SUBMITTER (NAME ONLY): Ana Rita Santos

TITLE: A Conversion Model for OCTA Vessel Density Metrics in Diabetic Eyes: AngioVue vs Angioplex

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Santos, T. Santos, R. Coimbra, I. Pais, I.P. Marques, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|A. Santos, C. Versos, Departamento de Ortóptica, Escola Superior de Saúde do Porto, Instituto Politécnico do Porto, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: To understand measurements variability between 2 different OCTA devices and to develop a conversion model that translate vascular metrics into a standardized and comparable value in patients with different stages of DR.

Methods: A cross-sectional study was conducted in 55 patients (n=108 eyes) with diabetes type 2 (68.1±9.3yrs), 37(67%) were males.

Each eye underwent 3x3mm OCTA scans in AngioVue (Optovue RTVue,Optovue Inc) followed by 3x3mm OCTA scans in Angioplex (Cirrus HD-OCT 5000,Zeiss Meditec Inc) both centred on fovea. The Foveal Avascular Zone(FAZ) area and perimeter and the binarized Vessel Density(bVD) in the Central area, Inner Ring (3mm ø centred on fovea) and full 3mm^2 area were collected from the Superficial Capillary plexus(SCP) images of both equipments. Agreement between AngioVue and Angioplex measurements was assessed by Intraclass Correlation Coefficient(ICC) and Bland-Altman plots. A conversion equation was established to transform bVD values from Angiovue in Angioplex-equivalent values. This equation was built using repeated-measures models with generalized estimating equations to account for the correlation in participants with 2 study eyes, with Angioplex measurement as the dependent variable and AngioVue measurement as the independent variable.

Results: Binarized VD values measured by AngioVue were significantly higher than those by Angioplex (inner ring: 42.9±4.8vs35.6±3.3; $p<0.001$). However, a good ICC between both equipments was found for FAZ metrics (0.66 (0.52-0.77) for area and 0.59 (0.45–0.70) for perimeter), showing a good agreement of these metrics independently of the device.

Regarding the conversion model between devices, the following equation was derived: Angioplex bVD=(Angiovue bVD x 0.45) + 16.3. With this equation,84% of the Angioplex-equivalent bVD values fell within 10% of the real measurements using Angioplex. The obtained difference between converted and real values of bVD was <7.21.

Conclusions: Despite the use of distinct algorithms to detect binarized retina VD between different OCTA equipments, we propose a conversion model to obtain comparable bVD measurements between AngioVue and Angioplex devices in diabetic eyes with distinct levels of severity. This conversion model opens important possibilities for clinical trials to pool data from different OCTA instruments, allowing comparison of results within and between groups that are using distinct instruments.

CONTROL ID: 3709121

SUBMITTER (NAME ONLY): PremNandhini Satgunam

TITLE: Repeatability of grating acuity and contrast sensitivity in children with cerebral visual impairment

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Satgunam, R. Sumalini, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|R. Sumalini, A. Subramanian, M. Conway, City University of London, London, London, UNITED KINGDOM|L. Lingappa, Rainbow Hospital, Hyderabad, INDIA|

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ABSTRACT BODY:

Purpose: Cerebral visual impairment (CVI) is a common cause of pediatric visual impairment globally. Children with CVI can have additional developmental delays in areas such as motor, cognition and speech. The location/extent of brain damage, frequency of seizures, medication can all contribute to the variability of clinical measurements in these children. Therefore it will be important to identify clinical tools with good repeatability to monitor and manage this condition. In this study, we aimed to determine the repeatability indices of 2 important clinical tests: grating acuity [Teller acuity cards (TAC), Peekaboo Vision app (PV)] and contrast sensitivity [Hiding Heidi cards (HH) and Ohio contrast cards (OCC)] tests in children with CVI.

Methods: A cross-sectional, prospective study was conducted on children with CVI visiting a paediatric neurology clinic in Hyderabad, India. Informed written consent was taken from parents. Grating acuity and contrast sensitivity tests were administered in a randomized sequence and testing time was recorded. Test-retest repeatability was carried out within 3.5 months on average.

Results: Thirty-two children (males: 22) with a mean age of 2.6±1.7 years (range: 9 months to 6.8 years) were recruited. Significantly different acuities were obtained with PV and TAC ($p<0.01$, 95% limits of agreement (LoA): -0.67 to 0.33 logMAR). Teller acuity cards (Coefficient of Repeatability (CR): 0.3) had better repeatability when compared to PV (CR: 0.83). Testing time with both acuity tests was found to be comparable ($p=0.76$). Significantly different contrast sensitivities were obtained with HH and OCC ($p=0.02$, 95% LoA: -0.31 to 0.47 logCS). Ohio contrast cards (CR: 0.32) had better repeatability when compared to HH (CR: 0.5). Significantly lesser time was taken to administer HH compared to OCC ($p<0.01$).

Conclusions: Repeatability was found to be better for TAC and OCC in measuring grating acuity and contrast sensitivity respectively. Differences in thresholding paradigms, number of cards depending on the step sizes measured and different types of stimuli could be the possible reasons for poor agreement between the tests. Choice of visual function tests for children with CVI should consider the repeatability measure, especially for longitudinal follow-ups.

CONTROL ID: 3709122

SUBMITTER (NAME ONLY): María Vaglienti

TITLE: Protective effect of Nitro-Oleic Acids in neovascularization, vascular regrowth and neurodegeneration in Oxygen-Induced Retinopathy model

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.V. Vaglienti, P.F. Barcelona, G. Bonacci, M.C. Sanchez, Departamento de Bioquímica Clínica- Facultad de Ciencias Químicas- UNC, Centro de Investigaciones en Bioquimica Clinica e Inmunologia, Cordoba, Córdoba, ARGENTINA|P.V. Subirada Caldarone, Instituto de Investigacion Medica Mercedes y Martin Ferreyra, Cordoba, Córdoba, ARGENTINA|B. Joray, Facultad de Ciencias Químicas-UCC, instituto de investigaciones en recursos naturales y sustentabilidad jose sanchez labrador S.J., Córdoba, Córdoba, ARGENTINA|M.C. Paz, UNC, UNITEFA-CONICET, Córdoba, Córdoba, ARGENTINA|

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ABSTRACT BODY:

Purpose: Inflammation, oxidative and nitrosative stress are involved in neovascular retinopathies (NR). Nitro-fatty acids are important electrophilic signaling mediators with anti-inflammatory, antioxidant and cytoprotective properties. Therefore, our aim is to evaluate the effect of Nitro-oleic acid (NO_2-OA) in a mouse model of oxygen-induced retinopathy (OIR).

Methods: OIR mouse model was used. Briefly, C57BL/6 mice (n=35) were exposed to 75% O_2 from P7 to P12, after which they were brought to room air (RA) for additional five (P17) or fourteen days (P26). Age-match mice maintained in RA (n=25) were used as controls. OIR mice were intraocular (i.o.) injected with 5 µM of NO_2-OA (n=22) or vehicle (n=13) at P12 and intraperitoneal (i.p) with 15 mg/Kg of NO_2-OA or vehicle at P14, P17, P20, P23. At P17 or P26 mice were sacrificed. Some eyes were fixed for whole mount staining of retina and microscopy and other retinas were used for Western blot or RT-PCR assays. Retinal functionality was assessed by scotopic electroretinography (ERG) in dark-adapted mice. Amplitudes and latencies of a- and b-waves from ERG were recorded at P17 or P26. Finally, the NO_2-OA effect on neovascularization was evaluated by tube formation assay in bovine aortic endothelial cells (BAEC). GraphPad Prism was used for statistical analysis.

Results: NO_2-OA induced vascular regrowth ($p<0.05$) and decrease pathological neovascularization ($p<0.001$) at P17 OIR. Interestingly, RT-PCR revealed a significant increase in VEGF levels in OIR mice respect to RA mice ($p<0.0001$), but not difference was found between NO_2-OA treatment and vehicle ($p=0.9978$). In addition, WB of neural retinas showed that NO_2-OA prevented glial stress by decreasing GFAP ($p<0.0001$) in OIR model at P17 ($p=0.3160$). In the other hand, NO_2-OA did not modify the ($p=0.0177$) levels of GS at P17 ($p=0.0003$). At P26, ERG shown that NO_2-OA treated mice prevented the decrease in b-wave amplitude ($p=0.1362$) as well as increasing the expression of total Caspase-3 ($p=0.0004$) as a marker of cellular protection. Finally, it was observed that NO_2-OA affected neovascularization by decreasing the total segment length ($p<0.0001$) and number of tubular structures ($p<0.0001$) in BAEC cells.

Conclusions: These findings suggest that NO_2-OA could be beneficial for retinal cells in order to attenuate vascular and non-vascular alterations in NR.

CONTROL ID: 3709139

SUBMITTER (NAME ONLY): Maria Luísa Ribeiro

TITLE: Characterization of two-year progression of risk phenotypes of diabetic retinopathy

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ribeiro, I. Marques, S. Ferreira, A. Santos, T. Santos, J.G. Cunha-Vaz, AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|M. Ribeiro, I. Marques, A. Santos, J.G. Cunha-Vaz, Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To characterize the two-years progression of two diabetic retinopathy (DR) risk phenotypes in type 2 diabetes (T2D).

Methods: A prospective longitudinal cohort study (CORDIS, NCT03696810) was conducted with 4 visits (baseline, 6-months, one-year and two-year). Demographic and systemic data included age, sex, diabetes duration, lipidic profile and hemoglobin A1c (HbA1c). Ophthalmological examinations including visual acuity (BCVA), color fundus photography (CFP) and optical coherence tomography (OCT and OCTA), identified the presence of nonproliferative diabetic retinopathy (NPDR). Phenotype classification was performed, at 6-month visit, based on microaneurysm turnover (MAT, on CFP) and central retinal thickness (CRT, on OCT). Only risk phenotypes B (MAT<6 and increased CRT) and C (MAT≥6 with or without increased CRT) were included. ETDRS grading was performed at the baseline and last visits based on 7-fields CFP.

Results: 133 T2D individuals were included in the study, 81 (60%) eyes classified as phenotype B and 52 (40%) eyes as phenotype C. Of these, 127 completed the two-year follow-up, 24 (19%) developed central-involved macular edema (CIME) and 2 clinically significant macular edema (CSME) (1.6%). In the two-year period, two-step severity progression (ETDRS) occurred only in one eye with phenotype C.

At baseline, eyes with phenotype C showed more capillary closure in the superficial capillary plexus (SCP), deep capillary plexus (DCP) and full retina (FR, p<0,001) and increased FAZ area (p<0,001), indicating more advanced microvascular disease and confirming the ischemia phenotype. During the two-year period both phenotypes, B and C, showed progression in GCL+IPL thinning (p<0,001) and decrease in vessel density in the DCP (<0,001). When analyzing the two-year progression of each phenotype, only phenotype C revealed significant decrease in BCVA (p=0,02) and enlargement of the FAZ (p=0,03). CSME developed only in phenotype C whereas CIME occurred in both risk phenotypes.

Conclusions: In the two-year period of follow-up both phenotypes B and C showed progression in retinal neurodegeneration associated with progression in capillary closure identified by progressive decrease in vessel density of the DCP. CIME developed in both phenotypes and CSME only in phenotype C.

CONTROL ID: 3709140

SUBMITTER (NAME ONLY): Fabiola Biasella

TITLE: Vitronectin and its interaction with plasminogen activator inhibitor 1 - a possible link to vascular changes in AMD pathology

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Biasella, C. Kiel, T. Strunz, U. Friedrich, B.H. Weber, Institute of Human Genetics, Universitat Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Structural and functional studies have implicated vitronectin (VTN), a human blood and extracellular matrix (ECM) protein, in the complex pathogenesis of age-related macular degeneration (AMD). Our aim was to further explore the role of this protein in AMD and the functional impact of the non-synonymous polymorphism rs704C>T in the VTN gene, significantly associated with AMD in a genome-wide association study (GWAS).

Methods: Based on the largest AMD GWAS dataset of the International AMD Genomics Consortium (IAMDGC), we performed an association analysis to refine the relationship of rs704 with AMD clinical subtypes in 16,144 cases and 17,832 controls. In vitro studies including protein interaction and activity assays, western blot analysis and immunofluorescence staining were conducted to investigate the effects of rs704 on VTN function, with a focus on the interaction of recombinant VTN isoforms (AMD risk-associated VTN_rs704:T and non-risk-associated VTN_rs704:C) with the binding partner and angiogenic regulator plasminogen activator inhibitor 1 (PAI-1), and their influence on PAI-1 production by cultured endothelial and retinal pigment epithelium (RPE) cells. In addition, a large-scale gene expression analysis was performed based on our retinal gene expression database (n=311) and the Genotype-Tissue Expression (GTEx) project (n=556).

Results: Our statistical analysis revealed an association of rs704 only with neovascular AMD (NVAMD; Q value <0.05). In in vitro assays, VTN_rs704:T showed a stronger binding to PAI-1 than VTN_rs704:C (1.50 ± 0.61-fold increase, p <0.05), while both isoforms equally sustained PAI-1 activity. Interestingly, exposure of endothelial and RPE cells to VTN isoforms resulted in a large accumulation of PAI-1 in the ECM compared to control-treated cells (p <0.05). In silico, gene expression of VTN and PAI-1 showed positive correlations and a statistically significant increase in human retinal and blood tissues aged 60 years and older.

Conclusions: Our findings link VTN function to the progression of NVAMD and suggest a mechanism whereby ageing and the AMD-associated rs704 variant may concomitantly alter angiogenesis-related processes regulated by VTN and PAI-1. This provides novel cues to understand NVAMD, eventually facilitating the development of target-based therapeutic options to prevent and cure the vascular complications in AMD.

CONTROL ID: 3709143

SUBMITTER (NAME ONLY): Ai Kuranami

TITLE: Age-related macular degeneration and new entity of pachychoroid neovasculopathy in Japanese patients

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kuranami, I. Maruko, R. Maruko, S. Nishihara, T. Iida, Tokyo Joshi Ika Daigaku, Shinjuku-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Pachychoroid neovasculopathy (PNV) have been recently noticed as a new clinical entity. On the other hand, PNV could not be a completely independent entity from the previous neovascular age-related macular degeneration (AMD) types, such as typical AMD, polypoidal choroidal vasculopathy (PCV), and retinal angiomatous proliferation (RAP), but some of each type might be determined to be PNV. In the current study, we retrospectively reviewed the clinical records of AMD patients and re-classified the AMDs to determine the prevalence of PNV.

Methods: One hundred and ten eyes of 100 consecutive patients diagnosed previously with AMD at Tokyo Women's Medical University Hospital were studied. All patients were Japanese over 50 years old, and the mean age was 75.6 years (72 males and 28 females). PNV was defined with macular neovascularization (MNV) detected just above the dilated choroidal vessels (Pachy-vessels), and choroidal thickness was not included in the definition. Locations of choroidal vessels, horizontal symmetric vortex vein, and watershed zone were evaluated on indocyanine green angiography (IA, HRA2, Heidelberg) and/or en face optical coherence tomography (OCT, Elite 9000, Zeiss). When polypoidal lesion was identified in IA, it was determined to be PCV. Subfoveal choroidal thickness (SCT) was also manually measured on OCT.

Results: Based on the current criteria, twenty-six patients (26.0%, 26 eyes) were diagnosed with PNV, 38 patients (38.0%, 44 eyes) with PCV, 29 patients (29.0%, 31 eyes) with typical AMD, and 7 patients (7.0%, 10 eyes) with RAP. All PNV cases (26 patients) diagnosed as typical AMD on the previous criteria. Asymmetric vortex vein and watershed zone shift were observed in 80.8% of PNV cases, which was significantly higher than in 40.0% of non-PNV cases ($P<0.01$). There was no significant difference in mean SCT between PNV and non-PNV cases (277±88μm vs 252±95μm, $P=0.21$).

Conclusions: According to our criteria, including the new entity of PNV, which excludes choroidal thickness as diagnostic index, PNV was identified in 26% of neovascular AMD in Japanese patients. The results of this study may have a significant impact on the treatment strategy for Japanese patients with MNV.

CONTROL ID: 3709144

SUBMITTER (NAME ONLY): Pere Català

TITLE: A single cell transcriptome analysis unravels the heterogeneity of primary cultured human corneal endothelial cells

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Protocols for the primary culture of human corneal endothelial cells (hCECs) have several limitations: cultures are heterogeneous, have a limited capacity to grow without negatively affecting the cells, are only successful if derived from donors younger than 40, and there is a lack of markers to identify the high quality from inferior cells. We hypothesized that by gaining transcriptomic information from individual cells, markers to enrich for high quality clinical-grade CECs can be identified and protocols improved using the molecular pathway–level information gained.

Methods: Four human donor corneas, with ages ranging from 24 to 34 years were used for this study. hCECs were isolated and cultured as described by Peh et al. 2015. hCECs from all donors at culture time points day 2 (passage 0), day 5 (passage 0), day 14 (passage 0), day 30 (passage 1) and day 46 (passage 2) were sequenced with 10x Genomics 3’ V3.1 protocol. The data from all samples were loaded in R (v.3.6.2), processed with Seurat package (v.3.2.0), and cells clustered using graph-based clustering.

Results: Approximately 85,000 hCECs were loaded to 10x genomics. Data of 62,000 sequenced cells revealed the main clusters observed during primary expansion of hCECs. The sequenced cells expressed typical endothelial markers such as ALCAM, PRDX6, TJP1, and ATP1A1. Pseudotime analysis revealed the dynamics and variations in hCEC during primary expansion. Differential expression analysis will be used to identify the major differences between cell clusters at early and late time points. This will allow the identification of markers to differentiate high quality to lower quality hCECs. Furthermore, differential analysis will allow the identification of altered pathways during primary expansion of hCECs.

Conclusions: This work provides the first single cell analysis of primary cultured hCECs depicting their heterogeneity. This research allows deep understanding on the process of primary expansion of hCECs and sets the basis for further improvement of protocols and therapies based on primary hCECs.

CONTROL ID: 3709145

SUBMITTER (NAME ONLY): Helena Feenstra

TITLE: Safety and efficacy of fovea-involving half-dose photodynamic therapy for chronic central serous chorioretinopathy

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.M. Feenstra, M.J. Lamme, E.H. van Dijk, C.J. Boon, Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|R.M. Diederen, R.O. Schlingemann, C.J. Boon, Ophthalmology, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|S. Fauser, Ophthalmology, Uniklinik Koln, Koln, Nordrhein-Westfalen, GERMANY|S.M. Downes, Ophthalmology, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|C.C. Hoyng, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Including the fovea in the treatment spot during half-dose photodynamic therapy (PDT) in chronic central serous chorioretinopathy (cCSC) still is a topic of controversy, since a risk of developing foveal atrophy after PDT has been previously suggested. We performed a retrospective study with data from prospective randomized controlled trials, to assess the risk of foveal atrophy, as well as the likelihood of structural and functional improvement on OCT, after half-dose PDT treatment of cCSC that included the fovea.

Methods: In the randomized controlled trials PLACE and SPECTRA, a total of 57 cCSC patients received half-dose PDT with a treatment spot that included the fovea at least partially, and were included in the current study. Optical coherence tomography (OCT) scans were analyzed for signs of foveal atrophy, as well as structural improvement, at baseline visit, at 8-12 weeks, 1, and 2 years after half-dose PDT. Fluorescein angiograms (FA) at baseline visit and at 8-12 weeks were analyzed for the presence of an RPE window defect. Main outcome measures were integrity of the external limiting membrane (ELM) and the ellipsoid zone (EZ). Secondary outcomes involved best-corrected visual acuity (BCVA) in Early Treatment of Diabetic Retinopathy Study (ETDRS) letters, and retinal sensitivity on microperimetry.

Results: The ELM was considered intact at baseline in 21/57 (36.8%) of patients, increasing to 56/57 (98.2%; $p<0.001$) at 1 year, and 50/51 (98.0%; $p<0.001$) at 2 years. The EZ was intact at first visit after SRF resolution in 5/57 (8.8%). At 1 year after half-dose PDT, 30/57 (52.6%) of patients had regained an EZ with a completely normal aspect ($p<0.001$), which increased to 32/57 (56.1%) at 2 years after baseline visit ($p<0.001$). None of the patients showed a deterioration of the foveal ELM or EZ after treatment. No window defects on FA were seen foveally either before- or after treatment. Mean BCVA and retinal sensitivity improved significantly at 1 year after treatment (+6.72 ±7.34 ETDRS letters, $p<0.001$, and +3.88 ±2.22 dB, $p<0.001$, respectively), compared to baseline.

Conclusions: In patients with cCSC who received half-dose PDT with inclusion of the fovea in the treatment spot, a significant improvement in structural and functional parameters was seen at 2 years of follow-up. None of the patients had evidence of development of PDT-associated foveal atrophy.

CONTROL ID: 3709146

SUBMITTER (NAME ONLY): Maria Kaukonen

TITLE: SaCas9 base editing as a treatment strategy for Rhodopsin-associated retinitis pigmentosa

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Gene replacement therapy has shown great promise in treating inherited retinal dystrophies, but its application to dominant diseases is limited. CRISPR-Cas9 base editing presents an alternative approach to correct dominant single nucleotide variants. We tested in vitro adenine and cytosine base editors (ABE, CBE) utilizing S. aureus Cas9 to treat the dominant RHO c.541G>A (p.E181K) mutation.

Methods: Available PAM sites were searched for the SaABE8e (Addgene #138500), KKH-SaABE8e (#138502) and the CBE SaBE4 (#100805), with single guide RNAs C[G>A]AGGGCCTGCAGTGCTCGTGtggaat and CAGGTACATCCCC[G>A]AGGGCCtgcagt; PAM sites in lower case letters. Transfections in HEK293 or patient fibroblasts with 700 ng base editor and 200 ng guide were performed using FuGene or Neon Electroporation kit. Editing efficiencies were determined 120h post-transfection by analyzing the sequencing data with EditR. Non-transfected cells and published guides were used as negative and positive controls.

Results: The RHO gene was successfully edited in HEK293 cells using SaABE8e and SaKKH-ABE8e constructs. For the SaABE8e, 45% editing efficiency was observed in guide position 12 and the SaKKH-ABE8e variant achieving 22% and 26% editing efficiencies of adenines at positions six and eight, respectively. However, editing at the adenine adjacent to the mutation site in each target sequence was not detected. The SaBE4 was confirmed to be active, achieving 19% editing with a published guide. Attempts were then made to introduce a mutant-allele specific stop codon by converting the C at guide position 11 into a T, thus converting a glutamine codon “CAG” into a stop codon “TAG”. Despite validation of both the SaBE4 construct and the guide, editing at the RHO locus was not detected in either HEK293 cells or patient fibroblasts.

Conclusions: The tested ABEs produced high editing efficiencies of the RHO gene. However, absence of editing at the adenine adjacent to the mutation site suggested the target base does not fall within the constructs’ editing window. Further optimizations for the guides or choosing alternative ABE with different PAM site are needed to correct the RHO c.541G>A mutation. The tested CBE did produce editing with a published guide, but need further optimization to efficiently edit the RHO locus.

CONTROL ID: 3709147

SUBMITTER (NAME ONLY): Marc Sirks

TITLE: Results of focal photocoagulation in polypoidal choroidal vasculopathy patients from a Dutch referral center

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report the outcomes of focal thermal laser photocoagulation in polypoidal choroidal vasculopathy (PCV) patients from a Dutch referral center.

Methods: We describe a retrospective series of 24 eyes with indocyanine green angiography (ICGA)-proven PCV who had received focal laser photocoagulation. Inclusion criteria were: 1) the presence of either one or a cluster of extrafoveal polyps in the early phase of ICGA, with or without a co-existing neovascular network, 2) the presence of visual symptoms, and 3) the performance of focal laser photocoagulation, but no intravitreal injections with anti-vascular endothelial growth factor (VEGF) medication for at least 6 weeks before laser photocoagulation.

Results: Twenty-four eyes of 22 patients were included. The mean age of patients was 72 years, with a female predominance (82%). The most common clinical features at presentation were exudates (88%), either serous or hemorrhagic pigment epithelial detachments (PEDs) (58%), and (sub)retinal hemorrhages (46%). During the mean total follow-up of more than 2 years, focal laser photocoagulation was applied once in 14 eyes (58%), and multiple times in 10 eyes (42%). Three months after laser photocoagulation, exudates were only seen in 17% of cases, serous or hemorrhagic PEDs in 4%, and hemorrhages in 4%. Over the first 3 months following laser photocoagulation, best-corrected visual acuity (BCVA) in Snellen improved 2 lines or more in 10 eyes (42%), decreased 2 lines or more in 4 eyes (16%), and remained stable (≤1 line change) in 10 eyes (42%). Only 5 remaining polyps were observed at the visit at 3 months after treatment and only 1 polyp was seen at 1 year after treatment. During the mean follow-up of 27 months, 7 of the 24 eyes (29%) had a polyp recurrence.

Conclusions: We observed a marked decrease of exudates, PEDs, and subretinal hemorrhages after focal laser photocoagulation in eyes with extrafoveal PCV, with a recurrence of polyps in only 25% of our cases, with a mean follow-up of 2 years. Visual acuity improved or stabilized in the majority of eyes. Monotherapy with focal laser photocoagulation may therefore still be a treatment option in PCV patients for whom photodynamic therapy or anti-VEGF medication is not available or for whom an intravitreal anti-VEGF injections treatment regimen is too intensive.

CONTROL ID: 3709149

SUBMITTER (NAME ONLY): Avril Watson

TITLE: Modelling monoallelic Stargardt disease with 3D retinal organoids

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Stargardt disease due to bi-allelic variants in ABCA4 (STGD1) is the leading cause of inherited maculopathy, yet ~35% of cases remain genetically unsolved with traditional sequencing methods. We hypothesize that the missing heritability is due to undiscovered RNA defects in ABCA4. We explore this hypothesis through induced pluripotent stem cell (iPSC)-disease modelling to derive a biologically relevant RNA source for long-read RNA sequencing (LRS).

Methods: iPSCs were generated from two monoallelic [CF1] cases with the complex heterozygous allele c.[5461-10T>C;5603A>T]. Whole genome sequencing (WGS) was conducted to exclude potential phenocopies. Resulting iPSC lines were differentiated alongside a bi-allelic STGD1 case (c.4892T>C and c.4539+2001G>A) and unaffected control using published 3D retinal organoid (RO) protocols to produce a biologically relevant in vitro model of STGD1 (n=2). ROs were characterised during development using immunostaining and quantitative PCR for common markers of the developing retina. ABCA4 expression was confirmed using Western blotting. Fluorescence was quantified using Image J (n=5 images/sample) with statistical analyses performed via two-tailed paired t-test (mean ± SEM).

Results: WGS on Patient 2 did not report any additional candidate variants in ABCA4 nor in other IRD-associated genes. However, c.5603A>T was identified in trans in Patient 1. All samples produced ROs with the major retinal cells present. A photoreceptor outer segment (POS) brush border formed apically on the RO, which increased from Day 180 onwards. ABCA4 protein was also visualised in the sample at the POS. At Day 120, a proportion of Recoverin^{+} photoreceptor cells in STGD1 were displaced towards the centre of the RO. Mislocalised expression was mirrored by rod and cone photoreceptors (Rhodopsin^{+} and OPN1MW/LW^{+} cells) which did not resolve by Day 230. Immunostaining with Caspase-3 reveals that this phenotype was not correlated with apoptosis.

Conclusions: We generated STGD1 ROs which develop POS and express ABCA4, validating the use of this model as a source of tissue-specific RNA. We report a novel disease-specific phenotype of mislocalised photoreceptors, occurring independent of apoptosis. Further work is required to characterise this model, but we believe it will aid with the drug-discovery process for STGD1. We are currently applying LRS to unveil the missing inheritance of remaining monoallelic cases in this study.

CONTROL ID: 3709160

SUBMITTER (NAME ONLY): Katie Curran

TITLE: UK Biobank retinal imaging grading: methods, baseline characteristics and findings for common ocular diseases.

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The UK Biobank (UKBB) study is a large, prospective cohort study including adults registered with the National Health Service. The aims of the present study were to describe the grading methods and baseline characteristics for participants who underwent retinal imaging, and to characterise individuals with retinal features suggestive of age-related macular degeneration (AMD), glaucoma and diabetic retinopathy (DR).

Methods: Non-mydriatic colour fundus photographs and macular optical coherence tomography (OCT) scans were acquired using a Topcon 3D OCT-1000 Mark II system (Topcon, Japan). Grading was performed by trained and certified graders and quality assured by clinicians of the Network of Ophthalmic Reading Centres UK (NetwORC UK – Belfast, Liverpool, and Moorfields Ophthalmic Reading Centres). Study-specific grading forms were created to capture retinal features including those associated with any AMD (at least one definite drusen on either imaging modality), glaucoma (based on colour fundus photographs only; ≥0.7 cup-disc ratio, ≥0.2 cup-disc ratio difference between the eyes, abnormal disc features (notching, inferior rim thinning or both) and/or disc haemorrhage in either eye) and DR (microaneurysms with or without other characteristic features of DR). Suspected cases of these conditions were

compared against the information provided by UKBB self-reported (verbal interview), linked hospital episode statistics and available primary care records.
Results: Among 68,517 UKBB participants who underwent retinal imaging, the median age at imaging was 58 years (interquartile range 51-64), 45.7% were men and 90.6% were of white ethnicity. Altogether, 64,266 (93.8%) participants had gradable colour fundus photographs and 68,465 (99.9%) had gradable OCT scans in at least one eye. Retinal features suggestive of any AMD, glaucoma and DR were identified in 15,178 (22.2%), 2,183 (3.2%) and 265 (0.4%) participants, of whom 125 (0.8%), 218 (10.0%) and 132 (49.8%) respectively had a recorded diagnosis.
Conclusions: The outcomes of grading of baseline images represents a rich resource that will aid detailed phenotyping of UKBB subjects and yields diagnostic information not captured by self-report and healthcare data linkage. Judicious use of the image analysis information generated will accelerate research across a range of areas including genetics and artificial intelligence.

CONTROL ID: 3709161

SUBMITTER (NAME ONLY): Sayantan Biswas

TITLE: Interactions between high-intensity light and optical refocus in the drive for hyperopia control.

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the synergetic impact of high-intensity light (HL) and optical refocus (RF) on lens induced hyperopia (LIH) in a chicken model.

Methods: One-day-old chicks (n=130) were assigned to 10 groups of 13 chicks each. Chicks were housed for 8 days in a 12/12h light-dark cycle (150 lux). In all groups, hyperopia was induced randomly in one eye from day 1 post-hatching (D1) until D8 using +10D lenses. The fellow eyes acted as uncovered control. Nine groups were exposed daily to continuous 2 hours (h), 4h or 6h of either HL (15,000 lux); RF (removal of +10D lens); or both (HL+RF). One control group remained without HL or RF interventions. Ocular axial length (AL), refractive error and choroidal thickness (CT) were measured on D1, D4 and D8 using ultrasonography, infra-red refractometry and optical coherence tomography. Outcome measures are expressed as inter-ocular difference (IOD=experimental-control eye) ± SEM and compared between groups and intervention durations using a 2-way ANOVA.

Results: By D8, LIH led to a significant decrease in AL (-0.42±0.03 mm), increased hyperopic refraction (+3.48±0.32 D) and choroidal thickening (+85.8±35.2 µm) in the control group (all, $P<0.001$). Exposure to 2h of HL, RF or HL+RF did not significantly affect outcome measures of LIH. HL was associated with an additional, duration-dependent, increase in hyperopic refraction, while only 6h of HL significantly decreased AL ($P=0.02$). RF caused a duration-dependent increase in AL, and decrease in hyperopic refraction (Fig. 1). When interventions were 2h or 4h long, HL+RF had a similar impact as RF on the AL and refraction of eyes with LIH. Conversely, 6h of HL significantly reduced the impact of RF on AL (HL+RF vs RF, $P<0.05$, Fig.1A). HL increased CT compared to RF ($P=0.007$) and HL+RF ($P=0.03$).

Conclusions: In eyes developing LIH, daily exposures to HL promotes axial shortening and hyperopia in a duration-dependent manner, whereas, RF promotes emmetropization and slows the development of LIH. Exposure to 6h of HL can modulate the drive of RF potentially through changes involving CT.

CONTROL ID: 3709163

SUBMITTER (NAME ONLY): Bettina Hohberger

TITLE: Glaucoma and Alzheimer: Neurodegenerative disorders show an adrenergic dysbalance

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is known as multifactorial neurodegenerative disorder with autoimmune components. One of these autoimmune phenomena targets the ß2 adrenergic receptor (ß2-AR; i.e. agonistic autoantibodies; ß2-agAAb) and is linked to the elevated IOP and an impaired retinal microcirculation. As the neurodegenerative disorder, Alzheimer's Disease (AD), is postulated to share a common molecular mechanism with glaucoma, the aim of the present study was to investigate autoimmune phenomena targeting the ß2-AR in patients with AD.

Methods: Sera of 11 subjects with AD and 18 subjects with primary open-angle glaucoma were analyzed for a seropositivity of functional autoantibodies against ß2-AR. AAbs were analyzed by frequency modulation of a specific rat cardiomyocyte bioassay in vitro. In addition, different species of amyloid beta (Aß) monomers were tested (Aß1-14, Aß10-25, Aβ10-37 Aß1-40, Aß1-42, Aβ28-40, and [Pyr]-Aß3-42). The study was approved by the local ethics committee and was done in accordance with the tenets of the Declaration of Helsinki. Informed consent was achieved.

Results: The results demonstrate that the long-chain [Pyr]-Aß3-42, representing a major neurogenic plaque component, exerted an activation in the bioassay, which was blocked by ICI118.551, indicating that the effect was realized via the ß2-AR. Contrary, none of the short-chain Aß (Aß1-14, Aß10-25, or Aβ28-40) showed any inhibitory or agonistic effect on ß2-AR. The long chain Aß1-40, Aβ1-42, and Aβ10-37, yet not the short-chain Aß peptides prevented the clenbuterol induced desensitization of the ß2-AR. In addition, we identified a seropositivity of functional AAb in AD patients, activating the ß2-AR like the ß2-agAAb found in patients with glaucoma.

Conclusions: As autoimmune mechanisms were reported to be involved in the pathogenesis of neurodegenerative disorders, we postulate that an overstimulation of the ß2-AR pathway can induce an adrenergic overdrive. This might play an important role in the multifactorial interplay of glaucoma and Alzheimer's Disease.

CONTROL ID: 3709167

SUBMITTER (NAME ONLY): Annie Wu

TITLE: Trends in Glaucoma Fellowship Surgical Experience

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Wu, Y. Zhao, D.S. Friedman, M.V. Boland, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Annie Wu: Commercial Relationship: Code N (No Commercial Relationship) | Yan Zhao: Commercial Relationship: Code N (No Commercial Relationship) | David Friedman: Commercial Relationship: Code N (No Commercial Relationship) | Michael Boland: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate US glaucoma fellow surgical experience with traditional filtering and microinvasive glaucoma surgeries (MIGS).

Methods: Association of University Professors of Ophthalmology (AUPO) case log data from 2008-2019 was reviewed and analyzed for year-to-year trends.

Results: From 2008 to 2019, mean primary trabeculectomy surgeries among glaucoma fellows decreased 17.6% from 30.1 to 24.8, which represented a 0.8% decrease per year (P=0.67). During the same time period, mean primary glaucoma drainage implant (GDI) surgeries increased 56.3% from 30.2 to 47.2, which represented a 4.3% increase per year (P<0.01). From 2014 to 2019, mean iStent cases increased from 3.7 to 11.7, which represented a 24.1% increase per year (P=0.03). Mean goniotomy cases from 2014-2019 increased from 0.2 to 8.6, which represented a 55.5% increase per year (P<0.01). From 2016 to 2019, mean Trabectome cases increased from 2.7 to 3.7, which represented a 16.3% increase per year (P=0.69), and mean gonioscopy-assisted transluminal trabeculotomy (GATT) cases increased from 1.7 to 4.7, which represented a 49.8% increase per year (P=0.24).

Conclusions: There are steadily increased cases of GDI, iStent, and goniotomy surgeries among US glaucoma fellows. The cases of primary trabeculectomy surgeries have been fluctuating with a possible downtrend.

CONTROL ID: 3709169

SUBMITTER (NAME ONLY): Jianzhong Chen

TITLE: Intact transthyretin proteoforms of intraocular origin in human subretinal fluid from rhegmatogenous retinal detachment

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chen, Department of Optometry and Vision Science, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|D. Cao, S. Fortmann, C.A. Curcio, R. Feist, J. Crosson, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Jianzhong Chen: Commercial Relationship: Code N (No Commercial Relationship) | Dongfeng Cao: Commercial Relationship: Code N (No Commercial Relationship) | Seth Fortmann: Commercial Relationship: Code N (No Commercial Relationship) | Christine Curcio: Commercial Relationship(s);Code F (Financial Support):Genentech/Hoffman LaRoche, Regeneron;Code I (Personal Financial Interest):MacRegen | Richard Feist: Commercial Relationship: Code N (No Commercial Relationship) | Jason Crosson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Rhegmatogenous retinal detachment leads to fluid between the photoreceptor outer segments and retinal pigment epithelium (RPE). Knowledge of the protein composition in this fluid may provide clues to retinal diseases such as age-related macular degeneration, which is believed to involve dysregulated lipid transfer between photoreceptors, RPE, and choroid.

Methods: Intact proteins were extracted from the subretinal fluids of five patients with rhegmatogenous retinal detachment and analyzed by tandem mass spectrometry. A publicly available retinal gene expression database was searched. Two human donor eyes with normal maculas were immunoprobed for transthyretin (TTR) with appropriate controls.

Results: Albumin, TTR, and apolipoprotein A-I were the three most abundant proteins in subretinal fluid. Remarkably, TTR relative to the other proteins was more abundant than its serum counterpart, suggestive of TTR being predominantly synthesized locally. Six post-translationally modified protein forms (proteoforms) of TTR were detected, with the relative amount of glutathionylated TTR being much higher in the subretinal fluid (12 - 43%) than values reported for counterparts in serum (< 5%) and cerebrospinal fluid (0.4 - 13%). Moreover, a putative TTR dimer of 32,428, most likely with glycosylation modifications, was detected as the fourth most abundant protein. The high abundance of TTR and putative TTR dimer in subretinal fluid was supported by single-cell RNA sequencing analysis, which showed strong signal for TTR in RPE. Immunohistochemistry further showed strong diffuse TTR immunoreactivity in choroidal stroma that contrasted with vertically aligned signal in the outer segment zone of the subretinal space and negligible signal in RPE cell bodies. Lower relative amounts of glutathionylated TTR and a putative TTR dimer in one AMD eye merits further investigation in more samples.

Conclusions: The high percentage of glutathionylated TTR suggests that glutathionylation is crucial for normal TTR function in the retina. RPE expression of TTR gene and compartmentalized immunoreactivity suggests that TTR is made intraocularly as well as in the liver for plasma. Lipid carriers like TTR may participate in pathways that when dysregulated lead to subretinal drusenoid deposit. Subretinal fluid from patients undergoing retinal detachment repair is a rich biofluid for discovery.

CONTROL ID: 3709176

SUBMITTER (NAME ONLY): Karolina Ploessl

TITLE: Nicotinamide and its role in reducing complement activation and oxidative stress in age-related macular degeneration

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Ploessl, A. Eifler, A. Ramadani, F. Schaetzler, B.H. Weber, Institute of Human Genetics, Universität Regensburg, Universitat Regensburg, Regensburg, Bayern, DE, academic, GERMANY|B.H. Weber, Insitute of Clinical Human Genetics, Universitatsklinikum Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Recent work suggests that the vitamin B3 derivative nicotinamide (NA) ameliorates an age-related macular degeneration (AMD) phenotype in retinal pigment epithelium (RPE) cells derived from induced pluripotent stem cells (iPSCs) (Saini et al., 2018). While NA is a frequent supplement in RPE culture media for its property to enhance iPSC-RPE differentiation, it may inadvertently disguise molecular phenotypes in cellular models of RPE pathologies. We therefore aimed to investigate the effects of NA depletion on RPE cell integrity and functionality as well as oxidative stress susceptibility in iPSC-RPE cell lines categorized into extremes of high or low genetic risk for AMD.

Methods: iPSC-RPE cells were cultivated on transwell inserts and depleted of NA one week after seeding. Oxidative stress was induced by sodium iodate (SI) treatment. RPE cell layer integrity and functionality was analyzed by transepithelial resistance (TEER) measurements, immunocytochemistry and a photoreceptor outer segment (POS) phagocytosis assay. mRNA expression of markers for RPE cell faith, complement cascade and oxidative stress response was measured by qRT-PCR and verified by Western Blot and ELISA.

Results: NA depletion had no influence on RPE monolayer integrity as shown by immunocytochemistry and TEER measurement. Upon NA depletion RPE markers BEST1 and RPE65 were down regulated, whereas expression of complement markers CFH and C3 and oxidative stress markers HMOX1 and NQO1 were increased. These changes were reversible by reintroducing NA. Intriguingly, cells depleted of NA showed an increased uptake of POS. Oxidative stress was induced by SI treatment. Cells depleted of NA did not show a more pronounced stress response than cells cultivated in presence of NA. Cell lines with different genetic AMD risk scores did not show differences for any of the parameters addressed.

Conclusions: While NA decreases baseline expression of oxidative stress response and complement cascade marker genes in iPSC-RPE the cellular responses to SI mediated oxidative stress remain unmodified. Additionally, RPE cells depleted of NA showed a much higher POS phagocytosis than cells cultivated with NA. It thus remains elusive if the beneficial effect of NA on oxidative stress and complement regulation makes it a suitable therapeutic agent for AMD.

CONTROL ID: 3709177

SUBMITTER (NAME ONLY): Vikram Ponnusamy

TITLE: Anxiety and depression in patients treated for proliferative diabetic retinopathy.

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Ponnusamy, P. Le, Y. Zhang, Ophthalmology, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy is associated with higher rates of anxiety and depression. We performed a retrospective case-control study to quantify the association between different interventions for the treatment of proliferative diabetic retinopathy (PDR), and anxiety and depression.

Methods: Medical records from The University of North Carolina Hospital System (2014-2020) were reviewed to identify patients diagnosed with PDR (n = 3572) , anxiety, and depression using ICD-9 and 10 codes. Furthermore, PDR patients that received treatment with intravitreal injection (IVI), pan-retinal photocoagulation laser (PRP), pars plana vitrectomy (PPV), retinal detachment repair (RDR), complex RDR, and removal of silicone oil were identified by CPT codes. Multiple logistic regression analysis was used to calculate the effect size of an odds ratio (OR) between each mental illness and PDR treatment. X^2 test of homogeneity and Fischer-exact test were used to determine statistical significance between groups. All P values received Bonferroni correction for multiple comparisons.

Results: Out of 3572 PDR patients, 648 had anxiety and 979 depression. IVI had lower odds of comorbid anxiety when compared to untreated PDR patients (OR 0.835, 0.738-0.944, P < 0.001). Similarly, there were reduced odds for comorbid depression when comparing between patients who received IVI (OR 0.584, 0.525-0.650, P < 0.001), PPV with endolaser (OR 0.725, 0.604-0.870, P < 0.001), or PRP (OR 0.589, 0.513-0.678, P < 0.001) to patients who had no intervention for PDR. However, RDR (OR 1.759, 1.044-2.966, P < 0.001) and complex RDR (OR 1.451, 1.032-2.040, P < 0.001) were associated with increased odds of comorbid anxiety when compared to patients with untreated PDR.

Conclusions: These findings further elucidate the relationship between mental health and diabetic retinopathy. Patients receiving surgical and non-surgical interventions for PDR have decreased odds of having comorbid anxiety and depression, with the exception of retinal detachment repair, which is associated with higher odds of anxiety. These findings emphasize the importance of multidisciplinary care in managing patients with diabetic retinal detachments.

CONTROL ID: 3709182

SUBMITTER (NAME ONLY): Paul Sladen

TITLE: AAV-RPGR Gene Therapy for RPGR-Associated X-Linked Retinitis Pigmentosa (XLRP): Human retinal organoid vector efficacy data

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Sladen, A. Naeem, T. Adefila-Ideozu, T. Vermeule, S. Busson, M. Michaelides, S. Naylor, A. Lane, T. Georgiadis, Pre-Clinical Development, MeiraGTx, London, UNITED KINGDOM|M. Michaelides, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mutations within the retinitis pigmentosa GTPase regulator (RPGR) are the most frequent cause of X-Linked Retinitis Pigmentosa (XLRP), a common and severe form of inherited retinal disease. XLRP is characterised by the progressive degeneration and loss of photoreceptors, leading to visual loss and, ultimately, bilateral blindness. Unfortunately, treatments for RPGR-associated XLRP are non-existent. Therefore, we sought to investigate the efficacy of $RPGR^{ORF15}$ gene supplementation in human RPGR-deficient retinal organoids (ROs).

Methods: Isogenic RPGR knockout (KO) induced pluripotent stem cells (iPSCs) were generated using established CRISPR/Cas9 gene editing methods. RPGR-KO iPSCs were differentiated into 3D ROs, which were utilised to test the RPGR clinical vector construct. Molecular, structural, and functional readouts included RPGR quantification, RPGR photoreceptor localization, RPGR glutamylation and ciliation assessment.

Results: Successful differentiation of RPGR-KO iPSCs was confirmed by qPCR and immunocytochemistry of major retinal and phototransduction markers. Viral transduction of RPGR-KO ROs with AAV-RPGR led to restoration of RPGR expression in human rods and cones. RPGR was localised at the photoreceptor cilium and led to marked improvements in several molecular readouts.

Conclusions: The RPGR transgene was correctly expressed, processed, and localised in human rods and cones following viral transduction of RPGR-deficient human ROs. These data agree with the reported Phase I/II trial positive results in patients with RPGR-associated XLRP.

CONTROL ID: 3709183

SUBMITTER (NAME ONLY): Lonneke Haer-Wigman

TITLE: Diagnostic genetic analysis of variants in the highly complex OPN1LW/OPN1MW gene cluster causal for mild to severe color vision deficiencies

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Haer-Wigman, A. den Ouden, R. Derks, M. Tjon-Pon-Fong, H. Yntema, M. Nelen, L. Vissers, K. Neveling, Department of Human Genetics, Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS|A. Hoekstra, R.V. r.vijzelaar@mrcholland.com, MRC Holland bv, Amsterdam, NETHERLANDS|M.M. van Genderen, D. Smailhodzic, Bartiméus Diagnostic Center for complex visual disorders,, Zeist, NETHERLANDS|J. Verheij, Medical Genetics, University Medical Center Groningen, Groningen, NETHERLANDS|H. Kroes, Medical Genetics, University Medical Center Utrecht, Utrecht, NETHERLANDS|M.M. van Genderen, Ophthalmology, University Medical Center Utrecht, Utrecht, NETHERLANDS|L. Haer-Wigman, A. den Ouden, R. Derks, M. Tjon-Pon-Fong, H. Yntema, M. Nelen, L. Vissers, K. Neveling, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS|D. Smailhodzic, The Rotterdam Eye Hospital, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Variants in the OPN1LW/OPN1MW gene cluster cause X-linked color vision deficiencies, such as the frequently occurring protanopia and deuteranopia or the more rare Bornholm eye disease and blue cone monochromacy. Genetic analysis of the cluster is extremely difficult, first due to the ~98% homology of the OPN1LW and OPN1MW genes, second because only the first two opsin genes in the cluster are clinically relevant, while the cluster can contain zero to as many as six gene copies and third because of the broad spectrum of causal variants.

Methods: A genetic assay was developed for the OPN1LW/OPN1MW gene cluster combining copy number analysis using multiplex ligation-dependent probe amplification (MLPA) and sequencing analysis using long-read circular consensus sequencing. The assay was tested on 50 clinical cases analyzed to confirm clinical diagnosis (n=43) or determine carrier status (n=7).

Results: Using the developed assay a broad range of pathogenic variants were detected, such as deletions of the LCR, hybrid genes, single variants (including 7 novel variants) and combinations of variants. In all 43 male cases in which a genetic confirmation of diagnosis was requested the genetic composition of the clinically relevant first and second gene in the OPN1LW/OPN1MW gene cluster could be determined. In 39 of these 43 cases the clinical diagnosis was genetically confirmed, in two cases it was unclear whether the detected variants were causal and in two causes no causal variants were detected. In the latter two cases the causal variants are most likely outside the OPN1LW/OPN1MW gene cluster. Indeed, in one of these cases variants in the ZNF644 gene were detected. In seven female samples carrier status could be determined, although in two samples parental samples were requested and analyzed to definitely conclude carrier status. Interestingly, in 4 of the 7 cases the causal allele arose de novo in the affected child.

Conclusions: The developed genetic assay for the OPN1LW/OPN1MW gene cluster is the first available diagnostic assay that can detect both structural and nucleotide variants with a straightforward analysis, as MLPA is a fast and efficient method for copy number analysis and the long read sequencing approach makes it possible to determine the genetic composition of the entire OPN1LW or OPN1MW gene in single sequencing reads.

CONTROL ID: 3709184

SUBMITTER (NAME ONLY): Celeste Limoli

TITLE:

What are the most common symptoms reported by patients presenting with neovascular age-related macular degeneration? A bicentre study

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Limoli, Ophthalmology, Universita degli Studi di Milano, Milano, Lombardia, ITALY|C. Limoli, S. Vujosevic, Eye Clinic, IRCCS MultiMedica, Milan, Lombardia, ITALY|L. O'Toole, M. Grehan, Ophthalmology, Bon Secours Hospital Dublin, Dublin, IRELAND|P. Nucci, S. Vujosevic, Biomedical, Surgical and Dental Sciences, Universita degli Studi di Milano, Milano, ITALY|

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ABSTRACT BODY:

Purpose: Neovascular age-related macular degeneration (nAMD) is a degenerative retinal disease that when untreated leads to severe visual loss. Prompt detection of the disease may achieve better therapeutic outcomes. This study aimed to ascertain the presenting symptoms of nAMD in 2 different population groups and examined how awareness interacts with clinical variables.

Methods: In this bicentre, cross-sectional study conducted from September to December 2021 in Milan and Dublin, patients with nAMD attending the intravitreal injection service were included. Four age-subgroups were considered: 60-69, 70-79, 80-89, >90. The patients completed an interviewer-administered questionnaire regarding their symptoms at the time of nAMD onset. Individuals were divided into group A composed of Italian patients and group B consisted of Irish patients. The 2 groups were compared using the Chi-square test with Yates correction for categorical variables (univariate analyses). P-values <.05 were considered statistically significant.

Results: 152 patients with nAMD were included in the study, 56 in group A and 96 in group B.

The most common age-subgroup was 80-89 years (46.7%); 95(62.5%) patients were females, while 57(37.5%) were males. The most frequent symptom at presentation was difficulty when reading (n=57,37.5%), followed by both drop in central vision in one eye (n=52,34.2%) and distortion (n=52,34.2%). Other presenting symptoms were a transient shadow upon wakening (n=26,17.1%), difficulty in going from light to dark (n=9,5.9%), and also in recognizing faces (n=6,3.9%). Notably, 44 patients (28.9%) were asymptomatic. Univariate linear regression analyses didn't reveal a significant association of awareness of the disease with age and sex. Interestingly, group A was more likely to be aware of the disease onset compared to group B X^2 (1,N=152)=4.483, p=.0342.

Conclusions: These findings show that almost a third of patients with nAMD are asymptomatic at the time of their first presentation. Symptom awareness was higher among the Italian cohort compared to the Irish group. nAMD patients should attend regular ophthalmic/optical coherence tomography monitoring rather than rely on subjective symptoms.

CONTROL ID: 3709186

SUBMITTER (NAME ONLY): James Panos

TITLE: Measurement of Distortion with Myopia Control Lenses Using a Novel Optical Instrument

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.G. Panos, B.S. Chieng, D. Winarso, A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|A. BACK, Vision CRC USA Inc., California, UNITED STATES|A. Ho, University of New South Wales School of Optometry and Vision Science, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: An increasing variety of myopia control spectacle lens (MCSL) designs are emerging. However their optical features potentially create distortion in the field of view affecting tolerance and compliance. The aim was to develop a novel bench device to measure this distortion and evaluate commercially available MCSLs.

Methods: An opto-electro-mechanical Lens Distortion Tester (LDT) was developed for evaluating Static Field (SF) and Horizontal Smooth Pursuit (HSP) distortion. The LDT includes a colour camera with a focusing lens, a test lens mount on an automatic pivoting arm, and a monitor to present a target object. The LDT can resolve micro to macro levels of distortion by adapting the optical layout.

Targets were black and white linear gratings in a range of spatial frequencies. Custom software controlled a pivoting arm for transverse angular lens movements to capture a sequence of output images. Post-processing analysis software was developed in Matlab whereby edge detection and deviation due to distortion was quantified by decomposition into frequency components.

Four commercially available spectacle lenses were evaluated; Hoya Single Vision (SV), Zeiss MyoVision, Hoya Miyosmart, and Essilor Stellest. Output of the distorted target edge was assessed using histogram plots. The frequency and magnitude of distortion was quantified across the field of view.

Results: The results presented in Fig.1 & 2 suggest consistent trends between SF and HSP:

— SV had the least amount of distortion spread evenly across the field, as represented by low magnitudes for all frequencies.

— MyoVision had the largest amount of low frequency (blue) distortion which increased to the peripheral field (i.e. peripheral drift).

— Miyosmart had a medium amount of distortion spread evenly across the field shown by low-medium (light blue) and medium (orange) frequencies (i.e. small jitter) in SF and HSP respectively.

— Stellest had a large amount of distortion increasing to the peripheral field with medium (orange) and low-high (light blue to green) frequencies (i.e. large jitter) in SF and HSP respectively.

Conclusions: The LDT can distinguish distortion characteristics between the various MCSL technologies. Each MCSL technology type (progressive power and lenslet) offers differing qualities and amounts of distortion. Miyosmart lenslets create the least distortion magnitude and change across the field of view when compared to other MCSL types.

CONTROL ID: 3709191

SUBMITTER (NAME ONLY): aisling mcglacken-byrne

TITLE: CLINICAL RESULTS OBTAINED WITH THE NEW PHYSIOL ISOPURE 123: AN ISOFOCAL OPTICAL DESIGN TO ACHIEVE FUNCTIONAL INTERMEDIATE VISION

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. mcglacken-byrne, J. Morris, E. Loane, Ophthalmology, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|

Commercial Relationships Disclosure: aisling mcglacken-byrne: Commercial Relationship: Code N (No Commercial Relationship) | James Morris: Commercial Relationship: Code N (No Commercial Relationship) | Edward Loane: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the clinical results obtained with the new PhysIOL Isopure 123: using an isofocal optical design to achieve functional intermediate vision

Methods: An observational study of patients with a isofocal IOL (PhysIOL Isopure 123) implanted between December 2020 and October 2021. Visual outcomes were assessed 1 month postoperatively; uncorrected and best-corrected distance visual acuity using logMAR at 4 metres, uncorrected and corrected intermediate (70cm) and reading/near visual acuity using a Jaeger chart

Results: Nineteen eyes of 18 patients were analysed. Mean preoperative distance visual acuity was 0.66 ± 0.71 logMAR. At the one-month post-operative follow-up visit, uncorrected distance visual acuity was 0.17 ± 0.17 logMAR and corrected distance visual acuity was 0.07 ± 0.12 logMAR. Two thirds (66%, n=12) of patients achieved uncorrected intermediate visual acuity (70cm) of N12 or better. Wearing their auto-refraction correction, sixty-six achieved N12 or better at 70cm and over half (53%) could read N10 or better at their comfortable near distance. There were no intra or post-operative complications of note. Mean post-operative spherical equivalent was -0.06 ± 0.04.

Conclusions: The results demonstrated that the PhysIOL Isopure 123 is able to restore near, intermediate, and distance visual function.

CONTROL ID: 3709194

SUBMITTER (NAME ONLY): Anne Celle

TITLE: Prospective natural history of retinitis pigmentosa due to RHO, PDE6A, or PDE6B mutations: interim analysis of the PHENOROD2 study

SESSION TITLE: Retinal Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Celle, A. Le Meur, D.C. Chung, SparingVision, Paris, FRANCE|S. Mohand-Said, J.A. Sahel, I.S. Audo, INSERM-DHOS CIC 1423, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts Centre d'investigation clinique, Paris, Île-de-France, FRANCE|S. Mohand-Said, J.A. Sahel, I.S. Audo, Centre de référence maladies rares REFERET, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To develop a deeper understanding of the progression of Retinitis Pigmentosa (RP), for the successful design of clinical trials assessing novel therapeutics.

Methods: PHENOROD2 is an ongoing prospective, multicentric, natural history study documenting functional and structural changes in patients with RP due to mutations in RHO, PDE6A, or PDE6B. An interim analysis was performed at baseline and 12 months in the first 44 patients enrolled at the national reference center for rare diseases (REFERET) of the Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts (Paris, France). One patient was lost to follow-up and was excluded from the analysis. Population demographics, visual acuity (VA), and kinetic visual field (V4e) were analyzed in the entire cohort and per genotype.

Results: Out of 43 patients, 32 (75%) carried a mutation in RHO, 7 (16%) in PDE6A, and 4 (9%) in PDE6B. Mean age at inclusion was 46 (12.2) years, and gender distribution was 53.5% males, 46.5% females.

At baseline, VA ranged between 20/13 and 20/800, with a mean of 0.14 (0.19) LogMAR (20/28) and 0.17 (0.22) LogMAR (20/30) in OD and OS, respectively. At 12 months, no significant changes were reported, although subjects with PDE6 variants showed a slight trend towards mild VA loss (+0.08 and +0.04 LogMAR in OD and OS, respectively).

At baseline, a mean visual field area of 5,532.4 (5,151.9) mm^2 was reported in both eyes of all patients (6,320.6 mm^2 in RHO patients, 2,675.2 mm^2 in PDE6A patients, and 4,226.9 mm^2 in PDE6B patients). At 12 months, a mean loss of -345.8 (1,572.8) mm^2 (-6.3%) was observed in all patients: -323.2 mm^2 (-5.1%) in RHO patients, -591.6 mm^2 (-22.1%) in PDE6A patients, and -96.85mm^2 (-2.3%) in PDE6B patients.

The small numbers of PDE6A and PDE6B patients did not allow for statistical analysis across groups.

Conclusions: Virtually no decrease in VA was observed after 12 months of follow-up in this population of patients with relatively spared VA at baseline, in alignment with the documented natural history of RP. However, a loss of visual field was reported over the same period. This suggests that visual field assessment may be more appropriate to monitor disease progression in the early stages. Future interim analyses including the entire PHENOROD2 cohort will help validate these preliminary observations.

CONTROL ID: 3709198
SUBMITTER (NAME ONLY): Elio Herzog
TITLE: Challenges in the characterization of the ocular surface microbiome
SESSION TITLE: Infection and Immunity
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Herzog, S. Wolf, M.S. Zinkernagel, D.C. Zysset-Burri, Departement of Ophthalmology, Inselspital Universitatsspital Bern, Bern, Bern, SWITZERLAND|I. Keller, S. Wolf, M.S. Zinkernagel, D.C. Zysset-Burri, Department for BioMedical Research, Universitat Bern Philosophisch-naturwissenschaftliche Fakultat, Bern, Bern, SWITZERLAND|E. Herzog, Graduate School for Cellular and Biomedical Sciences, Universitat Bern Philosophisch-naturwissenschaftliche Fakultat, Bern, Bern, SWITZERLAND|I. Keller, Interfaculty Bioinformatics Unit and Swiss Institute of Bioinformatics, Universitat Bern Philosophisch-naturwissenschaftliche Fakultat, Bern, Bern, SWITZERLAND|
Commercial Relationships Disclosure: Elio Herzog: Commercial Relationship: Code N (No Commercial Relationship) | Irene Keller: Commercial Relationship: Code N (No Commercial Relationship) | Sebastian Wolf: Commercial Relationship: Code N (No Commercial Relationship) | Martin Zinkernagel: Commercial Relationship: Code N (No Commercial Relationship) | Denise Zysset-Burri: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Since the ocular surface is continuously exposed to the environment, an important role of its microbiome is to protect the underlying tissue against colonization of pathogens. If left unchecked, the ocular surface microbiome (OSM) may itself cause disease by uncontrolled immune responses resulting in inflammatory processes. Due to the low abundance of microbial relative to host DNA, the generation of stable and reproducible sequencing data to characterize the human OSM is challenging.
Methods: To characterize the OSM by whole-metagenome sequencing, swabs of the lower conjunctiva were collected using standard cotton swabs compared to flocked nylon swabs. Total DNA was extracted by either the E.Z.N.A. MicroElute Genomic DNA (Omega) or the QIAamp DNA Microbiome (Qiagen) kit. The latter includes a mechanical lysis and host DNA depletion step. Samples were prescreened for bacterial DNA using RT-qPCR of 16S rRNA genes.
Results: More DNA was isolated using flocked swabs ($p=0.0378$, $n=21$). The majority of the identified taxa were bacteria (96.60 ± 1.74%), whereas 1.86 ± 1.38% and 1.54 ± 0.75% (SD) were viruses and eukaryotes, respectively. Using the Qiagen kit, a total of 112 species belonging to 71 genera in eight phyla were found compared to eleven species belonging to nine genera in three phyla isolated with the Omega kit (Fig. 1). The most abundant phyla were Proteobacteria and Actinobacteria, additionally Firmicutes if using the Qiagen kit. Extraction kits output differed in both, microbial composition and resolution (Fig. 2).
Fig. 1: Detected microbial phyla, genera and species using the E.Z.N.A. MicroElute Genomic DNA kit (Omega) vs. the QIAamp DNA Microbiome kit (Qiagen). The same three patients were sampled on consecutive days.
Fig. 2: The microbial composition on phylum (A) and species (B) level. The lower six samples are the same three subjects sampled on consecutive days extracted with either with the Omega (yellow) or Qiagen (green) kit.
Conclusions: Despite low microbial abundance of the OSM, preliminary data showed that robust sequencing data can be generated using flocked swabs to increase the DNA input and without 16S rRNA amplification to eliminate amplification bias and to include viral and fungal in addition to bacterial DNA. Microbial diversity depended on the DNA extraction kit, therefore positive controls with known microbial composition will be included in validation studies.

CONTROL ID: 3709202

SUBMITTER (NAME ONLY): Elena Gofas

TITLE: Detecting inflammatory cells in patients with Multiple Sclerosis using AO-SLO phase contrast imaging

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Gofas, N. Norberg, M. Paques, C. Vignal Clermont, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|Y. Beigneux, Hopitaux Universitaires Pitie Salpetriere-Charles Foix, Paris, Île-de-France, FRANCE|K. Grieve, Institut de la vision, Paris, Île-de-France, FRANCE|C. Louapre, Sorbonne University, Paris Brain Institute - ICM, Assistance Publique Hôpitaux de Paris, Inserm, CNRS, Hôpital de la Pitié Salpêtrière, CIC neurosciences, Paris, FRANCE|

Commercial Relationships Disclosure: Elena Gofas: Commercial Relationship: Code N (No Commercial Relationship) | Celine Louapre: Commercial Relationship(s);Code R (Recipient):Biogen, Novartis, Roche, Sanofi, Teva and Merck Serono;Code F (Financial Support):Biogen | Nathaniel Norberg: Commercial Relationship: Code N (No Commercial Relationship) | Ysoline Beigneux: Commercial Relationship: Code N (No Commercial Relationship) | Michel Paques: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Vignal Clermont: Commercial Relationship: Code N (No Commercial Relationship) | Kate Grieve: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is possible to find biomarkers in the retina that inform about the pathological state of other parts of the body. Neurodegenerative diseases could be diagnosed early by high-precision retinal imaging. However, many cells in the inner retina are too transparent to be detected by existing techniques. We have shown how multi-offset detection in Adaptive Optics Scanning Laser Ophthalmoscopy (AO-SLO) can capture variations in refractive index between retinal cells leading to images of ganglion and microglial cells in humans in vivo. A detector with the same offset distance was installed on a custom-modified AO-SLO Optical Coherence Tomography (OCT) device. The aim of this project was to detect transparent cellular biomarkers on patients suffering from multiple sclerosis (MS).

Methods: Images were acquired with the AO-SLO-OCT using a split-detector at 10 ADD offset distance. We imaged a total of 35 participants, 10 controls and 25 patients with MS. From the 25 patients, 20 were included in a therapeutic protocol, targetting patients with optic neuritis (ON) who received an electrical stimulation of the optic nerve; the other 5 patients (4 without ON) were included in an observational protocol. Patients were followed over several months and were imaged over different time periods. Quantitative biomarkers such as cell density, cell size and motion speed were extracted over time. AOSLO images were co-localized with simultaneously acquired AO-OCT cross sections to determine the retinal depth of cells.

Results: Inflammatory cells were detected on the retinal ganglion cell layer (GCL) in MS patients. We determined their depth through AO-OCT where highly reflective spots corresponded to the cells observed on the AOSLO images. The cell density peaked right after the ON and decreased over the following weeks. Cells were also detected on the control eye with no ON from the patients undergoing therapy and a few isolated cells were detected on some observational patients.

Conclusions: These cells specifically detected in the GCL which is targeted by MS degeneration, with a density that varies over time in relation to symptomatic attacks of the disease are a quantifiable biomarker of the state of the inflammation and could be correlated with other changes in this layer caused by MS. We aim to use this biomarker to evaluate the influence of the inflammatory response in MS on the demyelination process.

CONTROL ID: 3709203
SUBMITTER (NAME ONLY): Samuel Marks
TITLE: Devaluing privacy: medicine for AI in the public domain
SESSION TITLE: Public Health I
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S.I. Marks, G.W. Armstrong, D.S. Friedman, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S.I. Marks, G.W. Armstrong, D.S. Friedman, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: Samuel Marks: Commercial Relationship: Code N (No Commercial Relationship) | Grayson Armstrong: Commercial Relationship: Code N (No Commercial Relationship) | David Friedman: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Advocate and demonstrate a public domain methodology for the collection, analysis, and use of medical data. This is as opposed to keeping patient data private and siloed; the norm. Although privacy is attractive, we posit insufficient attention is targeted on the advantages of its inverse: the public domain. Public domaining medical information enables the advance of knowledge and understanding (through data-pooling and disparate expert analysis), and its sharing, regardless of financial and physical positions.
Methods: Recruit ophthalmologists who are department directors to allow their patients to be screened without the siloed gatekeeper approach. Each individual patient must explicitly give their informed consent, and, following a grace period of 2 months, be unable to withdraw their consent. New public-domain software systems are designed to facilitate this process. The medicolegal and other bureaucratic requirements for running these studies will also be placed in the public domain to aid replication.
Results: Initiating two studies at two departments at a major top-tier eye \& ear hospital in the United States, specifically: its ophthalmic emergency and glaucoma departments. Over 1,000 new patient records are expected to be collected and public-domained every month.
Conclusions: The culmination of patient data from disparate locations is greater than the sum of its parts… being a great boon for everything from epidemiological analyses to automated diagnoses through Machine Learning and Artificial Intelligence. Long term we hope others follow suit with the public domain methodology.

CONTROL ID: 3709210
SUBMITTER (NAME ONLY): Raymond Iezzi
TITLE: A porcine model of advanced age-related macular degeneration
SESSION TITLE: Animal Models of Age Related Macular Degeneration
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: R. Iezzi, J. Gandhi, A.D. Marmorstein, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|
Commercial Relationships Disclosure: Raymond Iezzi: Commercial Relationship(s);Code P (Patent):Mayo Clinic | Jarel Gandhi: Commercial Relationship(s);Code P (Patent):Mayo Clinic | Alan Marmorstein: Commercial Relationship(s);Code P (Patent):Mayo Clinic
ABSTRACT BODY:
Purpose: There are currently no large-mammal surgical models for geographic atrophy with choroidal neovascularization (CNV). Our goal was to develop a porcine surgical RPE (retina pigment epithelium) debridement model to study the time course of photoreceptor cell loss and choroidal remodeling. This model was developed to study the therapeutic potential of RPE sheet transplantation, delivered using erodible fibrin scaffolds in mitigating the effects of acquired RPE cell loss.
Methods: This research is compliant with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Six 2-month-old female domestic pigs (Sus scrofa domesticus), purpose-bred for medical research were used for this study. Animals were screened for overall health by a veterinarian and underwent pre-surgical ophthalmological examination to assure that the cornea and lens were clear and that there was no evidence of retinal dialysis or detachment in the operative eye. Three-port triamcinolone-assisted 25-gauge pars plana vitrectomy was performed with careful separation of the posterior hyaloid in the area centralis. A 41-gauge needle was used to create a retinal bleb, detaching the area centralis outside of the tapetum. Endodiathermy was applied along the proximal bleb and a 2mm retinotomy was created with vertical scissors. A nitinol wire or 5-0 proline loop was used to gently debride and remove a 5mm diameter region RPE cells without rupturing Bruch’s membrane. Fluid-air exchange was performed and 20% SF6 gas was injected. Animals underwent color fundus photos at 2 weeks post-op. Fundus photos, OCT and OCT angiography (OCTA) were also performed at 1,2,3,4 and 6 months post-op. Retinal histology was obtained at 2, 4 and 6 months, post-op.
Results: Debridement of RPE resulted in geographic atrophy with progressive loss of photoreceptors and rapid loss of choriocapillaris within 2 months in all eyes. Pachychoroidal changes were also observed in Sattler and Haller layers. OCTA revealed non-exudative type 1 CNV, initially at the edges of the debridement zone by 2 months. At six months, non-exudative filamentous type 1 CNV progressed toward the center of the debridement zone.
Conclusions: Surgical debridement of the RPE results in geographic atrophy and CNV, reproducing both forms of advanced AMD. This surgical model is useful as a means of testing the role of RPE and other cell replacement in treating advanced AMD.

CONTROL ID: 3709211

SUBMITTER (NAME ONLY): Michael Jaskolka

TITLE: Exploratory Safety Profile of EDIT-101, a First-in-Human in vivo CRISPR Gene Editing Therapy for CEP290-related Retinal Degeneration

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.C. Jaskolka, S. El-Husayni, B. Duke, A. Erlwein, R. Myers, L.A. Michaels, M. Shearman, K. Zhang, S. Mukherjee, Editas Medicine, Cambridge, Massachusetts, UNITED STATES|M.E. Pennesi, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|E.A. Pierce, Ocular Genomics Institute, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|E.A. Pierce, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Leber congenital amaurosis type 10 is a retinal degenerative condition that causes severe visual impairment. To restore vision, we developed EDIT-101, an adeno-associated virus type 5 encoding Staphylococcus aureus Cas9 (SaCas9) expressed under the photoreceptor-specific GRK1 promoter and two guide RNAs designed to excise the disease-causing CEP290 mutation, c.2991+1655A>G (CEP290-IVS26). Safety and tolerability of EDIT-101 is being evaluated in the ongoing BRILLIANCE (NCT03872479) trial, an open-label, Phase 1/2 single ascending dose study enrolling adults and children. Viral shedding in body fluids of EDIT-101 treated subjects is a key exploratory safety endpoint in the trial. To monitor this key safety assessment, a SaCas9-based real-time quantitative polymerase chain reaction (qPCR) assay was developed and validated.

Methods: We developed a qPCR assay to quantify EDIT-101 vector genomes in blood and tears by targeting the SaCas9 transgene. Assay validation was performed to establish linearity, reproducibility, limits of detection, biological matrix effects, and acceptance criteria for EDIT-101 detection in samples collected throughout the BRILLIANCE trial.

Results: The validated assay for blood and tears has a lower and upper limit of quantification (LLOQ & ULOQ) of 25 to $1x10^7$ double stranded EDIT-101 vector genomes, respectively, and a lower limit of detection (LLOD) of 10 vector genomes. No matrix effect or amplification above the LLOD was observed in the absence of EDIT-101. The assay is highly reproducible and specific with an efficiency of 92% to 103% and a $R^2 \geq 0.998$.

EDIT-101 vector genomes were only detected in a small number of clinical samples. The highest levels were observed the day after treatment, then rapidly dropped below the LLOQ. Vector genomes were only identified in tears collected from inside the lower eyelid of the treated, but not the untreated eye. Of the blood and tear samples tested, fewer blood samples contained detectable vector genomes. Levels of vector shed were minimal compared to the initial dose, indicating low risk to the patient or environment.

Conclusions: We developed a SaCas9-specific qPCR assay to evaluate viral shedding in the BRILLIANCE trial. Our data suggests observed EDIT-101 shedding is transient and at low levels of detection, with no risk of systemic viral persistence.

CONTROL ID: 3709214

SUBMITTER (NAME ONLY): Usha Chakravarthy

TITLE: Characterization of associations between macular atrophy and subretinal fibrosis in treated neovascular AMD : 7 year findings from the IVAN trial

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Chakravarthy, Ophthalmology, Belfast Health and Social Care Trust, Belfast, Belfast, UNITED KINGDOM|

Commercial Relationships Disclosure: Usha Chakravarthy: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis, Iveric Bio, Boehringer Ingelgheim;Code E (Employment):Hoffman La Roche

ABSTRACT BODY:

Purpose: To describe the frequency of fibrosis and macular atrophy (MA) detected by optical coherence tomography (OCT) and to characterize associations with visual acuity (VA) after exit from the inhibition of VEGF in age-related choroidal neovascularization (IVAN: ISRCTN92166560) trial.

Methods: Participants in the IVAN trial were randomized to either ranibizumab or bevacizumab and after exit received usual care consisting of treatment with licensed anti VEGF agents and followed for up to 7 years after enrolment. Visual acuity (VA) and image grading of the most recent OCT in 372 surviving participants were obtained from a study visit or from usual care records. Fibrosis was inferred from presence of hyperreflective material (HRM) on OCT and location categorized into none, subretinal only , subretinal pigment epithelial (sub-RPE) only, or combined (subretinal plus sub-RPE) Figure 1. Graders assigned the latter two categories only when they detected an intact RPE layer with HRM on its outer and or inner aspect. MA was identified from subsidence of the inner nuclear and or outer plexiform layer, thinning of the outer nuclear layer, or a band of hypertransmission of OCT signal. Observations were excluded from VA descriptives when VA was unavailable within 30 days of the OCT image.

Results: Tabulations of MA and HRM shown in Figure 1. MA was present in 90%, HRM in 82% and either in 96%. When MA was absent (n = 39) one third of study eyes had no HRM. Whereas when MA was present (n = 333) around one-fifth had no HRM. When HRM was subretinal, MA was detectable in 95.4% and absent in 4.6%. When HRM was sub-RPE only, MA was present in 85.8% and absent in 14.2%. Both VA and OCT were available in 319 (86%) study eyes. Examining associations of MA and HRM with VA, VA was best when MA was present with no HRM (median VA 65.0, IQR 45.0, 75.0) or MA present with HRM sub-RPE only (median VA 64.5, IQR 43.0, 72.0). In eyes with MA when HRM was subretinal, median VA was 33.0 letters (IQR 18.0, 62.0). In the absence of MA, VA was similar across the HRM groups.

Conclusions: High proportions of neovascular AMD eyes treated with anti VEGF agents over a sustained period that have subretinal fibrosis exhibit MA. A visible RPE layer was associated with a lower risk of an eye having MA and better VA.

CONTROL ID: 3709217

SUBMITTER (NAME ONLY): Robert Lavker

TITLE: Synthetic high density lipoprotein (HDL) nanoparticles: a novel class of therapeutics for corneal mustard keratopathy

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Lavker, N. Kaplan, V. Onay, K. Lu, H. Peng, Dermatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|K. McMahon, A. Calvert, C. Thaxton, Urology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Robert Lavker: Commercial Relationship: Code N (No Commercial Relationship) | Nihal Kaplan: Commercial Relationship: Code N (No Commercial Relationship) | Kaylin McMahon: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Calvert: Commercial Relationship: Code N (No Commercial Relationship) | Venus Onay: Commercial Relationship: Code N (No Commercial Relationship) | Kurt Lu: Commercial Relationship: Code N (No Commercial Relationship) | Colby Thaxton: Commercial Relationship: Code N (No Commercial Relationship) | Han Peng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Sulfur mustard (SM), a chemical warfare agent, can cause severe corneal inflammation and permanent damage in vision in exposed individuals. We have demonstrated that topical treatment of HDL NPs can attenuate inflammation resulting from chemical burns. We also have shown that systemic treatment with vitamin D3 can attenuate skin inflammation induced by UV irradiation. In this study, we tested the potential of topical application of HDL NPs and vitD3 as novel therapeutics in ocular injuries induced by nitrogen mustard (NM), which is an analog of SM and can mimic perturbations caused by SM.

Methods: Mouse corneas were exposed to 0.5% NM for 1min. Corneas were treated 1hr post wounding, topically with HDL NPs, or HDL NP complexed with vitamin D3 daily for 4 weeks. To evaluate corneal clarity, mouse corneas were imaged for haze scoring. To determine epithelial integrity, corneas were stained with fluorescein and imaged. RT-qPCR was performed to examine expression of pro-inflammatory genes (e.g., Il1b, Ccl2, Inos). Whole mount staining using CD31 was conducted to visualize vessel egress into the cornea.

Results: NM exposure caused perturbations in the anterior segment including corneal haze, epithelial cell death, severe inflammation (e.g., increased expression of Il1b, Ccl2, Inos), extensive corneal neovascularization, and conjunctivalization (e.g., goblet cells in cornea) in the central cornea. This suggests a compromise in the limbal epithelial stem cell niche and can lead to limbal epithelial stem cell deficiency. After NM injury, topical treatment with HDL NPs (1μM) significantly attenuated NM-induced detrimental effects, such as corneal haze and increased expression of pro-inflammatory genes. Interestingly, HDL NP- Vit D3 treatment further reduced: (i) the amount of corneal fluorescein staining; (ii) degree of haze; and (iii) pro-inflammatory cytokine and chemokine expression. This indicates that Vit D3 in combination with HDL NPs have a synergistic effect in the alleviation of NM-induced corneal damage.

Conclusions: We have established a mouse model mimicking SM injured cornea. Our findings strongly suggest that topical delivery of HDL NPs and HDL NP-Vit D3 to the cornea and limbus have vast treatment potential for corneal mustard keratopathy.

CONTROL ID: 3709218

SUBMITTER (NAME ONLY): Yu Lin

TITLE: STZ is toxic to rat retinal progenitors and suppresses their expansion

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lin, X. Ren, D. Chen, Sichuan University West China Hospital, Chengdu, Sichuan, CHINA|

Commercial Relationships Disclosure: Yu Lin: Commercial Relationship: Code N (No Commercial Relationship) | Xiang Ren: Commercial Relationship: Code N (No Commercial Relationship) | Danian Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: STZ is toxic to pancreatic b cells and thus can induce type 1 diabetes, but if it has any direct effects on retinal cells is unknown. The purpose of this study is to investigate the effects of systemic administered STZ on the retina of neonatal rats.

Methods: STZ or citrate buffer (control) were subcutaneously injected into neonatal rats at postnatal day 1, 3, and 5 (P1/3/5). Electroretinogram (ERG), hematoxylin and eosin (H&E) staining, immunofluorescent staining, flow cytometry, and RNA sequencing were performed to evaluate the effects of STZ on retinal function and structure, and retinal cell differentiation at different time-points after STZ administration, from P2-P70.

Results: At P21, STZ reduced the amplitudes of dark-adapted a wave and b wave, as well as the total oscillatory potentials (OPs) energy. HE staining showed abnormal retinal structures from P5, including rosettes at the peripheral retina and ONL extrusions at the central retina. The retina is much thinner, including ONL and INL. Immunofluorescent staining revealed that the numbers of early-born retinal cell types (ganglion cells, cone, horizontal cells and amacrine cells) were not changed, but the late-born retinal cell types (rod, bipolar cells and Müller cells) were significantly reduced. STZ induced cell death ($TUNEL^+$ or active $caspase\ 3^+$) of retinal progenitor cells (RPCs), from P2-P5 (mainly at P3-P4). EdU labeling and Ki67 staining found that STZ suppressed the proliferation of RPCs and delayed the cell cycle exit of RPCs. Flow cytometry showed that the G2/M phase of STZ rats reduced significantly. STZ also delayed the development of retinal deep vascular plexus (DVP) at P10.

Conclusions: STZ is toxic to rat RPCs, induces cell death and cell cycle arrest of this cell type.

CONTROL ID: 3709223

SUBMITTER (NAME ONLY): Karen Anderson

TITLE: STK-002, an Antisense Oligonucleotide (ASO) for the Treatment of Autosomal Dominant Optic Atrophy (ADOA), is Taken Up by Retinal Ganglion Cells (RGC) and Upregulates OPA-1 Protein Expression After Intravitreal Administration to Non-human Primates (NHPs)

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Anderson, A. Venkatesh, T. McKenty, D. Slate, Q. Lin, S. Ravipaty, S. Jacobson, A. Christiansen, R. Benmohamed, J. Hoger, G. Liau, Stoke Therapeutics Inc, Bedford, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Karen Anderson: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Aditya Venkatesh: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Taylor McKenty: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Deidre Slate: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Qian Lin: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Shobha Ravipaty: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Sarah Jacobson: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Anne Christiansen: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Radhia Benmohamed: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Jeff Hoger: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics | Gene Liau: Commercial Relationship(s);Code E (Employment):Stoke Therapeutics

ABSTRACT BODY:

Purpose: ADOA is the most common inherited optic neuropathy, starting in the first decade of life and resulting in severe and progressive visual decline due to loss of RGCs. Most patients harbor loss-of-function mutations in the OPA1 gene that lead to haploinsufficiency. Reduced OPA1 protein levels result in impaired mitochondrial function in RGCs leading to cell death. Currently, there is no treatment for patients with ADOA. Targeted Augmentation of Nuclear Gene Output (TANGO) ASOs, such as STK-002, reduce the inclusion of a non-productive, alternatively spliced exon in OPA1, and leverage the wild-type allele to increase productive OPA1 mRNA and protein. We previously demonstrated that TANGO ASOs can increase OPA1 protein levels in human cell lines, rabbit retina, and ADOA patient fibroblasts. In this study, we evaluated ASO localization and OPA1 protein levels in the retina following intravitreal administration of STK-002 to NHPs.

Methods: Cynomolgus monkeys (N=22) received bilateral intravitreal injections of vehicle or STK-002. Eyes were collected at 4 or 8 weeks after injection. Retinas were isolated for molecular analyses and whole globes were prepared for histology. Retinal OPA1 mRNA and protein were measured using qPCR (Taqman) and enzyme-linked immunosorbent assay (ELISA), respectively. A hybridization ELISA (HELISA) method was used to quantitate STK-002 levels in retina. Whole globes were sent for custom assay development and detection of STK-002 by miRNAscope™ in situ hybridization (ISH), and detection of OPA1 protein by immunofluorescence (IF).

Results: Retinal exposure of STK-002 increased in a dose-dependent manner and remained high at the last timepoint evaluated (Week 8). STK-002 also dose-dependently increased protein levels at Week 4, ranging from 31 to 47% compared to vehicle, and levels were maintained at Week 8. ISH and IF analysis demonstrated that both STK-002 and OPA1 protein levels increased in RGCs, the target cells for ADOA.

Conclusions: STK-002 produced a dose-dependent and persistent increase in OPA1 protein expression in the retinas of NHPs. ASO-induced increase in OPA1 protein levels in RGCs represents a potentially disease-modifying therapy for patients with ADOA.

CONTROL ID: 3709225

SUBMITTER (NAME ONLY): Clayton Santiago

TITLE: Single-cell RNA sequencing analysis of neurogenic competence in Müller glia in a rabbit retinal injury model

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.P. Santiago, M. Gimmen, S. Blackshaw, Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|Y. Lu, Y. Xin, M. McNally, C. Eberhart, J. Qian, M. Singh, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|T. Creamer, Basic Biomedical Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|L. Orzolek, Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|T. Zollner, W. Schubert, K. Nassar, Bayer AG, Wuppertal, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: The capacity for endogenous regeneration of retinal neurons after injury varies greatly among vertebrate species. For example, zebrafish Müller glia can regenerate all major retinal cell types after injury, while those in mice appear to lack this ability. The neurogenic potential of retinal glia in other mammalian model organisms is currently unknown. In this study, we aimed to identify genes and transcriptional networks involved in regulating neurogenic competence in a rabbit model of retinal injury.

Methods: Animal procedures were conducted in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by the Johns Hopkins Animal Care and Use Committee. Unilateral retinal injury was induced in Dutch Belted rabbits by vitrectomy, retinotomy, retinal detachment, platelet-rich plasma injection, and cryotherapy. At different time points after injury, extracted retinas were dissociated and processed to assess the transcriptional profile by single cell RNA sequencing (sc-RNAseq). Fellow eyes were used as non-injury controls.

Results: Retinas were harvested at time points ranging from six hours to 35 days after injury induction. We profiled >70,000 single cells in this study. All major retinal cells including neurons, glia, and retinal pigment epithelium cells were identified in the data sets using selected marker genes. We identified two trajectories of glial cells post-injury: the first expressing classical fibrotic markers (ACTA2 and COL1A1) and the second expressing several genes that are known to promote proliferation (MKI67, MYBL2, UBE2C, TOP2A and HMGA2) and neurogenic competence (ASCL1, GADD45G, KLF6, MSX2, OLIG2, HES6, BHLHE22 and NEUROG2).

Conclusions: Our high throughput transcriptomic analysis identified known fibrotic and neurogenic genes that were differentially expressed between control and injury states in the rabbit model. These findings may facilitate further research in large mammalian models on molecular pathways that could be targeted to induce neurogenesis in human Müller glia following retinal injury.

CONTROL ID: 3709226

SUBMITTER (NAME ONLY): Dustin Morley

TITLE: Multi-Device Pupil, Limbus, and Eyelid Segmentation using Deep Learning

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Morley, M. Evans, R&D, LENSAR, Orlando, Florida, UNITED STATES|

Commercial Relationships Disclosure: Dustin Morley: Commercial Relationship(s);Code E (Employment):LENSAR | Mike Evans: Commercial Relationship(s);Code E (Employment):LENSAR

ABSTRACT BODY:

Purpose: This study describes the application of deep learning methodology to identify the pupil, limbus, and eyelid boundaries in images from a variety of commercially available topographers with a single unified software approach.

Methods: 604 de-identified unique grayscale infrared iris images were obtained from a variety of commercially available topographers. All images had the boundaries delineating the pupil and visible iris annotated by hand using software tools. A custom pupil warping method was utilized to produce augmented copies of each image with the iris “stretched” to varying pupil shapes and sizes. A deep convolutional neural network based on the U-Net architecture was trained to label pixels from these images as belonging to the pupil, iris or neither. An active contours algorithm was developed to post-process the U-Net output into geometric curves and infer eyelid interference based on the shape of the iris contour. Performance was evaluated through two-fold cross-validation based on geometric center accuracy and dice coefficient (F1 score) of the final curve-bounded regions.

Results: The pupil and limbus were correctly identified in 603 of 604 unique eyes for a success rate of 99.8%. The pupil center error – defined as the Euclidean distance between the center-of-mass of the hand-labeled pupil region and the center of the best-fit ellipse to the identified pupil curve – was below 5 pixels in 98.7% of cases, below 10 pixels in 99.5% of cases, and below 15 pixels in 99.7% of cases (pixel scaling varies from approximately 0.03 to 0.045 mm per pixel). The similarly defined limbus center error was below 5 pixels in 69.2% of cases, below 10 pixels in 95.0% of cases, and below 15 pixels in 99.8% of cases. Dice coefficients measured above 0.95 in 95.6% of cases for the pupil, 98.2% for the composite iris region (including the pupil area), and 92.0% for the exclusive iris region (excluding the pupil area).

Conclusions: Modern deep learning technology is capable of segmenting iris images from a wide variety of diagnostic devices under a unified software approach, with a standardized image resizing scheme serving as the only device-specific operation. This technological advance has significant implications for device interoperability, as it can enable device software to handle images from multiple additional input devices with little or no modification.

CONTROL ID: 3709230

SUBMITTER (NAME ONLY): Darren Lee

TITLE: A novel and distinct TIGIT-dependent Treg subset provides resistance to relapsing uveitis through suppression of Th17 cells

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.J. Lee, T. McDonald, K. Peters, Ophthalmology/Dean McGee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|D.J. Lee, Microbiology and Immunology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Darren Lee: Commercial Relationship: Code N (No Commercial Relationship) | Trisha McDonald: Commercial Relationship: Code N (No Commercial Relationship) | Kayleigh Peters: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Experimental autoimmune uveitis (EAU) is used to gain a better understanding of human autoimmune uveitis. EAU-resolution is in part due to emergence of ocular antigen specific regulatory T cells (Tregs) that express T cell Immunoreceptor with Ig and ITIM domains (TIGIT). We have previously published that post-EAU TIGIT^{+} Tregs are distinct from post-EAU PD-1^{+} Tregs, and that Treg induction of PBMCs from uveitis patients induces significantly fewer TIGIT^{+} Tregs compared to controls. The role for TIGIT on Th17 cells over the course of EAU is not well understood.

Methods: IL-17-GFP and Foxp3-GFP reporter mice given TIGIT blocking antibody (Ab) at the onset of EAU and post-EAU mice were reimmunized for EAU. Flow cytometry analysis of TIGIT expression on Th17 and Tregs was done at the onset of EAU. Slit lamp examination and infiltration of Th17 and Tregs into the eye was done throughout disease and following reimmunization.

Results: We observed Th17 cells emerge in the eye beginning at the onset of EAU and diminish as EAU resolved. At the onset of EAU flow cytometry analysis of ocular T cells revealed 2-5-fold more TIGIT^{+} T cells in the FoxP3 compartment compared to the Th17 compartment. The reporter mice confirmed a persistence of Tregs in the eye compared to a decrease in Th17 cells as resolution of EAU occurred. Mice administered TIGIT blocking Ab showed no difference in the course of disease compared with control EAU mice. Reimmunization of EAU resulted in a significant increase in EAU of mice that received TIGIT blocking Ab compared to control EAU mice that received isotype Ab. Reimmunization of reporter mice that received TIGIT Ab showed diminished Tregs, and an increase of Th17 cells in the eye. In contrast, control reporter mice that received isotype had an increase in Tregs, and a decrease in Th17 cells in the eye.

Conclusions: This work suggests that TIGIT is needed for the induction of Tregs that emerge and persist in the eye over the course and resolution of EAU. Additionally, TIGIT signaling limits the migration of Th17 cells into the eye as resolution of EAU occurs. We also provide evidence that relapse of EAU may be due to an expansion of Th17 cells in the eye, and this expansion may be limited by TIGIT-dependent Tregs. The implication of this work is that TIGIT signaling may be an important mechanism that provides resistance to relapsing autoimmune uveitis.

CONTROL ID: 3709234

SUBMITTER (NAME ONLY): Giulia Midena

TITLE: In vivo intraocular biomarkers in uveal melanoma: an aqueous humor proteomic study.

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Midena, M. Bruno, G. Esposito, A. Micera, E. Midena, IRCCS – Fondazione Bietti, Roma, ITALY|R. Parrozzani, E. Midena, Department of Ophthalmology, University of Padova, Padova, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the presence of specific aqueous humour (AH) biomarkers in eyes affected by uveal melanoma (UM) and to correlate them with tumor genetic and clinical characteristics.

Methods: Seventy-two eyes affected by primary UM were included. Tumor thickness, serous detachment and largest basal diameter were specific clinical characteristics. During brachytherapy AH sample collection and transscleral fine needle aspiration biopsy were performed. AH samples were analyzed by microarray and western blotting techniques to quantify selected proteins. Cytologic material underwent fluorescence in situ hybridization for chromosome 3. The AH of thirty-six normal eyes, scheduled for cataract surgery, was used as control.

Results: Compared with the control group, significantly higher levels of Somatostatin Receptor Type 1 (SSTR1; p=0.027), Splicing Factor 3B subunit 1 (SF3B1; p=0.026), BRCA1 Associated Protein 1 (BAP1; p=0.012), Guanine nucleotide binding protein [G protein], q polypeptide (GNAQ; p=0.024), Human Melanoma Black (HMB45; p=0.017), Interleukin-6 (IL-6; p=0.049), IL-8 (p=0.007), Regulated upon Activation Normal T cell Expressed and Secreted (RANTES; p=0.009), Pigment Epithelium-Derived Factor (PEDF; p=0.049), Osteopontin (p=0.049), Epidermal Growth Factor (EGF; p=0.042), basic Fibroblast Growth Factor (bFGF; p=0.018), Macrophage Inhibiting Factor (MIF; p=0.008), Monocyte Chemoattractant Protein (MCP; p=0.022) were detected in UM group. A positive significant correlation was found between: tumor thickness and IL-8($p = 0.032$) and VEGF($p = 0.032$), degree of serous retinal detachment and IL-6 ($p = 0.021$), largest basal diameter and RANTES ($p = 0.031$). Monosomy 3 was detected in 34 cases (47%) and disomy 3 in 38 cases (53%). Statistically significant higher levels of inflammatory proteins were detected in eyes with monosomy 3 UM (p=0.049).

Conclusions: Selected biomarkers may be identified in the AH of eyes affected by UM. These findings not only confirm in vivo the possibilities offered by AH analysis in UM eyes, but suggest that AH evaluation may represent the liquid biopsy approach in UM diagnosis, prognosis and follow-up.

CONTROL ID: 3709235

SUBMITTER (NAME ONLY): Milica Margeta

TITLE: APOE4 impairs the response of neurodegenerative microglia and prevents neuronal loss in glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Margeta, K.M. Pitts, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|O. Butovsky, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Milica Margeta: Commercial Relationship(s);Code P (Patent):G3P | Kristen Pitts: Commercial Relationship: Code N (No Commercial Relationship) | Oleg Butovsky: Commercial Relationship(s);Code P (Patent):G3P

ABSTRACT BODY:

Purpose: The apolipoprotein E4 (APOE4) allele is associated with an increased risk of Alzheimer's disease and a decreased risk of glaucoma and age-related macular degeneration, but the underlying mechanisms remain poorly understood. Prior research has demonstrated that Apoe is a critical regulator of the microglial neurodegenerative (MGnD/DAM) molecular signature in disease. The goal of this study was to investigate the effect of human APOE alleles, APOE3 and APOE4, on microglial molecular signature and retinal ganglion cell (RGC) survival in glaucoma in order to test the hypothesis that the APOE4 allele is protective in glaucoma.

Methods: We investigated the microglial molecular signature in humanized APOE3 and APOE4 mice using the microbead (MB) glaucoma model. Retinal microglia were isolated one month after MB injection as CD11b+/Ly6C-/FCRLS+ cells and underwent Smart-Seq2 RNA sequencing. RGC survival was assessed in MB-injected APOE3 and APOE4 humanized mice using Brn3a+ cell body and PPD axon counts. As Galectin-3 (Lgals3) was found to be one of the strongly differentially expressed genes between APOE3 and APOE4 microglia, RGC survival was also evaluated in MB-injected Lgals3$^{-/-}$ mice and in wildtype mice intravitreally treated with Galectin-3 inhibitor TD139. Human retinal postmortem samples were genotyped for APOE and immunostained for Iba1 and Galectin-3.

Results: We have found that MB-injected APOE3 animals experience significant RGC loss and their microglia transition to MGnD molecular phenotype, characterized by upregulation of inflammatory cytokines, complement, and Lgals3. In contrast, MB-injected APOE4 animals were protected from RGC degeneration, and their microglia did not upregulate MGnD genes despite IOP elevation. Genetic and pharmacologic targeting of Galectin-3, the downstream effector of Apoe, also ameliorated RGC degeneration. Finally, Galectin-3 was upregulated in microglia in human APOE3 glaucoma samples, and its expression was attenuated in APOE4 glaucomatous retinas.

Conclusions: In this study we demonstrate that APOE4 impairs the response of neurodegenerative microglia and protects RGCs from glaucomatous degeneration. These results provide an explanation as to why the APOE4 allele is associated with a decreased risk of glaucoma and show that the APOE-Galectin-3 signaling pathway can be targeted to develop novel neuroprotective therapies for this blinding disease.

CONTROL ID: 3709236
SUBMITTER (NAME ONLY): Reed Pifer
TITLE: Low in vitro Serratia marcescens Adhesion to Lehfilcon A Contact Lenses
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Pifer, V. Harris, M. Crary, P. Shannon, Alcon Research Institute, Fort Worth, Texas, UNITED STATES|
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ABSTRACT BODY:
Purpose: Lehfilcon A is a new monthly replacement contact lens with a silicone hydrogel core and a Celligent® Technology water gradient surface with a ≥90% surface water content. The surface polymer, 2-methacryloyloxyethyl phosphorylcholine (MPC), creates a nanofiber structure on the lehfilcon A lens surface. MPC coatings protect against fouling by foreign substances, including microorganisms. Therefore, in this in vitro experimental study, we examined the ability of Serratia marcescens to adhere to lehfilcon A and leading monthly or bi-weekly replacement contact lenses.
Methods: We performed quantitative adhesion assays to evaluate the adherence of S. marcescens to seven contact lens materials (lehfilcon A, comfilcon A, senofilcon A, omafilcon B, fanfilcon A, balafilcon A, and senofilcon C). Individual contact lenses were incubated in the presence of S. marcescens and gently rinsed to remove non-adherent bacteria. Adherent bacteria were eluted from lenses via sonication and bacterial colony forming units (CFU) were enumerated by plating. CFUs were normalized to the surface area of each lens. Statistical analyses were performed as t-tests for differences in the mean log CFU/mm^2 between lens types without assuming equal standard deviation between groups. Bonferroni correction was used to account for multiple comparisons.

We performed fluorescent microscopy to qualitatively evaluate bacterial adherence to lehfilcon A and comparison lenses. The cell surface of live S. marcescens was stained with a protein-conjugating dye, 5(6)-Carboxytetramethylrhodamine succinimidyl ester (TAMRA-SE). Labeled bacteria were used in adhesion assays as described above, fixed with paraformaldehyde, and contact lenses were imaged using a TRITC filter.
Results: We observed lower densities of S. marcescens adhered to lehfilcon A (2.6 ± 0.3 log CFU/mm^2) relative to the next best performing lens material, comfilcon A (4.6 ± 0.3 log CFU/mm^2; $p < 0.0001$). This difference corresponds to ≥99.0% lower adhesion to lehfilcon A. In agreement, fluorescent microscopy visually demonstrated lower levels of bound bacteria to lehfilcon A vs alternative lens materials.
Conclusions: Our in vitro data suggests that S. marcescens adheres to lehfilcon A at low levels relative to comparable marketed contact lenses. These results add to the body of evidence that MPC coatings confer anti-fouling properties to medical devices.

CONTROL ID: 3709237

SUBMITTER (NAME ONLY): Majlinda Lako

TITLE: Conjunctival epithelial cells resist productive SARS-CoV-2 infection

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lako, R. Jackson, M. Georgiou, J. Collin, E. Stephenson, M. Haniffa, L. Armstrong, F.C. Figueiredo, R. Queen, Biosciences Institute, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|C. Hatton, J. Spegarova, C. Duncan, Translational and Clinical Research Institute,, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|H. Mudhar, B. Wagner, National Specialist Ophthalmic Pathology Service (NSOPS) Dept of Histopathology,, Royal Hallamshire Hospital, Sheffield, UNITED KINGDOM|P. Rooney, 5.NHS Blood and Transplant Tissue and Eye Services, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The ocular surface is a defined route of entry of several viral pathogens. Conjunctival epithelial cells, which express viral entry receptors ACE2 and TMPRSS2, constitute the largest exposed epithelium of the ocular surface tissue, and may represent a relevant viral entry route. An important unresolved question is whether SARS-CoV-2 can infect the conjunctival epithelial cells.

Methods: Adult human eyes from three female donors of 52, 78, and 80 years old were donated for research following informed consent. All tissue was provided by NHS Blood and Transplant Tissue and Eye Services or the Newcastle NHS Trust following ethical approval (18/YH/04/20). Conjunctival epithelial progenitors were expanded on 3T3 mitotically inactivated feeder cells and differentiated using an air-liquid interface (ALI) method. Single cell RNA-Seq, with complementary imaging and virological assays were used to define the cellular permissiveness of various epithelial cell types in the conjuctiva and determine the cell type specific innate immune response to SARS-CoV-2 infection.

Results: We generated an organotypic ALI model of conjunctival epithelium, composed of progenitor, basal and superficial epithelial cells and fibroblasts, which could be maintained successfully up to day 75 of differentiation. Using single-cell RNA Seq, with complementary imaging and virological assays, we observed that while all conjunctival cell types were permissive to SARS-CoV-2 genome expression, a productive infection did not ensue. The early innate immune response to SARS-CoV-2 infection in conjunctival cells was characterised by a robust autocrine and paracrine NF-Kβ activity, without activation of antiviral interferon signalling.

Conclusions: The data presented herein show that conjunctival epithelium is permissive to SARS-CoV-2 infection, but without evidence of productive viral replication. This study was performed in organotypic models derived from three different patients, with single cell RNA-Seq data obtained from the peak infection interval. Future work should assess changes in transcriptome of each conjunctival cell type in frequent intervals after infection and in a larger number of donors to get deeper insights into the refractory nature of these cell to viral propagation.

CONTROL ID: 3709238

SUBMITTER (NAME ONLY): Douglas Borchman

TITLE: Spectroscopic study of perfluorohexyloctane – human meibum interactions

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Vittitow, Clinical Affairs, Bausch and Lomb, Bridgewater, New Jersey, UNITED STATES|A. Ewurum, Chemistry, University of Louisville College of Arts and Sciences, Louisville, Kentucky, UNITED STATES|D. Borchman, S.R. Veligandla, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure: Douglas Borchman: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch + Lomb | Jason Vittitow: Commercial Relationship(s);Code E (Employment):Bausch + Lomb | Anthony Ewurum: Commercial Relationship: Code N (No Commercial Relationship) | Sravya Veligandla: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Perfluorohexyloctane (PFHO, NOV03) is under clinical investigation for the treatment of dry eye disease (DED) associated with meibomian gland dysfunction. We evaluated the physical properties of PFHO along with its in vitro effect on meibum from a human volunteer.

Methods: PFHO structure and interactions with standard lipid esters (LEs), a wax ester (WE), and with meibum from a 68-year old Caucasian volunteer without DED were studied using absorbance spectroscopies. Lipid composition and concentrations in the collected meibum were measured using nuclear magnetic resonance (NMR) spectroscopy. Evaporation rates were measured gravimetrically.

Results: PFHO is a liquid between -30°C and 70°C and evaporates at a rate of 0.137 ± 0.003 μm/min. When layered on top of physiological saline, PFHO inhibited the evaporation rate of saline by 84% ($P < 0.0001$). Stearylpalmitate and cholesterylstearate, two ordered LEs, were visibly insoluble in PFHO, whereas oleyloleate, a fluid WE, was soluble in PFHO. Addition of PFHO had a minimal effect on ordered LEs but increased the fluidity of the WE by 64%. Addition of PFHO to meibum (19:1, g:g) significantly increased the magnitude of the phase transition and decreased the cooperativity and minimum frequency of the phase transition of meibum but did not change the order of the lipids at physiological temperatures.

Conclusions: PFHO is a potential replacement for the tear film lipid layer in patients with DED: it significantly decreases the rate of evaporation, a property related to tear film stability. However, PFHO did not change the lipid order in meibum from a healthy volunteer. We speculate that PFHO could form a protective layer on the tear film surface that enhances tear film spreading as well as decreasing the rate of evaporation. Further in vitro rheological and in vivo evaporation rate studies are warranted along with interaction studies with meibum from DED patients.

CONTROL ID: 3709241

SUBMITTER (NAME ONLY): Ping Yang

TITLE: Cellular Uptake of Risuteganib via Endocytosis in Cultured Human RPE Cells

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Yang, R. Trimpey-Warhaftig, G.J. Jaffe, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|J. Koo, Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California, UNITED STATES|J. Park, H. Karageozian, V.H. Karageozian, Z. Shao, Allegro Ophthalmics, LLC, San Juan Capistrano, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Risuteganib (RSG) is a synthetic peptide that has shown promising efficacy in an intermediate dry age-related macular degeneration (AMD) phase 2 clinical study. We previously reported that RSG protected against retinal pigment epithelial (RPE) cell injury induced by hydroquinone (HQ), a major oxidant in cigarette smoke and atmospheric pollutants agents implicated in AMD pathogenesis. Herein, we investigate whether RPE cells take up RSG.

Methods: Cultured human RPE cells were transduced overnight with late endosome-GFP, mitochondria-GFP, or endoplasmic reticulum-GFP using CellLight Reagents (BacMam 2.0) at 40 particles per cell. Cells were washed, incubated with Alexa Fluor™ 555 alkyne, triethylammonium salt (AF555, 50uM, control) or RSG-Alexa Fluor™ 555 (RSG-AF555, 50uM, synthesized using Fmoc [the fluorenylmethoxycarbonyl protecting group] solid-phase peptide synthesis and N-Hydroxysuccinimidyl ester-amine reaction) for various times at 37°C or for 2.5 hours at 4°C. RSG co-localization with cell organelles were examined by confocal microscopy.

Results: A large amount of cytoplasmic dot-like staining was detected in RSG-AF555-treated cells while little staining was seen in AF555-treated cells 2.5 hours post-treatment. The cytoplasmic dot-like staining pattern in RSG-AF555-treated cells was dramatically reduced at 4°C when compared to 37°C at 2.5 hours post-treatment. RSG-AF555 accumulated in the cells as early as 30 minutes and remained for at least 21 hours. In RSG-AF555-treated cells, some RSG-AF555 dots were co-stained with late endosome and additional RSG-AF555 dots were co-stained with mitochondrial and endoplasmic reticulum 2.5 hours post-treatment.

Conclusions: Experiments at temperatures that permit and inhibit endocytosis suggest that cultured RPE cells take up RSG via endocytosis. Co-localization of RSG with cell organelles may be involved in RSG's protection against HQ-induced cell damage.

CONTROL ID: 3709243

SUBMITTER (NAME ONLY): Harsh Patel

TITLE: Ethylene-vinyl acetate (EVA) based implant for ocular inflammation

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Patel, E. Dobrzykowski, G. Ferrara, B. Wilson, C. Holmes, J. Haley, Long acting drug delivery, Celanese Corporation, Irving, Texas, UNITED STATES|S. Mathew, Analytical, Celanese Corporation, Irving, Texas, UNITED STATES|

Commercial Relationships Disclosure: Harsh Patel: Commercial Relationship: Code N (No Commercial Relationship) | Sanyo Mathew: Commercial Relationship: Code N (No Commercial Relationship) | Edward Dobrzykowski: Commercial Relationship: Code N (No Commercial Relationship) | Gerald Ferrara: Commercial Relationship: Code N (No Commercial Relationship) | Brian Wilson: Commercial Relationship: Code N (No Commercial Relationship) | Cyonna Holmes: Commercial Relationship: Code N (No Commercial Relationship) | Jeffery Haley: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Treatment for ocular inflammation includes intravitreally administered corticosteroid treatments which are plagued by inconsistent delivery and inability to maintain significant level of drug for a long period of time. This study proposes that sustained release of dexamethasone via a polymeric implant is an ideal solution for long term (> 6 months) delivery to treat chronic inflammation. This study demonstrates dexamethasone release from an EVA implant and highlights the ability to tune the release rate of a therapeutic with various loading percentages and polymer grades.

Methods: Powdered EVA with vinyl acetate contents of 28% and 40% were blended with dexamethasone at loading levels of 20% and 50%. These blends were compounded via hot melt extrusion (HME) on a 11mm twin screw extruder to produce four formulations. For each formulation, implants (N=6) were cut and weighed before placing them into Eppendorf conical tubes containing 5 mL buffer solution (pH =7.4). The tubes were placed into temperature-controlled incubators at 37 °C and 100 rpm. Samples were pulled at 1, 2, 7, 14, 21, 28 days and release were calculated via ultra-performance liquid chromatography (UPLC) method with thermo Fisher Scientific Vanquish UPLC equipped with an Ultra C18 column at 23 °C.

Results: All formulations demonstrated dexamethasone release at day one. 50% loaded formulations released dexamethasone at a higher concentration when compared to 20%-loaded formulations. EVA with 40% VA and 50% loaded with dexamethasone released 2.36 mg dexamethasone compared to 1.21 mg for EVA with 28% VA and loaded 20% at 28 days.

Conclusions: An EVA implant achieves sustained release of dexamethasone. Altering VA content is a tunable implant parameter that can be used to achieve the desired release profile of dexamethasone. The loading percentage has a larger effect on the release rate compared to the VA percentage in EVA. The demonstrated 1-month release rate, in tandem with modeling, provides evidence that an EVA implant can deliver dexamethasone for greater than 6 months.

CONTROL ID: 3709244

SUBMITTER (NAME ONLY): Jonathan Regenold

TITLE: Correlation between Diopsys® NOVA fixed-luminance flicker phase and Diagnosys® flicker implicit time

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Regenold, H. Ghoraba, H.L. Doan, M. Zaidi, J.J. Hwang, C. Or, I. Karaca, A. Akhavanrezayat, N. Than, C. Yasar, N. Yavari, S. Park, Y.H. Khan, A. Mobasserian, D.V. Do, Q.D. Nguyen, Byers Eye Institute, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|H.L. Doan, Truong Dai hoc Y khoa Pham Ngoc Thach, Ho Chi Minh, Ho Chi Minh, VIET NAM|

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ABSTRACT BODY:

Purpose: Diopsys® NOVA is a novel electroretinography (ERG) system that can perform flicker ERG testing. In this cross-sectional study, we assess the correlation between Diopsys® NOVA fixed-luminance flicker ERG phase and Diagnosys® Espion 2 flicker ERG implicit time measurements.

Methods: This study was a retrospective evaluation of patients with various retinal pathologies who underwent Diopsys® NOVA fixed-luminance and Diagnosys® Espion 2 flicker testing over a period of seven months. Patients who had an interim period of three or more months between the two tests were excluded. Patients who had any surgical intervention or change in disease activity between the two tests were excluded. Baseline patient characteristics including age, sex, and underlying diseases were collected. Pearson correlation coefficient was used for correlation analysis of values measured by the Diopsys® NOVA and the Diagnosys® Espion 2 flicker tests.

Results: The average Diopsys® phase measurement was 301.76 ± 38.02° while the average Diagnosys® implicit time measurement was 30.64 ± 4.28 milliseconds. A significant, strong negative correlation (r= -0.814, P<0.001) was observed between phase and implicit time measurements (Figure 1). Mean age of patients was 53.3 ± 24.1 years. 58% (n=7/12) of patients were female. Best corrected visual acuity ranged from 20/20 to hand motion. Ocular conditions included retinal vasculitis (n=7/22 eyes, 32%), melanoma associated retinopathy (n=2/22 eyes, 9%), panuveitis (n=2/22 eyes, 9%), autoimmune retinopathy (n=2/22 eyes, 9%), autoimmune optic neuropathy (n=2/22 eyes, 9%), non-proliferative diabetic retinopathy (n=2/22 eyes, 9%), age-related macular degeneration (n=2/22 eyes, 9%), tuberculous choroiditis (n=2/22 eyes, 9%), and retinal vein occlusion (n=1/22 eyes, 5%). Five patients (42%) had significant systemic associations including metastatic cutaneous melanoma, HLA-A29 positivity, tuberculosis, breast cancer, multiple sclerosis, and autoimmune hepatitis.

Conclusions: Higher Diopsys® NOVA fixed-luminance flicker ERG phase values are strongly correlated with lower Diagnosys® Espion 2 flicker ERG implicit time values. Our results suggest that Diopsys® NOVA fixed-luminance flicker ERG phase is consistent with Diagnosys® Espion 2 flicker ERG implicit time.

CONTROL ID: 3709246

SUBMITTER (NAME ONLY): Knut Stieger

TITLE: Increasing the amount of template favors HDR mediated DSB repair in photoreceptors in vivo following AAV mediated gene transfer

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Stieger, M. Knapp, D. Götzmann, A. Janise-Libawski, B. Gill, B. Fühler, T. Wimmer, B. Müller, Department of Ophthalmology, Justus Liebig Universitat Giessen, Giessen, Hessen, GERMANY|

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ABSTRACT BODY:

Purpose: Genome editing takes center stage in the development of new therapeutic applications for the treatment of inherited diseases. While a lot is known with regard to DNA repair processes and necessary modifications upon induction of a double strand break (DSB) at the target site in dividing cells in vitro, hardly anything is known in nondividing cells of different tissues in vivo, such as neurons. Therefore, the aim of the present study was to analyze the influence of template DNA quantity on the activity of nonhomologous endjoining (NHEJ) and homology directed repair (HDR) of DSBs in photoreceptor cells in vivo.

Methods: Sixteen hemizygous male or homozygous female mice (age: 2 months) of the C57BL/6-RPGR.^{tm1Sti} mouse line were injected subretinally with AAV2/8 vectors harboring the ISce-I homing endonuclease and a GFP frame linked by a T2A linker under the control of the rhodopsin kinase (Rk) promoter alone or together with a template (changing the ISce-I target site into a HindIII site) either in an all-in-one vector, or as two vectors at the ratio of 1:1 or 1:10 (endonuclease : template). Following euthanasia, GFP positive cells were enriched by FACS, and consequences of DNA repair activity studied at the target site by sanger sequencing and TIDE analysis.

Results: Between 10% (ISce-I vector alone), 15 and 17% (ISce-I and template all in one or 1:1 ratio, respectively) and 25% (ISce-I and template at 1:10 ratio) total editing activity was observed in targeted photoreceptor cells. While the NHEJ activity declined slightly from 10% (ISce-I vector alone) to 8% for the all in one vector and 6% for both vector combinations, the HDR activity increased from 8 and 9% for all in one vector and 1:1 ratio to 19% for the 1:10 ratio vector combination. Deletions and substitutions outnumbered insertions in NHEJ repair events and appeared to occur more often at the 5' site of the DSB.

Conclusions: Targeted DNA editing is possible in photoreceptor cells using the ISce-I homing endonuclease in vivo. The rate of HDR increases significantly with higher amounts of template. This correlation, which is known from in vitro experiments, has important implications in the design of therapeutic applications and may contradict the notion that all in one vectors are more efficient in gene transfer for genome editing applications.

CONTROL ID: 3709248

SUBMITTER (NAME ONLY): Timo Mulders

TITLE: Structure-function correlation of retinal photoreceptors in healthy subjects and PRPH2-associated Central Areolar Choroidal Dystrophy patients assessed by high-resolution scanning laser imaging and microperimetry

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Mulders, B. Klevering, C.B. Hoyng, T. Theelen, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|L. van der Zanden, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: High Magnification Module (HMM™, Heidelberg Engineering, Heidelberg, Germany) imaging is a novel technique, designed to visualize the retina at a cellular level. To assess the potential of HMM™ metrics as clinical endpoints for future trials, we evaluated correlations between structural HMM™ metrics, spectral-domain OCT (SD-OCT, Heidelberg Engineering, Heidelberg, Germany) and retinal sensitivity on MAIA microperimetry (MP, CenterVue, Padova, Italy) in healthy subjects and p.arg142trp PRPH2-associated Central Areolar Choroidal Dystrophy (CACD) patients.

Methods: We projected a default 10° MP grid on composite HMM™ images and performed automated cone density (CD), intercell distance (ICD) and nearest neighbor distance (NND) analysis at stimuli located at 3 and 5° retinal eccentricity. We averaged HMM™ metrics and MP sensitivity of each participant if located at similar eccentricity (3 or 5°) and meridian (superior, inferior, temporal or nasal) and calculated Pearson correlation coefficients. We manually measured outer retinal thickness (ORT) on SD-OCT in absolute scotomas and relative scotomas, outside of focal atrophy. We defined ORT as the distance between RPE/Bruch membrane and the external limiting membrane (ELM).

Results: We included 15 genetically confirmed CACD patients and 5 healthy subjects. All correlations of HMM™ metrics and MP sensitivity at 3° reached statistical significance and are depicted in table 1. With exception of the inferior meridian with a Pearson r of -0,577 (p= 0,015396) for ICD, we were unable to find significant correlations at 5°. We found ORT in absolute scotomas to be statistically significant thinner (p=0.033) compared to relative scotomas of the same subject and retinal eccentricity, while CD of the corresponding areas did not differ significantly (p=0.945).

Conclusions: We have established significant correlations between multiple structural metrics on HMM™ imaging and retinal sensitivity on MP in healthy subjects and p.arg142trp PRPH2-associated CACD patients. A multimodal approach combining SD-OCT with HMM™ imaging and MP may allow for detailed mapping of retinal photoreceptor integrity, which may be used as biomarkers in future clinical trials.

CONTROL ID: 3709249

SUBMITTER (NAME ONLY): Caroline Baumal

TITLE: Personalized treatment interval (PTI) dosing dynamics over 2 years in the phase 3 YOSEMITE and RHINE trials of faricimab in diabetic macular edema

SESSION TITLE: Diabetic Macular Edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.R. Baumal, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|J. Kitchens, Retina Associates of Kentucky, Kentucky, UNITED STATES|G. Jaffe, Duke Reading Center, Duke University, North Carolina, UNITED STATES|B. Gerendas, Vienna Reading Center, Medical University of Vienna, AUSTRIA|F. Abreu, K. Asik, A. Camino, Z. Haskova, Genentech, Inc., South San Francisco, California, UNITED STATES|N. Jain, Roche Products Ltd, Welwyn Garden City, Hertfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Dual inhibition of the angiopoietin-2 and vascular endothelial growth factor (VEGF)-A pathways with faricimab may extend treatment durability beyond current anti-VEGF therapies for diabetic macular edema (DME). The PTI algorithm in the phase 3 YOSEMITE/RHINE trials was a protocol-driven treat-and-extend regimen, designed to test the durability of faricimab by tailoring dosing intervals to individualized treatment response.

Methods: YOSEMITE/RHINE (NCT03622580/NCT03622593) were randomized, double-masked, active comparator–controlled trials of faricimab for center-involving DME. Patients were randomized 1:1:1 to faricimab 6.0 mg per PTI after a minimum of 4 initial every-4-week (Q4W) doses, faricimab 6.0 mg Q8W after 6 initial Q4W doses, or aflibercept 2.0 mg Q8W after 5 initial Q4W doses. In the PTI arms, patients received faricimab Q4W until central subfield thickness (CST) < 325 μm was achieved at or after week 12. Once CST < 325 μm was achieved, treatment intervals could be extended by 4 weeks (up to Q16W), maintained, or reduced by 4 or 8 weeks (as low as Q4W), based on prespecified CST and best-corrected visual acuity (BCVA) criteria. To maintain masking, all patients received sham injections at non–active dosing visits; however, CST and BCVA at sham injection visits were not used to determine PTI dosing intervals. Treatment intervals in the faricimab PTI arms were assessed through week 100.

Results: Among 1891 patients enrolled in YOSEMITE (N = 940) and RHINE (N = 951), 313 and 319 patients, respectively, were randomized to the faricimab PTI arms. At week 52, > 50% of patients in the PTI arms achieved Q16W dosing and > 70% achieved Q12W or Q16W dosing. Approximately two-thirds of patients achieved Q12W or Q16W dosing without an interval reduction below Q12W through week 52 (YOSEMITE, 68%; RHINE, 64%). The majority of patients who rapidly achieved Q16W dosing at week 32 (ie, the first timepoint that a patient could be extended to Q16W dosing) subsequently completed a full Q16W dosing cycle and remained on Q16W dosing at week 52. Faricimab treatment intervals through week 100 and PTI case studies will be presented at the meeting.

Conclusions: Treat-and-extend–based PTI dosing in YOSEMITE/RHINE optimized treatment intervals and demonstrated the durability of faricimab to meet the heterogeneous needs of patients with DME.

CONTROL ID: 3709251

SUBMITTER (NAME ONLY): Melina del Papa

TITLE: In vitro evaluation of sodium hyaluronate protective effect against benzalkonium chloride toxicity

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. del Papa, M. Passerini, Medical affairs, Laboratorios Poen, Ciudad Autónoma de Buenos Aires, Ciudad Autónoma de Buenos Aires, ARGENTINA|F. Sabbione, A. Vereertbrughen, J.G. Galletti, Innate Immunity, Institute of Experimental Medicine CONICET-ANM, Buenos Aires, Buenos Aires, ARGENTINA|

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ABSTRACT BODY:

Purpose: Long-term exposure to benzalkonium chloride (BAK) causes toxicity reactions on the ocular surface. Sodium hyaluronate (SH) has been postulated as a potential neutralizing agent for BAK-induced toxicity. The goal of this work was to evaluate the protective effect of SH on BAK-induced toxicity using an in vitro model.

Methods: The NAV14 cell line (SV40-immortalized murine conjunctival epithelium) was used. Cell monolayers were exposed to different concentrations of BAK (0.001%; 0.005%; 0.01%) and SH (0.2%; 0.3%; 0.4%) for 15 minutes; then, the cells were washed, and fresh culture media was added. Cell viability was evaluated after 2 h by resazurin reduction and lactate dehydrogenase (LDH) enzyme release. Also, cell migration and proliferation over 24 hours were determined by the scratch wound-healing assay. Data was analyzed by two-way ANOVA and is shown as mean±SD of two independent experiments with 4-6 replicates each. Statistical significance was defined as $p<0.05$.

Results: BAK induced a concentration-dependent decrease on cell viability (BAK 0.001%: 91±14%, BAK 0.005%: 45±9% and BAK 0.01%: 22±10% of control cells, $p<0.001$) and an increase in LDH release (no BAK: 0.22±0.02, BAK 0.001%: 0.31±0.02, BAK 0.005%: 1.14±0.05 and BAK 0.01%: 1.21±0.05, $p<0.001$). Conversely, SH neutralized these effects also in a concentration-dependent manner ($p<0.001$). In the presence of SH 0.4% (highest effect), cell viability was BAK 0.001%: 104±22%, BAK 0.005%: 109±9% and BAK 0.01%: 75±13% of control cells ($p<0.001$ for BAK 0.005-0.01%) while LDH release was no BAK: 0.24±0.03, BAK 0.001%: 0.26±0.01, BAK 0.005%: 0.37±0.02 and BAK 0.01%: 0.49±0.22, (vs no SH: $p<0.001$ for BAK 0.005-0.01%). BAK also reduced wound closure in vitro (after 24 h, no BAK: 76±14%, BAK 0.001%: 42±12%, BAK 0.005%: 17±16% and BAK 0.01%: 0.0% wound closure, $p<0.001$ for all BAK). Conversely, SH neutralized this effect in a concentration-dependent fashion ($p<0.001$). In the presence of SH 0.4% (highest effect), wound closure at 24 h was: no BAK: 81±15%, BAK 0.001%: 58±6%, BAK 0.005%: 63±10%, BAK 0.01%: 60±8% (vs no SH: $p<0.001$ for BAK 0.005-0.01%).

Conclusions: SH neutralized BAK toxicity on conjunctival epithelial cells in a concentration-dependent manner. SH 0.4% was even protective at the highest preservative concentration. These findings support the use of SH to mitigate BAK toxicity in patients, although more studies are needed.

CONTROL ID: 3709252
SUBMITTER (NAME ONLY): Julián García-Sánchez
TITLE:

Contrast sensitivity comparison of high myopic vs emmetropic patients using the Rabin Cone Contrast Sensitivity Test
SESSION TITLE: Myopia: Clinical Interventions and Diagnostics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. García-Sánchez, L. Rhoads Avila, R. Garcia-Santisteban, S. Peña-Aguilar, J. Leyva-Velarde, G. del Castillo Marquez, J. Serrano-Aguilar, G. Salcedo-Villanueva, Retina, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|L. Rhoads Avila, Medicine, Universidad La Salle, Mexico City, Mexico City, MEXICO|R. Garcia-Santisteban, Retina, Universidad Panamericana, Ciudad de Mexico, Ciudad de México, MEXICO|J. García-Sánchez, Medicine, Universidad Anahuac Mexico, Huixquilucan, Mexico, MEXICO|
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ABSTRACT BODY:
Purpose:

High myopes experience lower contrast sensitivity (CS). A fast and easy way to test for CS has been developed by the RCCST; however, baseline CS measurements using this system in patients with high myopia remain unknown. This study tested the hypothesis that CS will be lower in high myopic patients compared to emmetropic individuals.
Methods: Cross-sectional, comparative study. Twenty-five patients with high myopia (less than or equal to 6 D and/or >26.5mm axial length) aging between 18 and 50 years with a BCVA equal or better than 20/40 were enrolled. Postoperative patients or with any ophthalmological disease associated with myopia were excluded. RCCST, and A-mode ultrasound measurement of the axial length were performed in all participants. RCCST results were expressed in logarithmic units. Obtained data was later compared with our previous CS reports of emmetropic individuals. Mann-Whitney U test and Spearman's correlation were used for statistical analysis.
Results:

Twenty-five patients were included in group A (high myopic), of which 14 were women and 11 were men. This group had a mean age of 26.6 years, standard deviation (SD): 5.46, range: 18 - 36 (95% CI: 24.34 - 28.85) . The mean CS was 1.56, SD: 0.21, range: 0.90 - 1.75 (95% CI: 1.47 - 1.64).
Group B (emmetropic patients) was composed of 76 patients, with a mean age of 25.78 years, SD 4.69, range 18 - 39 years. Mean CS for group B was 1.62, 0.09 SD, 95% CI 1.60 - 1.65 (range: 1.25 - 1.98).
A comparison of mean CS using Mann-Whitney U Test, resulted in a non-significant Z-score of -0.422 (P= 0.673).
Spearman’s correlation between age and CS was performed for group A, resulting in a small, negative correlation, without statistical significance (Correlation Coefficient: -0.211; P= 0.311).
Group A presented a mean axial length of 27.11 mm, SD: 1.43, range: 25.41 - 31.01 (95% CI: 26.51 - 27.70).
Spearman’s test between contrast sensitivity and axial length resulted in a small, negative, non-significant correlation (correlation coefficient: -0.053; P= 0.801).
Conclusions: Our results are consistent with our hypothesis, CS in high myopic patients appear to be lower than in emmetropic patients, however the difference was not statistically significant. There is a small negative correlation between axial length and CS suggesting that high axial lengths may present lower CS.

CONTROL ID: 3709253

SUBMITTER (NAME ONLY): Melissa Toyos

TITLE: Phase 2 Study of the Efficacy and Safety of Recombinant Human Nerve Growth Factor (rhNGF) in Patients with Moderate-to-Severe Dry Eye

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Toyos, Toyos Clinic, Nashville, Tennessee, UNITED STATES|D. Wirta, Aesthetic Eye Care Institute & Eye Research Foundation, Newport Beach, California, UNITED STATES|J. Goosey, Houston Eye Associates, Houston, Texas, UNITED STATES|S. El-Harazi, Lugene Eye Institute, Glendale, California, UNITED STATES|F. Mantelli, Dompé, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye (DE) is a common condition that can profoundly impact patient (pt) quality of life. Pathogenesis is multifactorial, yet most therapies only address inflammation or tear film instability. Neurosensory abnormalities have been increasingly recognized as a key DE feature. A therapeutic agent targeting this etiology would be of great value as improving nerve health may be critical to restoring ocular homeostasis. This study evaluated the efficacy and safety of rhNGF in pts with DE.

Methods: This phase 2, randomized, vehicle (VEH)-controlled study enrolled pts ≥18 years with moderate-to-severe DE for ≥6 months. Pts were randomized 1:1:1 to receive the following drops in both eyes for 4 weeks (wks) + 12 wks follow up: 20 µg/mL rhNGF 3x/day (TID), 20 µg/mL rhNGF 2x/day (BID) + VEH 1x/day, or VEH TID. Primary endpoint was change from baseline in Schirmer test I without anesthesia at wk 4. Secondary endpoints included change in Symptom Assessment in Dry Eye (SANDE) scores. Treatment (tx)-emergent adverse events (TEAEs) were assessed throughout the study.

Results: In total, 261 pts were randomized to rhNGF TID (N=87), rhNGF BID (N=86), or VEH (N=88) arms. In the full analysis set, mean (SD) change from baseline in Schirmer test I at wk 4 was higher in the rhNGF BID than VEH arm (4.0 [8.1] vs 1.7 [5.8] mm, P=0.037). Rates of responders (score >10 mm/5 minutes) at wk 4 were also higher in the rhNGF TID (25.9%) and rhNGF BID (29.3%) arms compared with the VEH (11.9%) arm (P=0.028 and P=0.007, respectively). During follow up, the rhNGF TID arm had significantly greater mean (SD) SANDE score reductions, indicating greater symptom improvement, than the VEH arm at wk 8 (-27.2 [25.8] vs -16.9 [20.4], P=0.006), wk 12 (-27.9 [25.6] vs -16.4 [19.6], P=0.002), and wk 16 (-26.5 [25.7] vs -16.7 [19.7], P=0.008). More pts in the rhNGF arms than VEH arm reported ≥1 ocular TEAE in wks 1-4 (69.4% rhNGF TID, 65.5% rhNGF BID, 13.6% VEH); the most common was eye pain (63.5% rhNGF TID, 46.4% rhNGF BID, 4.5% VEH), which was mild and transient in most pts. No study drug-related serious AEs were reported.

Conclusions: After 4 wks of tx, rhNGF improved Schirmer test I scores and appeared to have clinically relevant enduring effects, with significantly improved DE symptoms up to 12 wks post-tx completion in the rhNGF TID arm. rhNGF was generally well-tolerated, and most TEAEs were mild.

CONTROL ID: 3709255

SUBMITTER (NAME ONLY): Leonard Coulibaly

TITLE: Progression dynamics of early versus advanced atrophic lesions in non-neovascular AMD using AI-based OCT analysis

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Coulibaly, P. Fuchs, D. Lachinov, O. Leingang, H. Bogunovic, G.S. Reiter, U. Schmidt-Erfurth, Ophthalmology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

Commercial Relationships Disclosure: Leonard Coulibaly: Commercial Relationship: Code N (No Commercial Relationship) | Philipp Fuchs: Commercial Relationship: Code N (No Commercial Relationship) | Dmitrii Lachinov: Commercial Relationship: Code N (No Commercial Relationship) | Oliver Leingang: Commercial Relationship: Code N (No Commercial Relationship) | Hrvoje Bogunovic: Commercial Relationship: Code N (No Commercial Relationship) | Gregor Reiter: Commercial Relationship: Code N (No Commercial Relationship) | Ursula Schmidt-Erfurth: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Atrophic lesion growth rates can vary during the progression of non-neovascular age-related macular degeneration (AMD) which might have potential influence on the use of complement inhibition. The purpose of this study is to investigate the progression of atrophic lesions as early as they arise in order to set a standard for the optimal time of first intervention.

Methods: Patients which had recently converted to atrophic late AMD were included and prospectively imaged using optical coherence tomography (OCT). The respective total areas of external limiting membrane (ELM) disruption and retinal pigment epithelial (RPE) loss on longitudinal OCT volumes were quantified using artificial intelligence (AI) algorithms. Freshly converted eyes were compared to eyes with advanced disease status using mixed effect models.

Results: Eighty-two eyes from 53 patients were included. The first cohort consisted of 30 eyes from 25 patients with a recent conversion to complete retinal pigment epithelium and outer retinal atrophy (cRORA) within 6 months. The second cohort consisted of 52 eyes from 28 patients with a conversion to cRORA at least two years prior to the first study visit. The study period encompassed two years with scheduled visits every 6 months. Mean (95%CI) square root progression of recent atrophy was 123.92 µm [76.88 – 170.86] and 126.08 µm [80.18 – 171.94] per year for ELM disruption and RPE loss, respectively. Mean square root progression of advanced lesions was 220.2 µm [187.46 – 252,68] and 219.2 µm [187 – 251.06] per year for ELM disruption and RPE loss, respectively. A significant difference regarding progression of ELM disruption (p=0.001) and RPE loss (p=0.001) between converted and advanced lesions was found.

Conclusions: Data on early disease progression in atrophic AMD is rare. Atrophic lesions from recently converted patients have a slower growth rate in comparison to patients in an advanced disease stage. These findings might play a crucial role in planning future treatments using complement inhibition. Individual disease monitoring in early AMD supported by AI-quantifications is necessary to capture the ideal point of care in non-neovascular AMD.

CONTROL ID: 3709259

SUBMITTER (NAME ONLY): Rowena Schultz

TITLE: Fluorescence lifetimes of subretinal pigment epithelial depositions are prolonged in a primary RPE cell culture model

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Schultz, D. Meller, M. Hammer, Clinic for Ophthalmology, Universitatsklinikum Jena, Jena, Thüringen, GERMANY|

Commercial Relationships Disclosure: Rowena Schultz: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Meller: Commercial Relationship: Code N (No Commercial Relationship) | Martin Hammer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Fluorescence lifetime imaging ophthalmoscopy (FLIO) is used to specify fundus autofluorescence of pathologic lesions such as drusen in AMD. However, the identification and full characterization of disease-related fluorophores in vivo is difficult. The purpose of this study was to measure fluorescence spectra and lifetimes of RPE and drusen-like sub-RPE deposits in an established in vitro model of primary RPE cell culture[1], which will enable down-stream fluorophore characterizations for a better understanding of in vivo FLIO findings.

Methods: Retinal pigment epithelium cells isolated from freshly enucleated porcine eyes were cultured on Transwell membranes for up to 8 weeks in Miller medium[2] supplemented with 0.5% and 1.5% human serum (upper and lower well, respectively). Two-photon-excited autofluorescence emission spectra and time-resolved autofluorescence measurements (500-700 nm, λ_{ex} = 960 nm) were recorded from the RPE cells as well as deposits generated by them. Decays were approximated by a series of three exponentials, with the amplitude-weighted mean (τ_m) utilized as the main parameter for statistical analysis (Wilcoxon test of deposits vs. surrounding RPE cells).

Results: Primary porcine RPE cells cultured with human serum survived 8 weeks and produced sub-RPE deposits (size: 693±292 μm^2, n=9) when cultured on 10-µm-thick Transwell membranes with 0.4-µm-diameter pores. The autofluorescence emission peak maximum of deposits was green-shifted compared to RPE (Median (IQR): 569 (0) nm vs. 636 (2.5) nm, Z = -2.9, p = 0.004) and the lifetimes were significantly prolonged (534 (583) ps vs. 81 (49) ps, Z = -2.8, p = 0.005).

Conclusions: The data suggest that sub-RPE deposit formation, initiated by porcine RPE cultured with human serum, leads to deposits with prolonged lifetimes comparable to drusen as seen in AMD histology.[3] This cell culture model of early AMD lesions provides a system for analysis of the fluorophore-composition of sub- RPE deposits and will help to better interpret FLIO imaging results.

1 Pilgrim et al., Invest Ophthalmol Vis Sci. 2017;58(2):708-719.

2 Maminishkis et al., Invest Ophthalmol Vis Sci. 2006;47(8):3612-3624.

3 Schultz et al., Invest Ophthalmol Vis Sci. 2020;61(11):9.

CONTROL ID: 3709264

SUBMITTER (NAME ONLY): Raksha Urs

TITLE: Ocular Blood-Flow in Neonates at risk for Retinopathy of Prematurity

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Urs, D.H. Jokl, J.D. Horowitz, O. Coki, L. Pinto, R.H. Silverman, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Plane-wave (PW) ultrasound with a linear array probe is capable of visualizing and measuring retrobulbar blood-flow. The goal of this study was to determine if PW ultrasound could be used to image and measure retorbulbar blood-flow velocities in preterm neonates and assess the association of these velocities with retinopathy of prematurity (ROP) stages and zone.

Methods: Ultrafast PW imaging of the perioptic region was performed with a Verasonics Vantage 128 ultrasound system using an 18 MHz linear array probe. Both eyes of 26 low-birthweight subjects at risk for ROP were scanned in the neonatal intensive care unit. Each scan was compounded from six scan angles, at a rate of 3000 compound scans/sec for 1.5 seconds, capturing at least two cardiac cycles. 16 subjects were scanned twice bringing the total number of eyes scanned to 84. All subjects had a birth-weight of less than 1500 g and a gestational age of less than 30 weeks. PW data were post processed to form color-doppler images and flow-velocity was measured in the central retinal artery (CRA), central retinal vein (CRV) and short posterior ciliary artery (SPCA) using spectrogram analysis. Findings were compared to ophthalmoscopic grading, with ultrasound and ophthalmoscopic findings masked until completion.

Results: Minimal change in arterial or venous flow was observed in stage 1 and 2 ROP, but systolic and diastolic flow velocities increased significantly ($p<.001$) compared to non-ROP at stage 3 in the CRA (from 39±14 mm/sec to 64±20 mm/sec systolic) and CRV (from 19±6 mm/sec to 31±12 mm/sec systolic) Systolic flow velocity increased as well in the SPCA (from 45±14 mm/sec to 58±15 mm/sec, $p=.007$). Resistance indices did not change significantly. Five stage-3 subjects with pre-plus disease did not have significantly different flow velocity than other stage-3 subjects. There was no correlation between flow velocity and blood pressure.

Conclusions: Flow velocities in the major orbital vessels increased at ROP stage 3. If plus disease is caused by high retinal flow velocities, its detection by PW ultrasound may represent a valuable tool to assess ROP risk in low birthweight neonates, especially because the exam can be performed more frequently than dilated ophthalmoscopy. With few pre-plus and no plus disease in this series, this hypothesis remains to be explored in a larger cohort.

CONTROL ID: 3709266

SUBMITTER (NAME ONLY): Valerie Harris

TITLE: Low in vitro Pseudomonas aeruginosa Adhesion to Lehfilcon A Contact Lenses

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Harris, R. Pifer, P. Shannon, M. Crary, Alcon Research Institute, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Valerie Harris: Commercial Relationship(s);Code E (Employment):Alcon | Reed Pifer: Commercial Relationship(s);Code E (Employment):Alcon | Paul Shannon: Commercial Relationship(s);Code E (Employment):Alcon | Monica Crary: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: Pseudomonas aeruginosa is the most common causative agent implicated in microbial keratitis. During contact lens wear, pathogens may be introduced into the ocular environment, which might cause adverse events. Lehfilcon A is a newly marketed contact lens with a water gradient surface composed of polymeric 2-methacryloyloxyethyl phosphorylcholine (MPC). MPC is reported to impart anti-biofouling properties onto coated substrates. Therefore, in this in vitro experimental study, we evaluated the ability of lehfilcon A to resist adhesion by P. aeruginosa.

Methods: Quantitative bacterial adhesion assays using five strains of P. aeruginosa were conducted to compare the adherence properties of lehfilcon A to five currently marketed contact lenses (comfilcon A, senofilcon C, samfilcon A, senofilcon A, fanfilcon A). Individual contact lenses were incubated in the presence of P. aeruginosa followed by gentle rinsing to remove non-adherent bacteria. Adherent bacteria were recovered from lenses by vigorous vortexing and eluted bacterial colony forming units (CFU) were enumerated by plating. CFUs were normalized to the surface area of each lens. Statistical analyses were performed as t-tests for differences in the mean log CFU/mm^2 between lens types without assuming equal standard deviation between groups. Bonferroni correction was used to account for multiple comparisons. Adherence of GFP-positive P. aeruginosa to contact lenses was qualitatively evaluated by fluorescent microscopy.

Results: Across five strains of P. aeruginosa, lehfilcon A allowed an average of 1.1 ± 0.1 log CFU/mm^2 fewer bacteria to bind to the lens compared to the next best performing contact lens material, senofilcon C. Across all strains, this corresponds to an average of 92.0% lower adherence by lehfilcon A compared to all lenses tested, or a difference greater than $2.2x10^5$ live bacteria per lens. Results from fluorescent imaging experiments support the quantitative results, with a clearly greater mass of P. aeruginosa adhering to non-MPC coated lenses.

Conclusions: Lehfilcon A has reduced P. aeruginosa adhesion relative to currently marketed monthly and bi-weekly contact lenses. Contact lenses that limit microbial adhesion coupled with effective contact lens care solutions may be an effective approach to reducing contact lens contamination.

CONTROL ID: 3709267

SUBMITTER (NAME ONLY): Suman Adhikari

TITLE: Correlation between the retinal layer thickness changes and diffusion tensor imaging measurements in Autosomal Dominant Alzheimer's disease

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Qiao, Y. Shi, Neuroimaging, University of Southern California Mark and Mary Stevens Neuroimaging and Informatics Institute, Los Angeles, California, UNITED STATES|J. Ringman, Neurology, Memory and Aging Center at the Keck School of Medicine of USC, California, UNITED STATES|M. Singer, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|S. Adhikari, A.H. Kashani, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|Y. Qiao, Fudan University Institute of Science and Technology for Brain-inspired Intelligence, Shanghai, CHINA|X. Jiang, Ophthalmology, USC Roski Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal degeneration occurs in Alzheimer's disease (AD), but its temporal association with intracranial pathology is unknown. This study investigated the association between OCT-derived retinal layer thickness and intracranial diffusion tensor imaging (DTI) measures of optic tracts among subjects with an Autosomal Dominantly inherited form of AD (ADAD).

Methods: Carriers of ADAD mutations (A431E_PSEN1 or V171I_APP or F388S_PSEN1) or non-carriers of the mutation from the same family were recruited from an NIH funded longitudinal study of ADAD. Outer nuclear layer (ONL), Ganglion Cell Layer (GCL), Inner Plexiform Layer (IPL) and GCIPL thickness were obtained using SD-OCT (Heidelberg Spectralis). The retinotopically mapped white matter tract integrity was measured along the optic tracts using previously described DTI measures including fractional anisotropy (FA), radial diffusivity (RD), mean diffusivity (MD), axial diffusivity (AD). The correlation between the retinal layer thickness and the DTI measures was assessed using generalized estimating equations to adjust for correlation between retinal measurements from two eyes of the same subject.

Results: Fifteen subjects with ADAD mutations (9 males, mean age 36yrs) and 4 non-carriers (1 male, mean age 37yrs) were recruited into the study. Six subjects with ADAD mutations were asymptomatic. FA was positively correlated with GCL (β=0.0017, P=0.01) and GCIPL complex (β=0.0008, P=0.03) thickness. RD was negatively correlated with GCL (β=-0.0105, P=0.002) and GCIPL complex (β=-0.0071, P=0.001) thickness. MD was negatively correlated with GCIPL complex (P=0.001) thickness. AD was positively correlated with GCL and GCIPL complex but not significant (P>0.05). The correlations between ONL thickness and DTI measures (FA, MD, AD and RD) were not significant (P>0.05).

Conclusions: GCIPL thickness was significantly associated with DTI measures of optic tract integrity. These findings support the hypothesis that the degeneration of ganglion cells in the retina is concurrent with a decrease in white matter integrity of the optic tracts in ADAD. The causal chain of events is a topic of further investigation.

CONTROL ID: 3709271

SUBMITTER (NAME ONLY): Victoria Koontz

TITLE: The differential role of distinct astrocyte populations in Persistent Fetal Vasculature (PFV) disease

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Koontz, S. Ghosh, N.A. Stepicheva, H. Liu, P. SHANG, O. Chowdhury, A. Strizhakova, R. Daley, S.L. Hose, D. Sinha, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, Ophthalmology, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|M. Yazdankhah, Regenerative Foundation, Neural Stem Cell Institute, Albany, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: PFV is a rare disease with limited treatment options, where the hyaloid artery does not regress normally after birth, potentially causing blindness in an otherwise normal child. We have shown that astrocytes in Nuc1 mutant (spontaneous mutation in Cryba1 gene that encodes for βA3/A1-crystallin) rats abnormally migrate and ensheath the hyaloid artery, likely due to abnormal lysosomal function and activated EGFR/mTORC1 signaling. Different astrocyte populations with anti/pro-inflammatory properties have been identified in human diseases and are linked to protective/neurodegenerative changes, respectively. Herein, we evaluated the importance of different astrocyte populations in our rat model, determining the roles of their underlying signaling pathways in the pathogenesis of PFV disease.

Methods: We performed scRNAseq analysis on optic nerve astrocytes from Nuc1 and WT rats. Western blot analysis evaluated the levels of mTOR and inflammatory signaling proteins. Astrocyte cell migration (wound healing assay), proliferation (Ki-67 expression) and phagocytosis (pHrodo internalization assay) were also assessed. βA1-mCherry construct was generated to overexpress the protein in astrocytes in vitro.

Results: scRNAseq analysis revealed two distinct astrocyte populations- astrocyte clusters 1 and 2 (AC1 and 2) in Nuc1 rats, but not in WT. AC1 showed increased expression of mTORC1 components like Raptor and downregulation of mTORC2 components like Rictor, with no increase in the levels of inflammatory genes. However, AC2 showed activation of both mTORC1/2 components and inflammatory mediators like CXCL14 and IL-2a. Interestingly, Lrp2 gene, which is linked with astrocyte activation in Parkinson's disease, as well as glial and cancer cell activation/migration, also was upregulated in AC2 but not in AC1 cells. These results were confirmed by western blots and the changes were rescued upon βA1-crystallin overexpression in AC2 cells. Induction of cell migration/proliferation and a reduction in phagocytic activity, known phenotypic changes during astrocyte activation in PFV disease were significant in AC2 cells and were rescued by βA1-crystallin overexpression.

Conclusions: We have identified a specific population of astrocytes which might be responsible for the pathogenesis of PFV disease: overexpression of βA1-crystallin in these astrocytes could have therapeutic importance for treating PFV disease.

CONTROL ID: 3709272

SUBMITTER (NAME ONLY): Ajay Ashok

TITLE: Epigenetic modulation following electrical stimulation in neurons

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ashok, W. Tai, A. Lennikov, K. Cho, D. Chen, Department of Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Ashok, T. Utheim, Department of Medical Biochemistry, Oslo University Hospital, Oslo, NORWAY|T. Utheim, Department of Ophthalmology, Oslo University Hospital, Oslo, NORWAY|

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ABSTRACT BODY:

Purpose: Epigenetic factors are known to influence neural development, functionality, and their response to pathophysiology. In recent times, electrical stimulation (ES) of cell and animal models have shown promising results in neural regeneration and recovery. However, the underlying mechanisms remains elusive. Our study will investigate if ES holds the promise to regulate DNA demethylation, a vital epigenetic event known to influence neuronal regeneration, using an in-vitro cell model.

Methods: PC12 cells acquired from ATCC were cultured and the effect of ES on DNA demethylases (ten-eleven translocation (TETs) proteins (TET1, TET2 and TET3)) was studied using qPCR. PC12 cells were incubated with 0, 5 and 100 ng/ml of nerve growth factor (NGF), a known inducer of neuronal differentiation, for 5 days and were also electrically stimulated for 20 min at 100 µA. Non-electrically stimulated cells were maintained as control. RNAs were collected 16 h post procedure and the changes in TETs gene expression were analyzed using qPCR. Additionally, lactate dehydrogenase (LDH) estimation assay was carried out to evaluate cytotoxicity in the experimental groups. Two-tailed Student's t-test was used for statistical analysis.

Results: qPCR revealed increased TET1 gene expression in cells exposed to ES relative to control cells. TET2 and TET3 amplification did not change significantly. LDH assay demonstrated no significant cytotoxicity in any treatment groups. Interestingly, increasing NGF concentration in PC12 cells exhibited similar induction of TET1 but not TET2 or TET3 expression, suggesting a possibly shared epigenetic event in ES and NGF-induced neuronal differentiation process.

Conclusions: Our results point to a possible regulation of TET1, a DNA demethylase, by ES in neurons. A comprehensive understanding of epigenetic regulation following ES in neuronal differentiation, development and homeostasis will help us unravel novel molecular pathways and pave the way to design blueprints for effective therapeutics to address neuronal protection, repair, and regeneration.

CONTROL ID: 3709274

SUBMITTER (NAME ONLY): Marta Gonzalez-Hernandez

TITLE: Optic Disc Area frequency distribution in a large sample of retinographic images

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To describe a new method to estimate the frequency distribution of optic nerve Disc Area, using digital retinographic images. Disc Area influences other morphological indices such as cup and rim, of interest in glaucoma (1). The immediate goal is to use this method in the Laguna ONhE application that allows estimation of hemoglobin distribution in the normal and glaucomatous optic nerve (2).

Methods: We analyzed 492,023 fundus images obtained with 7 fundus cameras (Table), mainly in Caucasian subjects. They were grouped by resolution and zoom. They were automatically segmented by identifying the inner edge of the Elschnig scleral ring. For this purpose, a neural network trained by Deep Learning previously described (3) was used. The number of pixels contained within the segmentation and their frequency distribution were calculated. The results of each camera, using different number of images, were compared with the global results using the Kolmogorov-Smirnov test to confront frequency distributions.

Results: The frequency distribution was Non-Gaussian, more limited in the small sizes than in the large ones. If the median is assigned a theoretical value of 1.95 mm^2(4) the 1^{th}, 5^{th}, 25^{th}, 50^{th}, 75^{th}, 95^{th} and 99^{th} percentiles would correspond to 1.29, 1.46, 1.73, 1.95, 2.20, 2.64 and 3.03 mm^2 in the whole data set (Figure 1). The overall differences were significant for the smaller series, but for each percentile their mean value was only 0.01mm^2 and the maximum 0.10mm^2, so they can be considered similar for practical purposes in all cameras. (Table).

Conclusions: By automatically segmenting the edges of the optic nerve and observing the frequency distribution of the number of pixels it delimits, it is possible to estimate the frequency distribution of the Disc Area in the population as a whole and that of each individual case.

References:

Jonas JB et al. Prog Retin Eye Res 2000;19:1-40

Gonzalez de la Rosa M et al. IOVS 2013;54:482-489

Gonzalez-Hernandez M et al. J Clin Med 2021;10:3231

Gonzalez-Hernandez M et al. Doctoral Thesis. University of La Laguna, Spain, 2017

CONTROL ID: 3709276

SUBMITTER (NAME ONLY): Safa Halouani

TITLE: Choriocapillaris flow impairment in hydroxychloroquine retinopathy: a quantitative comparative analysis using swept-source optical coherence tomography angiography

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Halouani, H. Le, N. HERDA, A. Miere, E. Souied, Ophthalmology, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|N. Terkmane, Ophthalmology, Hopital Henri Mondor, Creteil, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To quantitatively analyze choriocapillaris alterations using swept-source optical coherence tomography angiography (SS-OCTA) in eyes presenting with severe hydroxychloroquine (HCQ) retinopathy and to compare it with patients taking HCQ without toxic retinopathy and healthy controls.

Methods: In this cross-sectional study, macular 6x6 mm SS-OCTA scans were analyzed in eyes with either severe HCQ toxic retinopathy, or under HCQ without retinal toxicity, as well as in healthy age and sex-matched controls. The choriocapillaris en face slabs were extracted from the SS-OCTA device. En face choriocapillaris flow images were compensated with en face choriocapillaris structure images, followed by Phansalkar local thresholding using window radius 4 and 8 pixels. Percentage of flow deficits (FD %), as well as FD number, size, and total area, were computed for comparison.

Results: Seventy-six eyes of 38 patients under HCQ (mean age 49.89±11.68 years) and sixty eyes of 34 age-matched controls (mean age 54.30±14.85 years) were included in this study. Among the patients under HCQ, fourteen eyes (7 patients) presented with severe HCQ toxicity, while sixty-two eyes (31 patients) had no signs of toxicity. FD%, the average size of FDs, and the number of FDs were significantly different between the severe HCQ toxicity, no HCQ toxicity, and controls (p-value < 0.001 for all comparisons, for both radius 8 and 4 pixels). Compared to controls and eyes with no HCQ toxicity, the eyes with severe HCQ toxicity had a significantly higher FD% (p-value 0.009 and <0.001 for radius 8 pixels, p-value <0.001 and <0.001 using radius 4 pixels, respectively), a significantly lower number of FDs (p-value 0.005 and <0.001 using radius 8 pixels, p-value 0.005 and <0.001 using radius 4 pixels).

Conclusions: Our results suggest an involvement of the choriocapillaris in severe HCQ retinal toxicity, therefore expanding the current knowledge of the (inner) choroidal involvement in the pathogenesis of HCQ retinopathy.

CONTROL ID: 3709277

SUBMITTER (NAME ONLY): Ravnit Singh

TITLE: Functional Assessment of Hand-Eye Coordination in Individuals with Ultra-Low Vision Using Virtual Reality

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Singh, Johns Hopkins University Zanvyl Krieger School of Arts and Sciences, Baltimore, Maryland, UNITED STATES|A. Kartha, R. Sadeghi, C. Bradley, G. Dagnelie, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|C. Tran, T. Swanson, BaltiVirtual, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultra-Low Vision is defined as visual acuity ≤ 20/1600. Currently, there are no standardized tools available to assess hand-eye coordination in individuals with vision in the ULV range. The purpose of this study was to develop and validate a test to assess hand-eye coordination for people with ultra-low vision (ULV).

Methods: Eleven participants with ULV went through task stimulations requiring hand-eye coordination, such as flipping a light switch or placing silverware on a dinner table, using the VR Headset. Using a Leap Motion hand tracker, each participant was able to visualize their hand as they went about performing a task. The same task was presented at different visibility levels (high, medium, and low). Tasks were to be completed in 5 pre-defined steps (e.g., 5 defined steps to make a pancake). The results were then analyzed using the method of successive dichotomizations, a polytomous Rasch model, to estimate person measures (person ability) and item measures (task difficulty).

Results: Estimated item measures ranged from -3.49 to 3.97 logits with a mean of zero (by convention) and a SD = 1.8 logits (Fig 1). The most difficult item was sorting pills (3.97 logits) and the least difficult item was building a tower from high contrast blocks in decreasing size (-3.49 logits). Person measures ranged from -2.9 to 4.3 logits with a mean (SD) of 1.06 (2.09) logits. A t-test showed that the means of the distributions were not significantly different ($p = 0.2$). The items (tasks) were therefore well-targeted to the sample of persons.

Conclusions: The results show a mix of items with good spread of difficulty levels that can be used to assess hand-eye coordination in individuals with ULV with different levels of functional ability. We will continue testing in a larger sample of people using a reduced set of items by eliminating items with similar item measures to reduce redundancy and cut down testing times.

CONTROL ID: 3709281

SUBMITTER (NAME ONLY): Jason Betz

TITLE: Epidemiology and Risk Factors for Refractive Surgery Associated Ocular Pain

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Betz, A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Betz, A. Galor, Surgical Services, VA Miami Healthcare System, Miami, Florida, UNITED STATES|S. Aicher, H. Behrens, Department of Chemical Physiology & Biochemistry, Oregon Health & Science University, Portland, Oregon, UNITED STATES|B.M. HARKNESS, R. Stutzman, W. Chamberlain, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the frequency and risk factors for ocular pain after laser assisted in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK).

Methods: Prospective study of individuals undergoing refractive surgery. All individuals were seen prior to surgery and 3 months after surgery. Questionnaires regarding dry eye and ocular pain symptoms were completed at both time points. In addition, a comprehensive ocular surface assessment was performed at 3 months. The primary outcome measures were the frequency of ocular pain 3 months after surgery and risk factors for peristent pain. The latter were examined using multivariable forward stepwise logistic regression analyses.

Results: 58 individuals were enrolled into the study, with a mean age of 33±9 years (range 23 to 57); 65.5% (n=38) self identified as female, 74% as white, and 43% as Hispanic. The majory of individuals underwent bilateral (n=57) LASIK (n=52). Prior to surgery, 15.5% (n=9) of individuals indicated that they had any ocular pain (>0 rating of average pain intensity over a 1 week recall, range 0-10), with the majority reporting mild pain (n=7 with a score of 1). At 3 months, 33% (n=19) of individuals reported ocular pain (average intensity of pain over a 1 week recall >0), 10 with a score >1. This included 12 individuals (63%) who developed new ocular pain after surgery. The two factors that significantly predicted ocular pain after surgery (score>0) were ocular pain (odds ratio (OR)=3.15, 95% confidence interval (CI) 1.28-7.71, p = 0.01) and dry eye symptoms (Ocular Surface Disease Index, OR=1.12, 95% CI 1.0-1.26, p=0.05) before surgery. Pre-operative contact lens use (OR=0.16, 95% CI 0.03-0.90, p = 0.04) was protective against post-operative pain. When considering factors associated with pain intensity >1 at 3 months, pre-operative pain scores again predicted post-operative pain (OR=2.90, 95% CI 1.37-6.14, p=0.005) along with higher depression scores pre-surgery (Patient Health Questionniare-9, OR=1.38, 95% CI 1.08-1.75, p=0.01). Importantly, the majority (94%) of individuals were completely (70%) or somewhat (24%) satisfied with the results of their surgery.

Conclusions: A significant proportion of individuals report mild or greater post-operative pain 3 months after refractive surgery, with ocular pain prior to surgery being the most significant predictor for pain after surgery.

CONTROL ID: 3709282

SUBMITTER (NAME ONLY): Laura Garcia-Posadas

TITLE: Human Conjunctival MSCs produce extracellular vesicles that exhibit antioxidant activity in conjunctival epithelial cells

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To isolate extracellular vesicles (EVs) from human conjunctival mesenchymal stromal cells (Conj-MSCs) and analyze their effect on conjunctival epithelium.

Methods: Conjunctival stromal cells isolated from cadaveric donor tissues were cultured and analyzed to determine whether they could be defined MSC (n=5). Expression of MSC markers was analyzed by flow cytometry. Cells were cultured in adipogenic, osteogenic, and chondrocyte differentiation media, and stained with Oil Red, Von Kossa, and Alcian Blue, respectively, to determine multipotent capacity. Cells were grown at 70% confluence, secretome was collected after 48h with EVs-depleted FBS-supplemented medium and EVs were isolated by differential ultracentrifugation. EV morphology was evaluated by atomic force microscopy, size distribution analyzed by dynamic light scattering, and EVs were individually characterized by nanoflow cytometry. To analyze the effect on oxidative stress, the human conjunctival epithelial cell line IM-HConEpiC was exposed to 50 µg/ml Conj-MSCs-derived EVs for 3h (n=3), then loaded with 2′,7′-Dichlorofluorescin diacetate (30 min, 37°C) and finally exposed to 200 µM H_2O_2 to induce oxidative stress. Fluorescence was measured to quantify reactive oxygen species (ROS). Cell viability was determined by alamarBlue assay. Data were shown as mean ± standard deviation. One-way ANOVA was done to analyze differences.

Results: Cultured stromal cells fulfilled the criteria of MSCs: they adhered to plastic; expressed CD90 (99.95±0.03% positive cells), CD105 (99.04±1.43%), CD73 (99.99±0.19%), CD44 (99.93±0.05%), and lacked CD34, CD11b, CD19, CD45 and HLA-DR (0.82±0.91%); and differentiated in vitro into different lineages. Conj-MSCs EVs were morphologically round. Main EV subpopulations were <300nm, but larger differential subpopulations were also observed. EVs expressed CD9, CD63, CD81, and CD147 markers. H_2O_2 increased ROS by 1.61+0.31-fold ($p=0.0061$) compared to untreated cells set as 1, and Conj-MSC EVs decreased it to 0.42±0.46 ($p<0.0001$), in similar levels than adipose tissue-MSC-derived EVs (0.65±0.50; $p=0.0002$) and 250 µM ascorbic acid (0.50±0.59; $p<0.0001$), used as control. EVs did not affect cell viability.

Conclusions: Conj-MSC-derived EVs show no toxicity and promising antioxidant activity on conjunctival epithelial cells, warranting further research to determine their potential therapeutic effect.

CONTROL ID: 3709285

SUBMITTER (NAME ONLY): Cintia De Paiva

TITLE: Effects of Age and Genetic Diversity Background on Ectopic Lymphoid Structures in the Lacrimal Gland

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.S. De Paiva, K. Scholand, Z. Yu, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|K. Scholand, Biosciences, Rice University, Houston, Texas, UNITED STATES|H.P. Makarenkova, The Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We reported that aged C57BL/6 (B6) had increased lacrimal gland (LG) lymphoid infiltrates that are suggestive of ectopic lymphoid structures. However, B6 mice are T helper 1 prone mice. This study investigates the presence and composition of LG infiltrates in aged mice. We also analyse the diversity of mice with different genetic background.

Methods: Female B6 mice were used at 2-4, 12, and 24months (M) of age (n=10/age). A separate group of diversity outbred mice (DO, Jackson strain 009376) were used at 2-4 and 24M of age (n=9-10/age/sex). LGs were excised and used for histology, bulk RNA sequencing, or gene expression analysis using qPCR. Flow cytometry investigated B cell frequency. Eyes were excised for goblet cell density evaluation using PAS staining. The number of inflammatory foci (>50 cells) was counted under a 10X microscope lens. H&E-stained LGs were scanned, photographed, and image analysis calculated the focus score. The expression of B-cell-related genes was investigated by real-time PCR.

Results: Bulk RNA seq of aged B6 LGs showed upregulation of many inflammatory pathways. B-cell-related genes were among the top hits. A significant increase in B220+ cells was seen with aging from 8 to 12 to 24M in the LG (3, 20, and 38% among live cells, $P<0.05$). qPCR validation showed a significant increase in Cd19 (70 and 151-fold), Cd22 (46 and 138-fold) Cxcl13 (5 and 11-fold), Ltb (9 and 7-fold), Lta (4 and 5-fold), Glycam-1 (915 and 3095-fold), Ccl19 (11 and 15-fold) at 12 and 24M compared to young (all $P<0.05$ or lower). T helper follicular genes were also upregulated with aging: Cxcr5 (3 and 3-fold), Ccr7 (8 and 4-fold), Il21 (27 and 24-fold) (all $P<0.05$ or lower). Aged female DO mice have increased immune infiltrates in aged LGs (3.2±3.5 vs 0 focus score/4mm^2, $P<0.01$), but male DO mice do not (1.6±2 vs 0 focus score/4mm^2, $P>0.05$). Interestingly, female and male DO mice have decreased goblet cell density with aging (~35% loss compared to young DO, $P<0.01$ for both sexes).

Conclusions: Many pathways are altered in the aged LG in B6 mice, including B cell infiltration. There is an upregulation of B and T helper follicular-related genes as early as 12M of age. In addition, LG immune infiltrates preferentially accumulate in female mice, while goblet cell loss is observed in both sexes. These results show that age-related dry eye and LG infiltration is not exclusive of a mouse genotype.

CONTROL ID: 3709286

SUBMITTER (NAME ONLY): Nicole Pannullo

TITLE: Sox8 and Sox9 dominant-negative constructs promote photoreceptor specification while inhibiting generation of inner retinal cell types.

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pannullo, C.P. Santiago, M. Gimmen, L. Duncan, S. Blackshaw, Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sox8 and Sox9 are highly and specifically expressed in late-stage retinal progenitor cells (RPCs) and mature Muller glia (MG) and are predicted to repress proliferative and neurogenic competence in these cell types. We have developed dominant negative (DN) constructs of Sox8 and Sox9 to test their ability to alter the developmental trajectory in the murine retina. Constructs that promote an early-stage RPC cell fate and/or production of early-born retinal cell types will be used to reprogram adult Muller glia to early-stage RPCs that are competent to produce cone photoreceptors upon retinal injury in vivo.

Methods: DNs for Sox8 and Sox9 consisting of the DNA binding domain (DBD) only, DBD fused with a KRAB repressor (DBD+KRAB), and DBD fused with a VP48 activator (DBD+VP48) were designed. DNs were expressed in a pCAGIG construct downstream of a CAG promoter and upstream of an eGFP under the control of a bicistronic IRES element. Retinal explants were electroporated ex vivo to screen the DN constructs for their ability to alter the developmental trajectory in the retina. Retinal explants were electroporated with the DN constructs during late-stage retinal development (postnatal day(P)0-P8). The resulting phenotypes were analyzed using both scRNA-seq and immunohistochemistry.

Results: Retinal explants electroporated with the DBD and DBD+KRAB DN constructs at P0 showed phenotypes at P8 that were consistent with the known or predicted genetic loss of function of each cluster of paralogous genes, including a reduction in MG, bipolar and amacrine cell generation, and an increase in photoreceptor generation. Notably, these constructs also induce formation of a small number of cells expressing markers of cone photoreceptors.

Conclusions: These results suggest that suppression of Sox8 and Sox9 function is sufficient to shift the developmental trajectory of the retina to promote photoreceptor specification and induce expression of cone-specific markers. Since adult MG express many of the same TFs as late-stage RPCs, these DN constructs are potentially promising candidates for reprogramming MG to early-stage RPCs that are competent to produce cone photoreceptors upon retinal injury in vivo.

CONTROL ID: 3709296

SUBMITTER (NAME ONLY): So Yeon Uhm

TITLE: Comparison of Corneal Pachymetry and Anterior Chamber Dimension Between Hispanic and Non-Hispanic Populations

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Uhm, T. Do, B. Lam, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have shown that ocular anatomy may differ amongst ethnic groups. However, there are limited data on ethnic differences in corneal pachymetry and anterior chamber dimension. This study utilizes Pentacam data to compare corneal pachymetry and anterior chamber dimension between Hispanic and non-Hispanic White groups.

Methods: In this retrospective study, we analyzed Pentacam data from patients 50 years or older who underwent surgery for senile cataract. We included patients who were self-identified as Hispanic White or non-Hispanic White. Exclusion criteria included non-White race or multiethnic groups, history of surgery or trauma of cornea or anterior segment, or any abnormalities in these structures. The following parameters were compared between Hispanic Whites or non-Hispanic Whites: pupil center pachymetry, pachymetry at vertex, thinnest location, corneal volume, anterior chamber volume, and anterior chamber depth.

Results: This study consisted of 200 patients, including 103 Hispanic White individuals and 97 non-Hispanic White individuals. The mean age was 69.9 ± 7.4 years (range, 50-88 years), and there were 68 men and 132 women. There was no significant difference between Hispanic White and non-Hispanic White groups regarding age. There were no statistically significant differences between these two groups regarding pupil center pachymetry (546.2 ± 35.6 μm vs 548.2 ± 34.6 μm, P= 0.85), pachymetry at vertex (546.5 ± 35.3 μm vs 549.2 ± 34.7 μm, P=0.69), thinnest location (541.3 ± 36.1 μm vs 544.0 ± 33.5 μm, P=0.58), or corneal volume (59.4 ± 4.0 mm^3 vs 59.4 ± 3.8 mm^3, P=0.98). However, there were significant differences between Hispanic White and non-Hispanic White groups regarding anterior chamber volume (130.0 ± 45.6 mm^3 vs 146.6 ± 38.0 mm^3, respectively, P<0.001) and anterior chamber depth (2.6 ± 0.5 mm vs 2.7 ± 0.4 mm, respectively, P=0.01).

Conclusions: Although no significant differences exist in corneal pachymetry between Hispanic Whites and non-Hispanic Whites, anterior chamber depth and volume are significantly lower in Hispanic Whites compared with non-Hispanic Whites. Such anatomical differences should be considered during intraocular surgeries.

CONTROL ID: 3709297

SUBMITTER (NAME ONLY): Domenico Lepore

TITLE: Structural and functional ophthalmological follow-up of a preterm population: report at six years of age

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Lepore, B. Caproli, L. Hu, F. Giannuzzi, Ophthalmology, Universita Cattolica del Sacro Cuore Facolta di Medicina e Chirurgia, Roma, Lazio, ITALY|L. Orazi, G. Amorelli, D. Ricci, M. Petrianni, F. Amore, International Agency for the Prevention of Blindness, Rome, ITALY|F. Gallini, G. Vento, Pediatrics, Universita Cattolica del Sacro Cuore Facolta di Medicina e Chirurgia, Roma, Lazio, ITALY|F. Gallini, G. Vento, Pediatrics, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Lazio, ITALY|D. Ricci, M. Petrianni, F. Amore, Nat. Cen for Serv and Res on Low Vision, ITALY|

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ABSTRACT BODY:

Purpose: The aim of the study was to analyse structural and functional ophthalmological outcomes at six years of age in a population of children born with ≤32 weeks of gestational age (GA) and/or ≤1000grams of birth weight (BW) at the A. Gemelli University Hospital in Rome.

Methods: Per protocol, all preterm babies screened for acute ROP (following ICROP criteria) undergo at six year of age a full ophthalmologic and orthoptic examination. Different neurodevelopmental aspects were assessed By means of the Wechsler Intelligence Scale for Children (WISC) . A standard score below 79 was considered below average. Recently wide-field fundus retinography and oral ultra wide-field fluorescein angiography (UWFFA, OPTOS Inc USA) and OCT and OCT-A (Carl Zeiss, D) imaging were introduced in the protocol. Peripheral retinal vascular features highlighted by UWFFA were classified by three different graders and correlated with to clinical parameters such as BW, GA and acute ROP severity. Peripheral avascular retina (PAR) was also observed and classified form 1 to 3 based on its extent. Foveal Avascular Zone (FAZ) was observed with both OCT-A and UWFFA and correlated with visual acuity (VA).

Results: 45 preterm infants, 28.5% of the preterm population screened for ROP from January 2013 untill December 2014 were examined at a mean age of 6 years and 5 months. 72 eyes were previously diagnosed by various ROP stages. Mean age at examination was 6.14 years. 13 babies showed various degree of neurological disabilities and 17 various form of strabismus. ETDRS LogMar visual acuity ranged from 2 to 0. Peripheral retinal vasculature showed at WFFA a dichotomous pattern in 67% (n=55, shunting pattern in 21% (n=17) and finger-like pattern in 12% (n=10). One eye only showed a light leakage at the junction between vascular and avascular retina. PAR was present in 63% (n=29). FAZ was absent on 28,5% (n=24) of the OCTA images with a good accordance with WFFA images. No significant correlation was found with VA.

Conclusions: Dichotomous branching pattern and PAR are common peripheral vascular features in our population. These findings suggest the importance of a long term follow up in preterm children, especially those with specific peripheral vascular retinal features.

CONTROL ID: 3709299

SUBMITTER (NAME ONLY): Chau-Minh Phan

TITLE: Developing a novel in vitro eye model using 3D bioprinting for drug delivery studies

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Phan, W. David, P. Garg, L.W. Jones, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|C. Phan, W. David, L.W. Jones, Centre for Eye and Vision Research Limited, Hong Kong, ON, HONG KONG|

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ABSTRACT BODY:

Purpose: To develop an in vitro eye model using a novel 3D bioprinting method for testing the release of ophthalmic formulations to the posterior ocular region.

Methods: The eye model was designed using CAD software and includes both an anterior aqueous chamber and a posterior vitreous chamber. The vitreous chamber is surrounded by a blood chamber to mimic vessels that can be used to transport a blood-like substance. Three inlet ports control the flow of fluid into the chambers and the blood channels, and the three outlet ports allow fluids to exit these compartments. The eye model was 3D printed on a commercial mSLA printer (Photon Mono X, AnyCubic), which was retrofitted with a humidity and temperature control module to create a printing environment at 37°C and >80% humidity. The bioink formulation consisted of 10% gelatin methacrylate (GelMa). After printing, the models were incubated at 37°C to remove any uncured GelMa within any hollow compartments. For this study, phosphate-buffered saline was used as an aqueous and vitreous humour mimic. To evaluate the diffusion of a small hydrophilic molecule on the eye model, a contact lens (Air Optix) was soaked with a water-soluble red food dye for 1 hour and then placed on the eye model. The amount of dye in the anterior chamber, posterior chamber, and blood channels was measured using UV spectrophotometry after 24 hours.

Results: The entire model can be printed without any support structures within approximately 3 hours. The 3D printed eye model can also be autoclaved for testing that requires sterility. Because there were no diffusion barriers present in the current model, the red dye was detected in all three chambers after 24 hours. The highest concentration of dye was found in the anterior chamber, followed by the blood chamber and then the posterior chamber.

Conclusions: The prototype developed in this study can be used as a starting point to develop enhanced 3D printed eye models to test drug release kinetics of various devices and formulations. Future work will focus on adding the appropriate diffusion barriers to better simulate drug diffusion through ocular tissues.

CONTROL ID: 3709300

SUBMITTER (NAME ONLY): Gavin Arno

TITLE: Cas9 targeted long-read nanopore sequencing of ABCA4 and the OPN1LW/OPN1MW gene array for investigation of inherited retinal disease

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Arno, N. Jurkute, M. Michaelides, O.A. Mahroo, A.R. Webster, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|G. Arno, N. Jurkute, M. Michaelides, O.A. Mahroo, A.R. Webster, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|T. Boles, Sage Science Inc., Beverly, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Short, paired-end sequencing (next generation sequencing, NGS) enables interrogation of up to ~95% of the human genome. Several clinically relevant genes for inherited retinal disease (eg: OPN1LW/OPN1MW) and variants (eg: complex rearrangements) cannot be resolved by NGS technology including whole genome sequencing (WGS). We sought to investigate the use of Cas9 targeting of chromosomal segments (CATCH) with Oxford Nanopore Technologies (ONT) long-read sequencing for a WGS-intractable suspected ABCA4-retinopathy case and to sequence the NGS-intractable OPN1LW/OPN1MW gene array.

Methods: CATCH was performed for ABCA4 and the OPN1LW/OPN1MW array using CRISPR guide RNAs flanking the regions of interest followed by separation of high molecular weight DNA fragments using the SageHLS system (SAGE science). ONT MinION long-read sequencing was performed on resultant enriched DNA fragments.

Results: One patient with Stargardt disease was unresolved following WGS. A single heterozygous variant was identified (c.5715+5G>A) with no candidate non-coding or structural variants that could account for the second allele. CATCH-nanopore sequencing using CRISPR-guides flanking ABCA4 generated 337 on-target reads (chr1:93,992,834-94,121,148) and a maximal read depth of 50x. Interrogation of reads revealed a complex structural rearrangement comprising insertion of 689bp from the long non-coding RNA, LINC01500 at chr14q23.1, and an ~800bp long interspersed nuclear element (LINE) into intron 1 of ABCA4. Splice prediction (nnsplice) showed a potential 14bp pseudoexonwithin the inserted sequence.

Sequencing ofthe OPN1LW/OPN1MW gene array following CATCH enrichment for a control female subject generated a maximal read depth of 36x, and for a control male, 25x read depth, including full-length reads of up to ~233kb spanning the entire fragment enabling accurate haplotyping of the opsin arrays.

Conclusions: This study demonstrates that CATCH-nanopore sequencing is effective for cases intractable to NGS. We were able to generate significant enrichment for target regions and ultra-long reads spanning the entire targets. This study identified a complex structural rearrangement, missed by short-read WGS, in ABCA4 that may lead to cryptic splicing. Effective sequencing of the NGS-intractable OPN1LW/OPN1MW gene array is possible for variant detection in males with blue cone monochromacy.

CONTROL ID: 3709301

SUBMITTER (NAME ONLY): Hisashi Fukuyama

TITLE: Racial differences in presentation and outcomes of polypoidal choroidal vasculopathy in a multicenter clinical study

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Fukuyama, G.O. Bou Ghanem, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|J. Moir, D. Skondra, The University of Chicago Medicine, Chicago, Illinois, UNITED STATES|H. Fukuyama, F. Gomi, Hyogo Ika Daigaku, Nishinomiya, Hyogo, JAPAN|

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ABSTRACT BODY:

Purpose: To report the prevalence and clinical characteristics of polypoidal choroidal vasculopathy (PCV) at 3 tertiary referral centers, focusing on racial differences in Caucasians, African American, and Asian subjects.

Methods: We reviewed the medical records of patients diagnosed with treatment naïve exudative AMD between January 2016 and December 2020 at the following institutions: Northwestern University, University of Chicago, and Hyogo College of Medicine. We diagnosed PCV in this cohort based on fundus photos and OCT characteristics, defined as the presence of: two of the following three characteristics: sub-retinal pigment epithelium (RPE) ring-like lesion, complex RPE elevation, or sharp-peaked pigment epithelium detachment. We also report the visual and anatomic outcomes in patients who completed longitudinal follow-up of 12 months.

Results: A total of 123 patients with treatment-naïve PCV— 21 Caucasians, 18 African Americans, and 84 Asians— were identified. PCV prevalence in the overall AMD cohort was 6.89 % among Caucasian subjects, 33.3 % in African Americans, and 36.68 % in Asians. The prevalence of hard exudates and subretinal hemorrhage was highest in African American patients (55.6% and 72.0%) and considerably lower in Asians (32.1% and 38.1%) and Caucasians (14.3% and 33.3%). Baseline BCVA was also worse in African American patients (mean Log MAR: 0.793). Caucasian patients had significantly lower incidence of pachyvessels (28.6%) and more soft drusen (66.6%) compared to African Americans and Asians. Ninety-four patients — 20 Caucasian, 11 African American, and 63 Asians— were followed for more than one year. Mean BCVA (LogMar) improved significantly from baseline to month 12 (0.394 to 0.211) in the overall cohort (P<0.001), though this did not hold true for the Caucasian subgroup ((0.362-tp 0.361; P = 0.56).

Conclusions: We found significant differences in the prevalence and clinical characteristics of PCV amongst the three racial groups. These pathophysiologic differences deserve further study since they can have important impact on prognosis and treatment outcomes.

CONTROL ID: 3709303

SUBMITTER (NAME ONLY): Jade Moon

TITLE: Comparison of neovascularization detection in proliferative diabetic retinopathy using widefield swept source optical coherence tomography and fluorescein angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.Y. Moon, K.M. Wai, I. Garg, E.S. Lu, R. Zeng, J.B. Miller, Ophthalmology, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|J.Y. Moon, K.M. Wai, I. Garg, Y. Cui, R. Katz, Y. Zhu, E.S. Lu, R. Zeng, J.B. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|Y. Cui, Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|Y. Zhu, Ophthalmology, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|

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ABSTRACT BODY:

Purpose: We compare the ability of resident ophthalmologists to identify neovascularization (NV) in patients with proliferative diabetic retinopathy (PDR) using widefield (WF) swept source (SS) optical coherence tomography angiography (OCTA) and fluorescein angiography (FA) to help examine how easily this new technology could be more widely deployed to less experienced users.

Methods: Eyes with PDR based on clinical examination were imaged with 15mm x 15mm WF SS-OCTA and FA no more than 1 week apart. These images were scrambled to create a grading set consisting of anonymized SS-OCTA images of the retina slab with the corresponding B-scans (hereby referred to as SS-OCTA with corresponding B-scan), SS-OCTA images of the retina slab and the vitreoretinal interface (VRI) angio slab (hereby referred to as the VRI slab), and FA image set consisting of an early phase image and a late phase image (hereby referred to as FA) for each eye. After IRB approval, participants were asked to identify NV in each image and scored on the number of NV identified correctly. Additionally, participants were timed on how long they spent on each FA and VRI slab.

Results: 10 eyes from 10 patients were included in the study for a grading set consisting of 30 images. The mean number of neovascularization per image was 2.03. 11 resident physicians participated in the study. Overall, resident physicians correctly identified 65.6% of NV using FA, 50.8% of NV using SS-OCTA with corresponding B-scan, and 78.0% of NV using the VRI slab. There was no statistically significant difference in resident physician’s ability to detect NV across the three imaging modalities (P = 0.12). Participants spent an average of 4.8 seconds less for each VRI slab compared to FA (13.5 seconds versus 18.3 seconds, P = 0.04).

Conclusions: Detection rates of NV by resident physicians using SS-OCTA was comparable to that of using FA. Additionally, resident physicians were able to identify NV more quickly on VRI slab compared to FA. Our results suggest that SS-OCTA may be an appropriate imaging modality for the detection of NV in PDR patients, even with less experienced OCTA graders.

CONTROL ID: 3709305

SUBMITTER (NAME ONLY): Rose Trimpey-Warhaftig

TITLE: The novel secretome ST266 promotes survival of oxidant-stressed human RPE by a mechanism involving the Akt/mTOR/p70S6k/GSK-3b pathway

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Trimpey-Warhaftig, N. Besley, S. Lallier, P. Yang, G.J. Jaffe, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|H. Wessel, L. Brown, Noveome Biotherapeutics Inc, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress contributes to dysfunction and loss of retinal pigment epithelial (RPE) cells observed with age-related macular degeneration (AMD). ST266 is the biological secretome produced by a novel population of amnion-derived multipotent progenitor cells. We have previously shown that ST266 increases RPE cell survival and mitochondrial function after cells were treated with hydroquinone (HQ), hydrogen peroxide (H_2O_2), oxidants related to cigarette smoke, or all-trans Retinal (atRal), a pro-oxidant component of the retinoid cycle. Herein, we aim to determine the mechanism by which ST266 confers protection.

Methods: Cultured human RPE cells were pre-treated for 1h in the presence or absence of MK-2206, a known protein kinase B (Akt) inhibitor, treated with varying concentrations of H_2O_2, HQ, or atRal alone in serum-free media (SF-MEM) for 1.5h at 37^oC for WST-1 assay, followed by 1h or 24h treatment with STM100 (the media in which the amnion progenitor cells are grown) or ST266 (20% in STM100) for Western blot or WST-1 assay, respectively. Western blot analysis was performed to determine phosphorylation of Akt and its downstream targets p70 ribosomal S6 kinase (p70S6K), mammalian target of rapamycin (mTOR), and glycogen synthase kinase 3 beta (GSK-3B). Cell viability was measured with WST-1 reagent.

Results: ST266 significantly increased levels of phosphorylated Akt as well as its downstream targets p70S6k, mTOR, and GSK-3B ($p<0.05$). Addition of MK-2206 to STM100-treated cells virtually eliminated Akt phosphorylation, while the addition of MK-2206 to ST266-treated cells reduced Akt phosphorylation to near basal levels. ST266 significantly improved cell viability on average by 38%, 20%, and 29% in HQ-, H_2O_2-, and atRal-treated cells respectively compared to STM100 treated cells. This improved viability with ST266 was significantly reduced when MK-2206 was added to 17%, 7%, and 10% in HQ-, H_2O_2-, and atRal-treated cells respectively compared to STM100 treated cells ($p<0.05$).

Conclusions: When RPE cells were exposed to ST266, Akt phosphorylation increased as well as its downstream targets. ST266 improved cell viability after exposure to various oxidants, an effect that was significantly reduced when Akt activation was blocked. These data suggest that Akt is involved in the mechanism by which ST266 improves cell survival in oxidant-treated human RPE cells.

CONTROL ID: 3709306

SUBMITTER (NAME ONLY): Andrea Waksmunski

TITLE: Cross-Ancestry Glaucoma Genetic Risk Score in Hispanic Veterans in the Million Veteran Program

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Risk stratification for early detection of primary open-angle glaucoma (POAG) may mitigate severe disease outcomes, including irreversible vision loss, for millions globally. Genetic risk scores (GRS), which sum allelic effects, promise clinical utility for prediction of many complex diseases but are not generalizable across different ancestral groups. Moreover, although POAG burden is higher in Hispanic (HIS) individuals, most POAG genetic studies have been reported in individuals of non-HIS European ancestry (EUR). We aimed to evaluate POAG GRS performance in HIS Veterans in the Million Veteran Program (MVP).

Methods: We calculated GRS based on 127 published POAG-associated variants in HIS (382 cases and 2965 controls) and EUR (3382 cases and 58811 controls) Veterans in the MVP. Ancestry was defined using the Harmonized Ancestry and Race/Ethnicity (HARE) algorithm. We tested for association between the 127-variant (unweighted and weighted by published cross-ancestry effect estimates) GRS and POAG via logistic regression-based analyses with unadjusted and adjusted (age, sex, and 10 sample-specific principal components) models. We compared POAG case classification across GRS deciles and evaluated GRS model performance with receiver operator characteristic (ROC) curves and area under the curve (AUC) estimates. We also performed subset analyses of HIS with <50% EUR global genetic ancestry (GGA; determined via ADMIXTURE program).

Results: Unweighted and weighted GRS were significantly associated with POAG in HIS and EUR Veterans ($p<0.05$). Between the top decile and bottom 90%, we observed ~3-fold higher odds of POAG case classification for unweighted (odds ratios [OR], 95% confidence intervals [CI]: HIS: 2.70 [2.03-3.56]; EUR: 2.74 [2.51-2.98]) and weighted (HIS: 3.11 [2.35-4.07]; EUR: 3.03 [2.78-3.29]) GRS. We detected no statistically significant difference between GRS performance in ROC comparisons between HIS and EUR Veterans (AUC range 0.65-0.67). In GGA subset analyses of 220 cases and 1486 controls, ROC curves were comparable to the full HIS dataset.

Conclusions: POAG studies prioritizing diverse, non-EUR groups are crucial to ensure equitable clinical introduction of GRS for POAG prediction. We confirmed that a GRS of 127 POAG risk variants performed similarly in HIS and EUR MVP Veterans, regardless of majority EUR/non-EUR GGA.

CONTROL ID: 3709308

SUBMITTER (NAME ONLY): Levi Bonnell

TITLE: Predicting one-day post-cataract surgery intraocular pressure spikes using machine learning methods

SESSION TITLE: Using Technology for Care Delivery and Improvement

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Bonnell, K.L. Christopher, N. Mandava, A.M. Lynch, J.L. Patnaik, Ophthomology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Transient one-day postoperative intraocular pressure (IOP) spikes following cataract surgery are adverse outcome of cataract surgery and can lead to pain, corneal edema, glaucomatous nerve damage, anterior ischemic optic neuropathy, and vision loss. To our knowledge, no studies have combined known and unknown risk factors to predict IOP spikes. We performed a retrospective, observational cohort study to build a clinical prediction rule for one-day postoperative intraocular pressure spikes based on demographic, clinical, and ophthalmic data using machine learning methods.

Methods: First eye phacoemulsification cataract surgeries between January 2014 and June 2020 from the University of Colorado Cataract Outcomes Registry were included. Exclusion criteria were the absence of documented postoperative IOP. The presence of a one-day IOP spike was defined as an IOP ≥ 30 mmHg at the first day post-operative visit. The data were randomly split into two independent sets: a training set (80%) for development and tuning of the model and a test set (20%) to determine the final fit of the model. Random forests were used to build the clinical prediction model.

Results: A total of 7,676 first eye phacoemulsification cataract surgeries were included in the analyses. A random forest model with 75 variables produced the largest area under the receiver operator curve (0.80) in the training set and 0.71 (95% confidence interval 0.66, 0.79) in the test set, where 0.50 is no predictive power. Among the most influential predictors were surgery characteristics (cumulative dissipated energy, length of surgery, complex case, combined surgery), eye characteristics (eye diseases and measurements), baseline IOP, and race and sex of patient. The optimum operating point had a sensitivity of 0.78, specificity of 0.55 and a positive predictive value of 0.84.

Conclusions: A clinical prediction rule for postoperative IOP spikes can identify at-risk patients immediately after the surgery, allowing the surgeon to mitigate risk by providing prophylactic IOP lowering drops, ultimately reducing short-term pain and long-term sequalae. We also identified several novel risk factors for IOP spikes that warrant follow-up.

CONTROL ID: 3709310

SUBMITTER (NAME ONLY): Eric Enyong

TITLE: Non-caveolar Caveolin-1 in Müller glia regulate retinal innate immune responses

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.N. Enyong, M.H. Elliott, Physiology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|E.N. Enyong, J.M. Gurley, M.G. Agbaga, M.H. Elliott, Ophthalmology, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|M.G. Agbaga, Cell Biology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of Caveolin-1 (Cav1), the signature protein of caveolae, in regulation of innate immune response seems controversial, since Cav1 can either promote or suppress immune response in a cell-context manner. We speculate that caveolar and non-caveolar localization of Cav1 in different cells accounts for this paradoxical immune regulatory role. Here, we show that non-caveolar Cav1 in Müller glia enhance lipopolysaccharide (LPS)-induced interleukin-6 (IL-6) response, which can be blunted by either Cav1 silencing or sequestration into caveolae

Methods: To investigate the role of non-caveolar Cav1 in immune regulation, we either silenced Cav1 using Cav1-shRNA, or sequestered Cav1 into caveolae by expressing Cavin1/PTRF in MIO-M1 Müller glia and measured IL-6 response in tissue culture media by ELISA, with or without LPS stimulation. We used quantitative proteomics to identify immune-related pathways enriched in Cav1 immunoprecipitates from control and Cavin1/PTRF-expressing MIO-M1 Müller glia. Additionally we performed immunocytochemistry staining of MIO-M1 Müller glia using fluorescently labeled phalloidin to evaluate changes in filamentous actin (F-actin) when Cavin1/PTRF is expressed

Results: LPS stimulation of MIO-M1 Müller glia significantly increased IL-6 secretion into tissue culture media. Surprisingly, both Cav1 silencing or Cavin1/PTRF expression in MIO-M1 Müller glia significantly suppressed LPS-induced IL-6 response. Analysis of mass spectrometry data revealed significant differential association of different proteins with Cav1 when Cavin1/PTRF is expressed. Interestingly, we identified 18 genes in 11 of the 30 most enriched pathways for proteins with significantly increased association with Cav1 that were associated with immune-related pathways. These were distributed among seven distinct immune-related gene ontology (GO) functional categories including neutrophil activation, neutrophil degranulation, immune effector process and immune response. Furthermore, expression of Cavin1/PTRF in MIO-M1 Müller glia significantly reduced F-actin staining intensity

Conclusions: Our results suggest that non-caveolar Cav1 in MIO-M1 Müller glia enhance LPS-induced innate immune response. Expression of Cavin1/PTRF sequesters Cav1 into caveolae, which alters critical pathways involved in immune regulation, with remodeling of actin cytoskeleton as a potential mechanism

CONTROL ID: 3709312

SUBMITTER (NAME ONLY): Elyana Locatelli

TITLE: Relationships between serum levels of brain-derived neurotrophic factor and symptoms and signs of corneal nerve function

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine relationships between serum brain-derived neurotrophic factor (BDNF) and symptoms and signs of corneal nerve function.

Methods: Prospective study of individuals seen in the Miami Veterans Affairs eye clinic. All individuals completed questionnaires regarding ocular pain symptoms and underwent a comprehensive assessment of the ocular surface, including confocal microscopy. All individuals provided a blood sample which was analyzed for BDNF using R&D Free BDNF Quantikine ELISA Kit. Our primary goal was to examine relationships between neuropathic ocular pain symptoms and confocal microscopy findings and serum BDNF levels. These relationships were examined by correlational analysis, followed by multivariable forward stepwise linear regression analysis.

Results: 35 individuals were enrolled into this prospective study, with a mean age of 54±4 (range 48 to 63 years); 97% (n=34) self-identified as male, 60% as white, and 43% as Hispanic. BDNF levels ranged from 11.6 ng/ml to 50.5 ng/ml, with a mean of 30.5 ng/ml (standard deviation 9.0). BDNF levels were positively associated with Neuropathic Pain Symptom Inventory-modified for the eye (NPSI-E) scores ($r=0.33$, $p=0.05$) and corneal nerve beading density ($r=0.41$, $r=0.02$). When considering demographics, ocular symptoms, signs, and nerve metrics in a forward multivariable regression model, elevated levels of BDNF were associated with higher neuropathic pain symptoms (NPSI-E, standardized β 0.64, $p<0.005$) and higher corneal nerve beading density (minimum value of 6 scans from both eyes, standardized β 0.69, $p<0.005$). Elevated levels of BDNF were also associated with lower corneal sensation (measured with a cotton swab, standardized β -0.52, $p=0.001$) and corneal nerve fiber area (standardized β -0.40, $p=0.01$). This model explained 59% of variability in systemic BDNF levels. Of note, demographics and tear film metrics were not related to BDNF levels.

Conclusions: BDNF levels are related to higher neuropathic ocular pain symptoms and beading density (a measure associated with nerve metabolic activity).

CONTROL ID: 3709313

SUBMITTER (NAME ONLY): Hua Yang

TITLE: Differential expression of complement genes in mammalian eyes

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yang, M. Yuan, P. Gaurang, A. Sun, A. Latuszek, Y. Hu, J. Cao, C. Romano, Ophthalmology, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) results from a complex interaction of environmental and genetic risk factors. Genetic studies have shown complement genes are strongly associated with AMD. Rodent models based on expression of human genetic risk variants in complement genes have exhibited only limited phenotypic similarity to human disease. In the present study we have compared complement Factor H (CFH) and complement component 3 (C3) mRNA expression in different species eye (e.g. mouse, rat and human).

Methods: Paraffin sections or cryosections of mouse, rat and normal human donor eyes were used for in situ hybridization assay to determine the CFH and C3 expression. Manufacturer's (Advanced Cell Diagnostics) instructions were followed for RNAscope® experiments. CFH and C3
probes for different species were applied. Negative controls, e.g. DapB and positive probes or tissues (Liver), were included.

Results: In rodent eye (both rat and mouse), CFH mRNA is strongly expressed in the retinal pigment epithelium with some expression also found in inner nuclear (INL) and retinal ganglion cell (RGC) layers of the retina. C3 mRNA is expressed mainly in RGC, INL of retina, ciliary body, corneal epithelium with some expression is also found in rodent retinal pigment epithelium layer. However, in human eye, CFH and C3 mRNA are strongly expressed in the choroid. Some expression is also found in RGC, INL layer of retina, ONH, sclera, cornea endothelial and stroma; and ciliary body. There is no C3 or CFH signal detected in RPE cells.

Conclusions: The complement genes are present in ocular tissues, where they could play an important role in the pathogeneses of age-related macular degeneration. Our results show that complement factor H and C3 expression localization are quite different between human and rodent eyes. Rodent animal models based on manipulating CFH or C3 expression might not represent human disease because of these anatomic differences.

CONTROL ID: 3709315
SUBMITTER (NAME ONLY): Arthur Fernandes
TITLE: Age effects on ocular features of rhesus macaques
SESSION TITLE: IOLs and Presbyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A.G. Fernandes, A.D. Melin, Department of Anthropology and Archaeology, University of Calgary, Calgary, Alberta, CANADA|P. Alexopoulos, G. Wollstein, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|A. Burgos-Rodriguez, M.I. Martinez, Caribbean Primate Research Center, Universidad de Puerto Rico, San Juan, PUERTO RICO|M.J. Montague, Department of Neuroscience, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|L.J. Brent, Centre for Research in Animal Behaviour, University of Exeter, Exeter, Devon, UNITED KINGDOM|N. Snyder-Mackler, School of Life Sciences, Arizona State University, Tempe, Arizona, UNITED STATES|N. Snyder-Mackler, Center for Evolution and Medicine, Arizona State University, Tempe, Arizona, UNITED STATES|J. Danias, Department of Ophthalmology, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|J.P. Higham, Department of Anthropology, New York University, New York, New York, UNITED STATES|A.D. Melin, Alberta Children's Hospital Research Institute, Calgary, Alberta, CANADA|
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ABSTRACT BODY:

Purpose: Rhesus macaques (Macaca mulatta) are a valuable model in ophthalmology research, exhibiting visual systems that share many anatomical similarities with those of humans. The purpose of the current study is to investigate the effects of age on ocular features of a large cohort of free ranging rhesus macaques derived from animals originally introduced to Cayo Santiago/Puerto Rico in 1938.

Methods: A total of 172 animals (83 males and 89 females) from all ages (mean 13.1±5.7; range 0.7 to 26.2 years old) and mean weight of 16.0±7.6 pounds underwent a comprehensive eye exam, including slit-lamp biomicroscopy (HSL-600, MicroClear, Jiangsu, China), pachymetry (Pachmate 2, DGH Technologies, Exton, USA), axial length (vuPad, Sonomed Escalon, Lake Success, USA), and automated refraction (Topcon KR 7000S, Topcon, Tokyo, Japan). Each outcome variable was modeled as a function of age using multilevel mixed-effects models adjusted for animal sex and weight.

Results: Cataract of any degree (no evidence of traumatic cataract) was observed in 19 animals (11 unilateral and 8 bilateral cases) representing a frequency of 11.05% (95% CI: 6.78 – 16.71%). The mean pachymetry, axial length, and spherical equivalent were, respectively, 474.43±32.21 mm (median: 473.00), 19.49±1.24 mm (median: 19.46), and 0.30±1.70 D (median: 0.38). Age was significantly associated with cataract occurrence, pachymetry, axial length and spherical equivalent. For each 1 year increase of age, the odds of having cataract increased by 18% (OR= 1.18; 95%CI: 1.06 – 1.31; p=0.001), the pachymetry decreased by 1.11 mm (Coef.= -1.11; 95%CI: -2.00 to -0.23; p=0.013), the axial length increased by 0.03 mm (Coef.= 0.03; 95%CI: 0.01 to 0.05; p<0.001), and the spherical equivalent decreased by 0.12 D (Coef.= -0.12; 95%CI: -0.22 to -0.02; p=0.015).

Conclusions: Rhesus macaques have age-related ocular changes similar to those observed in human aging, including higher occurrence of cataract, decreasing corneal thickness, increasing axial length, and myopic shift. Our results are from a natural free-ranging population without medical intervention, which represents an excellent population for studying naturally occurring age-related eye diseases.

CONTROL ID: 3709316

SUBMITTER (NAME ONLY): Megan Cavet

TITLE: National physician survey on clinical practice patterns for the treatment of noninfectious uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Cavet, Medical Affairs, Bausch + Lomb, Rochester, New York, UNITED STATES|S. Hancock, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Noninfectious uveitis (NIU) often manifests as a persistent relapsing disease that may be challenging to treat. This survey was conducted to evaluate current treatment patterns for chronic and acute NIU among retina specialists and identify unmet needs associated with therapy for NIU and associated macular edema (ME).

Methods: An anonymized online survey on NIU practice patterns was designed and sent to ophthalmologists throughout the US. Screening questions limited respondents to retina specialists with retina/uveitis fellowship training and intravitreal injection experience. The survey consisted of questions related to respondent's location and specialty, occurrence of ME in association with NIU, NIU treatment patterns and therapeutic unmet needs. Responses were analyzed using descriptive statistics.

Results: Survey respondents (N=150) were evenly distributed geographically. Respondents reported ME secondary to 31% and 61% of acute and persistent NIU cases respectively, with an overall rate of 47%. Corticosteroids were the most common initial treatment for acute NIU (>90% of cases), mostly administered topically. Proportions of patients with unilateral/bilateral acute NIU receiving topical corticosteroids were 93%/91%, 51%/47% and 47%/46% for anterior, posterior and pan NIU, respectively. In persistent NIU, therapy was typically changed to another corticosteroid and/or a non-steroidal immunosuppressant. Among patients receiving corticosteroids for persistent NIU, periorbital delivery was the most common route of administration for unilateral/bilateral anterior NIU (59%/55%), while intravitreal delivery was most common for posterior NIU (64%/59%) and pan NIU (68%/63%). Respondents refrained from using corticosteroids in 20% of patients due to concern over elevated intraocular pressure (IOP) and considered elevated IOP, glaucoma and cataract risk to be moderately high concerns when selecting therapy (ranking of 4.0, 3.9, 3.5, respectively, on a 1-5 scale). A lower risk of IOP elevation was ranked as the greatest unmet need for corticosteroid therapies.

Conclusions: Survey results indicate that ME is commonly associated with NIU, and local corticosteroids are typically used first-line. However, physicians may limit use of corticosteroids due to risk of associated side effects such as cataract and IOP elevation; effective therapies with lower incidence of these adverse reactions are warranted.

CONTROL ID: 3709318

SUBMITTER (NAME ONLY): Raymond Oh

TITLE: Models of Autosomal Dominant Optic Atrophy (ADOA) using OPA1 haploinsufficient iPSCs and response to Targeted Augmentation of Nuclear Gene Output (TANGO) Antisense Oligonucleotides (ASOs) Treatment

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Oh, B. Slipp, A. Venkatesh, S. Ali, Z. Li, R.B. Hufnagel, I. Aznarez, G. Liau, J. Hoger, Stoke Therapeutics Inc, Bedford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: ADOA is the most common inherited optic neuropathy, resulting in severe and progressive visual failure due to loss of retinal ganglion cells (RGCs). Most patients harbor loss-of-function mutations in the OPA1 gene that lead to haploinsufficiency. Reduced OPA1 protein levels result in impaired mitochondrial function in RGCs leading to cell death. Currently, there is no treatment for patients with ADOA. TANGO ASOs reduce inclusion of a non-productive, alternatively spliced exon in OPA1, and leverage the wild-type (WT) allele to increase productive OPA1 mRNA and protein. To test TANGO ASOs on OPA1 expression and function in RGCs in a human ADOA model, we generated OPA1 haploinsufficient iPSCs for differentiating into retinal neurospheres.

Methods: OPA1 mutations were introduced in a WT human iPSC line using CRISPR-Cas9. Clones were assessed for karyotype, pluripotency, heterozygous mutation status, and OPA1 expression. Mutant and isogenic control WT retinal neurospheres were generated over 45 days of differentiation (PMID: 25640818). RGCs were assessed by immunofluorescent microscopy and single-cell RNA sequencing. Relative levels of OPA1 were assessed by qPCR, quantitative western, in situ hybridization, and immunohistochemistry. Reactive oxygen species (ROS) and viability of RGCs were assessed by flow cytometry. We evaluated neurospheres treated with TANGO ASOs by gymnotic delivery.

Results: Haploinsufficient OPA1 iPSC clones were generated with normal karyotype and pluripotency. Both OPA1 mutant and WT control neurospheres were generated with approximately 10-20% RGCs. OPA1 mutant cells had similar viability and increased cellular ROS levels compared to controls. ASO treatment of neurospheres increased OPA1 mRNA expression and OPA1 protein while reducing non-productive OPA1 mRNA.

Conclusions: iPSC-derived RGC-containing neurospheres provide a useful in vitro model to evaluate TANGO ASOs. TANGO ASOs were able to partially correct RNA and protein deficiencies in OPA1 mutant retinal neurospheres. Our results support that TANGO ASOs can potentially be used to treat ADOA caused by OPA1 haploinsufficiency.

CONTROL ID: 3709319

SUBMITTER (NAME ONLY): Chrystal Ferguson

TITLE: Ophthalmologists' Familiarity and Anticipated Use of Biosimilars Prior to the Launch of the First Biosimilar in Ophthalmology

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ferguson, Ophthalmology, Spherix Global Insights, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Chrystal Ferguson: Commercial Relationship(s);Code E (Employment):Spherix Global Insights

ABSTRACT BODY:

Purpose: The aim of this study is to assess, through a wirtten questionaire, ophthalmologists' knowledge, attitudes, current market use (bevacizumab biosimilars; not authorized in retinal conditions) and future market use (ranibizumab and aflibercept biosimilars) of biosimilars in ophthalmology.

Methods: In November 2021, US ophthalmologists (n=75) completed a 40-minute on-line survey. Ophthalmologists were required to be in practice between 2 and 40 years, spend at least 50% of their professional time in clinical practice seeing patients, and not be pediatric-focused.

Results: 61% of ophthalmologists are neutral towards biosimilars, while 24% are in-favor and 15% are against. 23% of respondents report their opinion has become more positive in the last two years, while only 6% report their opinion has become more negative. 29% of ophthalmologists surveyed are extremely familiar with the FDA biosimilar approval pathway while 44% are moderately familiar, and 27% are not familiar; 31% and 28% are extremely comfortable with the concepts of extrapolation and interchangeability respectively. 61% and 56% are aware of approved bevacizumab biosimilars (ABP 215 and PF-06439535 respectively) when given the options but reported use is only 2% (ABP 215) and 1% (PF-06439535) given bevacizumab is used off label and therefore retinal diseases would not qualify for extrapolation. 61% of surveyed ophthalmologists report low familiarity with SB11 (ranibizumab biosimilar and the first FDA approved biosimilar studied in retinal conditions) and only 16% were aware of the launch date in 2022. Respondents estimate a mean of 26% of ranibizumab patients will be switched to SB11 for any condition when it becomes available, but only estimate switching 10% of aflibercept patients to the biosimilar. 21% report being extremely likely to prescribe SB11 over ranibizumab while 12% report the same for aflibercept; however, 36% are not likely to prescribe SB11 over ranibizumab while 61% are not likely to prescribe the biosimilar over aflibercept.

Conclusions: Ophthalmologists are predominantly neutral towards biosimilars currently, and familiarity of the FDA approval pathway is modest. Bevacizumab biosimilars are not supported by ocular data influencing familiarity, comfort, and uptake. Biosimilars investigated in ophthalmologic conditions have potential for greater utility.

CONTROL ID: 3709320

SUBMITTER (NAME ONLY): Alexander Neugebauer

TITLE: Evaluation of Virtual-Reality based Gaze Training for Improved Visual Performance in Persons with Tunnel Vision

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Neugebauer, S. Wahl, ZEISS Vision Science Lab, Institute for Ophthalmology, University of Tuebingen, Tuebingen, GERMANY|I. Ivanov, S. Wahl, Carl Zeiss Vision GmbH, Aalen, Baden-Württemberg, GERMANY|K. Stingl, University Eye Hospital, Institute for Ophthalmology, University of Tuebingen, Tuebingen, GERMANY|K. Stingl, Center for Rare Eye Diseases, University of Tuebingen, Tuebingen, GERMANY|

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ABSTRACT BODY:

Purpose: Gaze training describes the method of encouraging a more effective gaze behavior in persons living with impairments to the visual field - such as Retinitis pigmentosa - through specifically designed visual tasks, thus improving the visual performance in everyday life. Recent advancements in the field of virtual reality in both technology and accessibility motivate new and adapted gaze training approaches. In this study, we aim to evaluate the potential of utilizing virtual reality devices in gaze training.

Methods: For this, a gaze training application for a wireless virtual reality headset was designed and developed. Seven visually healthy participants (aged 19-29, average 22.9±3.1) with simulated tunnel vision used the application over the course of two weeks for unsupervised at-home gaze training. The training consisted of three different visual tasks – navigation, target search and simultaneous tracking of multiple moving targets – each designed to encourage increased gaze movement. The results were analyzed using Linear Mixed Models. Participants were further asked to fill questionnaires regarding their experience with the training application and virtual reality device throughout the two-week training phase.

Results: Participants display an increase in effective gaze movements – measured by the perceived visual area over a fixed amount of time - over the course of the study, with an average linear increase of 14.3% in the navigation task and 19.0% in the search task from first to tenth session ($p<0.01$ in both tasks). In addition, it is found that increased effective gaze movements correlate with the performance in the navigation task ($p<0.01$). According to the questionnaires, the developed virtual-reality gaze training is intuitive, not straining and initially enjoyable, however the reported motivation during training decreases over the course of the study.

Conclusions: The improvements in gaze behavior and visual performance displayed by the participants with simulated tunnel vision suggest that similar results may be achieved in Retinitis pigmentosa patients, though it remains to be assessed whether these effects translate to real-world situations. Further, the complication-free execution of a two-week training phase and positive user feedback regarding ease-of-use of the application and virtual reality setup show their feasibility for unsupervised at-home training.

CONTROL ID: 3709322

SUBMITTER (NAME ONLY): Tatiana Getz

TITLE: Conditional late deletion of IRBP causes loss of retinal function and a slow retinal degeneration without myopic eye elongation

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Getz, M. Chrenek, C. Reid, D. Shelton, V. Summers, J.H. Boatright, J.M. Nickerson, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Germline knockout of IRBP (i.e., RBP3) results in severe myopia starting early in development (P7) followed much later by retinal degeneration (P25+). Here, we test the hypothesis that late deletion of IRBP expression should cause loss of photoreceptor function and retinal degeneration without an increase in eye axial length.

Methods: To conditionally delete IRBP late in rod photoreceptors specifically, we used Rho-iCRE75. Littermate controls without the Rho-iCRE75 driver, but with the $RBP3^{lox/lox}$ gene, were used for comparison. IRBP mRNA levels were measured by digital droplet RT-PCR. Retina function was measured with electroretinograms (ERGs). Fundus imaging and SD-OCT evaluated retina morphology in vivo. Eye axis and circumference dimensions were measured with noncontact micrometers at sub-micron accuracy and precision. ONL counts were conducted on H&E stained sections.

Results: By P30, IRBP gene expression levels were significantly decreased by about 90% in the Rho-iCRE75 $RBP3^{lox/lox}$ mice vs the $RBP3^{lox/lox}$ mice ($p<.0001$). At P60, the ERGs showed significant decreases in a-wave (~34%; $p<0.01$) and c-waves (~21%; $p<0.05$) for the Rho-iCRE75 $RBP3^{lox/lox}$ mice, while the b-wave trended about 13% lower but was not statistically significant. Fundus photographs and SD-OCT imaging showed no obvious pathology in any group. Eye axial length, equatorial width, fit diameter, and roundness were not significantly different between genotypes at either age group. Retinal arc lengths were not different at either age group. Interestingly, outer nuclear layer counts at P30 showed an 8% significant decrease of nuclei in Rho-iCRE75 $RBP3^{lox/lox}$ versus $RBP3^{lox/lox}$ mice ($p<0.05$).

Conclusions: 1. Loss of IRBP late (after rapid early eye growth is mostly complete) was not associated with myopic eye growth. 2. The eye may already be incompetent to experience abnormal eye elongation when IRBP was lost late. 3. Selectively early IRBP expression was sufficient to allow normal emmetropia in the mouse eye. 4. However, the late loss of IRBP profoundly decreased photoreceptor number and function soon after IRBP mRNA was lost. This suggests that IRBP independently controls photoreceptor maintenance and emmetropic eye growth, implying at least two different and independent mechanistic roles for IRBP.

CONTROL ID: 3709327

SUBMITTER (NAME ONLY): Laura Cushley

TITLE: Navigating the Unseen City: Stakeholder Opinions on Navigation of the Built Environment by Visually Impaired Individuals

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Cushley, K. Curran, T. Peto, Centre for Public Health, Queen's University Belfast, Belfast, Northern Ireland, UNITED KINGDOM|N. Galway, School of Natural and Built Environment, Queen's University Belfast, Belfast, Northern Ireland, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To assess how key stakeholders, including visually impaired individuals and ophthalmic professionals, perceive potential challenges and effects on visually impaired users navigating the built environment

Methods: Semi-structured interviews were conducted with 20 stakeholders including 3 town planners, 4 architects, 3 visually impaired individuals, 6 ophthalmic professionals including ophthalmologists and optometrists and 4 sight loss charities. All transcripts were analysed using NVivo version 11 and random transcripts from each category were analysed by a secondary analyst, to agree on themes and sub-themes. A senior researcher adjudicated themes and subthemes.

Results: Four main themes and twenty-three subthemes were identified (table 1). The main themes included barriers and enablers of the built environment, the impact of living with visual impairment, policy, regulation and guidance and future solutions and innovations. The issues mentioned most were isolation and loneliness (33 times), confidence (21 times), mental health (19 times), independence (13 times). This was echoed by all stakeholders with planning professionals stating, ‘it must restrict them going out psychologically which leads to a lack of interaction, makes them homebound which impacts their physical and mental health and wellbeing’. Charities stated that ‘People [feel] cut off from the rest of society stuck at home’. In addition, some of the biggest barriers and enablers to navigating the built environment were issues with pavements (58 times), street furniture (36 times), lighting (25 times), shared space (18 times) and pedestrian crossings (17 times). Visually impaired individuals felt that ‘we give so much space to cars and everyone else has to jostle on the pavement in fear of their death’. Town planners and architects echoed these concerns commenting ‘far too much space has been given over to the motor vehicle and now the space on footways in restricted’.

Conclusions: This study showed that there are potential challenges for people with a visual impairment when navigating the built environment, many of which ophthalmic professionals, built environment professionals, charities and visually impaired people agreed on. The results also showed how big an impact having visual impairment can have on moving around towns and cities and its effect on mental and physical health.

CONTROL ID: 3709329

SUBMITTER (NAME ONLY): Varsha Venkata Srinivasan

TITLE: Macula Ganglion Cell Inner Plexiform Layer and Circumpapillary Retinal Nerve Fiber Layer Thicknesses from Widefield Imaging are similar to Standard Scans

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Venkata Srinivasan, S. Das, N.B. Patel, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) inner retinal thickness measures of the macula and circumpapillary regions are important for determining onset and progression of experimental glaucoma in the non-human primate (NHP). Standard raster and circumpapillary scans have excellent repeatability but sample a limited region of the posterior pole. The purpose of this experiment was to determine the agreement and repeatability of inner retinal thickness measures from widefield imaging compared to standard scans

Methods: OCT scans (Spectralis HRA+OCT) were acquired from 30 NHPs with healthy eyes. 11 of these animals were imaged on at least 4 separate days to assess repeatability. Standard scans included a 20x20° raster scan centered on the macula, and a 12° diameter circular scan centered on the optic nerve head. Widefield imaging protocol included a 217 line, 55x45° raster scan centered on the macula. Scans were imported into MATLAB, and the inner retinal borders were delineated using a neural network-based image segmentation algorithm. For comparison, retinal nerve fiber layer (RNFL) thickness was determined from an interpolated 12° scan path from widefield thickness maps. For both standard and widefield scans, the ganglion cell inner plexiform layer (GCIPL) thickness was determined for a region of 16 degrees in diameter centered on the fovea.

Results: The average GCIPL thickness from standard raster scans was 72.7±4.3μm, and 73.7±3.7μm from widefield images (bias = -1.0μm, 95% LOA -4.4 to 2.4μm). Average circumpapillary RNFL thickness from the standard circular scan was 113.2±7.3μm, and 114.2±5.8μm for a similar interpolated path from widefield scans (bias = 1.0μm, 95% LOA -6.5 to 8.6μm). Repeatability (2.77xSw) for GCIPL thickness was 2.7μm and 3.2μm, and for RNFL thickness 5.2μm and 4.5μm, for standard and widefield scans respectively.

Conclusions: Inner retinal thickness measures from widefield imaging have good repeatability and are comparable to those measured using standard scans. One of the major advantages of using widefield imaging is that it encompasses most of the visual field sampled in perimetry.

CONTROL ID: 3709333

SUBMITTER (NAME ONLY): Vishal Swaminathan

TITLE: Outcomes of Early Onset Versus Delayed Rhegmatogenous Retinal Detachments after Acute Posterior Vitreous Detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Swaminathan, R. Israilevich, E. Cehelyk, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|J. Uhr, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|M. Salabati, R. Mahmoudzadeh, J. Hsu, The Retina Service, Mid Atlantic Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the anatomic and functional outcomes of eyes presenting with early onset versus delayed RDs following acute PVD.

Methods: This was a retrospective, comparative, interventional cohort study of patients who presented with delayed RDs (>42 days after initial presentation to a retinal specialist with acute PVD) compared to an age- and gender-matched control cohort who presented with early onset RDs (PVD and RD at initial visit to a retina specialist). All eyes underwent retinal detachment repair from October 1, 2015 to March 31, 2020. The primary outcome was the final attachment rate and single surgery anatomic success (SSAS) at 3 months.

Results: Seventy-one patients presented with delayed RDs and 147 matched controls presented with early onset RDs. Patients with delayed RD had a mean (SD) baseline logMAR VA of 0.20 (0.37) [Snellen, 20/32] at the initial presentation with an acute PVD, which then decreased to 0.50 (0.70) [Snellen, 20/63] at the time of RD diagnosis ($p<0.001$). The mean VA of the early onset RD group was 1.03 (0.92) [Snellen, 20/214]. There was a significant difference between the mean VA of these groups at the time of RD presentation ($p<0.001$). The mean VA was better at month 1 and 3 post-RD repair in the delayed RD group compared to that of the control group ($p=0.004$ and 0.03, respectively). No significant difference was found when comparing the mean VA at 6-months post-repair, 12-months post-repair, or at the final visit ($p=0.43$, 0.32, and 0.21 respectively). SSAS was 59/71 (83.1%) for the delayed RD group and 117/147 (79.6%) for the early onset RD group ($p=0.54$). In the delayed RD group, 31/71 (43.7%) eyes had a macula-off RD while in the control group 98/147 (67.5%) eyes were macula-off ($p=0.002$).

Conclusions: Delayed RDs occurring more than 6 weeks after initial presentation with an acute PVD generally had better VA at the RD diagnosis visit and faster post-surgical visual recovery compared to RDs diagnosed at the initial presentation to a retina specialist. While no significant difference in anatomic outcomes was seen between the two groups, a greater proportion of patients presented with macula on RDs in the delayed RD group, perhaps suggesting that RD warnings given at earlier visits may be beneficial.

CONTROL ID: 3709336

SUBMITTER (NAME ONLY): Maximilian McCann

TITLE: Hyperglycemia alters VEGF-induced permeability in retinal endothelial cells

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. McCann, Y. Li, A. Kazlauskas, Illinois Eye and Ear Infirmary, Department of Ophthalmology & Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|A. Kazlauskas, Department of Physiology & Biophysics, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although vascular endothelial growth factor (VEGF) drives vascular dysfunction in both non-diabetic (neovascular AMD) and diabetic (DME and PDR) settings, it remains an open question if hyperglycemia (a key element of the diabetic setting) influences VEGF-mediated permeability. The purpose of this study was to begin to address this question.

Methods: We studied the contribution of the renin-angiotensin-aldosterone system (RAAS) to VEGF-induced permeability in primary human retinal endothelial cells (HRECs), which were cultured for 10 days in either normal glucose (NG; 5 mM), or high glucose (HG; 30 mM) media, using transendothelial electrical resistance assay (TEER). Additionally, RNAseq analysis was performed on HRECs cultured in normal and high glucose conditions for 10 days.

Results: RNAseq analysis indicated that HG alone altered expression of over 2000 genes. Furthermore, VEGF altered expression of almost twice as many genes in HG versus NG cells. While many of the VEGF-regulated genes and pathways were unique to one glucose concentration, a small subset was altered by VEGF in both NG and HG cells. Follow-up laboratory-based experiments indicated that these common genes/pathways were probably not governing VEGF-driven permeability. Consequently, we considered if VEGF-mediated permeability was different between NG and HG cells. Indeed, it was. HG cells were more sensitive to VEGF-induced permeability. Furthermore, VEGF-induced permeability was in part dependent on RAAS in HG, but not NG cells. Our ongoing studies are focused on elucidating the underlying mechanism by which RAAS contributes to VEGF-induced permeability.

Conclusions: Hyperglycemia alters the way VEGF induces permeability in retinal endothelial cells. This realization, along with the underlying mechanism of this phenomenon, will guide development of individualized therapeutics for retinopathies in and outside the context of diabetes.

CONTROL ID: 3709338

SUBMITTER (NAME ONLY): ROBERT MITTRA

TITLE: Archway phase 3 trial of the Port Delivery System with ranibizumab (PDS) for neovascular AMD: end-of-study results

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The PDS is an innovative drug delivery system approved for neovascular age-related macular degeneration (nAMD) in the United States that includes an ocular implant for continuous delivery of a customized formulation of ranibizumab (RBZ) into the vitreous. The Archway trial (NCT03677934) evaluated safety and efficacy of the PDS for nAMD through 96 weeks (W).

Methods: Archway was a phase 3, randomized, active treatment–controlled trial. Patients (pts) with nAMD previously treated with and responsive to a mean of 5 anti–vascular endothelial growth factor injections were randomized 3:2 to PDS with RBZ 100 mg/mL with fixed 24W refill-exchanges (PDS Q24W), or intravitreal RBZ 0.5 mg injections every 4W (monthly RBZ) through W96. The trial evaluated noninferiority (NI) and equivalence of PDS Q24W versus monthly RBZ on a primary endpoint of best-corrected visual acuity (BCVA) change from baseline (BL) averaged over W36/40 (NI margin, –4.5 letters; equivalence margin, ±4.5 letters; previously presented) and key secondary endpoints of BCVA change from BL averaged over W60/64 and W88/92 (NI margin, –3.9 letters).

Results: PDS Q24W was noninferior to monthly RBZ at W60/64 and W88/92, with differences in adjusted mean (95% CI) BCVA change from BL of 0.4 (–1.4, +2.1) and –0.6 (–2.5, +1.3) letters between arms, respectively. Change in adjusted mean BCVA from BL averaged over W60/64 and W88/92, respectively, was –0.4 and –1.1 letters in the PDS Q24W arm and –0.8 and –0.5 letters in the monthly RBZ arm. Adjusted mean center point thickness change from BL was generally similar between arms through W96. During each of the 4 Q24W PDS treatment intervals, 98.4%, 94.6%, 94.8%, and 94.7% of PDS pts assessed did not receive supplemental RBZ treatment, respectively. The ocular safety profile of the PDS was generally unchanged from the primary analysis, with no new safety signals.

Conclusions: Archway end-of-study results support the continued efficacy of the PDS over 2 years. Archway BCVA results averaged over W60/64 and W88/92 were consistent with the primary analysis, with PDS Q24W noninferior to monthly RBZ. Through each of the 4 Q24W PDS treatment intervals, ~95% of PDS pts assessed did not receive

supplemental RBZ. Adverse events related to PDS procedures were well understood and manageable, with learnings continually implemented to optimize pt outcomes.

CONTROL ID: 3709343

SUBMITTER (NAME ONLY): Austin Igelman

TITLE: Characterizing the refractive error during the first 2 decades of life in patients with congenital stationary night blindness

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Igelman, T. Khuu, O. Uner, J. Grassmeyer, P. Yang, L. Wilson, D. Fredrick, M.E. Pennesi, Oregon Health & Science University, Portland, Oregon, UNITED STATES|T. Khuu, Elson S. Floyd College of Medicine, Washington State University, Spokane, WA, Washington, UNITED STATES|A. Tayyib, University of Toronto, Toronto, Ontario, CANADA|M. Reith, University Eye Hopsital, Center for Ophthalmology, University Tuebingen, GERMANY|B. Lorenz, Justus Liebig Universitat Giessen, Giessen, Hessen, GERMANY|E. O'Neil, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|E. O'Neil, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|S. Yassin, University of California San Diego, La Jolla, California, UNITED STATES|A. Stephenson, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|E. Krauss, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Congenital stationary night blindness (CSNB) is known to be associated with high myopia. However, there is only limited information on the natural history of refractive error and the variability by causal gene in patients with CSNB. We performed a multi-center, retrospective study to better characterize refractive error in CSNB.

Methods: In this multinational study 138 patients with a clinical and molecular diagnosis of CSNB age 1-20 years were included from 8 sites We conducted a retrospective longitudinal chart review including data on age, refractive error, and genotype. Refractive error was defined as spherical equivalent of refraction (SER). Inclusion criteria were at least 2 longitudinal SER measurements and a known genetic variant. Unpaired t-tests were used to evaluate the differences in SER and age of measurement between genes.

Results: The mean ± SD age in years at the youngest measurement was 6.70 ± 4.18, 5.03 ± 2.87, 3.88 ± 3.18, 3.80 ± 3.76, and 4.40 ± 2.80 for CACNA1F, NYX, TRPM1, GRM6, and GPR179 respectively. The mean ± SD age in years at the oldest measurement was 12.06 ± 4.79, 8.85 ± 8.62, 9.75 ± 4.84, 8.20 ± 5.11, and 8.80 ± 3.71 for CACNA1F, NYX, TRPM1, GRM6, and GPR179 respectively. The mean ± SD SER for the youngest measurement was -3.50D ± 5.01D, -6.51D ± 3.44D, -5.44D ± 3.14D, -5.28D ± 5.81D, -7.40D ± 2.26D for CACNA1F, NYX, TRPM1, GRM6, and GPR179 respectively. The mean ± SD SER for the oldest measurement was -4.79D ± 5.89D, -6.51D ± 3.44D, -7.54D ± 4.43D, -6.60D ± 6.54D, and -9.00D ± 3.56D for CACNA1F, NYX, TRPM1, GRM6, and GPR179 respectively. The two X-linked genes were CACNA1F and NYX. Age at the youngest measurement was not significantly different for CACNA1F vs NYX (p=0.120). Age at the oldest measurement was significantly older for CACNA1F vs NYX (p=0.032). The SER for NYX was significantly more myopic than CACNA1F (p=0.017, p=0.009) for the youngest and oldest measurements respectively.

Conclusions: Average age at the first measurement was not significantly different whereas the average age at the last visit was higher in CACNA1F than NYX. Despite that myopia increased as age increased, NYX had significantly higher myopia than CACNA1F at both the first and last measurement.

CONTROL ID: 3709345

SUBMITTER (NAME ONLY): GUANPING FENG

TITLE: In vivo measurement of light steering by single retinal cells optimizes phase-contrast AOSLO

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. FENG, Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|G. FENG, Q. Yang, K. Kunala, J. Schallek, Center for Vision science, University of Rochester, Rochester, New York, UNITED STATES|J. Schallek, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Phase-contrast adaptive optics scanning light ophthalmoscopy (AOSLO) enhances the visibility of translucent cells in the living retina. A model by Guevara-Torres suggests that the contrast is generated by the steering of light as it passes through refractive retinal cells that act as microscopic lenses. Here, we show for the first time, evidence that light is indeed bent by single retinal cells and laterally shifted at deeper retinal layers. This measurement provides information for detection optimization. Aperture patterns that favorably collect such steered light, can increase the contrast of translucent cells in the retina.

Methods: A digital micromirror device (DMD) was placed in the detection plane of a mouse AOSLO to image the light distribution in the retina. 796 nm light (241uW) was focused in the outer nuclear layer, while the detection plane was positioned conjugate to the deeper photoreceptor (PR)/RPE complex. The light distribution at the detector plane was imaged by turning on/off DMD facets to create a “flying” pinhole (~4.3 Airy disc diameter). A gradient descent algorithm optimized the aperture pattern by maximizing retinal image contrast (Brenner gradient, BG). Aperture pattern was trained on in vivo data from 3 adult C57BL/6J mice and was tested on a 4^{th} mouse.

Results: The light distribution was laterally shifted at deeper layers by as much as 6 μm consistent with a positive lens, showing that single translucent cells can lens and steer light (Fig.1). With the light distribution imaged, we could optimize the image contrast with an aperture pattern that highlights the lateral differences induced by cell steering. Starting from a random pattern, our algorithm iterated the aperture patterns to enhance the image contrast, which converged in 10 iterations (Fig. 2). Optimizing the BG in the horizontal direction, the trained aperture converged to an asymmetric pattern that resembled a split detector aperture that matched the differential light distribution seen by cell steering.

Conclusions: This strategy shows the first images of the directional steering of light by single retinal cells as light propagates to deeper retinal layers. We find that by optimizing the aperture this distribution of light can provide a further contrast improvement with the ultimate goal of providing intrinsic contrast for translucent cells in the retina.

CONTROL ID: 3709346

SUBMITTER (NAME ONLY): Diego Sbardella

TITLE: TAU-PROTEOFORMS IN AQUEOUS HUMOUR OF HEALTHY AND GLAUCOMA SUBJECTS AND ANALYSIS OF THE MOLECULAR PROPERTIES OF UB-TAU SPECIES IN VITRO

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Tau is a neuron-restricted microtubule-binding protein whose aggregation is pathognomonic of neurodegenerative diseases (tauopathies). Tau miss-sorting and accumulation has been proposed to be associated with glaucoma pathogenesis. Recently, tauopathies have been reported to display a distinguishable pattern of Tau ubiquitylation that affects protein sorting and aggregating fibril diversity. The conjugation of ubiquitin (Ub) to lysine (K) residues is a conserved post-synthetic modification each protein can be decorated within living cells, which regulates substrate sorting or clearance through the proteasome. Here we report identification of Ub-proteins and Tau proteoforms in the aqueous humor (AH) of healthy and glaucoma subjects and the characterization of the kinetics of digestion of enzymatically and semi-synthetically produced mono-Ub-Tau species by the 20S proteasome in vitro.

Methods: Western blotting and proteomics studies were applied to interrogate the repertoire of Ub-proteins and to identify Tau proteoforms in the AH of healthy (cataract) and glaucoma subjects (n=15). The Microtubule Binding Domain (MBD) of Tau has been conjugated to Ub (mono-) at different lysine residues, recapitulating proteoforms described in brain tissues post-mortem, through a semisynthetic strategy and fed to the 20S to figure out the dynamics of catalytic processing.

Results: Total Ub-proteins were frequent in the AH and display an average 2-fold increase in glaucoma vs healthy subjects ($p<0.0001$). Tau shows up as different proteoforms, including Ub-positive species matter of further investigation, in the AH of glaucoma subjects. Site-specific mono-ubiquitylated Tau-MBD species show greatly divergent kinetics of processing by the 20S.

Conclusions: Double the amounts of Ub-proteins are immune-detectable in the AH of glaucoma subjects compared to healthy controls. If confirmed on a larger sample size, the accumulation of specific Tau proteoforms, especially individual Ub-Tau species, may elucidate the mechanisms of metabolism within the retina and identify novel biomarkers for improved glaucoma management. The divergent pathogenicity of individual Ub-Tau proteoforms may also be associated with their dynamics of interaction with the 20S and differential propensity toward intrinsic resistance or optimized clearance to proteolysis

CONTROL ID: 3709350

SUBMITTER (NAME ONLY): Dominic Williams

TITLE: Novel DCN mutation in Armenian family with Congenital Stromal Corneal Dystrophy

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Williams, D. Chung, B. Glasgow, A.J. Aldave, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|A. Hovakimyan, A. Davtyan, Malayan Ophthalmologic Center, Yerevan, ARMENIA|

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ABSTRACT BODY:

Purpose: Congenital stromal corneal dystrophy (CSCD) is a rare congenital, dominantly inherited disorder characterized by diffuse stromal opacification. CSCD is associated with mutations in the decorin gene (DCN), which encodes one of the highly expressed small leucine rich proteoglycans in the extracellular matrix of the corneal stroma. As only 5 families with genetically confirmed CSCD have been reported, the identification of a novel pedigree provides the opportunity to better characterize the phenotype, ultrastructural features, clinical course and underlying genetic basis.

Methods: We report a novel Armenian family with affected individuals in 4 consecutive generations demonstrating clinical features consistent with CSCD. Consented individuals underwent slit lamp examination, optical coherence tomography and confocal microscopy. Genomic DNA was collected from saliva and all coding and adjacent intronic regions of DCN underwent PCR amplification and Sanger sequencing. In silico analysis was performed for identified mutations. Corneal tissue excised at the time of corneal transplantation underwent immunohistochemical and electron microscopic evaluation.

Results: Slit lamp examination of affected individuals showed bilateral, diffuse, panstromal corneal opacification. Two of the 6 individuals diagnosed with CSCD based on history and/or examination underwent genetic analysis; both demonstrated a novel heterozygous frameshift deletion in exon 8 of DCN (c.948delA (p.His317Thrfs*11)), predicted to cause a 33 amino acid truncation. The mutation was predicted to be damaging and disease causing by SIFT and Mutation Taster. Electron and light microscopic examination of an excised cornea demonstrated increased corneal thickness, stromal scarring, keratocyte loss and an irregularity of lamellar collagen spacing and fibril formation.

Conclusions: We report only the sixth affected pedigree with genetically confirmed CSCD, associated with a novel DCN frameshift mutation in an Armenian family. The clinical evaluation, multimodal imaging, and histopathological assessment of this family with CSCD broaden our understanding of the rare corneal disease.

CONTROL ID: 3709359

SUBMITTER (NAME ONLY): Ashutosh Jnawali

TITLE: Longitudinal changes in the retinal and choroidal thickness in young children at low and high risk for myopia

SESSION TITLE: Myopia: Structural Changes from Retina to Sclera

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Jnawali, K.L. Kerber, F.A. Vera-Diaz, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Earlier studies report an association of refractive error (RE) with retinal and choroidal thickness (RT and ChT respectively). However, it is not known whether these differences are present before the development of RE in children or develop as a consequence of the RE. We evaluated longitudinal changes in RT and ChT in young children who are at high or low risk of developing myopia as part of the Preventing myopia: Investigating Contributing factors to Nearsightedness In Children (PICNIC) study.

Methods: Children (n=23, age=7.6±0.9 years) were categorized as low risk (LR) (n=12, age=7.9±0.8 years, axial length, AXL=22.8±0.3mm, RE=1.1±0.3D) and high risk (HR) (n=11, age=7.4±1.0 years, AXL=22.5±0.8mm, RE=0.8±0.5D) for myopia, based on parental history and cycloplegic autorefraction at baseline. Wide-field SD-OCT (Spectralis, Heidelberg) radial scans centered on the fovea (55°, 12 lines) were collected at 3 points in time: baseline, 6 and 12 months. Images were processed in a custom Matlab program and corrected for lateral magnification using biometric data (Lenstar). RT and ChT were evaluated for retinal eccentricities of 1, 3, 5, 8 and 12 mm.

Results: At 12 months, AXL increased and RE decreased (less hyperopic) in the HR group ($p<0.05$ both) while only AXL increased in the LR group ($p<0.05$). At baseline, RT and ChT were not significantly different between the two groups at any eccentricity, although there was a trend for thicker choroid in the LR compared to the HR group at all eccentricities. There was also a significant increase in RT for the HR group at 1, 3 and 5 mm eccentricities, while RT increased at the central 1 mm only for the LR group ($p<0.05$ all). ChT increased significantly at all eccentricities for both groups, greatest superiorly (27.9±29.0 µm) and smallest nasally (19.9±20.7 µm) ($p<0.05$ both). Subfoveal ChT at 12 months increased significantly only in the LR group (26.2±27.8 µm, $p<0.01$).

Conclusions: At 12 months, there was greater ocular elongation and decreased hyperopia in children for HR of myopia, as predicted. Additionally, there were significant increase in RT and ChT, with different patterns of thickening for the HR and LR groups, which suggests differences in ocular growth patterns prior to myopia development. We will continue to follow up these children for 3 years, which will provide an understanding of changes associated with myopia development.

CONTROL ID: 3709360

SUBMITTER (NAME ONLY): Xufeng Zhao

TITLE: Natural-Language Diagnostic Report Generation by Multi-Modal AI for Macular Diseases

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhao, X. Gu, J. Yang, Y. Wang, Y. Chen, Ophthalmology, Peking Union Medical College Hospital, Dongcheng-qu, Beijing, CHINA|B. Li, W. Yu, Ophthalmology, Peking Union Medical College Hospital, Dongcheng-qu, Beijing, CHINA|C. Li, Ophthalmology, Dalian No.3 People's Hospital, Dalian, Liaoning, CHINA|X. Li, Key Lab of DEKE, Renmin University of China, Beijing, CHINA|J. zhao, J. Wang, Vistel AI Lab, Visionary Intelligence Ltd, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: To investigate a multi-modal approach to automatically generate natural-language diagnostic reports for macular diseases, by detecting varied lesions and diseases from color fundus photographs (CFP) and optical coherence tomography (OCT) images and accordingly synthesizing descriptions using natural-language processing (NLP) techniques.

Methods: Three pre-trained deep neural networks were used to detect variable retinal lesions from the CFP / OCT images and predict diagnosis from both modalities independently. A sanity check was performed to ensure the coherence between the detected lesions and the predicted diagnosis. Then a rule-based NLP algorithm descripted the lesions, reported diagnosis and recommended treatment (Fig. 1). A test set of 172 eyes from 127 subjects were successively acquired from July 2020 through September 2020 in our clinic, including 113 normal eyes and 59 abnormal eyes with epiretinal membrane (ERM), dry age-related macular degeneration (AMD), wet AMD and diabetic retinopathy (DR). Each eye consisted of one CFP and 12 radial OCT B-scans. Evaluation of the generated reports was conducted by comparing with the performance of two junior ophthalmologists. A questionnaire was designed and cooperatively judged by two retina specialists to quantitatively grade each report’s readability, correctness of diagnosis and recommendations (Fig. 1). All reports were anonymized to avoid potential bias. Sensitivity and specificity per class was also analyzed.

Results: AI-based NLP reports achieved higher grades in correctness of diagnosis (9.13 vs 9.03 points,) and recommendations (8.55 vs 8.50 points) compared to the junior ophthalmologists, but there was no statistically significance (P=0.43 and 0.85, respectively). For readability, both groups had a satisfactory performance (9.87 vs 9.88 points, P=0.87). Sensitivity of AI-reports and junior ophthalmologists was 0.74 (95% CI, 0.66 - 0.82) and 0.75 (95% CI, 0.67 - 0.83), respectively. Specificity of AI-reports and junior ophthalmologists was 0.94(95% CI, 0.91 - 0.98) and 0.97 (95% CI, 0.95 - 0.99), respectively (Fig. 2).

Conclusions: NLP algorithms-generated diagnostic reports for macular diseases based on multi-modal AI system can achieve similar performance as junior ophthalmologists, suggesting this emerging concept's potential in primary eye service.

CONTROL ID: 3709362

SUBMITTER (NAME ONLY): Ana Diego

TITLE: Anterior Eye Segment Imaging System for Teleophthalmology

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Diego, M. Abou Shousha, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Diego, Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|

Commercial Relationships Disclosure: Ana Diego: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Abou Shousha: Commercial Relationship(s);Code I (Personal Financial Interest):Heru, Inc.

ABSTRACT BODY:

Purpose: Teleophthalmology increases access to ophthalmic care, lowers screening barriers, and facilitates follow-ups. However, there is a need to develop better systems to evaluate diverse conditions remotely. This study aims to compare a portable anterior eye segment imaging system with the current standards method for ophthalmology examination.

Methods: The new imaging system consisted of two IMX219 Arducam autofocus sensors (Arducam, China, Nanjing) for Raspberry Pi V2 camera module connected to a Raspberry Pi Zero W (Raspberry Pi Foundation, UK, Cambridge) that clips to a HoloLens 2 (Microsoft, Redmond, WA). Twenty subjects from the Bascom Palmer Eye Institute clinic participated in the study. Anterior eye segment videos were recorded with the new system and a 720p FaceTime HD camera (Apple, Cupertino, CA). Afterward, an ophthalmologist evaluated the videos using a clinical eye examination form. This questionnaire assessed the presence of pathologies for the different eye structures and graded video quality based on identifying emergent findings. The video evaluations were compared with the standard slit-lamp clinical evaluation performed during the patient's visit.

Results: Thirty-five eyes were evaluated. The percentage sensitivity and specificity were 31.4% and 81.1%, respectively, for the HoloLens-RBPi videos and 13.7% and 39.9% for the web camera videos. Ocular structures such as the cornea, anterior chamber, iris, and lens were better evaluated with the HoloLens-RBPi videos (specificity 50%-88.5%, sensitivity 18.2%-40%). Conjunctiva and sclera had the highest sensitivity percentage for both modalities (73.3% HoloLens-RBPi and 66.7% Web Camera). The average grade for the HoloLens-RBPi videos was 3.17, and the web camera videos averaged 1.35 out of a 5 point scale.

Conclusions: Specificity percentages were higher than sensitivity percentages in both imaging modalities, indicating that video evaluations are less accurate for pathologies screening. Nevertheless, HoloLens-RBPi evaluations were statistically significantly better than the webcam evaluations. This study presented an alternative system to assess eye conditions for telemedicine, a system that provides more details than the current standard for eye evaluation performed through a webcam. Further developments will include improving camera and illumination quality, obtaining fundus images, automating camera positioning, and creating a program to access livestream images.

CONTROL ID: 3709363

SUBMITTER (NAME ONLY): Yuka Kihara

TITLE: Detecting Double Layer Sign (DLS) with OCT using Multi-Region Segmentation Visual Transformers (ViT)

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kihara, A.Y. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|Y. Shi, M. Shen, L. Wang, R. Laiginhas, X. Jiang, J. Liu, R. Morin, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami Health System, Miami, Florida, UNITED STATES|H. Fujiyoshi, Chubu University, Kasugai, JAPAN|

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ABSTRACT BODY:

Purpose: For the task of segmenting the double layer sign (DLS), an important feature of type 1 macular neovascularization (MNV) in age-related macular degeneration, we applied a Vision Transformer (ViT)-based model, which is now state of the art in many computer vision tasks. The ViT is convolution-free transformer architecture that can capture global interactions between elements of a scene and make better use of long-range dependencies.

Methods: Eyes were imaged using swept-source OCT angiography (SS-OCT, PLEX Elite 9000, Carl Zeiss Meditec, Dublin, CA) 6x6mm scans. The scans consisted of 500 A-scans per B-scan; each B-scan repeated twice at each of 500 B-scan positions along the y-axis. The SS-OCTA structural B-scans were manually annotated for the presence of a DLS and drusen (Dr) and used for training. We built a multi-region segmentation ViT that labelled both DLSs and Dr on a single B-scan image. In order to extend ViT from image classification to semantic segmentation, we depended on the output embeddings corresponding to image patches and obtained class labels from these embeddings with a pointwise linear decoder. For comparison, a convolutional (CNN) model was trained on the same dataset.

Results: A total of 251 eyes (211 patients) were included; 188 eyes with DLS and 63 eyes with drusen only (Dr) as controls. Our ViT model had 12 layers, 768 token sizes, and 12 heads. Mean Intersections over Union (IoU) between predicted and annotated masks for DLSs and Dr were 59.7%, 62.4% for the ViT model, and 44.9%, 52.8% for the CNN model, respectively. The transformer-based model significantly outperformed the CNN-based model.

Conclusions: We present a network that can detect DLS from structural B-scans alone using a purely transformer-based model and have applied it to a dataset with coarse annotations. To our knowledge, this is the first application of ViT segmentations in ophthalmic imaging.

CONTROL ID: 3709364

SUBMITTER (NAME ONLY): Federica Staurenghi

TITLE: Development of a minicircle gene therapy system for expanding treatment options of inherited retinal disease

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Staurenghi, M.E. McClements, A. Salman, R.E. MacLaren, Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|M.E. McClements, R.E. MacLaren, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: DNA minicircles (MC) are transgene DNA vectors produced as circular expression cassettes devoid of any bacterial plasmid DNA backbone. One or more transgenes can be expressed without the theoretical risk of immunogenic responses against the bacterial backbone sequence in the common plasmids. Their smaller size facilitates expansion of their cloning capacity and improves their delivery into cells; indeed, this technology offers a potential solution for the reduction in transfection efficiency translational barrier in gene therapy. The overriding aim was to study a novel gene therapy application, Minicircle (MC) DNA, that has not yet been fully explored as a possible promising treatment for genetic diseases in the eye.

Methods: Minicircles and plasmids carrying a CAG.GFP.WPRE.pA transgene were prepared with different transfection reagents used (FuGene and ViaFect) to identify optimal transfection conditions. HEK293 cells (Human Embryo Kidney cell line) and ex vivo retinal explants from wild-type (WT) mice were transfected with the MC and plasmid constructs and GFP expression was monitored by live cell imaging. Subretinal injections in WT mice assessed transfection reagent toxicity and transfection success of MC-treated eyes. Eyes were imaged using Scanning Laser Ophthalmoscope (SLO) and Optical Coherence Tomography (OCT) then harvested at 8 weeks post-injection.

Results: HEK293 cells maintained GFP expression from both MC and plasmid transfections for over a week post-treatment. Ex vivo retinal explants achieved GFP expression up to one week post-transfection, which was limited to MC treated samples. In vivo SLO assessments did not present any signs of toxicity in the retina up to 8 weeks post-injection. Similarly, OCT scans identified no significant differences in photoreceptor layer thickness of either inferior and superior retina between injection groups.

Conclusions: MC transfections achieved better outcomes in ex vivo studies than equivalent plasmid transfections. In vivo, neither the transfection reagents or the MC DNA induced retinal toxicity at the doses used. However, consistent evidence of reporter expression has yet to be achieved in vivo, indicating further investigations into the delivery method of MC DNA to the retina are required.

CONTROL ID: 3709366

SUBMITTER (NAME ONLY): Shiva Sabazade

TITLE: The Obesity Paradox in Uveal Melanoma: Body Mass Index >30 is associated with lower metastatic risk

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sabazade, A.H. Opalko, V. Gill, C. Herrspiegel, G. Stålhammar, Clinical Neuroscience Eye/Vision, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: To examine the association between metabolic factors and the risk of metastasis in uveal melanoma.

Methods: Data on patient body mass index, cardiovascular diseases, diabetes, use of anticoagulants, antihypertensives, diuretics, statins and hypothyroidism replacement therapy at the time of diagnosis were collected from all patients diagnosed with uveal melanoma at St. Erik Eye Hospital, Stockholm, Sweden from January 2009 through December 2017. The hazard ratio (HR) for metastasis was then calculated with Cox regressions. Obesity was defined as a BMI of 30.0 or above.

Results: Data on the presence of cardiovascular diseases, use of anticoagulants, antihypertensives and hypothyroidism replacement therapy was available for 683 patients. For 581 of these, body mass index (BMI) was available and for another 200, we also had data on the presence of diabetes type 1 and 2 and the use of statins, diuretics, metformin and insulin. A total of 465 patients (80%) were non-obese and a total of 116 patients (20%) were obese. In univariate Cox regression, tumor diameter (HR 1.2 per increasing mm, $p<0.0001$) and diabetes type 1 or 2 (HR 1.9, $p=0.05$) were associated with metastasis. Obesity was negatively correlated (HR 0.6, $p=0.04$). In multivariate Cox regression, tumor diameter (HR 1.2, $p<0.0001$) and obesity (HR 0.4, $p=0.006$) retained their significance

Conclusions: Obesity is associated with lower metastatic risk in uveal melanoma, independent of tumor size and diabetes.

CONTROL ID: 3709367

SUBMITTER (NAME ONLY): Rui Ma

TITLE: Transfer learning for optical coherence tomography angiography image segmentation

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ma, Y. Tao, M. Shyu, Electrical and Computer Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|L. Hao, X. Mendoza, M. Khodeiry, Y. Liu, R.K. Lee, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: While there have been multiple automatic segmentation techniques for different types of fundus images, few target specifically optical coherence tomography angiography (OCTA) images due to the difficulty of manual annotation during the data collection process, despite its importance in the diagnosis and treatment of various ophthalmic diseases. We developed and tested a deep learning approach to automatically segment the vascular structures in OCTA scans without the need for a large amount of manually traced images for training.

Methods: We pre-trained a deep learning-based image segmentation model, ResUNet, to automatically segment the axons and dendrites in retinal ganglion cell (RGC) images. A total of 110 RGC scans with manual annotations from human experts were used to develop this model, where 90 scans were used for training and the remaining 20 images were reserved as testing data. Next, transfer learning was applied by fine tuning the model on 4 manually annotated OCTA images, while 4 additional OCTA images were used for evaluation. Pre-processing and post-processing steps were applied to adjust the brightness and contrast of input images and segmentation outputs from the model.

Results: Our model can effectively and automatically segment the structures in both RGC and OCTA images. Quantitatively, our segmentation model achieves average foreground, background and overall accuracy of 0.689, 0.998 and 0.997 for the RGC images, and 0.662, 0.968 and 0.955 on the OCTA images, respectively.

Conclusions: Our model can successfully adapt the prior knowledge learned from axon and dendrite segmentation of RGC images to the segmentation of vascular structures in OCTA images.

CONTROL ID: 3709370

SUBMITTER (NAME ONLY): Josef Huemer

TITLE: Automated deep learning for detection and evaluation of posterior capsule opacification

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huemer, D. Sim, P.A. Keane, S. Wagner, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|M. Kronschlaeger, M. Ruiss, O. Findl, Hanusch-Krankenhaus, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To train and validate an automated deep learning system (DLS) on classifying high-resolution digital retroillumination images of posterior capsule opacification (PCO) and to discriminate between clinically significant and non-significant PCO.

Methods: For this retrospective register study, three expert observers graded two independent datasets totalling 279 images with no to severe PCO providing binary labels for clinical significance. The automated DLS was trained and internally validated with 179 images and externally validated with 100 images using Google Cloud AutoML Vision Application.

Results: Intraobserver variability κ (95% CI) for the three gradings for observer 1, 2 and 3 were 0.90 (0.86, 0.95), 0.94 (0.90, 0.97), and 0.88 (0.82, 0.93) respectively. Interobserver κ for the final grading for all three observers was 0.84 (0.78, 0.89) and for all nine gradings was 0.82 (0.76-0.86). Interobserver agreement was generally high, ranging from 0.85 (0.79-0.90) between observers 1 and 2 to 0.90 (0.85-0.94) for observers 1 and 3. On the internal validation dataset, sensitivity of the DLS was 0.89 at a specificity of 1 and the AUC was 0.98 (0.92-1). The external validation dataset consisted of 100 images, of which 63 were visually significant PCO. On external validation, sensitivity was 0.84 and specificity was 0.92. The AUC was 0.97 (0.93-0.99).

Conclusions: This automated DLS can provide highly accurate discrimination between clinically significant and non-significant PCO equivalent to human expert graders. The clinical value of this DLS as a potential decision support tool in different models of care warrants further clinical research.

CONTROL ID: 3709371

SUBMITTER (NAME ONLY): Ezigbobiara Umejiego

TITLE: Retina Gliosis and Hypercitrullination in a Novel Nitrogen Mustard Corneal Injury Model

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Umejiego, P. Bargagna-Mohan, R. Mohan, Neuroscience, UConn Health, Farmington, Connecticut, UNITED STATES|E. Umejiego, R. Mohan, University of Connecticut School of Medicine, Farmington, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Ezigbobiara Umejiego: Commercial Relationship: Code N (No Commercial Relationship) | Paola Bargagna-Mohan: Commercial Relationship(s);Code P (Patent):US Patent 8735178; US Patent 106690683 | Royce Mohan: Commercial Relationship(s);Code P (Patent):US Patent 8735178; US Patent 106690683

ABSTRACT BODY:

Purpose: Nitrogen mustard (NM) is a cytotoxic and alkylating agent with no antidote. As a potent vesicant, it causes debilitating eye injury in the anterior segment. However, its effect on the retina is unknown despite evidence of retinal deficits in humans exposed to the agent. Here, we studied NM's pathological effects in murine cornea and retina. We hypothesized that NM will cause degeneration of corneal Schwann cells (cSCs) and axons, and induce reactive gliosis and citrullination in injured mice retinas.

Methods: Adult C57LB/6 wild-type (WT) mice and PLP-eGFP transgenic (TG) mice were used (Bargagna-Mohan et al., J. Neurosci. Res., 2020). After sedation, 5 µL of 0.2% or 1.0% NM was applied for 5 min in the right eye to induce injury, and flushed with 5 mL of sterile saline. The left eye was used as control. Mice were euthanized at 5 and 14 days post-injury. TG mice eyes were dissected for immunohistochemical (IHC) analyses of whole mount corneas (WMCs) and cryosectioned posterior eye cups (PECs). Whole eyes of WT mice were cryosectioned for IHC analyses. WMCs were stained for axonal β3-tubulin and imaged for eGFP of cSCs, while PEC tissues were co-stained for GFAP and citrullination (F95 antibody). Epifluorescence microscopy was used for imaging.

Results: We found that 0.2% and 1.0% NM caused corneal injury and regression of stromal cSCs and axons, with no notable changes in the uninjured cornea. These findings were evident in the central and peripheral zones of the cornea, and were observed at both 5 and 14 days post-injury. In the injured retina, a global increase in reactive Muller glia with ample staining for GFAP was observed. Notably, the F95 antibody revealed increased citrullination in Muller glia at both 5 and 14 days post-injury time points at the 1.0% NM dose. Although the 0.2% NM dose caused corneal injury, retinal gliosis and increased citrullination were not observed. The cornea and retina responses to NM is consistent with our lab's findings from previous models of corneal injury.

Conclusions: Our initial results suggest that NM causes loss of corneal nerves leading to reduction in overall density, and increases Muller cell gliosis and citrullination of GFAP filaments in murine retinas. Our novel in vivo NM corneal injury model potentially supports real-life exposure and provides the first evidence that NM-induced retinal gliosis and hypercitrullination may be involved in retinal degeneration.

CONTROL ID: 3709377

SUBMITTER (NAME ONLY): Dimitrios Pollalis

TITLE: Exosome Delivery to Retina and Active targeting of CNV by RGD-conjugated exosomes

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Pollalis, G. Gopinadhan Nair, S. Lee, Ophthalmology, Dean McGee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|A.V. Nanda, The University of Oklahoma College of Medicine, Oklahoma City, Oklahoma, UNITED STATES|C. Kang, D. Kim, The University of Oklahoma College of Pharmacy, Oklahoma City, Oklahoma, UNITED STATES|S. Lee, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study assesses the transretinal penetration of intravitreally injected retinal tissue-derived naïve exosomes and the enhanced targeting of choroidal neovascularization (CNV) after decorating them with Arg-Gly-Asp (RGD), a well-known ligand for integrins which are essential in VEGF signaling in CNV.

Methods: Exosomes were recovered from either mouse Müller glial cell or whole mouse retina using differential ultracentrifugation. Their size, number, and morphology were characterized using nanoparticle tracking analysis (NTA) and transmission electron microscopy (TEM). Exosome markers were confirmed using an exosome detection antibody array. Intravitreal injection of fluorescent-labeled naïve or RGD-conjugated exosomes (5.3×10^7 exosomes/μl) were given to wild type (n =9) or laser-induced CNV mouse model (n= 9). Retinal uptake of exosomes was assessed by in vivo retinal imaging microscopy and fluorescent staining with DAPI, GSA, and anti-integrin α_v antibody of retinal sections or choroid/RPE flat mounts. Active targeting of CNV was assessed by comparing retinal uptake between areas with and without CNV and by colocalization analysis of RGD-conjugated exosomes with integrin α_v within CNV.

Results: We recovered an average of 2.1×10^9 particles/ml with a peak size of 140 nm from 10 whole mouse retinas, and 4.2×10^8 particles/ml with a peak size of 147 nm from the supernatant of primary cultured mouse Müller glia. Rapid retinal penetration of intravitreally injected exosomes was confirmed by retinal imaging microscopy at 3 and 24 hours post-injection. Intravitreally injected naïve and RGD-conjugated exosomes penetrated into inner and outer retinal layers including IPL, INL, OPL, and ONL at 1 and 7 days after injection. Intravitreally injected RGD-conjugated exosomes were exclusively delivered to the area of CNV including ONL, RPE, and choroid in laser-induced CNV mouse model with 89.5% of colocalization with integrin α_v. Exosomal origination between mouse Müller glia cell and whole mouse retina did not show differences in retinal penetration.

Conclusions: Intravitreally injected exosomes demonstrated good penetration in both inner and outer retina. Further, intravitreally injected RGD-conjugated exosomes were selectively delivered to the area of CNV. This suggests that RGD-conjugated exosomes have a great potential to serve as an intraocular drug delivery vehicle, allowing an active targeting strategy.

CONTROL ID: 3709378

SUBMITTER (NAME ONLY): Pawan Kumar Singh

TITLE: Role of Zika virus (ZIKV) in Glaucoma Pathobiology

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Singh, Ophthalmology/ Mason Eye Institute, University of Missouri School of Medicine, Columbia, Missouri, UNITED STATES|R. Kasetti, G. Zode, Department of Pharmacology and Neurosciences, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|A. Kumar, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Pawan Kumar Singh: Commercial Relationship: Code N (No Commercial Relationship) | Ramesh B Kasetti: Commercial Relationship: Code N (No Commercial Relationship) | Gulab Zode: Commercial Relationship: Code N (No Commercial Relationship) | Ashok Kumar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is classically viewed as a genetic and age-related disease and has rarely been associated with congenital infections. However, during the recent epidemics in Brazil, Zika virus (ZIKV) infection during pregnancy has been linked to cause glaucoma in infants. The aim of this study is to investigate the pathobiology of ZIKV induced glaucoma.

Methods: C57BL/6 wild type (WT) and IFNAR1$^{-/-}$ adult mice and pregnant dams were challenged with ZIKV strain PRVABC59 by anterior chamber (AC) and subcutaneous (s.c.) injections respectively. Intraocular pressure (IOP) was recorded at various time-points post-ZIKV infection. Trabecular meshwork (TM), retinal ganglion cells (RGCs) infectivity and cell death were assessed using immunofluorescence and TUNEL staining respectively. Axonal transport was measured by intravitreal injection of cholera toxin subunit B (CTB) and optic nerve imaging. For in vitro studies, human primary TM cells (HTMC) and GTM3 cell line were challenged with ZIKV at multiplicity of infection (MOI) 1 followed by measurements of innate antiviral responses using qPCR

Results: ZIKV infection caused increased IOP and the development of chorioretinal atrophy in both WT and IFNAR1$^{-/-}$ mouse eyes. AC inoculation of ZIKV caused infectivity in iridocorneal angle and TM, leading to the death of TM cells in the mouse eyes. ZIKV challenge resulted into RGC death and loss in the infected mice and neonate pups born from infected dams. ZIKV infection in IFANR1$^{-/-}$ mice caused optic nerve infectivity and disruption of anterograde axonal transport. ZIKV infection in mice induced autophagy in the anterior segment tissue, and autophagy inhibition using an FDA approved drug- Hydroxychloroquine (HCQ) attenuates ZIKV induced ocular pathology. HTMC and GTM3 cells were found to be permissive to ZIKV and evoked an innate antiviral response.

Conclusions: Our study for the first time showed experimental evidence of ZIKV induced glaucoma. Because of the similarity in glaucomatous pathologies in our study and other experimental glaucoma models, ZIKV infection can be used to study infectious triggers of glaucoma, currently, an understudied area of investigation.

CONTROL ID: 3709379

SUBMITTER (NAME ONLY): Erin NaPier

TITLE: Success of non-absorbable versus absorbable suture material for posterior fixation (Faden procedure) of the medial rectus

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. NaPier, Y. Schein, A. Spiller, G. Binenbaum, The Children's Hospital of Philadelphia Division of Ophthalmology, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Esotropia with a high accommodation to convergence ratio (AC/A) is commonly treated with medial rectus recession and/or posterior fixation sutures (Faden procedure). Posterior fixation sutures traditionally involve suturing the rectus muscle to the sclera at a point posterior to the insertion. This shortens the muscle's arc of contact and limits the muscle's movement through its soft-tissue pulley. The literature on posterior fixation sutures describes the use of non-absorbable sutures for fixation. We sought to compare the success rates and complication rates of non-absorbable versus absorbable suture materials for posterior fixation.

Methods: Retrospective cohort study of children who underwent a posterior scleral fixation procedure of medial rectus muscle for high AC/A strabismus. Exclusions included <3 months follow up and fixation performed by suturing to the surrounding pulley fascia. Children were divided into groups based on the use of non-absorbable and absorbable suture material, both with spatulated needles. The primary outcome was surgical success, defined as a reduction in high AC/A esotropia without the use of bifocal glasses.

Results: We studied 16 children who had a posterior fixation procedure (median age 5.1 years, range 2 to 8.5; median follow up 1.7 years, range 0.3 to 6.7). Seven (44%) children had fixation using a non-absorbable 5-0 Merseline suture and 9 (56%) children had fixation using an absorbable 6-0 Vicryl suture. Three of 7 (43%) treated using non-absorbable suture had surgical success, compared to 6 of 9 (67%) children treated with using absorbable suture (p=0.61, Fisher exact). There was 1 (17%) complication among the 7 children in the non-absorbable group and 0 among the 9 children in the absorbable group.

Conclusions: Absorbable sutures are as clinically effective as non-absorbable sutures when used for scleral posterior fixation of rectus muscles. Absorbable sutures obviate the need for placement of a long-lasting foreign material on the eye and provide surgeons with additional choice of suture material and accompanying spatulated needles.

CONTROL ID: 3709383

SUBMITTER (NAME ONLY): Milena Cioana

TITLE: Breast, Cervical and Colorectal Cancer Screening among Canadians with and without Self-Reported Visual Impairment

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Cancer screening can lead to early detection and reduced mortality. Due to barriers in reading, driving, and ambulating, individuals with visual impairment (VI) may participate in cancer screening less often than those without VI. This cross-sectional study compared participation rates in government-funded screening for breast, cervical and colorectal cancer in Canadians with and without VI, and examined associated sociodemographic factors.

Methods: Self-reported data on vision status and participation in mammography, pap smear, and fecal occult blood test was analyzed from the Canadian Community Health Survey 2013/2014 and 2017/2018. Participation in screening at the recommended age and time interval was compared between individuals with and without VI. Screening rates were also compared by level of household income and education, and having a family physician.

Results: Canadians with VI had lower participation rates in breast (53.0% [95% confidence interval [CI] 36.3-69.7%] vs. 67.0% [95% CI 64.5-69.4%]) and cervical (53.8% [95% CI 29.3-78.3%] vs. 76.2% [95% CI 74.0-78.3%]) cancer screening versus those without VI in 2013/2014. Colorectal cancer screening rates were similar for participants with and without VI (25.7% [95% CI 17.3-34.1%] vs. 24.7% [95% CI 23.7-25.6%]). Differences between the VI and non-VI groups across the three cancer screening categories persisted despite having a family physician. Lower levels of household income and education were associated with lower screening rates in the VI group for all cancer screenings examined. The 2017/2018 data similarly revealed a lower breast cancer (61.9% [95% CI 55.7-68.2%] vs. 69.4% [95% CI 66.3-72.5%]) and a comparable colorectal cancer screening rate (40.7% [95% CI 37.0-44.5%] vs. 38.0% [95% CI 36.4-39.5%]) in Canadians with versus without VI. Information on cervical cancer screening was unavailable in 2017/2018.

Conclusions: Canadians with self-reported VI appear to have lower participation rates in breast and cervical cancer screening than those without VI. Having a family physician did not impact the noticed lower participation rate. Smaller sample sizes in individuals with VI are likely responsible for the wide CI and non-significant differences observed. Policy-makers, organizations and clinicians should understand the unique barriers faced by individuals with VI, and facilitate adherence to screening guidelines.

CONTROL ID: 3709385

SUBMITTER (NAME ONLY): Monika Fleckenstein

TITLE: Individualized mesopic and dark-adapted fundus-controlled perimetry: Longitudinal changes in retinal sensitivity at the border of geographic atrophy.

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Fleckenstein, S. Schmitz-Valckenberg, Department of Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|L.A. von der Emde, F.G. Holz, S. Schmitz-Valckenberg, M. Pfau, Department of Ophthalmology, University of Bonn, Bonn, GERMANY|M. Pfau, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Monika Fleckenstein: Commercial Relationship(s);Code F (Financial Support):Spouse: Bayer, Carl Zeiss MediTec, Heidelberg Engineering, Novartis, Roche;Code C (Consultant/Contractor):Spouse: AlphaRET, Apellis, Bioeq, Katairo, Kubota Vision, Novartis, Oxurion, Pixium, Roche, SparingVision;Code R (Recipient):Spouse: Apellis, Heidelberg Engineering;Code O (Owner):Spouse: STZ GRADE Reading Center | Leon von der Emde: Commercial Relationship: Code N (No Commercial Relationship) | Frank Holz: Commercial Relationship(s);Code F (Financial Support):Acucela, Allergan, Apellis, Bayer, Bioeq/Formycon, CenterVue, Ellex, Roche/Genentech, Geuder, Heidelberg Engineering, IvericBio, Kanghong, Novartis, NightStarX, Optos, Pixium Vision, Zeiss;Code C (Consultant/Contractor):Acucela, Apellis, Bayer, Boehringer-Ingelheim, Bioeq/Formycon, Roche/Genentech, Geuder, Graybug, Gyroscope, Heidelberg Engineering, IvericBio, Kanghong, LinBioscience, Novartis, Oxurion, Pixium Vision, Stealth BioTherapeutics, Zeiss;Code O (Owner):STZ GRADE Reading Center | Steffen Schmitz-Valckenberg: Commercial Relationship(s);Code F (Financial Support):Bayer, Carl Zeiss MediTec, Heidelberg Engineering, Novartis, Roche;Code C (Consultant/Contractor):AlphaRET, Apellis, Bioeq, Katairo, Kubota Vision, Novartis, Oxurion, Pixium, Roche, SparingVision;Code R (Recipient):Apellis, Heidelberg Engineering;Code O (Owner):STZ GRADE Reading Center | Maximilian Pfau: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Pharmaceuticals

ABSTRACT BODY:

Purpose: To analyze mesopic and dark-adapted (DA) retinal sensitivity changes based on fundus-controlled perimetry (FCP) test patterns designed to the shape of geographic atrophy (GA).

Methods: A total of 40 patients (75.8 ± 8.5 years old; 21 females) were prospectively examined by mesopic, DA cyan, and DA red FCP with the S-MAIA device (CenterVue, Padua, Italy). Test points were placed along iso-hulls (i.e., contour lines) at even distances surrounding the GA boundary at −0.645°, 0.43°, 0.86°, 1.29°, 2.15°, and 3.01° with customized software. Retinal sensitivity was assessed in 40 eyes, with longitudinal data for 29 eyes with a median [IQR] of one follow-up visit [0;2] spanning 2.1 [1.9;2.3] years. Linear mixed model analysis was applied to estimate the change in sensitivity over time with “test point nested in eye” as a random effects term.

Results: At baseline, mesopic, DA cyan, and red testing showed a curvilinear relationship between sensitivity and distance to GA with more severely reduced light sensitivity in the proximity to GA (Figure 1). In the longitudinal analysis (Table 1), for mesopic testing, the estimated marginal mean [95% CI] for sensitivity change was -2.29 [-3.27;-1.31] dB/y at 0.43° and gradually less for more distant test points. For DA cyan testing, the most severe decline in sensitivity was observed for more peripheral loci at 2.15° with -1.38 [-2.09;-0.67] and at 3.01° with -1.38 [-2.09;-0.68] dB/y, due to a floor effect for DA cyan testing at 0.43°. The pattern of decline in DA red sensitivity paralleled the changes in mesopic sensitivity.

Conclusions: Individualized, lesion-tailored mesopic and DA cyan and red FCP testing in eyes with dry AMD detect advancing functional loss prior to GA development. Differential patterns of decline in sensitivity over time - depending on the distance from the GA border and on the mode of FCP testing - reveal a dynamic functional “fingerprint”: Early, pronounced rod-related sensitivity loss in a certain distance to the actual atrophic lesion along with late, pronounced mesopic sensitivity decline colocalizing with the atrophic lesion border. This data demonstrates in vivo the dynamic functional consequences of localized pathobiological processes in advancing GA progression.

CONTROL ID: 3709386

SUBMITTER (NAME ONLY): Jae-Hyun Jung

TITLE: Pedestrians Collision Detection Test for Peripheral Field Loss

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Jung, A.D. Hwang, A.R. Bowers, E. Peli, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Jung, A.D. Hwang, A.R. Bowers, E. Peli, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Safe mobility is difficult with peripheral field loss. Perimetry maps the field loss but cannot determine the effectiveness of residual field or visual aids in daily life, where multiple hazards may be on colliding and non-colliding paths. Simplistic collision detection tests included a single approaching pedestrian over a simple background. Realistic collision detection tests need to simulate complex real-world scenarios.

Methods: We reviewed videos of real-world walking in busy shopping malls to identify walking paths of pedestrians. These behaviors were modeled mathematically and implemented in a video-based pedestrian collision detection test using Unity 3D engine for patients with homonymous hemianopia (HH).

Results: A patient and a pedestrian walking straight on a collision course at constant speeds are defined by the initial bearing angles (α and β) from their walking paths (Fig. 1). If β is in the HH patient's blind side, the colliding pedestrian is not visible. We implemented colliding pedestrians: 1) approaching face-to-face colliding pedestrian (α<90°), where patient and pedestrian share social responsibility for avoiding a collision, and 2) overtaken colliding pedestrian (α>90°), in which the patient is solely responsible for avoiding the collision because the patient is outside the normal visual field of the overtaken colliding pedestrian (walking slower than the patient).

The first-person view of shopping mall walking with modeled pedestrians is displayed on a large screen matching the real-world perspective. In each trial, a lead child who guides the patient along the walking path and multiple non-colliding pedestrians (passing either in front of or behind the patient) are deployed with or without a colliding pedestrian (Fig. 2).

Conclusions: We characterized colliding/non-colliding pedestrian paths and developed the test, which may provide objective outcome measures for any type of field loss patients with and without field expansion aids.

CONTROL ID: 3709390

SUBMITTER (NAME ONLY): DRIRH KHARE

TITLE: The effects of diabetes on limbal epithelial cell-derived exosome cargos revealed by genomics and proteomics analyses

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. KHARE, A.J. Poe, Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|D. KHARE, A.J. Poe, S. Ghiam, A.V. Ljubimov, M. Saghizadeh, Regenerative Medicine Institute Eye Program, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|X.Y. Song, C. Santiskulvong, A. Rajewski, Genomics Core, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|S. Ghiam, A.V. Ljubimov, M. Saghizadeh, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the contents of diabetic (DM) and normal (N) primary limbal epithelial cell (LEC)-derived exosomes (Exos) using both genomic and proteomic analyses, and to identify their cargo differences.

Methods: Exos were isolated from age-matched human normal and DM LEC-conditioned media by ultracentrifugation. Total Exos RNA was isolated and subjected to Next Generation Sequencing (NGS) analysis. MiRNA libraries were prepared, sequenced, and aligned to GeneGlobe Data Analysis Center (Qiagen, Germantown, MD) followed by miRBase (release v21) mature and hairpin databases sequentially using Bowtie v1.2 (Langmead et al., 2009). For proteomics analysis, LEC-derived Exo lysates were reduced, alkylated, digested, and then labeled using 10-plex TMT isobaric tags and analyzed by tandem mass spectrometry. Pathway analysis was used to profile the molecular activities of the differentially expressed genes (DEG)/proteins cargos.

Results: The supervised analysis of NGS data identified a total of 2759 small RNAs including miRNA, piRNA, and snoRNA in all samples with the average threshold of more than one unique molecule identifier (UMI). Among these entities, 2422 were known miRNAs. A set of 87 (23 upregulated and 64 downregulated) miRNAs was identified as differentially expressed in DM-Exos vs. N-Exos (FC > 1.5 adjusted $p < 0.1$). Ingenuity pathway analysis of differentially expressed miRNA showed significant differences in insulin receptor signaling, cell cycle, regulation of EMT, chemokine, VEGF, planar cell polarity, and CXCR4 signaling pathways. Proteomics analysis showed a total of 2648 proteins associated with Exos in all samples. A set of 280 (26 upregulated and 254 downregulated) proteins was identified as differentially expressed in DM-Exos vs. N-Exos (FC > 2, $p < 0.05$). Pathway analysis of differentially expressed proteins showed significant differences in VEGF signaling, apoptosis, translation, metabolism, and cellular responses to stress pathways.

Conclusions: We identified normal and DM LEC-derived Exos' small RNAs and protein cargos and differentially expressed miRNAs and proteins in DM-Exos, which may have roles in disease state. Further studies are required to determine their functions in normal and diabetic cornea, which may help in developing more effective therapeutic approaches for corneal diseases such as diabetic keratopathy.

CONTROL ID: 3709392

SUBMITTER (NAME ONLY): Elvira Agron

TITLE: Effect of reticular pseudodrusen on progression to late age-related macular degeneration alongside traditional severity scales

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Agron, T.D. Keenan, E.Y. Chew, National Eye Institute, Bethesda, Maryland, UNITED STATES|T.E. Clemons, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Elvira Agron: Commercial Relationship: Code N (No Commercial Relationship) | Tiarnan Keenan: Commercial Relationship: Code N (No Commercial Relationship) | Traci Clemons: Commercial Relationship: Code N (No Commercial Relationship) | Emily Chew: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate reticular pseudodrusen (RPD) as a risk factor for progression to late age-related macular degeneration (AMD)

Methods: Color fundus photographs (CFP) of participants enrolled in the Age-Related Eye Diseases Study (AREDS) from annual study visits were graded for large drusen, pigmentary abnormalities, and late AMD. RPD presence was determined by deep learning grading of CFP. Proportional hazards regressions were performed that included traditional AMD severity scales (simplified severity scale (person) and 9-step scale (eye)) based upon the presence of drusen and pigmentary changes and RPD presence together. Outcomes were late AMD, geographic atrophy (GA) and neovascular AMD (NV).

Results: For the 9-step scale analyses 6959 eyes (3780 participants) with no late AMD at baseline were analyzed. For late AMD by eye, in a model including this scale and RPD together, the hazard ratio (HR) for RPD was 2.5 (95% confidence limit (CL): 2.1-3.1). In stratified models by the scale the RPD HRs were 5.1 and 1.8 for levels 1-6 and 7-8, respectively. For GA, the RPD HRs were 2.6 (2.2-3.4) (not stratified), 5.9 and 1.9 for levels 1-6 and 7-8, respectively. For NV, the HRs were 1.7 (1.3-2.2) (not stratified), 3.7 and 1.1 for levels 1-6 and 7-8. For the simplified scale analyses 3182 participants with no late AMD at baseline in either eye were analyzed. For late AMD, in a model including this scale and RPD together, the HR for RPD was 2.2 (1.8-2.6). In stratified models by the scale the RPD HRs were 3.2, 3.8, 2.3, and 1.6 for levels 0-1, 2, 3 and 4, respectively. For GA, the RPD HRs were 2.6 (2.1-3.2) (not stratified), 3.5, 4.9, 3.1 and 1.9 for levels 0-1, 2, 3 and 4, respectively. For NV, the HRs were 1.3 (0.9-1.8) (not stratified), 2.9, 3.03, 1.1 and 0.9 for levels 0-1, 2, 3 and 4. The Table includes the 95% CL of the models performed.

Conclusions: RPD represents an important third risk factor for progression to late AMD. This is true for both subtypes of late AMD, particularly for GA. However, the excess risk associated with RPD varies markedly by severity level. It carries highly increased risk at lower/moderate levels and less increased risk at higher levels. RPD status should be included in updated AMD classification systems, risk calculators, and clinical trials.

CONTROL ID: 3709394

SUBMITTER (NAME ONLY): Mojtaba Moharrer

TITLE: Using a low cost refraction kit to prescribe vision correction for myopic patients

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Uncorrected refractive error is treatable but it causes vision impairment in millions of people worldwide, due to lack of vision care resources. This study evaluate a low-cost Refractive Kit (RK) for measuring refractive error in people with myopia by lay persons, and effect of vision correction based on RK.

Methods: The RK is a booklet with 16 pages of Tumbling E letter chart and a tape measure which measures the far point of the myopic eye from -1.0 to -8 with 0.5 gap between each page. The distance is converted to spherical equivalent refractive error. 30 participants between the age of 18 to 40 years old were tested with RK and also standard non-cycloplegic subjective refraction. In addition, 71 participants in Mali were tested in a vision screening for Visual Acuity (VA) with and without spherical lens determined by a lay person using the RK.

Results: In the accuracy test, the refractive error according to standard test ranged from -7.25D to 0.5D with a mean of -3.0D. There were 11 eyes, with astigmatism of -1.75 CYL and worse, which were not able to read any of the RK chart. Excluding these eyes, the Pearson correlation coefficient between standard and RK measurement was 0.97. The mean of absolute error was 0.39, and the standard deviation of the absolute error is 0.37. Participants had a mean uncorrected Visual Acuity (VA) of 0.8, lowest VA of 1.30. Wearing spherical correction lens according to RK, corrected VA was improved to -0.04 significantly ($p < 0.001$). Among the 71 participants received vision screening in Mali, 23 were diagnosed with myopia, with uncorrected visual acuity of as low as 0.70 with average of 0.16. The measured refractive error using RK ranged from -1 to -5.5 diopters. The mean VA of these participants was improved to 0.03 ($p < 0.001$) with worse VA of 0.15 with spherical lens according to RK.

Conclusions: RK measurements were highly correlated with the measurement standard clinical refraction method for myopic eyes without strong astigmatism. While there is an error in RK measurement, spherical prescription based on low-cost RK can correct most eyes with impaired vision due to refractive error to normal range. RK has a potential to address the issue of uncorrected refractive error in areas lacking access to eyecare professionals.

CONTROL ID: 3709395

SUBMITTER (NAME ONLY): Poonam Mudgil

TITLE: Biophysical characteristics of human milk proteins for enhancing tear stability in dry eye

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Mudgil, Western Sydney University School of Medicine, Penrith South DC, New South Wales, AUSTRALIA|M. Pedler, E. McCourt, J. Petrash, Department of Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease affects millions of people worldwide and is prevalent in older people, females, contact lens wearers, and increasingly in the general population due to excessive use of visual display devices. Tear instability is the characteristic pathophysiology of the disease due to the inability of tears to form a stable film on the ocular surface, which leads to drying of the ocular surface. Enhancing tear stability is known to relieve symptoms of dry eye. Human breast milk (HBM) has been shown to contain proteins that enhance ocular surface healing following injury. In healthy tears, tear proteins increase tear stability by showing surface-active properties. The aim of this project was to study the biophysical characteristics of HBM proteins and compare them with the proteins found in tears as a first step to explore the use of HBM constituents for treatment of dry eye.

Methods: HBM samples were fresh frozen, then thawed, centrifuged, and aqueous recovered for lyophilisation. The aqueous containing proteins was used in the experiments. Pressure-area profiles and rheology of surface films of HBM proteins and tear proteins, namely, lysozyme and lactoferrin were studied using Langmuir trough technology on an artificial tear solution at the physiological pH and temperature of tears.

Results: Pressure-area profiles indicated that HBM proteins formed a highly compressible, non-collapsible surface film with a maximum surface pressure of 32mN/m. The surface films of lysozyme and lactoferrin were also compressible with the maximum surface pressures of 23mN/m and 17mN/m, respectively. Hysteresis was observed in all proteins with smallest in lactoferrin and highest in lysozyme.

Conclusions: HBM proteins are surface active and capable of reducing surface tension to increase the film stability. They are effective in smaller amounts, show higher surface pressure, and wider surface coverage than tear proteins lysozyme and lactoferrin. Overall, the biophysical experiments indicate that HBM proteins in smaller amounts would provide better protection to the tear film than the natural proteins of the tear film and can be effective in enhancing tear stability in dry eye.

CONTROL ID: 3709397

SUBMITTER (NAME ONLY): Anneli Savinainen

TITLE: A first in class Virus-Like Drug Conjugate (VDC) shows anti-tumor activity in Cancers that Commonly Metastasize to the Choroid

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Savinainen, R. Kines, C.C. Rich, Aura Biosciences, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: HPV-derived Virus Like Particles (VLPs) have been previously described to have the ability to selectively target a large panel of solid tumor types by binding to specifically modified heparan sulphate proteoglycans (HSPGs) on the tumor cell surface. The investigational VDC, belzupacap sarotalocan (AU-011), is composed of a modified VLP conjugated to a novel photosensitizer and is currently in phase 2 clinical trials for the treatment of primary choroidal melanoma. Upon light activation, AU-011 causes membrane disruption leading to acute cellular necrosis, tumor regression and an anti-tumor immune response in murine tumor models. With the ability to target a broad range of tumor types, AU-011 has the potential to treat tumors that metastasize to the choroid using the same treatment paradigm. We have previously shown anti-tumor activity of AU-011 in mouse models of breast and lung cancer. The purpose of this study was to expand to other cancer types that metastasize to the choroid as well as to explore the dose response.

Methods: In vitro efficacy was evaluated in a panel of cancer cell lines. Cells were treated with AU-011, and cell binding and cell killing were evaluated by flow cytometry. HSPG targeting was assessed by inhibiting HSPGs binding with exogenous heparin. In vivo efficacy was evaluated by utilizing EMT6 (breast), CT26 (colon) and RENCA (renal) syngeneic mouse models. Subcutaneous tumors were treated when they reached a size of ~50 mm^3. Treatment consisted of a single intravenous administration of AU-011 followed 12 hours later by external exposure to near-IR light. Tumor volumes were measured over time.

Results: In all cancer cell lines tested, the in vitro cell binding and cell killing potency were under 100pM. Cell binding and subsequent AU-011 mediated cell death was inhibited by heparin, demonstrating that AU-011 can bind to these tumor cell types in an HSPG-dependent manner. In vivo, AU-011 treatment demonstrated dose dependent activity and delay of tumor growth in EMT6, CT26, and RENCA murine tumor models.

Conclusions: These data demonstrate that AU-011 can bind to, and kill, cells derived from cancer types known to metastasize to the choroid. Furthermore, AU-011 showed dose dependent activity in vivo using cognate tumor models. The studies herein support further development of AU-011 for choroidal metastasis.

CONTROL ID: 3709399

SUBMITTER (NAME ONLY): Mai Nguyen

TITLE: Defective photoreceptor-to-bipolar cell synaptic transmission in novel knock-in mouse models of RP59

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.N. Nguyen, D. Chakraborty, S.J. Pittler, Optometry and Vision Science, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S.J. Fliesler, Ophthalmology, Biochemistry, and Neuroscience Graduate Program, SUNY The State University of New York, Buffalo, New York, UNITED STATES|S.J. Fliesler, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: RP59 (OMIM# 613861) is caused by mutations in the dehydrodolichyl diphosphate synthase (DHDDS) gene. We previously reported that knock-in mice with K42E and T206A DHDDS mutations do not exhibit overt retinal degeneration, but exhibit a “negative ERG” [normal a-wave and reduced (scotopic and photopic) b-wave amplitudes]. Here, we describe further characterization of two RP59 mouse models.

Methods: $Dhdds^{T206A/T206A}$ and $Dhdds^{T206A/K42E}$ knock-in mice (Nguyen et al., ARVO 2021) vs. age-matched WT ($Dhdds^{+/+}$) mice were assessed by quantitative retinal morphometry (SD-OCT) and electroretinography (ERG; 500 nm LED stimulus). Visual acuity (VA; spatial frequency) was assessed by OKR under scotopic and photopic conditions. Statistical significance (Student’s t-test) threshold was $p \leq 0.05$ ($N \geq 3$ SD-OCT, $N \geq 8$ ERG, $N \geq 3$ OKR).

Results: From PN 1- to PN 12-mo, neural retina full thickness declined <5% ($p \leq 0.05$), while INL thickness declined by 27% in $Dhdds^{T206A/T206A}$ and 30% in $Dhdds^{T206A/K42E}$ ($p \leq 0.01$), vs. WT mice. ERG b-to-a-wave amplitude (b/a) ratios declined (at 3-mo intervals) over the same time. At PN 12-mo: scotopic b/a ratios were reduced by ~25% in $Dhdds^{T206A/T206A}$ and by ~35% in $Dhdds^{T206A/K42E}$ mice, vs. WT values ($p \leq 0.01$). Photopic b/a ratios were also declined by ~33% in $Dhdds^{T206A/T206A}$ and by ~41% in $Dhdds^{T206A/K42E}$ mice, vs. WT values ($p \leq 0.01$). ERG c-wave amplitudes were like WT at PN 6-mo; however, at PN 12-mo, c-wave amplitudes were reduced by ~35% in both mutants, vs. WT mice ($p \leq 0.01$), and ERG d-wave amplitudes were reduced by ~35% in $Dhdds^{T206A/K42E}$ mice, vs. WT values ($p \leq 0.05$). Scotopic VA was reduced by ~15% and ~10%, respectively, in $Dhdds^{T206A/T206A}$ and $Dhdds^{T206A/K42E}$ mice, and photopic VA was reduced by ~15% and ~20.5%, respectively, in $Dhdds^{T206A/T206A}$ and $Dhdds^{T206A/K42E}$ mice, vs. WT values.

Conclusions: These results are consistent with defective rod- and cone-to-bipolar cell synaptic transmission (normal a-wave, reduced b- and d-waves) and compromised RPE and/or Müller cell responses (reduced c-wave) in these Dhdds mouse mutants.

CONTROL ID: 3709401

SUBMITTER (NAME ONLY): Itika Garg

TITLE: Widefield Swept-Source OCT Angiography (WF SS-OCTA) Vascular Metrics as Biomarkers for Renal Function in Diabetes Mellitus (DM) Patients

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Microvascular complications of DM (retinopathy, nephropathy and neuropathy) are closely interrelated and are an important cause of patient morbidity and mortality. We aim to evaluate the relationship between WF SS-OCTA quantitative metrics and the presence of albuminuria and serum creatinine in DM patients.

Methods: In this cross-sectional observational study between January 2019 and April 2021, 380 eyes of 234 patients were imaged on 100kHz WF SS-OCTA using 12x12mm angiogram centered on fovea. The ARI Network (Zeiss Portal) was used to calculate vessel density (VD), vessel skeletonized density (VSD), foveal avascular zone area, circularity, and perimeter; and ImageJ for non-perfusion area (NPA), Figure 1. We recorded glycosylated hemoglobin (HbA1c), serum urea, creatinine and urine albumin to creatinine ratio (ACR) within one year of imaging.

Results: The median patient age was 58.5 (50-65) years and 125 (53.4%) were males. Subjects had a median HbA1c 8.1 (7-9.3) %, median creatinine 0.98 (0.80-1.33) mg/dL and 111 (47.4%) patients had albuminuria (urine ACR >30mg/g). Using serum creatinine, estimated glomerular filtration rate (eGFR) was calculated, and 74 (31.6%) patients had chronic diabetic kidney disease (CDKD) i.e., eGFR <60mL/min/1.73m^2 (Figure 2). Using mixed effects multiple logistic regression model adjusting for age, smoking status, HbA1c, mean arterial blood pressure and duration of diabetes; NPA (Odd's ratio (OR)=1.14, 1.03-1.27; p=0.02) and whole retina VSD (OR=0.26, 0.08-0.10; p=0.02) were significantly associated with the presence of albuminuria. None of the OCTA metrics were significantly associated with serum creatinine. Also, NPA (OR=1.11, 1.00-1.23, p=0.047) and superficial VSD (OR=0.61, 0.37-0.99, p=0.047) were significant predictors for the presence of CDKD.

Conclusions: Herein, we see that NPA can serve as a potential imaging biomarker associated with deteriorating renal function (presence of albuminuria and CDKD). Due to OCTA having high-resolution and being depth resolved, quantitative OCTA metrics can leverage the changes at the retinal capillary level in patients with kidney damage.

Hence, this safe non-invasive device can be potentially useful for diagnosis and early management of various microvascular complications of DM.

CONTROL ID: 3709405

SUBMITTER (NAME ONLY): Joshua Disatham

TITLE: Gene Silencing by DNA Methylation Predicts Chromatin Regions and Transcription Factors Required for Lens Differentiation

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: A key epigenetic regulator of gene expression is gene silencing through DNA methylation at specific cytosines (mCG). mCG methylation governs chromatin configurations and DNA accessibility changes that modulate transcription factor function. It is well established that mCG methylation regulates the activities of individual genes and their cognate transcription factors but few studies have examined its role in global biological processes or employed it as a tool to predict key transcription factors. Here, we employed a multiomics analysis to establish a requirement for mCG methylation in gene expression events that hallmark lens cell differentiation.

Methods: The genome-wide relationships between mCG methylation, chromatin accessibility and transcript levels were compared between lens epithelial cells and fiber cells of embryonic day 13 chick lenses through integrated analysis of bisulfite sequencing, ATAC Seq and RNA Seq data. Bioinformatic interrogation of the data was used to predict functional DNA regulatory sites and transcription factor consensus representation across the chick genome.

Results: 7621 genomic loci exhibiting significant differences in mCG levels between lens epithelial and fiber cells were correlated with the differentiation state-specific expression of 1285 genes preferentially expressed in either lens fiber or lens epithelial cells (Pearson $r = -0.37$, $p < 1x10^{-42}$). mCG levels were inversely correlated with chromatin accessibility as determined by Assay for Transposase-Accessible Sequencing (ATAC-seq) (Pearson $r = -0.86$, $p < 1x10^{-300}$). Genes exhibiting altered regions of DNA methylation, chromatin accessibility and gene expression levels in fiber cells relative to epithelial cells include crystallins (CRYBA4, CRYBB1, CRYGN, CRYBB2), lens beaded filament proteins (BFSP1, BFSP2), transcription factors (HSF4, SOX2, HIF1A), and Notch signaling. Regions exhibiting cell-type specific DNA methylation changes were enriched with transcription factor binding sequences including HIF1A, SOX2, and the MAF family of transcription factors.

Conclusions: The results demonstrate that gene silencing through mCG methylation changes control chromatin accessibility and gene expression events that are required for lens differentiation. They also point to a role for mCG methylation in the regulated binding of transcription factors important for lens cell differentiation.

CONTROL ID: 3709407

SUBMITTER (NAME ONLY): Laura Le

TITLE: Anti-VEGF for diabetic retinopathy treatment: systematic review of randomized controlled trials

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Le, P. Latkany, Z. Haskova, N. Callaway, Genentech Inc, South San Francisco, California, UNITED STATES|N. Kothari, Texas Retina Associates, Dallas, Texas, UNITED STATES|N. Scott, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|M. Rodriguez, Vitreo-Retinal Associates of Worcester PC, Worcester, Massachusetts, UNITED STATES|N. Patel, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|N. Yannuzzi, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|N. Callaway, Stanford University Byers Eye Institute, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite widespread use for major ocular vasculature diseases, use of anti–vascular endothelial growth factors (VEGF) as primary treatment for nonproliferative diabetic retinopathy (NPDR) is debated. This study synthesized key efficacy results from pivotal clinical trials investigating anti-VEGF for primary treatment of DR.

Methods: A systematic literature search was conducted using Cochrane, PubMed, and clinical trial registers to identify clinical trials of DR that compared anti-VEGF monotherapy vs laser photocoagulation (any type), sham treatment, or clinical observation. Standard methodologies were used to identify, select, extract data from, and assess quality of the studies. Results of patient (pt) outcomes related to visual acuity (VA) and DR progression on Diabetic Retinopathy Severity Scale are reported.

Results: Among 975 publications, 13 met inclusion criteria for proliferative DR (PDR; n=5), diabetic macular edema (DME; n=6), and NPDR (n=2). At 2y, anti-VEGF resulted in better VA outcomes vs laser and sham in pts with PDR with or without DME, and pts with DME with variable baseline (BL) DR severity. In pts with NPDR without BL DME, anti-VEGF did not result in significant VA improvements vs sham. At longest follow-up across trials and indications, pts who received anti-VEGF generally showed higher rates of ≥2-step DR improvement on DRSS vs pts who did not (NPDR without BL DME at 2y, 52% vs 13%; PDR with or without DME at 5y, 46% and not evaluable; DME with variable BL DR severity at 3y, 38% vs 22%). Further, pts who received anti-VEGF showed lower rates of ≥2-step DR progression vs pts who did not (NPDR without BL DME at 2y, 4% vs 16%; PDR not reported; DME with variable BL DR severity at 3y, 3% vs 9%). In pts with NPDR without DME at BL, anti-VEGF injections were associated with lower rates of development of PDR and central-involved DME vs sham at 2y (4% vs 11%; 9% vs 21%).

Conclusions: A growing body of clinical trials shows that anti-VEGF injections can regress DR severity in moderately severe NPDR and PDR and reduce rates of PDR progression and DME development in NPDR without DME at BL. The strongest predictor of anti-VEGF efficacy on DR improvement is BL DR severity, which is independent of BL DME presence/absence; however, anti-VEGF effect on VA depends on BL DME presence/absence. This review supports future research on anti-VEGF for primary treatment of DR with or without DME.

CONTROL ID: 3709408

SUBMITTER (NAME ONLY): Mariam Mathai

TITLE: Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring - The ALOFT study

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Elman, Elman Retina Group, Pennsylvania, UNITED STATES|S. Reddy, M. Busquets, Retina Associates of Kentucky, Kentucky, UNITED STATES|B. Ladd, Virginia Eye Institute, Richmond, Virginia, UNITED STATES|A. Wagner, Wagner Macula & Retina Center, Virginia, UNITED STATES|G.E. Sanborn, J. Jacobs, Notal Vision Inc, Chantilly, Virginia, UNITED STATES|M. Mathai, R.A. Garfinkel, The Retina Group of Washington, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaluation of long-term visual acuity (VA) and performance of a monitoring strategy that includes a self-operated artificial intelligence enabled home monitoring system in conjunction with standard care for early detection of neovascular age related macular degeneration (nAMD) (ForeseeHome (FSH), Notal Vision Monitoring Center)

Methods: A retrospective review was performed of all iAMD patients monitored with FSH from 5 clinics from 8/2010-07/2020. Data included visual acuity (VA) at baseline, VA at conversion to nAMD during the monitoring period, VA at most recent visit, frequency of use, duration of monitoring, modality of CNV diagnosis (system alert vs detection by standard care means), and duration and number of treatments since conversion to most recent visit.

Results: 3334 eyes of 2123 patients were reviewed with a mean (SD) age of 74(8) years, monitored for mean (SD) duration of 3.1(2.4) years, with a total of 1,706,433 tests in 10,474 eye-monitoring years. A Kaplan-Meyer survival analysis predicted a mean (95%CI) 4.5(4.3-4.7) years of monitoring. The mean (SD) weekly FOU per patient was 5.2(3.4) and it was persistent over the usage period. 285 eyes converted while monitored at an annual rate of 2.72% and were treated with mean (SD) 17.3(16.5) injections over mean (SD) 2.7(2.0) years, with 6.4(3.1) injections per year for eye treated for > 1 year. The median VA at baseline and recent visit for eyes that did not convert were 20/27 and 20/34 with a median change of 0.0 letters. The median VA at baseline, conversion and recent visit for eyes that converted during the monitoring period were 20/30, 20/39 and 20/32 with a median change from baseline to conversion, baseline to recent and conversion to recent of -4, -4 and 0 letters, respectively. 52% of the conversions detected had a system alert prior to conversion. 48% of patients were detected by symptoms or routine visit. Patients experienced a non-nAMD alert on average every 4.6 years. At conversion and at recent visit the proportion (95% CI) of eyes that maintained ≥20/40 was 84%(78%-88%) and 82%(76%-86%) respectively.

Conclusions: Patients in the FSH monitoring program showed excellent long-term visual acuity years after conversion to nAMD, emphasizing the importance of early detection.

CONTROL ID: 3709411

SUBMITTER (NAME ONLY): David Veysset

TITLE: Retinal absorption measurements for laser therapy through interferometric imaging of the thermal expansion

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure: David Veysset: Commercial Relationship: Code N (No Commercial Relationship) | Yueming Zhuo: Commercial Relationship: Code N (No Commercial Relationship) | Junya Hattori: Commercial Relationship: Code N (No Commercial Relationship) | Mohajeet Bhuckory: Commercial Relationship: Code N (No Commercial Relationship) | Vimal Prabhu Pandiyan: Commercial Relationship(s);Code P (Patent):PCT/US2020/029984 | Ramkumar Sabesan: Commercial Relationship(s);Code P (Patent):PCT/US2020/029984 | Daniel Palanker: Commercial Relationship(s);Code P (Patent):PCT/US2020/029984

ABSTRACT BODY:

Purpose: Retinal laser therapy requires precise control of the temperature rise during the procedure, especially for the relatively narrow therapeutic window of the non-damaging thermal therapy. Heat deposition is primarily governed by the melanin concentration in the retinal pigment epithelium and pigmented choroid, which can vary locally within the retina and from patient to patient. It is therefore important to precisely determine the local absorption coefficients prior to the treatment. Here, we present a method for determining the optical and thermal properties of the retina, using phase-resolved optical coherence tomography (pOCT).

Methods: Optical path length changes (ΔOPL) following laser-induced heating and thermal expansion are measured using line-scan spectral-domain phase-resolved OCT. The sample is illuminated with a line field and the backscattered spatial profile is then imaged via an anamorphic configuration onto a high-speed camera, yielding B-scans, recorded at a maximum frame rate of 10 kHz. For the tissue heating, a 450-nm laser is used with 1-ms pulse duration.

Results: The method is demonstrated on a model retina (a multi-layer polymer-based tissue phantom) heated with a laser pulse focused onto an absorbing layer buried 60 μm below the surface. We monitor the thermal expansion as changes in the OPLs between multiple layers (e.g., the top and the absorbing surface planes), where both, the decrease of refractive index with temperature and the layers displacement contribute to ΔOPL. The absorption coefficient, the heat conductivity, and the thermal expansion coefficient of the model retina are determined by fitting a thermomechanical model to the experimental data, using the full lateral and temporal extent of the thermal deformations.

Conclusions: With this method, we demonstrate that the absorption coefficient can be determined with a precision of 2.5% and the temperature rise with a precision of about 0.2°C from a single 1 ms-long laser exposure, while the peak did not exceed 8°C during the pulse, which is well within the tissue safety range. We further discuss the temperature determination precision in the living eye with the present method.

CONTROL ID: 3709417

SUBMITTER (NAME ONLY): Shayna Sosnowik

TITLE: Decreased Coverage and Thickness of the Endothelial Glycocalyx in the Trabecular Outflow Pathway of Monkey Eyes with Laser-Induced Ocular Hypertension

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Though a non-uniform glycocalyx layer covers the endothelium of the trabecular outflow pathway in bovine and human eyes, the differences in glycocalyx morphology between regions of different flow types in normal and diseased eyes have not been explored. This study examined glycocalyx morphology in high- and low-flow regions in normal and laser-induced ocular hypertensive monkey eyes.

Methods: YAG laser photocoagulation burns were created along ~270 degrees of the trabecular meshwork (TM) of one eye (n = 6) or both eyes (n = 2) of each monkey, reducing outflow in these regions, until a consistent rise in intraocular pressure was noted. Portions of the TM were not lasered, allowing outflow. Unlasered eyes (n = 6) served as controls. Monkeys were euthanized ≥60 months after the last laser treatment. Eyes were enucleated and perfused at 15 mmHg to measure outflow facility, outflow pattern was labeled with fluorescein, then eyes underwent perfusion-fixation for glycocalyx labelling. Anterior segments were cut into ~36 radial wedges and processed for electron microscopy. Coverage and thickness of the glycocalyx were measured in the TM, Schlemm's canal (SC), collector channels (CCs), intrascleral veins (ISVs), and episcleral veins (ESVs) in non-lasered regions of laser-treated eyes and high- and low-flow regions of controls.

Results: Median outflow facility was significantly less in laser-treated eyes compared to controls ($P = 0.02$). A trend of increasing glycocalyx thickness from the TM to ESVs was noted in non-lasered regions of lasered eyes and controls. No significant differences were found in glycocalyx coverage and thickness between high- and low-flow regions of controls. In non-lasered regions of lasered eyes, glycocalyx thickness was less when compared to high-flow regions in SC and CCs and low-flow regions in CCs ($P < 0.05$), and coverage was less when compared to high-flow regions in TM and SC and low-flow regions in SC ($P < 0.05$). In lasered regions of laser-treated eyes, TM, SC, and CCs were partly to completely obliterated, and ISVs and ESVs rarely showed glycocalyx labeling.

Conclusions: Laser treatment of the TM resulted in a decrease in glycocalyx coverage and/or thickness in lasered and non-lasered regions. Whether these changes contribute to decreased outflow facility needs further investigation.

CONTROL ID: 3709421

SUBMITTER (NAME ONLY): Ewelina Pijewska

TITLE: Extraction of phase-based optoretinograms (ORG) from serial B-scans acquired by clinical-grade raster scanning OCT system

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pijewska, M. Meina, M. Szkulmowski, NCU, Nicolaus Copernicus University, POLAND|K.V. Vienola, P. Zhang, R.K. Meleppat, R.S. Jonnal, R.J. Zawadzki, University of California Davis, Davis, California, UNITED STATES|P. Zhang, Dalian University of Technology, Dalian, Liaoning, CHINA|

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ABSTRACT BODY:

Purpose: To present application of the modified Knox-Thompson phase-based method for extraction of the light-evoked functional responses of human retina imaged with optical coherence tomography (OCT).

Methods: The human volunteers were imaged in vivo with a clinical-grade OCT retinal imaging system, equipped with a controlled light stimulator, to allow ORG experiments. Before the testing volunteers were dark-adapted for over 5 minutes. The clinical-grade OCTs cannot resolve individual photoreceptors and instead probe a group of cells, resulting in limited phase information due to temporal speckle decorrelation. Implementation of the modified Knox-Thompson method allowed us to successfully extract phase-based ORG signals from the outer segment band (between IS/OS and COST).

Results: The phase-based ORG signals extracted from the same data sets, although more sensitive to retina motion and more computational demanding than ORG intensity-based methods, provided an order of magnitude higher sensitivity of detecting changes in retina layers positions. The cross-correlation of the phase difference between the measured layers of the object allowed identification of the intervals with strong phase correlation, thus allowing extraction of the ORG signal in a clinical setting.

Conclusions: Successful implementation of phase-based ORG signal analysis provided an order of magnitude higher sensitivity of detecting changes in retina layer positions. ORG signal analysis using clinical-grade raster scanning OCT systems is now possible, which should open a path to clinically friendly ORG probing.

CONTROL ID: 3709422

SUBMITTER (NAME ONLY): Amir Ali

TITLE: 3D-Bioprinted Outer Blood Retinal Barrier Model to Characterize the Role of Senescent Fibroblasts in Driving RPE Dysfunction

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ali, E. Nguyen, R. Hirday, R. Quinn, D. Bose, M. Kwak, J. Montford, T. Park, R. Sharma, K. Bharti, Ophthalmic Genetics & Visual Function Branch, National Eye Institute, National Institutes of Health Clinical Center, Bethesda, Maryland, UNITED STATES|A. Ali, School of Medicine, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chronic inflammation and tissue senescence have been implicated in the onset of dry age-related macular degeneration (AMD), but the role of choroidal fibroblasts in AMD pathogenesis is not well understood. To better understand the role of choroidal fibroblasts in AMD pathogenesis, we established an in vitro 3D bioprinted outer blood-retinal barrier (oBRB) model utilizing either iPSC fibroblasts or senescent adult fibroblasts and analyzed their effects on choroidal maturation and RPE functionality.

Methods: A 3D bioprinting system generated a model choroid tissue consisting of pericytes, endothelial cells (EC), and either iPSC-derived or senescent fibroblasts deposited on a PET transwell membrane. After 1 week of maturation, an iPSC-derived RPE monolayer was deposited on the opposite side of the PET membrane to complete the oBRB model. After 4 further weeks of maturation, the effects of iPSC-derived or senescent fibroblasts were evaluated using vasculature network area, transepithelial resistance (TER), PLVAP expression and Luminex analysis for tissue cytokine secretions in media. Two-way ANOVA and Tukey's Multiple Comparisons Test were utilized for analysis.

Results: Vasculature network area was significantly increased in iPSC versus senescent fibroblast tissues ($P \leq 0.0001$). Senescent fibroblasts increased PLVAP/GFP Colocalization in EC, indicating increased potential for fenestration formation in EC. TER values in RPE were significantly increased in iPSC vs. senescent tissues ($p \leq 0.0001$). The inclusion of senescent fibroblasts in tissues caused a significant increase in IL-1B, IL6 and IL8 in media.

Conclusions: Senescent choroidal fibroblast tissues have decreased choriocapillaris development and worsened RPE maturation and functionality compared to iPSC-derived tissues. Our work indicates a critical role of fibroblasts in RPE and choriocapillaris degeneration and in inflammatory processes associated with AMD pathogenesis.

CONTROL ID: 3709424

SUBMITTER (NAME ONLY): Iori Wada

TITLE: Signal Mechanisms of EMT and role of αB Crystallin Chaperone Peptide in the prevention of experimental PVR

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Wada, P.G. Sreekumar, C. Spee, R. Kannan, DOHENY EYE INSTITUTION, Pasadena, California, UNITED STATES|M.S. Ip, DOHENY EYE INSTITUTION, Los Angeles, California, UNITED STATES|R. Kannan, STEIN EYE INSTITUTE, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative Vitreoretinopathy (PVR) is characterized by the proliferation of retinal pigment epithelial (RPE) cells. In PVR, RPE cells undergo transformation into fibroblast-like cells by epithelial to mesenchymal transition (EMT). The purpose of this study was to investigate the role of αB crystallin (αBC) peptide on epithelial EMT in experimental PVR.

Methods: Subconfluent primary human RPE (hRPE) cells were stimulated by TGFβ2 (10 ng/ml) with or without αBC peptide (50 or 75 µg/ml) for 24h or 48h EMT/MET-associated markers were examined by RT-PCR and WB analysis. The effect of TGFβ2 on glycolysis and oxidative phosphorylation was determined in hRPE cells using Seahorse XF96 analyzer. PVR was induced in 6-8 week old male C57BL/6J mice by intravitreal administration of dispase (10 mg/ml) and PVR progression was studied on day 21. Expression of αSMA, E-cadherin (E-C), fibronectin (FN), and RPE65 in control and dispase-treated retina was determined by immunostaining on day 21.

Results: The EMT-associated αSMA and vimentin showed a significant upregulation with TGFβ2 stimulation at the gene (3- and 1.5-fold) and protein (2.5-fold) level. The protein expression of these markers was significantly suppressed by co-treatment with αBC peptide ($p < 0.05$ vs TGFβ2 alone). The mesenchymal epithelial transition (MET)-associated genes and proteins, E-C and SIRT1 were significantly downregulated by TGFβ2 (> 2-fold) and were restored by αBC peptide cotreatment. Mitochondrial oxygen consumption rate (OCR, pmol/min/total DNA) increased with TGFβ2 treatment for 24h or 48h and αBC peptide co-treatment caused a further increase in OCR for both time points. An increased deposition of αSMA and FN and a decreased expression of E-C and migration of RPE65 was observed 3 weeks after dispase administration by immunofluorescence.

Conclusions: Our findings suggest that αBC peptide may have therapeutic potential in preventing the proliferation of PVR by reversing the phenotype of EMT/MET and improving the mitochondrial function in RPE cells.

CONTROL ID: 3709427

SUBMITTER (NAME ONLY): Jennifer Bu

TITLE: Pupillary dilation and axial length in highly myopic patients

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Bu, R. Sella, R.R. Lian, J.Q. Hu, H.E. Gali, E. Walker, N.A. Afshari, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|R. Sella, E. Livny, Department of Ophthalmology, Rabin Medical Center, Petah Tikva, ISRAEL|

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ABSTRACT BODY:

Purpose: To determine how high myopia impacts pharmacological pupillary dilation, and to evaluate the relationship between the rate and extent of pharmacological pupillary dilation and axial length (AL).

Methods: Patients were recruited from Shiley Eye Institute at the University of California San Diego, and grouped into high myopes, defined as one or both eyes having a spherical equivalent (SE) refraction greater than -6 diopters (D) or AL>26mm, and controls (SE less than -6 D and AL<26mm). Inclusion criteria were: phakic, aged 21 to 100, and planning to get pharmacological pupillary dilation as part of their eye exam. Exclusion criteria were: current use of eye drops other than artificial tears, prior intraocular or refractive surgery, iris or angle abnormalities, history of eye inflammation, previous adverse reaction to dilating drops, or diabetes. Dilation was achieved with 1 drop of tropicamide 1% and phenylephrine 2.5% in each eye. Pupil size was measured utilizing a Colvard pupillometer and the Cirrus HD-OCT (manual measurement on anterior segment scans) at full and dim light prior to dilation, then 15 and 30 minutes after dilation. AL and keratometry were measured using the Zeiss IOLMaster 700. Two-sample t-tests and generalized estimating equations (GEE) models were performed using R software.

Results: Thirty-four patients (68 eyes) participated in the study. The average age was 49 years and 70.5% were females. Sixteen patients were high myopes (average SE -7.14 D, range -4.75 to -11) and 18 were controls (average -1.06 D, range +2 to -5.5). Fully dilated pupil size at 30 minutes was significantly correlated with both SE refraction ($r=-0.59$, $p < 0.001$) and AL ($r=0.44$, $p < 0.001$), indicating eyes with higher myopia, as measured by both AL and refractive error, dilated more. When grouped by AL, 16 eyes had AL>26 mm (range 26.03-28.58mm) and 48 eyes had AL<26 mm (range 22.77-25.99mm), with eyes>26mm dilating to a greater extent than eyes<26mm at both 15 ($p = .05$) and 30 minutes ($p < .0005$).

Conclusions: Highly myopic patients dilate to a larger pupillary size compared to other patients. The positive correlation between dilation and axial length may be explained by the difference in elasticity of the sclera and thickness of the iris in highly myopic eyes. Predicting dilation based on extent of myopia could facilitate intraocular surgery planning and reduce clinic wait times for myopic patients.

CONTROL ID: 3709428

SUBMITTER (NAME ONLY): Alyssa Grant

TITLE: Global Associations of Ambient Air Pollution and Glaucoma: A Systematic Review and Meta-Analysis

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Grant, G. Leung, E.E. Freeman, School of Epidemiology and Public Health, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|E.E. Freeman, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The hazardous effects of air pollution on the lungs and heart are well established. The effects on the eye, which is directly exposed to air pollution, are less known. The purpose of our study was to synthesize the existing evidence on the global associations of ambient air pollutants with glaucoma.

Methods: This work was conducted in accordance with the standards and guidelines of Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA). MEDLINE, EMBASE, and Scopus were searched for articles until September 30, 2021. Inclusion criteria included studies of adults, aged 40+ years, that provided measures of association between nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2), ozone (O_3), particulate matter (PM) less than 2.5μm in diameter ($PM_{2.5}$), and PM less than 10μm in diameter (PM_{10}) and glaucoma. Articles were screened, extracted, and graded for certainty of the evidence by two independent reviewers. Pooled odds ratio (OR) estimates and 95% confidence intervals (CI) were calculated using a random-effects meta-analysis model in which study weights were inversely related to the total variance and between-study variability was estimated using restricted maximum likelihood. PROSPERO registration ID: CRD42021250078.

Results: A total of 403 articles were identified. Of these, 4 studies including 181,801 people met the criteria for inclusion in our systematic review and meta-analysis. Consistent evidence for an association was found between $PM_{2.5}$ and glaucoma with 4 out of 4 studies reporting a positive association. The pooled OR for each 10 $\mu m/m^3$ increase of $PM_{2.5}$ on glaucoma was 1.18 (95% CI: 0.95-1.47). Inconsistent evidence was found for the associations between the other pollutants and glaucoma.

Conclusions: Current evidence suggests there may be an association between $PM_{2.5}$ and glaucoma. Strengths of the current study included the use of recent evidence in which large sample sizes were utilized while limitations included low response rates, the use of self-reported glaucoma measures, and cross-sectional study designs. More studies, especially those using longitudinal data, are needed and potential mechanisms should be explored by investigating interactions with genetic factors or inflammatory markers that may be involved in the causal pathway.

CONTROL ID: 3709431

SUBMITTER (NAME ONLY): Cameron Duic

TITLE: Association of hyperreflective foci with disease severity and functional impairment in age-related macular degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Duic, K. Hess, A. Thavikulwat, H. Wiley, T.D. Keenan, E.Y. Chew, C.A. Cukras, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze the presence of hyperreflective foci (HRF) across different severities of age-related macular degeneration (AMD) as well as to examine its correlation with other structural and functional AMD features, including reticular pseudodrusen (RPD), increased pigment and rod intercept time (RIT).

Methods: Participants older than 50 years with varying AMD severities (including no AMD) with multimodal imaging were included in this longitudinal single-center study (NCT01352975). Color fundus imaging was used to assess AMD severity and presence of increased pigment. Presence of RPD and HRF were detected on OCT volumes. One study eye per participant underwent dark adaptation (DA) testing measuring rod intercept time (RIT). The correlation of HRF with additional features of AMD were evaluated using linear and logistic mixed-effects models. HRF comparison at first and last visit was used for longitudinal analysis on AMD severity and RIT.

Results: A total of 1332 visits of 158 participants (292 eyes) with a mean baseline age of 72.3±9.14 years were included. HRF were detected more frequently in higher AMD severities. In a multivariable model, the presence of HRF was significantly associated with the presence of increased pigment (Odds ratio 397.42, $p<0.001$) and RPD (Odds ratio 10.38, $p=0.007$). Eyes with HRF demonstrated greater delays in DA (median 27.3 [IQR=16-40] mins), compared to eyes without HRF (13.5 [10-22] mins) but less than eyes with RPD only (40 [28-40] mins). The highest RIT values were found in eyes with both HRF and RPD present (40.0 [40-40] mins). Using linear mixed models, age and HRF explained a similar portion of the RIT variability in our cohort as age and RPD. Eyes that developed HRF demonstrated baseline RITs that were closer to eyes that had HRF at baseline compared to those that never developed HRF (29.2 [16-38], 38.45 [23-40] vs 12.8 [10-22] mins; Kruskal-Wallis). They also exhibited a greater change in AMD severity than those that did not change HRF grades.

Conclusions: The progressively increased presence of HRF in later AMD stages, in addition to its correlation with previously associated AMD biomarkers suggests that HRF is an important OCT feature adding to the understanding of disease progression. The presence of HRF was associated with delays in DA lending support that HRF is a marker for retinal pigment epithelium and photoreceptor dysfunction.

CONTROL ID: 3709434

SUBMITTER (NAME ONLY): Maxime Le Merdy

TITLE: Clinical Ocular Exposure Extrapolation Using PBPK Modeling and Simulation: Moxifloxacin Solution Case Study

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Le Merdy, V. Lukacova, Research, Simulations Plus Inc, Lancaster, California, UNITED STATES|M. Tan, A. Babiskin, L. Zhao, Office of Generic Drugs, Food and Drug Administration Office of Global Regulatory Operations and Policy, Silver Spring, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of generic ophthalmic drug products is challenging due to the complexity of the ocular system, difficulties with clinical measurements of drug concentrations at the site of action, and a lack of sensitive testing to evaluate the interplay of physiology with ophthalmic formulations. The rabbit eye physiology is comparable to human eye physiology and is commonly used as a preclinical model to investigate the impact of formulation changes on the ocular exposure of an Active Pharmaceutical Ingredient (API). The purpose of this study is to demonstrate the utility of an ocular physiologically based pharmacokinetic (PBPK) model for translation of ocular exposure from rabbit to human. Ophthalmic moxifloxacin (Mox) solution is presented as a case study.

Methods: The Ocular Compartmental Absorption and Transit (OCAT™) model within GastroPlus® v9.8.2 was used to build a PBPK for Mox ophthalmic solution that accounts for nasolacrimal drainage, ocular absorption, and distribution in the rabbit eye. The model was subsequently used to predict Mox exposure after ocular solution administration in humans. Drug-specific parameters were used as fitted and validated in the rabbit. The physiological parameters were adjusted to match human ocular physiology. Simulated human ocular PK profiles were compared with observed cornea and aqueous humor (AH) concentration data to assess the OCAT models' ability to predict human ocular exposure based on preclinical data.

Results: OCAT model simulations for rabbit well described the observed concentrations in the anterior segment (cornea, AH) of the eye following Mox solution administration of different doses and various administration schedules. After adjustment of physiological parameters to represent the human eye, the clinical ocular exposure (cornea, AH) following ocular administration of Mox solution at different doses and various administration schedules was predicted within 2-fold of observed exposures.

Conclusions: The OCAT model reasonably predicted Mox ocular exposure in humans. Even though more case studies for different types of APIs and formulations will be needed, the positive clinical extrapolation outcomes of Mox solution from this study represents an important step in the validation process of the extrapolation method used to predict human ocular exposure for other ophthalmic drug products using PBPK models.

CONTROL ID: 3709435

SUBMITTER (NAME ONLY): Fengyang Lei

TITLE: Compensatory expression of Crystallin γS in retinal microglia neutralizes endotoxin-induced neuroinflammation

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Lei, C. Zhou, N. Efstathiou, J. Chodosh, D.G. Vavvas, E.I. Paschalis, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|G.J. Wistow, Molecular Structure and Functional Genomics, National Eye Institute, Bethesda, Maryland, UNITED STATES|F. Lei, N. Cui, Y. Cai, H. Zhang, D. Weitz, Applied Physics, Harvard John A. Paulson School of Engineering and Applied Sciences, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore the origin of Crygs expression in the retina and assess its role against neuroinflammation

Methods: Retinal $CD45^{+}$ $CD11b^{+}$ cells from C57BL/6 mice were sequenced using single-cell RNAseq after inflammatory insult. Crygs expression was assessed using $CX3CR1^{+/EGFP}$ mice with immunohistochemistry and flow-cytometry. The function of Crygs was evaluated in $Crygs^{-/-}$ or wild-type mice that received recombinant murine Crygs (rCrygs) injection in the eye following acute retinal inflammation induced by ocular injection of LPS (10ng/mL) or ocular surface injury with NaOH. qPCR was used to quantify retinal inflammatory cytokines. The neutralizing effect of exogenous Crygs in LPS-mediated retinal inflammation was evaluated ex vivo in $CX3CR1^{GFP/+}$ mice using flow cytometry and immunofluorescent microscopy. Retinal lysates from AMD patients and healthy control were also analyzed by Western blot for Crygs expression

Results: Single cell RNAseq identified a subset of $CD45^{+}$ $CD11b^{+}$ retinal immune cells with compensatory expression of Crygs in response to inflammation. Studies in $CX3CR1^{GFP/+}$ mice showed that activated microglia express Crygs in response to injury. Administration of rCrygs in LPS injected mouse eyes led to significant suppression of TNF-α (65% suppression), IL-1β (60% suppression), and Crygs (95% suppression) within 24 hours, and reduced MHC-II expression in microglia from 51.6% to 12.27%. rCrygs was shown to mediate neuroprotection by physically binding to LPS, thereby disrupting its biologic activity. In a separate model of ocular alkali burn, deletion of Crygs gene exacerbated retinal TNF-α and IL-1β expression after injury while restoration of the gene in $CX3CR1^{+}$ cells by adoptive transfer suppressed inflammation in injured $Crygs^{-/-}$ mice. Lastly, we were able to detect expression of Crygs by Western blots in retinal extracts from patients with AMD, a condition known to have activated microglia, but not in normal controls.

Conclusions: Here we show for the first time that Crygs is expressed in retinal microglia during retinal inflammation or pathology. Its expression is compensatory in nature, leading to suppression of inflammation and associated retinal neurodegeneration. Further studies are required to assess the functional and therapeutic roles of Crygs in other retinal and CNS pathologies

CONTROL ID: 3709439

SUBMITTER (NAME ONLY): Brittany Perzia

TITLE: Telomerase gene promoter (TERT) mutation in recurrent uveal melanoma after secondary enucleation revealed by targeted next-generation sequencing

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. Perzia, J.S. Heng, J. Sinard, R. Lim, Yale University Department of Ophthalmology and Visual Science, New Haven, Connecticut, UNITED STATES|J. Sinard, Yale University Department of Pathology, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a paucity of data on the molecular mechanisms driving the local recurrence of uveal melanoma after enucleation, a rare event with devastating consequences. The purpose of this study was to characterize the tumor genetic profile in a patient with local recurrence of uveal melanoma in the intraorbital optic nerve in an anophthalmic orbit seven years after secondary enucleation.

Methods: Relevant clinical data and MRI imaging were reviewed. Biopsy of the recurrent tumor in the anophthalmic orbit was carried out. Archived primary tumor samples from prior enucleation and biopsy samples of the secondary recurrent tumor were obtained for histopathological analysis. Targeted next-generation sequencing (NGS) of biopsy samples of the secondary recurrent tumor was carried out using the Oncomine (Waltham, MA) Assay Targeted NGS Cancer Gene Panel to evaluate for DNA mutations and/or amplifications in 146 cancer-related genes as well as the presence of gene fusion mRNA transcripts involving 44 oncogenic driver genes.

Results: Primary tumor samples from the prior enucleation showed a uveal melanoma of mixed spindle and epithelioid cell types without extra-scleral extension or optic nerve invasion. Biopsy of the recurrent tumor showed mixed spindle and epithelioid cell types positive for MelanA and SOX10 on immunohistochemistry, consistent with malignant melanoma. Targeted NGS revealed somatic mutations in GNAQ (Q209L) and the telomerase gene (TERT) promoter (c.1-124C>T). No other mutations were detected in the remaining genes tested including BAP1 and SF3B1.

Conclusions: This is the first report of an activating TERT promoter mutation in local uveal melanoma recurrence. Future studies on genetic biomarkers in recurrent tumors may lead to rational strategies to reduce the local recurrence of uveal melanoma.

CONTROL ID: 3709442

SUBMITTER (NAME ONLY): Dieter Brandner

TITLE: Clinical Utility of MRI in Pediatric Patients with Uveitis and Optic Disc Edema

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Brandner, D. Bullock, M. Riskalla, K. Armbrust, J. Yamanuha, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|D. Brandner, Medical Scientist Training Program, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|D. Bullock, M. Riskalla, Department of Pediatrics, Division of Rheumatology, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|K. Armbrust, J. Yamanuha, Department of Ophthalmology and Visual Neurosciences, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Brain MRI for optic disc edema (ODE) is indicated in cases of presumed optic neuritis or suspicion for elevated intracranial pressure (ICP). The utility of brain MRI in pediatric patients with uveitis and optic disc edema is unknown and there are no guidelines for ordering neuroimaging in this setting. We conducted a retrospective review of 12 pediatric uveitis patients with ODE to assess the diagnostic yield of MRI in this population.

Methods: We identified pediatric patients with uveitis and ODE under the care of 2 uveitis specialists and 2 pediatric rheumatologists at the University of Minnesota between 2014 and 2021. Inclusion criteria were diagnosis of uveitis, clinically identified ODE, and an MRI performed within 60 days of identification of ODE. We reviewed retinal nerve fiber layer thickness by optical coherence tomography (RNFL-OCT), neurological symptoms, concurrent ocular medications, MRI findings, and whether MRI results impacted treatment.

Results: Twelve subjects met inclusion criteria. Nine (75.0%) had bilateral and three (25.0%) had unilateral ODE. Average age was 11 (range: 6-18 years). Neurologic symptoms manifested in 8 (66.7%) subjects. Brain MRI identified abnormalities in four (33.3%) subjects. Two of these individuals had elevated ICP treated with optic nerve sheath fenestration, one had pituitary enlargement unrelated to ODE, and one had nonspecific white matter hyperintensities. All subjects with abnormal MRI findings had bilateral ODE. Average RNFL thickness for the affected eye(s) was found to be 171 microns for those with negative MRI, 145 microns among those with abnormal MRI, and 124 microns for those with increased ICP. Uveitis was the presumptive cause of ODE in 11 (91.6%) of subjects.

Conclusions: Pediatric uveitis patients with optic disc edema may have an abnormal brain MRI even without substantial RNFL thickening or normal brain MRI even with significant RNFL thickening. This suggests that uveitic disc edema in pediatric patients is more nuanced and the decision to pursue neuroimaging cannot be dictated solely by RNFL OCT thickness.

CONTROL ID: 3709443

SUBMITTER (NAME ONLY): Han Peng

TITLE: Selective autophagy regulates limbal epithelial differentiation via controlling Notch1 protein degradation

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Peng, N. Kaplan, M. Liu, W. Yang, R.M. Lavker, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Selective autophagy, a highly regulated pathway specifically degrades certain cytosolic components that are recognized by selective adaptors. For example, selective autophagy degrades Notch1 protein via specific adaptors p62, which leads to inhibition of stem/progenitor cell differentiation in various tissues including neural cells. However, the role of selective autophagy in corneal/limbal epithelia remains unclear.

Methods: To determine the differentiation status of limbal epithelium, expression of differentiation markers (e.g., mucin1, PAI-2) as well as putative limbal epithelial stem cell markers (e.g., N-cad, K15) were determined by immunoblotting and immunostaining. 3D organotypic raft cultures of HLECs, a stratified limbal epithelial equivalent, were used to investigate the expression of differentiation markers (e.g., IVL, mucin1).

Results: Stem/TA cell-enriched HLECs were induced to differentiate by increasing the calcium concentration from 0.07mM to 1.6mM. Such calcium modulation reduced the expression of LC3II, as well as increased p62, indicating an inhibition of autophagy flux. Knockdown of autophagy-related genes (e.g., Beclin1, Atg5) enhanced HLEC differentiation as evidenced by increased expression of mucin1 and PAI-2 and reduced N-cad. This observation was confirmed using 3D organotypic raft cultures, which demonstrated that activation of autophagy by rapamycin inhibited the expression of IVL and mucin 1. To explore how autophagy regulates stem/TA cell-enriched HLEC differentiation, our single cell RNA seq investigation identified a group of novel stem/TA cell regulators including Bmal1 and Wdfy1. Inhibition of autophagy decreased stem cell regulators, Bmal1 and Wdfy1 in vitro and in vivo. Furthermore, knockdown of Bmal1 or Wdfy1 enhanced HLEC differentiation. Significantly, inhibition of Notch signaling, which is specifically and negatively regulated by selective autophagy, increased Wdfy1 expression. This suggests that attenuated autophagy induces differentiation of stem/TA cell-enriched limbal epithelial basal cells via controlling novel stem/TA cell regulators including Bmal1, Notch/Wdfy1.

Conclusions: Our observations suggest that a decrease in selective autophagy triggers the differentiation of stem/TA cell-enriched limbal epithelium into more differentiated limbal epithelial superficial cells.

CONTROL ID: 3709447

SUBMITTER (NAME ONLY): Hannah Doyle

TITLE: Boosting 2-Photon Vision with Adaptive Optics

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The 2-photon (2P) effect in vision occurs when light incident on the retina causes a direct photoisomerization of photoreceptor pigments involving two photons at a given wavelength, creating a percept of light corresponding to a 1-photon (1P) process at half that wavelength. Thus, a 2P effect elicited by 940-nm light may appear similar to 470-nm light. Typically, such an effect is achieved using pulsed lasers which compress photons in time. However, with adaptive optics (AO), we can also compress photons in space, further increasing the likelihood of 2P photoisomerization. We investigate the impact of AO correction on the 2P effect.

Methods: We scanned a focused spot of 940-nm light in a 0.9° x 0.9° raster pattern using an AO scanning laser ophthalmoscope. A supercontinuum light source was used with a ~20-ps pulse and an average power of 198.2 μW. We varied the focusing depth of the raster in and out of the plane of best focus and had subjects make a color and luminance match by tuning the color of a projector-generated square, thereby revealing the 2P effect's benefit from an AO correction.

Results: Subjects' matching data showed a clear increase in luminance and blue hue when the AO-corrected raster was focused on their photoreceptors. Their matches can be interpreted as having a relatively constant red component corresponding to 1P isomerizations at 940 nm superimposed with blue and green components that increase greatly as the raster comes into focus. For 3 subjects, a retinal irradiance of 0.29 W/cm^2 of 940-nm light elicited a percept equivalent to an irradiance of 94 nW/cm^2 of 470-nm light at best focus. Analysis of matching data yielded an average 1P luminance of 0.14 cd/m^2 with the luminance of the 2P effect peaking at 0.57 cd/m^2.

Conclusions: 2P vision was greatly enhanced by AO. As AO was used to focus a faintly-visible 940-nm scanning raster onto the retina, the raster appearance changed from red to blue, as if it were a mixture of 940- and 470-nm light. This effect was readily visible, despite our laser using pulses that are quite long compared to the conventional short-pulsed lasers used in 2P imaging (20 ps vs 200 fs). Our results are consistent with the hypothesis that this is a 2P isomerization process by the color appearance and by the strong focus dependency. These data set the technical specifications for future systems that aim to elicit even brighter color appearances via direct 2P activation of human photopigments.

CONTROL ID: 3709451

SUBMITTER (NAME ONLY): Nhuong-Sao Ton

TITLE: Endophthalmitis Following Intravitreal Injections of Anti-Vascular Endothelial Growth Factor Agents with 0.05% Aqueous Chlorhexidine versus 5% Povidone-Iodine as Ocular Antiseptics

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ton, M. Adam, Rocky Vista University College of Osteopathic Medicine, Parker, Colorado, UNITED STATES|M. Adam, Colorado Retina Associates, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Topical Povidone-Iodine (PI) is a widely used ocular surface antiseptic for intravitreal injections and is associated with significant ocular discomfort in some patients. In limited studies, aqueous chlorhexidine (CHX), as an alternative antimicrobial to PI, has been associated with a low post-injection endophthalmitis (PIE) rate and less ocular discomfort compared to PI. This study compares the rates and outcomes of PIE for patients pre-treated with 5% PI and 0.05% CHX.

Methods: This was a retrospective, single center, comparative cohort study of patients receiving intravitreal anti-VEGF injections from January 1, 2019, to November 30, 2021. Injection preparation with PI or CHX and cases of PIE were compiled using electronic health records and billing code data. The primary outcomes were the rate of endophthalmitis, culture results, and visual acuity. LogMAR visual acuity was determined at the time of causative anti-VEGF injection, endophthalmitis presentation, and 3-month follow-up.

Results: A total of 68,334 intravitreal injections were administered by 13 retinal specialists during the study period. 13 of 33,064 (0.0393%; 1 in 2,543 injections) cases of presumed endophthalmitis occurred in the PI group, and 9 of 35,270 (0.0255%; 1 in 3,918 injections) cases in the CHX group (OR=0.65; 95% CI 0.27–1.52; p=0.319; Table 1). For the PI group, there were 2 culture-positive endophthalmitis cases (0.00605%, 1 in 16,532), compared to 2 cases in the CHX group (0.00567%, 1 in 17,635) (OR=0.94; 95% CI 0.13–6.66; p=0.949; Table 1). No significant difference was observed in visual acuity between PI and CHX at causative injection (p=0.41), endophthalmitis encounter (p=0.45), and 3-month follow-up (p=0.45; Table 2).

Conclusions: There was no significant difference in the rate of PIE and visual acuity in the CHX group compared to the PI group. Further multicenter studies are needed to further evaluate the efficacy and safety of CHX compared to PI for intravitreal injection preparation.

CONTROL ID: 3709454

SUBMITTER (NAME ONLY): Jason Meyer

TITLE: Induction of reactivity in human pluripotent stem cell-derived astrocytes and their contribution to retinal ganglion cell degeneration

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Astrocytes closely associate with retinal ganglion cells (RGCs) in the nerve fiber layer of the retina and optic nerve, where they provide support for RGCs but can contribute to RGC neurodegeneration in a glaucomatous state. However, the mechanisms by which astrocytes promote neurotoxicity and contribute to neurodegeneration remain unclear. Importantly, human pluripotent stem cells (hPSCs) can serve as powerful tools for the in vitro analysis of human neurodegenerative diseases, including neuron-glia interactions.

Methods: Using hPSC-derived RGCs and astrocytes, we explored how reactive astrocytes contribute to RGC degeneration. Human pluripotent stem cells were differentiated into 3D retinal organoids or forebrain organoids for the subsequent isolation of retinal ganglion cells (RGCs) and astrocytes, respectively. The induction of a reactive astrocyte phenotype (“A1”) was promoted through incubation with a cocktail of recombinant proteins including C1q, TNFα and IL1α.

Results: Reactive astrocytes displayed profound morphological alterations exhibiting a hypertrophic profile and increased expression of reactive astrocyte-specific markers such as complement C3. Transcriptional analyses of reactive astrocytes revealed an upregulation of genes associated with the inflammatory pathway as well as cytokine signaling. Functionally, reactive astrocytes affected blood-brain barrier properties by reducing transendothelial electrical resistance and increasing barrier permeability. Moreover, the secretion of several pro-inflammatory cytokines was increased in reactive astrocytes. Consequently, the neurotoxic potential of reactive astrocytes was determined through co-cultures with hPSC-derived RGCs, in which reactive astrocytes promoted marked morphological alterations including neurite retraction and reduced neurite complexity.

Conclusions: The results of this study demonstrate that hPSC-derived astrocytes can be induced to acquire a reactive and dysfunctional profile with a predominant inflammatory and neurotoxic phenotype which leads to RGC neurodegeneration. Thus, the modulation of reactive astrocytes could offer a novel therapeutic strategy for glaucoma by restoring a more homeostatic state and reducting RGC neurodegenerative phenotypes.

CONTROL ID: 3709455

SUBMITTER (NAME ONLY): Anjalee Choudhury

TITLE: Impact of tumor necrosis factor receptor 1 (TNFR1) polymorphism on dry eye disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dry eye (DE) is a multifactorial disease with numerous presenting phenotypes and potential contributors. In order to deliver precision medicine, a better understanding of an individual's contributors to disease is needed. Genetic polymorphisms have previously been shown to influence disease presentation and course in diseases relevant to DE, such as in chronic pain syndromes. However, the impact of genetic polymorphisms on DE presentation and treatment response have not been well characterized. A previous study examined the impact of rs1800693 (chr12, alleles: T/C), a single nucleotide polymorphism (SNP) within the tumor necrosis factor receptor 1 (TNFR1) gene. Individuals with DE and homozygous alternate CC alleles were found to have a better symptomatic response to OCS-02 (a topical TNFα antibody) compared to those with a TC or TT alleles. Building on this data, in the current study, we examine the frequency of a CC genotype in a novel population, South Florida veterans, and investigate whether the presence of this genotype impacts disease phenotype and response to anti-inflammatory therapy.

Methods: Prospective study of 328 individuals with a variety of DE symptoms and signs who underwent genetic profiling for rs1800693 (TT, TC, CC). The frequency of genotype CC was examined as were relationships between genotype and phenotype and response to an anti-inflammatory agent.

Results: The mean age of the population was 61.7±9.8 years, 92% self-identified as male, 56% as white, and 21% as Hispanic. 13% (n=42) individuals had a CC genotype, which was equally distributed between races but was less common in Hispanics. The presence of a CC genotype (as compared to TT and TC) did not influence the DE phenotype with similar DE symptoms and signs between the groups. In all, 30 individuals (4 with CC) were treated with an anti-inflammatory agent. There was a trend for individuals with CC genotype to have a partial or complete response to treatment compared to the other two groups (100% vs 38.5%, p=0.07).

Conclusions: The presence of homozygosity of risk allele C (CC genotype) in a SNP within TNFR1 was noted in a minority of individuals with various aspects of DE. However, this genotype did not relate to DE phenotype but did impact treatment response. These finding suggest that current phenotyping strategies in DE are not sufficient to identify underlying contributors to disease, including potential genetic contributors.

CONTROL ID: 3709457

SUBMITTER (NAME ONLY): Yamini Attiku

TITLE: Comparison of Diabetic Retinopathy Severity Grading on ETDRS 7-field versus Ultrawide field Assessment

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Attiku, M.G. nittala, Y. He, S.B. Velga, S.R. Sadda, Doheny Eye Institute, Pasadena, California, UNITED STATES|C. Ramachandra, S. Bhat, K. Solanki, Eyenuk.Inc, Los Angeles, California, UNITED STATES|C. Jayadev, Narayana Nethralaya, Bangalore, Karnataka, INDIA|N. Choudhry, Vitreous Retina Macula Specialists of Toronto, Toronto, Ontario, CANADA|N. Choudhry, Department of Ophthalmology and Visual Sciences, University of Toronto, Toronto, Ontario, CANADA|S.R. Sadda, Department of Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the diabetic retinopathy severity level determined when considering only the ETDRS 7-Field region versus the entire ultrawide field (UWF) image

Methods: In this retrospective, cross-sectional study, UWF images (Optos 200Tx) were obtained from diabetic patients presenting to the retina clinic. An ETDRS 7-field overlay was superimposed on these UWF images to define the region covered by the ETDRS 7 standard fields. The images were graded on Eyenuk's web-based grading portal for the severity of DR, based on the region within the ETDRS 7-fields as well as based on the entire UWF image, using both the ICDR severity scale and the modified ETDRS DRSS scale from DRCR.net Protocol AA. In addition, the grader also determined whether the lesions were predominantly central lesions (PCL) or predominantly peripheral lesions (PPL) using both a single-field (PPL was assigned if any one peripheral field had more lesions than the corresponding ETDRS field) method and a global method (if entire region outside ETDRS 7-fields had more lesions than within ETDRS 7-fields).

Results: A total of 125 eyes from 81 patients were included in this analysis. The distribution of DR severity levels as assessed by ICDR is shown in Table 1, and by ETDRS DRSS in Table 2. Only 3 (2.4%) eyes had a discrepancy in DR severity level between the ETDRS 7-field region and the entire UWF region when using the ICDR classification system. Six (4.8%) eyes had a discrepancy in DR severity level between the ETDRS 7-field region and the entire UWF region when using the ETDRS DRSS Protocol AA classification system. The discrepancy was due to the presence of lesions [hemorrhages (n=1), neovascularization (n=2), scatter laser scars (n=2), and pre-retinal hemorrhage (n=1)] in the peripheral fields which were not identified in the ETDRS 7-fields. Thirty percent of the eyes were PPL by the single-field method and 10.5% were PPL by the global method.

Conclusions: Although, considering regions outside of the ETDRS 7-fields altered the DR severity level assessment in < 5% of cases in this cohort (which only had a proportion of patients with PPL), significant potential vision-threatening lesions including neovascularization and pre-retinal hemorrhage were missed. This highlights the importance of evaluating the entire UWF region when assessing patients with diabetic retinopathy.

CONTROL ID: 3709458

SUBMITTER (NAME ONLY): Yingchen He

TITLE: Letter and Word Recognition with Remapped Text

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. He, Department of Psychology, NC State University, Raleigh, North Carolina, UNITED STATES|D. Kang, C. Flowers, G.E. Legge, S. Engel, Department of Psychology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|C. Larson, Department of Ophthalmology and Visual Neurosciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Text remapping has been proposed to improve reading with central-field loss, where letters occluded by the scotoma are shifted in real-time to a location outside of the scotoma. However, remapped text deviates from horizontal lines, which may negatively affect reading. This study aims to test the feasibility of text remapping by evaluating letter and word recognition performance along unusual trajectories.

Methods: Stimuli were triplets of random letters (trigrams) and words of 3-8 letters (x-height = 1°), presented for 100 ms along trajectories of 13 letter positions. Two groups of college students respectively read trigrams (N = 16) and words (N = 12). Baseline performance was measured with a typical horizontal linear text trajectory passing through the fovea (0°). Four other trajectories were designed assuming a scotoma covering the central 5 letters: 1) Lowered-line: the entire line was lowered by 3.8°. 2) Step-down: the leftmost 4 letters remained at 0° but the rest were lowered by 3.8°. 3) V-shaped: the central 5 letters were lowered then raised along a diagonal, circumventing the scotoma. 4) Horizontal-gap: the line remained at 0° but skipping the central 5 letter positions. Recognition performance was normalized as a percentage of baseline. A linear mixed-effect model was fitted where Stimulus type (trigrams/words) and Trajectory were fixed effects and Participant was the random effect.

Results: Recognition of remapped text only reached 69.7% to 93.9% of baseline performance, consistent with the slower reading with central-field loss. The main effect of Trajectory was significant ($F_{3,72} = 117.58$, $p < .001$): Compared to the Lowered-line trajectory, the performance of the V-shape trajectory was significantly better whereas that of the Horizontal-gap trajectory was significantly worse (adjusted p's < .001). While contextual benefits were observed during word recognition at baseline, the effect of Stimulus type was not significant after normalization ($F_{1,24} = 0.075$, $p = .79$). No significant interaction was found ($F_{3,72} = 1.26$, $p = .30$), indicating that the trajectories affected letter- and word-recognition similarly.

Conclusions: A V-shaped trajectory produced better performance than horizontal trajectories in peripheral vision despite the unusual text arrangement. Text remapping may be a feasible way to improve reading in people with central-field loss by customizing text arrangements to make more effective use of peripheral vision.

CONTROL ID: 3709467

SUBMITTER (NAME ONLY): Deepayan Kar

TITLE: Morphology of the human retinal pigment epithelium (RPE) basal transport complex in fovea and parafovea revealed by volume electron microscopy

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kar, C.A. Curcio, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|O. Packer, Y.J. Kim, D.M. Dacey, Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|A. Pollreisz, Ophthalmology, Medical University of Vienna, AUSTRIA|

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ABSTRACT BODY:

Purpose: RPE basal infoldings are microvillous membrane specializations to optimize surface area for ion transport and exchange of metabolites with the choroidal circulation. The fovea is supplied by the choroid, while mixed rod-cone areas are supplied additionally by the retinal circulation. We hypothesize that the basal RPE will differ in areas with differing photoreceptor content. We investigated basal infoldings (BI) in foveal and parafoveal regions of human RPE.

Methods: Rapidly preserved foveal (~160 µm eccentricity) and parafoveal (~850 µm eccentricity) tissue from 21-year-old and 53-year-old organ donors, respectively, were vertically sectioned using scanning block-face EM at 5 x 5 x 50 nm voxel resolution. BI were manually reconstructed in 7.5 x 7.5 µm sampling regions at the basolateral RPE using TrakEM2. Morphometric analysis of density (# per mm of basal lamina) and surface area (mm^2 per sampling region) were performed using ImageJ and Dragonfly 2020.2 (Object Research Systems).

Results: BI resemble elongated filopodia that appear to originate and extend from a consistent level of the cell body and extend towards the RPE basal lamina (Figure). Foveal BI had fine ridge-like profiles (A1). Parafoveal BI were elaborate (D1) with whorls that extended as far as the nuclear envelope (D2, E2), in contrast to straighter and non-convoluted infoldings under the nuclei of foveal RPE (A2, B2). The density of BI was higher in the fovea than parafovea (4624 ± 594 vs. 2784 ± 359 infoldings/ mm, $P < 0.001$). The surface area was 39% higher in the fovea compared to parafovea (838.9 vs. 602.3 μm^2). We also identified electron-dense punctate material that tend to localize at the basal RPE cell body, in a regularly-spaced pattern (B2). The internal structure of this material resembled disorganized cristae of mitochondria.

Conclusions: Our initial findings suggest that the exchange capacity of foveal RPE may be significantly higher than parafoveal RPE. However, we cannot exclude that age difference in our samples could also be a factor in these morphological differences. To answer this question, ongoing studies will match regions and ages to the current samples (fovea of 21-year-old and parafovea of 53-year-old) and expand sample size with deep-learning assisted methods.

CONTROL ID: 3709474

SUBMITTER (NAME ONLY): Stephen Lesche

TITLE: Medicare Reimbursement Trends for Glaucoma Procedures: 2000 to 2020

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lesche, M. Asahi, H. Pakhchanian, A. Ahmed, D. Belyea, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|S. Francone, Georgetown University School of Medicine, Washington, District of Columbia, UNITED STATES|D. Pham, Touro University Nevada College of Health and Human Services, Henderson, Nevada, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Medicare reimbursements for glaucoma procedures have declined on average by 21% since the year 2000. These trends can help guide changes to Medicare policies and may explain the change in glaucoma practice patterns over time.

Methods: Reimbursement data from the Physician Fee Schedule look-up tool from the Centers for Medicare and Medicaid Services was compiled for Glaucoma procedures. Compensation trends for each CPT code were investigated after adjusting for inflation in 2020 US dollars from the unadjusted data between 2000 to 2020.

Results: The average adjusted reimbursement for the analyzed procedures decreased by 20.5% (95% confidence interval [CI], -15.4% to -25.6%) over the twenty-year period. On average, there was a 1.03% decrease in reimbursement rates per year (95% confidence interval [CI], -0.74% to -1.33%) with an adjusted CAGR of -1.35% (95% confidence interval [CI], -1.07% to -1.64%). Procedures with the largest decrease in reimbursement over the study period included CPT codes 65855 (Trabeculoplasty by laser surgery, 48.9%), 66761 (Iridotomy/iridectomy by laser surgery, 37.0%), and 66700 (Destruction ciliary body by diathermy, 32.37%). The only CPT code for which an increase in reimbursement rate was observed was 66762 (Laser iridoplasty by photocoagulation, 1.89%). These results show an overall declining rate in reimbursement for the glaucoma procedures analyzed in this study.

Conclusions: Medicare reimbursement for glaucoma procedures showed a significantly declining trend between 2000 to 2020. The varying trends seem to closely reflect the political and economic climate of the times. The declining trends previously led to some physicians refusing to take new Medicare patients. However, the legislative impact of the Consolidated Appropriations Act of 2020 brings hope for a future of rising Medicare reimbursement rates for Ophthalmology, and other medical specialties.

CONTROL ID: 3709476

SUBMITTER (NAME ONLY): Angus Grey

TITLE: Small molecule movement in the bovine lens – comparing and contrasting nutrient and pharmaceutical uptake and metabolism with MALDI mass spectrometry

SESSION TITLE: Lens Physiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To maintain tissue transparency, the ocular lens is avascular and operates a microcirculation that delivers nutrients and removes waste products from the lens nucleus. Breakdown of lens structure or function can lead to lens cataract. Globally, lens cataract is the leading cause of preventable blindness, yet the only ‘cure’ is surgical implantation of a synthetic lens. MALDI imaging mass spectrometry (IMS) has been used to map uptake of exogenous molecules to inform development of novel pharmaceutical approaches to delay or prevent the onset of cataract.

Methods: Bovine lenses were incubated from 5 min-20h in artificial aqueous humour containing stable isotopically-labelled (SIL) lens nutrients (glucose, glutathione) or pharmaceuticals. Axial cryosections (20mm) were analysed by negative and positive mode MALDI-FT-ICR IMS, respectively. Identical samples were microdissected into epithelium, outer cortex, inner cortex and nucleus regions. Gas chromatography mass spectrometry was then used on extracts of these lens regions to validate spatial distribution patterns observed by IMS, and confirm identities of small molecules observed by IMS. Liquid chromatography tandem mass spectrometry-based proteomics and immunohistochemistry were used to detect and localise specific small molecule transport proteins throughout the lens.

Results: For SIL lens nutrients, MALDI IMS showed signal first appeared in the peripheral epithelium and lens equator. Several members of the solute carrier family of integral membrane proteins (e.g. GLUT1, GLUT3) were also detected by proteomics and immunohistochemistry in this region. In contrast, uptake profiles for pharmaceuticals were less spatially directed than for lens nutrients. Rates of transport of pharmaceuticals throughout the lens were also different between pharmaceuticals with different physicochemical properties.

Conclusions: A combination of mass spectrometry techniques for protein, metabolite and pharmaceutical detection and mapping can be utilised to aid development of future therapeutic interventions that exploit lens physiological biochemistry to delay the onset of cataract.

CONTROL ID: 3709477

SUBMITTER (NAME ONLY): Ranit Karmakar

TITLE: Mobile-RetinaNet : A Computationally Efficient DeepNet for Retinal Fundus Image Segmentation for Use in Low-resource Settings

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Karmakar, S. Nooshabadi, Electrical and Computer Engineering, Michigan Technological University, Houghton, Michigan, UNITED STATES|A. Eghrari, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal fundus photography is used by physicians to detect and track different eye diseases such as glaucoma and diabetic retinopathy (DR). Manual segmentation is time-consuming and may introduce observational bias. This work presents a computer-aided automatic segmentation model for the retinal blood vessels and optic disc in retinal fundus images. Accurate automatic detection of these image features will reduce the manual effort while producing consistent results in clinical settings instantaneously.

Methods: The efficient use of bottleneck residual blocks on the U-Net like encoder-decoder convolutional neural network (CNN) architecture requires a significantly lesser number of floating-point operations (FLOPs) to achieve the desired accuracy. The model has been trained and tested on two publicly available retinal datasets, digital retinal images for vessel extraction (DRIVE) and child heart and health study in England (CHASE). The model's performance is compared with the prior art using widely used accuracy, sensitivity, specificity, and the area under the curve (AUC). For the OD segmentation, we proposed a fully automatic segmentation that uses classical image processing to localize the OD and then our network to do the semantic segmentation.

Results: For retinal vessel segmentation, we achieved an AUC score of 0.968 for the DRIVE dataset and 0.985 for the CHASE dataset which for the state-of-the-art is 0.986 and 0.991 respectively. With this small degradation in performance, our model needs 2.5 times a lesser number of parameters and 4.5 times fewer FLOPs. For OD segmentation, we achieved an AUC score of 0.950 and 0.981 for the DRIVE and CHASE datasets respectively

Conclusions: While deep learning models can be high resource-consuming, successfully developed a model that achieves very high efficiency for medical image segmentation task without loosing much accuracy.

CONTROL ID: 3709478

SUBMITTER (NAME ONLY): Stephen Hunter

TITLE: Evaluating the effectiveness of the PlusoptiX S12C photoscreener in detecting amblyopia risk factors in preschool children within one year of a mobile community vision screening program

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hunter, D. Suh, J. He, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Stephen Hunter: Commercial Relationship: Code N (No Commercial Relationship) | Donny Suh: Commercial Relationship: Code N (No Commercial Relationship) | Jody He: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To reduce the disease burden and increase early detection of amblyopia, the US Preventive Services Task Force recommends at least one vision screening for all children aged 3 to 5 years. The UCI EyeMobile for Children Program is a mobile community vision screening program designed to detect amblyopia or its risk factors in preschool children, and provide further eye care services including referral to ophthalmology if needed. We performed retrospective chart review to determine the effectiveness of our screening device in detecting amblyopia or its risk factors.

Methods: Children aged 30 to 72 months from 37 Orange County preschools underwent vision screening at their schools during the 2019 - 2020 school year. All screenings were conducted with the PlusoptiX S12C by two trained screeners using ROC 3 referral criteria. Children who failed the vision screening were given an appointment for a comprehensive eye examination on the UCI EyeMobile. Excluded from this group were those students absent from the school on the dates screening took place and those who had not provided signed consent forms. Amblyopia RF were determined using 2013 American Association for Pediatric Ophthalmology and Strabismus Vision Screening Committee Guidelines.

Results: A total of 5,226 children were screened during the 2019 - 2020 school year. 10.4% (546/5226) failed the photoscreening. 27.3% (149/546) were no-shows. 397 children were seen by an optometrist, of which 246 received complete comprehensive examinations including cycloplegic retinoscopy. 149 of these children were found to have at least one ARF, corresponding to a device positive predictive value (PPV) of 60.6% for detecting ambylogenic risk factors in the dilated group. Of the 151 children who were examined but did not undergo cycloplegic retinoscopy, 61 were found to have at least one ARF, corresponding to a PPV of 40.4% in the undilated group. The PPV for all 397 children examined was 52.9%.

Conclusions: Vision screening is crucial for the early detection and treatment of ambylopia. With a PPV of 52.9% for the detection of ambylopia and its risk factors, the PlusoptiX S12C is an adequate screening device for our program. We will consider modifying the device referral criteria as other studies have demonstrated this may lead to increased specificity and PPV.

CONTROL ID: 3709480

SUBMITTER (NAME ONLY): Hannah Youngblood

TITLE: Response of trabecular meshwork cells to estradiol under TGFβ2- and stretch-induced stress

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Youngblood, H. Yu, P.V. Schoenlein, Y. Liu, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|P.V. Schoenlein, Radiology, Augusta University, Augusta, Georgia, UNITED STATES|H. Xu, Population Health Sciences, Augusta University, Augusta, Georgia, UNITED STATES|Y. Liu, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The only modifiable risk factor for primary open-angle glaucoma, elevated intraocular pressure (IOP), is regulated by trabecular meshwork (TM)-related aqueous humor outflow. Estrogen signaling may play a role in lowering IOP. We sought to determine if 17β-estradiol (E2) treatment of primary human TM (HTM) cells could reverse the transcriptional profile induced by ocular hypertension (OHT)-inducing TGFβ2.

Methods: Primary HTM cells from 10 donors were cultured for >24 hours in estradiol-free medium before treating in the following groups: medium only, DMSO, 50nM E2, 10ng/mL TGFβ2, and 50nM E2 + 10ng/mL TGFβ2. For each cell line, treatments were performed simultaneously on cells cultured statically on plastic 6-well plates and cells undergoing cyclical stretch (1 cycle/sec) on a Flexcell Tension System for 24 hours. qRT-PCR was performed to assay the expression of 17 selected TGFβ2-responsive genes. The $\Delta\Delta C_t$ method followed by one-way ANOVA was used to calculate expression changes in response to treatments normalized to ACTB expression. Using relative fold changes, a linear mixed effect model was used to test for the overall effects of stretch and sex on gene expression, using treatment, stretch, and sex as covariates.

Results: Of the 17 TGFβ2-responsive genes profiled, TGFβ2 treatment significantly altered the expression of 4 genes in static and 8 genes in stretched HTM cells. Conversely, E2 treatment significantly altered the expression of 11 genes in static and BMP1 in stretched HTM cells. In several cases, genes that were significantly downregulated in response to TGFβ2 were significantly upregulated in response to E2 (e.g., SMAD2 and SMAD3 in static cells and BMP1 in stretched cells). Furthermore, in cells treated with both E2 and TGFβ2, E2 lessened or reversed the effects of TGFβ2 for several genes (e.g., NFATC1 and SMAD2 in static cells and BMP1, FST, GREM1, LAMC1, NFATC1, SMAD2, and SMAD3 in stretched cells). In addition to treatment response, nine genes were significantly impacted by stretch while two genes were significantly impacted by the sex of the cell donor.

Conclusions: TGFβ2 had more significant effects under stretch, suggesting that stretch may exacerbate TGFβ2 effects. In many cases, E2 was able to mitigate or reverse the transcriptional effects of TGFβ2. Therefore, E2 may ameliorate the effects of OHT-inducing TGFβ2 to reduce IOP, especially under conditions of mechanical stress.

CONTROL ID: 3709485

SUBMITTER (NAME ONLY): Xingjun Fan

TITLE: Lipid peroxidation induces ferroptosis in the lens epithelium

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Fan, Z. Wei, C. Hao, J. Huangfu, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|R. Srinivasagan, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|X. Zhang, Environmental and Public Health, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress is considered the central pathogenesis of age-related cataractogenesis. Aged and cataractous human lenses manifest with increased reactive oxygen species (ROS) formation, elevated lipid peroxidation, and accumulative intracellular redox-active iron. Interestingly, ample evidence suggests that there is no remarkable apoptosis present in aged and cataractous human lenses despite the profound disruption of redox homeostasis, raising an essential question regarding the existence of other cell death mechanisms. Here we sought to explore the role of lipid peroxidation in lens epithelial cell death.

Methods: Cell death pathways were explored using both in vitro cell aging model and ex vivo mouse lens capsule aging model. Lipid peroxidation and cell apoptosis markers were determined. Gene expression was performed by the deep sequencing approach.

Results: Here we show that the aging lens epithelium is susceptible to ferroptosis-mediated cell death via lipid peroxidation. We show that very low concentrations of system X_C^- inhibitor Erastin (0.5uM) and glutathione peroxidase 4 (GPX4) inhibitor RSL3 (0.1uM) can drastically induce human LEC (FHL124) ferroptosis in vitro and mouse lens epithelium ferroptosis ex vivo. Depletion of intracellular glutathione (GSH) in human LECs and mouse lens epithelium significantly sensitizes ferroptosis, particularly under the RSL3 challenge. Intriguingly, both human LECs and the mouse lens epithelium demonstrate an age-related sensitization of ferroptosis. Transcriptome analysis indicates that clusters of genes are up-or down-regulated in aged LECs, impacting cellular redox and iron homeostases, such as downregulation of both cystine/glutamate antiporter subunits SLC7A11 and SLC3A2 and iron exporter ferroportin (SLC40A1).

Conclusions: Here, for the first time, we are suggesting that LECs are highly susceptible to ferroptosis. Moreover, aged and cataractous human lenses may possess more pro-ferroptosis criteria than any other organ in the human body.

CONTROL ID: 3709486

SUBMITTER (NAME ONLY): Diego Alba

TITLE: Transient PERG extracted from Steady-State PERG in Glaucoma suspects

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Alba, V. Porciatti, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Toft-Nielsen, Jörvec Corporation, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To use the Continuous Loop Averaging Deconvolution (CLAD) technique to extract a per-stimulus PERG (Transient) from steady state (SS) PERG at jittered high-frequency stimulation rates, and compare CLAD PERG data from a pool of glaucoma suspects (N=23) with those of age matched controls (N=16).

Methods: PERG were recorded in response to contrast-reversal of horizontal gratings (LED display JÖRVEC Corp, mean luminance 800 cd/m^2, contrast ratio 99%) presented under 3 conditions: Conventional transient PERG at 3.91 rev/sec, conventional SS-PERG at 15.63 rev/sec, and jittered 'quasi' steady state (Q-SS) PERG at 15.63 mean rev/sec. Q-SS responses were deconvolved using CLAD (PMID: 25477321; 24618216), extracting the equivalent per-stimulus transient response at 15.63 rev/sec, obtaining a response with peaks and troughs similar to a conventional transient PERG. For conventional and deconvolved transient responses, waveform peaks (N35, P50, N95) were identified and latencies and amplitudes were measured. For conventional SS-PERG responses, analysis was done in the frequency domain, by looking at the phase and magnitude of the response at the frequency bin corresponding to the rate of stimulation (15.63 rev/sec).

Results: In all three conditions, there was a significant difference between the control and glaucoma suspect groups ($p<0.05$), with the CLAD deconvolved response having the most significant difference between the two groups. Receiver operator curves (ROC) generated for the three cases resulted in area under the curve (AUC) values of 0.789 for conventional transient responses (P50 to N95 amplitude), 0.683 for conventional SS PERG (SS magnitude) and 0.897 for deconvolved Q-SS responses (P50 to N95 amplitude).

Conclusions: Results show that while all the methods were effective differentiating between control and glaucoma suspect groups, the CLAD deconvolved responses had the highest specificity, suggesting that the CLAD technique unveils some clinically relevant information that is obscured in the SS response when using conventional analysis techniques. This has the potential to greatly expand the diagnostic utility of the PERG response.

CONTROL ID: 3709490

SUBMITTER (NAME ONLY): Marlyn Langford

TITLE: Distribution of gamma-glutamyltranspeptidase, aldose reductase, and biomarkers of oxidative stress in STZ-induced diabetic rat lens

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.P. Langford, T.B. Redens, Ophthalmology, LSU Health Shreveport, Shreveport, Louisiana, UNITED STATES|R. Eshaq, N. Harris, Molecular and Cellular Physiology, LSU Health Sciences Center, Shreveport, Louisiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate gamma-glutamyl transpeptidase (GGT, critical to glutathione recapture and cysteine-dependent cell proliferation), Xc- antiporter, (xCT, cysteine transporter), aldose reductase (AR, hyperglycemic oxidative stress marker), oxidized DNA [8-hydroxy-2'-deoxyguanosine (8-OHdG), and annexin V (marker of apoptosis) expression in streptozotocin (STZ)-induced diabetic cataractous and normal rat lens.

Methods: Gross ocular examinations were performed, and blood glucose levels were determined on control and diabetic rats. Bilateral eye enucleations were performed post euthanasia at 8 weeks and the eyes placed in 70% ethanol. Histopathology was determined on paraffin-embedded sections stained with hematoxylin and eosin. DAPI-treated sections were reacted with antibody to AR, GGT, 8-OHdG, and/or annexin V. The lens distributions were visualized using the immunohistochemical and immunofluorescent antibody methods, and digital images captured for comparative analysis.

Results: Cytopathological changes consistent with lens epithelial cells disorganization and lens cell hyperplasia were noted in hyperglycemic rat cataractous lenses. GGT was expressed by epithelial cells and diminished to undetectable levels within 1 mm of the control rat lens surface. AR and oxidized DNA (8-OHdG) were detected in normal lens beneath the lens cortex within lens fibers (1 mm from the surface). Xc-antiporter (xCT) expression was reduced in diabetic lens. Weak annexin V reactivity was detected in the lens epithelium. In the diabetic rat lens, GGT expression in epithelial cells was decreased, while GGT was detected on sub-capsular hyperplastic lens cells. Increased AR expression and oxidized DNA (8-OHdG) were detected in the sub-capsular hyperplastic lens fiber cells of diabetic rat lens. Oxidized DNA was detected in annexin V-positive lens epithelial cells of some diabetic lenses.

Conclusions: The sub-capsular cataractogenic changes in STZ-induced hyperglycemic diabetic rats were associated with increased expression of AR and GGT with oxidized DNA-positive hyperplastic lens fiber cells. The results support hyperglycemia-induced inhibition of epithelial-to-mesenchyme lens fiber cell differentiation and oxidative epithelial cell death as evidenced by annexin V expression.

CONTROL ID: 3709493

SUBMITTER (NAME ONLY): Jeff Huang

TITLE: Dermatologic UV-related cancers in the head and neck region are associated with exfoliation syndrome in a New York City-based clinic population

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, J.E. Geduldig, T.T. Tai, S. Ahmad, N. Chadha, K. Vinod, L.R. Pasquale, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|E.B. Jacobs, T.T. Tai, S. Ahmad, N. Chadha, D. Buxton, K. Vinod, R. Ritch, L.R. Pasquale, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|B.M. Wirostko, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|J. Kang, Brigham and Women's Hospital Channing Division of Network Medicine, Boston, Massachusetts, UNITED STATES|J.L. Wiggs, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Exfoliation syndrome (XFS) is a systemic disease in which extracellular matrix deposits (exfoliation material, XFM) are found in the anterior segment of the eye. Prior studies suggest that ocular UV radiation in early life is a risk factor for XFS. We performed a clinical survey study to assess the relationship between UV exposure in early life with XFS using UV-associated carcinomas [basal cell carcinoma (BCC), and squamous cell carcinoma (SCC)] history in specific regions of the body as a proxy for UV exposure.

Methods: Subjects were recruited for a one-time cross-sectional interview survey assessing age, sex, medical history, XFS diagnosis, eye color, hair color, likelihood of tanning or burning in early life, and history of BCC and/or SCC. Multivariate models adjusting for these covariates were performed.

Results: 321 subjects were recruited for the study (52.6% female, 96.2% white ethnicity, mean age: 72.6 years). 98 (30.5%) patients had XFS/XFG, 117 (36.5%) had primary open-angle glaucoma (POAG) and 106 (33.0%) were non-glaucomatous controls (Tbl. 1). After adjusting for the covariates, there was a 2-fold risk for having XFS with any history of BCC/SCC in the head and neck region versus POAG + controls (odds ratio (OR) = 2.05, 95% confidence interval (CI) = 1.04 – 3.89). Additionally, we observed a dose-response association where the chance of having XFS was higher by 67% with every BCC/SCC occurrence versus POAG + controls (OR = 1.67, 95% CI = 1.09 – 2.56). XFS versus control groups showed a 2.8-fold risk for XFS with any history of head/neck BCC/SCC (OR = 2.80, 95% CI = 1.12 – 7.02), and a 2-fold risk for each additional count of UV-related carcinomas (OR = 1.97, 95% CI = 1.09 – 3.58).

When BCC/SCC located anywhere on the body was considered, there were non-significant increased odds of XFS (OR = 1.65, 95% CI = 0.88 – 3.09).

There were no associations between head and neck BCC/SCCs and POAG compared to controls (OR = 1.15, 95% CI = 0.58 – 3.48).

Conclusions: Having BCC/SCC specifically in the head and neck region is associated with a 2-fold increase in risk for XFS/XFG. These findings support prior evidence that UV exposure may be a significant risk factor for XFS. In addition, these results provide further support for in vitro studies analyzing the effects of UV exposure in generating XFM and also strengthen recommendations for UV protection.

CONTROL ID: 3709494

SUBMITTER (NAME ONLY): Yvette Schein

TITLE: Risk Factors for Severe Retinopathy of Prematurity Among Low-risk Infants

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Schein, G. Binenbaum, Division of Ophthalmology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|Y. Yu, G. Ying, Scheie Eye Institute, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Postnatal Growth and ROP Studies (G-ROP-1&2) developed new ROP screening criteria with 100% sensitivity for type 1 and 30% fewer infants requiring exams. However, the criteria are slightly less sensitive for type 2. Currently under conventional screening criteria, outlier infants are identified with a subjective criterion of neonatologist judgment of a “poor postnatal course.” We identified risk factors for developing stage 2 and 3 in infants who were older, larger, or had faster weight gain than the G-ROP criteria to help neonatologists identify these outlying infants.

Methods: Secondary analysis of 2312 of 7483 infants in G-ROP-1 who did not meet the proposed G-ROP criteria. 5(0.2%) had stage 3; 57(2.5%) had stage 2. Medical and surgical comorbidities of prematurity during the first 28 postnatal days were evaluated using multivariable analysis.

Results: Factors associated with stage 2 or 3 ROP were no enteral feeding in first 3 weeks (aOR 5.6, 95% CI 2.6-12.1; 9 or more days on supplemental oxygen in first 4 weeks (aOR3.34, 2.0-5.6); NEC (aOR 4.2, 1.0-17.5); and IVH grade III/IV (aOR 2.6, 0.9-7.6). Risk of stage 2 or 3 increased with number of risk factors: 20/1575(1%) for 0; 34/636(5%) for 1; 7/51(14%) for 2; 1/3(33%) for 3.

Conclusions: NEC, IVH grade III/IV, 9 or more days on supplemental oxygen in first 4 weeks, and no enteral feeding in first 3 weeks are associated with increasing risk of stage 2 or 3 ROP. Counting the number of factors may help identify outlier infants requiring ROP examinations.

CONTROL ID: 3709498

SUBMITTER (NAME ONLY): Haakon Fjaervoll

TITLE: The Purinergic 2 X Receptor Agonists ATP, BzATP and 2MeSATP use ER Stores to Increase Cytosolic Free Calcium

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Fjaervoll, K. Fjaervoll, M. Yang, J. Bair, T. Utheim, D.A. Dartt, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|H. Fjaervoll, K. Fjaervoll, The Medical Student Research Program, Universitetet i Oslo Det medisinske fakultet, Oslo, Oslo, NORWAY|T. Utheim, Department of Medical Biochemistry, Oslo Universitetssykehus, Oslo, NORWAY|

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ABSTRACT BODY:

Purpose: Ionotropic purinergic receptors (P2XRs) are formed as hetero- or homotrimers from seven subunits, and are activated by extracellular nucleotides such as ATP. Upon activation, the P2XRs become permeable to cations, leading to activation of intracellular signaling pathways and an increase in cytosolic free calcium ($[Ca^{2+}]_i$). All P2XRs are present on cultured rat conjunctival goblet cells (CGCs). The purpose of this study was to investigate the source of the free cytosolic calcium in CGCs after the stimulation with ATP and the ATP analogues BzATP and 2MeSATP.

Methods: Goblet cells were cultured from rat conjunctival explants. First passage CGCs were incubated with the ratiometric fluorescent dye Fura 2-AM in: 1. buffer containing calcium or in calcium free buffer with or without 2 mM EGTA, or 2. calcium-containing buffer with or without the sarco/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) inhibitor thapsigargin (10^{-6} M) that depletes ER Ca^{2+} stores. The CGCs were then stimulated with the non-specific P2XR agonist ATP (10^{-7}-10^{-5} M) or the ATP analogues BzATP (10^{-7}-10^{-4} M) or 2MeSATP (10^{-7}-10^{-5} M), and $[Ca^{2+}]_i$ measured.

Results: $[Ca^{2+}]_i$ was significantly increased from baseline when stimulated with ATP (10^{-7}-10^{-4} M), BzATP (10^{-7}-10^{-4} M) or 2MeSATP (10^{-7}-10^{-5} M), with a maximal response for ATP at 10^{-5} M, BzATP at 10^{-4} M and 2MeSATP at 10^{-5} M in buffer containing calcium. The change in peak $[Ca^{2+}]_i$ was not significantly different in calcium free buffer, but was significantly reduced in the presence of 2 mM EGTA. The $[Ca^{2+}]_i$ increase in CGCs preincubated with thapsigargin was completely reduced for ATP at 10^{-4} M, BzATP at 10^{-4} M and 2MeSATP at 10^{-5} M.

Conclusions: We conclude that ATP and the ATP analogues BzATP and 2MeSATP increase $[Ca^{2+}]_i$ mainly through releasing ER calcium stores.

CONTROL ID: 3709499

SUBMITTER (NAME ONLY): Felicitas Bucher

TITLE: Oncostatin M reduces hypoxia-induced retinal neovascularization through Müller cell activation

SESSION TITLE: Blood flow and ischemia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Bucher, J. Rapp, P. Liang, G.R. Schlunck, H.T. Agostini, Eye Center, Medical Center, Faculty of Medicine, University of Freiburg, GERMANY|

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ABSTRACT BODY:

Purpose: Retinal neovascularization (NV) represents a common hallmark of retinal ischemic diseases in the context of diabetes or retinal vascular occlusion. While hypoxia is known to be a main driver of vascular endothelial cell proliferation and retinal neovascularization, it becomes more apparent that the inflammatory microenvironment and associated signaling pathways modulate hypoxia driven angiogenesis. In this study, we analyze the effect of Oncostatin M (OSM), a strong STAT3 activator with well-documented pro-angiogenic properties outside the eye, in a mouse model of hypoxia-induced retinopathy.

Methods: In the mouse model of oxygen-induced retinopathy (OIR) Bl6/J pups were subjected to hyperoxia between postnatal day (P) 7 and 12. Upon return to room air at P12 mice received intravitreal injections with 0.5µL of 100ng/µl OSM or PBS control. Retinal vascular phenotype following treatment was quantified at P17. Western blot analysis and immunohistochemical stainings on retinal cryosections for pSTAT3 were performed 12h post injection. Retinal vascular endothelial cells were isolated at P17 via cell sort using a CD31+/CD45- gating strategy and submitted for RNA sequencing.

Results: OSM reduced retinal NV in the OIR model by 65,2% compared to PBS-treated controls (N=11 mice, $p<0.05$). Western blot analysis showed a clear increase in pSTAT3 levels in retinal lysates 12 h post treatment. Immunohistochemical analysis visualized a positive pSTAT3 signal in the inner nuclear layer as well as GFAP upregulation in Müller cells suggesting a primary Müller cell response to OSM treatment. RNA sequencing of sorted vascular endothelial cells at OIR P17 revealed a downregulated angiogenic profile following OSM treatment (GSEA: GO angiogenesis, enrichment score 0.287 $p<0.05$).

Conclusions: OSM possesses therapeutic potential by a primary activation of Müller cells resulting in downregulation of angiogenic drivers in vascular endothelial cells.

CONTROL ID: 3709502

SUBMITTER (NAME ONLY): Frank Bucci

TITLE: A Contralateral Comparison of a Trifocal vs a Multifocal +3.25 IOL: Pt Preference, Visual Performance, & Predictors of Overall Satisfaction

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.A. Bucci, Bucci Laser Vision, Wilkes Barre, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Frank Bucci: Commercial Relationship(s);Code F (Financial Support):Johnson and Johnson

ABSTRACT BODY:

Purpose: To compare pt preference, visual performance, and overall satisfaction in pts receiving a trifocal (PanOptix) in one eye and a multifocal (Tecnis +3.25) in the opposite eye. To identify by regression analysis patient variables that predict pt preferences and overall satisfaction.

Methods: 30 KPE pts (60 eyes) were prospec. randomized to receive a PANO in one eye and a TMF +3.25 in the other eye. A pt questionnaire was administered to evaluate distance,intermediate, and near vision,halos,glare,and starbursts, and overall pt satisfaction. The M&S Clinical Trial Suite was used to assess letter acuity, sine wave, and bullseye contrast sensitivity. Metrics such as uncorrected visions, residual sph and cyl, angle kappa, HOAs, and pupil size were also evaluated. Regression analysis was used to identify objective and subjective variables acting as significant predictors of overall pt satisfaction and IOL preference.

Results: Pts signif preferred (p=.028) the TMF(18) to the PANO(7), and no preference(5). “Overall Satisfaction” was sig greater (4.70/5.00) for TMF vs (4.43/5.00) PANO (p=.05). Uncorrected distance vision was sig greater (p=.032) and best corrected dist acuity trended better (p=.059) for TMF eyes. The questionnaire revealed sig better (p=.05) responses for “frequency of glasses use at distance” and trended (p=.10) for “ability to function at distance without glasses” for TMF eyes. The objective varaibale of intermed (Jaeger) vision was sig better (p=.034) in PANO eyes. However, the subjective variable “frequency glasses use at intermed” trended (p=.10) for TMF eyes. For both TMF and PANO eyes, regression revealed that variables related to reading fine print and intermediate (Jaeger) vision were sig predictors of overall patient satisfaction. But for the PANO eyes only, 2 sine wave contrast sensitivity variables – “sine wave contrast sensitivity with glare” and “sine wave contrast sensitivity without glare” were both highly sig predictors of overall satisfaction in just the PANO eyes.

Conclusions: TMF was sig preferred to PANO (18 TMF,7 Pano,5 no pref). The “overall pt satisfaction” score by pt questionnaire was sig greater (p=.05) for TMF. Regression analysis strongly suggests that issues related to contrast sensitivity both with and without glare may be responsible for the significant preference for the TMF IOL.

CONTROL ID: 3709504

SUBMITTER (NAME ONLY): Myoungsup Sim

TITLE: Shear stress-induced autophagy regulates endothelial nitric oxide synthase (eNOS)/nitric oxide (NO) production via primary cilia in Schlemm's canal cells

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sim, K.M. Perkumas, W.D. Stamer, P.B. Liton, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Changes in intraocular pressure (IOP) are "sensed" by stretching of trabecular meshwork (TM) cells and shear stress on Schlemm's canal (SC) cells. We previously reported stretch-induced primary cilia (PC)-mediated activation of autophagy as a crucial physiological response for regulating IOP homeostasis in TM cells. Here we investigate the role of autophagy upon shear stress in SC cells.

Methods: Primary human SC cells (6 strains) and human umbilical vein endothelial cells (HUVECs) were subjected to shear stress (1~10 dyne/cm^2) for up to 24 h. Autophagy activation was monitored by measuring LC3-II and SQSTM1 levels, tandem fluorescent-tagged LC3 (tfLC3) or SQSTM1-RFP using western blot or live cell imaging. PC were detected by PC markers (acetylated-TUBA4A, IFT88 and 5HT$_6$-mcherry) and disrupted by chloral hydrate (2 mM for 3 day). The expression and activity of eNOS were measured by GFP under the control of eNOS promoter (eNOSpd-GFP) and phosphorylated eNOS (S1177). Autophagy was inhibited by bafilomycin A (50~100 nM) or siRNA targeting LC3B.

Results: Autophagy marker proteins (LC3 II and SQSTM1) significantly increase by approximately 2 fold ($p<0.05$, $n=6$) upon flow application (10 dyne/cm^2 for 24 h) in the SC cells. Time-lapse live imaging of tfLC3 and SQSTM1-RFP showed that autophagic activity increases and SQSTM1 is aggregated and continuously removed by autophagic vacuole-like structures upon shear stress. Immunochemical and live cell imaging analyses revealed the presence of PC in SC cells. Deciliation significantly prevented the increase in LC3-II levels by shear stress in SC cells (CNT vs deciliated: 2.36±0.58 vs 0.78 ±0.62, $n=4$, $p<0.05$). Time-lapse live imaging of eNOSpd-GFP and western blot showed that the transcription and phosphorylation of eNOS increase by shear stress, and removal of PC decreased eNOS phosphorylation in SC cells. Intriguingly, bafilomycin treatment decreased eNOS protein levels in HUVECs in a concentration-dependent manner, and LC3 knockdown decreased eNOS protein level of HUVECs in static and shear stress conditions (10 dyne/cm^2 for 24 h).

Conclusions: We demonstrate here for the first time the PC-mediated autophagy activation in response to physiological levels of shear stress in SC cells. Moreover, our data strongly suggest that the shear stress-induced autophagy regulates eNOS/NO production in SC cells.

CONTROL ID: 3709506

SUBMITTER (NAME ONLY): Lev Prasov

TITLE: Single cell RNA sequencing reveals the role of Myelin regulatory factor (MYRF) in regulating melanogenesis and cell structure during retinal pigment epithelial development.

SESSION TITLE: Single cell analysis in retinal research in health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Prasov, S.Q. Wang, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|L. Prasov, M.L. Brinkmeier, A. Yakoo, L.Y. Cheung, Human Genetics, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Lev Prasov: Commercial Relationship: Code N (No Commercial Relationship) | Michelle Brinkmeier: Commercial Relationship: Code N (No Commercial Relationship) | Su Wang: Commercial Relationship: Code N (No Commercial Relationship) | Athera Yakoo: Commercial Relationship: Code N (No Commercial Relationship) | Leonard Cheung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Variants in the transcription factor MYRF have been described in a cardiac urogenital syndrome and familial and sporadic nanophthalmos, but the mechanism of pathogenesis is unclear. Using a conditional mouse model of Myrf loss of function (Myrf fl/fl) in the early eye cup (RxCre), we previously showed that loss of Myrf leads to retinal degeneration and loss melanin pigment in the retinal pigment epithelial (RPE). Here, we identify specific gene expression changes caused by MYRF deficiency using single cell RNA sequencing (scRNAseq).

Methods: scRNAseq was conducted at 3 developmental timepoints (E13.5, E15.5, P0) using pools of eye cups from RxCre Myrf fl/fl or matched Myrf fl/fl littermates, and data were processed using CellRanger and Seurat. Histology, RNAscope in situ hybridization, and electron microscopy (EM) were used to validate gene expression findings.

Results: Cell clustering revealed that Myrf deficiency altered cell type distributions with reductions in RPE cells at all timepoints. Cell cycle dynamics were stable, consistent with increased cell death in mutants. There was also a compensatory increase in retinal progenitor (RPC) population at P0, without alteration in overall cell cycle dynamics. Differential gene expression analysis and PANTHER gene ontology-term analysis revealed down regulation of key pathways in mutant RPE cells, including melanosome biogenesis, cytoskeleton, and extracellular matrix. EM analysis and immunofluorescence staining of RPE flatmounts confirmed structural defects in RPE and disorganization of photoreceptor outer segments, loss of melanosomes, and alterations in novel structural proteins in the apical RPE. Compensatory upgregulation of Prss56, another gene implicated in nanophthalmos, was found in the RPC population.

Conclusions: These results suggest that MYRF plays a critical role in regulating RPE structure and function during development, which likely contributes to abnormal outer segment morphology and retinal degeneration in RxCre Myrf fl/fl mice. Compensatory gene expression changes in the retina may act maintain proper ocular size in mice. These studies inform molecular mechanisms of nanophthalmos and support a role for RPE in this condition.

CONTROL ID: 3709510

SUBMITTER (NAME ONLY): Michael Foster

TITLE: Long-term Outcomes in Neovascular Age-Related Macular Degeneration Eyes with Baseline Macular Atrophy on Anti-VEGF Treatment

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Foster, C.A. Urbano, C.M. Maatouk, M. Bui, G.L. Hom, B.L. Kuo, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|B.L. Kuo, R.P. Singh, K.E. Talcott, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies on long-term outcomes of neovascular age-related macular degeneration (nAMD) eyes on anti-vascular endothelial growth factor (anti-VEGF) injections are limited, especially if there is baseline macular atrophy (MA). This study aims to understand the long-term outcomes of nAMD eyes with baseline MA undergoing anti-VEGF injections.

Methods: This was a retrospective chart review of nAMD patients receiving at least twice-yearly anti-VEGF injections for nAMD for at least 5 years at Cole Eye Institute from 2012 to 2019. Measurements for sub-RPE illumination (SRI), foveal distance to atrophy (FDA), best visual acuity (BVA), and intraocular pressure (IOP) were collected annually. Eyes were excluded if subretinal fluid precluded reliable measurements or if one-year change in SRI or FDA was greater than 2 standard deviations from the cohort mean. 5-year change in BVA was regressed on combinations of six patient characteristics and baseline measures.

Results: A total of 232 eyes of 232 patients (83.9±9.0 years, 64% female) with nAMD and at least 5 years of follow-up (mean 6.0 years) with anti-VEGF injections were identified. 76% (n=178) had baseline MA. Baseline BVA was 67.2±13.9 letters for those with MA and 70.8±11.6 without MA (p=0.0971). Both groups experienced an initial non-significant improvement in average BVA before BVA began to decline (Table 1). Average BVA for patients with no MA peaked in year 1 (+3.0 from baseline, p=0.2289) while average BVA in patients with MA peaked in year 2 (+1.3 from baseline, p=0.0947). Additionally, differences in annual BVA change or BVA change from baseline are not statistically significant between groups without and with baseline MA (Table 1, p≥0.1324). Multiple linear regressions found baseline SRI (p=0.0026) and gender (p=0.0401) to be statistically significant regressors for 5-year change in BVA. Age, baseline FDA, baseline BVA, and baseline IOP were not significant regressors.

Conclusions: In nAMD patients treated with anti-VEGF injections, there was an initial non-significant improvement in vision before decline after two years of treatment. Differences in annual BVA change or BVA change from baseline are not statistically significant between groups without and with baseline MA, but gender and baseline SRI were found to be significant predictors of 5-year BVA change. Larger studies are needed to further explore these trends.

CONTROL ID: 3709511

SUBMITTER (NAME ONLY): SO GOTO

TITLE: Short-term induction and recovery from contact lens-induced myopia model in guinea pig

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. GOTO, Y. Zhang, Q. Zhu, C.F. Wildsoet, Optometry and Visual Science, University of California Berkeley, Berkeley, California, UNITED STATES|Q. Zhu, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: SO GOTO: Commercial Relationship: Code N (No Commercial Relationship) | Yan Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Qiurong Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Christine Wildsoet: Commercial Relationship(s);Code F (Financial Support):Alcon

ABSTRACT BODY:

Purpose: To characterize the guinea pig contact lens (CL) induced myopia model, the temporal profile of short-term ocular changes both during induction and after treatment is terminated.

Methods: To induce myopia, 2-week-old pigmented guinea pigs (New Zealand strain, n = 8) wore monocular -10 D rigid gas-permeable (RGP) CLs for one week, while the fellow eye served as a control. Ocular measurements were made at baseline, 3, and 7 days after initiation of CL wear. The CL treatment was then terminated on day 7, and additional measurements were made 3, 7, and 14 days later. Measurements included retinoscopy (spherical equivalent refractive error; SE), noncontact optical biometry (axial length, AL), and spectral-domain optical coherence tomography (choroidal and scleral thicknesses; ChT & ScT).

Results: Mean interocular differences (treated - fellow) in SE and AL were significantly different from baseline after 3 and 7 days of CL wear ($p < 0.0001$). ChT was also significantly reduced by day 7 of CL wear ($p = 0.004$). Interestingly, while both SEs and ALs of treated eyes recovered fully within 7 days of CL removal, the earlier ChT thinning, during the induction phase, was replaced by sustained thickening compared to baseline values, remaining significantly so on day 7 ($p = 0.009$), but returning to the normal by day 14. While ChT changes would have contributed to AL changes, they were much smaller in magnitude than AL changes in both phases. Interocular differences in ScT showed no significant changes.

Conclusions: The above patterns of myopia induction and recovery validate this negative RGP-CL model as an alternative to traditional spectacle lens models, at least for guinea pigs. The scaling mismatch between ChT and AL changes warrants further investigation in relation to underlying mechanisms.

CONTROL ID: 3709512

SUBMITTER (NAME ONLY): Boon Lin Teh

TITLE: Outcomes of conventional phacoemulsification surgery in Fuchs' endothelial dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Teh, A. Mylla Boso, Y. Ang, P. Papadakou, N. Tzoumas, F.C. Figueiredo, Department of Ophthalmology, Royal Victoria Infirmary, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UNITED KINGDOM|F.C. Figueiredo, Bioscience Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Fuchs' endothelial corneal dystrophy (FECD) is the most common corneal endothelial dystrophy and a major cause of visual impairment. FECD patients are at increased risk of endothelial cell density (ECD) loss during cataract surgery, requiring careful surgical consideration. We examine the predictive factors for corneal decompensation and the proportion of FECD patients requiring corneal transplant following conventional phacoemulsification surgery.

Methods: We retrospectively included all patients with FECD undergoing phacoemulsification and intraocular lens implantation by a single surgeon (FF) during 2015–2021 in a UK tertiary hospital, all conducted with soft-shell technique using DuoVisc®. We collected best-corrected visual acuity (BCVA), specular microscopy, and pachymetry measurements pre- and post-operatively, as well as complications and need for further corneal transplant. We excluded patients without pre- and post-operative specular microscopy measurements and those with follow-up of less than 2 months.

Results: 64 eyes of 51 patients were included. The mean age was 73 years (SD=9), 59% female. Median follow-up was 32 months (IQR=18). 13 (20.3%) eyes required Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) after cataract surgery, nine planned on listing and four unplanned. Median time between operations was 3 months (IQR=4). Of the 51 eyes not needing DSAEK, there was a significant change in mean BCVA (−0.13 logMAR, P=0.01) and central corneal thickness (CCT; +19.9μm, P<0.001) following cataract surgery. There was no significant change in ECD (−14%, P=0.16), hexagonality (−3%, P=0.23), or mean cell area (P=0.30). Using multilevel logistic regression adjusted for age, sex, and inter-eye correlation, we find that pre-operative CCT significantly predicts the risk of corneal decompensation (OR 1.01/μm, 95% CI 1.00–1.03, P=0.02) and need for corneal transplant post-cataract surgery (OR 1.04/μm, 95% CI 1.02–1.08, P=0.002). Kaplan-Meier analyses identify pre-operative CCT as a predictor of time-to-transplantation (P<0.001) with an optimal cutpoint value of 591μm.

Conclusions: Conventional phacoemulsification surgery with soft-shell technique has favourable visual outcomes in FECD. Careful counselling of FECD patients before cataract surgery is important with high pre-operative CCT being a significant risk factor for post-operative corneal decompensation and need for corneal transplantation.

CONTROL ID: 3709516

SUBMITTER (NAME ONLY): Hannah Cobb

TITLE: Pre-existing porcine anti-human antibodies: Implications for xenotransplantation studies

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mathias, A. Palestine, Ophthalmology, University of Colorado Health, Aurora, Colorado, UNITED STATES|V. Canto Soler, University of Colorado Gates Center for Regenerative Medicine, Aurora, Colorado, UNITED STATES|H. Cobb, S. Aparicio-Domingo, K. Li, M. Flores-Bellver, M. Mathias, V. Canto Soler, CellSight Ocular Stem Cell and Regeneration Program, Department of Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado, School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Xenotransplantation in animal models is a necessary step to reach clinical trials in humans. However, transplantation of human cells into animal models results in severe immune rejection responses. To determine the mechanisms underlying xenotransplant rejection in porcine models, we tested the hypothesis of the potential presence of pre-existing anti-human antibodies that could be responsible for immediate recognition and rejection of transplanted human cells.

Methods: Transplants containing neural retina and retinal pigmented epithelium (RPE) cells derived from human induced pluripotent stem cells (hiPSCs) were implanted in the subretinal space of P23H transgenic and Yucatan pigs. Blood was collected before transplantation (basal level) and weekly for 6 weeks post transplantation. Serum derived from blood was used as a probe in dot blot and western blot assays to attempt to quantify and identify the presence of porcine antibodies against human neural retinal cells, RPE cells, and undifferentiated hiPSC in the weeks prior to and post-surgery. Protein bands identified in western blots are currently being analyzed by mass spectrometry.

Results: Serum collected throughout the 6 weeks post transplantation resulted in positive dot blot signals of relatively equal intensity, inconsistent with a gradually increasing immune rejection process. Furthermore, positive signals were identified from naive serum, collected prior to transplantation, suggesting that the animals expressed pre-existing anti-human antibodies. Further analysis revealed a discrete number of distinct bands in samples corresponding to human neural retina, RPE, and hiPSC, suggesting that pigs expressed antibodies against specific human proteins. Naïve serum from both P23H transgenic and Yucatan pigs recognized equivalent molecular weight bands in neural retina (90kD, 70kD, and 45kD), RPE (70kD, and 45kD), and undifferentiated hiPSC (90kD, and 70kD) samples.

Conclusions: These studies suggest that xenotransplantation of hiPSC-derived retinal transplants in pigs is challenged by the presence of pre-existing anti-human antibodies in the naïve animal model. Follow-up studies will aim at identifying the specific human proteins against which pigs possess pre-existing immunity. Identification of these proteins would be instrumental in devising appropriate strategies to prevent xenotransplant rejection in pre-clinical porcine models.

CONTROL ID: 3709519

SUBMITTER (NAME ONLY): Arthi Bharadwaj

TITLE: Patient Adherence to Immunosuppressive Therapy for Chronic Inflammatory Eye Disease

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Bharadwaj, S. Kravets, J. Hallak, P. Bhat, A. Lobo, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|S. Kravets, Division of Epidemiology and Biostatistics, University of Illinois Chicago School of Public Health, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study investigates adherence rates to immunosuppressive therapy (IMT) for treatment of chronic noninfectious inflammatory eye disease (IED), the relationship between adherence to IMT and disease control, and factors associated with nonadherence in a tertiary care uveitis clinic.

Methods: Retrospective review of medical charts from 2015-2020 was conducted on patients with IED at 6 months, 1 year, and 2 years after initiation of IMT. Demographics and clinical characteristics regarding comorbidities, additional specialists, and medications were collected. Adherence rates and reasons for nonadherence were determined by review of chart notes and lab data. Exam findings were used to assess quiescence. A generalized linear mixed effects model was run to investigate the relationship between adherence and disease control.

Results: During the study period, 183 patients initiated IMT, with 178 included at 6 months, 170 at 1 year, and 126 at 2 years. The mean age was 44, 69% were female, 40% were Black/African American, and 39% had commercial insurance. Diagnoses included anterior uveitis (31%), intermediate uveitis (7%), posterior uveitis (13%), panuveitis (32%), and scleritis (17%). Types of IMT included Methotrexate (57%), Mycophenolate (26%), Adalimumab (6%), other (6%), and combination therapy (5%). More than one quarter of patients had at least one systemic comorbidity (27%) and took more than eight medications (26%). The adherence rate at 6 months and 1 year was 70% but dropped to 58% by 2 years. By 6 months, 46% of patients achieved quiescence, 56% by 1 year, and 64% by 2 years. Of patients who achieved disease control, 82% were adherent at 6 months, 78% at 1 year, and 65% at 2 years. Adherent patients have a 1.86 (95% CI 1.09, 3.20) times greater likelihood for disease control compared to nonadherent patients. At all time intervals, the primary reason for nonadherence was patient self-discontinuation due to insurance coverage issues or running out of medication. No specific demographic factors were significantly associated with nonadherence.

Conclusions: Patients on IMT for IED had steady adherence rates at 6 months and 1 year, with decreased adherence at 2 years. Patient adherence to IMT significantly correlates with disease quiescence, and nonadherence with uncontrolled ocular inflammation. Patient-centered interventions targeted to improving adherence may improve disease control in IED.

CONTROL ID: 3709524

SUBMITTER (NAME ONLY): Tasneem Sharma

TITLE: Spaceflight-Associated miRNAs Alters Expression of Targeted Genes in Ocular and Spinal Tissue Under Simulated Spaceflight Conditions

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.P. Sharma, R.C. Miller, S.P. ShahulHameed, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|T.P. Sharma, R.C. Miller, S.P. ShahulHameed, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|A. Kubik, N. Allen, E. Blaber, Rensselaer Polytechnic Institute, Center for Biotechnology & Interdisciplinary Studies, Troy, New York, UNITED STATES|S. Altinok, L.E. Oswalt, R. Sanchez-Hodge, J.C. Schisler, Pharmacology, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|S. Altinok, L.E. Oswalt, R. Sanchez-Hodge, J.C. Schisler, UNC McAllister Heart Institute, Chapel Hill, North Carolina, UNITED STATES|A. Beheshti, NASA Ames Research Center, Moffett Field, California, UNITED STATES|A. Beheshti, Broad Institute, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Spaceflight exposes humans to stress of microgravity and radiation, leading to immunosuppression, muscle atrophy, cardiovascular damage, and visual disturbances. Minimizing or mitigating these pathological changes is necessary for future deep space missions. Several spaceflight-related pathologies are associated with the altered expression of 13 miRNAs. Previously, we found increased expression of these spaceflight-associated miRNAs in rodents exposed to either simulated or real spaceflight and partial conservation in the space-flown twin of the NASA Twins Study. Moreover, small molecule inhibitors (antagomirs-Ag) targeting 3 spaceflight-associated miRNAs reduced vascular inflammation in human tissue exposed to simulated spaceflight. Here, we examined the effects of inhibiting these 3 spaceflight-associated miRNAs in mice before exposure to simulated spaceflight conditions.

Methods: We used 6 groups of 20 female mice: control, control + Ag, simulated gamma-cosmic rays (GCRs), GCRs + Ag, simulated space particle event (SPE), and SPE + Ag. Half of each group was housed with hindlimb unloading to simulate microgravity. Ag-treated mice were treated every 3 days, with the last treatment 24 hours before irradiation. We harvested the vertebral column and eyes. We isolated total RNA and used RT-qPCR to measure expression levels of 13 candidate genes.

Results: We identified 13 gene targets of 3 miRNAs via mirNET, mirWalk, and Cluepedia databases (Figure). Differences in relative expression of 13 genes was analyzed via Welch's unpaired t-test and two-way ANOVA. We found changes in spinal cord expression of 9 genes when treated with spaceflight-associated miRNA Ag ($p < 0.05$), several of which are involved in mitotic function, membrane organization, and phosphatase regulation. Conversely, in eyes we found that Ag treatment only changed expression of one gene (Zcchc9; sham vs SPE + Ag, $p< 0.05$; sham vs Sham + Ag $p< 0.05$), that encodes a zinc-finger containing protein phosphatase. However, simulated-spaceflight radiation and microgravity alone did not influence expression of the 13 target genes in the eye or spinal cord.

Conclusions: Our study demonstrates that inhibition of miRNAs in preclinical models of simulated spaceflight has potential for preventing biological damage.

CONTROL ID: 3709525

SUBMITTER (NAME ONLY): YINGZI XIONG

TITLE: Perceived Difficulties in Spatial Localization by People with Vision and Hearing impairment

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. XIONG, C. Farrington, N. Nguyen, G.E. Legge, Psychology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|Y. XIONG, G.E. Legge, Center for Applied and Translational Sensory Science, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|D. Brunt, Envision Research Institute, Wichita, Kansas, UNITED STATES|J. Nemargut, W. Wittich, School of Optometry, Universite de Montreal, Montreal, Quebec, CANADA|N. Nguyen, Human Factors & Ergonomics, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Spatial localization refers to the ability to determine the location of people and objects in relation to oneself. In previous psychophysical studies we have investigated the effect of vision and/or hearing impairments on spatial localization behavior. However, it is not known how people with sensory impairment judge the difficulty of spatial localization in real-life situations. We developed a spatial localization survey to assess participants' perceived difficulties in visual and auditory localization, as well as their sensory integration strategies in real-life scenarios.

Methods: The survey included 35 real-life scenarios with visual and auditory cues, e.g., "You are walking along a city sidewalk. A police vehicle is approaching with a siren sound and flashing lights. You need to determine which direction the police car is coming from". For each scenario, participants reported their perceived difficulties in completing the task solely by vision and solely by hearing, using a scale from 1-5 (1 = very easy; 5 = very difficult), and which sense (vision or hearing) they would primarily rely on. Data were collected from three groups—vision impairment (VI, N = 24); dual sensory impairment (vision and hearing/DSI, N = 15); and healthy controls (N = 26). Their mean acuities were 0.75, 0.52 and 0.0 logMAR; and mean hearing levels were 6.2, 30 and 5.8 dB, respectively.

Results: The VI and DSI group reported significantly higher visual difficulty scores than the control group. However, the DSI group did not show higher hearing difficulty scores than the control or VI group. When asked which sense the participants primarily relied on, the control group was consistently "vision dependent", while the VI and DSI groups had more participants who were "hearing dependent". Participants were primarily "vision dependent" until their acuity reached 1.0 logMAR (20/200), after which they were more likely to be "hearing dependent".

Conclusions: Vision impairment resulted in higher overall perceived difficulty in visual localization, while hearing impairment did not significantly affect the perceived difficulties in auditory localization. While healthy controls were primarily vision dependent, participants with VI or DSI adjusted their sensory dependence pattern in coping with vision impairment. Our survey provides a unified framework for assessing participants' reported vision and hearing function in daily activities.

CONTROL ID: 3709526

SUBMITTER (NAME ONLY): Joshua Glass

TITLE: Proteomic alterations after loss of IL-6 receptor in Müller glial cells in a conditional knockout mouse

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Glass, R. Robinson, T. Lee, G. Jones, W. Zhi, A. Sharma, S. Sharma, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|A. Sharma, Department of Population Health Sciences, Augusta University, Augusta, Georgia, UNITED STATES|S. Sharma, Department of Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cytokine interleukin-6 (IL-6) has two major signaling modalities, classical signaling and trans-signaling, which are generally considered anti-inflammatory and pro-inflammatory, respectively. IL-6 classical signaling is limited to cells expressing the membrane-bound IL-6 receptor (IL-6Rα), whereas trans-signaling is mediated through a soluble form of IL-6 receptor. To characterize the role of IL-6 signaling in retinal Müller glia, we generated a Müller-cell-specific Il6ra knockout (KO) mouse (Pdgfra-Cre Il6ra$^{fl/fl}$). In this study, proteomic analysis of Müller glial cells (MGCs) with and without IL-6Rα was performed to reveal the autocrine functions of IL-6 classical signaling in-vitro.

Methods: MGCs were isolated from wildtype C57BL/6J (WT) and KO mouse pups and cultured in-vitro. Comprehensive proteomic profiling of cell lysates from both groups was conducted using liquid chromatography-tandem mass spectrometry (LC-MS/MS).

Results: Proteomic profiling identified a total 1066 proteins, of which 79 proteins were significantly altered (33 upregulated and 46 downregulated) in MGCs from KO mice relative to WT. The top five upregulated proteins include PDZ and LIM domain protein 1 (Pdlim1: 5.25-fold), glycogen phosphorylase (Pygb: 3.36-fold), procollagen-lysine,2-oxoglutarate 5-dioxygenase 2 (Plod2: 3.24-fold), transgelin (Tagln: 2.87-fold), and acyl-coenzyme A thioesterase 9 (Acot9: 2.5-fold). The top five downregulated proteins include neprilysin (Mme: 0.12-fold), metalloreductase STEAP4 (Steap4: 0.17-fold), transmembrane glycoprotein NMB (Gpnmb: 0.19-fold), ectonucleotide pyrophosphatase/phosphodiesterase family member 5 (Enpp5: 0.26-fold), and alcohol dehydrogenase 1 (Adh1: 0.27-fold). Mitochondrial structure, cell metabolism, cytoskeletal structure, glycolysis, actin cytoskeletal signaling, and endoplasmic reticulum stress response were highly enriched gene ontology (GO) terms in the 79 altered proteins.

Conclusions: Elimination of IL-6 classical signaling via IL-6 receptor knockout in MGCs produced significant alterations in protein expression. This characterization reveals the autocrine functions of IL-6 classical signaling in-vitro and lays the groundwork for future experiments involving the functions of IL-6 in MGCs.

CONTROL ID: 3709527

SUBMITTER (NAME ONLY): Shruti Sharma

TITLE: Generation and characterization of a novel conditional knockout mouse to delineate the role of IL-6 trans-signaling in the retinal Müller glia

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sharma, R. Robinson, J. Glass, A. Sharma, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|S. Sharma, Department of Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|A. Sharma, Department of Population Health Sciences, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our recent studies in human retinal endothelial cells and diabetic mice indicate that the damaging effects of interleukin-6 (IL-6) in diabetic retinopathy (DR) are primarily mediated by IL-6 trans-signaling through its soluble IL-6 receptor (sIL-6R). The effects of IL-6 trans-signaling in Müller glial cells (MGCs) remain unclear, as MGCs also express the membrane-bound IL-6 receptor (IL-6Rα) and are thus capable of both classical and trans-signaling, making it difficult to discern the distinct effects of each signaling mechanism. To address this problem, we have generated a Müller-cell-specific Il6ra knockout (KO) mouse to eliminate IL-6 classical signaling in MGCs.

Methods: This conditional knockout mouse was created by crossing a mouse expressing a Müller-cell-specific Cre recombinase (C57BL/6-Tg(Pdgfra-cre)1Clc/J) with a floxed Il6ra mouse (B6;SJL-Il6ra$^{tm1.1Drew}$/J). Knockout specificity in MGCs was evaluated by immunohistochemistry of retinal sections. Visual function testing and live retinal imaging were performed using Phoenix MICRON™ Ganzfeld ERG system. Primary MGCs were isolated from wildtype (WT) and KO mice, and Il6ra KO was confirmed by RT-PCR, western blotting, and immunofluorescence staining.

Results: After successful breeding and genotyping, ~75% of F3-generation mice were positive for Cre recombinase and homozygous for floxed Il6ra. IL-6Rα protein expression was detected in WT Müller glia by immunofluorescence staining and confirmed to be absent in the KO mouse retina. Further, mRNA expression of the exon 5-6 region of the Il6ra gene, the region flanked by loxP sites, was not detected in KO MGCs. Western blotting and immunofluorescence staining for IL-6Rα confirmed its presence in WT MGCs and its absence in KO MGCs. Finally, we confirmed via H&E staining of retinal sections that KO mice possess normal retinal morphology. Preliminary visual function testing by ERG at 12 weeks of age showed a normal response to visual stimulus in KO mice, and fundus examination also showed no evidence of retinal lesions.

Conclusions: We have successfully generated a novel tissue-specific knockout mouse to isolate the specific effects of IL-6 trans-signaling in Müller glial cells. Use of this model will provide critical knowledge of the seemingly opposite roles of the two major IL-6 signaling modalities within the retina and retinal pathology.

CONTROL ID: 3709529

SUBMITTER (NAME ONLY): Kristen Pitts

TITLE: APOE and Galectin-3, markers of activated microglia, are elevated in the aqueous humor of glaucoma patients

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Pitts, C. Neeson, N. Hall, H. Falah, M. Margeta, D. Solá-Del Valle, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|N. Hall, M. Margeta, D. Solá-Del Valle, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Microglial activation has emerged as a critical event contributing to retinal ganglion cell loss in glaucoma. Apolipoprotein E (APOE), the major apolipoprotein in the brain, and Galectin-3 (Gal-3), a secreted carbohydrate-binding lectin, have been identified as molecules critical for microglial cytotoxicity in mouse models of glaucoma. In this study, we aim to examine the role of APOE and Gal-3 in human disease by analyzing their concentrations in aqueous humor (AH) collected from glaucoma patients and healthy controls.

Methods: AH was collected from 71 patients at the start of surgery, including 57 glaucoma patients undergoing various ophthalmic procedures and 14 control patients undergoing routine cataract surgery. APOE and Gal-3 levels were quantified by enzyme-linked immunosorbent assay and total protein concentration by bicinchoninic acid (BCA) assay. Patients' medical records were carefully reviewed to collect relevant preoperative data. Descriptive statistics, Pearson's correlation coefficient, and multivariate linear regression analyses were conducted to characterize associations between clinical and demographic variables and APOE and Gal-3 levels.

Results: APOE and Gal-3 levels were significantly elevated in the AH of glaucoma patients (1.64 +/- 1.45 µg/mL and 2.33 +/- 2.09 ng/mL, respectively) compared to controls (0.40 +/- 0.19 µg/mL, 0.92 +/- 0.81 ng/mL) [$p<0.001$; $p=0.004$]. APOE and Gal-3 levels were moderately positively correlated across the entire cohort ($r=0.65$, $p<0.001$). No association was observed between APOE and total protein or Gal-3 and total protein, indicating that APOE and Gal-3 levels were not increased in glaucomatous AH due to nonspecific protein accumulation ($p>0.3$). Multivariate linear regression analyses revealed significant associations between Gal-3 and maximum recorded intraocular pressure measurement ($p=0.009$), and between APOE and number of past ophthalmic surgeries ($p=0.031$).

Conclusions: Our findings demonstrate that APOE and Gal-3 are increased in the AH of glaucoma patients and significantly correlate with clinical measures of glaucoma severity. Thus, these molecules could serve as biomarkers to identify patients who may benefit from microglia-based neuroprotective glaucoma therapies.

CONTROL ID: 3709532

SUBMITTER (NAME ONLY): Dolly Padovani-Claudio

TITLE: Maternal diabetes, particularly Type 2 diabetes, is associated with increased odds of Stage 3-5 retinopathy of prematurity.

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Padovani-Claudio, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|A. Love, J. Sucre, S. Van Driest, Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|A. Lewis, L. Bastarache, Bioinformatics, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|J. Sucre, Neonatology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|S. Van Driest, Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) and diabetic retinopathy (DR) are leading causes of blindness. Retinal hypoxia, inflammation, and pre-retinal neovascularization characterize both conditions. Pregnancy, poor glycemic control, and diabetes mellitus (DM) duration are associated with worsening DR. On the other hand, low gestational age (GA), low birth weight (BW) and exposure to comorbidities like necrotizing enterocolitis (NEC) are risk factors for ROP progression. Pathologic similarities between ROP and DR posit that maternal DM (in-utero hyperglycemia) may increase a premature infant's risk of retinopathy progression to vision-threatening stages (Stage 3-5). However, the few studies that address this question describe conflicting results and no studies have reported data on specific maternal DM sub-types. Our study further explores the contribution of maternal DM-type to this potential association.

Methods: This retrospective cohort study included infants born between January 2004 and December 2017 with GA between 22 weeks 0 days and 30 weeks 6 days or with BW <1500g, who had documented staging on ROP screening, and who survived to at least day-of-life 30 and to 40 weeks corrected GA. The study investigated the association between Stage 3-5 ROP and maternal DM using multivariate analysis including GA, BW, year of birth, and NEC. A two-sided t-Test with $p<0.05$ was used for statistical significance.

Results: 2386 of 17066 infants met inclusion criteria. Of these 2386 infants, 1612 (67.5%) had Stage 0 (no ROP controls) and 242 (10.1%) had Stage 3-5 ROP. Maternal DM was found in 131 infants (8.1%) with Stage 0 ROP and 17 infants (7%) with Stage 3-5 ROP. In the multivariate analysis, a positive association with OR of 2.2 (95% CI: 1.0-4.3, p=0.03) was detected between Stage 3-5 ROP and maternal DM. Sub-analysis by DM-type suggested a significant association between Stage 3-5 ROP and maternal Type 2 DM (OR 3.7, 95% CI 1.3-10.1, p=0.012), but not with Type 1 DM (OR 5.9, 95% CI: 0.7-33, p=0.06) or with gestational DM (OR 1.1, 95% CI 0.4-3.0, p=0.859).

Conclusions: Our results suggest that maternal diabetes, particularly Type 2 DM, may confer an increased risk of developing vision-threatening ROP. Incorporating this risk factor to screening decisions may be valuable to preserve vision in at-risk infants.

CONTROL ID: 3709534

SUBMITTER (NAME ONLY): Caili Hao

TITLE: Aged Lens Epithelial Cells Suppress Proliferation and Epithelial-Mesenchymal Transition

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hao, Z. Wei, P. Gordon, J. Huangfu, X. Fan, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|X. Zhang, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|H. Yan, Xi'an Jiaotong University School of Medicine, Xi'an, Shaanxi, CHINA|

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ABSTRACT BODY:

Purpose: Posterior capsule opacification (PCO) is a frequent complication after cataract surgery, and advanced PCO requires YAG laser (Nd: YAG) capsulotomy, which often gives rise to more complications. Lens epithelial cell (LEC) proliferation and transformation (i.e., epithelial-mesenchymal transition (EMT)) are two key elements in PCO initiation and progression pathogenesis. While PCO marginally impacts aged cataract surgery patients, PCO incidences are exceptionally high in infants and children undergoing cataract surgery. The epigenetics of lens epithelial cell aging and its role in the discrepancy of PCO prevalence between young and older people have not been fully studied.

Methods: Here, we conducted a comprehensive differentially expressed gene (DEG) analysis of the young and aged lens epithelial cells (LECs) that originated from a cellular aging model. In vitro TGFb2 cell treatment and in vivo mouse cataract surgical models were used to validate our findings.

Results: We found that aged LECs decelerated rates of cell proliferation accompanied with dysregulation of cellular immune response and cell stress response. Surprisingly, we found that LECs systematically downregulated epithelial-mesenchymal transition (EMT)-promoting genes. The protein expression of several EMT hallmark genes, e.g., fibronectin, aSMA, and cadherin 11, were gradually decreased during LECs aging. We then confirmed these findings in vitro and found that aged LECs markedly alleviated TGFb2-mediated EMT. Importantly, we explicitly confirmed the in vitro findings from the in vivo mouse cataract surgery studies.

Conclusions: We propose that both the high proliferation rate and EMT-enriched young LECs phenotypic characteristics attribute to unusually high PCO incidence in infants and children.

CONTROL ID: 3709535
SUBMITTER (NAME ONLY): Steven Fliesler
TITLE: TMEM97 localization in the adult mouse retina
SESSION TITLE: Photoreceptor Biology, Protection and Degeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S.J. Fliesler, L.A. Skelton, S. Ramachandra Rao, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|S.J. Fliesler, L.A. Skelton, S. Ramachandra Rao, Ophthalmology, Biochemistry, and Neuroscience Program, University at Buffalo, Buffalo, New York, UNITED STATES|U. Wolfrum, Institute of Molecular Physiology, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|S. Martin, Chemistry, The University of Texas at Austin, Austin, Texas, UNITED STATES|
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ABSTRACT BODY:

Purpose: TMEM97 (Sigma-2 receptor) is a transmembrane protein that has been implicated in cell proliferation and death, cholesterol homeostasis and lipoprotein uptake. Its distribution and role in the retina are not well understood. Here, we examined TMEM97 distribution in the adult mouse retina.

Methods: Eyes from adult C57BL/6J wildtype (WT) and Tmem97 knockout (KO; Shen et al., 2021) mice were fixed in 4% paraformaldehyde/PBS, and cryosections (O.C.T.) were collected on glass microscope slides for immunohistochemistry (IHC) and probed with rabbit anti-TMEM97 (Invitrogen #PA5-2300 or Novus Biologicals #NBP1-30437), followed by fluorochrome-conjugated secondary antibodies (Abs), and examined by confocal fluorescence microscopy. Non-immune (normal) rabbit IgG (Sigma/Aldrich) served as a negative control. Markers of rod outer segments (ID4 anti-opsin), Müller glia (anti-glutamine synthetase (GS); BD, Clone 6 #610517), mitochondria (COX4-I1; #AF5814, Bio-Techne), cilia (chicken anti-rootletin; Tiansin Li, NEI), ECM (anti-IMPG1, #SC-377366) also were probed, using suitable secondary fluorochrome-conjugated Abs, and DAPI counterstain. Alternatively, WT mouse eyes were fixed in buffered mixed aldehydes, then embedded in LR White resin, and processed for immunoelectron microscopy, applying anti-TMEM97 Abs in combination with Nanogold-conjugated anti-rabbit Ab and silver enhancement (Wolfrum & Schmitt, 2000). Western blots (WB) of mouse neural retinas were probed with anti-TMEM97 Abs (ECL detection).

Results: WB analysis of retina lysates showed a single anti-TMEM97-positive band (M_r ~21 kDa), consistent with TMEM97. Prominent TMEM97 immunofluorescence labeling was found in the photoreceptor layer of the mouse retina, but no colocalization with rod opsin, COX4, GS, or IMPG1 was observed; occasional co-localization with rootletin in rods and RPE cells was observed, otherwise little or no RPE labeling. Focal and more diffuse labeling was observed in the OPL, IPL, and GCL. In both the INL and GCL we observed elongated staining that co-localized with rootletin. Tmem97 KO retinas exhibited no Tmem97 immunostaining. Immunoelectron microscopy confirmed TMEM97 localization in rod ciliary rootlets, and periciliary and centriolar material of retinal cells.

Conclusions: These findings are consistent with TMEM97 having a role in the structure and function of primary cilia in neural retina (especially photoreceptors) and RPE centrosomes.

CONTROL ID: 3709536

SUBMITTER (NAME ONLY): Joyce Kang

TITLE: Relationship between contrast sensitivity and visual field mean deviation

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kang, S. Freeman, S. De Arrigunaga, Y. Zhao, A.M. Roldan, T. Elze, D.S. Friedman, D. Liebman, M.M. Lin, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Chang, Genentech Inc, South San Francisco, California, UNITED STATES|D. Chang, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mean contrast sensitivity (CS) and area under the log CS function (AULCSF) parameters may help evaluate visual function in patients with glaucoma, yet they are rarely performed in routine clinical care. The quick CS function (qCSF) test (Adaptive Sensory Technology, San Diego, CA, USA) is a Bayesian adaptive procedure that estimates AULCSF by measuring CS at different spatial frequencies and modeling log CS as a function of stimulus size. We analyzed the relationship between qCSF test outputs and visual field mean deviation (MD).

Methods: In this observational study, subjects with visual acuity 20/40 or better and a diagnosis of glaucoma or glaucoma suspect performed the qCSF test. All subjects were reliable, experienced HFA testers. qCSF reports AULCSF and the individual CS recorded at 1.0, 1.5, 3.0, 6.0, 12.0 and 18.0 cycles per degree (CPD). We created a scatterplot with AULCSF as a function of each subject's MD and fit linear regression at each CPD to evaluate the effect of MD on CS, then adjusted for intraocular lens status.

Results: MD averaged -3.16 (± 3.90) dB for 54 eyes of 54 subjects with mean age 61 years (range 30-71) and was not correlated with AULCSF (P = 0.15, Figure 1). Better MD was associated with better CS at 1.0, 1.5, and 3.0 CPD (Figure 2), but these correlations were weak. When intraocular lens status was added to the model, it was correlated with CS at 1.0 and 1.5 CPD, and MD was no longer correlated with CS.

Conclusions: HFA MD and AULCSF were not correlated in this population with mostly early or no VF defects. MD was correlated with CS at lower CPD (1.0, 1.5, 3.0). This association was no longer statistically significant when adjusting for intraocular lens status. The mild glaucoma severity in this cohort may have limited the ability to detect a relationship between CS and MD, and any relationship was overshadowed by intraocular lens status. At higher CPD, CS is less correlated with MD and intraocular lens status. The results of this preliminary study were limited by the overall healthy population and apply only within the bounds of the tested cohort.

CONTROL ID: 3709537

SUBMITTER (NAME ONLY): Charles Zhang

TITLE: Patterns of gene expression vary among macular tissues and clinical stages of Age-related Macular Degeneration

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Zhang, J. Lillvis, B. Madow, M. Farkas, M.M. DeAngelis, University at Buffalo, Buffalo, New York, UNITED STATES|N.B. Haider, I.K. Kim, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.A. Owen, A. Shakoor, A.T. Vitale, John Moran Eye Center, Utah, UNITED STATES|T. Shaikh, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|L. Farrer, Boston University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gene expression varies among individuals and between tissues in the same person. Gene expression analyses in disease-affected tissues can help ascribe function to previously associated disease susceptibility variants in complex disorders such as age-related macular degeneration (AMD). We aimed to uncover patterns of differential gene expression between different disease stages to uncover the pathogenesis of AMD.

Methods: Utilizing well-characterized fresh human donor tissue from rapidly autopsied eyes, phenotyped and dissected according to a standardized protocol; the macula of the neural retina and separately the macula of the RPE/choroid. Analysis was performed on 27 donors (12 normals, 10 intermediate AMD and 5 neovascular AMD) that underwent poly A tail RNA-sequencing to identify differentially expressed genes (DEG) between the AMD subtypes.

Results: Following principal component analysis, DESeq2 pipeline analysis and correction with Benjamini -Hochberg, significant DEG within the macular RPE/choroid tissues was observed for 40 genes between intermediate AMD and normal eyes, 1,204 genes between neovascular AMD and normal eyes, and 1,194 genes between intermediate and neovascular AMD. Within the macular neural retina, 30, 41, and 50 genes were differentially expressed when comparing the same respective groups. Among genes associated with AMD from prior GWAS and candidate gene studies, expression was significantly higher for ABCA4, ABCA7, RORA and VTN in neovascular AMD versus normal macular RPE/choroid tissue; significantly lower for ABCA4, ABCA7, SPEF2 and significantly higher for TNFRSF10B and TRPM1 in intermediate versus neovascular AMD macular RPE/choroid. There was no overlap between significant DEG and tissue type. 16 pathways in the GSEA Hallmark collection were significantly enriched; 14 unique to the comparison of intermediate with normal eyes and 10 of those specific to the RPE/choroid tissue.

Conclusions: Our analysis demonstrates differential patterns of gene expression between AMD phenotypes in macula retina and RPE/choroid tissue with the later demonstrating greater variability underscoring the importance of assessing expression in a cell-type specific manner. Several genes and pathways were differentially expressed between phenotypes suggesting that clinical AMD may represent a spectrum of molecular pathophysiology.

CONTROL ID: 3709539

SUBMITTER (NAME ONLY): Tianxiao Huan

TITLE: Identifying Key Drivers Regulating the Metabolites Network of Age-related Macular Degeneration

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Huan, J.M. Seddon, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|M. Daly, Massachusetts General Hospital and Broad Institute, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Tianxiao Huan: Commercial Relationship: Code N (No Commercial Relationship) | Mark Daly: Commercial Relationship: Code N (No Commercial Relationship) | Johanna Seddon: Commercial Relationship(s);Code C (Consultant/Contractor):Laboratoires THEA;Code I (Personal Financial Interest):Gemini Therapeutics, Inc and Apellis

ABSTRACT BODY:

Purpose: Many circulating metabolites including lipids and fatty acids may be involved in the pathogenesis of age-related macular degeneration (AMD). However, conflicting results about their association with AMD have been reported and the relationship between metabolites and AMD remains largely unknown. Here we aim to provide an integrated perspective on the relationship and genetic basis of metabolites and AMD by leveraging the results of published genome-wide association studies (GWAS).

Methods: We curated published GWAS of human serum and plasma metabolites which identified quantitative trait loci for 300 metabolites (mQTLs). Summary statistics of AMD GWAS were derived from the International AMD Genomics Consortium. Two-sample Mendelian randomization (MR) was used to infer causal associations between metabolites and AMD using mQTLs as instrument variables.

Results: We built a metabolites network of AMD by cross-linking different metabolites with their shared SNP associations with AMD (P<5e-8). We found that four AMD risk loci near LIPC, CETP, APOE and MMP9 (PMID 20385826, 20888482, 21139980, 21447678) showed high pleiotropic effects on metabolites and each locus was associated with 20 metabolites on average. Some metabolites were related to multiple AMD risk loci, but the direction of association between metabolites and AMD conflicted at different loci. For example, rs17231506 in CETP was positively correlated with AMD (P=1.7e-8) and extra-large sized HDL (xl-HDL, P=6.7e-15), suggesting that xl-HDL was positively correlated with AMD. However, rs2070895 in LIPC was negatively correlated with AMD (P=1.8e-11) but positively correlated with xl-HDL (P=1.7e-9), suggesting that xl-HDL was negatively correlated with AMD. Results point to key regulatory genes that may balance levels of metabolites in AMD. MR analysis also showed that increased levels of Lyso-phosphatidylethanolamine (Beta=0.46, P=1.1e-18), docosatetranoic acid (Beta=1.4, P=3.5e-15), and m-HDL (Beta=0.67, P=6.9e-5) were associated with increased risk of AMD, and increased level of LDL, VLDL, and IDL (Beta=-0.37, P=4.6e-6) were associated with decreased risk of AMD.

Conclusions: Results provide evidence supporting potentially causal effects of many circulating metabolites on AMD, and pinpoint key regulators which may balance the metabolites network underlying AMD pathogenesis. Therefore, these findings may support new targets for AMD therapies.

CONTROL ID: 3709540

SUBMITTER (NAME ONLY): Kent Small

TITLE: Closure of Macular Holes With Topical Therapy and Why The Hydration Theory of Macular Hole Formation May Be Inaccurate

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.W. Small, J. Avetisjan, F. Shaya, Macula and Retina Institute, Glendale, California, UNITED STATES|K.W. Small, J. Avetisjan, F. Shaya, Molecular Insight Research Foundation, Glendale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Idiopathic macular holes are generally a surgical disease. While small, early macular holes may rarely close spontaneously, most require surgery for repair. Edema surrounding the edge of the hole is thought to be contributory and treating the edema is thought to possibly be able to close the hole. Herein, we report our experience with a non-surgical approach to repairing macular holes.

Methods: A retrospective chart review of 13 consecutive patients with macular holes from 2018-2021. Topical therapy consisted of a steroid, a non-steroidal and a carbonic anhydrase inhibitor. The setting was a solo retinal surgeon's practice. Follow-up ranged from 6 months to 2 years.

Data collected included size, stage and duration of macular hole, topical agents used and duration, grading scale of macular edema present, lens status and complications from topical or surgical therapy. The grading scale ranged from 0 (no intraretinal edema at all) to 4 (maximum, large amount of edema). If the hole failed to close after 3 months of topical therapy, intravitreal Ocriplasmin (Jetrea) was offered and / or vitrectomy with membrane peeling and fluid gas exchange. Best corrected visual acuities (BCVA) were converted to logMAR pre and post hole closure with topical therapy or surgery. SD-OCT images were captured of all patients.

Results: Seven of the 13 (54%) eyes initially treated topically experienced successful macular hole closure. Small holes (less than 230 microns) with better initial vision (0.474 vs 0.796 logMAR) were more likely to respond favorably to topical therapy (121 microns vs 499 microns). Additionally, holes with less surrounding edema responded better. Of the holes not responding to topical therapy, all were subsequently closed with pars plana vitrectomy (PPV), membrane peel and fluid / gas exchange.

Conclusions: Topical therapy is a reasonable first line treatment for macular holes with a better than 50% success rate. This is especially true for small, early onset holes with minimal or no edema. There was no apparent deleterious effect of a 1-3 month delay while treating with eye drops as surgery still had a very high success rate.

CONTROL ID: 3709543

SUBMITTER (NAME ONLY): Jimmy Chen

TITLE: Factors Involved in Developing an Open Electronic Health Record Glaucoma Dataset

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Data science research is dependent on large, well-compiled datasets. However, these datasets are difficult to acquire, and there are currently no best practices for sharing these data. An open dataset could address this gap, allowing researchers to investigate new hypotheses and develop more generalizable studies. This abstract describes factors considered in constructing such a dataset.

Methods: A dataset containing medical record numbers (MRNs) of glaucoma patients, providers and their specialty departments, visit identifiers and dates, raw progress notes and medication lists extracted from the EHR, and statistical analysis from a previously published manuscript was used (Chen et al, Ophthalmology Science, 2021). These progress notes and medication lists were previously manually annotated for medications names, frequency, route, and indication. Each dataset element was reviewed for protected health information (PHI). If PHI was present, a decision was made to remove or de-identify the data field. Example data fields, including PHI, and their rationale for inclusion/exclusion are described in Table 1.

Results: Patient MRNs, visit identifiers, and visit dates were the only data fields specifically with PHI, and were de-identified using an R library, anonymizer, which uses hash functions to encode identifying variables. Visit dates were shifted and truncated. Provider data was removed, and department data was included as is. Annotated medication data were paired with all data fields as a CSV and statistical code was included without modification. While medication lists were included as is, progress notes potentially contained PHI and required de-identification using a natural language processing algorithm, Philter (Python), with results verified by a clinician (JSC). These data could be uploaded to online data repositories such as Dryad or Figshare (Table 2), published as a Data Descriptor Article (Zarbin et al, TVST, 2021), and potentially used to develop or validate text-processing algorithms involving medication data.

Conclusions: Processing and uploading datasets for open-source dataset publication is a feasible, inexpensive process and could become standard practice to increase collaboration as well as dataset accessibility in vision research.

CONTROL ID: 3709544

SUBMITTER (NAME ONLY): Joshua Ehrlich

TITLE: The Joint Effect of Vision Impairment and Apolipoprotein E on the Hazard of Incident Cognitive Impairment

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.R. Ehrlich, Y. Zhou, G. Chung, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|J.R. Ehrlich, E. Ware, University of Michigan Institute for Social Research, Ann Arbor, Michigan, UNITED STATES|A. Kolli, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|G. Chung, School of Public Health, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have reported an association between vision impairment (VI) and cognitive health. Specifically, VI is associated with the development of cognitive impairment, a clinical precursor to dementia. However, most older adults with VI will not develop cognitive impairment or dementia. This study sought to determine whether the association of VI with incident cognitive impairment varies by ε4 carrier status of the Apolipoprotein E gene, a strong genetic risk factor for cognitive decline and dementia.

Methods: We used data from the population-based Aging, Demographics and Memory Study (ADAMS), which included adults aged 70 years and older. Vision impairment was defined as vision worse than 20/40 in the better seeing eye. Participants underwent a consensus panel assessment of cognitive function and were categorized as cognitively normal, cognitive impairment no dementia (CIND), or dementia. We constructed a Cox proportional hazards model to estimate the joint effects of VI and APOE-ε4 on the development of CIND among participants who were cognitively normal at baseline. Models were adjusted for age, sex, education, medical comorbidities, and for the competing risk of death.

Results: There were 196 participants included in this analysis. Both VI (HR=2.0, 95% CI 1.3-3.2) and APOE-ε4 (HR=1.7, 95% CI 1.2-2.6) were independently associated with incident CIND. The joint effect of VI and APOE-ε4 on incident CIND (HR=5.7, 95% CI 2.8-11.6) was significantly elevated compared to having no VI and no APOE-ε4 allele. However, there was no increase in the hazard of CIND among those with only VI or the APOE-ε4 allele (Figure).

Conclusions: The hazard of incident CIND among older adults with VI was elevated only among those who were carriers of the APOE-ε4 gene variant. These findings may be important for risk stratification and for targeting interventions to those at greatest risk.

CONTROL ID: 3709545

SUBMITTER (NAME ONLY): Patrick Yu-Wai-Man

TITLE: The phase III REFLECT trial: efficacy of bilateral gene therapy for Leber hereditary optic neuropathy (LHON) is maintained 2 years post administration

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: REFLECT is a Phase III randomized trial assessing the efficacy and safety of a bilateral intravitreal injection of lenadogene nolparvovec gene therapy for the treatment of Leber hereditary optic neuropathy (LHON) caused by the m.11778G>A mitochondrial DNA mutation in the MT-ND4 gene.

Methods: 98 LHON subjects carrying the m.11778G>A mutation, who were ≥ 15 years old at onset and with vision loss ≤ 365 days at enrollment, received a single intravitreal injection of lenadogene nolparvovec (9E10 viral genomes in 90 µL per eye) in the first-affected eye. The second-affected eye was randomly allocated to either gene therapy or placebo. Functional and structural parameters were monitored up to 2 years after treatment administration.

Results: 48 subjects were assigned to bilateral treatment with gene therapy and 50 to unilateral treatment (with the first-affected eye injected with lenadogene nolparvovec and the second-affected eye injected with placebo). Two years after injection, a statistically significant improvement in best-corrected visual acuity (BCVA) was reported from baseline in treated eyes. A significant improvement from the nadir was observed in all eyes, reaching +20 and +17 ETDRS letters in the first- and second-affected eyes, respectively, for bilaterally treated patients ($p<0.0001$), and +19 and +14 ETDRS letters in the first-treated and second-placebo eyes, respectively, for unilaterally treated patients ($p<0.0001$). A better average final BCVA was reported in subjects treated bilaterally compared to subjects treated unilaterally (+6 letters). A clinically meaningful improvement from the nadir of at least -0.3 LogMAR (+15 ETDRS letters) was reported in 73% of bilaterally treated subjects and 66% of unilaterally treated subjects, and 77% of bilaterally treated patients moved from off-chart BCVA at baseline to on-chart BCVA at 2 years.

Conclusions: The statistically significant improvement of BCVA from baseline and the nadir reported at 1.5 years post administration of lenadogene nolparvovec was maintained at 2 years. The improvement observed in placebo-treated eyes is consistent with the contralateral effect of a unilateral injection of lenadogene nolparvovec reported in the phase III trials RESCUE and REVERSE. The REFLECT results suggest a dose effect with bilateral injection of lenadogene nolparvovec.

CONTROL ID: 3709547

SUBMITTER (NAME ONLY): Brecken Blackburn

TITLE: Phase Decorrelation OCT for Monitoring Accelerated Crosslinking: Depth Resolution and Improved Scan Area

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Blackburn, M. McPheeters, M.W. Jenkins, W.J. Dupps, A.M. Rollins, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|W.J. Dupps, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: For assessing corneal biomechanics, resolving spatial heterogeneity both in depth and over a wide lateral field of view is advantageous to observe the effects of crosslinking procedures and diseases such as keratoconus – both of which vary as a function of corneal depth and lateral position. Phase decorrelation optical coherence tomography (PhD-OCT) is able to resolve the varying depth-dependent effects of different corneal crosslinking protocols and, through the use of a conical scanner, an improved ability to scan a wide field of view.

Methods: Ex vivo porcine corneas were imaged with both a typical telecentric scanner and the conical scan sample arm (following Beer et al., 2017) in conjunction with a 1310nm spectral domain OCT system. M-B scans were acquired and processed to extract the short-time complex decorrelation, as described in prior work (Blackburn et al., 2019). Crosslinking protocols were applied, including the Dresden protocol and accelerated protocols.

Results: Using the conical scanning system, there is no substantial degradation of image quality in the periphery and thus no corresponding degradation of the decorrelation signal. The preserved signal quality allows for decorrelation analysis further from the central cornea. Differences in the depth-profiles that were observed between varying crosslinking protocols correspond well with theory. The use of supplemental oxygen in accelerated protocols enhanced the crosslinking effect.

Conclusions: Conical focal plane scanners offer significant advantages for noise-sensitive OCT processing methods such as PhD-OCT to reliably extend their reach into the periphery of the cornea. PhD-OCT is demonstrated to provide depth-dependent information about crosslinking state.

CONTROL ID: 3709548

SUBMITTER (NAME ONLY): Ryutaro Akiba

TITLE: Rewiring of the adult midget pathway in a primate model of acute photoreceptor loss.

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The retinal fovea is responsible for high acuity vision. Within the primate fovea, each cone photoreceptor contacts a pair of ON and OFF midget bipolar cells (MBCs), forming the first synapses of the midget pathway. Foveal cone loss in retinal degenerative diseases such as macular degeneration is a major cause of blindness. Restoring vision in the fovea using cell-based therapies requires proper synaptic integration of new photoreceptors into the surviving midget circuitry. Thus, understanding how mature foveal circuits remodel after cone loss will be helpful for strategizing future therapies. Here, we used serial block face scanning electron microscopy (SBFSEM) to determine the connectivity of surviving foveal cones adjacent to regions of acute photoreceptor loss.

Methods: A region (200 µm by 500 µm) adjacent to the foveal pit of anesthetized 4-year-old Macaca fascicularis monkey was photocoagulated using a PASCAL laser (Topcon). The animal was euthanized 6 months later, the eye enucleated and the eyecup fixed in 4% glutaraldehyde in 0.1M cacodylate buffer. An unlasered retina from a 5-year-old Macaca fascicularis monkey served as a control. Samples were prepared for SBFSEM as previously described (Della Santina et al., 2015, Current Biology 26:2070-2077), and imaged using the VolumeScope (Thermo-Fisher). The samples, located 650 µm from the foveal center, were reconstructed using TrackEM2 software (NIH). Statistical analysis was carried out using Mann-Whitney U test.

Results: A single cone (n=10 cones) contacted a pair of ON and OFF MBCs in the control retina. A cone pedicle deprived zone (PDZ) was clearly visible 6 months after photocoagulation. As in control retina, ON and OFF MBCs within and adjacent to the PDZ were identified by their axonal stratification. At the PDZ border, ON MBCs (n=8) synapsed with single cones as in the control, whereas OFF MBCs (n=10) sometimes connected with 2 cones (average 1.6 ± 0.52; p=0.005 compared to control). Connectivity of individual cones with ON MBCs (0-3, average 1.07 ± 0.62, n=14 cones, p=0.041) and OFF MBCs (1-3, average 1.73 ± 0.90, n=11 cones, p=0.00006) increased significantly compared to the control.

Conclusions: The mature midget pathway in the primate retina rewires after acute cone loss. The extent of remodeling appears to differ between the ON and OFF pathways.

CONTROL ID: 3709551

SUBMITTER (NAME ONLY): RUTH ESKENAZI

TITLE: Sensitivity and specificity for the detection of Demodex mites with slit-lamp in patients with blepharitis.

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. ESKENAZI, N. Kahuam-López, A. Navas, C.A. Müller-Morales, E.O. Graue-Hernandez, cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: Demodex mites are the most common microscopic ectoparasite found in human skin, affecting 84% of the population older than 60 years. It is a common cause of chronic blepharitis. The gold standard for diagnosing a Demodex infestation is the visualization of the mite with light-microscopy examination. We tested the hypothesis that the detection of Demodex infestation in blepharitic patients by silt-lamp is a comparable tool for the detection of the pathogen.

Methods: Demodex infestation was evaluated in 22 patients with blepharitis. Two lashes with cylindrical dandruff were epilated from each lid. They were mounted on a glass slide with a drop of saline, a coverslip was mounted on each slide then placed on a strip of white paper and examined on a slit lamp (magnification x25) with a 90D lens attached. Mites were identified by their morphology and movement patterns. The number of mites per lash were documented. Thereafter the slides were transferred to the pathology laboratory to examined them under a light microscope, and the results were documented. The same procedure was followed with a control group (22 patients). The results were evaluated both per lash and per patient. The findings were expressed in number of mites and in positive (at least 1 mite identified per lash) or negative (no mite identified).

Results: 22 patients were included in the cohort, 11 men and 11 women with an average age of 54.8 years. A total of 176 epilated lashes were examined. The mean total Demodex count per lash was 0.9 ±1.3 mites by slit-lamp examination and 1.22 ±1.73 mites by light-microscopy. Corresponding values per patient were 7.3 ±4.4 and 9.7 ±7.18. The correlation between Demodex counts by using the slit lamp and light microscopy was midly-positive and statistically significant per patient (8 lashes, $r= 0.69$, $P<0.001$). Analysis of positive/negative results yielded 43.2% with a positive result for slit lamp and 51.7% for light-microscopy. The sensitivity of the slit lamp examination for the presence of Demodex per patient was 96.6%, with a specificity of 90.9%; the positive predictive value was 91.6% and the negative predictive value was 95.2%.

Conclusions: Our results are consisting with our hypothesis that Demodex infestation in patients with blepharitis and cylindrical dandruff can be confirmed using a slit lamp, and this technique is non-inferior than the light-microscopy examination.

CONTROL ID: 3709552

SUBMITTER (NAME ONLY): Claire Barnes

TITLE: Variability in elasticity of the crystalline lens

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Variability across individuals is rarely explored in perceptual and physiological research. We tested the hypothesis that inter-subject differences in the biomechanics of the human lens could be measured in vivo.

Methods: Inclusion criteria- age 44 through 55 years; best-corrected visual acuity (BCVA) of 20/20 or better in each eye; no abnormalities of the cornea, pupil or lens; no history of ocular trauma or surgery; and no sign of cataract in the undilated eye. Along with standard clinical exams, the test measures included distance-corrected near visual acuity (DCNVA), accommodative amplitude (AA) and the Near Acuity Visual Questionnaire (NAVQ, higher scores indicate greater difficulty with tasks such as reading small print). Longitudinal scans of the lens were performed with the Brillouin Optical Scanning System (BOSS^{TM}, Intelon Optics), to measure the axial thickness and elasticity ("longitudinal elastic modulus", LEM) of the lens.

Results: Of 33 subjects, binocular LEM values were obtained from 28 subjects (9 males) and monocular values from a further 4 (2 males). Subject age (mean±SD of 49.8±3.3 years) was significantly correlated with vertical cup-to-disc ratio (CDR), AA and DCNVA ($P \leq 0.001$). DCNVA also correlated with CDR and AA ($P < 0.001$). With eyes grouped by the degree of presbyopia (based on DCNVA, mild= 20/25 or 20/32; moderate= 20/40 or 20/50; severe= 20/63 or 20/80), analysis of variance tests showed the following significant differences in the clinical data: smaller CDR and greater AA for the mild group than the other two groups ($P < 0.001$) and higher IOP in the severe group than the moderate ($P = 0.007$). The NAVQ scores ranged from 0 to 100 (out of 100) and were significantly correlated only with DCNVA ($P = 0.006$). Compared with the clinical measures, LEM was positively correlated with AA ($P = 0.005$) and negatively correlated with DCNVA ($P = 0.02$) and spherical equivalence ($P = 0.03$). The BOSS data showed good repeatability within subjects (median variability within each eye of ≤6.1% for LEM and thicknesses) but varied considerably across subjects.

Conclusions: Across this small range of participant ages and BCVAs (20/15 to 20/20), differences were found between individuals in terms of self-reported difficulty with near vision and in lens elasticity and size, even for those of the same age and/or DCNVA. Thus, BOSS scans provide a non-contacting measure of individual differences in lens biomechanics.

CONTROL ID: 3709554

SUBMITTER (NAME ONLY): Jonathon Reynolds

TITLE: Vitamin C Reduces IGF-1 and VEGF Signaling in Retinal Endothelial Cells

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Reynolds, T.J. Alger, N. Islam, V.V. Manukyan, A.P. Sheppert, D.W. Sant, Biomedical Sciences, Noorda College of Osteopathic Medicine, Provo, Utah, UNITED STATES|G. Wang, Genetics, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glucose acts as a competitive inhibitor for vitamin C to cross the blood retinal barrier. Hyperglycemia reduces vitamin C levels in the eyes. Vitamin C acts as a cofactor for the Ten Eleven Translocation Oxidase (TET) enzymes, which are required for active DNA demethylation. Experiments were performed using primary, human retinal endothelial cells to elucidate the effects of vitamin C deficiency on the breakdown of the blood retinal barrier in diabetic retinopathy.

Methods: Primary human retinal endothelial cells were treated either with or without 50 micromolar vitamin C and RNA was extracted. Whole transcriptome sequencing (RNA-seq) was used to determine transcription changes genome wide. Pathway analysis was performed using EnrichR, GOrilla, and Gene Set Enrichment Analysis (GSEA).

Results: After treatment with vitamin C, 437 genes were found to have upregulated transcription and 308 genes were found to have downregulated transcription. Pathway analysis highlighted changes in several pathways that may elucidate changes that occur in retinal endothelial cells that may contribute to the pathogenesis of diabetic retinopathy, such as Insulin-like growth factor 1 (IGF-1) signaling, which was reduced after treatment with vitamin C. Although the contribution of IGF-1 to diabetic retinopathy has been largely attributed to stimulation of production of vascular endothelial growth factor A (VEGFA) in retinal pigment epithelial cells (RPE), knockout of IGF-1 receptors in retinal vascular endothelial cells was shown to reduce neovascularization in an oxygen-induced retinopathy mouse model. Additionally, VEGFA-VEGFR2 signaling pathways were reduced after treatment with vitamin C. New blood vessels from proliferative diabetic retinopathy have been found to regress after anti-VEGF treatments, and anti-VEGF is similar in efficiency to panretinal photocoagulation.

Conclusions: These data suggest that local vitamin C deficiencies in the eyes of diabetics affect signaling in the retinal endothelial cells which may contribute to the breakdown of the blood-retinal barrier in diabetic retinopathy. Specifically, vitamin C reduces IGF-1 signaling and VEGF signaling in retinal endothelial cells.

CONTROL ID: 3709555
SUBMITTER (NAME ONLY): Suzanne Michalak
TITLE: Longitudinal Choroidal Development in Preterm Infants
SESSION TITLE: Pediatric ophthalmology and imaging
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: While much is known about the timeline of retinal vascular development in preterm infants, little is known about the developmental trajectory of the choroid. We characterized changes in choroidal thickness from 30 to 60 weeks postmenstrual age (PMA) using optical coherence tomography imaging (OCT) in preterm infants.

Methods: Infants underwent imaging with investigational hand-held OCT as part of the prospective, observational, IRB-approved Study of Eye Imaging in Preterm InfantS (BabySTEPS). Average choroidal thickness across the central subfoveal 1 millimeter in each eye at each time point was measured using custom segmentation software. Eyes imaged at three or more distinct time points between 30 and 60 weeks PMA were included in the analysis. A segmented mixed model was used to analyze the change in choroidal thickness as a function of PMA.

Results: We included 1159 imaging sessions of 85 preterm infants (166 eyes). Average gestational age was 27.7 ± 2.6 weeks. Between 30 and 60 weeks PMA, choroidal growth follows a biphasic model, with a linear growth rate of 13.9 µm per week (95% confidence interval 12.8-14.0 µm) from 30 weeks until 38.2 weeks then cessation of growth, with a growth rate of -0.20 µm per week (95% confidence interval -1.48 to 1.07 µm) from 38.2 weeks to 60 weeks. Mean (±standard deviation) of choroidal thickness was 151.8 ± 38.9 µm at 31±1 weeks, 274.1 ± 86.0 µm at 41±1 weeks, and 301.0 ± 82.4 µm between 50 and 60 weeks.

Conclusions: The choroid experiences rapid linear growth from 30 weeks PMA until 38 weeks PMA, at which time the choroidal thickness is similar to that of a healthy adult. These foundational measurements will be essential as we learn more about choroidal development in preterm infants and the role of the choroid in ocular and retinal health.

CONTROL ID: 3709565

SUBMITTER (NAME ONLY): Akosua Boateng

TITLE: Dysregulation of Autophagy Occurs During Congenital Cataract Development in CRYβA1/A3-ΔG91 Mice.

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Boateng, R. Joseph, O.P. Srivastava, Optometry and Vision Science, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: CRYßA3/A1 is a lens-specific structural protein. However, in the RPE, recent evidence suggests that CRYßA3/A1 is also a lysosomal-resident protein where it controls autophagy and phagocytosis by regulating endolysosomal acidification via modulating the V-ATPase proton pump. G91-deletion (βA3ΔG91) is a common mutation in CRYßA3/A1 that causes autosomal dominant congenital cataract in humans. In this study, the purpose was to explore the molecular mechanism of βA3ΔG91-induced congenital cataract development.

Methods: We generated a βA3ΔG91 mouse model using CRISPR-Cas9 methodology at the UAB Transgenic & Genetically Engineered Models Core (TGEMs) facility. Comparative phenotypic- and biochemical characterizations of lenses from 1-month-old βA3ΔG91- and wild-type (WT) mice were performed. The methodologies used were non-invasive slit lamp examination, cellular migration assay, hematoxylin and eosin (H&E) staining, immunohistochemical (IHC) and western blot analyses and TUNEL assay. During the analyses, anti-βA3-, anti-p62-, anti-LC3- and anti-GAPDH antibodies were utilized.

Results: Slit-lamp examinations of lenses of 15-days- and 1-month old lenses showed that the βA3ΔG91 mice developed nuclear cataract and microphakia relative to age-matched WT mice. Scratch assay showed that βA3ΔG91 LECs had a relatively slower cellular migration rate than the WT cells. Comparative H&E- and Hoechst staining exhibited abnormally high number of nuclei and their debris in the inner and outer cortex of lenses of βA3ΔG91 than WT mice, suggesting an impaired nuclear degradation process. The IHC analyses showed ring-shaped overlapping expressions of LC3 A/B and CRYßA3 that were limited to the inner cortex of the βA3ΔG91 lenses. Additionally, βA3ΔG91 lenses also exhibited relatively higher p62 expression, lower CRYßA3 expression and greater apoptotic cells in the lens cortex in the TUNEL assay. These findings were further confirmed by western blot analyses.

Conclusions: The study shows an association of impaired autophagy in βA3ΔG91-lenses relative to WT lenses. It is probable that the presence of the greater autophagic cargo might be due to G91-deletion in βA3-crystallin and a lysosomal defect.

CONTROL ID: 3709568

SUBMITTER (NAME ONLY): David Birch

TITLE: Natural history of the progression of choroideremia; 24-month follow-up

SESSION TITLE: Retinal Degeneration

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Choroideremia (CHM) is a progressive, blinding X-linked chorioretinal dystrophy caused by mutations in the CHM gene encoding Rab escort protein-1. The purpose of our ongoing study (NCT02994368) is to evaluate the rate of progression of CHM using functional and anatomical assessments and to establish valid endpoints for future interventional trials.

Methods: Key eligibility criteria for this observational study include males age ≥ 14 years with a clinical and molecular diagnosis of CHM; best-corrected visual acuity (BCVA) score ≥34 ETDRS in the worst eye; presence of preserved ellipsoid zone (EZ) and outer nuclear layer within the central 10^{o} (using SD-OCT); and measurable visual fields. Each eye's disease stage was characterized based on preserved visual fields (VF) using the Goldmann III_{4e} spot size or equivalent; Type 1 is advanced with < 30 degree VF and Type 2 is early/intermediate with ≥ 30 degree VF. Both eyes were followed with semi-annual assessments for 24 months. Study assessments included BCVA, preserved fundus autofluorescence area (PFAF), and static perimetry (SP) with mean sensitivity, total hill of vision (V_{TOT}) and central vision (V_{30}) analyses. A central reading center graded PFAF images and visual fields.

Results: Subjects (n=55) were enrolled at 5 sites in the US and Canada; 4 subjects discontinued after the screening visit. The majority were non-Hispanic White (92.7%). Mean age ± SD was 32.8 ± 11.2 years. Most eyes at screening were assessed as Type 2 (81%); analysis by disease stage was limited due to the small proportion of Type 1 eyes (14%) enrolled. Subjects who completed the 24-month follow up visit (n=47, 85%) were included in the analysis. Baseline values and annualized rates of change are shown in Table 1. Correlations with PFAF area for SP mean sensitivity, SP V_{TOT}, and SP V_{30} at baseline are shown in Table 2. Analysis based on disease stage or pooled sample yielded similar results.

Conclusions: Similar to previous reports, BCVA remained stable, but PFAF and visual field parameters declined significantly over 24 months. Strong correlations were observed between PFAF area and visual field parameters at each visit. These findings have important implications for quantification and monitoring of structural and functional disease progression in CHM future interventional treatment trials.

CONTROL ID: 3709569

SUBMITTER (NAME ONLY): Jasmina Cehajic Kapetanovic

TITLE: Impaired glutamylation of ORF15 presents a unique phenotype in RPGR-related retinal dystrophy

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cehajic Kapetanovic, C. Martinez-Fernandez de la Camara, M.E. McClements, R.E. MacLaren, Nuffield Laboratory of Ophthalmology, Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|J. Cehajic Kapetanovic, C. Martinez-Fernandez de la Camara, J. Birtel, S. Rehman, P. Charbel Issa, R.E. MacLaren, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|J. Birtel, Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|P. Charbel Issa, Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|A.J. Lotery, Clinical Neuroscience Research Group, University of Southampton Faculty of Medicine, Southampton, Southampton, UNITED KINGDOM|A.J. Lotery, Ophthalmology, University Hospital Southampton NHS Foundation Trust, Southampton, Southampton, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To determine the genotype-phenotype correlation in patients with RPGR retinal dystrophy, the commonest form of X-linked and recessive retinitis pigmentosa. Post-translational glutamylation of photoreceptor-specific RPGR ORF15 by TTLL5 enzyme is essential for its function. TTLL5 needs to bind to ORF15 via the C-terminus to glutamylate RPGR. Since TTLL5 loss leads to cone-rod phenotype, in which normal RPGR would not be glutamylated, we hypothesise that the phenotype of distal RPGR mutations would merge with TTLL5 retinal dystrophy.

Methods: We conducted a retrospective study of 102 male patients with RPGR disease at three specialist centres and recorded results of ophthalmic examination, retinal imaging, microperimetry and molecular genetic analysis by next-generation sequencing. In vitro assays were performed to assess the level of RPGR glutamylation in distal mutations and analyse the level of interaction with TTLL5 in these mutant constructs compared to wild-type RPGR.

Results: Of 102 male patients with genetically confirmed RPGR variants, 99 were deep phenotyped. 13 patients had advanced disease with pan-retinal photoreceptor dysfunction. 64 out of remaining 86 patients (74%) had predominant rod-cone phenotype, 18/86 (21%) had cone-rod, 3/86 (3%) had cone only phenotype and 1/86 (1%) patients had mixed cone and cone-rod phenotype. Most mutations associated with cone-rod phenotype were in the distal part of the ORF15 region and those with cone only phenotype were in the very distal part including the basic domain. In-vitro glutamylation assay showed that all tested truncating mutations with a predominant cone phenotype (n=3) had reduced levels of glutamylation, with variable degree of interaction with TTLL5 enzyme.

Conclusions: Mutations found at the proximal N-terminus of RPGR are associated with predominant rod-cone phenotype, with increasing cone involvement towards the distal C-terminus and a predominant cone phenotype associated with the very distal mutations. In-vitro studies demonstrate the importance of glutamylation for normal functioning of RPGR, as the very distal mutations that result in almost full-length normal RPGR, reduce glutamylation and lead to retinal disease with cone phenotype. The application of RPGR with reduced glutamylation in gene therapy clinical trials may convert a rod-cone dystrophy into a cone dystrophy phenotype.

CONTROL ID: 3709573

SUBMITTER (NAME ONLY): Alexander Schuster

TITLE: Association of commonly used systemic medications with glaucoma prevalence and intraocular pressure across Europe: the E3 Consortium

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate the association of common systemic medication use with intraocular pressure and glaucoma prevalence in the European population.

Methods: We examined associations of systemic medication use with intraocular pressure and glaucoma prevalence in a meta-analysis of multiple cohort studies of the European Eye Epidemiology (E3) consortium. IOP measurement method and glaucoma ascertainment were according to individual study protocols. Multivariable regression (linear for IOP and logistic for glaucoma prevalence) was carried out in each study and results pooled using random effects meta-analysis. Age, sex, body-mass index and diabetes were included as co-variables. Associations of antidiabetic medications were evaluated only in diabetic subjects.

Results: A total of 46,845 participants from 11 population-based studies from the E3-consortium were included. In the meta-analysis of our fully-adjusted multivariable models, beta-blocker usage was associated with a lower IOP (all beta-blockers: Beta=-0.33 mmHg, 95% confidence interval (CI)=-0.58 to -0.08; non-selective betablockers: Beta=-0.56, 95% CI=-0.92 to -0.21; selective betablockers: Beta= -0.40, 95% CI=-0.64 to -0.16). In the meta-analysis of our fully-adjusted multivariable models, usage of calcium-channel blockers was positively associated with a higher glaucoma prevalence (all calcium-channel blockers: OR=1.25, 95% CI=1.05 to 1.50; selective calcium-channel blockers with mainly vascular effects: OR=1.27, 95% CI=1.05 to 1.53; selective calcium-channel blockers with direct cardiac effects: OR=1.54, 95% CI=1.07 to 2.21). Usage of RAS-inhibitors, diuretics, alpha-agonists, statins, fibrates,

non-selective monoamine reuptake inhibitors, selective serotonin reuptake inhibitors, and antidiabetic medications was not associated with IOP or glaucoma.

Conclusions: Our study supports and quantifies the known IOP-lowering effect of systemic beta-blockers, but there was no evidence of an IOP-lowering effect of other commonly used systemic medications. The usage of calcium-channel blockers (both with vascular and direct cardiac effects) was associated with a higher prevalence of glaucoma but not with higher IOP. Further studies are required to probe whether this harmful association of calcium-channel blockers with glaucoma is causal.

CONTROL ID: 3709574

SUBMITTER (NAME ONLY): Jie Meng

TITLE: PEDF exerts neuroprotective effects on retinal ganglion cells via PEDF receptors

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Meng, S. Bürger, A. Zwanzig, M. Beck, P. Wiedemann, F. Ziemssen, J. Unterlauft, E. Wolfram, Eye Hospital, Universitat Leipzig, Leipzig, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: The aim of this study was to investigate expression and regulation of two of several receptors for PEDF, patatin-like phospholipase 2 gene product/PEDF-R and laminin receptor (LR), in serum-starved RGCs under hypoxia, which is a relevant pathological condition in retinal neurodegenerative diseases such as glaucoma or ischemic retinopathies, and explore their involvement in the survival of retinal neuronal cells. Changes in the expression of some neuroprotective factors (PEDF, VEGF, BDNF) and anti-apoptotic Bcl-2 family members (Bcl-2, Bcl-x_L), when reducing the expression of PEDF receptors. In addition, we have also evaluated whether ERK1/2 signaling pathway was involved in the process which PEDF exerts pro-survival effects on retinal ganglion cells.

Methods: Using RGCs isolated from mice eyeballs and the immortalized retinal cell line R28 as the main research objects. Immunocytochemical Staining, RNA Interference, qPCR, and western blot techniques, were used to detect the expression levels of PEDF-R and Laminin-R under different stimulations. After knocking out PEDF-R and LR genes with interfering RNA, the expression level of neuroprotective factors and anti-apoptotic Bcl-2 family-related factors were detected. Western blot technology was also used to explore the phosphorylation level of ERK1/2 signaling pathway.

Results: RGCs and R28 cells express both PEDF-R and LR. PEDF and VEGF exposure, as well as the presence of Müller cells, enhance the expression of both receptors. These expression trends were the same under hypoxic conditions. After knocking down PEDF-R and LR, the anti-apoptotic Bcl-2 family members' (Bcl-2, Bcl-x_L) and neuroprotective mediators' (PEDF, VEGF, BDNF) expression was significantly reduced. PEDF treatment enhanced the phosphorylation level of ERK1/2 in R28 cells.

Conclusions: The enhancement of PEDF-R and Laminin R under hypoxia sensitizes retinal neurons to interaction with PEDF, which leads to increased cell viability through induction of anti-apoptotic Bcl-2 family members, expression of secretable pro-survival factors, and suppression of apoptosis. ERK1/2 signaling pathway might be involved in the PEDF's action. Elucidating PEDF-R, Laminin R function and signaling pathways regulating receptor-promoted RGC survival may be helpful in developing more efficient treatment options for retinal neurodegenerative diseases.

CONTROL ID: 3709577

SUBMITTER (NAME ONLY): Yiming Lu

TITLE: Laser speckle flowgraphy correlates with the OCT-derived choroidal metrics in healthy human eye

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lu, H. Zhou, X. Zhou, Y. Chen, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R.K. Wang, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the dominant source of the laser speckle flowgraphy (LSFG) signals using optical coherence tomography (OCT) derived retinal and choroidal metrics.

Methods: LSFG, OCT and OCT angiography (OCTA) imaging were performed using a custom-designed LSFG system and a commercial swept-source OCT (SSOCT) system. Mean LSFG map was obtained to enhance the signal-to-noise ratio by averaging individual LSFG maps over multiple cardiac cycles. Standard 6-by-6 mm OCTA map of the retina was generated by the SSOCT system. Choroidal vasculatures were visualized from OCT scans using an attenuation correction method. Large retinal vessels were identified using the retinal OCTA image and the corresponding vessel areas were excluded from LSFG, retinal and choroidal data, leaving the background area for analysis. Two-dimensional metrics maps, including retinal thickness (RT), vessel area density (VAD), vessel skeleton density (VSD), vessel complexity index (VCI), vessel diameter index (VDI), and vessel perimeter index (VPI) of the retina, and choroidal thickness (CT), choroidal vessel volume (CVV), and choroidal vessel index (CVI), were obtained for the quantification analysis. Topographic correlation analysis was then performed between the maps of LSFG and the retinal and choroidal metrics.

Results: 10 normal subjects (6 females and 4 males, age range: 24~35 years old) without any known eye diseases were involved in this study. The mean LSFG map exhibited good accordance with the CT and CVV maps. In comparison, the retinal metrics presented generally homogenous distribution of values which was different from the mean LSFG map (Figure 1). Statistically, LSFG signals were significantly correlated with CT and CVV (Spearman's correlation coefficient, $\rho > 0.6$ and p-value < 0.01), but were generally not correlated with all the retinal metrics and CVI ($|\rho| < 0.5$ and p-value > 0.05).

Conclusions: LSFG signals were correlated with the choroidal thickness and vessel volume, suggesting the choroidal blood flow are the dominant source of the LSFG signal.

CONTROL ID: 3709582

SUBMITTER (NAME ONLY): Antoni Vallbona Garcia

TITLE: Reduced mitochondrial DNA copy number in peripheral blood lymphocytes of POAG patients

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vallbona Garcia, C.A. Webers, T.G. Gorgels, University Eye Clinic Maastricht, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|A. Vallbona Garcia, I. Hamers, F. van Tienen, I. de Coo, H. Smeets, Toxicogenomics, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|H. Smeets, T.G. Gorgels, Research school of mental health and neuroscience, Universiteit Maastricht, Maastricht, Limburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Glaucoma is a group of complex optic neuropathies, which cause vision loss in more than 70 million people worldwide. Its pathophysiology is not fully understood. Since retinal ganglion cells (RGCs) have a high energy demand, suboptimal mitochondrial function may put the survival of these neurons at risk. In the present study, we explored if peripheral blood lymphocytes (PBL) mitochondrial DNA (mtDNA) quantity or quality could reflect a role for mitochondrial impairment in development of primary open angle glaucoma (POAG).

Methods: We have selected four age- and sex-matched groups, namely POAG patients with high intraocular pressure at diagnosis (high tension glaucoma: HTG; n=98), normal tension glaucoma patients (NTG, n=37), ocular hypertensive controls (n=9), and cataract controls (n=32), all without remarkable comorbidities. PBL DNA was isolated and mtDNA copy number was assessed by qPCR quantification of mitochondrial D-loop and nuclear B2M gene. MtDNA copy number comparison between the groups was conducted using Kruskall-Wallis test combined with Dunn's multiple comparison test in GraphPad Prism and R software (V4.1.2). In addition, the presence of the common 4,977 base pair mtDNA deletion was assayed by a sensitive PCR, which amplified the region containing the specific breakpoints in the mitochondrial genome.

Results: Analysis of the mtDNA copy number revealed a significant reduction in HTG patients (median mtDNA copies per cell: 60.82, interquartile range (IQR): 47.75-80.26) compared with NTG patients (median mtDNA copies per cell: 76.77, IQR: 62.30-99.54, p-value < 0.01) and cataract controls (median mtDNA copies per cell: 85.90, IQR: 71.82-105.1, p-value < 0.001), but not with ocular hypertensive controls (median mtDNA copies per cell: 77.22, IQR: 67.98-109.8). The common 4,977 base pair mtDNA deletion was not detected in any of the participants.

Conclusions: The mtDNA copy number was reduced in PBL-DNA of HTG patients. Most likely, this reflects a suboptimal mitochondrial function, which together with ageing and/or high intraocular pressure, may lead to mitochondrial dysfunction during life in RGCs and may contribute to glaucoma pathology in some HTG patients. These patients may be amenable for a mitochondria-targeted drug treatment.

CONTROL ID: 3709583

SUBMITTER (NAME ONLY): Tom Buckley

TITLE: Bi-allelic inheritance of dominant and recessive RP1 mutations raises challenges for genetic counselling

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Buckley, P. Clouston, M. Shanks, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|J. Cehajic Kapetanovic, R.E. MacLaren, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To report on the presence of both dominant and recessive RP1-related retinitis pigmentosa in different members of the same non-consanguineous family.

Methods: In this case series, three members of the same family - the daughter, father and mother - were investigated. They underwent clinical assessment by dilated fundus examination and multimodal imaging. Molecular analysis of 111 genes associated with retinitis pigmentosa and retinitis pigmentosa-like phenotypes was undertaken probing the RP1 gene capturing the coding exons and 10 base pairs of the flanking introns of the 111 genes. Putative pathogenic variants were confirmed by Sanger sequencing.

Results: The 38-year-old father was diagnosed with an asymptomatic mild phenotype of rod-cone dystrophy detected by his optometrist, which was subsequently confirmed to be caused by a previously described dominant RP1 c.2613dupA mutation. He was reassured that his 11-year old daughter had a 50% chance of inheriting the same mutation and that the condition, if she had it, would most likely be mild. Clinical phenotyping of his daughter however showed a severe case of early onset cone-rod dystrophy. The mother was asymptomatic and clinically normal. Sanger sequencing of the RP1 gene in the daughter confirmed the presence of biallelic mutations – the dominant c.2613dupA variant from her father and a novel c.3843dupT truncating variant inherited from her mother, both located in exon 4 of the RP1 gene.

Conclusions: Mutations in exon 4 of RP1 are known to cause differential dominant and recessive disease. The novel c.3843dupT variant is likely to act in an autosomal recessive manner, since the heterozygous mother is clinically unaffected. Its pathogenicity is also supported by the previously reported c.3843delT mutation at the same nucleotide and results in a similarly truncated RP1 protein. The father is mildly affected by a known dominant variant which truncates the RP1 protein more proximally. However, inheritance of both variants in a compound heterozygous state in the daughter resulted in a much more severe, early onset cone-rod phenotype, in a pattern akin to recessive disease. This raises challenges for genetic counselling and development of gene-based therapies for RP1 mutations.

CONTROL ID: 3709584

SUBMITTER (NAME ONLY): Charles Evers III

TITLE: What are the smallest clinically visible drusen in aging and age-related macular degeneration (AMD)? A histology and fluorescein angiography study

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.D. Evers III, J.D. Messinger, C.A. Curcio, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|L. Chen, The First Affiliated Hospital of Chongqing Medical University, Chongqing, Sichuan, CHINA|D. Cabral, K. Freund, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|K. Freund, Department of Ophthalmology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|D. Cabral, CEDOC - NOVA Medical School, Universidade NOVA de Lisboa, Lisbon, PORTUGAL|R. Dolz-Marco, Unit of Macula, Clinica Oftalvist, Valencia, SPAIN|

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ABSTRACT BODY:

Purpose: High resolution optical coherence tomography (HR-OCT) provides unprecedentedly detailed views of retina and choroid. Small perturbations of retinal pigment epithelium-basal lamina-Bruch's membrane band (RPE-BL-BrM) represent earliest stages of AMD. To inform the interpretation of HR-OCT-anchored multimodal imaging, we identified small drusen by histology and fluorescein angiography.

Methods: We surveyed Project MACULA (https://projectmacula.org/) an online resource of epoxy-resin histology of human donor eyes (N=54, aged-normal; N=24 early-intermediate AMD; N=13 geographic atrophy). Nodular drusen located between RPE- BL and inner collagenous layer of BrM were solid, globular, and homogeneously stained with toluidine blue. They lacked overlying basal laminar deposit (BLamD, between RPE and native BL) and basal mounds (soft drusen material within BLamD). Soft drusen material in any location was granular and light grayish brown. In images acquired with an oil immersion objective, base widths of single (non-confluent) nodular drusen were measured using FIJI. In one eye with non-exudative neovascular AMD, an area of punctate hyperfluorescence in late-phase fluorescein angiography (FA) 11 years before death (PMID 32247535) was mapped in histology.

Results: In 104 images from 43/92 eyes, small lesions included nodular drusen, 53 images; small soft drusen, 8; BLamD / basal mounds, 33; multilayer BLamD / BLinD-drusen, 10. The Figure shows that the range of nodular drusen (N=128) widths was 2.2 to 110 μm (median, 13.0 μm; interquartile range 7.7, 20.0 μm). In the eye with late phase FA, 91 similar-sized nodular drusen were found in an area with small circles of uniform fluorescence.

Conclusions: In two samples, 90% and 95% of nodular drusen (92% total) have base width <30 μm, a size just visible in color fundus photography (CFP; PMID 10365048). Results support reports that CFP reveals depigmentation over drusen and underestimates drusen dimensions, relative to histology and OCT (PMID 32568988, 33411474). The FA appearance is consistent with staining of individual drusen. Whether these deposits resemble cuticular drusen with "starry sky" angiograms needs further research (PMID 7525362, 10365048, 20924263, 28964580). Direct visualization of a sequence from numerous small drusen to soft drusen (PMID 17270675, 25905023) may be possible.

CONTROL ID: 3709585

SUBMITTER (NAME ONLY): Gui-Shuang Ying

TITLE: Dynamic Prediction Model for Treatment-requiring Retinopathy of Prematurity

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Ying, Y. Yu, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|G. Binenbaum, Ophthalmology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior risk models for retinopathy of prematurity (ROP) have been based on risk factors assessed at a single time point, even though risk factors can change over time. We sought to develop and validate a dynamic prediction model for treatment-requiring ROP (TR-ROP) using time-updated risk factors in two large, broad-risk cohort studies of premature infants.

Methods: Secondary analyses were performed using data from the G-ROP-1 study (retrospective, 7483 infants from 29 hospitals, 2006-2012) for model development and data from the G-ROP-2 study (prospective, 3980 infants from 41 hospitals, 2015-2017) for model validation. The outcome was development of TR-ROP (e.g., type 1 or treated ROP). Risk factors considered for the prediction model included birth weight [BW], gestational age [GA], gender, race, oxygen use, Sepsis/NEC, thrombocytopenia, maternal or donor milk feedings, weight gain rate, a time-updating previously validated ROP severity score, and postmenstrual age (PMA). Univariable and multivariable repeated measures logistic regression models were performed to identify predictive risk factors. Area under the ROC curve (AUC) was calculated to evaluate the prediction model performance.

Results: TR-ROP occurred in 524 (7.0%) of G-ROP-1 infants (median GA 28 wks; median BW 1099g) and 256 (6.4%) of G-ROP-2 infants (median GA 28 wks; median BW 1072g). Using G-ROP-1 data, a dynamic prediction model (Table 1) was developed that included BW ($p<0.001$), race ($p<0.001$), week of first enteral feeds during the first 6 weeks of life ($p<0.001$), time-updating thrombocytopenia ($p=0.004$), NEC/sepsis ($p=0.004$), slow weight gain ($p=0.004$), ROP severity score ($p<0.001$), PMA, and interaction term between ROP severity score and PMA ($p<0.001$). This prediction model had an AUC of 0.88, which was significantly higher than a prediction model based on BW and GA only (AUC=0.77, $p<0.0001$). A prediction model that included significant predictors (BW, GA, race, ROP severity score, PMA, and interaction between ROP severity score and PMA) that were available in both the G-ROP-1 and G-ROP-2 datasets had an AUC of 0.86 in G-ROP-1 and 0.87 in G-ROP-2 (Table 2).

Conclusions: Our developed and validated dynamic prediction model that considers time-updating ROP severity score and other traditional and novel risk factors may provide a tool for dynamically identifying high risk premature infants that are likely to develop TR-ROP.

CONTROL ID: 3709586

SUBMITTER (NAME ONLY): Alexander Reese

TITLE: Multimodal imaging case series of acute macular neuroretinopathy secondary to COVID-19 infection

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Reese, Augusta University and University of Georgia Medical Partnership, Athens, Georgia, UNITED STATES|G.D. Lee, H. Cho, S. Koh, R. Komati, Georgia Retina, PC, Sandy Springs, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Understanding of the ocular manifestations of coronavirus disease 2019 (COVID-19) is continuing to develop. While ocular symptoms, chiefly conjunctivitis, have been reported, retinal pathologies have been suggested as a rarer complication and are hypothesized to derive from a combination of the inflammatory and vasculopathic effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Using a retrospective, observational case series design, we describe a series of four eyes in three patients with acute macular neuroretinopathy (AMN) and paracentral acute middle maculopathy (PAMM) associated with COVID-19 illness.

Methods: Our practice's electronic medical record (EMR) was retrospectively queried for patients from April 2020 to December 2021 who had been diagnosed with AMN or PAMM and COVID-19 illness. Three patients were identified by this method. Patient demographic information, physical exam, optical coherence tomography (OCT), infrared reflectance (IR), and fluorescein angiography (FA) studies were all used for analysis.

Results: Imaging signs of AMN were revealed in four eyes in three female patients, aged 22, 32, and 64 years old, all with confirmed symptomatic COVID-19 corresponding to the start of visual symptoms. The average onset of visual symptoms from COVID-19 illness was 14 days (range 0–56). 4/4 eyes were symptomatic for scotomata. Average logMAR visual acuity was 0.024 (Snellen 20/21, range 0–0.097). 4/4 eyes demonstrated typical findings of AMN: IR imaging with prominent dark petaloid or ovoid parafoveal lesions and corresponding disruption of the ellipsoid zone on OCT (Fig. 1). FA imaging did not show any abnormal fluorescence pattern. Autofluorescence in 1/4 eyes demonstrated hyperautofluorescence corresponding to the abnormal area on IR imaging (Fig. 2). Two month follow-up showed persistent symptoms of scotomata with unchanged findings on follow-up imaging in 100% of cases.

Conclusions: This series demonstrates that, although rare, SARS-CoV-2 infection may result in microvasculopathic injuries to the retina, namely AMN and PAMM.

CONTROL ID: 3709591

SUBMITTER (NAME ONLY): Daniel LEMAITRE

TITLE: Treatment Outside the Recommended Guidelines for Retinopathy of Prematurity (ROP): Prevalence, Characteristics and Issues.

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. LEMAITRE, A. Barjol, Y. Abdelmassih, G. Martin, F. Metge, T. Chapron, G. Caputo, La Fondation Adolphe de Rothschild, Paris, Île-de-France, FRANCE|D. LEMAITRE, Medicine, Sorbonne Universite, Paris, Île-de-France, FRANCE|C. Farnoux, Pediatric, Assistance Publique - Hopitaux de Paris, Paris, Île-de-France, FRANCE|T. Chapron, Centre de Recherche en Epidemiologie et Statistiques Sorbonne Paris Cite, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To assess the prevalence and characteristics of preterm infants with Retinopathy Of Prematurity (ROP) treated outside the recommendation guidelines.

Methods: In this retrospective monocentric cohort, we included all premature babies treated in our department for ROP by photoablative laser or anti-VEGF intravitreal injection. Main outcome was treatment of both eyes for ROP less severe than type 1.

Results: A total of 114 children received treatment for ROP in our department, among them 32 (28.1%) children received treatment for off-label indications. The off-label indications were persistent stage 2 or 3 ROP that showed no evidence of regression after 41 weeks of corrected gestational age (11 children; 34.4%), pre-plus stage (11 children; 34.4%), difficulties in disease staging (7 children; 21.9%), type 2 ROP with plus disease (2 children; 6.2%), and logistical difficulties (1 child, 3.1%). In the off-label treated group, mean gestational age was 25.3±1.4 weeks and mean birth weight was 734±174 grams. Off-label treated children were older (40.6±7.0 weeks vs. 37.4±3.6 weeks; p=0.002) and received less laser impacts (1460±207 vs. 2007±171 impacts; p=0.03). In the group treated inside the guidelines, 10 babies received bilateral treatment with one eye less severe than type 1 ROP.

Conclusions: To resume, in our cohort 28.1% of babies received treatment for ROP less severe than type 1. Main indications for off-label treatment were the persistence of active ROP during follow-up and the presence of pre-plus stage disease. If thisOur data suggests the need to update ROP treatment criteria to reflect real-life practices. Additional studies are required to evaluate long-term impact of a treatment outside the recommended indications and to establish revised treatment guidelines.

CONTROL ID: 3709595

SUBMITTER (NAME ONLY): Julia Owen

TITLE: Deep-learning Embedding of Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO) for Macular Telangiectasia Type 2 and Age-Related Macular Degeneration

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Owen, C.S. Lee, A.Y. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|L. Sauer, P.S. Bernstein, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fluorescence lifetime imaging ophthalmoscopy (FLIO) allows for unprecedented temporal resolution of the macular fluorescence signal. Current visualization techniques for FLIO rely on hand-adjusted parameters that may not be reproducible. Here we fully-automate the visualization of FLIO data by embedding in a lower dimensional space, merging 1-D autoencoder and classification deep learning networks.

Methods: FLIO images were collected from healthy (n=91), MacTel (n=128) and AMD (n=30) eyes for the short (f1) and long (f2) spectral channels (each with 1024 time bins). The images were patient-split 80/20 into training and validation sets. Labels for vessels were segmented using a threshold on the mean across time. A parafoveal window of 64x64 pixels was extracted from each train subject and each pixel time course (f1 and f2) was truncated to 512 time points and labeled as either: Healthy, MacTel, AMD, or vessel. The f1 and f2 time courses were embedded into two dimensions with parallel autoencoders linked through a 4-class classification head (see Figure 1A). The whole validation images (256x256) were embedded into four dimensions (two each for f1 and f2) and visualized.

Results: We achieved a validation accuracy of 80.0% and correlation coefficients of 0.911 and 0.957 between the true and decoded time courses for f1 and f2, respectively (Fig 1B). The examples of the decoded time courses are more smooth but preserve the shape of the true FLIO time courses (Fig 1C). The example MacTel embeddings show changes in the perifoveal area while the example AMD embeddings show a more widespread alteration throughout the macula (Fig 2).

Conclusions: Utilizing autoencoders linked with a classification head, we created an embedding that is sufficient to recover the original signal (autoencoder) and is designed to be disease specific (classification). This fully-automated approach may enable FLIO to be used as a biomarker in future clinical studies.

CONTROL ID: 3709596

SUBMITTER (NAME ONLY): Arum Wu

TITLE: NANOBODY rescues adRP phenotype in a P23H adRP cell model, suggesting therapeutic potential

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Wu, D. Salom, C. Sander, P.D. Kiser, K. Palczewski, Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|E. Pardon, J. Steyaert, Structural Biology Brussels, Vrije Universiteit Brussel, Brussels, Brussels, BELGIUM|E. Pardon, J. Steyaert, VIB-VUB Center for Structural Biology, Vrije Universiteit Brussel, Brussels, Brussels, BELGIUM|P.D. Kiser, Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|K. Palczewski, Chemistry, Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Treatment for autosomal dominant retinitis pigmentosa (adRP) by gene therapy is challenging, due to genetic heterogeneity. We used innovative NANOBODY® technology to test our hypothesis that nanobodies (Nbs), due to their nano-scale size, would efficiently stabilize P23H mutant RHO and restore rhodopsin homeostasis without cellular toxicity in an in vitro HEK293 cell model of RP. We also characterized the thermodynamics and crystal structure of the Nb-RHO complexes to assess the binding stability and identify the interface between the Nb and its target.

Methods: 29 Nbs were raised against native bovine rod outer segments (ROS). After confirming their binding affinity to native bovine ROS by gel shift assay, selected Nbs were expressed intracellularly in bovine wild type (WT)-RHO cells, or P23H-RHO HEK293 cells. Accumulation of mutant RHO by the Nbs was evaluated by Western blot and UV-visible spectroscopy, relative to controls with non-binding Nb. The stability of the antigen-antibody interactions was analyzed by spectroscopy at different temperatures and pH in light or dark conditions over the period of 11 days. Crystal structures of the Nb-RHO complexes were collected and analyzed along with the results from alanine-scanning mutagenesis in Nb-complementarity-determining regions.

Results: Among the 29 Nbs, 4 Nbs showed a gel shift, indicative of binding to native bovine ROS in a dose-dependent manner. Nb-RHO complexes maintained an equilibrium between ground and active states for 11 days after bleaching in the dark, at 4 ^{o}C or room temperature (RT). Under light conditions, the complexes were still stable at 4 ^{o}C, but gradually bleached and degraded at RT. While P23H-RHO levels were lower compared to WT-RHO by Western blot, intracellular co-expression of Nb in P23H cells significantly increased RHO protein levels ($P<0.05$), relative to the non-binding Nb control. Crystal structure and alanine-scanning results revealed the binding epitopes of Nb to RHO in its extracellular loop II and the N-terminal tail, explaining the action mechanism on mutant P23H stabilization.

Conclusions: Intracellular expression of Nbs rescues the mutant RHO phenotype in an in vitro HEK293 adRP model, suggesting therapeutic potential of the nanobody technology. Since there are few treatment options for RHO-adRP, NANOBODY technology might offer a new treatment option regardless of a patient’s genetic background.

CONTROL ID: 3709598

SUBMITTER (NAME ONLY): Kaitlin Scholand

TITLE: The effects of heterochronic parabiosis in the aged eye and lacrimal gland

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Scholand, R. Sampige, G. Govindarajan, C.S. De Paiva, Ocular Surface Center, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|A.F. Mack, M.E. Maniskas, L.D. McCullough, BRAINS Research Laboratory, Department of Neurology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is associated with inflammation and oxidative stress. In the eye and lacrimal gland (LG), increasing age is associated with chronic inflammation, a greater infiltration of immune cells, and tissue damage. Heterochronic parabiosis is an experimental method used to identify how soluble serum factors impact aging and disease. We investigated if heterochronic pairing of mice (young to aged) could modulate age-related eye and LG alterations.

Methods: Male and female PepBoy mice 4 months of age were surgically joined to either another PepBoy or a C57BL/6J (B6) mouse aged 18 months. Pairings were either isochronic (young to young or aged to aged) or heterochronic (young to aged), all same-sexed. Mice were evaluated 2 months post-surgery. General appearance and focus score were investigated in H&E-stained LG sections (n=21 male pairs; n=5 female pairs). LGs were analyzed by qPCR for inflammatory and T and B-cell related markers (n=5 male pairs; n= 6 female pairs).

Results: There were significant increases in focal score in aged-aged pairings compared to young-young pairings (Kruskal-Wallis test; $P<0.0001$). In male LGs, there was a significant increase in focal score in both mice in the heterochronic young-aged pairing (2±2 vs 3±2 focus score/4mm^2) compared to the isochronic young-young and young non-parabiotic (0.8±0.7 and 0±0 focus score/4mm^2, respectively, at least $P<0.01$). There were significant increases in mRNA fold expression of Ctss (3-fold), Ciita (MHC II,3-fold), Cd19 (57-fold), Ccl19 (3.67-fold), and Ifng (IFN-γ,7-fold) by age (young-young vs. aged-aged) in aged female pairs. There were significant sex-related changes in mRNA fold in Cxcl13 (13-fold) and Il1b (2-fold) in isochronic pairs (at least $P<0.05$ for all). Interestingly, we found significant fibrosis in 36% of the aged parabiotic male LGs, irrespectively of pairing.

Conclusions: Our results indicate that serum soluble factors from young mice for 8 weeks were not enough to reverse inflammation and infiltrating immune cells in aged tissues. It is possible that a longer duration of parabiosis is needed. This suggests that age-related changes in the LG microenvironmental/architecture participate in perpetuating inflammation. Therapies that aim at improving cellular health may have a stronger impact on improving inflammation and cellular inflammation in LGs than parabiosis.

CONTROL ID: 3709599

SUBMITTER (NAME ONLY): Monica Melo

TITLE: Association of variants in the FOXC1, ATXN2 and TXNRD2 genes with primary open angle glaucoma in a Brazilian population

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.B. Melo, T.R. Rodrigues, B.B. de Souza, V.H. Bertozzo, J.N. Castro, Center for Molecular Biology and Genetic Engineering, University of Campinas, Campinas, São Paulo, BRAZIL|V.P. Costa, J.C. Vasconcellos, Ophthalmology, Faculty of Medical Sciences, University of Campinas, Campinas, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Primary Open Angle Glaucoma (POAG) is the main cause of irreversible blindness worldwide, being described as a neurodegenerative disease of multifactorial etiology. Thus, the identification of genetic and environmental factors is of utmost importance for early diagnosis and to establish an appropriate clinical management. Multiethnic Genome Wide Association Studies (GWAS) identified single nucleotide variants (SNVs) in the FOXC1, ATXN2 and TXNRD2 genes that may be associated with the pathophysiology and endophenotypes of POAG. However, to our knowledge, these variants have not been investigated in admixed populations, such as the Brazilian population. The aim of this case-control study was to investigate the association of the variants rs2745572 (FOXC1), rs7137828 (ATXN2) and rs35934224 (TXNRD2) as risk factors for the development of POAG in a Brazilian cohort from the Southeast.

Methods: This study comprised 506 cases and 501 controls. Variants rs2745572 and rs35934224 were genotyped through Taqman® assay and validated by Sanger sequencing in 10% of the samples. Variant rs7137828 was genotyped exclusively by Sanger sequencing. Genetic association was estimated through Chi-Square and Logistic Regression tests.

Results: The case group was consisted of 50.99% males, while the control group was composed by 43.11% males (p=0.011). There was no statistical difference in age between cases and controls. The primary research outcome has revealed that the variant rs7137828 (ATXN2), was associated with an increased risk for development of POAG in the presence of the T allele (p=0.0025). Through multivariate logistic regression adjusted for gender, the TT genotype was associated with an increased risk for development of POAG compared to the CC genotype (p=0.006; OR=1.717; IC95%=1.169-2.535). There was no significant association of rs2745572 (FOXC1) and rs35934224 (TXNRD2) variants for alleles and genotypes with POAG.

Conclusions: Our data indicate an association of the variant rs7137828 in homozygosity as well as in the presence of the T allele with an increased risk for POAG in a Brazilian cohort. If validated in additional sub-populations from the country, this finding may enable the development of relevant strategies for early diagnosis of glaucoma in the future.

CONTROL ID: 3709600

SUBMITTER (NAME ONLY): Michael Carbone

TITLE: Comparison of Average Interval between Anti-Vascular Endothelial Growth Factor (Anti-VEGF) Injections in Diabetic Retinopathy, Retinal Vein Occlusions, and Wet Age-Related Macular Degeneration

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.W. Carbone, D. Marino, C. Miller, A. Miller, C. McCrossin, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|M.W. Carbone, Ohio University Heritage College of Osteopathic Medicine, Athens, Ohio, UNITED STATES|C. Miller, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|A. Miller, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To calculate and compare the average interval between Anti-VEGF injections for patients with diabetic retinopathy (DR), retinal vein occlusion (RVO), and wet age-related macular degeneration (wAMD).

Methods: All data was collected by the practice management of Retina Associates of Cleveland, Inc. Data was collected from patients who received Anti-VEGF injections of Aflibercept (AFL), Bevacizumab (BEVA), Brolucizumab-Dbll (BROL), and Ranibizumab (RAN) from July 2020 through July 2021 and includes patient number, injection service dates, injection service ID's, procedure codes, and primary diagnoses. The patients selected were those injected unilaterally and diagnosed with DR, RVO, or wAMD. The number of days between injection service dates were calculated for each patient. The data set was then organized by primary diagnosis and average number of days between Anti-VEGF injection.

Results: From July 2020 through July 2021, 14,911 patients were injected unilaterally. There were 1,313 DR patients with an average interval between injections of 70 days. There were 2,809 RVO patients with an average interval between injections of 54 days. There were 10,789 wAMD patients with an average interval between injections of 55 days. When comparing average interval between Anti-VEGF injections for DR versus RVO, a two-tailed t-test calculates a p-value of $p<0.01$. When comparing average interval between Anti-VEGF injections for DR versus wAMD, a two-tailed t-test calculates a p-value of $p<0.01$. Lastly, when comparing average interval between Anti-VEGF injections for RVO versus wAMD, a two-tailed t-tests calculates a p-value of $p=0.25$.

Conclusions: The results of this study suggest that patients diagnosed with RVO or wAMD have a shorter interval of time between injections when compared to patients diagnosed with DR. There does not appear to be a significant difference in average injection intervals between patients with RVO and wAMD.

CONTROL ID: 3709603

SUBMITTER (NAME ONLY): Hyeck Soo Son

TITLE: In Situ Injection and Transduction of Human Limbal Stem Cells Using Adeno-Associated Viruses

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Son, A.S. Jun, J.W. Foster, M. Roy, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited corneal dystrophies may cause severe visual impairment. While phototherapeutic keratectomy or corneal transplantations may provide symptomatic relief, the procedures are associated with high infection and recurrence rates. Gene therapies may provide an alternative and a potentially permanent treatment. Adeno-associated viruses (AAVs) have emerged as the vectors of choice for ocular gene therapy thanks to their established safety profile. This study aimed to investigate limbal injections into human cadaveric tissues using 1) trypan blue as a visual guide and 2) two AAV serotypes to test the in situ transduction efficiency of human limbal stem cells (LSCs).

Methods: Human cadaveric corneal tissues were fixed on an artificial anterior chamber (Katena, Parsippany, NJ, USA). Trypan blue (50-µl) was injected into the limbal region using a beveld 34-gauge needle (JBP Nanoneedle, South Korea) and a 1-ml syringe (BD Syringe, Franklin Lakes, NJ, USA). In parallel, 50-µl of AAV serotypes 1 and DJ (10^{11} genome copies(GC)/mL diluted in phosphate-buffered saline) harboring enhanced green fluorescent protein (eGFP) gene were injected into separate human cadaveric corneal tissues using the same injection technique. Tissues injected with AAV-eGFP were cultured for 2 weeks using the “air-lift” method and evaluated for immunohistochemical staining. Expression of eGFP as well as recombinant stem cell marker p63 was analyzed using a confocal microscope.

Results: Histological assessment showed trypan blue staining of the sub-limbal region, confirming that LSCs can be targeted using the injection technique. Immunohistochemical analysis of the corneal tissues injected with AAV serotypes 1 and DJ show that LSCs co-stain p63alpha, eGFP, and DAPI.

Conclusions: The injection technique could successfully target human LSCs in a reproducible manner, and led to effective transduction of LSCs with AAV serotypes 1 and DJ. Thus, we demonstrate that in situ injection of limbal cells may provide a feasible mode for corneal genetic therapy.

CONTROL ID: 3709604

SUBMITTER (NAME ONLY): William Ridder

TITLE: Comparison of the Recommended ISCEV and a Modified Analysis Protocol for the PhNR Test.

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.H. Ridder, Southern California College of Optometry, Marshall B. Ketchum University, Fullerton, California, UNITED STATES|J. Farmer, Diagnosys, LLC, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: William Ridder: Commercial Relationship(s);Code C (Consultant/Contractor):Abbvie;Code C (Consultant/Contractor):Ionis Pharmaceuticals;Code C (Consultant/Contractor):jCyte, Inc. | Jeff Farmer: Commercial Relationship(s);Code E (Employment):Diagnosys, LLC

ABSTRACT BODY:

Purpose: Several studies have reported that glaucoma patients have abnormal Photopic Negative Response (PhNR) results compared to normal subjects. The International Society for Clinical Electrophysiology of Vision (ISCEV) released an extended protocol standard for PhNR in 2018. The purpose of this study was to compare the standard ISCEV PhNR protocol to a similar protocol modified to enhance the performance of the method in detecting glaucomatous damage.

Methods: Thirty-three subjects were enrolled in this study (12 glaucoma, 10 glaucoma suspects, and 11 control subjects). PhNR tests were conducted with a Diagnosys E3 mobile system (Diagnosys LLC, Lowell, MA) with a monocular ColorBurst stimulator. ISCEV PhNR tests utilized all parameters specified by the ISCEV requirement including 1 cd•s/m^2 red flashes on a 10 cd/m^2 blue background, 1 Hz stimulation frequency, bandpass filters of 0.3 to 300 Hz, and an average of at least 50 recordings. Modified ISCEV PhNR tests used the same parameters as the ISCEV tests with exceptions of 2 cd•s/m^2 red flashes at 1 or 4 Hz stimulation frequency, 5 to 45 Hz bandpass filters and novel, objective sweep selection parameters. All subjects were dilated and PhNRs were conducted with Burian-Allen bipolar electrodes. According to ISCEV standards, the PhNR relative to baseline, a-wave and b-wave response amplitudes and PhNR-baseline/b-wave amplitude ratios were measured. Coefficients of variation and 2-sample t-test were used to assess the data from one randomly chosen eye per subject.

Results: The modified analysis protocol for the PhNR-baseline amplitude resulted in a decrease in the average coefficient of variation for all conditions (Average ISCEV protocol CV = -63% and Modified analysis CV = -41%). The modified analysis resulted in the glaucoma suspects being significantly different from the glaucoma subjects (1 and 4 Hz stimuli with ISCEV analysis p values were 0.083 and 0.838, respectively and with the modified analysis were 0.004 and 0.018, respectively).

Conclusions: The modified analysis protocol resulted in a decrease in within group data variability which resulted in a significant difference between the PhNR-baseline data for the glaucoma subjects and glaucoma suspects. Thus, the modified analysis protocol may result in greater test sensitivity making it a better diagnostic tool.

CONTROL ID: 3709605

SUBMITTER (NAME ONLY): Tara O'Rourke

TITLE: Visual Performance of Non-Diffractive Extended Depth of Focus and Neutral Aspheric Monofocal Intraocular Lenses

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. O'Rourke, S. Pantanelli, O. Bolognia, A. Longenecker, E. Lehman, K. Scruggs, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare binocular distance, intermediate, and near visual acuity and patient reported outcomes of non-diffractive extended depth of focus (ND-EDOF; Alcon Vivity) and neutral aspheric monofocal (Bausch & Lomb enVista) intraocular lenses.

Methods: This was a prospective, single-center, patient and assessor-masked clinical study. Qualified subjects were randomized to receive either the ND-EDOF or monofocal IOL in both eyes, targeted for emmetropia. Post-operatively, subjects underwent examination at regularly scheduled intervals through 3 months. The primary endpoint was the mean logMAR best-distance corrected visual acuity at intermediate (DCIVA; 66 cm) tested in binocular photopic conditions. Secondary endpoints included binocular best-corrected distance (BCDVA; 4 m) and best-distance corrected near (DCNVA; 40 cm) visual acuity. Subjects' outcomes will also be assessed by way of questionnaires evaluating visual disturbances and spectacle dependence.

Results: Fifty-six subjects have been enrolled to date. Thirty (ND-EDOF = 15; monofocal = 15) and 20 (ND-EDOF = 9; monofocal = 11) subjects have completed the one- and three month study visits, respectively. At one month, the binocular BCDVA, DCIVA and DCNVA's were -0.003 ± 0.09, -0.019 ± 0.12, and 0.03 ±0.13 for the ND-EDOF lens and -0.016 ± 0.05 ($p = 0.83$), 0.17 ± 0.12 ($p = 0.0009$), and 0.17 ± 0.14 ($p = 0.0126$) logMAR for the monofocal IOL, respectively. This equates to two lines of improvement compared to the monofocal lens results. Clinically speaking, the ND-EDOF IOL resulted in 93% of patients obtaining 20/25 or better at intermediate and 87% obtaining 20/25 or better at near. This compares with 40% at intermediate and 47% at near for the same thresholds in patients implanted bilaterally with the monofocal.

Conclusions: The ND-EDOF had similar distance vision and provided two lines of improvement for both intermediate and near vision when compared to the monofocal IOL with a neutral aspheric optical profile.

CONTROL ID: 3709606
SUBMITTER (NAME ONLY): Maria de los Angeles Ramos Cadena
TITLE: Longitudinal changes in structural and functional measurements along the glaucoma severity spectrum
SESSION TITLE: Structure-Function Relationship
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: M. Ramos Cadena, G. Wollstein, T. Lee, J. Hu, J.S. Schuman, Ophthalmology, NYU Langone Health, NYU Grossman School of Medicine, New York, New York, UNITED STATES|G. Wollstein, J.S. Schuman, Department of Biomedical Engineering, NYU Tandon School of Engineering, Brooklyn, New York, UNITED STATES|T. Lee, J. Hu, Population Health, NYU Langone Health, New York, New York, UNITED STATES|F. Lavinsky, Ophthalmology, Universidade do Vale do Rio dos Sinos, Sao Leopoldo, RS, BRAZIL|I. Conner, Ophthalmology, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|
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ABSTRACT BODY:
Purpose: Previously we described the longitudinal glaucoma relationship between structure and function using a broken stick analysis approach to identify the location where the rate of change accelerates or decelerates. In that analysis we used each measurement point as an independent point, aggregated all eyes from all visits, and treated longitudinal data as cross-sectional. Using improved statistical methodology, we accounted for repeated measurements and the use of data from both eyes in the longitudinal model. The purpose of this study is to identify the locations of tipping points and rates of change before and after them in structural and functional measurements.
Methods: Subjects with comprehensive ophthalmic examination and 5 or more visits with qualified visual fields (VF; Humphrey Field Analyzer; Zeiss, Dublin, CA) and OCT (Cirrus HD-OCT; Zeiss) with ONH and macular scans were enrolled. Segmented mixed models that account for repeated measurements were utilized to estimate the tipping points and the difference-in-slope. The number of tipping points was determined by identifying the optimal model using Bayesian information criterion.
Results: 216 eyes (164 open angle glaucoma, 45 glaucoma suspect, and 7 healthy eyes) of 145 subjects were analyzed (Table). Retinal nerve fiber layer (RNFL), and ganglion cell inner retinal layer (GCIPL) decreases and cup to disc ratio (CDR) increases since early stages of the disease were measured (Figure). Unlike previous cross-sectional reports, visual field mean deviation (MD) also decreases along with structural parameters since early stages of the disease. RNFL thinning stalls beyond MD<-15.63dB (Figure A) while GCIPL keeps decreasing (B), and CDR slowly increases (C) throughout the functional damage range. Direct comparison between the structural parameters shows that RNFL thinning decelerates in advanced disease compared to both GCIPL and CDR and GCIPL thinning decelerates compared to CDR.
Conclusions: Structural and functional measurements (RNFL, GCIPL, CDR and MD) are useful to evaluate glaucoma change from early stages of the disease. As glaucoma progresses and RNFL reaches its minimal measurable level GCIPL, CDR and MD remain useful to evaluate the disease. The clinical routine for following subjects with glaucoma should account for the ability to measure relevant parameters at various stages of disease.

CONTROL ID: 3709607

SUBMITTER (NAME ONLY): Mitchell Sullivan

TITLE: Circumpapillary retinal nerve fiber layer axon density is reduced in experimental glaucoma eyes.

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sullivan, M. Gondo, N.B. Patel, Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Mitchell Sullivan: Commercial Relationship: Code N (No Commercial Relationship) | Margaret Gondo: Commercial Relationship: Code N (No Commercial Relationship) | Nimesh Patel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Histological studies show that there is good correspondence between optical coherence tomography (OCT) determined circumpapillary retinal nerve fiber layer (RNFL) thickness and total retrobulbar axon counts. However, these relationships don't include differences in axon size and distribution with circumpapillary location and disease. The purpose of this study was to determine the variability in axon size and density for six circumpapillary regions, in the non-human primate experimental glaucoma model.

Methods: Four animals with unilateral experimental glaucoma were included in this study. Following endpoint OCT imaging, animals were euthanized, and perfusion fixed with 4% paraformaldehyde. The eyes were enucleated and circumpapillary tissue ~600µm from the rim margin, for the temporal, superior-temporal, superior-nasal, nasal, inferior-nasal and inferior-temporal regions, was dissected. This tissue, was then placed in 2% glutaraldehyde/2% paraformaldehyde and processed for serial block face scanning electron microscopy (SBFSEM). 20x20x20µm SBFSEM volumes were obtained from each block at 100nm, and all axons were delineated for three frames (frame 10, 100, and 190) using imageJ.

Results: Endpoint OCT circumpapillary average RNFL thickness for experimental eyes were 49µm, 52µm, 76µm, and 84µm. For control eyes, the temporal sector had the highest axon density (1.9-3.2 axons/μm^2), while the superior-nasal sector had the lowest (0.9-1.3 axons/μm^2). This difference was maintained in eyes with experimental glaucoma. Although the mean axon diameter in eyes with experimental glaucoma (0.34±0.45µm) was less than that of control eyes (0.36±0.43µm, $p<0.01$), axon density in experimental glaucoma was reduced (control eyes 1.67 axons/μm^2, experimental 1.27 axons/μm^2, $p=0.023$).

Conclusions: To estimate retinal ganglion cell content from in vivo OCT RNFL scans, both circumpapillary location and stage of experimental glaucoma need to be considered. Although in vivo OCT measures of the temporal NFL are the thinnest, it has the smallest axons and greatest density. The smaller axon diameters in glaucomatous eyes could reflect a change in axon morphology, or a selective loss of larger axons.

CONTROL ID: 3709611

SUBMITTER (NAME ONLY): Nathaniel Mullin

TITLE: Non-random cellular distribution of the mitochondrial 3243A>G variant in the human retina and choroid and its impact on disease phenotype.

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.K. Mullin, A.P. Voigt, M.J. Flamme-Wiese, X. Liu, K.L. Wieland, E.M. Stone, B.A. Tucker, R.F. Mullins, University of Iowa Institute for Vision Research, Iowa, UNITED STATES|N.K. Mullin, A.P. Voigt, M.J. Flamme-Wiese, X. Liu, K.L. Wieland, E.M. Stone, B.A. Tucker, R.F. Mullins, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The dynamics of mitochondrial genome partitioning in complex tissues such as the retina have implications for how mitochondrial variants cause disease. In this study, we sought to understand how the most common pathogenic mitochondrial variant (m.3243A>G) is distributed across ocular cell types in eyes from patients with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), and how this distribution relates to gene expression in ocular cells. We hypothesized that in the eyes of MELAS patients with severe retinal atrophy, the photoreceptors and retinal pigment epithelium (RPE) would harbor high levels of m.3243G.

Methods: We profiled the proportion of the m.3243A>G variant in single cells from the retina, RPE, and choroid of a MELAS patient, as well as from a healthy control donor. Chromatin accessibility and heteroplasmy were assessed using the mitochondrial single-cell assay for transposable chromatin by sequencing (mt-scATACseq), which captures both nuclear and mitochondrial DNA reads. The transcriptomes of single cells from the same samples were profiled in parallel using single-cell RNA sequencing (scRNAseq). Data were analyzed using Seurat and Signac in R.

Results: We find that the proportion of the pathogenic m.3243G allele is neither evenly nor randomly distributed among ocular cell types. While all classes of neural retinal cells and the RPE exhibited a high degree of heteroplasmy, endothelial and lymphocyte populations of the choroid are near homoplasmic for the wildtype m.3243A allele. Single cell gene expression analysis reveals that the presence of the m.3243G allele in neural retinal cells deranges expression of pathways involved in energy metabolism and the response to oxidative stress. However, many of the same pathways in choroidal cell classes homoplasmic for the wildtype allele are also dysregulated.

Conclusions: This work illuminates the non-random segregation of a pathogenic mitochondrial variant in the retina and choroid and demonstrates that the m.3243A>G variant causes non-cell autonomous tissue dysfunction in the complex and metabolically linked light sensing tissue of the eye. Expanding our understanding of the mechanisms that underlie the non-random partitioning of m.3243A>G will enhance management of this and potentially other mitochondrial diseases.

CONTROL ID: 3709613
SUBMITTER (NAME ONLY): Timothy Yap
TITLE: Glaucoma rose plots: redesigning circumpapillary progression analysis
SESSION TITLE: Imaging in glaucoma
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: T.E. Yap, P. Bloom, M. Cordeiro, E. Normando, Imperial College Ophthalmology Research Group, Imperial College London, London, London, UNITED KINGDOM|B. Davis, Central Laser Facility, Rutherford Appleton Laboratory, Didcot, Oxfordshire, UNITED KINGDOM|M. Cordeiro, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|P. Bloom, E. Normando, Glaucoma, Western Eye Hospital, London, London, UNITED KINGDOM|
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ABSTRACT BODY:

Purpose: To improve the detection of disease progression with novel analysis and display of circumpapillary optical coherence tomography (OCT) progression data.
Methods: Glaucoma rose plot analysis (RPA) was developed to automatically analyse and display progression analysis of circumpapillary retinal nerve fibre layer (cRNFL) OCT data. A clustering technique was employed to allow circumferential statistical determination of progressing regions of varying widths, without the use of predefined sectors. Results were presented in the form of an angular histogram for each eye.

RPA was evaluated using data from primary open-angle glaucoma (POAG) or POAG suspect eyes and compared to a gold-standard determined by three clinicians' assessment of OCT series and linear regression plots. Each eye was graded as 'progressing' or 'stable/unaffected'.

Rose plots were assessed using objective and subjective methods to confirm their relevance and practical application. Objectively, the area of red rose petals was compared. Subjectively, rose plots were assessed by three masked assessors as suspicious of progression or not, with time to diagnosis compared against sequential linear regression of global and sectoral cRNFL values.
Results: A total of 743 scans making up registered series from 98 eyes were analysed. The mean ± SD number of visits was 8.5 ± 3.8 μm in the progressing eyes, and 7.1 ± 2.8 μm in the stable or unaffected eyes ($p = 0.06$). Rose plots were able to distinguish progressing eyes from stable or unaffected eyes with area under receiver-operating characteristic curve (AUROC) of 0.968 (95% CI 0.92-1.00) compared to 0.706 (95% CI 0.585 – 0.826) using global cRNFL thickness. Furthermore, agreement on progression status between clinician graders using RPA was greater than when assessing OCT scans and linear regression plots (Fleiss' kappa = 0.86, 95% CI 0.81 – 0.91 compared with 0.66, 95% CI 0.54 – 0.77), with progression detected 8.7 months sooner than traditional linear regression methods ($p<0.0001$).
Conclusions: Glaucoma RPA is a representative and intuitive progression analysis tool that can improve the reproducibility and speed with which progression is detected. As RPA is a statistical (deterministic) technique not dependent on deep learning, this should facilitate rapid clinical translation.

CONTROL ID: 3709615

SUBMITTER (NAME ONLY): Mohit Mohit

TITLE: Up-scaling and humanization of retinal organotypic culture as a model for intraocular efficiency and toxicity analyses.

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: New intraocular drugs still need to be tested in in vivo models before becoming approved. Available retina cultures are only of limited value to replace in vivo studies due to a short life time, a small number of samples gained per retina, and mostly they are of animal origin. We aimed to prolong the duration of a retina organotypic culture, to increase the number of samples harvested per retina, and to humanize the system from pig to human retina. The enhanced model offers the analysis of efficiency and toxicity of intraocular drugs while replacing animal experiments according to 3R and being highly transferable to human patients.

Methods: Retinae derived from pig (from a local slaughterhouse 5-8h post-sacrifice) or from human donor eyes (from the Lions Gift of Sight Eyebank 2-5d post-enucleation); both were cultured in serum free Ames' medium supplemented with growth factors (1% N2, 1% B-27) for 14d at 21°C. Retinae were analyzed for viability performing a PI staining, a CytoTox-Glo® and a TUNEL assay. Morphology was assessed in flatmounts by a customized score (0=no damage to 3=severe damage, cell loss) and in cross sections after histological staining, while cell-type-specific degradation and inflammation were evaluated by immunofluorescent staining (rhodopsin, GFAP, Iba-1).

Results: The combination of hypothermia, cell-protective growth factors, optimized tissue processing, and the harvest of 6 mm small punch-samples (12-24 samples/retina) preserved retinal structure for 14d in pig and human cultures as quantified by the modestly increasing score from 0.56 to 1.91 (pig) and 1 to 1.95 (human) (0 vs. 14d); and qualitatively assessed in H&E-stained sections. Viability decreased moderately over time (0 vs. 14d: 20.6 vs. 39.1 mean grey value [PI^+ cells], 2690 vs. 2002 AU [LDH-release]; 2.5 vs. 135 apoptotic cells/section). Immunohistology confirmed presence of photoreceptors up to day 11 and a low activation of Muller and microglia cells in both, pig and human retina.

Conclusions: Summarized, pig and human neural retinas (central & peripheral parts) can be cultured for 14d preserving key cell types and structure. Degradation, cell loss and inflammatory cell activation are modest, allowing efficiency and toxicity analyses. The enhanced model is suitable to evaluate the benefit of new intraocular treatments while using less animals and improving transferability to humans.

CONTROL ID: 3709621

SUBMITTER (NAME ONLY): Gurbani Kaur

TITLE: Comparison of Retinal Degeneration in GUCY2D- and CRX-related Autosomal Dominant Cone-Rod Dystrophy

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare cone structure and function in patients with autosomal dominant-cone rod dystrophy (AD-CRD) due to genetic mutations in retinal guanylate cyclase (GUCY2D), which encodes a protein that modulates calcium metabolism, and in the homeodomain transcription factor (CRX) that regulates photoreceptor differentiation.

Methods: Refractive error, best corrected visual acuity, short-wavelength autofluorescence fundus photos, and spectral domain optical coherence tomography (SD-OCT) were obtained from all subjects. Confocal and split-detector adaptive optics scanning laser ophthalmoscopy (AOSLO) images were acquired from one patient each with GUCY2D and CRX mutations and stable fixation. Cone spacing was calculated using a density recovery profile method and Z-scores were used to report standard deviation (std dev) from the normal mean at the eccentricity of the measured cones; < 2 was within normal limits. Differences between groups were assessed by Student's t-test (GraphPad PRISM-9 software).

Results: Our cross-sectional study included 14 eyes of 7 AD-CRD patients (3 with GUCY2D and 4 with CRX mutations); the groups were not different in age (GUCY2D mean ± std dev: 51.3 ± 17.8 years, and CRX 41.0 ± 3.8, P = 0.3). Though both groups displayed reduced visual acuity and central scotomas, CRX patients had better visual acuity (P = 0.013) and less myopic refractive error (P = 0.0075) than GUCY2D patients. Fundus autofluorescence revealed retinal pigment epithelial mottling in early stages and bull's eye maculopathy in advanced disease in both groups. SD-OCT revealed outer retinal layer thickness loss with foveal atrophy in all but one GUCY2D patient and ellipsoid zone irregularity in CRX patients. AOSLO images showed no evidence of cone structure at the anatomical fovea for either CRX- or GUCY2D-related AD-CRD. In the eyes with CRX-related AD-CRD, cone spacing Z scores were within normal limits (0.76 ± 0.70; n=3 regions), while in the eyes with GUCY2D-related AD-CRD, Z-scores were abnormal (5.2 ± 5.3; n=10 regions).

Conclusions: AD-CRD differs in disease severity as evidenced by worse visual acuity, greater myopic refractive error and more abnormal cone spacing in GUCY2D patients relative to similarly aged CRX patients. High resolution retinal imaging showed cone loss in all imaged patients and may aid in diagnosis and disease severity monitoring in patients with GUCY2D and CRX-related AD-CRD.

CONTROL ID: 3709624

SUBMITTER (NAME ONLY): Zubin Mishra

TITLE: Comparison of OCTA Axial Profiles in Healthy Eyes and Eyes with Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: While in standard transverse en-face image analysis, optical coherence tomography angiography (OCTA) is averaged over predefined retinal vascular slabs, in axial OCTA analysis, the signal is averaged over the transverse directions, and the resulting axial profiles are subsequently analyzed in depth. Axial profile analysis may provide a more sensitive method for detecting microvasculature changes with disease at different depths even in high-speed OCT acquisitions at lower transverse resolution (preserving the high original OCT resolution axially). In this study, we sought to compare axial profiles in healthy eyes with eyes afflicted with diabetic retinopathy (DR).

Methods: The study cohort includes 17 healthy eyes and 18 eyes with DR. Among the 18 DR eyes, 4 had mild non-proliferative (NP) DR, 9 had moderate NPDR, and 5 had diabetic macular edema (proliferative (P) DR or NPDR). OCTA macular images were captured with the Spectralis OCT2 (Heidelberg Eng.) using a scan pattern size of ~5.8mm x 5.8 mm (20° x 20°; 512 x 512 pixels). Axial signals were quantified from specific retinal layers: NF - nerve fiber, GC - ganglion cell, IP - inner plexiform, IN - inner nuclear, and OP - outer plexiform. Axial signals were quantified within fovea-centered concentric rings with radii 1.5°- 2° (paracentral), 3°- 3.5° (pericentral), and 4.5° - 5° (peripheral).

Results: Fig.1 compares axial profiles in eyes from healthy subjects and DR patients. Fig. 2 compares DR subcategories. Compared to healthy eyes, overall axial signal reduction was observed in DR eyes and DR subcategories. Blunting of axial signal peaks in GCL and in IPL-INL (intermediate capillary plexus) in paracentral ring was observed in DR eyes compared to healthy eyes. Additionally, both intermediate and deep (INL-OPL) peaks were blunted in DR eyes in pericentral and peripheral rings. Significant differences were not observed among eyes with different DR stages.

Conclusions: Axial profile analysis can distinguish normal and DR eyes, providing new insights into disease pathophysiology. The parafoveal OCTA signal was attenuated in DR eyes at multiple flow layers. These observations warrant further investigation with a larger study cohort.

CONTROL ID: 3709626

SUBMITTER (NAME ONLY): Cheng-Rong Yu

TITLE: IL-12p35 is constitutively expressed in the retina and suppresses uveitis in the mouse

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Yu, M. Kang, C.E. Egwuagu, Molecular Immunology Section, Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|Y. Jittayasothorn, Immunoregulation Section, Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|L. Dong, Genetic Engineering Core, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: IL-27 (IL-27p28/Ebi3) and IL-35 (IL-12p35/Ebi3) are members of the IL-12 family of cytokines that suppress experimental autoimmune uveitis (EAU) and experimental autoimmune encephalomyelitis (EAE), two autoimmune diseases that serve as mouse models of human uveitis and multiple sclerosis (MS), respectively [1,2]. IL-27 is constitutively expressed in the retina and upregulation of IL-27 by microglia cells contributes to suppression of uveitis [3,4]. Because IL-27 and IL-35 share the Ebi3 subunit and are functionally and structurally similar, we generated IL-12p35 (il12a) reporter mice and investigated whether IL-35 is also constitutively expressed in the retina.

Methods: We used CRISPR-Cas9 technology to generate il12a knock-in reporter mice driven by endogenous il12a promoter and yfp-gene cassette (venus-bGH/PA) was inserted into exon 1 of il12a. Founder mice were back-crossed for several generation and mice expressing IL-12p35 and yellow fluorescent protein (YFP) were identified by FACS, qPCRs, Western blotting, FACS, ELISA, immunohistochemistry and confocal microscopy. EAU was induced in control or IL-12p35/YFP reporter mice and disease severity was assessed as previously described [3,4]. The YFP reporter mouse was used to trace IL-12p35-expressing cells during immune response to EAU.

Results: We have shown that retinal cells constitutively express the IL-12p35 subunit and its expression was down-regulated during the onset of EAU. We further show that the IL-12p35-YFP knock-in mice, deficient in p35 expression, developed a more severe EAU in comparison to wild-type controls.

Conclusions: Our results show that p35 or IL-35 are constitutively expressed by retinal cells. Thus, similar to IL-27, IL-35 might also suppress inflammatory responses in the retina and confer protection against prolonged inflammation in the retina during uveitis.

1. Choi, J.K., et al. IL-12p35 Inhibits Neuroinflammation and Ameliorates Autoimmune Encephalomyelitis. Front Immunol 8, 1258 (2017).

2. Wang, R.X., et al. Interleukin-35 induces regulatory B cells that suppress autoimmune disease. Nat Med 20, 633-641 (2014).

3. Choi, J.K., et al. IL-27-producing B-1a cells suppress neuroinflammation and CNS autoimmune diseases. Proc Natl Acad Sci U S A 118(2021).

4. Amadi-Obi, A., et al. T(H)17 cells contribute to uveitis and scleritis and are expanded by IL-2 and inhibited by IL-27/STAT1. Nat Med 13, 711-718 (2007).

CONTROL ID: 3709627

SUBMITTER (NAME ONLY): Joanne Li

TITLE: Combining adaptive optics with erythrocyte mediated angiography reveals preferential sites of erythrocyte stasis within the choriocapillaris

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Li, A.J. Bower, L. Huryn, J. Tam, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|J. Pottenburgh, V. Chen, O. Saeedi, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics (AO) can be used to visualize autologously-reinjected, indocyanine green (ICG)-loaded erythrocytes (erythrocyte mediated angiography, EMA) in the living human eye. In this study, we introduce an improved approach to longitudinally map erythrocytes in stasis within the choriocapillaris.

Methods: EMA was performed annually for four years in one subject, with images acquired at various timepoints after injection using a Heidelberg Spectralis Scanning Laser Ophthalmoscope (SLO). For three of the visits, AO imaging was performed on the same day as the EMA procedure to obtain higher resolution images of the erythrocytes in stasis. AO enhanced ICG angiography (AO-ICGA) was also performed to map out the choriocapillaris in the foveal region (PMID 30456310). All images were co-registered and locations of cells in stasis identified using both SLO and AO were combined for further analysis.

Results: Erythrocytes in stasis were observed at all visits. Across the four-year follow-up, a total of 54 cells in stasis were identified by SLO and/or AO within the foveal choriocapillaris network mapped using AO-ICGA. Remarkably, 100% of these cells were localized to pixels corresponding to the choriocapillaris vessel lumens, which would be highly unlikely to occur by random chance ($p<0.01$, one-sided binomial test, with the probability of success set at 68% - the overall percentage of pixels that corresponded to choriocapillaris lumens). The observation of cells in stasis within the choriocapillaris (as opposed to retinal capillaries) was further corroborated using AO images acquired over a series of different focal planes throughout the retina (~35 μm step size). Interestingly, when comparing locations at which cells in stasis were observed over the four years, there were positions within the choriocapillaris network at which cells in stasis was observed across multiple visits, suggesting that these may be preferential sites of erythrocyte stasis within the choriocapillaris.

Conclusions: The combination of AO with EMA enables erythrocytes to be mapped to the choriocapillaris network at fine spatial resolution, a first step towards unraveling the peculiarities of how cells flow through the choriocapillaris meshwork. We demonstrate, for the first time, longitudinal assessment of erythrocytes in stasis at the single capillary level.

CONTROL ID: 3709628

SUBMITTER (NAME ONLY): Ryan McNabb

TITLE: Autonomous Robotically Aligned OCT Enables Remote, Telehealth Retinal Imaging and Angiography

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.P. McNabb, A. Song, K. Roh, S. Schuman, G.J. Jaffe, J.A. Izatt, A.N. Kuo, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|P. Ortiz, M. Draelos, J.A. Izatt, A.N. Kuo, Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmic OCT currently requires patients to position themselves in chin or forehead rests for stabilization with the system operator in close proximity. Robotically aligned OCT (RAOCT) enables remote patient imaging by autonomously aligning itself to a freely seated patient while the imager is physically elsewhere.

Methods: Face and pupil tracking cameras triangulated 3D eye and pupil motion enabling real-time autonomous robotic alignment of a custom 32° FOV retinal SSOCT (1040nm) system (Fig. 1A&C). In conjunction with robotic alignment, we introduced a network layer to the acquisition hardware stack: Zoom© for 2-way A/V communication and NoMachine© for encrypted IP-to-IP, GPU accelerated remote PC and hardware control (Fig. 1B), enabling kilometer-scale distances between imager and patient. The imager instructed patients (where to look, when to blink), began/ended OCT acquisition, and verified image quality. We acquired remote RAOCT retinal volumes from healthy and diseased eyes at the Duke Eye Center on 17 individuals (seated, without chin/forehead rest) under an IRB approved protocol with the imager 10.8 km away at a satellite clinic (Fig. 1D).

Results: Using autonomous robotic alignment, we remotely acquired (10.8 km) OCT and OCTA images in healthy and diseased eyes. Retinal capillaries surrounding the foveal avascular zone are well resolved in a 15° FOV OCTA image (Fig. 2A). In Fig. 2C&D are the thickness map and B-scan from a patient with cystoid macular edema (CME), epiretinal membrane (ERM), and a schisis cavity. Healthy retinas (n=14 eyes) had a mean foveal thickness of 272±1 μm with an intra-subject repeatability of ±1.7 μm; diseased retinas (n=17) had a mean thickness of 308±91 μm and a repeatability of ±1.6 μm.

Conclusions: We demonstrate OCT and OCTA imaging with kilometer-scale distance between imager and patient. This can serve as a foundation for telehealth retinal OCT without physically present technicians or physicians.

CONTROL ID: 3709630

SUBMITTER (NAME ONLY): Douglas Devries

TITLE: Phentolamine Ophthalmic Solution Reverses Pharmacologically Induced Mydriasis in Healthy Subjects: Subgroup Analyses in the Pivotal Phase 3 MIRA-2 Randomized Controlled Trial

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Devries, J.S. Pepose, A. Kolli, K. Rahmani, R. Patel, M. Sooch, E. Lazar, A. Khatri, M. Brigell, Ocuphire, Farmington Hills, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pharmacologically-induced mydriasis (PIM) typically lasts 6-24 hours, during which patients may experience ocular discomfort decreased visual performance. Pre-specified sub-group analyses of the MIRA-2 Phase 3 trial assessed the efficacy and safety of 0.75% phentolamine ophthalmic solution (POS) to expedite the reversal of PIM.

Methods: The MIRA-2 trial was a randomized, double-masked, placebo-controlled, multi-center, 1 day Phase 3 clinical trial. Healthy subjects were randomized 1:1 to POS or Placebo (two drops in the study-eye, and one drop in the fellow-eye) one hour after PIM with phenylephrine, tropicamide, or Paremyd (hydroxyamphetamine and tropicamide combination), with 3:1:1 randomization to mydriatic agents, respectively. The primary efficacy endpoint was the percentage of subjects' study eyes returning to ≤ 0.2 mm from baseline pupil diameter (PD) at 90 min post-treatment (with POS vs placebo, compared by logistic regression). Analyses of this efficacy endpoint were stratified by study- vs fellow-eye, by iris color, and by mydriatic agent.

Results: Ninety-four subjects were randomized to POS (mean age 34 years, 62% female) and 91 were randomized to placebo (mean age 33 years, 55% female). More study-eyes treated with two drops of POS had reversal of mydriasis at 90 min compared to placebo (49% vs 7%; $p<0.0001$). This difference between POS and placebo was similar in fellow-eyes which received one drop (48.9% vs 5.5%; $p < 0.0001$). Significant differences were observed both in those with light (56% vs 2%; $p < 0.0001$) and dark (43% vs 11%; $p < 0.0001$) irides at 90 min. Significant differences between POS and placebo were seen with phenylephrine at all time points from 1 to 6 hours, including at 90 min (79% vs 18%; $p < 0.0001$); and in subjects dilated with longer lasting tropicamide or Paremyd at each time point from 2 hours (24% vs 0%; $p < 0.05$) to 6 hours (97% vs 28%; $p < 0.0001$).

Conclusions: Both one and two drops of POS had rapid onset of effect, significantly reducing PD within 90 min or less. POS had benefits across common mydriatic agents and across iris colors, providing a potential treatment to reverse PIM.

CONTROL ID: 3709640

SUBMITTER (NAME ONLY): Pingting Liu

TITLE: Neuroprotection of SARM1 Inhibition in Traumatic and Glaucomatous but not in EAE Optic Neuropathies

SESSION TITLE: Neuroprotection and neuroregeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Liu, H. Huang, W. Chen, F. Fang, L. Li, X. Feng, L. Liu, D. Liu, R. Dalal, Y. Sun, Y. Hu, Stanford University, Stanford, California, UNITED STATES|K. Ling, F. Rigo, Ionis Pharmaceuticals Inc, Carlsbad, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: SARM1 deletion is neuroprotective in many but not all neurodegenerative disease models. Optic neuropathy is a group of optic nerve (ON) diseases with progressive degeneration of ON and retinal ganglion cells (RGCs). Here we tested the neuroprotection potentials of two gene therapy strategies for SARM1 inhibition, antisense oligonucleotide (ASO) and CRISPR-mediated gene knockdown, comparing with germline SARM1 deletion, in three optic neuropathy mouse models.

Methods: Mice intravitreal injection was used for retina local ASO delivery or AAV-mediated RGC-specific CRISPR SARM1 knockdown. After SARM1 inhibition, three optic neuropathy models, traumatic ON crush (ONC), silicone oil-induced ocular hypertension (SOHU) glaucoma, and experimental autoimmune encephalomyelitis (EAE)/optic neuritis, were generated. To evaluate the neuroprotective effects of these SARM1 inhibition strategies, in vivo spectral-domain optical coherence tomography (OCT) imaging and post-mortem retina and ON histological analysis were used to estimate survival retinal ganglion cells (RGC) and axons; Pattern electroretinogram (PERG) recording was used to analyze RGC function in response to a visual stimulus.

Results: This study reveals that retinal local SARM1 ASO delivery and AAV-mediated RGC-specific CRISPR knockdown of SARM1 achieve similar neuroprotective effects as SARM1 straight KO: SARM1 inhibition only protects ON but not RGC soma after traumatic ONC injury, however, it protects both RGC soma and axons in SOHU glaucoma model. And these two gene therapy strategies of SARM1 inhibition have no neuroprotective effect on RGCs and ONs in the EAE/optic neuritis model.

Conclusions: Our studies suggest that SARM1 inhibition by local ASO delivery or AAV-mediated CRISPR is a promising neuroprotective gene therapy strategy for traumatic and glaucomatous optic neuropathies, but not for demyelinating optic neuritis.

CONTROL ID: 3709641

SUBMITTER (NAME ONLY): Anthony Gjyzeli

TITLE: Association Between Retinal Hemorrhage and Visual Acuity in the Study of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2)

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gjyzeli, S. Whittier, A. Domalpally, B.A. Blodi, R. Voland, S. Watson, Wisconsin Reading Center, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|I.U. Scott, The Pennsylvania State University, University Park, Pennsylvania, UNITED STATES|M.S. Ip, Doheny Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|N. Oden, P.C. Van Veldhuisen, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|A. Au, D. Sarraf, Jules Stein Eye Institutes, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The type of retinal hemorrhage (heme) in central and hemi-retinal vein occlusions (CRVO/HRVO) may serve as a biomarker of visual acuity. Our study investigated association between superficial heme (within nerve fiber layer (NFL)) and deep heme (below the NFL) and visual acuity letter score (VALS) in participants of the Study of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2). We hypothesized that superficial heme is associated with worse visual acuity VALS both at baseline and at 6 months, following fixed monthly intravitreal anti-VEGF injections.

Methods: 304 eyes with gradable baseline CFP were graded to determine the proportion of superficial and deep heme within a 9 subfield grid (Figure). Field 9 was ungradable in >10% of eyes and not included in the analysis; Field 1 is over the optic nerve and was analyzed for peripapillary superficial heme (PSH) only. The predominant type of heme in each location was categorized as peripapillary superficial heme (PSH) in Field 1 - 5; macular superficial heme (MSH) and macular deep heme (MDH) in Fields 6 - 8. Predominance was assigned based on the highest proportion of heme in each location (superficial vs deep in all fields; PSH vs MSH vs MDH).

Results: Predominantly superficial compared to predominantly deep retinal hemorrhage at baseline was associated with worse VALS at baseline (48.9 vs 53.1; $p = 0.03$) but greater VALS at 6 months (71.1 vs 66.2; $p = 0.029$). When stratified for predominance based on location, there was no significant difference in baseline VALS between MSH, PSH and MDH (47.8, 49.5, and 53.1 respectively; $p < 0.18$). At 6 months, after adjusting for age, gender, race and ethnicity, subjects with MSH had higher VALS (69.8) than those with PSH (65.4) or MDH (65.2, $p = 0.02$). Subjects with MDH and MSH had greater increases in VALS from baseline to 6 months than subjects with PSH (20.7, 23.0, and 13.6 respectively; $p < 0.001$).

Conclusions: Superficial heme at baseline, specifically in the peripapillary location, has a worse VALS outcome in eyes with CRVO/HRVO. This suggests that assessment of type of heme in CRVO/HRVO may be a biomarker of VALS and peripapillary heme may correlate with worse VALS outcomes.

CONTROL ID: 3709642

SUBMITTER (NAME ONLY): Hailey Levi

TITLE: Dynein Dysregulation Due to the Absence of NUDC leads to Mitochondrial Mislocalization and Dysfunction in Rod Photoreceptors

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.J. Levi, M. Hubbard, M. Garner, A. Gade, A.K. Gross, Neurobiology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|T. Hollingsworth, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|K. Jiang, A. Swaroop, Neurobiology Neurodegeneration & Repair Laboratory, National Eye Institute, Bethesda, Maryland, UNITED STATES|N. Nelson, G. Ying, W. Baehr, B.W. Jones, Ophthalmology/Visual Science, The University of Utah, Salt Lake City, Utah, UNITED STATES|D. Benefield, G. Rowe, Medicine, Division of Cardiovascular Disease, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mitochondrial stress impairs the function of photoreceptors and can lead to retinal degeneration and blindness. Microtubules and the cytoplasmic dynein complex are necessary for proper trafficking and localization of cargo, including mitochondria. We have identified Nuclear Distribution Protein C (NUDC), a known regulator of cytoplasmic dynein, to be critical in rod and cone photoreceptor health. We hypothesize that the absence of NUDC causes a dysregulation in dynein movement along microtubules leading to mitochondrial and protein mislocalization, as well as cellular stress and cell death.

Methods: We generated a floxed Nudc mouse and bred it to the rod-specific Opsin-iCre75 mouse to produce $Nudc^{+/-}$ or $Nudc^{-/-}$ in rods. To characterize the effect of NUDC loss on mitochondria in the retina of these mice, we performed a combination of assays including: Optical Coherence Tomography (OCT) to uncover retinal thickness in vivo; Transmission Electron Microscopy (TEM) to investigate the ultrastructure of mitochondria in rods; quantitative RT-PCR (qRT-PCR) to measure changes in transcripts of selected mitochondrial genes; immunohistochemistry (IHC) to reveal localization of key proteins involved in phototransduction, mitochondrial fission/fusion, and unfolded protein response (UPR) pathways; and seahorse assays to assess mitochondrial respiration in freshly dissected ex vivo retinal tissues.

Results: At P21, OCT analysis revealed retinal degeneration progressing through P42. TEM demonstrated an increased number of mitochondria scattered throughout the inner segment in $Nudc^{-/-}$ rods, rather than localized in the ellipsoid as in wild type. qRT-PCR showed no change or decrease in mRNA levels of genes associated with mitochondrial fission, but IHC revealed an upregulation of gliosis via GFAP in Müller glia and rhodopsin mislocalization in photoreceptors in the absence of NUDC. Additionally, altered mitochondrial respiration and mitochondrial reserve capacity were observed with Nudc deletion in P21 rods.

Conclusions: We have demonstrated that, in the absence of NUDC, mitochondria are mislocalized and exhibit compromised function in rod photoreceptors. We detect an upregulation of proteins involved in the UPR and in the inflammatory response concomitant with retinal degeneration, underscoring the importance of microtubule trafficking by NUDC in the overall health of photoreceptors.

CONTROL ID: 3709644

SUBMITTER (NAME ONLY): Ayesha Patil

TITLE: Exfoliation Syndrome and Exfoliation Glaucoma in the Navajo Nation

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Exfoliation syndrome (XFS) is a common identifiable cause of secondary open-angle glaucoma[1]. Estimates gathered over a decade ago on the prevalence of glaucoma in Native American populations hover around 6%; however, data is lacking regarding the burden of XFS in this population[2,3]. In 1971, Faulkner et al. estimated the prevalence of XFS in a sample of 50 Navajo Native Americans over the age of 60 as 38%[4]. Given that XFS can cause irreversible blindness secondary to glaucoma, this study aims to identify the current prevalence of XFS among Navajo Nation residents within the Four Corners region of the United States.

Methods: A retrospective chart review was conducted from 2016-2021 for patients aged 18 and older, examined in partnership with the Utah Navajo Health System and the Moran Eye Center. All patients with XFS or XFG diagnosed by slit lamp exam were identified through chart review. Additionally, patient demographic information and ocular/systemic comorbidities were gathered.

Results: Of the 1,152 patient charts available for review, eight patients (11 eyes) were diagnosed with XFS with three patients (4 eyes) demonstrating concomitant XFG. Of the patients with XFS, three had bilateral disease, three were right eye, and two were left eye. Within this XFS population, 50% of the patients identified as male, with a mean age of 73 years. Of patients with XFS, 38%, 50%, and 13% were seen at the Montezuma Creek, Monument Valley and Navajo Mountain sites respectively. Average presenting IOP in XFS eyes was 19.54 mmHg (n=11) and 18 mmHg (n=4) for non-XFS fellow eyes. The overall prevalence of XFS was 0.7% and the overall prevalence of XFG was found to be 0.26%. The rate of XFG among patients with XFS was 37.5%.

Conclusions: Compared to Faulkner's study of the Navajo Nation residents in 1971, our findings show a considerably lower prevalence of XFS at 0.7%. We present the largest population-based study to date of XFS and XFG among this population. The discrepancy of our findings compared to Faulkner's could be due to variation in diagnostic and inclusion criteria, clinician-dependent factors, and perhaps most critically, differences in study populations. The difference could indicate unique genetic and epigenetic factors within a single ethnic group that spans a large geographic area of the American Southwest, which has not been investigated to date.

CONTROL ID: 3709647

SUBMITTER (NAME ONLY): Ely Manstein

TITLE: The Effect of Foot Reflexology on Intraocular Pressure in Primary Open-Angle Glaucoma and Ocular Hypertension Patients

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Manstein, D. Patel, A. Krane, D. Yu, J.D. Henderer, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|P. Kung, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|D. Cohen, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: A recent pilot study demonstrated that foot reflexology can temporarily lower intraocular pressure (IOP) in ocular hypertension (OHTN) patients, however this study lacked a control and a more robust study is necessary to confirm its effect. We performed a prospective randomized controlled clinical trial to see if a shoe insert could be designed to both duplicate the effects seen by foot reflexology in OHTN patients and lengthen the treatment effect beyond the 90-120 minute treatment effect suggested by the original pilot data. We also performed a pilot study to see if foot reflexology could lower IOP in primary open angle glaucoma (POAG) patients.

Methods: This is a pilot study in POAG patients undergoing selective laser trabeculoplasty and a prospective therapeutic trial in OHTN patients recruited from the Temple Ophthalmology clinic. OHTN patients underwent a one-month medication washout. POAG patients performed a 5-minute foot massage on a massage board. OHTN patients performed a 5-minute foot massage with 3D-printed shoe inserts (study insert) or sham inserts. IOP was checked by a masked investigator pre-massage and 5-, 30-, 60-, 90- and 120-minutes post-massage. On two separate days, OHTN patients wore either study inserts or sham inserts for the full day. IOP was measured at 8 AM before wearing the inserts and again at 4 PM.

Results: For the 18 POAG patients, IOP significantly decreased after 5-minute foot massage by 1.9 mmHg (10.1%, p=0.02) and 3.1 mmHg (18.0%, p=0.01) in the right and left eyes compared to baseline. For the 12 OHTN patients, the 5-minute study insert massage significantly decreased IOP by 2.7 mmHg (12.3%, p=0.003) and 2.2 mmHg (10.2%, p=0.004) in the right and left eyes. The sham insert massage significantly decreased IOP by 1.9 mmHg (7.9%, p=0.03) in the right eye. The difference between the study inserts and sham inserts was not significant. During the all-day trial, IOP decreased 1.6 mmHg (7.1%) and 2.3 mmHg (10.3%) for the right and left eyes. Neither was significantly different from the sham.

Conclusions: 5-minute foot reflexology temporarily lowers IOP in some POAG and OHTN patients. The study insert did not lower IOP in OHTN patients more than the sham. Perhaps a different application of foot reflexology or a different version of the insert would be more effective and remains a topic for future research.

CONTROL ID: 3709648

SUBMITTER (NAME ONLY): Melissa Chang

TITLE: Evaluating scleral vessel density changes before and after ab interno trabeculotomy using IOL Master 500 : a case series

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.Y. Lin, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|M. Chang, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Melissa Chang: Commercial Relationship: Code N (No Commercial Relationship) | Ken Lin: Commercial Relationship(s);Code C (Consultant/Contractor):Zeiss, Johnson and Johnson

ABSTRACT BODY:

Purpose: This case series demonstrates a proof of concept using automated machine learning to quantify the change in limbal episcleral vessel morphology in glaucoma patients who undergo trabeculotomy ab interno (Trabectome). Currently there are no reliable noninvasive methods to quantify changes in anatomy after minimally invasive glaucoma surgeries (MIGS). Intraocular pressure (IOP) and gonioscopy remain the two parameters that surgeons can assess for MIGS efficacy. One type of MIGS, Trabectome, is thought to decrease IOP by decreasing aqueous humor outflow resistance. Sclera images may offer a methodology for assessing changes seen noninvasively as a result of Trabectome.

Methods: This study retrospectively analyzed 3 eyes from 2 patients who underwent combined Trabectome with phacoemulsification cataract surgery by 1 surgeon in a hospital setting. Images were taken immediately before and 1 month after the procedure using the Zeiss IOLMaster 500. The open-source image processing package Fiji (ImageJ mirror) was used to load images that were cropped to rectangles of the sclera-only nasal region. The Fiji plug-in Trainable Weka Segmentation was used with 4 reference patients' images from a different dataset to train a model to identify scleral vessels from sclera. The trained model was then applied to study images to calculate the % area of scleral vessels. 3 rectangles of each patient's eye were cropped from the nasal region to optimize either width, height, or most salient vessels, and averages and standard deviations were calculated using Microsoft Excel 2021.

Results: The first patient's right eye had an average % area of scleral vessels compared to white sclera of 9.10±0.27% pre-procedure, and 8.72±0.30% post-procedure. The second patient's right eye had an average % area of 13.75±0.83% pre-procedure compared to 7.18±0.72% post, and left eye average of 12.77±1.21% pre-procedure compared to 11.05±0.65% post. All three eyes had greater than 30% IOP reduction after Trabectome.

Conclusions: Overall there was a decrease in visible sclera vessel area across all three patients who underwent the Trabectome surgery. This presumably is due to less blood and more aqueous in these episcleral vessels following Trabectome. The images captured noninvasively with the IOLMaster 500 along with the machine learning model may be useful adjunctive tools to assess surgical outcomes following MIGS.

CONTROL ID: 3709652

SUBMITTER (NAME ONLY): Han Woong Lim

TITLE: Quantitative evaluation of optic nerve atrophy using diffusion tensor imaging

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Lim, E. Hong, J. Yang, Y. Yeon, H. Cho, W. Lee, Ophthalmology, Hanyang University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|H. Lim, E. Hong, J. Yang, Y. Yeon, H. Cho, W. Lee, Hanyang Vision Research Center, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To quantitatively investigate the microstructural properties of the optic nerve (ON) in vivo using diffusion tensor imaging (DTI) in patient with unilateral optic atrophy (OA) and to determine the association between the ON diffusion properties and retinal nerve fiber layer (RNFL) thickness of optic nerve head (ONH).

Methods: Diffusion magnetic resonance imaging (MRI) was scanned from 6 patients with unilateral OA (OA group) and 11 control subjects (control group). ONs were tracked and a central tract was extracted from optic nerve head to orbital apex along the ON length. To obtain quantitative values of ON microstructure from tensor derived-metrics, fractional anisotropy (FA; a measure of diffusion directions), mean diffusivity (MD; a measure of averaged diffusivity), axial diffusivity (AD; a measure of diffusion in the major axes), and radial diffusivity (RD; a measure of diffusion in radial axes) were computed in the atrohpic (affected) and non-affected ONs of patients with unilateral OA and both ONs of controls. In control group, the averaged measurements of both ONs in each subject were used for statistical analysis. RNFL thickness was measured using optical coherent tomography and the correlation between the tensor measures and RNFL thickness was also analyzed.

Results: FA of atrophic ON was lower than that of non-affected and control ONs (Atrophic[A], 0.136 ± 0.059; Non-affected[N], 0.384 ± 0.048; Control[C], 0.389 ± 0.053). MD and RD of atrophic ONs were higher than those of non-affected and control ONs (MD, A, 0.988 ± 0.247; N, 0.658 ± 0.058; C, 0.687 ± 0.079; RD, A, 0.920 ± 0.247; N, 0.510 ± 0.054; C, 0.532 ± 0.078). However, AD of atrophic ON did not show significant differences to that of non-affected and control ONs (A, 1.123 ± 0.252; N, 0.955± 0.080; C, 0.998 ± 0.094; A vs N, P = 0.152; A vs C, P = 0.155). All DTI measures of atrophic ON except for AD showed a significant correlation with RNFL thickness of ONH; FA showed the strongest correlation, followed by RD and MD (FA, R^2 = 0.936, P < 0.001; RD, R^2 = 0.795, P < 0.001; MD, R^2 = 0.655, P = 0.001; AD, R^2 = 0.183, P = 0.073).

Conclusions: We quantitatively analyzed the optic nerve using DTI and identified differences in DTI measures between atrophic and normal ONs. Additionally, the significant correlation between DTI measures and RNFL thickness suggests the applicability of DTI as a clinical tool to evaluate the optic nerve.

CONTROL ID: 3709656

SUBMITTER (NAME ONLY): Heberto Quintero

TITLE: Restoration of mitochondrial axonal transport by adaptor supplementation prevents neurodegeneration and rescues visual function in glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Alarcon-Martinez, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|H. Quintero, Y. Shiga, N.A. Belforte, S. El Hajji, D. Villafranca-Baughman, F. Dotigny, A. Di Polo, Department of Neuroscience, Universite de Montreal, Montreal, Quebec, CANADA|H. Quintero, Y. Shiga, N.A. Belforte, S. El Hajji, D. Villafranca-Baughman, F. Dotigny, A. Di Polo, University of Montreal Hospital Research Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Mitochondria distribution in retinal ganglion cells (RGC) is crucial for homeostasis and neurotransmission. Here, we tested the hypotheses that: i) mitochondrial axonal transport deficits contribute to energetic imbalance and RGC damage in glaucoma, and ii) supplementation of the adaptor protein Disc1 (Disrupted in Schizophrenia 1) restores mitochondrial mobility, prevents energy decline, and rescues RGC function

Methods: Ocular hypertension (OHT) was induced by intracameral injection of magnetic microbeads in Thy1-CFP-MitoS mice. RGC-specific Disc1 levels were increased using recombinant adeno-asociated virus (AAV.Disc1). Two-photon laser scanning microscopy was used to i) record mitochondrial movement along RGC axons followed by kymograph analysis, and ii) measure axonal ATP levels using the sensor Ateam. Mitochondrial volume in single RGC axons was quantified using confocal microscopy and Imaris software. RGC density was quantified in RBPMS-stained retinas using a stereological approach. RGC function was assessed by measuring light-evoked positive scotopic threshold responses (pSTR) and using the optomotor reflex assay for visual acuity.

Results: Live imaging of mitochondrial mobility along RGC axons showed a reduction of anterograde transport in glaucomatous eyes (OHT-2 weeks: 40% decrease, t-test $p<0.001$, n=14/grp). Transport deficits were accompanied by a decrease in mitochondrial volume in RGC axons, both in the retina and the myelination transition zone (~50% reduction vs. sham, t-test $p<0.001$, n=16/grp). Intravitreal administration of AAV.Disc1 fully restored mitochondrial mobility and volume in RGC axons subjected to OHT (ANOVA $p<0.01$, n=10/grp). Remarkably, enhanced mitochondrial transport restored axonal ATP levels preventing energetic decline (ANOVA $p<0.05$, n=4/grp) and promoted robust RGC survival (ANOVA $p<0.001$, n=10/grp). Furthermore, AAV.Disc1 prevented loss of light-evoked pSTR responses (ANOVA $p<0.01$, n=12/grp) and improved visual acuity relative to sham animals (ANOVA $p<0.01$, n=8/grp).

Conclusions: Glaucomatous damage disrupts mitochondrial anterograde transport along RGC axons leading to mitochondria depletion and energy decline. Disc1 adaptor supplementation improved mitochondrial anterograde transport, replenished axonal mitochondria, rescued energy homeostasis, and restored light-evoked responses and visual acuity in glaucoma.

CONTROL ID: 3709658

SUBMITTER (NAME ONLY): Maria Constanza Tripolone

TITLE: Assessment of flickering chromatic pupillometry in patients with risk of glaucoma

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tripolone, L. Issolio, P. Barrionuevo, Instituto de Investigación en Luz, Ambiente y Visión, Consejo Nacional de Investigaciones Cientificas y Tecnicas, San Miguel de Tucumán, Tucumán, ARGENTINA|L. Issolio, Departamento de Luminotecnia, Luz y Visión, FACET, Universidad Nacional de Tucuman, San Miguel de Tucuman, Tucumán, ARGENTINA|C. Agüero, A. Lavaque, D. Pérez, Centro de Especialidades Oftalmológicas, San Miguel de Tucumán, Tucumán, ARGENTINA|

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ABSTRACT BODY:

Purpose: Chromatic pupillometry is increasingly used for assessing human retinal function through measurements of pupil responses to different colored light stimuli. The discovery of intrinsically photosensitive retinal ganglion cells (ipRGCs) adds a new dimension to the detection and monitoring of retinal and optic nerve disorders, including open-angle glaucoma (OAG) through pupillometry. However, the detection of pre-perimetric glaucomatous deficits still remains a challenge. We hypothesize that early damage in OAG risk could be reflected in affected flickering pupil responses.

Methods: All participants underwent ophthalmological assessments and were classified in healthy controls (HG) and OAG risk patients (GR). The GR group was characterized with high intraocular pressure and/or a family history of OAG with no pre-existing OAG; assessed by OCT and ERG. Pupillary recordings were obtained using a lab-made photostimulator-pupillometer system with monochromatic stimuli of blue (468 nm), green (516 nm), and red (632 nm). Flickering sinusoidal stimuli of 1Hz frequency and 10s duration were presented in an integrating sphere-like dome with a Lambertian inner surface at two modulation levels: 100% and 70%. Each participant was monocularly tested and was light-adapted to the mean chromaticity during 60 s., previous to the stimulus onset. In the frequency domain, amplitude (mm) and phase (degrees) parameters were assessed. In the temporal domain (% initial diameter), initial constriction, and post pulse plateau parameters were evaluated.

Results: The amplitude was significantly reduced ($p<0.05$) in GR group for green (100%), red (100%), and red (70%). The phase was significantly reduced ($p<0.05$) in the GR group for blue (100%), green (100%), red (100%), blue (70%), and green (70%). The Initial Constriction was higher ($p<0.01$) in the HC group for blue (100%), green (100%), red (100%), and red (70%) with respect to the GR group. No significant differences were found for the post pulse response parameter.

Conclusions: We found differences in transient pupil responses between healthy control and glaucoma risk groups, especially for high-modulation red and green stimuli. These results suggest that flickering chromatic pupillometry can reveal early changes in patients with potential OAG, not detected by other clinical methods. Furthermore, early signs of OAG might contain detriments in cone afferences to ipRGCs.

CONTROL ID: 3709662

SUBMITTER (NAME ONLY): Darlene Dartt

TITLE: Evaluating the effect of titaminates in a metal-organic engineered bioactive film on growth of conjunctival epithelial cells

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Dartt, C. Lee, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Murali, O. Nilsen, Chemistry, Universitetet i Oslo, Oslo, NORWAY|D.A. Dartt, C. Lee, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Infections, autoimmune diseases, trauma or chemical/thermal burns can scar the conjunctiva, requiring transplantation. The purpose of this study is to explore the biological potential of a class of bioactive films named titaminates and identify the ideal candidate for use in development of a functional conjunctival equivalent for transplantation to repair the conjunctiva.

Methods: Titaminates were produced by a molecular layer deposition (MLD) technique on a plain glass coverslip using titanium (T) combined with amino acids (X). Four titaminates (TD (aspartic acid), TGD (glycine aspartic acid), TG (glycine), and TC (cysteine)), a zinc variant (ZnC), and unmodified glass coverslip (NT) were tested using six different epithelial cell preparations cultured from human and rat conjunctiva. Each cell preparation was defined by its nativity (primary (p) or first passage (f)), tissue origin (human (Hu) or rat), and cell type (goblet cell (Gob) or mixture of goblet, stratified squamous, and undifferentiated cells (Mix)). For primary cells, an explant was cultured directly on each biofilm. Fold outgrowth was calculated from the cell area and the explant size. First passage cells were prepared by passaging 50,000 primary cells per film. Proliferation capacity was measured using colorimetric redox indicator resazurin.

Results: TG was the optimum bioactive film for supporting primary cell growth. Fold outgrowth of pHuMix on TG was 70-fold, which was substantially higher compared to that of the second-best biofilm TGD at 33-fold, or NT at 7-fold. Fold outgrowth of pHuGob on TG was about 15-fold, which was higher than TGD at 9-fold and NT at 11-fold. TG was also one of the top three for the first passage cells. fHuGob on TG showed the highest proliferation capacity both at 24 and 48 h. The proliferation capacity of fHuMix, fRatGob, and fRatMix on TG was similar to that on TC, TGD, and TD, which were all higher than ZnC and NT. For all first passage cells, the area cultured by cells did not correlate with the proliferation capacity. For proliferation capacity TC> TGD >TG > NT > TD. ZnC was notably inferior in every measurement.

Conclusions: We conclude that titaminates support the construction of a functional conjunctival equivalent when multiple conjunctival cell types are used and that TG is the best performing scaffold used.

CONTROL ID: 3709663

SUBMITTER (NAME ONLY): Laura Periman

TITLE: Bilateral Effect of OC-01 Nasal Spray for Treatment of Dry Eye Disease Signs & Symptoms in Subjects with Mild, Moderate & Severe Dry Eye Disease, as Determined by Baseline Eye Dryness Score

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.M. Periman, S. Maiti, Periman Eye Institute, Seattle, Washington, UNITED STATES|A.G. Kabat, L. Hendrix, A. Gibson, Oyster Point Pharma, Princeton, New Jersey, UNITED STATES|A.G. Kabat, Salus University, Elkins Park, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: OC-01 (varenicline solution) nasal spray is a cholinergic agonist that pharmacologically neuro-activates the trigeminal parasympathetic pathway (TPP) to result in increased basal tear production for the treatment of signs & symptoms of dry eye disease. Unilateral activation of the TPP via a single nostril may facilitate bilateral tear production; however, OC-01 was administered to each nostril BID in the ONSET-1 and ONSET-2 clinical trials. Herein, we report bilateral outcomes, and also outcomes by subgroup symptom severity.

Methods: 891 adult subjects with Eye Dryness Score (EDS, range 0-100) were randomized to either OC-01 0.06 mg, 0.03 mg or vehicle control (VC); at baseline, 200 had EDS <40 and 691 had EDS ≥40. The study eye was defined as the eye meeting all inclusion/exclusion criteria at screening. If both eyes qualified, then the eye with the greatest increase in Schirmer's Test Score (STS, mm) upon mechanical stimulation, or (if no difference) the eye with the lower basal STS, was selected. Analysis of covariance (ANCOVA) using a last observation carried forward (LOCF) approach assessed mean changes from baseline in STS at Week 4.

Results: Mean changes from baseline in STS were greater for eyes treated with OC-01 as compared to VC at week 4. Outcomes in the <40 EDS cohort were: 0.06 mg, 11.0 (± 10.0, p<0.01); 0.03 mg, 8.4 (± 10.0, p=0.01); VC, 4.1 (± 6.5). For the ≥40 EDS group, outcomes were similar: 0.06 mg, 9.2 (± 9.0, p<0.01); 0.03 mg, 9.9 (± 9.7, p<0.01); VC, 3.9 (± 7.1).

OC-01 treated subjects also showed statistically significant differences in percent achieving ≥10 mm STS change from baseline as compared to VC at Week 4. Outcomes in the <40 EDS cohort were: 0.06 mg, 37.3% (OR 6.40, p<0.01); 0.03 mg, 30.9% (OR 3.02, p=0.03); VC, 18.5%. For the ≥40 EDS group, outcomes were similar: 0.06 mg, 39.2% (OR 3.10, p<0.01); 0.03 mg, 38.8% (OR 3.17, p<0.01); VC, 17.9%.

Conclusions: Pharmacologic neuro-activation of the TPP via BID administration of OC-01 to each nostril demonstrated consistency in bilateral basal tear production improvements, regardless of baseline EDS severity. OC-01 was generally tolerable under conditions of the study. The most common adverse reaction was sneezing (82%-84%) and, in >5%, cough, throat irritation & nasal irritation.

CONTROL ID: 3709664
SUBMITTER (NAME ONLY): Walid Raslan
TITLE: Efficacy and Safety of Subthreshold laser Treatment for Chronic Central Serous Chorioretinopathy
SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: W. Raslan, S. Younis, Ophthalmology - Medical Retina, Western Eye Hospital, London, London, UNITED KINGDOM|
Commercial Relationships Disclosure: Walid Raslan: Commercial Relationship: Code N (No Commercial Relationship) | Saad Younis: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Chronic central serous chorioretinopathy (CSR) is a disease characterized by focal fluid accumulation underneath the neuroretina. This can cause irreversible vision loss due to progressive and permanent photoreceptor damage and/or RPE atrophy. The complex and multifactorial pathogenesis of CSR, is still uncertain and the effective treatment for CSR is still not fully explored.

Subthreshold laser has been used to treat CSR and has shown some efficacy in CSR patients with subfoveal and extrafoveal leakage sites.
Our research aims to assess the response and safety of subthreshold laser 577-nm (SML) treatment in patients with chronic CSR.
Methods: - We performed a retrospective study of 11 eyes of 11 patients diagnosed with chronic CSR treated with one or two sessions of sub-threshold yellow laser.
- Patients received subthreshold micropulse yellow laser photocoagulation at 5% duty cycle at a reduced energy level from the micropulse laser test burns with Laser exposure time of 20 ms, and the spot diameter was 100 microns.
- Inclusion criteria:
> CSR suffered for a minimum of 6 months
> No previous treatment
> No loss of vision
> Presence of subretinal fluid secondary to chronic CSR when the treatment was performed

- Data collected: age, gender, laterality, duration of the CSR, best-corrected visual acuity (BCVA) pre and post-treatment, central retinal thickness (CRT) pre and post-treatment, retina changes post-treatment.
- Cirrus HD-OCT scan, fundus autofluorescence, and fundus colour photos were used to collect clinical findings.
Results: - Two third of the patients responded to treatment
- The mean CRT measured by OCT pre- treatment changed from 355 +/- 84 µm to 294+/-67 µm post-treatment (P=0.056), showing an 18% average reduction in fluid height
- There was no evidence of retinal pigment epithelium or retinal damage on SD-OCT, FFA, or fundus autofluorescence
- The BCVA changed from 0.57 +/-0.27 LogMAR pre-treatment to 0.46 +/- 0.31 (P=0.11)
Conclusions: - Subthreshold laser photocoagulation is an effective treatment option for chronic CSCR
- There was no evidence of retinal damage after treatment
- The BCVA didn’t improve much, probably because of the chronic nature of the disease in our patients
- We may try this treatment with acute CSCR, in such cases we expect better results
- Future research with larger samples is required

CONTROL ID: 3709666

SUBMITTER (NAME ONLY): Bartosz Szczesny

TITLE: Oxidative stress induces Z-DNA binding protein 1-dependent activation of microglia via mtDNA released from retinal pigment epithelial cells.

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Szczesny, J. Saada, R. McAuley, M. Marcatti, T. Tang, M. Motamedi, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress, inflammation, and aberrant activation of microglia in the retina are commonly observed in ocular pathologies. In glaucoma or age-related macular degeneration, the chronic activation of microglia affects retinal ganglion cells and photoreceptors, respectively, contributing to gradual vision loss. However, the molecular mechanisms that cause activation of microglia in the retina are not fully understood.

Methods: We used cultured differetiated ARPE-19 cells, human brain microglia and various cellualr and molecular biologu techniques including: proximity ligation assay, DNA damage analysis, qPCR, RT-qPCR, IP, Nanoparticle Tracking Analysis, ELISA.

Results: Here we show that exposure of retinal pigment epithelial (RPE) cells to chronic low-level oxidative stress induces mitochondrial DNA (mtDNA)-specific damage, and the subsequent translocation of damaged mtDNA to the cytoplasm results in the binding and activation of intracellular DNA receptor Z-DNA binding protein 1 (ZBP1). Activation of the mtDNA/ZBP1 pathway triggers the expression of pro-inflammatory markers in RPE cells. In addition, we show the enhanced release of extracellular vesicles (EVs) containing fragments of mtDNA derived from the apical site of RPE cells induces a pro-inflammatory phenotype of microglia via activation of ZBP1 signaling.

Conclusions: Collectively, our report establishes oxidatively damaged mtDNA as an important signaling molecule with ZBP1 as its intracellular receptor in the development of an inflammatory response in the retina. We propose that this novel mtDNA-mediated autocrine and paracrine mechanism for triggering and maintaining inflammation in the retina may play an important role in ocular pathologies. Therefore, the molecular mechanisms identified in this report are potentially suitable therapeutic targets to ameliorate development of ocular pathologies.

CONTROL ID: 3709667

SUBMITTER (NAME ONLY): Rakesh Radhakrishnan

TITLE: Dissecting the role of the Motor Protein MYO1C in Rhodopsin trafficking for Visual Function

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Radhakrishnan, G.P. Lobo, Ophthalmology and Visual Neurosciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Rakesh Radhakrishnan: Commercial Relationship: Code N (No Commercial Relationship) | Glenn Lobo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The proper trafficking of the visual chromophore Rhodopsin, from its site of synthesis the Photoreceptor Inner Segments (IS) to the Outer Segments (OS), represents a critical event for visual function in humans. Mistrafficking or mislocalization of rhodopsin to other photoreceptor compartments due to mutations in Opsin or defects in its transporters, can lead to retinal phenotypes that are observed in Usher Syndrome (USH) and Retinitis Pigmentosa (RP). We recently identified a role for an unconventional motor protein, Myosin 1C (MYO1C), in the transport of Rhodopsin to the OS. The purpose of this study was to explore the mechanistic role for MYO1C in the transport of Rhodopsin, which could have clinical implications for retinal phenotypes in RP and USH.

Methods: Myo1c knockout mice showed mislocalized Rhodopsin in photoreceptors that manifested in a loss of visual function. This suggests a possible interaction between these two proteins. The MYO1C-Rhodopsin putative interaction was predicted by HADDOCK 2.4 docking using available crystal structures of mouse MYO1C and bovine Rhodopsin. MYO1C-Rhodopsin interaction was confirmed using an overexpression system in COS1 and ARPE19 cell lines. Further, the pmCherry MYO1C deletion constructs and GFP Rhodopsin were generated and co-transfected in cell lines for co-localization analysis. The Pearson's correlation was measured and Acceptor Photobleach Förster Resonance Energy Transfer (FRET) was performed to confirm the physical interactions.

Results: The docking analysis of MYO1C and Rhodopsin indicated an interaction at the MYO1C IQ and post IQ domain region with Rhodopsin C'-terminus. In a cell culture system, a positive interaction between MYO1C and Rhodopsin was observed by immunofluorescence and quantified by Pearson's correlation and FRET. The C-terminal domain deletion constructs of MYO1C showed defects in the interaction with rhodopsin, implying a possible MYO1C C-terminus post IQ domain region interaction with Rhodopsin.

Conclusions: The importance of MYO1C C-terminal interaction with Rhodopsin C-terminal was confirmed in vitro. Our analysis has clinical implications for somatic mutations in the Rhodopsin C-terminus domain implicated in RP, possibly due to loss of MYO1C interaction and transport. Thus, it would be interesting to investigate and screen for genetic variants in the C-terminus of Myo1c and Rhodopsin in patients with USH and RP.

CONTROL ID: 3709669
SUBMITTER (NAME ONLY): Cara Schachter
TITLE: COVID Involvement in Eyecare Professionals
SESSION TITLE: Public Health I
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C.J. Schachter, E. Sherry, L.S. Azeez, D. Mojica, A. Kheirkhah, Department of Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|
Commercial Relationships Disclosure: Cara Schachter: Commercial Relationship: Code N (No Commercial Relationship) | Emily Sherry: Commercial Relationship: Code N (No Commercial Relationship) | Leen Azeez: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Mojica: Commercial Relationship: Code N (No Commercial Relationship) | Ahmad Kheirkhah: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: The SARS-CoV-2 pandemic has been an ongoing area of study in scientific, clinical, and pharmaceutical communities. Although it is known that many in medical fields developed COVID, it is unknown how COVID has involved eyecare professionals. The purpose of this study is to evaluate COVID involvement in eyecare professionals.
Methods: In this cross-sectional study, an anonymous questionnaire survey was distributed among eyecare professionals. Their experiences with COVID exposure, testing, and infection were evaluated.
Results: 92 eyecare professionals answered the survey, consisting of 25 ophthalmologists, 7 ophthalmology residents, 6 optometrists, 48 ophthalmic technicians, and 6 ophthalmology clinic administrative staff. These included 33 men and 56 women; 3 preferred not to disclose their sex. The mean age was 42.0 ± 12.2 years (range, 21-75 years). Of these, 11 (12.0%) have been COVID positive with symptoms, and none were COVID positive without symptoms. The positive rate was 0% in ophthalmologists, ophthalmology residents, and optometrists, 20.8% in ophthalmic technicians, and 16.7% in administrative staff. Of people without COVID (n=81), 15 (18.5%) had been exposed to a COVID-positive individual, 39 (48.1%) had tested negative for COVID, and 27 (33.3%) had not yet been tested for COVID.
Conclusions: Only a small percentage of eyecare professionals have developed symptomatic COVID. The rate of symptomatic COVID was significantly lower in ophthalmologists, ophthalmology residents, and optometrists evaluated in this study compared to the general population. Such low rates may be due to using proper protective measures, including suitable workplace protocols.

CONTROL ID: 3709670

SUBMITTER (NAME ONLY): Westin Wong

TITLE: The Vascular Theory of Glaucoma - Quantifying Blood Vessels in Cadaveric Optic Nerve Head Specimens

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wong, B. Landis, N. Noyce, A.C. Pappas, Rocky Vista University College of Osteopathic Medicine, Parker, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Westin Wong: Commercial Relationship: Code N (No Commercial Relationship) | Brianna Landis: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Noyce: Commercial Relationship: Code N (No Commercial Relationship) | Anthony Pappas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Damage to axons in the optic nerve head (ONH) likely contributes to vision loss in patients with glaucoma. While the mechanism of axonal injury has not been fully elucidated, vascular factors have long been considered to play a role. Despite efforts to link determinants of ocular blood flow to the development of glaucoma, a simple quantification of the ONH blood supply has not been previously performed. Here, we quantified blood vessels in sections of ONHs obtained from cadaveric donors with and without glaucoma to determine whether deficiencies in ONH vascularity are associated with glaucomatous disease.

Methods: Six ONHs were recovered from four cadaveric donors; of which, one ONH had a history of glaucomatous disease of unknown subtype. The remaining ONHs were obtained from donors with no offered history of ophthalmic disease. All ONHs were sectioned serially (5 μm thick) and stained with an antibody targeting the endothelial cell marker, CD31. 10x images were acquired from each quadrant of the ONHs, and vascularity (i.e., the number of CD31-positive blood vessels) was quantified manually by a blinded observer. Six serial sections per ONH were analyzed. CD31-positive structures were included in our analysis if they exhibited either: 1) a clear and obvious lumen, or 2) 20 μm of uninterrupted staining. The central retinal vessels were excluded from our analysis.

Results: Vascularity within the supero-medial, infero-medial, and infero-lateral quadrants were similar between glaucomatous and non-glaucomatous ONHs. However, the supero-lateral quadrant of the glaucomatous ONH exhibited a consistently lower number of blood vessels ($\mu = 16.0$, SE = 1.7; n = 6 images from 1 eye) compared to the supero-lateral quadrants of non-glaucomatous ONHs ($\mu = 27.8$, SE = 5.3; n = 24 images from 4 eyes).

Conclusions: Our results raise the possibility that glaucomatous ONHs exhibit reduced vascularity. This could reflect either: 1) a lower number of blood vessels entering the nerve parenchyma, 2) a reduction in the amount branching within the vascular bed, and/or 3) vascular remodeling following axonal damage. Further research with increased sample size is needed to confirm our findings.

CONTROL ID: 3709671

SUBMITTER (NAME ONLY): Ahmed Salman

TITLE: In vitro characterisation of spontaneously immortalised Non-Human Primate Müller glia cell lines as a potential source for cell replacement therapies for retinal degenerative eye disease

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Salman, A. Barnard, R.E. MacLaren, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|A. Bolinches Amoros, A. Russell, Department of Pharmacology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|D. Moralli, P. Brijka, C. Green, Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|S. Davies, Department of Chemistry, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Ahmed Salman: Commercial Relationship: Code N (No Commercial Relationship) | Aranxta Bolinches Amoros: Commercial Relationship: Code N (No Commercial Relationship) | Alun Barnard: Commercial Relationship: Code N (No Commercial Relationship) | Daniela Moralli: Commercial Relationship: Code N (No Commercial Relationship) | Paulina Brijka: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Green: Commercial Relationship: Code N (No Commercial Relationship) | Steve Davies: Commercial Relationship: Code N (No Commercial Relationship) | Angela Russell: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Müller glia, which are astrocyte-like radial cells that play a pivotal role in maintaining retinal homeostasis, are considered to be the main glial cells in the retina. Their expression spans along the retina providing general structural support to retinal neurones and blood vessels. Among several other functions, they prevent aberrant photoreceptors migration into the subretinal space and facilitate glutamate uptake to keep its extracellular concentration below toxic levels.

In lower vertebrates such as fish and amphibians, the injured retina shows a regeneration potential which is believed to stem from Müller glia. Although this regeneration potential is common for all vertebrates, it is, however, absent in mammalian systems for unknown reasons. Although various Müller glia cell lines have been described in the literature including those derived from human and rat, to our knowledge, no non-human primate (NHP) Müller glia cell line is currently available.

Methods: A spontaneously immortalised Müller glia cell line was established from a primary culture of neural retina of a Macaque monkey dissociated using a papain dissociation reagent. The cells were cultured, passaged and eventually immortalised without the presence of growth factors. The cells were examined for expression of Müller glia and other markers by immunocytochemistry and RT-PCR and differentiated with growth factors known to stimulate cells differentiation.

Results: Here we report a spontaneously immortalised Müller glia cell line isolated from rhesus macaque monkeys, grown under normal culture conditions and could be expanded indefinitely without the presence of growth factors. The cell line exhibits normal morphology and expressed Müller glia markers among other stem cell markers when examined with immunocytochemistry and RT-PCR. When cultured in the presence of growth factors that stimulate cell differentiation, they altered their gene expression profile by expressing a combination of retinal neuronal markers

Conclusions: Our observations indicate that the non-human primate retina harbours a population of cells that express both Müller glia and stem cell markers, which can be useful for future cell replacement therapies.

CONTROL ID: 3709672

SUBMITTER (NAME ONLY): Berthold Pemp

TITLE: Isolated dominant optic atrophy with childhood onset in a family with the heterozygous SDHA mutation c.1351C>T

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Pemp, C. Mitsch, A. Reitner, Department of Ophthalmology, Medical University of Vienna, Vienna, AUSTRIA|W.M. Schmidt, Center of Anatomy & Cell Biology, Neuromuscular Research Department, Medical University of Vienna, Vienna, AUSTRIA|

Commercial Relationships Disclosure: Berthold Pemp: Commercial Relationship(s);Code C (Consultant/Contractor):Chiesi;Code F (Financial Support):Chiesi;Code R (Recipient):Chiesi, Santen | Wolfgang Schmidt: Commercial Relationship: Code N (No Commercial Relationship) | Christoph Mitsch: Commercial Relationship(s);Code R (Recipient):Bayer, Novartis, Takeda | Andreas Reitner: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Heterozygous mutations in the nuclear encoded gene for the succinate dehydrogenase complex flavoprotein subunit A (SDHA) of the mitochondrial respiratory chain complex II (CII; succinate-ubiquinone oxidoreductase) have been described in a rare syndrome including predominantly adult onset bilateral optic atrophy, progressive neurological impairment, and in some cases cardiomyopathy. They may disturb the electron transfer from succinate to ubiquinone and cause partial CII deficiency. Here, we describe a family featuring optic atrophy with autosomal dominant inheritance as the only symptom in multiple generations, segregating a pathogenic mutation in the SDHA gene, previously described in patients with progressive optic atrophy, ataxia, and myopathy.

Methods: Clinical examinations included visual acuity testing, automated threshold perimetry, OCT-based measurement of peripapillary retinal nerve fiber layer (pRNFL) thickness and macular ganglion cell layer (mGCL) thickness, laboratory tests, cranial MRI, neurological and cardiological examination. Genetic analysis was performed by exome sequencing in the index patient and subsequent confirmation by conventional DNA sequencing in all affected individuals.

Results: Four male patients, two adults and two children aged 7 and 9, from two generations of the same family presented with bilateral optic atrophy, central visual field defects, severely reduced pRNFL thickness (37-48 µm) and moderately reduced mGCL thickness (23-31 µm). Genetic analysis revealed the heterozygous missense mutation NM_004168.4:c.1351C>T p.(Arg451Cys) within the SDHA gene, affecting a highly conserved arginine residue in the FAD/NAD(P)-binding domain of SDHA. No other mutations in known optic atrophy genes were detected in the index patient. Cranial MRI, metabolic laboratory tests, neurological and cardiological examinations were all unremarkable.

Conclusions: Information in this pedigree adds isolated dominant optic atrophy with childhood onset to the phenotype spectrum of heterozygous mutations in SDHA, which are known to cause a syndrome characterized by neurodegeneration with ataxia and late-onset optic atrophy (NDAXOA, OMIM #619259). Although being a rare cause, we advise to include SDHA in gene sequencing panels for dominant optic atrophy.

CONTROL ID: 3709674

SUBMITTER (NAME ONLY): Derek Hu

TITLE: Cardiovascular disease burden in patients presenting with HZO

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hu, A. Yan, D. Chan, A. Rains, J.Y. Zhang, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|D. Skondra, A. Farooq, Ophthalmology and Visual Science, The University of Chicago Medicine, Chicago, Illinois, UNITED STATES|F. Alenghat, Cardiology, The University of Chicago Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Herpes zoster ophthalmicus (HZO) has been associated with increased rates of composite cardiovascular (CV) events, though the mechanism by which varicella zoster virus (VZV) reactivation induces this risk is unclear. We performed a retrospective study to examine baseline CV risk profiles in HZO patients.

Methods: Patients who presented at our tertiary care academic center for initial HZO management between 1/1/2009 and 12/31/2019 were identified. We excluded those under 18 years of age or with only one recorded clinical encounter. A control cohort of patients presenting during the same timeframe was randomly selected and matched for age, race, and gender. Patient variables were abstracted through manual chart review and Epic SlicerDicer up until initial HZO presentation (pre-diagnosis). Subjects were also tracked for one year past the date of initial HZO presentation (post-diagnosis) for CV event occurrence. Statistics were performed with chi-squared and t-test analyses.

Results: 289 HZO patients were identified during the study period. 43 patients with only one clinical encounter were excluded, leaving a final HZO cohort of 246 patients. Pre-diagnosis HZO patients were more likely than controls to have BMIs in the healthy category (35% vs. 26%; p=0.03) and less likely to fall under the obese category (24.8% vs. 33.3%; p=0.04). No differences in blood pressure values or smoking status were found between cohorts. Hemoglobin A1c (p=0.73) and lipid panel (p=0.13) values also did not differ between cohorts pre-diagnosis. Rates for hypertension medications (46.7% vs. 48.4%; p=0.72), statins (35.4% vs. 37.4%; p=0.64), and aspirin therapy (26.4% vs. 24.4%; p=0.61) were similar between cohorts pre-diagnosis. None of the traditional CV comorbidities or composite CV events (p=0.50) were elevated in HZO patients before their initial diagnosis. Strikingly, rates of composite CV events were also not increased in the year following HZO diagnosis in our cohort (p=0.89).

Conclusions: Although HZO episodes have been associated with increased risk of CV events, the baseline CV disease burden was not elevated in our HZO cohort nor was the 1-year rate of CV events after diagnosis. This suggests that increased HZO-related CV risk, if present, may be driven by productive VZV infection sequelae. An improved understanding of the risk profiles and disease progression of HZO patients may inform novel screening and prevention methods.

CONTROL ID: 3709675

SUBMITTER (NAME ONLY): Sanjana Basak

TITLE: OptiDicer reduces long CUG RNA accumulation in corneal endothelial cells from patients with Fuchs' dystrophy

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Basak, H. Uehara, B.K. Ambati, University of Oregon, Eugene, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Sanjana Basak: Commercial Relationship: Code N (No Commercial Relationship) | Hironori Uehara: Commercial Relationship: Code N (No Commercial Relationship) | Balamurali Ambati: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Fuchs' endothelial corneal dystrophy (FECD) is a genetic disease which leads to eye pain, significant loss of vision and corneal lesions called guttae. Late-onset FECD is characterized by the expanded repeat trinucleotide sequence (CTG)n (n>30-40) in the TCF4 gene. The accumulation of CUG RNA in the nucleus forms cytotoxic RNA foci. Recently, we developed a recombinant variant of DICER, OptiDicer, which can degrade double-strand RNA through RNaseIII activity. In this study, we examined whether OptiDicer can decrease CUG RNA accumulation in corneal endothelial cells from patients with Fuchs' dystrophy.

Methods: F35T cells, Human corneal endothelial cells from an FECD patient with (CTG)n n>1000, were used in this study. pCMV-NLS-OptiDicer (Nuclear localization signal conjugated OptiDicer) was transfected by Lipofectamine-3000 in an Fibronectin coated 8-well chamber slide. As a control, we used D2A-OptiDicer (which has no RNaseIII activity by introducing two alanine scanning mutations in OptiDicer). Two days post transfection, the cells were fixed by 4% PFA, and then subjected to in situ hybridization using Alexa647 conjugated (CAG)8 2O-methyl RNA probes in order to detect CUG RNA accumulation. The images were obtained with an EVOS fluorescence microscope, and the number of CUG RNA accumulation was counted.

Results: The transfection efficiency was estimated as 50%. We did not find significant cell loss by pCMV-NLS-OptiDicer or pCMV-D2A-OptiDicer transfection. Accumulation of CUG RNA was counted in 276 OptiDicer transfected and 222 D2A-OptiDcier transfected F35T cells. The average number of CUG RNA accumulation was 1.9+/-1.4 in OptiDicer-F35T and 2.9+/-1.7 in D2A-OptiDicer control F35T ($p<0.001$), respectively.

Conclusions: We found that OptiDicer significantly decreased CUG-RNA accumulation in late-onset FECD patient derived corneal endothelial cells, although the low transfection efficiency may underestimate OptiDicer effect. Our result suggests OptiDicer can be a potential treatment for long CUG RNA repeat derived FECD. Future studies will explore OptiDicer in other cell lines from FECD patients with other transfection methods.

CONTROL ID: 3709680

SUBMITTER (NAME ONLY): Corinna Cozzitorto

TITLE: Col4a1 mutations alter periocular mesenchyme cell migration that may contribute to anterior segment dysgenesis in mice.

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Cozzitorto, Z. Peltz, L. Flores, M. Mao, L. Della Santina, D.B. Gould, Ophthalmolgy, University of California San Francisco, San Francisco, California, UNITED STATES|D.B. Gould, Anatomy, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in collagen type IV alpha 1 (COL4A1) and alpha 2 (COL4A2) cause a multisystem disorder characterized by variable cerebrovascular, ocular, renal, and neuromuscular manifestations. The affected tissues are mainly derived from two distinct embryonic origins: the neural crest cells (NCCs) and the mesoderm germ layer. The periocular mesenchyme (POM) is a transient migratory embryonic tissue of NCCs and paraxial mesoderm derivation. It gives rise to anterior segment structures such as the corneal endothelium and stroma, trabecular meshwork, and ciliary muscle. Morphogenetic defects of these structures can impair aqueous humor outflow, leading to elevated intraocular pressure and glaucoma development. Approximately one-third of patients with COL4A1 and COL4A2 mutations have ocular anterior segment dysgenesis (ASD), including congenital glaucoma resulting from dysgenesis of POM-derived structures. POM terminal differentiation has been the major focus of ASD research, but the cellular mechanisms are still unclear. We hypothesize that Col4a1 mutation may alter POM biology underlying ASD.

Methods: Immunofluorescence and confocal microscopy were performed on control and Col4a1 mutant mouse embryos at embryonic day (E) 9.5 and E10.5 using antibodies against SOX10 to label migratory NCCs, and FOXC1 and PITX2 to label the POM and prospective corneal stroma at E12.5.

Results: SOX10 labeling revealed that Col4a1 mutant and control embryos had similar numbers of migrating cranial NCCs at both E9.5 and E10.5. However, compared to control littermates, cranial NCCs moving towards the eye region in E9.5 mutants showed abnormal migration, forming a less cohesive migratory stream. On the other hand, within the POM of E9.5 and E10.5 Col4a1 mutant embryos, NCCs clustered more closely. POM analysis at E12.5 revealed that $FOXC1^{+}$, but not $PITX2^{+}$, POM cells migrate less cohesively within the prospective corneal stroma of Col4a1 mutant embryos compared to controls.

Conclusions: In agreement with our hypothesis, our results show for the first time that Col4a1 mutations lead to cranial NCC and POM migratory defects without affecting cell numbers. Further examinations are needed to understand both the molecular causes and consequences of the uncovered migratory phenotype. Future work will analyze the mesodermal contribution to ASD in Col4a1 mutants.

CONTROL ID: 3709682

SUBMITTER (NAME ONLY): Kenneth Lam

TITLE: Automatic identification of Microaneurysms in Diabetic Retinopathy patients utilizing an nnU-Net

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Lam, A. Yaghy, A. Camacho, N.K. Waheed, New England Eye Center, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|L. Husvogt, A. Maier, Pattern Recognition Lab, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Microaneurysms (MA) are early clinical signs seen in patients with non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). They result from capillary wall outpouching, can bleed, and result in vision loss. The advent of optical coherence tomography angiography (OCTA) has allowed for the noninvasive detection of MAs as compared to fluorescein angiography. Herein, we developed an nnU-Net that automatically identifies MAs on OCTA en face images.

Methods: Patients with early, intermediate, and severe NPDR as well as PDR, who were imaged on the ZEISS PLEX Elite 9000 using a field size of 6x6 mm, were retrospectively enrolled from the New England Eye Center. We isolated the automatically segmented superficial and deep capillary layers of the OCTA en face images. Two expert graders independently and manually labeled MA using the EXACT web-based labeling tool. Utilizing the labeled data, we trained a 2D nnU-Net (a self-configuring deep learning tool that utilizes heuristic and data-based rules to choose suitable hyper-parameters) to detect MA. Both the network topology and training process are guided by empiric rules that take into account image dimension, modality, and annotations. Furthermore, we adapted parameters of the nnU-Net to fit the specific needs of MA detection. We evaluated different loss functions and training parameters.

Results: 111 eyes from 60 patients with DR were included for analysis. Preliminary tests on the network utilized the superficial capillary layer labeled by one expert grader. 16 images were held back for testing and the network achieved a per-pixel accuracy score of 99% on the test data. These results are preliminary and do not include all of the data and annotations yet.

Conclusions: Detection of MA in the superficial capillary plexus images from the PLEX Elite system is feasible using annotations generated from both the EXACT labeling tool and nnU-Net and it achieves a per-pixel accuracy score of 99%.

CONTROL ID: 3709684

SUBMITTER (NAME ONLY): De-Quan Li

TITLE: IL-37 prevents corneal barrier disruption by inhibiting TNF-α/CTSS signaling in primary human corneal epithelial cells under hyperosmotic stress

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Li, Y. Zhang, J. Li, X. Chen, S.C. Pflugfelder, C.S. De Paiva, Ocular Surface Center, Cullen Eye Institute, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|Y. Zhang, X. Chen, Eye Hospital, School of Optometry and Ophthalmology, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|J. Li, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To explore novel role and molecular mechanism of a natural anti-inflammatory cytokine interleukin (IL) 37 in preventing corneal epithelial barrier disruption from hyperosmolar stress as occurs in dry eye.

Methods: Primary human corneal epithelial cells (HCECs) were cultured from fresh donor limbal explants. An in vitro dry eye model with hyperosmolar stress was established by switching HCECs from isosmolar (312mOsM) to hyperosmolar medium (350-500 mOsM) alone or with rhIL-37, some cells were treated with TNF-α, for different periods (2-48 hours). The expression of cytokines and cathepsin S, and barrier protein integrity were evaluated by RT-qPCR, ELISA, and immunofluorescent staining with confocal microscopy.

Results: The integrity of epithelial barrier was significantly disrupted in HCECs exposed to hyperosmolar medium, as shown by immunofluorescent images of tight junction (ZO-1, occludin and claudin-1) and adheren junction (E-cadherin) proteins. The opposite responses were observed between TNF-α stimulated and IL-37 suppressed in HCECs exposed to hyperosmolarity. Cathepsin S, encoded by CTSS gene, was found to directly disrupt epithelial barrier. Interestingly, CTSS expression was significantly induced by TNF-α and hyperosmolarity, while exogenous rhIL-37 inhibited TNF-α and CTSS expression at mRNA and protein levels following hyperosmolar stress. rhIL-37 further restored barrier protein integrity, observed in 2D and 3D confocal immunofluorescent images, in HCECs under hyperosmolar stress.

Conclusions: Our findings demonstrate a novel signaling pathway by which the anti-inflammatory cytokine IL-37 suppresses TNF-α and CTSS stimulated corneal epithelial barrier disruption under hyperosmotic stress. This study provides new insight into mechanisms disrupting or preventing corneal barrier in dry eye disease.

CONTROL ID: 3709690

SUBMITTER (NAME ONLY): Omar Halawa

TITLE: Gender-based differences in Medicare reimbursements among ophthalmologists persist across time

SESSION TITLE: Health Economics and Health Care Delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Halawa, M.V. Boland, N. Zebardast, Harvard Medical School, Boston, Massachusetts, UNITED STATES|O. Halawa, S. Sekimitsu, M.V. Boland, N. Zebardast, Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Sekimitsu, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Omar Halawa: Commercial Relationship: Code N (No Commercial Relationship) | Sayuri Sekimitsu: Commercial Relationship: Code N (No Commercial Relationship) | Michael Boland: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss;Code C (Consultant/Contractor):Meditec;Code C (Consultant/Contractor):Topcon | Nazlee Zebardast: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Evaluate differences in Medicare reimbursements between men and women ophthalmologists between 2013 and 2019.

Methods: The Centers for Medicare and Medicaid Services Physician and Other Supplier Public Use File was used to determine total reimbursements and number of charges submitted by MD or DO ophthalmologists between 2013 and 2019. Reimbursements were standardized to account for geographic differences in Medicare reimbursement per service. Billing codes were grouped into service categories including outpatient office visits and eye examinations, diagnostic testing, laser and surgery. Data from the American Community Survey (ACS) were used to determine zip-code-level socioeconomic characteristics (unemployment, poverty, income, and education) for the location of each physician's practice. A multivariable linear regression model was used to evaluate differences in annual reimbursements by gender, accounting for calendar year, years of experience, total number of services, ACS zip-code data, and proportion of procedural services.

Results: Among 20,730 ophthalmologists who received Medicare reimbursements between 2013 and 2019, 15,722 (75.8%) were men. The most common billing codes submitted were for outpatient visits and eye examinations (17.7 million charges/year), diagnostic imaging of the retina (5.9 million charges/year), intra-vitreal injection (3.1 million charges) and removal of cataract with insertion of lens (2.3 million charges). Compared to men, women ophthalmologists received lower median annual reimbursements ($95,042.73, IQR 29,548.99-206,034.7 for women vs. $199,044.10, IQR 77,230.51-397,937.60 for men, $p<0.001$, Figure 1) and billed for a lower annual number of services (1,232, IQR 432-2484 vs. 2,302, IQR 988-4,252, respectively $p<0.001$). After adjustment for covariates, women ophthalmologists received $20,239.80 less in reimbursements than men (95% confidence interval -18,732.28 to -21,747.32, $p <0.001$). The greatest disparity in reimbursements was seen in vitreoretinal surgery, with women ophthalmologists earning 0.27 cents for each dollar earned by men (Figure 2).

Conclusions: Women ophthalmologists received less reimbursements from Medicare than men over time and across all categories of billing codes. Disparities in reimbursement persisted after controlling for physician and practice characteristics.

CONTROL ID: 3709696

SUBMITTER (NAME ONLY): Lili Xie

TITLE: Identification of a putative receptor for the myeloid cell-derived growth factor oncomodulin and its role in CNS and PNS regeneration

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Xie, Y. Yin, S. Peterson, S. Jayakar, L. Benowitz, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|J. Oses-Prieto, A. Burlingame, University of California San Francisco, San Francisco, California, UNITED STATES|J. Li, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. Rasband, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although the optic nerve, like other mature CNS pathways, cannot regenerate when injured, this failure can be partially reversed by inducing sterile inflammation in the eye. Previous work from our lab showed that this phenomenon is mediated in large part by oncomodulin (Ocm), a 12 kDa Ca++-binding protein that is secreted by myeloid cells. Ocm also induces outgrowth from dorsal ganglion neurons (DRGs) and may play a role in the conditioning lesion effect, whereby injury to a peripheral nerve enhances the ability of DRG neurons to extend central and peripheral axons into spinal cord and sciatic nerve respectively. So we aim to identify the Ocm receptor (Ocm-R) and explore its role in CNS and PNS regeneration.

Methods: Biotinylation by antibody recognition (BAR) followed by mass spectrometry were used to identify Ocm-R candidates. Co-immunoprecipitation and Biacore studies were used to reveal the direct interaction between Ocm and Ocm-R. Ocm-R expression in RGCs and DRG neurons were manipulated by CRISPR-Cas9 and aav2/9-short hairpin RNA (shRNA) targeting Ocm-R respectively. Ocm-R expression in cell line was overexpressed by plasmid transfection.

Results: We now report the isolation of a likely Ocm receptor (Ocm-R). Knock-down of Ocm-R in RGCs leads to the loss of Ocm binding to RGCs and a substantial loss of inflammation-induced regeneration after optic nerve injury without affecting regeneration induced by other means (pten deletion in RGCs). Conversely, ectopic expression of Ocm-R in cells with low baseline expression results in high Ocm binding. Moreover, Ocm-R knockdown reduces conditioning lesion induced DRGs neurons' central and peripheral axon regeneration.

Conclusions: Oncomodulin and its receptor enable the conditioning lesion induced CNS and PNS regeneration.

CONTROL ID: 3709697

SUBMITTER (NAME ONLY): Jonathan Halim

TITLE: Telemedicine for Diabetic Retinopathy Screening in Low- and Middle-Income Countries: A Systematic Review and Bibliometric Analysis

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Halim, Barts Health NHS Trust, London, England, UNITED KINGDOM|J. Xie, V. Chaudhary, McMaster University, Hamilton, Ontario, CANADA|S. Sivaprasad, NIHR Moorfields Biomedical Research Centre, London, England, UNITED KINGDOM|

Commercial Relationships Disclosure: Jonathan Halim: Commercial Relationship: Code N (No Commercial Relationship) | Jim Xie: Commercial Relationship: Code N (No Commercial Relationship) | Varun Chaudhary: Commercial Relationship: Code N (No Commercial Relationship) | Sobha Sivaprasad: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Populations of low- and middle-income countries (LMICs) have poorer access to eye care due to fewer ophthalmologists per capita. Telemedicine enables remote diabetic retinopathy screening and widely improves access. This study aims to evaluate the current role of telemedicine for diabetic retinopathy screening in LMICs.

Methods: A systematic search of PubMed, Embase, Web of Science, and Cochrane Central was undertaken. Studies were included if they involved the use of telemedicine, as defined by the American Association of Telemedicine (ATA), for diabetic retinopathy screening among populations in LMICs. The outcomes reflected the quality of telemedicine according to ATA categories, screening personnel, location, and system used.

Results: Of 301 studies retrieved, 38 were included, involving a total of 206,725 individuals, and comprising 34 cross-sectional studies, 3 randomised controlled trials, and 1 cohort study. The publication year ranged from 2007-2021. The studies were from Bangladesh, Brazil, Cameroon, China, Costa Rica, India, Iran, Kenya, Lebanon, Mexico, Nepal, Peru, Zambia, and Zimbabwe. ATA Category 2 and 3 clinical validation for screening were attained in 61% (n = 23) and 18% (n = 7) of the studies, with the remaining 21% (n = 8) being ATA Category 1. The majority of studies (n = 20) appointed either technicians or nurses as image acquisition personnel, while image graders largely involved ophthalmologists (n = 35). The most common location of screening were hospitals (n = 18), followed by health centres (n = 11), mobile clinics (n = 10), and primary care clinics (n = 9). A median of 2 pictures (range = 1-7) were taken in each study, the majority being non-stereo (n = 31). Nineteen studies used non-mydriatic imaging, 14 utilised mydriasis, and 4 performed dilation as needed. Whilst 55% (n = 21) of the studies involved opportunistic screening programmes, 45% (n = 17) were systematic screening programmes integrated within the healthcare system, and 71% (n = 27) comprised follow-up pathways.

Conclusions: A variety of telemedicine tools have been attempted in LMICs and have successfully screened a large number of individuals. However, more funding and infrastructure are needed for these programmes to be integrated into the healthcare system for systematic population-level screening.

CONTROL ID: 3709698

SUBMITTER (NAME ONLY): Hironori Uehara

TITLE: Gene knockdown of Col8a2 in mouse corneal endothelium by non-homologous end joint repair using adenovirus-mediated Crispr/Cas9

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Uehara, X. Zhang, B.K. Ambati, Phil and Penny Knight Campus for Accelerating Scientific Impact, University of Oregon, Eugene, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gene knockdown by NHEJ (non-homologous end joint repair) using Crispr/Cas9 can be useful for various eye diseases such as Fuchs' endothelial corneal dystrophy (FECD). In this study, to evaluate Crispr/Cas9 efficacy in corneal endothelium, we examined the indel (insert/deletion) rate in mouse corneal endothelium after adenovirus-mediated Crispr/Cas9 using deep sequencing. Also, we infected adenovirus-Cas9 targeting Col8a2 to human donor corneas and evaluated its safety.

Methods: Adenovirus encoding Cas9 and guide RNA targeting Col8a2 gene (Ad-Cas9-Col8a2gRNA) was injected into anterior chamber in C57BL6/j mice. Mutations of Col8a2 are responsible for early-onset FECD. The genomic DNA (gDNA) was purified from the dissected corneal endothelium. PCR was performed at the gRNA target site. The PCR products were subjected to deep sequencing, and the indel rates were calculated. In human donor corneas, paired corneas were treated with Ad-Cas9-Col8a2gRNA or mock. One week post infection, the corneal endothelial cell density was evaluated by alizarin red staining.

Results: Immunostaining showed that Ad-Cas9-Col8a2gRNA ($6.3x10^6$ vg) significantly decreased 91 ± 33 % of COL8A2 expression in the corneal endothelium compared to the non-injected control corneas ($p<0.01$, N=4). By deep sequencing, the rates of insertion and deletion were 20.0 ± 4.0% and 3.6 ± 0.5% respectively, and the total indel rate was 23.7 ± 4.5%. However, these values may be an underestimate due to inclusion of genomic DNA from stromal cells which were not infected with adenovirus through anterior chamber injection. Therefore, the adjusted indel rate was estimated as 102.5±16.3%. Although this value does not have direct evidence, the immunostaining of COL8A2 in the cornea supports this estimation. In human corneas, we confirmed Cas9 protein expression in corneal endothelium by immunostaining and the indels by PCR/restriction enzyme digestion. We did not find significant difference of corneal endothelial cell density by adenovirus infection (2978 ± 85 cells/mm^2 in mock and 2982 ± 157 cells/mm^2 in Ad-Cas9-Col8a2gRNA).

Conclusions: In this study, we showed the indel rate in mouse corneal endothelium by adenovirus mediated Crispr/Cas9 and safety of this vector in human donor corneas. Our result indicates the gene knockdown by Crispr/Cas9 can be useful for genetic corneal endothelial cell diseases such as FECD.

CONTROL ID: 3709699

SUBMITTER (NAME ONLY): Dong Liu

TITLE: NMNAT2 and NAD^+ are Downregulated in Glaucomatous RGCs and Overexpression of NMNAT2 Rescues Glaucomatous Neurodegeneration

SESSION TITLE: Neuroprotection and neuroregeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Liu, F. Fang, P. Zhuang, X. Feng, P. Liu, H. Huang, L. Li, W. Chen, L. Liu, Y. Sun, Y. Hu, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|H. Jiang, J. Ye, Radiation Oncology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|F. Fang, Ophthalmology, Central South University, Changsha, Hunan, CHINA|

ABSTRACT BODY:

Purpose: Emerging evidence suggests that redox factor NAD^+ decline is a hallmark of aging and neurodegenerative diseases. This study tested the hypothesis that modulating glaucomatous RGC intrinsic NMNAT2 levels which is the key enzyme in the NAD^+ biosynthetic process, is a promising gene therapy for glaucomatous neurodegeneration.

Methods: We first profiled the translatomes of RGCs in naïve and silicone oil-induced ocular hypertension (SOHU)/glaucoma mice by RiboTag mRNA sequencing. NMNATs mRNA levels were then validated in SOHU glaucomatous RGCs by in situ hybridization. NAD^+ levels in retina and optic nerve were acquired by LC/MS based NAD^+. RGCs soma and axon survival were evaluated by in vivo optical coherence tomography (OCT) imaging and post-mortem retina wholemounts and ON sections histological analysis. Visual function were evaluated by the pattern electroretinogram (PERG) and optokinetic tracking response (OKR) test.

Results: Deep sequencing of translating mRNAs isolated from RGC ribosomes reveals that all three isoforms of NMNATs can be detected in RGCs but NMNAT2 is the most abundant isoform, which is significantly decreased in glaucomatous RGCs ($p < 0.0001$). In ON crush neuropathy model, AAV2 mediated RGC-specific overexpression of NMNAT2Δex6 promotes RGC soma and axon survival, comparable with cytNMNAT1 in axonal protection while marginally better in soma protection ($p < 0.05$). In SOHU glaucoma model, RGC-specific overexpression of NMNAT2Δex6 promotes dramatic survival of both RGC somata and axons possibly by significantly restoring NAD^+ levels in glaucomatous retinas ($p < 0.05$) and ONs ($p < 0.01$). In terms of visual function, the peak-to-trough (P1-N2) amplitude ratio of the SOHU eyes to contralateral eyes in PERG increased significantly after NMNAT2 overexpression in RGCs ($p < 0.0001$) and also significantly preserves visual acuity of the glaucomatous eyes in OKR test ($p < 0.0001$).

Conclusions: Taking advantage of our recently developed SOHU mouse glaucoma model and RGC-specific AAV promoter, mSncg, we found decreased NMNAT2 expression in glaucomatous RGCs, which may lead to NAD^+ decline in RGCs and ONs. We further demonstrated that modulating RGC intrinsic levels of NMNAT2 by an AAV2-mSncg vector represents a potent gene therapy strategy for protecting both RGC somata and axons in traumatic ON injury and SOHU glaucoma model.

CONTROL ID: 3709704

SUBMITTER (NAME ONLY): Solomon Gibson

TITLE: Htr1b is required for normal mouse vision and retinal physiology

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gibson, B.J. Frankfort, Department of Neuroscience, Baylor College of Medicine, Houston, Texas, UNITED STATES|S. Gibson, G. Shen, P.M. Pitale, Y.H. Park, M. Polo Prieto, B.J. Frankfort, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Little is known about the mechanisms by which serotonin (5HT) functions in the retina. Using publicly available RNA sequencing data, we have identified 5HT receptor 1b (Htr1b) as a likely mediator of 5HT in retinal ganglion cells (RGCs). In this study, we investigate the expression and function of Htr1b in the retina and RGCs.

Methods: 8-week wild-type mice were used to determine gene (Htr1b) expression. RNAscope in situ hybridization (ISH) was performed on retinal cryosections and imaged using confocal microscopy.

Whole field flash electroretinograms (ERGs) were used to record scotopic and photopic amplitudes in 22 mice (8 $Htr1b^{-/-}$; 8 $Htr1b^{+/-}$; 6 WT). Positive scotopic threshold response (pSTR), b-wave, and a-wave amplitudes were recorded. Visual behavior was evaluated in $Htr1b^{-/-}$ mice and controls by assessing the scotopic and photopic optokinetic response. Gratings of variable spatial frequency or contrast were presented to evaluate spatial frequency threshold and contrast sensitivity threshold, respectively. We performed retinal histology and in vivo SD-OCT imaging on 8-week $Htr1b^{-/-}$ animals to quantify retinal layer thickness. Retinal layers (GCL, IPL, INL, OPL, and ONL) were measured as a percentage of total retinal thickness and compared to age and sex-matched wild-type controls.RGC numbers were determined from whole-mount retinas which were prepared and visualized with confocal microscopy. RBPMS-positive cells were counted semi-automatically using an ImageJ extension. Total cell density was normalized to image size.

Results: ISH showed that Htr1b RNA is primarily restricted to the GCL layer. $Htr1b^{-/-}$ mice showed reduced ERG amplitudes and OKR thresholds compared to control mice. The pSTR slope (amplitude/light intensity) was reduced by 40% (P=0.0035). With OKR testing, scotopic contrast sensitivity thresholds were diminished by 10%-15% (P=0.0334). Histology, SD-OCT imaging, and RGC counts showed no observable alterations in the retinal morphology of $Htr1b^{-/-}$ mice.

Conclusions: Our results show that loss of Htr1b function results in abnormal retinal physiology and visual function despite overtly normal retinal structure and RGC counts. Collectively, these experiments suggest that Htr1b plays an important and previously unrecognized role in 5HT action in the retina. More research is needed to understand 5HT action and its potential impact on retinal disease.

CONTROL ID: 3709706

SUBMITTER (NAME ONLY): Ashley Sun

TITLE: Augmented Intelligence Integrated into the Electronic Medical Record to Improve Cataract Refractive Outcomes: A Pilot Study

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sun, J.J. Kudrna, N. Cannon, T. O'Rourke, K. Goodling, S. Pantanelli, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intraocular lens (IOL) power calculations for cataract surgery remain an imperfect science with known shortcomings in eyes with extreme biometric measurements. The purpose of this study was to investigate whether an augmented intelligence (AI)-based clinical decision aid integrated into the electronic medical record (EMR) improved prediction accuracy of the SRK/T formula in eyes undergoing cataract surgery.

Methods: This was a retrospective consecutive case series compared SRK/T and AI-modified SRK/T predictions on eyes in which monofocal IOLs were implanted in adult subjects. The testing dataset included 116 eyes of 79 patents, implanted with an MX60E IOL. Exclusion criteria included corneal or intraocular opacities of any kind other than cataract, history of other intraocular surgery, post-operative refraction recorded outside study period (21-90 days following surgery), or post-operative best-corrected vision worse than 20/30. A tool was built into the EMR that analyzes biometric data and makes recommendations from the peer-reviewed literature on how to adjust refractive targets for eyes with short or long axial lengths (AI-AL), flat or steep keratometries (AL-K), or shallow or deep anterior chamber depths (AI-ACD). Primary endpoints included standard deviation (SD) of the prediction error (PE) for both SRK/T and AI-modified SRK/T predictions. Secondary endpoints include mean absolute prediction error (MAE), and proportion of eyes with post-operative spherical equivalent (SE) within 0.25 and 0.50 diopters (D) of predicted.

Results: SRK/T + AI-K improved upon the original SRK/T formula based upon several metrics. The SDs of the signed PEs were 0.657 and 0.623 D for the SRK/T and SRK/T + AI-K, respectively. MAEs for the same were 0.455 and 0.420 D, respectively ($p < 0.0003$). The proportion of eyes with post-operative SE within 0.25 and 0.50 D of predicted were 39.7% and 69.8% vs. 44.0% and 72.4%, respectively ($p < 0.0002$ for both). Other adjustments of the SRK/T formula based on AL and ACD did not result in meaningful improvements.

Conclusions: An AI-based clinical decision aid integrated into an EMR may help to refine prediction accuracy of SRK/T. Further validation is needed in more eyes and consideration of multiple biometry measurements simultaneously.

CONTROL ID: 3709708

SUBMITTER (NAME ONLY): Sayan Ghosh

TITLE: Crosstalk between metabolism and inflammation in dry age-related macular degeneration

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ghosh, P. SHANG, N.A. Stepicheva, H. Liu, O. Chowdhury, V. Koontz, A. Strizhakova, R. Daley, S.L. Hose, D. Sinha, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The dry form of age-related macular degeneration (AMD), one of the leading causes of blindness in the elderly, has now been established as a multifactorial disease. Cellular metabolic alterations and chronic inflammation have been identified as two major pathological factors that contribute to the progression of dry AMD. In this study we evaluated the crosstalk between metabolic changes and inflammation induction in a mouse model that shows a dry AMD-like phenotype with the intent to target specific molecules in a pathway that would rescue both the metabolic insult and inflammation, thereby halting the progression of the disease.

Methods: RNAseq analysis was performed on RPE cells from cultured wild type RPE explants overexpressing βA1-, βA3- or βA3/A1-crystallin via adenoviral RFP constructs. To compare the metabolic gene profile/intermediates in the RPE cells at the early and advanced stages of disease progression in a mouse model, scRNAseq (cells from the sub-retinal space) and metabolomics/lipidomics (RPE cells) analyses were performed on 3, 10 and 15 month old Cryba1-floxed and cKO mice; data were confirmed with western blotting. βA3 KO and Cryba1 cKO mice were fed a high fat diet (HFD) to induce metabolic stress and resulting changes in signaling mediators and histopathology assessed.

Results: Metabolomics studies revealed a significant increase in the levels of intermediates known to induce mTORC1 signaling, like aspartate and betaine, in cKO RPE relative to controls. Lipidomic profiling showed elevated fatty acids (FAs) in cKO RPE, owing to the activation of the mTORC1-dependent FA synthesis pathway. We identified IL-17 signaling pathway activation as the link between these metabolic changes and chronic inflammation induction in the RPE of our mouse model during disease progression. Further, HFD treatment in our mouse models exacerbated the alterations in IL-17 levels and FA synthesis, and induced lipid droplet accumulation in the RPE cells.

Conclusions: We have now established the onset of IL-17 mediated inflammatory signaling as the link between cellular metabolic alterations and chronic inflammation in a mouse model of dry AMD. It is known that IL-17 is upregulated in the RPE of human AMD patients. Hence, targeting IL-17 and/or molecules of this signaling pathway could be an avenue for future therapeutic interventions to delay the progression of dry AMD.

CONTROL ID: 3709711

SUBMITTER (NAME ONLY): Andrew Jo

TITLE: Retinal bipolar cells make inhibitory synapses onto amacrine cells

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Jo, S. Deniz, J. Xu, S.H. DeVries, Y. Zhu, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Andrew Jo: Commercial Relationship: Code N (No Commercial Relationship) | Sercan Deniz: Commercial Relationship: Code N (No Commercial Relationship) | Jian Xu: Commercial Relationship: Code N (No Commercial Relationship) | Steven DeVries: Commercial Relationship: Code N (No Commercial Relationship) | Yongling Zhu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Amacrine cells (ACs) are the least understood cell class in the retina due to the lack of genetic access and limited accessibility for patch-clamp recording. In this study, we combined mouse genetics, genetic profiling, functional imaging, and electrophysiology recording to discover new AC types and analyze their functional properties.

Methods: We use Cre/tTA intersectional genetics to identify new AC types, followed by analyzing their genetic profiles with single cell RNA sequencing (scRNA-seq), and then characterize their functional properties and circuit roles with GCaMP and iGluSnFr imaging, combined with electrophysiology recording.

Results: With Slc32a1-iCreER/Scg2-tTA intersectional strategy, we identified a new narrow-field AC subtype in the mouse retina, named Scg2-AC2. To our surprise, Scg2-AC2 showed light responses unexpected from morphological features. Scg2-AC2 stratified in the ON layer, but was activated by light decrement (OFF) in the surround and inhibited by light increment (ON) in the center. The ON center inhibition was created by sign-inverting mGluR8 activated by glutamate released from ON bipolar cells. The OFF surround activation was mediated by a wide-filed AC that received excitation from sustained OFF bipolar cells in the OFF sublamina and then made gap junction connections with Scg2-AC2 and activated it in the dark.

Conclusions: This study discovered a new AC type inhibited by bipolar cells via glutamate transmission. The structure and function correlation of Scg2-AC2 positions its potential role in “crossover inhibition” between ON and OFF channels by carrying OFF inhibition to the ON channel to enhance light sensitivity of RGCs in the dark.

CONTROL ID: 3709712

SUBMITTER (NAME ONLY): Hanna Luong

TITLE: Identification of Choroidal Vascular Abnormalities in Patients with Hereditary Hemorrhagic Telangiectasia (HHT)

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Luong, O. Houghton, Mayo Clinic School of Medicine - Scottsdale Campus, Scottsdale, Arizona, UNITED STATES|

Commercial Relationships Disclosure: Hanna Luong: Commercial Relationship: Code N (No Commercial Relationship) | Odette Houghton: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Reported rates of ocular involvement in HHT and recommendations regarding ophthalmic surveillance are variable. Our study sought to evaluate the prevalence of ocular imaging in patients with HHT at a large academic medical institution, characterize the choroidal vascular changes on indocyanine green angiography (ICGA) and optical coherence tomography (OCT), and present the first images of ocular HHT with ultra-widefield ICGA and enhanced-depth imaging (EDI) OCT.

Methods: Retrospective review of patients with HHT who were seen in the ophthalmology clinic at any of the Mayo Clinic sites (MN, AZ, and FL) between October 22, 2011 to October 22, 2021.

Results: Of the 71 patients with HHT identified, 7 individuals had appropriate imaging defined as radial or raster spectral-domain OCT scans and/or ICGA. 4 patients were female and 3 were male. 57% of patients, which included all male patients with imaging, had enlarged choroidal vessels detected on OCT (Image 1) and/or ICGA (Image 2). 43% of patients had both choroidal and retinal vascular changes, which consisted of pre-capillary vascular loop, capillary drop out/ischemia with telangiectasia and microaneurysms, and tortuosity of the retinal veins. The mean age for individuals with and without choroidal findings was 67 ± 11 years and 45 ± 24 years, respectively. Patients with choroidal changes included the endoglin gene mutation and displayed symptoms of gastrointestinal arteriovenous malformations (AVM) and facial and mucocutaneous telangiectasias. In contrast, one patient without choroidal changes had the activin A receptor type-like kinase 1 gene mutation and no signs or symptoms of HHT. A similar proportion of those with and without choroidal abnormalities had epistaxis and pulmonary AVMs.

Conclusions: To our knowledge, this study is the first to illustrate choroidal vascular changes in HHT with ultra-widefield ICGA and EDI OCT. The small number of patients suggests a low incidence of choroidal vascular abnormalities. Those with choroidal vascular abnormalities appear to have corroborating retinal vascular changes as well as a greater number and severity of systemic symptoms than patients without choroidal findings.

CONTROL ID: 3709716

SUBMITTER (NAME ONLY): Yixiao Wang

TITLE: Transcription factor Nfe2l1 sets proteasomal levels in the retina

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, A. Snell, J. Jinde, E. Colvin, F.M. Dyka, E. Lobanova, Department of Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|E. Colvin, Campbell University School of Osteopathic Medicine, Buies Creek, North Carolina, UNITED STATES|E. Lobanova, Department of Pharmacology and Therapeutics, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Multiple studies suggested that alterations in the cellular ability to maintain healthy proteome contribute to vision loss. The majority of proteins in any cells are degraded by Ubiquitin-Protein System (UPS), a complex cellular network that includes hundreds of proteins working in concert with chaperone and autophagy systems. A potentially efficient strategy to manipulate such complex cellular system is to target transcriptional factor(s) or pathways controlling the expression levels of its key components. Previous studies established transcriptional factor Nfe2l1 (Nuclear factor erythroid-2-like 1) as an activator of proteasomal gene expression in response to lethal concentrations of proteasomal inhibitors in cancer cells lines. Other studies suggested that Nfe2l1 instead regulates genes related to redox and anti-inflammatory response, cell regeneration and protection from cholesterol toxicity. Here, we used mouse genetics to define regulatory gene networks of Nfe2l1 in the retina.

Methods: To understand the role of Nfe2l1, we studied retinal phenotypes of mice overexpressing or lacking Nfe2l1. Levels of proteasomes and other proteins were assessed using RNA-seq, qRT-PCR and WB. The proteasomal activity was measured using fluorogenic peptidase assay. Health, function, and structural changes of the retina were evaluated with OCT, ERG, morphometric and microscopic analysis.

Results: Nfe2l1 overexpression increases levels and activity of proteasomes in the retina without affecting retinal morphology or function. Whole retina knockout of Nfe2l1 reduces the pool of proteasomes and their activity. This leads to progressive thinning of the retina, loss of photoreceptors and other retinal neurons with particularly pronounced loss of ganglion and horizontal cells. Transcriptional studies uncovered that in addition to proteasomal subunits, Nfe2l1 regulates critical autophagy genes, ubiquitin ligases, deubiquitinating enzymes and chaperones.

Conclusions: Nfe2l1 is a powerful master regulator of proteostasis in the retina and controls expression of proteasomal components, wide range of proteins involved in the degradation of ubiquitinated proteins, chaperones and autophagy. The basal activity of Nfe2l1 sets proteolytic capacity of retinal neurons and plays an important role in retinal health. These findings warrant further studies of Nfe2l1 in the retina and support exploring an enhancement of this pathway with therapeutic goals.

CONTROL ID: 3709718

SUBMITTER (NAME ONLY): Jaeryung Oh

TITLE: Comparison of axial length measurement in eyes with chorioretinal diseases using spectral-domain optical coherence tomography-based device and partial coherence interferometry

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Oh, Y. Kim, C. Yun, S. Ahn, Department of Ophthalmology, Korea University College of Medicine and School of Medicine, Seoul, Foreign, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Only a few studies have evaluated the reliability and comparability of axial length measurement using various ocular biometry devices in eyes with chorioretinal diseases. Partial coherence interferometry has been most widely used to measure the axial length of the eye, but devices using various principles have recently been developed. We compared the axial length measurement between partial coherence interferometry and spectral-domain optical coherence tomography (SD-OCT)-based devices.

Methods: This instrument validation and comparative study, which was conducted prospectively and retrospectively, included patients with various chorioretinal diseases and healthy subjects. All patients underwent axial length measurement using a recently introduced SD-OCT-based device (HOCT-1F; Huvitz Co., Ltd., Anyang-si, South Korea) and a partial coherence interferometry (IOLMaster, version 5.4, Carl Zeiss Meditec). We compared the axial lengths measured by two devices and evaluated their agreement using the intraclass coefficient (ICC) and the Bland-Altman plots with 95% limits of agreement (LOA).

Results: A total of 151 eyes of 87 patients were included, and the mean age was 63.3 ± 10.0 years. Of 151 eyes, 22 were healthy controls and 129 had chorioretinal diseases. The mean axial length measured by OCT-based device and partial coherence interferometry was 23.72 ± 0.88 mm and 23.63 ± 0.91 mm, respectively. The mean difference in axial length between the two devices was significant both in healthy controls ($P = 0.0048$) and in eyes with chorioretinal diseases ($P < 0.001$). However, the axial length measured by two devices showed excellent agreement both in healthy controls (ICC = 0.992) and in eyes with chorioretinal disease (ICC = 0.991). In Bland-Altman analysis, the mean difference of axial length in healthy controls and in eyes with chorioretinal disease was 0.099 ± 0.144 (95% LOA, -0.183–0.381) and 0.088 ± 0.168 mm (95% LOA, -0.241–0.146), respectively.

Conclusions: The new SD-OCT-based device showed a good agreement with partial coherence interferometry. Axial length measured by SD-OCT-based devices are compatible, but some correction factor is required.

CONTROL ID: 3709721

SUBMITTER (NAME ONLY): Isabel Moreno

TITLE: Hyaluronan supports the limbal stem cell phenotype during ex vivo culture

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Moreno, S. Puri, M. Sun, X. Lin, T.F. Gesteira, V.J. Coulson-Thomas, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|S. Puri, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|T.F. Gesteira, Optimvia, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hyaluronan (HA), an integral component of the limbal stem cell niche (LSCN), has been shown to be instrumental in maintaining limbal stem cells (LESCs) in vivo. Here, we investigated whether human LESCs also express HA in vitro. HA is known to assist LESCs in vivo, therefore, we also investigated whether this endogenous matrix supports ex vivoexpansion of LESCs and whether the addition of exogenous HA can further support LESCs.

Methods: Primary human LESCs (hLESCs) were isolated from donor human corneas and a mouse corneal epithelial progenitor (TKE2) cell line was obtained. The HA extracellular matrix was identified in vitro through immunocytochemistry, flow cytometry, and a red blood exclusion assay. LESCs were cultured onto HA coated petri dishes or in the presence of HA through media supplementation. Cell viability, proliferation, cell size, colony formation capacity (CFC), and putative stem cell marker expression were investigated.

Results: Both hLESCs and TKE2 cells present a HA rich ECM in vitro which is essential for maintaining viable LESCs. Providing exogenous HA as supplemented media increased LESC proliferation, CFC, and putative LESC marker expression.

Conclusions: Exogenous and endogenous HA preserve the LESC phenotype supporting ex vivo expansion. The presence of HA in the ECM creates a specialized niche for LESCs both in vitro and ex vivo, therefore, supplementing hLESCs with HA can become an accessible and affordable option for clinical applications.

CONTROL ID: 3709722

SUBMITTER (NAME ONLY): Elliot Choi

TITLE: In vivo base editing rescues cone photoreceptors in a mouse model of early-onset inherited retinal degeneration

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.H. Choi, S. Suh, Medical Scientist Training Program, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|E.H. Choi, S. Suh, A. Foik, H.O. Leinonen, S.W. Du, Z. Dong, K. Palczewski, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|G. Newby, S. Banskota, X.D. Gao, A. Raguram, S. Kohil, D.R. Liu, Merkin Institute of Transformative Technologies in Healthcare, Broad Institute, Cambridge, Massachusetts, UNITED STATES|T.V. Hoang, S. Blackshaw, Department of Neuroscience, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|D. Lyon, Department of Anatomy and Neurobiology, University of California Irvine, Irvine, California, UNITED STATES|D.R. Liu, Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts, UNITED STATES|K. Palczewski, Department of Physiology and Biophysics, University of California Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Leber congenital amaurosis (LCA) is the most common cause of inherited retinal degeneration in children. LCA patients with RPE65 mutations show accelerated cone photoreceptor dysfunction and death, resulting in early visual impairment. It is therefore crucial to develop a robust therapy that not only compensates for lost RPE65 function, but also protects photoreceptors from further degeneration. Here, we sought to answer whether base editing could rescue cone photoreceptor's survival and function.

Methods: We first screened for a combination of evolved ABE variants and sgRNAs to enhance the on-target correction rate and reduce bystander base editing. Then, we packaged the selected ABE variant and sgRNA into a lentivirus and subretinally delivered it to rd12 or rd12Gnat1$^{-/-}$ mice at 3-weeks-old. We assessed the DNA correction, RPE65 rescue, survival of S-opsin- and M-opsin-positive cones (S-cones and M-cones), and localization of S-opsins and M-opsins on retinal wholemount and cross-section staining. Furthermore, we evaluated cone function in treated rd12Gnat1$^{-/-}$ mice with electroretinography and visual cortex recordings. Lastly, we used single-cell RNA-sequencing to examine the impact of base editing on cone photoreceptors.

Results: Subretinal delivery of ABE and sgRNA corrected up to 40% of Rpe65 transcripts and preserved significantly higher numbers of S-opsin- and M-opsin-positive cones compared to the age-matched control group. The retinal cross-sections of the treated mice revealed correct localization of S-opsins and M-opsins in the cone outer segments. The photopic ERG waveforms from S- or M-cones from the treated rd12Gnat1$^{-/-}$ mice exhibited a prominent b-wave, whereas untreated eyes did not respond. Long-term protection of cone photoreceptors and function was also evident in older mice at 6 months of age. Furthermore, single-cell RNA-seq of the treated retinas revealed rescue of the gene expressions associated with cone phototransduction and survival.

Conclusions: Our results show that base editing can rescue the function and survival of cone photoreceptors, which has been a major challenge in the treatment of inherited blindness. These findings provide a foundation for a potential one-time treatment for LCA that confers long-lasting retinal protection, and warrant development of base editing for clinical application.

CONTROL ID: 3709723
SUBMITTER (NAME ONLY): Yoonjee Park
TITLE: Long-term Dose-controllable Drug Delivery Implant
SESSION TITLE: Drug delivery
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y. Park, W. Kao, Opthalmology, University of Cincinnati College of Medicine, Cincinnati, Ohio, UNITED STATES|Y. Park, X. He, Z. Yuan, Chemical Engineering, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|
Commercial Relationships Disclosure: Yoonjee Park: Commercial Relationship: Code N (No Commercial Relationship) | Xingyu He: Commercial Relationship: Code N (No Commercial Relationship) | Zheng Yuan: Commercial Relationship: Code N (No Commercial Relationship) | Winston Kao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Repetitive intravitreal injections of drug or intravitreal injections of sustained-release corticosteroid implants (Ozurdex, Retisert, and Iluvien) are the current standard of care for the chronic diseases. However, these methods involve complications due to the high initial dose at the time of injection, known as burst release.
In this study, we have developed a size-exclusive nanoporous biodegradable poly lactic glycolic acid (PLGA) capsule for dosage-controllable drug delivery implants to avoid the burst release and control the dose only when needed.
Methods: We have developed a biodegradable PLGA implant enclosing light-activated liposomal drug (methotrexate). The PLGA implant has nano-sized pores where methotrexate (MTX) was released through when activated by laser, leaving the liposomal drug in the capsule. We have optimized the porosity and the pore size for MTX release kinetics, and tested the stability and the safety for 6 months in vivo rabbit eyes. We also irradiated near infrared laser (NIR, 1064 nm) through the lens of rabbit eyes to release MTX and fluorescence dye for visualization. The MTX release by laser was quantified based on in vivo imaging.
Results: We created a pore size less than 5 nm to selectively release drug molecules only upon laser irradiation leaving the liposomal drug inside the capsule ($p<0.05$). We observed the nanopore size increased during degradation over 6 months in physiological conditions via scanning electron microscopy.
Shrinkage of the implant structure, observed on Day 180, was attributed to the degradation process. No adverse event due to the implant was observed on the retina via fundus, ultrasound exam and histology, during the 6 months. The implant did not seem to interfere with vision of the rabbits, based on their behavior. The location and position of the implant was not significantly changed.
Lastly, the dose released in vivo by laser followed the first-order kinetics and daily/weekly dose was clinically relevant (~50 ug per week).
Conclusions: We successfully showed effective drug release from a nanoporous PLGA implant using pulsed NIR laser irradiation both in vitro and in vivo. The drug delivery system was safe and stable against leakage for 6 months. The light-activated drug delivery system that we developed will provide tightly-controlled release without burst release. Thus, the drug delivery system could be potentially used for long-term posterior eye disease treatment.

CONTROL ID: 3709724

SUBMITTER (NAME ONLY): Kari Vienola

TITLE: Phase-based optoretinography with clinical-grade OCT using tissue velocity

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.V. Vienola, R.J. Zawadzki, R.S. Jonnal, Department of Ophthalmology and Vision Science, University of California Davis, Sacramento, California, UNITED STATES|R.J. Zawadzki, Department of Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In blinding diseases of the retina, loss of visual function may occur long before structural changes are observed. The emerging field of optoretinography (ORG) promises non-invasive, objective assessment of functional, stimulus-evoked responses in the retina. Here we present a novel ORG approach to facilitate and accelerate ORG applications in the clinical setting.

Methods: The swept-source optical coherence tomography (SS-OCT) system uses a source centered at 1060 nm with a 100 kHz A-scan rate and 100 nm bandwidth (Fig. 1). The beam is scanned horizontally over the retina to acquire a series of B-scans. The stimulus source is a fiber-coupled light emitting diode at 555 nm, configured to deliver 30 ms flash. The system was configured to acquire 250 A-scans over each 2.5° scan, resulting in a B-scan rate of 400 Hz and sampling density of ~333 mm^{-1} the retina. Prior to imaging, the subjects were dark-adapted for five minutes. The stimulus flash was delivered after the first 0.25 s of OCT acquisition. A time window of five B-scans (t = 10 ms) was used to do a linear fit of the complex signal over time at each pixel. The angle of the fit to the complex signal reveals local tissue velocity, which was recorded as a function of time relative to the stimulus onset.

Results: The results shown in Fig. 2 used a stimulus power of 42 μW, isomerizing 66% of photopigment in the predominant L- and M-cones in a 1.2° circular region. All three subjects showed reproducible differential velocities (between IS/OS and COST) consistent with the previously reported stimulus-evoked contraction (< 10 ms) and elongation (10-50 ms) phases of the outer segment ORG response.

Conclusions: The results are consistent with previous ORG responses acquired from photoreceptor's outer segments using adaptive optics OCT (AO-OCT). Including time for dark adaptation, imaging, and processing, functional responses can be measured and visualized within ten minutes providing a feasible clinical pipeline for larger scale ORG studies.

CONTROL ID: 3709725

SUBMITTER (NAME ONLY): Jehwi Jeon

TITLE: Natural intravital branch retinal artery occlusion model for investigating retinal microglia in ischemic reperfusion injury

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Jeon, S. Kim, E. Kong, Y. Kim, P. Kim, Korea Advanced Institute of Science and Technology, Daejeon, Daejeon, KOREA (THE REPUBLIC OF)|S. Kim, J. Yang, J. Lee, J. Lee, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To establish a natural and reproducible branch retinal artery occlusion (BRAO) mouse model by using intravital confocal retinal microscopy and to analyze pathophysiologic changes of the retinal microglia in Ischemic-Reperfusion (IR) injury after BRAO modeling.

Methods: Rose bengal (75mg/kg) was injected to 7 weeks-old transgenic mice (CX3CR1-GFP, for microglial visualization). 561nm laser was projected to a specified single vessel to induce photo-thrombosis for 27 seconds by custom-built video-rate confocal microscopy. Thrombosis was recorded in real time and intravital retinal images were longitudinally acquired for 7 days. Immunohistochemistry, fluorescence associated cell sorting (FACS) analysis and RT-qPCR were performed to observe IR injury related reactions of retinal microglia.

Results: Establishment of reproducible BRAO modeling was archived. Blocked perfusion in the targeted artery by embolism occlusion and the formation of ischemic area were reliably observed in all BRAO induced model. Dynamic alteration in the molecular profiles of immune cell infiltrated to the ischemic lesion were prominently activated at 3 days after BRAO modeling. Especially, Nox2 RNA expression, CD86 expression and microglial morphology changes were peaked at that time. The time point is co-related with the reperfusion with thrombus self-resolution. At day 7 with restored reperfusion in large vessel, CX3CR1 signal was slightly decreased but the number of CX3CR1+ microglia were significantly increased around ischemic area. These microglia were focally recruited from optic disc through nerve fibers and large veins. And most of the CX3CR1-GFP (+) cells had no CCR2 expression.

Conclusions: Our study successfully demonstrated a reproducible BRAO modeling with technical advantages of precise control of the time points and selection of a specific single target vessel. The role of retinal microglia in IR injury after BRAO could be analyzed. It will be a useful experimental tool to investigate the pathophysiology of BRAO.

CONTROL ID: 3709730

SUBMITTER (NAME ONLY): Katie Flaharty

TITLE: Association between neighborhood deprivation and clinic appointment attendance in a free glaucoma screening program

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Flaharty, J. Cho, D. Musch, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|M. Lu, L. Niziol, J. Aliancy, P. Hicks, M.A. Woodward, A. Elam, J. Zhang, L. Johnson, A.K. Bicket, D. John, P. Newman-Casey, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|M. Kershaw, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate which participant and neighborhood characteristics are associated with not showing up for a free glaucoma screening appointment.

Methods: Participant demographics were extracted from the University of Michigan electronic health record and distance between residence and clinic site was calculated using a geographical information system. Neighborhood level characteristics obtained from the United States Census included median household income (HHI), percent of households whose rent burden is 30% or more of their income, percent of household income spent on energy costs, percent of households without vehicles, and area deprivation index (ADI). Demographic and neighborhood characteristics were summarized and compared between participants who attended their screening visits (shows) and those who did not (no-shows). Logistic regression was used to model the probability of no-show for each neighborhood characteristic and distance while adjusting for age, sex, ethnicity, and race.

Results: 1431 participants were scheduled for screening appointments between July 2020 to November 2021. Participants were on average 54.1 years old (SD=14.5), 60% female, 51% Black, 37% White, 9% Latinx, and lived an average of 7.7 miles from each clinic (SD=8.1). Participants lived in neighborhoods with an average median HHI of $49,200 (SD=30,200), where an average of 46.8% of households were rent burdened (SD=23.9%), 5.0% (SD=2.7%) were energy burdened, 11.7% (SD=6.0%) had no vehicle, and the mean ADI was 6.8 (SD=3.2, 1-10 scale where 10 is the most deprived). The no-show rate was 23% (n=330/1431). After adjusting for demographics, a 1% increase in energy burden (odds ratio, OR=1.08, p=0.003), households without a vehicle (OR=1.02, p=0.197), a 5% increase in rent burden (OR=1.04, p=0.023), and a 1-point increase in ADI (OR=1.08, p=0.002) were associated with higher odds of no-show. A 10-mile increase in distance to clinic (OR=0.85, p=0.135) and a $10k increase in median HHI (OR=0.90, p<0.001) were associated with lower odds of no-show.

Conclusions: Higher neighborhood levels of poverty were associated with higher odds of no-showing to a free glaucoma screening appointment, after adjusting for age, sex, race, and ethnicity. Providing communities with high poverty rates additional holistic support to attend free eye care services will help enable early detection and treatment for glaucoma.

CONTROL ID: 3709731
SUBMITTER (NAME ONLY): Masumi Asahi
TITLE: US National Trends in Ophthalmic Procedures During the COVID-19 Pandemic
SESSION TITLE: Public Health I
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Asahi, M. Dalal, The George Washington University Department of Ophthalmology, Washington, District of Columbia, UNITED STATES|H. Pakhchanian, S. Rosenberg, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|C. DeYoung, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|I. Liu, Augusta University, Augusta, Georgia, UNITED STATES|S. Bellur, National Eye Institute, Bethesda, Maryland, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|
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ABSTRACT BODY:

Purpose: To evaluate the relationship between COVID-19 case volume and ophthalmic procedural volume during the pandemic.
Methods: A retrospective cohort study using TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple large health organizations in the United States. Monthly Current Procedural Terminology (CPT)-specific volumes per HCO were clustered chronologically to calculate average volumes into three-month seasons to calculate average volumes. Seasonal averages from a combination of 2018 and 2019 data were used to provide a baseline comparison to pre-pandemic procedural volume. An aggregate of the total pandemic period (March 2020 - August 2021) was compared to the corresponding figures in pre-pandemic timeframes.
Results: 670,541 unique ophthalmic procedures from among 573 HCOs between March 2018 and August 2021 were included. Intravitreal injections was the most prevalent procedure with 320,106 occurrences. Phacoemulsification cataract surgery was the second most prevalent (N = 176,095) procedure with 144,816 uncomplicated (82.2%) and 31,279 complicated (17.8%). Intravitreal injections had the highest mean seasonal volume per HCO for each of the five COVID-19 pandemic seasons. From March 2020 – August 2021, a mean pandemic volume of 266.7 (SD = 15) was observed, a 5% decrease ($p<0.05$) in procedures compared to pre-pandemic mean of 280.8 (SD = 26.1).

During the five COVID-19 pandemic seasons, the seasonal mean volume almost always differed from pre-pandemic comparisons. Spring 2020 exhibited the sharpest seasonal decrease in procedural volume (88%). Spring 2021 had the largest count of significant increase in procedure volume (18%). Aggregate mean volume per HCO showed significant decreases for 11 out of 17 procedures in the 12-month March 2020-February 2021 timeframe and significant decreases for 10/17 procedures over the 18-month March 2020-August 2021 timeframe. A relative inverse relationship between COVID-19 case volume and ophthalmic procedure volume was observed.
Conclusions: This study highlights the relative inverse relationship between COVID-19 cases and ophthalmic procedure volume in the US. Reduction in procedural volume may result in delayed care with potential for vision loss. Awareness and understanding of these trends could help ophthalmologists prepare should a similar cycle occur in the setting of the omicron and future variants.

CONTROL ID: 3709734

SUBMITTER (NAME ONLY): Amir Akhavanrezayat

TITLE: Efficacy and safety of tocilizumab in the management of non-infectious uveitis: a systematic review and meta-analysis of before-after clinical trials

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Akhavanrezayat, H. Ghoraba, Q.D. Nguyen, Department of Ophthalmology, Byers Eye Institute, Stanford University School of Medicine, California, UNITED STATES|S. Samadi, F. Jafari, A. Mohammadpour, Department of Clinical Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, IRAN (THE ISLAMIC REPUBLIC OF)|M. Sadeghi, Department of Epidemiology, Faculty of Health, Mashhad University of Medical Sciences, Mashhad, IRAN (THE ISLAMIC REPUBLIC OF)|A. Mohammadpour, Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, IRAN (THE ISLAMIC REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: The use of tocilizumab (TCZ), an interleukin-6 inhibitor, to treat non-infectious uveitis (NIU), one of the leading causes of preventable blindness worldwide, has generated considerable controversy. Therefore, we performed a systematic review and meta-analysis (MA) of existing literature to determine the efficacy and safety of TCZ in NIU treatment.

Methods: A comprehensive online search was conducted using PubMed, Web of Science, Embase, Scopus databases and reference lists of pertinent studies for pre-post clinical trials published through October 2021. Overall, 2614 records were identified, of which 991 were duplicates. Subsequently, unrelated studies were excluded by title and abstract screening (n=1594) and full-text assessment (n=21). Ultimately, 5 of the 8 relevant studies included in the systematic review were eligible for inclusion in the MA. We recorded all reported adverse events (AE) and considered the mean difference in best-corrected visual acuity (BCVA) before and after TCZ treatment as the visual outcome. Weighted mean difference (WMD) with 95% confidence interval (CI) was employed as pooled estimation of intervention efficacy using random-effects MA. Heterogeneity was assessed using Cochran's Q test and quantified with the I^2 statistic. Sensitivity analysis was performed to evaluate the robustness of the MA findings using Stata version 14 software.

Results: Pooled data of 46 patients (77 eyes) of the 5 included trials were meta-analyzed. In these studies, which had a mean follow-up of 14.58 months, 8 mg/kg TCZ was administered monthly to treat refractory uveitis-related macular edema, cystoid macular edema and juvenile idiopathic arthritis. TCZ AEs requiring dose lowering/discontinuation were reported in 2 cases (mild neutropenia and community-acquired pneumonia). Between-study heterogeneity was low (I^2 =18.7%,p=0.29) and mean LogMAR BCVA significantly improved after TCZ therapy (WMD=-0.26 (CI=-0.41to-0.10))(Fig1). Our MA supports a statistically significant improvement in BCVA, indicating a robustness of the finding.

Conclusions: TCZ has statistically been demonstrated to be effective in NIU management with almost negligible AEs. This finding may provide clinicians with sufficient information to consider TCZ as a possible therapeutic option for eligible NIU patients.

CONTROL ID: 3709736

SUBMITTER (NAME ONLY): Shrinivas Pundlik

TITLE: Head Scanning of Patients with Homonymous Hemianopia at Street Crossings

SESSION TITLE: Vision Impairment: Impact on Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Pundlik, E. Peli, K. Houston, G. Luo, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Pundlik, E. Peli, K. Houston, G. Luo, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Kumar, Computer Science, Stony Brook University, Stony Brook, New York, UNITED STATES|

Commercial Relationships Disclosure: Shrinivas Pundlik: Commercial Relationship(s);Code C (Consultant/Contractor):Boston Eye Diagnostics;Code O (Owner):EyeNexo LLC | Ayush Kumar: Commercial Relationship: Code N (No Commercial Relationship) | Eli Peli: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Houston: Commercial Relationship: Code N (No Commercial Relationship) | Gang Luo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Head scanning may be critical for safe walking, especially for patients with homonymous field defects (HFDs). The study investigated differences in head scanning behaviors between left and right HFD.

Methods: 13 patients (7 Left HFD, 6 Right HFD) walked along two urban routes (each about 0.5 miles long) containing among them 7 different street crossing locations without pedestrian signal, while wearing a mobile gaze (eye + head) tracking system that also captured synchronized scene videos. Time points corresponding to street crossing instances (including approach and crossing phases) were manually identified in the scene videos. Large horizontal head scans (> 20°) relative to torso were counted. Based on the direction of crossing traffic (Left, Right, or Both) at each intersection, scanning behavior was classified as either safe – at least one scan towards the direction of traffic, or unsafe – lack of scanning towards the traffic direction. For crossings with 2-way traffic, scanning in both directions were required to be considered as a safe scan. The proportion of crossings with unsafe scanning was compared between Right & Left HFD patients using a Poisson regression model.

Results: A total of 197 non-signalized crossing instances totaling 55 minutes were annotated, yielding 350 head scans (average of 1.78 scans/crossing). The majority (66%) of crossing instances had one-way traffic (29% from Left and 37% from Right). The proportions of crossing instances with traffic from the left side, right side, and both sides were 30%, 40%, 30%, respectively for Left HFD group, and were 28%, 34% and 38% for Right HFD group, respectively. The proportions of traffic direction experienced was not significantly different between the two patient groups (χ^2 = 1.4, p = 0.5). However, the proportion of crossing instances with unsafe scanning in Right HFD patients (0.74) was 62% higher than Left HFD patients (0.46), which was statistically significant (β = 1.62, 95% CI: 1.12 - 2.34, p = 0.01).

Conclusions: In this study, where direct measurement of head scanning was performed during real-world walking scenarios, Right HFD patients had more instances of unsafe scanning behavior compared to Left HFD patients when crossing non-signalized intersections.

CONTROL ID: 3709737

SUBMITTER (NAME ONLY): Ujjaldeep Jaggi

TITLE: Role of macrophage sub-populations in ocular HSV-1 infection.

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Jaggi, H. Matundan, H. Ghiasi, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To understand the mechanism of macrophage subtypes on ocular HSV-1 infection, we previously demonstrated that altering macrophage polarization from resting stage (M0) towards M2 leads to reduction in both primary and latent infection in comparison to induction of M1 in ocularly infected mice. Based on these observations, we implemented studies using $M1^{-/-}$, $M2^{-/-}$, transgenic mice lacking autophagy in their M1 or M2 and compared them to wild type (WT) mice.

Methods: We constructed two different transgenic mice by blocking autophagy in M1 macrophages with γ34.5 gene expressed under the control of NOS2 promoter (M1) or ARG1 promoter (M2). Both male and female $M1^{-/-}$, $M2^{-/-}$, transgenic mice lacking autophagy in the M1, transgenic mice lacking autophagy in the M2 and WT control mice were ocularly infected with $2X10^5$ PFU/eye of virulent HSV-1 strain McKrae or avirulent strain KOS with or without corneal scarification. Mice were evaluated for severity of eye disease, viral titers in the eye and latency-reactivation. Bone marrow experiments were conducted to validate the phenotype of mice and in-vitro viral titers. Detailed screening of various genes, cytokines and chemokines were analyzed by nanostring and Luminex.

Results: Increased viral titers ($P<0.05$) and mortality was recorded for $M1^{-/-}$ mice as compared to WT group and $M2^{-/-}$ mice. Viral titers, corneal scarring and mortality were restored on adoptive transfer of M1 macrophages to $M1^{-/-}$ mice with no impact on latency-reactivation. $M2^{-/-}$ mice showed delayed reactivation ($P<0.001$) compared with WT mice. Loss of M1 macrophages in $M1^{-/-}$ mice resulted in enhanced inflammatory response as validated by nanostring and Luminex analysis as compared to other mice groups. We have also shown that blocking autophagy in M1 macrophages increased viral titers and eye disease ($P<0.05$) in ocularly infected mice compared with mice lacking autophagy in their M2 macrophages or WT mice.

Conclusions: Our studies elucidate the importance of M1 macrophages in controlling the virus replication in the eyes of infected mice, preventing mortality and eye disease. We also found the importance of autophagy in protection from virus replication and eye disease in transgenic mice lacking autophagy in their M1 but not their M2 macrophages. Therefore, our data conclude the importance of M1 but not M2 macrophages in protection against ocular HSV-1 infection.

CONTROL ID: 3709738

SUBMITTER (NAME ONLY): Vivian Qin

TITLE: Utilization of Instagram by ophthalmology residency programs in the era of COVID-19

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Qin, L. Wushanley, V. Lee, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|A. Chen, University of Pennsylvania School of Arts and Sciences, Philadelphia, Pennsylvania, UNITED STATES|H. Bashir, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|D. Hsu, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Vivian Qin: Commercial Relationship: Code N (No Commercial Relationship) | Amy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Hasan Bashir: Commercial Relationship: Code N (No Commercial Relationship) | David Hsu: Commercial Relationship: Code N (No Commercial Relationship) | Lily Wushanley: Commercial Relationship: Code N (No Commercial Relationship) | Vivian Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Social media has become an increasingly utilized tool in academic medicine and in ophthalmology, especially as COVID-19 pandemic restrictions limit in-person interactions. We performed a cross-sectional study of publicly available accounts on the social media platform Instagram to describe the use of Instagram by academic ophthalmology residency programs in the United States over time and analyzed the impact of the COVID-19 pandemic on ophthalmology's social media presence.

Methods: Accredited ophthalmology residency programs as of November 2021 were identified using the Accreditation Council for Graduate Medical Education (ACGME) database and were reviewed to identify programs with an affiliated publicly available Instagram account. For each account, the number of posts, followers, and followed accounts were calculated, as well as the year of creation. For the top six ophthalmology Instagram accounts, as determined by number of followers, each post after 2018 was classified into one of six categories (Award/Publication, Department Highlight, Flyer/Holiday, Informal/Candid Group Photo, Medical, or Miscellaneous), and the number of likes and comments was calculated with assistance of a Python script. A two-tailed independent t-test was utilized to analyze user engagement by likes and comments before and after January 2020.

Results: Of the 124 ophthalmology residency programs, 78 (62.9%) were identified as having an affiliated Instagram account, 60 accounts (48.4%) were created during the years 2020 or 2021, and 62 (50.0%) accounts focused specifically on promoting the residency training program. Of the top six accounts with the most followers, post categories that received the most engagement were "Medical" and "Informal/Candid Group Photo" while those that received the least engagement were "Flyer/Holiday" and "Miscellaneous." User engagement on posts as measured by likes and comments increased across multiple post categories after January 2020.

Conclusions: Social media presence of ophthalmology residency programs on Instagram increased substantially in 2020 and 2021. As a result of the COVID-19 pandemic restricting in-person interactions, residency programs have used alternative platforms to reach applicants. Given the increasing use of such applications, social media will likely continue to become an important aspect of professional engagement in ophthalmology.

CONTROL ID: 3709743

SUBMITTER (NAME ONLY): Bora Kim

TITLE: Long-term effects of simultaneous transplantation of both human induced pluripotent stem cell-derived retinal pigment epithelial cells and photoreceptors in Pde6b knockout rats

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kim, J. Yang, J. Lee, Ophthalmology, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|B. Kim, University of Ulsan, Ulsan, KOREA (THE REPUBLIC OF)|J. Yang, Ophthalmology, Dongguk University Ilsan Hospital, Goyang, Gyeonggi-do, KOREA (THE REPUBLIC OF)|E. Kang, Stem Cell Center, Asan Institute for Life Sciences, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Retinal degenerative disorders, including age-related macular degeneration and retinitis pigmentosa (RP), are characterized by the irreversible loss of photoreceptor cells and retinal pigment epithelial (RPE) cells; however, the long-term effect of implanting both human induced pluripotent stem cell (hiPSC)-derived RPE and photoreceptor for retinal regeneration has not yet been investigated. In this study, we evaluated the long-term effects of hiPSC-derived RPE and photoreceptor cell transplantation in Pde6b knockout rats to study RP.

Methods: We differentiated skin fibroblast-derived hiPSC into RPE and photoreceptor cells and verified in vitro. Pde6b knockout rats were generated by using CRISPR-Cpf1 technology. After, differentiated hiPSCs were injected into the subretinal space of the right eyes of rats before the appearance of signs of retinal degeneration at 2–3 weeks of age. Ten months after transplantation, we evaluated the cells using fundus photography, optical coherence tomography, and histological evaluation.

Results: Following transplantation of hiPSC-derived retinal cells no abnormal cell proliferation was observed. A relatively large number of transplanted cells persisted during the first 4 months; subsequently, the number of these cells decreased gradually. Notably, immunohistochemical analysis revealed that the hiPSC-derived retinal cells showed characteristics of both RPE cells and photoreceptors of human origin after transplantation. Functional analysis of vision by scotopic electroretinogram revealed significant preservation of vision after transplantation.

Conclusions: Our study suggests that the transplantation of hiPSC- derived retinal cells, including RPE cells and photoreceptors, has a potential therapeutic effect against irreversible retinal degenerative diseases.

CONTROL ID: 3709746

SUBMITTER (NAME ONLY): Nishaant Bhambra

TITLE: A Novel Method to Measure Retinal Displacement Using Ultra-Widefield Fundus Autofluorescence Imaging

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.(. Bhambra, C. Francisconi, S. Marafon, N. Figueiredo, V. Juncal, K. Brosh, R.H. Muni, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|R. Hillier, Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To introduce a novel method to measure retinal displacement in 3D using ultra-widefield fundus autofluorescence (UWF-FAF) imaging.

Methods: Images were acquired from patients presenting with primary macula-off RRD treated with pneumatic retinopexy (PnR) or pars plana vitrectomy (PPV). A coordinate grid was applied at the OD center of each UWF-FAF image. Two masked graders selected corresponding points on the retinal vasculature and retinal vessel printings (RVPs) within Zone 1, a circular region centered on the fovea with a radius extending to the center of the optic disk (Figure 1). 2D UWF-FAF images were projected to a 3D projection using OD and fovea coordinates. Vertical, horizontal, and diagonal arc distances between corresponding vessel and RVP pairs were calculated (Figure 2). Vector displacements of the RVP to vessel were calculated and averaged within Zone 1.

Results: 170 retinal vessel-RVP pairs were identified from 54 UWF-FAFs. Mean retinal displacement in Zone 1 was 0.36±0.38 mm with an absolute mean angle of displacement of 94.93±41.48° and directionality of displacement of 191.84±97.39°. Mean Zone 1 displacements were 0.44±0.42 mm and 0.21±0.27 mm in PPV (n=34) and PnR (n=19) eyes respectively, and was significantly greater in PPV eyes than PnR eyes (p=0.041). Between groups no significant difference in mean angle of displacement or directionality was found.

Conclusions: We present a novel method of quantitatively assessing displacement of retinal tissue that considers retinal curvature, via retinal vessels and RVPs on UWF-FAF.

CONTROL ID: 3709749

SUBMITTER (NAME ONLY): Christopher Kaler

TITLE: BAP1-mediated transcriptional influence on normal eye development

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Kaler, D. Rodriguez, University of Miami School of Medicine, Miami, Florida, UNITED STATES|S. Kurtenbach, Bascom Palmer Eye Institute, Sylvester Comprehensive Cancer Center, and Interdisciplinary Stem Cell Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|J. Harbour, UT Southwestern Medical Center, Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Christopher Kaler: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Rodriguez: Commercial Relationship: Code N (No Commercial Relationship) | Stefan Kurtenbach: Commercial Relationship: Code N (No Commercial Relationship) | J. William Harbour: Commercial Relationship(s);Code C (Consultant/Contractor):Castle Biosciences

ABSTRACT BODY:

Purpose: Uveal Melanoma (UM) is an aggressive ocular cancer that leads to metastatic death in ≈50% of patients. UM can be divided into two prognostic groups based on molecular landscape: class 1 UM, associated with EIF1AX or SF3B1 variants and low metastatic risk, and class 2 UM with loss-of-function mutations in BAP1 [breast cancer type 1 (BRCA1)–associated protein 1]. BAP1 is known primarily as a tumor suppressor gene implicated in renal cell carcinoma as well as class 2 UM, and recently has been associated with the process of normal eye development. Related to this latter role, BAP1 normally interacts with HDAC1 (histone deacetylase subunit 1), a critical component of the NuRD (nucleosome remodeling and deacetylase) complex, which normally mediates embryonic lineage commitment and cell differentiation through DNA histone deacetylation and chromatin remodeling. Preliminary data from our laboratory strongly suggests that absence of BAP1 disrupts the normal association between HDAC1 and two NuRD complex proteins, CHD3 and CHD4 (Chromodomain Helicase DNA binding protein 3 and 4), DNA-binding proteins with helicase and nucleosome remodeling activities. Here, we further explore the impact of the BAP1-NuRD complex interaction by directly abrogating CHD3 and 4 and comparing downstream expression of biomarkers associated with BAP1 loss.

Methods: We remodeled HEK293 cells and normal melanocytes by siRNA knockdown of CHD3 and CHD4. We used Western blotting and densitometry to quantitate expression of HDAC4 (histone deacetylase subunit 4), a molecular signature of BAP1 loss, in these CHD3/CHD4 knockdown cells.

Results: Western blotting confirmed selective, efficient knockdown of CHD3 and CHD4. Western blots of HEK293 cells with CHD3 or CHD4 knockdown documented increased HDAC4 expression in both conditions compared to cells treated with an siRNA scramble as control. Experiments in progress include assessment of other molecular signatures of BAP1 loss, including the pluripotency marker NANOG, after siRNA knockdown of CHD3 and CHD4 in melanocytes.

Conclusions: These data support the potential involvement of BAP1 in recruitment of NuRD complex components and imply that differences in BAP1 expression may mediate transcriptional events involved in normal and abnormal eye development, via NuRD (Figure). Insights from this research may also be relevant to HDAC inhibitor therapy, previously suggested as promising treatment options for class 2 UM.

CONTROL ID: 3709752

SUBMITTER (NAME ONLY): Jila Noorikolouri

TITLE: Central Serous Chorioretinopathy associated with Ocular Tuberculosis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Noorikolouri, C. Leal, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Jila Noorikolouri: Commercial Relationship: Code N (No Commercial Relationship) | Christian Leal: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: .To report two cases of central serous chorioretinopathy (CSCR) associated with ocular tuberculosis (TB) and improvement following the standard anti-TB treatment

Methods: The first case was a 61 years-old native of India male who presented with recurrent iridocyclitis and episcleritis of the left eye. Fundus exam and macula Optical Coherence Tomography (OCT) revealed subretinal fluid (SRF) and pigmentary changes in the right eye suggestive for CSCR. The normal CXR and the positive quantiferon gold test indicated presumed ocular TB.

The second case was a 47-year-old Mexican male who presented with occlusive retinal vasculitis of unclear etiology and chronic CSCR in both eyes and positive quantiferon gold test.

Both patients subsequently started anti-TB treatment with a two-month course of moxifloxacin 400mg, rifampin 600mg, isoniazid 300mg, pyrazinamide 1500mg, and vitamin B6 50mg daily. Pyrazinamide was discontinued in the first patient after a week of pruritic rash. Both patients ultimately remained on rifampin 600mg, isoniazid 300mg, and B6 50mg daily for a planned treatment course of 9 months.

Results: First patients showed resolution of SRF in 2 months with no recurrence of either the fluid in the right eye and iridocyclitis and episcleritis of the left eye at subsequent follow-up visits, by the end of 7 months ant-TB treatment.

In the second case, the SRF resolved completely in the right eye in 3 months and the left eye in 5 months without recurrence by the end of ani-TB treatment.

Conclusions: Ocular TB may present as CSCR and improve with the standard anti- TB treatment. Large long-term clinical observations are required to confirm this association and response to the treatment.

CONTROL ID: 3709761
SUBMITTER (NAME ONLY): José Vargas
TITLE: Fall-related longitudinal changes in gait among glaucoma patients
SESSION TITLE: Vision Impairment: Impact on Driving and Mobility
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: J.G. Vargas, A. Mihailovic, P.Y. Ramulu, Wilmer Eye Institute / Glaucoma, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|
Commercial Relationships Disclosure: José Vargas: Commercial Relationship: Code N (No Commercial Relationship) | Aleksandra Mihailovic: Commercial Relationship: Code N (No Commercial Relationship) | Pradeep Ramulu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine the effect of falls on gait in glaucoma patients and to examine if falls lead to gait changes reflective of more cautious walking.

Methods: The GAITRite Electronic Walkway (CIR Systems Inc) was used to characterize participants' baseline gait and to record subsequent changes during three follow-up visits. Study visits were performed once a year. Gait parameters examined included stride length, stride length coefficient of variation (CV), stride velocity, stride velocity CV, base of support, base of support CV and cadence. Participants were classified into fallers and non-fallers based on the prospective falls data collection during the first year of the study. Assessment of longitudinal gait changes for each gait parameter in relation to faller status was evaluated using generalized estimating equation (GEE) models to account for within-individual clustering. Models controlled for age, race, gender, integrated visual field sensitivities, polypharmacy, and comorbidities.

Results: The 240 participants had a mean age of 71 years (SD = 7.6); about half of the participants were male and one-third were Black. Stratified analyses by fall status showed that over the course of the study stride length became shorter in both non-fallers and fallers (β = -0.08 z-score unit/year, β = -0.09 z-score unit/year, respectively, $p<0.001$ for all), while stride velocity slowed only among fallers (β = -0.08 z-score unit/year, $p=0.003$) and variability in stride velocity decreased only among non-fallers (β = -0.07 z-score unit/year, $p=0.009$). Base of support, cadence, base of support CV and stride length CV remained unchanged over the study period for both groups ($p>0.05$ for all). No differences in the longitudinal change in gait parameters over time were noted for fallers as compared to non-fallers ($p>0.05$ for all).

Conclusions: Among glaucoma patients, both faller and non-fallers seemed to have adopted a more cautious gait over time, though fallers did not appear to change their gait significantly more than non-fallers. Further studies with longer observation time are needed to evaluate this relationship.

CONTROL ID: 3709763

SUBMITTER (NAME ONLY): Laura Magana Hernandez

TITLE: Hybrid rod-cone anatomical characteristics revealed in the ultrastructural features and synaptic architecture of the functionally plastic pure-rod retina

SESSION TITLE: Photoreceptors and the OPL

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Magana Hernandez, E. Alvarez, D. Umbertus, J. Robles, E. Rose, D. Brown, I. Anastassov, San Francisco State University, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our research is aimed at understanding how the pure-rod retina of the elasmobranch Little skate (L. erinacea) can perform rod and cone functions with a monotypic population of photoreceptors. The skate retina allows us to describe the properties of rod circuitry within the context of a functional, evolutionarily optimized visual system, where all downstream components co-evolved to process signals from a single cell type. Here, we reveal the ultrastructural characteristics of a hybrid rod, its postsynaptic partners, and the wiring in the OPL of a pure-rod retina.

Methods: SB-3DEM was performed on individual retinal samples of the little skate. The datasets analyzed are from a region of interest (ROI) in the OPL and from a full cross-section of the skate retina. The ROI dataset XYZ dimensions are 27.6µm x 27.6µm x 21.5µm with a voxel size of 4.5nm x 4.5nm x 70nm. The full cross-section dataset dimensions are 88µm x 304µm x 21.8 µm with a voxel size of 10nm x 10nm x 70nm. 3D reconstructions and measurements were done with Reconstruct and Amira3D software.

Results: ~12-14 anatomically distinct invaginating processes diverge from rod terminals. These are presumed to belong to ON bipolar and horizontal cells. Additionally, ~3-4 processes made basal contacts outside of the invagination and are presumed to belong to OFF bipolar cells. However, it is also possible that there is a switched basal and invaginating identity for ON and OFF bipolar cells, respectively (as seen in some amphibians). The skate rod does not have an axonated terminal and exhibits ~4-6 telodendria (~2-18 µm), which can be traced to neighboring rods, or unidentified postsynaptic processes. Putative synaptic contacts along telodendria are presumed based on local neurotransmitter vesicle clusters along the length of telodendria.

Conclusions: Skate rod terminal morphology suggests a hybrid rod-cone anatomy. The lack of cones in skates may explain why rods are able to light-adapt and process visual information typically in the domain of cones. To fulfill the function of cones, while also retaining rod capabilities, the rod may need to make extra contacts with neighboring rods and other retinal neurons. We hypothesize that the anatomical hallmarks we see in our data suggest that skate rods have a hybrid rod-cone architecture, which also extends to the downstream circuitry.

CONTROL ID: 3709765

SUBMITTER (NAME ONLY): Takuhiro Hayakawa

TITLE: Short-term efficacy of switch therapy to brolucizumab in Japanese patients with neovascular age-related macular degeneration

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Hayakawa, T. Matsuki, K. Akiyama, K. Watanabe, T. Noda, Ophthalmology, National Hospital Organization Tokyo Medical Center, JAPAN|M. Sasaki, Tachikawa Hospital, JAPAN|K. Akiyama, M. Sasaki, T. Noda, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, JAPAN|

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ABSTRACT BODY:

Purpose: To report the short-term efficacy of switch therapy to brolucizumab in Japanese patients with neovascular age-related macular degeneration (nAMD) recalcitrant to aflibercept or ranibizumab therapy.

Methods: Design: Prospective case series.

Participants: Fifteen eyes of 15 patients with nAMD unable to extend treatment intervals beyond 8 weeks under aflibercept or ranibizumab therapy were enrolled.

Patients were switched to brolucizumab therapy, and the treatment intervals were reassessed based on the recurrence of fluids under the treat and extend protocol.

The best-corrected visual acuity converted to logarithm of the minimum angle of resolution (logMAR) unit, central foveal retinal thickness (CRT), height of subretinal retinal fluid (SRF) at the central fovea, maximum height of pigment epithelial detachment (PED), and the presence or absence of SRF and IRF were compared at baseline (after the last injection before switch therapy) and after the second intravitreal injection of brolucizumab (IVBr).

Results: The CRT(P=0.006), height of SRF (P=0.012) and maximum height of PED(P=0.001) improved significantly from baseline after the second IVBr. The visual acuity did not significantly improved from the baseline after the second IVBr (P=0.799). The proportions of eyes with SRF changed from 80% to 27% ($P = 0.012$, χ^2: 6.40)and the proportions of eyes with IRF changed from 6.7% to 13.3% ($P = 0.318$, χ^2: 1.00). There were three cases of intraocular inflammation without vision loss after the second IVBr.

Conclusions: The switch therapy to brolucizumab resulted in early anatomical response for Japanese patients with nAMD recalcitrant to aflibercept or ranibizumab therapy.

CONTROL ID: 3709766
SUBMITTER (NAME ONLY): Jeff Rabin
TITLE: Color Correcting Lenses Enhance Cone VEPs in Color Deficiency
SESSION TITLE: Vision assessment and Clinical applications
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: J.C. Rabin, F. Silva, N. Trevino, H. Gillentine, L. Liqing, L. Inclan, G. Anderson, E. Lee, H. Vo, University of the Incarnate Word Rosenberg School of Optometry, San Antonio, Texas, UNITED STATES|
Commercial Relationships Disclosure: Jeff Rabin: Commercial Relationship: Code N (No Commercial Relationship) | Frances Silva: Commercial Relationship: Code N (No Commercial Relationship) | Natalie Trevino: Commercial Relationship: Code N (No Commercial Relationship) | Harper Gillentine: Commercial Relationship: Code N (No Commercial Relationship) | Li Liqing: Commercial Relationship: Code N (No Commercial Relationship) | Loary Inclan: Commercial Relationship: Code N (No Commercial Relationship) | Gary Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Erica Lee: Commercial Relationship: Code N (No Commercial Relationship) | Harrison Vo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Extended wear of color correcting lenses (CCLs, www.enchroma.com) improves suprathreshold color perception in hereditary color vision deficiency (CVD) even when CCLs are removed (Werner et al. 2020, doi.org/10.1016/j.cub.2020.05.054). We reported similar results at threshold and suprathreshold levels including cone visual-evoked potentials (VEPs, Rabin et al. 2022, doi:10.1038/s41433-021-01924-0). Our purpose was to further assess VEPs as a metric of CCL efficacy.

Methods: 13 CVDs (9 deuteranomalous, 4 protanomalous, age 32±14,13-66; CVD confirmed by Ishihara, anomaloscope, cone CS) provided informed consent to participate in our initial before-after design. Each subject was given a CCL appropriate for their CVD and tested without and with CCLs at baseline and 11-14 days after wearing CCLs (2.5±1.8 avg. hrs./day). Average cone specific pattern-onset VEPs (Rabin et al. 2016, doi:10.1167/tvst.5.3.8, 1 deg. checks specific to CVD and normal cones) were recorded to 75 pattern onsets without and with CCLs. Data normality allowed for ANOVA and t-tests (Bonferroni correction for multiple comparisons).

Results: In CVDs immediate wear of CCLs yielded robust VEPs with increased amplitudes ($F=8.8$, $P<.005$) and decreased VEP latencies ($F=7.2$, $P<.01$) in response to the deficient cone stimulus compared to measures without wearing CCLs. Yet immediate use of CCLs had no effect on amplitude ($F=0.2$, $P>.68$) or latency ($F=0.6$, $P>0.43$) in response to the stimulus for the CVDs' normal cone type indicating cone selectivity of this effect. Baseline mean VEP amplitudes for the CVD cone type without CCLs (3.6 μV) was significantly less than mean amplitude with CCLs (6.4 μV, $P<.002$). Baseline latency without CCLs (119.9 msec) was greater than with CCLs (90.8 msec, $P<.02$). After 12 days of CCL wear, 67% of CVDs showed increased VEP amplitude without wearing CCLs (mean increase 2.7 μV) and 75% showed decreased VEP latency (mean decrease 38.3 msec), but changes were not significant when compared to baseline measures without CCLs ($P>0.38$).

Conclusions: Cone VEPs provide an objective metric of color with use of CCLs. While immediate impact of CCLs on VEPs improved amplitude 2X and decreased latency 30 msec., long term effects occurred in some but not all CVDs, likely due wearing time variations, non-optimal matching of available CCLs to patient needs, and CVD severity. Future studies will include improved CCLs and control measures to address these issues.

CONTROL ID: 3709767

SUBMITTER (NAME ONLY): Ramanath Bhandari

TITLE: Characterizing a Novel Bispecific Platform (Surrobody) for use in Back of the Eye Disease

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Several back of the eye diseases are mediated through multiple complex pathways with cross-talk. Having the ability to bind multiple targets with a single molecule may prove especially beneficial, bringing gains in efficacy of treatment. The purpose of this study is to characterize a novel bispecific platform (surrobody) for use in back of the eye disease. This study describes the structure of the novel platform and characterizes its Chemistry, Manufacturing, and Controls(CMC) characteristics through use of Size Exclusion Chromatography (SEC), its pharmacokinetic half-life (PK) in cynomolgus monkeys, and its thermostability after 12 months of storage at various temperatures.

Methods: All experiments were performed in accordance with the ARVO statement for Use of Animals in Ophthalmic and Vision Research. Three cynomolgus monkeys were administered an intravenous dose of Bispecific surrobody (10 mg/kg). Serum was tested over a 28 day period, with PK values then calculated. SEC was used to characterize the product after HEK293F transfection which showed high expression. Thermostability was assessed by holding Bispecific Surrobodies at room temperature, -80°C , and 4°C for 12 months and then assessing half maximal effective concentration via Enzyme Linked Immunosorbent Assay (ELISA).

Results: PK in cynomolgus monkeys was found to be 6.04 days for the Bispecific Surrobody as compared to 10.88 days for the control antibody using ELISA. SEC revealed single peaks indicating high levels of heterodimeric bispecific product formation. ELISA testing revealed no loss of activity of the Bispecific Surrobody with storage between -80°C

and room temperature for 12 months.

Conclusions: This novel bispecific platform has several desirable characteristics for a potential therapeutic agent. Its CMC characteristics show single peaks on SEC indicating high levels of heterodimeric bispecific product. Its full length constant fragment (Fc) affords long half-life as demonstrated in serum of cynomolgus monkeys on par with typical antibody half-life. Additionally, its thermostability at room temperature and ability to withstand a freeze-thaw cycle without losing efficacy points to its durability and potential to do away with cold chain logistics required for current generation therapeutics. Further study of the platform is warranted as the potential to develop into a next generation therapeutic exists.

CONTROL ID: 3709773
SUBMITTER (NAME ONLY): Ernesto Sabogal
TITLE: Factors associated with follow up to eye care after teleophthalmology evaluation of diabetic patients
SESSION TITLE: Telehealth
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: To report on demographic and systemic health related factors associated with follow-up eye care for diabetic patients from safety net primary care clinics in one health system who received a teleophthalmology evaluation.

Methods: A retrospective analysis on prospectively obtained cross sectional data for patients who underwent teleophthalmology evaluation at six urban safety net primary care clinics from 2015-2021 was performed. Demographic factors included age, race, ethnicity, sex, and health insurance. Systemic health factors included BP, smoking status, HbA1c, level of diabetic retinopathy (DR) and distance VA. Patients diagnosed with DR post screening were identified as having vision threatening (VTDR) (presence of diabetic macular edema (hard exudates), severe non-proliferative DR or worse) or non-vision threatening DR (NVTDR). Predictor variables associated with dependent variables at $p<0.20$ were included in single and multivariate logistic regressions at a $p<0.05$ significance level.

Results: Of patients (n=1229) evaluated via teleophthalmology, 702 (57%) scheduled follow up eye care appointments. 396 (56%) patients kept their appointments.

More African Americans (62%) made appointments than whites (49%), or those classified as other races (59%) ($p<0.001$). More Hispanics (62%) made appointments than non-Hispanics (56%) ($p<0.05$). Medicare Advantage (59%) ($p<0.006$), Medicare/Medicaid (62%) ($p<0.02$), and Medicaid managed plan holders (62%) ($p<0.003$) were more likely to make appointments than the uninsured (44%). More patients with VTDR (79%) ($p<0.001$) or NVTDR (66%) ($p<0.05$) made appointments than those without DR (55%).

Older age ($p<0.02$) was associated with keeping appointments. More nonsmokers (61%) ($p<0.03$) kept appointments than smokers (51%). More Medicare insurance plan holders (59%) kept appointments than commercial plan holders (51%) ($p<0.03$). VTDR ($p=0.19$) and NVTDR ($p=0.30$) patients were not more likely to keep appointments than those without DR.

Conclusions: Follow-up to eye care following primary care based vision screening and telehealth evaluation for retinopathy in patients with diabetes remains a challenge. Patients diagnosed with DR were more likely to make but not keep follow up appointments. More support to increase appointment adherence in low income, safety net patients is required, especially if they are younger, smoke, or have commercial insurance.

CONTROL ID: 3709776

SUBMITTER (NAME ONLY): Michael Yu

TITLE: A Novel Approach to Estimating Choroidal Lesion Thickness Using 2D Optomap Images

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Yu, M. Heiferman, E. Korot, P. Mruthyunjaya, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|M. Heiferman, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tumor thickness is a well-established risk factor for transformation of choroidal nevus (CN) into choroidal melanoma (CM) and thus plays an important role in risk stratification of melanocytic choroidal lesions (MCL). Currently, B-scan ultrasonography is the most reliable method for measuring tumor thickness, but its utility in screening may be limited. Herein, we describe a novel technique for rapid extraction of tumor thickness data from 2D ultra-widefield (UWF) dual-wavelength scanning laser ophthalmoscope Optomap images (Optos PLC, Dunfermline, Fife, Scotland, UK).

Methods: A consecutive series of patients seen in the Ocular Oncology Service at the Byers Eye Institute (Stanford University, Palo Alto, CA) with clinically diagnosed MCL underwent complete clinical examination, UWF imaging, and standardized B-scan ultrasonography (Eye Cubed, Ellex Medical, Adelaide, Australia). The UWF images were post-processed to isolate the green-wavelength-only image. Using Image J (National Institutes of Health, Bethesda, MD, USA), average pixel intensities within the lesion and of the adjacent retina were obtained, and the difference between both values calculated (“pixel intensity difference”; average lesion intensity minus average adjacent retina intensity). The pixel intensity difference was then plotted against the reference standard for tumor thickness as measured by standardized B-scan ultrasonography. The significance of the relationship between both variables was assessed by linear regression analysis.

Results: A total of 141 MCL (16 CM and 125 CN) of 141 patients were evaluated. Mean ultrasonographic thickness was 1.2 mm (median: 0.8, range: 0.5-7.3). Mean pixel intensity difference was 6.7 (median: 3.8, range: -20.0 – 55.0). The linear correlation coefficient for tumor thickness to pixel intensity difference was 0.85 ($p<0.001$), indicating a strong positive correlation between tumor thickness and tumor brightness on green-wavelength imaging (Figure 1). Coefficient of determination (R^2) was 0.74. A pixel intensity difference threshold of >10 conferred a 100.0% sensitivity and 97.4% specificity for detection of tumors with thickness >2 mm.

Conclusions: Choroidal tumor thickness can be rapidly and reliably estimated using 2D UWF images. With additional validation, this method could augment future high-throughput screening and risk stratification of MCL with UWF images alone.

CONTROL ID: 3709779

SUBMITTER (NAME ONLY): Ching-Yu Cheng

TITLE: Retinal photograph-based deep learning predicts biological age, and stratifies morbidity and mortality risk

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ageing is an important risk factor for a variety of human pathologies. Biological age (BA) may better capture ageing-related physiological changes, compared to chronological age (CA). We developed a deep-learning (DL) algorithm to predict BA based on retinal photographs and evaluated the performance of our new ageing marker in the risk stratification of mortality and major morbidity in general populations.

Methods: We first trained a DL algorithm using 129,236 retinal photographs from 40,480 participants in the Korean Health Screening study to predict the probability of age being ≥65 years (“RetiAGE”) and then evaluated the ability of RetiAGE to stratify the risk of mortality and major morbidity among 56,301 participants in the UK Biobank. Cox proportional hazards model was used to estimate the hazard ratios (HRs).

Results: In the UK Biobank, over a 10-year follow up, 2,236 (4.0%) died; of them, 636 [28.4%] were due to cardiovascular diseases (CVDs) and 1,276 [57.1%] due to cancers. Compared to the participants in the RetiAGE first quartile, those in the RetiAGE fourth quartile had a 67% higher risk of 10-year all-cause mortality (HR=1.67 [1.42-1.95]; Figure), a 142% higher risk of CVD mortality (HR=2.42 [1.69-3.48]), and a 60% higher risk of cancer mortality (HR=1.60 [1.31-1.96]), independent of CA and established ageing phenotypic biomarkers. Likewise, compared to the first quartile group, the risk of CVD and cancer events in the fourth quartile group increased by 39% (HR=1.39 [1.14-1.69]) and 18% (HR=1.18 [1.10-1.26]), respectively. The best discrimination ability for RetiAGE alone was found for CVD mortality (c-index=0.70, sensitivity=0.76, specificity=0.55). Furthermore, adding RetiAGE increased the discrimination ability of the model beyond CA and phenotypic biomarkers (increment in c-index between 1 and 2%).

Conclusions: The DL-derived RetiAGE provides a novel, alternative approach to measure ageing.

CONTROL ID: 3709781

SUBMITTER (NAME ONLY): Trong Phat Do

TITLE: Comparison of Corneal Tomograpic Parameters Between Hispanic and Non-Hispanic Populations

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Do, S. Uhm, B. Lam, A. Kheirkhah, Department of Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously, it has been shown that ocular anatomy may be different in different ethnicities. However, little is known about differences in corneal tomography between Hispanic and non-Hispanic populations. This study aims to compare corneal tomographic parameters as measured by Pentacam between Hispanic and non-Hispanic White populations.

Methods: In this retrospective study, we analyzed Pentacam data from patients who underwent surgery for senile cataract. We included patients 50 years or older who were self-identified as Hispanic White and non-Hispanic White. We excluded patients with corneal or anterior segment surgery or trauma, or any abnormality in these structures. The following parameters were compared between the Hispanic White and non-Hispanic White groups for both anterior and posterior corneal surface: steep keratometry (K1), flat keratometry (K2), mean keratometry (Km), maximum keratometry (Kmax), amount of astigmatism, axis of steep meridian, and type of astigmatism.

Results: This study consisted of 200 patients, including 103 Hispanic White individuals and 97 non-Hispanic White individuals. The mean age was 69.9 ± 7.4 years (range, 50-88 years), and there were 68 men and 132 women. There were no statistically significant differences between Hispanics and non-Hispanics regarding K1, K2, Km, Kmax, amount of astigmatism, and steep axis in both front and back corneal surfaces. There were also no significant differences in type of corneal astigmatism (with-the-rule, against-the-rule, or oblique) in front or back corneal surfaces between these two groups. There were significant differences between right and left eyes in corneal front steep axis (73.8 ± 49.9 deg vs 104.3 ± 49.7 deg, respectively, $P<0.001$) and corneal back steep axis (97.8 ± 22.8 deg vs 82.8 ± 21.7 deg, respectively, $P<0.001$). However, no differences existed in corneal front and back steep axes between Hispanics and non-Hispanics.

Conclusions: There are no significant differences in corneal tomographic parameters, including keratometry and degree and amount of astigmatim in front and back corneal surfaces between Hispanic and non-Hispanic White patients.

CONTROL ID: 3709782

SUBMITTER (NAME ONLY): Dean Psarakis

TITLE: Factors influencing visual satisfaction and willingness to wear myopia control spectacles

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate adaptation and factors associated with vision satisfaction and willingness to wear (WTW) Miyosmart spectacles.

Methods: Twenty-five myopes aged 18-35 years were recruited. In phase 1, subjects wore single vision (SV) and Miyosmart spectacles bilaterally for 1 hour each. Objective variables assessed were; visual acuity (VA) and contrast sensitivity (CS), in high (HI) and low illumination (LI) on and off-visual axis. Subjective variables included; dynamic vision disruption rating (DVDR), vision ratings (VR) for clarity, ghosting, haloes (on and off-axis), overall visual comfort and VR in various scenarios including; reading, screen use, walking, moving eyes/head and overall vision satisfaction (OVS) (1-10 scale). WTW was indicated as yes/no. Multivariate analysis considered all variables using generalised estimating equations for OVS. Odds ratios (OR) determined variables associated with WTW. In phase 2, subjects wore Miyosmart for 2 days and all subjective VR were given before and after wear. Paired t-tests were used to assess changes.

Results: Phase 1 was completed by 24 subject and phase 2, 21. At a univariate level, all variables other than on-axis VA (high and low contrast in HI and LI) and on-axis CS were significantly correlated with OVS and WTW (all $p<0.05$). WTW was 83% in SV and 8% in Miyosmart. Multivariate analysis indicated higher OVS was associated with higher scores in VR for moving eyes/head (r=0.88), reading (r=0.83), overall visual comfort (r=0.78) and CS off-axis (r=0.63), with a model r2=0.85 (all p£0.01). WTW was associated with higher OVS (OR=3.4), lower DVDR (OR=0.59) and near ghosting (OR=0.1) (all p=0.01). After 2 days of wear, there were significant improvements in VR for distance (0.76±1.45), distance off to side (1.38±2.13), when walking (1.33±2.33), moving eyes/head (1.38±2.27), reading (1.19±2.44), screen use (1.62±3.28), and OVS (1.81±2.04). There was also a significant reduction in ghosting on screens (1.62±1.46) and reading (1.43±3.04) (all $p<0.05$). WTW increased to 38%.

Conclusions: Subjective evaluation of visual tasks that depend on peripheral and dynamic vision have a higher correlation with wearability for the Miyosmart lens in an adult population, with significant adaptation occurring after only 2 days. These findings may assist in evaluating the performance of, as well as predicting adaptation in such lens designs.

CONTROL ID: 3709783

SUBMITTER (NAME ONLY): Nick Di Girolamo

TITLE: Delineating goblet cell metaplasia in a murine model of limbal stem cell deficiency

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Maintaining corneal health and transparency are necessary pre-requisites for exquisite vision; a function ascribed to stem cells (SCs) nestled within the limbus. Perturbations to this site or depletion of its SCs, results in limbal stem cell deficiency (LSCD). Whilst characterizing a murine model of this disease, we discovered a rare and unreported phenomenon on the cornea; goblet cell metaplasia (GCM). Our goal was to unravel the mechanism through which it transpires.

Methods: C57BL/6 (n=138) and aged matched K14CreER-Confetti (n=30) mice were used. Partial and total LSCD was induced by mechanical debridement. Suture-induced (n=6) and nu/nu athymic (n=3) mice were employed as acute and chronic models of corneal neovascularization. Mice were clinically evaluated and procured tissue assessed after PAS-staining, immunofluorescence for the presence of keratins (K8, K12, K13, K14), mucins (MUC5AC) and blood vessels (CD31), and cell proliferation (BrdU/EdU).

Results: In mapping the evolution of LSCD, PAS^{+}/$MUC5AC^{+}$ GCs were not detected in the region spanning the bulbar conjunctiva-limbus suggesting they did not migrate from their forniceal cull-de-sac. Rather, they appeared 7 days post-injury, arising from K8 conjunctival precursors which invaded the cornea as part of conjunctivalization. Fluorescence intensity for K12 in the central cornea decreased concomitant with elevated MUC5AC and CD31 compared to controls (15.14 v 37.94, $p<0.0001$; 31.12 v 11.03, $p<0.0001$; 27.38 v 20.23, $p<0.0001$, respectively). GCs strongly correlated with blood vessels ($r=0.95$, $p=0.004$). In Confetti mice, multicolored GC rosettes formed indicating that they have a K14 ancestry. In the absence of limbal damage but amidst an acute or chronic corneal neovascular response, GCs were not detected.

Conclusions: This first report on GCM on the murine cornea dismisses the theory that these cells emigrate as a component of conjunctivalization. While neovascularization encouraged GCM, it was not the principal driver, rather a breach in the limbal barrier was necessary to initiate metaplasia. Whether GCM manifests in corneas of patients with LSCD is yet to be determined, nonetheless it should be investigated to determine whether this type of cell identity change can be suppressed or corrected pharmacologically to prevent sequela such as the formation of vision-obstructing mucous plaques.

CONTROL ID: 3709791

SUBMITTER (NAME ONLY): Jian Sun

TITLE: A Bayesian deep learning model for age-related macular degeneration screening

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sun, DZNE, GERMANY|S. Yousefi, Department of Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|S. Yousefi, Department of Genetics, Genomics, and Informatics, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a reliable deep learning construct for screening of age-related macular degeneration (AMD) based on fundus photographs.

Methods: We developed a Bayesian convolutional neural net (BCNN) to detect AMD and to quantify the predictive uncertainty based on fundus photographs. We utilized 60,511 fundus photographs from the age-related eye disease study (AREDS) to develop models for detecting four levels of disease severity including healthy, small drusen, large drusen, and late AMD and used the 7448 fundus images in the holdout dataset to independently validate the findings. We further evaluated our models based on 20 images collected from a hospital in Japan. We compared the accuracy of the BCNN model with a conventional deep convolutional neural net (DCNN), which used similar architecture as the BCNN model. We also evaluated the relationship between the accuracy and predictive uncertainty of the BCNN model based on input training data with varying size.

Results: Based on the holdout testing dataset, the AUC of the BCNN model in distinguishing four levels of severity was 0.88 (95%CI: 0.86-0.90), and the quadratic Cohen's kappa was 0.86. The AUC of the DCNN model in distinguishing four levels of severity was 0.85 (95%CI: 0.83-0.87), and the quadratic Cohen's kappa was 0.83. For BCNN model, the predictive uncertainty of correct predictions was significantly lower than that of incorrect predictions.

Conclusions: We developed a BCNN model that was more accurate than classical DCNN model in detecting AMD. The proposed BCNN generates prediction uncertainty in addition to prediction likelihood. A lower predictive uncertainty corresponds to a higher confidence of the model in the provided outcome. This feature is critical for currently black-box CNN models and may assist physicians in making more informed clinical decisions.

CONTROL ID: 3709802

SUBMITTER (NAME ONLY): Erica Shelton

TITLE: Assessing the role of social determinants of health in children receiving a vision test using national data from the National Survey of Children's Health

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To identify how social determinants of health relate with the likelihood of a parent or guardian reporting a child has had a vision test within the last 12 months

Methods: National data from the 2016-2020 National Survey of Children's Health were obtained through the National Survey of Children's Health online database. The analysis looked at age, sex, race, household income status, household education status, insurance status, family resilience, and reported adverse childhood events as indirect measures of social determinants of health. Data for each measure across each year were evaluated using a chi square test, while differences over the five years were analyzed through a multiyear logistic regression.

Results: The odds of reporting a vision test decreased by 10% each year. Age, sex, income status, adverse childhood events, and insurance status demonstrated a significant correlation with reporting a vision test for a child in each of the 5 years analyzed (all $p < 0.05$). Family resilience did not show a significant correlation with reporting a vision test for a child in each of the 5 years analyzed. Males were less likely to have a reported vision test and the likelihood of a reported vision test increased with age. Data from 2016-2018 showed that over 50% of the people who reported being uninsured still reported a vision test, but in 2019 and 2020 less than 50% of those who are uninsured reported a vision test.

Conclusions: Social determinants of health impact children's likelihood of receiving vision care and understanding how these determinants impact this likelihood allows for better policy and programs to achieve visual health equity for children.

CONTROL ID: 3709803

SUBMITTER (NAME ONLY): Xiayin Zhang

TITLE: From phenotype to genotype: glaucoma and psychiatric disorders

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To measure the phenotypic and genotypic associations between glaucoma and psychiatric disorders.

Methods: A total of 169, 362 participants from the UK Biobank cohort were included in the phenotypic analysis, participants underwent detailed questionnaire and standardized physical examinations between 2006 and 2010 and were followed up until 2021. Multivariable Cox regression models were used to investigate the relationship between glaucoma and incident psychiatric disorders. A total of 674,296 samples of glaucoma cohorts and 449,203 samples of psychiatric disorders cohorts from previous genome-wide association studies were included in the genotypic analysis. The conditional/conjunctional false discovery rate methodology was utilized to estimate the specific overlapping loci between glaucoma and psychiatric disorders. Gene expression analysis in the human brain and aqueous humor outflow pathways was further offered to provide independent experimental evidence. The associations of the identified overlapping loci with phenotypes were further validated among the UK biobank participants.

Results: A total of 5,527 participants had glaucoma at baseline. The multivariable-adjusted hazard ratio (HR) (95%confidence interval [CI]) for glaucoma associated with total four psychiatric disorders was 1.11 (1.03-1.21). Specifically, the presence of glaucoma was significantly associated with increased risk of an incident anxiety disorder (HR, 1.33; 95% CI 1.09-1.62). We identified ten independent genomic variants shared between glaucoma and anxiety disorder and between glaucoma and major depressive disorder, encompassing variants predicted to regulate genes expressed in human aqueous humor outflow pathways and the brain. The independent genomic variants rs7310615, rs9820228, rs9831374, rs7784849, rs2193255, rs72963135, and rs11030381 were validated to correlate with both glaucoma and the traits of psychiatric disorders in the UK biobank.

Conclusions: We found that glaucoma was associated with an increased risk of developing anxiety disorder in the UK longitudinal database. Consistently, we found genetic evidence supporting the shared biological basis of comorbidity between glaucoma and psychiatric disorders. This study adds to the body of literature implicating shared genetic architecture as a potential etiology for relationships between glaucoma and psychiatric disorders, and provides insight on their pathogenesis and novel therapeutic targets.

CONTROL ID: 3709804

SUBMITTER (NAME ONLY): Louis Pasquale

TITLE: Metabolite and lipid biomarkers associated with intraocular pressure and inner retinal morphology: results from the UK Biobank

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.R. Pasquale, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|J.L. Wiggs, T. Elze, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A. Khawaja, Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|J. Kang, J. Lasky-Su, O. Zeleznik, Medicine, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|J. Kim, Epidemiology, Harvard T.H. Chan School of Public Health, Massachusetts, UNITED STATES|P.G. Hysi, Ophthalmology, King's College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To assess the relation between intraocular pressure, macular retinal nerve fiber layer (mRNFL) thickness, macular ganglion cell inner plexiform layer (mGCIPL) thickness and measured metabolites with emphasis on lipids, lipoproteins and their subclasses, amino acids, and ketone bodies in the UK Biobank.

Methods: We analyzed 167 non-fasting serum metabolites measured by NMR (Nuclear Magnetic Resonance; Nightingale, Finland; version 2020). The sample sizes varied by outcome: 28,780, 10,763, and 10,763 participants, respectively, with data on corneal compensated intraocular pressure (IOPcc), mRNFL, mGCIPL and metabolomics. We used multiple linear regression models adjusting for various covariables (such as age, sex, body mass index, smoking status, diabetes, coronary artery disease, beta blocker use, and statin use) with individual metabolites (probit transformed) as the predictor for each outcome. The reported estimates represent the difference in each outcome variable for each standard deviation increase in the probit-transformed metabolite values. We considered false discovery rates (FDR<0.05) for metabolite classes and number of effective test (NEF<0.05) for individual metabolites as significant after correction for multiple testing.

Results: Overall, associations with mGCIPL were not significant after correction for multiple testing (NEF>0.07). Total branched chain amino acids were associated with lower IOP (-0.17mmHg; 95% confidence interval (CI): -0.12, -022; NEF p-value=4.3E-10) but had null associations with OCT parameters (NEF p-value=1.0). Total concentration of lipoprotein particles was associated with higher IOP (0.11mmHg; 95% CI: 0.05, 0.16; NEF p-value=0.02) and thinner mRNFL (-0.18 microns; 95% CI: -0.27,-0.09; NEF p-value=0.02). Several lipoprotein components (cholesterol, cholesterol esters, phospholipids) carried on LDL and HDL were associated with higher IOP (FDR<0.05) and some were also associated with thinner mRNFL (example: cholesterol esters in small HDL particles: -0.19 microns; 95%CI: -0.28,-0.09; NEF p-value=0.03). Interestingly, cholesterol and cholesterol esters carried on VLDL particles were associated with lower IOP and thicker mRNFL (FDR <0.05 for both).

Conclusions: Higher serum levels of LDL and HDL as well as many of their components were associated with higher IOP and thinner mRNFL in a large population based sample.

CONTROL ID: 3709813

SUBMITTER (NAME ONLY): Ajay Kuriyan

TITLE: Racial and Gender Disparities in Enrollment and Participation in Diabetic Macular Edema Clinical Trials in the United States

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Kuriyan, T. Bowe, R.R. Soares, C. Huang, M.A. Khan, A. Chiang, M. Cohen, M. Klufas, O.P. Gupta, Y. Yonekawa, D. Xu, Mid Atlantic Retina/Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|B.K. Williams, Cincinnati Eye Institute, Cincinnati, Ohio, UNITED STATES|J. Sridhar, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Numerous studies have raised concerns that clinical trial cohorts are frequently demographically different from the population undergoing treatment post FDA approval. Our study describes the racial and ethnic composition of the cohorts of diabetic macular edema
(DME) clinical trials and compares this to the racial and ethnic composition of patients undergoing treatment for DME from the (Intelligent Research in Sight) IRIS ® Registry.

Methods: This is a retrospective cohort study comparing the racial/ethnicity and gender composition of patients undergoing treatment for DME from the (Intelligent Research in Sight) IRIS ® Registry and participants in Diabetic Retinopathy Clinical Research (DRCR) Retina Network clinical trials and industry sponsored trials that met the following inclusion criteria: conducted in the United States of America, Phase III completed, data reported between Jan 1, 2000, and Jan 1, 2020, and demographic information reported with results.

Results: Twenty-two clinical trials met our inclusion criteria. Seventeen were part of the DRCR and five were industry-sponsored trials. Compared to the enrollment fraction of 4.94% among Whites, lower enrollment fractions were found in Black patients (3.99%, odds ratio [OR] 0.816,
confidence interval [CI] 0.786-0.867, P< 0.001) and in Hispanic patients (2.81%, OR 0.579, CI 0.541-0.620, P<0.001). Men were more likely to enroll in the clinical trials compared to women (enrollment fraction, 4.11% vs 3.64%, respectively, OR 1.22, CI 1.074-1.172, P < 0.001).

Conclusions: DME clinical trials have a higher relative proportion of White and male subjects when compared to the population undergoing treatment for DME. Further efforts should consider measures to encourage clinical trial recruitment that is reflective of the DME population undergoing treatment to ensure generalizability of clinical trial results.

CONTROL ID: 3709818

SUBMITTER (NAME ONLY): Sara Aghajari

TITLE: Recording multifocal ERGs using a custom-built gaze-contingent system

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Aghajari, A. Taylor, F.A. Vera-Diaz, T. Panorgias, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P.J. Bex, Northeastern University College of Science, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recording mfERG using commercial devices requires the subject's sustained fixation at a specific location, which is not always attainable. We used our custom-built gaze-contingent system (GCS) to test the feasibility of recording mfERG in the presence of normal eye movements.

Methods: ERG responses were recorded in young adults (n=7) with a commercial device (Diagnosys) and also with the GCS under two conditions: Fixed and GC. The stimulus consisted of a central disk (radius = 2.5°) with 5 surrounding concentric rings (inner radii = [2.5°-12.5°], outer radii = [5°-15°], step size = 2.5°), and was presented on an LCD monitor (refresh rate = 75Hz). The m-sequence (m-seq) had 2^{12}-1 states, each lasting 39.9ms (1 stimulus frame, and 2 filler frames), and the m-seq lag between the rings was 256 states.

The GCS consisted of a 1401 DAQ system, and a 1902 amplifier (CED UK), a Bits# stimulus generator (CRS UK) alongside MATLAB and Psychtoolbox for stimulus generation, and an Eyelink eye tracker (2KHz sampling rate, SR Research CA) for monitoring gaze. In Fixed mode, the stimulus and fixation point were centered at the screen, while in GC mode, they were updated based on the gaze location at the beginning of the previous stimulus frame. An unfilled 2×2° square centered on the screen designated the permissible extent of gaze locations. If the gaze moved beyond this area, the edges changed color to warn the subject, and the affected m-seq states were repeated. To remove blink artifacts, all states presented 0.7sec prior until 3sec after a blink detection were re-tested. Computation of the mfERG responses required cross-correlation of the ERG signal and the stimulus luminance time-series. A photodiode at the top-left corner of the screen rendered the m-seq based on the luminance of the central stimulus.

Results: A repeated measure correlation (rmcorr) analysis indicated: 1) A high correlation between the P1 latencies measured with the 2 modes of the GCS ($r = 0.84$, $P < 0.001$), 2) An agreement between the commercial device and the GCS-GC mode in terms of P1 latencies ($r = 0.35$, $P = 0.037$), 3) No significant correlations for N1 latencies.

Conclusions: Our results suggest that making the stimulus GC does not affect P1 timings, and our measurements are not qualitatively different from the commercial devices. Therefore, this approach can be used with unstable fixation and to improve the spatial specificity of the mfERG technique.

CONTROL ID: 3709819

SUBMITTER (NAME ONLY): Ju Yi Hung

TITLE: A Pilot Study on Novel Ptotic Eye Dataset: Automated Prediction of Horizontal Corneal Diameter on Digital Photos of Taiwanese Ptotic Patients by Convolutional Neural Networks (CNNs)

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hung, Ophthalmology, Taipei Medical University Hospital, Taipei, TAIWAN|J. Hung, C. Fuh, Computer Science and Information Engineering, National Taiwan University, Taipei, TAIWAN|K. Chen, Biomedical Engineering, National Cheng Kung University, Taipei, Taiwan, TAIWAN|P. Chandrashan, D. Myung, A. Kossler, Stanford University School of Medicine, Byers Eye Institute at Stanford, Palo Alto, California, UNITED STATES|S. Liao, Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan, TAIWAN|S. Liao, College of Medicine, National Taiwan University, Taipei, Taiwan, TAIWAN|C. Hsu, Ophthalmology, Tri-Service General Hospital, Taipei, Taiwan, TAIWAN|

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ABSTRACT BODY:

Purpose: To present the preliminary results of automated measurements for horizontal corneal diameter (white-to-white distance) by a trained deep learning-based artificial intelligence(AI) model.

Methods: A novel dataset of healthy and ptotic eye images was used to develop a deep learning U-net-based model, which performs automated segmentation of the iris. A total of 100 ptotic eyes from the dataset were used for training, with another 100 ptotic eyes utilized for testing the AI model after adequate training. Iris edges were detected automatically based on the results of AI segmentation, then a circle and its center are simulated and represented mathematically in accordance with partially visible iris edges of ptotic eyes. Therefore, A horizontal corneal diameter, white-to-white distance, was calculated using the radius of the simulated circle for ptotic eyes. The AI predicted white-to-white distance was then compared with an attending physician manual measuring the white-to-white distance on the same 100 testing dataset to provide a comparison.

Results: From the 100 image test results predicted by our trained convolutional neural networks (CNNs) model, the mean of the horizontal corneal diameter in ptotic eyes was 11.99mm (range 10.77mm - 13.61mm, SD 0.514). The results of manual measurement by one attending physician in the same 100 test dataset showed that the mean was 12.21mm (range 11.05mm - 13.43mm, SD 0.486). The manual and AI-predicted measurements were well correlated (Pearson $r = 0.66$, $p < 0.01$).

Conclusions: Using our novel ptotic eye dataset, the CNN-based AI model demonstrated its potential to predict the horizontal corneal diameter (white-to-white distance) for ptotic digital photos. Further training on the AI model and careful validation for accuracy both need to be performed and presented in the future.

CONTROL ID: 3709822

SUBMITTER (NAME ONLY): Anna Heinke

TITLE: Quantitative evaluation of morphological changes in anti-VEGF treated choroidal neovascularization due to age related macular degeneration using optical coherence tomography angiography.

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Heinke, W.R. Freeman, D.G. Bartsch, L. Cheng, C. Galang, A. Warter, F. Kalaw, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|A. Heinke, W.R. Freeman, D.G. Bartsch, L. Cheng, C. Galang, A. Warter, F. Kalaw, Joan and Irwin Jacobs Retina Center, La Jolla, California, UNITED STATES|H. Zhang, T. Nguyen, C. An, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to determine if clinical response to anti-VEGF intravitreal injection therapy correlated to quantitative changes of CNV area and vascularity in OCTA.

Methods: 10 eyes of 10 patients (4 males, 6 females, mean age 75,1 y. o) with CNV were enrolled in the study. The inclusion criteria were presence of CNV confirmed with OCT, OCTA and FA in patients with initially active disease. A comprehensive ophthalmological exam was performed and OCTA was performed with Heidelberg Spectralis or Optovue using high resolution scans during the initial disease activity. The follow-up scan was performed after the successful response, i.e. at the presence of major reduction of sub- or intraretinal fluid or disappearance. CNV area was manually delineated and measured using Image J (area of selection in square milimeters). The CNV vascularity was measured using AngioTool by determining area of the vessels and was determined as a percentage of area occupied by vessels inside the explant area. Paired analysis was performed to compare the parameters at baseline and at the follow-up. The images were overlaid using the opencv(CV2) package in Python to look for morphological changes before and after the treatment.

Results: Analysis of vascularity of the lesion showed a decrease from 34% to 23% (p=0.002). The pre-and post-treatment mean CNV area was 74.26 before versus 66.57 square milimeters after treatment (p=0.1621). The analysis of overlaid images showed that in most cases morphology of the vessels changes with narrowing of the vessels and fewer vessels after the injection.

Conclusions: We found that the CNV vessel percentage area correlates with clinical response to anti-VEGF, and it decreases significantly after the successful treatment. Treatment effect may thus be due to reduced lumen and permeability. The reduction in vascular percentage may be due to reduction in vascular lumen and number of vessels. OCTA thanks to its ability to image the dynamics of neovascular changes may be a useful additional method in determining the optimal intervals of anti-VEGF injection.

CONTROL ID: 3709825

SUBMITTER (NAME ONLY): Taku Yamamoto

TITLE: Interleukin-1β regulates αB-crystallin phosphorylation and mRNA expression in retinal Müller cells under diabetic conditions

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yamamoto, S. Kase, K. Kikuchi, S. Ishida, Laboratory of Ocular Cell Biology and Visual Science, Department of Ophthalmology, Hokkaido University Faculty of Medicine and Graduate School of Medicine, Sapporo, Hokkaido, JAPAN|

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ABSTRACT BODY:

Purpose: The phosphorylation of αB-crystallin/CRYAB, one of small heat shock proteins also known as HSPB5, modulates its molecular dynamics and chaperone activity. Hyperglycemia and chronic inflammation play pivotal roles in the pathology of diabetic retinopathy, in which biological alterations of retinal glial cells are one of the key elements. However, αB-crystallin expression changes remain elusive in retinal glia cells under various diabetic stimuli. Here, we show interleukin (IL)-1β, an inflammatory cytokine upregulated in diabetic retinopathy, regulates the phosphorylation and mRNA expression of αB-crystallin in Müller cells.

Methods: Human Müller cells (MIO-M1) were used to evaluate changes in gene and protein expression with real-time quantitative PCR, enzyme linked immunosorbent assay (ELISA) and immunoblot analyses. Retinal tissues, isolated from the Spontaneously Diabetic Torii (SDT) fatty rat, a type 2 diabetic animal model with obesity, were examined by double-staining immunofluorescence.

Results: Real-time PCR and ELISA showed that CRYAB mRNA and αB-crystallin protein expression decreased in 50mM high glucose medium compared with 50mM mannitol. CRYAB transcripts expression was downregulated with 10ng/ml IL-1β (fold change; 24 hours = 0.33, 48h = 0.38, $p < 0.01$). AlphaB-crystallin serine 59 residue was phosphorylated with IL-1β application, which was inhibited following CRYAB siRNA induction in MIO-M1 cells. There was co-localization of glial fibrillary acidic protein (GFAP) with αB-crystallin and phosphorylated αB-crystallin at serine 59 in Müller cells in retinal specimens of SDT fatty rats.

Conclusions: CRYAB mRNA expression and the phosphorylation of αB-crystallin serine 59 residue were modulated by IL-1β in Müller cells under diabetic conditions, suggesting that αB-crystallin contributes to the pathogenesis of diabetic retinopathy.

CONTROL ID: 3709829

SUBMITTER (NAME ONLY): Rachel Israilevich

TITLE: Rhegmatogenous Retinal Detachment Repair Clinical Outcomes in Pseudophakic Eyes with Multifocal versus Monofocal Lenses

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Israilevich, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|A. Shahlaee, M. Salabati, R. Mahmoudzadeh, T. Wakabayashi, Y. Yonekawa, M. Klufas, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare anatomic and visual acuity (VA) outcomes of rhegmatogenous retinal detachment (RRD) repair in pseudophakic eyes with multifocal versus monofocal intraocular lenses (IOLs).

Methods: This was a single-institution, retrospective case-control study evaluating all pseudophakic eyes with multifocal IOLs undergoing primary RRD repair with pars plana vitrectomy (PPV) or PPV with scleral buckle (PPV+SB) from 1/1/13-9/1/21. A 1:1 monofocal IOL control group was matched based on age, gender, macula status, primary surgeon, and timing of surgery. Eyes with baseline PVR were excluded. Outcomes included single surgery anatomic success (SSAS) rate at 90 days after surgery, and VA at baseline and final visit after primary RRD repair.

Results: Seventy-one eyes had multifocal IOLs at primary RRD surgery during the study period and were eligible for analysis. Both the multifocal and control groups included 71 eyes, and mean age was 64.8 ± 8.5 and 64.5 ± 8.8 years, respectively (p=0.85). Primary PPV and PPV+SB was performed on 66 (93%) and 5 (7%) multifocal eyes, respectively, vs. 60 (84.5%) and 11 (15.5%) control eyes (p=0.11). Mean follow-up was 773 ± 588 days in the multifocal group vs. 793 ± 565 days in the control group (p=0.84). Overall SSAS was achieved in 55 (77.5%) multifocal eyes vs. 63 (88.7%) control eyes (p=0.073). Primary PPV and PPV+SB resulted in SSAS in 50 (75.8%) and 5 (100%) multifocal eyes vs. 53 (88.3%) and 10 (90.9%) control eyes (p=0.068, p=1.00, respectively). In surgical failures, the mean number of RRD surgeries was 2.4 ± 0.7 in the multifocal group vs. 2.1 ± 0.4 in the control group (p=0.33). Mean baseline logMAR VA was 0.95 ± 0.89 (20/178) in multifocal eyes vs. 0.95 ± 0.92 (20/178) in control eyes (p=0.84), and at final visit was 0.27 ± 0.34 (20/37) in multifocal eyes vs. 0.28 ± 0.43 (20/38) in control eyes (p=0.83). The most common cause of surgical failure in both groups was post-operative PVR which developed in 8 (53.5%) of multifocal and 5 (71.4%) of control failures (p=0.65).

Conclusions: In pseudophakic RRDs undergoing primary surgical repair, there was a trend towards higher SSAS in eyes with monofocal IOLs, but no statistically significant difference in SSAS or PVR development in eyes with multifocal vs. monofocal IOLs. Visual outcomes were similar in both groups and significantly improved compared to baseline.

CONTROL ID: 3709835

SUBMITTER (NAME ONLY): Xiaoqin Huang

TITLE: An objective and easy-to-use glaucoma severity classification system based on artificial intelligence

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Huang, S. Yousefi, Department of Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|F. Saki, QUALCOMM Inc, San Diego, California, UNITED STATES|M. Wang, T. Elze, Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. Boland, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L. Pasquale, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, UNITED STATES|C.A. Johnson, Department of Ophthalmology & Visual Sciences, University of Iowa Hospitals and Clinics, Iowa, UNITED STATES|S. Yousefi, Department of Genetics, Genomics, and Informatics, University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a simple and easy-to-use glaucoma staging system based on visual fields (VFs) and to evaluate the system using an independent validation dataset.

Methods: We developed an unsupervised k-means algorithm to identify clusters with similar VFs (Fig. 1). We annotated the clusters based on their respective mean deviation (MD). To establish an objective criterion for glaucoma staging, we computed optimal MD thresholds that discriminated clusters with the highest accuracy based on Bayes minimum error principle. We validated the entire pipeline based on an independent validation dataset and evaluated the accuracy of the staging system based on the identified MD thresholds (Fig. 1).

Results: k-means model discovered four clusters with 6784, 4034, 1541, and 872 VFs and average MDs of 0.0 dB (±1.4: SD), -4.8 dB (±1.9), -12.2 dB (±2.9), and -23.0 dB (±3.8), respectively. The supervised Bayes minimum error classifier identified optimal MD thresholds of -2.2 dB, - 8.0 dB, and -17.3 dB for discriminating normal eyes and eyes at the early, moderate, and advanced stages of glaucoma (Fig. 2). Approximately 2.2% of normal eyes and eyes in the early stage of glaucoma had VF loss in at least one of the four central VT test locations. The accuracy of the glaucoma staging system based on the identified MD thresholds with respect to the initial k-means clusters was about 94%.

Conclusions: We used unsupervised and supervised machine learning models to develop an objective glaucoma staging system without expert intervention. We discovered that MDs of approximately -2 dB, - 8 dB, and -17 dB provide the optimal thresholds for staging glaucoma to four severity levels. The proposed staging system is unbiased, easy-to-use, and consistent, thus may be used in glaucoma research and clinical practice to improve glaucoma care.

CONTROL ID: 3709838

SUBMITTER (NAME ONLY): Rachael Allen

TITLE: Dopamine treatment delays diabetic retinopathy onset in a retrospective study

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of blindness, and world-wide prevalence is expected to increase. Dopamine treatment protects against early neuronal dysfunction in DR in both animal models and people and acts as an anti-angiogenic in models of acute lung injury, cancer, and irritable bowel syndrome. Whether dopamine functions as an anti-angiogenic to reduce clinically-recognized vascular pathology in DR is unknown. Here, we used a retrospective study of Veterans with diabetes to determine whether taking L-DOPA or dopamine agonists delayed DR onset.

Methods: A retrospective analysis of medical records was used to identify patients diagnosed with diabetes, with or without a history of treatment with levodopa or dopamine agonists. The primary outcome was the time interval between initial diabetes diagnosis and DR diagnosis. Patients with >100 days of dopamine prescriptions during the time period between diagnoses (dopamine group, n=424) were compared against patients with no history of dopamine prescriptions (untreated group, n=9952). Other factors compared across groups were age at diabetes diagnosis, gender, race, tobacco usage, co-morbidities, blood sugar control, and insulin/hypoglycemic usage with unpaired t-tests for continuous variables and Chi-square tests for categorical variables. A multivariate linear model was utilized to assess the relative impact of dopamine treatment and other factors on the time to develop DR in Veterans with diabetes. Statistical assessments were performed using RStudio version 1.4.

Results: Dopamine treatment delayed DR onset in Veterans with diabetes by 1.5 years (6.802 vs. 8.381 years, $p<0.001$). On average, the dopamine group was older (55.01 vs. 57.24, $p<0.001$), with a higher proportion of female patients (female: 6.4% vs. 3.8%, $p<0.001$) and a higher Elixhauser co-morbidity score with van Walraven weighting (5.552 vs. 3.338, $p<0.001$). There was no difference in average HbA_{1c} between groups. The primary dopamine drugs taken included D2-like agonists (77.4%), dopamine precursors (20.7%), and dopamine degradation enzyme inhibitors (1.9%).

Conclusions: Veterans with diabetes who took L-DOPA and dopamine agonists showed delayed onset of vascular pathology associated with DR. This research demonstrates the value of long-term dopamine treatment for DR. Future research will include a prospective study to examine the protective effects of L-DOPA on vascular pathology in DR.

CONTROL ID: 3709839

SUBMITTER (NAME ONLY): Clemence Bonnet

TITLE: Wnt signaling pathway in the human limbus: a comprehensive mapping by single mRNA detection

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Bonnet, M. Ruiz, S. Gonzalez, C. Tseng, S.X. Deng, Cornea, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|C. Bonnet, J. Bourges, F.F. Behar-Cohen, Cornea, Hopital Cochin, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To evaluate the in situ spatial mRNA expression of 4 Wnt ligands (WNT2, WNT6, WNT11, WNT16B), 4 Wnt inhibitors (dickkopf WNT Signaling Pathway Inhibitor 1 [DKK1], secreted frizzled-related protein 5 [SFRP5], frizzled-related protein [FRZB], WNT inhibitory factor 1 [WIF1]), and frizzled7 (Fzd7), that have been shown previously upregulated in the limbus by differential gene profiling using q-RT-PCR.

Methods: The V2 fluorescent RNAscope (ACD, Newark, California) was performed on fresh frozen tissue sections from 5 human corneas with less than 8 hours of death to preservation time and intact epithelium. Positive signals were quantified using Imaris software.

Results: All 4 Wnt ligands, 4 Wnt inhibitors, and Fzd7 were preferentially expressed in the basal layer of the cornea and limbus compared to the suprabasal layer ($P<0.05$). When compared with the basal corneal epithelial layer, all 4 Wnt ligands, FRZB, and Fzd7 were preferentially expressed in the basal limbal epithelial layer in a decreasing gradient manner towards the superficial layers ($P<0.05$). No gradients were found for DKK1, WIF1, and SFRP5 expression. All 4 Wnt ligands, 4 Wnt inhibitors, and Fzd7 were also detected in the limbal stroma ($P<0.05$). Fzd7 was preferentially expressed in the basal limbal epithelial layer of the superior limbus compared with other limbal quadrants ($P<0.05$).

Conclusions: Wnt ligands are expressed in a gradient manner towards the superficial layers. Both paracrine and autocrine Wnt signaling pathways are involved in LSCs regulation, suggesting that a fine tuning of Wnt signaling exists to control LSC differentiation and proliferation.

CONTROL ID: 3709844

SUBMITTER (NAME ONLY): Mai Tsukikawa

TITLE: Repeatability and Agreement of Optical Coherence Tomography Measurements Obtained with the Spectralis OCT2 and the New Spectralis OCT3

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tsukikawa, A.A. Jammal, H. Tseng, F. Medeiros, S. Asrani, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Spectralis OCT3 (Heidelberg Engineering, Heidelberg, Germany) is a new OCT device capable of faster image acquisition at 125,000 Hz, compared to 85,000 Hz of the current Spectralis OCT2. The purpose of this study was to evaluate the repeatability and agreement of optic disc and retinal nerve fiber layer (RNFL) parameters obtained by these 2 devices.

Methods: Normal and glaucoma eyes of adult subjects were recruited. OCT scans were obtained 3 times on the same day with the Spectralis OCT2 and Spectralis OCT3, by the same examiner. Sectoral and global RNFL thickness as well as global minimum rim width (MRW) and Bruch's membrane opening area (BMOa) were measured. Repeatability was assessed by the coefficient of variation (COV) with bootstrapped 95% confidence interval (CI) for each parameter of each device. Bland-Altman plots were constructed to assess interdevice agreement.

Results: Included were 20 eyes from 20 subjects, with mean ± standard deviation (range) of 73.7 ± 18.0 µm (42.3 to 111.7 µm) for global RNFL, 219.0 ± 63.0 µm (86.3 to 358.3 µm) for global MRW, and 2.10 ± 0.5 mm^2 (1.45 to 3.24 mm^2) for BMOa measured by the Spectralis OCT2. Both Spectralis OCT2 and OCT3 showed similarly low COVs [95% CI] for global RNFL thickness (1.1% [0.4% to 1.9%] vs. 0.9% [0.6% to 1.2%], respectively), global MRW (1.0% [0.6% to 1.5] vs. 1.1% [0.8% to 1.4%], respectively), and BMOa (0.7% [0.5% to 0.9%] vs. 0.9% [0.6% to 1.2%], respectively). Bland-Altman 95% limits of agreement were -3.7 to 5.1 µm for RNFL, -5.0 to -3.9 µm for MRW, and -0.06 to 0.07 mm^2 for BMOa, demonstrating good interdevice agreement for all parameters.

Conclusions: We found excellent intravisit repeatability of measurements for both devices. Bland-Altman limits of agreement were low, suggesting that measurements are potentially interchangeable between devices.

CONTROL ID: 3709846

SUBMITTER (NAME ONLY): Tsz Wing Leung

TITLE: Internal optics failed to compensate for increased corneal astigmatism in myopic children over a 2-year period

SESSION TITLE: Myopia and refractive error development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Leung, R. Chun, Y. Li, C. To, C. Kee, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|T. Leung, R. Chun, C. Kee, Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Hong Kong, HONG KONG|C. To, Centre for Eye and Vision Research (CEVR), HONG KONG|

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ABSTRACT BODY:

Purpose: It has been shown that the internal optics can partially compensate for corneal aberrations to maintain the overall aberration of the entire eye at a lower level. However, optical compensation reported in previous studies was based on cross-sectional data collected from adults with fully developed eyes. Longitudinal evidence from children whose eyes are rapidly developing is still lacking. This study investigated longitudinal interactions of corneal and internal aberrations on the ocular aberrations in myopic children.

Methods: Myopic Chinese children (n = 69, age: 8-10 years) were included. Their ocular and corneal wavefront aberrations were measured using an aberrometer incorporated with a corneal topographer at baseline and after two years. Internal aberration was calculated by directly subtracting the corneal aberration from the ocular aberration. Compensation factor (CF) was calculated, using root mean square error (RMSE), to indicate the effectiveness of internal optics to counterbalance the corneal aberrations: CF = 1 – (ocular aberration RMSE / corneal aberration RMSE). Axial length was measured using a partial coherence interferometer.

Results: Ocular lower-order astigmatism RMSE was significantly increased by 0.21±0.03 μm during myopic eye growth, accompanied by 0.18±0.03 μm increase in corneal lower-order astigmatism (paired t-tests, $P < 0.001$). The CF was dropped from 0.51 to 0.38, suggesting that compensation from the internal optics became less effective. When investigating individual Zernike coefficients, there was a significant increase in negative corneal H/V astigmatism (paired t-test, $P < 0.001$) but no significant change for the compensatory positive internal H/V astigmatism (unpaired t-test, $P = 0.07$), resulting in a more negative ocular H/V astigmatism (paired t-test, $P < 0.001$). While myopia progressed over the two-year follow-up period, H/V astigmatic change was not significantly associated with axial elongation (Pearson’s correlation, $P = 0.26$).

Conclusions: The increased ocular lower-order astigmatism indicates that the internal optics failed to compensate for the increased corneal astigmatism in children during myopic eye growth. Further works are required to understand the associated mechanism underlying the astigmatic changes in children.

CONTROL ID: 3709849

SUBMITTER (NAME ONLY): Taibo Li

TITLE: The Impact of Bilateral Visual Field Patterns on Quality of Life Parameters

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Li, J. Sabharwal, P.Y. Ramulu, J. Yohannan, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|C. Bradley, A. Mihailovic, J. Sabharwal, P.Y. Ramulu, J. Yohannan, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|L.Q. Shen, M. Wang, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.Q. Shen, M. Wang, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual field (VF) is the gold standard for assessing visual function. Archetypal analysis has been applied to unilateral VF to define specific patterns of loss. However, bilateral VF changes have larger impact on patient function. Therefore, we aim to 1) generate distinct archetypes of bilateral VF loss, and 2) assess the impact of archetypes of bilateral VF loss on patient function.

Methods: To develop archetypes for bilateral VF loss, we assessed 15,663 unique patients with bilateral 24-2 VFs obtained on the same day. Included VFs had false positives <15%, false negative <25% for moderate glaucoma and <50% for severe glaucoma, and fixation losses <10%. We decomposed each bilateral VF into 25 distinct archetypes (i.e. distinct patterns of bilateral VF loss) using elbow plot analysis. To assess the impact of the bilateral VF loss on patient function, we used an independent dataset with 229 patients who had bilateral VF data and had undergone functional testing to generate quality of life (QOL) data on reading speed and composite scores. We performed linear regression with projected archetype coefficients as the independent variable and QOL metrics as the dependent variable and applied Bonferroni correction for multiple testing.

Results: Among the 25 archetypes derived from bilateral VF data, twelve show VF defects in similar spatial locations in two eyes (Figure 1). The most represented archetypes are AT 3 (normal), AT10 (superior peripheral OD), and AT 21 (superior peripheral OS, Figure 2). In the clinical evaluation cohort, AT3 (normal, p = .002), AT5 (bilateral superior and inferior arcuate defects, p = .001), AT7 (diffuse bilateral loss p = .001), and AT11 (inferior bilateral loss, p = .001) are significantly associated composite score, while AT3 (p = .04), AT7 (p = .04), and AT11 (p = .04) are associated with reading speed.

Conclusions: Patients with a greater percentage of bilateral normal archetype tend to have improved QOL and higher reading speed. Whereas, patients with greater amounts of diffuse bilateral depression and inferior VF loss have worse QOL and lower reading speed. Bilateral VF archetypal analysis presents a useful framework to characterize subgroups of glaucoma patients, which can allow clinicians to better understand the impact of glaucoma on individual patients.

CONTROL ID: 3709850

SUBMITTER (NAME ONLY): Erika Aguzzi

TITLE: Improving integration of transplanted human stem cell derived retinal ganglion cells

SESSION TITLE: Neuroprotection and neuroregeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.A. Aguzzi, K.Y. Zhang, A. Nagalingam, X. Chang, D.J. Zack, T.V. Johnson, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma causes progressive retinal ganglion cell (RGC) death. The mammalian retina lacks regenerative capacity, but RGC replacement and optic nerve regeneration hold potential for restoring vision in glaucoma and other optic neuropathies. Here, we characterize a barrier to donor human stem cell-derived RGC integration following intravitreal transplantation in vivo. We demonstrate that the internal limiting membrane (ILM) impedes the migration of transplanted RGCs into the recipient retina.

Methods: We differentiated RGCs from human embryonic stem cells using established methods. To circumvent the ILM, we intravitreally injected the nonspecific protease Pronase-E (or saline, negative control) in immunodepleted mice of both sexes. We verified that Pronase-E digests the ILM without affecting the survival of endogenous retinal neurons or glia. In complementary experiments, we transplanted human RGCs in Lama1^{nmf223} mice of both sexes, which harbor a point mutation in the Lama-1 gene, and which exhibit developmental ILM defects. Samples sizes included ≥15 mice per group and experiments were replicated at least twice by masked investigators. We assessed donor RGC survival and engraftment using 3D reconstructions of confocal z-stacks.

Results: Donor RGC survival progressively decreased ($p<0.0001$) from 6h to 14d post transplantation and was not altered by proteolytic or transgenic ILM disruption. Overall survival rates were ≤1%, commensurate with prior published work. Migration of surviving donor RGC somas into the recipient RGC layer was ≥5-fold greater after proteolytic($p<0.02$) and transgenic ($p<0.003$) ILM disruption. Intriguingly, surviving RGCs spontaneously grew axons towards the optic nerve head (Figure). Extension of dendrites into the recipient inner plexiform layer (IPL) was observed exclusively following ILM disruption (Figure).

Conclusions: These observations advance our understanding of the barriers to human RGC engraftment and synaptogenesis within the adult mammalian retina, and may provide a target for clinically translating regenerative medicine approaches to optic neuropathy. Ongoing work aims to improve donor RGC survival and to characterize the functional connectivity of donor RGCs within the host retinal neurocircuitry.

CONTROL ID: 3709854

SUBMITTER (NAME ONLY): Matthew McPheeters

TITLE: Functional imaging of the murine corneal nerves longitudinally and in vivo

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. McPheeters, B. Blackburn, W.J. Dupps, A.M. Rollins, M.W. Jenkins, Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|W.J. Dupps, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|M.W. Jenkins, Pediatrics, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Numerous diseases detrimentally affect corneal nerves. Corneal nerve dysfunction has been linked to dry eye syndrome onset, neurotrophic keratopathy, and other diseases. The morphology and histology of corneal nerves in health and disease has been extensively studied. However, studies of corneal nerve function have been limited (e.g., electrical recordings of ciliary nerves or calcium reporter dyes in ex vivo corneas). Here, we demonstrate functional imaging of corneal nerves over time, as well as stimulus-response.

Methods: We made a cre-lox mouse line expressing GCaMP6f against the Nestin promoter for expression in corneal nerves. We imaged corneas in vivo (mice under isoflurane) with a custom confocal imaging system and an air objective. We applied drops of KCl solution (0.3 M) and tetracaine (0.5%) to the cornea while imaging.

Results: Fig. 1 shows a demonstration of basal corneal nerve signaling in the same cornea over the course of a month. This demonstrates how functional imaging might be used to study nerve activity changes in response to ocular surgeries or pharmaceutical treatments. Fig. 2 shows a demonstration of in vivo calcium imaging where corneal nerves respond to a stimulus. Repeated stimulus and response characterization is one way that the response of corneal nerves could be characterized over time.

Conclusions: The in vivo demonstration of longitudinal imaging and stimulus-response builds upon previous work to develop a model system to study how corneal nerve responses change over time. This will facilitate better studies and understanding of factors that could slow the development of neuropathies. It may also help in the development and testing of new clinical interventions and therapies.

CONTROL ID: 3709860

SUBMITTER (NAME ONLY): Viet Chau

TITLE: Phylogenic and Genomic Analysis of HSV-1 Ocular Isolates Recovered From Keratoconjunctivitis

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Chau, D. Miller, N. Yannuzzi, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Kolb, C.R. Brandt, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is limited data on the prevalence and genetic diversity of the herpes simplex virus type 1 (HSV-1) virulence genes in ocular isolates. Phylogenetic and genomic analyses of 9 HSV-1 conjunctival isolates were performed to help better understand genetic variability amongst common virulence genes in ocular herpetic disease.

Methods: Whole genome sequencing of 9 HSV-1 isolates recovered in tissue culture from conjunctival scrapings collected between 2004 and 2015 from patients with viral kerato-conjunctivitis were screened using the PacBio Sequel II platform. A phylogenetic network was generated using a multiple sequence alignment method, combining the 9 viral isolate sequences along with 160 global HSV-1 sequences. Protein sequence analyses of common virulence genes (thymidine kinase [TK], DNA polymerase, and ICP22) were performed.

Results: Of the 9 samples, 8 mapped to the American-European clade, whereas the remaining one, closely aligned with the African clade. Both TK and DNA polymerase protein sequencing analyses revealed multiple single nucleotide polymorphisms (SNPs). The majority of these have been previously described, none however are known to confer antiviral resistance. One novel TK SNP (P300S) was found in two viral isolates and the potential effect of the polymorphism on TK and antiviral resistance has yet to be determined. Two novel DNA polymerase SNPs (T929A and R1001Q) were found, which have yet to be described in the literature. The impact on DNA polymerase and acyclovir susceptibility is also unknown. Analysis of ICP22 protein sequences did not reveal any novel protein coding SNPs, however two isolates contained an A78D change, which may affect nucleotidylation of the ICP22 protein.

Conclusions: Whole genome sequencing along with phylogenetic and genomic analyses are powerful tools for understanding genetic variability amongst ocular conjunctival HSV isolates. Identification of novel and common recurrent polymorphisms may help understand drivers of herpetic pathogenicity and factors that may influence virulence in ocular disease.

CONTROL ID: 3709865

SUBMITTER (NAME ONLY): Anvit Rai

TITLE: Test of the Robustness of an OCT-based Method for Identifying Glaucomatous Damage Across Different Instruments

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rai, S. La Bruna, J. Kerr, G. Mao, E. Tsamis, D.C. Hood, Psychology, Columbia University, New York, New York, UNITED STATES|A. Rai, Medical student, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|E. Tsamis, A. Leshno, C.G. DeMoraes, G.A. Cioffi, J.M. Liebmann, D.C. Hood, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test the Columbia University (CU) OCT-based method [1,2] for distinguishing glaucomatous damage from healthy controls by applying it to scans from different OCT instruments.

Methods: OCT glaucoma reports [3] were analyzed from 116 eyes from a prospective, observational, case-control study, included 54 healthy controls (HC), 32 early (EG, 24-2 mean deviation (MD) >-6dB), 12 moderate (MG, MD <-6dB and >-12dB), and 18 advanced glaucoma (AG, MD <-12dB). Eyes were scanned with two commercially available OCT instruments from different manufacturers, A and B. Each instrument uses different technology (swept-source vs. spectral-domain), segmentation algorithms, and normative data. A set of reports was generated for each device. These reports [3] included thickness and probability (p-) maps from both the retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL), as well as a circumpapillary (cp) b-scan image and cpRNFL thickness plot. Four graders, experienced with the CU OCT-based method, categorized each eye as glaucoma (G), not glaucoma (NG), or uncertain (UNC) based upon clearly defined rules (Fig. 1).[1,2] Disagreements were adjudicated. Eyes with grades of UNC were treated as G in calculating specificity and sensitivity, as both grades require additional testing.

Results: For 113 (97%) of the 116 eyes, the grades were identical (Table 1). All 3 disagreements involved an UNC grade for either the A or B report. After combining eyes with UNC and G grades, the specificity for the 54 HC eyes was 98% (A) and 96% (B), while the sensitivity for the 62 G eyes was 100% for both A and B instruments.

Conclusions: The CU OCT-based method showed consistency across instruments from different manufacturers, with different normative groups and different algorithms. The sensitivity and specificity suggested that this method may help physicians distinguish glaucomatous eyes from healthy controls using OCT. 1. Liebmann et al; 2022; 2. Hood et al., PRER, 2022; 3. Hood PRER, 2017.

CONTROL ID: 3709867

SUBMITTER (NAME ONLY): Gustavo Gameiro

TITLE: Do blinking parameters in essential blepharospasm patients become similar to normal subjects after botulinum toxin injections?

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A comprehensive analysis of blinking in essential blepharospasm (EB) rather than assessing the global eyelid movements (anomalous eyelid movements + blinking) frequency is clinically relevant to understand the complexity of this condition and the effect of treatment in blinking parameters. This study focuses on objectively evaluating blinking kinematics of EB patients before and after treatment, as well as comparing those parameters to controls.

Methods: Patients with moderate to severe disease and matching-age controls were enrolled. Patients were followed up before and 15 days after the administration of onabotulinumtoxinA (BTX). A high-speed camera and micro-LED were used to register a 3-minute video of eyelid movements (blinking + anomalous eyelid spasms). Movements correspondent to blinking were isolated and a custom-made software was used to objectively evaluate them. Outcomes were blinking frequency, mean amplitude of blinking and mean maximum velocity of eyelid closing (MVEC) during blinking. T-student tests were used to compare different groups and paired-t tests, to compare measurements before and after treatment in the EB group.

Results: 24 eyes from 12 patients with EB and 13 eyes of 13 control subjects were included in this study. Table 1 summarizes the findings (presented as mean ± standard deviation). Baseline EB blinking frequency was significantly higher ($p<0.0001$) and MVEC during blinking was significantly lower ($p=0.0019$), when compared to control subjects', whereas a significant difference was not observed for blinking amplitude ($p=0.6585$) before treatment. After BTX injections, all parameters significantly reduced when compared to baseline measurements in the EB group ($p=0.032$ for blinking frequency; $p<0.001$ for amplitude and $p<0.001$ for MVEC). Although the blinking frequency significantly reduced after treatment, a significant difference was still observed, when compared to the control group ($p=0.0195$). Blinking amplitude ($p=0.0098$) and maximum velocity ($p<0.0001$) were significantly lower when compared to the control group.

Conclusions: Our results show that all assessed blinking parameters significantly differed from control subjects after treament, likely reflecting alterations due to the disease itself and due to the effect of botulinum toxin in orbicularis oculi muscle.

CONTROL ID: 3709869

SUBMITTER (NAME ONLY): Meera Sivalingam

TITLE: Outcomes of Eyes Lost To Follow up with Proliferative Diabetic Retinopathy That Recieved Combination Panretinal Photocoagulation and Intravitreal Anti-Vascular Endothelial Growth Factor.

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sivalingam, A. Obeid, D. Parikh, P. Brower, J. Hsu, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the outcomes of eyes with proliferative diabetic retinopathy (PDR) that were lost to follow up (LTFU) after receiving a combination of panretinal photocoagulation (PRP) and intravitreal anti-VEGF therapy.

Methods: Eyes with PDR receiving combination therapy (PRP + anti-VEGF within 3 months of one another) that were LTFU for greater than 6 months were identified. Clinical data (including visual acuity) was then evaluated at different timepoints.

Results: A total of 250 eyes were eligible for analysis. Eyes were LTFU for a mean total of 305 (SD 142) days. Mean logMAR at the date LTFU was 0.62 (SD 0.56). LogMAR was significantly worse at the return from LTFU visit [0.82 (SD 0.70) $p<0.001$)] and the final visit [0.81 (0.75) $p<0.001$]. On the initial visit 201 (79.8%) of patients had diabetic macular edema (DME), 20 (7.9%) had neovascular glaucoma (NVG) , 22 (8.7%) had tractional retinal detachments (TRD), and 140 (55.6%) had vitreous hemorrhage (VH). On the return visit 197 (78.2%) of patients had DME, 30 (11.9%) had NVG, 26 (10.3%) had TRDs, and 143 (56.7%) had VH. On the final visit 184 (73.0%) of patients had DME, 27 (10.7%) had NVG, 35 (13.9%) had TRDs, and 122 (48.4%) had VH.

Conclusions: There was a significant, albeit a minimal decline in the visual acuity of eyes that received combination therapy and were LTFU. This may have been attributed to worsening DME or increase in the prevalence of anatomic complications.

CONTROL ID: 3709876

SUBMITTER (NAME ONLY): Rohini Nair

TITLE: Characterization of retinal architecture in a systemic HL/EL double knockout mouse model

SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.M. Nair, Y. Song, B.A. Bell, K. Zhang, J.L. Dunaief, V.R. Chavali, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|D.J. Rader, Departments of Genetics, Medicine, and Pediatrics, the Cardiovascular Institute, and the Institute for Translational Medicine and Therapeutics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: There have been several reports of impaired lipid metabolism in age-related macular degeneration (AMD) pathogenesis. Large-scale genome-wide association studies in AMD patients have identified genes, including LIPC (HL), CETP, APOE, and ABCA1, that play a role in the generation, transport, and metabolism of high-density lipoprotein (HDL) particles. Additionally, increased systemic lipid levels have been correlated with increased AMD risk, the exact role of which has not been explored. With the premise of dysregulated lipid metabolism as a risk factor for degenerative retinal disorders, our study aims to explore the age-related effect of systemic loss of two lipases, Hepatic Lipase (HL) and Endothelial Lipase (EL) on retinal ultrastructure and function.

Methods: The HL/EL DKO mice on a C57BL/6J background were aged for up to 14 months. Retinal structure and function were assessed using histology, electroretinography, and spectral-domain optical coherence tomography at 7 and 12 months. To investigate retinal pathology and lipid deposits with aging, histological and ultrastructural analysis were performed at 14 months in comparison to wild-type C57BL/6 mice.

Results: The HL/EL DKO mice showed a significant reduction, with age, in all the three-wave responses (rod-a, b, and cone-b) when compared to controls. Small punctate, hyperreflective foci were observed in the retinas of HL/EL DKO mice at 12 months. There was a significant reduction in the number of S-opsin expressing cones in the DKO mice when compared to the controls. Retinal expression of Glutamine Synthetase (mGS) and cellular retinaldehyde–binding protein (mCRALBP) was also found to be reduced in DKOs. The DKO mice showed a marked accumulation of neutral lipids and unesterified cholesterol droplets in the choroidal and sub-RPE region when stained using Oil Red O and BODIPY suggesting deregulated lipid clearance. Ultrastructural analysis of HL/EL DKO mice also showed multiple lipid droplets below the Bruch's membrane (BrM). Additionally, we observed disrupted and swollen RPE basal infoldings in the DKO mice.

Conclusions: Systemic loss of HL and EL leads to degenerative retinal changes and accumulation of lipids in the RPE/BrM/choroid in aged HL/EL DKO mice, sharing features with AMD pathophysiology. Further studies are warranted to understand the role of dysregulated lipid metabolism in inducing age-related degenerative retinal changes.

CONTROL ID: 3709877

SUBMITTER (NAME ONLY): Haiwen Gui

TITLE: Explaining Deep Learning Models for Low Vision Prognosis

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Gui, Stanford University School of Medicine, Stanford, California, UNITED STATES|B. Tseng, W. Hu, S.Y. Wang, Byers Eye Institute, Department of Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low vision rehabilitation improves quality-of-life for visually impaired patients, but referral rates fall short of national guidelines. Automatically identifying patients with poor visual prognosis from electronic health records (EHR) could allow targeted referrals to low vision services. The purpose of this study was to build, understand, and explain deep learning artificial intelligence models that predict visual prognosis using EHR data.

Methods: We identified 5547 patients with low vision (defined as best documented visual acuity (VA) <20/40) from EHR from 2009-2018, with ≥ 1 year of follow-up. From the EHR, we extracted ophthalmology free-text notes and structured data, such as demographics, billing/procedure codes, medications, and eye exam findings. To predict whether low vision patients would still have low vision a year later, we developed deep learning models that used 1) structured inputs, 2) free-text progress notes represented by standardized clinical concepts extracted using named entity recognition (NER), and 3) a combination of the two. Performance metrics including area under the receiver operating curve (AUROC) and F1 score were evaluated on a held-out test set. We then evaluated models using Local Interpretable Model-Agnostic Explanations to determine which input features were most important to the predictions.

Results: Among the 5547 patients, 40.7% (N=2258) never improved to better than 20/40 over one year of follow-up. Our single-modality model based on structured inputs predicted low vision prognosis with AUROC of 80% and F1 score of 70%. Our model combining NER text and structured inputs achieved an AUROC of 79% and F1 score of 63%. Explainability studies revealed that important features for predicting low vision prognosis included features clinicians also rely upon, such as best visual acuity and the presence or absence of irreversible ophthalmic findings, as shown in Fig1.

Conclusions: Deep learning models often suffer from a lack of transparency. Our explainability analyses provide insight into the medical context surrounding low vision prognosis and are a vital step towards increasing clinicians' trust in these models.

CONTROL ID: 3709879

SUBMITTER (NAME ONLY): Congxiao Zhang

TITLE: Targeted deletion of interferon regulatory factor 5 gene in mice triggers choroidal neovascularization

SESSION TITLE: Animal Models of Age Related Macular Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Zhang, R. Quinn, E. Nguyen, J.G. David, K. Bharti, OSCTRS/OGVFB, National Eye Institute, Bethesda, Maryland, UNITED STATES|N. Fernando, Neuro-Immune Regulome Unit (NIRU), National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Choroidal neovascularization (CNV), an advanced form of age-related-macular-degeneration (AMD), is associated with gradual loss of choroidal integrity. However, the molecular mechanisms of CNV initiation and the loss of choroidal integrity remain unexplored. Signaling molecules that help maintain local immune cell populations and regulate local inflammation are suggested to contribute to CNV. Interferon regulatory factor 5 (IRF5) is a transcription factor known for modulation of inflammation and for promoting macrophage subtype polarization between M1 (proinflammatory) and M2 (proangiogenic). Here, we aim to dissect the function of IRF5 in CNV development by characterizing a IRF5 knockout (IRF5null) mouse model.

Methods: Loss of IRF5 expression in RPE/choroid was verified by qRT-PCR and immunohistochemistry with antibody against IRF5. Ocular structures were evaluated live using optical coherence tomography (OCT) and fluorescein angiography, and histologically using light and confocal microscopy. Immune cell populations were characterized by flow cytometry and immunohistochemistry with lineage specific and activation markers, including CD11b, CD11c, F4/80, CD86, CD206, CD14, MHCII, Ly6c. Retina physiology was studied by electroretinography (ERG).

Results: IRF5 null homozygous eyes displayed an increase in the number of immature macrophages. Phenotypically, IRF5 null mice showed normal gross anatomical structure at birth. By 9 months of age, choroidal /RPE morphological defects include overgrowth of new choroidal vessels that invade sub-RPE/Bruch's membrane, degeneration of RPE overlying CNV, and overt presence of migratory cells, presumably phagocytes, in the subretinal space. These changes were concomitant with a reduction in the response amplitudes in the a- and b- waves of ERG.

Conclusions: Loss of IRF5 is sufficient to induce CNV in the eye and compromise choroid/RPE/retina homeostasis. These findings indicate an important role for the IRF5 in controlling immune regulation in the posterior part of the eye. IRF5 null eyes can serve as a model for studying early events in AMD pathogenesis.

CONTROL ID: 3709881

SUBMITTER (NAME ONLY): Kei Takahashi

TITLE: Molecular characterization of MAP9 in primary cilia as a modifier of canine RPGRIP1 cone-rod dystrophy

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Takahashi, G.D. Aguirre, K. Miyadera, Department of Clinical Sciences and Advanced Medicine, University of Pennsylvania School of Veterinary Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: A form of canine cone-rod dystrophy (cord1) has been associated with a homozygous insertion in RPGRIP1 ($RPGRIP1^{ins/ins}$) as the primary disease locus with a homozygous deletion in MAP9 ($MAP9^{del/del}$) as a modifier prompting early disease onset. Both gene products are suggested to play important roles in the photoreceptor connecting cilia. However, the role of MAP9 in primary cilia nor the effect of its modifier variant is not fully understood. We aim to characterize the molecular function of MAP9 in photoreceptor primary cilia.

Methods: MAP9 expression in the connecting cilia was evaluated by immunohistochemistry using $RPGRIP1^{ins/ins}$ canine retinal cryosections with/without the $MAP9^{del/del}$ modifier. The role of MAP9 in cilia was studied in an in vitro primary cilia model. Cultured 661w cells were serum-starved for 48h to induce post-mitotic ciliogenesis. RNA was extracted from $MAP9^{+/+}$ and $MAP9^{del/del}$ canine retinas followed by reverse transcription, and wild type and mutant MAP9 cDNA (MAP9-Wt and MAP9-Mut) were subcloned into expression vectors. 661w cells were transfected with the vectors and then assessed for subcellular localization of MAP9 using immunocytochemistry.

Results: MAP9 was localized at the base of connecting cilia in in $RPGRIP1^{ins/ins}$ canine retinas of all MAP9 genotypes. However, MAP9 expression was decreased in the presence of the $MAP9^{del/del}$ modifier. Cultured 661w cells showed that endogenous MAP9 was localized as two juxtaposing puncta. Upon ciliogenesis, there was cilia extension from one of the two MAP9-positive puncta where MAP9 signals extend into the cilia structure. RPGRIP1 signals were comparable with and without ciliogenesis, forming loose aggregates corresponding to the site of the base of cilia. Overexpressed MAP9 proteins exhibited broad cytoplasmic expression but with increased signals corresponding to the site of RPGRIP1 aggregates. Interestingly, the lengths of primary cilia were significantly increased in cells transfected with MAP9-Wt than those with MAP9-Mut.

Conclusions: Ex vivo and in vitro colocalization suggests that MAP9 interacts directly or indirectly with RPGRIP1 in photoreceptor primary cilia. MAP9 might play an important role in the formation and functional regulation of primary cilia. The MAP9-Mut protein may lack normal MAP9 function resulting in altered cilia characteristics leading to the accelerated disease onset observed in cord1 dogs.

CONTROL ID: 3709886

SUBMITTER (NAME ONLY): Theodore Leng

TITLE: Characterizing real-world functional outcomes in patients with geographic atrophy: An IRIS Registry Analysis

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Leng, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|D.S. Borkar, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|M. Hatfield, S. Li, M. Gallivan, Verana Health, California, UNITED STATES|P. Joshi, A. McKeown, Apellis Pharmaceuticals Inc, Crestwood, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Geographic atrophy (GA) impairs visual function and patient quality of life (QoL). However, real-world data (RWD) on correlations between GA progression and functional decline are lacking. To address this gap, we performed a retrospective cohort analysis of patient notes to assess the feasibility of quantifying vision-related QoL (VR-QoL) and patient-reported outcomes (PRO) in GA.

Methods: Documentation of VR-QoL was assessed in a random sample of GA patient notes from the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight), a real-world electronic health record (EHR) dataset. Two cohorts were studied: (1) incident GA cases in 2019 analyzed on the date of diagnosis, and (2) prevalent GA cases first diagnosed in 2016 with notes at Year 3 of follow-up. Notes were searched for keywords associated with visual function, mental health, mobility, and independence. For frequently documented functional outcomes, clinical context was analyzed in 50 relevant notes per word.

Results: The mean age of incident (n=101) and prevalent (n=97) GA patients was 80.6 years (SD=7.5) and 81.9 years (SD=6.3), respectively. 54% of incident and 62% of prevalent patients had subfoveal GA; 27 – 39% had concomitant glaucoma or cataract. The majority of patients were managed by retina specialists. Functional outcomes were rarely documented in patient notes: keywords “reading” and “driving” were found in <10% of records. “Low vision” was mentioned in <3% of notes, while “anxiety / depression” was noted in <2%. “Mobility / independence / disability” were not found. 64% of driving-related notes discussed trouble driving or night driving; 44% of reading-related notes indicated impairment, while 32% discussed reading glasses or aids. 74% of low-vision-related notes recommended a low vision consultation.

Conclusions: VR-QoL and PROs are infrequently documented in the EHR by ophthalmologists. Sparse documentation limits the use of standalone EHR note data for QoL/PRO assessment. Retina specialists often refer GA patients to low vision specialists, who may be more likely to monitor and document changes in VR-QoL. While regulatory agencies have advocated for the use of patient-centered outcomes in clinical trials, real-world assessment of PROs is lacking, necessitating improved tools to collect RWD on patient QoL.

CONTROL ID: 3709889

SUBMITTER (NAME ONLY): Arunkumar Ranganathan

TITLE: Macular Carotenoids Lutein (L) and Zeaxanthin (Z) Protect Human Retinal Pigment Epithelial (RPE) Cells from Cobalt chloride-Induced Hypoxia Stress.

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ranganathan, B. Li, P.S. Bernstein, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Arunkumar Ranganathan: Commercial Relationship: Code N (No Commercial Relationship) | Binxing Li: Commercial Relationship: Code N (No Commercial Relationship) | Paul Bernstein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Hypoxia-induced oxidative stress is one of the vital factors that activate the pathogenic mechanism of retinal diseases such as diabetic retinopathy and retinopathy of prematurity. Cobalt chloride ($CoCl_2$) is a commonly used hypoxia mimetic agent that induces oxidative stress-mediated apoptosis by generating reactive oxygen species (ROS). Most retinal diseases are irreversible with no effective treatment; therefore protecting the RPE cells from hypoxia stress is an effective therapeutic way to prevent or slow down the progression of retinal diseases. L and Z are potent antioxidants and can be used as an effective therapy for the treatment of hypoxia-induced oxidative stress. In this study, we evaluate the protective effect of L and Z from $CoCl_2$-induced hypoxia stress.

Methods: To determine the anti-hypoxia effect of L and Z, ARPE-19 cells were pretreated with 1, 2, and 5 μM of L and Z for 24 h and then incubated with and without 8mM $CoCl_2$ for 4 h. Cell viability was measured by incubating cells with 0.5 mg/ml MTT solution for 2 h in dark and measured at 550 nm. To determine ROS levels, cells were pretreated with 1, 2, and 5 μM of L and Z for 24 h, and then incubated with 2 μM 5-(and 6)- chloromethyl-dichlorodihydrofluorescein diacetate (CM-H_2DCFDA) reagent. Cells were measured at Ex/Em: 485nm/535nm.

Results: ARPE-19 cells treated with $CoCl_2$ result in reduced cell viability and increased ROS levels compared to the untreated $CoCl_2$. Cells pretreated with L and Z before $CoCl_2$ treatment efficiently attenuate $CoCl_2$ induced cytotoxicity and ROS levels in a dose-dependent manner (1-5 μM). Pretreatment with 5 μM of L significantly increase the cell viability by 1.3 fold and decrease the ROS levels by 1.7 fold. Pretreatment with 5 μM of Z significantly increased the cell viability by 1.5 fold and decreased the ROS levels by 2.2 fold compared to control (without carotenoid treatment).

Conclusions: L and Z protect ARPE-19 cells from $CoCl_2$-induced hypoxia stress and attenuate cytotoxicity and ROS levels. Z had a comparatively better protective effect relative to L. This may be due to their better antioxidant activity, but a further detailed study is warranted. Macular carotenoids alone or in combination with other nutrients can be used in the prevention of hypoxia-related retinal diseases.

CONTROL ID: 3709890

SUBMITTER (NAME ONLY): Karen Torrejon

TITLE: Blood-Retinal -Barrier 3D Model Using Microfabricated Porous Scaffolds

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.Y. Torrejon, A. Unser, H. Afzaal, H. Williams, F. Ahmed, Glauconix Biosciences Inc, Albany, New York, UNITED STATES|P.A. D'Amore, Schepens Eye Res Inst of Mass. Eye & Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of therapies that target blood-retinal barrier (BRB) disruption is hindered by a lack of reliable in vitro models that recapitulate the biology and pathophysiology of BRB-related diseases. We aimed to engineer a model of the human BRB and to validate the model by inducing changes in permeability and testing agents currently employed in the clinic.

Methods: Scaffolds coated with hyaluronan-based hydrogel were seeded with primary human retinal microvascular endothelial cells (hRMVECs) and allowed to grow for 7 days. Scaffolds were inverted, primary human pericytes (PCs) were added and were grown for an additional 6 days. The cocultures were treated with TNF-α (5 ng/mL) or IL1β (10 ng/mL) for 72 hrs then exposed to bevacizumab (0.25 ng/mL), aflibercept (500 ug/mL), prednisolone (100 nM), dexamethasone (100 nM) and/or VEGF-121 (100 ng/mL for 6 days. Expression of endothelial and pericyte markers was examined by immunofluorescence and barrier function was assessed by measuring transendothelial cell resistance (TEER).

Results: The scaffolds supported the growth of the cocultures into a 3D structure. The endothelium expressed CD31, VE-cadherin, ZO1 and VWF whereas the PCs expressed NG2, PDGFR-β and NGFRP75. The TEER day 11 was 223.9±26.5 $\Omega*cm^2$ (N=9). Compared to monocultures, the constructs displayed enhanced expression of VE-cadherin (***P<.001, N=6), CD31 (**P<.005, N=6), PDGFR-β and NG2. Treatment with TNF-α or IL1β decreased ZO-1 and F-actin labeling and led to disrupted localization of VE-cadherin. Endothelial morphology changed from cobblestone to spindle-shaped, and F-actin was localized to the edges and tips of the cells, suggesting cell motility. Treatment with a combination of VEGF neutralizing agents and steroids rescued VE-cadherin expression and its localization at cell junctions, suggesting restoration of barrier integrity. VEGF neutralization alone led to more cytoplasmic localization of VE-cadherin.

Conclusions: These results demonstrate the feasibility of creating a 3D model of the BRB with key physiological and biological characteristics that will be valuable for screening therapeutics as well as understanding the development and maintenance of the BRB.

CONTROL ID: 3709892

SUBMITTER (NAME ONLY): Nish Patel

TITLE: Safety and outcomes of intraoperative intravitreal injection of dexamethasone after air-fluid exchange in pars plana vitrectomy for diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Patel, V. Kasetty, T. Looysen, A. Hamad, Ophthalmology, Henry Ford Hospital, Detroit, Michigan, UNITED STATES|S. Ketkar, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endolaser (EL) can cause significant inflammation as well as serous choroidal and retinal detachments. A 2003 study noted improvement in postoperative (PO) inflammation after a single intravitreal injection of dexamethasone (DEX) following pars plana vitrectomy (PPV). However, none of these patients underwent air-fluid exchange (AFE). We aim to determine the safety and efficacy of intraoperative intravitreal injection of DEX after AFE in PPV with EL for diabetic retinopathy (DR).

Methods: A retrospective consecutive study was conducted over a one-year period. 23 eyes (21 patients) met inclusion criteria for the study: subjects 18 years of age or older who intraoperatively received a single intravitreal injection of DEX (0.2 mg) after PPV with AFE and EL for DR complications. Data analysis was performed with SAS 9.4 (SAS Institute Inc, Cary, NC, USA).

Results: The mean logMAR best corrected visual acuity (BCVA) at the pre-operative visit was 1.45 (median=1.30, SD=1.03). Twenty-two (95.7%) eyes had an intraocular pressure (IOP) in the normal range (0- 21) at this visit, and one eye had an IOP of 25. No eyes had significant anterior chamber (AC) inflammation prior to PPV. After AFE, two (8.7%) eyes were left under C_3F_8 gas, one (4.3%) under SF_6 gas, and two (8.7%) under silicone oil (SO). Median improvement in BCVA was noted at the PO one month (-0.7, p=0.0277) and three month (-0.9, p=0.0150) visits. Seventeen (94.4%) eyes had an IOP in the normal range at the three month PO visit; one (5.6%) had an IOP of 22. No eyes demonstrated significant AC inflammation at the PO one and three month visits. Three (13.0%) eyes required an intravitreal injection within six months after PPV. The mean central retinal thickness per optical coherence tomography was 367.61 µm (median=302.0, SD=181.9) at a mean PO period of 153.7 days (median=174.00, SD=64.3). Five (21.7%) eyes exhibited choroidal detachments on PO day one; all of which self-resolved by week one. Three (13.0%) eyes underwent repeat PPV: one for proliferative vitreoretinopathy, one for vitreous hemorrhage, and one for SO removal.

Conclusions: A single intravitreal injection of DEX after PPV with EL and AFE appears to be safe. Further studies comparing groups that receive intravitreal DEX to those that do not are warranted to assess the effectiveness of this intervention in improving PO outcomes.

CONTROL ID: 3709894
SUBMITTER (NAME ONLY): Gloria Nashed
TITLE: Inadequacy of ICD Codes for Phenotyping Inherited Retinal Diseases
SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G. Nashed, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|S. Gangaputra, M.A. Brantley, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|
Commercial Relationships Disclosure: Gloria Nashed: Commercial Relationship: Code N (No Commercial Relationship) | Sapna Gangaputra: Commercial Relationship: Code N (No Commercial Relationship) | Milam Brantley: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRDs) are a diverse group of diseases that can possibly lead to blindness. Ongoing clinical trials are testing the potential for gene therapy as treatment for certain IRDs. Physicians treating IRD patients should know which patients qualify for these trials. However, one barrier for identifying these patients is the limited scope of ICD codes for IRDs. In this retrospective chart review, we use peripheral and macular IRDs to test the hypothesis that some retinal dystrophies are not well represented in current ICD nomenclature compared to more well-known IRDs like retinitis pigmentosa (RP) and Stargardt disease (STGD).

Methods: This study was conducted with approval of the Vanderbilt University Medical Center Institutional Review Board/Ethics Committee. Manual chart review was performed for 250 patients who were isolated from the Vanderbilt Eye Institute electronic health record based on ICD10 H35.52 (peripheral retinal dystrophies) and for 281 patients who were isolated based on ICD10 H35.50 or H35.53 (macular dystrophies). Phenotypes of peripheral disease that were analyzed include RP, rod-cone dystrophy, and Usher syndrome. Phenotypes of macular disease that were analyzed include STGD, macular pattern dystrophy, vitelliform dystrophy, Sorsby fundus dystrophy (SFD), and cone/cone-rod dystrophy. The proportion of patients whose ICD designation aligned with the diagnosis made by an IRD specialist was then calculated for each phenotype.

Results: In the peripheral disease group, the percentage of accurate diagnoses are as follows: 70.8% for RP, 4.8% for rod-cone dystrophy, and 7.6% for Usher syndrome. In the macular disease group, the percentage of accurate diagnoses are as follows: 14.9% for STGD, 31.3% for macular pattern dystrophy, 1.07% for vitelliform dystrophy, 1.4% for SFD, and 8.9% for cone/cone-rod dystrophy.

Conclusions: Our results reveal low concordance between the clinician’s diagnosis and the ICD codes for peripheral and macular IRDs, even including well-known diseases such as RP, STGD, and macular pattern dystrophy. This suggests that current ICD nomenclature is unable to adequately encompass many IRD phenotypes, making big data analysis challenging for these diseases. More specific ICD10 codes are needed to phenotype these IRD patients to help physicians more readily identify those who qualify for IRD clinical trials.

CONTROL ID: 3709896

SUBMITTER (NAME ONLY): Jennifer Lopez

TITLE: Subretinal Deposits in Young Patients Treated with Voretigene Neparvovec-rzyl for RPE65-mediated Retinal Dystrophy

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lopez, M.S. Borchert, T. Lee, A. Nagiel, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|J. Lopez, M.S. Borchert, T. Lee, A. Nagiel, Ophthalmology, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Jennifer Lopez: Commercial Relationship: Code N (No Commercial Relationship) | Mark Borchert: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Lee: Commercial Relationship: Code N (No Commercial Relationship) | Aaron Nagiel: Commercial Relationship(s);Code C (Consultant/Contractor):Consultant for Biogen, REGENXBIO, Novartis, and Allergan Retina.

ABSTRACT BODY:

Purpose: To report the phenomenon of subretinal deposits and discuss its possible causes in 3 young patients treated with voretigene neparvovec-ryzl (VN) for RPE65-mediated retinal dystrophy.

Methods: This is a retrospective interventional case series at a single tertiary referral center.

Results: We report a series of 3 young patients ages 22 months, 2 years, and 5 years old who developed subretinal deposits following subretinal VN treatment for RPE65-mediated retinal dystrophy. All 3 patients underwent bilateral surgery with each eye treated 7-10 days apart. At post-operative week 1, curvilinear subretinal deposits were noted inferior to the original bleb location in all three patients. In the 5-year-old patient, more extensive sheets of subretinal white deposits were observed in the inferior periphery of both eyes with no signs of inflammatory leakage on fluorescein angiography. All three patients experienced improved visual function with treatment, and both the macular and inferior subretinal deposits have improved or resolved over the follow-up period.

Conclusions: We describe subretinal deposits following VN in three young children as a phenomenon not well described in the clinical trials. The appearance and location of the deposits suggest that blebs migrate after air-fluid exchange and that there may be transient subretinal inflammation at the time of treatment. These findings may inform the delivery parameters and safety profile of AAV-based gene therapy in young children, and in general, as the number of retinal gene therapy trials continues to grow.

CONTROL ID: 3709898

SUBMITTER (NAME ONLY): KARLA BARRERA

TITLE: Association of the insertion / deletion polymorphism of the angiotensin converting enzyme gene with the presence and severity of diabetic retinopathy

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.E. BARRERA, S. ROJAS JUAREZ, Retina, Hospital Fundacion Nuestra Señora de la Luz IAP, Cuauhtémoc, Ciudad de México, MEXICO|H.J. Pérez, Centro de investigación biomédica, Hospital Fundacion Nuestra Señora de la Luz IAP, Cuauhtémoc, Mexico City, MEXICO|

Commercial Relationships Disclosure: KARLA BARRERA: Commercial Relationship: Code N (No Commercial Relationship) | Hector Pérez: Commercial Relationship: Code N (No Commercial Relationship) | SERGIO ROJAS JUAREZ: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The I / D polymorphism of the angiotensin converting enzyme (ACE) gene has been the main gene that predisposes to the development of diabetic retinopathy (DR). Activation of I/D is associated with increased ACE activity in plasma, and this elevated activity accelerates the development of DR; however, the evidence for this association is limited and, to date, no association between severity and polymorphism has been demonstrated. A retrospective, observational and analytical case-control study performed to determine whether the deletion / insertion polymorphism of the gene encoding ACE is related to the presence and severity of DR, and to identify the allele with the highest risk.

Methods: 90 subjects were studied in each group. Study group: subjects with a diagnosis of DR at any stage according to ETDRS. Control group: subjects without: DR, retinal involvement, ocular pathology caused by microvascular etiology, diabetes mellitus or systemic arterial hypertension.

DNA was obtained, ECA gene was identified by amplification of the polymorphic region of the gene, with the PCR technique, using specific oligonucleotides and they were analyzed by electrophoresis. Comparative analysis of allelic and genotypic frequencies was performed with Fisher's exact test and the odds ratio was calculated.

Results: DNA analysis has been performed on 28 control patients and 32 patients with diabetic retinopathy.

27 control subjects and 32 patients with DR were studied. The metabolic measurement results were significantly higher in patients. The most frequent allele in patients was insertion (I), when compared with the deletion allele (D), a 3.22-fold risk of presenting DR was obtained in patients with genotype I/I (p 0.007). Frequency of allele I in patients was 73%, in controls 57% (p = 0.013), OR was 2.04. Regarding severity, genotype I/I its being higher in study group with greater severity according to the ETDRS (p <0.0001).

Conclusions: The I / D polymorphism plays a determining role in the development and progression of DR, however more genetic studies are needed on the ACE polymorphism and its etiopathogenic association with DR. The results obtained in this study carried out in the Mexican population were found to differ from those reported in the bibliography. (DNA study and statistical analysis with final n: 180, will be carried out in the next weeks)

CONTROL ID: 3709900

SUBMITTER (NAME ONLY): Irina Sverdlichenko

TITLE: Anemia and idiopathic intracranial hypertension: a retrospective observational and case-control study

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Sverdlichenko, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|W. Yu, Division of Ophthalmology, Department of Surgery, McMaster University, Hamilton, Ontario, CANADA|E. Margolin, J. Micieli, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|J. Micieli, Kensington Vision and Research Centre, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The relationship between anemia and idiopathic intracranial hypertension (IIH) continues to be controversial. The goal of the present study was to: 1) Determine the relative prevalence of anemia in IIH patients compared to age and sex-matched controls attending neuro-ophthalmology clinics and 2) To compare the initial and final visual outcomes of IIH patients with and without anemia.

Methods: 123 consecutive IIH patients were recruited from tertiary neuro-ophthalmology clinics and matched by age and sex to 113 non-IIH neuro-ophthalmology controls. Retrospective chart review obtained information on demographics, symptoms and visual function at presentation and final follow-up. Complete blood counts (CBC) were collected within 6 months of diagnosis and 3 months of final follow-up and anemia diagnosis was made based on hemoglobin <120g/L for women and <130g/L for men. Anemia was further classified as mild (hemoglobin >110g/L), moderate (hemoglobin 80-109g/L), and severe (hemoglobin <80g/L). The study protocol was approved by the appropriate institutional research ethics board.

Results: More IIH patients than controls met criteria for anemia (22.8%, 28/123 versus 10.6%, 12/113, p=0.01), with an odds ratio of 2.48 (95% CI 1.19-5.16). IIH patients had a significantly lower mean hemoglobin than controls (127.6g/L ± 18.0 versus 133.0g/L ± 11.8, p<0.01) and 17.9% (5/28) of anemic IIH patients had severe anemia compared to zero in the control group. When comparing the 28 IIH patients with anemia to the 95 IIH patients without anemia, there were no differences between groups in terms of sex, age, body mass index (BMI) or symptomatology. IIH patients with anemia were more likely to have mild-to-moderate visual acuity impairment (logMAR 0.3-1; 14.3%, 8/56 eyes versus 3.7%, 7/190 eyes, p=0.01) and worse Humphrey mean deviation (-5.7dB + 8.1 versus -3.4dB + 4.2, p=0.048) compared to non-anemia IIH patients at presentation. At final follow-up, there was no difference in visual acuity, but Humphrey mean deviation continued to be worse among anemic IIH patients (-5.6dB + 6.4 versus 3.2dB + 5.7, p=0.045).

Conclusions: Anemia is more prevalent among IIH patients compared to neuro-ophthalmology controls and may influence the initial and final visual function in IIH patients. As a CBC is a widely available test, we suggest that this test be obtained in all patients with new papilledema.

CONTROL ID: 3709903
SUBMITTER (NAME ONLY): Niranjana Kesavamoorthy
TITLE: Fluorescent lifetime imaging microscopy of fixed mice retina
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Kesavamoorthy, H. Ameri, Ophthalmology, USC Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|J.A. Junge, S. Fraser, Department of Biological sciences, University of Southern California Dana and David Dornsife College of Letters Arts and Sciences, Los Angeles, California, UNITED STATES|
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ABSTRACT BODY:
Purpose: To study retinal mouse metabolic states ex-vivo using novel tissue preparation and fluorescent lifetime imaging microscopy (FLIM).
Methods: Wild type C57BL/6J mice were included in the study. Following euthanasia and enucleation, corneas were removed, and eyecups were fixed overnight in a 4% Paraformaldehyde (PFA) solution. The next day, eyecups were embedded in polyacrylamide, and 200 µm thick retinal sections were made using a vibratome. Images were taken using the Leica SP8 DIVE FALCON for multiphoton FLIM measurements of metabolic states and tissue structure, using the phasor approach to FLIM analysis. Tissue excitation was performed with 740 nm light from our ultrafast tunable laser at ~500 µW power. FLIM was collected simultaneously on two hybrid detectors from ~425-475 nm for NADH and ~530-650 nm for FAD, retinoids and hemoglobin.
Results: The percentage of bound NADH was ~50% in the retinal pigment epithelium, ~55% in the photoreceptor layer and 60-70% in the inner retina, indicating higher glycolysis in the outer retina and higher oxidative phosphorylation in the inner retina. This finding in fixed tissues, recapitulated previous findings of live-tissue metabolic FLIM NADH measurements. Additionally, our study showed that the hemoglobin signal in the vasculature has a distinct FLIM profile allowing visibility of retinal capillaries on 3-dimensional images as they penetrate the retina and form capillary plexus at different layers. This novel tissue preparation, imaging, and analysis pipeline enable the reconstruction of metabolic states of tissue layers, cells, stroma, and vasculature in 3 dimensions, without the need for staining techniques.
Conclusions: FLIM of retinal sections in mice showed a predominance of glycolysis in the outer retina and oxidative phosphorylation in the inner retina. With additional autofluorescence excitation and emission strategies, FLIM could be used to define the structure and metabolism of healthy versus diseased retinas.

CONTROL ID: 3709907

SUBMITTER (NAME ONLY): Chifune Kai

TITLE: Association between severity grading and visual function in patients with Fuchs endothelial corneal dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kai, Y. Oie, N. Nishida, S. Doi, C. Fujimoto, S. Asonuma, T. Soma, S. Koh, R. Kawasaki, K. Nishida, Ophthalmology, Osaka Daigaku, Suita, Osaka, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the relationship between severity grading and visual function in patients with Fuchs endothelial corneal dystrophy (FECD).

Methods: This prospective study included 49 eyes of 27 patients with FECD and 10 eyes of 10 normal subjects in the outpatient clinic in the Department of Ophthalmology at Osaka University Hospital. Subjects with cataract N3 or more, and after keratoplasty were excluded. We determined modified Krachmer grade for each subject, and evaluated corrected distance visual acuity (CDVA), contrast sensitivity (AULCSF), and central corneal thickness (CCT). We analyzed the association between the severity grading evaluated using modified Krachmer grade or CCT and visual function shown as CDVA or AULCSF.

Results: For FECD patients, the average age was 63.1±11.3 years. 22 female and 5 male patients were included. The average CDVA, AULCSF and CCT of the patients were 0.02±0.16 (logMAR), 0.98±0.27, 580±47μm, respectively. There were significant differences in CDVA and AULCSF between modified Krachmer grades ($p = 0.0002$, $p < 0.0001$, respectively). Especially, the differences between grade 0 and 3, 4, or 5 were significant by Steel-Dwass analysis (CDVA: $p = 0.03$, $p = 0.003$, $p = 0.02$, AULCSF: $p = 0.004$, $p = 0.0006$, $p = 0.04$, respectively). There were also significant differences in CDVA and AULCSF between CCT grades ($p < 0.0001$, both). Particularly, the differences between normal eyes and CCT of <550 μm, or between 550-599 μm and ≥ 600 μm were significant by Steel-Dwass analysis (CDVA: $p = 0.002$, $p = 0.002$, AULCSF: $p = 0.03$, $p = 0.0004$, respectively).

Conclusions: It was suggested that the visual function was significantly impaired in FECD patients with modified Krachmer grade 3 or worse. This threshold can be considered for surgical indication of endothelial keratoplasty in terms of visual function. However, CCT might not be suitable for an indicator of surgical intervention because visual function was significantly affected even in patients with normal CCT.

CONTROL ID: 3709909

SUBMITTER (NAME ONLY): Yukari Nakano

TITLE: Effect of inter-pulse interval on suprachoroidal-transretinal stimulation efficiency in retinal prosthesis

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Nakano, Y. Terasawa, Artificial Vision Institute, R&D Div, Nidek Co., Ltd., Gamagori, Aichi, JAPAN|T. Ueno, R&D Div, Nidek Co., Ltd., Gamagori, JAPAN|H. Sawai, Department of Health Sciences, School of Nursing, Osaka Prefecture University, Habikino, Osaka, JAPAN|

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ABSTRACT BODY:

Purpose: We previously reported that stimulation efficiency of retinal prosthesis decreases during suprachoroidal-translationally applied trains of stimulus pulses at the frequency of 20 Hz [Y. Nakano, et al. IOVS 2020;61:2210]. To understand the underlying mechanism that led to the decrease, we have investigated how inter-pulse interval (IPI) affects electrical stimulation efficiency in acute animal experiments.

Methods: Field potentials were recorded from the right superior colliculus of healthy adult rats (Long-Evans, n = 7) anesthetized with urethane. Paired-pulse trans-retinal electrical stimulation (TES) at an IPI of 20-200 ms was focally delivered to the sclera of the left eyeball. Each pulse was cathodic-first biphasic, with no gap term (Fig. 1). The amplitudes of evoked potentials (EPs) to the second TES pulse were compared with those to the first one.

Results: The second EPs were significantly suppressed ($p < 0.05$, paired t-test) by 35% of the first EPs at 60 ms and 80% at 100 ms, of IPI. The relative amplitude of the second EP to the first, recovered at 200 ms, is shown in Fig. 2.

Conclusions: In this study, the length of IPI affected the EP of the second pulse. In the future, we will investigate the IPI that can minimize the decrease in EP after the second pulse, during continuous stimulation.

CONTROL ID: 3709911

SUBMITTER (NAME ONLY): Han Yu Zhang

TITLE: Myopia control effect of Defocus Incorporated Multiple Segments (DIMS) spectacle lens is influenced by baseline relative peripheral refraction

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zhang, C. Lam, W. Tang, C. To, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|H. Zhang, C. Lam, C. To, Centre for Eye and Vision Research (CEVR),, HONG KONG|M. Leung, Discipline of Optometry and Vision Science, University of Canberra, Canberra, Australian Capital Territory, AUSTRALIA|H. Qi, Hoya Corporation, JAPAN|P. Lee, Department of Health Sciences, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Study if baseline relative peripheral refraction (RPR) profile influences myopia progression in Chinese myopic children wearing Defocus Incorporated Multiple Segments (DIMS) compared to single vision (SV) spectacle lenses.

Methods: Data from a 2-year randomized controlled trial were analyzed retrospectively. Peripheral refraction at 10°, 20°, and 30° nasal (10N, 20N, 30N) and temporal (T) retina were measured for the DIMS and SV group. Subjects were subdivided into two subgroups according to baseline RPR: myopic RPR (RPR ≤ 0 D) and hyperopic RPR (RPR > 0 D) subgroup. Myopia progression and axial elongation over 2 years were compared further between myopic RPR and hyperopic RPR subgroup within the SV and DIMS group.

Results: 79 subjects and 81 subjects in the DIMS and SV group were investigated respectively. The comparison between myopic RPR and hyperopic RPR at 10N and 20N was presented as other positions did not show statistically significant results. In the SV group, no statistically significant differences were noted in myopia progression (mean difference: -0.26±0.14 D, p=0.06) and axial elongation (mean difference:0.04±0.05 mm, p=0.48) between the myopic RPR (n=27) and hyperopic RPR (n=54) 10N subgroups. There was also no significant difference in myopia progression (mean difference: -0.25±0.20 D, p=0.19) and axial elongation (mean difference: 0.08±0.08 mm, p=0.27) between myopic RPR (n=11) and hyperopic RPR (n=70) subgroups at 20N. However, in the DIMS group, children with myopic RPR at 10N (n=27) showed significantly more myopia progression (mean difference: -0.36±0.14 D, p=0.009) and more axial elongation (mean difference: 0.16±0.05 mm, p=0.001) than the children with hyperopic RPR at 10N (n=52). And myopic RPR at the 20N subgroup (n=12) showed significantly more myopia progression (mean difference: -0.40±0.16 D, p=0.01) and more axial elongation (mean difference: 0.15±0.07 mm, p=0.02) than the hyperopic RPR at 20N subgroup (n=67).

Conclusions: The baseline RPR profile showed no influence in myopia progression of the SV lens wearers. DIMS lens wearers showed better efficacy in myopia control in children with relatively more baseline hyperopic RPR than children with relatively baseline myopic RPR. This suggests that using customized peripheral myopic defocus based on individual baseline RPR may help to improve myopia control effects.

CONTROL ID: 3709913

SUBMITTER (NAME ONLY): Yu Huang

TITLE: Retinal vascular features as new biomarkers for aortic aneurysms and aortic dissections

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Huang, X. Zhang, Z. Zhu, X. Zhang, S. Tang, X. Shang, C. Li, M. He, Guangdong Provincial People's Hospital Department of Ophthalmology, Guangzhou, Guangdong, CHINA|D. Shi, M. He, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: The onset and progression of aortic aneurysms are asymptomatic, which eventually becomes a life-threatening event when the vessel wall is dissected or ruptured. The screening and diagnosing of aneurysms are expensive and sometimes invasive. Retinal vascular features (RVFs) are measured easily and non-invasively, they reflect the systemic vascular properties as well as the clinical risk factors for aneurysms, hence they can be the potential biomarkers for aortic aneurysms and dissections. In this study, we used the genetic information of aneurysms as the genotypes and RVFs as phenotypes and conducted a phenome-wide association study (PheWAS), in order to identify novel imaging biomarkers which can assist the early diagnosis of aortic aneurysms.

Methods: The study was conducted within the UK Biobank participants. Digital retinal fundus images from the right eyes were used. A machine learning method was used to extract the RVFs, which resulted in 91 quantitative features. Genetic risk scores (GRS) for abdominal, thoracic and intracranial aneurysms were generated by PLINK and SNPs representing 4 different Marfan genes (FBN1, COL16A1, LOC728241 and LOC441376) were extracted. The R package 'PheWAS' was used and age, sex, blood pressure and BMI were adjusted as covariates.

Results: A total number of 50380 participants were included. In the PheWAS, after Bonferroni correction, 6 RVFs which represent the vessel caliber, complexity or tortuosity were associated with abdominal aneurysm, and 'artery_calibre' and 'number_of_vascular_tree' (ntree_a) were associated with thoracic (β=0.06, P=4.41e-05) and intracranial (β=-0.09, P=9.92e-05) aneurysms respectively. The 'ntree_a' was shared between abdominal and intracranial aneurysms. For Marfan genes, 'mean_artery_curve_angle' (CurveAngle) was common for all 4 genes (FBN1:β=-0.09, P=4.30e-10; COL16A1:β=-0.07, P=4.28e-08; LOC728241:β=-0.05, P=1.26e-04; LOC441376:β=0.07, P=1.75e-05), and 'ntree_a' was shared by 3 genes (FBN1:β=-1.52, P=3.53e-14; COL16A1:β=-0.04, P=2.71e-04; LOC728241:β=-0.04, P=4.27e-04) (Figure 1). Among the overall traits, 'ntree_a' and 'CurveAngle' were the most common RVFs (Figure 2).

Conclusions: The PheWAS identified several RVFs that are associated with different types of aneurysms. Among them, 'ntree_a' and 'CurveAngle' are most commonly identified by different aneurysms, suggesting they are potential vascular biomarkers for aneurysms.

CONTROL ID: 3709916

SUBMITTER (NAME ONLY): Sachin Phakey

TITLE: Impact of COVID-19 on ophthalmic surgery in Australia

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Phakey, L.L. Lim, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|A.J. Hall, Ophthalmology, Alfred Health, Melbourne, Victoria, AUSTRALIA|A.J. Hall, Department of Surgery, Central Clinical School, Monash University, Clayton, Victoria, AUSTRALIA|L.L. Lim, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Sachin Phakey: Commercial Relationship: Code N (No Commercial Relationship) | Anthony Hall: Commercial Relationship: Code N (No Commercial Relationship) | Lyndell Lim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The effect of coronavirus disease 2019 (COVID-19) on ophthalmic surgical case numbers in Australia and globally remains poorly characterised. Increased incidence of COVID-19 in Australia between March and April 2020 led to a national lockdown and elective surgery restrictions. The aim of this population-based study was to quantify the early impact of COVID-19 on ophthalmic surgery in Australia, comparing surgical service rates in 2019 and 2020.

Methods: Retrospective analysis of the number of ophthalmic surgical services in 2019 and 2020 in all Australian States and Territories, as recorded by Medicare (Australian Government-funded universal health insurance scheme subsidising healthcare costs for Australian residents). Monthly surgical service rates were calculated and Poisson regression was used to compare the change in service rates between months.

Results: Between March and April 2020, surgical service rates decreased for: cataract surgery (by 71%, 95% CI: 70-72%), cataract surgery with minimally invasive glaucoma surgical device insertion (by 71%, 95% CI: 65-75%), pterygium removal (by 67%, 95% CI: 60-72%), corneal transplantation (by 31%, 95% CI: 9-48%), and collagen crosslinking for corneal ectasias (by 35%, 95% CI: 18-48%). Comparatively, service rates for these surgeries did not differ or decreased less between March and April 2019. Interestingly, glaucoma filtration surgery rates decreased between March and April in 2020 (by 44%, 95% CI: 29-56%) and also in 2019 (by 45%, 95% CI: 31-55%), whilst retinal detachment surgery rates were unchanged between these months in 2020 (crude decrease 9%, 95% CI: -28 to 16%) and 2019 (crude decrease 11%, 95% CI: -26 to 9%).

Conclusions: Despite relatively low rates of COVID-19 community transmission in Australia in 2020, ophthalmic surgical service rates decreased during months in lockdown and with restrictions, largely for non-time-critical conditions. These data may have health planning implications as the pandemic continues, with future lockdowns and restrictions possible, especially as COVID-19 variants emerge.

CONTROL ID: 3709917

SUBMITTER (NAME ONLY): Livia Brier

TITLE: Anti-TNFα conjugates for treatment of posterior chronic non-infectious uveitis

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Brier, A. Twite, A. Barnebey, M. Mahomed, W.M. Jackson, Valitor, Inc, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chronic non-infectious uveitis (NIU) can result in nerve damage and vision loss. Most patients are treated using corticosteroids, which can lead to serious side effects. Intravitreal (ITV) administration of biologic TNFα inhibitors can substantially reduce the need for steroids. However, these products were not designed or validated for ITV use, and off-label ITV treatment with existing TNFα inhibitors is not recommended. Valitor is developing an anti-TNFα biologic specifically designed for ITV administration with a projected treatment frequency of only 2-3 times per year as a steroid-sparing treatment for chronic NIU.

Methods: We synthesized multivalent protein (MVP) conjugates comprising multiple copies (i.e. valency) of anti-TNFα antibodies bound to soluble hyaluronic acid biopolymers. We determined MVP binding affinity to TNFα using biolayer interferometry and cell bioassays. We assessed the ITV half-life of MVPs by delivering 50 µL of fluorescently-tagged MVP to rabbit eyes and measuring the amount of drug remaining in the eye after over time. We also evaluated the efficacy of anti-TNFα MVPs in a rat model of experimental autoimmune uveitis (EAU). Ocular inflammation was induced in rats by injecting 50 µg of interphotoreceptor retinoid-binding protein in 200 µL of complete Freund's adjuvant. At early stages of disease onset (6 and 8 days after induction), we delivered either 12.6 µg anti-TNFαMVPs, 40 µg of dexamethasone (dex), or vehicle control via 5 µL ITV injection. We assessed inflammation by ocular examination and ocular tissue histopathology.

Results: Based on binding affinity measurements, we found that MVP potency increased directly with valency, and at high valency, the potency of MVPs were substantially (~100X) greater than the unconjugated protein controls. The ITV half-life of the MVPs was also to 6-8 times longer than unconjugated therapeutics. EAU inflammation in rats treated with anti-TNFα MVPs was similar to those treated with dex, and both treatments reduced inflammation compared to the vehicle control.

Conclusions: The MVP platform appears capable of increasing the potency and ITV durability of anti-TNFα inhibitors. By generating a sustained anti-inflammatory response with minimal systemic exposure, we expect our anti-TNFα MVP conjugates will enable a better overall safety profile compared other current treatment strategies for chronic NIU.

CONTROL ID: 3709920

SUBMITTER (NAME ONLY): Hannah Yoon

TITLE: Assessment of Corneal Epithelial Thickness in Patients after Hematopoietic Stem Cell Transplantation

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.H. Yoon, E. Shorter, C. Mun, J. Mun, A. Garcia, S. Jain, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare epithelial thickness in patients who developed ocular Graft Versus Host Disease (definite oGVHD) after hematopoietic stem cell transplantation (HSCT), and those who did not (none oGHVD).

Methods: In this retrospective chart review, patients with GVHD who underwent corneal epithelial thickness mapping at the Illinois Eye and Ear Infirmary between July 1, 2021 and October 15, 2021 were identified. Records were reviewed for corneal epithelial thickness data measured by optical coherence tomography (Optovue Avanti), Schirmer 1 test without anesthetic, corneal and conjunctival staining, and ocular surface disease index (OSDI) scores. Mean ± SD values of each corneal epithelial thickness variable (central 2mm, superior epithelial thickness 2-7mm, inferior epithelial thickness 2-7mm, standard deviation) were calculated for the definite and none oGHVD groups. Correlations of epithelial thickness and standard deviation to the signs and symptoms of dry eye were calculated.

Results: There were 136 definite oGVHD eyes and 40 none oGVHD eyes. The mean (± SD) central, superior, and inferior corneal epithelial thicknesses were 50.90 (± 6.60) um, 46.08 (± 7.21) um, and 52.15 (± 6.81) um in the definite oGHVD group, and 51.96 (± 4.01) um, 48.6 (± 4.71) um, and 53.36 (± 4.72) um in the none oGVHD group. The superior corneal epithelium was thinner in definite oGVHD eyes compared to none oGVHD eyes ($p = 0.048$), while there was no statistical difference in central or inferior epithelium. The variability of epithelial thickness (measured as standard deviation) was higher in definite oGVHD eyes (4.64 ± 2.23) compared to none oGVHD eyes (2.90 ± 1.08; $p < 0.0001$). OSDI scores were higher for patients with definite oGVHD (28.29 ± 23.79) compared to those without oGVHD (14.12 ± 17.21; $p = 0.001$). OSDI scores negatively correlated with superior epithelial thickness (Pearson coefficient = -0.207, $p = 0.007$) and positively correlated with epithelial thickness variability (Pearson coefficient = 0.228, $p = 0.003$).

Conclusions: In this series, eyes with definite oGHVD exhibited thinner superior corneal epithelial thicknesses and higher variability in epithelial thickness compared to eyes without oGVHD. Corneal epithelial mapping may be an objective and efficient method of diagnosing ocular GVHD.

CONTROL ID: 3709921

SUBMITTER (NAME ONLY): Jayant Iyer

TITLE: 5-Year progression of primary angle closure after treatment: the Primary Angle Closure Study (PACeS)

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is no recent evidence on progression rates of Primary Angle Closure (PAC) to Primary Angle Closure Glaucoma (PACG). We aimed to study the 5-year progression rates of treated PAC to PACG or acute primary angle closure (APAC).

Methods: A retrospective cohort study of 79 PAC subjects was performed. PAC was defined as iridotrabecular contact of 180 degrees or more, in the presence of raised intraocular pressure or peripheral anterior synechiae, without evidence of glaucomatous optic neuropathy. Data on intraocular pressure (IOP), gonioscopy, treatment instituted and time of progression to PACG or APAC were analyzed. In subjects with bilateral PAC, one eye per subject was randomly chosen for analysis.

Results: Of the 79 PAC subjects, 58 (73.4%) subjects were female and all subjects were of Chinese descent. All eyes were treated - 76 underwent initial laser peripheral iridotomy (LPI) and 3 underwent lens extraction as a primary procedure. During the follow-up period, 30 were started on IOP-lowering medications, and another 21 underwent cataract extraction. 14 of the eyes that underwent cataract extraction required medications. None of the eyes developed APAC. Only 4 eyes progressed to PACG over 5 years of follow-up, 3 of which remained phakic at time of progression.

Conclusions: These results suggest that the risk of progression of treated PAC to PACG is low. Our findings reveal lower rates of 5-year progression compared to previously published data. We found that cataract extraction reduces the likelihood of requiring glaucoma medications at 5 years.

CONTROL ID: 3709923

SUBMITTER (NAME ONLY): Zhengyang Xu

TITLE: Calcium responses to optogenetic stimulation decay faster in primate retinal ganglion cells after photoreceptor ablation

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: A number of vision restoration therapies aim to restore light sensitivity to retinal ganglion cells (RGCs) following extended periods of blindness. In rodent models of retinal degeneration, physiological changes in RGCs after photoreceptor (PR) loss have been reported but this has not been investigated in primates. By expressing both a calcium indicator (GCaMP6s) and an optogenetic actuator (ChrimsonR) in foveal RGCs of a macaque, we use in vivo imaging to assess changes in RGCs in the weeks and years following PR loss.

Methods: AAV2-CAG-GCaMP6s and AAV2-CAG-ChrimsonR-tdTomato were co-injected into the vitreous. Cones were ablated with a Mai-Tai pulsed laser (0.8 x 0.7o, 106 ms, 120-150mW, 730 nm) delivered through an adaptive optics scanning light ophthalmoscope (AOSLO). GCaMP fluorescence from 218 RGCs in two eccentricity matched regions of the fovea was collected using AOSLO and tracked over 10 weeks. In the first location (long-term deafferented) PR input was removed 2 years prior to recording, while in the second location (short-term deafferented) PR input was removed 1 week prior to recording. A 0.5 s, optogenetic stimulus (1 mW, 640 nm) was delivered to the RGCs, the GCaMP fluorescence was recorded for 90 s, and the decay fitted with an exponential model.

Results: Optogenetic responses in RGCs persisted for over 2 years following PR ablation. The mean time to peak calcium response did not differ significantly between the long-term (1.43±0.17s SD) and the short-term (1.45±0.30s SD) deafferented RGCs (unpaired t-test, $p=0.05$, $n=654$). The mean decay constant of the calcium response decreased 2.1 fold (2.5±0.5 s to 1.2±0.2 s SD) in the 8 weeks post PR ablation ($p<0.001$, paired t-test, $n=109$), with 87% of the decrease occurring within the first 5 weeks. The decay constant did not decrease further from week 8-10.

Conclusions: By expressing both an optogenetic actuator and a calcium indicator in foveal RGCs, we tracked the development of altered RGC physiology in vivo in the weeks and years following PR loss. The presence of optogenetic responses 2 years after PR loss and the stability of the rise time are promising for vision restoration therapies targeting RGCs, however, the 2.1 fold reduction of the calcium response decay constant suggests that restored activity may be impacted by changes in the inner retina weeks after PR loss.

CONTROL ID: 3709926

SUBMITTER (NAME ONLY): Susana Chung

TITLE: Local analysis reveals lower light sensitivity and thicker retinal layers of the amblyopic eyes near the fovea

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Visual deficits associated with amblyopia are often attributed to a cortical origin, with little contribution from the retina. Yet, controversial results have been reported in relation to whether the retinal structures and functions differ between the two eyes in amblyopia. The goals of this study were to compare light sensitivity and thickness of various retinal layers in local retinal regions, and to evaluate the correlations between sensitivity and layer thicknesses, between the amblyopic (AE) and the fellow (FE) eyes of observers with amblyopia.

Methods: Sixteen observers with amblyopia (age: 14 to 72 years, 7 with strabismic amblyopia and 9 with anisometropic amblyopia) participated in this study. Light sensitivity was measured at 37 retinal locations within the central 10° of the visual field for each eye of the observers using a MAIA microperimeter. The 37 locations included the center of the fixation location, and eccentricities at 1°, 3° and 5° along 12 meridians from fixation. Retinal structures were imaged using a Spectralis OCT, with 97 B-scans covering the central 20° of the visual field. En-face retinal images obtained using MAIA and Spectralis for the same eye were co-registered using custom-written software and thickness of the various retinal layers were extracted at each of the 37 retinal locations.

Results: Results were analyzed using linear mixed-effects models (observer as a random effect). Neither light sensitivity nor retinal layer thicknesses depended on the type of amblyopia. Sensitivity was 0.58 dB [SE 0.11] lower in the AE than in the FE. The difference in sensitivity between the two eyes was largest for retinal locations at 1° from fixation. Retinal layers were generally thicker in the AE than in the FE. Layer thickness was significantly correlated with light sensitivity across the central 10° (accounting for repeated measurements) for 6 of the 8 layers for FE, but only 2 of the 8 layers for AE.

Conclusions: Analyzing the function and structures of the retina for local regions, rather than pooling over much larger regions as in previous studies, revealed lower sensitivity and thicker retinal layers of the AE near the fovea, compared with the FE. Additionally, the AE showed an absence of correlations between sensitivity and layer thicknesses that were observed in the FE. These findings suggest that the retina may play a role in limiting vision in the AE.

CONTROL ID: 3709934

SUBMITTER (NAME ONLY): Daisuke Nagasato

TITLE: Foveal thickness fluctuation on visual and morphologic outcomes in anti-vascular endothelial growth factor treatments for branch retinal vein occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine the effects of foveal thickness (FT) fluctuation (FTF) of visual and morphologic outcomes in anti-vascular endothelial growth factor (VEGF) treatments with pro re nata regimen for Branch retinal vein occlusion (BRVO)- macular edema (ME).

Methods: We conducted a retrospective, observational case series (2012-2021) at a multi-center retinal practice among 309 treatment-naïve patients (309 eyes) with BRVO. FT was assessed via optical coherence tomography (OCT) at each study visit. We evaluated the logarithm of the minimal angle of resolution best corrected visual acuity (logMAR BCVA) and the defect length of the foveal ellipsoid zone (EZ) band measured via OCT.

Results: At baseline, the mean logMAR BCVA was 0.30±0.30 and the mean FT was 503±162 μm. The number of anti-VEGF injections for BRVO-ME was 5.8±4.6 during the mean follow-up period (50.6±22.2 months). At the final examination, the mean logMAR BCVA and FT values were significantly improved compared with the baseline. Multiple regression analyses showed that age, baseline logMAR BCVA, and FTF were significantly associated with the final logMAR BCVA (β=0.20, 0.35, and 0.30, respectively). FTF (divided into Groups 0-3 in ascending order of FTF) was significantly associated with the logMAR BCVA and the defect length of the foveal EZ band at the final examination. The defect lengths of the foveal EZ band were longitudinally shortened in Groups 0-1 and were slightly prolonged in Groups 2-3. The logMAR BCVA maintained improvements in Groups 0-1, and worsened slightly in Groups 2-3.

Conclusions: FTF was significantly associated with visual acuity and foveal photoreceptor status. Thus, we conclude that morphologic and functional prognoses of eyes with BRVO may be improved by identifying the characteristics of eyes with a larger FTF and consequently controlling the FTF more strictly.

CONTROL ID: 3709935

SUBMITTER (NAME ONLY): Bhav Parikh

TITLE: Decoding transcriptional response of stem cell-derived retinal pigment epithelial cells after subretinal transplantation at single cell resolution

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Visual dysfunction in age-related macular degeneration (AMD) is associated with the degeneration of retinal pigmental epithelial cells (RPEs). Several ongoing clinical trials are testing cell replacement therapy as means to halt AMD progression, using human pluripotent stem cell (hPSC)-derived RPEs. Although grafted cells pre-transplantation are routinely characterized, it is unknown how these cells respond transcriptionally post-transplantation. In this study, we dissected the single cell transcriptomic changes in hPSC-RPEs after transplantation.

Methods: Two sources of hPSCs, embryonic (ESCs) and induced (iPSCs), were differentiated to generate RPEs, which were characterized at the mRNA, protein, and functional level to confirm their resemblance to native counterparts. 1-month-old hPSC-RPEs were then either grown further for a month in vitro or subretinally implanted into immunocompetent Dutch Belted rabbits and followed-up for an additional month. At 2 months, both in vitro and in vivo transplanted cells were harvested for single cell RNA sequencing (scRNA-seq).

Results: The in vitro 1-month-old hPSC-RPE cells expressed RPE signature markers, secreted cytokines in a polarized fashion, and demonstrated barrier function and phagocytosis. These 1-month-old cells were successfully xenografted subretinally into immunocompetent hosts and displayed maintenance of overlying retinal structure, and retinal function. There was absence of adverse reactions against both sources of RPEs. ScRNA-seq of in vitro RPEs from both sources revealed a similar heterogenous population consisting of a spectrum of varying maturity states, from progenitor to late RPE. Profiling of RPE after subretinal transplantation unravelled robust in vivo maturation towards late RPE state.

Conclusions: In this work, we generated high quality, functional RPEs from two different hPSC sources. Subretinal transplantation of these cells into an immunocompetent host did not elicit an adverse reaction, highlighting hPSCs as a promising cell source to treat AMD. Furthermore, scRNA-seq performed on subretinally transplanted hPSC-RPEs uncovered the favorable maturation of a heterogenous in vitro RPE population towards a homogenous adult state. Overall, our findings provide a high-resolution perspective on a stem cell-based product intended for future clinical use.

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CONTROL ID: 3709936

SUBMITTER (NAME ONLY): Tatsuya Nakagawa

TITLE: RNA-Seq based transcriptome analysis of corneal endothelial cells derived from the patients with Fuchs endothelial corneal dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: We previously reported an RNA-Seq dataset of corneal endothelium derived from healthy subjects (Tokuda Y, et al. Sci Data, 2020). The purpose of this present study was to elucidate the genetic alternations and potential signaling pathways related to the pathophysiology of Fuchs endothelial corneal dystrophy (FECD) by utilizing an RNA-Seq of corneal endothelium obtained from the patients with FECD.

Methods: Corneal endothelial cells were isolated from patients with FECD (n=10) and healthy controls (n=7). RNA-Seq libraries were generated using the SMARTer® Stranded Total RNA-Seq Kit v2, and then sequenced by using a paired-end 100-bp read protocol. Genes were considered as differentially expressed genes (DEGs) with adjusted P-value (< 0.05) and Log_2 Fold Change (≥ 1.0 or ≤ -1.0). Variation or similarity of gene expression was then confirmed by principal component analysis (PCA). For enrichment analysis, gene ontology (GO), Reactome, and KEGG pathways were investigated by use of R software.

Results: Among a total of 24,636 genes detected by RNA-Seq, 2,366 genes were identified as DEGs in FECD (1,092 upregulated and 1,274 downregulated genes). PCA revealed the presence of two visual groups composed of control and FECD, respectively. For downstream analysis, 1,706 DEGs (696 upregulated and 1,010 downregulated genes) were extracted by confirming gene annotations. GO analysis indicated enrichment of extracellular structure organization, extracellular matrix (ECM) organization, response to oxidative stress, and apoptotic signaling pathway. Consistently, Reactome pathway analysis indicated the dysregulation of ECM related pathways. KEGG pathway analysis demonstrated the involvement of the phosphatidylinositol 3-kinase (PI3K)/Akt and mitogen-activated protein kinase (MAPK) signaling pathways.

Conclusions: The current study presented additional evidence that ECM dysregulation and oxidative stress are involved in the pathophysiology of FECD, and that the PI3K/Akt and MAPK signaling pathways might be interesting targets for elucidating the pathophysiology as well as drug discovery, though future in vitro and in vivo FECD-model "wet experiments" will be necessary.

CONTROL ID: 3709937

SUBMITTER (NAME ONLY): Rachael Heath Jeffery

TITLE: A natural history study of functional and structural outcome measures in PRPH2-associated retinal dystrophy

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.C. Heath Jeffery, J.A. Thompson, I. Constable, I. McAllister, T.L. McLaren, J.N. De Roach, T.M. Lamey, F.K. Chen, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Progression rates of PRPH2-associated retinal dystrophy have not been described. We used structural and functional outcome measures to establish disease progression rates in best-corrected visual acuity (BCVA), total lesion size (TLS), dark autofluorescence (DAF) area, total macular volume (TMV) and mean macular sensitivity (MMS).

Methods: In this retrospective case series, patients with confirmed heterozygous pathogenic PRPH2 variants, 6 monthly serial BCVA, ultra-widefield (UWF) fundus autofluorescence (FAF), optical coherence tomography and MAIA microperimetry with at least 1 year of follow up were included. Linear regression was performed for each eye of each subject to determine the rate of change. Changes in TMV and MMS were compared to a cohort of normal controls.

Results: A total of 12 patients (mean baseline age=55, F:M=4:8) from 10 unrelated families were followed for a mean (SD, range) of 4.7 (2.1, 1.0-8.5) years. The overall mean (SD) BCVA decline was 0.91 (1.86, OD) and 2.93 (5.34, OS) letters/year with no significant interocular difference (p=0.28). Mean (SD) effective radius expansion rates in TLS and DAF were 0.16 (0.13) and 0.10 (0.08) mm/year and 0.15 (0.14) and 0.11 (0.05) mm/year in OD and OS respectively. Mean (SD) TMV decline was 0.079 (0.053, OD) and 0.071 (0.047, OS) mm^3/year with no significant interocular difference (p=0.25). Healthy controls (N=42, mean age=51) showed a mean decline of 0.006 mm^3/year. Overall MMS change was +0.38 (OD) and -0.72 (OS) dB/year. Four patients showed a bilateral MSS decline of 1.90 (OD) and 1.31 (OS) dB/year. Five patients showed a bilateral MSS increase of 0.61 (OD) and 0.49 (OS) dB/year attributed to learning effects. Healthy controls (N=41, mean age=51) showed a mean (SD) MSS decline of 0.02 dB/year.

Conclusions: Patients with PRPH2-associated retinal dystrophy showed slow expansion rates in UWF-FAF derived TLS and DAF area. OCT-derived TMV may serve as an important quantitative outcome measure for future therapeutic clinical trials. Functional outcome measures however warrant further investigation given their large variability and significant learning effects.

CONTROL ID: 3709938

SUBMITTER (NAME ONLY): yasufumi tomioka

TITLE: Detection of Cellular Senescence in Conjunctival Epithelium from Elderly Individuals and Role of Ocular Senescent Cells in the Disruption of Barrier Function

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. tomioka, K. Kitazawa, K. Numa, N. Yokoi, C. Sotozono, Kyoto Prefectural University of Medicine, JAPAN|K. Kitazawa, K. Numa, J. Campisi, Buck Institute for Research on Aging, Novato, California, UNITED STATES|J. Campisi, E O Lawrence Berkeley National Laboratory, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although changes in the ocular surface microenvironment are known to occur during aging, it remains unclear whether cellular senescence at the ocular surface contributes to age-related phenotypes. Here, conjunctival tissue samples obtained from elderly subjects (aged 65 years or older) and irradiated primary conjunctival epithelial cells (CjECs) were used to determine the potential role of ocular senescent cells.

Methods: Our study involved 10 conjunctival tissue samples obtained from 10 healthy elderly subjects [4 males and 6 females; mean age: 68.5 years (range: 65-81 years)], and primary CjECs obtained from human donor eyes that were cultured and X-irradiated at 10 Gy. Tissue samples and irradiated CjECs were examined using immunostaining or western blotting for $p16^{INK4a}$ expression (an important marker of cellular senescence) and for the senescence-associated beta-galactosidase (SA-βgal). We also investigated the expression of protein zonula occuludens-1 (ZO-1) in the epithelial barrier, and barrier function of the irradiated CjECs was evaluated via transepithelial electrical resistance (TEER). Student's t-test was used for statistical analysis.

Results: Expression of $p16^{INK4a}$ was observed in 6 (60%) of the 10 conjunctival tissue samples, with an average positive rate of 12.3% in each sample, while no $p16^{INK4a}$ expressing cells was detected in the other 4 tissue samples, and this expression was not sex-dependent. ZO-1 expression was reduced in tissue samples showing $p16^{INK4a}$-positivity but was retained in tissue samples where $p16^{INK4a}$ was undetectable. In irradiated CjECs, there was a significant increase in $p16^{INK4a}$ expression and SA-βgal activity (and a decrease in ZO-1 expression) both at RNA and protein levels compared to control cells ($P<0.05$). Moreover, compared with non-irradiated CjECs, TEER was significantly reduced in irradiated CjECs ($P<0.05$).

Conclusions: We report here the presence of senescent cells in the conjunctival epithelium of elderly subjects, the acquisition of senescent phenotypes in CjECs induced to senescence upon irradiation, and the contribution of ocular senescent cells in the decrease of epithelial barrier function.

CONTROL ID: 3709940

SUBMITTER (NAME ONLY): Navid Manafi

TITLE: Relationship Between Macular Vessel Density Metrics and Lesion Distribution in Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic eyes with predominantly peripheral lesions (PPL) have been suggested to be at higher risk for progression to proliferative diabetic retinopathy (PDR). Retinal nonperfusion is known to increase with increasing severity of diabetic retinopathy. We sought to evaluate the relationship between macula vessel density metrics on optical coherence tomography angiography (OCTA) with lesion distribution in eyes with DR.

Methods: Patients with DR presenting to three tertiary care centers (Aravind Eye Hospital (326 eyes), LV Prasad Eye Institute (86 eyes), Sankara Nethralaya (86 eyes)) who underwent both Optos ultrawidefield (UWF) pseudocolor imaging and macular OCTA (Cirrus Angioplex, 6x6 mm) were included in this retrospective analysis. The distribution of DR lesions was assessed by comparing each of the peripheral ETDRS extended fields (3-7) against their corresponding ETDRS field. An eye was determined to have predominantly peripheral lesions (PPL) if any peripheral field had a greater severity or extent of lesions compared to its corresponding central ETDRS field; otherwise, it was classified as predominantly central lesions (PCL). After correction for segmentation errors, en face OCTA images from the superficial and deep capillary plexuses (SCP and DCP) were exported and analyzed using Image J. Perfusion density (PD) and vessel length density (VLD) were calculated following binarization (PD) and skeletonization (VLD). PD and VLD of the SCP and DCP were compared between eyes with PPL and PCL DR lesion distribution.

Results: Total of 404 eyes were included in this study (62.1% PCL and 37.9% PPL). There was no significant difference, however in mean SCP PD (30.45 in PPL eyes and 30.95 in PCL eyes; p=0.415) or in DCP PD (34.13 in PPL and 34.22 in PCL; p=0.480). There was also no significant difference in SCP VLD (11.53 in PPL and 11.73 in PCL; p=0.394) or DCP VLD (14.49 in PPL and 14.47 in PCL; p=0.307).

Conclusions: Though predominantly peripheral lesions are thought to be associated with a higher risk of progression, eyes with PPL do not have worse macular perfusion. OCTA analysis of the retinal periphery will be necessary to determine whether eyes with PPL have more severe peripheral nonperfusion.

CONTROL ID: 3709943
SUBMITTER (NAME ONLY): Farid Thomaz Neto
TITLE: Melatonin protects mitochondria in Non-AMD cybrids and AMD cybrids
SESSION TITLE: Cell biology of retinal diseases
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: F.J. Thomaz Neto, N. Salimiagdam, B.D. Kuppermann, M. Kenney, Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|F.J. Thomaz Neto, N. Salimiagdam, B.D. Kuppermann, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Among elderly people in developed countries age-related macular degeneration (AMD) is the leading cause of progressive vision loss. Hallmark features of AMD are an accumulation of drusen in the Bruch's membrane and dysfunction of retinal pigment epithelial (RPE) cells. Oxidative stress is an important factor contributing to the damaged RPE cells. Multiple studies provide evidence that melanin is an important antioxidant factor which leads to reduction of the reactive oxygen species (ROS). Melatonin also has anti-inflammatory, antitumor, and antiangiogenic properties.

Evaluate melatonin protection in Non-AMD cybrids and in AMD cybrids.

Methods: AMD patients and age-matched non-AMD individuals provided platelets that were combined with mitochondria-deficient (Rho0) ARPE-19 cells. The resultant Cybrid cell lines have identical nuclei but mitochondria from different individuals. Cybrids were cultured in 96-well plates (10,000 cells/well) and treated with Melatonin 200 μM for 24 hours. Ethanol was used as vehicle-control. ROS levels and cellular metabolism were measured by the H2DCFDA and MTT assays, respectively. After adding 100 μl H2DCFDA solution/well, plates were read via the fluorescent plate reader with the excitation (EX, 492nm) and emission (EM, 520nm) wavelengths. For cell metabolism, 10 μl of MTT assay reagent was added per well and plates were incubated in 37°C for 3 hours. After adding 100 μl/well of DMSO, plates were analyzed (signal at 570 nm and reference at 630 nm) with the absorbance plate reader. – Statistics were calculated using Student T-test.

Results: ROS levels of non-AMD and AMD cybrids with melatonin declined to 90.50 ± 3.79 ($P < 0.0001$, n=4) and 84.50 ± 1.55 ($P < 0.0001$, n=4) versus Ethanol groups (100.8 ± 0.478, n=4) and (99.75 ± 1.75, n=4), respectively. MTT Assay levels of non-AMD and AMD cybrids with Melatonin improved to 129 ± 2.97 ($P < 0.0001$, n=4) and 132.3 ± 2.78 ($P < 0.0001$, n=4) versus Ethanol groups (100.8 ±0.478, n=4) and (99.75 ±1.75, n=4), respectively.

Conclusions: Non-AMD cybrids and AMD cybrids treated with melatonin had significantly increased cellular metabolism and lower levels of ROS, demonstrating that melatonin could protect cells against oxidative stress.

CONTROL ID: 3709945

SUBMITTER (NAME ONLY): Kapil Mishra

TITLE: Newly Diagnosed Central Serous Chorioretinopathy: Demographics and Epidemiology from the IRIS® Registry (Intelligent Research in Sight)

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mishra, A. Brant, S. Pershing, A.T. Perlroth, H. Bair, C. Xu, D.V. Do, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|K. Mishra, A. Brant, A.T. Perlroth, H. Bair, C. Xu, D.V. Do, Byers Eye Institute, Stanford University, Spencer Center for Vision Research, California, UNITED STATES|S. Pershing, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine demographics and visual acuity for patients with newly diagnosed central serous chorioretinopathy (CSCR) as captured in the IRIS Registry.

Methods: We identified patients with a new diagnosis of CSCR between 2017 and 2018 in the IRIS Registry. We investigated patient characteristics (age, sex, and race/ethnicity) associated with CSCR, and visual acuity (VA) at time of first diagnosis and routine follow-up visits. We processed multivariate regressions to analyze the odds of developing CSCR relative to all patients in the IRIS Registry database.

Results: 28,323 patients were newly diagnosed with CSCR between 2017 and 2018 in the IRIS Registry. The majority of patients with new CSCR were male (68.54%), and the decade with the most CSCR diagnoses was 51-60 years (23.68%). Mean VA at time of diagnosis was 0.29 logMAR (about 20/40) which decreased only slightly to 0.33 logMAR 1 year following diagnosis. Compared to patients in the IRIS Registry without CSCR, patients with CSCR were more likely to be of Asian (Odds ratio (OR) 1.65, $p < 0.001$) or Hispanic descent (OR 1.5, $p < 0.001$) using White as a reference, and were more likely to have Commercial (OR 1.12, $p < 0.001$) or Military (OR 1.29, $p < 0.001$) insurance compared to Medicare, Medicaid (using no insurance as a reference).

Conclusions: According to the IRIS Registry, patients with newly diagnosed CSCR were most commonly middle-aged male, of Asian or Hispanic descent, and with commercial or military insurance. Initial VA at diagnosis was 20/40, and this was relatively stable 1 year following diagnosis.

CONTROL ID: 3709952

SUBMITTER (NAME ONLY): Kazuyo Ito

TITLE: Real-Time, Clinician-Free Detection of Staphyloma Presence and Apex Location in a Cohort of Highly Myopic Eyes With an Ultrasound-Based Algorithm

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Ito, Y. Dan, J.D. Yu, Q.V. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS Medical School, Singapore, SINGAPORE|T.H. Lye, J. Mamou, F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|R.H. Silverman, Q.V. Hoang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultrasound is a commonly available tool to assess the properties of the posterior eye, allowing us to characterize morphological changes. Here, the present study investigates the use of curvature in a simple algorithm to achieve automated (clinician-free) staphyloma detection, as well as pinpoint the location of staphyloma apexes—locations known to be prone to pathologic change.

Methods: 46 individuals (emmetropic, highly myopic (HM) or pathologic myopia) were enrolled in this study (axial length (AxL) range: 22.3-39.3mm) yielded 130 images in total. 10 MHz US B-scan images were acquired while subjects fixated in primary gaze. Eyes were clinically classified into two groups – a non-staphyloma group (composed of eyes that were either emmetropic or HM without staphyloma) and a staphyloma group. On each US image, an intensity-based segmentation algorithm automatically tracked the posterior eyewall. Local curvature (K) of the posterior eyewall and distance (L) of the posterior eyewall to the US transducer were calculated. The location of the staphyloma apex was also automatically estimated. The area under the receiver operator characteristic (AUROC) curve was used to evaluate the diagnostic ability of eight local statistics derived from K, L and AxL. The performance of binary classification (i.e. presence or absence of staphyloma) was assessed at an optimal cut-off point and compared with the performance of junior clinicians.

Results: A fully-automated algorithm was able to detect the posterior eyewall and quantify the non-uniformity of the posterior eye shape with a good classification performance of AUROC > 0.70 for most parameters derived from local curvature (K). The best classifier (the combination of AxL, standard deviation of K, and the standard deviation of L) yielded a diagnostic validation performance of 0.897, which was comparable to the diagnostic performance of junior clinicians. Our method localized the staphyloma apex with an average error of 1.35+/-1.34 mm.

Conclusions: Our fully-automated method enables staphyloma detection with performance comparable to that of junior clinicians. Combined with real-time data acquisition capabilities of US, this method has the potential to be employed as a screening tool for clinician-free in-vivo staphyloma detection.

CONTROL ID: 3709953

SUBMITTER (NAME ONLY): Sang Woo Moon

TITLE: Anterior segment optical coherence tomography imaging of filtering blebs after trabeculectomy with amniotic membrane transplantation in patients with primary open-angle glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Moon, H. Kim, T. Kim, J. Lee, Ophthalmology, Pusan National University Hospital, Busan, KOREA (THE REPUBLIC OF)|S. Moon, J. Lee, Biomedical Research Institute, Pusan National University Hospital, Busan, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To analyse anterior segment optical coherence tomography (AS-OCT) imaging of the filtering bleb after trabeculectomy with amniotic membrane transplantation (AMT) and evaluate intrableb structural parameters associated with intraocular pressure (IOP) control.

Methods: Ninety-six patients with primary open-angle glaucoma who underwent fornix-based trabeculectomy with AMT (AMT group; 85 eyes, 69 patients) or without AMT (control group; 31 eyes, 27 patients) were included. Intrableb structural parameters including bleb height, bleb wall thickness, striping layer thickness, bleb wall reflectivity, fluid-filled space area/height/score, and microcyst formation were evaluated on horizontal and vertical AS-OCT scans at least one year after trabeculectomy. Surgical success was defined as an IOP ≤ 18 mmHg and IOP reduction ≥ 20% without medication. Logistic regression analyses were performed to determine intrableb parameters associated with IOP control.

Results: Patients with successful IOP control had greater bleb height, bleb wall and striping layer thickness, lower bleb wall reflectivity, and more frequent microcyst formation (all ps ≤ 0.023) in both groups. In the AMT group, the patients with successful IOP control had greater fluid-filled space area and score (all ps ≤ 0.043). Multivariate logistic regression analysis showed that lower bleb wall reflectivity alone was associated with successful IOP control in the control group [odds ratio (OR) = 0.812, p = 0.017]. Greater fluid-filled space score (OR = 8.016, p = 0.027), lower bleb wall reflectivity (OR = 0.913, p = 0.003), and microcyst formation (OR = 16.202, p = 0.041) were associated with successful IOP control in the AMT group.

Conclusions: Hyporeflective bleb wall was associated with successful IOP control after trabeculectomy regardless of AMT. However, the extent of the fluid-filled space was associated with successful IOP control only after trabeculectomy with AMT.

CONTROL ID: 3709954

SUBMITTER (NAME ONLY): Kaveri Thakoor

TITLE: Evaluation of a Deep Learning Model on a Real-World Clinical Glaucoma Dataset

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Thakoor, S. La Bruna, P. Sajda, D.C. Hood, Columbia University, New York, New York, UNITED STATES|A. Leshno, E. Tsamis, G. De Moraes, N. Harizman, J.M. Liebmann, G.A. Cioffi, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate a deep learning model (DLM) for detecting glaucoma based upon OCT probability maps by applying it to eyes from a university-based clinical practice. We asked if the DLM diagnosis accurately reflects the diagnosis made by OCT experts using a full OCT report, and if it had the potential to aid in the clinical diagnosis.

Methods: The model: A DLM [1] was previously trained and validated on OCT retinal nerve fiber layer probability maps (RNFL p-maps) (Fig. 1A) from good quality scans of patients without obvious co-morbidities or extreme refractive errors. The real-world data: OCT scans were obtained from 99 eyes from 59 patients visiting a university-based, glaucoma practice. 4 eyes with unreadable scans were excluded. Unlike the eyes used to train the DLM, the 95 eyes were older (55 eyes, aged 70 to 98 years), with a range of disease severity, and various co-morbidities (e.g., ERM, AMD, high myopia). The analysis: The DLM output ranges from 0% (H: healthy) to 100% (G: optic neuropathy consistent with glaucoma). Eyes were categorized as H (≤5%), G (≥95%), or UNC (uncertain), and compared to the grading of a Hood report (Fig. 1B) by 4 OCT experts (OCT-E), who rated each eye H, G, or UNC. G and UNC judgments were combined, as both require follow-up. To assess the potential value of the DLM, a glaucoma expert made a clinical decision (CD) of H, G, or UNC (suspect) twice for each eye, first (CD1) based upon past chart notes, visual fields, and OCT scans, except for the recent Hood report, and again (CD2) to see if the OCT Hood report with the DLM output and heatmap (Fig. 1B, 1C) would alter CD1.

Results: The DLM decision agreed with the OCT-E decision in 95% of the eyes; all 5 disagreements involved an UNC judgment. Of the 9 eyes with a CD1 of UNC (suspect), CD2 changed to G in 3 and H in 3, in agreement with the DLM. Of the 7 eyes with a CD1 of H, but a DLM grade of G, CD2 changed to “probably G” in 4 (e.g., Fig. 1B) and UNC in 2. Of the 6 eyes with a CD1 of G, but a DLM grade of H, CD2 changed to H in 1, and in 4 eyes, the CD2 noted that other factors such as ERMs or retinal disease probably contributed.

Conclusions: The DLM output based upon the RNFL p-map showed excellent agreement with the OCT-E decisions based upon the complete OCT report (Fig. 1B). A post-hoc analysis suggested that the DLM has the potential to aid in clinical diagnosis. [1] Thakoor et al., IEEE TBME, 2021.

CONTROL ID: 3709958

SUBMITTER (NAME ONLY): Ramin Khoramnia

TITLE:

Safety and effectiveness of the fluocinolone acetonide intravitreal implant (ILUVIEN): Final study results from the European IRISS registry study

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Khoramnia, Department of Ophthalmology, Ruprecht Karls Universitat Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|T. Peto, School of Medicine, Dentistry and Biomedical Sciences, Centre for Public Health, Belfast, Belfast, UNITED KINGDOM|S.R. Taylor, Department of Ophthalmology, University of Surrey, Surrey, UNITED KINGDOM|J. Paulo Castro de Sousa, Ophthalmology Department, Leiria Hospital Center, Leiria, PORTUGAL|C. Bailey, Bristol Eye Hospital, Bristol, Bristol, UNITED KINGDOM|U. Chakravarthy, Centre for Public Health, Queen's University of Belfast, UNITED KINGDOM|L. Hill, Statistical Consultant, Montana, UNITED STATES|

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ABSTRACT BODY:

Purpose:

To report the final study results from the IRISS study with a focus on outcomes in patients with diabetic macular edema (DME).

Methods:

The IRISS study is a European 5-year post-authorisation registry study conducted in a total of a total of 556 patients (N=695 eyes) and studied for up to five-and-a-half years after being treated with the fluocinolone acetonide (ILUVIEN) implant.

Safety assessments included the occurrence of intra-ocular pressure (IOP) events and their management, and effectiveness included changes in best-recorded visual acuity (VA) with a focus on outcomes based on median duration of DME.

Results:

From the 695 eyes that were included, the majority (96.7%) had diabetic macular edema (DME) and had a mean follow-up of 37.8 months (up to a maximum of 65.0 months).

The focus here is therefore on the IOP outcomes and changes in VA reported in the DME population.

In patients with DME, 35.1% of eyes required IOP-lowering medication with a mean of 13.3±11.6 months (mean±SD) to the first IOP-lowering medication.

5.5% of eyes required IOP-lowering procedures (4.3% surgery and 1.2% non-penetrating) were required to control pressure with a mean of 25.9±10.6 months to the first procedure (surgery or non-penetrating).

A rise in pressure of ≥10 mm Hg and of >30 mm Hg was observed in 15.3% and 14.7% eyes, respectively.

Mean VA increased from a baseline of 52.3 letters to 57.5 letters at Month 36, with consistent improvements observed between months 12 and 36.

Subgroup analysis, based on median DME duration, showed improved VA changes in patients where the median duration was less than the median.

Conclusions: This study confirms the favourable long-term benefit-to-risk profile of the fluocinolone acetonide implant with additional benefits observed in patients with DME that were treated earlier.

CONTROL ID: 3709960

SUBMITTER (NAME ONLY): chenchen wang

TITLE: Nectin-1 and NMHC-IIB: major mediators of HSV-1 entry into corneal nerves.

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. wang, Y. He, Q. Liang, K. Hu, Nanjing University, Nanjing, Jiangsu, CHINA|

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ABSTRACT BODY:

Purpose: To investigate the cellular receptors and molecular mechanisms of herpes simplex virus type 1 (HSV-1) entry into corneal nerves.

Methods: Immunofluorescence was performed to determine the distribution and expression of HSV-1 entry receptors in corneal nerves of healthy mice, including nectin-1, herpes virus entry medium (HVEM), non-muscle myosin heavy chain IIA (NMHC-IIA), NMHC-IIB, and myelin-associated glycoprotein (MAG). Quantitative real-time Polymerase Chain Reaction (qPCR) were used to further analyze the expression of HSV-1 receptors in trigeminal ganglion (TG) from healthy and Herpes Simplex Keratitis (HSK) mice. Enzymatic digestion and density gradient centrifugation was used to isolate TG to single TG neurons. Antibody antagonism and siRNA techniques were employed to investigate the functional receptors mediating HSV-1 entry into cultured TG neurons from mice in vitro. Subconjunctival injection of specific antibodies was then performed to further explore the roles of functional receptors in vivo.

Results: We observed that Nectin-1, HVEM, NMHC-IIA and NMHC-IIB were expressed in healthy corneal nerves, but MAG not. MAG was only expressed on the myelin sheaths in TG, and was nearly unexpressed in cultured TG neurons. On day 3 post-infection, the expression of nectin-1, HVEM and NMHC-IIB in TG was significantly increased, while NMHC-IIA was decreased. HSV-1 entry was significantly inhibited in Nectin-1 or NMHC-IIB knockdown TG neurons in vitro, but had little inhibitory effect in HVEM or NMHC-IIA knockdown TG neurons. Also, in vivo antibody antagonism of nectin-1 or NMHC-IIB inhibited HSV-1 entry into corneal nerves and reduced virus replication in TG.

Conclusions: Nectin-1, HVEM, NMHC-IIA, and NMHC-IIB were expressed in corneal nerves of healthy mice. However, nectin-1 and NMHC-IIB may play the predominant role in mediating HSV-1 entry.

CONTROL ID: 3709962

SUBMITTER (NAME ONLY): Jeffrey Peterson

TITLE: Improving Rose Bengal Photodynamic Antimicrobial Therapy efficacy by validating predictive model

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Peterson, E. Arrieta, K.D. Leviste, P.A. Sepulveda Beltran, F. Manns, J. Parel, Ophthalmic Biophysics Center, Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|I.E. Kochevar, Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, UNITED STATES|K.J. Mintz, B.C. Ferreira, R.M. Leblanc, Department of Chemistry, University of Miami, Coral Gables, Florida, UNITED STATES|K.J. Mintz, Department of Materials Science and Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|F. Manns, Department of Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|J. Parel, Brien Holden Vision Center, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Antimicrobial resistant and atypical infectious keratitis has been effectively treated with experimental Rose Bengal Photodynamic Antimicrobial Therapy (RB-PDAT). RB-PDAT creates antimicrobial singlet oxygen ($^1O_2$) by exciting Rose Bengal (RB) photosensitizer with green light. A proof-of-concept chemistry kinetics model was previously developed (Peterson et al., 2021) to predict $^1O_2$ distribution within the cornea during RB-PDAT for a given set of input parameters (light dose, RB concentration, and application time). Although developed using experimental data, the model had not yet been validated using direct $^1O_2$ dose measurement. Validation and fitting of this model will enable optimization of $^1O_2$ dose by optimizing RB-PDAT treatment parameters.

Methods: 4 groups of 3 donor eyes were treated with different RB concentrations (0.054, 0.12, 0.58, 1.2 mM). Donor eyes were treated with 20% dextran for 24 hours to de-swell the cornea and then treated with RB for 30 min. A $^1O_2$ dosage measurement system previously developed for RB-PDAT (Peterson et al., 2021) was used to measure $^1O_2$ generated during green light stimulation (at 10^7 mW/cm^2) before and after RB treatment. Measured $^1O_2$ signal was normalized and compared with normalized $^1O_2$ level predicted by chemical kinetics model for the corresponding RB concentrations at 6 and 12 mW/cm^2 at 525 nm (irradiances typical for RB-PDAT used to compare because solver is unstable beyond 30 mW/cm^2). All values normalized to respective $^1O_2$ value at 1.2 mM. The model was solved numerically in MATLAB.

Results: Predicted normalized $^1O_2$ values were within a standard deviation of measured $^1O_2$ signal at every RB concentration except at RB concentration of 0, where a non-zero $^1O_2$ signal was observed. Comparing normalized predicted $^1O_2$ signal values with mean normalized measured $^1O_2$ dosimeter signal showed relative error ranging from 9.5% to 80.9% and 10.6% to 62.6% at 6 and 12 mW/cm^2 respectively. Highest error is seen at 0.054 mM for all conditions when excluding 0 mM RB (100% error as model assumes no $^1O_2$ production).

Conclusions: We show a proof-of-concept predictive model for $^1O_2$ dose generated during RB-PDAT, capable of testing a range of experimental parameters which can be used for optimizing RB-PDAT clinical efficacy. While limited due to variability of experimental data, early results demonstrate reasonable correlation between measured and predicted $^1O_2$ levels.

CONTROL ID: 3709966

SUBMITTER (NAME ONLY): Lachlan Knight

TITLE: Quality of life in children and adults with childhood glaucoma: An interview study

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Knight, B. Ridge, J.E. Craig, E. Souzeau, Ophthalmology, Flinders University, Bedford Park, South Australia, AUSTRALIA|L. Knight, Ophthalmology, Women's and Children's Hospital Adelaide, North Adelaide, South Australia, AUSTRALIA|S.E. Staffieri, Ophthalmology, The Royal Children's Hospital Melbourne, Parkville, Victoria, AUSTRALIA|S.E. Staffieri, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|M. Prem Senthil, College of Nursing and Health Sciences, Flinders University Caring Futures Institute, Bedford Park, South Australia, AUSTRALIA|

Commercial Relationships Disclosure: Lachlan Knight: Commercial Relationship: Code N (No Commercial Relationship) | Bronwyn Ridge: Commercial Relationship: Code N (No Commercial Relationship) | Sandra Staffieri: Commercial Relationship: Code N (No Commercial Relationship) | Jamie Craig: Commercial Relationship: Code N (No Commercial Relationship) | Mallika Prem Senthil: Commercial Relationship: Code N (No Commercial Relationship) | Emmanuelle Souzeau: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The psychosocial impact of childhood glaucoma has not been well described due to the complexity, variability and rarity of the disease. We performed an exploratory qualitative study to report and compare the quality of life issues encountered by children and adults with childhood glaucoma.

Methods: A qualitative research methodology (interpretive phenomenology) was applied and data were collected through semi-structured interviews. Children (aged 8 to 17 years) and adults (aged ≥18 years) were recruited from the Australian and New Zealand Registry of Advanced Glaucoma. NVivo-12 software was used to inductively analyze and code data to identify quality of life themes.

Results: Eighteen children (mean age 12.4 ± 3.1 years; 33% female) and 47 adults (mean age 40.0 ± 15.3 years; 55% female) were interviewed. Eleven quality of life themes were identified. Coping strategies was the most prominent theme in either cohort. Shared adaptive coping strategies included peer support, resilience and having a positive relationship with the ophthalmologist. Maladaptive coping behaviors, including treatment nonadherence and clinical nonattendance, appeared to begin in children aged 13 to 17 years and were most prominent in adults aged <40 years. Adults experienced a more significant threat to emotional well-being than children which included feeling misunderstood due to disease rarity, being self-conscious of the physical manifestations of glaucoma and feeling anxious of possible disease progression. Meanwhile, children were more concerned with inconveniences related to clinic waiting times and pupillary dilatation. The effect of childhood glaucoma on family planning was a novel QoL theme in adults and included worry for their child to inherit the condition. This led to genetic counseling-seeking behaviors. Mobility issues were infrequently experienced by either cohort.

Conclusions: The psychosocial impact of childhood glaucoma extends beyond the clinical environment and is minimized by the use of coping strategies. Our data suggest that older children may require additional social and ophthalmic support as they transition into adulthood whilst genetic counseling and family planning options should be timely discussed. This study supports the development of a childhood glaucoma-specific patient reported outcome measure for assessment of the psychosocial impact of childhood glaucoma.

CONTROL ID: 3709967

SUBMITTER (NAME ONLY): OREN GABBAY

TITLE: USING THE TEAR FILM IMAGER FOR COVID19 DETECTION – A PILOT STUDY

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. GABBAY, G. Kleinmann, Ophthalmology, Edith Wolfson Medical Center, Holon, ISRAEL|O. GABBAY, G. Kleinmann, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|

Commercial Relationships Disclosure: OREN GABBAY: Commercial Relationship: Code N (No Commercial Relationship) | Guy Kleinmann: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A key challenge in limiting the spread of Covid-19 is the absence of a fast non-invasive tool to detect infected individuals in the general population. Using polymerase chain reaction (PCR) testing, it has been demonstrated that SARS-CoV-2 is present in the tear film of patients with ocular symptoms. The presence of virions in or next to the lipid layer of the tear film would theoretically cause a measurable interruption of the normal tear bi-layer structure.

The goal of this pilot study is to test the hypothesis that a specialized version of Tear Film Imager (vTFI) could be used for detection of infected individuals, in a quick, non-invasive manner.

It is important to note that vTFI findings are not specific to SARS-Cov-2, and similar enveloped virions might cause a comparable disturbance.

Methods: In our pilot study, twenty eyes of ten patients that were hospitalized due to Covid-19 infection in a designated quarantine department were compared to twenty eyes of ten healthy control patients. The study was approved by the Wolfson medical center's Institutional Review Board. All participants had a nasopharyngeal PCR swab confirming infection status up to 72 hours prior to examination by vTFI. Any patients with chronic viral infection (i.e. HIV, HBV etc'), corneal abnormalities, or corneal/refractive surgery were excluded to ensure uniformity of the data and focus on virion detection

Results: Using vTFI 16 out of 20 healthy eyes correctly tested negative. 15 out of 20 Covid-positive eyes were correctly identified positive using TFI. In total 70% of the control group were correctly categorized by TFI algorithm as healthy (positive if one eye positive) and 80% of the Covid-infected individuals were positively identified.

Conclusions: Identification of Covid-19 status from the tear film layer using ultra-fast non-invasive vTFI shows promise and a larger sample blinded study should be performed to assess its implementation in an outpatient setting. Being a non-specific test, the use of vTFI is not dependent on special primers and may offer a modality for diagnosing individuals suspected of being infected with other emerging pathogens.

CONTROL ID: 3709968

SUBMITTER (NAME ONLY): Meira Fogel Levin

TITLE: Pentosan-associated maculopathy: Early detection using OCT angiography and choriocapillaris flow deficit analysis.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Fogel Levin, A. Santina, A. Au, A. Wong, N. Abraham, A. Lu, S. Somisetty, V. Romero Morales, S.R. Sadda, D. Sarraf, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|M. Fogel Levin, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|G. Corradetti, S.R. Sadda, Doheny Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pentosan maculopathy may progress despite discontinuation of the drug exposure. The identification of earlier imaging markers of toxicity may be critical to prevent vision loss. Hence, we compared the choriocapillaris flow deficit (CC FD) from optical coherence angiography (OCT) angiography in eyes of patients treated with high cumulative dosages of pentosan polysulfate sodium (PPS) with no signs of retinal toxicity versus healthy age-matched controls

Methods: Patients treated with PPS for interstitial cystitis with a cumulative dosage of more than 1000 grams underwent multimodal imaging screening to exclude evidence of PPS maculopathy or other retinal abnormalities. All study patients and age-matched healthy controls completed OCT angiography (OCTA) using the Solix device (Solix; Optovue Inc, Fremont, California, USA), with a 3x3 mm volume cube scan centered on the fovea. En face OCTA images at the level of the CC were exported, and CC FDs were computed and compared between groups.

Results: Fifteen patients treated with PPS and fifteen age-matched controls were included. The mean PPS cumulative dose was 1974±666.4 grams over a mean of 17.6 ±6.8 treatment years. All patients had visual acuity of 20/25 or better and normal fundus autofluorescence (FAF), OCT, multicolor, near-infrared reflectance (NIR), and ultra-widefield fundus color and AF images. The CC FD was 32.7±3.6% in the PPS group compared to 28.6±4.3% in the control group (p=0.023).

Conclusions: PPS treated patients show significant CC flow impairment before the development of overt signs of macular toxicity compared to healthy age-matched controls. Thus, the choroid may be the earliest manifestation of ocular toxicity, predating the development of clinically evident RPE injury. The subsequent RPE disruption may be the result of choriocapillaris impairment or primary PPS toxicity. Regardless, assessment of the CC on OCTA may be a useful tool for early detection of toxicity, though further longitudinal studies are required.

CONTROL ID: 3709969

SUBMITTER (NAME ONLY): Naoto Suzuki

TITLE: Trial study on applying focal macular electroretinogram function on the microperimetry system

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Suzuki, Mechanical Engineering, National Institute of Technology, Numazu College, Numazu, Shizuoka, JAPAN|

Commercial Relationships Disclosure: Naoto Suzuki: Commercial Relationship(s);Code F (Financial Support):Japan Society for the Promotion of Science

ABSTRACT BODY:

Purpose: This study aims to investigate cryptogenic diseases including macular dystrophy. The decline in visual sensitivity of the retina has been measured using microperimetry, the retinal layer causing this decline has been identified using multifocal electroretinogram (ERG). Instead of the multifocal ERG, a focal macular ERG function has been applied on the microperimetry.

Methods: This apparatus is made of illumination and photographic optical systems separated by a mirror with a hole. Additionally, it is made of a microperimetry optical system and an ERG optical system separated by a cold mirror. The apparatus consists of an Edmund infrared camera EO-50231, a lens with a 25-mm focal length, a halogen lamp, an objective lens with a 50-mm focal length, four double convex lenses with a 100-mm focal length, two aperture stops, a mirror, a 45° cold mirror, a 12.1-inch high brightness monitor with 2,000 cd/m2, and an artificial eye. A differential amplifier with gain 10, high-pass filter with a 21.2-Hz cut-off frequency, 50-Hz notch filter, and two non-inverting amplifiers with gains 1001 and 11 have been deployed in this study. Moreover, this study used the National Instruments' I/O device USB-6216, shielded connector block SCB-68A, the Nihon Kohden's plate electrode NE-113A, the Nihon Kohden's electromagnetic shield sheet Y049, and the LabVIEW 2018 software for data retrieval. To conduct the focal macular ERG, a DynaScan's 49-inch ultrahigh brightness liquid crystal display (LCD) with 3,500 cd/m2 has been prepared. The focal macular ERG software was developed using C++ Builder 10.2.

Results: On the ultrahigh brightness LCD, the ERG software could show three sizes of stimulus spot circles: 5°, 10°, and 15° in diameters. Moreover, a function, which could adjust size of the stimulus spot circle, has been added as the diameter was changed from 1° to 15°.The stimulus spot circle could be shown as the circle's center was similar to an examination target's center of the microperimetry. The software showed a flicker stimulation as the frequency was changed from 10 Hz to 100 Hz.

Conclusions: The focal macular ERG function is expected to identify the retinal layer causing visual alterations at specific points throughout the retina. Further work towards preclinical animal testing and clinical evaluation are required.

CONTROL ID: 3709971

SUBMITTER (NAME ONLY): Tomoaki Murakami

TITLE: Clinical Relevance of Parafoveal Intercapillary Space Spectrum and Foveal Avascular Zone in Diabetic Retinopathy without Macular Edema

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Murakami, N. Terada, K. Ishihara, Y. Dodo, K. Nishikawa, K. Kawai, K. Morino, A. Tsujikawa, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the clinical significance of intercapillary space spectrum on swept source optical coherence tomography angiography (SS-OCTA) images in diabetic retinopathy (DR).

Methods: We retrospectively reviewed consecutive 96 eyes of 82 patients suffering from DR without macular edema. Automatic image processing of en-face OCTA images provided the quantitative parameters and location of intercapillary spaces within central 2 mm circle The parafoveal areas were divided into 40 sectors according to the distance and octant. We evaluated how the intercapillary spaces are associated with logarithm of the minimum angle of resolution (logMAR) and feasible to diagnose diabetic macular ischemia.

Results: Among several quantitative parameters, total counts of the intercapillary spaces showed most significant correlation to logMAR ($\rho = -0.408$, $P<0.001$). The size thresholding did not improve the statistical association, whereas numbers of the spaces in 2 highly significant sectors showed better associations with logMAR ($\rho = -0.488$, $P<0.001$). Multivariate regression analyses revealed that both the FAZ area ($\beta=0.226$, $P=0.043$), and the number of the intercapillary spaces ($\beta=-0.270$, $P=0.014$) were related to logMAR. The clustering using the FAZ area and the intercapillary spaces revealed two major clusters, one of which might be proposed as diabetic macular ischemia. Subsequent receiver operating characteristic analyses demonstrated that the intercapillary spaces (area under the curve [AUC] = 0.999) rather than the FAZ area (AUC =0.785) discriminated these two clusters.

Conclusions: Both enlarged FAZ and decreased interapillary spaces contribute to visual impairment and propose an objective and quantitative diagnosis of diabetic macular ischemia in DR without macular edema.

CONTROL ID: 3709974

SUBMITTER (NAME ONLY): Sophie Frank

TITLE: Advances in photoreceptor quantification moving from conventional to high-resolution SPECTRALIS optical coherence tomography

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Frank, H. Bogunovic, O. Leingang, P. Fuchs, L. Coulibaly, G.S. Reiter, U. Schmidt-Erfurth, Department of Ophthalmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: High-Resolution SPECTRALIS OCT is based on a shorter central wavelength and a larger spectral bandwidth providing an axial resolution of up to 3 µm compared to 7 µm in conventional OCT imaging with an identical lateral resolution. The purpose of this study was to investigate efficacy in retinal morphology accessibility on the photoreceptor (PR) level in intermediate age-related macular degeneration (iAMD).

Methods: Patients with iAMD were imaged using a 6x6mm scan pattern (97 B-scans) for standard SPECTRALIS HRA+OCT and the investigational device SPECTRALIS High-Res OCT, both by Heidelberg Engineering, Germany. PR thickness was measured using a previously trained deep learning algorithm for segmenting PR layer (inner border of the ellipsoid zone to retinal pigment epithelium) and manually corrected if necessary. Overall PR thickness and drusen maps were computed for all patients. PR loss area and thickness were compared between devices and areas using mixed effect models.

Results: Twenty-nine eyes from 23 patients were included. Mean PR loss in the central 1 mm area was higher on the standard OCT with 0.07 mm^2 compared to 0.04 mm^2 on the High-Res OCT (p=0.049). Parafoveal (1-3 mm) PR loss was 0.32 mm^2 and 0.16 mm^2 on the standard OCT and the High-Res OCT, respectively (p=0.032). Perifoveal (3-6 mm) PR loss was 0.08 mm^2 on the standard OCT and 0.05 mm^2 on the High-Res OCT (p=0.029). Mean overall PR thickness was 26.46 µm on the standard OCT compared to 32.23 µm on the High-Res OCT. Mean PR thickness in drusen areas was 26.30 µm and 32.39 µm in non-drusen areas. The PR layer was generally thinner on the standard OCT ($p<0.001$) and in drusen areas ($p<0.001$).

Conclusions: High-Res OCT with superior axial resolution is able to identify the condition of the PR level in iAMD with higher precision. High resolution improves the distinction of retinal layers on OCT imaging promoting the understanding of retinal disease particularly in its early stage. Higher axial resolution might therefore be better suited to investigate disease pathomechanisms, progression to advanced macular atrophy and valid therapeutic targets.

CONTROL ID: 3709978

SUBMITTER (NAME ONLY): Vasily SMIRNOV

TITLE: VSX2 variants are responsible for bipolar cell dysfunction with distinct lens and chorioretinal alterations.

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.M. SMIRNOV, C. Condroyer, A. Antonio, J.A. Sahel, I.S. Audo, C. Zeitz, Sorbonne Université, INSERM, CNRS, Institut de la Vision., Paris, FRANCE|V.M. SMIRNOV, Universite de Lille, Lille, Hauts-de-France, FRANCE|M. Robert, Ophthalmology Department, Hôpital Universitaire Necker-Enfants Malades, F-75015 Paris, France, Paris, FRANCE|M. Robert, Borelli Centre, UMR 9010, CNRS-SSA-ENS Paris Saclay-Paris University, F-91190 Gif-sur-Yvette, France, Paris, FRANCE|J. Rozet, I. Perrault, Laboratory of Genetics in Ophthalmology (LGO), INSERM UMR1163, Institute of Genetic Diseases, Imagine and Paris Descartes University, F-75015 Paris, France, Paris, FRANCE|J.A. Sahel, Department of Ophthalmology, The University of Pittsburgh School of Medicine, Pittsburg, Pennsylvania 15213, United States, Pittsburg, Pennsylvania, UNITED STATES|I.S. Audo, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Centre de Référence Maladies Rares REFERET and INSERM-DGOS CIC 1423, F-75012 Paris, France, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Congenital stationary night blindness (CSNB) is a group of genetically and clinically heterogeneous retinal disorders, usually manifesting with infantile nystagmus, reduced visual acuity, variable degree of myopia and poor visual behavior in dim light. The diagnosis is done on the basis of full-field electroretinogram (ffERG) features. Most of the patients are characterized by an electronegative Schubert-Bornschein-type of ffERG, showing either a signal transmission defect from photoreceptor to all bipolar cells (incomplete (ic)CSNB) or selectively affecting rod and cone ON-bipolar cells (complete (c)CSNB). The goal of this study was to identify the gene defect in a family with non-syndromic CSNB with peculiar characteristics.

Methods: Three patients from two unrelated families have been clinically and genetically explored by state-of-the-art methods.

Results: Patients had infantile nystagmus, low stable visual acuity, myopia and night blindness. Two older patients had bilateral lens luxation and underwent lens extraction. All patients presented atrophic peripheral chorioretinal changes. The ffERG revealed an electronegative Schubert-Bornschein appearance, but combining characteristics of incomplete and complete CSNB, affecting rod and cone ON- and OFF-bipolar cells. Whole exome and Sanger sequencing identified in each index case a novel homozygous variant (respectively c.595C>T p.(Arg199Cys) and c.698C>T p.(Pro233Leu)) in VSX2 co-segregating with the phenotype in available family members.

Conclusions: Variants in VSX2 can lead to different phenotypes, either defects of early ocular development (anophthalmia, microphthalmia and coloboma) or peculiar CSNB with lens luxation and chorioretinal changes, described herein. VSX2 is a major regulator of early ocular development and is highly expressed in bipolar cells in adult retina. Further studies are needed to understand the pathogenic mechanisms associated with variants in VSX2 leading to two distinct phenotypes.

CONTROL ID: 3709979

SUBMITTER (NAME ONLY): Chunmei Wang

TITLE: Ocular antibiotics susceptibility of multidrug-resistant Staphylococcus isolated from ocular anterior segment

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Wang, J. Yue, S. Jian, S. Liu, H. Zhang, Zhengzhou University People's Hospital, Zhengzhou University, Zhengzhou, Henan, CHINA|C. Wang, J. Yue, Y. Niu, S. Jian, S. Liu, H. Zhang, Henan Eye Hospital, Henan Provincial People's Hospital, Zhengzhou, Henan, CHINA|Y. Niu, Henan University People's Hospital, Henan University, Zhengzhou, Henan, CHINA|

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ABSTRACT BODY:

Purpose: To study the five common ocular antibiotics susceptibility of multidrug-resistant Staphylococcus isolated from conjunctival sac, cornea, eyelid margin and lacrimal sac in the ocular anterior segment.

Methods: 67 isolates were collected from patients from January 2018 to May 2019 at Henan Eye Hospital and identified by DL-STAPH Staphylococcus. Levofloxacin, tobramycin, clindamycin fusidic acid and cefazolin sodium were purchased from Dalian Meilun Biotechnology Co., Ltd.and Shenzhen China Resources Jiuxin Pharmaceutical Co., Ltd.. Ocular antibiotics susceptibility of multidrug-resistant Staphylococcus was determined by the Minimum Inhibitory Concentration methods according to the guidelines of Clinical and Laboratory Standards Institute.

Results: 35 methicillin-resistant Staphylococcus (MRS), 30 beta-lactamase-producing Staphylococcus (β-Lac) and 2 β-Lac MRS isolates were identified from 67 multidrug-resistant Staphylococcus. MRS isolates accounted for 80.00%,75.00%, 44.19% and 42.86%, and β-Lac isolates accounted for 20.00%, 20.00%, 53.49% and 42.86% in lacrimal sac, cornea, conjunctival sac and eyelid margin respectively. The drug-resistant Staphylococcus epidermidis was the major isolates in eyelid margin (57.14%) and conjunctival sac (46.51%). Meanwhile, the drug-resistant Staphylococcus aureus was the major isolates in lacrimal sac (40.00%) and cornea (33.33%). The susceptibility rates of cefazolin sodium, fusidic acid, levofloxacin, clindamycin and tobramycin against 35 MRS isolates were 74.29%, 68.57%, 34.29%, 34.29% and 31.43% respectively. The susceptibility rates of cefazolin sodium against MRS isolates were 100% in cornea, eyelid margin and lacrimal sac. The susceptibility rates of cefazolin sodium, fusidic acid, levofloxacin, tobramycin and clindamycin against 30 β-Lac isolates were 90.00%, 76.67%, 56.67%, 53.33% and 26.67% respectively. The susceptibility of cefazolin sodium and fusidic acid against β-Lac isolates were higher than MRS isolates.

Conclusions: Our results indicate that cefazolin sodium and fusidic acid may be considered a reliable alternative for the treatment of multidrug-resistant staphylococcus in the ocular surface, especially of β-Lac drug-resistant staphylococcus.

CONTROL ID: 3709981

SUBMITTER (NAME ONLY): Mengya Zhao

TITLE: Spp1 drives retinal ganglion cell resiliency in glaucomatous neuropathy

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Zhao, K. Toma, B. Kinde, Y. Han, X. Duan, University of California San Francisco, San Francisco, California, UNITED STATES|Y. Hu, Stanford University, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) loss subject to elevated intraocular pressure (IOP) represents the leading cause of irreversible vision loss in glaucoma patients. Understanding how different RGC types respond to sustained IOP elevation can provide insight into key molecular players involved in neuroprotection and shed light on potential therapeutic targets for the treatment of glaucoma.

Methods: Chronic IOP elevation was achieved using the silicone oil-induced ocular hypertension under-detected (SOHU) model. Silicone oil was injected into the anterior chamber of mice 8–10 weeks of age and a saline control into the contralateral eye. The IOP was monitored once weekly for up to 6 weeks after SO injection using the tonometer. AAV-mediated Secreted Phosphoprotein 1 (Spp1) knockdown or overexpression in RGCs occurred at 8 weeks of age. Mice were sacrificed at 1 week and 4 weeks post-SOHU surgery for RGC subtype-specific immunohistochemistry (IHC) analysis. Spp1 expression was also assessed by IHC in post-mortem human retina, as well as an enzyme-linked immunosorbent assay (ELISA) to quantify Spp1 in the aqueous humor (AH) from patients with glaucoma.

Results: αRGCs and intrinsic-photosensitive RGCs (ipRGCs) are uniquely resilient in the context of chronically elevated IOP. The preferential resiliency was, in part, driven by elevated expression of Spp1. Our past work showed that Spp1 promotes optic nerve regrowth in combination with growth factors. Elimination of Spp1 from RGCs using either a Spp1 mutant or AAV-mediated Spp1 knockdown led to a significant decrease of αRGC survival. In contrast, overexpression of Spp1 in Foxp2-positive RGCs (F-RGCs) led to enhanced neuroprotection of this RGC subclass, which is highly susceptible to increased IOP. In post-mortem human retina, we found that Spp1 is also enriched in human RGC subsets, particularly in the central regions of the retina, as potential markers for human parasol RGCs. SPP1 quantification by ELISA from AH of patients with glaucoma showed that Spp1 levels are correlated with the severity of glaucoma.

Conclusions: Our study revealed a novel role for Spp1 in promoting RGC resiliency in mouse models of glaucomatous neuropathy. Spp1 levels correlate with the severity of optic neuropathy in patients with glaucoma. Our data indicated that Spp1 may be a relevant biomarker as well as a therapeutic target for promoting neuroprotection in patients with glaucoma.

CONTROL ID: 3709983

SUBMITTER (NAME ONLY): Joveeta Joseph Ruben

TITLE: Temporal analysis in Transcriptomic profile identifies immune markers and modulation of key pathways in Murine Model of Multi-Drug Resistant (MDR) Pseudomonas aeruginosa endophthalmitis

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Joseph Ruben, P. NAIK, M.N. Naik, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Increasing incidences of multidrug-resistant (MDR) P. aeruginosa (PA) causing endophthalmitis threaten our ability to manage this vision threatening condition. Understanding host-pathogen interactions is central for improving clinical outcomes. In this study, temporal dynamics of immune response in mouse model of MDR-PAendophthalmitis was investigated by transcriptome analysis.

Methods: C57BL/6 mice were infected with MDR-PA and susceptible (S-PA) and disease progression and severity was monitored at 6h and 24h post infection (p.i). The extent of retinal damage was assessed by H&E staining. Microarray analysis was performed using SuperPrint G3 Mouse Gene Expression v2 chip and the differential gene expression analysis was performed with limma package in R (v4.0.0.) /Bioconductor (v3.11). A computational pipeline then selected differentially expressed genes at both the time points and clustered them into groups with distinct temporal patterns associated with molecular functions and pathways.

Results: Histological analysis revealed significant difference in retinal architecture and vitreous infiltrates. In comparison to S-PA, MDR-PA revealed altered expression of 923 genes at 6h and 2220 genes at 24h. Further, 23% and 76% of these altered genes and their downstream interacting proteins showed time specific expression (6h and 24h respectively), indicating its association with disease progression. Adhesion proteins like Desmocollin-2,-3, Protocadherin 10, Integrin beta-3, and Cadherin-22 were upregulated during 6h, while growth factors like fgf11, fgf9, and regulator of G protein signalling were downregulated. At 24h. Lipocalin along with TNF receptor-associated factor 1 and GFAP was found to be upregulated at 24h. Histopathological changes and DEG's suggest that the magnitude of upregulation was stronger at 24h. Major clustering of genes at 24h involved in disease progression involved: inflammasome signalling, dysregulated ubiquitination, complement cascade, extracellular matrix remodelling.

Conclusions: The transcriptional differences between the two time points reveal that distinct genes contributes to disease severity and provided novel insights by extending the number of molecular determinants and functional pathways that underpin host associated damage.

CONTROL ID: 3709987

SUBMITTER (NAME ONLY): Yong-Seok Song

TITLE: Cytochrome P450 1B1 regulates ocular oxidative stress through modulation of iron homeostasis by retinal endothelial cells

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Song, I. Zaitoun, N. Sheibani, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|C.M. Sorenson, Department of Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|Y. Song, I. Zaitoun, C.M. Sorenson, N. Sheibani, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Yong-Seok Song: Commercial Relationship: Code N (No Commercial Relationship) | Ismail Zaitoun: Commercial Relationship: Code N (No Commercial Relationship) | Christine Sorenson: Commercial Relationship: Code N (No Commercial Relationship) | Nader Sheibani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Cytochrome p450 1B1 (CYP1B1) is a CYP enzyme, found primarily in extrahepatic tissues including the eye, with important roles in tissue development and homeostasis. CYP1B1 metabolizes both exogenous and endogenous molecules including 17β-estradiol and arachidonic acid. We previously showed that CYP1B1 deficiency results in increased oxidative stress mitigating angiogenesis in vivo and in retinal endothelial cells (REC) in vitro. The aim of the current study was to determine the molecular mechanisms by which CYP1B1 modulates ocular redox homeostasis. We propose this is accomplished through the regulation of ocular iron homeostasis.

Methods: REC are major regulator of ocular iron homeostasis and express all the iron regulator proteins. REC isolated from wild-type C57BL/6J and Cyp1b1-deficient ($Cyp1b1^{-/-}$, same background) mice were used for in vitro studies. Expression levels of genes involved in iron homeostasis were assessed by RT-qPCR and Western blot analysis. Intracellular iron levels were determined using fluorescent probes. Lipid peroxide production was examined by immunofluorescence staining. Ferroptosis sensitivity was assessed by incubation of cells with different concentrations of erastin, a ferroptosis inducer, using an MTS assay. For in vivo studies, $Cyp1b1^{-/-}$ mice were intraperitoneally injected with estrogen receptor alpha antagonist methyl-piperidino-pyrazole (MPP) or iron chelator deferoxamine (DFO) during oxygen-induced ischemic retinopathy (OIR).

Results: $Cyp1b1^{-/-}$ REC showed increased levels of bone morphogenetic protein 6 (BMP6), which drove hepcidin expression and decreased ferroportin levels resulting in increased intracellular iron accumulation. The intracellular iron levels in REC were confirmed by Calcein and FerroOrange staining. The increased iron levels in$Cyp1b1^{-/-}$ REC were concomitant with increased levels of lipid peroxidation and enhanced sensitivity to ferroptosis. These changes in $Cyp1b1^{-/-}$ REC and $Cyp1b1^{-/-}$ mice were reversed by incubation with iron chelator DFO or MPP.

Conclusions: Our findings establish that CYP1B1 expression maintains ocular redox homeostasis through estrogen receptor signaling impacting iron homeostasis by modulation of BMP6 levels in the endothelium. Lack of Cyp1b1 results in increased intracellular iron levels, enhanced lipid peroxidation, and oxidative stress.

CONTROL ID: 3709989

SUBMITTER (NAME ONLY): Maria Weller

TITLE: Longterm porcine retinal explants as an alternative to in vivo experimentation

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Weller, B. Müller, K. Stieger, Experimental Ophthalmology, Justus Liebig Universitat Giessen, Giessen, Hessen, GERMANY|

Commercial Relationships Disclosure: Maria Weller: Commercial Relationship: Code N (No Commercial Relationship) | Brigitte Müller: Commercial Relationship: Code N (No Commercial Relationship) | Knut Stieger: Commercial Relationship(s);Code C (Consultant/Contractor):SpliceBio, CoaveTx;Code F (Financial Support):CoaveTx

ABSTRACT BODY:

Purpose: The porcine retina represents an optimal model system for inherited retinal dystrophies due to the anatomical similarities to the human retina, including a cone enriched visual streak. As large animal models require significant infrastructural and financial resources, the organotypic retina culture might pose a good model system to study gene therapeutic approaches prior to in vivo application. However, to this date it appeared to be difficult to reproduce good quality explants that can be kept in culture long enough to enable viral vector mediated genome editing experimentation. Our protocol allows to keep explants in culture for up to 20 days with good morphological preservation.

Methods: Two to four retinal explants per eye were obtained from the visual streak and transferred onto a polycarbonate membrane insert with the photoreceptors facing down. They were cultured for up to 28 days with Neurobasal-A medium containing 100 or 450 mg/dl glucose at 37°C and 5% CO_2. We supplemented the medium with combinations of fetal calf serum, B-27 with or without Insulin and N-2. Explants were analyzed using confocal laser scanning microscopy after immunofluorescent (IF) labeling with antibodies against glial fibrillary acidic protein, glutamine synthetase, protein kinase C alpha, rhodopsin, and short-wave-sensitive opsin 1, all counterstained with 4',6-Diamidino-2-phenylindol (DAPI).

Results: We were able to keep explants in culture up to 20 days with only little degradation as seen after IF at different harvesting time points. Best results were attained using Neurobasal-A medium containing 100 mg/dl glucose, 2x B-27 containing Insulin, 1x N-2, 1x L-Glutamine and 1x antibiotic-antimycotic, and a medium change every 48 hours. Eyes treated with heat for decontamination purposes by the butcher showed significantly less good preservation compared to those obtained without heat treatment. Keeping the eyes in ice cold medium until right before preparation and minimizing transport time gave the best results.

Conclusions: Using a standardized protocol, porcine retinal explants represent an easy to handle intermediate model between in vitro and in vivo experimentation. Using pig eyes from a local butcher renders this model system easily reproducible and contributes to the implementation of the 3R principle by Russell and Burch. This model system is currently tested with standard gene therapy vectors for efficient gene transfer.

CONTROL ID: 3709993

SUBMITTER (NAME ONLY): Michael Elman

TITLE: Performance of AI-based Notal OCT Analyzer (NOA) in retinal fluid volume quantification from repeated self-imaging with Home OCT in eyes with neovascular age-related macular degeneration (nAMD)

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Elman, S. Schechet, Elman Retina Group, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Michael Elman: Commercial Relationship(s);Code F (Financial Support):National Eye Institute;Code F (Financial Support):Apellis Pharmaceuticals;Code F (Financial Support):Alimera Sciences, Inc;Code F (Financial Support):Clover Therapeutics ;Code F (Financial Support):Neurotech Pharmaceuticals;Code F (Financial Support):NGM Biopharmaceuticals, Inc;Code F (Financial Support):Novartis Pharmaceuticals, Inc;Code I (Personal Financial Interest):Notal Vision | Sidney Schechet: Commercial Relationship(s);Code C (Consultant/Contractor):Alimera Sciences

ABSTRACT BODY:

Purpose: To evaluate the performance of NOA in 2 different aspects, precision of fluid volume quantification on consecutive in-clinic self-imaging as well as agreement with reference office OCT scans acquired in the same visit

Methods: The NOA is a deep learning algorithm that analyzes scans of the Notal Vision Home OCT (NVHO). The data is comprised of 242 NVHO volume scans acquired from 47 patients and 88 eyes with nAMD. Repeatability of fluid volume was calculated for all eyes with at least two repeats via coefficient of variance (CV). Retinal fluid agreement with manually annotated Cirrus scans was evaluated on a subset of the data and was estimated globally and spatially. Global agreement estimation was calculated with Pearson correlation coefficient (PCC) and Lin's concordance correlation coefficient (CCC). Spatial agreement was calculated with 2D correlation of the fluid thickness maps and on gridded versions of the original maps. All analysis was performed on eyes with clinically meaningful retinal fluid volume greater than 3 nanoliter

Results: NOA repeatability performance was evaluated on a set of scans from 26 eyes resulting in a CV of 4.1%. NOA agreement with Cirrus was evaluated on a subset of 23 eyes with an expert annotation of retinal fluid in the Cirrus scans. The PCC and CCC of retinal fluid volume between Cirrus and the NVHO with NOA were 0.984 and 0.975 respectively. For spatial agreement, the median (IQR) 2D correlation was 0.869 (0.769-0.940) and the median (IQR) 2D correlation of the maps with grids with densities of 20x20,10x10 was 0.841 (0.720-0.941) and 0.915 (0.757-0.963), respectively

Conclusions: The results validate the performance of the home OCT system comprised of a device and an AI-based algorithm. The low CV allows for accurate retinal fluid quantification with small variation in clinically meaningful amounts of retinal fluid. The high PCC and CCC of fluid volume and spatial correlation confirm that the same pathologies were accurately identified by NOA and the reference office OCT. Overall, the results present further evidence for the ability of the Notal Vision Home OCT to remotely monitor nAMD disease activity

CONTROL ID: 3710004

SUBMITTER (NAME ONLY): Mohajeet Bhuckory

TITLE: 3-dimensional subretinal prosthesis with single-cell resolution

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In patients with geographic atrophy, planar subretinal photovoltaic implants with 100μm bipolar pixels provided prosthetic acuity up to 20/460, closely matching the pixel size. In rats, similar implants with 75 and 55μm bipolar pixels also demonstrated grating acuity matching the pixel pitch. However, stimulation threshold increases with decreasing size of bipolar pixel in planar implants, and it exceeds the electrode charge injection limit with pixels smaller than 40μm. To overcome this limitation, we developed 3-dimensional honeycomb-shaped electrodes. Retinal cells migrating of the into the honeycomb wells should experience a nearly uniform vertical electric field, resulting in a significantly lower stimulation threshold, independent of the pixel width. Here, we investigate the structural integration of the inner retinal cells with the wells matching the single cell size.

Methods: The 1 mm wide, 30 μm thick implants with 10 μm deep wells were fabricated in silicon, with wells diameter of 6, 8, 10 and 12 μm. Devices were implanted beneath the degenerate rat retina (RCS, p180-300) for 6 weeks, and then examined with confocal imaging of retinal whole mounts. The integration was quantified by counting the DAPI-positive nuclei within the wells. The cells populating the wells and the immune response were assessed on immunolabelled whole mounts with various cellular markers.

Results: The fraction of cell-filled wells increased with the pixel width: from 22% in 6 and 8 μm wells to 70% in 12 μm wells. The 10 μm wells had the best integration, with 60% of its cavities containing single cells, while in the 12 μm implants, more than half of the wells had more than one nucleus. The immune reaction to the implants was as mild as with planar arrays: 6% of the 10 μm wells were populated by IBA1 positive cells (microglia).

Conclusions: Honeycomb-shaped subretinal prostheses with 10 μm wide wells enable individual inner retinal neurons to migrate into the cavities that can contain active electrodes of individual pixels, which should allow single-cell stimulation. Since pixel size of 10 μm geometrically corresponds to visual acuity of about 20/40, this approach may enable highly functional restoration of central vision in patients with advanced age-related macular degeneration.

CONTROL ID: 3710008

SUBMITTER (NAME ONLY): YongUn Shin

TITLE: Differential expression of aqueous humor microRNAs in central retinal vein occlusion and its association with matrix metalloproteinases

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Shin, E. Hong, H. Yu, H. Cho, Hanyang University, Seongdong-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To investigate the differential expression of microRNAs (miRNAs) in aqueous humor of patients with central retinal vein occlusion (CRVO) and its association with aqueous humor matrix metalloproteinase (MMPs) activity.

Methods: A total of 18 subjects, including 10 naïve CRVO patients (CRVO group) and 8 control subjects (control group) who were scheduled for intravitreal injection and cataract surgery, respectively, were included. The aqueous humor samples collected at the beginning of each procedure were analyzed. First, a microarray composed of 84 microRNAs was performed to find differentially expressed miRNAs in the CRVO aqueous humor, which were further analyzed using a bioinformatics tool to identify directly related cytokine/proteins in CRVO. Finally, MMP-2 and -9 were selected and the aqueous humor MMP-2 and -9 activities were detected using gelatin zymography.

Results: Eight miRNAs (hsa-mir-16-5p, hsa-mir-142-3p, hsa-mir-19a-3p, hsa-mir-144-3p, hsa-mir-195-5p, hsa-mir-17-5p, hsa-mir-93-5p, and hsa-mir-20a-5p) were significantly downregulated in CRVO group compared to control group. Bioinformatics showed a direct relationship between down-regulated miRNAs, CRVO disease, and the following proteins: MMP-2, MMP-9, tumor necrosis factor (TNF), transforming growth factor-beta 1 (TGFB1), caspase 3 (CASP3), interleukin-6 (IL6), interferon-gamma (IFNG), and interleukin-1-beta (IL1B). Gelatin zymography analysis showed significantly increased MMP-2 and -9 activities in aqueous humor of the CRVO group compared to that of the control group ($p < 0.01$).

Conclusions: This study was the first to investigate the differentially expressed miRNAs and the activity of associated MMPs in aqueous humor of CRVO patients. MMP-2 and -9 were directly related to down-regulated miRNAs, and their activities have significantly increased in the aqueous humor of CRVO patients. Therefore, the relevant miRNAs and MMPs in aqueous humor could serve as potential biomarkers or therapeutic targets in CRVO.

CONTROL ID: 3710011

SUBMITTER (NAME ONLY): Dan Mejlachowicz

TITLE: Chronic systemic dexamethasone regulates the mineralocorticoid/glucocorticoid pathways balance in rat ocular tissues

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Mejlachowicz, M. Zola, M. Naud, F. Jaisser, M. Zhao, F.F. Behar-Cohen, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|M. Zola, F.F. Behar-Cohen, Opthalmology, Hopital Cochin, Paris, Île-de-France, FRANCE|R. Gregorio, Universidade Federal de Minas Gerais, Belo Horizonte, MG, BRAZIL|

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ABSTRACT BODY:

Purpose: Central serous chorioretinopathy (CSCR) is a rare ocular side-effect of glucocorticoids (GCs). But contrarily to the other GCs-induced side effects, the route of GCs administration influences the risk of CSCR. The nasal, articular, oral and dermal routes favor CSCR but not the high and sustained intraocular GCs. To evaluate potential involvement of the hypothalamic-pituitary-adrenal axis (HPA) brake, we studied the corticosterone ocular levels and the corticoid receptors balance after chronic systemic dexamethasone treatment in rats.

Methods: Lewis rats were untreated (N=7) or received systemic injection of either dexamethasone (N=16) or saline (N=5) daily for 5 days. Baseline levels of corticosterone were measured by Elisa at baseline and at 5 days in the serum and the ocular media and dexamethasone levels were measured at 5 days in the serum and ocular media. The expression level of Nr3c1, Nr3c2, 11-bhsd1 and 2 were measured in the neural retina, retinal pigment epithelium (RPE)/choroid and iris/ciliary body. The expression of mineralocorticoid-induced genes was evaluated in the neural retina: Enac-a, Kir4.1 and Aqp4 and in the RPE/choroid: Shroom 2, Ngal, Mmp9, Omg, Ptx3, Plaur and Fosl-1.

Results: After dexamethasone injection, corticosterone level significantly dropped in serum ($p<0.0001$) and in ocular media ($p<0.002$). After saline injection, serum corticosterone also dropped. In the neural retina, the expression of Nr3c1 encoding GR was down-regulated after treatment with dexamethasone ($p<0.01$) or saline ($p<0.001$), which was also seen for Nr3c2 encoding MR ($p<0.001$) but the Nr3c2/Nr3c1 expression balance did not change significantly. In the RPE/choroid of dexamethasone treated rats, a significant increase in the Nr3c2/Nr3c1 ($p<0.01$) and 11β-hsd2/11β-hsd1 ($p<0.05$) ratio was measured showing hyperactivation of MR pathway. In the retina, Enac-a, Kir4.1, Aqp4 were down-regulated after dexamethasone treatment ($p<0.05$). In RPE/choroid, the expression of Plaur ($p<0.01$) and Fosl-1 ($p<0.05$) was increased and Omg was reduced ($p<0.05$) after dexamethasone treatment, in line with MR overactivation.

Conclusions: The HPA axis brake resulting from systemic chronic dexamethasone causes a significant reduction of systemic and ocular corticosterone and an imbalance of corticoid receptors expression in the RPE/choroid towards overactivation of MR, which could favor the occurrence of CSCR.

CONTROL ID: 3710012

SUBMITTER (NAME ONLY): Nathaniel Norberg

TITLE: Enhanced visualization and progression tracking of gaze dependent features in adaptive optics ophthalmoscopy.

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Grieve, M. Paques, Sorbonne Université, INSERM, CNRS, Institut de la Vision, Paris, FRANCE|E. Rossi, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|E. Rossi, Bioengineering, University of Pittsburgh Swanson School of Engineering, Pittsburgh, Pennsylvania, UNITED STATES|N. Norberg, K. Grieve, M. Paques, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: We previously reported a novel method for visualizing drusen using flood illumination adaptive optics (FIAO) ophthalmoscopy that exploits gaze-dependent contrast variations to detect drusen with high contrast and resolution [Rossi et al. TVST 2021;10(14):19]. Here we expand on that method by comparing gaze-dependent FIAO images to adaptive optics scanning laser ophthalmoscopy (AOSLO) and extend this approach to other maculopathies: pigment epithelial detachment, subretinal drusenoid deposits (SDDs), retinal pigment epithelium (RPE) atrophy, small hard exudates, serous retinal detachment and poppers maculopathy.

Methods: A FIAO fundus camera (rtx1, ImagineEyes, France) was used to acquire a 4°×4° fovea-centered image and then its internal fixation target was moved to obtain 4–8 additional, overlapping images, with gaze displaced by +/- 2° vertically and horizontally (n=182 eyes). Custom software registered images and calculated the standard deviation (SD) of each pixel across areas of overlap. A subset of patients were imaged following the same protocol on AOSLO (PSI, Massachusetts) for multimodal comparison and investigation into gaze dependent imaging (GDI) in scanning technology.

Results: Gaze-varying structures were not detected in controls. GDI is effective if each image is in focus and precisely aligned. With GDI in FIAO, drusen were detected in patients with high contrast and clear structural delineation. While GDI of drusen shows a bright annulus, GDI of pigment epithelial detachment showed an irregular bright annulus; SDDs and RPE atrophy were lower contrast than drusen; small hard exudates showed punctuate gaze-dependent variability, while serous retinal detachment and poppers maculopathy did not show enhanced contrast by GDI. Gaze-dependent AOSLO detected drusen (figure) with differences in contrast between split and confocal modalities.

Conclusions: Gaze-dependent imaging in FIAO and AOSLO images allowed for visualization of microstructural features such as drusen via contrast enhancement. Our method shows individual drusen delineation that furthers our capacity to detect, map, measure, and monitor progression of drusen. Multi-modal comparison is essential to build a correct and complete interpretation of gaze dependent retinal structures, therefore extension of our method to scanning technology is beneficial, despite the difficulties of removing scan related-distortions.

CONTROL ID: 3710013

SUBMITTER (NAME ONLY): Gerhard Garhofer

TITLE: Altered retinal oxygen metabolism in patients with multiple sclerosis

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Garhofer, M. Kallab, N. Hommer, A. Schlatter, D. Schmidl, L. Schmetterer, Department of Clinical Pharmacology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|G. Bsteh, P. Altmann, Department of Neurology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|M. Pfister, R.M. Werkmeister, Center for Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Functional changes in the neural retina have been proposed to be associated with multiple sclerosis pathogenesis and progression. The aim of the present study was to assess retinal oxygen extraction and total retinal blood flow in patients with diagnosed relapsing multiple sclerosis (RMS) and history of unilateral optic neuritis (ON).

Methods: A total of 16 RMS patients and 18 healthy control subjects participated in this cross-sectional study. Retinal oxygen extraction was calculated using retinal oxygen saturation values obtained from the oxygen module of the retinal vessel analyzer (RVA, Imedos, Germany) and total retinal blood flow data measured with a custom-built Doppler optical coherence tomography (DOCT) system. Measurements were performed in both eyes of RMS patients (MS+ON eye referring to the eye with history of optic neuritis and MS-ON eye referring to the eye with no history of optic neuritis). One eye from each healthy subject was used as control.

Results: Retinal oxygen extraction was lowest in MS+ON eyes (1.8 ± 0.2 µl O_2/min), higher in MS-ON eyes (2.1 ± 0.5 µl O_2/min) and highest in healthy eyes (2.3 ± 0.6 µl O_2/min; p = 0.031 between groups). Total retinal blood flow was lower in MS+ON eyes (33.2 ± 6.0 µl/min) as compared to MS-ON eyes (38.3 ± 4.6 µl/min) and healthy eyes (37.2 ± 4.7 µl/min; p = 0.010 between groups).

Conclusions: The present study found retinal oxygen extraction to be reduced in eyes of patients with RMS. This reduction seems to be more pronounced in eyes with history of optic neuritis. The role of this reduction in retinal oxygen extraction in the disease process and whether it is a cause or consequence needs to be further investigated.

CONTROL ID: 3710016

SUBMITTER (NAME ONLY): Kaihua Hou

TITLE: A Comparison of Clinician and Deep Learning Performance at Detecting Visual Field Worsening

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hou, P. Herbert, M. Unberath, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|C. Bradley, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|C.A. Johnson, M. Wall, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|J. Sabharwal, P.Y. Ramulu, J. Yohannan, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the ability of a Deep Learning Model (DLM) and clinicians to identify Visual Field (VF) worsening among a large cohort of glaucoma patients.

Methods: We conducted a retrospective longitudinal study of glaucoma patients across multiple glaucoma providers with at least seven reliable VFs. The clinicians' decision of the presence of VF worsening in each eye was made at the time of the last VF in the series during routine clinical care. We trained a 2D convolutional Long Short-Term Memory DLM to predict VF worsening from the series of VFs for each eye(Figure 1). The reference standard for defining VF worsening used to train/test the DLM and evaluate clinician performance was defined as worsening in at least 4 out of the 6 trend-based and event-based algorithms: Mean Deviation (MD) slope, Visual Field Index (VFI) slope, Point Linear Regression (PLR) slope, Advanced Glaucoma Intervention Study (AGIS) score, Guided Progression Analysis (GPA), and Collaborative Initial Glaucoma Treatment Study (CIGTS). We split the data into 80%, 10%, and 10% for training, validation, and testing respectively for our DLM. The performance of the DLM and clinician at identifying VF worsening was evaluated in the test set using Area Under the Receiver Operating Characteristic Curve (AUROC).

Results: A total of 8,705 eyes from 5,099 patients were included. Adapting the reference standard criteria of VF worsening, a total of 869 eyes (10%) were found to have worsening VFs over time. The DLM had an AUROC of 0.94 (95% CI: 0.93, 0.99) for detecting VF worsening on the test set. In contrast, the clinician decision had an estimated AUROC of 0.63 (95% CI: 0.56, 0.70) on the test set.

Conclusions: A DLM was trained to identify VF worsening with good classification performance. The performance of the DLM at identifying VF worsening was superior to the performance of clinicians during routine clinical care.

CONTROL ID: 3710017

SUBMITTER (NAME ONLY): Anran RAN

TITLE: Federated Deep Learning for Classifying Glaucomatous Optic Neuropathy from Optical Coherence Tomography Volumetric Scans: A Privacy-preserving Multi-national Study

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. RAN, P.P. Chan, N.C. Chan, O. Wong, C. Tham, C.Y. Cheung, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|X. Wang, P. Heng, Department of Computer Science and Engineering, The Chinese University of Hong Kong, Hong Kong, HONG KONG|P.P. Chan, O. Wong, C. Tham, Hong Kong Eye Hospital, Hong Kong, HONG KONG|N.C. Chan, Prince of Wales Hospital, Hong Kong, HONG KONG|H. Yung, Tuen Mun Hospital, Hong Kong, HONG KONG|R.T. Chang, S.S. Mannil, Department of Ophthalmology, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|Y. Tham, C. Cheng, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: We aim to develop privacy-preserving deep-learning (DL) models with federated learning (FL), a technique taking advantage of datasets across multiple “clients” (i.e., different end-users or centers) without centralizing or sharing data, to classify glaucomatous optic neuropathy (GON) from 3D optical coherence tomography (OCT) volumetric scans.

Methods: This is a multi-national study. We collected datasets of OCT scans from 7 eye centers. Each dataset was a “client” and split into training, tuning, and testing sets with a ratio of 7:1:2. We experimented with three kinds of DL architectures to develop 3D FL-Models. Figure 1 illustrates the FL process, which consists of a “central server” and 7 local clients. The central server maintains a “Global Model” and coordinates clients’ updates on their local models. To be specific, each client trained locally on its own training set and then updated the model parameters to the central server after one training epoch. The central server aggregated the updates from each local model to refine the Global Model and then redistributed the updated Global Model to all the clients. Subsequently, each client continued fine-tuning locally with its tuning set based on the updated Global Model. This process repeated back and forth until the Global Model converged which was then tested on each client’s testing set. For performance comparison, we used all data from 7 clients to develop Joint-Models which served as the upper bound and were tested on the same testing sets as FL-Models.

Results: We used 8,436 volumetric scans from 2,192 patients (Table 1). FL-Models developed by three architectures achieved the area under the receiver operating curve (AUROC) values with ranges of 0.784-0.993, 0.805-0.996, and 0.809-0.991 in 7 clients, respectively. Joint-Models achieved AUROC values of 0.775-0.997, 0.807-0.999, and 0.822-0.996, respectively. In each client, the FL-Models had accuracy, sensitivity, and specificity similar to corresponding Joint-Models (Table 2).

Conclusions: The 3D FL-Models showed performance non-inferior to Joint-Models and achieved good generalizability without sharing any patient data among multiple centers. Our results demonstrated that the FL technique can ensure data security and enhance the feasibility of implementing DL-based OCT analysis to identify GON in real-world clinics.

CONTROL ID: 3710019

SUBMITTER (NAME ONLY): Ka-Yan Mak

TITLE: Diagnostic Contribution of Genes with Treatments or Interventional Clinical Trials in a Large Retinal Dystrophy Cohort

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mak, K. Kämpjärvi, K. Wells, J. Känsäkoski, P. von Nandelstadh, R. Perez, M. Gandia, S. Vattulainen-Collanus, M. Mikk, M. Muona, I. Saarinen, S. Tuupanen, J. Koskenvuo, Blueprint Genetics, a Quest Diagnostics Company, Espoo, FINLAND|K. Gall, A. Scocchia, J. Hathaway, Blueprint Genetics Inc, a Quest Diagnostics Company, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the recent past, vision loss secondary to inherited retinal disease (IRD) was considered ‘incurable.’ Progress in both gene therapy and the molecular characterization of IRDs has led to a rapid increase in the number of gene-specific treatments as well as planned and ongoing interventional clinical trials for ocular disease. Perhaps less apparent is how diagnostic genetic testing, such as with next-generation sequencing (NGS), informs the opportunity for gene-specific treatments and interventional clinical trials for IRD. Here, we assess how NGS-based panel results impact access to targeted treatment and clinical trials in a large cohort of patients with IRD.

Methods: We carried out a retrospective analysis of test results from 18,026 deidentified patients who were tested consecutively with an IRD-related panel at Blueprint Genetics (Table 1). The target regions included coding exons, intronic regions ± 20 bps from the exon-intron boundaries and clinically significant noncoding variants. Copy number analysis was done bioinformatically from the NGS data using 2 different pipelines, including 1 proprietary pipeline developed for the detection of small, exon-level CNVs. Variant interpretation was performed according to American College of Medical Genetics guidelines. Clinical information, demographics, and results were extracted from the internal laboratory database.

Results: The median coverage of all target regions was 99.91% at >20X while the median sequencing depth was 210X. The median age at testing was 46 years. Males made up 48.4% (8,730) of the cohort while females made up 51.1% (9,203). Sex was not specified in 0.5% (93) patients. A molecular diagnosis was made in 9,156 (50.8%) patients while a variant of unknown significance (VUS) favoring pathogenic was identified in an additional 973 (5.4%) patients. A total of 214 genes were involved in the molecular diagnoses of IRD. In particular, diagnoses involving the 14 genes for which therapy or clinical trial is available accounted for 41.7% of the total diagnoses (Table 2).

Conclusions: For every 5 patients who received a molecular diagnosis for their IRD in this cohort, 2 have a diagnosis involving a gene/specific variant that may allow them to access treatment or a clinical trial.

CONTROL ID: 3710020

SUBMITTER (NAME ONLY): Connie Ho

TITLE: Predictors of glaucomatous progression in patients with small and large optic discs

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To identify factors associated with visual field (VF) progression in glaucoma patients with small and large optic discs.

Methods: We performed a retrospective review of glaucoma patients with small and large optic discs from the UCLA Stein Glaucoma Division from 1993-2019. Disc size was defined by optical coherence tomography (OCT) or Heidelberg Retinal Tomography (HRT) values with disc area ≤1.3 mm^2 (5^{th}%) and ≥2.9 mm^2 (95^{th}%). Patient charts were reviewed for demographics, diabetes, cardiovascular disease, autoimmune disease, glaucoma type, and ocular comorbidities. VF deterioration was measured by the Glaucoma Rate Index (GRI),[1] and eyes were categorized into fast (GRI<-6) or slow (GRI>-6) progressors. Logistic regression models were performed with all covariates as predictors and GRI<-6 as the outcome.

Results: Of 4,505 patients with eligible disc photos, the study population included 331 eyes with small discs (mean GRI=-3.7) and 234 with large discs (mean GRI=-3.8). In small discs, female gender was associated with increased progression (adjusted odds ratio [aOR]=3.14, 95% confidence interval [CI]=1.71,5.99), while other types of glaucoma (versus primary open angle glaucoma) were associated with decreased progression (aOR=0.11, CI=0.02,0.40). In large discs, increased intraocular pressure (IOP) range was associated with increased progression (aOR=1.35, CI=1.12,1.66). Characteristics associated with large discs included vasospastic phenotype[2] (aOR=0.37, CI=0.18,0.7) and certain races/ethnicities (Black: aOR=0.05, CI=0.02,0.12; Hispanic: aOR=0.1, CI=0.04,0.24; Asian: aOR=0.23, CI=0.14,0.38; Other: aOR=0.35, CI=0.21,0.6) (aORs calculated as small versus large). Potential associations between some covariates and progression may have been undetected due to low proportions of affected patients and insufficient statistical power.

Conclusions: Multiple characteristics were associated in glaucoma patients with small and large discs, as well as with their disease progression. Further investigation of discernible glaucoma phenotypes would be beneficial to improve disease prognostication, treatment, and interpretation of complex genetic associations.

References:

1. Caprioli J, et al. A Method to Measure the Rate of Glaucomatous Visual Field Change. Transl Vis Sci Technol. 2018;7(6):14.

2. Alizadeh R, et al. A Phenotype of Primary Open-Angle Glaucoma with Systemic Vasospasm. J Glaucoma. 2018;27(11):987-992.

CONTROL ID: 3710021

SUBMITTER (NAME ONLY): Valeria Lo Faro

TITLE: Post-GWAS investigation of multi-ancestry meta-analysis reveals enrichment of epithelial to mesenchyme-like transition genes in primary open-angle glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) is a complex ocular disease characterized by death of retinal ganglion cells and atrophy of the optic nerve head that, if untreated, leads to blindness. Previous studies have shown that POAG has a genetic etiology component, however, the identification of all the causative genetic factors has proven to be challenging. Investigation of the underlying genetics and cell types involved in POAG can contribute to a better understanding of the disease mechanisms. In our study, we conducted post-GWAS analyses oriented to the investigation of pathway, gene, tissue, and cell types prioritization in a multi-ancestry POAG cohort.

Methods: We used results generated from a large-scale genome-wide association POAG meta-analysis, conducted in subjects sourced from 15 global biobanks participating in the Global Biobank Meta-Initiative (GBMI), a collaboration of global biobanks. A total of 26,848 cases and 1,460,599 controls from six ancestries were analyzed. We evaluated if the genomic loci were implicated in POAG map specific cell types using Linkage Disequilibrium Score Regression (LDSC), and compared results obtained from Data-driven Expression Prioritized Integration for Complex Traits (DEPICT) analyses. GeneMANIA was used to investigate gene interaction. In order to prevent spurious findings, false discovery rate method was used for multiple testing corrections.

Results: The significant results from LDSC pointed to mesenchymal, vascular and adipocytes cell types, showing consistency with the results also obtained in tissue-enrichment analysis from DEPICT. Furthermore, gene-prioritization identified 54 genes that were used to construct interaction networks. Potential hub genes identified were BMP2, CPE, FERMT2, FOXC1, MYBPC3, PARVA, SEMA3C, SIX4, TGFB2, TGFBR3, and TPM1. Nine of these genes have a role in epithelial to mesenchyme-like transition cellular mechanism.

Conclusions: Our findings promote the potential role of the epithelial to mesenchyme-like transition in POAG and contribute to improving the biological mechanisms underlying this condition. Further experimental studies are required to investigate this potential contribution with respect to POAG pathogenesis and to identify novel target genes.

CONTROL ID: 3710023

SUBMITTER (NAME ONLY): Karis Little

TITLE: Characterising retinal neurovascular dysfunction in a mouse model of Alzheimer's disease combined with Type 2 diabetes

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Type-2 diabetes (T2D) is associated with increased risk of Alzheimer's disease (AD). Commonly affected pathways centre around the neurovascular unit (NVU). Glial pathology, neurodegeneration and vascular damage are hallmarks of both diabetic retinopathy (DR) and AD. Therefore, retinal pathology may be useful to understand brain changes in T2D and AD. We assessed retinal pathology in mice models of AD and T2D, and a crossed model of AD/T2D to understand the pathogenesis of this important co-morbidity.

Methods: The NVU was assessed in retinal tissue from WT, APP/PS1, db/db and APP/PS1xdb/db mice at 14 and 26 weeks old. Immunohistochemistry staining was carried out to assess gliosis (GFAP), acellular capillaries (Isolectin-B4/Collagen 4), and Müller cell potassium/ water homeostasis (Kir4.1, AQP4). Changes to neuronal populations were assessed by staining for Calbindin (Horizontal cells), Brn3a (Retinal Ganglion cells) and Cone-arrestin (Cone-photoreceptors).

Results: We observed NVU dysfunction in APP/PS1xdb/db retina including significant Müller cell gliosis at 14 weeks ($p<0.05$). Müller cells showed alteration of Kir4.1 and AQP4 localisation in APP/PS1 and db/db retina which was more apparent in APP/PS1xdb/db mice at 26 weeks. APP/PS1 x db/db mice had significantly more acellular capillaries than WT mice at 14 weeks ($p<0.01$). A significant decrease in retinal ganglion cells was observed at 26 weeks in db/db ($p<0.05$) and APP/PS1 x db/db mice ($p<0.05$) compared to WT. Horizontal cells were significantly reduced in APP/PS1 ($p<0.05$) and APP/PS1xdb/db ($p<0.05$) retina at 26 weeks. A significant decrease in the number of Cone arrestin^{+} cells in the APP/PS1xdb/db retina was observed at both 14 ($p<0.001$) and 26 weeks ($p<0.001$) vs WT. The number of DAPI^{+} cells in the outer nuclear layer was significantly reduced in APP/PS1xdb/db mice compared to APP/PS1 ($p<0.001$) and db/db ($p<0.05$) alone.

Conclusions: We observed evidence of NVU dysfunction APP/PS1xdb/db retina, which appeared to be more severe than APP/PS1 or db/db alone. This occurs alongside severe cognitive impairment in this model (1). APP/PS1xdb/db had increased gliosis and dysregulation of water and ion homeostasis together with retinal neurodegeneration features. Further studies are required to characterise the changes of the NVU in the retina and brain during diabetes related neurodegeneration. (1) Infante-Garcia et al. 2016

CONTROL ID: 3710024

SUBMITTER (NAME ONLY): Mathias Gallardo

TITLE: Evaluating an OCT-based Algorithm of Central Subfield Thickness Estimation on AMD and DME patients

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the accuracy of an algorithm to estimate Central Subfield Thickness (CST) from OCT volumes for patients with AMD or DME.

Methods: We collected OCT volumes from two groups of patients, respectively including exudative AMD (541) and DME (1’568) patients. We refer to them as the AMD group and DME group. All patients received an anti-VEGF treatment, were treated and monitored between 01/2013 and 06/2021. We found 3’974 OCT volumes for the AMD group and 11’501 OCT volumes for the DME group. The algorithm to be evaluated relies on the CE-marked Discovery® layer segmentation algorithm (RetinAI Medical AG, Switzerland) and computes the average retinal thickness in the central-1mm region from the ETDRS grid. For each OCT volume, the true CST was measured independently by two graders and a third grader in case of disagreement. The annotations were performed by the Bern Photographic Reading Center (Inselspital, Universitätsspital Bern, Universitätsklinik für Augenheilkunde, Bern, Switzerland). After removing the ungradable OCT volumes and considering the 99^{th} percentile of the thicknesses, the AMD group comprises of 3’894 OCT volumes (537 patients) and the DME group of 11'269 OCT volumes (1’526 patients).

Results: We reported a strong correlation between the annotated values of CSTs and the predicted ones from the algorithm (R2=0.96) for both groups. We observed that the algorithm tends to over-estimate the retinal thickness in general, leading however to a small mean absolute error (prediction - annotation), 3.19µm (95% CI, 2.6–3.8µm) and 10.68µm (95% CI, 10.4–11µm) for AMD and DME groups, respectively. Indeed, relatively to the median annotated CSTs (302µm and 310µm), these errors represent 1.06% and 3.44% of the total retinal thickness for AMD and DME cohorts, respectively. We observed that 5.4% (210/3’894) samples are located outside the 95% limits of agreement for AMD and 5.1% (574/11 269) samples are located outside the 95% limits of agreement in DME.

Conclusions: We report very good performances for CST estimation on OCT volumes with AMD and DME. This unveils the potential of such algorithms to support clinical decision making and to envision new strategies to facilitate annotation for clinical trials. To understand the sources of the difference in CST errors between the two groups, we plan to analyze the ETDRS alignment and to consider the presence of fluids and other biomarkers.

CONTROL ID: 3710028

SUBMITTER (NAME ONLY): Masaru Takeuchi

TITLE: Adalimumab Treatment for Recurrence of Ocular Inflammation in Patients with Vogt-Koyanagi-Harada Disease: a multicenter study

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We investigated efficacy and safety of adalimumab (ADA) treatment for exacerbation or recurrence of Vogt-Koyanagi-Harada (VKH) patients.

Methods: This is a retrospective, multi-centre cohort study. Medical records of 70 VKH patients who received ADA treatment for more than 6 months were retrospectively investigated for best corrected visual acuity (BCVA), aqueous flare counts, subfoveal choroidal thickness (SFCT), indocyanine green angiography (ICGA) score, corticosteroid doses, and presence or absence of immunosuppressors at baseline before the initiation of ADA and 6 months later. Adverse events were recorded.

Results: The mean age of VKH patients was 54.8 ± 15.1 years and male/female ratio was 34/36. SFCT, ICGA scores, and corticosteroids and cyclosporine doses were significantly reduced by ADA treatment for 6 months compared to baseline, while LogMAR visual acuity and flare counts were also improved without being statistically significant. When sub-classified into VKH patients with the presence of sunset glow fundus (SGF) and without SGF, SFCT, ICGA scores, and mean corticosteroid doses were significantly lower after ADA treatment for 6 months, but the difference was not significant for LogMAR visual acuity and flare counts compared to baseline in the group without SGF. In the group with SGF, LogMAR visual acuity, ICGA scores and mean corticosteroid doses were significantly lower, but the difference was not significant for flare counts and SFCT when compared to baseline. Adverse events were observed in 17.1%, in which infection including tuberculosis was at 7.14% and psoriasis was at 2.86%. ADA treatment was continued in 91.4%.

Conclusions: ADA was shown to be effective to achieve remission of VKH disease refractory to conventional immunosuppressive treatments, and was generally well tolerated with few serious adverse events.

CONTROL ID: 3710036

SUBMITTER (NAME ONLY): Filippo Amore

TITLE: Usability and Adherence to the EyeFitness telerehabilitation software in visually impaired patients. Preliminary results of a multicentre study

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Amore, V. Silvestri, M. Sulfaro, M. Guidobaldi, P. Piscopo, National Reference Centre Service, Research, Prevention of Blindness and Vision Rehabilitation - WHO Collaborating Centre, ROMA, ITALY|G. Villani, Cooperativa Sociale QUID - Progetto Yea. Riabilitazione Visiva per Ipovedenti di Verona, Verona, ITALY|G. Giacomelli, Department of Neuroscience, Psychology, Drug Research and Child Health, University of Florence, Careggi Teaching Hospital, Florance, ITALY|G. Carnovale Scalzo, Department of Ophthalmology, Magna Graecia University, Catanzaro, Catanzaro, ITALY|F. Perna, Ophthalmology Clinic, Department of Medicine and Science of Ageing, University G. D'Annunzio Chieti-Pescara, Chieti, Chieti, ITALY|S.N. Markowitz, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Telerehabilitation is a new way of providing web-based services to chronic patients who receive rehabilitative care at home with remote supervision by trained staff. It allows to increase the frequency and intensity of care provided to the patient.

The purpose of this study was to evaluate the usability of the EyeFitness telerehabilitation software and patients' adherence to treatment

Methods: 44 visually impaired subjects of various etiologies, 19 males and 22 females, mean age 53 4 years (SD= 19, 5 years, Range= 22-89 years), were enrolled. The home training using the EyeFitness software was conducted for 5 days a week, for a total of 6 weeks. The software was individually configured for each patient, choosing the exercises according to the eye disease, the patient's residual perceptive abilities (visual acuity and contrast sensitivity) and the specific visual skills to be enhanced. Recruitment and monitoring of the progress was conducted from five rehabilitation centers. The Post-Study System Usability Questionnaire (PSSUQ) was administered after the use of the software

Results: Patients had good adherence: one had a poor participation and only two interrupt the training before the end of the program; these were excluded from the analysis.The average overall completion rate for the 41 patients included in the analysis was 97,2% (SD= 5,2), indicating that the average patient completed their prescribed exercises 5 days per week over the course of their enrollment in the program. The PSSUQ indicator showed that patients were satisfied with the EyeFitness software, with an overall average score of 1,85 (SD= 0,96, Range= 1,04 - 2,86). The three sub-scales revealed positive opinions on system quality (mean score 1,45, SD= 0,87, Range= 1,19-2,025), information quality (mean score 1,77, SD= 1,5, Range= 1,25-4,23), and interface quality (mean score 2,01, SD= 1,32, Range= 1,82-2,55). Providers also commented favorably on the experience and found this approach useful in supporting traditional in-person vision rehabilitation

Conclusions:

Preliminary results show that both participants and providers gave positive assessments to the feasibility and acceptability of telerehabilitation sessions. The software could be a viable approach for visually impaired individuals who have difficulty attending traditional rehabilitation programs at the low vision center

CONTROL ID: 3710040

SUBMITTER (NAME ONLY): Soojin Kim

TITLE: Endothelial heterogeneity in the inner and outer blood-retinal barrier

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The blood-retinal barrier (BRB) has two components: inner and outer barrier. The neurovascular unit of the retina plays key roles in the inner BRB. Choroid, the major components of the outer BRB provides oxygen and nourishment to the retina. Retinal and choroidal blood vessels come in different morphologies and have distinct organotypic characteristics that enable them to execute tissue–specific functions. In this study, we investigated endothelial heterogeneity across the distinct vascular beds in the eye.

Methods: We evaluated molecular and functional differences between primary human retinal endothelial cells (HRECs) and human choroidal endothelial cells (HCECs) in terms of angiogenic and vasculogenic properties, permeability, and transcytosis. We performed tube formation assay, cell migration assay, in vitro permeability assay, microfluidic sprouting assay, and transcriptome analysis.

Results: HRECs showed higher proliferation and migration activity than HCECs, but the tube formation ability did not show a significant difference. HCECs displayed earlier sprouting angiogenesis but the overall speed was faster and more stable in HRECs under angiogenic stimuli. HRECs expressed higher adherens junctional proteins than HCECs, but the tight junctional genes and transcytosis related genes were more in HCEC. Angiopoietin-2 was predominantly expressed in HRECs, but VEGF receptors were higher in HCECs. PDGFB was higher in HRECs than HCECs which correlates to the less pericytes coverage in choroidal blood vessels. Our data indicate that HCECs is a quiescent endothelium but can be stimulated under the angiogenic environment, and have a specialized transcriptome for trans-endothelial molecular transport.

Conclusions: Retinal and choroidal blood vessels constitute two distinct BRBs under the endothelial heterogeneity: The outer BRB, size-selective barrier with vascular transcytosis for metabolic support, and the inner BRB, forming tight barriers, composes organotypic vasculature and maintains homeostasis in the eye.

CONTROL ID: 3710043

SUBMITTER (NAME ONLY): Kristian Lisbjerg

TITLE: Disease progression of retinitis pigmentosa caused by PRPF31 variants: A retrospective study with up to 36 years follow-up

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Lisbjerg, L. Kessel, Department of Ophthalmology, Rigshospitalet, Kobenhavn, DENMARK|M. Bertelsen, K. Gronskov, Department of Clinical Genetics, Rigshospitalet, Kobenhavn, DENMARK|J.P. Holtan, Department of Ophthalmology, Oslo Universitetssykehus, Oslo, NORWAY|L. Kessel, Department of Clinical Medicine, Kobenhavns Universitet, Kobenhavn, DENMARK|

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ABSTRACT BODY:

Purpose: The disease progression of retinitis pigmentosa (RP) differs between individuals and between different genetic subtypes. We performed a retrospective clinical study to characterize the natural disease progression in PRPF31-related autosomal dominant retinitis pigmentosa (RP11).

Methods: We identified individuals with RP11 and collected retrospective data from disease onset to present date including genetics, demographic data, Goldmann visual field areas, and visual acuity measures. Visual fields were evaluated as summed squared degrees and best corrected visual acuities were converted to logMAR. We performed linear mixed model regression analysis on the longitudinal data to evaluate the annual disease progression in visual fields, and we used survival analysis to evaluate the age when a person first meets legal blindness criteria.

Results: We included information on 46 subjects with RP11. Our study population represented 17 unique PRPF31 variants. Median age of disease onset was 10 years (range 5-65). Follow-up spanned from 0-36 years with a median of 8 years. Goldmann visual field areas decreased by 9.7% (95% CI 7.4 – 11.9) with Goldmann target IV4e and by 7.5% (95% CI 4.8 – 10.1) with target III4e per year. Best corrected visual acuity tends to decrease with age, however it did not decline to less than 20/200 in any of our cases. Survival analysis showed that half of the RP11 patients had reached legal blindness by the median age of 57 years (95% CI 41-75 years).

Conclusions: In retinitis pigmentosa caused by PRPF31 variants, disease onset is most frequently in early childhood with a variable disease progression depending on onset of symptoms. Visual field area deteriorates faster than best corrected visual acuity, and visual field loss is the main reason for legal blindness in our study population. Visual acuity naturally declines with age, but individuals with RP11 maintain a fair and relatively stable central visual acuity until late state disease in high age. This study characterizes the progression of retinitis pigmentosa caused by PRPF31 variants and can aid conduction of future prospective trials, and to advice and inform RP11 patients in a clinical setting.

CONTROL ID: 3710045

SUBMITTER (NAME ONLY): Yusuke Sano

TITLE: Identification of two putative fusion genes in eyelid and conjunctival tumors

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Sano, Y. Fujii, N. Funatsu, Kyushu Daigaku Igakubu Daigakuin Igakukei Gakufu Daigakuin Igaku Kenkyuin, Fukuoka, JAPAN|M. Akiyama, M. Tanabe, E. Seki, K. Yamana, H. Yoshikawa, K. Sonoda, Kyushu Daigaku, Fukuoka, Fukuoka, JAPAN|A. Fujimoto, Tokyo Daigaku, Bunkyo-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Transcriptome sequencing enables us to reveal fusion genes associated with carcinogenesis and gene expression patterns relevant to classification of cancers. The aims of this study are to identify fusion genes of eyelid and conjunctival malignant tumors, and to assess the characteristics of eyelid and conjunctival tumors among various cancer types by comprehensive cross-tumor gene expression analysis.

Methods: Twenty-three eyelid sebaceous carcinoma (SeC), three basal cell carcinoma (BCC), and three conjunctival squamous cell carcinoma (SCC) samples obtained at Kyushu University Hospital were included in this study. NovaSeq 6000® (Illumina) was used for RNA-sequencing. For detecting fusion genes and counting mapped reads, Genomon2.6.3 and HTSeq0.12.4 were used, respectively. The read counts were normalized for sequence depth and transcript length to assess gene expression level. We integrated publicly available transcriptomic data from 9,924 samples across 36 cancer types, with our 29 samples of RNA sequencing data for gene expression analysis in pan-cancers. The gene expression levels of 19,853 protein-coding genes were examined for differences among tumor types.

Results: We identified 130 pairs of fusion genes in SeC, 5 pairs in BCC, and 9 pairs in SCC, respectively. The fusion genes identified in multiple cases of the same cancer type included HOXC11-CRNDE fusion gene identified in 4 cases of SeC and TMBIM4-RPL14 fusion gene identified in 2 cases of BCC. In SCC cases, fusion genes detected in multiple cases were not identified. In the gene expression analysis of pan-cancer, eyelid and conjunctival tumors appeared to formed a unique cluster by dimensionality reduction using t-SNE. In addition, eyelid and conjunctival tumors exhibited gene expression patterns similar to those of squamous cell carcinomas of various primary organs.

Conclusions: HOXC11-CRNDE fusion and TMBIM4-RPL14 fusion may be associated with carcinogenesis of eyelid and conjunctival malignant tumors.

CONTROL ID: 3710051

SUBMITTER (NAME ONLY): Alexander Kolesnikov

TITLE: Knockout of Nr2e3 protects against photoreceptor degeneration in two mouse models of retinitis pigmentosa

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kolesnikov, V. Kefalov, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|D. Murphy, J. Corbo, Pathology and Immunology, Washington University in St Louis, Saint Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: In many retinal diseases such as retinitis pigmentosa (RP), single gene mutations cause rod photoreceptor death which is later followed by cone death. Traditionally, therapeutic efforts have aimed to reintroduce a normal copy of the mutated gene. However, RP is caused by mutations in dozens of different rod-specific or rod-enriched genes. Thus, there is a strong motivation to develop gene-independent therapies that could be used to treat a wide range of genetic forms of RP. While previous studies have shown the feasibility of this approach by targeting the rod-specific transcription factor Nrl, this disrupts gene expression and cases major changes in rod morphology and physiology. We tested the hypothesis that a more subtle approach, the knockout of Nr2e3 (a rod-specific transcription factor downstream of Nrl) will protect photoreceptors against degeneration in two different models of RP.

Methods: Rods in Nr2e3-deficient (rd7) mice are hybrid cells that ectopically express a subset of cone genes in addition to the normal complement of rod genes. We crossed rd7 mice with rhodopsin knockout ($Rho^{-/-}$) or rod phosphodiesterase (rd10) mutant mice. Retinal function and morphology were analyzed at different ages by in vivo electroretinography and immunohistochemistry. Scotopic and photopic visual acuity and contrast sensitivity were evaluated from optomotor behavior tests. RNA-seq analysis was performed to determine differential gene expression in wild type and rd7 retinas.

Results: ERG recordings revealed that M-cone function was preserved at wild-type levels for up to 6 months in $Rho^{-/-}$;rd7 mice, in contrast to control $Rho^{-/-}$ animals where it deteriorated gradually and was fully absent by 4 months. This result correlated with greatly extended survival of both rods and cones and maintenance of photopic vision in the $Rho^{-/-}$;rd7 mice. A similar degree of rod and cone structural and functional protection was observed in rd10;rd7 mice despite the very rapid retinal degeneration in rd10 mice. RNA-seq analysis showed up-regulation of several cone genes in rd7 retinas which might mediate protection against retinal degeneration.

Conclusions: Knockout of Nr2e3 slows retinal degeneration and ameliorates secondary cone death in two distinct models of RP. The therapeutic mechanism may involve the upregulation of one or more cone-enriched genes in rods.

CONTROL ID: 3710053

SUBMITTER (NAME ONLY): Jihye Ahn

TITLE: The composition of water in contact lens depend on the pH

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Ahn, Y. SamYoung, M. Choi, Optometry, Seoul National University of Science and Technology, Nowon-gu, Seoul, KOREA (THE REPUBLIC OF)|M. Choi, Convergence Institute of Biomedical Engineering and Biomaterials, Seoul National University of Science and Technology, Nowon-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Among contact lens materials, ionic materials have pK_a values which affects the degree of protonation by pH of swelling media. As a result of these degree of protonation, physical properties of contact lens can be altered including diameter, equilibrium water content. In this study, physical properties of contact lenses and state of water in contact lenses were examined depend on the pH.

Methods: The 1-Day ACUVUE MOIST (Johnson& Johnson Inc.) and SofLens (Bausch + Lomb Inc.) were used. PBS buffer solutions at pH from 5.8 to 8.2 were used though out the study. The diameter, equilibrium water content, and the quantity of freezable water (W_f) and non-freezable water (W_{nf}) in the contact lens at each pH condition was measured.

Results: The etafilcon A material contact lens showed decreased diameter, equilibrium water content, and the quantity of W_f with decreasing pH below 7.0. The quantity of W_{nf} tended to decrease with increasing pH. Hilafilcon B did not show specific trend in changes of diameter, equilibrium water content, and W_{nf} and W_f .

Conclusions: The diameter and equilibrium water content of the contact lens have decreased due to dehydration of the contact lens. The composition of W_{nf} and W_f showed conflicting results, which implies that dehydration can significantly change the ratio of water composition. Since the ratio of W_{nf} and W_f of the contact lens may vary, research should be conducted to reveal the correlation between these properties and the state of water in contact lens.

CONTROL ID: 3710055
SUBMITTER (NAME ONLY): Maria Miranda
TITLE: Dutasteride: possible new treatment in retinal degenerations
SESSION TITLE: Tissue, drug and genome engineering
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Miranda, A. Cantó, J. Martínez, V. Hernández-Rabaza, T. Olivar, I. Almansa, Ciencias Biomédicas, Universidad CEU Cardenal Herrera Facultad de Ciencias de la Salud, Alfara, Valenciana, SPAIN|
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ABSTRACT BODY:

Purpose: The interactions between gonadal steroid hormones and the retina have received limited attention, though it has been suggested that they may play a protective role in retinal diseases. The purpose of this work was to study the repurposing of one drug (dutasteride) for retinitis pigmentosa (RP) treatment. Dutasteride (DUT) is a 5α-reductase inhibitor that have not been associated with increases in serum testosterone levels. Furthermore, modulation or inhibition of 5α-reductase activity increases levels of neuroprotective steroids. We also studied the action mechanisms that provide DUT with a neuroprotective role in RP. To this end, the changes that dutasteride induce on markers of inflammation, and glutathione (GSH) metabolism in the retina of rds mice were studied.

Methods: Animals were treated in accordance with the ARVO statement for the use of animals in ophthalmic and vision research. Rds mice were treated intraperitoneally with DUT on postnatal days 11, 13, 15, 17 and 19 and euthanized on day 21. Hematoxylin-eosin, TUNEL, and rod and cone immunohistochemistry were performed to determine if DUT was able to delay photoreceptor death. Immunohistochemical techniques were used to study changes in retinal microglia (Iba-1) morphology and distribution. Degree of inflammatory cells activation was evaluated by measuring expression of CD68. Possible modifications of other glial cells were also studied with GFAP (glial fibrillar acid protein). Finally, GSH localization was examined, and western blot analysis was performed to determine retinal GSH synthesis and transport.

Results: DUT increased photoreceptor survival in rds mice. An increase in iba-1 positive cells was found in rds retinas and DUT normalized the number, migration and the length and number of branches in these cells ($p<0,01$). DUT decreased in CD68 and GFAP expression (more than 50% of increase in rds retina). Finally, DUT was also able to ameliorate the observed alterations in GSH metabolism in rds retina.

Conclusions: DUT may be used to ameliorate retinal micro and macroglial activation in RP, as well as alterations in the metabolism of the most important intracellular antioxidant.

CONTROL ID: 3710057

SUBMITTER (NAME ONLY): Rebekkah Hitti-Malin

TITLE: Single-molecule Molecular Inversion Probes allow cost-effective targeted sequencing of all genes and loci associated with macular diseases.

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.J. Hitti-Malin, S. Roosing, C. Dhaenens, A.I. Den Hollander, D. Panneman, E.G. Boonen, L. de Rooij, M. Guimaraes Ramos, M. van de Vorst, A. Hoischen, F.P. Cremers, Department of Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|R.J. Hitti-Malin, S. Roosing, D. Panneman, F.P. Cremers, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|C. Dhaenens, Lille Neuroscience & Cognition, Universite de Lille Faculte de Medecine, Lille, Hauts-de-France, FRANCE|A.I. Den Hollander, Department of Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|G. Farrar, The School of Genetics & Microbiology, The University of Dublin Trinity College, Dublin, IRELAND|B. de Koning, Department of Clinical Genetics, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|C. Gilissen, A. Hoischen, Radboud Institute of Molecular Life Sciences, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases are clinically and genetically heterogeneous. Amongst these are macular diseases (MDs) characterized by central vision loss. Inherited MDs (iMDs) are relatively rare and generally present at an early age, while age-related MD (AMD) is more prevalent and occurs later in life. The clinical and genetic heterogeneity in MDs makes a clear diagnosis challenging. The use of cost-effective single molecule Molecular Inversion Probes (smMIPs) to sequence ABCA4 in patients with Stargardt disease identified many coding and non-coding variants, but ~57% remained unsolved (Khan et al., 2020; PMID: 32307445). We hypothesized that the missing heritability may be revealed by smMIPs-based sequencing of all MD-associated genes.

Methods: We used 17,394 smMIPs designed by Molecular Loop Biosciences (USA) to sequence the coding regions of 105 iMD and AMD-associated genes, known pseudo-exons, and the mitochondrial genome. DNA libraries of 384 iMD samples previously investigated for variants in ABCA4, were pooled for sequencing on the NovaSeq 6000 platform. Variant filtering prioritized autosomal recessive variants with an allele frequency of ≤0.5% in population databases, and autosomal dominant variants with an allele frequency of ≤0.1%. Variants with a Franklin-ACMG classification of class 3-5 were selected.

Results: Across NovaSeq SP sequencing runs, an average nucleotide coverage of 680× was observed. Sequencing data for 104 iMD probands, who previously were shown not to carry two alleles in ABCA4, have been fully analysed. Across these 104 probands, 132 candidate variants in 40 genes, comprising two CNVs and 130 SNVs or indels, were identified. Of the SNVs or indels, 19 were class 5 variants (pathogenic), 21 class 4 variants (likely pathogenic) and 90 class 3 variants (VUS). Forty probands were considered to be genetically solved by disease causing variants in 24 genes, achieving a diagnostic yield of 38% within this ABCA4-pre-screened cohort.

Conclusions: Utilising smMIPs to target MD-associated genes and loci is a cost-effective approach. Further analysis will identify known and novel variants in iMD-associated genes, which will offer an accurate clinical diagnosis to patients and their families in addition to revealing new genetic associations for MDs.

CONTROL ID: 3710058

SUBMITTER (NAME ONLY): Kelsey Stuart

TITLE: Association of alcohol consumption with glaucoma and related traits

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.V. Stuart, R. Luben, K. Madjedi, P. Patel, P. Foster, A. Khawaja, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UNITED KINGDOM|R. Luben, MRC Epidemiology Unit, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|A. Warwick, UCL Institute of Cardiovascular Science, University College London, London, London, UNITED KINGDOM|K. Madjedi, Department of Ophthalmology, University of Calgary, Calgary, Alberta, CANADA|M. Lentjes, School of Medical Sciences, Örebro University, Örebro, SWEDEN|

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ABSTRACT BODY:

Purpose: Habitual alcohol consumption is an important modifiable risk factor associated with a multitude of adverse health outcomes, but evidence for the associations with glaucoma and related traits are unclear. We performed a cross-sectional observational study of UK Biobank participants as an understanding of these relationships may have important clinical and public health implications.

Methods: Participants (aged 39–72 years) were categorized according to self-reported drinking behaviors. Quantitative estimates of alcohol intake were derived from touchscreen questionnaires and food composition tables. We included participants with data on intraocular pressure (IOP) (n=109,097), inner retinal OCT measurements (n=46,414) and glaucoma (n=173,734). Ocular parameters were measured as part of a comprehensive eye examination and glaucoma case ascertainment was through a combination of self-report and linked national hospital records. Multivariable linear, logistic and restricted cubic spline regression were used to model associations. All analyses were adjusted for key sociodemographic, medical, anthropometric and lifestyle factors.

Results: Compared to never/infrequent drinkers, regular drinkers had higher IOP (+0.15mmHg; P<0.001) and non-significant trends towards a thinner retinal nerve fiber layer (RNFL), thinner ganglion cell–inner plexiform layer (GC–IPL) and higher odds of glaucoma. Former drinkers had a higher odds of glaucoma (OR 1.44; P=0.006). In regular drinkers, alcohol intake was associated with all outcomes in a dose-dependent manner. Compared to the lowest alcohol intake quintile (median 17g/week), participants in the highest quintile (median 278g/week) had higher IOP (+0.26mmHg; P<0.001), thinner RNFL (-0.41µm; P<0.001), thinner GC–IPL (-0.81µm; P<0.001) and higher odds of glaucoma (OR 1.30; P=0.008) (P_{trend} ≤0.003 for all). There was evidence for non-linearity with an apparent threshold effect at approximately 50g/week for RNFL, GC–IPL and glaucoma. No differential effect by sex or alcoholic beverage type was observed.

Conclusions: Alcohol intake was consistently and adversely associated with glaucoma and related traits, and at levels below current UK and US drinking guidelines. If further studies support a causal relationship, this may inform lifestyle advice for people with or at risk of glaucoma.

CONTROL ID: 3710059

SUBMITTER (NAME ONLY): Amrish Selvam

TITLE: Pigment Epithelial Detachment Vascularity Index (PEDVI) in Neovascular Age-Related Macular Degeneration: An Image Processing Approach

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Selvam, J. Ong, M.N. Ibrahim, J.A. Sahel, K.K. Vupparaboina, J. Chhablani, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|A. Kuchhal, Fox Chapel High School, Pittsburgh, Pennsylvania, UNITED STATES|M.A. Rasheed, University of Waterloo School of Optometry and Vision Sciences, Waterloo, Ontario, CANADA|M. Patel, BJ Medical College, Ahmedabad, Gujarat, INDIA|S. Manne, Department of Electrical Engineering, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: To provide an automated method of characterizing the presumed vascularity of pigment epithelial detachments (PEDs) in neovascular age-related macular degeneration (nAMD) and to quantify the areas of serous, neovascular, and fibrous tissues within PEDs.

Methods: A retrospective dataset of 28 high-resolution spectral-domain OCT (SD-OCT) B-scans taken from 22 patients with nAMD with presence of fibrovascular PED, were analyzed for this experiment. B-scans were acquired using the Heidelberg Spectralis device with a resolution of 1536x1536 in pixels. Exclusion criteria included drusenoid PEDs. For pre-processing, shadow compensation and linear standardization were applied. PEDs were segmented and then filtered using 2D kernels to create a series of generated images. A PED vascularity index score (PEDVI) was calculated for each pixel within the PED using a function of generated images. Pixels within the PED were classified as serous, neovascular, or fibrous based on PEDVI and respective areas were calculated. Accuracy of segmentation and classification within the PED were graded independently twice by two expert clinicians in masked fashion on a scale of 0-100.

Results: Of the 28 eyes, 15 had serous fluid, 24 had neovascular tissue, and 16 had fibrous tissue within a PED. Inter-observer reproducibilities were 0.99, 0.78, 0.94, and 0.79 for grader 1; 0.95, 0.78, 0.79, and 0.74 for grader 2; intra-observer repeatabilities were 0.90, 0.73, 0.84, and 0.81 for accuracy of segmentation, and classification of serous, neovascular, and fibrous respectively. Mean inter-grader reproducibility and intra-grader repeatability were 0.85 ± 0.10 and 0.82 ± 0.07 respectively. The mean graded scores were 96.88 ± 8.81, 92.67 ± 7.84, 93.44 ± 8.12, and 92.89 ± 8.25 for segmentation, serous, neovascular, and fibrous respectively. Mean total PED area, and when present, mean serous, neovascular, and fibrous areas in mm^2 were 0.26 ± 0.44, 0.218 ± 0.462, 0.108 ± 0.102, and 0.061 ± 0.077 respectively.

Conclusions: PEDVI scores calculated from a kernel-based image processing approach demonstrates potential for quantifying PEDs and approximating relative sizes of serous, neovascular, and fibrous tissue. An automated algorithm for segmentation is underway.

CONTROL ID: 3710065

SUBMITTER (NAME ONLY): Rong Lu

TITLE: RNA Sequencing and Bioinformatic Analysis on Retinoblastoma Revealing Cell Cycle Deregulation being a Key Process in Retinoblastoma Tumorigenesis

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lu, H. Ma, C. Nie, Y. Gao, J. Li, Z. Tang, Y. Chen, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To reveal targetability of polo-like kinase 1 (PLK1) with a small molecular inhibitor ON-01910.Na using retinoblastoma, an intraocular malignancy that lacks targeted therapy, as a disease model.

Methods: Transcriptomic analysis on patient retinoblastoma tissues was done to find key pathway and to select key factor of retinoblastoma. Subsequently, antitumor activity of ON-01910.Na, the drug targetting the selected key factor, was investigated in both cellular and animal levels.

Results: Transcriptomic analysis on patient retinoblastoma tissues suggested that cell cycle progression was deregulated and confirmed that PLK1 pathway was upregulated. In the investigation of antitumor activity of ON-01910.Na, a PLK1 inhibitor, it was found that cytotoxicity induced by ON-01910.Na was tumor specific and dose dependent in retinoblastoma cells, while nontumor cells were minimally affected. In three-dimensional culture, ON-01910.Na demonstrated efficient drug penetrability with multilayer cell death. Posttreatment transcriptomic findings revealed that cell cycle arrest and MAPK cascade activation were induced following PLK1 inhibition and eventually resulted in apoptotic cell death. In Balb/c nude mice, a safe threshold of 0.8 nmol intravitreal dosage of ON-01910.Na was established for intraocular safety, which was demonstrated by structural integrity and functional preservation. Furthermore, intraocular and subcutaneous xenograft were significantly reduced with ON-01910.Na treatments.

Conclusions: Local treatment of ON-01910.Na may be a novel, effective modality benefiting patients with PLK1-aberrant retinoblastoma.

CONTROL ID: 3710069
SUBMITTER (NAME ONLY): Clara Mestre
TITLE: The effect of anisometropia on reflex vergence movements
SESSION TITLE: Eye movements and nystagmus
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Mestre, K. Bonnen, T. Candy, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|S. Neupane, Department of Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|L. Wilcox, Centre for Vision Research, York University, Toronto, Ontario, CANADA|D. Giaschi, Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, British Columbia, CANADA|
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ABSTRACT BODY:
Purpose: Anisometropia is a risk factor for atypical binocular development associated with strabismus and amblyopia. The goal of this study was to understand the impact of different degrees of simulated anisometropia on vergence eye movements.
Methods: Participants viewed a cartoon character (2deg wide) displayed dichoptically on a 68x41deg gray background with varying amounts of retinal disparity. Spherical defocus of 1, 2 or 4D was applied to one or both eyes' stimuli using convolution with the Point Spread Function adjusted for the subject's pupil size. Eye movements were recorded with an Eyelink 1000. In condition 1, a step change in disparity (0-8deg) was introduced and displayed for 320ms, followed by a blank screen. Open-loop vergence amplitude was used to estimate the reflex response. In condition 2, retinal disparity varied between ±4deg relative to the screen with quasi-random velocities for 40s. Cross-correlations between stimulus and vergence velocities were computed.
Results: 22 youth and adults (15-51yrs) and 16 typically developing children (4-8yrs) participated in condition 1. With no defocus, open-loop vergence peaked for ±2deg disparity for both groups. Median (IQR) amplitudes were similar at 0.33 (0.19) deg convergence and -0.40 (0.23) deg divergence for adults, and 0.50 (0.51) deg and -0.42 (0.43) deg for children. Bilateral defocus had no effect. However, 4D of unilateral defocus reduced convergence and divergence amplitudes, especially for children (0.28 (0.33) deg and -0.36 (0.30) deg, respectively). Condition 2 was completed by 18 typical youth and adults (16-53yrs). The median (IQR) peak correlation of 0.61 (0.14) with no defocus decreased to 0.33 (0.41) with 4D unilateral defocus, while the decrease was smaller with 4D bilateral defocus (0.57 (0.23)). The median (IQR) latency of 183 (40) ms with no defocus increased to 198 (40) ms and 223 (40) ms with 4D of bilateral and unilateral defocus, respectively.
Conclusions: Our results confirm that unilateral defocus has a more detrimental effect than bilateral defocus on reflex vergence movements especially in children, which emphasizes the importance of similar retinal images for binocular development. For adults, the sustained responses required in condition 2 were especially affected. Although 1D of anisometropia can be associated with amblyopia, 2 to 4D are needed to disrupt this reflex oculomotor system and compromise accurate alignment for this small central stimulus.

CONTROL ID: 3710072

SUBMITTER (NAME ONLY): Jiayun Wang

TITLE: Surgical anatomy of the small animal eye - 3D reconstruction and ablation effect

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, P. Walter, S. Baumgarten, Ophthalmology, Rheinisch-Westfalische Technische Hochschule Aachen, Aachen, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Retinal prostheses help to restore vision in patients with degenerative retinal diseases, and require safe insertion. To prevent intra-/postoperative complications, e.g. retinal tearing and detachment, we performed an anatomical, histological study to describe safe insertion sites into the eye in mice, rats, and rabbits as well as in vivo experiments to observe the effect of laser- and cryo-ablation on the insertion sites. We pursue a better understanding of the surgical anatomy of the insertion sites and surgical feasibility of the implantation of retinal stimulators.

Methods: Four 15-28 weeks C57BL/6J wild-type(wt) mouse eyes, four 12-16 weeks rd10 mouse eyes, six 28 weeks Brown Norway rat eyes and twelve Chinchilla Bastard rabbit eyes went under histological processing. Three-dimensional (3D) data sets were created with two approaches: One was to create a rotationally symmetric 3D model of the eyeball by rotating a central sagittal section through the corneal apex and posterior retinal pole 360°. The second was that acquired images were subjected to image registration to align multiple scenes into one integrated image. The data was also used to reconstruct the eyes' anatomy in a virtual reality platform.

Laser- and cryo-ablation were performed in six wt mice, six rd10 mice, six Brown Norway rats and six Chinchilla Bastard rabbits. The effect of ablation was examined after 3 weeks by funduscopic effect control and histological processing of the treated areas.

Results: 3D models of mouse, rat and rabbit eyes were successfully established. We observed atrophy of the inner retinal layers as an effect of laser- and cryo-ablation. No retinal detachment occurred in the treated areas.

Conclusions: 3D models of small animal eyes can help to simulate surgical interventions of the implantation procedure of retinal stimulators. Laser- and cryo-ablation of the insertion sites may greatly contribute to a successful implantation procedure. These projects lead to safer implantation of microsystems into the eye.

CONTROL ID: 3710075

SUBMITTER (NAME ONLY): Ines Marques

TITLE: Characterization of two-year progression of capillary closure in nonproliferative diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.P. Marques, M. Ribeiro, S. Ferreira, A. Santos, T. Santos, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|I.P. Marques, M. Ribeiro, A. Santos, J.G. Cunha-Vaz, Coimbra Institute for Clinical and Biomedical Research (iCBR), Universidade de Coimbra Faculdade de Medicina, Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To characterize the two-year progression of capillary closure in different diabetic retinopathy (DR) risk phenotypes in type 2 diabetes (T2D).

Methods: A prospective longitudinal cohort study (CORDIS, NCT03696810) was conducted with 4 visits (baseline, 6-months, one-year and two-year). Demographic and systemic data included age, sex, diabetes duration, lipidic profile and hemoglobin A1c (HbA1c). Ophthalmological examinations including visual acuity (BCVA), color fundus photography (CFP) and optical coherence tomography (OCT and OCTA) identified nonproliferative diabetic retinopathy (NPDR). Phenotype classification was performed, at 6-month visit, based on microaneurysm turnover (MAT, on CFP) and central retinal thickness (CRT, on OCT). Only risk phenotypes B (MAT<6 and increased CRT) and C (MAT≥6 with or without increased CRT) were included. ETDRS grading was performed at the baseline and last visit based on 7-fields CFP.

Results: 133 T2D individuals were included in the study, 81 (60%) eyes classified as phenotype B and 52 (40%) eyes as phenotype C. Of these, 127 completed the two-year follow-up with 24 (19%) developing central-involved macular edema (CIME) and 2 (1.6%) clinically significant macular edema (CSME).

At baseline, eyes with phenotype C showed more capillary closure in the superficial capillary plexus (SCP), deep capillary plexus (DCP) and full retina (FR), p<0,001) and increased FAZ area (p<0,001), indicating more advanced ischemic disease. During the two-year follow-up period, the decrease in skeletonized vessel density indicating capillary closure, occurred mainly in the DCP in both phenotypes. Positive associations with the increased capillary closure were identified with GCL+IPL thinning (representing neurodegeneration) and decreased BCVA.

Conclusions: Significant progression in capillary closure was identified by a decrease in vessel density in the deep capillary plexus occurring in both phenotypes and in the different ETDRS levels. Eyes developing CIME had less decrease in vessel density of the SCP at baseline.

CONTROL ID: 3710081

SUBMITTER (NAME ONLY): Javier Lozano-Sanroma

TITLE: Dry eye disease treated with plasma rich in growth factor. Morphometric analysis of corneal innervation.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lozano-Sanroma, A. Barros Suárez, J. Queiruga Piñeiro, A. Poo López, Optometry, Instituto Oftalmologico Fernandez-Vega, Oviedo, Asturias, SPAIN|I. Alcalde, J. Merayo-Lloves, L. Fernandez-Vega Cueto-Felgueroso, Instituto Universitario Fernandez-Vega, Oviedo, SPAIN|J. Merayo-Lloves, L. Fernandez-Vega Cueto-Felgueroso, Universidad de Oviedo, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: This study examined the effect of plasma rich in growth factor treatment (PRGF), on subbasal nervous plexus innervation of patients diagnosed with dry eye disease (DED).

Methods: A prospective, observational study was conducted analyzing 31eyes images of 31 patients with DED (22 women and 9 males) aged 53.4±8.5 years (range 36 to 71 years). Subjects underwent microscopy confocal in vivo (IVMC) before (bf) and after (af) 3 months of treatment with PRFG. At least 3 images of each eye were selected and the following subbasal central nervous plexus parameters were measured with ACC Metrics software: Corneal Nerve Fiber Density (CNFD), Corneal Nerve Branch Density (CNBD), Corneal Nerve Fiber Length (CNFL), Corneal Nerve Fiber Total Branch Density (CTBD), Corneal Nerve Fiber Area (CNFA), Corneal Nerve Fiber Width (CNFW) and Corneal Nerve Fractal Dimension (CNFrD). Data analysis was performed with SPSS® software for Windows 22.0 (SPSS® Inc, Chicago, IL.). The normality of the sample was checked with the Shapiro-Wilk test and the results were compared to the t test or the Wilcoxon test based on the distribution of the data. The differences were considered statistically significant for $P<0.05$

Results: The mean and their standard deviations obtained for the variables analyzed were: CNFDbf: 17,854±1,311 and CNFDaf: 18,590±1,699 fibers/mm2, CNBDbf: 21,847±2,465 and CNBDaf: 24,591±3,310 branches/mm2, CNFLbf: 12,324±0,548 and CNFLaf: 12,828±0,789mm/mm2, CTBDbf: 37,728±3,428 and CTBDaf: 41,187±5,124 branches/mm2, CNFAbf: 0.00598±0.00277 and CNFAaf: 0.00596 ± 0.00332 mm2 by mm2, CNFWbf: 0.0223±0.0030 and CNFWaf: 0.0224±0.0029 mm2 by mm2, CNFrDaf: 1,471±0,006 and CNFrDbf: 1,463±0,02. Differences versus before and after treatment values were not statistically significant in all values analyzed.

Conclusions: Nervous plexus parameters improved after treatment with PRGF, although without being statistically significant. Further studies should include a larger sample.

CONTROL ID: 3710084

SUBMITTER (NAME ONLY): Manuel Chacon

TITLE: Performance assessment of QobuR-RhCE – a cruelty-free in vitro cornea model

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chacon, N. Vázquez, M. Persinal-Medina, S. Alonso-Alonso, I. Alcalde, J. Merayo-Lloves, A. Meana, Instituto Universitario Fernández-Vega - Fundación de Investigación Oftalmológica - Universidad de Oviedo, Oviedo, SPAIN|

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ABSTRACT BODY:

Purpose: To replace the Draize eye irritation test (OECD Test Guideline 404), several test methods based on reconstructed cornea-like epithelium (RhCE) have been developed and adopted in the OECD TG 492. The objective of this study was to define the essential structural, functional and procedural elements and to stablish the experimental procedures and evaluate the performance assessment of QobuR-RhCE, an in-house cruelty-free RhCE model to be used for the evaluation of eye hazard

Methods: QobuR-RhCE consists in normal human corneal epithelial cells cultured at the air-liquid interface forming a stratified squamous epithelium resembling a native human corneal epithelium

Essential test method components consisting of structural, functional and procedural elements were evaluated and standardized. These components included unique characteristics of the test method (i.e. histology), critical procedural details (i.e. barrier function) and quality control measures

Performance assessment was evaluated in accordance with the revised performance standards for the assessment of proposed similar or modified in vitro reconstructed human cornea-like epithelium and the minimum list of reference chemicals was evaluated on QobuR-RhCE. In addition to standard cell viability evaluation, we describe a secondary endpoint based on Transepithelial Electrical Resistance (TEER) that could be of use to better discriminate between irritants and non-irritants

Accuracy, specificity, sensitivity and within-laboratory reproducibility (WLR) were calculated according to the OECD Performance Standards for the assessment of proposed similar or modified in vitro RhCE test methods for Eye Hazard

Results: As result, the proposed method scored 93.3% sensibility, 60% specificity, 76.7% accuracy and 96.7% WLR, providing a similar performance in comparison to the validated reference methods. The inclusion of TEER as a barrier disruption predictor provided additional information for safety assessment that could be of interest during the evaluation of particular chemical products such as borderline chemical products, colored compounds or direct MTT reducers

Conclusions: The results of this study suggest that QobuR-RhCE test method is capable of fulfilling the performance standards as described in OECD TG 492 for similar in vitro RhCE test methods for eye hazard, suggesting that QobuR-RhCE is a reliable method for predicting eye irritation

CONTROL ID: 3710089

SUBMITTER (NAME ONLY): Francisco Burgos-Fernandez

TITLE: Deep learning for eye fundus diagnosis based on multispectral imaging

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.J. Burgos-Fernandez, F. Díaz-Doutón, M. Vilaseca, J. Pujol, Universitat Politecnica de Catalunya, Barcelona, Catalunya, SPAIN|F.J. Burgos-Fernandez, B. Ly, M. Sermesant, Inria Centre de Recherche Sophia Antipolis Mediterranee, Sophia Antipolis, Provence-Alpes-Côte d'Azu, FRANCE|M. Sermesant, Electrophysiology and Heart Modelling Institute (IHU, Liryc), Pessac, FRANCE|

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ABSTRACT BODY:

Purpose: A new deep-learning based method for automatic eye fundus diagnosis using multispectral images is proposed. The method discriminates between healthy and diseased eyes exploiting the potential of multispectral data. Among other pathologies, those mainly considered were age-related macular degeneration (ARMD), glaucoma and diabetic retinopathy as the leading causes of vision loss affecting the retina.

Methods: We analyzed 68 healthy and 68 diseased eyes from 89 subjects, 63% females and 37% males (19-95 years); only patients with retinal and/or choroidal pathologies were included. For each eye, 15 images from 400 nm to 1300 nm were acquired with a novel multispectral fundus camera. The deep learning network was adapted from that developed by Ly et al. (Ly B. et al. Lect. Notes Comput. Sc., vol. 12738, 2021) for sustained ventricular arrhythmia prediction, which involves a conditional variational autoencoder (CVAE) and a classifier model. The low dimensional features generated by the encoder are the inputs for the classifier and the decoder, which reconstructs the original sequence of 15 spectral images. These features contain information of healthy and diseased structures such as drusen, scars, edemas and neovascularization. The error between the encoder-decoder outputs is used to improve the performance of the network. The dataset was divided in training/validation (80% data) and test (20% data) datasets.

Results: The multispectral images offered very relevant information of healthy (Fig. 1 left) and diseased (Fig. 1 right) eye fundus structures to be used as input data for the proposed algorithm. The CVAE ran for 85 epochs leading to a classification accuracy of 96.43%, a loss of 0.20, a sensitivity of 92.86% and a specificity of 100.00% when discriminating between healthy and diseased fundus of the test dataset.

Conclusions: The proposed CVAE for the automatic classification of healthy and diseased eyes from multispectral eye fundus images produced an excellent outcome, highlighting the power of an encoder-decoder network and the significant information retrieved from multispectral images in the visible and near-infrared beyond 900 nm, a relatively unexplored range. Future work will focus on differentiating among pathologies by means of approaches such as attention maps, which help identifying abnormal structures.

CONTROL ID: 3710091

SUBMITTER (NAME ONLY): Suzanne de Bruijn

TITLE: Revisiting WGS data reveals previously overlooked structural variants disrupting IRD-associated genes

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. de Bruijn, K. Neveling, R.J. Hitti-Malin, J. Corominas, J. Reurink, H. Kremer, M. Nelen, C. Gilissen, F.P. Cremers, A. Hoischen, S. Roosing, Department of Human Genetics, Radboudumc, Nijmegen, NETHERLANDS|H. Kremer, R.J. Pennings, Department of Otorhinolaryngology, Radboudumc, Nijmegen, NETHERLANDS|A. Hoischen, Department of Internal Medicine, Radboudumc, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Structural variants (SVs) play an important role in the development of inherited retinal diseases (IRDs). Although the identification of SVs has significantly improved with the arrival of whole genome sequencing (WGS), we hypothesize that the involvement of SVs in IRDs is larger than currently anticipated. In this study, we revisited short-read WGS (srWGS) data from an IRD cohort to identify gene-disruptive SVs. Prioritization criteria were re-established to allow optimal detection and interpretation of SVs.

Methods: Optical genome mapping (OGM) was performed to improve SV detection in srWGS-negative cases. OGM identified a pericentric 173 Mb inversion in a monoallelic USH2A case. One breakpoint of this inversion is located within USH2A and disrupts the coding region of the gene. Retrospectively, the variant could be observed in srWGS data but was previously deemed false positive, mainly because of the unexpected large size of the variant. The identification of this extremely large inversion urged us to revisit our srWGS data and reestablish SV quality and filtering criteria. In total srWGS data of 425 IRD cases were screened for disruptive SVs affecting IRD-associated genes.

Results: Reanalysis of srWGS data revealed large inversion events that were overlooked during initial analyses, including a 5.8 Mb USH2Aand 4.1 Mb EYS inversion. The EYS inversion was identified in a case that was previously considered genetically solved, as this individual harbors compound heterozygous EYS variants of which one variant of unknown significance (Pt-12, Fadaie et al., PMID:34795310). The identification of the SV prompted us to revise this genetic diagnosis and emphasizes the need for complete genome analysis including SV detection. Additionally several small homozygous or heterozygous deletions were identified affecting e.g. EYS and PRPF31. The corresponding samples are now considered genetically solved.

Conclusions: Our data confirm a significant contribution of small and large SVs to the mutational landscape of IRDs and thus possibly also of other inherited disorders. The optimized prioritization protocol significantly improved SV identification from srWGS data, as it yielded several pathogenic SVs that were missed during previous analyses. This strongly suggests that more attention should be paid to SV identification and interpretation, and that the current contribution of SVs is still underestimated.

CONTROL ID: 3710097
SUBMITTER (NAME ONLY): Hailong He
TITLE: Ophthalmic screening of young rhesus and cynomolgus monkeys in China
SESSION TITLE: Animal models of human ocular disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: H. He, Z. Jin, Beijing Institute of Ophthalmology, Beijing, Beijing, CHINA|
Commercial Relationships Disclosure: Hailong He: Commercial Relationship: Code N (No Commercial Relationship) | Zi-Bing Jin: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To examine the ocular refraction parameters of young rhesus and cynomolgus monkeys in the natural growth and development conditions of China.
Methods: In this cross-sectional study, 26 rhesus monkeys and 12 cynomolgus monkeys, aged 2-5 years old, were selected. Spherical equivalent (SE), axial length (AXL), anterior chamber depth (ACD), lens thickness (LT) and vitreous chamber depth (VCD) were measured by automatic computer optometry and A-scan ultrasonography. A fundus camera and OCT were also performed to exclude ocular diseases. T-test was used to compare the continued normal distribution data. Wilcox on Rank-Sum test was used to compare the non-normal distribution data. Spearman's correlation and logistic regression analysis were used to identify the factors associated with AXL. $P<0.05$ was considered statistically significance.
Results: Two rhesus monkeys were excluded for abnormal eye development. For remaining 24 rhesus monkeys, SE was 0.01±1.08 D, AXL was 19.57±0.85 mm, ACD was 3.36±0.77 mm, LT was 4.08±0.74 mm, VCD was 12.11±0.55 mm for right eyes and 0.27±1.22 D, 19.59±0.84 mm, 3.59±1.23 mm, 4.22±0.66 mm, 12.11±0.72 mm for left eyes. For 12 cynomolgus monkeys, SE was -0.52±0.92 D, AXL was 18.24±0.56 mm, ACD was 3.59±0.27 mm, LT was 3.23±0.23 mm, VCD was 11.41±0.78 mm for right eyes and -0.38±1.03 D, 17.98±0.51 mm, 3.57±0.59 mm, 3.22±0.38 mm, 11.12±0.70 mm for left eyes. The SE of 48 rhesus monkeys eyes was 0.14±1.15D and -0.45±0.96 D for 24 cynomolgus monkeys eyes, there was a significant difference between the two groups ($t=2.174$, $P<0.05$). The AXL of 48 rhesus monkey eyes was 19.80±0.95 mm and 18.02±0.99 mm for 24 cynomolgus monkey eyes, there was a significant difference between the two groups ($Z=-5.734$, $P<0.05$). The AXL of 72 rhesus and cynomolgus monkeys' eyes were included. Spearman's correlation showed that ACD, LT, ACD, strain, gender, age and weight were statistically significantly associated with AXL ($R=0.396$, 0.558, 0.717, -0.681, -0.456, -0.421, 0.657, $P<0.05$). The results of logistic regression analysis showed that ACD, LT and VCD were statistically significantly associated with a longer AXL (Beta=0.663, 0.704, 0.669, $P<0.05$).
Conclusions: This study found there was significant difference in SE and AXL between the rhesus and cynomolgus monkeys. ACD, LT and VCD were statistically significantly associated with axial elongation. The ocular parameters could provide a foundation for future research.

CONTROL ID: 3710101

SUBMITTER (NAME ONLY): Birgit Govers

TITLE: Posterior vitreous membrane findings on OCT in patients with collagen type IV abnormalities

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. Govers, S. Keijser, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|J. de Hoog, Ophthalmology, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|

Commercial Relationships Disclosure: Birgit Govers: Commercial Relationship: Code N (No Commercial Relationship) | Joeri de Hoog: Commercial Relationship: Code N (No Commercial Relationship) | Sander Keijser: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The pathological mechanisms of abnormal collagen type IV predisposing to macular hole formation in Alport syndrome are hypothesized to be related to a weakened internal limiting membrane. However, deviant collagen type IV might also predispose to macular hole formation in these patients due to vitreous cortex abnormalities. We aim to describe the posterior vitreous structures visible on optical coherence tomography (OCT) imaging in a case series of patients with collagen type IV mutations.

Methods: An observational case series of OCT-findings in three patients with collagen type IV abnormalities.

Results: In two patients diagnosed with Alport syndrome and in one patient with a possibly pathogenic genetic variant in COL4A3 we observed a remarkable posterior vitreous cortex with a vitreoschisis-like appearance on OCT. One of these patients developed a rhegmatogenous retinal detachment and one patients developed a macular hole.

Conclusions: These vitreous cortex findings are possibly related to abnormal collagen type IV and might additionally be associated with pathological mechanisms of macular hole formation in Alport syndrome. Future studies might confirm the presence of abnormal collagen type IV in the vitreous cortex in macular hole patients with Alport syndrome.

CONTROL ID: 3710102

SUBMITTER (NAME ONLY): James Wawrzynski

TITLE: Intravitreal Cerliponase alfa for the treatment of CLN2 type Batten Disease related retinal dystrophy: A first in man report of ocular enzyme replacement

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Wawrzynski, P. Gissen, R. Henderson, Institute of Child Health, University College London, London, London, UNITED KINGDOM|J. Wawrzynski, P. Gissen, R. Bowman, R. Bower, C. Gan, L. Harding, D. Thompson, R. Henderson, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|A. Mortensen, Batten Disease Family Association, Farnborough, Hampshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: CLN2 type Batten Disease is a fatal neurodegenerative condition of childhood that is associated with retinal dystrophy and blindness. Intracerebroventricular infusion of Cerliponase alfa (rhTPP1) greatly slows the rate of neurodegenerative decline but not retinopathy. In 2020 intravitreal administration of rhTPP1 was shown to slow retinal degeneration in a canine model of CLN2. We report on the first-in-man use of intravitreal rhTPP1 for the treatment of CLN2 type Batten Disease associated retinal dystrophy.

Methods: 8 children (4 female) aged 5-9 with genetically and clinically confirmed CLN2 Batten Disease were prospectively enrolled. Patients were selected if they were currently in the retinal degenerative phase of the condition. Enrolled children are undergoing 8-weekly intravitreal injections of rhTPP1 (0.2mg in 0.05ml) into the right eye for a total of 12 to 18 months. The left eye is untreated and acts as a paired control.

The primary outcome is safety based on the clinical detection of intraocular complications and in particular uveitis. A secondary outcome is central foveal thickness (CFT) and paracentral macular thickness (PMT) measured by spectral domain OCT (Heidelberg Spectralis Flex).

Results: Participants have had between 2 and 4 intravitreal injections and 4-6 months of followup so far. No adverse reactions (uveitis, raised IOP or media opacity) have been detected. The mean baseline CFT was 81µm (right), 87µm (left). The CFT has reduced by 16% in right eyes and 20% in left eyes. The mean baseline PMT was 213µm (right), 213µm (left). The PMT has reduced by 4% (right) and 7% (left).

A paired t-test showed that the difference between the rate of foveal and paracentral retinal thinning between left and right eyes was not statistically significant (p= <0.05) at this early stage in the trial.

A statistically significant difference between the PMT over time (but not CFT) was found for both right (p=0.046) and left (p=0.015) eyes (paired t-test).

Conclusions: Intravitreal rhTPP1 appears safe with no evidence of uveitis detected. Rapid retinal thinning is seen in untreated eyes, confirming that patients are in the degenerative phase of the condition. A slower rate of retinal thinning is seen in treated eyes, although a statistically significant difference is not seen at this early stage in the trial.

CONTROL ID: 3710105

SUBMITTER (NAME ONLY): Kentaro Kawai

TITLE: Clinically significant nonperfusion areas in diabetic retinopathy on widefield optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kawai, T. Murakami, Y. Mori, K. Ishihara, Y. Dodo, N. Terada, K. Nishikawa, K. Morino, A. Tsujikawa, Department of Ophthalmology and Visual Sciences, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: To examine the distribution of nonperfusion areas (NPAs) and its clinical relevance in diabetic retinopathy (DR) of different severities using widefield optical coherence tomography angiography (OCTA).

Methods: One hundred and forty-two eyes in 113 patients with diabetes (27 eyes with no DR [NDR], 71 with nonproliferative DR [NPDR], and 44 eyes with proliferative DR [PDR]) were prospectively participated. We obtained nominal 20 × 23mm (1614 × 1856 pixels) OCTA images using Xephilio OCT-S1. We evaluated NPAs within the 20mm-diameter circle centered on the fovea. After automatic detection of vessel edges using an ImageJ plug-in (Canny edge detection), the image was divided into regions of interest (ROIs) of 10 × 10 pixels, and ROIs without the edges were defined as NPAs. The frequency of the NPAs were calculated for each ROI. The ROIs with greater differences in the frequency than the third quartile were defined as significant areas. We evaluated area under the receiver operating characteristic curve (AUC) for DR severity discrimination using the NPA rates.

Results: The differences in the NPA rates between NDR and NPDR in each ROI were 1.4% (interquartile range [IQR], 0.0-2.7). Within central 10 mm, 34.5%, 13.8%, 7.1%, and 5.2% in temporal, superior, nasal, and inferior quadrants corresponded to the significant areas. The percentages outside it were 36.2%, 27.2%, 27.2%, and 30.3% in individual quadrants. The AUCs of NPA rates in total or significant areas to discriminate NPDR from NDR were 0.772 (95% confidence interval [CI], 0.687-0.856) and 1.000 (95% CI, 1.000-1.000), respectively. Further comparative study revealed that the differences in the NPA rate between NPDR and PDR in each ROI were 5.8 % (IQR, 1.9-10.2). The percentage of significant area was 0.0% in the quadrants other than the temporal subfield within central 10mm, while the percentages of significant area outside it were 39.1%, 36.5%, 19.8%, and 38.7%, respectively. The AUCs of NPA rate was 0.887 (95% CI, 0.828-0.946) and 0.946 (95% CI, 0.906-0.986) in the total and significant areas, respectively.

Conclusions: Clinically significant NPAs on widefield OCTA images might be useful in diagnosing NPDR and PDR as well as suggest the processes of vasoregression in DR.

CONTROL ID: 3710107

SUBMITTER (NAME ONLY): Yayu Chen

TITLE: The prevalence of binocular vision dysfunctions in Taiwanese non-presbyopia adults

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, Department of Optometry, Da-Yeh University, Dacun, Changhua, TAIWAN|

Commercial Relationships Disclosure: Yayu Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Refractive error is associated with binocular vision dysfunctions. Although the myopia rate of young adults in Taiwan has already reached nearly 90%[1], the prevalence of binocular vision dysfunctions in Taiwan is still unclear. Thus, the purpose of this study is to investigate the prevalence of binocular vision dysfunctions in non-presbyopia adults in Taiwan.

Methods: A total of 107 healthy non-presbyopia adults aged between 20 to 40 years old were included in this study. All participants were corrected refractive errors and examined accommodative tests and binocular vision tests. The collected data were analyzed and categorized into 7 types of vergence dysfunctions and 2 types of accommodative dysfunctions by using the diagnostic criteria of Ma et el.[2]

Results: The results showed that 48.6% of all participants were normal binocular vision and 51.4% were abnormal binocular vision (including vergence dysfunctions and accommodative dysfunctions). In the vergence dysfunctions, there were 15.0% were basic exophoria (BXO), 8.4% were convergence insufficiency (CI), 5.6% were divergence insufficiency (DI), 3.7% were fusional vergence dysfunction (FVD), 2.8% were basic esophoria (BSO), 1.9% were convergence excess (CE), and 1.9% were divergence excess (DE). In the accommodative dysfunctions, there were 8.4% were accommodative insufficiency (AI) and 3.7% were accommodative infacility (AIF).

Conclusions: In conclusions, this study indicated that 39.3% of the participants were vergence dysfunctions and 12.1% were accommodative dysfunctions. BXO and AI is the most common type in vergence dysfunctions and accommodative dysfunctions, respectively.

1. Ophthalmology, 2021, 128(2): 290-301.

2. J Ophthalmol, 2019, 5904903.

CONTROL ID: 3710110

SUBMITTER (NAME ONLY): Christian Burri

TITLE: Real-Time Optical Coherence Tomography Controlled Microsecond Laser Retinal Microsurgery: First In-vivo Results

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Reliable mild photocoagulation and selective retina therapy (SRT) selectively damaging the retinal pigment epithelium (RPE) while sparing the neuroretina, the photoreceptors as well as the choroid are highly demanded. However, due to the inter- and intraindividual variability of RPE and choroidal absorption, optical microsurgery requires reliable real-time laser dosing to prevent unwanted overexposure and extended damage of the neuroretina. In this experiment optical coherence tomography (OCT) was implemented to detect minimal damage, and a laser feedback control algorithm was used for real-time dosing. For the first time in-vivo experiments on rabbits were performed with microsecond laser pulses of varying duration.

Methods: Pigment rabbit eyes (n=6) were exposed to laser pulses of 4, 8, 12, and 20 µs in duration (wavelength, 532 nm; ramp-mode, maximum 15 pulses; repetition rate, 100 Hz). Therefore, a system with a scanning laser ophthalmoscope and spectral-domain OCT (Heidelberg Engineering) extended with a prototype laser (Meridian Medical) was used. For each laser lesion, the increasing ramp's end energy was individually controlled in real-time using OCT dosimetry (central wavelength, 870 nm; scan rate, 80 kHz). Within 1 hour after irradiation, retinal changes were assessed with fluorescein angiography (FA), indocyanine green angiography (ICGA), color fundus photography (CFP) and OCT.

Results: OCT dosimetry utilizing the control algorithm can interrupt the ramp-mode in real-time for each lesion individually. The preconditioned algorithm enabled treatment with a clearly visible breakdown of the blood-retinal barrier (BRB) according to FA and ICGA imaging and barely visible treatment lesions according to CFP. OCT B-scans through the treated areas provided a first indication of the morphological tissue impact. Preliminary evaluation shows that the algorithm stopped the laser at 4 µs at a ramp end energy of 53 µJ (corresponds to 13/15 pulses), at 8 µs at 68 µJ (5/15 pulses), at 12 µs at 74 µJ (7/15 pulses), and at 20 µs at 100 µJ (1/15 pulses).

Conclusions: The novel system with OCT based laser dosing proved to induce minimal visible damage and BRB breakdown in a wide range of pulse durations. The new irradiation scheme and algorithm are being optimized and tested in multiple subjects to further limit unwanted damage and enable pure RPE selective laser microsurgery in real-time.

CONTROL ID: 3710111

SUBMITTER (NAME ONLY): Sunny Ohia

TITLE: EFFECT OF HYDROGEN SULFIDE-RELEASING COMPOUNDS ON LIPOPOLYSACCHARIDE-INDUCED INFLAMMATION IN CULTURED PORCINE IRIS-CILIARY BODY EXPLANTS

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Ohia, A. Okolie, F. Muili, Y. Njie-Mbye, Pharmaceutical Sciences, Texas Southern University, Houston, Texas, UNITED STATES|C.A. Opere, Pharmacy Sciences, Creighton University School of Pharmacy and Health Professions, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evidence from literature demonstrates that exogenous administration of hydrogen sulfide (H_2S) decreases inflammation in retinal pigment epithelial cells exposed to homocysteine (Ravi et al. 2021, EER 212:108759). Since lipopolysaccharide (LPS) has been reported to induce inflammation in cultured human iris-ciliary body (ICB) explants (Brito et al. 2004, EER 79:203), we investigated the pharmacological actions of H_2S-releasing compounds on LPS-induced inflammation in cultured porcine ICB explants (using Tumor Necrosis Factor-alpha, TNFα, as a marker).

Methods: Freshly isolated porcine ICB explants were cut into quadrants and cultured in Roswell Park Memorial Institute (RPMI) 1640 medium containing 1% penicillin-streptomycin. Explants were then exposed to different concentrations of LPS for 20 h. When used, H_2S-releasing compounds, sodium hydrosulfide (NaHS) and GYY4137 were added to media 15 mins and 30 mins, respectively, before the end of the incubation period. Concentrations of TNFα in culture supernatants were measured using ELISA kit purchased from Sigma-Aldrich.

Results: Different concentration of LPS tested elicited increases in TNFα production in cultured ICB explants over basal levels (7.21 ± 0.29 ng/g; n = 6). For instance, LPS 10 ng/ml, 25 ng/ml, and 50 ng/ml enhanced TNFα production up to 10.36 ± 0.23 ng/g (n = 6), 12.32 ± 0.40 ng/g (n = 5) and 11.80 ± 1.11 ng/g (n = 5), respectively. In the presence of LPS (25 ng/ml), a fast-releasing H_2S compound, NaHS (5 μM and 50 μM) caused significant ($p < 0.001$) decreases in LPS-induced TNFα production by 22.7 % ± 3.6 % (n = 6) and 26.5 % ± 5.3 % (n = 5), respectively. Likewise, the slow-releasing H_2S compound, GYY4137 (1 μM and 10 μM) evoked significant ($p < 0.001$) reductions of LPS-induced TNFα production by 25.0 % ± 3.7 % (n =5) and 19.9% ± 1.8 % (n = 4), respectively.

Conclusions: We conclude that LPS can induce an inflammatory response in the cultured porcine ICB explants. Both fast- and slow-releasing H_2S compounds reduced LPS-induced TNFα production in the ICB explants suggesting an anti-inflammatory action of this gas in the anterior uvea.

CONTROL ID: 3710112

SUBMITTER (NAME ONLY): Michael Moussa

TITLE: Impact of fresh carrier graft thickness on aqueous leak after Boston Keratoprosthesis implantation in an ex-vivo model

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Moussa, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|E. Hellier, R. Bashshur, Eversight Eye Bank, Ann Arbor, Michigan, UNITED STATES|R.R. Sayegh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|P. Agarwal, Mid Yorkshire Hospitals NHS Trust, Wakefield, Wakefield, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Various carriers for the Boston Keratoprosthesis (KPro) have been proposed, however the optimal parameters of these grafts remain to be elucidated. One important parameter is the thickness of the carrier grafts. We examine the impact of corneal thickness on aqueous leak after KPro implantation in Life4C-preserved fresh corneal grafts.

Methods: Using a femtosecond laser, corneal donor buttons were mounted on an artificial anterior chamber and cut to various thicknesses. Anterior segment OCT was used to measure the thickness before and after the cut creation. A dermatologic punch was used to make a central hole and the KPro was assembled in the standard fashion. The assembled corneal construct was mounted onto the anterior chamber which was attached to a phacoemulsification machine with the intraocular pressure (IOP) set at the lowest setting of 20 mmHg. The IOP was gradually increased and a fluorescein strip was used to check Seidel positivity.

Results: The thicknesses of the tested corneal grafts were measured to be 79 µm, 242 µm, 389 µm, 414 µm, 435 µm, and 702 µm. When connected to the phacoemulsification machine, the fresh corneas of 79 µm and 242 µm were Seidel positive at 20 mmHg, while the remaining fresh corneas remained Seidel negative even at maximal IOP (80 mmHg).

Conclusions: A minimal corneal carrier graft thickness between 242 µm and 435 µm is required to avoid intraoperative leak during KPro implantation using fresh corneas. This is thinner than our previously reported range for ethanol-preserved corneas. Additional experiments are needed to further narrow down this range and compare to preserved carrier grafts.

CONTROL ID: 3710113

SUBMITTER (NAME ONLY): Juan Bueno

TITLE: Structural Organization of the Sclera in Chicks after Deprivation Myopia Measured Using Second Harmonic Generation Microscopy

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Bueno, R. Martinez-Ojeda, E.J. Fernandez, P. Artal, Universidad de Murcia, Murcia, Murcia, SPAIN|M.P. Feldkaemper, Universitatsklinikum Tubingen Forschungsinstitut fur Augenheilkunde, Tubingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: The outer layer of the sclera is a dense connective tissue mainly composed of collagen fibers. Abnormal eye growth during myopia progression is associated with extracellular matrix (ECM) restructuring and scleral thinning. Second Harmonic Generation (SHG) microscopy allows visualizing collagen-based tissues without the use of markers. In this work, we obtained SHG images from scleral tissues to objectively quantify possible changes in collagen organization as a function of different amounts of induced deprivation myopia in chicks.

Methods: A SHG microscope operating in backscattering-mode was used to image chick scleral tissues in 26 eyes from areas close to the optic nerve head. Unstained scleral punches of both control and deprived (mean refraction=-8D) eyes were used in the experiment. Myopia was induced by placing a translucent diffuser in one of the chickens' eyes for one week. Two SHG imaging modalities were employed: Tomographic (XZ or YZ), and regular XY images. The former allowed direct estimation of the scleral thickness, while the latter were used to characterize the collagen fiber structural dispersion by means of Fourier and Radon transforms.

Results: Scleral collagen fibers provided strong SHG signals for analysis. We did not find differences in scleral thickness as a function of ocular refraction. On the opposite, fiber structural dispersion significant increased with refraction (R=0.48, p=0.01) and decreased with axial length (R=0.67, p=0.0002). The structure of scleral collagen fibers ranged between a non-organized and a quasi-aligned (with a dominant direction of the fibers) distribution.

Conclusions: SHG microscopy imaging provided a high-resolution visualization of individual collagen fibers of the chicken sclera with different levels of induced myopia. A significant decrease in fiber structural dispersion was associated to a higher myopic refraction. Nevertheless, the thickness of the control sclerae and that of deprived eyes were similar. This technique allows quantifying alterations during myopia induction, providing a useful tool for a better understanding of the emmetropization processes.

CONTROL ID: 3710116

SUBMITTER (NAME ONLY): Alexander Shpak

TITLE: Glial cell line-derived neurotrophic factor in patients with primary open-angle glaucoma and age-related cataract

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Shpak, A.A. Troshina, The S. Fyodorov Eye Microsurgery Federal State Institution, Moscow, RUSSIAN FEDERATION|A.B. Guekht, T.A. Druzhkova, Moscow Research and Clinical Center for Neuropsychiatry of the Healthcare Department of Moscow, Moscow, RUSSIAN FEDERATION|N.V. Gulyaeva, Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: The role of glial cell line-derived neurotrophic factor (GDNF) in pathogenesis of primary open-angle glaucoma (POAG) is not clear. The aim of the study was to measure the content of GDNF in the aqueous humor, lacrimal fluid, and blood serum in patients with POAG and age-related cataract.

Methods: We examined 30 patients (30 eyes) with POAG and age-related cataract. Forty-seven previously examined patients of similar age and sex with age-related cataract (47 eyes) served as a control (Shpak AA, et al. IOVS 2021, 62; ARVO e-abstract 718). Collection of stimulated lacrimal fluid was performed by a pipette on the day preceding surgery; the aqueous humor of the anterior chamber and the blood were sampled during the phacoemulsification of a cataract. The concentration of GDNF was measured using an enzyme immunoassay RayBio® Human GDNF ELISA Kit (RayBiotech, USA) on a ChemWell 2910 automatic analyzer (Awareness Technology Inc., USA).

Results: Compared to controls, at the earlier stages of POAG (stages 1-2 according to classification by Mills et al., 2006), GDNF concentration (median [interquartile range]) was significantly decreased ($P<0.05$ – $P<0.001$) in all studied biological fluids: in aqueous humor (46 [14-57] vs. 83 [59-119]), lacrimal fluid (176 [96-238] vs. 314 [244-422]) and serum (163 [128-202] vs. 196 [174-239]) pg/mL. In later stages 3-4, the GDNF levels increased, however, in the aqueous humor and lacrimal fluid remained significantly reduced in comparison with controls. An inverse correlation with the perimetric index VFI was found for the content of GDNF in lacrimal fluid ($r=-0.47$; $P=0.01$) and serum ($r=-0.40$; $P=0.03$); a direct correlation was found between the GDNF levels in serum and aqueous humor ($r=0.47$; $P=0.01$).

Conclusions: In patients with POAG, GDNF level in the aqueous humor, lacrimal fluid, and blood serum is significantly decreased, especially in the earlier stages of the disease. In subsequent stages, reduction of GDNF level in the aqueous humor and lacrimal fluid is less pronounced, however the level of GDNF in these media remains significantly reduced compared to patients without glaucoma. An inverse correlation with the perimetric index VFI was found for the content of GDNF in lacrimal fluid and blood serum, as well as a direct correlation of GDNF levels in the blood serum and aqueous humor.

CONTROL ID: 3710122

SUBMITTER (NAME ONLY): Ting XIAO

TITLE: DNAJC30 disease-causing gene variants in a large Central European cohort of patients with inherited optic atrophy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. XIAO, S. Kieninger, N. Weisschuh, S. Kohl, B. Wissinger, Molecular Genetics Laboratory, University Hospital Tübingen Institute for Ophthalmic Research, GERMANY|F. Tonagel, Centre for Ophthalmology, University Hospital Tübingen Clinic of Ophthalmology, GERMANY|K. Rüther, Facharztpraxis für Augenheilkunde, GERMANY|U. Kellner, Zentrum für Seltene Netzhauterkrankungen, AugenZentrum Siegburg, GERMANY|W. Lagrèze, Eye Centre, University of Freiburg Medical Centre, GERMANY|P. Mazzola, T. Haack, Institute of Human Genetics and Applied Genomics, University of Tübingen, GERMANY|T. Haack, Centre for Rare Diseases, University of Tübingen, GERMANY|P. Kroisel, Diagnostic & Research Institute of Human Genetics, Medical University of Graz Diagnostics & Research Center for Molecular BioMedicine, AUSTRIA|T. Brockmann, S. Knappe, Department of Ophthalmology, Universitätsmedizin Rostock, GERMANY|U. Kellner, RetinaScience, GERMANY|

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ABSTRACT BODY:

Purpose: Leber's hereditary optic neuropathy (LHON) has been considered a prototypical mitochondriopathy and a textbook example for maternal inherited disease. However, recently, an autosomal recessive form of LHON (arLHON) has been described, caused by disease-causing variants in the nuclear encoded gene DNAJC30. We performed a retrospective screening of DNAJC30 in a large series of genetically unsolved patients clinically diagnosed with LHON patients or other forms of inherited optic atrophy (OA). We compiled and compared the prevalence, patients' demography and clinical findings with those linked to mtDNA variants.

Methods: 1202 patients (1197 index patients and 5 affected family members, male: female ratio 1.8:1) were retrospectively selected for DNAJC30 screening, including 800 patients with a clinical diagnosis of LHON and 402 patients with OA. Genomic DNA samples of patients were used for screening of the coding sequence of DNAJC30 gene and its flanking untranslated regions by PCR amplification and subsequent Sanger sequencing. Pathogenicity of variants was assessed by in silico software prediction, allele frequency, and segregation analysis. Microsatellite marker analysis was performed to analyze the founder effect for the variant c.152A>G;p.(Tyr51Cys). Clinical examinations include visual acuity measurement, slit lamp examination, perimetry, indirect ophthalmoscopy, optical coherence tomography and color vision (Ishihara plates and Farnsworth-Munsell Dichotomous D-15 test).

Results: We identified likely pathogenic variants in 2.9% (35/1202) patients. The missense variant c.152A>G;p.(Tyr51Cys) accounted for 90% of disease-associated alleles in our cohort. Marker analysis provided strong evidence for a founder effect and a common origin of this mutation. Furthermore, we identified two novel pathogenic variants in DNAJC30: the nonsense variant c.610G>T;p.(Glu204*) and the in-frame deletion c.230_232del;p.(His77del). Clinical investigation of the patients with arLHON revealed a younger age of onset, a more frequent bilateral onset and an increased clinically relevant recovery compared to LHON associated with disease-causing variants in the mitochondrial DNA (mtLHON).

Conclusions: This study expands previous findings on arLHON and emphasizes the importance of DNAJC30 in the genetic diagnostics of LHON and OA in European patients.

CONTROL ID: 3710125

SUBMITTER (NAME ONLY): zi jin

TITLE: Laser speckle contrast imaging derived retinal hemodynamics abnormalities in Alzheimer's disease

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. jin, C. zhou, Peking University Shenzhen Graduate School, Shenzhen, Guangdong, CHINA|C. jiang, J. li, X. chen, Peking University Shenzhen Hospital, Shenzhen, Guangdong, CHINA|Q. ren, Peking University, Beijing, Beijing, CHINA|Y. yang, Y. lu, Hebei University, Baoding, Hebei, CHINA|

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ABSTRACT BODY:

Purpose: Laser speckle contrast imaging (LSCI) is a promising technique for measuring the retinal hemodynamics because LSCI is capable of imaging large field of retinal blood flow in just a few seconds. This study aims to evaluate retinal hemodynamics abnormalities in Alzheimer's disease (AD) through our custom-built LSCI.

Methods: 83 Patients with AD and 75 healthy age and sex-matched subjects were recruited in the study. All subjects underwent medical history, blood pressure measurement, the Montreal Cognitive Assessment (MOCA), best-corrected visual acuity, intraocular pressure (IOP), and custom-built LSCI. Based on the laser speckle phenomenon, the LSCI was used to measure the retinal blood flow. A laser diode at 850 nm wavelength was used for LSCI. An annular fiber bundle was adopted for uniform retinal illumination. The retinal speckle pattern images were captured by the CMOS camera (M3ST507M-H, DO3THINK, GuangDong, China) with 1224 pixels X 1024 pixels at a frame rate of 80 fps for a 5-second measured period. Then, LSCI algorithm was proposed to calculate the laser speckle contrast (LSC) value to represent the blood velocity. The relative blood flow of the optic nerve head area was chosen to obtain the retinal blood flow pulsatility curve (Fig. 1). According to the pulse-waveform analysis, the quantitative parameters can be calculated, such as flow acceleration index (FAI). The eye with better corrected visual acuity was selected for the LSCI.

Results: There was no significant difference between the groups for systolic blood pressure, diastolic blood pressure, mean blood pressure, IOP, and ocular perfusion pressure. No difference in patients with diabetes mellitus, and hypertension was observed between two groups. Compared to controls, the parameters corrected visual acuity (0.86±0.19 vs 0.93±0.19, p=0.05), MOCA scores (15.9±7.0 vs 28.1±1.5, p<0.01)), and FAI (1.17±0.39 versus 1.33±0.54, p=0.05) were significantly lower in AD (Fig. 2).

Conclusions: The present study demonstrates significant differences in retinal hemodynamics between AD patients and healthy subjects through LSCI. FAI may be a useful indicator for early detection of AD.

CONTROL ID: 3710137

SUBMITTER (NAME ONLY): Martin Menten

TITLE: Discovery of imaging biomarkers for healthy aging and age-related macular degeneration using counterfactual generative adversarial networks

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: There is a lack of clinically usable biomarkers for the diagnosis and prognosis of age-related macular degeneration (AMD). Visualizing the effect of healthy and pathological aging on the retina may aid the discovery of novel imaging biomarkers for AMD. To this end, we explore the use of deep learning to synthesize counterfactual OCT images that reflect hypothetical scenarios in which age, sex or disease stage of the scanned subject are changed while the subject's identity remains fixed.

Methods: We developed a counterfactual generative adversarial network (GAN) that alters existing OCT images to visualize the retina at a different, operator-selectable age, sex or AMD disease stage. Two datasets, which have been curated for the PINNACLE study, were used for GAN training and validation: 175,869 OCT images of predominantly healthy participants in the UK Biobank population study and 57,875 images of AMD patients undergoing treatment at Southampton Eye Unit. The visual quality of the counterfactuals was quantified by conducting a Turing Test, in which five expert ophthalmologists were asked to distinguish between real and artificially generated OCT images. Additionally, we measured whether the generated images faithfully depict the counterfactual age and sex and preserve the subject identity by predicting these demographics using independently trained ResNet-50 neural networks.

Results: The generated counterfactuals were indistinguishable from real OCT images in most cases (Turing Test accuracy: 76.6%±18.4%). The GAN realistically modified image features associated with subject age and sex (correlation between counterfactual and predicted age: Pearson's R of 0.86±0.02; agreement between counterfactual and predicted sex: 79.7%±5.8%), while preserving subject identity in 88.8%±6.4% of counterfactuals. Several observed retinal changes were linked to plausible biomarkers, such as thinning of retinal layers with aging or increase in drusen size with progressing AMD.

Conclusions: We have demonstrated the ability of GANs to generate realistic counterfactual OCT images, which can be used to visualize the individual course of retinal changes caused by healthy or pathological aging.

CONTROL ID: 3710140

SUBMITTER (NAME ONLY): Juliane Hammer

TITLE: Adult zebrafish atoh7 mutants lack retinal ganglion cells resulting in structural changes of the optic tectum and altered social interactions

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hammer, P. Röppenack, S. Yousuf, H. Grandel, A. Machate, M. Fischer, S. Hans, M. Brand, Developmental Genetics, Center for Regenerative Therapies Dresden, Zentrum fur Regenerative Therapien Dresden, Dresden, Sachsen, DE, academic/medres, Dresden, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Atoh7 plays a major role in the development of retinal ganglion cells and the optic nerve and mutations in ATOH7 have been associated with multiple ocular disease traits in humans. In zebrafish, atoh7 mutants fail to generate retinal ganglion cells during embryogenesis, until 6 days post fertilization. Here we characterized adult atoh7 mutants to explore the consequences of missing retinal output on retinal and tectal structure, as well as visually-mediated behaviors.

Methods: We raised atoh7 mutants to adulthood under adjusted feeding and holding conditions and systematically characterized their phenotype at 10 to 12 months of age. The histological structure of retina and tectum was monitored using histology and immunohistochemistry. We performed measurements of retinal thickness and analysis of blood vessel distribution using optical coherence tomography. Further, visually-mediated behavior was assessed using a dark-light place preference test, a social preference test, and the optokinetic response assay. The influence of vision on shoaling behavior was analyzed using the idTracker software.

Results: Adult atoh7 mutants display a darker body pigmentation and significantly reduced body size. Likewise, their retina is significantly thinner (more than 10 %) as they lack all retinal ganglion cells, and therefore, neither possess a nerve fiber layer, nor form an optic nerve. In addition, the distribution of retinal blood vessels is altered in atoh7 mutants. The optic tectum of atoh7 mutants is reduced in size by 25 % and contains less white matter, as well as exhibits a disrupted layering. Applied behavioral assays confirm that adult atoh7 mutants are blind, and show changes in their social behavior.

Conclusions: We find that retinal ganglion cells are still lacking at the adult stage of zebrafish atoh7 mutants resulting in the absence of the optic nerve and a failure of the optokinetic response. Moreover, we conclude that missing innervations of the optic tectum and the associated lack of visual input are the likely cause of structural changes of the optic tectum and subsequent alterations in social interactions.

CONTROL ID: 3710141

SUBMITTER (NAME ONLY): Jennifer Landry

TITLE: Comparison of Biosimilar Molecules to Bevacizumab for Treatment of Neovascular Disease

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Landry, M. Sprouse, T. Issa, T. Stout, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|J. Landry, M. Sprouse, T. Issa, T. Stout, Clayton Foundation for Research, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neovascular diseases of the retina represent a significant disease burden with diabetic retinopathy being the leading cause of blindness in the western world. The development of anti-VEGF drugs revolutionized the treatment of these diseases and significantly improved outcomes. In recent studies, bevacizumab has been proven to be noninferior to Ranibizumab, making anti-VEGF more accessible to patients. New biosimilar molecules to bevacizumab have been approved for use in cancer patients but have yet to be approved in the eye. The goal of this study is to demonstrate that these molecules are safe and effective at reducing neovascularization in the eye.

Methods: Mouse and rabbit models were used to investigate efficacy and safety, respectively, of two novel anti-VEGF biosimilars. Animals were randomized to receive either bevacizumab, Mvasi or Zirabev in one eye; contralateral eyes served as saline or no treatment controls. For the efficacy arm of the study, adult C57BL/6J mice received four laser burns per eye to induce choroidal neovascularization (CNV). Intravitreal anti-VEGF treatments were administered 4,10, and 14 days post-injury followed by fundus fluorescein angiography (FA) and OCT weekly. For the safety study, adult New Zealand White rabbits received a single intravitreal anti-VEGF treatment. Animals were followed weekly with both photopic and scotopic ERG in addition to OCT at endpoint.

Results: CNV was observed in all groups indicated by fluorescein leakage at each laser-induced lesion. No difference was observed in the change of overall area or mean gray value between injury and endpoint among biosimilar treatments. Further, no difference was observed in the change of area and depth of lesions post biosimilar treatment. Regarding safety, no significant changes were seen in A or B wave amplitude over the 4 weeks across all groups. When compared with the contralateral eye controls (saline only), none of the eyes treated with anti-VEGF showed a decrease in amplitude in either photopic or scotopic ERG.

Conclusions: To date, we have seen no difference in the efficacy of bevacizumab, Zirabev and Mvasi. Further, there have been no adverse structural changes and no changes in retinal function. We conclude that these drugs may be suitable alternatives to bevacizumab but will need to be further investigated through a clinical trial.

CONTROL ID: 3710146

SUBMITTER (NAME ONLY): Antoine Sassine

TITLE: Analysis of Architectural Retinal Changes Utilizing Intraoperative OCT Following Surgical Intervention with the Sharkskin Forceps

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.G. Sassine, Y. Cakir, K.E. Talcott, S.K. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess for retinal alterations immediately following membrane peeling procedures with the Finesse Sharkskin ILM Forceps (Alcon, Ft Worth, TX) using intraoperative optical coherence tomography (iOCT).

Methods: A post-hoc analysis of the IRB-approved prospective DISCOVER iOCT study was performed to evaluate iOCT findings in eyes that underwent membrane peeling procedures with the Finesse Sharkskin Forceps, an FDA-cleared handheld membrane peeling device. The forceps were utilized as part of the standard-of-care surgical procedure. In the DISCOVER study, a standardized imaging iOCT protocol is utilized with imaging obtained at various pre-determined time points in the surgery. Pre-peel and post-peel iOCT video and images were evaluated for each eye to assess for post-peel anatomic alterations. Surgical video/iOCT correlation was conducted to evaluate the etiology of anatomic alterations, such as instrument-tissue interaction vs indirect peeling forces.

Results: Thirty-two eyes were included in the analysis with a primary diagnosis of either epiretinal membrane for 22 eyes (69%) and full thickness macular hole for 10 (31%). Ten eyes (31%) underwent complete membrane peeling with Sharkskin Forceps, and 22 eyes (69%) underwent combined peeling with membrane loop-induced edge initiation with peel completion performed with the Sharkskin Forceps. Three eyes (9%) had focal retinal alterations identified on iOCT following tissue-instrument interaction with Sharkskin Forceps demonstrating focal full thickness retinal elevations. Two eyes (6%) had focal inner retinal elevations and one eye (3%) had a full-thickness retinal elevation that were not related to direct tissue-instrument interaction but rather indirect peeling forces. All of these alterations were subclinical (i.e., not visible without iOCT). No intraoperative adverse events occurred.

Conclusions: iOCT-identified architectural alterations related to direct-tissue instrument interaction was relatively infrequent (<10%) with similar frequency to previously reported alterations with other surgical instruments. Further longitudinal comparative research is needed to better understand clinical impact of various peeling methods.

CONTROL ID: 3710147

SUBMITTER (NAME ONLY): Azza Dammak

TITLE: Development of a new intraocular hypertension animal model with gold nanoparticles.

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Dammak, C. Pastrana, F. Huete, C. Carpena Torres, G. Carracedo, Department of Biochemistry and molecular biology, Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|A. Dammak, C. Pastrana, C. Carpena Torres, G. Carracedo, Department of Biochemistry and molecular biology, Ocupharm Diagnostics, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: The aim of this study was to develop a new rabbit model of chronic intraocular hypertension produced by Gold Nanoparticles (GNP) with characteristics similar to human chronic glaucoma and to evaluate different inflammation and oxidative stress biomarkers related with glaucoma.

Methods: Six rabbit were used to the animal model development, n=3 for study group and n=3 for control group. The ocular hypertension model was developed by making multiple intraocular injections of 100 µl of PBS +GNP (80nM concentration) in study group and only PBS in the control group. Increasing intraocular pression (IOP) protocol was developed during a period of 4 weeks by series of four intra-anterior chamber weekly injections. After intracameral injection period, another 4 weeks were stablished without treatment before to measure IOP recovery. IOP was measured weekly by TonoVet tonometer. For biomarkers evaluation, Six rabbit were used to the animal model development, n=3 for study group and n=3 for control group. Following the animal model developed with GNP, it was extracted 100µl of aqueous humor before to inject the PBS+ GNP solution (study group) or only PBS (control group). Osteopontin and diadenosine tetraphosphate were analyzed by HPLC. Data are represented as mean ± SD and p value<0.05 were consider statistically significant.

Results: The IOP was increased in the study group from 12,4 ± 1.1 mmHg at the baseline to 18,2 ±1,3 mmHg after 4 weeks of injections, being the trend statistically significant (p<0.05). The increasing was constant, being around 2 mmHg each week.

However, no differences were found in control group for any measurement, keeping in similar values during all experiment. The IOP recovery in the study group was completed after 4 weeks without GNP injections. Regarding biomarkers evaluation, it was found a significant increasing of Osteopontin after 4 weeks of GNP injections, from 0.0042 ± 0.03 nM to 0.07 ± 0.04 nM (p<0.05). No changes were found in the control group. For Diadenosine tetraphosphate , no differences were found between groups.

Conclusions: The ocular hypertension animal model with GNP seems to be a great option to study the different potential biomarkers of Glaucoma. New long term studies to analyze the effect of GNPs in the ganglion cells density are needed to convert this hypertension model to a glaucoma model.

CONTROL ID: 3710150

SUBMITTER (NAME ONLY): Ana Isabel Jimenez

TITLE: Phase I of SYL1801, a new siRNA delivered in eye drops for age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Jimenez, R&D, Sylentis, SPAIN|V. Ruz, B. Vargas, Regulatory, Sylentis, SPAIN|A. Bleau, Clinical Operations, Sylentis, SPAIN|

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ABSTRACT BODY:

Purpose: The objective of this study is to determine safety, tolerability and pharmacokinetic (PK) profile of different doses of SYL1801 ophthalmic solution in healthy volunteers. SYL1801 is a small interfering ribonucleic acid (siRNA) inhibitor of NRARP (Notch-Regulated Ankyrin Repeat Protein) synthesis, a key regulator of choroidal neovascularization.

Methods: This is an observer-masked, parallel groups, time-lagged study comprised of two treatment intervals: single ascending dose (SAD) and multiple ascending dose (MAD). Four different dose levels of SYL1801 were evaluated: 10 mg/mL q.d. (once daily), 25mg/mL q.d., 50 mg/mL q.d. and b.i.d. (twice daily). SAD intervals included three subjects per cohort and consisted of one treatment day, while MAD intervals had six subjects per cohort treated for 7 consecutive days. Administration in eye drops at Day 1 (through Day 7 for MAD interval) was conducted in one randomly chosen eye. Follow up visits were performed 24 and 72 hours after last administration.

Primary outcomes were ocular tolerability at the site of administration (cornea and conjunctiva) 72 hours after last instillation of SYL1801 and primary PK parameters determination. Secondary outcomes included ocular tolerability at 1 and 24 hours, electrocardiography, laboratory parameters, secondary PK parameters and adverse event (AE) occurrence. PK samples were collected 2, 15, 30 minutes, 1, 4 and 24 hours after last administration (LLOQ: 1 ng/mL).

Results: A total of 36 healthy volunteers were allocated into one of the different administration schedules and completed the study. Preliminary reports after study close-out showed that 4 possibly related AEs (blepharitis in 2 subjects; queratitis, hyperemia and ocular irritation, in 1 subject each) were reported; all of them were mild and resolved in less than 72 hours. PK parameters could not be determined given SYL1801 was only detected in one study sample. No cumulative effect was observed

Conclusions: This study provides evidence that SYL1801, a new siRNA administered in eye drops for retinal diseases, is safe and well tolerated. Few related AEs occurrence together with limited systemic bioavailability supports good safety profile. This, together with in vitro and in vivo efficacy data, further supports clinical development of SYL1801.

CONTROL ID: 3710152

SUBMITTER (NAME ONLY): Karla Alejandra Ruiz Ceja

TITLE: Meta-analysis of human retinal transcriptome data: a powerful tool to gain insight into the genomic organization of inherited retinal disease genes

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Ruiz Ceja, D. Capasso, D. di Bernardo, S. Banfi, Telethon Institute of Genetics and Medicine, Napoli, Campania, ITALY|D. di Bernardo, Department of Chemical Engineering and Industrial Engineering, Universita degli Studi di Napoli Federico II, Napoli, Campania, ITALY|S. Banfi, Department of Precision Medicine, Universita degli Studi della Campania Luigi Vanvitelli, Napoli, Campania, ITALY|D. Capasso, School for Advanced Studies (SSM), Genomics and Experimental Medicine program, Universita degli Studi di Napoli Federico II, Napoli, Campania, ITALY|

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ABSTRACT BODY:

Purpose: To gain insight into the genomic organization and transcript composition of inherited retinal disease (IRDs) genes using publicly available RNA-Seq datasets obtained from the human retina.

Methods: We retrieved from publicly available expression databases 177 bulk RNA-Seq human retina data from non-visually impaired post-mortem donors (Pinelli et al., PMID:27235414 and Ratnapriya et al., PMID:30742112). After quality control analysis, we retained only 161 of them. We then re-analyzed the whole datasets using an ad-hoc designed pipeline. RNA-Seq alignments were assembled at a single sample level and merged to generate an Observed Transcriptome that allowed us to create a single set of assembled transcripts. Transcript expression levels were quantified by scaling TPM (Transcript Per Million) abundance estimates per sample (scaled TPM), and transcripts with less than one median TPM were filtered out. We selected a subset of newly identified candidate transcripts for independent validation by Reverse Transcriptase (RT-)PCR. cDNAs were obtained from RNA extracted from human retina and blood samples. Obtained RT-PCR products were sequenced to assess their identity.

Results: We focused our analysis on 219 IRD genes and identified a total of 3367 putative novel transcripts. The latter were the results of a) partial intron retentions, b) exon skipping and extension, and, in fewer cases, c) novel exon additions and d) connections with other transcriptional units. RT-PCR analysis carried out on a selected subset of putative novel transcripts revealed an overall 50% rate of experimental validation.

Conclusions: This is, to the best of our knowledge, the most comprehensive and extended meta-analysis of IRD genes carried out on RNA-Seq data. Our work provides a reliable expression quantification of IRD transcripts in the human retina, including the identification of novel ones, and paves the way towards a better understanding of the organization of their transcriptional units and, possibly, of the molecular mechanisms underlying inherited retinal diseases.

CONTROL ID: 3710153

SUBMITTER (NAME ONLY): Laura Celotto

TITLE: Single cell RNA sequencing reveals heterogeneity of Müller glia-derived progenitors and partial recapitulation of the developmental retinogenesis program in the light injured zebrafish retina

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Celotto, F. Rost, S. Hans, M. Brand, Center for Regenerative Therapies Dresden, Zentrum fur Regenerative Therapien Dresden, Dresden, Sachsen, DE, academic/medres, GERMANY|

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ABSTRACT BODY:

Purpose: In zebrafish, retinal progenitors (RP) derive from Müller glia (MG) and restore the entire retinal architecture upon lesion. Detailed information on the underlying genes orchestrating this process is missing. Here, we profile the transcriptome of RPs and MGs and track their differentiation in the early regenerating zebrafish retina.

Methods: Adult zebrafish expressing mCherry in MG and GFP in all proliferating cells were used. Retinae of either untreated controls or light lesioned animals were dissociated at 44 hours post lesion (hpl), 4 and 6 days post lesion (dpl). Subsequently, mCherry as well as mCherry/GFP double-positive cells were isolated via Fluorescence Activated Cell Sorting and single cell RNA sequencing (scRNAseq) was performed using 10x Genomics. To validate the results of the scRNAseq, we applied immunohistochemistry and in situ hybridization.

Results: Bioinformatic analysis of 11690 cells identified 15 different cell clusters. Four clusters represent MG. Two clusters contain resting, gfap-positive MG, which are found at all four time points. The others contain reactive, proliferating and reactive, non-proliferating MG obtained at 44 hpl and 4 dpl, respectively. Heterogeneous RP clusters appear at 4 and 6 dpl. Multipotency markers, like pax6a, pax6b, rx1 and vsx2, are expressed in early RPs and resting or reactive MG. Both, early RPs and reactive MG upregulate proliferative, Notch-related and inflammatory markers, like pcna, her4.1 and hmgb2b. A second cluster of RPs is proliferative and expresses early neurogenic markers like atoh7 and pou2f2a. A third RP cluster upregulates markers of several neuronal lineages, like onecut1, onecut2 (horizontal cells), otx5 (photoreceptors) and neurod4 (amacrine cells). Retinal ganglion cells, horizontal cell RPs (pcna, lhx1a, prox1) and photoreceptor RPs (pcna, nr23, thrb) branch from neurogenic RPs already at 4 dpl. Red and blue cones derive from photoreceptor RPs as well as amacrine and bipolar cells from neurogenic RPs at 6 dpl. Rods were not present in the sampled progeny.

Conclusions: MG and early RPs have highly similar transcriptomes, whereas neurogenic and fate restricted RPs initiate markers of retinogenesis in the regenerating retina. Regenerated progeny arises following the developmental retinogenic order.

CONTROL ID: 3710154

SUBMITTER (NAME ONLY): Chia-Yu Wang

TITLE: The Effect of Intracameral Cefuroxime after Routine Cataract Surgery on Macular Thickness and Perfusion Status

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wang, Y. Peng, Ophthalmology, Taipei Tzu Chi Hospital, New Taipei City, TAIWAN|C. Cheng, National Taiwan University College of Medicine, Taipei, TAIWAN|

Commercial Relationships Disclosure: Chia-Yu Wang: Commercial Relationship: Code N (No Commercial Relationship) | Chun-Yao Cheng: Commercial Relationship: Code N (No Commercial Relationship) | Yi-Jie Peng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the safety of intracameral cefuroxime (ICI) 1mg/0.1ml at the end of routine phacoemulsification procedure, we designed a retrospective observational study to evaluate the early changes in retinal thickness (MRT), superficial capillary plexus (SCP) and deep capillary plexus (DCP) by optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) after uncomplicated phacoemulsification.

Methods: 27 eyes of 27 Asian adults were included: 13 eyes with ICI cefuroxime (CEF group) (67.5±12.7 years old); 14 eyes without ICI cefuroxime (Control) (69.93±8.32 years old). All subjects underwent a complete examination including best-corrected visual acuity (BCVA), slit lamp, fundoscope, OCT and OCTA scan before surgery (T0), 1 day (T1), 7 days (T7) and 30 days (T30) after surgery. The retinal thickness was defined as the average thickness in the central, inner and outer circle of the ETDRS grid. We exported OCTA images into ImageJ software (Figure 1). After subtracting the fovea avascular zone (FAZ), we made a 3mm diameter circle centered on the fovea to analyze vessel density (VD) and skeleton density (SD) of SCP and DCP respectively. Independent t test was used to compare parameters between two groups.

Results: (Table 1) Before surgery, there was no significant difference of the mean VD and SD both in SCP and DCP between two groups. (Figure 2) At T1, the mean VD and SD in DCP increased significantly in CEF group compared to controls (29.63±3.24 % vs 25.93±2.30 %; P=0.003 and 8.15±0.91 % vs 7.40±0.64 %; P=0.025, respectively). At T30, the mean VD and SD in DCP elevated again in CEF group (29.89±2.99 % vs 27.73±2.56 %; P=0.054 and 8.11±0.75 % vs 7.52±0.54 %; P=0.026, respectively). Otherwise, there was no difference of mean BCVA, MRT and VD/SD in SCP between groups.

Conclusions: This study elucidates that VD and SD in DCP increase significantly at postoperative day 1 and day 30 in eyes with ICI cefuroxime after cataract surgery. Although the safety of prophylactic ICI cefuroxime is widely accepted nowadays, cefuroxime may still induce subclinical macular perfusion changes without affecting the postoperative visual acuity and macular thickness.

CONTROL ID: 3710156

SUBMITTER (NAME ONLY): Jacob Smith

TITLE: Characterizing extremely negative reviews of ophthalmologists on yelp.com

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.F. Smith, M. Qureshi, O. Adeleye, H. Luong, Mayo Clinic School of Medicine - Scottsdale Campus, Scottsdale, Arizona, UNITED STATES|J. Shen, Ophthalmology, Mayo Clinic Arizona, Scottsdale, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patient satisfaction with the care experience is a critical element of overall high quality healthcare delivery, and patients increasingly utilize online crowd-sourced physician rating tools to evaluate and select a physician. We performed a retrospective characterization of one-star reviews on yelp.com. We hypothesized that most reviews would be nonclinical in nature and that complaints referencing a procedural episode would be largely clinical in nature.

Methods: A search was performed for reviews on yelp.com using the keyword “ophthalmologist” for the top 8 most population-dense metropolitan areas in the United States. One-star reviews were classified as procedural or nonprocedural. Complaints were analyzed and categorized as clinical or nonclinical.

Results: 5,532 reviews were assessed, of which 477 (8.6%) were one-star reviews to be analyzed. These reviews amounted to 1,120 distinct complaints, 287 (25.6%) were clinical in nature and 833 (74.4%) were nonclinical. The most common clinical complaints were technical incompetence/error (50; 17.4%), unsatisfactory result (46; 16.0%), and complication (43; 15.0%). The most common nonclinical complaints were office staff interpersonal (182; 21.8%), wait time (174; 20.9%), and physician interpersonal (141; 16.9%). Patients reporting an ophthalmologic procedure (surgery, injection, etc.) wrote 64 reviews resulting in 193 (17.2%) complaints. Nonprocedural patients wrote 413 reviews resulting in 927 (82.8%) complaints. Compared with nonprocedural reviews, procedural reviews were more likely to relate a clinical complaint (93.8% procedural vs. 28.6% nonprocedural, $P < 0.001$).

Conclusions: The majority of one-star reviews of ophthalmologists in highly populated urban areas included in this study focused on nonclinical complaints unrelated to a procedure performed by the clinician being reviewed, confirming our hypothesis. Procedural complaints were more likely to include a clinical component to the review. These findings can help clinicians identify and address unique healthcare delivery challenges in the field of ophthalmology.

CONTROL ID: 3710161

SUBMITTER (NAME ONLY): Joy Willemse

TITLE: Imaging the orientations of fibers of the human retina and peripapillary sclera with polarization-sensitive optical coherence tomography

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Willemse, V. Zoutenbier, J. de Boer, Vrije Universiteit Amsterdam Faculteit der Betawetenschappen, Amsterdam, Noord-Holland, NETHERLANDS|F.D. Verbraak, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Information on the structure and direction of the scleral collagen and retinal nerves might be helpful in the diagnosis and monitoring of glaucoma, age-related macular degeneration (AMD) and high myopia. In this pilot study, polarization sensitive-OCT (PS-OCT) is used to image the orientation and birefringence of these fiber structures in the eye in these patient groups.

Methods: A depth-multiplexed fiber-based PS-OCT system will be used to extract quantitative and local information on optic axis, birefringence, and depolarization from the retina and peripapillary sclera. The setup contains a swept-source laser centered at 1060 nm with a repetition rate of 200 kHz. Data of glaucoma, wAMD and high myopia patients will be obtained.

Results: By segmentation of the RNFL, Henle's fiber layer and the first 180 µm of sclera, orientation en face images of the different structures can be created (Fig. 1). As the orientation of the retinal nerves is known to be radially from the optic nerve head, absolute orientations of Henle's fiber layer and the sclera could be extracted, as shown in Fig 1. d) and f). The first layer of sclera collagen fibers is oriented approximately parallel to the retinal nerves. A ring structure can be recognized around the optic nerve head, where the orientation of the collagen fibers is circular.

Conclusions: PS-OCT has been used to successfully extract optic axis orientation of the retinal nerves, Henle's fiber layer and the sclera locally in 3D in vivo. The PS-OCT system will be used to detect pathological changes in fiber structures associated with disease. PS-OCT imaging of myopia, wAMD and glaucoma can improve our understanding of retinal biomechanics and structural alterations in different disease stages.

CONTROL ID: 3710163

SUBMITTER (NAME ONLY): Joshua Millar

TITLE: Multimodal mass spectrometry imaging of key biomarkers to study age-related macular degeneration

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Millar, S. Campbell, C. Duckett, L. Cole, Biomolecular Sciences Research Centre, Sheffield Hallam University, Sheffield, South Yorkshire, UNITED KINGDOM|S.L. Doyle, Trinity College Institute of Neuroscience, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Proteins associated with the innate immune system alongside essential and non-essential trace metals are associated with age-related macular degeneration (AMD) onset. Determining the location of innate immune receptors thought to be involved in disease pathogenesis is important when assessing how best to target these receptors. Non-specificity of antibody staining is a challenge for certain immune receptors, e.g. NLRP3. Here mass spectrometry imaging (MSI) has been used to identify and spatially characterise both proteomic and metallomic species within ocular tissue.

Methods: Proteomic data was acquired from mouse ocular tissue prepared on a HTX M3+, trypsin was applied at 25 $\mu l min^{-1}$. 5 $mg ml^{-1}$ of CHCA matrix was applied with variable flow rates. Analysis was conducted using SELECT SERIES MRT and SYNAPT MALDI-MS instruments (Waters Corporation, Manchester, UK) within the mass range 700 to 2000Da. Metallomic analysis was conducted on the same ocular tissue using a NexION 350X ICP-MS (PerkinElmer, Manchester, UK) coupled to an UP-213 laser ablation (LA) system (New Wave Research, Freemont, CA, USA). The ICP-MS was run in Kinetic Energy Discriminatory (KED) mode utilising a variable laser spot size (6 & 40µm), 46% laser energy and a repetition rate of 22Hz.

Results: Investigations are currently underway to interpret the spatial distribution of key biomarkers associated with AMD pathology within mouse ocular tissues. MALDI-MS has exhibited the distribution of NLRP3 and associated proteins in mouse retinal tissue. Current preliminary data suggests the presence of peptides of interest including tentative identifications of peptides associated with the NLRP3 inflammasome. Additionally, LA-ICP-MS has been used to characterize accumulation of both essential and non-essential metals within mouse ocular tissues, utilizing high resolution mass spectrometry to identify determine spatial distribution of key trace metals within the mouse chorio-retinal microanatomy.

Conclusions: This study exhibits the capabilities of multimodal MSI, and how when utilised in an interdisciplinary manner, MALDI-MSI and LA-ICP-MSI have potential to inform on unknown biological mechanisms of retinal degeneration.

CONTROL ID: 3710164

SUBMITTER (NAME ONLY): Immanuel Seitz

TITLE: Neural plasticity of the human visual system reflects treatment effect in gene therapy for Achromatopsia

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I.P. Seitz, M. Fischer, K. Bartz-Schmidt, Centre for Ophthalmology, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|M. Erb, T. Ethofer, Department of Biomedical Magnetic Resonance, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|M. Fischer, Oxford Eye Hospital and Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|A. Rina, Neurology, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|A. Rina, Visual and Cognitive Neuroscience, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|G. Keliris, Bio-Imaging Lab, Universiteit Antwerpen, Antwerpen, BELGIUM|G. Keliris, Max-Planck Institute for Biological Cybernetics, Physiology of cognitive processes, Tübingen, Germany, GERMANY|

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ABSTRACT BODY:

Purpose: Achromatopsia (ACHM) is an inherited retinal disease marked by total cone photoreceptor dysfunction. Tübingen University Hospital completed a Phase I/II clinical trial evaluating the safety and efficacy of an AAV-based, subetinal gene therapy (GT) in adults affected by ACHM due to mutations in CNGA3. One year after GT for ACHM, patients demonstrated a significant, yet not clinically relevant, improvement of best-corrected visual acuity (BCVA) and contrast sensitivity (CS). Because ACHM patients are affected from birth, we hypothesized, that beyond retinal restitution of CNGA3 bioactivity, neural plasticity of the visual system could be a limiting factor in treatment response. To test this hypothesis, patients underwent diffusion tensor imaging (DTI), an established surrogate for white matter (WM) integrity and organization, prior to, and one year after GT.

Methods: Nine patients were examined by a single operator, using a Siemens PRISMA 3T MRI device and a 64-channel head coil. Data processing relied on FSL and SPM12. Using DTI, we measured fractioned anisotropy (FA), a scalar value between 0 and 1, which denotes the directionality of diffusion, and mean diffusivity (MD), the mean speed of diffusion along all tensors. DTI, BCVA and CS measurements were taken prior to, and 1 year after GT. We then performed a voxel-wise regression analysis for ΔFA and ΔMD vs. ΔBCVA and ΔCS along the visual system, with a significance threshold of $p<0.05$, and rejection of small clusters (<25 voxels).

Results: DTI imaging revealed multiple clusters (n=12) along the visual system, in which WM changes [ΔFA, ΔMD] and clinical treatment response [ΔBCVA, ΔCS] one year after GT displayed a moderate to strong (R^2=0.47-0.74), and significant ($p<0.05$) correlation. This was the case for both BCVA (vs. FA R^2=0.48-0.56, n=4 vs. MD R^2=0.47-0.72, n=4), and CS (vs. FA R^2=0.48-0.74, n=3, vs. MD R^2=0.66, n=1).

Conclusions: Despite a low effect size in adult ACHM patients, DTI revealed a significant correlation between the degree of BCVA and CS improvement, and the degree of WM plasticity in key areas of the visual system, one year after GT. This supports the notion, that neural plasticity might indeed be a limiting factor in the treatment response of adult ACHM patients. Based on these results, it seems sensible to treat younger patients, which harbor greater potential for a remodeling of the visual system.

CONTROL ID: 3710165

SUBMITTER (NAME ONLY): Jose Sahel

TITLE: Optogenetics in the clinic: safety and efficacy updates on the phase 1/2 clinical trial PIONEER

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Boulanger-Scemama, Ophthalmology, Fondation Ophtalmologique Rothschild, Paris, FRANCE|C. Pagot, C. de Montleau, E. Gutman, Institut de la Vision, StreetLab, Paris, FRANCE|M. Taiel, GenSight Biologics SA, Paris, Île-de-France, FRANCE|J.A. Sahel, J.N. Martel, Ophthalmology, UPMC, UPMC, Pittsburgh, PA, US, health/system, Pittsburgh, Pennsylvania, UNITED STATES|S. Degli Esposti, Moorfields Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, National Institute for Health Research, London, UNITED KINGDOM|J.A. Sahel, I.S. Audo, A. Arleo, A. Delaux, J. de Saint Aubert, J. Duebel, S. Picaud, D. Dalkara, Institut de la Vision, Sorbonne Université, Inserm, CNRS, Paris, FRANCE|I.S. Audo, E. Boulanger-Scemama, INSERM-DGOS CIC 1423, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, FRANCE|B. Roska, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Evaluate the GS030 optogenetic therapy in subjects with end-stage non-syndromic retinitis pigmentosa.

Methods: The GS030 optogenetic therapy combines an intravitreal injection of gene therapy with the use of a medical device. The GS030 gene therapy vector expresses channelrhodopsin ChrimsonR-tdTomato in retinal ganglion cells. The light-stimulating goggles encode the visual scene and project corresponding light pulses to activate the retinal ganglion cells. PIONEER is an international open-label dose-escalation clinical study of GS030 for the treatment of late-stage retinitis pigmentosa.

Results: 9 patients were injected with increasing doses of gene therapy: 3 received 5E10 viral genomes (vg)/eye, 3 received 1.5E11 vg/eye, and 3 received 5E11 vg/eye. Started 8 weeks after injection, the use of light-stimulating goggles was well tolerated. The main ocular adverse event related to gene therapy was mild intraocular inflammation responsive to corticosteroid treatment. Following systematic visual training with the goggles, two patients were able to locate and touch small objects on a table. One of these 2 patients underwent EEG recording during a visual test, which showed vision-related cortical activity.

Conclusions: GS030 demonstrates a good safety profile up to 2.5 years after vector administration, and preliminary efficacy assessment shows partial functional recovery in two patients.

CONTROL ID: 3710166

SUBMITTER (NAME ONLY): Byung Soo Kang

TITLE: High Myopia Induced by Bilateral Form Deprivation Is Highly Synchronized in Both Eyes of Chickens: a pilot study

SESSION TITLE: Myopia: Mechanism of Emmetropization and Eye Growth

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Kang, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|B. Kang, T. Leung, S.A. Vyas, C. Kee, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|C. Kee, Research Centre for SHARP Vision, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Form-deprivation and lens-induced myopia are two well-established models for experimental myopia research. Although both paradigms induce axial myopia, form-deprivation myopia is induced by the absence of clear vision and the axial elongation can progress continuously with large inter-subject variability (open-loop); whereas lens-induced myopia by imposing hyperopic defocus stops when eyes receive a clear focal image (closed-loop). This pilot study investigated whether the refractive development in both eyes was independent of each other under the bilateral form-deprivation condition.

Methods: At day 5 post-hatching (P5), White Leghorn chicks were randomly assigned to receive either unilateral (UFD, n=5) or bilateral form deprivation (BFD, n=5) by covering one (right eye) or both eyes with translucent diffusers. At the onset and over the 9-day treatment period, refractive state and ocular axial dimensions were measured longitudinally (P5, P7, P10, P12, and P14) using a modified Hartinger refractometer and a high-resolution A-scan ultrasonographer, respectively. Two-way repeated measures ANOVA was used for statistical analysis. All parameters were expressed as mean±SD.

Results: Both treatment and duration showed significant main effects on spherical-equivalent refractive error (SE) development (Treatment effect: $F(3,16)= 4.19$, $p<0.05$; Duration effect: $F(1,19)= 36$, $p<0.001$). Regardless of the treatment received, form-deprived eyes showed a rapid myopic shift in refractive state and vitreous chamber elongation (Fig 1A&B). Interestingly, the high myopia induced by BFD paradigm was highly synchronized in both eyes: the interocular difference in SE and vitreous chamber depth (VCD) were: P10: SE= 0.97±2.61D, VCD= −29.21±37.03μm; P12: SE= −0.08±1.84D, VCD= 7.78±83.87μm; P14: SE= 2.19±0.83D, VCD= 43.29±51.74μm (Fig 2A&B).

Conclusions: Refractive development in both eyes was synchronized under bilateral form deprivation in chickens. Further studies are warranted to understand the mechanism of inter-ocular synchronization and its potential role in form deprivation myopia.

CONTROL ID: 3710168

SUBMITTER (NAME ONLY): Heiko Stino

TITLE: Comparison of neovascularization (NV) detection in proliferative diabetic retinopathy (PDR) between single-capture wide-field optical coherence tomography angiography (WF-OCTA) and ultra-widefield fluorescein angiography (UWF-FA)

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Stino, A. Sedova, S. Sacu, U. Schmidt-Erfurth, A. Pollreisz, Department of Ophthalmology, Medizinische Universitat Wien, Vienna, Vienna, AUSTRIA|M. Niederleithner, T. Schmoll, R.A. Leitgeb, Center for Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Vienna, Vienna, AUSTRIA|T. Schmoll, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the detection rate of retinal NVs in eyes with PDR between UWF-FA and WF-OCTA systems.

Methods: In this ongoing prospective study patients with NV at the disc (NVD) or elsewhere (NVE) detected on UWF-FA (California, Optos) were recruited from our outpatient clinic. Single-capture 65° (18x18 mm) WF-OCTA-imaging was performed using a Zeiss PLEX Elite prototype (Carl Zeiss Meditec GmbH) at an A-scan rate of 1.7 mHZ; and an axial and lateral resolution of 9 µm and 20 µm, respectively. Angiograms were visually enhanced using a deep learning-based algorithm for denoising. WF-OCTA B-scans were examined for blood flow signals above the internal limiting membrane by two retina specialists.

Results: 38 eyes of 26 patients with PDR detected on UWF-FA were included until December 2021. 36 eyes (94.7%) had at least one NV within the 18x18mm WF-OCTA. A total of 141 NVEs were detected on UWF-FA of which 41 (29.1%), 50 (35.5%), 28 (19.9%), and 22 (15.6%) were located superotemporal, inferotemporal, superonasal, and inferonasal, respectively. Significantly more NVEs occurred in the temporal compared to the nasal quadrants ($p < 0.05$). 87 NVEs (61.7% of all NVEs) were detected using single-capture WF-OCTA. Compared to UWF-FA the number of NVEs detected on WF-OCTA in the superotemporal, inferotemporal, superonasal, and inferonasal quadrants was 35 (85.4%), 40 (80%), 5 (17.9%), and 7 (31.8%), respectively.

Conclusions: Single-capture WF-OCTA allows correct classification of PDR in 95% of individuals by detecting at least one NV within the observed field. On UWF-FA NVEs were most prevalent in the temporal fields with a majority of them detected on WF-OCTA scans. Quick and non-invasive WF-OCTA imaging has the potential to replace FA as a single diagnostic tool in clinical routine in the evaluation of PDR activity.

CONTROL ID: 3710170

SUBMITTER (NAME ONLY): Ziv Rotfogel

TITLE: Oxidative stress facilitates exogenous mitochondria internalization and survival in retinal ganglion precursor-like cells

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Rotfogel, K. Ben-Yaakov, M. Sharvit-Bader, D. Raz, W. Ghannam, Y. Haim, A. Marcovich, H. Leiba, A. Eisenberg-Lerner, M. Aharoni-Simon, Ophthalmology Research Laboratory, Kaplan Medical Center, Rehovot, ISRAEL|Z. Rotfogel, A. Marcovich, H. Leiba, Faculty of Medicine, Hadassah Medical School, Hebrew University of Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: Mitochondrial dysfunction is highly implicated in various acute, chronic and genetic disorders of the visual system, owing to the high demand of energy supply of ocular cells and their constant exposure to oxidative stress. Recently, Mitochondrial transplantation (MitoPlant) has emerged as a novel therapeutic modality for the treatment of ischemia/reperfusion insults. It was previously shown that MitoPlant temporarily protects retinal ganglion cells from cell death during ocular ischemia. Here, we characterized MitoPlant dynamics in retinal ganglion precursor-like cells, by evaluating uptake and survival of mitochondria in recipient cells under oxidative stress.

Methods: We developed a new method for detection of transplanted mitochondria using qPCR, based on a difference in the mtDNA sequence of C57BL/6 and BALB/c mouse strains. We applied this approach together with flow cytometry and imaging techniques to evaluate mitochonrial transplantation dynamics in 661W cells in steady state conditions and under oxidative stress.

Results: We demonstrate that exogenous mitochondria are substantially internalized as early as three hours after transplantation, and that the levels of exogenous mitochondria decline in recipient cells after twenty four hours. Interestingly, exposure of the target cells to moderate oxidative stress prior to MitoPlant dramatically enhanced mitochondrial uptake and extended the survival of mitochondria in recipient cells by more than three fold.

Conclusions: We developed a new research tool that enables following exogenous mitochondrial survival within recipient cells and demonstrate that oxidative stress significantly enhances exogenous mitochondria uptake and survival in retinal ganglion precursor-like cells. These results may promote delineating MitoPlant mechanism and the development of tools to prolong mitochondrial survival, thereby offering novel opportunities for the use of MitoPlant as a promising therapy for chronic and genetic mitochondrial diseases.

CONTROL ID: 3710172

SUBMITTER (NAME ONLY): Philipp Luedtke

TITLE: Characterization of subconjunctival murine fibroblasts and human Tenon fibroblasts

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Luedtke, E. Molinski, M. Binter, C. Framme, R. Meister, J. Tode, H. Fuchs, Ophthalmology, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Excessive wound healing after glaucoma filtration surgery (GFS) is primarily caused by the transformation of subconjunctival Tenon fibroblasts into increased extracellular matrix-producing myofibroblasts. The extracellular matrix forms a barrier that causes inadequate absorption of excess aqueous humor by the conjunctiva and increases intraocular pressure. To test future fibrosis inhibitors in vivo after GFS in a mouse model, murine subconjunctival fibroblasts (mSCFs) were isolated and compared to human Tenon fibroblasts (hTFs).

Methods: Methods:

(1) Tissue samples were taken from the subconjunctival space of C57BL/6 mouse eyes (n=3) or tenon from humans undergoing trabeculectomy surgery (n=3). Both cell types were compared morphologically, by immunocytochemistry (ICC) and Western blot analysis. An outgrowth of cells from both tissues was observed 5 to 7 days after initial culture and could be successfully expanded until passages 5-7.

(2) ICC staining of Vimentin, α-SMA, Collagen I (Col1), and Collagen VI (Col6) was performed with both cell types after 5 days of treatment without or with TGF-beta (10 ng/ml) to induce fibrosis or with the TGFBR2-inhibitor SB431542 (10 ng/ml) to block fibrosis induction.

(3) Western blots of α-SMA (with and without TGF-beta treatment for 5 days) and Col1 (without treatment) were performed.

Results: The ICC analysis revealed that Col1 was present in every cell line in the perinuclear region's cytoplasm in mouse and human cultures. Extracellular Col1 could not be detected. Col6 could also be seen in the perinuclear area, and structures of Col6 connecting neighboring cells could be detected in all analyzed cell types. Vimentin showed a filamentous distribution in mSCFs and hTFs. As expected, the number of α-SMA-positive cells was increased in both cell types after 5 days of TGF-beta exposure. Western blots analysis showed higher α -SMA protein expression in TGF-beta treated mSCFs and hTFs compared to untreated or SB431542-treated cells.

Conclusions: MSCFs and hTFs have a filamentous distribution of Vimentin. Both show Col1 and Col6 expressions in the perinuclear region. Both cell types share the origin and ability to transform into myofibroblasts as TGF-beta treatment for 5 days induced α-SMA protein compared to untreated or SB431542-treated cells. The similarities between mSCFs and hTFs are essential for conducting trabeculectomy or subconjunctival scarring studies.

CONTROL ID: 3710173

SUBMITTER (NAME ONLY): Giovanni William Oliverio

TITLE: The efficacy of a netilmicin/dexamethasone gel combination in the treatment of posterior blepharitis in moderate-severe dry eye patients.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Oliverio, L. Inferrera, E. Imelde, P. Aragona, Biomedical Sciences, Universita degli Studi di Messina, Messina, Sicilia, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the safety and efficacy of netilmicin/dexamethasone fixed combination in the treatment of meibomian gland dysfunction (MGD)-associated posterior blepharitis.

Methods: In this observational and controlled study were enrolled 40 patients with MGD and symptoms of dry eye disease. Two groups were established: 20 patients (group 1) received netilmicin 3 mg/ml and dexamethasone 1 mg/ml eye gel two times daily, whereas in group 2 (20 patients) received vehicle two times daily for 15 days. Patients underwent at baseline, and after 15 and 45 days Symptom Assessment in Dry Eye (SANDE) questionnaire, Visual Analogue Rating Scale (VARS) for dry eye symptoms, Keratograph 5M (Oculus, Germany) was used to assess non-invasive tear film breakup time (NIBUT), tear meniscus height (TMH), ocular redness and meibography score. Moreover, fluorescein tear-film breakup time (T-BUT), fluorescein ocular surface staining, lid margin evaluation including hyperemia, edema and meibum expressibility and quality examinations were carried out. Furthermore, intraocular pressure (IOP) and best-corrected visual acuity (BCVA) were considered as safety parameters

Results: In group 1, at 15 and 45 days there were statistically significant changes in VARS and SANDE score ($p < 0.0001$) as well as lid margin parameters, T-BUT and fluorescein ocular surface staining ($p < 0.0001$). No significant changes in BCVA and IOP were noted at the end of the study. Comparing the two groups, a significant improvement of SANDE was observed at 15 days in group 1 as well as lid margin parameters, BUT and fluorescein ocular surface staining at 15 and 45 days (all $p < 0.0001$).

Conclusions: Netilmicin/dexamethasone combination is effective and safe to treat MGD-associated posterior blepharitis improving both symptoms, and ocular surface signs.

CONTROL ID: 3710174

SUBMITTER (NAME ONLY): Jan Ness

TITLE: Transcriptomic and Immunocytochemical comparison of 2D and 3D in vitro angiogenesis assays

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.N. Ness, J. Rapp, J. Wolf, P. Liang, H.T. Agostini, G.R. Schlunck, C. Lange, F. Bucher, Eye Center, Universitatsklinikum Freiburg, Freiburg, Baden-Württemberg, GERMANY|M. Hug, Hospital Pharmacy, Universitatsklinikum Freiburg, Freiburg, Baden-Württemberg, GERMANY|J. Rapp, J. Wolf, P. Liang, H.T. Agostini, G.R. Schlunck, C. Lange, F. Bucher, Albert-Ludwigs-Universitat Freiburg Medizinische Fakultat, Freiburg, Baden-Württemberg, GERMANY|J.N. Ness, M. Hug, Institute for Pharmaceutical Sciences, Albert-Ludwigs-Universitat Freiburg Fakultat fur Chemie und Pharmazie, Freiburg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Retinal vascular diseases represent one of the most common causes for vision loss in the western world. To study angiogenic processes and identify novel therapeutic targets, researchers utilize a variety of in vitro angiogenesis assays in either 2D or 3D settings. Interestingly, research results from 2D and 3D in vitro assays do not necessarily align. In this study, we compare transcriptomic and immunocytochemical changes in vascular endothelial cells from common 2D and 3D in vitro angiogenesis assays to unravel advantages and disadvantages and, based on this, the preferred use of the respective assay.

Methods: The 2D Migration Assay and 3D Spheroid Sprouting Assay were both performed using human umbilical vein endothelial cells (HUVEC). Human VEGF165 was used to stimulate the endothelial cell migration and sprouting. We applied RNA Seq analysis to assess the transcriptomic modulations in HUVECs following stimulation with hVEGF165 in the respective 2D and 3D setting. Immunocytochemistry was used to characterize differences at the protein level in the assays performed.

Results: In both 2D and 3D assays, genes related to angiogenesis, migration and vascular development were enriched after stimulation with hVEGF165. Interestingly, in the 3D setting vascular endothelial cells showed a clearer transcriptomic shift in response to hVEGF165 treatment (foldchange: 3.96, differentially expressed genes (DEG): 763) than in the 2D setting (foldchange: 1.34, DEG: 167). Upregulation of common proangiogenic genes including KDR and VCAM1 was comparable in both assays. In contrast, transcriptomic changes related to cell-matrix interaction and glycolysis were both significantly increased only in the 3D setting. Immunocytochemical stainings revealed that exclusively in the 3D setting, vascular endothelial cells were able to generate an in vivo like tip cell behavior visualized by localized CD34 expression in the spheroid sprouts.

Conclusions: Our data underline that the transcriptomic profile of vascular endothelial cells and their responsiveness to VEGF and most likely other test substances is influenced by the assay microenvironment. For scientific questions regarding matrix interactions or glycolytic switches researchers should consider the 3D setting. For high throughput screening experiments and investigations of main angiogenic pathways the 2D setting may be sufficient.

CONTROL ID: 3710179

SUBMITTER (NAME ONLY): Matthias Marten Mauschitz

TITLE: Association of lipid-lowering drugs, anti-diabetic drugs, non-steroidal anti-inflammatory drugs, and levodopa with age-related macular degeneration in Europeans: A meta-analysis of the European Eye Epidemiology (E3) – consortium

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Mauschitz, R.P. Finger, Department of Ophthalmology, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|A.K. Schuster, Department of Ophthalmology, Universitatsmedizin der Johannes Gutenberg-Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|A.P. Khawaja, MRC Epidemiology Unit, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|M. Bikbov, Ufimskij naucno-issledovatel'skij institut glaznyh boleznej, Ufa, Bashkortostan, RUSSIAN FEDERATION|R.E. Hogg, Centre for Experimental Medicine, Institute of Clinical Science, Queen's University Belfast, UNITED KINGDOM|F.G. Rauscher, Leipzig Research Centre for Civilization Diseases (LIFE), Leipzig University, GERMANY|F. Topouzis, Ophthalmology, Aristoteleio Panepistemio Thessalonikes, Thessaloniki, Central Macedonia, GREECE|C. Brandl, Ophthalmology, Universitatsklinikum Regensburg, Regensburg, Bayern, GERMANY|C. Creuzot-Garcher, Ophthalmology, University Hospital Dijon, FRANCE|C. Delcourt, Bordeaux Population Health Research Center, FRANCE|H. Hense, Epidemiology, Universitatsklinikum Munster, Munster, Nordrhein-Westfalen, GERMANY|R. Silva, Ophthalmology, Centro Hospitalar e Universitário de Coimbra, PORTUGAL|S. Piermarocchi, Neuroscience, University of Padova, ITALY|K. Ritchie, Institut national de la santé et de la recherche médicale, FRANCE|M. Gran Erke, Ophthalmology, Oslo Universitetssykehus, Oslo, NORWAY|

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ABSTRACT BODY:

Purpose: Changes in lipid metabolism, chronic inflammation and increased oxidative stress have been discussed as patho-etiogenetic drivers in age-related macular degeneration (AMD). Systemic medication, such as lipid-lowering drugs (LLD) and anti-diabetic drugs, affect these pathways and may therefore also play a role in AMD pathogenesis. We aimed to investigate associations of commonly used systemic drugs with AMD prevalence in the European population.

Methods: We included 38,694 adults from 14 population-based studies from the European Eye Epidemiology (E3) consortium. We performed multivariable logistic regression modelling to examine medication use association with prevalence of AMD as well as late AMD. Analyses were carried out separately by study and results pooled using random effects meta-analysis. We conducted these analyses separately for LLD, anti-diabetic drugs, non-steroidal anti-inflammatory drugs (NSAID), and L-Dopa.

Results: Between studies, mean age ranged from 61.5 ± 7.1 to 82.6 ± 3.8 years and prevalence ranged from 12.1% to 64.5% and from 0.5% to 35.5% for any and any late AMD, respectively. In the meta-analysis of our multivariable models, LLD and anti-diabetic drugs were associated with lower AMD prevalence (OR 0.85, 95% confidence interval

(CI)=0.79 - 0.91 and OR 0.78, 95% CI=0.66 - 0.91). We found no association with late AMD or with any other medication.

Conclusions: Our study shows an association of LLD and anti-diabetic drug use with lower AMD prevalence across multiple European cohorts. Our findings support the importance of metabolic processes in the complex etiology of AMD.

CONTROL ID: 3710182

SUBMITTER (NAME ONLY): Jia Yin

TITLE: Peripheral Sensory Nerves Inhibit Corneal Angiogenesis via alpha-Melanocyte-Stimulating Hormone

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yin, S. zhu, L. Liu, K. Pang, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Yin, S. zhu, L. Liu, K. Pang, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiogenesis in the normally avascular cornea underlies common corneal diseases. Corneal sensory nerves, derived from the trigeminal ganglion (TG), are master regulators of ocular surface homeostasis. Here we seek to determine whether corneal nerves directly modulate angiogenesis and investigate the role of neuropeptide alpha-Melanocyte-Stimulating Hormone (α-MSH).

Methods: TG neurons were isolated from C57BL/6 mice and cultured in Neurobasal A medium. A co-culture system was set up by placing TG neurons in in the top chamber of a transwell and vascular endothelial cells (VEC, MILE SVEN1 cell line) in the bottom chamber. VEC proliferation, migration, and tube formation were determined with and without TG neurons. In vivo corneal angiogenesis was induced by placing intrastromal sutures in BALB/C mouse corneas.

Results: Presence of TG neurons in co-culture decreased VEC proliferation by 35% (P=0.008) and migration by 20% (P=0.046). Similarly, conditioned media (CM) of TG neurons reduced VEC proliferation (P<0.0001), migration (p=0.017), and the number of junctions (P=0.004) and length of tubes (P=0.001) formed by VEC. Topical application of neuron CM led to a 76% reduction in suture induced-corneal angiogenesis in vivo (P=0.025). More than 80% of TG neurons and 90% of subbasal corneal nerves express α-MSH. α-MSH (100nM) reduced VEC proliferation, migration, and tube formation in vitro and subconjunctival injection of α-MSH reduced corneal angiogenesis by 56% (P=0.008) in vivo. Antagonizing α-MSH signaling with Agouti-signaling protein or siRNA knock-down in TG neurons reversed the inhibitory effects of neuron CM on VEC proliferation, migration, and tube formation.

Conclusions: TG neurons and corneal nerves express anti-angiogenic neuropeptide α-MSH, which plays a critical role in the direct modulation of corneal angiogenesis by peripheral sensory nerves.

CONTROL ID: 3710185

SUBMITTER (NAME ONLY): Nicholas Johnson

TITLE: The use of ocular coherence tomography (OCT) for early glaucoma screening in patients with diabetes

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Johnson, P. Gupta, T. Lee, J. Rosdahl, Department of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Though there are no population-based screening recommendations for glaucoma, screening in at-risk populations has proven beneficial. Ocular coherence tomography (OCT) is a popular tool for assessing structural damage from glaucoma. The purpose of this study is to determine the utility of OCT for glaucoma screening in a population of diabetic patients. These results may inform future screening practices for early detection of glaucoma.

Methods: In this prospective study, patients with diabetes were screened for diabetic eye disease at a Duke primary care clinic over six months. The current study is a post-hoc analysis of OCT data collected from these patients. Glaucoma suspects (GS) were identified based on abnormal retinal nerve fiber layer (RNFL) thickness on OCT. Two-dimensional fundus photos of GS were graded by two independent raters for cup-to-disc ratio (CDR), image quality, and presence of optic disc notching, rim thinning, or disc hemorrhage.

Results: Of the 807 subjects that were screened, 50 patients (6.2%) were identified as GS due to abnormal RNFL thickness in at least one eye. The cohort of GS was 44% female and 70% white. Mean RNFL thickness for GS was significantly lower than mean RNFL in the total screening population ($p<0.001$). Median CDR for GS was 0.44. Twenty-eight eyes of 17 GS were marked as having optic disc notching or rim thinning by at least one grader, while 13 eyes of 7 GS were marked by both graders. Racial differences showed that mean CDR was significantly higher in non-whites than whites ($p<0.001$). Patient age was negatively correlated with RNFL ($r=-0.29$, $p=0.004$).

Conclusions: The aim of this study was to determine the percentage of diabetic patients categorized as GS by OCT and elicit how many suspects also showed clinical signs of glaucomatous damage. Results of this study suggest that in a sample of diabetic patients, a small but clinically significant minority may be flagged as GS based on OCT. Nearly one-fifth of these suspects demonstrated clinical signs of glaucoma on fundus evaluation. The construction of screening guidelines for glaucoma remains an important discussion in primary prevention of the disease. These results suggest that screening with OCT may be warranted in certain populations to allow for earlier diagnosis and treatment, particularly in older, non-white patients with diabetes.

CONTROL ID: 3710190

SUBMITTER (NAME ONLY): Sraboni Chaudhury

TITLE: Novel PKM2 activators for photoreceptor neuroprotection: identifying potential clinical candidates

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chaudhury, E. Weh, H. HAGER, T.J. Wubben, C.G. Besirli, Ophthalmology and Visual Sciences,, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|J. RECH, B. WATCH, INTERNAL MEDICINE, University of Michigan, ANN ARBOR, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a lack of successful treatment options that prevent photoreceptor cell death. We have shown that reprogramming photoreceptor metabolism via activation of PKM2 is a novel therapeutic strategy for neuroprotection. The low aqueous solubility and structural features of current PKM2 activators limit their ability to be translated to the bedside. The goal of this study was to develop the next generation of small molecule PKM2 activators, with improved solubility and in vivo potency for ocular delivery.

Methods: To address the structural limitations of current PKM2 activators, medicinal chemistry efforts focused on a pyridazinoindolone heterocyclic core with a range of functional groups. 49 novel analogues were developed, and solubility of the compounds was tested at pH 7.4. The ability to activate PKM2 was tested with human recombinant PKM2 enzyme, in vitro in 661W cells, and in vivo in rat retina via intravitreal (IVT) injection, oral gavage, or intraperitoneal injection (IP), using a continuous, enzyme-coupled assay that measures the depletion of NADH via absorbance at 340 nm.

Results: All compounds showed nanomolar potency with recombinant PKM2 and in vitro in 661W cells. MCTI-566 was identified as a highly soluble PKM2 activator with aqueous solubility of 385 µg/mL and an AC_{50} = 83 ± 9 nM. When injected intravitreally, MCTI-566 retained PKM activation as compared to tool compound and known selective PKM2 activator, ML-265. Interestingly, a single oral dose of ML-265 (50 mg/kg) produces similar PKM activation in the retina as a single intravitreal injection of ML-265 (1 mM) and retains 100% increased PKM activation after 1 week. Likewise, a single IP dose (50 mg/kg) of MCTI-566 produced similar PKM activation in the retina as compared to a single IVT injection of ML-265 (1 mM) and retained 100% increased PKM activation in the retina after 1 week.

Conclusions: This study developed the next generation of PKM2 activators with improved aqueous solubility while maintaining nanomolar potency. Successful commercial development of MCTI-566 would be transformative for ophthalmology, as a novel PKM2 activator could potentially be the first therapeutic to stop photoreceptor death and improve vision in currently untreatable eye conditions. Future studies will assess ocular and systemic toxicity and in vivo efficacy.

CONTROL ID: 3710192

SUBMITTER (NAME ONLY): Shanlee Stevens

TITLE: Clinical and optical coherence tomography comparison between ocular surface squamous neoplasia and squamous metaplasia

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. Stevens, D. Reyes-Capo, U. Patel, V. Tang, R.A. Abou Khzam, A. Choudhury, S.R. Dubovy, C.L. Karp, A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Galor, VA Miami Healthcare System, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the clinical characteristics and high-resolution optical coherence tomography (HR-OCT) findings between corneal squamous metaplasia and ocular surface squamous neoplasia (OSSN).

Methods: A retrospective case control study of eight patients, four with histologically confirmed squamous metaplasia and four with histologically confirmed OSSN, that presented to the Miami Veterans Administration Medical Center and Bascom Palmer Eye Institute between 2016 and 2020, was performed. Clinical characteristics, HR-OCT findings, and pathology were evaluated and compared.

Results: Four patients with squamous metaplasia and four with OSSN were evaluated. In the metaplasia group, 75% were male, two were white, and two were black. In the OSSN group, all four were white males. All lesions were opalescent and occurred at the limbus; however, the borders were more smooth and rounded in the metaplastic lesions compared to OSSN. HR-OCT findings were indistinguishable between the two groups. The attached figure compares the slit lamp photograph, HR-OCT, and pathology between a case with squamous metaplasia (top row) and a case with OSSN (bottom row).

Conclusions: There is overlap in clinical characteristics and HR-OCT findings between corneal squamous metaplasia and OSSN, highlighting one limitation of HR-OCT. As such, if a corneal opacity has some but not all HR-OCT findings of OSSN, squamous metaplasia should also be considered. A biopsy may be indicated to further evaluate and guide treatment.

CONTROL ID: 3710193

SUBMITTER (NAME ONLY): Gagan Kalra

TITLE: Association of Aqueous Cytokine Expression with Quantitative Leakage Patterns on Ultra-widefield Angiography in the PRIME Study

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Kalra, K.E. Talcott, S.K. Srivastava, J. Reese, J.P. Ehlers, Ophthalmology, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|G. Kalra, K.E. Talcott, S.K. Srivastava, J. Reese, J.P. Ehlers, Ophthalmology, The Tony and Leona Campane Center for Excellence in Image-Guided Surgery and Advanced Imaging Research, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|C.C. Wykoff, Ophthalmology, Retina Consultants of Texas, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the link between aqueous cytokine expression and quantitative leakage phenotypes on ultra-widefield fluorescein angiography (UWFA) in diabetic retinopathy (DR).

Methods: Patients with DR enrolled in the prospective randomized PRIME trial were included in this study. Baseline aqueous samples were analyzed for cytokine expression using a multi-plex ELISA assay for 54 cytokines. UWFA scans from the same visit were utilized for automated machine learning-enhanced quantitative analysis to obtain perivascular leakage index (PLI) and general leakage index (GLI) with manual correction, as needed. Perivascular leakage was denoted by hyperfluorescence within 5 pixels of the segmented vascular tree. Generalized leakage was all other leakage beyond the specified distance from the vessel. Pearson's correlation was used to study the correlation between leakage metrics obtained from UWFA and 16 high expression cytokines found in >80% of the samples.

Results: Thirty-seven DR eyes without edema were included in this study. Significant correlations of panretinal PLI with ANGPTL4 (r=0.36, p=0.028) and angiostatin (r=0.37, p=0.025) were identified. Additionally, panretinal GLI significantly correlated with ANGPTL4 (r=0.40, p=0.015), IFNg (r=0.35, p=0.035), and CXCL16 (r=0.33, p=0.047). Foveal PLI significantly correlated with TNFa (r=0.40, p=0.015). Foveal GLI significantly correlated with VEGF-D (r=0.33, p=0.043), IL12p70 (r=0.34, p=0.039), and IL-17 (r=0.43, p=0.007). PlGF correlated significantly with foveal PLI/GLI ratio (r=0.48, p=0.002) and ANG-2 correlated significantly with panretinal PLI/GLI ratio (r=0.58, p=0.002). Additional correlation trends were identified with panretinal PLI with HB-EGF (r=0.32, p=0.051) and follistatin (r=0.28, p=0.097). Panretinal GLI trended towards significant correlation with VEGF-A (r=0.28, p=0.091), HGF (r=0.28, p=0.097), IL-17 (r=0.28, p=0.090), and TNFb (r=0.28, p=0.092. Foveal PLI/GLI ratio showed correlation trend for ANG-2 (r=0.28, p=0.097).

Conclusions: In this analysis, PLI and GLI on UWFA demonstrate differential significant correlations with aqueous cytokine expression in eyes with DR. Further investigation with larger datasets is warranted to substantiate these associations and evaluate the potential role for these signals for treatment response.

CONTROL ID: 3710194

SUBMITTER (NAME ONLY): Brian Perkins

TITLE: Notch inhibition promotes regeneration and immunosuppression supports cone survival in a zebrafish model of inherited retinal dystrophy

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.D. Perkins, P. Song, J. Fogerty, S. Grabinski, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|P. Boyd, D. Hyde, Biological Sciences, University of Notre Dame, Notre Dame, Indiana, UNITED STATES|T.V. Hoang, S. Blackshaw, Neuroscience, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|J.S. Mumm, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Müller glia (MG) in several zebrafish models of chronic photoreceptor degeneration fail to re-enter the cell cycle and regenerate lost cells. Our goals were to determine the transcriptional and cellular responses to chronic degeneration and to identify mechanisms that prevent regeneration in cep290 and bbs2 mutant zebrafish.

Methods: RNA-seq, single-cell RNA-seq, and qRT-PCR were used to assess gene expression changes. Immunohistochemistry was performed on retinal cryosections to monitor retinal cell types. Acute injury was generated by exposing animals to high intensity light. Dexamethasone and irf8 mutant zebrafish were used for temporary and chronic immune suppression, respectively. The gamma-secretase inhibitor RO4929097A was used to inhibit Notch signaling. A minimum of 6 animals per group were tested. Data was quantified and analyzed using ANOVA with post hoc comparisons.

Results: Zebrafish cep290 and bbs2 mutants exhibit progressive photoreceptor degeneration beginning at 3 months of age. Degeneration leads to an immune response with accumulation of 4C4+/L-plastin+ cells in the outer nuclear layer (ONL) and subretinal space and the upregulation of inflammatory signaling pathways. Both mutants exhibit increased numbers of PCNA+ cells in the ONL but only a 2-fold increase in the number of proliferating Müller glia. At 1 month of recovery following acute light damage, the density of regenerated photoreceptors in cep290 or bbs2 mutants at all ages remained significantly lower than that of wild-type animals. In irf8;cep290 double mutants, which possessed significantly fewer microglia, there was reduced inflammation and cone degeneration was rescued. Finally, single-cell RNA-sequencing revealed sustained notch3 expression in MG of cep290 mutants and inhibition of Notch signaling induced MG to re-enter the cell cycle in both mutants.

Conclusions: Zebrafish cep290 and bbs2 mutants progressively lose cones beginning by 3 months of age. Regeneration of lost cones occurs only following acute damage, suggesting that the mutants retain the ability to stimulate reprogramming and proliferation of Müller glia. Finally, we show that inhibition of Notch signaling releases that constraint. Our results indicate that therapies to suppress microglia function may prolong photoreceptor survival and that triggering regeneration requires more than inflammation alone.

CONTROL ID: 3710195

SUBMITTER (NAME ONLY): Suzanne Yzer

TITLE: Treatment of Peripapillary Pachychoroid Syndrome

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yzer, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|S. Yzer, A. Pothof, J. Martinez, Rotterdam Eye Hospital, Rotterdam, NETHERLANDS|F.F. Behar-Cohen, Hopital Cocin Opthalmopole, Paris, FRANCE|

Commercial Relationships Disclosure: Suzanne Yzer: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Pothof: Commercial Relationship: Code N (No Commercial Relationship) | Jose Martinez: Commercial Relationship: Code N (No Commercial Relationship) | Francine Behar-Cohen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the treatment response to topical steroidal eye drops in peripapillary pachychoroid syndrome (PPS)

Methods: In an observational study we examined 15 patients (21 eyes) with a diagnosis of PPS. Patients were followed for 2-10 years prior to topical steroidal treatment without any signs of reduction of the cysts, even upon the more classical treatments like photodynamic therapy or oral acetolozamide. All included patients received topical Pred Forte 10mg/ml (PF) 3-times daily for four weeks. Upon a good response (absence of cysts) the topical steroids were tapered off by one drop a month.

Results: Of the included 21 eyes, baseline visual acuity (VA) was 20/30. The median choroidal thickness was 202um at 3mm nasal of the fovea, 369um 1.5 nasal of the fovea, and 430um subfoveal. All patients showed a good anatomical response to topical steroids on OCT. Six patients experienced prolonged reduction of cysts even when dosage was reduced to once daily. On tapering of PF, 3 patients (4 eyes) had recurrence of cysts that subsequently disappeared when dosage was increased. The VA improved in 9 eyes, remained unchanged in 5 and decreased in 3 eyes. Seven eyes experienced elevated IOP (range 26-32mmHg), for which in 2 eyes PF was discontinued upon which cysts recurred.

Conclusions: In this observational study for recalcitrant cystic changes secondary to PPS we saw a favorable response to topical steroids in all 15 cases (21 eyes). During tapering off of the steroidal drug recurrence of the cysts was seen that disappeared again upon increasing the topical drugs. The disappearance of the cysts resulted in better reading vision and better contrast but only mildly improved VA. Topical steroids may be a viable treatment option in PPS.

CONTROL ID: 3710199
SUBMITTER (NAME ONLY): Desmond Adler
TITLE: Customized Epi-On Crosslinking Algorithms for Automated Keratoconus Treatment Planning
SESSION TITLE: Keratoconus and corneal biomechanics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D.C. Adler, M. Smirnov, B. Tavakol, Z. Hill, D. Usher, Glaukos Corp, Burlington, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: Desmond Adler: Commercial Relationship(s);Code E (Employment):Glaukos Corp.;Code I (Personal Financial Interest):Glaukos Corp. | Mikhail Smirnov: Commercial Relationship(s);Code E (Employment):Glaukos Corp.;Code I (Personal Financial Interest):Glaukos Corp. | Behrouz Tavakol: Commercial Relationship(s);Code E (Employment):Glaukos Corp.;Code I (Personal Financial Interest):Glaukos Corp. | Zachary Hill: Commercial Relationship(s);Code E (Employment):Glaukos Corp. | David Usher: Commercial Relationship(s);Code E (Employment):Glaukos Corp.;Code I (Personal Financial Interest):Glaukos Corp.

ABSTRACT BODY:

Purpose: Customized crosslinking treatments for keratoconus enhance visual and keratometric outcomes compared to non-customized treatments by tailoring the ultraviolet (UV) light pattern to the corneal geometry of the individual patient. Currently, physicians manually customize UV patterns using heuristics. Here, we assess 12 automated epi-on treatment planning algorithms in an in silico study to identify which have the greatest potential for aberration reduction and corneal flattening while eliminating user subjectivity.

Methods: 20 digital corneas were created using 3D tomography from keratoconic subjects. 12 planning algorithms were applied to each cornea representing 4 input maps (anterior tangential curvature, pachymetry, anterior and posterior elevation) and 3 scaling parameters (small, medium, and large UV zones). Each algorithm automatically detected and segmented the keratoconic defect and created stacked UV dose patterns of 11, 13, and 15 J/cm^2 fit to the individual corneas.

A photochemical-biomechanical model simulated epi-on treatment effects and predicted post-op corneal shapes. Outputs included change in max corneal curvature (Kmax), cone location and magnitude index, keratoconus severity index, vertical coma (VC), astigmatism, and spherical and higher-order aberrations. Comparisons were made to non-customized 9mm UV spots and manually-customized treatments.

Results: In silico analysis showed a spectrum of corneal flattening and aberration reduction tradeoffs. Pachymetry-based algorithms generated UV patterns that were central, circular, and gave the largest predicted change in Kmax (-2.4D). Elevation algorithms were peripheral, elliptical, and gave the largest predicted change in VC (-0.6um). Tangential curvature algorithms gave a balance between Kmax (-2.3D) and VC (-0.5um). All algorithms outperformed a 9mm spot (-0.2D Kmax, -0.1um VC) and manual customization (-1.7D Kmax, -0.3um VC).

Conclusions: Automated UV treatment plans may outperform non-customized and manually-customized crosslinking treatments for keratoconus while eliminating subjectivity.

CONTROL ID: 3710200

SUBMITTER (NAME ONLY): Deshea Harris

TITLE: OK-101, A Novel Chemerin Receptor Agonist, Ameliorates Neuropathic Corneal Pain in a Mouse Model of Ciliary Nerve Ligation

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.L. Harris, F. Qiu, A. Sultan, P. Hamrah, Center for Translational Ocular Immunology and Department of Ophthalmology, Tufts Medical Center and Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|R. Patil, G.S. Jacob, OKYO Pharma Ltd, New York, New York, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Deshea Harris: Commercial Relationship: Code N (No Commercial Relationship) | Fangfang Qiu: Commercial Relationship: Code N (No Commercial Relationship) | Ayesha Sultan: Commercial Relationship: Code N (No Commercial Relationship) | Raj Patil: Commercial Relationship(s);Code E (Employment):OKYO Pharma Ltd. | Gary Jacob: Commercial Relationship(s);Code E (Employment):OKYO Pharma Ltd. | Pedram Hamrah: Commercial Relationship(s);Code S (non-remunerative):Novartis, Oyster point, Dompe;Code C (Consultant/Contractor):Kala, Novartis, Dompe, Clementia, Novaliq, Santen, OKYO, Eyenovia

ABSTRACT BODY:

Purpose: The purpose of the study was to evaluate the ability of OK-101, a novel chemerin receptor agonist, to improve neuropathic corneal pain (NCP). We investigated the efficacy of lipidated (L) and non-lipidated (NL) OK-101 in an NCP mouse model of ciliary nerve ligation.

Methods: NCP was induced by ligation of the ciliary nerve and confirmed by stimulation with 5M hyperosmolar saline (HS) and eye wiping response (counts/30 sec) on day 3. The integrity of the corneal epithelium was revealed by corneal fluorescein staining (CFS, Grade 0-3 in 5 regions on a 0-15 severity scale). Mice were divided into groups and given either L- or NL-OK-101 with a frequency of either 6/6 or 3/6 times/day or balanced salt solution (BSS) vehicle control. Gabapentin (100mg/kg i.p.) given on days 4, 7, 10 and 14 after surgery was used as a positive control. Treatment duration was for a total 11 days and efficacy measured by 5M HS and eye wiping. Safety measures included blink reflex due to mechanical stimulation by Cochet-Bonnet esthesiometer and CFS performed at 7, 10 and 14 days post surgery.

Results: NCP was established as demonstrated by increased eye wipes after ligation compared to naïve mice (36.65±6.45 vs. 13.74±3.18 counts/30 sec; $p<0.0001$) with no difference in CFS ($p>0.05$). Both compounds at either frequency did show an analgesic effect by inhibiting the hypersensitivity to 5M HS compared to BSS at day 14 (L-OK-101 at 3/6 17.5±0.78 and 6/6 15.4±0.73; NL-OK-101 at 3/6 16.8±0.88 and 6/6 14.6±0.75 vs. BSS 27.2±0.68 counts/30 sec; $p<0.0001$). Additionally, L- and NL-OK-101 at 6/6 and NL-OK-101at 3/6 times per day inhibited corneal nociceptor sensitization similar to gabapentin at day 14 (14.6±0.75, 15.4±0.73 and 16.8±0.88 vs 13.2±0.80 counts/30 sec, respectively). Both L- and NL-OK-101 at either frequency showed statistically significant ($p <0.05$) recovery of mechanical sensitivity threshold on par with gabapentin and significantly better than vehicle control ($p <0.01$) at days 7 and 10. Both the compounds showed no effect on corneal epithelial integrity compared to gabapentin or BSS (0.56±0.45 vs. 0.78±0.60 or 0.66±0.50 on the severity scale).

Conclusions: Topically administered OK-101 was effective in reducing NCP in a ciliary nerve ligation mouse model suggesting OK-101 could be a potential therapeutic target for the treatment of neuropathic corneal pain.

CONTROL ID: 3710204
SUBMITTER (NAME ONLY): Yifan Lu
TITLE: Quantitative WF SS-OCTA and visual outcomes in RAO
SESSION TITLE: OCT Angiography Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y. Lu, R. Zeng, R. BAJAJ, R. Katz, J.B. Miller, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Cui, Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|Y. Lu, E.S. Lu, R. BAJAJ, J.B. Miller, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|Y. Zhu, Ophthalmology, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|R. Le, Wenzhou Medical University Eye Hospital, Wenzhou, Zhejiang, CHINA|J.C. Wang, Northern California Retina Vitreous Associates Inc, Mountain View, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Retinal artery occlusion (RAO) is an emergency that can lead to poor visual outcomes and is associated with an increased risk of cerebral stroke and cardiovascular events. Fluorescein angiography is the traditional diagnostic tool for RAO; however, wide-field swept-source optical coherence tomography angiography (WF SS-OCTA) is able to provide quick and non-invasive angiographic information with a wide field of view. In this study, we looked for associations between OCT-A vascular metrics and visual acuity (VA) in patients with prior diagnosis of RAO.

Methods: Patients with diagnoses of central or branched RAO were included. A 6 x 6mm Angio and a 15 x 15mm AngioPlex Montage OCT-A image were obtained for both eyes in each patient using the Zeiss Plex Elite 9000 WF SS-OCTA device. Each 6 x 6mm image was divided into nine Early Treatment Diabetic Retinopathy Study (ETDRS) subfields. The average measurement of the central foveal subfield, inner ring, and outer ring was calculated for each parameter. Non-perfusion area (NPA) was manually measured using 15 x 15mm Montage images. A linear regression model was utilized to identify a correlation between the imaging metrics and VA. A P-value less than 0.05 was considered to be statistically significant.

Results: 25 subjects were included in the study. For RAO eyes, there was a statistically significant negative correlation between VA and retinal thickness as well as superficial capillary plexus vessel density (VD). A negative correlation was found between VA and deep capillary plexus VD without statistical significance. There was a positive correlation between VA and choroidal thickness as well as choroidal volume without statistical significance. No significant correlation was found between VA and the above metrics in contralateral eyes. For NPA measurements, no significant correlation was found.

Conclusions: This is the first study to investigate the utility of WF SS-OCTA in RAO and to demonstrate correlations between various retinal vascular imaging metrics and visual outcomes. Further investigations should explore the associations between these imaging findings and cardiovascular risk as RAO patients are at elevated risk for symptomatic stroke. The results of this study provide a basis to understand the structural changes involved in visual outcomes in RAO. Furthermore, they may help guide management of RAO and prevention of cerebral stroke and cardiovascular accidents in patients with RAO.

CONTROL ID: 3710213

SUBMITTER (NAME ONLY): Chi-Hsiu Liu

TITLE: A Mutation-Independent CRISPR/Cas9-based 'Knockout and Replace' Strategy to Treat Rhodopsin-Associated Autosomal Dominant Retinitis Pigmentosa

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Liu, P. Wolf, R. Dong, Y. Huang, D. Tabbaa, E. Marco, B. Duke, A. Pinilla, A. Pant, R. D'Souza, J. Newmark, G. Giannoukos, K. Zhang, A. Timmers, M. Shearman, M. Allocca, Editas Medicine, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rhodopsin-associated autosomal dominant retinitis pigmentosa (RHO-adRP) is an inherited retinal disease that results in blindness due to photoreceptor degeneration. Over 150 mutations in the RHO gene are known to cause RHO-adRP. Using a dual AAV system, Editas Medicine is exploring potential therapy with a highly efficient CRISPR/Cas9 to knockout aberrant endogenous rhodopsin and replace it with an exogenous functional rhodopsin (KO&R).

Methods: The specificity of a human and non-human primate (NHP) cross-reactive Cas9 guide was tested using human retina explants transduced with the KO&R. Pharmacokinetics and pharmacodynamics of the KO&R were assessed in humanized mRho$^{hRHO/+}$ mice. Efficacy was measured in NHPs by comparing knockout (KO) only and KO&R versions of the dual AAV system delivered via subretinal injection. A miniRHO promoter was used to drive Cas9 as well as RHO expression while restricting editing and replacement of RHO expression to the rod photoreceptors. On- and off-target editing was assessed using Next Generation Sequencing. Endogenous and replacement RHO levels were quantified using NanoString and tandem mass spectrometry. Morphological and functional readouts were assessed by histopathology and electroretinography.

Results: No off-target editing was observed in human retina explants after transduction with the KO&R. The KO&R achieved maximal levels approximately 6 weeks post-dose and remained stable for at least 13 weeks post-dose in mRho$^{hRHO/+}$ mice. The KO&R levels displayed a dose response reaching a plateau at a dose of 6E12 vg/ml. Studies in NHP demonstrated nearly 100% knockout of endogenous RHO, and replacement RHO produced over 30% of normal RHO protein. The KO&R-injected eyes showed restoration of RHO expression in the outer segments and retention of normal photoreceptor structure and function (ERG analysis) compared to the KO-injected eye.

Conclusions: Editas characterized and demonstrated high efficacy of a CRISPR/Cas9-based KO&R therapeutic strategy for RHO-adRP. The experimental therapy is mutation-agnostic and could be a potential one-time treatment to permanently suppress the toxic gain of function associated with mutated RHO. The efficacy of our KO&R gene editing therapy in NHP supports continued advancement of this approach toward treating patients.

CONTROL ID: 3710214

SUBMITTER (NAME ONLY): Ren-Juan Shen

TITLE: Long-read high-throughput sequencing uncovers rare structural variations in syndromic optic atrophy

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Shen, Y. Li, Z. Jin, Beijing Institute of Ophthalmology, Beijing, Beijing, CHINA|R. Shen, Y. Li, Z. Jin, Beijing Tongren Hospital, Beijing, Beijing, CHINA|

Commercial Relationships Disclosure: Ren-Juan Shen: Commercial Relationship: Code N (No Commercial Relationship) | Yang Li: Commercial Relationship: Code N (No Commercial Relationship) | Zi-Bing Jin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Next generation sequencing (NGS), that is, short-read sequencing (SRS), has been widely used in identifying pathogenic mutations in inherited eye diseases (IEDs). However, the approximate diagnosis rate using SRS is around 52%, which is probably due to novel genes, or variants that may be missed by SRS approaches, such as structural variants (SVs) and variants in introns or regulatory regions. In this study, we performed long-read sequencing (LRS) to re-evaluate the disease-causing mutations of IED patient whose genetic etiology remained unclear after SRS.

Methods: Long read sequencing around 30X genome coverage using the PacBio Sequel II system was performed on a Chinese family with a proband diagnosed with syndromic optic atrophy. Comprehensive bioinformatic analysis was then conducted, followed by trio-based segregation analysis and pathogenicity analysis.

Results: Genome-wide SV calling yielded a total of 130520 SVs, with de novo SVs of 12188. Among them, we determined a novel 1447-bp de novo heterozygous deletion located in the NR2F1 gene which was segregated with the phenotype of optic atrophy and epilepsy. The de novo deletion spans the 5’ UTR and the first exon along with partial intron 1, resulting in haploinsufficiency of NR2F1,which has been reported to be the etiology of autosomal dominant Bosch-Boonstra-Schaaf optic atrophy syndrome (BBSOAS).

Conclusions: The genetic etiology of the family with syndromic optic atrophy was successfully identified using LRS and we reported a novel SV associated with BBSOAS. Overall, this study has shown that SVs may contribute to the genetic etiology of syndromic optic atrophy, and that SV analyses should be included in the genetic workflow of IED. It also demonstrates the potential value of long-read sequencing in identifying SVs in patients with IEDs.

CONTROL ID: 3710217

SUBMITTER (NAME ONLY): Li Liu

TITLE: TNFAIP3 may be key to TLR4-activation of the inflammasome in the retinal vasculature

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Liu, Y. Jiang, J.J. Steinle, OVAS, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Li Liu: Commercial Relationship: Code N (No Commercial Relationship) | Youde Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Jena Steinle: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine whether tumor necrosis factor, alpha-induced protein 3 (TNFAIP3) regulated toll-like receptor 4 (TLR4) actions on the NOD-like receptor protein 3 (NLRP3) inflammasome.

Methods: Western blotting was done on retinal lysates from TLR4 floxed and endothelial cell specific TLR4 knockout mice for TNFAIP3, TLR4, and NLRP3 pathway proteins. Retinal endothelial cells (REC) were grown in normal and high glucose and treated with TNFAIP3 siRNA, followed by Western blotting for TLR4 and NLRP3 pathway proteins.

Results: Loss of TLR4 in endothelial cells increased TNFAIP3 levels, while decreasing NLRP3 pathway proteins. High glucose culturing conditions increased TLR4 and NLRP3 proteins, which were increased by TNFAIP3 siRNA.

Conclusions: Data demonstrate that TLR4 regulates NLRP3 pathway proteins. TNFAIP3 can regulate TLR4 and the NLRP3 pathway. TNFAIP3 may offer a new target for therapeutic development against retinal inflammation

CONTROL ID: 3710220

SUBMITTER (NAME ONLY): Melita Kaltak

TITLE: QR-1011 corrects splicing in the Stargardt disease type 1-causing variant ABCA4 c.5461-10T>C

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Kaltak, P. de Bruijn, K. Dulla, G. Platenburg, J. Swildens, ProQR Therapeutics NV, Leiden, Zuid-Holland, NETHERLANDS|M. Kaltak, R.W. Collin, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|S. Lee, D. Piccolo, M.E. Cheetham, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: ABCA4 c.5461-10T>C is the third most common Stargardt disease type 1 (STGD1)-causing variant, for which no treatment is available. It leads to exclusion of exons 39 and 40, resulting in out-of-frame ABCA4 transcripts and a severely reduced production of wildtype ABCA4 protein. Here, we investigated the restoration of wildtype splicing by QR-1011, an antisense oligonucleotide (AON), as a therapeutic approach using in vitro cell models.

Methods: The effect of target-specific AONs was investigated by transfection (n=3) of HEK293 cells using a splice-predictive midigene model carrying the mutation. Isoform-specific digital PCR (dPCR) was used for absolute quantification of correct transcript as a percentage of all measured ABCA4 transcripts. Subsequently, QR-1011, the best performing AON, was studied in 3 dimensional CRISPR-Cas9 edited or patient-derived human retinal organoids (ROs), both homozygous for c.5461-10T>C. ROs (n=6 or 8 per group) were treated once with either QR-1011 or a control AON and harvested after 8 weeks. The quantification of transcripts by dPCR was accompanied by immunohistochemistry (IHC) and Western Blot (WB) analysis to identify rescue of wildtype ABCA4 protein expression post-AON treatment. Statistical analysis was performed with either two-tailed Student’s t-test or one-way ANOVA with Dunnett’s multiple comparisons test.

Results: In midigene-transfected cells, QR-1011 achieved 51,8±2,4% (mean±SEM; p<0,0001 vs. control) of correct transcript and was selected as best splice-modulating AON. In CRISPR-Cas9 edited ROs, QR-1011 corrected 37,9±2,1% (p<0,0001) of the full-length ABCA4 isoform after 8-weeks, while patient-derived ROs contained 46,04±7,1% (p<0,0001) of wildtype transcript after similar treatment. By contrast, in both control groups, only 3% of wildtype ABCA4 transcripts were detected. Furthermore, IHC and WB analysis of treated ROs revealed rescue of wildtype ABCA4 protein, which was localized in outer segments of photoreceptor cells, as opposed to control samples where no protein was observed.

Conclusions: QR-1011 treatment resulted in splice correction in both midigene and organoid models. Moreover, when administered to ROs, QR-1011 restored the production of ABCA4 protein. These results show the ability of QR-1011 to correct aberrant splicing caused by the c.5461-10T>C mutation in ABCA4 and highlight its therapeutic potential for STGD1.

CONTROL ID: 3710222

SUBMITTER (NAME ONLY): David Bates

TITLE: MFAP4 reduces vascular leakage in a Rabbit Model of Choroidal Neovascularization (CNV)

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Bates, J.J. Hua, A.P. Lynch, A.V. Benest, University of Nottingham, Nottingham, Nottinghamshire, UNITED KINGDOM|A. Schlosser, B. Pilecki, U. Holmskov, G.L. Sorensen, Syddansk Universitet, Odense, Syddanmark, DENMARK|

Commercial Relationships Disclosure: David Bates: Commercial Relationship(s);Code C (Consultant/Contractor):Exonate Ltd;Code P (Patent):Exonate Ltd;Code I (Personal Financial Interest):Exonate Ltd;Code O (Owner):Exonate Ltd | Jing Hua: Commercial Relationship: Code N (No Commercial Relationship) | Anders Schlosser: Commercial Relationship(s);Code P (Patent):US9988442B2 | Amy Lynch: Commercial Relationship: Code N (No Commercial Relationship) | Bartosch Pilecki: Commercial Relationship: Code N (No Commercial Relationship) | Uffe Holmskov: Commercial Relationship(s);Code P (Patent):US9988442B2 | Andrew Benest: Commercial Relationship: Code N (No Commercial Relationship) | Grith Sorensen: Commercial Relationship(s);Code P (Patent):US9988442B2

ABSTRACT BODY:

Purpose: Purpose: New treatment strategies are needed to improve the disease management for patients who respond poorly to anti-VEGF treatments. Microfibrillar-associated protein 4 (MFAP4) is an extracellular matrix protein and a ligand for avb3 and avb5 integrins. We previously showed that anti-MFAP4 antibodies (anti-MFAP4) effectively block pathological angiogenesis and inflammation in a mouse model of laser-induced choroidal neovascularization and in a rat model of diabetic retinopathy. Here, we report the efficacy of anti-MFAP4 in a rabbit model of CNV.

Methods: CNV lesions were induced in 18 brown HyD rabbits by subretinal injection of 50µl of MatriGel containing 100ng FGF2 and 100ng LPS. Bruch's membrane was perforated with a 30G micro-lancet to ensure a small subretinal hemorrhage from the choroidal vessels. The growth of lesions was observed using optic and fluorescein angiogram (FA) modules of a Heidelberg Spectralis. Once CNV growth had reached measurable size after one month, animals received 50µl intravitreal injections of anti-MFAP4 (2mg), ranibizumab (Lucentis 0.5mg) or remained as untreated controls. Lesions were then measured one and two months after the treatments using FA. Three of the control animals and one of the ranibizumab animals were lost to imaging due to cloudiness.

Results: The vascular area of the CNV lesions were significantly reduced after 1 month ($p<0.05$), 2 months ($p<0.001$) and were sustained for 6 months after intravitreal injection with 2mg anti-MFAP4 (n = 12 of 6 rabbits). The 0.5mg Lucentis-treated (n = 10 of 5 rabbits) group had reduced lesion size only after 4 and 6 months compared with initial measurement. (2-way ANOVA with post hoc Tukey test). At each time point the anti-MFAP lesion size was smaller than anti-VEGF lesion size ($p<0.001$, two way ANOVA)

Conclusions: We demonstrated a single intravitreal injection of anti-MFAP4 effectively reduced the CNV lesion size in the rabbit model. Using MFAP4 as alternative target to VEGF could be used as novel strategy, particularly in patients who respond poorly to anti-VEGF treatments.

CONTROL ID: 3710223

SUBMITTER (NAME ONLY): Katja Hatz

TITLE: Geographic atrophy in AMD - prognostic factors based on long-term follow-up

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.B. Hatz, L. Hoffmann, L. Cedro, Vista Klinik AG, Binningen, SWITZERLAND|K.B. Hatz , Universitat Basel, Basel, Basel-Stadt, SWITZERLAND|

Commercial Relationships Disclosure: Katja Hatz: Commercial Relationship(s);Code F (Financial Support):Roche, Novartis, Bayer, Allergan | Laura Hoffmann: Commercial Relationship: Code N (No Commercial Relationship) | Luca Cedro: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: So far, the natural course of geographic atrophy (GA) progression in age-related macular degeneration (AMD) has primarily been investigated by fundus photography and fundus autofluorescence (FAF) imaging. The aim of this long-term retrospective, observational clinical study was to show the enlargement rate (ER) of GA, defined as complete retinal pigment epithelium and outer retinal atrophy (cRORA) and to find predictors of progression.

Methods: All patients available in the database of Vista Eye Clinic Binningen, Switzerland, with follow-up of at least 24 months and existing GA in at least one eye, regardless of neovascular AMD (nAMD) being present initially or in the course of disease, were included. SD-OCT and FAF evaluations were performed according to a standardized protocol. The cRORA area ER (mm2/yr), the cRORA square root area ER (mm/yr), the FAF GA area and the condition of the outer retina (inner-/outer segment line (IS/OS) and external limiting membrane (ELM) disruption scores) were determined.

Results: 210 eyes of 133 patient (65% females) were included. Mean follow-up time was 4.0±2.3 (range 2-10) years. 109 (52%) eyes were classified as primary or secondary nAMD, 101 (48%) as exclusively dry AMD. The primary lesion was unifocal in 151 (72%) and multifocal in 59 (28%) eyes. A strong correlation was observed between the area of cRORA (SD-OCT) and the FAF GA area ($r= 0.925$; $p<0.001$). Mean ER was 1.44±1.6 mm2/yr and mean square root ER 0.29±0.19 mm/yr. There was no significant difference in mean ER between eyes without (dry AMD) and with intravitreal anti-VEGF injections (nAMD) (0.3±0.19 mm/yr vs. 0.28±0.20 mm/yr; $p=0.466$). Eyes with a multifocal GA pattern at baseline had a significantly higher mean ER compared to eyes with a unifocal pattern (0.34±0.19 mm/yr vs. 0.27±1.19 mm/yr; $p=0.008$). There were moderate significant correlations between ELM and IS/OS disruption scores and visual acuity at baseline, 5 and 7 years (all r values ca. -0.5; $p<0.001$). In multivariate regression analysis, a scattered cRORA pattern at baseline ($p=0.022$) and a smaller baseline lesion size ($p=0.036$) were associated with a higher mean ER.

Conclusions: SD-OCT evaluated cRORA area might serve as a GA parameter comparable to traditional FAF measurement. The dispersion pattern and baseline lesion size might be predictors of ER, whereas anti-VEGF treatment seems not to be associated with ER.

CONTROL ID: 3710225

SUBMITTER (NAME ONLY): Palaiologos Alexopoulos

TITLE: Lamina Cribrosa Microstructure in Non-Human Primates with Naturally Occurring Peripapillary Retinal Nerve Fiber Layer Thinning

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Alexopoulos, Z. Ghassabi, R. Zambrano, T. Lee, A. Vellappally, E. Shemuelian, H. Ishikawa, J.S. Schuman, G. Wollstein, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|A.G. Fernandes, A.D. Melin, Anthropology & Archaeology, University of Calgary, Calgary, Alberta, CANADA|T. Lee, J. Hu, Population Health, New York University, New York, New York, UNITED STATES|H. Ishikawa, Ophthalmology, Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|A. Burgos-Rodriguez, M.I. Martinez, Caribbean Primate Research Center, Universidad de Puerto Rico, San Juan, PUERTO RICO|J.S. Schuman, Biomedical Engineering and Electrical & Computer Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|A.D. Melin, Medical Genetics, Alberta Health Services, Edmonton, Alberta, CANADA|J.P. Higham, Anthropology, New York University, New York, New York, UNITED STATES|J. Danias, Ophthalmology & Cell Biology, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|G. Wollstein, Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The lamina cribrosa (LC) is hypothesized to be the site of initial axonal damage in glaucoma with the peripapillary retinal nerve fiber layer (RNFL) thickness is widely used as a standard metric for quantifying this damage. The purpose of this study was to determine in vivo changes in the microstructure of the LC in eyes of non-human primates (NHP) with naturally occurring RNFL thinning.

Methods: Spectral-domain OCT scans (Leica, Chicago, IL) of the optic nerve head (ONH) were acquired in vivo from a colony of 50 adult rhesus monkeys, suspected of having high prevalence of naturally occurring glaucoma. The circumpapillary global and quadrant RNFL thickness was analyzed using a custom automated segmentation software. From the set of 100 eyes, the 10 eyes with the thinnest global RNFL values were selected as the study group, while 10 eyes with RNFL values around the 50^{th} percentile were used as the control group. A previously described automated segmentation algorithm was used for LC microstructure analysis. The LC microstructure was analyzed globally and in the following volumetric sectors: quadrants, central and peripheral lamina, and 3 depth slabs (anterior, middle, posterior; Figure). Beam thickness/pore diameter ratio (BPR) and connective tissue volume fraction (CTVF: beam volume/total volume) were calculated globally and in sectors.

Results: 20 eyes (15 animals) were analyzed (Table 1). While no significant difference was detected between groups for age, weight or disc size, the study group had significantly thinner RNFL than the control group ($p<0.01$). The study group had significantly larger BPR and CTVF compared with the control group (Table 2). Significant sectoral differences between study and control group RNFL thickness were noted for BPR and CTVF in the nasal and temporal quadrants, central LC, and in LC depth. Across eyes, the global RNFL thickness was moderately negatively correlated only with the global CTVF (lower RNFL thickness associated with higher CTVF; $r^2=0.63$, $p=0.045$).

Conclusions: Eyes with thinner circumpapillary RNFL had thicker LC BPR and CTVF globally and in various sectors when compared to eyes with normal RNFL thickness. Whether these LC changes are the cause of RNFL damage or the result of remodeling of the LC requires further investigation.

CONTROL ID: 3710226

SUBMITTER (NAME ONLY): Friederike Kortuem

TITLE: Adaptive optics ophthalmoscopy in retinitis pigmentosa: typical patterns

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.C. Kortuem, M. Kempf, L. Kuehlewein, C. Kortuem, E. Zrenner, K. Stingl, Universitatsklinikum Tubingen, Tubingen, Baden-Württemberg, GERMANY|F. Nasser, Universitat Leipzig, Leipzig, Sachsen, GERMANY|M. Paques, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|S. Kohl, B. Wissinger, M. Ueffing, Universitatsklinikum Tubingen Forschungsinstitut fur Augenheilkunde, Tubingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Due to advances in optics, electronics and computation, morphological changes of the photoreceptor mosaic can be made visible by adaptive optics ophthalmoscopy (AOO). Retinitis pigmentosa (RP) is a degenerative retinal disease that affects primarily the rod photoreceptors followed by the loss of cone receptors. This paper aims to present typical findings in RP with the adaptive optics flood illumination retinal camera rtx1.

Methods: 174 patients with syndromic or non-syndromic RP were examined with the commercially available adaptive optics flood illumination retinal camera rtx1 and spectral domain optical coherence tomography (OCT) and fundus autofluorescence (FAF) imaging at the Center for Ophthalmology, University of Tuebingen. AOO patterns were studied in the context of multimodal retinal imaging.

Results: Five different patterns in RP could be observed: 1) unspecific atrophy, 2) central visibility of cones, 3) “puffy” cones, 4) the “cheetah” pattern, and 5) atrophic pigment clumping. These patterns in AOO correlated with findings on OCT and FAF imaging. We hypothesize that these patterns represent specific stages of photoreceptor degeneration in RP.

Conclusions: AOO provides an additional dimension to high-resolution retinal imaging in RP, enabling to determine patterns of retinal degeneration. Future evaluation of cone photoreceptor mosaic using AOO imaging is warranted to determine changes on an even more microscopical level, e.g. photoreceptor integrity.

CONTROL ID: 3710227

SUBMITTER (NAME ONLY): Yi-Hsing Chen

TITLE: Diabetic ocular environment facilitates the invasion of Klebsiella pneumoniae to Human Retinal Pigment Epithelial Cells: via suppression of NFkB and MAPK pathway

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, Y. Hwang, Chang Gung Medical Foundation, Taoyuan, TAIWAN|Y. Chen, University College London School of Life and Medical Sciences, London, London, UNITED KINGDOM|C. Shen, Chang Gung University, Taoyuan, Taoyuan, TAIWAN|

Commercial Relationships Disclosure: Yi-Hsing Chen: Commercial Relationship: Code N (No Commercial Relationship) | Chia-Rui Shen: Commercial Relationship: Code N (No Commercial Relationship) | Yih-Shiou Hwang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) serves as an outer blood retinal barrier during Klebsiella pneumoniae (KP) infection in endogenous endophthalmitis. Nevertheless, the pathogen-associated molecular patterns and the specific adhesion molecules used of RPE cells upon interaction with KP are yet been reported. In this study, we investigate the changes of diabetic ocular environment facilitate the development of KP invasion to the eye.

Methods: In this study, we investigated the ability of KP to invade human RPE cells (ARPE-19) in in vitro diabetic condition (in 27.5mM and 17.5mM glucose culture medium). Adhesion and invasion assays were undertaken to investigate roles of tight junction proteins, adhesion molecules, acute inflammatory molecules (IL-1, IL-6, IL8) and molecules involved in the pathogen-associated molecular patterns via ELISA and western blot studies. The results were validated via RNA sequencing on ARPE-19 cells.

Results: We concluded that KP adhesion and invasion to RPE were increased in hyperglycemic condition via breaking down specific tight junction pathway proteins and enhancing specific adhesion molecules including vascular cell adhesion protein 1 (VCAM-1) and activated leukocyte cell adhesion molecule (ALCAM). Furthermore, toll-like receptor 4 (TLR4) was enhanced for pattern recognition and NF-kB and MAPK pathway were involved during KP infection.

Conclusions: This is the first study to highlight the pattern recognition, adhesion molecules engaged, and signal transduction pathway during KP invasion to the eye in diabetic ocular condition in vitro. The results suggest a strong rationale for between endogenous endophthalmitis and systemic KP infection for individuals with diabetes mellitus.

CONTROL ID: 3710229

SUBMITTER (NAME ONLY): Sarah Miller

TITLE: Global Current Practice Patterns for the Management of Traumatic Optic Neuropathy and Orbital Floor Fractures

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Miller, A. Chen, A. Liu, F. Woreta, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|A. Shah, M. Gardiner, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M.J. Fliotsos, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|P. Meeralakshmi, Aravind Eye Hospital, Madurai, Tamil Nadu, INDIA|G. Justin, Duke Medicine, Durham, North Carolina, UNITED STATES|R. Low, R.V. Agrawal, Tan Tock Seng Hospital, Singapore, SINGAPORE|J. Auran, Columbia University Irving Medical Center, New York, New York, UNITED STATES|K. Cavuoto, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|Y. Yonekawa, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|A.K. Hoskin, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|R.J. Blanch, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Facial trauma can have a variety of sequelae, including orbital floor fractures and traumatic optic neuropathy. Although these injuries are common, their management is controversial. Our goal was to summarize management practices at international high-volume eye trauma centers and identify areas of alignment and discrepancy.

Methods: An online survey was conducted from August 2020 to January 2021 to obtain a census of management paradigms for orbital floor fractures and traumatic optic neuropathy at high-volume eye trauma centers globally. Trauma experts responded on behalf of general practices at their institutions.

Results: Response rate was 85.7% (36/42); 3 of the responding centers were excluded from analysis due to low case volume. Of the responding institutions, 54.5% (n=18/33) routinely administered systemic antibiotics for orbital floor fractures, with oral amoxicillin and clavulanic acid (n=13/18, 72.2%) and oral cefalexin (n=4/18, 22.2%) being most common. Only 27.3% (n=9/33) of respondents administered systemic steroids, most of whom utilized oral steroids (n=7/9, 77.8%). Respondents considered the optimal timing for surgical repair of orbital floor fractures to be on average 11.46 ± 8.46 days from presentation, with oculoplastic surgeons participating in performing the repair at 72.7% (n=24/33) of responding institutions and oral and maxillofacial surgeons at 57.6% (n=19/33) of centers. Most experts did not routinely admit patients with isolated orbital fractures on presentation (n=26/33, 78.8%); however, 48.5% (n=16/33) of respondents admitted patients after the repair for an average of 3.50 ± 1.96 days. For cases of traumatic optic neuropathy, 63.6% (n=21/33) of respondents routinely administered systemic steroids, with 57.1% (n=12/21) preferring intravenous administration. High dose steroids (methylprednisolone 1gm daily) were used by 36.4% (n=12/33) of responding centers and moderate doses (prednisone 1 mg/kg daily) were preferred by 21.2% (n=7/33).

Conclusions: While experts largely agreed on administering antibiotics for orbital floor fractures and steroids for traumatic optic neuropathy, responding trauma experts differed on many aspects of optimal management paradigms. Further investigations are needed into best treatment regimens to institute evidence-based care in ophthalmic trauma.

CONTROL ID: 3710231

SUBMITTER (NAME ONLY): Jason Myers

TITLE: Synthetic Nuclease Resistant Enhanced Hammerhead Ribozymes for Nucleic Acid Ocular Therapeutics

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Myers, J.M. Sullivan, Ophthalmology (Ross Eye Institute), University at Buffalo, Buffalo, New York, UNITED STATES|J. Myers, J.M. Sullivan, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure: Jason Myers: Commercial Relationship(s);Code P (Patent):Research Foundation of SUNY, Veterans Administration | Jack Sullivan: Commercial Relationship(s);Code P (Patent):Research Foundation of SUNY, Veterans Administration (8,252,527 and 8,450,473)

ABSTRACT BODY:

Purpose: We are investigating enhanced hammerhead ribozymes (EhhRzs) that exceed the turnover rate of historical minimal hhRzs (mhhRzs). Small synthetic nuclease resistant EhhRzs are great candidates for intraocular therapeutics. The inner limiting membrane (ILM) which provides a structural boundary between the vitreous and retina allows diffusional entry of small nucleic acids for retinal therapies.

Methods: Substrate RHO-266 RNA is 15 nt long with a 5' FAM and 3' BHQ1 (IDT); cleavage at CUC 266 results in liberation of quenched fluorescence which is quantified optically in real time. Synthetic EhhRzs are generated by IDT. Cleavage reactions are initiated by mixing EhhRz with substrate RNA in assay buffer (10 mM Tris-HCl, pH 7.5 with 0.5 mM Mg^{2+}) and optically measured at 37°C in a qRT/PCR machine. Nuclease assays are performed in 10% Normal Human Serum (NHS) or recombinant RNase A (100nM) at 37°C. Data are analyzed in Origin.

Results: Chemical modifications (2'-O-Methyl, 2OMe) throughout the EhhRz (except for core nucleotides: G5,G8,G12, A9,A15.1), provides nuclease resistance at 24hrs, but catalytic activity is abolished (1/min vs unmodified 283/min, p=7.30E-12). Locked nucleic acid (LNA) residues incorporated at the 5 and 3' ends with 2OMe occupied residues in the EhhRz (except for U4, G5,8,12, A9, A15.1, and stem) resulted in catalytic activity (382/min) but lacked nuclease resistance (p=1.11E-6). Antisense oligos designed to protect regions of the EhhRz core demonstrated nuclease protection and provided evidence of susceptibility at U4. An EhhRz incorporating 2OMe, LNA, 2'-Fluor C in the stem, and 2'-Amino U4, maintained strong catalytic activity (112/min) and nuclease resistance at 24hrs.

Conclusions: Chemically-modified EhhRzs that provide nuclease protection while retaining enhanced catalytic activity contribute a useful tool for synthetic nucleic acid ocular therapeutics. These studies incentivize novel chemical biological approaches to further enhance catalytic activity while preserving nuclease insensitivity and extended tissue and cellular half-lives. Synthetic EhhRzs with increased catalytic activity support function under Michaelis-Menten conditions ([S] >> [E]) that allow for robust target mRNA knockdown at lower levels of therapeutic delivery (and toxicity).

CONTROL ID: 3710233

SUBMITTER (NAME ONLY): Bo Kyoung Kim

TITLE: Optn can protect Ripk1-dependent cell death in the retina by selective autophagy.

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kim, Chemistry and chemical engineering, Ecole Polytechnique Federale de Lausanne, Lausanne, SWITZERLAND|B. Kim, P. Westenskow, F. Roudnicky, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|D. Vucic, Genentech Inc, South San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Bo Kyoung Kim: Commercial Relationship(s);Code F (Financial Support):F.Hoffmann-La Roche;Code E (Employment):pRED, I2O, Ophthalmology | Peter Westenskow: Commercial Relationship(s);Code E (Employment):F.Hoffmann-La Roche | Domagoj Vucic: Commercial Relationship(s);Code E (Employment):Genentech | Filip Roudnicky: Commercial Relationship(s);Code E (Employment):F.Hoffmann-La Roche

ABSTRACT BODY:

Purpose: As glaucoma occurs from multifactorial causes, studying glaucoma causative mutation leading to a monogenic form of glaucoma would help better understand glaucoma development. Here, we tested if glaucoma may sensitize cells to death induced by cell stressors.

Methods: Gene editing

CRISPR/Cas9-mediated deletion of genes was performed by electroporation of Cas9 RNP in 661w.

OPTN E50K cell line generation

To generate cell lines harboring Optn-WT and Optn-E50K, PhiC31 integrase system was adapted following the manufacturer's protocol.

Ischemia-reperfusion injury model

The needle was connected to a 0.9 % NaCl reservoir and hung it up to sustain the pressure of the mice eye. After 45 minutes of ischemia induction by pressure.

Results: Optn-KO and Optn-E50K sensitize cells to TNFα-dependent necroptosis.

Optn-KO and Optn-E50K are more susceptible to necroptosis stimuli TBE (TNFα, BV6, Emricasan) and TTaE (TNFα, Takinib, Emricasan) confirmed by lactate dehydrogenase (LDH) release. GNE684, a small molecule Ripk1 inhibitor, suppressed LDH release. WB analysis confirmed that the phosphorylation of Ripk1, Ripk3, and Mlkl, the core axis of necroptosis, were induced more prominently in Optn-KO and Optn-E50K under necroptosis stimuli also in the glaucoma experimental mice model. Only necroptosis conferred this susceptibility of Optn-KO and Optn-E50K but not apoptosis such as doxorubicin or staurosporine. Thus, we confirmed that Optn can protect cells against TNFα-mediated necroptosis, and Optn-E50K is a loss-of-function mutation in the cell death context.

mRNA levels of TNFα and RIPK3 are elevated in the retina from glaucoma patients.

TNFα and RIPK3 showed a well correlated transcript-to-translation ratio. The transcript level of TNFα and RIPK3, a critical component of necroptosis, are upregulated in the glaucomatous retina compared to the non-glaucomatous retina. These data could underline the connection to necroptotic cell death in glaucoma pathogenesis.

Conclusions: Here, we showed that the Optn-E50K variant, a glaucoma causative mutation in an autosomal dominant pattern sensitizes cells to TNFα-mediated necroptosis. This study may suggest implications of TNFα in glaucoma pathogenesis in both subtypes, intraocular pressure (IOP) –related and non-IOP-related glaucoma, and inform possible future therapy for neuropathies in the retina.

CONTROL ID: 3710236

SUBMITTER (NAME ONLY): Alexander Black

TITLE: Evaluation of Visual Outcomes of Toric IOL with Non-Frosted Haptics, a Single Surgeon Series

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Black, S. Dana, A. Kahn, C. Buznego, W. Trattler, Florida International University Herbert Wertheim College of Medicine, Miami, Florida, UNITED STATES|S. Schadt, Larkin Community Hospital Graduate Medical Education, South Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Alexander Black: Commercial Relationship: Code N (No Commercial Relationship) | Shiran Dana: Commercial Relationship: Code N (No Commercial Relationship) | Amanda Kahn: Commercial Relationship: Code N (No Commercial Relationship) | Samuel Schadt: Commercial Relationship: Code N (No Commercial Relationship) | Carlos Buznego: Commercial Relationship: Code N (No Commercial Relationship) | William Trattler: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate visual outcomes of 103 consecutive Toric intra-ocular lens (IOL) placement procedures from 2017-2019 at a single center using an FDA-approved Toric IOL with non-frosted haptics.

Methods: We conducted a retrospective chart review of consecutive monofocal Toric IOL's from a single manufacturer, performed at a single surgery center by a single surgeon. All patients underwent femtosecond laser capsulotomy with placement of 2 marks on the anterior capsule 180 degrees apart on the target axis. Iris registration technology aided identification of the steep corneal axis at the capsular plane for alignment and accounted for head positioning during laser. IOL powers were planned with Barrett Toric calculator. Pre- and post-operative data points were recorded and analyzed. Patients with reduced best-corrected-visual-acuity (BCVA) due to pre-existing retinal (epiretinal membrane) and corneal (keratoconus or Fuch's dystrophy) conditions were excluded from the final analysis. Four eyes were excluded due to lack of follow up, and 18 eyes were that were targeted for near were excluded as well.

Results: 103 consecutive surgeries were evaluated. The mean cohort age was 72 years old and 56% female and 44% male. 67% of patients identified as non-Hispanic white, 26% identified as Hispanic and 7% did not report. After application of all exclusion criteria, our final cohort included 74 eyes, of which 58 eyes (78.4%) achieved our goal of 20/30 or better uncorrected visual acuity (UCVA). Of the 16 eyes (21.6%) that did not achieve the goal of 20/30 UCVA or better, 9 of 16 (56%) had >0.75D residual astigmatism, and 12 of 16 (75%) had >0.50D of myopic spherical equivalent. 5 eyes (6.8%) underwent post-operative IOL rotation for axis correction, and 5 eyes (6.8%) underwent laser vision correction adjustments. No patients underwent IOL exchange.

Conclusions: While Toric IOLs with unfrosted haptics have potential to provide excellent UCVA for patients undergoing cataract surgery, the 6.8% rate of return to the OR for repositioning the toric IOL to the correct axis in our study population is high. Frosted haptics potentially improve visual outcomes by increasing rotational stability through a textured surface creating more friction between the haptic and the capsular bag. Our future goal is to evaluate outcomes in a matched cohort of eyes with monofocal toric IOLs that have frosted haptics.

CONTROL ID: 3710237

SUBMITTER (NAME ONLY): Andres Serrano

TITLE: Aqueous Humor of Failed Corneal Grafts Induce Inflammasome Activation in Endothelial Cells

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Serrano, A. Gomez-Bedoya, A. Tovar, G. Amescua, F. Cabot, C.L. Karp, A.L. Sabater, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. de Rivero Vaccari, Neurological Surgery, University of Miami Miami Project to Cure Paralysis, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: High levels of proinflammatory cytokines in the aqueous humor (AqH) have been associated with corneal graft failure (CGF) and endothelial cell loss after corneal transplant. Pyroptosis is a recently described caspase-1-dependent proinflammatory programed cell death mechanism. Pyroptosis is triggered upon inflammasome activation, which is a multiprotein complex comprised by the protein apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC); a nucleotide oligomerization domain-like receptor (NLRs); and procaspase-1. In the present study, we assessed caspase-1 levels in primary human corneal endothelial cells (PhCEC) following exposure to the AqH of patients with CGF and from healthy patients.

Methods: PhCEC were incubated in vitro for 60 minutes with the AqH of patients with CGF (n=4) who underwent corneal transplantation and healthy patients who underwent cataract surgery (n=4). The levels of caspase-1 in PhCEC were determined by ELISA 24 hours following exposure. A specific caspase-1 inhibitor (Ac-YVAD-cmk) was used to assess downregulation in these cells.

Results: Protein levels of caspase-1 were significantly higher in PhCEC incubated with the AqH of patients with CGF than those incubated with the AqH of healthy eyes ($p<0.0043$), and with the group with no AqH exposure ($p<0.0008$). The last two groups did not show differences between them ($p=0.58$). Additionally, levels of caspase-1 were significantly downregulated by the caspase-1 inhibitor Ac-YVAD-cmk in PhCEC exposed to the AqH of patients with CGF ($p<0.0017$) but showed no differences in other groups.

Conclusions: AqH of patients with CGF induced inflammasome activation in corneal endothelial cells and was downregulated by Ac-YVAD-cmk, suggesting that pyroptosis may play an essential role in the pathogenesis of endothelial cell death that leads to CGF. These findings reassert the importance of further studies of this pathway for therapeutic purposes.

CONTROL ID: 3710241
SUBMITTER (NAME ONLY): Masanobu Iida
TITLE: The effect of binocular blindness in critical period on visual white matter pathways: a single case study
SESSION TITLE: Retinal and central processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Iida, S. Ogawa, H. Horiguchi, S. Nakadomari, Y. Masuda, T. Nakano, ophthalmology, Tokyo Jikeikai Ika Daigaku, Minato-ku, Tokyo, JAPAN|H. Takemura, Division of Sensory and Cognitive Brain Mapping, Department of System Neuroscience, Seirigaku Kenkyujo, Okazaki, Aichi, JAPAN|H. Takemura, Department of Physiological Sciences, School of Life Science,, Sogo Kenkyu Daigakuin Daigaku, Miura-gun, Kanagawa, JAPAN|A. Miyazaki, Global Education Center, Waseda Daigaku, Shinjuku-ku, Tokyo, JAPAN|M. Osawa, T. Kinjo, K. Matsumoto, Brain Science Institute, Tamagawa Daigaku, Machida, Tokyo, JAPAN|K. Yoshikawa, Yoshikawa Eye Clinic, Machida, JAPAN|S. Nakadomari, Kobe Shiritsu Kobe Eye Center Byoin, Kobe, Hyogo, JAPAN|
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ABSTRACT BODY:
Purpose: This study aimed to analyze the effect of binocular blindness in critical periods on visual white matter pathways.
Methods: We have previously reported that diffusion MRI measurements along early visual white matter pathways (the optic tract; OT and optic radiation; OR) acquired from patients of adult-onset eye diseases (glaucoma, leber hereditary optic neuropathy, and cone-rod dystrophy) differ from those acquired from healthy controls (Ogawa et al., 2014; Takemura et al., 2019). However, few studies have analyzed how early blindness affects tissue properties of visual white matter pathways. Here, we acquired diffusion MRI from a male in their 40s with congenital glaucoma (CG) who went binocular blind around 7 to 8 years old using 3T MRI (SIEMENS Trio Tim). We compared his diffusion measurements along OT and OR with age matched healthy controls (n=25, female=11) and glaucoma groups (n=10, female=4). Datasets obtained from healthy controls and glaucoma subjects were already analyzed in a previous study (Ogawa et al., 2021).
We applied probabilistic tractography to identify the OT and OR (Sherbondy et al., 2008). We then estimated fractional anisotropy (FA) along the OT and OR in all subjects, and then compared FA of CG from that of other groups.
Results: The diffusion measurements in the OT and the OR of CG were significantly different from those of the other two groups. In both OT and OR, CG showed significantly smaller FA compared with those in the glaucoma group (OT: $d' = 3.75$, $p = 0.03$; OR: $d' = 5.40$, $p = 0.001$) and the healthy controls (OT: $d' = 5.26$, $p = 0.005$; OR: $d' = 7.68$, $p < 0.001$).
Conclusions: Our preliminary analysis suggests that white matter tissue changes occurring in CG is significantly bigger than those in the glaucoma group. The results raise a possibility that the complete loss of binocular visual input occurred during the visual critical period may cause bigger changes in the microstructure of visual pathways.

CONTROL ID: 3710243

SUBMITTER (NAME ONLY): Magda Meester

TITLE: Lifestyle score for patients with age-related macular degeneration to promote change

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Meester, E.F. Thee, C. Brussee, M. van Veen, S. de Koning-Backus, C.C. Klaver, Ophthalmology, Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

Commercial Relationships Disclosure: Magda Meester: Commercial Relationship: Code N (No Commercial Relationship) | Eric Thee: Commercial Relationship: Code N (No Commercial Relationship) | Corina Brussee: Commercial Relationship: Code N (No Commercial Relationship) | Marianne van Veen: Commercial Relationship: Code N (No Commercial Relationship) | Sheila de Koning-Backus: Commercial Relationship: Code N (No Commercial Relationship) | Caroline Klaver: Commercial Relationship(s);Code R (Recipient):Thea Pharma, Bayer;Code C (Consultant/Contractor):Bayer

ABSTRACT BODY:

Purpose: Doctors find it challenging to address lifestyle changes in patients with age-related macular degeneration (AMD) despite the current insight that a healthy lifestyle can reduce risk of progression by half. We developed an easy to use lifestyle scoring form for patients with intermediate or unilateral late AMD who are still at risk for severe visual loss.

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Methods: Scoring forms were created based on risk estimates for lifestyle factors from validated studies. Patients ascertained from the clinic and patient organizations received scores for smoking, Mediterranean diet, exercise, and BMI. Each healthy outcome received a point; the maximum score was 13 points. We determined tertiles of total genetic risk by genotyping the 52 known common risk variants.

Results: In an ongoing AMD lifestyle study, we analyzed the scores from the first 38 AMD patients with intermediate or unilateral late AMD. Of these, 16 (42%) had a total lifestyle score ≤ 6; only 2 (6%) scored ≥ 10. Low scores were mainly driven by non-adherence to the Mediterranean diet, with low vegetable and fish intake being most prominent. The majority (56%) of patients had a genetic risk in the highest tertile.

Conclusions: This lifestyle form provides an easy tool to gain insight about the lifestyle of AMD patients, and can help motivate them to improve their daily habits to reduce the impact of their genetic risk.

CONTROL ID: 3710244

SUBMITTER (NAME ONLY): Francesco Cinque

TITLE: Equivalent choroidal thicknesses between eyes of patients with unilateral neovascular age-related macular degeneration who have been treated with anti-vascular endothelial growth factor: a paired eyes comparative study

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Cinque, F. van den Tillaart, C.C. Klaver, C.C. Hoyng, Y.T. Lechanteur, Ophtalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|C.C. Klaver, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Controversy exist regarding the effects of treatment of neovascular (NV) age-related macular degeneration (AMD) with anti-vascular endothelial growth factor (VEGF) on choroidal thickness (CT). We performed a cross sectional study to investigate the possible differences in choroidal thickness (CT) between the treated NV eyes and the untreated non-NV (NNV) eyes of patients with unilateral NV AMD.

Methods: A total of 164 eyes of 82 consecutive patients were selected from an ongoing prospective cohort study of patients with unilateral NV AMD. Patients had a mean age of 74.5 years (standard deviation [SD] 7.7) and 51/82 were female. Patients had to have unilateral NV AMD for which they received anti-VEGF treatment (currently or in the past). Two researchers (FT and FC) independently measured CT on spectral domain enhanced-depth imaging optical coherence tomography images using the calliper function in Heidelberg Eye Explorer (version 2.6.4.0, Heidelberg Engineering, Heidelberg, Germany). CT was measured at the fovea as well as 1500 µm and 3000 µm from the fovea in both the temporal and nasal direction. Interclass correlation coefficients (ICC) and Bland-Altman plots were calculated to check for intergrader reliability. The average value of the two measurements was then used. Differences between CT in NV and NNV eyes were assessed using a paired-samples T-test. Associations of CT with variables of interest were assessed through Pearson’s correlation coefficient analysis.

Results: ICC was above 0.941 across all measurement points. Bland-Altman plots revealed no intergrader bias. Average CT (SD) was 223.4 (107.8)µm and 233.4 (109.4)µm for NNV and NV eyes, respectively (P = .16). Age was significantly but weakly correlated with subfoveal thickness with a correlation coefficient of -.258 (P =.019). The amount of injections was not associated with CT (correlation coefficient - 0.01, P =.957).

Conclusions: In this cohort of unilateral AMD patients there appears to be no difference in choroidal thicknesses of NV eyes treated with anti-VEGF compared to the fellow NNV eye.

CONTROL ID: 3710246

SUBMITTER (NAME ONLY): Oliver Gardiner

TITLE: Can deep learning models understand natural language descriptions of patient symptoms following cataract surgery?

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.W. Gardiner, M. Chowdhury, E. Lim, A. Higham, N. de Pennington, Ufonia Limited, Oxford, Oxfordshire, UNITED KINGDOM|A. Higham, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|E. Lim, Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: As cataract surgery numbers rise, follow up demands place further strains on hospital services. This study uses data collected using an automated telephone platform Dora, which asks patients symptom-based questions to elicit postoperative concerns. We compare the ability of different machine learning techniques to understand patients' descriptions of their symptoms during a cataract surgery follow up with Dora.

Methods:

The training and test datasets were collected from two non-overlapping patient populations who used Dora as part of ethically approved research studies across 3 diverse UK hospitals. The training dataset was augmented with members of the public using the Dora platform. All participants consented to their data being used and the data was fully anonymised. The datasets consist of transcribed utterances of patients describing their symptoms in response to questions like "is your eye red?". Each utterance was labelled with an intent, for example, "gritty" or " red eye" from a total of 24 different intents. Two ophthalmologists independently labelled the dataset and resolved conflicts to establish ground truth labels.

We compared 5 different deep learning and traditional machine learning models; the optimal hyperparameters for each were determined using a grid search and 4-fold cross-validation on the training set. The models were then trained on the entire training dataset and their performance evaluated on the test set.

Results: The training dataset included 1558 unique utterances from 191 patients and 254 members of the public. The test dataset had 255 unique utterances from 142 patients. The best performing model was the Dual Intent and Entity Transformer (DIET) classifier using word embeddings from BERT as presented in Table 1.

Conclusions: Deep learning models have the potential to accurately classify patient intents as part of a natural language conversation, with the DIET classifier performing best. Particularly in this low-data domain, the models benefit greatly from pretrained language models such as BERT. These models can thus be used to deliver autonomous clinical conversations for cataract surgery follow up.

CONTROL ID: 3710247

SUBMITTER (NAME ONLY): David Abram

TITLE: Retinal biomarkers for potential diagnosis of late stage of Alzheimer's Disease

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Abram, T. Sein, V. Bondarenko, Touro University Nevada College of Osteopathic Medicine, Henderson, Nevada, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alzheimer's Disease (AD) is a common neurological disorder affecting millions of individuals worldwide. We performed an experimental model and attempted to identify retinal biomarkers that can be used for a noninvasive diagnosis of this brain disorder.

Methods: Cryosections of brains and retinas from cadavers were analyzed. 2 cadavers without a history of neurodegenerative disease (1 male, 1 female) and 4 cadavers affected by AD (2 males, 2 females) were used. The structures of the brain specifically focused on were the prefrontal cortex (PFC), hippocampus, temporal lobe, visual cortex. Each tissue section was immunostained with antibodies against total tau (TT), phospho-tau 181 (PT181), phospho-tau 205 (PT205), and beta-amyloid (BA). Every stained section was then microscopically analyzed to compare and contrast each marker using optical density (OD) measurements.

Results: Retina samples of AD cadavers expressed a statistical significance increase in OD of the TT marker when compared to normal cadavers (AD = 0.37 OD ± 0.179, Normal = 0.01 OD ± 0.0049). In regards to the brain structures, only the TT markers in PFC were found to have statistical significant increases in OD value (AD = 0.28 OD ± 0.0621, Normal = 0.04 OD ± 0.0423). TT, PT181, PT205, and BA also expressed slight increases in OD in several brain structures of the AD cadavers but were not found to be statistically significant.

Conclusions: There is a significant increase in the TT marker in the retina with similar findings in the PFC. This suggests that using TT as a marker in the PFC and retina has the highest potential to aid in diagnosing AD, with a possibility of studying the progression of AD through TT in different areas of the brain in future research.

CONTROL ID: 3710248

SUBMITTER (NAME ONLY): Mario Matthaei

TITLE: Correlation of clinical fibrillar layer detection with corneal thickness in advanced Fuchs endothelial corneal dystrophy eyes.

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Matthaei, O. Özer, M. Mestanoglu, A. Howaldt, T. Clahsen, S. Siebelmann, N. Reinking, C. Cursiefen, B. Bachmann, Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Central geographic subendothelial deposits in the form of a fibrillar layer (FL) are formed in advanced stages of Fuchs endothelial corneal dystrophy (FECD). Previous studies demonstrated a decrease in corneal endothelial cell (CEC) density and an increase in corneal backscatter in the FL area. The present study investigated the association of clinical FL detection with alterations in corneal thickness.

Methods: Analysis of patients (n=96) presenting for Descemet membrane endothelial keratoplasty (DMEK) for advanced FECD at the Department of Ophthalmology, University Hospital of Cologne, Germany. Slit lamp biomicroscopy with FECD grading was followed by Scheimpflug imaging with en face backscatter analysis and tomography / pachymetric analysis. FL dimensions were measured and correlation with tomographic / pachymetric values was performed. Formal approval to conduct this study was obtained from the Ethics Committee of the University of Cologne (No. 16.424). The research adhered to tenets of the Declaration of Helsinki.

Results: A FL was detected in 74% of all eyes (n=71). FL dimension measures (mean + SD) were for area 9.97+-5.13 mm^2, for maximum caliper diameter 4.38+-1.07 mm, for maximum vertical caliper diameter 3.50+-0.93 mm, and for maximum horizontal caliper diameter 4.09+-1.10 mm. Pachymetric values in FL-positive versus FL-negative eyes were for central corneal thickness (CCT) 614.59+-51.82 µm and 575.12+-48.38 µm (p=0.001), for corneal thickness at the apex (ACT) 613.97+-51.57 µm and 575.20+-46.15 µm, for peripheral corneal thickness at 1mm (PCT_{1mm}) 615,73+-49,95 µm and 580,20+-44.21 µm (p=0.002), for PCT_{2mm} 625.15+-47.63 µm and 599.07+-40.85 µm (p=0.017), for PCT_{3mm} 651.04+-46.32 µm and 635.04+-39.86 µm (p=0.128) and for PCT_{4mm} 695.07+-51.75 µm and 686.00+-43.20 µm (p=0.435), respectively. Correlation analysis indicated a weak correlation for the FL maximum vertical caliper diameter with ACT and PCT_{1mm} values.

Conclusions: Scheimpflug en face backscatter detection of a FL is associated with increased corneal thickness within the central 2 mm of advanced FECD eyes. Combined with our previous studies showing reduced CEC count and increased light scattering in the FL area this provides further evidence that the detection of a FL may qualify as a criterion for intervention in FECD patients in the future.

CONTROL ID: 3710249

SUBMITTER (NAME ONLY): Giovanna Guidoboni

TITLE: Physiology-informed machine learning to enable precision medical approaches of intraocular pressure and blood pressure management in glaucoma

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Guidoboni, D. Zou, R. Nunez, R. Rai, J. Keller, Electrical Engineering Computer Science, University of Missouri, Columbia, Missouri, UNITED STATES|G. Guidoboni, M. Lin, Mathematics, University of Missouri, Columbia, Missouri, UNITED STATES|C. Wikle, Statistics, University of Missouri, Columbia, Missouri, UNITED STATES|E.L. Robinson, School of Social Work, University of Missouri System, Columbia, Missouri, UNITED STATES|A. Verticchio, B.A. Siesky, A. Harris, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision loss in many open-angle glaucoma (OAG) patients continues despite successful treatment lowering intraocular pressure (IOP). The reasons remain elusive. Here, we show that mathematical modeling and machine learning (ML) can help identify subgroups of OAG patients whose disease process entails different relative contributions of IOP and blood pressure (BP).

Methods: 115 OAG patients were assessed every 6 months over a 7-year period for IOP, systolic and diastolic blood pressures (SBP, DBP), heart rate (HR), structural and hemodynamic evaluations via ocular coherence tomography (OCT), Heidelberg Retinal Tomography (HRT), Heidelberg Retinal Flowmetry (HRF), and Color Doppler Imaging (CDI). Fuzzy c-means (FCM) clustering was applied to the dataset comprising: (i) IOP, SBP, DBP, HR measured at the first visit for each patient in the IGPS study; and (ii) individualized estimates of vascular pressures and resistances obtained via a validated mathematical model (Guidoboni et al, IOVS, 2014). FCM is part of ML and the mathematical model is based on physiology, leading to physiology-informed ML. Follow-up visits and data from OCT, HRT, HRF and CDI were not used for clustering.

Results: While the data for IOP and mean arterial pressure (MAP) for the first visit of each IGPS patient do not exhibit any particular pattern (Fig.1a), the physiology-informed ML method revealed 3 distinct clusters. The slanted lines separating the clusters result from the nonlinear interplay that IOP and BP have on ocular hemodynamics captured by the mathematical model. Fig. 2 shows that the cluster membership based on the first visit is associated with different clinical outcomes after 4 years (p values obtained with the 2-sample paired Wilcoxon signed rank test for medians; p <= 0.05 in bold). Cluster 1 shows minimal progression, whereas Cluster 2 shows marked structural progression accompanied by significant hemodynamic changes. Cluster 3 exhibits significant changes only in HRT and HRF markers, but not in OCT and CDI.

Conclusions: This study suggests that the proposed physiology-informed ML approach can identify and quantify the relative contributions of IOP and BP on the OAG risk for patient subgroups. Thus, this approach may enable precision medical approaches of IOP and BP management in OAG.

CONTROL ID: 3710252

SUBMITTER (NAME ONLY): Enton Lam

TITLE: Photoreceptors modulated retinal angiogenesis via SOCS3

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Lam, T. Wang, D.I. Tsirukis, S. Kaneko, Y. Sun, Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a major cause of vision loss and blindness in children. In ROP, the onset of neovascularization (NV) is at around 32-weeks gestational age, regardless of gestational age at birth, which coincides with the development of rod outer segments and full rod function. Photoreceptors may play an important role in ROP pathogenesis. Yet, the molecular and cellular mechanisms through which photoreceptors control retinal NV in ROP are largely unknown. We aim to investigate the role of photoreceptors in controlling retinal angiogenesis via suppressor of cytokine signaling 3 (SOCS3).

Methods: The Cre/LoxP system was used to generate rod photoreceptor specific Socs3 knockout mice (Socs3 cKO) by crossing Socs3 flox/flox mice with Rhodopsin improved Cre mice (Rho-iCre) and Socs3 overexpression mice (Socs3 cOE) by crossing Socs3 OE flox/flox mice with Rho-iCre mice. The oxygen induced retinopathy (OIR) mouse model was used as a ROP preclinical model. Mice were exposed to 75% oxygen from postnatal day (P)7 to P12 and returned to room air from P12 to P17. Retinas were enucleated, fixed, and stained with endothelial cell marker isolectin B4 at P17 for phenotypical analysis. NV and vaso-obliteration (VO) was quantified using Image J. Real-time PCR and western blot were used to validate the efficacy of Socs3 overexpression and knockout. Immunohistochemistry was used to determine protein localization in the retina. Results are reported as mean ± SEM, and statistical analyses were performed with GraphPad Prism (v8.0).

Results: In the OIR model, SOCS3 expression was highly induced in the photoreceptor layer. The efficacy of photoreceptor Socs3 overexpression and knockout was validated. Cre recombination of Socs3 in the outer nuclear layer of the retina was confirmed using Rho-iCre driven mTmG reporter mice. In the OIR model, SOCS3 deficiency in rod photoreceptors significantly increased NV by 25% ($p<0.01$, n=18-20) without influencing VO ($p>0.05$) compared to controls. Conversely, SOCS3 overexpression significantly decreased NV by 28% ($p<0.01$, n=17-20) but not VO ($p>0.05$) compared to littermate controls. Pharmacologic treatment with SOCS3 activator naringenin suppressed retinal neovascularization.

Conclusions: Our data strongly suggests that rod photoreceptor SOCS3 mediates neovascularization in the OIR model. Activation of photoreceptor SOCS3 may be a potential therapeutic for treating retinal angiogenesis.

CONTROL ID: 3710260

SUBMITTER (NAME ONLY): Nicole Himebaugh

TITLE: Ex Vivo Analysis of Ultraviolet Light Transmission in Select Species

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Himebaugh, B.C. Gilger, A. Oh, Clinical Sciences, NC State University College of Veterinary Medicine, Raleigh, North Carolina, UNITED STATES|B. Ekesten, Swedish University of Agricultural Sciences, Uppsala, Uppsala, SWEDEN|K. Weninger, Physics, NC State University College of Sciences, Raleigh, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Different species block varying amounts of wavelengths in the ultraviolet (UV) spectrum to protect the retina. However, evolution of UV vision in some mammalian species is thought to aid in environmental navigation, communication, and foraging behavior. Specifically, dogs and cats are suspected to have UV vision although the percent transmission (%T) of UV light reaching the retina is not clearly defined. The aim of this study is to assess the transmission of the UV spectrum (200-400 nm) through enucleated globes of different species (dogs, cats, rabbits, pigs, and humans) using spectrophotometry.

Methods: Globes (n=6-10 per species) from animal models were analyzed within 24 hours of death. Human globes (n=2) were acquired from an eye bank. For spectrophotometry, a 5-10 mm circular area of sclera and choroid from the posterior aspect of the globe was removed under a surgical microscope. The retina remained intact to mimic the path of light through the living eye. The %T of wavelengths from 200-800 nm were measured through the ocular media (cornea, aqueous humor, lens, and vitreous humor) and retina of dogs, cats, pigs, rabbits, and humans. The %T within the UV range (200-400 nm) and UV-Visible range (200-800 nm) were compared between species. Data was analyzed using area under the curve and ANOVA with significance set at $p<0.05$.

Results: Compared to other species, there was a significantly larger amount of UV %T in globes of dogs and cats ($p<0.0001$). Cats transmitted the highest percentage of UV light with over 59% transmission at 400 nm whereas dogs transmitted 27% of light at 400 nm. At 350 nm, cats transmitted 30% of light and dogs transmitted 9%. There was also a significantly larger amount of UV %T in globes of rabbits compared to pigs ($p=0.0021$) and humans ($p=0.0150$). Rabbits transmitted 27% of light at 400nm and less than 1% at 350 nm. Humans and pigs did not differ significantly in the amount of UV %T ($p=0.9985$) and transmitted less than 1% of light below 400nm.

Conclusions: Dogs and cats have significantly higher transmission of wavelengths below 400 nm through their ocular media and retina compared to rabbits, pigs, and humans. This suggests that these crepuscular species can take advantage of UV light both in nature and under artificial lighting conditions. Results from this study will support further vision research in cats and dogs. These results may be used to train companion, working, and service animals.

CONTROL ID: 3710264

SUBMITTER (NAME ONLY): Shahin Nasr

TITLE: Amblyopia Impacts on Activity within Human V2/V3 Thin and Thick Stripes during Binocular Summation

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Nasr, B. Kennedy, A. Nabasaliza, R.B. Tootell, Radiology, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|S. Nasr, R.B. Tootell, Radiology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Skerswetat, N. Aycardi, P.J. Bex, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|D.G. Hunter, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Nabasaliza, D.G. Hunter, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: In normally-sighted individuals, visual acuity benefits from binocular summation. However, this effect is weakened in amblyopic individuals, especially for high spatial frequency (SF) stimuli (Pardhan and Gilchrist, 1992). To clarify the underlying disorder, we examined the function of thick and thin stripes in human V2 (and V3) during monocular and binocular perception. In normally sighted individuals, these stripes respond differentially to low- vs. high-SF components (Tootell and Nasr, 2017).

Methods: Six strabismic and five anisometropic (best-corrected visual acuity in the amblyopic eye 20/60 to 20/300) individuals, aged 19-55 years old, participated in this study. Using high-resolution fMRI (7T; voxel size = 1 mm isotropic), we localized thin and thick stripes across V2/V3 (Figure 1A). Then, we measured the activity within these stripes as subjects were presented with high (99%) and low (5%) contrast gratings of 0.1–5.8 cycle/deg., either monocularly or binocularly.

Results: For monocularly presented high-contrast stimuli, thin and thick stripes showed a preference for high-SF (Figure 1B) and low-SF (Figure 1C), respectively. This preference did not vary based on the stimulated eye. When presented binocularly, low-SF (but not high-SF) gratings evoked a significantly stronger response, compared to when the same stimuli were presented monocularly ($p<0.01$). When normalized relative to the averaged response, this effect was significantly stronger in thin compared to thick stripes ($p<0.05$).

For low-contrast stimuli, high-SF gratings evoked a stronger response when presented to fellow- compared to amblyopic-eye (Figure 1D-E). However, only the response to low-SF gratings benefited from binocular summation.

Conclusions: In amblyopic individuals, the impact of binocular summation is limited to the response to low-SF gratings and appeared to be stronger in V2/V3 thin (relative to thick) stripes.

CONTROL ID: 3710273

SUBMITTER (NAME ONLY): Fabian Braeu

TITLE: AI-based Clinical Assessment of Optic Nerve Head Robustness from 3D Optical Coherence Tomography Imaging

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To develop a clinically applicable approach to assess the robustness of an individual optic nerve head (ONH) from a standard 3D optical coherence tomography (OCT) scan by predicting how it would deform under a hypothetical acute change in intraocular pressure (IOP).

Methods: 316 subjects had their ONHs imaged non-invasively with 3D optical coherence tomography (OCT) before and after acute IOP elevation through ophtalmo-dynanometry – a method to raise IOP via globe indentation. We then categorized each ONH as robust or compliant. To do so, a 3D digital volume correlation algorithm was applied to both OCT volumes of each ONH to extract an IOP-induced average effective strain in the lamina cribrosa region (E_{eff}). 169 subjects were considered to exhibit robust ONHs ($E_{eff} < 4\%$) and 147 were classified as compliant ($E_{eff} > 4\%$). Learning from these biomechanical data, we compared three algorithms to assess ONH robustness strictly from a baseline (undeformed) OCT volume: (1) a point cloud classification network, (2) a decision tree ensemble, and (3) an autoencoder in combination with a fully connected binary classification network. For each method, 253 subjects were used for training and 63 for testing. To evaluate the performance of our algorithms in predicting ONH robustness, we used the area under the receiver operating characteristic curve (AUC).

Results: All three methods were able to assess ONH robustness from 3D structural information alone. The point cloud classification network (AUC: 0.77) performed slightly better than the decision tree ensemble (AUC: 0.69) and the autoencoder (AUC: 0.68).

Conclusions: We introduce a novel machine learning based method to assess ONH robustness strictly from a standard 3D OCT scan. Our proposed approach may have wide clinical interest because it does not require new hardware (it can be combined with any existing OCT device) and can assess ONH robustness without the need of performing complex biomechanical tests. Longitudinal studies should establish if ONH robustness estimated by the herein presented technique helps to predict and better understand the development and progression of glaucoma. Our method will soon be improved by incorporating a larger biomechanical dataset.

CONTROL ID: 3710277

SUBMITTER (NAME ONLY): Jeremias Galletti

TITLE: Effects of Cathepsin S inhibition in the Aged Lacrimal Gland

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.G. Galletti, Innate Immunity, Institute of Experimental Medicine CONICET-ANM, Buenos Aires, Buenos Aires, ARGENTINA|J.G. Galletti, K. Scholand, Z. Yu, C.S. De Paiva, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|W. Haap, T. Ferreira, Roche Pharma Research and Early Development, F. Hoffmann-La Roche Ltd, Basel, SWITZERLAND|K. Scholand, Department of Biosciences, Rice University, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously shown that aged C57BL/6J (B6) mice have increased cathepsin S in tears, lacrimal gland lysates, and spleen. High cathepsin levels have been linked to the generation of autoreactive T cells. This study investigated the effects of cathepsin S inhibition on age-related dry eye disease in B6 mice.

Methods: Female B6 mice aged 15.5 to 17 months were randomized (n=16/group) to receive either a medicated diet formulated by mixing the cathepsin S inhibitor (R05461111, 262.5mg/kg chow, Roche, Switzerland) or standard diet (placebo) for 12 consecutive weeks. Eye draining lymph nodes and lacrimal glands (LGs) were excised and prepared for either histology or assayed by flow cytometry to quantify infiltrating T cells. The number of inflammatory foci (>50 cells) was counted under a 10X microscope lens. Image analysis of scanned H&E-stained LGs was used to calculate focus score/4mm^2 and foci area (μm^2). Eyes and adnexae were collected and processed for histology. Goblet cell density was investigated in PAS-stained sections. Expression of Tnf, Ifn, Il12, and Cxcl10 was investigated by real-time PCR in LG and conjunctiva.

Results: Compared to the standard diet, mice subjected to cathepsin S inhibition showed a decrease in CD4$^+$IFN-γ$^+$ (49.6±9 vs. 35±7.5%) and an increase in CD4$^+$Foxp3$^+$ (9.2±4 vs. 19.4±5 %) cells in the LGs (n=5/group, P<0.05 or lower). A similar non-statistically significant trend was observed in ocular draining nodes. The frequency of total CD45$^+$IL-12$^+$ cells was decreased in cathepsin S-inhibitor diet LGs, accompanied by a decrease in frequency and activation (CD86 expression) in CD45$^+$CD11c$^-$MHC II$^+$CD11b$^+$F4/80$^+$ cells. While there was no change in focus score between the treatment groups (2.2±0.7 vs. 2.62±0.7 focus score/4mm^2), a significant increase in conjunctival goblet cell density was observed in the inhibitor-treated animals (45±5.5 vs. 30±7.8 goblet cells/mm, P <0.01) compared to the standard diet. Significant lower levels of Ifn, Tnf, Il12 (range 25-40% decrease) were observed in LG, while low levels of Ifn, Il12, and Cxcl10 (range 40-70% decrease) were present in the conjunctiva in the inhibitor-treated mice.

Conclusions: Altogether our results indicate that therapies aimed at reducing cathepsin S can improve age-related dry eye disease. Further studies with a longer duration are needed to evaluate the role of cathepsin S in the formation of inflammatory foci in the aged lacrimal gland.

CONTROL ID: 3710278

SUBMITTER (NAME ONLY): catherine Jamison

TITLE: Assessing choroidal thickness in eyes with idiopathic serous epithelial detachments in UK Biobank

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Idiopathic serous epithelial detachments (SPEDs) are part of the spectrum of central serous chorioretinopathy (CSCR). This study presents imaging characteristics of those with idiopathic SPED compared to those without in UK Biobank (UKBB), a prospective cohort study.

Methods: UKBB is a biomedical database with over 500,000 UK participants aged 40-69 years. Of these, colour and optical coherence tomography (OCT) gradable images were obtained using spectral domain OCT (Topcon- 1000, Topcon, Japan) in 68517 participants. The images were graded masked by trained and certified graders.

Idiopathic SPED cases were selected for detailed grading; number of SPEDs, height, base diameter and location of the largest SPED, sub-foveal choroidal thickness (SFCT), maximum choroidal thickness (MCT), and greatest (vertical) choroidal vessel diameter (CVD) on the foveal scan.

A control-group of an equal number of pathology free UKBB eyes were graded using the same method. T-tests were used for comparisons, using SPSS v26.

Results: Of the 68517 available retinal images, 109 eyes (85 patients) had at least one idiopathic SPED, 12 patients had bilateral SPEDs. 76% of eyes had one SPED, 17% had two SPEDs, 4% three, 2% four and 2% over 5. Mean SPED height was 100.2μm (range 23-501) and mean base diameter 483.97μm (119-1961).

Extra-foveal SPEDs were present in 73%, 19% were juxta-foveal and 8% sub-foveal (geometric centre of the fovea). There was a slight predilection for superior and nasal presentation but this was not significant.

There was a significant difference in mean SFCT between groups, 355μm (141-567) for those with SPED and 265 μm (111-443) for those without ($p<0.001$). With SPED the mean MCT was 414 μm (190-567), 320 μm (176-458) for those without ($p<0.001$). CVD was also significantly different; 191 μm (108-439) for SPED eyes and 165 μm (93-267) for non-SPEDs ($p<0.001$).

Conclusions: SFCT and MCT were significantly higher in those with SPEDs than those without. Additionally CVD of the largest gradable vessel (foveal scan) was significantly greater in those with SPEDs, signifying choroidal vascular changes in those with SPED. The weakness of the study was that no enhanced depth imaging was available for this cohort, however we demonstrated the feasibility of using this image set for SPED analysis.

CONTROL ID: 3710282

SUBMITTER (NAME ONLY): Anton Lennikov

TITLE: Electric stimulation reduces microglia proinflammatory activity in vitro

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lennikov, M. Yang, K. Chang, L. Pan, D.Y. Shu, K. Cho, M. Saint-Geniez, D.A. Dartt, D. Chen, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|T. Utheim, Ophthalmology, Oslo University Hospital, Oslo, NORWAY|A. Lennikov, K. Chang, T. Utheim, Medical Biochemistry, Oslo University Hospital, Oslo, NORWAY|

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ABSTRACT BODY:

Purpose: Electrical stimulation (ES) employing a low-intensity electric current with minimal tissue heating presents a potential therapeutic modality that can be applied noninvasively to the eye. However, the cellular level effects of the ES on several retinal cell types are largely unexplored. In this study, we evaluated the effects of ES on microglia (MG) and human retinal endothelial cells (HREC) in vitro.

Methods: Primary brain MG was isolated from adult C57BL/6 mice. The resulting cultures were subjected to ES (biphasic, 300 μA, 20 Hz) for 1 hour. The activation profile of MG was studied by immunostaining, RT-PCR, and cytokine arrays. Calcium flux in response to ATP 10^{-7} M stimulation (120 sec) was measured by Fura-2. MG cells oxygen consumption and mitochondria activity were studied through high-resolution respirometry (Seahorse XF24, Agilent), JC-1 mitochondria membrane potential assay, and cellular ATP content quantification. The effect of ES on primary human endothelial cells (HREC) angiogenic activity was investigated using migration and tube formation assays combined with a measure of VEGFA expression. Findings were validated using the choroidal explant sprouting assay.

Results: ES reduced the expression of proinflammatory cytokines, including IL-6, TNFα, COX-2, and ATP-induced Ca2+ flux in the MG cells ($p<0.05$). Seahorse XF24 analysis of ES MG cells indicated reduced basal ($p<0.05$) and maximal ($p<0.05$) respiration and ATP production ($p<0.01$). Proton leak was not significantly affected compared to control cultures ($p>0.05$), suggestive of a lack of mitochondria damage. The results were confirmed by reduced cellular ATP content ($p<0.01$) and reduced JC-1 mitochondrial potential in the ES MG cells. In HREC, endothelial cells migration ($p<0.01$) and tube formation ($p<0.01$) were suppressed by ES, vascular outgrowth from choroidal explants was also reduced ($p<0.05$). Western blotting and immunostaining analysis of ES HREC further confirmed reduced VEGFa expression.

Conclusions: ES inhibits MG activity by reversibly depolarising mitochondrial potential and ATP production. The lack of ATP reduces Ca^{2+} flux in response to proinflammatory stimuli due to depletion of endoplasmic reticulum (ER) Ca2+ depo. ES also reduces the angiogenic potential of HREC by suppressing VEGF expression and choroidal vessels ex-vivo. These data suggest the therapeutic potential of biphasic ES in inflammatory and neovascular diseases of the eye.

CONTROL ID: 3710283

SUBMITTER (NAME ONLY): Matthieu Duot

TITLE: An integrative analysis using iCLIP-seq and RNA-Seq to identify genes post-transcriptionally regulated by the cataract-linked RNA-binding protein CELF1 in the lens

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Celf1 encodes an RNA-binding protein (RBP) that post-transcriptionally regulates gene expression by distinct mechanisms, including alternative splicing. Germline knockout (KO) or lens-specific conditional knockout (cKO) Celf1 mice develop lens defects and early-onset cataract. We sought to identify RNA targets of CELF1 protein in the lens, particularly those regulated at the level of alternative splicing, and whose mis-regulation upon CELF1-deficiency may contribute to lens defects and cataract.

Methods: We performed integrative analysis using multiple omics-based approaches to identify Celf1-regulated downstream RNA targets in the lens. Individual-nucleotide resolution UV crosslinking and immunoprecipitation (iCLIP) followed by high-throughput RNA-sequencing (iCLIP-seq) identified CELF1 protein-RNA binding sites in adult mouse wild-type (WT) lens. This data was analyzed in the context of RNA-seq data on Celf1 KO or Celf1 cKO and control mouse lenses, which identified mis-regulated candidate genes with alternative splicing events.

Results: Integrative analysis of iCLIP-seq and RNA-seq data allowed the prioritization of 22 RNAs whose splicing pattern is likely directly controlled by CELF1 protein in the lens. Of these, seven RNAs that encode proteins linked to cytoskeleton (e.g. ABLIM1, ANK2, CLTA, CTNNA2, SPTBN1, SEPTIN8, YWHAE) were validated by RT-PCR to have mis-expressed alternative splice isoforms in Celf1 KO lens. Normal lens fiber cell differentiation involves cytoskeleton modifications that are necessary for their characteristic morphology and organization, which is found to be perturbed in Celf1-deficient lens. Thus, abnormal splicing of these cytoskeletal protein-encoding RNAs may contribute to the cataract pathology in Celf1 KO lenses.

Conclusions: Integrative analysis using iCLIP-seq data generated on WT lens (for identifying RNA binding sites of CELF1 protein) and RNA-seq data generated on Celf1 KO and Celf1 cKO lens (for identifying genes with mis-regulated alternative splicing event) led to prioritization of targets that are linked to the cytoskeleton and whose altered expression may explain distinct aspects of the lens pathology and cataract resulting from Celf1 deficiency.

CONTROL ID: 3710284

SUBMITTER (NAME ONLY): Abhinav Thareja

TITLE: Improving the penetration of Dexamethasone to the posterior segment of eye using topically applied penetration enhancing agents

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Disease and damage in the posterior segment of the eye are a major global cause of blindness. Topical eye-drop treatments are less effective because therapeutic molecules penetrate ocular tissue barriers poorly. We investigated penetration enhancement of the most commonly used anti-inflammatory drug, dexamethasone sodium phosphate (DSP), after topical delivery with three penetration enhancing agents (PEAs) — an in-house synthesized novel helical polymer and two commonly used cell penetrating peptides (CPPs), TAT and Penetratin.

Methods: Trans-corneal penetration of the three PEAs and DSP formulations with PEAs were assayed ex-vivo in a rapid and cost-effective screening model of excised porcine cornea and quantified using UV & fluorescence spectroscopy for PEAs and by high performance liquid chromatography (HPLC) for DSP. Immunostaining of corneal sections with tight junction markers, ZO-1 and Claudin-5, assessed the integrity of tight junctions and also provided a reference for visualizing the internalized PEA in corneal epithelium by confocal microscopy. Trans-epithelial electrical resistance (TEER) measurements for the corneal epithelium before and 60 minutes after application were used to determine the integrity of corneal barriers and barrier function. Furthermore, in-vitro cytotoxicity of PEAs was performed by the MTT assay in ARPE-19 and HCE-2 cells, whilst immunocytochemistry (ICC) was used in assays involving adult rat primary retinal cultures.

Results: All three PEAs effectively crossed the cornea individually. There was almost 15-fold enhancement of DSP trans-corneal permeation after topical application with PEAs. Confocal microscopy after immunostaining showed retention and epithelial internalization of PEAs on corneal epithelial surfaces while also revealing intact tight junctions. TEER measurements confirmed that there was no damage to the integrity of barrier function after PEA/DSP application. Finally, MTT assays and ICC showed no toxicity in ARPE-19, HCE-2 cells, or primary rat retinal cells, respectively.

Conclusions: Topically applied novel polymers, TAT and Penetratin all increased trans-corneal penetration efficiency of DSP without causing any damage to the corneal barrier integrity or in-vitro toxicity. This can potentially increase the bioavailability of DSP in the posterior segment tissues.

CONTROL ID: 3710292

SUBMITTER (NAME ONLY): Jose Villa-Carpes

TITLE: Retinal and Choroidal Thickness at Different Eccentricities in the Myopic Eye

SESSION TITLE: Myopia: Structural Changes from Retina to Sclera

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Myopia progression might alter the morphology of the posterior eye, particularly the neural retina and the choroid. In this work we investigated whether, and eventually to what extent, the amplitude of myopia correlates with both retinal and choroidal thickness measured with a commercial swept-source optical coherence tomography (OCT) instrument.

Methods: Retinal OCT images from 42 myopes (25 females and 17 males; mean age: 27.1±4.0 years) were acquired around the fovea. Subjects were distributed into three groups according to their objective refraction: low myopia (>-1D), moderate myopia (-1D to -4,5D] and high myopia [-4,5D to -12D]. The OCT images were digitally processed, correcting geometrical distortions and curvature, with a custom MATLAB^{TM} software adopting the Bruch membrane as the reference plane for intra-retinal distances. From the so-processed images, retinal and choroidal thicknesses were semi-manually obtained at four different eccentricities along the horizonal meridian (fovea, 2.25mm nasal; 2.25 and 3.38mm temporal from fovea) using ImageJ^{TM}. Three measurements were obtained from each location.

Results: Thicknesses of both retina and choroid followed a normal distribution (Shapiro-Wilk test). Foveal retinal thickness did not correlate with refraction in any group. On the opposite, certain linear correlation (R=0.45) appeared for sub-foveal choroidal thickness. When the groups were considered, the mean sub-foveal choroidal thickness was statistically different in the high myopia group (ANOVA test). Nasal and temporal retinal thickness exhibited a moderate association with refraction, with significant differences between low-moderate myopia and high myopia groups. Neither nasal nor temporal at 3.38 mm choroidal thickness correlated with ocular refraction. Nevertheless, significant differences between low and high myopia groups were found at 2.25-mm temporal location.

Conclusions: A significant decrease in sub-foveal choroidal thickness was found in the high myopia group with no variations in foveal thickness between groups. Retinal thickness correlated with refraction at 2.25mm eccentricity, nasal and temporal locations, with high myopes exhibiting lowest values. Retinal and choroidal thicknesses show differences as a function of refraction and eccentricity, which might be a marker for myopia evolution, also serving to evaluate current treatments.

CONTROL ID: 3710293

SUBMITTER (NAME ONLY): Rosellina Guarascio

TITLE: The role of light in the pathogenesis of rhodopsin retinitis pigmentosa

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Li, R. Chen, Baylor College of Medicine, Houston, Texas, UNITED STATES|R. Guarascio, K. Hau, R. Asfahani, K. Ziaka, H. Poultney, D. Athanasiou, M. Aguila, M.E. Cheetham, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Autosomal dominant Retinitis Pigmentosa (adRP) is an inherited retinal degenerative disease that initially affects rod photoreceptors function and survival. The first gene identified to cause adRP was RHO, which encodes for rhodopsin, a G-protein coupled receptor involved in the detection of low level light and the consequent activation of rods phototransduction cascade. We focused our attention on a common UK pathogenic rhodopsin amino acid substitution, RHO^{M39R}. Here we have investigated the effect of light on retinal function and degeneration in both RHO^{M39R} and Rho^{M39R} models.

Methods: To investigate the role of light in retinal degeneration, we used two different models: Rho^{M39R} knock-in (KI) mice and $RHO^{M39R/+}$ human iPSC-derived retinal organoids (hROs). Different levels of light exposure were investigated as a modifier of disease. Optic Coherence Tomography (OCT) and Electroretinogram (ERG) were performed on mice to characterise mouse retina thickness and activity, respectively. Electron microscopy was performed to characterise the ultrastructure of the retina. Rhodopsin protein levels were analysed by western blotting. RNAseq was performed to evaluate changes in the retinal transcriptome, while immunohistochemistry was used to analyse rhodopsin localization and retina degeneration in both mouse retina and hROs.

Results: 3 weeks old $Rho^{M39R/+}$ KI mice reared in ambient light had impaired retinal function by ERG, while the thickness of the outer nuclear layer (ONL) was comparable to control $Rho^{+/+}$. By contrast, rearing in reduced ambient light exposure, protected the ERG function of $Rho^{M39R/+}$ animals. Exposure to bright light (max intensity: 30 $cd*s/m^2$) through repeated ERG, caused a progressive decrease in ONL thickness and in retinal activity. 3 week old $Rho^{M39R/M39R}$ KI mice raised in ambient light showed severely compromised retinal function, reduced ONL thickness and altered outer segment (OS) morphology. Moreover, a single exposure to bright light significantly decreased the ONL thickness of $Rho^{M39R/M39R}$ KI retina within 24h, while inducing the expression of apoptotic genes by 3h. 170-200 days old $RHO^{M39R/+}$ hROs showed signs of retinal degeneration and mistrafficking of rhodopsin compared to control $RHO^{+/+}$ hROs.

Conclusions: The combined study in both KI mice and human ROs can provide insights into the role of light in sector RP in mammalian models and the ability to develop new therapies to treat RP patients.

CONTROL ID: 3710297
SUBMITTER (NAME ONLY): Matthew McHarg
TITLE: Anti-drug antibodies to monoclonal TNF inhibitors in non-infectious uveitis
SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. McHarg, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|M. McHarg, S. Bellur, W. Kongwattananon, S. Vitale, H. Sen, S. Kodati, National Eye Institute, Bethesda, Maryland, UNITED STATES|
Commercial Relationships Disclosure: Matthew McHarg: Commercial Relationship: Code N (No Commercial Relationship) | Sunil Bellur: Commercial Relationship: Code N (No Commercial Relationship) | Wijak Kongwattananon: Commercial Relationship: Code N (No Commercial Relationship) | Susan Vitale: Commercial Relationship: Code N (No Commercial Relationship) | H Nida Sen: Commercial Relationship(s);Code E (Employment):NEI Intramural Research Program | Shilpa Kodati: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: This study aimed to investigate the association between circulating drug levels and anti-drug antibodies (ADAs), clinical response, and concurrent immunomodulatory treatment (IMT) in patients with non-infectious uveitis treated with TNF-α inhibitors.
Methods: A retrospective study was conducted at the National Eye Institute. Patients who underwent anti-adalimumab or anti-infliximab immunoassay testing for the presence of ADAs were included. Chart review was performed for demographic and laboratory data.
Results: Forty-two adalimumab and 12 infliximab patients were included. In the adalimumab group, mean duration since diagnosis and duration of therapy of 84.2 and 30.6 months, respectively. In the infliximab group, mean duration since diagnosis and duration of therapy was 92.5 and 20.9 months, respectively. 35.8% of all adalimumab patients had ADAs with a mean antibody level (MAL) of 97.3 AU/mL. No infliximab patients developed ADAs.

When divided based on clinical response, 54.8% of adalimumab patients were complete responders with a mean drug level (MDL) of 11.4 mcg/mL, 14.3% were partial responders with MDL 9.7 mcg/mL, and 30.9% were non-responders with MDL 6.8 mcg/mL. ADAs were present in 21.7% of complete responders (MDL 4.1 mcg/mL and MAL 73.4 AU/mL), 50% of partial responders (MDL 2.1 mcg/ML and MAL 250.2 AU/mL), and 53.8% of non-responders (MDL 2.2 mcg/mL and MAL 35.3 AU/mL). In the infliximab group, MDL was 27.2 mcg/mL.

MDL and MAL were also analyzed based on use of concurrent IMTs. ADAs were present in 20.0% of patients on mycophenolate mofetil, 38.5% on methotrexate, and 53.8% on monotherapy. MDL and MAL were 12.57 mcg/mL and 50.33 AU/mL for the mycophenolate group, 9.02mcg/mL and 42.8 AU/mL for methotrexate, and 6.78mcg/mL and 147.34 AU/mL for monotherapy, respectively.
Conclusions: ADAs were observed in 35.8% of adalimumab and 0% of infliximab patients. In the adalimumab cohort, complete responders had a higher MDL and lower ADA compared to partial and non-responders. Notably, when antibodies were present, MDL was lower regardless of clinical response, suggesting that a complete clinical response is associated with higher drug levels even when ADAs are present. Lastly, patients who used IMTs concurrently had a higher MDL and lower frequency of ADA in the adalimumab group, suggesting a benefit over monotherapy. Additional research is required to better understand the impact of ADAs in non-infectious uveitis.

CONTROL ID: 3710300

SUBMITTER (NAME ONLY): Jiwoong Lee

TITLE: The effect of amniotic membrane transplantation on trabeculectomy in patients with pseudoexfoliation glaucoma

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Lee, T. Kim, H. Kim, S. Moon, Pusan National University School of Medicine, Busan, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To evaluate the effect of amniotic membrane transplantation (AMT) on trabeculectomy in patients with pseudoexfoliation glaucoma (PXG)

Methods: We reviewed the medical records of patients with PXG who underwent fornix-based trabeculectomy with Mitomycin C with or without AMT. Kaplan-Meier survival curves were compared with log-rank test in AMT group and control group. All patients had follow-up of at least 12 months. Surgical success was defined by following 4 criteria. (1) Criteria A: intraocular pressure (IOP) ≤ 18 mmHg and IOP reduction 20% without medication; (2) Criteria B: IOP ≤ 15 mmHg and IOP reduction 25% without medication; (3) Criteria C: IOP ≤ 18 mmHg and IOP reduction 20% with or without medications; (4) Criteria D: IOP ≤ 15 mmHg and IOP reduction 25% with or without medications. Kaplan-Meier survival curves were compared with log-rank test in AMT group and control group. Cox proportional hazard models were used to estimate the influence of AMT on surgical success accounting for confounding variables.

Results: 52 eyes with AMT (AMT group) and 33 eyes without AMT (control group) were included in this retrospective study. Cumulative success rates were 86.5% at 12 months and 83.8% at 24 months for AMT group, and 63.6% and 56.3% for control group by criterion A. Complete success rates were significantly greater for AMT group than for control group by criteria A and B (P = 0.017, P = 0.005, respectively). Cumulative success rates were 92.1% at 12 months and 89.0% at 24 months for AMT group, and 75.1% and 62.8% for control group by criterion C. Qualified success rates were significantly greater for AMT group than for control group by criteria C and D (P = 0.047, P = 0.021, respectively). On multivariable Cox regression analyses, AMT was associated with higher success rate with all criteria for complete and qualified success (P ≤ 0.04 for all). Avascular bleb developed in 7 eyes (21.2%) of control group while there were no eyes with avascular bleb in AMT group (P = 0.004).

Conclusions: In patients with PXG, trabeculectomy with AMT for target IOP ≤ 18 mmHg or ≤ 15 mmHg was more successful than trabeculectomy without AMT. Avascular bleb was found only after trabeculectomy without AMT.

CONTROL ID: 3710303

SUBMITTER (NAME ONLY): Guorong Li

TITLE: Outflow segmentation patterns and pilocarpine induced outflow changes with age

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Li, A. Wilson, C. Bowes Rickman, W.D. Stamer, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age is a critical risk factor for ocular hypertension in glaucoma. But, how age affects the regulation of conventional outflow is unclear. The aim of this study was to determine the effect of age on outflow in the presence or absence of pilocarpine (PILO).

Methods: C57BL/6J mice (1-30 month-old) were used for the study. Green fluorescence beads (0.1um) were perfused intracamerally at pressures 15, 20, 25 and 30 mmHg for 10 min at each pressure in live mice. Pressure was set by a column of fluid connected to a cannulation needle, and outflow (OF) was calculated at each pressure level by the volume leaving the column during 10 min intervals. For PILO studies, 1% PILO was applied topically to one eye just before pressure steps. After perfusions, mice were immediately euthanized. Anterior segment flat mounts were imaged by confocal microscopy.

Results: Regardless of age, the inferior quadrant displayed the least amount of tracer in the majority of the eyes. Overall fluorescence intensity decreased in an age dependent manner, with a greater percentage of low flow regions found in eyes of older mice. Eyes treated with PILO showed increased fluorescence intensity in inferior quadrants, especially in aged eyes. However, age did not significantly change averaged OF across all pressures measured in vivo. As expected, PILO significantly increased mean OF in both young and aged eyes (young: 0.36±0.09 vs 0.52±0.14 ul/min, p=0.02, n=7-33; aged: 0.4±0.12 vs. 0.57±0.14 ul/min, p=0.03, n=6-27). Interestingly, PILO effects in young mice was rapid, increasing OF during the first 10 min by 79% at 15 mmHg (0.45±0.17 vs. 0.80±0.37 ul/min, p=0.04) and by 57% during the next 10 min at 20 mmHg (0.34±0.14 vs. 0.53±0.27 ul/min, p=0.11). In contrast, we observed no increase in OF in old mice for the first 20 min of PILO at IOP 15 or 20 mmHg. The last 20 min of PILO perfusion was different in old mice, significantly increasing OF by 67-69% (25 mmHg=0.39±0.15 vs 0.66±0.16 ul/min, p=0.006; 30 mmHg=0.41±0.11 vs. 0.69±0.17 ul/min, p=0.009). By comparison, PILO had no significant effects in young mice over the last 20 min.

Conclusions: Labeled high flow regions were reduced with age, which is consistent with the lower outflow detected in aged human eyes. In addition, age also impacted the effects of PILO on outflow tissues, where young mice showed a rapid response and aged mice had a slower and more constant response.

CONTROL ID: 3710304

SUBMITTER (NAME ONLY): Alexandra Blomfield

TITLE: The nuclear receptor REV-ERBα regulates retinal vessel regeneration in a mouse model of oxygen-induced retinopathy

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Blomfield, F. Yemanyi, C. Liu, S. Huang, K. Bora, M. Maurya, J. Chen, Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ischemic proliferative retinopathies, like retinopathy of prematurity and diabetic retinopathy, are often blinding and treatment options are limited. Current treatments focus primarily on reducing pathological neovascularization (NV) in the second phase of disease without addressing vessel loss in the first phase. We aimed to investigate the latter by assessing the role of REV-ERBα, a nuclear receptor and transcriptional repressor with a cellular cytoprotective effect, in promoting vessel regeneration in a mouse model of oxygen-induced ischemic retinopathy (OIR).

Methods: Wild-type (WT) and systemic REV-ERBα knockout (KO) mice were analyzed for developmental retinal angiogenesis at post-natal day (P) 5 and P10 for superficial and deep vessel network. In OIR, mice were kept in 75% oxygen from P7-P12 and returned to room air until P17. Vascular morphology was assessed in retinal flat mounts with isolectin (endothelium marker) staining. The effects of REV-ERBα on angiogenesis and endothelial cell (EC) function were analyzed in sprouting assays of aortic rings isolated from REV-ERBα KO mice and in human retinal microvascular endothelial cells (HRMECs) treated with REV-ERBα agonists (SR9009 and SR9011). Expression levels of potential REV-ERBα target genes involved in angiogenesis and antioxidant defense were analyzed in HRMECs and mouse retinal tissue.

Results: REV-ERBα KO retinas displayed normal developmental angiogenesis when compared to WT, with no significant difference observed in superficial vascular area at P5 or in deep layer vessel morphology at P10. In the OIR model, REV-ERBα KO mice showed a substantially greater area of retinal vaso-obliteration at both P12 and P17, as well as a substantially greater area of pathological NV at P17. REV-ERBα KO aortic ring explants had significantly reduced sprouting when compared to WT. Treatment with REV-ERBα agonists increased vascular tube formation in HRMECs in both normal and H_2O_2-treated conditions. Expression of Nrf2, a master regulator of antioxidant response, was significantly decreased in REV-ERBα KO retinas, while in HRMECs treated with REV-ERBα agonists, Nrf2 expression was increased.

Conclusions: Our results suggest that genetic deficiency of REV-ERBα may impede vascular regeneration in retinopathy, without impacting developmental angiogenesis, possibly through dysregulation of EC oxidative stress response.

CONTROL ID: 3710310

SUBMITTER (NAME ONLY): Markus Schranz

TITLE: Tracking of fibrosis growth in neovascular age related macular degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schranz, P.K. Roberts, M. Hollaus, G. Mylonas, S. Sacu, U. Schmidt-Erfurth, University Clinic for Ophthalmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|A.R. Motschi, M. Pircher, C.K. Hitzenberger, Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To track retinal fibrosis (RF) growth in a group of treatment naïve eyes with neovascular age related macular degeneration (nAMD) over a follow up period of one year using a polarization sensitive optical coherence tomography prototype (PS-OCT).

Methods: In this prospective observational study, patients with treatment naïve nAMD were included and treated according to a treat and extend regimen with intravitreal aflibercept.

At baseline and month 12 each patient underwent

PS-OCT & color fundus photography (CFP) imaging.

PS-OCT technology depicts retinal fibrosis based on its birefringence, where fibrotic lesions appear as columns of uniform axis-orientation.

A new algorithm was used to automatically detect retinal fibrosis in single B-scans and subsequently calculate the area of the fibrosis within the image.

Results: We analyzed 54 eyes with treatment naïve MNV due to AMD.

The mean age was 76.9 years, 62.5% of patients were diagnosed with type 1, 20.83% with type 2 and 16.67 with type 3 MNV, respectively.

At baseline only 1 eye showed retinal fibrosis, in this eye fibrosis size increased from 2.4mm^2 to 3.1 mm^2 (increase by 30%).

At year 1, fibrotic tissue was detected in 5 more eyes, within those eyes

mean fibrosis area increased significantly from 0 to 4.51 ± 1.15mm^2 ($p<0.05$).

Four out of 6 eyes with fibrosis were diagnosed with type 2 MNV.

Conclusions: In our study cohort around 10% of patients developed retinal fibrosis within one year.

Retinal fibrosis occurred more likely in type 2 MNV than in different MNV types.

This PS-OCT prototype combined with the new algorithm offers a precise and objective method to detect, measure and track fibrosis growth in nAMD.

CONTROL ID: 3710314

SUBMITTER (NAME ONLY): Hector Sandoval

TITLE: A Retrospective Study of Refractive Changes in Diabetic and Non-Diabetic Veterans in an Urban Setting

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Sandoval, I. Dersu, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|Y. Yang, W. Hou, Stony Brook University, Stony Brook, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Changes in refractive errors are common among diabetics with an increased prevalence of both hyperopia and myopia. However, it is unknown whether refractive errors are associated with changes in eye health or comorbid conditions. The purpose of this retrospective study was to characterize the refractive error changes among diabetic subjects in an urban setting and investigate the relationship between refractive error and eye health or comorbid conditions.

Methods: Medical records from 300 subjects were reviewed over an average time span of 9 years at Brooklyn Veteran's Affairs Hospital. Subjects were chosen with eye visits in 2021 with a 3-year minimum eye visit history and were excluded if they had previous cataract surgery. Spherical equivalents for baseline and last refractive errors were collected as well as cup-to-disk (C/D) ratios, glaucoma status, body mass index (BMI), and presence of hypertension, hyperlipidemia, coronary artery disease, chronic kidney disease. Chi-square t-test, multiple linear regression, and logistic regression were used for statistical analysis.

Results: Diabetics mean baseline refraction was -0.12 (1.68) right eye (OD) and -0.21 (1.79) left eye (OS) and mean last refraction was 0.13 (1.91) OD and 0.05 (1.88) OS. Non-diabetic subjects mean baseline refraction was -0.16 (2.11) OD and -0.22 (2.22) OS and mean last refraction was 0.08 (2.42) OD and 0.03 (1.12) OS. Refractive error changes among diabetic subjects were 0.25 (0.81) OD and 0.26 (0.88) OS and among non-diabetic subjects 0.24 (1.12) OD and 0.25 (0.86) OS. Using multiple regression, there was a statistically significant negative association between C/D ratio OD and OD refractive change ($\beta = -0.7$; $p = 0.05$) and between BMI and OS refractive change ($\beta = -0.03$; $p = 0.007$). Further analysis showed 1 unit increase in baseline OD/OS refraction was associated with a 0.33 ($p = 0.04$) and 0.31 ($p = 0.07$) decrease in BMI respectively. There were no statistically significant associations between refractive error differences and the remaining covariates.

Conclusions: In our study population, a refractive error shift was observed from myopia to hyperopia and refraction error difference was negatively associated with C/D ratio and obesity. No difference was found between refraction error difference among diabetic vs non-diabetic subjects and there was no statistically significantly association with other comorbidities.

CONTROL ID: 3710315

SUBMITTER (NAME ONLY): Yassin Nayel

TITLE: A modified photographic grading system for trachomatous scarring

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Nayel, B. Munoz, S.K. West, M.A. Wolle, Dana Center for Preventive Ophthalmology, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|Y. Nayel, American University of the Caribbean School of Medicine BV, Cupecoy, SINT MAARTEN (DUTCH PART)|H. Mkocha, Kongwa Trachoma Project, Kongwa, TANZANIA, UNITED REPUBLIC OF|

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ABSTRACT BODY:

Purpose: To assess a new modification of a previously published photographic four-step severity grading scale (S1-S4) for trachomatous scarring (TS).

Methods: A cross-sectional study was conducted of adult women in Kongwa, Tanzania. Images of the everted eyelids were taken and graded for the presence and severity of TS. The previously published severity scale for TS defines S3 as ‘conjunctival scarring occupying at least one third but less than 90% of the upper eyelid’. In the new modification, S3 was subdivided into two categories: 1) S3A - scarring covering at least one third but less than 50% of the upper eyelid conjunctiva, and 2) S3B - scarring covering at least 50% but less than 90% of the upper eyelid conjunctiva. The feasibility, reliability, and ease of use of this new grading modification were evaluated. This new categorization was then applied to images taken of the same women 3 years prior as part of a longitudinal study, to evaluate whether it could help detect prior undetected progression.

Results: A total of 5397 eyes of 2712 subjects were included in this study. We report on a subset of these eyes, 4412 eyes of 2217 subjects. Of the eyes graded, 761 (17.5%) were graded as S3. 87 of the S3 eyes were re-graded using the modified grading scheme; 29 (33.3%) were S3A, and 58 (66.7%) were S3B. 64 eyes were noted to also have been graded as S3 3 years prior. To evaluate whether splitting the S3 category might help detect more progression, these eyes were re-graded using the modified grading scheme; 22% of the eyes were noted to have progressed from S3A to S3B. Interobserver agreement using the modified grading system on a set of 36 images was an unweighted kappa of 0.60.

Conclusions: The modified photographic TS grading system is both easy to implement and reliable; it is also able to help detect more progression of scarring. This more nuanced modified TS grading system will be beneficial for future studies analyzing trachomatous scarring in photographs.

CONTROL ID: 3710317

SUBMITTER (NAME ONLY): Raghavi Sudharsan

TITLE: Disease-driven Prolactin Isoform Expression in Canine Inherited Retinopathies

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sudharsan, G.D. Aguirre, W.A. Beltran, Clinical Sciences & Advanced Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently identified a novel Prolactin transcript lacking the first exon (PRLΔE1) that is highly upregulated in photoreceptors (PR) in two non-allelic canine early-onset retinal degenerations (RD): PDE6β-RCD1 and RPGR-XLPRA2. Expression of PRLΔE1 in the two models correlated with the onset of cell death and increased steadily as retinal degeneration progressed. This short PRL isoform was also identified in human retinas. We have now expanded our study of expression of PRLΔE1 to other canine retinopathies, including RPGR-XLPRA1, NPHP5-LCA, RHO-ADRP, CNGB3-ACHM3, and in RPGR retinas post gene augmentation therapy.

Methods: Retinal PRL expression was probed by RNA in situ hybridization (RNA-ISH, RNAscope, ACDBio) performed on OCT embedded normal and mutant retinal sections. RPGR immunolabeling was performed following PRL RNA-ISH in RPGR -XLPRA1 and -XLPRA2 retinas that had received AAV-RPGR gene therapy.

Results: PR-specific expression of PRLΔE1 was observed in the following canine models of progressive inherited retinal degeneration (IRD): RPGR-XLPRA1 and NPHP5-LCA. In RPGR-XLPRA2 carrier retinas that undergo random X-inactivation, patches of PRLΔE1 expression correlated with patches of PR degeneration. However, we did not observe expression of PRLΔE1 24 hrs and 2 wks after light exposure that triggers acute rod loss in the canine RHO-T4R model of adRP. No PRLΔE1 expression was seen either in the CNGB3-ACHM3 retina that undergoes extremely slow cone degeneration. In RPGR-XLPRA1 and RPGR-XLPRA2 dogs subretinally-injected with an AAV-RPGR vector, PRLΔE1 was completely absent in treated PRs while robust expression was seen in diseased/untreated areas.

Conclusions: PRLΔE1 expression has now been found in 4 different canine models of IRD with a protracted loss of PRs. PRLΔE1 expression correlates with the onset of retinal degeneration and is sustained as PR cell death progresses. Corrective gene therapy in RPGR mutant dogs that prevented further retinal degeneration and PR cell loss also completely ceased PRLΔE1 expression in these retinas. Additional studies are underway to characterize the function of PRLΔE1 in IRD.

CONTROL ID: 3710318

SUBMITTER (NAME ONLY): Archana Jalligampala

TITLE: Successful late-stage disease treatment of P23H human RHO (hRHO) using ARCUS nuclease gene editing in a pig model of Autosomal Dominant Retinitis Pigmentosa (adRP)

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 1

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Jalligampala, J.M. Noel, O.N. Jacobs, A.L. Bradley, W. Wang, M.H. Jabbar, J. Prestigiacomo, M.A. McCall, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|N. Hasan, M.A. McCall, Anatomical Sciences and Neurobiology, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|J. Smith, V. Bartsevich, K. Viles, D. Jantz, Precision Biosciences Inc, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The P23H mutation in the rhodopsin (RHO) gene represents the most common form of adRP in North America. We previously showed successful gene editing using the ARCUS nuclease, RHO 1-2, a meganuclease, in a TgP23HhRHO pig model of adRP when treatment began at postnatal days, P3-7. This time-point corresponds to mid-stage human adRP, where many rod photoreceptors are present. However, from birth, untreated TgP23H pigs have no rod isolated ffERG response. To determine how late in adRP Rho1-2 gene editing continues to be successful, we evaluated its therapeutic efficacy when treatment began at P18 or P30 when fewer rods remain.

Methods: RHO 1-2 mRNA was packaged in a self-complementary AAV5 vector with a GRK1 promoter and was delivered subretinally (40 µl) to both eyes of TgP23H pigs at P18 and P30. Eyes from untreated animals served as control. The efficacy of $2x10^{10}$vg (n:eyes=8, P18; n=6 P30) and $6x10^{10}$vg (n=2 eyes, P30) on retinal structure and function were assessed at regular post injection intervals through 20 weeks post-injection (wpi). Fundus imaging, clinical exams, and OCTs assessed RHO 1-2 tolerability and retinal structure. Full-field ERGs assessed retinal function. At final time-point, the animals were euthanized and the retinal sections were processed for immunohistochemistry/confocal microscopy to assess the photoreceptor morphology.

Results: Treatment with RHO 1-2 was well tolerated, with no signs of an immune response. Treatment with both concentrations of RHO 1-2 (2 or $6x10^{10}$vg) rejuvenated a rod isolated ffERG b-wave response as early as 8wpi (~9uV). Mean b-wave amplitudes increased until 17wpi (~13-20uV) and were maintained through 20wpi. There is a strong correlation between rod isolated function and rod morphology. RHO 1-2 treated Tg P23H rods, have elongated inner and outer segments (IS/OS) and correctly localized rhodopsin. In contrast, untreated areas in the same retina or untreated Tg retinas have almost no rods and those that remain have no IS/OS and mislocalized rhodopsin.

Conclusions: Our results show that ARCUS nuclease RHO1-2 gene editing of the P23H hRHO allele rejuvenated rods even in late-stage disease. This approach arrested rod degeneration and rejuvenated rod structure and function in TgP23HhRHO pig model of adRP. These findings expand the therapeutic window for RHO 1-2 to retina late-stage adRP.

CONTROL ID: 3710319

SUBMITTER (NAME ONLY): Elisabetta Pilotto

TITLE: Hyper-reflective Retinal Foci as an in vivo imaging biomarker of microglia activation in Von Hippel-Lindau disease

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pilotto, T. Torresin, M. Bacelle, E. Midena, Department of Ophthalmology, University of Padova, Padova, ITALY|E. Pilotto, Padova University Hospital, ERN Eye Center, Padova, Padova, ITALY|G. Midena, E. Midena, IRCCS – Fondazione Bietti, Rome, Rome, ITALY|

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ABSTRACT BODY:

Purpose: Von Hippel-Lindau (VHL) disease is caused by a mutation of the VHL gene and characterized by the development of retinal hemangioblastomas (RH). Current pathophysiologic mechanisms of RH development and progression are still insufficient to predict RH behavior. VHL gene is involved in the cellular response to hypoxia and in many intracellular signaling pathways expressed both in angiogenesis and inflammation. Optical coherence tomography (OCT) allows to identify hyper-reflective retinal foci (HRF) known as aggregates of activated microglial cells as possible in vivo biomarker of local inflammation. The aim of the present study was to investigate the presence of HRF in patients with genetically confirmed VHL disease.

Methods: In this cross-sectional study, patients with VHL underwent complete ophthalmological examination and OCT with HRA + OCT Spectralis. HRF were manually identified and calculated in inner (IR), outer (OR) and full retina. Age-matched healthy subjects were enrolled as controls.

Results: 113 eyes of 63 VHL patients and 56 eyes of 28 healthy subjects were evaluated. HRF number was significantly higher in VHL than in controls in IR (28.06 ± 7.50 vs 25.25 ± 6.64, p=0.042). No difference was observed in OR and in full retina (OR: 7.73 ± 2.59 vs 7.95 ± 2.51, p = 0.599; full retina: 35.79 ± 8.77 vs 33.20 ± 7.47, p = 0.093).

Conclusions: Retinal microglial activation, documented by the increase of HRF, characterizes VHL eyes. The role of activated microglia in the retina of VHL eyes needs to be better investigated, mainly considering local VHL disease manifestations.

CONTROL ID: 3710324

SUBMITTER (NAME ONLY): Zia Chaudhuri

TITLE: Magnetic resonance imaging analysis of age-related distance esotropia in geriatric Indian subjects

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Chaudhuri, Department of Ophthalmology, Lady Hardinge Medical College, New Delhi, Delhi, INDIA|Z. Chaudhuri, P. Kataria, Vision Research Laboratory, Atal Bihari Vajpayee Institute of Medical Sciences & Dr Ram Manohar Lohia Hospital, New Delhi, Delhi, INDIA|U. Garga, Y. Singh, Department of Radio-Diagnosis, Atal Bihari Vajpayee Institute of Medical Sciences & Dr Ram Manohar Lohia Hospital, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Cross-sectional assessment of extraocular muscles (EOM) and adnexa by high-resolution surface coil orbital magnetic resonance imaging {(MRI), 1.5T Seimens Symphony} was performed in symptomatic Indian geriatric subjects with small-angle horizontal diplopia at distance, diagnosed as having age-related distance esotropia (ARDE). These MRI parameters was compared with similar image derivations in age matched asymptomatic and younger subjects.

Methods: 9 ARDE subjects (18 orbits) of average age 77.2±3.6 years (8 males) were imaged fixating at a central target. 2mm thick contiguous quasi-coronal image planes perpendicular to the orbital axis were analysed for EOM pulley locations, EOM cross sections and LR-SR band length while quasi-sagittal and axial planes were used to measure rectus EOM length, all by Image J software as per published norms. A comprehensive ophthalmic and neurological evaluation was performed in all subjects. The comparative control groups comprised 10 age matched asymptomatic subjects (20 orbits) of average age 67±4.7 years (7 males)–Group 1; 13 middle-aged subjects (26 orbits) of average age 48±4.7 years (7 males)–Group 2 and 12 young subjects (24 orbits) of average age 26±7.8 years (6 males)–Group 3.

Results: The average LR-SR band length in Group 1, 2 and 3 respectively were 12.8±3.2mm, 10.3±1.7mm and 8.7±1.8mm as compared to 14.4±2.8mm in the ARDE group (p=0.06, ≤0.0001, ≤0.00001). The angulation of the long axis of the lateral rectus (LR) muscle to the globe vertical axis was 23 ± 7.4^{o} (Group 1), 7.5 ± 8.8^{o} (Group 2) and 1.2 ± 7.9^{o} (Group 3) as compared to 22.4 ± 11.3^{o} in the ARDE group (p=0.8, ≤0.0001, ≤0.00001). The rectus EOM length was similar in all groups. Unilateral LR-SR band rupture was observed in one ARDE subject (Figure 1A-E).

Conclusions: The significant rectus EOM elongation and characteristic LR-SR band rupture observed in $2/3^{rd}$ cases of ARDE patients in the Caucasian population was not observed in a similar symptomatic geriatric Indian cohort. However, age-related progressive LR-SR band lengthening and increased angulation of the LR muscle to the globe probably accounted for the loss of LR functioning as an abductor at distance and consequent ARDE (Figure 2A-E).

CONTROL ID: 3710326

SUBMITTER (NAME ONLY): Ruben Hemelings

TITLE: Pointwise visual field estimation from opposing macular optical coherence tomography B-scan pairings using a 2D convolutional neural network

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Hemelings, J. Van Eijgen, E. Christinaki, I. Stalmans, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|D. Wong, J. Chua, L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|J. Van Eijgen, I. Stalmans, Katholieke Universiteit Leuven Universitaire Ziekenhuizen Leuven Campus Gasthuisberg Dienst Ophthalmology, Leuven, Flanders, BELGIUM|G. Garhofer, Medizinische Universitat Wien Universitatsklinik fur Klinische Pharmakologie, Wien, Wien, AUSTRIA|D. Wong, L. Schmetterer, Nanyang Technological University, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Deep learning approaches have been successfully applied to estimate visual field (VF) information from optical coherence tomography (OCT) scans. We retrospectively assessed the potential of pointwise VF estimation from opposing macular OCT B-scan pairs using a 2D convolutional neural network (CNN).

Methods: Data were retrospectively collected from two European glaucoma clinics (C1 and C2). Inclusion criteria consisted of paired SPECTRALIS® macular OCT volume scans (61 B-scans) and Humphrey Field Analyzer (HFA) 24-2 SITA Standard VF exams. C1 consisted of 1516 OCT-VF pairs from 850 eyes of 485 individuals while C2 encompassed 35 OCT-VF pairs from the same number of eyes. OCT-VF pairs of C1 were split as 60% training, 20% validation, and 20% testing, while the data from C2 was used as an external test set. The validation and test sets were filtered on HFA reliability indices.

Macular B-scans were assigned from 0 (most inferior scan) to 60 (most superior scan), with B-scan 30 intersecting the fovea (Figure 1). Four opposing B-scan pairings were used as model input to a custom ResNet-50 CNN that was adapted to the prediction of 52 continuous values. The four experiments were named after their B-scan pairing: 00-60, 10-50, 20-40, and 30-30. Individual models were ensembled through prediction averaging. Model performance was evaluated using Pearson’s r, as well as the percentage decrease in mean absolute error from baseline (MAEdecr). The latter was defined as the MAE when the mean value per VF point would be predicted.

Results: Baseline MAE for the test sets in C1 and C2 were 7.57dB and 9.38dB, respectively. For C1, the 10-50 B-scan pair performed the best [r=0.71(0.65-0.76), MAEdecr=33%], although the difference with 00-60 and 20-40 setups was not significant. The CNN trained with 30-30 B-scan pairs performed significantly worse [r=0.65(0.58-0.71), MAEdecr=29%]. Prediction averaging yielded the best performance [r=0.73(0.68-0.78), MAEdecr=35%]. Performance on the 32 OCT-VF data points of C2 was significantly lower.

Conclusions: Opposite macular B-Scan pairs performed similar in the task of 52 HFA 24-2 SS threshold value estimation using a custom 2D CNN. The middle B-Scan that intersects the fovea performed significantly worse. Future experiments should investigate the added-value of including all B-Scans using a 3D CNN for automated VF estimation.

CONTROL ID: 3710329

SUBMITTER (NAME ONLY): Andres Angel Calderon-Garcia

TITLE: Evaluation of gene expression in conjunctival epithelial cells associated with contact lens wear and discomfort.

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Calderon-Garcia, L. Valencia-Nieto, C. Valencia-Sandonís, M. Blanco-Vázquez, A. López-de-la Rosa, I. Fernández, C. García-Vazquez, C. Arroyo-Del Arroyo, M. González-García, A. Enriquez-De-Salamanca, IOBA-Institute of Applied Ophthalmobiology, University of Valladolid, Valladolid, SPAIN|I. Fernández, M. González-García, A. Enriquez-De-Salamanca, CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine), Carlos III Health Institute, Valladolid, SPAIN|

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ABSTRACT BODY:

Purpose: To confirm, in a larger population, results from a study of conjunctival epithelial cells gene expression associated to contact lens (CL) wear (CLW) and discomfort (CLD).

Methods: Thirty-six subjects were recruited in this new study in order to complete the data from the 24 ones enrolled in a previous study done by our group (López-de la Rosa et al., Ocul Immunol Inflamm, 2019). Therefore, a total of 60 subjects were included in this analysis: 40 CLWs, further divided into 20 asymptomatic CLW (ACLW) and 20 symptomatic CLW (SCLW) according to the CLDEQ-short form, and 20 non-CLWs. The exclusion criteria were extended or continuous CL wear (overnight use) and the presence of dry eye disease. CL wearers had to be CL users for at least 6 months before being included in the study. Conjunctival impression cytology was used to collect bulbar conjunctival epithelial cells. Expression of 84 genes related to neuropathic and inflammatory pain was analysed by RT-PCR using a commercial PCR array. The effect of CL wear and discomfort between non-CL and CL-wearers and between ACLW and SCLW was analysed. Additionally, a gene set enrichment analysis was performed in order to assign biological meaning to the genes differentially expressed.

Results: 6 genes were found to be significantly upregulated in the CL wearers compared to the non-wearers: CD200, EDN1, PTGS1 and TNF, involved in modulation of pain responses, P2RX7 related to pain conduction, and GRIN1, involved in synaptic transmission. Regarding CLD, 11 genes were found to be significantly downregulated in SCLW subjects compared to ASCLW: BDKRB1, DBH, PDYN, PTGS1 and TNF, related to pain responses modulation, CACNA1B, GRIN1, GRM1 and HTR1A, related to synaptic transmission, and ADORA1 and P2RX3, involved in pain conduction.

Conclusions: The present study confirms previous findings of the increased expression of CACNA1NB and PTGS1 genes in conjunctival epithelium associated with CLW, and also includes the finding of EDN1, P2RX7 and TNF upregulated genes. Additionally, this study also confirms the previously reported alteration in ADORA1, BDKRB1, CACNA1B, HTR1A, PTGS1, and PYDYN genes associated with CLD. Additionally, DBH, GRIN1, GRM1 and TNF genes have been also found to be significantly altered in CLD. CL wear and CLD might be responsible for, or related to, changes in several pain-related gene expression in conjunctival epithelial cells.

CONTROL ID: 3710330

SUBMITTER (NAME ONLY): Jingjing Jiang

TITLE: Botulinum Toxin A for Horizontal Concomitant Strabismus in Chinese Children: A Pilot Study

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Jiang, L. Li, Department of Ophthalmology, Beijing Children's Hospital, CHINA|

Commercial Relationships Disclosure: Jingjing Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Li Li: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: For childhood strabismus, early surgical intervention improves both motor and sensory outcomes. Botulinum toxin type A (BTA) injection is an alternative to incisional surgery that is fast, less invasive, and preserves a more normal biomechanical construct. This study was undertaken to assess recruitment potential for a randomized controlled trial to assess the safety and effectiveness of BTX-A for horizontal concomitant strabismus in children in our institution.

Methods: Records of all children, all less than age 18 years, treated with BTX-A for horizontal concomitant strabismus at Beijing Children's Hospital between December 2014 and December 2020 were reviewed retrospectively. Bilateral injections of BTX-A (Henli, 2.5u/0.1ml) were made into the medial or lateral rectus muscles under general anesthesia. Reinjection was permitted if initial alignment was not satisfactory. Patients were followed at least 12months after the last injection. Success was defined as a final misalignment <10 PD, or a final misalignment < 20 PD if there was evidence of binocular single vision.

Results: 71 patients were included. Mean age at initial treatment was 52.15 ± 39.31months. 52 had esotropia and 19 had exotropia. The mean follow-up period was 25.82±14.76 months. The mean number of botulinum toxin injection per patient was 1.27 ± 0.48. A total of 53 patients (74.65%) received one injection, 17 patients (23.94%) two injections, one patient (1.41%) three injections. 51 patients (71.83%) showed successful alignment at the last visit after the final injection. The mean amount of esodeviation before injection was 46.35 ± 20.7 PD at distance and 46.73 ± 20.53 PD at near. At the final follow-up, the mean esodeviation was 11.56 ± 14.88 PD at distance and 12.31 ± 14.47 PD at near ($p < 0.001$). The mean amount of exodeviation before injection was 44.21 ± 16.52 PD at distance and 46.84 ± 14.45 PD at near. At the final follow-up, the mean exodeviation was 16.32 ± 20.40 PD at distance and 17.42 ± 20.01 PD at near ($p < 0.001$). 20 patients (28.17%) developed transient ptosis after injections, vertical deviations were seen in 3 patients (4.23%), Subconjunctival haemorrhage was seen in 5 patients (7.04%). All these adverse events had resolved in all cases within 3 months.

Conclusions: BTA is an effective treatment for management of horizontal strabismus in children. Additional study of this unique cohort is warranted.

CONTROL ID: 3710339

SUBMITTER (NAME ONLY): John Kunzeman

TITLE: Assessing Inhibition of HUVEC Migration by a Novel VEGF-A and Angiopoietin-2 Bispecific Protein (RO-634)

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kunzeman, Southern Illinois University School of Medicine, Springfield, Illinois, UNITED STATES|J.L. Olson, A. Jones, J. Morgenstern, A. Strong, S. Droho, N. Mueller, M. Huvard, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|S. Bevers, Department of Structural Biology and Biochemistry, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|P.K. Kaiser, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|A.M. Khanani, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|J.S. Heier, OCB, Boston, Massachusetts, UNITED STATES|N. Gupta, Glenwood High School, Chatham, Illinois, UNITED STATES|A. Sinha, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|R. Bhandari, Eye Institute, Springfield Clinic LLP, Springfield, Illinois, UNITED STATES|L. Xu, Independent Research Consultant, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate how a novel vascular endothelial growth-factor A (VEGF-A) and angiopoietin-2 (Ang-2) bispecific protein (surrobody), RO-634, inhibits human umbilical vein endothelial cell (HUVECs) migration by assessing wound closure post exposure to VEGF-A in laboratory models.

Methods: HUVEC cells were purchased and grown in a 5% CO_2 humidified incubator at 37°C. Endothelial Cell Medium was used for optimal proliferation. Culture-inserts were used to evaluate HUVEC migration potential. Thirty-five thousand HUVEC cells were seeded into a bifurcated chamber and incubated overnight. Eighteen hours after initial seeding, the culture inserts were removed and cells were washed 3x with 1x PBS. After washing, media containing 40 ng of VEGF-A was added along with either bevacizumab, aflibercept, or RO-634. Cells were incubated with the desired medium for 12 hours. The percent change in wound closure was calculated using an image of the same area over the two designated timepoints. This process was repeated in triplicate.

Results: At 12 hours, HUVEC cells exposed to 40 ng of VEGF-A and aflibercept demonstrated a 70% reduction in VEGF-induced HUVEC migration compared to no treatment. HUVEC cells exposed to 40 ng of VEGF-A and bevacizumab demonstrated a 22% reduction in VEGF-induced HUVEC migration compared to no treatment. HUVEC cells exposed to 40 ng of VEGF-A and RO-634 demonstrated a 68% reduction in VEGF-induced HUVEC migration compared to no treatment. The difference in reduction in VEGF-induced HUVEC migration between aflibercept and RO-634 was insignificant ($p=0.93$). The results are shown in figure 1.

Conclusions: This data suggests that novel bispecific protein (surrobody), RO-634, is effective at preventing HUVEC migration post exposure to VEGF-A and is superior at preventing cell migration when compared with bevacizumab in this experiment. There is no statistically significant difference between aflibercept and RO-634 in preventing cell migration of endothelial cells.

CONTROL ID: 3710341

SUBMITTER (NAME ONLY): Eric Romanowski

TITLE: In Vitro Evaluation of REMOGEN® OMEGA for HLA-DRA and MMP-9 Modulation and Cytotoxicity to Human Ocular Surface Cells

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.G. Romanowski, N.A. Stella, R.M. Shanks, The Charles T. Campbell Ophthalmic Microbiology Laboratory, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Eric Romanowski: Commercial Relationship(s);Code F (Financial Support):TRB Chemedica | Nicholas Stella: Commercial Relationship(s);Code F (Financial Support):TRB Chemedica | Robert Shanks: Commercial Relationship(s);Code F (Financial Support):TRB Chemedica

ABSTRACT BODY:

Purpose: REMOGEN® OMEGA (REM) (TRB Chemedica) is a topical, preservative-free emulsion of essential fatty acids (eicosapentaenoic acid and docosahexanoic acid), vitamin E, glycerol, polyacrylic acid, and polymers that is used for treating symptoms and signs of dry eye and/or ocular surface damage, due to diseases such as superficial keratitis, Sjögren syndrome or primary dry eye syndrome. The goals of the current study were to determine whether pretreatment with REM affects the production of HLA Class II histocompatibility antigen (HLA-DRA) and matrix metalloproteinase 9 (MMP-9) by human corneal limbal epithelial (HCLE) cells after stimulation with lipopolysaccharide (LPS) as well as the overall cytotoxicity to HCLE cells. HLA-DRA and MMP-9 have been implicated as biomarkers of ocular inflammation in dry eye disease.

Methods: For the cytotoxicity assays, HCLE cells were incubated for 6 h with a 2-fold dilution series of REM (50%-0.1953%) or a mock solution. Cells were assessed for cytotoxicity using Presto Blue (Invitrogen). For the ELISA assays, HCLE cells were pretreated for 24 h with 50% REM or a mock solution, washed, then treated with or without LPS (10 mg/ml). ELISA assays for HLA-DRA (MyBiosource.com) and MMP-9 (Life Technologies-ThermoFisher) were carried out using the manufacturers' instructions. Statistical analysis (ANOVA with Dunnett's and Tukey's Post-test) was performed with GraphPad Prism.

Results: No significant differences in cytotoxicity were demonstrated among the mock treated and the REM concentrations at 6 h ($n=4$ for each concentration, $p>0.05$). REM pretreatment of HCLE cells stimulated with LPS significantly reduced MMP-9 production (85.1%; $n=4$, $p<0.01$) and HLA-DRA production (52.5%; $n=5$, $p<0.001$) compared to mock-pretreated cells.

Conclusions: After 24 h of pretreatment, REM significantly reduced MMP-9 and HLA-DRA production by the ocular surface HCLE cell line. Despite a high concentration up to 50% and extended exposure, there was no statistically significant loss of ocular surface cell viability caused by REM. REM appears to be nontoxic and anti-inflammatory to HCLE cells in vitro.

CONTROL ID: 3710342

SUBMITTER (NAME ONLY): Anton Hommer

TITLE: The effect of antibiotic eye drops on the nasal and pharyngeal microbiome in healthy subjects

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.B. Hommer, Hommer Ophthalmology Institute, Vienna, AUSTRIA|A.B. Hommer, G. Garhofer, M. Zeitlinger, A. Nussbaumer-Proell, D. Schmidl, Department of Clinical Pharmacology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|I. Klymiuk, Division of Cell Biology, Histology and Embryology, Gottfried Schatz Research Center, Medizinische Universitat Graz, Graz, Steiermark, AUSTRIA|S. Trajanoski, Core Facility Computational Bioanalytics, Medizinische Universitat Graz, Graz, Steiermark, AUSTRIA|

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ABSTRACT BODY:

Purpose: In clinical practice, topical ophthalmic antibiotics are commonly prescribed for numerous indications such as bacterial conjunctivitis, keratitis, blepharitis, dacryocystitis and also as prophylactic treatment after ocular surgeries. Due to the anatomical connection through the nasolacrimal duct it is possible that antibiotic eye drops also have an effect on the nasal and pharyngeal bacterial composition. This was investigated in the present study.

Methods: Twenty healthy volunteers were randomized into four treatment groups to receive different antibiotic eye drops or topical lubricants as control. Five subjects received gentamicin eye drops, 5 received ciprofloxacin eye drops, 5 received povidone eye drops unpreserved and 5 received povidone eye drops preserved with benzalkonium chloride (BAC). Subjects self-administered the assigned eye drops 4 times daily for one week. Nasal and pharyngeal swabs were taken before the first administration and after the last dose. Illumina next-generation sequencing (NGS) based 16S rRNA analysis was performed on all samples to gain information about the nasal and pharyngeal bacterial microbiome. Bacterial richness data were provided as operational taxonomic units (OTUs).

Results: None of the administered eye drops had a relevant effect on the pharyngeal microbiome. In contrast, a numerical increase in bacterial richness in nasal swabs was found after antibiotic treatment. In particular, nasal bacterial richness increased from 163 ± 30 to 243 ± 100 OTUs with gentamicin treatment ($p = 0.06$) and from 114 ± 17 to 144 ± 45 OTUs with ciprofloxacin treatment ($p = 0.31$). In the povidone group, nasal bacterial richness only changed from 177 ± 41 to 186 ± 63 OTUs ($p = 0.88$) while in the povidone + BAC group, it almost remained identical (148 ± 50 vs. 148 ± 39 OTUs, $p= 1.0$).

Conclusions: Although not statistically significant, the results of the present study point towards a potential effect of topical antibiotics on the nasal bacterial flora, while no effect on the pharyngeal microbiome was found. To confirm these results, larger studies including more subjects are needed.

CONTROL ID: 3710343

SUBMITTER (NAME ONLY): Sihame Doukkali

TITLE: Bilateral Sequential and Simultaneous Rhegmatogenous Retinal Detachments: Analysis of the Anatomical and Functional Outcomes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Doukkali, M. Hébert, E. You, M. Ghasempourabadi, S. Bourgault, M. Caissie, É. Tourville, A. Dirani, Centre universitaire d'ophtalmologie - Université Laval, Hopital du Saint-Sacrement, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: There are few reports regarding outcomes in sequential and simultaneous bilateral rhegmatogenous retinal detachment (BRRD) repair. We performed this retrospective cohort study to assess the anatomical and functional outcomes in BRRD repair.

Methods: Patients diagnosed with BRRD between 2014 and 2020 at the CHU de Québec – Université Laval were reviewed. We excluded patients with other etiologies (e.g., diabetic retinopathy, tractional retinal detachment (RD), exudative RD) and patients with previous vitreoretinal surgeries. There were 218 eyes of 109 patients. Of these, 86 (79%) were male and median [Q1, Q3] age at presentation for the first eye was 60 [54, 66] years. Data include patient demographics, preoperative characteristics, intraoperative management, single surgery anatomic success (SSAS), complications, and final pinhole visual acuity (PHVA) in logarithm of the minimal angle of resolution (logMAR).

Results: Of the 109 patients included, 92% (n=100) had sequential BRRD and 8% (n=9) simultaneous BRRD. Simultaneous BRRD patients were more likely to have high myopia (simultaneous: 78% vs. sequential: 23%; $p<0.001$) and half of them (n=5, 56%) had unilateral symptoms only. Between first and second eye RD, median [Q1, Q3] duration of symptoms was shorter for the second eye compared to the first (first: 7 [3, 15] days vs. second: 4 [2, 10] days; p=0.028). Second eyes also had less retinal tears (first: 2.94 ± 2.76 tears vs. second: 2.38 ± 1.79 tears; p=0.031) and better median [Q1, Q3] PHVA at presentation (first: 0.46 [0.14, 2.30] vs. second: 0.24 [0.06, 0.95]; p=0.012). SSAS was 92% (n=100) and 93% (n=101) for the first and second eye, respectively (p=1.00). Both eyes improved visual acuity with comparable PHVA at 3 months (first: 0.30 [0.14, 0.48] vs. second: 0.34 [0.13, 0.70]; p=0.36). Final PHVA was however better for the first eye (first: 0.14 [0.04, 0.30] vs. second: 0.20 [0.04, 0.43]; p=0.010). Complication rates were similar between both eyes (first: n=1, 1% vs. second: n=2, 1.8%).

Conclusions: In this BRRD cohort, SSAS was similar for both eyes. The subsequent eye was more likely to be treated earlier with less advanced presentations, but at 3 months, PHVA was not significantly different between eyes. Difference in final PHVA may be attributable to longer follow-up in first eyes.

CONTROL ID: 3710346

SUBMITTER (NAME ONLY): Tzu-yu Chiu

TITLE: Dacryocystitis: an update on microbiology and drug susceptibility

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chiu, C. Lin, Ophthalmology, Kaohsiung Medical University Chung Ho Memorial Hospital, Kaohsiung, TAIWAN|T. Chiu, Kaohsiung Medical University School of Medicine, Kaohsiung, TAIWAN|C. Lin, Kaohsiung Municipal Siaogang Hospital, Kaohsiung, TAIWAN|

Commercial Relationships Disclosure: Tzu-yu Chiu: Commercial Relationship: Code N (No Commercial Relationship) | Chia-Ching Lin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: More accessible medical environments may change the microbiology of dacryocystitis. The aim of our study was to identify the changing trends in microorganisms in lacrimal sac infections and examine their susceptibilities against currently recommended antibiotics.

Methods: Patients who admitted under diagnosis of dacryocystitis between 2011 and 2021 at Kaohsiung Medical University Hospital, a tertiary medical center, were retrospectively reviewed. The pus cultures collected from these patients were then evaluated to determine the types of microorganisms and their antimicrobial susceptibilities.

Results: In this study, a total of 67 patients hospitalized with dacryocystitis were evaluated, which was more common in females than in males (83.58% vs 16.41%).

From 65 pus samples, 64 microorganisms were isolated. The rate of positive culture was 87.7% and mix culture was 10.76%. The proportion of gram positive and negative isolates was nearly equal (51.56% vs 46.88%). The three most frequently isolated microorganisms were Staphylococcus aureus (23.43%) followed by Pseudomonas aeruginosa (20.31%), Staphylococcus epidermidis (7.81%) and Escherichia Coli (7.81%). An incidence of oxacillin-resistance Staphylococcus species in was 65.21%. Sensitivity of common antibiotics for aerobic bacteria is 34.10% in ampicillin-sulbactum, 50% in cefazolin, 29.63% in erythromycin and 48.14% in tetracycline.

Conclusions: Staphylococcus species, especially S. aureus, is the major pathologic microorganism in dacryocystitis. Vancomycin, cefoperazone-sulbactum and imipenum are the most sensitive antibiotics against most common isolated microorganisms in our study. The high prevalence of oxacillin-resistance and increasing isolation of Pseudomonas aeruginosa, could provide us a reference for empirical antibiotics selection.

CONTROL ID: 3710347

SUBMITTER (NAME ONLY): Zsolt Ablonczy

TITLE: CCN5 gene delivery is beneficial in a sodium-iodate challenge model of dry age-related macular degeneration

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Ablonczy, S. Niles, C. Schillo, M. Patil, H. Patterson, Preclinical, Ora, Inc, Andover, Massachusetts, UNITED STATES|S. Im, K.M. Woo, W.J. Park, Olive Biotherapeutics, Gwangju, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Loss of vision in severe dry age-related macular degeneration (AMD) is secondary to retinal pigment epithelium and photoreceptor damage. The CCN family of matricellular proteins are key signaling molecules involved in many vital biological functions, including cell proliferation, angiogenesis, fibrosis, and wound healing. Recently, it has been shown that CCN5 (WISP-2) is efficacious in a laser induced choroidal neovascularization model. This is the first study assessing the efficacy of CCN5 gene delivery in a rat sodium-iodate challenge model.

Methods: Brown-Norway rats received a single 5 µL intravitreal or subretinal of either AAV2-GFP ($5*10^{10}$ vg/eye) or AAV2-CCN5 in two doses ($1*10^{10}$ or $5*10^{10}$ vg/eye). Naïve animals and intravitreally-delivered Met12 peptide (50 µg/eye) served as control. Sodium-iodate ($NaIO_3$) was injected intravenously 3 weeks following AAV injections. Electroretinography (ERG), fundus imaging, autofluorescence, and optical coherence tomography (OCT) was used to evaluate the condition of the injected eyes for up to 4 weeks after sodium-iodate challenge. At the conclusion of the study, eyes were collected for histology. Data were expressed as means ± SEM and analyzed using one-way ANOVA.

Results: No significant changes, other than the uniform expression of GFP across the retina in the AAV2-GFP group, was observed between AAV injection and $NaIO_3$ challenge. After $NaIO_3$ administration, lesions appeared on fundus images and on OCT in a week, and increasingly worsened till the end of the study in the AAV2-GFP group and ERG amplitudes gradually decreased for up to 50% of naive animals by day 28. In contrast, the high dose AAV2-CCN5 group performed just as well as naïve. The low dose AAV2-CCN5 group performed slightly but not significantly worse than the high dose group. Results with subretinally- or intravitreally-delivered AAV2-CCN5 were not significantly different in any applicable groups.

Conclusions: $NaIO_3$ challenge can reaibly induce RPE and photoreceptor loss and is considered to model these dry-AMD symptoms. Our study demonstrated that AAV-mediated delivery of CCN5 to the retina was tolerable and equally beneficial for protecting against damage induced by $NaIO_3$. These results pave the way to begin to utilize intravitreally- or subretinally-delivered CCN5 therapy for the treatment of severe dry-AMD and geographic atrophy.

CONTROL ID: 3710348

SUBMITTER (NAME ONLY): Jason Colasanti

TITLE: Investigating the role of miR-34a in choroidal neovascularization

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Colasanti, R.S. Apte, Ophthalmology, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Jason Colasanti: Commercial Relationship: Code N (No Commercial Relationship) | Rajendra Apte: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a leading cause of vision loss in the elderly, and its prevalence is growing rapidly due to the increasingly aging global population. Choroidal neovascularization (CNV) is the aberrant growth of blood vessels beneath the retina that characterizes the most severe form of AMD. Mechanisms underlying the improper vascularization of the choroid are not entirely understood. A handful of microRNAs become dysregulated in ocular tissue during the progression of AMD and of these miR-34a may play a significant role due to its involvement in many gene pathways relating to inflammation, angiogenesis, and cellular senescence. Although a positive correlation has been previously established between miR-34a and CNV in the ocular tissue of patients suffering from wet AMD, there has yet to be a causal link made between the two. Therefore, we hypothesized that the upregulation of miR-34a in ocular tissue with age promotes CNV.

Methods: To investigate the role of miR-34a in CNV, we used an experimental mouse model of laser-induced CNV. Further analysis using bulk-RNA sequencing analysis of choroidal cell lysates revealed downstream targets of miR-34a likely to be implicated in the progression of CNV.

Results: Using whole-body miR-34a$^{-/-}$ mice we found that CNV lesions were significantly decreased in the absence of miR-34a compared to wild-type controls. Additionally, preliminary RNA-seq analysis revealed genes that are potential downstream targets of miR-34a in the context of laser-induced CNV.

Conclusions: Ultimately, we found that miR-34a may promote CNV by downregulating key genes that regulate angiogenesis in the choroid. Investigating the underlying mechanisms of miR-34a in promoting CNV will lead to an improved understanding of AMD pathogenesis and may provide novel treatment strategies for this debilitating disease.

CONTROL ID: 3710349

SUBMITTER (NAME ONLY): Arathy Kartha

TITLE: Visual Wayfinding in people with Ultra Low Vision using Virtual Reality

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kartha, R. Sadeghi, G. Dagnelie, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|R. Sadeghi, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|T. Swanson, BaltiVirtual, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: People with ultra-low vision (ULV) use echolocation and white cane for navigation and wayfinding. There is very little information about how their limited vision can be useful in efficient and safe navigation in unfamiliar settings and environments. The purpose of this study was to develop and calibrate a virtual reality tool for assessing visual wayfinding in people with ULV.

Methods: 15 participants with ULV completed wayfinding tasks in three settings – a street crossing, a cafeteria, and a metro station in virtual reality. Each of these scenarios were presented under different levels of visual clutter to present a range of visual demands and cognitive loads. Task completion times and number of collisions were recorded. Habitual cane users (n=7) were tested with and without cane. Visual acuity was estimated for all participants using the Berkeley Rudimentary Vision Test.

Results: The mean number of collisions ranged from 0.7 to 5.3 among participants across different scenes. The number of collisions increased with increasing clutter and there was a significant association between the number of collisions and estimated visual acuity (R^2 = 0.6, $p<0.05$). Mean task completion times ranged from 25.6 to 87.2s across different scenes and was significantly associated with estimated visual acuities (R^2 = 0.75, $p< 0.005$). We did not observe a speed vs. accuracy trade-off probably because participants were asked to walk at their normal walking speeds. Participants had more total number of collisions without cane (80) than with cane (54) which was statistically significant ($p<0.05$). Similarly, the mean task completion times were higher for without cane (478.2s) compared to with cane (342.9 s) which was also statistically significant ($p<0.05$).

Conclusions: Overall, we found that performance in the wayfinding test presented in virtual reality was consistent with visual acuity of our participants with ULV and could be used as a reliable functional mobility assessment for ULV once calibrated. This test could also be used as a rehabilitation tool to improve wayfinding in people with ULV by training to reduce the number of collisions in the safety of virtual environment. Even though there were no real obstacles to detect, we found that using a cane provided an advantage for habitual users.

CONTROL ID: 3710358

SUBMITTER (NAME ONLY): Roger Goldberg

TITLE: Efficacy of intravitreal pegcetacoplan in patients with geographic atrophy (GA): 12-month results from the phase 3 OAKS and DERBY studies.

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate the efficacy of monthly or every-other-month (EOM) intravitreal pegcetacoplan compared with sham in patients with GA secondary to age-related macular degeneration.

Methods: OAKS (NCT03525613) and DERBY (NCT03525600) are phase 3, randomized, double-masked, sham-controlled studies. Enrolled patients were ≥60 years old, with best-corrected visual acuity ≥24 letters, and GA area between 2.5 and 17.5 mm^2, including foveal and extrafoveal lesions. The primary endpoint for both studies was change in GA lesion size from baseline to Month 12 measured by fundus autofluorescence. Safety measures included incidences of ocular and systemic adverse events.

Results: OAKS and DERBY enrolled 637 and 621 patients, respectively. OAKS showed statistically significant reductions in GA lesion growth vs sham in the monthly and EOM arms by 22% (p=0.0003) and 16% (p=0.0052), respectively. The results of DERBY did not reach statistical significance: pegcetacoplan decreased GA lesion growth vs sham by 12% (p=0.0528) and 11% (p=0.0750) in the monthly and EOM arms, respectively. In a prespecified pooled analysis, reductions were 17% (p<0.0001; nominal) and 14% (p=0.0012; nominal) in monthly and EOM arms vs sham. In a prespecified analysis of extrafoveal GA lesions, growth was reduced by 35% (p<0.0001; nominal) and 21% (p=0.0159; nominal) in OAKS and by 16% (p=0.0712; nominal) and 25% (p=0.0028; nominal) in DERBY in the monthly and EOM arms, respectively, compared with sham. In a prespecified analysis of foveal GA lesions, growth was reduced by 16% (p=0.0324; nominal) and 16% (p=0.0179; nominal) in OAKS and by 7% (p=0.3611; nominal) and increased by 1% (p=0.8993; nominal) in DERBY in the monthly and EOM arms, respectively, compared with sham.

Conclusions: Monthly and EOM pegcetacoplan met the primary endpoint in OAKS, with positive trends also observed in DERBY. Pegcetacoplan demonstrated greater efficacy in patients with extrafoveal lesions at baseline. Taken together with the positive results from the well-controlled phase 2 FILLY study, these findings support the efficacy of pegcetacoplan in slowing the progression of GA lesions.

CONTROL ID: 3710363

SUBMITTER (NAME ONLY): Mihai Mititelu

TITLE: Redefining the Spectrum of Pentosan Polysulfate Retinopathy: Multimodal Imaging Findings from a Cross-Sectional Screening Study

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mititelu, A. Dieu, S. Whittier, J.W. Pak, R. Voland, K. Boyd, J. Gottlieb, G. Crabtree, A. Domalpally, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|D. Giles, Obstetrics and Gynecology, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is growing evidence of a direct association between Pentosan polysulfate (PPS) (the only FDA approved oral medication for the treatment of interstitial cystitis) therapy and the development of macular changes. Using multimodal retinal imaging, we describe an expanded spectrum of findings among PPS users.

Methods: Thirty-nine participants who were current or recent users of PPS underwent a brief eye exam answered a comprehensive medical and ophthalmic questionnaire, including dosage and duration of PPS exposure. Multimodal imaging including color fundus photography, fundus autofluorescence (FAF) and spectral domain optical coherence tomography (SD-OCT) was obtained. Images were evaluated by expert graders at the Wisconsin Reading Center. Abnormalities were categorized as definitive toxicity (DT) if seen on both FAF and SD-OCT and questionable toxicity (QT) if seen on either FAF or SD-OCT.

Results: The mean PPS daily dose of the study cohort was 282mg (88-400mg), while the mean cumulative dose was 915g (19-3650g) over a mean period of 8.8 years (2 months-25 years). DT was identified in 24 (31%) of eyes and QT in 8 (10%) of eyes. A total of 16 (41%) participants had at least one eye graded as DT, while bilateral DT was seen in 8 (20.5%) participants. Retinal pigment epithelium (RPE) abnormalities (thickening and/or thinning) were present in all DT eyes. RPE atrophy was seen in 7 (18.0%) eyes, predominantly outside the central subfield. SD-OCT features include the presence of a flying-saucer sign and consistent interdigitation zone abnormalities ranging from thickening to disruption. FAF abnormalities were seen in 22 (91.6%) eyes, and in 18 (75%) eyes these were found outside the central subfield and extending beyond the arcades. Predominant hypoautofluorescence was present in 13 (54.1 %) eyes, compared to 3 (12%) eyes with predominant hyperautofluorescence and 5 (20.8%) eyes with a predominant mixed appearance.

Conclusions: A PPS retinopathy prevalence of 41% is higher than previously reported and suggests a wider phenotypic spectrum of structural abnormalities among PPS users. The RPE and outer retina are the most common areas of macular changes, with a constellation of findings often seen outside the macula. The subtle and atypical findings in this cohort should prompt clinicians to consider lowering the threshold for diagnosing PPS retinopathy.

CONTROL ID: 3710367

SUBMITTER (NAME ONLY): Sari Yordi

TITLE: Bacillary Detachment in Neovascular AMD: Incidence, SD-OCT Compartmental Features, and Response to Anti-VEGF Therapy in the HAWK Study

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yordi, K. Wise, L. Lunasco, H. Cetin, K. Talcott, S.K. Srivastava, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|J. Hu, R. Zahid, Novartis AG, East Hanover, New Jersey, UNITED STATES|S. Yordi, K. Wise, L. Lunasco, H. Cetin, K. Talcott, S.K. Srivastava, J.P. Ehlers, The Tony and Leona Campane Center for Excellence in Image-Guided Surgery and Advanced Imaging Research, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bacillary detachment (BD) is a unique optical coherence tomography (OCT) signature that has been traditionally described primarily in inflammatory disorders. A previous analysis identified BD in neovascular age-related macular degeneration (nAMD) in the Phase 2 OSPREY study. The goal of this analysis was to evaluate BD incidence, clinical features, and response to anti-vascular endothelial growth factor (VEGF) therapy in a large Phase 3 nAMD study.

Methods: This was a post hoc analysis of the spectral domain (SD)-OCT images collected during the 48-week anti-VEGF treatment period from the randomized clinical trial HAWK in participants with nAMD. BD was defined on SD-OCT as a hyporeflective space above a hyperreflective linear structure continuous with the ellipsoid zone (EZ) band (Figure 1). Characterization of compartmental parameters, including retinal metrics and retinal fluid volumes, was performed using a machine-learning-augmented feature extraction platform. Fluid contained within the BD was identified as subretinal fluid for this analysis. This hypothesis-generating analysis did not adjust for multiple comparisons and was treatment agnostic.

Results: A total of 72/656 eyes (11%) had BD at baseline on SD-OCT. Compared to eyes without BD at baseline, BD eyes demonstrated significantly higher mean central subfield thickness (CST, 498 µm vs 366 µm; $p<0.001$), total retinal fluid volume (1.14 mm^3 vs 0.53 mm^3; $p<0.001$), subretinal fluid volume (1.01 mm^3 vs 0.37 mm^3; $p<0.001$), macular total retinal fluid index (TRFI, 0.09% vs 0.05%; $p<0.001$), and lower EZ-retinal pigment epithelium (RPE) CST (2.42 mm^3 vs 4.64 mm^3; $p<0.001$), respectively. After a single anti-VEGF injection, resolution of BD was noted in 94.4% of eyes at Week 4.

Conclusions: BD was identified in a significant proportion of nAMD eyes and was associated with higher baseline fluid volumes and CST. Anti-VEGF therapy resulted in a rapid and dramatic resolution of BD lesions in nearly 95% of eyes with a single injection.

CONTROL ID: 3710373

SUBMITTER (NAME ONLY): Joseph Branco

TITLE: Archetypal Longitudinal Visual Field Analysis of Optic Neuritis and Idiopathic Intracranial Hypertension in a “Real World” Clinical Setting

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Branco, E. Solli, M.J. Kupersmith, Neurology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.R. Pasquale, M.J. Kupersmith, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|W. Jui-Kai, R.H. Kardon, Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

ABSTRACT BODY:

Purpose: We recently used archetypal analysis (AA), a form of unsupervised machine learning, to derive quantifiable patterns, or archetypes (AT), of visual field (VF) loss from the optic neuritis treatment trial (ONTT) and idiopathic intracranial hypertension treatment trial (IIHTT) datasets. Our purpose was to derive new AT models for VFs from clinic-based ON and IIH cases. For both ON and IIH, we hypothesized: 1. The new AT model would resemble our prior AT model; 2. Baseline AT1 (normal VF pattern) weight would be associated with outcome VF mean deviation (MD); 3. AA would reveal residual patterns of VF defects in eyes with MD≥-2.00 dB at outcome.

Methods: We derived two AT models: one based on 446 VFs from 142 patients with acute ON, and the other based on 798 VFs from 120 patients with IIH and VF loss (Fig. 1). We compared these ATs to the ONTT and IIHTT-derived ATs. We compared outcome MD values between patients with baseline AT1 weights above and below the mean using the Mann-Whitney U test. We assessed change in MD over time in each group using the Wilcoxon signed rank test. We determined the number of VFs with abnormal AT weights in eyes with MD≥-2.00 dB at outcome.

Results: For ON, the two ATs of greatest relative weight (RW; 52.7%, 6.32%) resembled those derived from the ONTT (40.2%, 9.43%). For IIH, the three ATs of greatest RW (51.8%, 8.50%, 7.11%) resembled those derived from the IIHTT (30.9%, 23.9%, 5.89%). For ON VFs with baseline AT1 weights < the mean, the improvement in MD (12.9 dB, $p<0.001$) was greater than for those with baseline AT1 weights > the mean (2.61 dB, $p<0.001$). Outcome AT1 weight and MD did not differ between the two groups. For IIH VFs with baseline AT1 weights < the mean, the improvement in MD (2.01 dB, $p<0.001$) was greater than for those with baseline AT1 weights > the mean (0.77 dB, $p<0.001$). On average, VFs with baseline AT1 weights > the mean reached better MD values (-1.26 dB vs. -3.69, $p<0.001$) at outcome than those with baseline AT1 weights < the mean (Fig. 2). For VFs with MD≥-2.00 dB at outcome, 19/45 ON and 44/88 IIH VFs had an abnormal AT.

Conclusions: AA identified reproducible and quantifiable patterns from “real world” IIH and ON VFs. Baseline AT1 weight is associated with VF outcome. AA can indicate residual defects in VFs at outcome.

CONTROL ID: 3710374

SUBMITTER (NAME ONLY): Lourdes Grassi

TITLE: Phenotypic Expression of the Optic Disc in Primary Open Angle Glaucoma

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Grassi, E. Bouris, E. Morales, J. Caprioli, Glaucoma, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|D. SALAZAR, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|A. De Gainza, Hospital Italiano de Buenos Aires, Buenos Aires, Federal District, ARGENTINA|

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ABSTRACT BODY:

Purpose: We performed a retrospective study to identify demographic and ocular characteristics associated with six identifiable optic disc phenotypes in Primary Open Angle Glaucoma (POAG) patients.

Methods: Records of patients from the UCLA Stein Glaucoma Division between 1997 and 2019 were reviewed; included were those with a diagnosis of POAG, one disc photo within two years of a visual field (VF), ≥ 2 VFs with Mean Deviation (MD) > -10dB, Pattern Standard Deviation (PSD) probability <0.05, and a Cirrus Optical Coherence Tomography (OCT) with optic disc area between 1.14 and 3mm^2. Poor quality images were excluded. The photos were classified independently by three masked glaucoma specialists into disc phenotypic subgroups, according to standard reference photographs: 1) Concentric rim thinning, 2) Focal rim thinning, 3) Acquired pit of the optic nerve (APON), 4) Tilted (with or without peripapillary atrophy (PPA)), 5) Extensive PPA, and 6) Broad rim thinning. Covariates included age, race/ethnicity, sex, family history of glaucoma, smoking status, hypertension, cardiovascular disease, diabetes, visual acuity (LogMAR), IOP, refractive error, number of medications, central corneal thickness (CCT), visual field MD and PSD, disc area and RNFL thickness. Multinomial Logistic Regression analysis included all covariates.

Results: In 420 eyes of 420 patients, phenotypes included 127 Concentric thinning (30%), 117 Focal thinning (28%), 95 Broad thinning (23%), 45 Tilted (11%), 22 Extensive PPA (5%) and 14 APON (3%). Variables with statistically significant differences ($p < 0.05$) between phenotypes included sex, race, age, refraction, mean PSD, disc area, RNFL. Phenotype traits of interest included 1) Females were more likely to have Focal Thinning, APON and Broad Thinning; 2) Asians were more frequently tilted; 3) African descent were more likely to have Concentric thinning; and 4) APON was less likely to have cardiovascular disease and diabetes.

Conclusions: This study reports six phenotypic classifications of POAG patients, with emergence of different and ocular and systemic differences between phenotypes. Future refinement of phenotypes should allow improved individualization of patient care and enhance genetic associations.

CONTROL ID: 3710378

SUBMITTER (NAME ONLY): Daniel Cohen

TITLE: Machine Learning-based Prediction for Development of New Hydroxychloroquine Retinopathy based on Quantitative Outer Retinal SD-OCT Features and Clinical Variables

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Cohen, G. Kalra, K.E. Talcott, S. Kaiser, O. Uguegbu, S.K. Srivastava, J.P. Ehlers, Ophthalmology, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|D. Cohen, G. Kalra, K.E. Talcott, S. Kaiser, O. Uguegbu, M. Hu, S.K. Srivastava, J.P. Ehlers, Ophthalmology, The Tony and Leona Campane Center for Excellence in Image-Guided Surgery and Advanced Imaging Research, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|M. Hu, Department of Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Identifying eyes without current hydroxychloroquine (HCQ) retinal toxicity that are at high-risk to progress to toxicity could facilitate clinician intervention for HCQ dosing modifications. The purpose of the current study is to analyze predictive capability of a machine learning (ML)-based model for identifying eyes that progressed to HCQ toxicity by using a combination of quantitative higher-order SD-OCT features and baseline clinical variables.

Methods: This was an IRB-approved retrospective cohort study of 371 subjects on HCQ without evidence of toxicity where data was collected at baseline and final screening visits. OCTs from all timepoints were analyzed with an automated multi-layer compartmental segmentation system to provide quantitative outer retinal parameters. A selection of baseline clinical features (i.e., cumulative HCQ dose, duration of therapy) and quantitative SD-OCT biomarkers (e.g., volumetric ellipsoid zone (EZ) integrity and compartmental measurements) were compared between eyes that progressed to toxicity (progressors) and eyes that did not progress (nonprogressors). A random forest classifier with 10-fold cross validation was trained using baseline features selected based on univariate analysis.

Results: This analysis includes 371 subjects on HCQ with 21 progressing to hydroxychloroquine retinopathy. Baseline features showed highly statistically significant differences in means between progressors and non-progressors: partial EZ attenuation percentage (9.4±8.7% vs 5.6±3.7 %; $p<0.0001$, panmacular ONL volume (3.4±0.6 mm3 vs 4.0±0.5 mm3 ; $p<0.0001$), panmacular EZ volume (1.0±0.2 mm3 vs 1.2±0.2 mm3 ; $p<0.0001$), ONL-RPE thickness 1 mm nasal to fovea (116.4±21.2 µm vs 128.6±17.8 µm; $p<0.0045$), and daily HCQ dose (5.3±1.4 mg/kg vs 4.8±1.5 mg/kg; $p=0.02$). The random forest classifier demonstrated a mean area under curve of 0.89 (0.77-0.94) with sensitivity and specificity of 90% and 80% respectively in identifying progressors.

Conclusions: Combining targeted quantitative SD-OCT biomarkers with HCQ dose enabled the development of a highly discriminating ML-based classification model for the prediction of progression to HCQ toxicity. Future research will be focused on analyzing this model in external datasets and prospective studies.

CONTROL ID: 3710382

SUBMITTER (NAME ONLY): Eyad Shihabeddin

TITLE: Transcriptomic evidence of stress and remodeling in a degenerating/regenerating Zebrafish model of Retinitis Pigmentosa

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shihabeddin, H. Wei, J. Wu, Ophthalmology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|E. Shihabeddin, A. Santhanam, J. O'Brien, Vision Science, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited retinal degenerative diseases, such as Retinitis Pigmentosa (RP), show progressive loss of rods and cones until the individual becomes blind. While rods are lost, downstream neurons are still functional and undergo remodeling as degeneration progresses. While individual cell types have been studied in retinal degenerative models, it remains unclear how the whole retina is affected. To better understand retinal plasticity during degeneration/regeneration (deg/reg), we generated and characterized a transgenic zebrafish (Zf) model expressing the P23H rhodopsin mutation. We hypothesize single cell analysis of P23H Zf will allow us to assess how each cell type is affected during the progression of RP.

Methods: Single cell RNA sequencing analysis was performed separately on WT and P23H retinas. TSNE clusters were generated through Seurat. Cytoscape, and String pathway analysis tools were used to identify pathways for each cell type.

Results: All cell types are found across WT and P23H TSNEs, however, P23H retinas display distinct differences in gene expression. Rods in the P23H retinas show higher levels of oxidative stress genes and markers involved in the misfolded protein pathway. Since Zf regenerate retinal neurons, P23H retinas maintain ~40% of rods compared to WT. Cones in the P23H model don’t undergo cell death, but express increased levels of stress. Retinal neurons downstream of photoreceptors show evidence of remodeling. Rod BPCs increases in genes involved in dendritic self-avoidance and decreases in genes involved in axon targeting. Horizontal cells (HCs) show increases in genes involved in axon remodeling. RGCs from P23H retinas show upregulation of genes involved with postsynaptic glutamatergic receptors. Surprisingly, cones in P23H retinas also have increased expression of genes regulating circadian rhythm.

Conclusions: Photoreceptor deg/reg impacts predominant functions of downstream retinal cell types. While rods are continuously deg/reg, downstream neurons display synapse remodeling activity. Rod BPCs and HCs undergo rewiring, implying a constant state of forming new synapses with newly formed rods. RGCs seem to upregulate their glutamatergic receptors so that there is increased sensitivity in the retinal circuitry. Overall, the retinal environment adjusts so that living photoreceptors may be utilized to maintain rod photoreceptor signal transduction.

CONTROL ID: 3710383

SUBMITTER (NAME ONLY): Davide Piccolo

TITLE: Investigation of ABCA4 missense variant plasma membrane trafficking in cell models.

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Piccolo, C. Zarouchlioti, J. Bellingham, M.E. Cheetham, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: A potential strategy to treat inherited diseases that are associated with protein misfolding is to correct folding, restore the three-dimensional structure and enhance traffic. Here we investigate the plasma membrane localisation of ABCA4 protein using an in vitro cell model, which could be used as a screen for drugs that positively affect folding.

Methods: The trafficking of the ABCA4 was investigated at 37^0C in vitro by transient transfection of HEK293 and CHO cells using plasmids encoding for the wild-type (WT)-ABCA4 protein and four missense variants, provided by Professor Molday, UBC, Canada. The expression levels of the proteins was assessed by Western Blot (WB) and the cell surface expression was evaluated by immunocytochemistry (ICC) using an antibody against an extracellular epitope. In order to determine whether the traffic and folding were temperature-sensitive, the same experiments were performed at reduced temperature (30^0C). A quantitative assay was developed to monitor the membrane protein plasma membrane traffic. Statistical analysis was performed with two-tailed Student's t-test.

Results: At 37^0C the expression level of the WT-ABCA4 assessed by WB did not show a significant difference to the missense variants. Plasma membrane staining was observed only in few cells expressing WT-ABCA4. When cells were grown at 30^0C, the steady-state protein levels and the plasma membrane signal of the WT and the missense variants were increased. The plasma membrane specificity of the quantitative assay and the ability to detect pharmacological rescue of protein folding was confirmed using WT rhodopsin (RHO) and the misfolding P23H-RHO variant. In this assay WT-ABCA4 showed an increase in plasma membrane signal compared to all the missense variants, except A1038V, suggesting it is not associated with mistrafficking.

Conclusions: Reduced growth temperature can enhance the plasma membrane traffic of WT and missense variants of ABCA4 in cultured cells, suggesting that some of these variants are temperature sensitive misfolding variants that might be amenable to pharmacological rescue. The assay we developed is able to quickly and robustly detect plasma membrane localization, which could be used as a surrogate marker for correct folding and trafficking, and has potential use for high-throughput screening of small molecules able to restore ABCA4 folding.

CONTROL ID: 3710384

SUBMITTER (NAME ONLY): Marlene Hollaus

TITLE: Early changes of photoreceptor layer thickness following surgery in eyes with epiretinal membranes analyzed by deep-learning

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hollaus, M. Georgopoulos, J. Iby, O. Leingang, H. Bogunovic, U. Schmidt-Erfurth, S. Sacu, Medizinische Universitat Wien Universitatsklinik fur Augenheilkunde und Optometrie, Wien, Wien, AUSTRIA|J. Brugger, Medizinische Universitat Wien Zentrum fur Medizinische Statistik Informatik und Intelligente Systeme, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To analyze short-term changes of mean photoreceptor thickness (PRT) on the ETDRS-Grid after vitrectomy and membrane peeling in patients with epiretinal membrane (ERM) using deep-learning.

Methods: Forty-eight patients with idiopathic ERM were included in this prospective study. Healthy fellow eyes served as control. Study examinations comprised best-corrected visual acuity (BCVA) and spectral-domain optical coherence tomography before surgery, 1 week, 1 month and 3 months after surgery. Mean PRT was assessed using an automated algorithm and correlated with BCVA and central retinal thickness (CRT).

Results: Regarding PRT, a significant decrease from baseline to week 1 in the central 1mm (38.23µm±6.88µm to 32.13µm±5.61µm, $p<0.001$), 3mm (34.52µm±4.09µm to 29.78µm±4.24µm, $p<0.001$) and 6mm (32.40µm±3.69µm to 28.17µm±3.72µm, $p<0.001$) disc area as well as a significant increase at month 3 in the 6mm (32.40µm±3.69µm to 32.99µm±2.60µm, $p=0.031$) disc area of the study eye compared to the fellow eye (at baseline 40.82µm±5.62µm, 36.29µm±4.61µm and 33.46µm±4.68µm in the 1mm, 3mm and 6mm disc area, respectively; at week 1 40.35µm±4.91µm, 36.79µm±3.63µm and 33.97µm±4.12µm in the 1mm, 3mm and 6mm disc area, respectively; at month 3 33.07µm±4.15µm in the 6mm disc area) were observed. Changes in PRT in the central 1mm, 3mm and 6mm disc area after 1 week correlated negatively with the change in BCVA (0.30±0.24 logMar to 0.25±0.17 logMar; $rs=-0.350$, $p=0.034$; $rs=-0.337$, $p=0.041$ and $rs=-0.343$, $p=0.038$, respectively) and CRT (449.90µm±78.97µm to 462.20µm±52.53µm; $rs=-0.604$, $p<0.001$; $rs=-0.399$, $p=0.013$ and $rs=-0.344$, $p=0.034$, respectively). Visual acuity increased significantly from baseline (0.30±0.24 logMar) to month 3 (0.15±0.16 logMar, $p<0.001$).

Conclusions: Application of an automated algorithm across a 6mm grid with different sections allows for a comprehensive evaluation of the photoreceptor layer in the macula. Early changes of PRT allow prediction about postoperative functional and even morphological outcomes.

CONTROL ID: 3710387

SUBMITTER (NAME ONLY): Andreia Goncalves

TITLE: Regulation of intracellular heme modulates retinal angiogenesis

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Goncalves, X. Liu, D.A. Antonetti, Department of Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|N. Santander, T. Arnold, Department of Pediatrics, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the heme transporter FLVCR2 cause Fowler syndrome, a prenatal lethal disease characterized by proliferative vasculopathy leading to glomeruloid bodies in the brain and retina. We hypothesize that intracellular heme content represents a completely novel regulator of angiogenesis regulating endothelial tip to stalk differentiation.

Methods: Primary culture of retinal endothelial cells (BREC) were used to test the effect of siRNA to FLVCR2. Cell proliferation was assessed by EdU incorporation or ki67 immunostaining. Tube formation was determined by Matrigel assay in vitro and in retinal explants ex vivo. Heme synthesis was inhibited by using succinylacetone (SA) and induced by 5-Aminolevulinic acid (5ALA). VEGF signaling and cleaved NOTCH product were determined by Western blot. Endothelial-specific knockout of FLVCR2 was achieved by Cdh5-Cre recombination in mice.

Results: Knockdown of FLVCR2 in BREC led to increased proliferation and tube formation, coincident with a 50% decrease in intracellular heme content. Inhibiting heme biosynthesis with SA was able to mimic the effects of FLVCR2 knockdown. Conversely, adding back the heme precursor 5ALA or membrane soluble hemin reversed the effects of FLVCR2 knockdown and SA, respectively. Decreasing intracellular heme levels by either FLVCR2 knockdown or SA did not alter VEGF signaling, nor did it alter mitochondrial function as measured by Seahorse. NOTCH signaling pathway was increased by FLVCR2 knockdown and blocking NOTCH cleavage with gamma-secretase inhibitor DAPT was able to completely prevent the increase in cell proliferation and tube formation. In retinal explants decreased intracellular heme levels promoted increased sprout length but only when provided after tip cell formation and initiation of angiogenesis. In a similar manner, inducing endothelial-specific FLVCR2 knockout at post-natal day 7 led to the formation of glomeruloid structures and hypoxia in the superficial capillary plexus of the retina. Additionally, systemic administration of SA lead to an underdevelopment of the deep capillary plexus in the retinas of wild-type mice.

Conclusions: Together, these results suggest that low levels of intracellular heme in retinal endothelial cells promote the stalk cell phenotype increasing proliferation and tube formation and reveal heme as a novel regulator of retinal angiogenesis.

CONTROL ID: 3710388

SUBMITTER (NAME ONLY): Darby Roberts

TITLE: An ex vivo porcine cornea-based assay as a model for predicting equine keratitis fungi drug sensitivity

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Roberts, C. Ludwig, M. Cullen, J.H. Salmon, B.C. Gilger, Department of Clinical Sciences, NC State University, Raleigh, North Carolina, UNITED STATES|M. Cubeta, Center for Integrated Fungal Research, NC State University, Raleigh, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fungal keratitis (FK) is an infectious disease of the cornea that is increasing in prevalence worldwide. To combat increasing prevalence and improve current therapies, broad-spectrum antifungal agents and models that reliably assess efficacy of topical applied drugs are needed. Current models such as in vitro minimum inhibitory concentration assays can be challenging to interpret due to the lack of established drug breakpoints for many fungal species. These in vitro methods may also fail to correlate well with in vivo application. The purpose of this research is to compare an ex vivo corneal model for antifungal drug efficacy to recent results from a gold-standard MIC assay, with the hypothesis that this method will provide an accurate evaluation of therapeutic efficacy that is better representative of fungal colonization and corneal infection.

Methods: Archived isolates of Aspergillus flavus, A. fumigatus, Fusarium falciforme, and F. keratoplasticum, sourced from equine FK patients at North Carolina State University, were used for this study. Disinfected porcine cadaver globes were inoculated via intrastromal injection with approximately 500,000 conidia of A. flavus, A. fumigatus, F. keratoplasticum, or F. falciforme. Corneas were excised and incubated in Dulbecco's Modified Eagle Cell Culture Medium (DMEM) with either amphotericin B (AMB), luliconazole (LUL), natamycin (NAT), or voriconazole (VOR) at a concentration equivalent to 0.0X, 0.25X, 1.0X or 2.0X of the previously reported MIC. Radial fungal growth was monitored by imaging corneas and measuring area of colonization by pixel count every 12 hours for 72 hours total.

Results: All antifungal drugs examined significantly inhibited growth of A. fumigatus and F. keratoplasticum at or below the MIC at all time points. With few exceptions, all drugs inhibited growth of A. flavus below the MIC at all time points. AMB did not inhibit growth of F. falciforme, while all other drugs inhibited growth at or below the MIC for all time points except for LUL at 24 hours.

Conclusions: Inhibition of radial fungal growth in corneas injected with conidia and incubated in AMB, LUL, NAT, or VOR corresponded well with in vitro MICs in each isolate. With few exceptions, ex vivo fungal growth was significantly inhibited at one-half of the established MIC.

CONTROL ID: 3710394

SUBMITTER (NAME ONLY): Zelia Corradi

TITLE: Antisense oligonucleotide-based rescue of complex splicing defects in ABCA4

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Corradi, L. de Rooij, R.J. Hitti-Malin, A. Garanto, R.W. Collin, F.P. Cremers, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|Z. Corradi, R.J. Hitti-Malin, R.W. Collin, F.P. Cremers, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|A. Garanto, Pediatrics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The ABCA4 gene, implicated in Stargardt disease (STGD1), has a high percentage of splicing altering pathogenic variants, some of which leading to complex defects. Antisense oligonucleotides (AONs) have shown promising results in targeting splicing altering variants. Here, we selected two regions in ABCA4, containing four variants, leading to complex splicing defects on which we performed AON-based rescue studies.

Methods: Three variants were selected in intron 13, i.e. c.1938-619A>G and c.1938-621G>A that lead to inclusion of a pseudoexon (PE2) on their own or together with a second PE (PE1), located upstream, and c.1938-514A>G that results in the inclusion of PE3 or PE3 and PE1 together (Figure 1). Three novel AONs were designed to target PE2 and PE3, while PE1 was targeted using a previously tested AON1 with adjustments in the sugar moieties (Sangermano et al. Genet Med. 21:1751-1760; 2019). Variant c.6148-84A>T in intron 44 was selected as it resulted in either inclusion of a short PE (PE4) or of a longer PE (PE5) together with exon 44 skipping. All AONs had a phosphorothioate backbone and a 2'-O-methoxyethyl sugar modification. AON efficacy was assessed using in vitro splice assays in HEK293T cells using midigene constructs containing the variants of interest. (Figure 1: Schematic representation of variants in intron 13 (a) and intron 44 (b) causing complex splicing defects. The blue squares represent the PE inclusions. In green, the positions targeted by the AONs used in the study are shown).

Results: Treatment with AON1 for all intron 13 variants successfully promoted PE1 exclusion. AON2 and AON3 efficiently corrected the splicing defects caused by variants c.1938-619A>G and c.1938-621G>A, including the PE1 insertion, while AON4 showed no effect. Aberrant splicing due to c.1938-514A>G was completely corrected by AON3 and partially (~80%) by AON4. Surprisingly, AON2, not targeting PE3 directly, was also able to partially correct PE3 insertion. For intron 44 splicing defects, AON5 showed a partial effect while AON6 was able to completely restore normal splicing.

Conclusions: AON-based splicing modulation is a promising approach to target complex splicing defects in ABCA4. Different variants localized in specific regions can be efficiently targeted by a single AON when the related PEs share part of their sequence.

CONTROL ID: 3710398

SUBMITTER (NAME ONLY): Sara Touhami

TITLE: Anatomic and functional prognosis of vitreo-retinal surgery in non-exudative uveitic retinal detachment.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Touhami, A. Mainguy, B. Bodaghi, Sorbonne Université, Paris, FRANCE|A. Mainguy, M. Weber, Ophthalmology, Nantes University, FRANCE|

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ABSTRACT BODY:

Purpose: Study the anatomic and functional outcomes of surgery in uveitic non-exudative retinal detachment (NERD).

Methods: Retrospective case series of consecutive eyes with uveitic NERD undergoing surgery between January 2012 and December 2019.

Results: 75 eyes of 70 patients were included. The etiology of intraocular inflammation causing NERD was infectious in 73.3% of cases, immune in 9.3% of cases, tumoral in 2.7% of cases and idiopathic in 14.7% of cases. Posterior and panuveitis accounted for 96.4% of included eyes. Proliferative vitreoretinopathy (PVR) was present in 28.2% of eyes at baseline. The first surgery consisted in vitrectomy alone, scleral buckling alone (SB) or both in respectively 88%, 4% and 8% of cases. Reattachment rate was 75 % after 1 surgery (100% in case of SB) and 89.3% after ≥ 2 surgeries. The mean best corrected visual acuity (BCVA) was 1.5±0.8 logMAR at presentation improving to 1.1±0.9 logMAR at the last follow up (36.6±23.5 months). At the last follow up, 66,6% of eyes reached a countable BCVA (≥20/400 Snellen). After multivariate analysis, the predictive factors of final BCVA≥20/400 were: having baseline BCVA≥20/400(OR=6.1,p=0.01), inactivity of baseline ocular inflammation (OR=0.2 for active inflammation, p=0.015) and absence of retinal detachment (RD) relapse during the follow up (OR=0.1 for RD relapse, p=0.001). The predictive factors of final retinal reattachment were: having baseline BCVA≥20/400(OR=11.3, p=0.05), and absence of relapse within the first 6 weeks of surgery (OR=0.1 for RD relapse, p=0.03).

Conclusions: When managed properly, uveitic NERD has a good anatomic outcome especially when SB is used. For the first time, presence of active inflammation at the time of RD seems to cause the poorest visual outcomes. This should urge physicians adopt the most adequate perioperative anti-inflammatory strategy.

CONTROL ID: 3710399

SUBMITTER (NAME ONLY): Ebrahim Abdul Shukkur

TITLE: Therapeutic efficacy of Tβ4/VIP as a combination treatment against hyperglycemia-induced changes in human corneal epithelial cells using real-time ECIS® monitoring

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Abdul Shukkur, H. Kani, T. Ebrahim, A. Stambersky, J. Win, Y. Wang, A. Ibrahim, T. Carion, G. Sosne, E.A. Berger, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Roughly 425 million people are diagnosed with diabetes, which is the leading cause of adult-onset blindness. Despite the prevalence of diabetic retinopathy, 70% of adult diabetic patients develop visually debilitating corneal complications, including impaired wound healing. Unfortunately, treatment for diabetes-induced corneal damage remains limited. The current project seeks to begin investigating a peptide-based combination therapy, thymosin β4 and vasoactive intestinal peptide (Tβ4/VIP), to restore high glucose-induced damage to the corneal epithelium.

Methods: The electric cell-substrate impedance sensing (ECIS®) system was used for real-time monitoring of barrier function and wound healing of human telomerase-immortalized corneal epithelial cells (HUCLs). HUCLs were seeded (60,000 cells/well) in DMEM/F12 media supplemented with 10% FBS, 1% pen/strep in a 96-well array plate. Upon confluency, cells were serum starved for 12-16 h before treatment with normal glucose (5mM; NG) or high glucose (25mM; HG) + Tβ4 (0.1%) and VIP (5nM). Total resistance of the HUCL monolayer across a range of frequencies (250-64,000 Hz) was measured over time to assess barrier integrity. For the wound healing assay, a precise electrical wound (250 μm diameter) was induced. Cell migration was monitored by recording the time required to reform a monolayer. To confirm these findings, Western blot was used to assess protein levels of select markers (ZO-1, occludin and claudin-1) associated with the corneal epithelial tight junction complex.

Results: Barrier integrity was significantly impaired under HG conditions and restored with Tβ4/VIP treatment; whereas, Tβ4 and VIP monotherapies were not effective. This was further supported by reduced levels of tight junction proteins after HG exposure compared to NG, which were enhanced with Tβ4/VIP treatment. Likewise, wound healing was significantly impaired under HG conditions as evidenced by reduced migration velocity. Remarkably, Tβ4/VIP significantly improved cell migration velocity despite HG conditions and restored barrier function similar to that observed under NG conditions.

Conclusions: These results support the premise that Tβ4 works synergistically with VIP to enhance the therapeutic activity with potential for significant impact regarding the treatment of diabetes-induced complications of the cornea.

CONTROL ID: 3710402

SUBMITTER (NAME ONLY): Dillon Brown

TITLE: Form deprivation (FD) and exogenous all-trans retinoic acid (atRA) result in similar myopigenesis and scleral phenotypes in mice

SESSION TITLE: Myopia: Mechanism of Emmetropization and Eye Growth

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Brown, C.R. Ethier, M.T. Pardue, Coulter Department of Biomedical Engineering, Georgia Institute of Technology College of Engineering, Atlanta, Georgia, UNITED STATES|D. Brown, Q. Paulus, M.T. Pardue, Center for Visual and Neurocognitive Rehabilitation, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|J. Yu, P. Kumar, M.A. Kane, Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, Maryland, UNITED STATES|M. Kowalski, J. Patel, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|J. Patel, Department of Orthopaedics, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual stimuli influence myopic axial elongation via a retina-to-sclera signaling cascade, ultimately triggering scleral remodeling and influencing biomechanics; however, it is still unclear which signaling molecules relay myopigenic cues across the posterior eye wall. Here, we show that ocular outcomes between mice exposed to FD and those treated with oral atRA are highly comparable, suggesting a role for atRA in myopigenic retinoscleral signaling.

Methods: Male C57 Bl/6J mice (4 wks of age) were subjected to unilateral FD (n=15), leaving the contralateral eye untreated (Contra; n=15). Additional mice received daily delivery of icing sugar pellets (Ctrl, 2.5 g/kg, n=11) or sugar+atRA (RA, 25 mg atRA/kg, n=17) via a voluntary feeding paradigm. Refractive error (RE) was measured prior to and at the conclusion of treatment (FD: 3 wks, RA: 2 wks). After sacrifice, sclerae were isolated and used to quantify either tensile stiffness (unconfined compression and biphasic modeling; Brown et al., J Royal Soc Int, 2020) or glycosaminoglycan (GAG) and DNA content (dimethylmethylene blue and picogreen assays).

Results: Contra and Ctrl eyes were not significantly different on any outcome measure, and all animals had comparable RE at baseline. Both FD and oral atRA caused relative myopia to develop vs. controls (FD: -4.3D, $p<0.001$; RA: -5.6D, $p<0.001$). The changes in RE were accompanied by significantly decreased scleral tensile stiffness (34% and 32% lower in the FD and RA groups vs controls, respectively, FD: $p<0.001$, RA: $p<0.001$). Neither the degree of myopia ($p=0.29$) nor decrease in stiffness ($p=0.92$) differed between atRA vs. FD. Neither scleral GAG nor DNA content significantly differed between any group.

Conclusions: FD, a myopigenic visual cue, and oral atRA both induce myopia and comparably alter scleral properties in mice. The unchanged scleral DNA content suggests oral atRA is not influencing biomechanics via altered cellular proliferation; thus, the decreased stiffness may be due to scleral remodeling. GAGs were hypothesized as a biomechanically relevant remodeling target that may overlap between the two treatments; however, GAG content of the entire sclera was not measurably affected by either treatment. Work is ongoing to better characterize scleral GAGs via immunohistochemistry and to measure atRA concentrations in FD-treated eyes.

CONTROL ID: 3710413

SUBMITTER (NAME ONLY): James Deom

TITLE: Retrospective analysis of the common uses of loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension in clinical practice

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Deom, The Dry Eye Center of North Eastern Pennsylvania, Pennsylvania, UNITED STATES|J. Deom, Hazleton Eye Specialists, Pennsylvania, UNITED STATES|S. Kannar, Kannarr Eye Care, LLC, Pittsburg, Kansas, UNITED STATES|P. Vollmer, Vita Eye Clinic, North Carolina, UNITED STATES|P. Vollmer, Synvenio Group, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: James Deom: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch & Lomb | Shane Kannar: Commercial Relationship(s);Code C (Consultant/Contractor):AbbVie (Allergan), Johnson and Johnson, Alcon, Cooper, Bausch & Lomb, Vision Source, Novartis, Osmotica | Patrick Vollmer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Use of a combination corticosteroid and antibiotic product is common in ocular inflammatory conditions for which corticosteroid therapy is indicated and there exists a risk of superficial bacterial infection. Combination loteprednol etabonate 0.5% and tobramycin 0.3% (LE/T) has been evaluated for blepharokeratoconjunctivitis in two trials, but there has been limited reporting on real-world use of this combination product. We report on the use of LE/T in our practices including prescribing patterns and outcomes.

Methods: This was a retrospective chart review conducted at 3 optometric practices in the USA. Data were collected from cases in which LE/T was used and data was recorded for the period commencing with therapy with a minimum of one follow-up visit (within 2 months). Data abstracted included patient demographics, diagnosis, LE/T dosing regimen, pre- and post-treatment ocular signs, and symptoms, intraocular (IOP) pressure measurements, adverse event (AE) reports, and visual acuity, and any notations as to resolution of baseline condition. Primary outcomes included IOP elevations and AEs.

Results: A total of 98 patient charts were extracted, and data from 87 patient charts (115 LE/T treated eyes) were included in the analysis. Mean (SD) years of age was 45.6 (19.7), most patients were white (83.9%), and just over half were female (58.6). Most eyes (94 of 115) had data for only one related follow-up visit; 20 had data for two. Common baseline conditions were conjunctival injury/corneal abrasion (25.3%), keratitis (19.5%), viral conjunctivitis (16.1%), and blepharitis/MGD (11.5%). The most common LE/T dosing regimen was one drop four times daily. Mean IOP (SD) at baseline was 15.1 (4.3) mm Hg and 15.8 (4.1) mm Hg at the first follow up visit. No adverse events were recorded, and there were no changes in visual acuity with treatment. Where recorded, most patients (88.2%) were noted as having their condition resolved or resolving at the first follow up visit.

Conclusions: LE/T appears to have been well-tolerated when used for the management of various ocular inflammatory conditions encountered in optometric practice. Most patient charts reflected the resolution of the baseline condition with the use of LE/T.

CONTROL ID: 3710415

SUBMITTER (NAME ONLY): Natalie Hudson

TITLE: Characterisation of three novel animal models of geographic atrophy

SESSION TITLE: Animal Models of Age Related Macular Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Hudson, J. O'Callaghan, C. Delaney, A. Reddy, K. Byrne, S. Doyle, M. Campbell, The University of Dublin Trinity College, Dublin, IRELAND|

Commercial Relationships Disclosure: Natalie Hudson: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey O'Callaghan: Commercial Relationship: Code N (No Commercial Relationship) | Conor Delaney: Commercial Relationship: Code N (No Commercial Relationship) | Avril Reddy: Commercial Relationship: Code N (No Commercial Relationship) | Kieva Byrne: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Doyle: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Campbell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recently, we have been developing novel approaches to elucidate the early initiating factors that may underlie retinal degeneration in the pathology of dry age-related macular degeneration (AMD), and specifically its end-stage Geographic Atrophy (GA). We have discovered that altered expression of a key tight junction component, claudin-5, found at the inner blood-retinal barrier (iBRB) can lead to an atrophy-like appearance in the retinal pigment epithelium (RPE). Here, we sought to further develop novel animal models with varying claudin-5 expression levels, and iBRB integrity, to assess the damage observed and downstream changes that lead to RPE atrophy.

Methods: We have developed three novel animal models that vary in the expression levels of claudin-5 and induce retinal degeneration within different time frames. These animal models are: 1) RNAi based inducible claudin-5 knockdown mice, 2) Cldn5+/- mice and 3) C57BL6/J mice sub-retinally injected with adeno-associated virus (AAV) vectors expressing shRNA targeting claudin-5. Each model has been characterised to determine the effect of constant claudin-5 suppression on retinal and RPE integrity at different time points in retinal degeneration. In-life imaging of mice was carried out by optical coherence tomography (OCT) to examine retinal and RPE integrity and fundus fluorescein angiography (FFA) to assess retinal blood vessel integrity. In addition, electroretinography (ERG) has been carried out to determine electrophysiological activity. Immunohistochemical, histopathological, protein and transcript analysis was undertaken following sacrifice to further characterise these models.

Results: Assessment of these three mouse models shows that RPE atrophy progression varies depending on the level and length of time of claudin-5 expression at the iBRB and is exacerbated when addition of high cholesterol chow was provided.

Conclusions: Each of the three models developed provide unique characteristics that enable us to determine changes that are arising at the varying stages of disease progression, which may aid us in understanding GA pathology in humans. Targeting the inner retinal vasculature by stabilising and regulating claudin-5 expression may have therapeutic potential for preventing GA onset and development.

CONTROL ID: 3710416

SUBMITTER (NAME ONLY): Rinki Ratnapriya

TITLE: Artificial neural network-based classification of Age-related Macular Degeneration using gene expression profiles.

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ratnapriya, H. Nakajima, D. Christl, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Rinki Ratnapriya: Commercial Relationship: Code N (No Commercial Relationship) | Hosei Nakajima: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Christl: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Gene expression dysregulation is emerging as a dominant model in complex diseases. However, accessing the transcriptome profiles in large disease and non-disease cohorts are challenging, which present significant limitation in identifying genes and pathways involved in the disease process using existing methods such as differential gene expression analysis. The purpose of this study was to apply machine learning methods to uncover gene expression signatures associated with Age-related Macular Degeneration (AMD).

Methods: RNAseq data from 453 donor retina belonging to normal and AMD patients were used to establish and test the model for AMD classification. We investigated three feature selection methods and tested seven machine learning models using 10 folds cross-validation to find the best model. To train the models, the data was randomly split into 70% training data and 30% test data. The training data was then further split for a 10 times cross validation repeated 5 times. Sensitivity, specificity, accuracy, and Matthews Correlation Coefficient (MCC) were used to compare the performance of the machine learning models. We used a combination of pathways analysis, co-expression regulation networks, and recursive feature selection methods to identify the candidate with higher discriminative power.

Results: Most classifiers performed well achieving 70-80% accuracy. Among seven machine learning models used, eXtreme Gradient Boosting (xgb) linear yielded the highest accuracy (82%) in differentiating the advanced AMD from controls based on 555 genes/features. The sensitivity and specificity for gene expression predictions to differentiate AMD from non-AMD was 80% and 82% respectively with an MCC score of 0.63. These features were enriched for genes in immune response, complement and extracellular matrix and connected to known AMD genes through co-expression networks and gene expression correlation.

Conclusions: Our work demonstrates the merits of machine learning approaches for disease classification and suggests the key role of gene expression changes in AMD despite a small patient population. Gene regulatory networks are sufficiently interconnected with individual genes having a small impact on the disease outcome. Thus, our method provides an opportunity to regain the holistic view of the AMD that is lost in experimentally tested reductionist approaches.

CONTROL ID: 3710417

SUBMITTER (NAME ONLY): Fatemeh Rajaii

TITLE: Single Nuclear RNA Sequencing of Thyroid Eye Disease Retrobulbar Fat Reveals Fibroblasts Undergoing Adipogenesis In Vivo

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Rajaii, J. Han, N. Mahoney, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|D. Kim, S. Blackshaw, Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|T. McCulley, Ophthalmology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Fatemeh Rajaii: Commercial Relationship(s);Code C (Consultant/Contractor):Horizon Therapeutics;Code I (Personal Financial Interest):Horizon Therapeutics | Dong Won Kim: Commercial Relationship: Code N (No Commercial Relationship) | Jeong Han: Commercial Relationship: Code N (No Commercial Relationship) | Timothy McCulley: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Mahoney: Commercial Relationship(s);Code C (Consultant/Contractor):Horizon Therapeutics | Seth Blackshaw: Commercial Relationship(s);Code F (Financial Support):Genentech

ABSTRACT BODY:

Purpose: Orbital fibroblasts are targets of the immune response in thyroid eye disease (TED). In vitro work has shown that in response to immune activation, orbital fibroblasts produce cytokines and undergo adipogenesis. In this study, we use single nuclear RNA sequencing (snRNA-Seq) to characterize and compare gene expression and cell types present in orbital fat isolated from control patients and those with TED.

Methods: We performed nRNA-Seq on retrobulbar fat from three control patients undergoing resection of prolapsed orbital fat and three patients with TED undergoing orbital decompression. TED patients had clinical activity scores ranging from 0-3.

Results: We identified multiple cell types in control patients and those with TED using snRNA-Seq, including fibroblasts and adipocytes (Figure 1a). TED patients have a higher proportion of adipocytes than controls (Figure1b), and TED-specific adipocytes expressed higher levels of adipocyte-enriched/specific genes, FKBP5 and PLIN5 (Figure 1c). TED patients show a reduced proportion of fibroblasts (Figure 1a) and reduced expression in fibroblast-enriched genes (Figure 2a). In addition, we identified fibroblast subtypes that express markers that we have described previously during adipogenic differentiation in vitro, such as PPARG and PDE3B (Figure 2b). In addition, gene expression changes in orbital fibroblasts undergoing adipogenesis match closely to our previous observations in vitro.

Conclusions: We demonstrate evidence of hyperplasia within orbital adipocytes and fibroblasts in TED patients. We identify in vivo changes in gene expression in TED orbital fibroblasts that are consistent with our current in vitro model of orbital adipogenesis.

CONTROL ID: 3710421

SUBMITTER (NAME ONLY): Bhavana Chhunchha

TITLE: Lens epithelial cell Prdx6 deficiency activates ROS-Inflammasome pathway-driven cell death

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Chhunchha, D.P. Singh, Ophthalmology and Visual Sciences, University of Nebraska Medical Center College of Medicine, Omaha, Nebraska, UNITED STATES|E. Kubo, Department of Ophthalmology, Kanazawa Medical University, Kanazawa, Ishikawa, JAPAN|

Commercial Relationships Disclosure: Bhavana Chhunchha: Commercial Relationship: Code N (No Commercial Relationship) | Eri Kubo: Commercial Relationship: Code N (No Commercial Relationship) | Dhirendra Singh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Augmentation of oxidative stress-induced inflammation due to deterioration of antioxidant defense with advancing age is suggested to be associated with aging-related blinding diseases. The multifunctional antioxidant protein Peroxiredoxin 6 (Prdx6) provides cytoprotection and delays lens opacity by regulating reactive oxygen species (ROS) homeostasis. Herein, we showed, for the first time, that Prdx6-deficiency in mouse (m) lens epithelial cells (mLECs) causes ROS-induced Nlrp3 inflammasome activation-mediated inflammatory cell death.

Methods: $Prdx6^{-/-}$ (a model for aging) and $Prdx6^{+/+}$ LECs-derived from Prdx6-deficient and wild-type of 12 months old mice lenses were treated or untreated with N-acetylcysteine (NAC) or Prdx6, and then exposed to H_2O_2 (0-100μM) for different periods. ROS levels were quantified by H2-DCF-DA dye and cell death was evaluated by LDH (a marker for pyroptotic cell death) and MTS assays. Western blot or ELISA and real-time PCR were used to monitor expression or activation of Prdx6, NF-κB, IκBα, Nlrp3 inflammasome (Nlrp3, ASC, caspase-1) activation, IL-1β, and gasdermin-D in $Prdx6^{+/+}$ and $Prdx6^{-/-}$ LECs lysates or cell culture supernatant. SN50, a NF-κB inhibitor was used to block NF-κB activation. Two-tailed Student's t-test and one–way ANOVA were used for statistical analysis.

Results: Compared to $Prdx6^{+/+}$, $Prdx6^{-/-}$ LECs bearing elevated ROS showed markedly increased expression and activation of Nlrp3 and inflammatory proteins; caspase-1, IL-1β, ASC, NF-κB and gasdermin-D with elevated caspase-1 activity, IL-1β secretion and gasdermin-D cleavage involved in cell death/pyroptosis. These factors and cell death were further increased in $Prdx6^{-/-}$ LECs in response to H_2O_2. Under these conditions, a supply of Prdx6 or NAC or SN50 to $Prdx6^{-/-}$ LECs attenuated ROS-driven aberrant activation of Nlrp3, the inflammatory factors, and therapeutically reduced caspase-1 activation, release of IL-1β and LDH, and suppressed cell death ($p<0.001$). Coupled with a significantly the lower vulnerability of $Prdx6^{+/+}$ LECs, these results revealed that Prdx6-deficiency caused ROS-dependent activation of Nlrp3 inflammasome assembly and pyroptosis in LECs.

Conclusions: Our findings underscore the importance of Prdx6 in the redox-signaling network of Nlrp3 inflammasome activation regulating LECs homeostasis as its deficiency is associated with ROS/Nlrp3 inflammasome activation-dependent pyroptotic cell death.

CONTROL ID: 3710424

SUBMITTER (NAME ONLY): Xiaoyu Tang

TITLE: A novel HIF1α inhibitor KC7F2 attenuates oxygen-induced retinal neovascularization

SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Tang, K. Cui, P. Wu, Y. Xu, X. Liang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: KC7F2 is a novel molecule compound that can inhibit the translation of hypoxia-inducible factor 1α (HIF1α). The purpose of the present study was to investigate whether KC7F2 played a role in oxygen-induced retinal neovascularization (RNV).

Methods: Oxygen-induced retinopathy (OIR) models in C57BL/6J mice and Sprague-Dawley rats were used for in vivo study. After intraperitoneal injections of KC7F2, RNV was detected by immunofluorescence and hematoxylin-eosin staining. Retinal inflammation was explored by immunofluorescence. EdU incorporation assay, cell counting kit-8 assay, scratch test, transwell assay and matrigel assay were used to evaluate the effect of KC7F2 on the proliferation, migration and tube formation of human umbilical vein endothelial cell (HUVEC) induced by vascular endothelial growth factor (VEGF) in vitro. Protein expression was examined by Western blot.

Results: KC7F2 treatment (10 mg/kg/d) in OIR mice significantly attenuated pathological neovascularization ($p=0.0005$), and decreased the number of preretinal neovascular cell nuclei ($p=0.0071$), without changing avascular area ($p=0.3583$), which showed the same trends in OIR rats. Consistently, after the KC7F2 intervention (10 μM), cell proliferation was inhibited in VEGF-induced HUVEC ($p=0.0172$), which was in agreement with the trend observed in retinas of OIR mice ($p<0.0001$). Meanwhile, KC7F2 suppressed VEGF-induced HUVEC migration ($p=0.0003$) and tube formation ($p=0.0135$), and decreased the density of leukocytes ($p=0.0027$) and microglia ($p=0.0001$) co-localizing neovascular areas in the retinas. Moreover, HIF1α-VEGF pathway activated in retinas of OIR mice and hypoxia-induced HUVEC, was suppressed by KC7F2 treatment.

Conclusions: The current study showed the anti-angiogenic effect of KC7F2 via HIF1α-VEGF pathway, suggesting that it might be an effective drug for RNV treatment.

CONTROL ID: 3710425

SUBMITTER (NAME ONLY): Elin Strachan

TITLE: Developing a Zebrafish Model of Dominant Optic Atrophy

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Strachan, B.N. Kennedy, N. O'Sullivan, SBBS, University College Dublin, Dublin, IRELAND|

Commercial Relationships Disclosure: Elin Strachan: Commercial Relationship: Code N (No Commercial Relationship) | Breandan Kennedy: Commercial Relationship: Code N (No Commercial Relationship) | Niamh O'Sullivan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic Atrophy (OA) is a hereditary neurodegenerative disease characterised by progressive sight loss. This is associated with the irreversible degeneration of retinal ganglion cells. Most cases are associated with dominant mutations in the gene OPA1 (optic atrophy 1), a protein essential for mitochondrial fission – many OA patient fibroblasts have previously been noted to have varying mitochondrial dysfunction. It is unclear why mitochondrial dysfunction leads to retinal ganglion cell death, and there is currently no treatment for OA. I aim to create a zebrafish model of optic atrophy in order to understand the pathogenic mechanisms leading to sight loss in this condition.

Methods: I have designed pairs CRISPR guides to target commonly mutated regions of the zebrafish Opa1 gene, to create a large deletion. This deletion is predicted to cause a loss of function in the resulting protein. These guides were injected into 1-4 cell stage zebrafish embryos, and I subsequently performed optokinetic response assays to determine the presence of a visual defect in the resulting crispants.

Results: I was able to validate the presence of the predicted deletion through PCR and sequencing. Optokinetic response assays revealed a significant reduction in visual acuity in 5dpf crispants compared to siblings without deletion events. I am in the process of raising a subset of the crispants to produce a stable heterozygous line to repeat and validate these experiments.

Conclusions:

I have designed and validated CRISPR guides to create a large deletion in the Opa1 gene. Crispants injected with these guides display a reduction in visual acuity consistent with sight loss seen in patients with loss of OPA1 function. This is a positive early indication this model could be used to study the pathogenicity of loss of function Opa1 mutations. The visual phenotype could additionally be used to screen for modulators of Opa1 function in future.

CONTROL ID: 3710426

SUBMITTER (NAME ONLY): Raghu Krishnamoorthy

TITLE: The Endothelin Receptor Antagonist Macitentan Acts through both Vascular and Cellular Mechanisms to Promote Neuroprotection of Retinal Ganglion Cells in Rodents.

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.R. Krishnamoorthy, B. Kodati, W. Zhang, D.L. Stankowska, Pharmacology and Neuroscience, NTERI, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|S.H. Chavala, CIRC Biosciences, Inc.,, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Raghu Krishnamoorthy: Commercial Relationship: Code N (No Commercial Relationship) | Bindu Kodati: Commercial Relationship: Code N (No Commercial Relationship) | Sai Chavala: Commercial Relationship: Code N (No Commercial Relationship) | Wei Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Dorota Stankowska: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The endothelin system has been shown to be a contributor to neurodegeneration in rodent models of glaucoma. The purpose of this study was to determine if the endothelin receptor antagonist, macitentan, could promote neuroprotection by blocking endothelin-1 (ET-1) mediated vasoconstrictive changes as well as reduce RGC loss and axonal injury during ocular hypertension.

Methods: Adult retired breeder male and female Brown Norway rats were either untreated or treated with macitentan (5 mg/kg body wt) in dietary gels three days per week. Following the treatments, the rats were intravitreally injected in one eye with 4 ml of 500 mM ET-1 and the retinal vasculature was imaged in a Micron IV retinal imaging system. In a parallel set of experiments IOP was elevated in one eye of Brown Norway rats and the animals were treated with macitentan for 4 weeks in dietary gels. Pattern ERG analysis, RGC counts and PPD staining of optic nerve sections were carried out.

Results: ET-1 administration produced rapid vasoconstrictive effects in retinal arteries that occurred 5 min after intravitreal administration and recovery began to occur 20 minutes post-injection. Rats treated with macitentan in the diet abrogated the ET-1 mediated vasoconstrictive effects or delayed its onset. Following IOP elevation in rats, untreated rats exhibited a significant 32% loss of RGCs, compared to naïve rats. Dietary administration of macitentan (5 mg/kg) significantly ($p<0.01$) enhanced the survival of RGCs (5% RGC loss), significantly ($p<0.01$) protected against optic nerve axonal injury and a trend towards preservation of PERG amplitude (not significant).

Conclusions: Blocking both ET_A and ET_B receptors by oral administration of the endothelin receptor antagonist, macitentan, may protect from hypoxic injury as well as promote RGC survival during ocular hypertension. Endothelin receptor antagonists could potentially act through both vascular and cellular mechanisms to promote neuroprotection in glaucoma.

CONTROL ID: 3710432

SUBMITTER (NAME ONLY): Quan Nguyen

TITLE: Suprachoroidal triamcinolone acetonide injectable suspension for macular edema associated with uveitis: Outcomes by anatomic subtypes in PEACHTREE

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q.D. Nguyen, Byers Eye Institute, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|B. Kapik, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Quan Nguyen: Commercial Relationship(s);Code F (Financial Support):Clearside Biomedical Inc | Barry Kapik: Commercial Relationship(s);Code E (Employment):Clearside Biomedical Inc;Code I (Personal Financial Interest):Clearside Biomedical Inc | Thomas Ciulla: Commercial Relationship(s);Code E (Employment):Clearside Biomedical Inc;Code I (Personal Financial Interest):Clearside Biomedical Inc

ABSTRACT BODY:

Purpose: Triamcinolone acetonide injectable suspension for suprachoroidal use (SCS-TA) provides targeted steroid delivery to the choroid/retina while minimizing exposure in nontarget tissues. The PEACHTREE Study evaluated SCS-TA for macular edema (ME) secondary to noninfectious uveitis (NIU). In these post-hoc analyses, we evaluated the efficacy and safety of SCS-TA in subjects from PEACHTREE categorized by discreet anatomic subtype of uveitis.

Methods: In PEACHTREE, 160 NIU subjects with ME were randomized 3:2 to SCS-TA or sham procedure at baseline and week 12 and were followed for 24 weeks. Subjects diagnosed with NIU of any anatomic subtype, including anterior-, intermediate-, posterior-, and pan-uveitis, were included. Herein, efficacy endpoints, including changes in best corrected visual acuity (BCVA), central subfield retinal thickness (CST), and safety endpoints, including adverse event (AE) reports and intraocular pressure (IOP), were evaluated in subjects diagnosed with NIU in a single anatomic location.

Results: Of subjects in the SCS-TA and control arm, 13 vs 7 had anterior uveitis, 21 vs 15 had intermediate uveitis, 20 vs 11 had posterior uveitis, and 30 vs 24 had panuveitis. Across NIU subtypes, at week 24, SCS-TA-treated subjects showed significant improvements from baseline in BCVA ranging from 12.1 to 15.9 letters, while control subjects showed changes ranging from -1.6 to 9.1 letters, with significant between-treatment differences among subjects diagnosed with posterior- or pan-uveitis ($P \leq 0.024$). Similarly, changes in CST ranging from -120.1 to -189.0 µm were observed in SCS-TA-treated subjects vs -20.3 to 10.2 µm in control subjects, with significant between-treatment differences among intermediate-, posterior- and pan-uveitis subtypes ($P \leq 0.014$). Reports of AEs appeared similar between treatments by anatomic subtype. At week 24, SCS-TA-treated subjects showed IOP changes of 0.5 to 3.1 mm Hg compared to -1.2 to 1.7 mm Hg in control subjects.

Conclusions: Treatment with SCS-TA resulted in significant BCVA improvements from baseline in all anatomic NIU subtypes and was significantly better vs control in posterior- and pan-uveitis. Significant improvements in CST from baseline were observed vs both baseline and control for most anatomic NIU locations. Safety findings were comparable across discreet NIU subtypes.

CONTROL ID: 3710433

SUBMITTER (NAME ONLY): Evan Scott

TITLE: Assessing Off-Target Interactions Between Schlemm's Canal-Targeted Nanocarriers and the Cornea Endothelium

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Scott, M. Vincent, M. Johnson, Northwestern University, Evanston, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Evan Scott: Commercial Relationship: Code N (No Commercial Relationship) | Michael Vincent: Commercial Relationship: Code N (No Commercial Relationship) | Mark Johnson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Nanoscale drug carriers (i.e. nanocarriers) can be designed to both target as well as avoid specific cell types during therapy. With a goal of developing an IOP-lowering agent with minimal off-target effects, we designed FLT4-targeted latrunculin A-laden nanocarriers (t-LatA-NCs) that bind specifically to Schlemm's canal cells. This targeted glaucoma therapeutic enhances uptake compared to non-targeted nanocarriers (nt-LatA-NCs) and significantly lowers IOP in mice via intracellularly delivered LatA, a known cell-softening agent that decreases outflow resistance in the eye[1]. Here, we examine the toxicity and non-specific binding of these nanocarriers to corneal endothelial cells in vitro and in situ.

Methods: An immortalized bovine cornea endothelial cell line (BCE C/D-1b, ATCC, Manassas, VA) was exposed to t-LatA-NCs or free drug (effective LatA concentrations up to 2.5 mM) for 24 hours. Cytotoxicity was examined using the MTT (3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide) assay. Nine human corneoscleral rims from six donors were obtained from Eversight (Chicago, IL). Corneas were isolated from rims and were incubated with dye-loaded nt-NCs or t-NCs (18 µg LatA /ml), or PBS for 2 hours. Afterwards, single cell suspensions were prepared and analyzed by flow cytometry to examine whether the FLT4-binding peptide modulates the extent of micelle internalization by the cornea endothelium. NC uptake was quantified by determining the percentage of CD325 (N-Cadherin) positive cells that internalized the dye-loaded micelles.

Results: LatA was non-toxic to bovine corneal endothelial cells in vitro. The t-LatA-NCs consistently enhanced corneal endothelial cell viability above the free drug treatment group ($p<0.05$). Human corneal endothelial cells showed minimal uptake of NCs, and there was no significant difference between t-LatA-NCs and nt-LatA-NCs (see Fig., 2.3 ± 0.8% vs 1.7 ± 0.5%, respectively, $p>0.3$).

Conclusions: Our results demonstrate that our optimized cell softening glaucoma nanotherapy is non-toxic to bovine cornea endothelial cells in vitro. Furthermore, FLT4 targeting ligands did not enhance uptake by the human cornea endothelium in situ.

CONTROL ID: 3710436

SUBMITTER (NAME ONLY): Elizabeth Moloney

TITLE: Collagen type 1-containing PHEMA hydrogels support enhanced viability and biointegration of human keratocytes.

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.B. Moloney, T. Ritter, REMEDI, National University of Ireland Galway, Galway, Galway, IRELAND|A. Pandit, CURAM, National University of Ireland Galway, Galway, Galway, IRELAND|T. Ritter, College of Medicine Nursing and Health Science, National University of Ireland, Galway, IRELAND|E.B. Moloney, A. Pandit, College of Science and Engineering, National University of Ireland, Galway, IRELAND|L. Sánchez-Abella, B. Palla Rubio, D. Dupin, I. Loinaz, CIDETEC, Basque Research and Technology Alliance, Donostia-San Sebastián, SPAIN|M. González, E. Larra, AJL Ophthalmic, Alava, SPAIN|

Commercial Relationships Disclosure: Elizabeth Moloney: Commercial Relationship: Code N (No Commercial Relationship) | Laura Sánchez-Abella: Commercial Relationship: Code N (No Commercial Relationship) | Beatriz Palla Rubio: Commercial Relationship: Code N (No Commercial Relationship) | Maria González: Commercial Relationship: Code N (No Commercial Relationship) | Damien Dupin: Commercial Relationship: Code N (No Commercial Relationship) | Eva Larra: Commercial Relationship: Code N (No Commercial Relationship) | Iraida Loinaz: Commercial Relationship: Code N (No Commercial Relationship) | Abhay Pandit: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Ritter: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate if the production of PHEMA (poly(2-hydroxyethyl methacrylate)), a biomaterial previously used in artificial corneas, with biomacromolecules enhances viability and integration of human corneal keratocytes (HCK).

Methods: Several varieties of PHEMA-based hydrogels were prepared with 0.05% collagen (COL-I), 0.1% COL-I, 0.2% COL-I, or 0.1% COL-I in combination with 0.025% hyaluronic acid (HA). Samples were individually sterilized by beta-irradiation prior to use in vitro. HCK were seeded at a density of $2x10^4$ cells/cm^2 onto the top surface of hydrogel discs of different compositions. Viability at 5 days post-seeding was measured by quantifying ATP released from metabolically viable cells. Infiltration of cells into the porous biomaterial was quantified by counting the number of DAPI-stained nuclei in horizontal cryosections of HCK-seeded hydrogel buttons. To determine whether corneal cells exposed to the various hydrogels alter their secreted MMP profile, conditioned media was collected 6 days post-seeding for semi-quantification of MMPs using an antibody array dot blot approach.

Results: Only PHEMA-based hydrogels prepared in the presence of 0.1% COL-I alone supported statistically significant enhanced viability of HCK across three independent assays ($p<0.05$) when compared to viability on unmodified PHEMA hydrogels (n=6 samples per hydrogel, per assay; One-way ANOVA, with Dunnett's multiple comparison test). Preliminary data suggested that collagen-only modified PHEMA hydrogels (0.1% or 0.2% COL-I) encouraged deeper infiltration of cells into the biomaterial. MMP levels secreted from HCK grown on modified hydrogels were expressed as fold-change compared to levels observed from cells grown on unmodified samples ($p<0.01$, one-way ANOVA, with Tukey's multiple comparison test). MMP 1 and MMP 3 levels were significantly increased in all modified hydrogels samples, whereas MMP8, MMP10, and MMP13 remained constant across all samples. COL-I-only hydrogels elicited a significant decrease in MMP2 levels, whereas MMP9 levels were only significantly reduced when HCKs were cultured on hydrogels containing both HA and COL-I.

Conclusions: By supporting enhanced survival of HCK in vitro, PHEMA hydrogels containing 0.1% COL-I may allow for improved biointegration of hydrogel-based keratoprosthesis in diseased eyes.

CONTROL ID: 3710439
SUBMITTER (NAME ONLY): Brian Blais
TITLE: Modeling amblyopia treatment responses through principles of synaptic plasticity
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
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Commercial Relationships Disclosure: Brian Blais: Commercial Relationship: Code N (No Commercial Relationship) | Eric Gaier: Commercial Relationship(s);Code C (Consultant/Contractor):Luminopia, Stoke Therapeutics Inc.;Code P (Patent):Luminopia | Scott Xiao: Commercial Relationship(s);Code O (Owner):Luminopia;Code P (Patent):Luminopia
ABSTRACT BODY:
Purpose: Amblyopia is a common cause of visual impairment that results from unequal visual inputs during development. The imbalance is known to manifest through synaptic alterations in visual cortex that shift ocular dominance. Understanding the effects of amblyogenic drivers and their reversal with synaptic plasticity could enable improvements in amblyopia treatment efficacy. This study uses a specific model of activity-dependent neural plasticity, the Bienenstock, Cooper, and Munro (BCM) model, to compare the dynamics of amblyopia recovery at the neuronal level under several treatment protocols, including optical correction, patching, atropine penalization, and binocular therapies.
Methods: We use a model of the single cortical cell receiving natural scene stimuli from two channels representing each eye. Thalamocortical synaptic modification obeys the BCM learning rule where competition between the two eyes drives changes in ocular dominance. Anisometropic amblyopia is modeled by blurring input to the affected eye, and the fix (with glasses) rebalances the structure of inputs. Patching is modeled with unstructured activity (noise) in the fellow eye, and atropine penalization uses both noise and blurred input to the fellow eye. Binocular therapies involving contrast modification and dichoptic masks are modeled with established input filters.
Results: Imbalanced structure of inputs produce a long-lasting ocular dominance shift in favor of the fellow eye that recovers partially when input is re-balanced. We can drive recovery by shifting the difference between inputs in favor of the affected eye, and the rate of recovery increases with greater input disparity. The rate of recovery is greater with patch and atropine treatment models as compared to contrast disparity alone. Addition of dichoptic masks enhances the rate of recovery with the binocular treatment model, comparable to traditional therapies. The efficacy of binocular therapy is directly dependent on the size of the dichoptic masks and level of contrast disparity.
Conclusions: The BCM principles of activity-dependent synaptic plasticity are sufficient to model the ocular dominance shifts underlying the development of and recovery from amblyopia. The importance of the dichoptic masks and contrast disparity levels on the efficacy of the binocular therapy model suggests that these parameters require precise refinement to optimize amblyopia recovery.

CONTROL ID: 3710441

SUBMITTER (NAME ONLY): Harsh Bandhey

TITLE: Exploring Deep-Learning on SD-OCT images as an Effective Mitigation Technique for Hydroxychloroquine-Induced Retinal Toxicity

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Bandhey, Q. Gao, M. Pajic, Electrical and Computer Engineering, Duke University, Durham, North Carolina, UNITED STATES|A. Del Risco, J. Rathinavelu, School of Medicine, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|M. Hadziahmetovic, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is no precise method of individualized risk assessment and automated screening for macular retinopathy due to hydroxychloroquine (HCQ) induced retinal toxicity. We propose the explorative analysis of deep learning methods on spectral-domain optical coherence tomography (SD-OCT) to detect retinopathy before topographical fundus damage and further predict individualized SD-OCT-based risk assessment for HCQ toxicity.

Methods: Clinical Data from 73 patients on HCQ treatment, including SD-OCT, multifocal electroretinogram (mfERG), and autofluorescence (FAF) images, were collected and classified as normal vs. abnormal according to overall clinical assessment and mfERG results (as per Figure 1).

For detection of HCQ induced retinopathy, an Inception-v3 model was trained on augmented images from corresponding “normal” and “abnormal” SD-OCT images using transfer learning on ImageNet pre-trained weights. Performance improvement on Image preprocessing techniques such as Contrast Limited Adaptive Histogram Equalization (CLAHE) and Block Matching and 3-D (BM3D) Filtering were also analyzed.

For prediction of risk of HCQ toxicity, a Long Short Term Memory-based Classifier is proposed with the same structured data as shown below in Figure 2.

Results: For detection, on preprocessed images augmented from 228 “abnormal” SD-OCTs and 128 “normal” SD-OCTs with a 80-20 train-test split, the Inception-v3 model gave a precision of 0.72, recall of 0.92, F1 score of 0.81 and an Accuracy of 0.81 for detecting “abnormal” conditions.

Contrast Limited Adaptive Histogram Equalization (CLAHE) significantly improved the performance. However, Block Matching and 3D Filtering (BM3D) was too slow to be performed on an augmented dataset. For prediction, we had only three patients with advanced “bull’s eye” maculopathy presented over a period of time; thus, prediction analysis could not be performed.

Conclusions: Explorative analysis of deep-learning methods on SD-OCT shows that effective screening methods could be developed for early macular retinopathy detection due to HCQ toxicity with proper Image preprocessing. DL-based HCQ toxicity risk predictors require a larger dataset, and further analysis is required for this task.

CONTROL ID: 3710444

SUBMITTER (NAME ONLY): Alan Chew

TITLE: Clinical profile and visual outcome predictors in exogenous endophthalmitis in a referral center in Mexico City

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ledesma-Gil, R. Cano-Hidalgo, F. Graue-Wiechers, Retina, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|A. Chew, L. Haro-Morlett, G. Ornelas-Hall, E. Villalobos-Gonzalez, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: Exogenous endophthalmitis (EE) is the most serious complication of penetrating eye surgeries and open globe trauma (OGT). It is crucial to know the associated factors that will determine the final visual prognosis. The aim of the present study was to describe the epidemiological, clinical profile and visual outcomes (VO) predictors in patients with EE in a referral ophthalmology center.

Methods: Retrospective, observational clinical study. Patients diagnosed with EE between January 2018 to September 2021 were included. Data collected included demographic characteristics, endophthalmitis origin, culture samples, microbiological diagnosis, initial and final best corrected visual acuity (BCVA), and treatment received. Major outcome was change in BCVA after endophthalmitis treatment and associated factors. T-test and Fisher's exact test for statistical analysis were used.

Results: Seventy-three patients with EE were included. Surgery associated (SA) was the most common cause responsible for 39 cases (53.4%), followed by keratitis associated 18 cases (24.6%) and trauma associated (TA) 16 cases (21.9%). Gram-positive bacteria predominated in positive cultures (n= 35 [54.3%]). There was a statistically significant difference at mean age between TA group 41.1 ±18.7 years and SA group 59.9 ±20.9 years (p= 0.002).

Final logMAR BCVA in the TA group was 4 ±0.9 (Snellen, light perception [LP]) and in the SA group was 2.7 ±1.7 (Snellen, Hand Motion [HM]). Fourteen (35.8%) patients in the SA group had a final BCVA ≥ 20/400; whereas in the TA group all patients had a final BCVA ≤ CF.

Risk factors for non-improving BCVA after EE included OGT (p= 0.007) and initial BCVA of LP or worse (p <0.0001) in the SA group. There was no statistical difference in the final VO in patients that were treated with intravitreal injection (II) and those treated with vitrectomy (VTM) (p =0.40). Although 6 patients (75%) treated with VTM had an improvement in final BCVA compared with 12 (57.1%) of the patients just treated with II, this could be due to the sample number. We observed a tendency of diminishing cases of TA endophthalmitis after covid era, this could be associated with the isolation measures recommended.

Conclusions: Surgery associated EE had a better visual prognosis than those with trauma associated EE. The initial BCVA is a meaningful indicator for final VO, being favorable when is better than HM.

CONTROL ID: 3710447

SUBMITTER (NAME ONLY): Gregory Konar

TITLE: Knockdown of ptbp1 induces proliferation of immune cells in zebrafish retina

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Konar, Z. Flickinger, S. Sharma, W. Lyon, J. Patton, Biological Sciences, Vanderbilt University, Nashville, Tennessee, UNITED STATES|S. Nevills, Interdisciplinary Graduate Program in the Biomedical Sciences, Vanderbilt University, Nashville, Tennessee, UNITED STATES|T.S. Rex, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Polypyrimidine tract binding protein (PTB) is an alternative splicing factor that can alter splice site selection. Knockdown of PTB can convert cultured fibroblasts to neurons and glial-like cells into neurons in the cortex and dentate gyrus of adult mice. In the retina, knockdown of PTB was proposed to convert Müller glia (MG) into retinal ganglion cells, but this has been questioned due to apparent nonspecific uptake of AAV vectors. We sought to determine the effect of knockdown of PTB after intravitreal injection into zebrafish.

Methods: We injected antisense oligonucleotides (ASOs) targeting PTB into 1016tuba1a:GFP transgenic fish that express GFP in dedifferentiated MG and proliferating progenitor cells during retina regeneration. We then immunostained retinal sections with antibodies against GFP, against Lcp1, a marker of leukocytes and macrophages, and also antibodies against Proliferating Cell Nuclear Antigen (PCNA), and/or co-injection of EdU to detect proliferation.

Results: Intravitreal injection of antisense oligonucleotides (ASOs) targeting PTB in zebrafish produced a robust proliferative response 72 hours post injection. However, few, if any, of the proliferating cells detected after injection of ASOs targeting PTB co-localized with GFP in 1016tuba1a:GFP fish. At 1 week post PTB ASO treatment we detected co-labeling of Lcp1 and EdU in 31 of the 69 EdU^+ cells compared to just 1 of 5 EdU^+ cells in PBS treated retinas ($p=0.026$) or 3 of 8 EdU^+ cells in GFP ASO treated retinas ($p=0.049$).

Conclusions: In response to PTB knockdown, there is activation of immune type cells, which may include microglia and/or type 1 or 2 macrophages. Activation of the immune system aligns with previous work showing that PTB regulates inflammatory responses in mammals. Further experiments are needed to precisely identify the proliferating cells observed after ASO targeting of PTB, but our results support a role for inflammation in response to decreased levels of PTB.

CONTROL ID: 3710449

SUBMITTER (NAME ONLY): Raman Prasad Sah

TITLE: Impact of zone geometry on the introduction of myopic defocus in young eyes wearing multizone lenses.

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sah, D. Meyer, P.S. Kollbaum, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|X. Cheng, N.A. Brennan, Johnson & Johnson Vision Care Inc, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Multizone soft contact lenses (SCL) have been shown effective to control myopia progression in young eyes due to proposed introduction of myopic defocus. This project investigated the myopic defocus introduced and how this varied as a function of lens geometry.

Methods: Ten healthy young adult, myopic subjects were binocularly fitted with each of 4 contact lenses in a random order. Lenses included single vision (SV), concentric-ring dual-focus (DF), center-distance multifocal (MF), and a new multi-zone optical design with RingBoost^{TM} (RB) technology. A Shack-Hartmann aberrometer was modified to allow open field binocular viewing and capture full natural pupil wavefront aberrations of right eyes at 4 target vergences (TVs) between -0.25 and -4.00 D. Wavefront data were processed using a custom MATLAB program. Eye plus lens defocus was quantified as the difference between the measured refractive state (RS) and target vergence (TV) based on the average of all lenslet samples within each zone of the multizone designs throughout the entire pupil and compared to equivalent (theoretical) zone areas of SV. Defocus measures of all samples throughout the natural pupil were then used to calculate the percentage of the pupil that contained myopic defocused light for each lens. Myopia was defined as -0.50 D or more myopia, and hyperopia +0.75 D or more hyperopia.

Results: At -0.25 D TV on average only 11.44% of the pupil was myopic with SV, whereas 62.44%, 84.23%, and 50.39% of the pupil was myopic for the DF, MF, and RB designs, respectively. At -4 D TV, all lenses exhibited a systematic decrease in the percentage of pupil area with myopic defocus (SV: 2.81%; DF: 18.05%; MF: 5.32% and RB: 26.33%), but more of the pupil remained myopic with the multizone lenses compared to SV.

Conclusions: Multizone lenses introduced significant amounts of myopic defocus at all viewing distances, however, the magnitude and proportion of defocus was influenced by the lens zone geometry along with viewing distance dependent changes in pupil sizes. Lens with the RingBoost^{TM} (RB) technology retained relatively higher levels of myopic defocus at near viewing.

CONTROL ID: 3710450

SUBMITTER (NAME ONLY): Elizabeth Bierlein

TITLE: The role of retinal BDNF on the development of the dorsolateral geniculate nucleus

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Bierlein, M.J. Van Hook, Dept of Ophthalmology & Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

Commercial Relationships Disclosure: Elizabeth Bierlein: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Van Hook: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Brain-derived neurotrophic factor (BDNF) is a key regulator of nervous system plasticity with important roles in the development and maintenance. Within the visual system, the role of retinal BDNF transported to the dorsolateral geniculate nucleus (dLGN), the visual relay center of the thalamus, has not been characterized. Therefore, our goal was to determine whether retinal BDNF influences the development of the dLGN by selectively deleting retinal BDNF using Cre-lox technology.

Methods: We used a mouse line with Cre expression specific to the retina (Chx10-Cre) crossed with BDNFfl/fl mice to selectively delete BDNF from the retina. To test for visual system function differences between Chx10-Cre;BDNFfl/fl (cKO) and control (C57Bl/6J or BDNFfl/fl mice) of both sexes, we analyzed eye tracking abilities in an optomotor (OMR) task using stimuli of varying spatial frequency (n=46) or contrast sensitivity (n=31) and recorded electroretinograms (ERGs) to analyze any retinal differences (n=26 eyes). We also analyzed mEPSCs (n=41) as well as sholl analysis (n=21) in neurobiotin-filled dLGN thalamocortical (TC) neurons. Additionally, we analyzed binocular segregation using intravitreally-injected cholera toxin b (CTb) traces in young mice (n=10).

Results: Results from OMR showed that cKO mice spent less time tracking than controls (spatial frequency: p=0.02; cKO n = 24, ctr n = 22 mice, unpaired t-test; contrast sensitivity: p=0.02; cKO n = 18, ctr n = 13 mice, unpaired t-test), however, there were no differences in outer retinal light responses (p=0.7 A wave, p=0.9 B wave; cKO n = 10 eyes, ctr n = 16 eyes, unpaired t-test). cKO TC neurons had a higher frequency (p=0.02) and lower area in cKO mEPSCs (p=0.046), (cKO n = 19 cells, 9 mice; ctr n = 22 cells, 12 mice, nested t-test nested t-test). Sholl analysis of TC neurons indicated that cKO TC neurons were significantly less complex than control neurons (p=0.03, -7.183 ± 3.066 SEM; cKO n = 11 cells, 6 mice; ctr n = 10 cells, 4 mice). Additionally, CTb analysis suggested no significant differences in binocular segregation (p=0.97; cKO n = 5 mice; ctr n = 5 mice, unpaired t-test).

Conclusions: These results suggest that retinal BDNF plays a role in the structure and function of the dLGN. These results further our understanding of both developmental and neurodegenerative processes in the visual system.

CONTROL ID: 3710451

SUBMITTER (NAME ONLY): Frank Spors

TITLE: Field of View Measurements in Low Vision Telescopes

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Spors, N. Ghazaryan, B. McAllister, College of Optometry, Western University of Health Sciences, Pomona, California, UNITED STATES|

Commercial Relationships Disclosure: Frank Spors: Commercial Relationship: Code N (No Commercial Relationship) | Nane Ghazaryan: Commercial Relationship: Code N (No Commercial Relationship) | Bennett McAllister: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this study was to determine the accuracy of the visual field of view claims by low vision telescope manufacturers for commonly prescribed telescopes in a setting that can be easily duplicated in a clinical Low Vision practice.

Methods: The useful visual fields of 20 telescopes were determined based on measurements in one observer which had an intact visual field. The visual fields were measured by the investigator as dynamic visual fields using a tangent screen set up at 2, 4, and 6 meters and a standardized Goldmann target size of 2mm. To avoid experimental bias, the manufacturer-stated fields of view were not known by the investigators prior to concluding all measurements. Statistical analysis was conducted using repeated-measures ANOVA with Dunnett's multiple comparisons test and a P value of < .05 was considered statistically significant. A difference of more than 1 degree was considered clinically meaningful.

Results: Statistically significant differences were found between the manufacturer-stated visual field angles and the measured field angles for measuring distances of 2 m (P = .0.0004) and 4 m (P = 0.0.0183), but not for 6 m (P = 0.1431).

At 2 m, the measured visual field angles (mean 13.12 degrees, SD 3.802) were substantially larger than the manufacturer-stated visual field angles (mean 11.08 degrees, SD 3.163). This difference was clinically meaningful.

At 4 m, the measured visual field angles (mean 12.41 degrees, SD 3.766) were substantially larger than the manufacturer-stated visual field angles (mean 11.08 degrees, SD 3.163). This difference was clinically meaningful.

At 6 m, the measured visual field angles (mean 11.88 degrees, SD 3.449) were slightly larger than the average of the manufacturer-stated visual field angles (11.08 degrees, SD 3.163). This difference was considered clinically not relevant.

Conclusions: For the 20 measured telescopes, the manufacturer-stated field angles are appropriate for a distance of 6 m. At shorter distances of 2 m and 4 m, the manufacturer-stated visual field angles underestimate the measured visual field angles. Since telescopes are inherently designed for seeing distant objects, the manufacturer-stated visual field angles are reliable.

CONTROL ID: 3710452

SUBMITTER (NAME ONLY): Yi-Jie Peng

TITLE: Tight Adherent Feature on Optical Coherence Tomography may Predict Postoperative Visual Outcome in Epiretinal Membrane Eyes

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Peng, Ophthalmology, Taipei Tzu Chi Hospital, Taipei, TAIWAN|T. Lai, Ophthalmology, En Chu Kong Hospital, New Taipei City, TAIWAN|

Commercial Relationships Disclosure: Yi-Jie Peng: Commercial Relationship: Code N (No Commercial Relationship) | Tzu-Ting Lai: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the predictive parameter among preoperative measurements that best predicts postoperative visual outcome in the epiretinal membrane (ERM) surgery.

Methods: Thirty-three consecutive patients with idiopathic unilateral ERM patients between 2015 and 2018 were enrolled. Moreover, age-matched healthy eyes were selected as the control group. Based on preoperative optical coherence tomography (OCT), we further divided the patients with ERM into two groups: type 1, loosely attached ERM, and type 2, tight adherent ERM. We documented the vision and thickness of various retinal layers: nerve fiber layer, ganglion cell layer, inner plexiform layer (GCL+IPL), inner nuclear layer (INL), outer retinal layer (ORL), and retinal pigment epithelium/Bruch complex layer before and after the surgery. We analyzed the eyes that underwent combined ERM and cataract surgery or ERM surgery with subsequent cataract surgery. The association between postoperative visual acuity and these variables was analyzed using multiple linear regression analysis.

Results: We identified 11 eyes with type 1 adhesion and 22 eyes with type 2 adhesions. Both groups demonstrated significantly thicker GCL+ IPL thicknesses than the controls. The postoperative best-corrected visual acuity (BCVA) in type II patients was worse than type I pateints ($p=0.026$). The preoperative GCL + IPL and INL layers were significantly thicker in type II patients ($p=0.005$ and $p= 0.033$, respectively) than in type I patients. Multiple linear regression analysis showed that GCL+IPL thickness was an independent predictor of postoperative visual acuity (VA).

Conclusions: Idiopathic ERM demonstrated significantly thicker inner retinal layers (GCL + IPL and INL). However, the ORL thickness was similar between the normal eyes and ERM eyes. The preoperative GCL + IPL and INL layers were significantly thicker in patients with type II ERM than that in patients with type I ERM. Preoperative GCL + IPL thickness is an independent prognostic factor for the ERM surgery.

CONTROL ID: 3710453

SUBMITTER (NAME ONLY): Joost Brinks

TITLE: Sex Hormones in Males and Females with Active Central Serous Chorioretinopathy

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Brinks, E.H. van Dijk, R. Tsonaka, O.C. Meijer, C.J. Boon, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|C.J. Boon, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To assess the role of sex hormones in male and female patients with central serous chorioretinopathy (CSC), a disease with a pronounced male predilection.

Methods: A total of 206 chronic CSC patients (183 males, 23 females) and 59 healthy controls (29 males, 30 females) were enrolled. Serum testosterone, estradiol, albumin, and sex hormone-binding globulin levels were determined using immunoassays. The free fraction of testosterone and the free testosterone/estradiol-ratio were calculated.

Results: No differences in the levels of total testosterone and estradiol were observed between CSC patients and healthy controls. Albumin levels were found to be lower in male CSC patients compared to controls (controls 47.8 g/L, patients 46.0 g/L, adj. p = 0.006). Only in females with CSC, sex hormone-binding globulin levels were found to be lower (controls 94.2 nmol/L, patients 50.4 nmol/L, adj. p = 0.001), together with a higher free testosterone/estradiol-ratio (controls 0.06, patients 0.18, adj. p = 0.018).

Conclusions: In this study, we did not find evidence for a disturbance in sex hormone levels in males with CSC. The lower levels of sex hormone-binding globulin in females with CSC, leading to a disturbed free testosterone/estradiol-ratio, warrants further investigation into the role of androgens in females with CSC.

CONTROL ID: 3710455

SUBMITTER (NAME ONLY): Bilal AlWattar

TITLE: Relationship of Multifocal Electroretinographic Responses and Macular Layer Volume in Eyes Treated for Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.K. AlWattar, J.K. Patel, A.B. Fulton, J.D. Akula, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|B.K. AlWattar, A.B. Fulton, J.D. Akula, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M.I. Fonseca, A. Nouck-a-Nwal, Northeastern University, Boston, Massachusetts, UNITED STATES|P. Altschwager, Pontificia Universidad Catolica de Chile Facultad de Medicina, Santiago, CHILE|

Commercial Relationships Disclosure: Bilal AlWattar: Commercial Relationship: Code N (No Commercial Relationship) | Jagvi Patel: Commercial Relationship: Code N (No Commercial Relationship) | Mariana Fonseca: Commercial Relationship: Code N (No Commercial Relationship) | Alexandra Nouck-a-Nwal: Commercial Relationship: Code N (No Commercial Relationship) | Pablo Altschwager: Commercial Relationship: Code N (No Commercial Relationship) | Anne Fulton: Commercial Relationship: Code N (No Commercial Relationship) | James Akula: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is marked attenuation in the amplitudes of N1 and P1 in the mfERG responses of eyes with a history of severe (i.e., treated) ROP; N1 and P1 in eyes with a history of mild (i.e., untreated) or no ROP differ little from term-born controls (Altschwager et al., 2017). We aimed to determine the cellular origins of these previously reported deficits.

Methods: We measured the moment-by-moment association of response amplitude and the volume of retinal layers in the respective retinal regions stimulated by the standard 103 scaled hexagonal mfERG elements. Adolescent and adult subjects (N=45) participated. Each element was aligned to its corresponding area on the OCT; stimuli falling on the fovea and on the optic nerve head were excluded. The OCT volumes were segmented into “photoreceptor,” “postreceptor,” and “inner” retinal layers. Linear mixed-effects modeling was used to derive estimated coefficients (voltage/volume) for each layer throughout the full 80-ms standard epoch in subjects with (a) no history of ROP (N=26), (b) a history of ROP too mild to require treatment (N=15), and (c) severe ROP treated with laser photoablation (N=4).

Results: Overall, volume of the photoreceptor layer was attenuated while the inner layer was enlarged in the severe retinae. The modeling revealed no marked differences in the mfERG-to-OCT relationships among subjects with no history of ROP or a history of mild ROP. However, it suggested that the marked attenuation in the amplitudes of N1 and P1 in the mfERG responses of severe ROP subjects results mostly from a combination of decreased cornea-negative postreceptor potentials and a latency shift in cornea-positive postreceptor potentials that flatten P1 (but do not much change its implicit time). Also, because the contribution of the inner retina was most significant in the interval between the prominent troughs/peaks of the intact response, it did not rescue N1 and P1 amplitudes. Across all groups, photoreceptor retinal responses differed little.

Conclusions: Model results were in good overall agreement with previous interpretations of the origins of the mfERG. The marked mfERG abnormalities in eyes with severe ROP are probably mediated in large part by changes in bipolar cell function. There was no evidence of dysfunction in the macular cones.

CONTROL ID: 3710456

SUBMITTER (NAME ONLY): Alberto Castillo

TITLE: Prevalence and clinical characteristics of neurotrophic keratopathy in a Hispanic population in northeastern Mexico.

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Castillo, J.E. Valdez, D. Loya-Garcia, R.E. Ruiz, J.E. Arreola, Instituto de Oftalmologia y Ciencias Visuales, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To evaluate the prevalence and clinical characteristics of neurotrophic keratopathy (NK) in northeastern Mexico.

Methods: Cross-sectional study in which NK patients admitted to our ophthalmology clinic between 2015-2021 were consecutively enrolled. Data regarding demographics, clinical characteristics, and comorbidities were collected at the time diagnosis of NK was made. General descriptive analyzes were performed using measures of central tendency and comparative analysis using Student's T test for quantitative data and Fisher's test or chi-square distribution for qualitative data. $P < 0.05$ was considered statistically significant.

Results: Results: In the period from 2015 to 2021, a total of 74,056 patients were treated and of these 42 had a diagnosis of neurotrophic keratitis. The prevalence found was 5.67 [CI95 3.95 ~ 7.38] in 10,000 cases. The mean age observed was 59 ± 17.21 years (Table 1), occurring more frequently in males in 59% and with corneal epithelial defects in 66.7% (Table 1). The most frequent antecedents were the use of topical medications in 90% (Table 1), the presence of diabetes mellitus 2 in 40.5% (Table 1) and systemic arterial hypertension in 26.2% (Table 1). The associated clinical characteristics that were observed more frequently were visual acuity deficiency in 81% (Table 1) followed by foreign body sensation in 50% (Table 1). A greater association of developing corneal ulceration was found in females while males only presented corneal epithelial alterations (Table 2). Furthermore, no association was observed with the use of contact lenses (Table 2). Among the clinical characteristics, the absence of ocular pain, redness and constant tearing were associated with the progress of the disease (Table 2).

Conclusions: Neurotrophic keratitis is an underdiagnosed disease with a broad clinical spectrum. The antecedents that were contracted corroborate what was reported in the literature as risk factors. The prevalence of the disease in this geographical area was not reported, so it is expected to increase over time when searching for it intentionally.

CONTROL ID: 3710457

SUBMITTER (NAME ONLY): Tapanmitra Ravi

TITLE: Automatic image skeletonization to characterize ZO-1 distribution in the corneal endothelium following hypothermia and oxidative stress

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ravi, Computer Science & Engineering, Dayananda Sagar College of Engineering, Bangalore, Karnataka, INDIA|M. Thanuja, S.H. Ranganath, Chemical Engineering, Siddaganga Institute of Technology, Tumkur, Karnataka, INDIA|A. C, Biotechnology, Siddaganga Institute of Technology, Tumkur, Karnataka, INDIA|S.S. Kuruvadi, Data Science, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|P. Shilpashree, Electronics and Communication Engineering, Siddaganga Institute of Technology, Tumkur, Karnataka, INDIA|S.P. Srinivas, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: ZO-1 binds to Claudins at the apical junctional complex as an intracellular scaffold protein. Thus, it manifests contiguously at the cellular periphery in the endothelium with an intact barrier function. However, stressful stimuli, such as hypothermia, oxidative stress, and allograft rejection, break down the perijunctional actomyosin ring (PAMR) concomitant with the destruction of ZO-1 organization (insets in Fig.). This study aims to quantify such disruptions of ZO-1 through combined immunocytochemistry, confocal microscopy, and automatic image skeletonization.

Methods: Porcine eyes were subjected to hypothermia (4 °C; 3-7 days) or oxidative stress (100 μM; H_2O_2 for 60 min). Next, images of PAMR and ZO-1 were registered by immunocytochemistry combined with confocal microscopy at the focal plane of ZO-1. The images were then subjected to automatic segmentation by (U-Net)-based deep learning workflow to delineate ZO-1 distribution at the cellular periphery. Finally, the segmented images were skeletonized using the scikit-image (python) implementation of the Zha84 method, and the corresponding outputs were analyzed for estimating the distribution of branch lengths.

Results: In untreated cells, ZO-1 was contiguous with tricellular junctions. At moderate hypothermic stress, the linear edges were disrupted along with the loss of tricellular links. The linear edges broke down into smaller pieces and punctate blobs at severe stress levels. The severity of the impact on ZO-1 generally paralled those on PAMR. The U-Net led to reliable segmentation with an F1 score of 82%, IoU of 77%, and an accuracy of 94%. Subsequent skeletonization and determination of branch lengths showed a skewed distribution profile compared to those for untreated cells (Fig.) with the frequency of appearance of small segments increasing significantly with higher stress levels.

Conclusions: We have developed a workflow to quantify the ZO-1 disruption patterns in response to hypothermia and oxidative stress in the corneal endothelium.

CONTROL ID: 3710461

SUBMITTER (NAME ONLY): Reece Mazade

TITLE: Single-cell recordings reveal modulation of ON and OFF retinal signals in the myopic murine eye

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Mazade, M.T. Pardue, Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|R. Mazade, M.T. Pardue, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Reece Mazade: Commercial Relationship: Code N (No Commercial Relationship) | Machelle Pardue: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Visual pathways that signal luminance increments (ON pathway) and decrements (OFF pathway) have been suggested to differentially influence myopia progression and are more weakly driven by defocused stimuli. However, inner retinal signals (including those from ON and OFF pathways) have not been directly studied electrophysiologically in myopic eyes. Here, we investigate how responses from single inner retinal neurons are modulated in myopia.

Methods: Lens-induced myopia (LIM) in C57BL/6J mice was generated unilaterally by placing a -10D lens over the OD eye, leaving the OS eye as a contralateral control (LIM, n=29). Refractive errors (RE) were measured in animals before lens placement and at the end of the treatment period (>2 weeks). A subset of mice were left untreated as naïve controls (Ctrl, n=9). Retinas were collected and prepared for whole-cell voltage clamp recordings. A white OLED screen (max luminance: ~2,000 cd/m^2) was used to generate full-field, 500 ms duration flash stimuli. Light-evoked ON and OFF excitatory and inhibitory responses were measured from single dark-adapted bipolar (BC) and amacrine cells (AC), identified via fluorescent labeling.

Results: All LIM mice developed a myopic shift (ΔRE OD - OS) after 2 weeks (-2.7±0.2 D, $p<0.001$) whereas Ctrl mice did not. The average ON and OFF excitatory response across all recorded cells was ~50% weaker in myopic (n=14 cells) than non-myopic eyes (Ctrl + LIM OS eyes, n=12 cells; $p=0.034$). Interestingly, myopia affected ON- and OFF-driven inhibition in opposite directions. Combining all recorded cells, ON inhibition decreased ~28% and OFF inhibition increased ~42% in myopic (ON n=23, OFF n=20 cells) compared to non-myopic eyes (ON n=14, OFF n=12 cells; $p<0.001$). In myopic eyes, ACs, cone BCs, and rod BCs primarily contributed to reduced ON inhibition while ACs and OFF cone BCs primarily contributed to increased OFF inhibition.

Conclusions: Our results provide direct electrophysiological evidence suggesting modulation of inner retinal ON and OFF responses in myopic eyes. On average, LIM led to weaker ON and OFF excitatory drive, weaker ON-driven inhibition, and stronger OFF-driven inhibition to inner retinal neurons. Our preliminary findings suggest that retinal dysfunction in myopia includes altered ON/OFF retinal balance and supports our ongoing investigation of the effects of myopia on visual signaling in all retinal cell types.

CONTROL ID: 3710463

SUBMITTER (NAME ONLY): Rohit Khanna

TITLE: Incidence, Visual Impairment and Blindness due to Retinitis Pigmentosa in Rural Population in India: 15 Year Follow-up of the Andhra Pradesh Eye Disease Study cohort

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.C. Khanna, S. Marmamula, A. Mettla, P. Giridhar, S. Banerjee, K. Shekhar, G.N. Rao, Allen Foster Research Centre for Community Eye Health Research Centre, Gullapalli Pratibha Rao International Centre for Advancement of Rural Eye care, L V Prasad Eye Institute, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|D. Parameswarappa, S. Jalali, Srimati Kanuri Santhamma Center for Vitreo - Retinal Diseases, L V Prasad Eye Institute, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|S. Chakrabarti, Brien Holden Eye Research Centre, L V Prasad Eye Institute, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: The Andhra Pradesh Eye Disease Study III (APEDS III) represents a 15 year follow up of a cohort of participants who were initially evaluated in APEDS I from 1996-2000. It included the surviving participants from all age groups (n=5395; 83.6%) belonging to three rural areas of APEDS I. The present study was aimed to assess the incidence, visual impairment (VI) and blindness due to Retinitis Pigmentosa (RP) in this rural Southern Indian cohort.

Methods: Following a detailed interview, all the participants underwent a comprehensive eye examination including fundus photography and diagnostic tests. Visual acuity (VA) was measured using a standard logarithm of minimum angle of resolution (logMAR) chart at a distance of three meters. Unaided, presenting, pinhole and best-corrected VA were also recorded. All participants with RP of APEDS I were followed up until APEDS III. Descriptive statistics using mean ± standard deviation with inter-quartile range (IQR) were calculated. Main outcome measures were RP incidence, VI and blindness as per World Health Organization criteria.

Results: At baseline (APEDS I), 7771 participants residing in three rural areas were examined. There were 9 cases of RP with mean age at baseline of 47.33 ± 10.89 years (IQR 39-55). There was a male preponderance (6:3) and the mean best-corrected visual acuity (BCVA) of 18 eyes from nine participants was 1.2 ± 0.72log MAR (IQR 0.7-1.6). Over a mean follow-up duration of 15 years, 5395/7771 (69.4%) were reexamined, which included 7 RP participants from APEDS I. Additionally, 2 new cases of RP were identified that provided an overall incidence of 370/million in 15 years (24.7/million per year). The mean BCVA of 14 eyes of seven patients who were reexamined in APEDS III was 2.17±0.56log MAR (IQR 1.8-2.6) and 5 of these 7 patients developed incident blindness during the follow-up period.

Conclusions: The overall incidence of RP was relatively high in the Southern Indian population and this information would be valuable in planning for future eye care strategies to address and prevent this condition.

CONTROL ID: 3710464

SUBMITTER (NAME ONLY): Shusheng Wang

TITLE: A CRISPR-based inducible system for VEGF repression for AMD

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Wang, Y. Tong, Y. Wu, J. Ma, Z. Zhang, Cell and Molecular biology, Tulane University School of Science and Engineering, New Orleans, Louisiana, UNITED STATES|S. Wang, Ophthalmology, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure: Shusheng Wang: Commercial Relationship(s);Code P (Patent):Tulane University | Yao Tong: Commercial Relationship: Code N (No Commercial Relationship) | Yinga Wu: Commercial Relationship: Code N (No Commercial Relationship) | Jing Ma: Commercial Relationship: Code N (No Commercial Relationship) | Zunyi Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the primary cause of irreversible blindness in the elderly. The current paradigm for wet AMD treatment is monthly intravitreal injection of anti-VEGF antibodies, which poses a significant economic burden to the patients. Continuous blocking of VEGF may have adverse effect in choroid capillaries and the ciliary body. We propose a gene therapy approach to drive inducible and reversible VEGF repression using a CRISPR-based system, which could avoid repetitive intravitreal injection while achieving controllable VEGF repression.

Methods: ARPE-19 and mouse RPE cell lines were engineered to express Cas9-Krab reversibly as controlled by doxycycline (Dox), which was confirmed by Western blot analysis and immunostaining. A series of guide RNA pairs targeting human (mouse) VEGF promoter were used in screening to identify guide RNAs that can repress VEGF expression. constitutively expressed. Real-time PCR and ELISA were employed to quantify the VEGF expression before and after Dox treatment in the system. Laser injury model is being used to evaluate the efficacy of the approach in vivo.

Results: Induction and dosage-response of Cas9-Krab expression were confirmed by Western blot analysis and immunostaining. In addition, Cas9-Krab can be reinduced in the same cells within 12 hours 7 days after the first induction. Guide RNAs have been screened to target VEGF promoter RPE cells. Up to 90% reduction of VEGF mRNA and protein expression has been achieved in the system.

Conclusions: We have established a CRISPR-based reversible VEGF repression system, which could be used to treating retinal diseases including AMD and diabetic retinopathy. (This research has been supported by a grant from BrightFocus Foundation)

CONTROL ID: 3710475
SUBMITTER (NAME ONLY): Ellis Tibbs
TITLE: The role of Granzyme B in Ocular Graft versus Host Disease
SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Tibbs, X. Cao, Microbiology and Immunology, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|E. Tibbs, S. Sajjan, S. Sunshine, X. Cao, Marlene and Stewart Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|
Commercial Relationships Disclosure: Ellis Tibbs: Commercial Relationship: Code N (No Commercial Relationship) | Seema Sajjan: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Sunshine: Commercial Relationship: Code N (No Commercial Relationship) | Xuefang Cao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular graft versus host disease (oGVHD) affects 40-60% of patients who have undergone allogeneic hematopoietic stem cell transplant resulting in debilitating eye disease characterized by decreased vision, pain, and dry eye disease (DED). The mechanisms underpinning inflammation in oGVHD are not completely understood. Granzyme B (GzmB) is a serine protease associated with granule mediated perforin dependent pathway leading to apoptosis. GzmB is thought to be involved in multiple autoimmune diseases such as Systemic Lupus Erythematous, scleroderma, which share similarities to GvHD. We hypothesize that the production of GzmB increases the severity of oGvHD, playing a critical role in oGVHD pathogenesis via perforin dependent and independent mechanisms.
Methods: We conducted an allogeneic hematopoietic stem cell transplant using a mouse model. This study included four groups; T and B cell depleted Bone Marrow (TBCD-BM) only, TBCD-BM+Splenocytes (BM+Spl), TBCD-BM+Splenocytes+IL-2c (BM+Spl+IL2), and TBCD-BM+Splenocytes(-CD8depl)+IL-2c (BM+Spl-CD8+IL2). CD8depl is a group in which CD8 T cells were depleted from the spleen prior to transplantation. IL-2c is a complex of murine IL-2 cytokine and IL-2 monoclonal antibody which activate T-cells. GvHD and oGvHD was scored for the duration of the experiment to determine the progression of GvHD and oGvHD. The individual scores for cornea staining, eyelid, eyelid fur, and cornea haze are used to determine the overall oGvHD score by combining the values and then taking the average within the groups at each time point. Grade 1 refers to the least severe and Grade 4 refers to the most severe. In addition, we collected tissue from the cornea, eyelid, conjunctiva, and lacrimal gland from the mice and quantified the gene expressions of GzmB, Arg-1, TNFα, and IFNγR using RT-qPCR.
Results: BM+Spl-CD8+IL2 group showed a significant increase (75%, p=0.013) in oGvHD severity compared to BM+Spl. In fact, the BM+Spl+IL2 group showed a 7.5% increase in oGvHD compared to BM+Spl though this was not significant. BM+Spl+IL2 showed an increase in GzmB, IFNγR, Arg-1 expression in the conjunctiva (36, 3, and 3-fold), the eyelid (42, 7, and 2-fold), and the cornea (38, 33, 1.2-fold) compared to TBCD-BM only.
Conclusions: The presence of IL-2c which promotes GzmB production of T cells increases the severity of oGvHD. Further investigation of GzmB in oGvHD is warranted as a potential target for therapy.

CONTROL ID: 3710476

SUBMITTER (NAME ONLY): Marcel Bernucci

TITLE: Spectrally resolving S, M, and L cone sensitivities across the visible spectrum using AO-OCT optoretinography with a supercontinuum laser

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bernucci, K. Kurokawa, Y. Liu, F. Zhang, J. Crowell, D.T. Miller, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|K. Kurokawa, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|F. Zhang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The differential responses of S, M, and L cones to short, medium, and long wavelengths of light produce human color vision. Objective methods have been developed to examine cone spectral responses but remain limited. Previously, we developed an adaptive optics optical coherence tomography (AO-OCT) method that used the cone optoretinogram to identify spectral types of individual human cones with unprecedented sensitivity, accuracy, and efficiency [1]. Here, we extend this approach to measuring cone sensitivities across the visible spectrum by controlling the wavelength and strength of stimulation with a supercontinuum laser.

Methods: AO-OCT volumes of 1°×0.8° at 3.8° temporal retina were acquired repeatedly over 5s at 10 Hz for one color normal subject. AO-OCT cone optoretinograms were observed 2.5s after stimulation with flashes of 450, 480, 520, 545, 570, 600, and 635 nm light. Flashes consisting of 5-8 power levels (0.23-31μW) were generated by a supercontinuum laser and controlled by an acousto-optic tunable filter, both spectrally (<1.8 nm bandwidth) and temporally (60 ms flash duration except at 450 and 480 nm that needed longer exposures). Cone spectral types were classified and the mean cone response following stimulus was obtained for the different flash strengths and wavelengths. After compensating for lenticular and macular absorption, the mean cone response as a function of flash strength was fit to a power law from which cone spectral sensitivities were extracted.

Results: Twenty spectral sensitivity measurements were acquired in total. We compared our measurements to Stockman & Sharpe's well-recognized psychophysical cone fundamentals using an iterative function to find the offset producing the minimum total difference between our sensitivity measurements and that of the normalized psychophysical data. Our measurements produced a least-squared error for S, M, and L cones of 0.00, 0.017, and 0.022, respectively, using all seven wavelengths with the exception of 480 nm for S cones. To date we have determined confidence intervals (CIs) for L and M cones of <0.083 and <0.074, respectively, for 545, 570, and 600 nm and for L cones of ±0.034 at 635 nm.

Conclusions: We have developed an objective method that provides highly specific and sensitive measurements of cone sensitivity across the visible spectrum.

[1] Zhang, et al. PNAS 2019 116 (16) 7951-6

CONTROL ID: 3710477

SUBMITTER (NAME ONLY): John Sheppard

TITLE: Efficacy of NOV03 (Perfluorohexyloctane) on Signs and Symptoms of Dry Eye Disease associated with Meibomian Gland Dysfunction: The Mojave study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Sheppard, Virginia Eye Consultants, Norfolk, Virginia, UNITED STATES|F.K. Kurata, East West Eye Institute, Los Angeles, California, UNITED STATES|A. Epitropoulos, The Eye Center of Columbus, Columbus, Ohio, UNITED STATES|S. Krösser, Novaliq GmbH, Heidelberg, Baden-Württemberg, GERMANY|J. Vittitow, Clinical Affairs, Bausch + Lomb, Bridgewater, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the efficacy and safety of NOV03 (100% perfluorohexyloctane; F6H8) an investigational, novel, water-free, preservative-free sterile eye drop dosed four times a day (QID) compared to hypotonic saline eye drops for the treatment of the signs and symptoms of dry eye disease (DED) associated with Meibomian gland dysfunction (MGD).

Methods: Mojave was a Phase 3, multicenter, randomized, comparator-controlled, double-masked study conducted in subjects ≥18 years with DED associated with MGD. Eligible subjects were randomized 1:1 to NOV03 or hypotonic saline and instilled 1 drop QID into both eyes for approximately 57 days. Efficacy was assessed at Day 15, Day 29, and Day 57. Primary efficacy endpoints were the change from baseline (CFB) in total corneal fluorescein staining (tCFS; primary sign) and in VAS dryness score (primary symptom) at Day 57. The study eye was the eye with the worse tCFS score at baseline. Safety endpoints included adverse events (AEs), visual acuity, biomicroscopy, fundoscopy and intraocular pressure.

Results: A total of 620 subjects were randomized and treated (n=311 NOV03; n=309 saline). Mean age was 53.6 years, and the majority of subjects were female (78.7%). On Day 57, mean (SD) CFB in tCFS (–2.3 [2.8] NOV03 group vs –1.1 [2.9] saline group) and eye dryness VAS score (–29.5 [28.6] NOV03 group vs –19.0 [27.2] saline group) were statistically significantly different in favor of NOV03 ($P<0.001$ for both). Few subjects experienced ocular AEs in the study eye (9.6% NOV03 group, 9.7% saline group). Blepharitis, mostly mild, was the only AE that occurred in a >1% higher proportion of subjects treated with NOV03 vs saline (1.6% vs 0.3%). Other safety assessments were unremarkable.

Conclusions: In this Phase 3 study of subjects with DED associated with MGD, NOV03 eye drops demonstrated statistically significant improvements over hypotonic saline eye drops in both the primary sign (tCFS) and the primary symptom (VAS dryness) endpoints. NOV03 appeared well tolerated in this population. Efficacy and safety findings were consistent with those reported in a previous Phase 3 study (Gobi).

CONTROL ID: 3710479

SUBMITTER (NAME ONLY): Birgit Lorenz

TITLE: Current management of patients with RPE65 mutation-associated Inherited Retinal Degenerations (RPE65-IRD) in Europe. Results of a 2-year follow-up multinational survey by the European Vision Institute Clinical Research Network (EVICR.net) and the European Reference Network for Rare Eye Diseases (ERN-EYE)

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lorenz, Department of Ophthalmology, University Hospital Bonn, Bonn, GERMANY| B. Lorenz, Justus-Liebig-University, Giessen, GERMANY|J. Tavares, J.P. Marques, AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|J.P. Marques, Department of Ophthalmology, Centro Hospitalar e Universitário de Coimbra, Coimbra, PORTUGAL|I. van den Born, Rotterdam Eye Hospital, Rotterdam, NETHERLANDS|K. Stingl, Center for Ophthalmology, University of Tuebingen, University Eye Hospital, Tuebingen, GERMANY|E. Pilotto, Department of Ophthalmology, University of Padova, Padova, ITALY|P. Charbel Issa, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UNITED KINGDOM|P. Charbel Issa, Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UNITED KINGDOM|D. Leroux, H. Dollfus, CARGO & ERN-EYE management, Hôpitaux Universitaires de Strasbourg, Strasbourg, FRANCE|H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel, Basel, SWITZERLAND|H.P. Scholl, Department of Ophthalmology, University of Basel, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To evaluate the current management of RPE65-IRD in Europe since market authorization of Voretigene Neparvovec (VN, Luxturna™) in 2018. To date, over 200 patients have been treated outside the USA, of which about 90% in Europe. We conducted among all EVICR.net centers and ERN-EYE health care providers (HCPs) the second multinational survey on management of IRDs in Europe with a special focus on RPE65-IRD.

Methods: An electronic survey questionnaire with 48 questions specifically addressing RPE65-IRD (2019 survey [1]) was developed and sent to 126 EVICR.net centers and ERN-EYE HCPs. Statistical analysis was performed with Excel and R.

Results: The overall response rate was 44%; 26 sites follow RPE65-IRD patients. Table 1 compares data with the 2019 survey[1]. By June 2021, 8/26 centers have treated 57 RPE65-IRD cases (1 – 19/site, median 6), and 43 await treatment (range 0 - 10/site, median 5). The overall age range was 3 – 52 years, and 172 patients do not (yet) qualify for treatment (2 - 60/site, median 15). Main reasons were too advanced (54% on average) or mild disease (18% on average). Only 38% of centers participate in the PERCEIVE registry (EUPAS31153, http://www.encepp.eu/encepp/viewResource.htm?id=37005). Table 2 summarizes objective and subjective outcomes for 12 items. Quality of life and full field stimulus test (FST) improvements had the highest scores.

Conclusions: This second multinational survey on management of RPE65-IRD of EVICR.net sites and ERN-EYE HCPs in Europe indicates that RPE65-IRD is diagnosed more reliably in 2021 compared to 2019. By June 2021, 8/26 sites reported detailed results. Main reasons for non-treatment were too advanced or mild disease. Patient satisfaction

with treatment was 40%. Detailed results were not available in 50 to 80% of the 12 outcome items.

1. Lorenz B, et al. Ophthalmic Res. 2021;64(5):740-753. doi:10.1159/000515688

CONTROL ID: 3710480

SUBMITTER (NAME ONLY): Whitney Stuard

TITLE: IGFBP-3 regulates metabolic activity and mitochondrial morphology through a biphasic response in corneal epithelial cells during hyperosmolar stress

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.L. Stuard, M. Kabaalioğlu Guner, D.M. Robertson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Whitney Stuard: Commercial Relationship: Code N (No Commercial Relationship) | Melis Kabaalioğlu Guner: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Robertson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Hyperosmolarity of the precorneal tear film plays a key role in the underlying pathobiology of dry eye disease (DED). The insulin-like growth factor binding protein-3 (IGFBP-3) is a pleiotropic protein present in the precorneal tear film and is downregulated in response to hyperosmolar stress (H-stress) in corneal epithelial cells (CECs). The purpose of this study was to evaluate the role of IGFBP-3 in mitochondrial morphology and metabolic activity in CECs and corneal epithelium exposed to H-stress.

Methods: Telomerase-immortalized human corneal epithelial (hTCEpi) cells were cultured in isotonic keratinocyte basal media (KBM, 330 mOsm) or KBM with osmolarity values up to 450 mOsm, with or without recombinant human (rh)IGFBP-3 for 2 or 24 hours. Mitochondrial respiration, morphology, and dynamics were analyzed using a seahorse metabolic flux analyzer, real-time PCR, and transmission electron microscopy. Expression and localization of IGFBP-3 and type I IGF-receptor (IGF-1R) were analyzed using subcellular fractionation/immunoblotting. Protein translation was quantified with a SUnSET assay. Injection of 20 mU of botulinum toxin B into the exorbital lacrimal gland of C57BL6/N mice was used to induce DED. DED was confirmed using a phenol red thread test and by corneal staining using fluorescein. After 21 days of DED, mice were treated topically with balanced salt solution with or without rhIGFBP-3. IGFBP-3 expression in the corneal epithelium was assessed using an IGFBP-3 ELISA and immunofluorescence.

Results: H-stress decreased IGFBP-3 expression in vitro and in vivo. Intra- and extracellular levels of IGFBP-3 parallel mitochondrial respiration in CECs under H-stress. At 2 hours of H-stress, IGFBP-3 induced mitochondrial translocation of IGF-1R. At 24 hours, there was a stress-mediated decrease in oxidative phosphorylation that was blocked by the addition of exogenous IGFBP-3. Treatment with IGFBP-3 also promoted IGFBP-3 nuclear localization, mitochondrial hyperfusion, and protein translation. In vivo, exogenous IGFBP-3 restored CEC health.

Conclusions: These data show that IGFBP-3 mediates mitochondrial structure and function through an early and late biphasic response. These findings could pave the way for novel therapeutics for diseases in ocular tissues, such as DED, with underlying mitochondrial and metabolic dysfunction.

CONTROL ID: 3710481

SUBMITTER (NAME ONLY): Rajiv Rangan

TITLE: miRNA Profiling of Optic Nerve Head Astrocytes Exposed to Cyclic Stretch

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Rangan, T. Tovar-Vidales, North Texas Eye Research Institute, Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Rajiv Rangan: Commercial Relationship: Code N (No Commercial Relationship) | Tara Tovar-Vidales: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is the primary risk factor for glaucoma, a leading cause of irreversible blindness consequent to retinal ganglion cell (RGC) degeneration. Elevated IOP induces biomechanical aberrations within ocular tissues – including the transmission of stretch through the lamina cribrosa (LC) region of the optic nerve head (ONH), the initial site of RGC damage. ONH astrocytes (ONHA), a primary cell type of the LC, respond to stretch in a manner that promotes pathological extracellular matrix (ECM) remodeling (fibrosis) and mechanical damage of RGC axons within the ONH. A complex set of molecular mechanisms regulate ECM remodeling. Part of this regulation may involve microRNAs (miRNAs), small molecules that inhibit protein expression by binding to and silencing mRNA. In this study, we examined miRNA expression profiles of ONHA exposed to cyclic stretch. We hypothesized that cyclic stretch would increase expression of miRNAs that silence anti-fibrotic protein translation and decrease expression of miRNAs that silence pro-fibrotic protein translation, promoting a net-fibrotic molecular signaling environment.

Methods: Primary human normal ONHA cell strains (n=3) were exposed to 0-12% cyclic stretch for 24 hours; controls were exposed to 0% stretch. RNA samples were collected from stretched and control cells. miRNA PCR arrays were used to determine expression changes for miRNAs associated with fibrosis. Expression fold changes were normalized to SNORD68. The bioinformatics tool TargetScan was used to predict mRNA targets for dysregulated miRNAs. Western blotting of conditioned medium was used to compare TGFβ2, fibronectin, and transglutaminase 2 expression between control and stretched ONHA.

Results: miR-146b-5p was upregulated by +5.97-fold (P = 0.029) in stretched ONHA. Predicted mRNA targets for miR-146b-5p are involved in fibrosis and cell survival, among other functions. Preliminary data indicates the upregulation of secreted proteins associated with fibrosis (TGFβ2, fibronectin, transglutaminase 2) by stretched ONHA.

Conclusions: Stretch modulates miRNA expression in cultured human ONHA, miR-146b may mediate ECM alterations and other pathological changes at the LC. Future experimental directions will include assessing co-expression of other miR-146 family miRNAs, validating putative mRNA targets and elucidating the mechanisms by which specific miRNAs and their targets modulate ECM remodeling.

CONTROL ID: 3710484

SUBMITTER (NAME ONLY): Laura Schaefer

TITLE: Metagenomic sequencing of Sjögren syndrome and healthy gut microbiota reveals differential bacterial species that correlate with disease severity

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Schaefer, F.S. Midani, C.M. Trujillo-Vargas, R.A. Britton, Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas, UNITED STATES|L. Schaefer, F.S. Midani, R.A. Britton, Center of Metagenomics and Microbiome Research, Baylor College of Medicine, Houston, Texas, UNITED STATES|C.M. Trujillo-Vargas, Grupo de Inmunodeficiencias Primarias, Universidad de Antioquia Facultad de Medicina, Medellin, COLOMBIA|S.C. Pflugfelder, C.S. De Paiva, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Laura Schaefer: Commercial Relationship(s);Code I (Personal Financial Interest):Mikrovia, Panabio, Tenza Inc. | Firas Midani: Commercial Relationship: Code N (No Commercial Relationship) | Claudia Trujillo-Vargas: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Pflugfelder: Commercial Relationship(s);Code F (Financial Support):Yuyu Pharma, Santen, Dompe;Code C (Consultant/Contractor):Allergan, Dompe, Kala, Kowa, Novatis Pharma AG, Senju | Robert Britton: Commercial Relationship(s);Code C (Consultant/Contractor):Tenza Inc.;Code I (Personal Financial Interest):Mikrovia, Panabio, Tenza Inc. | Cintia De Paiva: Commercial Relationship(s);Code F (Financial Support):Yuyu Pharma, Roche, Allysta

ABSTRACT BODY:

Purpose: A growing number of studies show that homeostasis of the ocular surface is impacted by the intestinal microbiome, and several 16S sequencing studies have demonstrated dysbiosis of the intestinal microbiota in Sjögren Syndrome (SS) patients. In this study, we utilized metagenomic sequencing to perform a deeper analysis of the intestinal microbiome to identify differential bacterial species using stools collected from sex- and age-matched subjects.

Methods: Age-matched healthy (n = 20), dry eye (n = 4) and SS (n = 7) female patients were enrolled at the BCM Alkek Eye Center. Ocular disease severity was scored following International Dry Eye Workshop guidelines. Patients were supplied with stool collection kits and submitted samples within 24 hours post-collection. High quality DNA was prepared for metagenomics sequencing from stool aliquots using DNEasy Powersoil Pro kits. Sequencing, annotation, and initial analysis were performed by Diversigen with their BoosterShot Shotgun Sequencing service. We further analyzed the data using the vegan and randomForest packages in R statistical software.

Results: Shannon alpha diversity and observed operational taxonomic units (OTUs) were significantly decreased in SS ($P<0.05$). Observed OTUs inversely correlated with ocular severity score (Spearman's $r=-0.37$, $P<0.05$). Using Bray-Curtis beta diversity analysis, we found significant separation between healthy and SS groups (PERMANOVA $R^2=0.08$, $P<0.05$), but not between healthy and dry eye groups. We investigated taxonomic differences using the Random Forest machine learning algorithm. At the phylum level, Bacteroidetes ($P<0.05$) and Actinobacteria ($P<0.01$) contributed the most to community differences. At the species level, SS patients were distinguished by significant increases in Bacteroides caecimuris, Mediterranea masilliensis, Bacteroides coprophilus and Clostridium_sp_7_3_54FAA and a significant decrease in Bifidobacterium bifidum compared to healthy controls (all $P<0.01$), and these species changes correlated with disease severity.

Conclusions: Our metagenomic data confirm that the SS gut microbiome is less diverse, and that reduced diversity correlates with increased ocular disease severity. In addition, we have identified specific bacterial species that are either depleted or enriched in SS patients and correlate with ocular surface disease severity.

CONTROL ID: 3710487

SUBMITTER (NAME ONLY): Irona Khandaker

TITLE: Longitudinal characterization of foveal RA signaling in human Retinal Organoids

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Khandaker, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Irona Khandaker: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Induced pluripotent stem cells (iPSCs) derived human retinal organoids (hRetOrg) have emerged as a powerful system for studying retinal diseases while formation of a fovea has not been yet achieved in current methods. We hypothesize that foveated-hRetOrg can be generated if in vivo developmental molecular programs underlying fovea formation, namely Retinoic Acid (RA) signaling, are recapitulated in this in vitro system. We therefore settled to longitudinally characterize RA signaling in hRetOrg during retinogenesis period.

Methods: We established a hRetOrg culture system generated from a human control iPSC line, IMR(90)-4, based on Zhong et al. 2014 and Cowan et al. 2020 methods. We collected hRetOrg from the beginning of retinogenesis at week (W) 5 up to fully differentiated stages at W21 for gene expression analysis by qRT-PCR, in situ hybridization and immunohistochemistry. We also employed electroporation technique to perform localized transfections in defined hRetOrg domains using customized electrodes and chambers.

Results: We confirmed recapitulation of in vivo retina developmental key points in our hRetOrg cultures, such as formation of eye-field at day (D) 7, optic vesicle –like configurations at D16 and optic cup-like structures at D25. Around W5, neural retinal cells spontaneously began to differentiate following in vivo birth dating orders. Immunohistochemistry analysis of W21 hRetOrg showed Rhodopsin, SW, and M/LW cone expressions in outer segment-like structures confirming full differentiation of photoreceptors in our cultures. Regarding RA signaling analysis, we found that RA synthesizing enzymes ALDH1A1 (dorsally expressed in vivo) and ALDH1A3 (ventrally expressed in vivo) are expressed in non-overlapping domains with slightly different dynamics. Expression of RA degradative enzymes is more complex and highly variable among organoids. Additionally, we also developed an efficient gene transfection method of hRetOrg via electroporation for precise spatiotemporal regulation of expression of any gene of interest.

Conclusions: This study thoroughly characterizes RA signaling in current hRetOrg cultures during retinogenesis period, constituting a reference where upon genes of interest can be manipulated in order to recapitulate in vivo patterns of foveal molecular mechanisms, which ultimately can lead to the formation of foveated-hRetOrgs.

CONTROL ID: 3710488

SUBMITTER (NAME ONLY): Nikki Khandwala

TITLE: Characteristics of treatment-requiring retinopathy of prematurity in a screening program at Aravind Eye Hospital, India

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Khandwala, E. Cole, R.V. Chan, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|M. Oh, S. Ostmo, J. Campbell, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Subramaniam, P. Shah, Aravind Eye Care System, Madurai, Tamil Nadu, INDIA|

Commercial Relationships Disclosure: Nikki Khandwala: Commercial Relationship(s);Code F (Financial Support):NIH Grant P30 EY001792 | Emily Cole: Commercial Relationship: Code N (No Commercial Relationship) | Minn Oh: Commercial Relationship: Code N (No Commercial Relationship) | Prema Subramaniam: Commercial Relationship: Code N (No Commercial Relationship) | Susan Ostmo: Commercial Relationship: Code N (No Commercial Relationship) | Parag Shah: Commercial Relationship: Code N (No Commercial Relationship) | Robison Chan: Commercial Relationship(s);Code F (Financial Support):Research to Prevent Blindness;Code F (Financial Support):R01EY19474 grant from the National Institutes of Health (Bethesda, MD);Code F (Financial Support):P30EY001792 grant from the National Institutes of Health (Bethesda, MD);Code F (Financial Support):USAID;Code F (Financial Support):SEVA;Code C (Consultant/Contractor):Alcon ;Code O (Owner):Siloam Vision | J. Peter Campbell: Commercial Relationship(s);Code F (Financial Support):Research to Prevent Blindness (New York, NY);Code F (Financial Support):R01EY19474 grant from the National Institutes of Health (Bethesda, MD);Code F (Financial Support):P30EY001792 grant from the National Institutes of Health (Bethesda, MD);Code F (Financial Support):USAID;Code F (Financial Support):SEVA;Code F (Financial Support):P30EY10572 grant from the National Institute of Health (Bethesda, MD);Code C (Consultant/Contractor):Boston AI ;Code O (Owner):Siloam Vision

ABSTRACT BODY:

Purpose: The International Classification of Retinopathy of Prematurity (ICROP) defines the classification of ROP for clinical trials and treatment guidelines, however ICROP has historically been predominantly influenced by ROP pathology in the US and Europe. Since ROP phenotypes can vary especially in low-and-middle-income countries (LMIC), there is a gap in knowledge as to how applicable ICROP classifications are to treatment in LMIC. In this study, we evaluate the ICROP classifications of all babies treated for ROP at the Aravind Eye Hospital (AEH) in South India.

Methods: A retrospective study was performed on all treatment-requiring (TR) ROP at AEH between April 2019 and November 2020. As part of routine tele-ROP screening, disease was documented by Retcam Shuttle and graders recorded the level of disease by ICROP criteria using a web-based data management system iTeleGENx (Chicago, IL, USA). Diagnosis of TR-ROP and any treatment received were recorded.

Results: A total of 204 eyes of 104 babies were diagnosed with TR-ROP out of 2700 babies (3.9%) screened for ROP during the time interval. The mean ± standard deviation (SD) gestational age was 30 ± 2 wks and average birth weight was 1270 ± 285 g. Using ICROP criteria and current treatment guidelines, 184 eyes of 94 babies (89.5%) were treated according to guidelines with either zone 1, with plus (37.2%), zone 2, stage 3, with plus (42.6%) or zone 1, stage 3 (4.3%). 20 eyes of 10 babies (9.6%) who received treatment had Type 2 ROP ICROP characteristics, presenting with zone 2 stage 3, pre-plus ROP (80%).

Conclusions: We found that approximately 90% of babies were treated according to guidelines established by the ICROP and Early Treatment for ROP (ETROP) study, suggesting that despite demographic and phenotypic differences, the ICROP informs clinical diagnosis and management in LMIC.

CONTROL ID: 3710490

SUBMITTER (NAME ONLY): Christopher Henry

TITLE: Suprachoroidal triamcinolone acetonide injectable suspension for macular edema associated with uveitis: Visual and anatomic outcomes by age

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.R. Henry, Retina Consultants of Texas, Houston, Texas, UNITED STATES|B. Kapik, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Christopher Henry: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch and Lomb, Clearside Biomedical | Barry Kapik: Commercial Relationship(s);Code E (Employment):Clearside Biomedical Inc;Code I (Personal Financial Interest):Clearside Biomedical Inc | Thomas Ciulla: Commercial Relationship(s);Code E (Employment):Clearside Biomedical Inc;Code I (Personal Financial Interest):Clearside Biomedical Inc

ABSTRACT BODY:

Purpose: Safety and efficacy of triamcinolone acetonide injectable suspension, for suprachoroidal use (SCS-TA) in the treatment of macular edema (ME) associated with noninfectious uveitis (NIU) was previously demonstrated in the Phase 3 PEACHTREE study. This post-hoc analysis evaluated the impact of age on treatment outcomes from that study.

Methods: Subjects with ME secondary to NIU (N=160) were randomized 3:2 to receive a suprachoroidal injection of SCS-TA (4 mg) or a sham procedure in the study eye at baseline and Week 12 and were followed for 24 weeks. Subjects received rescue therapy based on preestablished criteria. Anatomical and visual outcomes, incidence of adverse events, and intraocular pressure (IOP) elevations were evaluated at each visit. A post-hoc analysis was performed to stratify best corrected visual acuity (BCVA, ETDRS letters), central subfield thickness (CST, μm), need for rescue and incidences of IOP and cataract by subject age (≤50 and >50 years).

Results: In the SCS-TA vs control arms, 46 vs 33 subjects were ≤50 years and 50 vs 31 subjects were >50 years of age. Similar proportions of subjects had persistent NIU (>3 month duration) in both age groups, while time since ME diagnosis was shorter in the younger age group (50.5 vs 90.0 weeks in the SCS-TA arm). Change from baseline (CFB) in BCVA was greater with SCS-TA vs control in both age groups at all visits. At Week 24, in subjects ≤50 and >50 years of age, respectively, the CFB in BCVA was 15.2 and 12.5 ($P<0.001$ for both) and between treatment differences were 9.4 and 12.5 ($P\leq0.014$ for both). In both age groups, CFB in CST was greater with SCS-TA vs control at all visits; between treatment differences were -148.3 and -120.2 in subjects ≤50 and >50 years of age ($P\leq0.008$ for both). The rescue rate for SCS-TA vs control was 8.7 vs 66.7% and 18.0 vs 77.4% in subjects ≤50 and >50 years of age, respectively. Incidences of IOP elevation ≥10 mm Hg from baseline at any post-baseline visit in the SCS-TA vs control arms were 15.2 vs 18.2% and 16.3 vs 16.1% in the ≤50 and >50 year age groups, respectively. Cataract rates in the SCS-TA vs control arms were 8.7 vs 9.1% and 6.0 vs 3.2% in subjects ≤50 and >50 years of age, respectively.

Conclusions: These data suggest that SCS-TA is effective and well tolerated in the treatment of ME associated with NIU irrespective of patient age.

CONTROL ID: 3710491

SUBMITTER (NAME ONLY): Ariel Kantor

TITLE: Development of CRISPR-Cas9 repressors for targeted epigenome editing

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kantor, A. Salman, M.E. McClements, R.E. MacLaren, Nuffield Laboratory of Ophthalmology, University of Oxford Nuffield Department of Clinical Neurosciences, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Ariel Kantor: Commercial Relationship: Code N (No Commercial Relationship) | Ahmed Salman: Commercial Relationship: Code N (No Commercial Relationship) | Michelle McClements: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Epigenome editing utilizing the CRISPR (clustered, regularly interspaced, short palindromic repeats)-Cas9 platform has emerged as a promising alternative to cleavage-dependent gene editing, providing a novel approach for targeted control of gene expression. Previous work has shown that fusing several transcriptional regulators to dCas9 in tandem can achieve a synergistic increase in activity, although the additional payload of an epigenetic effector molecule limits AAV-based delivery strategies.

Methods: We developed a novel 105-aa MeCp2 repressor effector comprised of the MeCp2 transcriptional repressor domain (TRD). We first designed gRNAs to target the epigenome editor systems with both S. aureus (Sa) and C. jejuni (Cj) Cas9 proteins to a HEK293 cell line harboring a proline-glutamate-serine-threonine-rich (PEST) destabilized-GFP (dGFP) sequence and measured dGFP expression by fluorescence spectroscopy. To validate our epigenetic editor using a clinically relevant target, we next employed a dual luciferase (Firefly-Renilla) assay system to screen gRNAs against neural retina leucine zipper (NRL), a transcription factor dictating a rod cell phenotype in photoreceptors. Oligonucleotides encoding the relevant sequence were cloned into a reporter construct, and then co-transfected into HEK-293T cells with plasmids expressing the dSaCas9-repressor and relevant gRNA sequence to NRL.

Results: At 48-hour and 96-hour timepoints, we observed a ~20% reduction in dGFP expression with the dSaCas9 bipartite KRAB-MeCp2 repressor, in comparison to no detectable dGFP knockdown with a non-targeting gRNA control. Following in silico design and screening in a dual luciferase assay, significant knockdown was observed against NRL across 5 of 6 tested repressor effector combinations, with the best gRNA achieving 57.6% luciferase knockdown

Conclusions: Our results confirm the development and in vitro validation of a novel bipartite repressor effector that can be packaged all-in-one in AAV. No discernible epigenetic repression was detected with the CjCas9 protein. To facilitate in vivo epigenetic editing, we generated AAV8 for both dSaCas9-KRAB and dSaCas9-KRAB-MeCp2 repressor systems. Future studies will evaluate the utility of Cas9-mediated repressors in retinal organoids and in an Nrl.EGFP mouse model.

CONTROL ID: 3710496

SUBMITTER (NAME ONLY): Oksana Persidina

TITLE: Effects of normal aging on the mouse retina assessed by full-field flash and flicker electroretinography.

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Persidina, J. Park, T. Nguyen, J. McAnany, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Oksana Persidina: Commercial Relationship: Code N (No Commercial Relationship) | Jason Park: Commercial Relationship: Code N (No Commercial Relationship) | Tara Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | J Jason McAnany: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate changes in the electroretinogram (ERG) that accompany normal aging in mice. Previous studies have shown that the flash ERG a- and b-wave amplitudes decrease with increasing age in mice. By contrast, the effect of age on the flicker ERG has not been reported in mice, despite its utility for assessing cone pathway function. This study compared the effects of normal aging on single flash and flicker ERGs in C57BL/6J mice.

Methods: ERGs were recorded from a single cohort of wild type C57BL/6J mice at 5, 10, and 30 weeks of age (9 to 10 mice per age group) using conventional techniques. Dark-adapted flash ERGs were recorded across a broad range of luminance (-3.0 to 2.0 log $cd*s*m^{-2}$); a- and b-wave amplitude and implicit time (IT) were calculated from these responses. In addition, the light adapted flicker ERG elicited by sinusoidally modulated light was measured across a range of temporal frequencies (2 to 31 Hz). Fourier analysis was applied to extract amplitudes and phases from the flicker responses. Analysis of variance was used for statistical comparisons of amplitude and timing among age groups.

Results: There were significant differences in the a-wave amplitude ($F = 73.31$, $p < 0.001$) and b-wave amplitude ($F = 134.72$, $p < 0.001$) for the three age groups. From week 5 to week 30, the amplitudes of both components decreased by a factor of approximately 1.8. There were no significant age-related differences in the implicit time of these components (both $F < 2.29$, $p > 0.10$). There were significant differences in the fundamental amplitude of the flicker ERG ($F = 46.85.00$, $p < 0.001$) and in the second harmonic amplitude ($F = 9.79$, $p < 0.001$) for the three age groups. From week 5 to week 30, the amplitudes of both components decreased by a factor of approximately 1.8. There were no significant age-related differences in the phases of these components (both $F < 2.64$, $p > 0.08$).

Conclusions: Age scales the single flash and flicker ERG similarly, reducing response amplitude by nearly half from 5 to 30 weeks without affecting response timing. Although similar declines in rod and cone photoreceptor function could explain these findings, changes in ocular resistance with age may provide an alternative explanation. Age-related loss of ERG amplitude should be considered in studies that involve mice of different ages.

CONTROL ID: 3710498

SUBMITTER (NAME ONLY): Erin Robinson

TITLE: Artificial intelligence-integrated approaches in ophthalmology: A qualitative pilot study of provider understanding and adoption of AI

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.L. Robinson, School of Social Work, University of Missouri, Columbia, Missouri, UNITED STATES|G. Guidoboni, J. Keller, University of Missouri, Columbia, Missouri, UNITED STATES|A. Verticchio, B.A. Siesky, A. Harris, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|R. Zukerman, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore the understanding and adoption of artificial intelligence (AI) applications within clinical ophthalmology.

Methods: For this exploratory pilot study, semi-structured one-on-one interviews (N=18) were conducted with ophthalmologists, ophthalmology residents, fellows, and medical professionals involved in the diagnosis and treatment of eye diseases. An interview guide informed by prior research of an interdisciplinary team and clinical expertise steered the question-asking process. Virtual interviews lasted approximately 30 minutes and were analyzed with a qualitative content analysis approach.

Results: The majority of participants were white (56%), male (61%), and aged 25-44 years (Mean=32.3). 78% were affiliated with academia and 38% were attending physicians with 1-11 years of practice. Analysis revealed all participants believed that AI informed practice was vital in ophthalmology, with many participants describing it as the “future of the profession.” While all participants were able to discuss specific applications of AI to the field, such as diagnosing diabetic retinopathy and glaucoma, very few participants had used AI in their own practice. A balance between the ‘computer and the clinician’ was noted. Identified disadvantages of an AI-integrated practice include: machine learning techniques can be subject to human data collection bias, a lack of ‘big data’ to help inform AI models, lack of buy-in from the profession, and a perceived lack of access to AI in rural areas. Participants envision integrating AI into future practice as a tool to help guide decision making and to save time. No substantial differences or patterns in responses were noted across participant demographics.

Conclusions: Participants exhibited foundational knowledge of AI in clinical ophthalmology practice and how AI can be leveraged in their future work. However barriers to adoption and integration of AI to practice were widely noted. Looking forward, additional training on specific AI driven models to increase clinician knowledge and adoption are recommended for actualization of AI improvements in clinical practice.

CONTROL ID: 3710500

SUBMITTER (NAME ONLY): Samuel Du

TITLE: Delivery of genome editors to the mouse eye using engineered virus-like particles

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.W. Du, S. Suh, E.H. Choi, G. Palczewska, K. Palczewski, Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|S.W. Du, K. Palczewski, Physiology & Biophysics, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|S. Banskota, A. Raguram, D.R. Liu, Broad Institute, Cambridge, Massachusetts, UNITED STATES|S. Banskota, A. Raguram, Chemistry & Chemical Biology, Harvard University, Cambridge, Massachusetts, UNITED STATES|S. Suh, E.H. Choi, D.R. Liu, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Precision genome editing could advance greatly the treatment of inherited retinal diseases (IRDs), as shown by the reversion of IRD-causing mutations by CRISPR/Cas9 and restoration of visual function in animal models. However, before broader human application, it is imperative to improve the safety profile of vectors for genome editor delivery to minimize deleterious off-target and bystander effects, which can occur when they are expressed over prolonged periods of time. As genomic DNA edits are permanent, a one-time treatment with transiently delivered genome editors should be sufficient to correct an IRD mutation. One such promising method is the administration of genome editors as preformed proteins and ribonucleoproteins encapsulated within virus-like particles (VLPs).

Methods: All animal procedures were approved by the IACUC at UC Irvine and conformed to the recommendations of the American Veterinary Medical Association Panel on Euthanasia and ARVO.

We developed engineered VLPs (eVLPs), an improved VLP platform for packaging and delivering genome editor proteins and RNPs. eVLP possess many of the same advantages as viral vectors, including cell-type tropism and large cargo capacity, but offer significant safety advantages over lentiviral and AAV vectors, such as decreased off-target and bystander editing, and no risk of genomic integration. We exploited the property of Moloney murine leukemia virus which accommodates C-terminal fusion of proteins to its gag structural protein to ensure proper and controlled packaging of genome editors within the eVLPs.

Results: We produced eVLP constructs carrying Cre recombinase or adenine base editors (ABEs). eVLPs efficiently delivered their cargoes to cell lines in vitro. When injected subretinally, eVLPs effected genomic changes in the RPE, such as loxP recombination and A to G nucleotide changes, as assessed by imaging and ERG. Importantly, these eVLPs correct mutations with similar on-target and substantially lower bystander and off-target editing compared to virally delivered ABEs.

Conclusions: By iteratively modifying the surface glycoprotein of eVLPs, we will screen for eVLPs which facilitate the delivery of genome editors to photoreceptors, which historically have been difficult to target with enveloped viruses. We hope the adaptation of this technology will enable the broader application of genome editors to the mouse and human eye.

CONTROL ID: 3710501

SUBMITTER (NAME ONLY): Ramesh Periasamy

TITLE: Improving retinal vascular endothelial cell tropism through rational rAAV capsid design.

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vascular endothelial cells (VEC) are essential for retinal homeostasis and their dysfunction underlies pathogenesis in diabetic retinopathy (DR) and exudative age-related macular degeneration (AMD). Studies have shown that recombinant adeno-associated virus (rAAV) vectors can deliver the gene to neural cells of the retina, yet targeting VECs remains extremely challenging. In this study, we developed rAAV capsid mutant vectors with improved tropism to target retinal VEC through the incorporation of endothelial targeting peptides into the viral capsid.

Methods: rAAV2/2, 2/2[QuadYF-TV], and rAAV2/9 serotype vectors (n=10, capsid mutants per serotype) expressing GFP were generated by inserting heptameric peptides (7AA) designed to increase endothelial targeting at positions 588 (2/2 and 2/2[QuadYF-TV] or 589 (2/9) of the virus protein (VP1-3). The packaging and transduction efficiency of the VEC targeting vectors was assessed on HEK293T cells to confirm infectivity. Subsequently, each vector (MOI=75000) was administered to ex vivo primary bovine VECs. After 72 hours, cells were labeled with CD31, and transduction efficiency was quantified using flow cytometry. Following identification of a mutant (EC5) with improved endothelial tropism, AAVs vectors were administered intra-ocularly and intravenously in C57Bl/6j mice under isoflurane anesthesia. After 4-months, cSLO imaging was performed to assess tropism before the eyes and organs (heart, liver, lungs, and brain) were collected for post-mortem histology.

Results: All capsid mutant rAAV vectors generated were found to transduce HEK293T cells leading to expression of GFP, indicating insertions did not adversely affect packaging. The EC5 mutant demonstrated increased transduction of CD31+ primary bovine VECs in all serotypes, with a fold change of 1.7, 2.7- and 3.6-times higher transduction efficiency when incorporated in the rAAV2/9, 2/2, and 2/2[QuadYF-TV] capsids, respectively. cSLO imaging demonstrated visible expression of GFP in the retinal vasculature following intravenous administration for EC5 mutant vectors versus unmodified controls.

Conclusions: The generation of rAAV vectors targeting retinal VECs could improve gene therapy treatment for DR and AMD. Our findings suggest that incorporating endothelial targeting peptide into rAAV capsid could improve tropism and allow delivery of therapeutic transgenes efficiently to the retinal VECs.

CONTROL ID: 3710507

SUBMITTER (NAME ONLY): Jay Oh

TITLE: Herpes Simplex Virus Type 1 Does Not Stimulate Parthanatos During Infection of ARPE-19 Cells

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Oh, R.D. Dix, Biology, Georgia State University, Atlanta, Georgia, UNITED STATES|R.D. Dix, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Jay Oh: Commercial Relationship: Code N (No Commercial Relationship) | Richard Dix: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Parthanatos is a caspase-independent cell death pathway whose contribution to retinal disease during the pathogenesis of acute retinal necrosis (ARN) or progressive outer retinal necrosis (PORN) caused by herpes simplex virus type 1 (HSV1) remains unclear. Grady et al (2012) showed that parthanatos is simulated during HSV1 infection of primary human fibroblasts. Our laboratory also has shown that key parthanatos proteins are stimulated within retinitis-susceptible eyes of mice with retrovirus-induced immunosuppression (MAIDS) after murine cytomegalovirus infection (Oh et al, 2019). These observations prompted us to investigate the possibility that parthanatos might also operate during HSV1 infection of human retinal cells. We, therefore, performed a pilot study to test the hypothesis that parthanatos-associated PARP-1 and PAR proteins are stimulated during HSV1 infection of ARPE-19 cells.

Methods: Monolayers of ARPE-19 cells were inoculated with either HSV1 [KOS] (moi = 10) or maintenance medium (negative control) and harvested at 1, 2, and 3 days postinfection. Monolayers of uninfected ARPE-19 cells were treated with hydrogen peroxide (H_2O_2) (500 uM) for stimulation of parthanatos (positive control) and harvested at 2 hrs after treatment. HSV1-infected, mock-infected, and H_2O_2-treated cells were lysed and subjected to western blot analysis for detection of PARP-1 and PAR proteins.

Results: H_2O_2-treated ARPE-19 cells showed stimulation of PARP-1 and especially PAR that is essential for the operation of parthanatos. Whereas PARP-1 protein was stimulated in both mock-infected and HSV1-infected ARPE-19 cells at relatively equal amounts at all times investigated, stimulation of PAR protein was not detected in either mock-infected or HSV1-infected ARPE-19 cells at all times investigated.

Conclusions: Although parthanatos can operate in ARPE-19 cells as suggested by stimulation of PARP-1 and PAR following H_2O_2-treatment, we provide new evidence that HSV1 infection may inhibit the operation of parthanatos in ARPE-19 cells, possibly through virus-encoded suppressors as seen during apoptosis and necroptosis (Guo et al, 2015). Our findings also suggest that stimulation of parthanatos during HSV1 infection is cell-type specific. Our pilot study provides proof-of-principle for further investigations to determine the role of parthanatos during the pathogenesis of HSV1-induced ARN and PORN.

CONTROL ID: 3710508

SUBMITTER (NAME ONLY): Sarah Kim

TITLE: Precise quantification of episcleral venous flow rates in human subjects before and after netarsudil 0.02%

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Kim, University of Maryland at College Park, College Park, Maryland, UNITED STATES|V. Chen, J. Pottenburgh, O. Saeedi, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|M. Cruz, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Netarsudil, a Rho-kinase inhibitor and norepinephrine transporter inhibitor, is known to lower episcleral venous pressure, however, its precise effect on flow rates has not been studied. We have recently developed erythrocyte mediated angiography, EMA, a technique in which autologous fluorescently labeled erythrocytes are reinjected into a human subject permitting the observation and precise quantification of flow rates. The purpose of this study was to quantify the short- and long-term effects of netarsudil on episcleral venous flow rates in treatment-naïve ocular hypertensive and glaucoma suspect subjects using EMA.

Methods: This prospective study enrolled treatment-naive ocular hypertensive and glaucoma suspect patients. All subjects underwent anterior segment EMA, conventional indocyanine green angiography, and applanation tonometry at baseline, 1 hour after drop instillation, and 1-2 weeks after once daily topical netarsudil use. A MATLAB program we developed was used to track erythrocytes on EMA angiograms. Vessel diameter was measured using the Automated Retinal Image Analyzer program. Changes in erythrocyte velocity, vessel diameter, estimated blood flow, and IOP were assessed using two-sample unpaired t-tests.

Results: Twelve episcleral vessels of nine eyes of seven patients were analyzed. IOP was reduced from 15.6±3.4 to 10.7±4.1mmHg at 1-hour (p=0.017) and 11.1±4.3mmHg at 1-2 week(s) after therapy initiation (p=0.007). Mean erythrocyte velocities did not differ significantly in this sample from baseline (2.2±1.0 mm/s), at one hour (3.1±1.4mm/s, p=0.063), or at 1-2 weeks (1.8±1.4 mm/s, p=0.219). However, vessel diameter increased from 62.7±14.5um to 100.2±32.3um (p=0.003) after one hour and 85.8±30.9um (p=0.008) after 1-2 weeks. Episcleral blood flow increased significantly from 0.45±0.28μL/min to 1 hour post eyedrop (2.06±02.41μL/min, p=0.033), but not after 1-2 weeks (0.74±0.94μL/min, p=0.121).

Conclusions: We found that netarsudil 0.02% resulted in significant IOP reduction and associated increase in episcleral venous flow rates in treatment-naïve glaucoma suspect patients. This is the first study to our knowledge that quantified the change in episcleral venous blood flow in vivo after a pharmacologic intervention, which can be assessed using EMA. This technology has the potential to offer novel biomarkers for treatments that target the conventional outflow pathway.

CONTROL ID: 3710509

SUBMITTER (NAME ONLY): Gideon Obasanmi

TITLE: Granzyme B Proteolyzes Thrombospondin-1 in RPE Cells and Choroidal Neovascularization

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Obasanmi, E.Y. Tian, E. To, J.Z. Cui, J.A. Matsubara, Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|M.R. Zeglinski, D. Granville, Department of Pathology, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: An imbalance of pro and anti-angiogenic factors contributes to the pathology of neovascular AMD (nAMD). Thrombospondin-1 (TSP-1) is a potent inhibitor of angiogenesis induced by pro-angiogenic factors such as vascular endothelial growth factor (VEGF). Granzyme B (GrB) is a serine protease whose extracellular activity is increased in the outer retina and choroid of human eyes with choroidal neovascularization (CNV) from nAMD. This study determines the effects of GrB on TSP-1 in silico, and in cell-free cleavage assays, human eyes, RPE culture, and an explant choroid sprouting assay (CSA).

Methods: Mapping of human TSP-1 protein sequences for potential GrB cleavage sites was performed with GraBCas while the prediction of cleavage product size was done with the Compute pI/Mw tool from ExPASy. To confirm predictions, cell-free cleavage assays were done by digesting rhTSP-1 with rhGrB in 50 mM Tris, pH 7.5 for 2 hours at 37^{O}C. Electrophoresis was performed on the digestion products, followed by Coomassie Brilliant Blue staining and imaging. CNV donor eye tissue sections were probed by immunohistochemistry for GrB and TSP-1. RPE cells were stimulated with GrB. CSA using RPE-choroid-sclera explants from 3-month-old C57BL/6J mice was established and cultured with rhTSP-1 (1 µg) or rhGrB (100nM) treatments. Images of CSA explants were captured and sprouting morphometry was quantified Western blot (WB) was used to assess TSP-1 expression in RPE cell culture and CSA supernatant.

Results: In silico analysis predicted six potential GrB cleavage sites in the N- and C-termini and within type III repeats of TSP-1. Cell-free cleavage assays shows that GrB cleaves TSP-1 with double fragments ranging ~100kDa and triple fragments between 63-75kDa. An inverse relationship of GrB and TSP-1 was confirmed in RPE and choroid of CNV eyes, with higher GrB and lower TSP-1 immunolabelling. WB showed significantly reduced expression of TSP-1 in GrB-treated RPE cell culture ($p<0.05$) and CSA supernatant ($p<0.05$) compared with controls. Vascular sprouting area was significantly reduced in TSP-1 treated CSA ($p<0.05$) compared with controls.

Conclusions: GrB cleavage of antiangiogenic factors such as TSP-1 may contribute to CNV development in nAMD via pro-angiogenesis. Future studies are required to investigate whether the pharmacological inhibition of extracellular GrB could mitigate CNV in nAMD by conserving intact TSP-1.

CONTROL ID: 3710515

SUBMITTER (NAME ONLY): Brian Gutermuth

TITLE: Late-Onset Orbital Infection Following Blowout Fracture Repair with a Medpor Titan Implant: A Case Report

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Gutermuth, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|R. Beaulieu, Ophthalmalology, Kresge Eye Institute, Detroit, Michigan, UNITED STATES|R. Beaulieu, Consultants in Ophthalmic and Facial Plastic Surgery, Southfield, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Brian Gutermuth: Commercial Relationship: Code N (No Commercial Relationship) | Robert Beaulieu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report a case of late orbital infection with aspergillus and multiple bacteria species nine months after orbital floor fracture repair using the Titan Medpor implant.

Methods: Observational case report

Results: A 40 year-old male with a non-contributory past medical and ocular history presented with diplopia and right-sided enophthalmos after sustaining trauma to the orbit. Examination was relevant for moderate limitation in downgaze and exophthalmometry readings of 19.5 mm on the right and 22 mm on the left. His exam was otherwise unremarkable. CT imaging revealed a right orbital floor fracture with herniation of orbital contents into the maxillary sinus. Surgical repair achieved proper coverage of the fracture edges by a Medpor Titan orbital implant, which is a sheet of titanium mesh embedded within a porous polyethylene matrix with a solid barrier surface facing the orbital contents. Post-operatively, he had full extraocular motility, resolution of his diplopia and enophthalmos, and equal exophthalmometry measurements at one day, one week, and two months. He returned to clinic on post-operative month nine with complaints of right eye gaze-evoked amaurosis on upgaze, intermittent diplopia, and a pressure sensation on upgaze. Exam revealed full extraocular motility, 1 mm of hyperglobus on the right, and exophthalmometry readings of 22.5 mm on the right and 22 mm on the left. CT imaging of the orbits with and without contrast demonstrated a malpositioned orbital implant with a peri-implant capsule and fluid collection. He underwent orbital implant removal with drainage of the fluid collection. Cultures revealed the presence of non-fumigatus Aspergillus, along with rare Staphylococcus epidermidis and Neisseria sicca.

Conclusions: Our case presents two uncommon orbital pathologies. The first being the occurrence of late orbital infection in an immunocompetent patient with an otherwise uncomplicated recovery. The second is a culture-proven orbital infection with Aspergillus spp. after an orbital floor repair with a porous polyethylene comprised implant. Post-operative orbital infection with Aspergillus sp. has no clearly defined incidence, with only a few case reports describing the complication. We use this case to bring awareness to these rare occurrences and the need to have high suspicion of late-onset implant infection in patients with orbital signs after fracture repair.

CONTROL ID: 3710516

SUBMITTER (NAME ONLY): Danica Joseph

TITLE: Long term outcome and prognostic indicators in Posner Schlossman Syndrome

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.M. Joseph, P.J. McCluskey, Sydney Hospital and Sydney Eye Hospital, Sydney, New South Wales, AUSTRALIA|L.L. Lim, P. Samalia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|L.L. Lim, P. Samalia, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|J. Wells, Canberra Hospital, Canberra, Australian Capital Territory, AUSTRALIA|P.J. McCluskey, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|E. Paul, Public Health and Preventative Medicine, Monash University, Melbourne, Victoria, AUSTRALIA|A.J. Hall, Alfred Hospital, Melbourne, Victoria, AUSTRALIA|A.J. Hall, Surgery, Central Clinical School, Monash University, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine the incidence of and risk factors for progression in patients with Posner Schlossman Syndrome (PSS) by assessing time to progression (TTP).

Methods: This retrospective multi-centre study reviewed long-term follow-up data of PSS patients across five Australian institutions between 1990 and 2020. Initial presentation clinical data, demographics, frequency of PSS relapse without progression, antiviral usage and anterior chamber (AC) tap results were recorded. Progression was defined as development of chronic secondary glaucoma, chronic uveitis or permanent corneal or endothelial failure. Relapse without these features was not counted as progression. TTP was taken as the time from initial presentation to the first detection of progression. Cox proportional hazards regression and Kaplan-Meier analysis were used to estimate the risk of disease progression and compare progression free survival among different groups.

Results: 102 consecutive patients (68 men and 34 women) met the inclusion criteria. Follow-up ranged from 0-31 years with a mean of 5.0 years. 47 of 102 patients met the criteria for progression with development of chronic glaucoma (n=39), chronic inflammation (n=22) or permanent endothelial failure (n=4). TTP varied from 0–11 years with a median of 0.8 years. 46 of 102 patients underwent an AC tap of which 28 were positive (viral DNA identified) and 18 negative. Median progression free survival in tap-positive patients was 2.6 years compared to 5.3 years in the tap-negative group.

On univariate analysis, higher age at presentation was associated with increased risk of progression (HR 1.03 per year of increased age, $p<0.0001$), whilst immunocompetence (HR 0.36, $p=0.037$) and white ethnicity showed a reduced risk of progression (HR 0.36). On multivariate analysis increased age at presentation (HR 1.03 per year, $p=0.002$) and a positive AC tap (HR 2.8, $p=0.001$) showed increased risk of progression while white ethnicity (HR 0.27, $p=0.02$) was protective.

Conclusions: The long-term prognosis of PSS is reasonable. The majority of patients do not progress by 5.0 years. Increasing age at presentation and a positive AC tap are associated with increased risk of progression and white ethnicity is associated with reduced risk. This information might be used to guide management of patients with PSS.

CONTROL ID: 3710517

SUBMITTER (NAME ONLY): Viviana Barquet-Piza

TITLE: Effect of Prostaglandin Analogues on Corneal Hysteresis in Treatment Naïve Racially Diverse Patients

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Barquet-Piza, M. Giovingo, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|J. Nelson, Des Moines University, Des Moines, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal hysteresis (CH) has been shown to be an independent risk factor for the development and progression of glaucoma. Topical Prostaglandin Analogues (PGA) are a common first-line treatment for open-angle glaucomas. Previous studies have found that high CH values are associated with a lower rate of visual field loss, while low CH have been identified as an independent risk factor for development and progression of glaucoma. PGA's have been demonstrated to increase CH through several mechanisms including reduced central corneal thickness, increased keratocyte density, and lower intraocular pressure. The aim of this study is to investigate if starting PGA treatment alters corneal hysteresis in a treatment naïve, racially diverse group of patients.

Methods: A total of 38 eyes from 19 patients were analyzed. Patients with a diagnosis of either primary open angle glaucoma, ocular hypertension, normal tension glaucoma, or anatomically narrow angle who were treatment naïve were included. CH measurements were taken with the Ocular Response Analyzer (ORA) prior to PGA use and after PGA use. CH measurements with waveform score lower than 3.5 were excluded. Demographic data for the patients was also obtained.

Results: Paired T-Test were completed to examine variance between untreated and treated CH values for each patient. Significant increases in CH were observed after PGA use in both right eye (OD) ($p=0.02$) and left eyes (OS) ($p=0.002$). There was an average CH increase of 1.08 (SD=+1.70) OD and 1.13 (SD=+1.28) OS. 57.89% of the study population identified as African American/Black, 26.32% Hispanic, 10.53% White, and 5.26% Asian.

Conclusions: These findings demonstrated a significant increase in CH after starting PGA use in a predominantly Black and Hispanic population. This increase in CH could lead to a reduction in glaucoma progression, as well as identify a possible modifiable risk factor for glaucoma that was previously not considered, particularly in populations that are already at higher risk, and identify a new therapeutic effect of PGA. Further studies are necessary to determine if the effects of PGA on CH persist long term.

CONTROL ID: 3710522
SUBMITTER (NAME ONLY): Mahbubul Shihan
TITLE: Depth-dependent structural responses of mouse lens fiber cells during whole lens shape changes
SESSION TITLE: Lens Biology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M.H. Shihan, J. Parreno, V.M. Fowler, University of Delaware, Newark, Delaware, UNITED STATES|S.K. Biswas, W. Lo, Morehouse School of Medicine, Georgia, UNITED STATES|
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ABSTRACT BODY:

Purpose: Two common age-related lens pathologies, cataracts, and presbyopia are linked to age-dependent increases in lens stiffness. The mouse lens has dramatic alterations in fiber cell shapes and organization with lens age, along with increased lens stiffness. However, little is known about the relationship between observed depth-dependent cellular structures, and lens biomechanical properties. We aimed to determine lens fiber cell macro-to-nanoscale structural deformation during and after lens compression as a function of radial depth.

Methods: Freshly dissected 8-week-old mouse lenses were compressed by application of 10 glass coverslips (CS). Images of lenses were taken with an Olympus SZ11 dissecting microscope with a digital camera, followed by fixation for scanning electron microscopy (SEM). Images of mouse fiber cells under compression and after recovery were captured by a JEOL 820 scanning electron microscope. Image analysis was performed using ImageJ.

Results: Morphometrics analysis revealed that at 10 CS load (29% axial strain), lens axial diameter, aspect ratio, and volume decreased compared to controls while equatorial diameter increased, as expected. Upon release of load, equatorial diameter and aspect ratio recovered completely, while axial diameter and volume recovered partially. SEM revealed that cortical fiber bundle curvature increased under compression (10CS), compared to controls and recovered lenses, while nuclear fiber bundle curvature was unaffected. The paddles and protrusions of outer cortical fibers were severely distorted by compression, with a near absence of paddle-associated protrusions in the compressed lens compared to controls, while this phenomenon was rescued in the recovered lens. Notably, in SEM images of the inner cortex, the nanostructures of fiber cells were unaffected by compression, resembling the morphology of controls and recovered lenses.

Conclusions: Our study reveals that gross lens shape change caused by mechanical strain results in ultrastructural-level changes of the lens fiber cells in a depth-dependent fashion such that the nanostructures of fiber cells are deformed in the outer cortex, but little to no deformation in the inner cortex and nucleus of the lens. This provides critical information to expand current biomechanical models of lens shape changes in terms of presbyopia and cataracts.

CONTROL ID: 3710523

SUBMITTER (NAME ONLY): Elsayed Elbasiony

TITLE: Mast cells augment neutrophil activation and their secretion of tissue-damaging factor

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Elbasiony, W. Cho, Y. Guan, A. Singh, S. Mittal, S. Chauhan, Department of Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Excessive neutrophil activation and secretion of their effector molecules result in tissue damage during ocular inflammation. Previously, our study demonstrated that mast cells initiate neutrophil recruitment to the ocular surface following injury. Here, we investigated whether mast cells promote activation of neutrophils to secrete tissue-damaging effector molecule.

Methods: Bone marrow cells were harvested from femurs and tibias of Balb/c mice and cultured for 3-4 weeks in the presence of IL-3 (10 ng/ml) and SCF (50 ng/ml) to generate mast cells. Neutrophils were magnetically sorted from the bone marrow cells of Balb/c mice using a neutrophil isolation kit (>95% purity). Mast cells were co-cultured with neutrophils at 1:1 ratio for 3 hours. Thereafter, neutrophils were harvested to evaluate the expression of their activation markers, CD11b and Ly6G, using flow cytometry. Supernatants of the co-cultures were collected to assess the activity of myeloperoxidase (MPO), an enzyme involved in neutrophil-mediated collateral tissue damage, using a colorimetric assay kit.

Results: Neutrophils co-cultured with mast cells expressed a significantly higher level of maturation marker CD11b (5-fold increase) ($P=0.0002$), compared to neutrophils cultured in medium alone. Similarly, a significant 48% increase in the expression of Ly6G by neutrophils was observed in the presence of mast cells compared to neutrophils cultured alone ($p=0.008$). In addition, a significant 50% increase in MPO activity was observed in neutrophils when cultured in the presence of mast cells, compared to control neutrophil cultures ($p=0.03$).

Conclusions: Our data demonstrate that mast cells amplify neutrophil activation and promote the secretion of tissue damaging myeloperoxidase enzyme.

CONTROL ID: 3710524
SUBMITTER (NAME ONLY): Alex Nixon
TITLE: Ratio of Refractive Error Change to Axial Elongation in Young Myopes
SESSION TITLE: Myopia epidemiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Nixon, W. Shamp, E. Maynes, X. Cheng, N.A. Brennan, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|M.A. Bullimore, University of Houston College of Optometry, Houston, Texas, UNITED STATES|
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ABSTRACT BODY:

Purpose: With increasing use of axial length to monitor myopia progression, the ratio of refractive error (RE) change to axial elongation (AE) has important clinical implications. However, the true value of the ratio and how age and axial length affect it remain uncertain. We conducted a systematic review and meta-analysis to model the ratio.
Methods: A systematic search was performed using Ovid Medline, EMBASE, and Cochrane Central Register of Controlled Trials. The following combined terms were used: “myopia” or “myopic” and “child” or “children” and “progression” or “longitudinal” or “follow-up” or “shift” and “axial”. Studies containing simultaneous RE change and AE in untreated eyes were identified. Other data collected were mean baseline age, standard deviation (SD) of AE, SD of RE change, sample size and proportion of Asian subjects in the study population. Due to desired statistical properties, the natural logarithm of the magnitude of mean refractive error change versus mean axial elongation was analyzed with a weighted multivariable linear mixed effects meta-analysis model, including three levels of random effects to account for all variability. The standard inverse variance method was used for weighting. Baseline values for mean RE and mean AE were included in the model as covariates.
Results: A total of 67 studies with 86 different subpopulations and 167 evaluations contained complete data sets. The model is plotted in the Figure and covariates summarized in the Table. The overall weighted mean ratio was 2.04 [95%CI: 1.96, 2.12] D/mm. No covariates were statistically significant. Prediction intervals were relatively large, potentially reflecting variability in refractive error.
Conclusions: This work sets a benchmark for clinical expectations with respect to the ratio between RE change and AE in myopic children. The lack of apparent impact of age on the ratio may reflect counterbalance between physiologic growth observed in younger children and a decreased ratio, anticipated from optical calculations, in longer eyes of older children. Interpretation should take into account limitations of using aggregated rather than individual subject data.

CONTROL ID: 3710532

SUBMITTER (NAME ONLY): Hadar Naidorf Rosenblatt

TITLE: Efficiency of anti-VEGF drug switch in patients who did not respond to a series of Bevacizumab injections

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Naidorf Rosenblatt, Z. Rotfogel, Ophthalmology, Kaplan Medical Center, Rehovot, ISRAEL|A. Ganon, Ophthalmology, Yitzhak Shamir Medical Center Assaf Harofeh, Zerifin, Center, ISRAEL|

Commercial Relationships Disclosure: Hadar Naidorf Rosenblatt: Commercial Relationship: Code N (No Commercial Relationship) | Aya Ganon: Commercial Relationship: Code N (No Commercial Relationship) | Ziv Rotfogel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: When patients with macular edema due to pathologies like neovascular age-related macular degeneration (nAMD) and diabetic retinopathy (DR) fail to show significant improvement within the first 3 to 6 months of initiating anti vascular endothelial growth factor (anti-VEGF) treatment, they are often switched to a different anti-VEGF agent. However, the benefits of such a switch were not well established. We examined the effectiveness of anti-VEGF agent switching in eyes with retinal pathologies that show poor response to Bevacizumab Intra-vitreal injections.

Methods: We retrospectively compared the results of the central macular thickness (CMT) and visual acuity (VA) between eyes with sub-optimal response to at least three Bevacizumab injections that continued retreatment with Bevacizumab versus those that switched to Aflibercept or Ranibizumab injections. 59 eyes were investigated: 21 eyes with Diabetic retinopathy (DR)- group A, 28 eyes with neovascular age-related macular degeneration (nAMD)- group B. Group C composed of group A and group B and 10 more eyes with either retinal vein occlusion or pseudophakic cystoid macular edema. Groups were divided into subgroups- groups A1 (8 eyes), B1(14 eyes), and C1 (25 eyes) continued to be treated with Bevacizumab. Groups A2, B2, C2 consisted of patients that switched to aflibercept or Ranibizumab injections and included 13, 14, and 34 eyes respectively.

Results: In all eyes where treatment has been switched to either Aflibercept or Ranibizumab, a decrease of CMT was seen; 38.5 (SD 46.2); 92.6 (SD 106.8), and 82.1 (SD 115.6) microns in groups A2, B2, and C2 respectively. However,a mean increase of 1.63 microns (SD 87.3) was found in the CMT of eyes in group A1; and a mean decrease in CMT of 5.71 (SD 111.7) and 2.12 (SD 94.9) microns was found in group B1 and C1 respectively. The difference in CMT was statistically significance between groups B1 versus B2 and between C1 versus C2 groups ($p=0.025$, $p=0.004$, respectively). A similar trend was seen between groups A1 versus A2 but statistical significance was not achieved. Analysis of the visual acuity revealed no significant difference between all groups.

Conclusions: Our results may indicate that switching between anti-VEGF agents is indeed an effective strategy to treat eyes with sub-optimal response to Bevacizumab injections.

CONTROL ID: 3710533

SUBMITTER (NAME ONLY): Roberto Nunez

TITLE: Clarifying the roles of high and low blood pressure in glaucoma via physiology-informed machine learning

SESSION TITLE: Blood flow and ischemia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Nunez, R. Rai, J. Keller, M. Lin, D. Zou, G. Guidoboni, Engineering, University of Missouri System, Columbia, Missouri, UNITED STATES|E.L. Robinson, Social Work, University of Missouri System, Columbia, Missouri, UNITED STATES|G. Guidoboni, Mathematics, University of Missouri System, Columbia, Missouri, UNITED STATES|A. Harris, A. Verticchio, B.A. Siesky, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|C. Wikle, Statistics, University of Missouri System, Columbia, Missouri, UNITED STATES|M. Szopos, Mathematics, Universite de Paris, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Both high and low blood pressure (BP), together with intraocular pressure (IOP), are risk factors for glaucoma. The underlying physiological mechanisms for both high and low BP as a risk factor remain elusive. Here a novel physiology-informed machine learning (ML) approach combines physiology-based mathematical modeling and unsupervised clustering to discern the impact that abnormal BP may have on glaucoma.

Methods: 115 open angle glaucoma (OAG) patients were assessed for: IOP, systolic and diastolic BP (SBP, DBP), heart rate (HR), and color Doppler imaging (CDI) of peak-systolic and end-diastolic velocity (PSV, EDV) of the ophthalmic artery (OA) and central retinal artery (CRA). For each patient, IOP, SBP, DBP, and HR were fed to a validated mathematical model (Guidoboni et al, IOVS, 2014) which estimates hemodynamic variables unavailable from instrumentation. The enhanced dataset and the model-estimated variables are fed to a Fuzzy c-means (FCM) clustering algorithm to identify patient clusters with similar ocular hemodynamics.

Results: The FCM clustering algorithm revealed 3 clusters plotted in the IOP-MAP plane in Fig.1 (left) (MAP=mean arterial pressure = 2/3DBP+1/3SBP). Fig.1 (right) shows that ocular perfusion pressure (OPP = 2/3MAP-IOP) is high in cluster 2 and low in cluster 3. The PSV medians in the CRA are similar for all clusters (<10%), while the PSV median in the OA of cluster 2 was ~22% higher than in clusters 1 and 3 (see Fig.2 (top)). On the other hand, cluster 3 exhibits higher vascular resistance in the venules and central retinal vein (Fig.2 (bottom)).

Conclusions: High and low BP may contribute to glaucoma in different ways, depending also on the IOP level. The bigger discrepancy in PSV medians in OA with respect to CRA may indicate that patients in cluster 2 need a stronger autoregulation engagement to maintain homeostasis, thereby limiting their capacity to accommodate physiological BP fluctuations. High venous resistance in cluster 3 might render those vessels susceptible to venous collapse. The technology for measuring venous resistances is currently unavailable and our results indicate that its development might be an important goal for the study of glaucoma.

CONTROL ID: 3710535

SUBMITTER (NAME ONLY): Nooshin Mojab

TITLE: FundusNet, A self-supervised contrastive learning framework for Fundus Feature Learning

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Mojab, M. Alam, J. Hallak, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose:

To introduce a model called FundusNet which learns visual representations of Fundus images that can be employed in other downstream tasks of ophthalmic imaging applications to further improve the generalization performance.

Methods:

We employ a self-supervised learning approach formulated as a contrastive learning framework by incorporating a broad family of data augmentation. This could potentially lessen the sensitivity of the model to domain-specific information in the data and therefore improve upon the generalization of learned features that can be used across different domains. In the contrastive learning framework, the representations are learned by maximizing the agreement between the two augmented views of the same data input. This framework consists of four main components, augmented views, base encoder, projection head, and contrastive loss.

We evaluate the quality of the learned representation for a downstream task of glaucoma detection and compare our method to a fully supervised method and transfer learning method using a pre-trained network on non-medical images, ImageNet and CIFAR. We employ a subset of the I-ODA dataset for unsupervised pre-training which learns the base encoder model. I-ODA is a real-world multi-domain ophthalmic imaging dataset from which we isolated 14k fundus photos with 6000 glaucoma and 8000 non-glaucoma images.

Results:

Our method archives the performance accuracy of 84.87% outperforming the strongest supervised baseline by ~2% and self-supervised baseline by ~4.6%. Among the supervised baselines, the custom-designed method achieves a better result over off-the-shelf ResNet. This shows that specifically designed networks are usually very important to the success of supervised methods which could limit their generalization capacity, especially for real-world clinical applications. The superior performance of FundusNet over transfer learning that uses pre-trained networks on ImageNet shows that transfer learning performs the best when the nature of target data is similar to the one used for pretraining.

Conclusions:

FundusNet addresses the limitation of transfer learning with non-medical images for ophthalmic imaging applications that face a shortage of labeled data. Self-supervised learning is able to achieve a more general representation and hence improve the generalization performance as opposed to fully supervised methods.

CONTROL ID: 3710538

SUBMITTER (NAME ONLY): Lindsay Rhodes

TITLE: The AL-SIGHT Program: Evaluating Change in Patient Knowledge about Glaucoma and Attitudes about Eye Care

SESSION TITLE: Public Health I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Alabama Screening and Intervention for Glaucoma and eye Health through Telemedicine (AL-SIGHT) program provided evidence-based eye health education tailored for patients at-risk for glaucoma in rural primary care clinics. The education program was based on the InCHARGE eye health education program designed for African Americans and materials from Prevent Blindness and NEI's National Eye Health Education Program. This study investigated the impact of the first year of AL-SIGHT's eye health education on at-risk patients' knowledge about glaucoma and attitudes about eye care.

Methods: Three federally qualified health centers in rural, underserved communities in Alabama enrolled participants with one or more risk factors: Black or Hispanic ≥ 40 years, White ≥ 50 years, diabetes, a pre-existing glaucoma diagnosis, and/or a family history of glaucoma. Participants were administered a 7-question survey to assess their knowledge and attitudes on glaucoma and eye care prior to delivery of the education program and ocular imaging. Follow-up surveys were administered 6 weeks and 6 months after the initial visit by telephone call or web-based survey. Participant changes of survey responses from baseline to 6-week and 6-month follow-ups were compared using McNemar's test.

Results: 209 participants completed the 6-week follow-up survey. Overall, there was a 56% improvement in knowledge but only a 9% improvement in attitude from baseline. 87 participants complete the 6-month follow-up survey. There was a 68% improvement in knowledge and a 13% improvement in attitude from baseline. Tables 1 and 2 describe the change in knowledge about glaucoma and attitudes about eye care at the 2 time points for each question.

Conclusions: AL-SIGHT's eye health education program improved knowledge about glaucoma at both the 6-week and 6-month timepoints. The program also had a slight improvement in attitudes about eye care, but these questions had a high percentage correct at baseline. It is encouraging that the 6-month results showed that the improved knowledge was maintained, although the sample size was smaller. Efforts will be made to stress to participants that a complete glaucoma exam consists of much more than just measuring eye pressure.

CONTROL ID: 3710540

SUBMITTER (NAME ONLY): Matthew Griffin

TITLE: Indications Cited when Initiating Scatter Laser Photocoagulation in Proliferative Sickle Cell Retinopathy

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.T. Griffin, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|M.T. Griffin, R. Mahmoudzadeh, D. Xu, J. Light, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sickle cell disease (SCD) is the most common inherited blood disorder, affecting 100,000 people in the United States and 3.2 million people globally. In proliferative sickle cell retinopathy (PSR) retinal capillary non-perfusion (CNP) leads to retinal neovascularization (NVE) that may progress to vitreous hemorrhage (VH) or tractional retinal detachment (TRD) and vision loss. Scatter laser photocoagulation is the gold standard for managing PSR but published guidelines predate the use of ultra-widefield imaging (UWFI) which allows for earlier detection of peripheral CNP and NVE. Little to no data exists on current practice patterns in PSR. We compiled data on laser photocoagulation in PSR to examine practice patterns at Wills Eye Hospital from 2014 to 2021.

Methods: Clinical charts from the Wills Eye Hospital Retina Service/Mid Atlantic Retina Group from 2014 to 2021 were retrospectively reviewed. Patients with SCR were identified using ICD-10 codes for SCD (H57.1), other non-diabetic proliferative retinopathy (H35.20, H35.21, H35.22, H35.23), and retinal disorders in diseases classified elsewhere (H36). Charts were reviewed to confirm the diagnosis of SCR and at least one documented laser treatment of at least one eye (CPT codes 67145, 67227, 67228). Exclusion criteria included comorbid diabetic or hypertensive retinopathy as well as uveitis and retinal vasculitic disease. Clinical data including VA, IOP, imaging/exam findings, prior laser status, length of follow-up, genotype, and patient demographics were recorded. The indications for initiating laser as documented by retina specialists were reported as our primary outcome.

Results: 97 scatter laser procedures performed by 30 retina specialists on 79 eyes (N = 79) (40 OD, 39 OS) in 55 patients (mean age 43.3) were identified. Primary indications for laser among all eyes were NVE/CNP (68.4%), VH (21.5%), and TRD (10.1%). Indications cited among treatment naïve eyes (n = 64) were NVE/CNP (67.2%), VH (20.3%), and TRD (12.5%). Patient characteristics are reported in Figure 1.

Conclusions: Retina specialists frequently elect to perform scatter laser photocoagulation in PSR based on peripheral NVE and CNP. Current practice patterns guided by UWFI may lead to earlier initiation of laser in PSR. Further study is warranted to evaluate the effectiveness of these treatment decisions and identify best practices for preventing vision loss in PSR.

CONTROL ID: 3710542

SUBMITTER (NAME ONLY): Timothy P.H. Lin

TITLE: Early Rate of Optical Coherence Tomography Angiography Changes is Associated with Normal Tension Glaucoma Progression Risk

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Lin, B. Shen, A. Ling, P.P. Chan, C. Tham, C. Cheung, Ophthalmology, The Chinese University of Hong Kong, Hong Kong, HONG KONG|O. Wong, T. Sit, Statistics, The Chinese University of Hong Kong, Hong Kong, HONG KONG|P.P. Chan, C. Tham, Hong Kong Eye Hospital, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Currently, the causal and temporal relationships between the degeneration in retinal vasculature and glaucoma remain ill-defined. This study evaluated the early rate of changes in optical coherence tomography angiography (OCTA) metrics in a cohort of normal tension glaucoma (NTG) eyes, and their relationships to the subsequent risk of glaucoma progression.

Methods: Three hundred and thirty-four eyes from 167 NTG patients with a follow-up period of ≥24 months were included. A swept-source OCT was used to acquire OCTA images of the peripapillary region with a scan area of 3mm x 3mm centered on the optic disc. An automated customized program was used for quantitative analysis to compute the circumpapillary vessel density (cpVD) after the removal of retinal arterioles and venules from the raw OCTA images. Early longitudinal changes of OCTA metrics from baseline to 1 year were determined for each eye. The relationship between the rate of OCTA metrics decay determined from 3 time points (0, 6, and 12 months) in the first year of follow-up to the subsequent risk of glaucoma progression was evaluated. We further attempted to define cut-off values of rate of OCTA decay in the early follow-up phase that would stratify eyes into high risk of glaucoma progression in the subsequent follow-up period.

Results: Twenty-seven eyes (8.08%) developed visual field deterioration over a mean follow-up period of 35.58 ± 5.56 months. Each 1% elevation of the annual rate of cpVD decay in the first year of follow-up was associated with more than 40% risk of glaucoma progression (RR [CI], Temporal cpVD: 1.46 [1.02-2.09]; Nasal cpVD: 1.64 [1.21-2.21]; Global cpVD: 1.48 [1.09, 2.01]) (Table). The Kaplen-Meier curves illustrate that NTG eyes with faster rates of cpVD decay the were associated with significantly higher risk of glaucoma progression, compared to eyes with slower rates of cpVD decay.

Conclusions: This study demonstrated the significant associations between early changes in cpVD as measured by OCTA and the subsequent risk of NTG progression. The findings provided evidence to support the prognostic value of retinal vasculature analysis and a novel perspective for such interpretation in the clinical settings.

CONTROL ID: 3710544

SUBMITTER (NAME ONLY): Richard Dix

TITLE: An experimental mouse model of AIDS-related progressive outer retinal necrosis (PORN) shows evidence for subclinical herpesvirus encephalitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.D. Dix, J. Oh, Biology, Georgia State University, Atlanta, Georgia, UNITED STATES| R.D. Dix, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Richard Dix: Commercial Relationship: Code N (No Commercial Relationship) | Jay Oh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Progressive outer retinal necrosis (PORN) in AIDS patients is a variant of acute retinal necrosis (ARN) in immunocompetent patients. ARN caused by herpes simplex virus type 1 (HSV1) has been associated with subclinical herpes simplex encephalitis (HSE). We therefore sought to develop a new animal model of HSV1 retinal necrosis in mice with retrovirus-induced immunosuppression (MAIDS) that mimics AIDS-related PORN and investigate the possible development and pathogenesis of subclinical HSE during HSV1 PORN as seen during HSV1 ARN.

Methods: Following anterior chamber inoculation of right eyes of groups of C57BL/6 mice with MAIDS with 10^4 PFU of either HSV1 [KOS] or HSV1 [H299] (ARN-associated clinical isolate), the inoculated right eyes, right brain halves, left brain halves, and uninoculated left eyes were collected at 3, 5, 7, or 10 days postinfection (pi) and subjected to standard plaque assay or histopathologic analysis.

Results: Histopathologic analysis of HSV1 [KOS]- or HSV1 [H299]-infected right eyes of mice with MAIDS at 10 days pi revealed retinal disease reminiscent of AIDS-related PORN in ~80% of inoculated animals whereas all uninoculated left eyes showed normal retinal architecture. Although HSV1 [KOS]- or HSV1 [H299]-infected right eyes of MAIDS mice showed consistently high amounts of infectious virus ranging from 10^3 to 10^5 PFU, right brain halves in comparison showed little ($<10^2$ PFU) to no detectable infectious virus. Significantly, none (0%) of the HSV1 [KOS] or HSV1 [H299] uniocular-infected animals showed evidence for acute HSE.

Conclusions: We have successfully developed a clinically relevant mouse model for AIDS-related HSV1 PORN using mice with MAIDS that also shows evidence for subclinical HSE. The mouse model is not virus strain dependent. Studies are ongoing to define with greater clarity the development of subclinical HSE during MAIDS-related HSV1 PORN and identify those factors of innate immunity that prevent or minimize virus spread from retina to brain and protect against acute HSE development with focus on macrophages and related cytokines/chemokines as well as programmed cell death pathways.

CONTROL ID: 3710545

SUBMITTER (NAME ONLY): Armando Oliver

TITLE: HLA-A29-Associated Retinal Vasculitis Without Choroidal Lesions

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Oliver, M. Pappaterra, C. Amaral, S. Muns, D. Duran, V. Marrero, G.A. Requejo, F. Marrero, E. DeJesus, Ophthalmology, Universidad de Puerto Rico Recinto de Ciencias Medicas, San Juan, Puerto Rico, UNITED STATES|C. Amaral, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|M. Ryan, M. Riskalla, D. Koozekanani, Ophthalmology, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|M. Pappaterra, Ponce Health Sciences University, Ponce, Puerto Rico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Birdshot retinochoroidopathy (BSRC) is characterized by multifocal choroidal lesions, retinal vasculitis, and macular edema. However, some patients may present with HLA-A29-associated retinal vasculitis without choroidal lesions. We aim to test the hypothesis that these patients may share clinical features with birdshot retinochoroiditis, including the need for systemic immunosuppressive therapy.

Methods: A retrospective medical chart review of patients who were HLA-A29 positive and had retinal vasculitis, yet no birdshot lesions was performed. Demographic, clinical, and therapeutic data were entered into a new database for analysis.

Results: Five patients who had HLA-A29-associated retinal vasculitis without choroidal lesions were identified. The median age at presentation was 52 years (range 14 - 71); 60% were female. At presentation, four patients had a visual acuity of 20/50 or better in both eyes. All eyes had mild vitritis, while 3 eyes (30%) had cystoid macular edema. One patient presented with bilateral optic nerve swelling. All patients required treatment with systemic steroids and immunosuppressive therapy.

Conclusions: HLA-A29-associated retinal vasculitis without choroidal lesions appears to share many clinical features with birdshot chorioretinitis, including the need for systemic immunosuppressive therapy. Whether this entity represents an early form of birdshot retinochoroiditis or a more localized variant of the disease is a topic for further studies.

CONTROL ID: 3710546

SUBMITTER (NAME ONLY): Signe Jeppesen

TITLE: Redistribution but no changes in total retinal blood two months after branch retinal vein occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.K. Jeppesen, Aarhus Universitet, Aarhus, Midtjylland, DENMARK|S.K. Jeppesen, T. Bek, Ophthalmology, Aarhus Universitetshospital, Aarhus, DENMARK|

Commercial Relationships Disclosure: Signe Jeppesen: Commercial Relationship: Code N (No Commercial Relationship) | Toke Bek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate regional distribution and total blood flow in retinal vessels within two months after branch retinal vein occlusion (BRVO).

Methods: Retinal blood flow was studied in the four main arcade arterioles and venules in 40 normal persons (18 males and 22 females) aged (mean±SD, range) 34.5±7.7, 24-57 years and in thirteen patients with BRVO (6 males and 7 females) aged (mean±SD, range) 54.3±7.0, 41-62 years at the time of referral and after one and two months using Doppler OCT (Medical University, Vienna, Austria).

Results: The total blood flow in the four arcades showed no significant differences among arterioles and venules and no significant difference among the normal and BRVO patients (two-way ANOVA, $p>0.39$), and in the BRVO patients the total blood flow showed no significant changes over time ($p>0.44$). At referral and after one month there was no significant difference between the blood flow in the affected and the non-affected temporal arcade vessels ($p>0.20$ for all comparisons), but after two months the blood flow difference between the non-affected and the affected temporal venule in BRVO patients had increased significantly ($p=0.04$). During the same period, there was no significant changes in central retinal thickness, best corrected visual acuity or in the oxygen saturation in the affected vessels ($p>0.15$ for all comparisons).

Conclusions: Restitution of the retina until two months after referral for BRVO can be accompanied with changes in the distribution of but not in total retinal blood flow.

CONTROL ID: 3710548

SUBMITTER (NAME ONLY): Jason Park

TITLE: Comparison of retinal structure and cyst location in X-linked retinoschisis and enhanced S-cone syndrome

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Park, R.A. Hyde, J. McAnany, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|F.T. Collison, College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|F.T. Collison, The Chicago Lighthouse, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular schisis is commonly observed in individuals with X-linked retinoschisis (XLRS) and enhanced S-cone syndrome (ESCS). The schisis can occur in several retinal layers in XLRS, perhaps most commonly in the inner nuclear layer (INL), whereas the schisis location in ESCS is less documented. The present study quantified retinal layer thickness as an approach to infer the location of macular schisis in XLRS and ESCS.

Methods: Horizontal macular B-scans (9 mm width) were acquired from 22 control subjects (25 to 50 yo, 14 males), 9 subjects with XLRS (18 to 50 yo; all genetically confirmed), and 6 subjects with ESCS (16 to 48 yo; 3 males; 5 genetically confirmed). The thickness of the INL, outer nuclear layer plus outer plexiform layer (OPL+ONL), and outer segments of the photoreceptors (OS+) was calculated from the scans using a semi-automated approach. For each layer, thickness was averaged throughout the scan and ANOVA on ranks was used to compare mean thickness for the three subject groups.

Results: Eight of 9 XLRS subjects and 5 of 6 ESCS subjects had macular schisis by OCT imaging. The INL was abnormally thick for all XLRS subjects, and ranged from normal to abnormally thin for all but one ESCS subject. As a group, the INL was significantly thicker than normal for the XLRS subjects ($Q = 3.85$, $p < 0.05$), but not significantly different from normal for the ESCS subjects ($Q = 1.75$, $p > 0.05$). Conversely, the OPL+ONL was abnormally thick for all ESCS subjects and abnormally thin for all XLRS subjects. The mean OPL+ONL was significantly thicker than normal for the ESCS subjects ($Q = 3.62$, $p < 0.05$) and significantly thinner than normal for the XLRS subjects ($Q = 2.81$, $p < 0.05$). The OS+ was abnormally thin for all but one XLRS subject, and ranged from borderline-thin to thick for the ESCS subjects. As a group, the OS+ was significantly thinner than normal for the XLRS subjects ($Q = 3.85$, $p < 0.05$), but not significantly different from normal for the ESCS subjects ($Q = 0.16$, $p > 0.05$).

Conclusions: In this sample of subjects, macular schisis was predominately located in the INL of XLRS subjects and in the OPL+ONL of ESCS subjects. Additionally, photoreceptor thinning appears to be a common characteristic of XLRS that is less apparent in ESCS. These data may provide an additional objective approach to differentiate between XLRS and ESCS.

CONTROL ID: 3710555

SUBMITTER (NAME ONLY): Oren Yehezkel

TITLE: A Prospective, Multicenter, Randomized, Masked, Controlled Pivotal Trial to Assess the Safety and Efficacy of an Eye-Tracking-Based Treatment for Amblyopia Under Binocular Conditions versus-Patching- Interim Results

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Yehezkel, A. Moshkovitz, NovaSight Ltd, Airport city, ISRAEL|T. Wygnanski-Jaffe, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|M. Belkin, Goldschleger Eye Research Institute, Sheba Medical Center The Goldschleger Eye Institute, Tel Hashomer, Tel Aviv, ISRAEL|T. Wygnanski-Jaffe, Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, ISRAEL|

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ABSTRACT BODY:

Purpose: Introduction: A pivotal RCT study was conducted to evaluate the safety and efficacy of a novel treatment for amblyopia using the CureSight, a binocular- eye-tracking- based device compared with the golden standard of amblyopia treatment-patching.

Methods: 103 participants children aged 4-9 with anisometropic, strabismic or mixed amblyopia watched an internet content of their choice on the CureSight screen five times a week for 90 minutes vs. 7 days a week of 120 minutes of patching over 16 weeks . An eye tracker with a sampling rate of 90 Hz was used to identify the gaze position of each eye. During the treatment, patients wore anaglyph glasses over their habitual correction spectacles. Binocular stimulation movies using any internet or educational content were presented with the images of both eyes superimposed and the foveal area of the non-amblyopic eye blurred to a visual acuity of two lines below the acuity of the non-amblyopic eye. Best-corrected visual acuity (BCVA) at near and distance, stereo acuity, contrast sensitivity and reading performance were assessed. Primary efficacy endpointof the study was the mean change in distance BCVA of the amblyopic eye from baseline after binocular CureSight treatment, compared to that of patching. The secondary efficacy endpoint was the change from baseline to week 16 in in both study groups: stereo acuity test score, binocular distance and near BCVA and the amblyopic eye near VA.

Results: Interim analysis of the pivotal study was conducted after approximately 90% of the evaluable cohort subjects completed the 16-week follow-up visit. The primary outcome results were defined as “favorable” according to the statistical analysis plan (CP ≥ 90%) for the pre-planned analysis with 87 completed subjects.

Conclusions: The full study results are expected during February 2022 and will be presented at the conference.

CONTROL ID: 3710556

SUBMITTER (NAME ONLY): Judith Zavala

TITLE: In vitro biocompatibility panel for PEGDA intraocular drug delivery devices

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zavala, F. Robles-Saucedo, C. Guerrero-Beltrán, J.E. Valdez, Escuela de Medicina, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|L. Dávila, University of California Merced, Merced, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: PEGDA drug delivery devices (PDDD) have potential for the treatment of chronic vitreoretinal diseases, surpassing the ocular barriers, and sustaining the drug release. In vivo models are the most used to analyze the potential of PDDD. However, there are cellular biomarkers that can be analyzed in vitro to prevent non desired effects in preclinical studies. Here, we analyzed the acute cell response in vitro in terms of cell viability, cytotoxicity, apoptosis, and necrosis in cells exposed to PDDD.

Methods: PDDD were 3D bioprinted at Lawrence Livermore National Laboratory. Endothelial cells SVEC 4-10 (ATTC®) were used in three groups: control (non-treated), negative control (treated with 15% DMSO), and treated (exposed to PDDD). For the cytotoxicity test, a second negative control was used (treated with 5% DMSO). SVEC 4-10 cells (5,000/100mL per well) were incubated in a 96-well plate with or without a ~2.4 mg piece of PDDD for 24h to determine cell viability (with Cell Titer Blue, Promega) and cytotoxicity (with LDH assay kit, Pierce). For apoptosis analysis (with Annexin V kit, ThermoFisher Scientific), 200,000 cells/well in a 12-well plate were used. The results were analyzed using GraphPad Prism 8.01 software.

Results: The viability of cells exposed to PDDD was 70.9%, with significant difference when compared to the control ($p = 0.0383$). The cytotoxicity measured by LDH activity was 2.17% ($p = 0.0123$). The early apoptosis was 24.1% in the treated cells and 15.9% in the control, while the late apoptosis was 3.4% and 2.7% respectively. There was no difference in the necrosis analysis (0.1% in treated and non-treated cells).

Conclusions: The exposure to PDDD decreased the cell viability and increased the cytotoxicity near to the acceptable treshold. The apoptotic activity increased in 10% in the treated cells, however, the viability decrease is not attributed to necrotic events. This in vitro biocompatibility panel allows the adjudgment making in the composition of the PDDD before using it in preclinical models. Additionally, this panel can be complemented with the analysis of oxidative stress, genotoxicity, and inflammatory markers.

CONTROL ID: 3710557

SUBMITTER (NAME ONLY): Henry Chen

TITLE: Neuroprotection of retinal ganglion cells using two vector approach for expression of TrkB receptor and agonist ligand

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Chen, A. Latuszek, Y. Hu, B. Patel, G. Patel, J. Cao, C. Romano, Ophthalmology, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

Commercial Relationships Disclosure: Henry Chen: Commercial Relationship(s);Code E (Employment):Regeneron | Adrianna Latuszek: Commercial Relationship(s);Code E (Employment):Regeneron | Ying Hu: Commercial Relationship(s);Code E (Employment):Regeneron | Brijeshkumar Patel: Commercial Relationship(s);Code E (Employment):Regeneron | Gaurang Patel: Commercial Relationship(s);Code E (Employment):Regeneron | Jingtai Cao: Commercial Relationship(s);Code E (Employment):Regeneron | Carl Romano: Commercial Relationship(s);Code E (Employment):Regeneron

ABSTRACT BODY:

Purpose: Tropomyosin receptor kinase B (TrkB) is an effective target for neuroprotection in experimental glaucoma models. Supplying agonist ligands, such as brain-derived neurotrophic factor (BDNF) and neurotrophin-4 (NT4), by protein or gene therapy in glaucoma models has been shown to protect retinal ganglion cells (RGCs). However, long-term protection is hindered by TrkB down-regulation and truncated TrkB isoforms. Previous experiments have demonstrated when both TrkB and BDNF are expressed and given to the eye before optic nerve injury, RGC death is delayed. For this experiment, we are using a two-vector approach to confirm the necessity of both the receptor and ligand for the long-term neuroprotection of RGCs.

Methods: Adeno-associated viruses (AAVs) were made by our Viral Vector Technologies AAV Production Core. For in vitro protein quantification, HEK-293 cells were transduced with AAVs. Supernatant and lysate were collected three days afterward for ELISAs. Adult C57BL/6J mice or adult Sprague Dawley rats were used. The eyes were intravitreally injected with AAV2 vectors expressing TrkB, proBDNF, NT4, or a combination of AAVs. Three weeks after AAV injection, optic nerve injury was performed. Two or four weeks after injury, animals were sacrificed, eyes were collected, retinas were dissected, immunofluorescently stained for Brn3a and flat-mounted to count the RGC number.

Results: In vitro transduction of HEK-293 cells after 3 days of AAV treatment shows increased expression of TrkB, BDNF, or NT4. In vivo treatment of the combination of AAV2-TrkB with either AAV2-proBDNF or AAV2-NT4 significantly increases the survival of RGCs up to 78% two or four weeks after severe optic nerve injury compared to up to 46% in single AAV in both mice and rats.

Conclusions: Intravitreal administration of the combination of separate vectors encoding AAV2-TrkB and either AAV2-BDNF or AAV2-NT4 shows a significant neuroprotective effect after optic nerve injury in mice and rats, greater than achieved with ligand- or receptor-providing vectors alone.

CONTROL ID: 3710558

SUBMITTER (NAME ONLY): Suva Roy

TITLE: Light-sheet imaging of large-scale neural population activity in the retina.

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Roy, M. Rudzite, M. Scalabrino, G. Field, Neurobiology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|D. Wang, Y. Gong, Biomedical Engineering, Duke University Pratt School of Engineering, Durham, North Carolina, UNITED STATES|A. Sher, Physics, University of California Santa Cruz Division of Physical and Biological Sciences, Santa Cruz, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The visual signal entering the mouse retina is distributed across ~14 different bipolar cell (BC) types and then across ~40 different retinal ganglion cell (RGC) types. Each of these cell types are specialized to perform a specific computation for extracting relevant features of the visual world. To understand how these computations are implemented in neural circuits, we need to measure neural population activity in distinct BC and RGC types. Existing technologies are limited in scope in measuring population neural activity across synaptic tiers.

Methods: We have developed a single-photon light-sheet imaging system for measuring large-scale population activity of retinal cells. We used retinas from transgenic mice: Ai148;PVCre and Ai148;PCP2Cre expressing GCaMP6f in RGCs and BCs respectively. Cone photoreceptors expressing S-opsin were targeted for UV pattered and full-field stimulation. A semi-automated algorithm was used to characterize functionally distinct RGCs and BCs based on their spatiotemporal calcium footprints.

Results: The performance of the system was optimized by imaging fluorescent beads and axonal varicosities of individual RGCs. Axial resolution was obtained as ~20-30um, indicating clear laminar separation between the excitation light-sheet and the photoreceptor layer on which the visual stimulus was focused. We routinely imaged somatic activity of 200-300 RGCs (n=5 mice), and ~20-50 BCs (n=2 mice). Using different stimuli, we were able to drive different patterns of calcium activity, that allowed us to classify RGCs into 8-10 types in this mouse line, in agreement with previous anatomical findings. We further imaged visual stimulus evoked calcium activity in the synaptic terminals of multiple BCs simultaneously, and were able to distinguish different BC types from their inter-terminal and intra-terminal activity patterns.

Conclusions: Our platform provides a low-cost high-throughput solution for imaging calcium fluorescence dynamics in large populations of retinal cells at somatic and synaptic resolutions and classifying them based on their response characteristics. These findings have potential implications for revealing how visual signals are transformed at the synapses of functionally distinct BCs and RGCs.

CONTROL ID: 3710560

SUBMITTER (NAME ONLY): Seema Banerjee

TITLE: Relation Between Real-World Home Physical Activities and Cadence with Home Environment in Glaucoma Patients.

SESSION TITLE: Vision Impairment: Impact on Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Banerjee, A. Mihailovic, P.Y. Ramulu, Wilmer eye institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior research has not described the relationship between physical activity at home and the home environment in persons with visual impairment. Here we investigate the association between (1) the number and frequency of fall-related home hazards and (2) poor lighting with home physical activity in patients with glaucoma.

Methods: In this cross-sectional study, participants were 57 years or older at recruitment and diagnosed with primary glaucoma or were glaucoma suspects. Seven areas of participants' homes were evaluated (bedroom, bathroom, living room, kitchen, dining room, hallway, and indoor stairs) for fall hazards using the Home Environment Assessment for Visually Impaired (HEAVI). Based on these data, the total number of hazards, frequency of hazards, and average home lighting were calculated. Physical activity at home (average daily: steps, moderate to vigorous (MV) activity minutes, and peak cadence) was estimated from 7 days of GPS data (to confirm home location) and accelerometer data (to gauge activity). Negative binomial regression models were used to evaluate the relationship between each measure of home PA with metrics of the home environment. Models controlled for age, race, gender, integrated visual field sensitivity, comorbidities, and polypharmacy.

Results: One hundred fifty-three participants were included in the analysis with a mean age of 71 years (SD=7.8); half were male and about a third were Black. For every 0.1 log unit increase in average home lighting, significant increases of 3% in average daily peak cadence ($p=0.008$) and a 12% increase in MV activity ($p=0.03$) were observed. Furthermore, the average number of steps taken at home daily increased in homes with more home hazards (22% more steps/10 additional home hazards, $p=0.04$) and it was not associated with average home lighting ($p>0.05$). The frequency of hazards was not associated with any activity metric ($p>0.05$ for all)

Conclusions: The home environment, in particular lighting at home, may influence home physical activity in those with glaucoma. Further research is needed to better understand this relationship and how we may improve the PA at home using home modifications to improve home safety.

CONTROL ID: 3710561

SUBMITTER (NAME ONLY): Junghun Kweon

TITLE: Multiscale imaging of mouse corneal endothelial cell damage induced by elevated intraocular pressure

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kweon, Y. Zhang, B.S. brenner, R. Fang, H. Zhang, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|C. Sun, Mechanical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|J.L. Goldberg, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hexagonal-shaped corneal endothelial cells (CECs) are essential in maintaining corneal transparency for clear vision. In glaucoma patients, abnormal CEC function caused by high intraocular pressure (IOP) can contribute to vision loss. We developed a multi-scale imaging workflow to determine whether we could identify morphological and structural variations at at the nanoscopic level using a mouse model of high IOP induced by anterior chamber cannulation

Methods: We cannulated the left eyes of wild-type (WT) mice using anterior chamber puncture, and controlled the IOP to be 40 mmHg by adjusting the height of the syringe; right eyes served as controls. We first used a custom visible-light optical coherence tomography (vis-OCT) to monitor the overall corneal damage in real-time. After one hour of hypertension treatment, we sacrificed the mice, isolated their corneas, and processed one half for single-molecule localization microscopy (SMLM) and the other half for scanning electron microscopy (SEM)

Results: The vis-OCT images of control corneas showed a typical normal stroma (Fig. 1A). Increased corneal thickness was observed (Fig. 1B) with typical edematous appearance after maintaining 40 mmHg IOP for one hour. SMLM images showed the typical hexagonal structures of CECs in controls (Fig. 1C). However, after hypertension treatment, the intercellular tight junction structures labeled by ZO-1 became distorted dramatically, showing variations including extended filaments (Fig. 1E) or discontinuous and thinner junctional structures (Fig. 1D) between CECs. Using SEM, we identified similar hexagonal structures of CECs as showed in SMLM (Fig. 1F). Meanwhile, we observed the junctional structural variations on the surface level of CECs in hypertensive corneas, validating SMLM imaging results (Fig. 1G)

Conclusions: We imaged corneal flat-mounts to reveal nanoscopic variations in CECs in hypertension mouse models using vis-OCT, SMLM, and SEM. Such disruptions of the intercellular junctional structure of CECs in corneas may contribute to the loss of transparency and vision damage in glaucoma patients with high IOP

CONTROL ID: 3710568

SUBMITTER (NAME ONLY): J Jason McAnany

TITLE: Spatial summation is altered throughout the macula in juvenile X-linked retinoschisis

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. McAnany, J.C. Park, R.A. Hyde, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: J Jason McAnany: Commercial Relationship: Code N (No Commercial Relationship) | Jason Park: Commercial Relationship: Code N (No Commercial Relationship) | Robert Hyde: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previous studies suggest that the fovea of individuals with juvenile X-linked retinoschisis (XLRS) may be functionally similar to that of the normal periphery. We evaluated this hypothesis by determining the relationship between contrast threshold and stimulus size across the visual field in XLRS subjects.

Methods: Nine subjects with XLRS and 10 age-similar, visually-normal individuals participated. Thresholds were measured at 15 locations along the horizontal meridian of the visual field using a commercially available Octopus visual field perimeter. The field locations were grouped into four regions based on eccentricity from fixation: peripheral (10^{o}-60^{o}), perifoveal (5^{o}-10^{o}), parafoveal (2^{o}) and foveal. Stimulus area ranged from 0.01 deg^{2} to 2.32 deg^{2} (Goldmann sizes I to V). Thresholds for the control and XLRS groups were compared statistically by analysis of variance with Bonferroni-corrected pairwise comparisons. The relationship between threshold and stimulus size was described using a spatial summation model to quantify the critical area of spatial summation beyond which threshold is independent of stimulus size.

Results: For measurements in the periphery and perifovea, thresholds were modestly elevated for the XLRS group (less than 2.5x). Threshold differences between groups were significant in the periphery and perifovea for the size I to IV stimuli ($p < 0.02$), but not for the size V stimulus ($p > 0.06$). Threshold elevations were larger in the parafovea (4.7x) and fovea (8.4x) for the XLRS group, and pairwise comparisons indicated significant differences for all stimulus sizes ($p < 0.001$). XLRS thresholds measured in the fovea, parafovea, and perifovea did not differ significantly from those measured from the peripheral field of the control group ($p > 0.09$). The critical area for spatial summation was significantly larger for all field regions for the XLRS group compared to the control group ($p < 0.002$).

Conclusions: Spatial summation characteristics of the XLRS fovea, parafovea, and perifovea are similar to those of the normal periphery, suggesting abnormally large receptive field sizes in XLRS. The data indicate that scaling stimulus size can equate thresholds for the XLRS and controls subjects throughout all areas of the visual field.

CONTROL ID: 3710572

SUBMITTER (NAME ONLY): Reeti Gulati

TITLE: Effect of the Rho-kinase Inhibitor Netarsudil on Corneal Neovascularization in an Alkali-Burn Mouse Model

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.K. Gulati, Medical School, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|T. Janetos, S. Basti, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Reeti Gulati: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Janetos: Commercial Relationship: Code N (No Commercial Relationship) | Surendra Basti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal neovascularization (CNV) is a consequence of a variety of ocular pathologies including infectious and autoimmune etiologies. RhoA and its downstream effector ROCK play an important role in the development of neovascularization. Previous research has shown promise in treating CNV using both RhoA and ROCK inhibitors. We tested the hypothesis that Netarsudil treatment in an alkali burn injury mouse model will decrease CNV.

Methods: Wild type mice of age 3-6 months were divided into treatment and control groups. Alkali burn injury was performed on the right eye to induce CNV. One week after burn, anterior segment photography was done to ensure similar levels of baseline CNV between treatment and control groups. The treatment group was treated with the rho-kinase inhibitor, Netarsudil solution (0.02%; 0.02 mg/mL), brand name Rhopressa, at a frequency of once-a-day for 4 weeks. The control group was treated with balanced saline solution (BSS) in a similar manner. At the end of treatment, mice were euthanized for final anterior segment photography and corneal immunostaining was performed using CD31 to quantify CNV.

Results: A total of 5 mice have been treated thus far (3 in treatment group, 2 in control group). Anterior segment photos shortly after alkali burn show similar levels of baseline CNV (Figure 1). Immunostaining results at this stage indicate no significant difference in percent CNV between the treatment and control groups at four weeks (Figure 2). There was a large range in percent corneal neovascularization in the mice treated with Netarsudil.

Conclusions: This study is designed to evaluate whether inhibition of rho-kinase can regress established CNV in an alkali burn injury mouse model. Our experiment at this stage indicates no significant difference in CNV in the mice treated with Netarsudil versus BSS. A treatment goal of 30 mice is currently underway as a larger sample size of mice is needed to power conclusions. Final results have the potential to impact future research directions for treatment of CNV.

CONTROL ID: 3710573

SUBMITTER (NAME ONLY): Hanh Truong

TITLE: The Ciliary Transition Zone Protein Tectonic1 Forms a Membrane Ciliary Barrier in Mouse Rod Outer Segments

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Truong, J.R. Willer, J. Martinez-Marquez, A. Travis, J.N. Pearring, Ophthalmology, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Light is detected by the outer segment compartment of retinal photoreceptors. The outer segment is an adapted primary cilium, which are thin microtubule-based organelles that relay extracellular signals to the cell through receptors enriched in the ciliary membrane. The distinct protein composition of the cilium is maintained by a membrane diffusional barrier, formed by transition zone proteins. While previous work has shown that membrane proteins utilize ciliary transport carriers (such as TULP, IFT, and BBSome) to enter and exit the cilium, the molecular components of the diffusion barrier remain unknown. Tectonic1 (Tctn1), an extracellular protein, forms a large complex with other ciliary proteins at the transition zone and has been shown to regulate ciliary membrane composition in primary cilia. We hypothesize that Tctn1 forms a diffusion barrier that maintains the unique membrane-associated protein composition of the photoreceptor outer segment.

Methods: To study Tctn1 in rod photoreceptors, a conditional Tctn1floxed mouse was generated through CRISPR gene targeting. This $Tctn1^{flox/flox}$ mouse was then crossed to an iCre75 mouse, which specifically expresses Cre recombinase in rod photoreceptors, to then generate our rod-specific Tctn1 knock-out mouse ($iCre;Tctn1^{f/f}$).

Results: We found that ciliary outer segment formation is normal in the absence of Tctn1; however, proteins typically excluded from the outer segment are now accumulating within the outer segment of $iCre;Tctn1^{f/f}$ rods. Mislocalization of these proteins in the outer segment is detrimental to rod health as photoreceptor degeneration occurs by 6 months. Interestingly, we show that the abundance and localization of ciliary transport carriers are not affected by the loss of Tctn1 which would suggest that Tctn1 acts as a physical gate at the transition zone.

Conclusions: Together, our results show that Tctn1 is part of the membrane ciliary gate. We are now testing whether the loss of Tctn1 impacts the diffusional rate of membrane proteins through the transition zone, allowing them to sneak by the exit machinery. Ultimately, my work has helped to understand how the transition zone functions as a membrane gate within photoreceptors and primary cilia in general.

CONTROL ID: 3710574

SUBMITTER (NAME ONLY): Chi Mong Or

TITLE: Repeatability of electroretinogram measurements

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Or, H. Ghoraba, M. Zaidi, A. Akhavanrezayat, J. Regenold, G. Uludag, C. Yasar, S. Park, N. Than, J.J. Hwang, Q.D. Nguyen, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Electroretinography (ERG) plays a vital role in the diagnosis of various eye diseases. The International Society for Clinical Electrophysiology of Vision (ICSEV) has published guidelines standardizing the acquisition of ERG. However, repeatability of ERG measurements has not been clearly elucidated. In this study, we aim to assess the repeatability of ERG measurements as performed using ICSEV guidelines.

Methods: 98 consecutive patients with various ocular conditions and a recent ERG were included in our study. Full-field ERG (Diagnosys, LLC) was performed by a single examiner, with repeat measurements recorded as per ICSEV guidelines. The magnitudes of the A and B waves, along with their respective latencies, under each testing condition were collected. Statistical tests of repeatability including coefficient of variation and intraclass correlation coefficient (ICC) were employed. Statistical analysis was performed using MedCalc software.

Results: Using the coefficient of variation, A and B wave latencies and magnitudes had very good repeatability (<10) under the Scotopic 3 and 10 conditions. A wave latency, B wave latency and B wave magnitude measurements under Scotopic 0.01 conditions also had very good repeatability. A wave latency and B wave magnitude under both photopic conditions had good repeatability (10-20). A wave magnitude under both photopic conditions and the A wave magnitude under Scotopic 0.01 had poor repeatability (>30). Using the ICC, the scotopic 3 and 10 measurements had the best repeatability, with multiple measures demonstrating excellent repeatability. Measurements under scotopic 0.01 conditions also had good to excellent repeatability. The photopic measurements had varied repeatability scores, with the A wave magnitude and latency under photopic 3 conditions demonstrating poor reliability.

Conclusions: ERG measurements had variable repeatability using the standard protocol, with those under scotopic 3 and 10 conditions demonstrating the highest degree of repeatability. Further studies are required to elucidate this and explore the repeatability of ERG measurements in different patient populations.

CONTROL ID: 3710577

SUBMITTER (NAME ONLY): Albert Xiong

TITLE: Inhibition of miR-21 prevents abnormal angiogenesis and subretinal fibrosis in an experimental model of choroidal neovascularization

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Xiong, M. Thounaojam, M. Bartoli, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|Q. Yang, Y. Huo, Vascular Biology Center, Augusta University, Augusta, Georgia, UNITED STATES|R. Jadeja, P.M. Martin, Biochemistry and Molecular Biology, Augusta University, Augusta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Albert Xiong: Commercial Relationship: Code N (No Commercial Relationship) | Menaka Thounaojam: Commercial Relationship: Code N (No Commercial Relationship) | Qiuhua Yang: Commercial Relationship: Code N (No Commercial Relationship) | Ravirajsinh Jadeja: Commercial Relationship: Code N (No Commercial Relationship) | Pamela Martin: Commercial Relationship: Code N (No Commercial Relationship) | Yuqing Huo: Commercial Relationship: Code N (No Commercial Relationship) | Manuela Bartoli: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Choroidal neovascularization (CNV) and consequent sub-retinal fibrosis remain sight-threatening conditions with a significant percentage of patients being resistant to anti-VEGF-based treatments or presenting frequent recurrences. MicroRNA-21-5p (miR-21) is a non-coding RNA with pro-angiogenic and pro-fibrotic abilities that our group and others have previously studied for its pathogenic implications in diabetic and oxygen-induced retinopathy. Here, we have investigated the effects of blocking miR-21 in an experimental model of CNV.

Methods: CNV was induced in C57Bl/6J mice by laser injury of Bruch's membrane and analyzed at different time points. MiR-21 inhibition was achieved by intraorbital injection of miR-21 Locked Nucleic Acid (LNA) inhibitor. As control, we used mice subjected to CNV that were injected with scramble antagomir or age-matched normal mice. Immunohistochemistry was performed to visualize retinal histopathological changes (hematoxilin/eosin staining) and to assess vascular density and distribution (isolectin B4), fibrotic progression (collagen I), and reactivity to alpha smooth muscle actin (alpha SMA) antibodies suggesting epithelial to mesenchymal transition (EMT). Quantitative RT-PCR was used to assess miR-21 levels in the different experimental groups.

Results: In untreated CNV mice neovascularization was observed to peak around day 14 post-injury before mildly regressing at day 21. Collagen I (Col1) staining showed that in CNV mice fibrosis progressed further beyond 14 days. In CNV mice treated with miR-21 inhibitor (a.miR-21), Col1 and Isolectin B4 stained areas were noticeably smaller beyond the 7-day post-injury time point as compared to untreated CNV mice or mice treated with scramble antagomir. Quantification of the fibrosed area through measurement of the Col1 stained areas in maximum projection images confirmed these findings. Expression of fibrosis and EMT markers (alpha SMA) were significantly downregulated in a.miR-21 injected mice. SD-OCT-based analysis also evidenced that a.miR-21 rescued retinal thickness and decreased neovascular lesions in CNV mice. Lastly, H&E staining confirmed improved retinal architecture in a.miR-21 treated CNV mice.

Conclusions: Our data indicate miR-21 as a novel player in CNV induction and progression and suggest its inhibition as a new therapeutic strategy for this potentially blinding condition.

CONTROL ID: 3710578

SUBMITTER (NAME ONLY): Seongjin Lim

TITLE: Optical coherence tomography angiography (OCTA) demonstrates displacements of large disc and peripapillary vessels during horizontal duction

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lim, J.L. Demer, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES| S. Lim, A. Tran, J.L. Demer, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Seongjin Lim: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Tran: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Demer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It has been proposed that eye-movement related deformation of optic nerves could induce mechanical stress in the optic disc from which the retinal vasculature emerges. To study this phenomenon quantitatively we used OCTA for high-resolution 3D imaging of larger disc and peripapillary vessels during horizontal duction.

Methods: Eight eyes of 5 normal adults were imaged in the 3×3 mm^2 region centered on the disc using the Heidelberg Spectralis scanner in central gaze, and in 35° ab- and adduction. Deep learning was employed for automatic identification of blood vessels and Bruch's membrane. Furthermore, we applied 3D scale-invariant feature transformation (SIFT) to extract feature points for the blood vessels. Among paired feature points in different gaze positions, we filtered for points with a distance <100 µm from large vessels. We registered vascular feature points to compute their displacements relative to the center of Bruch's membrane opening (BMO). We reconstructed the plane of Bruch's membrane whose normal vector defines the Z-axis (anterior-posterior). The X-axis (temporal-nasal) was defined by a line from BMO center to the fovea, and the Y-axis was perpendicular to X and Z.

Results: In adduction, feature points in nasal disc and peripapillary region were displaced farther temporally by 10±9 µm (mean±SD), significantly more than 2±11 µm in the temporal region (p=0.0011, n=8 eyes); this indicates horizontal compression of the vascular arbor from the nasal side. Adduction also resulted 13±15 µm anterior displacement in nasal region that was significantly larger than 5±13 µm in the temporal region (p=0.0157), indicating tilting of the vascular arbor. However, in abduction temporal and anterior displacements were similar in the nasal and temporal regions, indicating absence of both horizonal compression and tilting of the vascular arbor.

Conclusions: OCTA demonstrates that both ab- and adduction induce 3-dimensional deformations of major blood vessels emerging from the optic disc, but only in adduction is the vascular arbor tilted and horizontally compressed. These findings are consistent with optic nerve tethering in adduction but not abduction.

CONTROL ID: 3710579

SUBMITTER (NAME ONLY): Nikolas London

TITLE: Faricimab in neovascular age-related macular degeneration: updated week 48 efficacy, safety, and durability in the phase 3 TENAYA and LUCERNE trials

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Dual inhibition of angiopoietin-2 and vascular endothelial growth factor-A with faricimab, a bispecific antibody designed for intraocular use, may promote vascular stability and durable efficacy in patients with neovascular age-related macular degeneration (nAMD). Here we report updated week 48 results of the phase 3 TENAYA (NCT03823287) and LUCERNE (NCT03823300) trials, comparing efficacy, safety, and durability of faricimab with aflibercept in patients with nAMD.

Methods: Patients with nAMD (pooled N = 1329) were randomized 1:1 to faricimab up to every 16 weeks (Q16W; n = 665) or aflibercept every 8 weeks (Q8W; n = 664). After 4 initial doses every 4 weeks (Q4W), faricimab-treated patients were treated Q8W, every 12 weeks (Q12W), or Q16W based on prespecified central subfield thickness (CST) and best-corrected visual acuity (BCVA) criteria at weeks 20 or 24. The primary endpoint was mean change from baseline in BCVA averaged over weeks 40, 44, and 48. Secondary efficacy endpoints, including visual and anatomic outcomes and safety, were assessed Q4W through week 48.

Results: Faricimab up to Q16W treatment resulted in comparable visual acuity outcomes compared to aflibercept Q8W, including noninferior BCVA gains averaged over weeks 40–48 (+6.2 and +5.9 Early Treatment Diabetic Study letters, respectively). Anatomical outcomes were also comparable between treatment arms, including mean reductions in CST from baseline averaged over weeks 40–48. Regarding durability, at week 48, 45.3% of faricimab-treated patients were on Q16W dosing and 78.7% were on Q12W dosing or longer. Representative cases of patients achieving Q16W dosing and associated retinal images will be presented. Faricimab was well tolerated, with low rates of intraocular inflammation and no vasculitis or occlusive retinitis events reported.

Conclusions: Pooled data from TENAYA/LUCERNE demonstrate that through week 48, faricimab up to Q16W offered durable vision gains and meaningful anatomic improvements that were comparable with aflibercept Q8W and was well tolerated.

CONTROL ID: 3710581

SUBMITTER (NAME ONLY): Xiaolin Wang

TITLE: Mesopic and Scotopic Light Sensitivity Loss Associated with Intraretinal Hyperreflective Foci in Age-related Macular Degeneration

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Intraretinal hyperreflective foci (IHF) on optical coherence tomography (OCT) in eyes with intermediate age-related macular degeneration (AMD) are associated with a higher risk for progression to advanced AMD. This study evaluates the impact of IHF on cone- and rod-mediated vision in patients with intermediate AMD using mesopic and scotopic microperimetry and correlate the findings with retinal structures revealed by multimodal imaging including adaptive optics scanning laser ophthalmoscopy (AOSLO).

Methods: In a retrospective study involving 225 eyes of 141 subjects with AMD, IHF were identified on spectral domain OCT B-scans in 123 eyes of 69 subjects, aged 77.3 ± 7.3 years old. Lesions associated with AMD such as drusen and subretinal drusenoid deposits (SDD) were assessed by color fundus photographs, infrared reflectance, blue-light autofluorescence, and OCT. Cone photoreceptor structure was examined by AOSLO. Cone- and rod-mediated sensitivity was tested using a microperimeter (MP1-S, Nidek) under mesopic and scotopic conditions in 16 eyes of 16 subjects with intermediate AMD (grades 5 to 8 in the AREDS 9-step severity scale). Mesopic and scotopic light sensitivity tested in the retinal areas with and without IHF but with a similar SDD/drusen load were compared in the same eye.

Results: Retinal areas with IHF exhibited significantly reduced mesopic (16.92 ± 5.59 dB vs. 18.62 ± 4.73 dB, $p = 0.0003$) and scotopic (8.31 ± 5.72 dB vs. 9.70 ± 5.63 dB, $p = 0.0087$) light sensitivity, in comparison to those without IHF. AOSLO revealed disrupted cone photoreceptor structure in areas with IHF and the photoreceptor mosaic was largely not visible in regions with IHF (Figure).

Conclusions: IHF are associated with significant loss of visual function and photoreceptor degeneration in eyes with intermediate AMD. Larger prospective longitudinal studies are required to investigate the pathogenesis and sequence of events leading to the development of IHF and associated photoreceptor loss.

CONTROL ID: 3710583

SUBMITTER (NAME ONLY): Zahra Mohtashami

TITLE: Analysis of 1-month-old MOTS-c in H2O; Using High Resolution Mass Spectrometry

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Mohtashami, M. Ozgul, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|B. Katz, Chemistry, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: MOTS-c peptide is one of the mitochondrial derived peptides which represent a new class of biologically active molecules with potential to protect retinal cells from oxidative stress associated with retinal pathology. State-of-the-art techniques can be used to analyze stability of intact MOTS-c peptide and identify MOTS-c fragments for possible use in future therapeutic investigation of age-related macular degeneration.

Methods: Stability analyses was done by High-Resolution Mass Spectrometry (HRMS). During this process the MOTS-c solutions with a concentration of 12.5 µg/ml were stored at 4°C and 37°C for 30 days.

Mass spectrometric analysis was performed using Xevo G2-XS Quadrupole Time-of-Flight mass spectrometer (HRMS) coupled to UPLC. The UPLC method used 30 minutes linear gradient at 0.3 mL/min from 97% A to 97% B where A is 0.1% Formic Acid in water and B is 100% Acetonitrile. For HRMS analysis, positive electrospray ionization mode was utilized. A capillary transfer temperature of 300°C and a spray voltage of 3.0 kV were used to accomplish ionization. A resolution of 30,000 Full Width at Half Maximum was used for a full scan experiment within a range of 100–2000 m/z as well as 15,000 FWHM with an isolation window adjusted to 2.0 m/z for. Leucine Enkephalin was used as a lock mass for nominal mass correction, and a CsNaI ladder was used to calibrate the detector.

Results: In MOTS-c peptide with molecular weight of 2173.11g/mol, the main ions of +5, +4 and +3 were formed at 435.84, 544.54 and 725.72 m/z (Figure 1). In MOTS-c, oxidation of methionine remained constant upon incubation of MOTS-C in water for 30 days at 37^{O}C. Intact MOTS-c peptides without oxidation were detected at the highest intensities. HRMS spectrums of MOTS-c stability in HPLC water are presented in Figures.

Conclusions: It is the first time that 1-month stability properties of MOTS-c peptide and its oxidation and degradation products have been analyzed in detail using advanced HRMS technologies. The data suggest that intact MOTS-c peptides in HPLC water represent a more stable form than Humanin-G peptides in water. The results may help researchers design better in vitro and in vivo experimental parameters to further understand the critical role of MOTS-c in physiological conditions and human diseases.

CONTROL ID: 3710587

SUBMITTER (NAME ONLY): Louis DEBILLON

TITLE: Birdshot chorioretinitis in patients aged 80 and older

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. DEBILLON, E. Bousquet, P. Duraffour, S. Kecili, D. Monnet, A. Brézin, Hopital Cochin, Paris, Île-de-France, FRANCE|J.E. Thorne, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Birdshot chorioretinitis (BSCR) is a chronic uveitis that can lead to a progressive loss of visual acuity and field over time. The aim of this study was to assess the manifestations of the disease in patients >80 years old.

Methods:

Among the patients with BSCR prospectively followed in our cohort (ClinicalTrials.gov Identifier: NCT05153057), we focused our analyses on those examined at age >80 years. Patients were assessed in a standardized manner including visual symptoms, best-corrected visual acuity (BCVA), dilated ophthalmic examination, visual field testing (Humphrey 30-2), fundus autofluorescence (FAF), fluorescein angiography and SD-OCT. When multiple visits occurred after age 80, data from the most recent visit were used. Active inflammation was defined by the presence of macular edema and/or vitritis and/or vasculitis and/or papillitis. Confluent atrophy was defined as hypoautofluorescent spots on FAF.

Results:

As of October 2021, 37 of 442 patients (8.8%, 74 affected eyes) were >80 years old at the most recent clinical visit. Mean age was 84.0 ± 3.7 years (range 80-93 years) and 24 (64.9%) patients were female. The mean disease duration was 22.4 years. Mean LogMAR BCVA was 0.53 ± 0.77 (range 0 – 2.3) in affected eyes, with 32 patients (86.5%) having 20/40 or better vision in at least one eye. Thirty-two patients (86.5%) received treatment during follow up. Systemic corticosteroids, immunosuppressants, and corticosteroid injections [intravitreal or sub-tenon] were previously prescribed in 24 (64.9%), 16 (43.2%) and 21 (56.8%) patients respectively. Thirty-three patients (89.2%) were receiving no treatment and 57 eyes (81.4%) in 30 patients (85.7%) had no active inflammation at the most recent visit. Confluent atrophy in the posterior pole was observed in 30 (42.8%) eyes in 17 patients (48.6%). Patients with confluent atrophy had significantly worse mean BCVA (LogMAR 1.0±0.94 vs 0.13±0.15, $p<0.0001$), longer mean disease duration (26.9±9.8 vs 17.6±9.0 years, $p=0.0005$), thinner mean central macular thickness on SD-OCT (245.6±117.2 vs 268.0±48.8 µm, $p=0.002$) and worse visual field mean deviation (-15.1±7.7 vs -6.8±6.0 dB, $p=0.0003$).

Conclusions: The majority of patients with BSCR aged >80 have preserved BCVA of 20/40 or better in at least one eye over several decades of disease duration. Confluent atrophy in the posterior pole was correlated with worse visual function in these patients.

CONTROL ID: 3710588

SUBMITTER (NAME ONLY): Liya Xu

TITLE: Identifying DNA methylation signatures of retinoblastoma via aqueous humor, a novel ocular liquid biopsy

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Xu, J.L. Berry, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|L. Xu, J.L. Berry, Opthalmology, University of Southern California, Los Angeles, California, UNITED STATES|H. Li, G. Liang, Urology, University of Southern California, Los Angeles, California, UNITED STATES|D. Weisenberger, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tissue biopsy of Rb can cause tumor spread, so it is contraindicated. We demonstrated that aqueous humor (AH), an ocular fluid, is a high-yield liquid biopsy source enabling in vivo detection of tumor-derived cell-free DNA (cfDNA), thus overcoming the contraindication to biopsy. In ~13% of Rb patients, tumor progression is driven by epigenetic deregulation of tumor-promoting pathways without detectable genomic alterations. However, epigenetic studies have been done only on primary tumors from surgically removed eyes. The frequency and effect of epigenomic regulation in eyes that have been saved with therapy are unclear due to a complete lack of access to in vivo tumor tissue. Therefore, epigenetic analysis of AH cfDNA is highly desired to understand the broader spectrum of Rb tumorigenesis and prognosis.

Methods: We included 16 AH samples and 4 Rb tumors from 12 patients with 14 Rb eyes in the study. We conducted global DNA methylation profiling of tumor tissues from surgically removed Rb eyes and AH samples collected from different clinical stages and treatment outcomes using the Illumina Infinium EPIC DNA methylation BeadArray platform. Publicly-available DNA methylation data of normal retina, Rb eyes, and Rb patients were obtained from Gene Expression Omnibus (GEO, GSE57362) for cell-type DNA methylation comparisons.

Results: Our preliminary studies revealed a high degree of concordance in genome-wide differential DNA methylation patterns between paired AH and tumor samples. Integrating our data with large public datasets, we identified reliable Rb DNA methylation signatures in AH cfDNA that have potential diagnostic and prognostic applications. We also identified DNA hypermethylation of the RB1 promoter, which may serve as an efficacious target of DNA methylation inhibitors. By integrating DNA methylation data with gene expression data, we identified over 300 differentially expressed genes potentially directly regulated by DNA methylation in Rb tumorigenesis.

Conclusions: Our findings set the stage for exploring epigenetic markers using AH cfDNA specimens, including identifying potential prognostic markers and therapeutic targets to ultimately improve the clinical management of Rb patients.

CONTROL ID: 3710589

SUBMITTER (NAME ONLY): Swetha Bindu Velaga

TITLE: Longitudinal Assessment of Area of Reticular Pseudodrusen in Eyes with Age-Related Macular Degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the change in the area of reticular pseudodrusen (RPD) over a two year period in eyes with age-related macular degeneration (AMD).

Methods: AMD eyes with RPD enrolled in the Amish Eye Study (AES) with baseline and two year follow-up infrared reflectance (IR) images were eligible for this analysis. Eyes were excluded for poor quality images, extension of RPD beyond the margins of the image, or if they developed geographic atrophy at the month 24 visit. Thirty-degree IR images and volume OCTs (6x6mm, 512x97, ART=9, fovea-centered) were obtained using the Spectralis HRA+OCT. Using the instrument software, a certified grader delineated the RPD area (mm^2) on the IR image using the free hand tool, and measured the choroidal thickness on the OCT at the foveal center as well as at 3500 µm superior and inferior to the foveal center. Measurements were performed on both baseline and Month 24 images. 30% of eyes were randomly selected for reproducibility analysis by a second masked grader. The change over two years was assessed using paired t tests.

Results: Of 1332 eyes (666 subjects) enrolled in the AMISH eye study, a total of 108 eyes (from 54 subjects) were noted to have RPD and from these 35 eyes of 22 subjects were included in the final analysis (32 eyes were excluded due to extension of RPD to the image border, 19 due to poor image quality, and 22 due to development of GA). The mean age of included subjects was 72.7 ± 9.1 (range: 3.5 – 84) years and 13 were female (37%). Mean subfoveal choroidal thickness at baseline was 194.58 ± 79.2 µm. RPD area was increased significantly ($p < 0.001$) at month 24 (17.67 ± 9.59 mm^2) compared to baseline (11.44 ± 7.96 mm^2) with a mean increase of 6.23 ± 4.64 mm^2. There was no significant change at 2 years, however, in choroidal thickness in any of the regions: superior ($p = 0.09$), subfoveal ($p = 0.26$) and inferior ($p = 0.52$). Intraclass correlation (ICC) for RPD area between the two graders was 0.997 with a mean difference of 0.49 mm^2.

Conclusions: In this longitudinal natural history analysis, we observed an increase in RPD area of >6mm^2 over two years despite no significant change in choroidal thickness. These findings may provide new insight into the evolution and lifecycle of RPD.

CONTROL ID: 3710591

SUBMITTER (NAME ONLY): Oluchi Ihionu

TITLE: Demographic Factors Associated with Differential Access to Treatment in Keratoconus Patients at a U.S. Urban Safety Net Hospital

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Ihionu, M. Arsiwala, N. Sanayei, H.J. Lee, Boston University School of Medicine, Boston University School of Medicine, Boston, MA, US, academic/medsch, Massachusetts, UNITED STATES|J. Samra, Biostatistics, Boston University School of Public Health, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is limited information regarding the influence of demographic factors on keratoconus outcomes. The purpose of this study is to examine the effects of race/ethnicity, primary patient language, health insurance, and area deprivation index (ADI) on rates at which patients receive two different keratoconus interventions: corneal collagen crosslinking (CXL) and medical contact lenses (CL). Our primary hypothesis was that patients who live in more impoverished areas, as determined by ADI, have lower access rates to CXL and CL, and that other demographic factors could influence this access to treatment as well.

Methods: Electronic medical records of keratoconus patients at Boston Medical Center from 2012-2020 were retrospectively examined to obtain CXL and CL treatment records, race/ethnicity, primary language, insurance (private, public, or none), and home address. National ADI quintile was determined by address, and patients were categorized as 1st, 2nd, or 3rd quintiles and above (most disadvantaged). Logistic regression models were used to calculate odds ratios for keratoconus treatment adjusted for age, ADI, insurance, race/ethnicity, and language. Chi-square likelihood ratios were used to test for associations between demographic factors and odds of treatment. Post-hoc analyses were performed using Tukey's method at a 5% family-wise error rate.

Results: 572 charts were reviewed, and 32 patients were excluded due to incomplete records. Of 540 remaining KCN patients, 42 received CXL and 213 received and/or had a history of CL. There was no significant association between ADI and CXL treatment (p=0.688) or CL access (p=0.912). Multivariate analyses showed that patients whose primary language was not English were less likely to have CL access relative to patients whose primary language was English (ORadj=0.65, 95% CI 0.45-0.93, p=0.021). Insurance status (p=0.002) and race/ethnicity (p=0.003) had significant associations with CXL treatment in multivariate models. When adjusted for all other factors, including insurance status, White patients were more likely to receive CXL relative to Black patients (ORadj=8.54, 95% CI 2.82-27.09) and patients with private insurance were more likely to receive CXL than those without insurance (ORadj=10.00, 95% CI 2.59-66.22).

Conclusions: Our data demonstrate disparities in keratoconus treatment access for disadvantaged groups.

CONTROL ID: 3710593

SUBMITTER (NAME ONLY): Aman Patel

TITLE: Central corneal steepening is associated with vaccinia nummular keratitis

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Patel, H. Choudhry, M. Dastjerdi, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: About 20 patients develop ocular complications per 1 million smallpox immunizations, usually through autoinoculation, in which the patient transfers Vaccinia from the immunization site to the eye. We observed central corneal steepening (CCS) that occurred in the setting of Vaccinia virus-associated nummular keratitis.

Methods: A 40-year-old healthy male with no significant past ocular or medical history who was vaccinated against smallpox in 2003 was examined. Within 2 weeks of vaccination, he developed a diffuse skin rash and bilateral eye redness. He later experienced progressive decline in his corrected distance visual acuity. After undergoing an eye exam, he was informed that the blurry vision was associated with smallpox vaccination. He also developed significant nearsightedness and astigmatism.

Results: Recently, his vision with corrective glasses of OD=-6.50- 2.50 x 140; 20/30, and -5.00- 2.50 x 130; 20/60. Pupils, ocular motility, confrontation visual field, external exam, lids, and conjunctiva were unremarkable. There were no symblepharon, tear film, or function abnormalities. Bilateral, fine peripheral corneal neovascularization and multiple peripheral coin shape opacities (subepithelial/anterior stroma) that spared the central corneas were noted. Some of these opacities coalesced. Pentacam tomography revealed significant CCS similar to central keratoconus in each eye (Fig. 1). Anterior segment optical coherence tomography demonstrated subepithelial and anterior stromal lesions that were confined to superficial peripheral corneal layers without involvement of deeper corneal layers and the visual axis (Fig. 2). A plausible explanation for the patient's stable myopic shift and astigmatism is that inflammation caused structural changes in the corneal mid-periphery. This process may be similar to the myopic refractive changes seen in conductive keratoplasty, in which heat-induced shrinking of peripheral collagen lamellae causes CCS.

Conclusions: Significant CCS can occur in the setting of mid-peripheral nummular keratitis, which presumably mimics the conductive keratoplasty biomechanical changes in the corneal mid-periphery that led to the CCS.

CONTROL ID: 3710594

SUBMITTER (NAME ONLY): Vikram Sharma

TITLE: Promoting PKM2 tetramerization to treat RPE epithelial-to-mesenchymal transition in proliferative vitreoretinopathy

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Sharma, M. Goswami, Q. Zhang, S. Chaudhury, K. Li, C.G. Besirli, J.M. Miller, T.J. Wubben, Opthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|A. Andren, C.A. Lyssiotis, Molecular & Integrative Physiology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|H.B. Durumulta, Children's Hospital Medical Center, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) represents the greatest risk of failure of retinal detachment repair surgery. No pharmacotherapies have prevented the formation of PVR, so a significant unmet need exists. The epithelial-to-mesenchymal transition (EMT) of retinal pigment epithelial (RPE) cells is critical in PVR pathogenesis. Increased glycolysis is a hallmark of RPE EMT. Pyruvate kinase M2 (PKM2) is a key regulator of glycolysis that exists in different oligomeric states, dimer and tetramer, and has been implicated in glycolytic reprogramming of cells. Small molecule modulators of PKM2, like ML-265, induce tetramerization reducing glycolytic reprogramming. We assessed the therapeutic potential of pharmacologically inducing PKM2 tetramerization in preventing PVR.

Methods: To mimic the loss of cell contact observed in the PVR process and stimulate EMT, primary human fetal RPE (hfRPE) were seeded at 10% density. Expression of EMT markers, PKM2, and mediators of glycolytic reprogramming and proliferation were assessed. A continuous, enzyme-coupled assay that measures the depletion of NADH measured PK activity. Targeted metabolomics assessed the impact of ML-265 on the metabolic profile of hfRPE. The therapeutic potential of ML-265 in attenuating RPE EMT and PVR was evaluated in in vitro assays. ML-265 toxicity was assessed via transepithelial electrical resistance (TEER) and cell death markers.

Results: Low seeding density of hfRPE demonstrated a fibroblastic-like PVR phenotype (hfRPE EMT) with induction of EMT markers α-SMA and NCAD. PKM2 but not PKM1 expression was increased. Yet, overall PK activity was decreased and the phosphoenolpyruvate (PEP) to pyruvate ratio was increased in hfRPE EMT suggesting PKM2 is in the low activity, dimeric state. ML-265 treatment increased PK activity >3-fold in hfRPE EMT. ML-265 induced a decrease in glycolytic intermediates and the expression of HIF1A, GLUT1, and PDK1in hfRPE EMT. ML-265 decreased the proliferation of EMT hfRPE cells and the expression of MYC and CCND1 as well as inhibited EMT hfRPE-mediated gel contraction with a reduction in α-SMA expression. Exposure to ML-265 did not reduce TEER or increase annexin or PI staining in differentiated hfRPE.

Conclusions: This study suggests that pharmacologically inducing PKM2 tetramerization may be an innovative therapeutic strategy for PVR.

CONTROL ID: 3710595

SUBMITTER (NAME ONLY): Carolina Bernal-Morales

TITLE: Multiple sclerosis associates reduced retinal fractal dimension

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the association between multiple sclerosis (MS) and retinal fractal dimension (FD), a retinal vascular geometric index of complexity.

Methods: A retrospective cohort study with data from 96,992 patients, of which 250 had multiple sclerosis seen at a tertiary ophthalmic institution in London, United Kingdom. Retinal fractal dimension was extracted from macular-centered colour fundus photographs using the Vascular Assessment and Measurement Platform for Images of the Retina. Multivariable linear regression evaluated the association between retinal FD and multiple sclerosis adjusting for age, sex, hypertension and diabetes mellitus.

Results: Patients with multiple sclerosis were younger (61.6 +/- 12.8 years of age versus 68.2 +/-12.5, $p<0.001$) and more likely to be female (72.4% versus 50.9%, $p<0.001$) but less likely to be diabetic (32.4% versus 47.5%, $p<0.001$) or hypertensive (73.6% versus 80.1%, $p<0.001$). Retinal FD was similar regardless of MS status (non-MS: 1.511+/-0.032 versus MS: 1.514 +/- 0.032, $p=0.23$). After adjustment for age, sex, hypertension and diabetes mellitus, retinal fractal dimension was reduced in patients with MS (b -0.0043, 95% confidence interval: -0.008, -0.0006, $p=0.024$).

Conclusions: Retinal FD is reduced in people with MS. It remains unclear whether FD may be related to disease severity and therapeutics and further work should characterize its role in dynamic disease modelling.

CONTROL ID: 3710596

SUBMITTER (NAME ONLY): Muneeswar Gupta Nittala

TITLE: Predictors for Growth of Geographic Atrophy over 12 Months

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nittala, A. Hariri, S. Velaga, S.R. Sadda, Doheny Eye Institute, Pasadena, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the relationship between characteristics of geographic atrophy (GA) lesions at baseline and Month 6, on the growth rate of atrophy over 12 months.

Methods: A total of 82 eyes of 82 subjects with geographic atrophy (GA) and 12 months of follow-up data at the Doheny Image Reading Center were included in this retrospective analysis. All subjects had undergone blue light fundus autofluorescence (FAF) imaging at baseline, Month 6, and Month 12. To be included in this analysis, the total GA lesion area was required to be between 2.54 and 17.78 mm^2, and in multifocal cases, at least one of the lesions was required to be larger than 1.27 mm^2. Areas of definite decreased autofluorescence (at all visits) corresponding to GA were manually segmented using planimetric reading center software. Lesion location (subfoveal vs nonfoveal), number, morphology (multifocal, horseshoe, ring, single), perimeter, and circularity index were measured at baseline and at month 6. Development of new/distinct lesions, as well as merger of two or more lesions at Month 6, were also assessed. These lesion characteristics at baseline and month 6 were correlated with the month 12 GA growth rate by linear regression analysis.

Results: Of 82 eyes included in this analysis, 50 were multifocal. Baseline GA area and annual growth rate of GA were 8.06 ± 4.06 mm^2 and 2.02 ± 1.13 mm^2 respectively. The average number of atrophic lesions at baseline was 3.8 ± 3.7 and this decreased to 3.5 ± 3.5 at month 12 ($p = 0.58$). The average perimeter of the lesions at baseline was 20.61 ± 10.90 mm and this increased to 20.74 ± 10.42 mm at month 6, but the difference was not significant ($p = 0.94$). In addition, the increase in CI from 0.34 ± 0.21 at baseline to 0.37 ± 0.21 at month 6 was also not statistically significant ($p = 0.41$). Figure 1 illustrates the Descriptive Regression Coefficients for GA area growth at month 12. Factors associated with a faster enlargement of GA are shown in Figure 2.

Conclusions: Although many baseline lesion characteristics can influence the enlargement rate of GA, their predictive value is small compared to the prior growth rate. This suggests that a “run-in” period prior to randomization may be useful for standardizing treatment arms in interventional trials.

CONTROL ID: 3710597

SUBMITTER (NAME ONLY): Arthur DeCarlo

TITLE: GABAergic but not Glutamatergic Modulators Microinjected into the Suprachiasmatic Nucleus Elevate IOP

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. DeCarlo, B.C. Samuels, Ophthalmology, The University of Alabama at Birmingham Department of Medicine, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Arthur DeCarlo: Commercial Relationship: Code N (No Commercial Relationship) | Brian Samuels: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of blindness in adults. Elevations and fluctuations in intraocular pressure (IOP) are thought to be risk factors for development and progression of glaucoma. This research targets the hypothalamic suprachiasmatic nucleus (SCN) in an attempt to identify new pharmacological targets for regulating IOP. The SCN lies above the pituitary gland at the base of the brain. It makes direct neural connections to the retina and to other more caudal nuclei, such as the dorsomedial hypothalamic and perifornical areas, which our lab has identified as playing a potential role in IOP regulation. The SCN is the primary modulator of circadian rhythms and is well situated to modulate IOP diurnal rhythms, thus it is of significant interest.

Methods: Male Sprague-Dawley rats (n=35) were placed under mild isoflurane anesthesia at midday. Using a stereotactic surgical approach, a 75 nL injectate of a chemical neurotransmitter agonist, antagonist, or control solution was delivered to the SCN while recording IOP, heart rate (HR), blood pressure (MAP), and intracranial pressure (ICP).

Results: The net increase of IOP in response to the $GABA_A$ antagonist bicuculline methiodide (BMI) injected into the SCN was similar (+6.8 +/- 1.2 mm Hg, n=8) to previously reported responses by the dorsomedial hypothalamus (+7.1 +/- 1.9, n=9) or by the raphe pallidus (+7.4 +/- 1.4, n=8) to BMI injection. The IOP response of the SCN to the glutamate receptor agonist, NMDA, was low (+4.7 +/- 0.8 mm Hg, n=8), and the response to the glutamate receptor antagonist, MK 801, was also low (+5.0 +/- 0.5, n=5). However, IOP was markedly raised (+14.3 +/- 2.4 mm Hg, n=5) by injecting a standard PBS solution of 0.1M phosphate buffer with added 154 mM NaCl (579 mM calculated osmolarity), though there was an absence of corresponding increases in ICP, HR, or MAP. Further investigation using a 0.9% NaCl injectate (308 mM calculated osmolarity) did not show IOP stimulation (+4.0 +/- 1.1 mm Hg, n=4), nor did injection of an artificial CSF solution (311 mM calculated osmolarity) raise the IOP (+5.4 +/- 1.3, n=5).

Conclusions: IOP regulation appears to be mediated by GABAergic and not glutamatergic neuronal pathways in the SCN, but neural conductivity associated with extracellular hyperosmolarity may play a significant role in SCN IOP regulatory activity.

CONTROL ID: 3710598

SUBMITTER (NAME ONLY): Olivia Cundy

TITLE: Clinical consensus on the classification of keratic precipitates

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Keratic precipitates (KPs) are a feature of ocular inflammation. KP morphology has been described as a vital diagnostic clue for different forms of inflammatory disease, yet there is no agreed morphology classification system. We aimed to undertake a rapid review to identify the most commonly used descriptors for KP morphology, and to describe the degree of consensus around slit-lamp based descriptions of KP morphology amongst a group of paediatric uveitis specialists.

Methods: Rapid literature review (search term: “keratic precipitates”) to identify the descriptive terms used for KPs, and frequency of use, in the published literature. REDCap image based electronic survey of KP morphology undertaken by members of the United Kingdom’s Paediatric Ocular Inflammation Group (POIG), who were asked to indicate KPs type present in each image. Degree of consensus for each of the 29 images in the survey was analysed for each KP morphological parameter with a threshold set at 80% agreement.

Results: The rapid review identified 469 papers, of which 259 used descriptive terms for keratic precipitates. The most commonly used descriptors (total 76 terms identified) were ‘mutton-fat’ (n=93 papers), ‘fine’ (n=76), ‘stellate’ (n=40), ‘large’ (n=33) and ‘medium’ (n=32).

The response rate for the survey was 26/32 (81.%). Consensus was met for the descriptive terms ‘large’ (consensus reached for 25/29 images, median consensus 91%, range 58 – 100%), mutton-fat (23/29, median 91%, range 54 – 100%), stellate (25/29, 90%, 57 – 100%), but not for the terms fine/dust (12/27, 74%, 50 – 96%) or medium (11/27, 73%).

Conclusions: This survey reveals an absence of clinical consensus around the classification of KPs using size (fine V medium), although there is evidence of good consensus on the appearance of large, stellate and mutton-fat KP. Harmonisation of clinical nomenclature is a key foundation for multi-centre research such as the currently underway POIG supported UNICORN (UK Uveitis in Childhood Prospective National Cohort study). These findings work will support future attempts to create consensus based nomenclature for this important diagnostic sign.

CONTROL ID: 3710599

SUBMITTER (NAME ONLY): Steven Pittler

TITLE: Ultrastructural changes in the RPE and outer retina in a mouse knock-in model of RP59

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.J. Pittler, J.D. Messinger, Optometry and Vision Science, Vision Science Research Center, University of Alabama at Birmingham, BIRMINGHAM, Alabama, UNITED STATES|S. Ramachandra Rao, S.J. Fliesler, Ophthalmology, Biochemistry, and Neuroscience Graduate Program, SUNY-University at Buffalo, BUFFALO, New York, UNITED STATES|S. Ramachandra Rao, S.J. Fliesler, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|D.M. Sherry, Cell Biology and Pharmaceutical Sciences, University of Oklahoma, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: A subset of defects in the DHDDS gene, which is required for protein glycosylation, cause retinitis pigmentosa 59 (RP59). We previously generated a knock-in model of the most prevalent DHDDS mutation, K42E. Here, we describe new findings obtained by ultrastructural and light level analyses to assess the fine structure of the mutant mouse retina and RPE.

Methods: Eyes from 6 homozygous K42E and 3 WT mice at 18 mo were used in this study. Histological analysis was performed using semithin sections stained with toluidine blue. Transmission electron microscopy (TEM) was performed on ultrathin (80-100 nm) sections prepared from mixed aldehyde-fixed, epoxy-embedded tissues using standard conditions. TUNEL staining was performed using paraffin-embedded tissue sections to assess cell death.

Results: Histological analysis revealed that the K42E retina was comparable to WT retina in all layers except the OPL, where patchy invasion by rod nuclei was observed and processes of second-order neurons were reduced, especially in the periphery. Pyknotic nuclei were observed in the ONL and INL, and TUNEL staining revealed several dying cells in the mutant retina compared to WT. At the TEM level, most rod and cone terminals showed normal presynaptic ultrastructure, with synaptic ribbons decorated with synaptic vesicles anchored to the plasma membrane and contacted post-synaptic processes from horizontal and bipolar cells. However, some photoreceptor cell bodies and terminals displayed darkened cellular material, consistent with impending cell death. Basal infoldings on the RPE adjacent to Bruch’s membrane were frequently disorganized and severely degenerated RPE was occasionally observed in K42E mice.

Conclusions: Perturbations in the RPE and OPL and cell loss in the Dhdds K42E mouse retina are consistent with previously described ERG deficits in this RP59 model. These results suggest that defective RPE function and signal transmission between photoreceptors and inner retinal neurons may be major contributors to the etiology of RP59.

CONTROL ID: 3710601

SUBMITTER (NAME ONLY): Lara Skelton

TITLE: Altered astrocyte morphology and intermediate filament distribution in the rat optic nerve following acoustic blast overpressure exposure

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glial and neuronal responses to acoustic blast overpressure (ABO) exposure have been studied extensively in the brain and retina, but remain relatively uncharacterized in the optic nerve. We examined the expression and distribution patterns of GFAP, synemin, nestin and neurofilament-M (NF-M) in rat optic nerve following ABO relative to unexposed controls, to ascertain basal and post-blast distribution of these major intermediate filament (IF) cytoskeletal components.

Methods: Anesthetized adult male Long-Evans rats were subjected to ABO exposure, with the blast directed at the right side of the head (Allen et al., 2018, 2021). Optic nerves were harvested at 1 wk post-ABO alongside non-exposed, age/sex-matched controls, and fixed in PBS-buffered PFA. Transverse cryosections (O.C.T. embedment) were prepared, subjected to antigen retrieval, and processed for confocal microscopy immunofluorescence histochemistry (IHC) using polyclonal antibodies (Abs) against GFAP, nestin, and NF-M, and monoclonal antibodies against synemin (clone A8), with suitable fluor-conjugated secondary Abs. Local thickness mapping and particle analysis of synemin immunolabeling through z-stacks was performed in FIJI ImageJ™. Statistical analysis: Student's t-test, significance threshold $p<0.05$ (N=3/group).

Results: GFAP, nestin and synemin were robustly expressed in control optic nerve astrocytes, with overlapping distribution through the IF cytoskeleton. Astrocytes were evenly distributed through control transverse optic nerve sections. Synemin partially co-localized with GFAP and nestin IF and appeared to form fine cytoskeletal structures along the astrocytic cell processes. At 1 wk post-ABO, astrocytes appeared heterogeneous, with a sub-population exhibiting hypertrophic cell processes, and were re-distributed more centrally in the optic nerve. Co-labeling for axons using anti-NF-M identified distinct axonal bundles that appeared ordered and regularly spaced in control optic nerves. At 1 wk post-ABO, peripheral disturbance to the axon bundles was observed. Local thickness analysis revealed a ~1.5-fold increase in particle size of cytoskeletal synemin through the astrocytic processes.

Conclusions: Astrocytes undergo morphological and distribution changes in the rat optic nerve following ABO, accompanied by altered synemin localization through the IF cytoskeleton.

CONTROL ID: 3710603

SUBMITTER (NAME ONLY): David Buickians

TITLE: Retinal Vessel Tortuosity Indices (VTIs) as a potential biomarker of idiopathic intracranial hypertension(IIH): Baseline analysis of the IIH treatment trial

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Buickians, H. Moss, Ophthamology, Stanford University School of Medicine, Stanford, California, UNITED STATES|H. Moss, Neurology & Neurological Sciences, Stanford University School of Medicine, Stanford, California, UNITED STATES|D. Dahshan, School of Medicine, Marshall University Joan C Edwards School of Medicine, Huntington, West Virginia, UNITED STATES|M. Shahidi, A. Nankali, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|S.E. Feldon, Ophthalmology, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Changes in optic nerve head swelling (papilledema) are delayed following intracranial pressure (ICP) changes in IIH. Retinal vascular changes may occur more quickly and are therefore a potential non-invasive, quantitative biomarker for ICP changes in IIH. The purpose of this study is to characterize retinal vessel tortuosity in a cohort of untreated IIH subjects.

Methods: Peripapillary arteriolar and venular tortuosity indices (aVTI, vVTI) were measured for 4 arterioles and 4 venules in a region of interest 4.5-6.4mm centered on the optic nerve on retinal photographs centered on the optic nerve from the baseline visit (prior to treatment) of study eyes in subjects who completed IIHTT follow up (n=126). VTI was measured using custom software that uses a clustering algorithm to identify center lines of each selected vessel. Curve magnitudes were then calculated by the ratio of vessel segment length to straight length between inflection points which establish a dimensionless VTI. For each subject, VTI was averaged for each vessel type and compared with other baseline parameters from the IIHTT (demographics, IOP, ICP, BP, other photographic parameters) using Pearson correlation and linear regression(LR).

Results: VTI measurements for ≥3 arterioles and/or venules were successful for 101 eyes. aVTI was 0.14 +/- 0.05 and vVTI was 0.12 +/ -0.07. vVTI was associated with gender(r=0.23,p= 0.02 LR), IOP(r=0.28,p=0.005 LR), ICP(r=0.17,p=0.08 LR), optic nerve elevation area(r=0.18,p=0.087 LR) and average venule diameter(r=0.27,p=0.006 LR). aVTI was associated with average arteriole diameter(r=0.19,p=0.06 LR). All other comparisons had slopes with p>0.1.

Conclusions: vVTI and aVTI could be measured on the majority of photographs of untreated papilledema. Cross sectional analysis showed weak correlations with other markers of IIH and local pressures. Analysis of association between VTI change and IIH treatment response are needed to assess the potential of retinal VTI as a marker of disease treatment.

IIHTT Clinical Trial NCT01003639

CONTROL ID: 3710604

SUBMITTER (NAME ONLY): Navita Lopez

TITLE: Microglia utilize both CR3 and Mertk receptor pathways to eliminate RGCs in the embryonic retina

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Lopez, S.R. Anderson, M.L. Vetter, Neurobiology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Navita Lopez: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Monica Vetter: Commercial Relationship(s);Code C (Consultant/Contractor):Roche

ABSTRACT BODY:

Purpose: Microglia are the resident myeloid cells of the CNS that serve multiple roles during development. We previously showed that these phagocytes are responsible for the elimination of a subset of newborn retinal ganglion cells (RGCs) in the embryonic retina. This is partly dependent on microglial recognition of RGCs by complement receptor 3 (CR3); however, we hypothesize that additional receptor pathways are involved. Here we investigate the role of the TAM receptor tyrosine kinases, which are known to facilitate phagocytosis. Embryonic retinal microglia express two members of this family, Mertk and Axl. Microglial-mediated phagocytosis of excess neurons is a pivotal process in neural development, and we hypothesize that embryonic retinal microglia utilize both CR3 and TAM receptors to recognize and eliminate a subset of viable newborn RGCs in the developing retina and regulate RGC density.

Methods: We used B6. Mertk$^{-/-}$, Axl$^{-/-}$ and Mertk$^{-/-}$Axl$^{-/-}$ mice to assess the role of TAM receptors in embryonic RGC elimination. Retinal whole mounts were collected at P0, when excess RGCs would persist, and we performed RBPMS immunostaining and confocal imaging then quantified RGC density. To determine if multiple receptor pathways cooperate to contribute to embryonic RGC elimination, we used Mertk$^{-/-}$, CD11b$^{-/-}$ (CR3) and Mertk$^{-/-}$ CD11b$^{-/-}$ mice and analyzed RGC number at P0 in whole mount retinas.

Results: We find that genetic ablation of Mertk resulted in an increase in RGC density at birth compared to wildtype controls. Mertk$^{-/-}$ mice showed an 8.95% increase in RGC density at P0 (n=12; p=0.005). Mice deficient in both Mertk and Axl, resulted in a 11.81% increase in RGC density (n=12; p<0.0001), similar to Mertk$^{-/-}$ alone, suggesting that Mertk is primarily responsible. We show that with knockout of both Mertk and CD11b, there is an additive effect, with a 19.78% increase in RGC density (n=4; p<0.0001).

Conclusions: Shortly after RGCs are generated, a non-apoptotic subset is eliminated by phagocytic microglia. We show that multiple microglial receptor pathways contribute to the embryonic elimination of RGCs, and we establish that Mertk and CR3 cooperate in this process. Future studies will define the properties of RGCs targeted for elimination.

CONTROL ID: 3710608

SUBMITTER (NAME ONLY): Javier Zarranz-Ventura

TITLE: Real impact and reasons for anti-VEGF treatment delay during Covid-19 pandemic lockdown in neovascular age-related macular degeneration: A national study

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zarranz-Ventura, Hospital Clinic de Barcelona, Barcelona, Catalunya, SPAIN|J. Zarranz-Ventura, R. Martin-Pinardel, Institut d'Investigacions Biomediques August Pi i Sunyer, Barcelona, Catalunya, SPAIN|R. Gallego Pinazo, Clínica Oftalvist, Valencia, Valencia, SPAIN|L. Gomez, Novartis Pharmaceuticals, SPAIN|J. Escobar, Hospital Dos de Maig, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: To assess the visual impact and reasons for treatment delay during the COVID-19 pandemic lockdown in neovascular age-related macular degeneration (nAMD) patients in ongoing anti-VEGF therapy.

Methods: Retrospective, national, multicentre, observational study in nAMD patients treated with anti-VEGF therapy and registered in the Fight Retinal Blindness (FRB) Spain platform prior to lockdown. Study cohort was divided in timely treated patients (TTP) and delayed treatment patients (DTP). Mean change in best corrected visual acuity (BCVA, in ETDRS letters) from the last follow-up visit (FUV) before lockdown (BLD) (baseline [BL] visit) to the first FUV after lockdown (ALD) was assessed. A specific questionnaire was distributed to the participant centers to investigate further the reasons for treatment delay in all individual cases.

Results: A total of 245 eyes fulfilled the eligibility criteria, from which 39.6% were TTP (n=97) and 60.4% were DTP (n=148). TTP presented greater baseline and final BCVA compared to DTP (64.1 vs 58.7 letters, p=0.023, and 63.6 vs 57.1, p=0.004). BCVA loss was significantly greater for DTP vs TTP (-2.0 vs -0.6 letters, p=0.016). For DTP cohort, the primary reason for visit delay was patient decision (48.2%) followed by limited hospital clinic capacity (42.7%). When patients decided not to attend scheduled visits, the main reason was fear to Covid-19 infection (49.4%).

Conclusions: This study provides relevant data about the impact on visual outcomes of Covid-19 pandemic lockdown on nAMD patients and specifically provides new additional information regarding the main reasons for treatment and visits delay from both patients and healthcare service delivery perspectives.

CONTROL ID: 3710609

SUBMITTER (NAME ONLY): Shweta Modgil

TITLE: 2-Fluoro-N-(2-(5-hydroxy-1H-indol-3-yl)ethyl)nicotinamide (HIFN) protects against vision loss from closed-globe ocular trauma by activating tropomyosin-related kinase B (TrkB)

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Modgil, P. Iuvone, Department of Opthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|C.L. Walker, F.E. McDonald, Department of Chemistry, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: A small molecule activator of TrkB, HIOC, has been shown to protect against vision loss following ocular blast injury (Dhakal et al, J Neurotrauma 2021;38:2896). In this study, we assessed the protective effects of a fluoropyridine analog of HIOC.

Methods: Using HIOC as a lead structure, an analog (HIFN) containing fluorine substituted pyridine was synthesized. Adult male C57BL/6J mice were subjected to blast overpressure injury at ~20psi. Within 30 minutes of blast, animals were administered intraperitoneally either vehicle, HIFN or HIOC (40mg/kg). The treatment was continued for another 6 days. Contrast sensitivity at a spatial frequency of 0.064c/d and visual acuity (spatial frequency threshold) were measured using the optomotor response. Scotopic electroretinogram (ERG) and pattern ERG (spatial frequency of 0.155 c/d, 2.1 contrast reversal/sec and mean luminance of 50cd/m^2) were recorded. TrkB activation was assessed by western blot analysis of TrkB phosphorylation. Animals were administered with TrkB specific inhibitor, ANA-12 (0.5mg/kg), 2.5 h prior to treatment with compound.

Results: HIOC and HIFN both reduced the visual acuity ($p \leq 0.05$ vs Blast-Veh) and contrast sensitivity deficits after blast ($p \leq 0.05$ vs Blast-Veh). The protection of contrast sensitivity afforded by HIFN was better than that by HIOC at 7-week post blast ($p \leq 0.05$). No effects of blast, HIFN, or HIOC were observed in the scotopic ERG a-wave or b-wave amplitudes. At 8-week post blast there was a significant decline in P1 and N2 wave amplitude of pERG in Blast-Veh group ($p \leq 0.001$). HIFN and HIOC treatment reduced the decline in P1 amplitude ($p \leq 0.05$ vs Blast-Veh). HIFN and HIOC showed a trend to increase the N2 amplitude compared to vehicle, but the effects were not statistically significant ($p=0.06$ vs Blast-Veh). HIFN activated TrkB at a concentration of 10 nM in NIH/3T3 cells expressing human TrkB. The TrkB inhibitor, ANA-12, blocked the protective effects exhibited by HIFN and HIOC in blast animals.

Conclusions: HIFN protects against blast-induced vision loss and retinal ganglion cell damage, as assessed by pERG. HIFN appears to preserve contrast sensitivity better than HIOC, although this needs to be assessed at different drug doses. The protective effects of HIFN are due to activation of TrkB receptor.

CONTROL ID: 3710611

SUBMITTER (NAME ONLY): David Burgoyne

TITLE: Effect of N0651 on ocular inflammation in endotoxin-induced uveitis and autoimmune uveitis in the rat.

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Burgoyne, E. DeBruin, N. Hatfield, J. Langlands, Naegis Pharmaceuticals Inc., British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Uveitis is a common cause of visual disability and blindness. Experimental models of uveitis have been developed in rats by injection of endotoxin (endotoxin induced uveitis; EIU) or immunization with ocular antigens (experimental autoimmune uveitis; EAU). N0651 is a novel compound inhibiting the production of leukotrienes C4 and B4 (LTC4/B4) with greater potency than zileuton. Studies were undertaken to evaluate the effect of N0651 on measures of inflammation in EIU and EAU in the rat.

Methods: EIU was induced in Lewis rats by injection of 75 µg LPS into the hind paw. Levels of inflammation in the eye were assessed after 24 hrs by clinical score and histologically. N0651 (30 mg/kg) and prednisolone (2 mg/kg) were administered orally at the time of LPS challenge and 6 hrs post challenge.

EAU was induced in Lewis rats by injection of R16 peptide (30 µg) in 200 µL of complete Freund's adjuvant in the base of the tail. Clinical signs of disease were evident 6 days after immunization. Animals were treated with N0651 topically 4 times daily (10 µL/eye; 0.5% solution) plus a single daily oral dose (30 mg/kg) after ocular clinical signs of uveitis were observed.

Results: In the EIU model, N0651 (30 mg/Kg) reduced the clinical scores from 7 to 4 (max possible score 7), and histological examination of eyes showed N0651 reduced cell content and fibrin content in the aqueous humor and cornea. The effect on clinical score was comparable to that seen with prednisolone, however, the effect on both cell content and fibrin deposition in the cornea were minimal.

In the EAU model, clinical scores were reduced after topical + oral N0651 compared to control (median 1.25 vs 2.75; maximum possible score 4). Histological scoring of the posterior segment demonstrated lower disease severity (median 2 vs 3.75; maximum possible score 4), and reduced retinal thickness in N0651 treated animals compared to untreated (139.5 vs 185.5 nm).

Conclusions: N0615 affords protection against development of uveitis in both the EIU and EAU models,demonstrating effects at both the anterior and posterior segments in each model, respectively.

CONTROL ID: 3710612

SUBMITTER (NAME ONLY): Rosa Dolz-Marco

TITLE: High axial resolution optical coherence tomography images show important features in patients with age-related macular degeneration

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Dolz-Marco, R. Gallego Pinazo, Unit of Macula, Oftalvist, Valencia, Valencia, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the clinical benefit of high axial resolution optical coherence tomography (OCT) images in patients diagnosed with age-related macular degeneration (AMD) using a research OCT prototype (High-Res OCT, Heidelberg Engineering, Germany) with 3 µm optical resolution.

Methods: Patients diagnosed with AMD undergoing routine macular evaluation were scheduled for High-Res OCT imaging. The examination included OCT, OCT angiography, fundus autofluorescence, and multispectral images acquired with commercially available OCT device (SPECTRALIS) and High-Res OCT images acquired using the research prototype. Findings observed on the High-Res OCT images were compared and correlated with the conventional OCT and multimodal approach.

Results: One-hundred eleven eyes of 63 patients were included. A better delineation of retinal layers was achieved with increased contrast between layers in the High-Res OCT images. The status of the outer retinal bands (external limiting membrane, photoreceptors ellipsoid and interdigitation zones) and the content of the retinal pigment epithelium (RPE) detachment both in neovascular and non-neovascular cases were better assessed in High-Res images when compared to conventional OCT. A significant split between the RPE layer and Bruch's membrane was observed in the majority of cases (84%) in the foveal area and also extending throughout the macula and was not evident on conventional OCT.

Conclusions: High-Res OCT images provided a detailed representation of structures in the retina not seen with conventional OCT axial resolution (about 7 µm). A better delimitation between layers was observed, and better assessment of important biomarkers in AMD cases was achieved, which might be beneficial in the improvement of segmentation algorithms and clinical evaluation of these cases.

CONTROL ID: 3710613

SUBMITTER (NAME ONLY): Stephanie George

TITLE: Elucidating strain-dependent responses of Shroom3 in lens epithelial cell proliferation

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. George, H.L. Chandler, T.F. Plageman, The Ohio State University College of Optometry, Columbus, Ohio, UNITED STATES|H.L. Chandler, The Ohio State University College of Veterinary Medicine, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Stephanie George: Commercial Relationship: Code N (No Commercial Relationship) | Heather Chandler: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Plageman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The mechanisms underlying an increased lens size due to lens epithelial cell proliferation in presbyopia remain unknown. Biomechanical strain is hypothesized to be a contributor, as the zonules attach to the lens germinative zone. Shroom3, a cytoskeletal protein, is necessary for ocular development and facilitates lens placode invagination. Preliminary studies demonstrate that Shroom3 mutants lack ventral optic cup closure, illustrating the significance of Shroom3 in epithelial folding, fusion, and potentially, proliferation. We hypothesize inducing intercellular strain through Shroom3 overexpression increases proliferation in vitro.

Methods: Model epithelia, Madin-Darby canine kidney (MDCK) cells, were transfected with Shroom3 to create a stable line (pTre3-Shroom3-mCherry) inducible with doxycycline with dual selection hygromycin/G418. Once cells reached confluence on glass coverslips, EdU was incorporated into cells for 18 hours and fixed with paraformaldehyde. Cells were imaged throughout the coverslip centrally and peripherally (n=5) using Zeiss Axio Observer (N=3). MDCK wildtype (wt) cells were used to control for the effect of doxycycline. The number of nuclei and EdU^{+} cells were counted using ImageJ. Statistical analysis was performed using two-tailed Student's t-test.

Results: SHROOM3 overexpression resulted in significantly reduced mitosis, as shown through nuclei counts ($p \leq 0.001$) and percentage of EdU^{+} cells ($p \leq 0.001$). The addition of doxycycline affected proliferation differently depending on the location of cells on the coverslip. Peripheral $doxycycline^{+}$ wt cells showed decreased proliferation ($p \leq 0.05$) compared to pTre3g-Shroom3-mCherry $doxycycline^{-}$ cells, but not compared to peripheral $doxycycline^{-}$ wt cells. Central $doxycycline^{+}$ wt cells showed decreased proliferation ($p \leq 0.05$) compared to $doxycycline^{-}$ wt cells but not to pTre3g-Shroom3-mCherry $doxycycline^{-}$ cells.

Conclusions: Our results contradict our hypothesis and instead show that Shroom3 decreases proliferation. Although doxycycline affected proliferation both centrally and peripherally, results were not consistent between cells with/without doxycycline; our results can be attributed to SHROOM3 expression levels. Future experiments will apply these methods to in vivo models.

CONTROL ID: 3710616

SUBMITTER (NAME ONLY): Tea Soon Park

TITLE: Generation of choroid and RPE cells from iPSC with CFH knockout for modeling of AMD

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Park, R. Quinn, R. Hirday, A. Ali, E. Nguyen, D. Bose, R. Sharma, K. Bharti, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Complement factor H (CFH) inhibits the alternate pathway of the complement system. Compromised CFH expression causes immune system imbalance and complement-mediated damage to healthy cells. CFH expression and activity changes are associated with increased risk of age-related macular degeneration (AMD), but the relative contributions of CFH from the retinal pigmented epithelium (RPE) and the choroid are not known. Here we aim to study the effects of CFH in choroid versus RPE using CFH knockout (KO) iPSCs and the 3D bioprinting technique.

Methods: iPSC line from a healthy donor (wildtype, WT-iPSC) was genetically modified to generate a CFH-KO-iPSC using CRISPR/Cas9 technology. Both WT- and CFH-KO-iPSC lines were differentiated into RPE, endothelial cells (EC), pericytes, and fibroblasts and validated by immunophenotyping. Capillary formations by iPSC-derived cells were assessed by a hydrogel tubulogenesis assay combining ECs, pericytes, and fibroblasts matured for 3 weeks. 3D-bioprinting was performed on a biodegradable PLGA scaffold for choroid formation and the RPE monolayer seeded on the other side of the scaffolds. Live images of GFP expression from ECs were documented for capillary formation and maturation for 5 weeks after 3D-bioprinting.

Results: All differentiated cell components from WT- and CFH-KO-iPSC were cryopreserved and thawed successfully prior to functional validation and 3D bioprinting. CD31+ EC was verified by acetylated-Dil-LDL uptake, hydrogel tubulogenesis, and expression of CD146 and vWF, ETV2, PLVAP, CA4, and RGCC. Pericytes were differentiated from CD31- cells with TGF-b3 and PDGF-bb and confirmed the expression of PDGFR-b, NG2, CD44, and a-SMA. Fibroblasts were differentiated from pericytes and expressed vimentin, connexin43, and collagen-I. EC, pericytes, and fibroblasts were assembled into capillary-like structures in 3D hydrogel tubulogenesis assay up to 3 weeks. Bruch's membrane formation in bioprinted tissues was confirmed by the expression of fibronectin, collagen-I, laminin, and elastin.

Conclusions: Our results show that all four cell components (RPE, EC, pericytes, and fibroblasts) were differentiated from WT- and CFH-KO-iPSC with compatible protein expressions. Using these cell components we generated 3D-bioprinted ex-vivo choroid-RPE system that provides as a tool to investigate the disease mechanism and the role of anaphylatoxins in RPE versus the choroid.

CONTROL ID: 3710618

SUBMITTER (NAME ONLY): Vanessa Raphtis

TITLE: Ocular Pulse Amplitude (OPA) in Canine ADAMTS10-Open-Angle Glaucoma (ADAMTS10-OAG)

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Raphtis, D. Sharma, A. Anderson, C. Harman, A.M. Komaromy, Michigan State University, East Lansing, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect of the G661R missense mutation in the ADAMTS10 gene on ocular pulse amplitude (OPA) in dogs.

Methods: Animals studied included 39 glaucomatous and 14 unaffected control male and female dogs between the ages of 6 months and 12 years (median: 3.2 years). Dogs were sedated with butorphanol and midazolam and average of both right and left eye were measured. Intraocular pressure (IOP) was measured with the Icare® Tonovet rebound tonometer. The Reichert Model 30™ Pneumotonometer was used to measure OPA, deviation index, and pulsation rate. During each session, measurements were taken twice, once for acclimation to the probe and noise of the pneumotonometer, and a second time for actual data collection. Central corneal thickness (CCT) measurements were taken via Accutome® PachPen, and A-scan biometry assessed with DGH Technology Scanmate. Data analysis was conducted with ANOVA, ANCOVA and regression models.

Results: Mutant dogs had a significantly lower OPA of 4.24 +/- 2.05 mmHg (mean +/- SD) compared to 6.54 +/- 2.83 mmHg of normal dogs (p=0.002). There was no significant age effect, and OPA was not correlated with any other parameters, including CCT. As expected, mutant dogs displayed a greater mean IOP of 25.04 +/- 8.04 mmHg compared to 15.25 +/- 3.59 mmHg of normal dogs.

Conclusions: The lower OPA in ADAMTS10-mutant dogs corresponds to previously documented weaker and biochemically distinct posterior sclera. OPA measurement could be a valuable in vivo clinical tool to assess individuals' scleral biomechanics, and therefore their susceptibility to IOP elevation.

CONTROL ID: 3710623

SUBMITTER (NAME ONLY): Maggie Lin

TITLE: Physiological variations in intraocular pressure: mathematical modeling outputs versus clinical data from patients with glaucoma and healthy controls

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Lin, G. Guidoboni, R. Nunez, Electrical Engineering and Computer Science, University of Missouri, Columbia, Missouri, UNITED STATES|A. Harris, A. Verticchio, B.A. Siesky, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|G. Guidoboni, Mathematics, University of Missouri, Columbia, Missouri, UNITED STATES|D. Coll, M. Szopos, Mathematiques Appliquees a Paris 5, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is a major risk factor for open angle glaucoma (OAG). During each heartbeat, IOP exhibits pulsations described as ocular pulse amplitude (OPA). OPA has been shown to be relevant in glaucoma as IOP and OPA are affected by several factors, including systolic and diastolic blood pressure (SBP, DBP), tissue biomechanics, and aqueous humor (AH) flow. Here, we use a mathematical model to investigate how IOP and OPA are influenced by variations in SBP, DBP, and model parameters characterizing tissue biomechanics and AH flow in comparison with clinical data.

Methods: The model calculates IOP and OPA from the balance between AH inflow and outflow, the pulsatile BP inputs, and the deformability of ocular tissues. Two simulation scenarios are considered (health and disease), with the latter characterized by an outflow facility reduced by 70% with respect to baseline. In both scenarios, physiological variations are included in SBP and DBP as normal distributions [SBP~ N (124.1, 11.1) and DBP ~ N (77.5, 7.1)]. Variations in all other model parameters were assumed to follow a uniform distribution [± 15% with respect to published baseline values (Szopos et al 2016, Stefanoni et al 2018)].

Results: The table in Fig.1 compares model predictions for IOP and OPA with clinical data on 90 healthy subjects (Cheng et al, 2017) and 115 glaucoma patients. In both health and disease, model results are within the same range of clinical data. Fig. 2 shows the scatterplots of OPA versus pulse pressure (PP=SBP-DBP) as computed by the model (a) and measured clinically (b) on glaucoma patients. When fitted with a linear regression, both computed and measured data had a positive slope of 0.0265 and 0.0122, respectively.

Conclusions: The model proved capable of simulating IOP and OPA in health and disease. OPA was predicted to increase with PP as evidenced by clinical data on glaucoma patients. These data suggest mathematical modeling approaches may help clinicians confirm and/or discriminate OAG disease.

CONTROL ID: 3710624

SUBMITTER (NAME ONLY): Manqi Pan

TITLE: Factors influencing chorioretinal biomechanical responses to IOP

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pan, S. Kwok, J. Liu, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Liu, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Manqi Pan: Commercial Relationship: Code N (No Commercial Relationship) | Sunny Kwok: Commercial Relationship: Code N (No Commercial Relationship) | Jun Liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A positive intraocular pressure (IOP) stretches the ocular shell and its inner lining: the chorioretinal tissue. Interestingly, chorioretinal folds occur under certain conditions despite the stretch created by IOP. In this study, we developed a computation model to determine which biomechanical factors most influenced chorioretinal stresses and strains and the implications for chorioretinal folds.

Methods: A computational model of the eye with two layers, the sclera and the chorioretina, was developed (Fig. 1A). Seven input factors including scleral/chorioretinal thickness, scleral/chorioretinal Poisson's ratio, scleral/chorioretinal modulus, and IOP were independently varied within the reported ranges in the human eye (Fig. 1B). The mean in-plane stress and strain of the chorioretina were quantified as outcome measures. Input factors were ranked based on their relative influence on the outcome measures.

Results: Under all simulated conditions, the chorioretinal tissue experienced a positive in-plane strain but a negative in-plane stress (Fig. 1C, D). The 3 inputs that had largest influence on chorioretinal stress were, ranked in order, IOP, scleral modulus, and chorioretinal Poisson's ratio (Fig. 2). The 3 inputs that had largest influence on chorioretinal strain were, ranked in order, scleral modulus, IOP, and chorioretinal Poisson's ratio (Fig. 2). The mean in-plane stress within the chorioretina during IOP change from 10 to 30 mmHg was -1.15 to -3.46 kPa. The mean in-plane strain within the chorioretina was 1.13% to 0.14% when sclera modulus changed from 1 to 9 MPa.

Conclusions: The chorioretinal tissue experiences a negative in-plane stress which may underlie localized folding. This stress is strongly dependent on IOP, while sclera modulus has the largest effect on the in-plane strain. Changes in either may induce chorioretinal folds, consistent with clinical observations. These results provide new biomechanical insights into chorioretinal folds.

CONTROL ID: 3710625

SUBMITTER (NAME ONLY): Bani Antonio-Aguirre

TITLE: Risk of cystoid macular edema after cataract surgery in retinitis pigmentosa: an analysis of United States claims from 2010 to 2018.

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Antonio-Aguirre, B.K. Swenor, M.S. Singh, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|B.K. Swenor, Johns Hopkins Disability Health Research Center, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|J.K. Canner, Johns Hopkins Surgery Center for Outcomes Research, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cataract surgery is commonly performed in patients with retinitis pigmentosa (RP), but concern exists regarding the possibly heightened risk of postoperative cystoid macular edema (CME). We evaluated the association between RP and postoperative CME after cataract extraction (CE).

Methods: We analyzed eight years of longitudinal data from the IBM MarketScan® database (2010 – 2018) and included patients aged 18 to 65 years who underwent single-phase CE. We excluded CME and diabetic macular edema cases at baseline. Incident postoperative CME in the same eye that underwent CE was assessed. A mixed-effects Cox model estimated the hazard ratio (HR) and 95% confidence intervals (CI) for the association between CME and RP, controlling for sex, age, diabetes, hypertension, epiretinal membrane (ERM), and retinal vein occlusion. Johns Hopkins University Institutional Review Board approved this project.

Results: The cohort included 468,123 subjects and 615,645 eyes: 124 with RP and 615,521 without RP. Median follow-up was 9.06 months (95% CI, 9.06 – 9.09). Postoperative CME was reported in 4,933 eyes (0.8%). Subjects with RP had 4.83 times the risk of CME (95% CI, 2.13 – 10.92; P<0.001) than those without RP but with similar characteristics. On average, RP cases developed CME 3.9 weeks later than those without RP (95% CI, 2.04 – 6.5; P<0.001). In the cohort, baseline ERM was associated with higher risk of postoperative CME (HR, 4.30, 95% CI, 3.12 – 5.93; P<0.001). Age was inversely associated with CME; subjects aged 55 to 65 had 52% lower risk of postoperative CME (95% CI, 39% – 62%; P<0.001) than those aged 18 to 34. However, when stratified by RP status, neither baseline ERM nor age had the same effect in RP eyes. In these subjects, ERM had a protective effect (HR, 0.12; 95% CI= 0.48 – 0.97; P=0.004), and age did not significantly influence the risk, although it had a bimodal distribution.

Conclusions: Postoperative CME among RP patients may be significantly higher than candidates without RP but otherwise similar characteristics. In addition, CME in RP patients may have a delayed presentation, necessitating longer follow-up. Understanding this risk will facilitate clinician-patient communication regarding treatment recommendations and vision-impacting complications. Future research should focus on interventions to reduce CME risk in RP patients.

CONTROL ID: 3710631

SUBMITTER (NAME ONLY): Charles Bouchard

TITLE: Indications and Outcomes of Surgery for High Myopia: STAAR Intraocular Collamer Lens (ICL) vs. LASIK

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.S. Bouchard, K. Kirk, Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|Y. Ren, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Charles Bouchard: Commercial Relationship: Code N (No Commercial Relationship) | Kent Kirk: Commercial Relationship: Code N (No Commercial Relationship) | Yanhan Ren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although the ICL is more invasive than laser-assisted in situ keratomileusis (LASIK), it is indicated for patients with very high myopia, commonly over -7D. ICL is associated with certain risks including cataract and glaucoma which may develop years after surgery requiring additional procedures. In this study, we examined the outcome and safety profile of ICL vs. LASIK at 1 week, 1 month, and 1 year postoperatively.

Methods: In this retrospective study, we examined records from a single surgeon (KK) as well as 2 patients with post ICL complications requiring ICL removal. An important aim of this study was to use the 1 year follow up data since this is one of the standard ICL follow up visits. We hypothesized that the FDA approved ICL (2005) would have a comparable target refractive outcome and safety profile when compared to LASIK.

Results: There were a total of 45 ICL eyes and 65 LASIK eyes. Preoperatively, ICL patients had a significantly higher manifest refraction spherical equivalent (MRSE) and cycloplegic refraction spherical equivalent (CRSE) than LASIK patients ($p<0.05$). For patients who received the ICL implants, the average MRSE at 1-week, 1-month, 1-year post-op was -0.37D±(0.13), -0.29D±(0.09), -0.53D±(0.15); and -1.60D±(0.16), -0.36D±(0.15), -0.36D±(0.07) for patients who received LASIK. The differences in post-op MRSE between ICL and LASIK were not statistically significant ($p>0.05$). The only significant differences were 1 month LogMAR best corrected visual acuity and 1 year LogMAR distance uncorrected visual acuity ($p<0.05$), in which LASIK had better visual acuity. Common postoperative findings in both groups were refractive target deviations and punctate keratitis. Reoperation rates in the ICL and LASIK groups were 21.4% and 10.8% respectively, which was not statistically significant ($p>0.05$). 42.6% of ICL patients underwent the procedure during the COVID-19 pandemic compared to 26.2% of LASIK.

Conclusions: Our results demonstrate that ICL is safe and effective for patients with high myopia. Although ICL patients had a significantly higher preoperative MRSE compared to the LASIK group, the ICL patients were able to achieve similar refractive targets. There were no cases of glaucoma or cataract at 1 year in the ICL group. In conclusion, ICL surgery is as safe and effective as LASIK surgery in correcting patients with high myopia, regardless of pre-operative refractive error.

CONTROL ID: 3710632

SUBMITTER (NAME ONLY): Sana El Hajji

TITLE: Insulin promotes RGC dendrite regeneration through ribosomal protein S6 kinase activation leading to restoration of neuronal function in glaucoma

SESSION TITLE: Neuroprotection and neuroregeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. El Hajji, N.A. Belforte, Y. Shiga, F. Dotigny, A. Di Polo, Department of Neuroscience, Universite de Montreal, Montreal, Quebec, CANADA|S. El Hajji, N.A. Belforte, Y. Shiga, F. Dotigny, A. Di Polo, Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: We previously demonstrated that insulin promotes RGC dendrite regeneration through activation of the mTOR pathway. However, the precise mechanisms of insulin-mediated regeneration and the effect of insulin on vision restoration are not well understood. Here, we asked: 1) what are the mTOR downstream effectors responsible for insulin-induced dendritic regrowth? 2) does insulin restore RGC function and visual responses in glaucoma?

Methods: Ocular hypertension (OHT) was induced by injection of magnetic microbeads in Thy1-YFP mice. Daily insulin or saline eye drops started at 2-weeks after OHT induction, when there is marked dendritic retraction, and dendrites were imaged and reconstructed 1 or 4 weeks later. The role of the mTORC1 downstream effectors, S6K and 4EBP1, was assessed by loss of function using targeted siRNAs. RGC survival and function were evaluated using complementary methods: i) quantification of RBPMS-positive neurons, ii) single-RGC calcium dynamics using two-photon microscopy live imaging in transgenic mice carrying the calcium indicator GCaMP6f, and iii) optomotor reflex assays.

Results: Insulin promoted a substantial increase in RGC dendritic length and complexity in glaucomatous eyes (n=6 mice/group, ANOVA, $p<0.001$). siRNA-based knockdown of S6K impaired insulin-mediated RGC dendrite regeneration, while 4EBP1 silencing had no effect. Intriguingly, S6K increased mTORC2 activity through phosphorylation of mSIN1 enhancing RGC dendrite regeneration. Insulin promoted robust RGC survival at 3 and 6 weeks of OHT induction relative to saline (OHT-3wks, insulin: 2057±34 RGC/mm^2, vehicle: 1679±66 RGC/mm^2, N=3-6 mice/group, ANOVA, $p<0.001$). Importantly, insulin restored light-evoked RGC calcium dynamics (n=6 mice/group, $p<0.01$) and improved visual acuity (N=5-8 mice/group, ANOVA, $p<0.01$) in glaucoma

Conclusions: Our data show that S6K is a key signaling component required for insulin-mediated RGC dendrite regeneration, an effect that is enhanced by cross-talk with mTORC2 through mSIN1 activation. Importantly, insulin prevents RGC loss while restoring light-evoked responses and visual acuity. These findings support a critical role for insulin as a pro-regenerative therapy and identify downstream targets to restore RGC connectivity and function in glaucoma

CONTROL ID: 3710633

SUBMITTER (NAME ONLY): Ruixue Liu

TITLE: High speed adaptive optics ophthalmoscopy for noninvasive characterization of hemodynamics in retinal vessels of various diameters in the living human eye

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop high speed and high resolution retinal imaging for precise measurement of the flow dynamics in the smallest to largest vessels in the living human retina.

Methods: An adaptive optics (AO) enhanced line scan imaging system employing a low coherent superluminescent near-infrared diode (λ=795 nm) as the imaging light source and a high speed line camera was designed to image the retina in a near-confocal mode. An anamorphic imaging mechanism was adopted to increase light collecting efficiency and ensure adequate digitization of optical resolution. To image the blood flow in vessels with a diameter < 10 μm, retinal images were acquired with a full 2D raster scanning mode of 512 lines/frame. Blood velocity was measured by the spatiotemporal traces of the red blood cells. To image blood flow in vessels with a diameter > 10 μm, the scanner was programmed to stop across the vessel in a frame thereby directly generating the spatiotemporal traces of the red blood cells within the vessel in this frame. The blood velocity profile across vessel lumen was measured by the slope of the spatiotemporal traces at different radial positions.

Results: With the full 2D raster scanning mode, the instrument produced retinal images with cellular level resolution at a frame rate of 400 frames/second (FPS) with a digitization of 512×512 pixels over a field of view of 1.2 deg ×1.2 deg. This mode allows for the red blood cells flowing the capillaries directly imaged. Blood velocity in vessels with a diameter up to 200 μm can be measured with the partial 2D mode.

Conclusions: The continuous velocity of the erythrocytes measured by high spatiotemporal resolution retinal imaging renders the fine profile of the erythrocyte movement. In-vivo study of high order hemodynamics that reflects the overall mechanical property of retinal vasculature is underway.

CONTROL ID: 3710634

SUBMITTER (NAME ONLY): Tara Nguyen

TITLE: Pattern electroretinogram and photopic negative response amplitudes are correlated in C57BL/6J mice.

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.T. Nguyen, J.C. Park, J. McAnany, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Measurements of the pattern electroretinogram (pERG) and of the photopic negative response (PhNR) have been used to evaluate inner-retinal function in humans and in animal models of disease. The purpose of this study was to determine the correlation between these two electrophysiological measures using a commercially-available electrophysiology system.

Methods: 6-month-old, wild-type C57BL/6J female mice were tested (N = 9). Stimuli were generated by a Celeris rodent ERG system (Diagnosys, LLC, MA, USA), which was also used to record the ERG signals. The PhNR was elicited by a 20-cd-s-m^{-2} white flash presented against a 40 cd/m^2 green adapting field. The flashes were presented at a rate of 2 Hz and 200 response were averaged for analysis. The PhNR was calculated as the amplitude of the trough following the b-wave divided by the b-wave amplitude (PhNR/b). The pERG was elicited by a contrast reversing bar stimulus (bar width: 0.06 cycles/degree; mean luminance: 50 cd/m^2; reversal rate: 2.1/sec); 400 sweeps were averaged for analysis. The pERG waveform was characterized by a positive peak (P) followed by a negative trough (N). pERG amplitude was defined in two ways: 1) baseline to N (“N”); 2) P-to-N.

Results: The PhNR amplitude ranged from 2.6 to 11.3 μV and the latency ranged from 91.1 to 182.5 ms. The PhNR/b amplitude ratio ranged from 0.08 to 0.20. The pERG N ranged from 0.8 to 3.7 μV, whereas the pERG P-to-N ranged from 2.0 to 8.2 μV. The coefficient of variation (standard deviation/mean) was 0.30, 0.49, and 0.44 for the PhNR/b, P-N, and N amplitudes, respectively. The PhNR/b ratio was not correlated with pERG P-to-N ($r = 0.25$, $p = 0.52$), but was correlated significantly with pERG N ($r = 0.70$, $p = 0.04$).

Conclusions: The significant correlation between the PhNR/b ratio and the pERG N component suggests that these measures may share a common retinal source. Although the variability among measures is similar, PhNR measurement may have practical advantages over pERG recordings in rodent models.

CONTROL ID: 3710635
SUBMITTER (NAME ONLY): Sofía De Arrigunaga
TITLE: Learning curve on tablet-based visual field tests during one week of daily testing
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: S. De Arrigunaga, J. Kang, Y. Zhao, S. Freeman, A.M. Roldan, T. Elze, M.M. Lin, D. Liebman, D.S. Friedman, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Chang, Genentech Inc, South San Francisco, California, UNITED STATES|D. Chang, Stanford University School of Medicine, Stanford, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Frequent home-based visual field (VF) testing using portable perimetry devices, such as the tablet-based Melbourne Rapid Fields (MRF, M&S Technologies, Niles, IL, USA), has been proposed to improve earlier detection of glaucoma progression. This pilot observational study evaluated MRF in terms of test reproducibility.

Methods: Subjects who were either glaucoma suspects or who had a glaucoma diagnosis were recruited during regular clinic visits. After a training session in the office with MRF, subjects were loaned tablets with pre-installed MRF software and instructed to take VF tests at home daily for one week as a training period, then weekly thereafter for three months. To assess a learning effect during the first week, longitudinal analysis with a fixed effects model was used to calculate the change of the group mean over time for test performance as measured by mean deviation (MD) and pattern standard deviation (PSD), and an asymptotic regression model was fit to the first five tests.

Results: Fifty-two subjects with a mean age of 62 years (range 30-79) are included in this analysis. There was a significant learning effect between the first and second test, as evidenced by a significant difference in MD (0.63 dB, CI = [0.06, 1.21], P = 0.031) and PSD (-0.58 dB, CI = [-1.05, -0.12] P = 0.013). The average MD and PSD of the second and third tests was similar to that of subsequent tests during the first week. Similarly, in an asymptotic regression model, 99.5% of the asymptote was reached for MD and PSD already after the second test, which indicates that nearly all learning had been completed prior to the second test.

Conclusions: Preliminary results show a strong learning effect from the first MRF test done independently by subjects. As we look to operationalize the use of new VF devices for at home monitoring, these data suggest that an average of the second and third MRF tests can be used as a baseline measure. Participants seem to reach a performance “steady state” starting with their second test.

CONTROL ID: 3710639

SUBMITTER (NAME ONLY): Sasan Moghimi

TITLE: Prediction of Glaucoma Development from Glaucoma Suspect with OCT Structural Measurements using Artificial Intelligence

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Moghimi, V. Mohammadzadeh, T. Nishida, E. Walker, G. Mamoudinezhad, J. Wu, L.M. Zangwill, R.N. Weinreb, Viterbi Family Department of Ophthalmology, Hamilton Glaucoma Center, Shiley Eye Institute, La Jolla, California, UNITED STATES|J.M. Liebmann, Department of Ophthalmology, Edward S. Harkness Eye Institute, Columbia University Medical Center, 2Bernard and Shirlee Brown Glaucoma Research Laboratory, New York, New York, UNITED STATES|C.A. Girkin, Bernard School of Medicine, University of Alabama-Birmingham, Birmingham, Alabama, UNITED STATES|T. Javidi, University of California San Diego Jacobs School of Engineering, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the ability of macular and circumpapillary retinal nerve fiber (cpRNFL) change rates and clinical/demographic factors to predict development of glaucoma from glaucoma suspects (GS) through elastic net regression (ENR) and machine learning (ML) models.

Methods: 162 eyes of 146 patients with GS were included. The eyes were required to have characteristic glaucomatous optic nerve changes without visual field (VF) defects. Development of glaucoma was defined as having VF glaucoma hemifield test outside normal limit and pattern standard deviation 5% in 3 consecutive exams. Global and sectoral rates of change of macular ganglion cell/inner plexiform layer (GCIPL) and cpRNFL OCT were calculated with linear mixed-effect models. The ENR and ML models, gradient boost model (GBM), support vector machine (SVM) and Naïve Bayes (NB) were fit for structural rates of change and clinical/demographic parameters in order to predict the development of glaucoma in GS. Parameter tuning with Grid Search Method and 5-fold cross validation were applied for each ML model.

Results: 47 eyes developed glaucoma based on the study criteria. The average follow-up time was 2.3 and 2.1 years for glaucoma and GS eyes, respectively. The rates of average GCIPL were significantly faster in the eyes that converted to glaucoma (= –0.10, P<0.001) and the average cpRNFL rates was not significant (= –0.15, P=0.152). Predictive factors that were selected by ENR were average, minimum, superior and temporal superior GCIPL change rates and average intraocular pressure (IOP) during follow-up (AUC (95% confidence interval (CI)=0.71 (0.62, 0.80)). Parameters with highest relative importance from GBM were average GCIPL rates, average IOP during follow-up, age, axial length temporal superior and temporal inferior GCIPL and temporal cpRNFL change rates (Figure 1). The AUC (95% CI) for prediction of glaucoma development was 0.91 (0.86, 0.97), 0.87 (0.81, 0.92) and 0.82 (0.75, 0.89) for GBM, SVM and NB, respectively (Figure 2).

Conclusions: Development of glaucoma in glaucoma suspect eyes can be predicted from longitudinal macular and cpRNFL OCT data and average IOP during follow-up with clinically relevant accuracy. The proposed models may assist clinicians to predict better the development of glaucoma.

CONTROL ID: 3710640

SUBMITTER (NAME ONLY): Aytan Musayeva

TITLE: The inflamed corneal bed microenvironment abrogates the graft-protective function of regulatory T cells

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Musayeva, T. Blanco, H. Nakagawa, S. Wang, H. Alemi, G. Ortiz, S. Lee, T.H. Dohlman, Y. Chen, S. Chauhan, J. Yin, R. Dana, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously shown a correlation between Treg dysfunction and enhanced APC maturation in the graft site of recipients at high-risk (HR) of rejection, at early stages after corneal transplantation. Herein, we investigated graft site environment-induced function changes of Treg in HR recipients.

Methods: High risk (HR) and low risk (LR) allogeneic corneal transplantations were performed using C57BL/6 mice as donors and BALB/c as hosts. On days 3 and 7, post-transplantation $CD4^{+}CD25^{+}FoxP3^{+}$ Tregs and prototypical phenotypic maturation markers on $CD11b^{+}MHC\text{-}II^{high}$ APCs were assessed. Bone marrow GM-CSF-generated $CD11b^{+}$ APCs were preconditioned with Tregs FACS-sorted from the graft-site of HR or LR in the presence of LPS (100ng/ml) and IL-2 (10ng/ml) and sonicated allogenic splenocytes (1:20:21) for 48 hours. Then, Tregs were removed, and $CD4^{+}CD25^{-}$ naïve T cells were added for 5 days. Next, MACS-sorted naïve Tregs from naïve mice were cultured with IL-6, with or without anti-IL-6R antibody for 12 hours, and co-cultured as above. Tregs from LR recipients were injected in newly HR host, and vice versa. Readouts included flow cytometry, ELISA, RT-PCR, and clinical follow-up.

Results: Treg frequencies and their expression levels of FoxP3 were significantly lower in HR compared to LR ($p<0.01$). The frequency of $FoxP3^{+}$ Treg expressing alpha E integrin (CD103) was significantly lower in HR vs. LR ($p<0.001$) as well as the expression of IL-6R ($p<0.001$). Frequencies of $MHC\text{-}II^{high}$, CD80, CD86, and CCR7 in $CD11b^{+}$APC, as well as IFN-g production by CD4+ T cells, $^{+}$ T cells were found significantly higher when APCs were preconditioned with Treg from HR recipients vs. LR ($p<0.001$). This was recapitulated when APCs were preconditioned with naïve Treg pretreated with IL-6. Finally, adoptive transfer of Treg from LR to HR recipient mice suppressed the expression of maturation markers in the grafted cornea ($p<0.001$) and led to 55% allograft survival ($p<0.0001$); while adoptive transfer of HR Treg to LR host increased the expression of those markers ($p<0.001$) and led to 100% allograft survival ($p<0.0001$).

Conclusions: These results demonstrate that the transplant environment alters the regulatory function of the graft site’s early infiltrated Treg, and suggest that highly functional Treg could be a potential therapeutic approach to improve survival in HR corneal transplants.

CONTROL ID: 3710641

SUBMITTER (NAME ONLY): Juliette Wohlschlegel

TITLE: Stimulation of neurogenic regeneration from human Müller glia

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wohlschlegel, A. Haugan, C. Finkbeiner, D. Hoffer, T. Reh, Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: In mammals, loss of retinal cells due to disease or trauma is an irreversible process which leads to blindness. Interestingly, regeneration of retinal neurons is a well-established process in some non-mammalian vertebrates and is driven by the Muller glia (MG) which are able to re-enter the cell cycle and reprogram into neurogenic progenitors upon retinal injury or disease. Progress has been made to “translate” this mechanism to mammals to promote retinal regeneration. A breakthrough in the field was the demonstration that MG can generate new neurons in vivo in the adult mouse retina after the overexpression of the pro-neuronal transcription factor Ascl1. In this study, we show that the same strategy could be applied to regenerate retinal neurogenic progenitors using human MG in vitro.

Methods: In human fetal development, MG appear following a temporal central to periphery gradient in the retina and, can first be identified at Day 73 in the center and later (D100) in the periphery. We have developed protocols for obtaining in vitro 2D cultures of MG dissociated from stem cell-derived organoids over 150 days of age. MG cultures were characterized with immunostaining and single cell RNA sequencing (scRNA-seq). We used lentivirus mediated gene delivery for over-expression of ASCL1 (CMV-ASCL1-GFP). The addition of EdU to the culture combined with GFP allowed us to track newly generated cells to control for any surviving neurons from the initial dissociation of the organoids. To determine whether ASCL1 induces neurogenesis in human MG, we used scRNA-seq analysis and Immunolabeling (IHC) for neuro-specific antibodies and EdU.

Results: IHC analysis showed that MG are present in retinal organoids around Day 180. MG derived from organoids can be grown and passaged in 2D cultures, are of good purity and contain only few surviving neurons. MG can also be frozen for cell banking. When infected with a lentivirus driving ASCL1-GFP, the human MG can be reprogrammed to a neurogenic state as assessed with IHC, and by using scRNA-seq. Our study demonstrates for the first time that Ascl1 can reprogram human MG into neurogenic progenitor cells in vitro.

Conclusions: Our work demonstrates the first evidence of regenerative capacity of MG in human.

CONTROL ID: 3710642

SUBMITTER (NAME ONLY): Sriganesh Ramachandra Rao

TITLE: Generation of novel, tractable conditional knockout models of RP59

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dehydrodolichyl diphosphate synthase (DHDDS) catalyzes the committed step for dolichol synthesis, required for protein N-glycosylation. Its mutations underlie RP59 (OMIM# 613861). Here, we describe development of novel RP59 mouse models, using Bestrophin1 (BEST1)- and cone-rod homeobox (CRX) Cre-driven Dhdds ablation.

Methods: Dhdds$^{flx/flx}$ mice were bred against BEST1-Cre or CRX-Cre mice and against ZsGreen reporter mice to achieve Dhdds ablation in RPE/Müller glia cells or photoreceptor (PR)/bipolar (BP) cell progenitors, respectively. Controls: wildtype (WT) C57BL/6J mice, and CRX-Cre and BEST1-Cre mice bred against ZsGreen reporter mice. Western blot (WB) ±PNGase-F was performed on retinas from PN 4-wk old Dhdds KO vs. WT mice, probing with anti-RHO (1D4). Ectopic Cre expression was monitored using a blue light box. Immunohistochemistry (IHC) against RHO, GFAP, and GLUL, and ERG analysis was performed on all mouse lines (N=3/group). Statistical analysis: Student's t-test, $P<0.05$ (significance threshold).

Results: CRX-Cre mice expressed Cre in PR and BP cells. BEST1-Cre-ZsGreen mice showed Cre activity in RPE/Müller cells, with "leaky" expression in BP cells. Whole body green fluorescence revealed ectopic expression. Dhdds ablation using the ectopic BEST1-Cre line led to panretinal degeneration. ERG outcomes were a function of Cre expression in individual lines. BEST1-Cre Dhdds$^{flx/flx}$ mice exhibited significantly decreased ERG responses, vs. controls.. Remnant retinal cells in leaky Best1-Cre Dhdds$^{flx/flx}$ mice were mostly ZsGreen-negative. Dhdds deletion in PR/BP progenitor cells caused early-onset retinal degeneration with null ERG responses at PN 4-wk. IHC and TUNEL analysis of PN 4-wk KO retinas revealed >90% loss of PR and BP cells. However, WB (RHO+) results were comparable for mutant vs. WT retinas, indicating no protein N-glycosylation defect.

Conclusions: Use of a ZsGreen reporter background afforded confirmation of targeted vs. ectopic Dhdds, highlighting the importance of including a fluorescent reporter background in studies involving Cre-LoxP system-dependent, spatially restricted ablation of target genes. Retinal degeneration, rather than dysplasia, was observed, despite initiation of early-onset Dhdds ablation. These findings suggest that PR and BP cells are highly sensitive to loss of CPT activity.

CONTROL ID: 3710643

SUBMITTER (NAME ONLY): Markus Kuehn

TITLE: T-cell profiling of glaucoma patients

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Kuehn, R.H. Kardon, O.W. Gramlich, VA Center for the Prevention and Treatment of Visual Loss, Iowa City, Iowa, UNITED STATES|M.H. Kuehn, H. Zeng, W. Alward, Y.H. Kwon, J.H. Fingert, N. Sears, R.H. Kardon, O.W. Gramlich, Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accumulating evidence suggests an involvement of adaptive immune responses in the pathophysiology of glaucoma. The purpose of this study was to determine if differences in the T-cell populations exist between patients with primary open angle glaucoma (POAG) and age-matched controls.

Methods: Peripheral blood mononuclear cells (PBMC) were obtained from POAG patients (n=60) and age matched controls (n=40). T-cells were then profiled by fluorescence assisted cell sorting (FACS) using a panel of 29 cell surface markers. In a second experiment, PBMC were stimulated with phorbol myristate acetate (PMA) and ionomycin and analyzed using a panel of 18 cytokine markers. Data were collected on a Cytek® Aurora equipped with five lasers and 64 detectors and analyzed with SpectroFlo and FlowJo software. Data are given as frequencies of total cell number in each sample.

Results: Few differences between POAG and control samples were detected among unstimulated T cell populations. However, there is a significant increase of naïve CD4 T cells in POAG patients (POAG: 4114%; controls: 3415%; P=0.036). However, upon ex vivo stimulation several significant differences in CD4 cell populations are apparent. These include increased frequencies in POAG samples of CD4 T cells expressing CD154 (POAG: 6511%; controls: 537%; P=0.017), naïve CD4 T cells numbers expressing IFN (POAG:10.5%; controls: 0.40.1%; P=0.001), and TNF (POAG: 136%; controls: 73%; P=0.003). Likewise, there was a significant increase in IL-17A expressing central memory cells (POAG: 0.6 controls 0.4 P=0.049). In contrast, a significant decrease in IL-21 (POAG:2 ctrls:5P=0.0002) and IL-17 (POAG: 0.2 controls: 0.4P=0.011) effector memory cells was detected in the POAG cohort. No differences in the CD8 T cells population between POAG and control samples were observed.

Conclusions: Our data suggest that trafficking of central memory cells and/or effector CD4 memory cells is altered in POAG patients. Additionally, the T cell activation threshold is reduced in POAG patients. These findings indicate that T cells in POAG patients are more likely to actively contribute to pro-inflammatory signaling than those of controls.

CONTROL ID: 3710653
SUBMITTER (NAME ONLY): Jan Tode
TITLE: A New Model for Glaucoma Filtering Surgery in Mice
SESSION TITLE: Surgery and Wound Healing
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: J. Tode, M. Binter, E. Molinski, S. Hempel, C. Framme, H. Fuchs, P. Luedtke, Ophthalmology, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|M. Heider, Animal Research, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|
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ABSTRACT BODY:

Purpose: Fibrosis is a glaucoma filtration surgery (GFS) problem that often demands reoperation. At present, different antifibrotic drugs are used to inhibit fibrosis with unsatisfactory results. Only a few GFS mouse models for drug research exist. These are difficult to perform and complicated by the big murine lens, which can easily be damaged while penetrating the anterior chamber. We designed the first GFS mouse model without anterior chamber penetration, leaving the lens safely untouched.

Methods: Baseline intraocular pressure (IOP) was measured under inhalation anesthesia. Then, surgery was performed in six C57BL/6J mice under general anesthesia. A 27G needle was inserted into the conjunctiva and slid forward subconjunctivally close to the limbus. The sclera was penetrated, and a fistula was created between the posterior chamber and subconjunctival space. Afterwards, clinical examination and IOP-measurement under inhalation anesthesia followed every two days for two weeks.

Results: Postoperatively, a filtering bleb was seen in every mouse (n=6). Mean IOP decreased from 14.2 mmHg (±3.0 SD) at baseline to 8.33 mmHg (±0.9) on day two after surgery. The conjunctiva was elevated until day two in every mouse. Between days four and eight, pigment and stronger conjunctival injection were seen at the fistula, as well as a significant IOP rise. From day eight onwards, IOP stayed at baseline values; the GFS bleb was flat again.
Mean IOP values (±SD) during follow-ups were: 11.5 mmHg (± 3.7) at day 4, 13.0 mmHg (±2.7) at day 6, 9.6 mmHg (±2.0) at day 8, 13.2 mmHg (±1.2) at day 10, 14.4 mmHg (±0.2) at day 12, and 15.2 mmHg (±2.8) at day 14. No infectious complications were seen.

Conclusions: We developed a new, inexpensive, easy to perform, reproducible GFS mouse model, which can be used for fibrosis research or antifibrotic drug screening in vivo. It works without penetration of the anterior chamber, leaving the large murine lens untouched and thereby minimizing complications.

CONTROL ID: 3710654
SUBMITTER (NAME ONLY): Kaitlyn Rutter
TITLE: Photoreceptor mitochondria can be transferred and turned over by Müller glia
SESSION TITLE: Photoreceptors and disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K.M. Rutter, R.A. Hutto, S.E. Brockerhoff, Biochemistry, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|S.E. Brockerhoff, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|
Commercial Relationships Disclosure: Kaitlyn Rutter: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Hutto: Commercial Relationship: Code N (No Commercial Relationship) | Susan Brockerhoff: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To maintain vision throughout a lifetime, photoreceptors must remain viable despite chronic stress, including oxidative stress. Photoreceptors may have specialized stress adaptations, such as maintaining healthy pools of mitochondria, to remain robust and functional. We exposed zebrafish to systemic or cone-specific stressors and evaluated the impact on cone mitochondria.
Methods: We generated transgenic zebrafish with fluorophores targeted to cone mitochondria (Tg(gnat2:Su9-mKate2); Tg(gnat2:Su9-TagBFP)). Zebrafish larvae were exposed to cold stress (16°C), cone-specific oxidative stress (using the transgenic line Tg(gnat2:Su9-KillerRed)), or 1.2 mM chloramphenicol starting at 3 or 4dpf. At 6dpf, larvae were imaged live using confocal microscopy.

To assess cone mitochondria localization, we used a triple transgenic fish expressing a cone mitochondrial marker, a Müller glia marker (Tg(GFAP:TdTomato)) and a cone cytosol marker (Tg(gnat2:EGFP)).

To assess mitophagy, we used larvae co-expressing the BFP mitochondria marker and an autophagosome marker fluorescently tagged under the Müller glia promotor (Tg(GFAP:EGFP-mCherry-LC3)). Results reported as mean ± SEM.
Results: Cone mitochondria were rarely seen outside the ellipsoid region, but this was increased post all stressors. 23.6% ± 1.6% (n = 44 zebrafish) of mislocalized cone mitochondria co-localized with Müller glia after cold stress. This occurred to a lesser extent in unstressed conditions (14.0% ± 3.7%; n = 38 zebrafish). Of the mislocalized mitochondria in Müller glia, 4.5% ± 3.0% co-localized with unacidified LC3, 33.2% ± 5.7% co-localized with acidified LC3, and 48.4% ± 9.0% were proximal to LC3 post cold stress (n = 10 zebrafish).
Conclusions: Photoreceptor mitochondria adapt to chronic stress by migrating away from the dense mitochondrial cluster in the ellipsoid region. These mitochondria can leave the cell and be taken up by Müller glia cells. Some cone mitochondria are likely undergoing mitophagy since they are associated with autophagosomes in Müller glia.

CONTROL ID: 3710656

SUBMITTER (NAME ONLY): Kristin Hösel

TITLE: Clinical and functional effect of intravitreal injection of anti-IL-6 antibody on experimental autoimmune uveitis (EAU) in mice

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hösel, B. Chasan, C. Ehlken, J. Roider, Ophthalmology, Universitatsklinikum Schleswig-Holstein, Kiel, Schleswig-Holstein, GERMANY|S. Rose-John, Biochemie, Christian-Albrechts-Universitat zu Kiel, Kiel, Schleswig-Holstein, GERMANY|J. Tode, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|

Commercial Relationships Disclosure: Kristin Hösel: Commercial Relationship: Code N (No Commercial Relationship) | Büsra Chasan: Commercial Relationship: Code N (No Commercial Relationship) | Christoph Ehlken: Commercial Relationship: Code N (No Commercial Relationship) | Jan Tode: Commercial Relationship: Code N (No Commercial Relationship) | Stefan Rose-John: Commercial Relationship: Code N (No Commercial Relationship) | Johann Roider: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the functional and clinical effect of intravitreally injected anti-IL-6 antibody for the treatment of experimental autoimmune uveitis (EAU) in mice.

Methods: EAU was induced in 17 female B10.RIII mice by Inter-Photoreceptor-Binding-Protein (IRBP) in complete Freund's adjuvant, boosted by Pertussis toxin. Anti-IL-6 antibody was intravitreally injected on day 10, 13 and 16 after EAU induction (day 0) into the randomized treatment eye and isotype antibody likewise into the fellow control eye. Visual acuity testing via Optodrum and clinical scoring via fundus imaging (6 EAU grades) was done single-blinded on day 0, 10, 13, 16 and 18.

Results: Uveitis developed in all 17 mice. Visual acuity was significantly higher in treated eyes compared to the fellow control eyes on day 13, 16 and 18. The greatest effect was seen on day 16 and 18 ($p < 0.001$, t-test). Clinical uveitis score was significantly reduced in treated eyes compared to the fellow control eyes on day 13, 16 and 18 with greatest effect on day 18 ($p = 0.003$, Wilcoxon-test).

Conclusions: Intravitreal anti-IL-6 treatment significantly attenuates experimental autoimmune uveitis in mice. The effect was seen clinically and functionally. Further studies are needed to evaluate intravitreal anti-IL-6 application as a therapy concept for the treatment of non-infectious uveitis in humans.

CONTROL ID: 3710659

SUBMITTER (NAME ONLY): Ana De-La-Mata

TITLE: Bone marrow- and adipose tissue-derived mesenchymal stem cells partially restore corneal and limbal epithelial phenotype in a rabbit model of limbal stem cell deficiency

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. De-La-Mata, S. Galindo, M. Lopez-Paniagua, J. Herreras Cantalapiedra, C. García-Vazquez, B. Marceñido, M. Calonge, T. Nieto-Miguel, IOBA -Institute of Applied Ophthalmobiology, Universidad de Valladolid, Valladolid, Castilla y León, SPAIN|A. De-La-Mata, S. Galindo, M. Lopez-Paniagua, M. Calonge, T. Nieto-Miguel, CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine), Instituto de Salud Carlos III, Valladolid, SPAIN|C. García-Vazquez, Regional Center for Regenerative Medicine and Cell Therapy, SPAIN|J. Herreras Cantalapiedra, Department of Ophthalmology, Clinic University Hospital, Valladolid, SPAIN|

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ABSTRACT BODY:

Purpose: Limbal stem cell deficiency (LSCD) occurs as a result of limbal stem cell damage and/or sclerocorneal limbal niche destruction. Our research group has recently demonstrated that transplantation of both bone marrow- and adipose tissue-derived mesenchymal stem cells (BM-MSCs and AT-MSCs) in a LSCD rabbit model reduces the development of corneal opacity, and partially restores the tissue structure of the damaged ocular surface. The aim of this work was to study the effect of BM-MSC and AT-MSC transplantation on the corneal and limbal epithelial phenotype of a rabbit model of ocular surface failure due to LSCD.

Methods: A total LSCD model was developed in 15 New Zealand white rabbits through 360 surgical limbal peritomy after N-heptanol-based denudation of the corneal surface. Three weeks after the injury, 10 rabbits were transplanted with 250,000 human MSCs on amniotic membrane (5 with BM-MSCs; 5 with AT-MSCs) and 5 non-transplanted animals formed the untreated group. At the end of the follow-up (11 weeks), immunofluorescence studies in ocular surface tissue sections were done to analyze the expression of corneal (CK3, E-cadherin) and limbal (CK15, p63) epithelial cell specific markers. Fluorescence intensity was measured using ImageJ software in 2 tissue sections per rabbit.

Results: E-cadherin expression was similar in untreated LSCD eyes and healthy control eyes, but it significantly increased in LSCD eyes after BM-MSC transplantation. The expression of CK3, CK15 and p63 was significantly reduced in untreated LSCD eyes compared to healthy control eyes, but transplantation of both BM-MSCs and AT-MSCs in LSCD eyes induced a partial (CK15) or an almost full (CK3 and p63) recovery of their expression levels. Nevertheless, the expression levels achieved were in general higher in the eyes treated with BM-MSCs than in those treated with AT-MSCs.

Conclusions: Although the effect of BM-MSC transplantation seems slightly superior, transplantation of both BM-MSCs and AT-MSCs in a LSCD rabbit model partially restores corneal and limbal epithelial phenotype. Therefore, both types of MSCs seem valid alternatives for the treatment of LSCD.

CONTROL ID: 3710661

SUBMITTER (NAME ONLY): Hanna De Bruyn

TITLE: Full-Field Rod-Mediated Electroretinographic (ERG) Responses in Stargardt Disease

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. De Bruyn, J. Akula, K. Malendowicz, A.B. Fulton, Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|J. Akula, A.B. Fulton, Department of Ophthalmology, Harvard University, Cambridge, Massachusetts, UNITED STATES|I. Mihalek, Department of Molecular Medicine and Biotechnology, Sveuciliste u Rijeci, Rijeka, CROATIA|

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ABSTRACT BODY:

Purpose: To assess rod-mediated ERG responses to full-field stimuli in pediatric patients with biallelic variants in ABCA4. Typically, the conspicuous clinical feature in ABCA4 retinal disease is maculopathy.

Methods: Of our 44 patients with biallelic variants in ABCA4, 40 had at least one ERG test. The age at ERG test was 1.26–22.12 (median: 11.09) years, except for one patient who was tested at age 58 years. The variants in ABCA4 ranged from double nulls (producing no protein) to less severe. We calculated the amplitude and sensitivity of the rod photoresponse (R_{rod} and S_{rod}) from the a-wave and the postreceptor activity (V_{max}, $1/\sigma$) from the b-wave.

Results: Among those with double null variants, nearly all (92.5%) had R_{rod} values below the 95% prediction limit for normal (PLN), and 67.5% had S_{rod} values below the PLN. By contrast, among those with mild mutations, the rod photoresponse deficits were uncommon. As for the postreceptor response parameters, even in the case of the double nulls, deficits in V_{max} were less frequent. All values of the postreceptor response parameters (V_{max}, $1/\sigma$) were normal in those with mild variants in ABCA4.

Conclusions: Significant deficits in rod-mediated ERG responses to full-field stimuli are common, even though the obvious clinical feature is maculopathy. The frequent deficits in rod photoreceptor activity are likely indicators of the pathobiology of ABCA4 retinal disease. ABCA4 is expressed in both rods and cones.

CONTROL ID: 3710664

SUBMITTER (NAME ONLY): William Waldock

TITLE: Risk of ischaemic stroke following diagnosis of proliferative diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Waldock, Imperial College London, London, London, UNITED KINGDOM|S. Wagner, N. PONTIKOS, A. Petzold, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A.K. Denniston, University Hospitals Birmingham NHS Foundation Trust, Birmingham, Birmingham, UNITED KINGDOM|M. Cortina-Borja, J. Rahi, University College London Institute of Child Health, London, London, UNITED KINGDOM|A.K. Denniston, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|J. Rahi, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|P.A. Keane, NIHR Biomedical Research Centre at University College London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To characterize the incidence rate of iscahemic stroke in patients following a new diagnosis of proliferative diabetic retinopathy (PDR) at a regional ophthalmic institution in London, United Kingdom.

Methods: Methods: A historical cohort study of all patients >= 40 years of age and newly diagnosed with proliferative diabetic retinopathy between January 1st 2008 and March 31st 2018 linked with national data on hospital admissions using the Hospital Episode Statistics database. Ischaemic stroke was defined as code I63/I64 using the International Classification of Diseases 10th Revision. Incidence rates with 95% confidence intervals were calculated using the Poisson distribution and adjusted hazard ratios (HR) modelling incidence of stroke against fixed covariates of age, sex, ethnicity and socioeconomic deprivation was through Cox proportional hazard modelling and Fine-Gray competing risks regression.

Results: Results: A total of 2537 patients (1544 male, 61.9%) with a mean age of 60.5 +/- 10.6 were newly diagnosed with PDR during the eligible period. Among the cohort, 72 had an incident iscahemic stroke with a crude rate of 1123.3 (883.4-1403.1) per 100,000 person-years at risk. Men (59.6 +/- 10.6 years) were younger at diagnosis than women (62.0 +/- 10.5, p <0.001); those with greater socioeconomic deprivation were also diagnosed at a younger age (most deprived decile 58.8 +/- 10.6 versus least deprived decile 62.2 +/- 11.8, p<0.001). On adjusted analysis, age alone was associated with greater hazards of incident stroke (HR 1.05, 1.03-1.08).

Conclusions: Discussion: Greater socioeconomic deprivation and male sex are associated with a younger age of PDR diagnosis. Following diagnosis, incidence of iscahemic stroke is higher with greater age but does not appear to be associated with ethnicity, sex or socioeconomic deprivation.

CONTROL ID: 3710665

SUBMITTER (NAME ONLY): Jose Javier Garcia-Medina

TITLE: Pointwise correlations between different intraretinal layer thicknesses and retinal sensitivity as assessed by OCT and microperimetry in healthy and glaucomatous eyes

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Garcia-Medina, Hospital General Universitario Jose M Morales Meseguer, Murcia, Murcia, SPAIN|L. Lopez-Canovas, Hospital General Universitario Reina Sofia, Murcia, Murcia, SPAIN|V. Zanon-Moreno, European University of Valencia, Valencia, Valencia, SPAIN|M.D. Pinazo-Duran, Universitat de Valencia, Valencia, Comunitat Valenciana, SPAIN|M. Del-Rio-Vellosillo, Hospital Clinico Universitario Virgen de la Arrixaca, El Palmar, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To assess the pointwise relationship between macular function and structure in healthy and glaucomatous eyes for inner and outer segmentations assessed by OCT.

Methods: 72 eyes were included and divided into two groups: control group made up of 27 eyes and a primary open-angle glaucoma (POAG) group of 45 eyes. All eyes underwent retinal sensitivity assessment with microperimetry MP-1 and the structure was studied with OCT (Spectralis). The following automatic segmentations were considered: outer retinal layer, ganglion cell layer (GCL), inner plexiform layer (IPL), GCL+IPL and ganglion cell complex (mRNGL+GCL+IPL). Microperimetry maps were exactly superimposed over OCT maps considering anatomical references by using Overlay2 software. Punctual thicknesses for each considered segmentation were obtained in correspondence with every point of assessed macular sensitivity. The displacement of the ganglion cells of the retina were considered for inner retinal segmentations. Structure-function associations were calculated by using Spearman correlation. Significant correlation maps were plotted.

Results: Healthy group did not show significant correlations in any of the considered segmentations. In contrast, we found positive significant correlations for inner retinal layers but not for outer retinal layer. This significant correlations followed different patterns: peripheral for mRNFL, paracentral in temporal area for GCL, IPL and GCL+IPL and combined for mRNGL+GCL+IPL. The highest number of significant correlations were obtained for mRNGL+GCL+IPL.

Conclusions: There are specific patterns of significant pointwise structure-function correlation in macula for inner retinal layers in POAG.

CONTROL ID: 3710671

SUBMITTER (NAME ONLY): Mala Upadhyay

TITLE: Oxidative stress-induced RPE and retinal cell death involves multiple regulated cell death pathways.

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Upadhyay, C. Milliner, V.L. Bonilha, Ophthalmic Research, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Mala Upadhyay: Commercial Relationship: Code N (No Commercial Relationship) | Caroline Milliner: Commercial Relationship: Code N (No Commercial Relationship) | Vera Bonilha: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To dissect oxidative stress-related cell death pathways in RPE and retina using the $NaIO_3$ mouse degeneration model.

Methods: Three-month-old C57BL/6J mice received a single tail vein injection of 10 mg/Kg $NaIO_3$; the DJ-1 KO mice were also analyzed as a model of increased sensitivity to oxidative stress. This concentration of $NaIO_3$ induces degeneration only in the DJ-1 KO mice. Parallel groups of mice were injected with PBS. Retina and RPE were isolated, lysed, and analyzed by LC-MS/MS. Panther analysis tool and Ingenuity Pathway Analysis were used to analyze the proteomics data. Main observations were further assayed by Western blotting, immunohistochemistry, confocal microscopy, and histology in mice injected with increasing concentrations of $NaIO_3$ (10-30 mg/Kg).

Results: Proteomics data analyses suggested cell death and survival as one of the top modulated molecular and cellular functions in RPE and retina of C57BL/6J and DJ-1 KO mice injected with 10 mg/Kg $NaIO_3$ compared to PBS injected equivalent. Apoptosis and necroptosis pathways were analyzed using active caspase-3 (acas3) and p-MLKL immunostaining. In PBS-injected mice, we observed increased acas3 reactivity in the DJ-1 KO mice compared to C57BL/6J mice; p-MLKL was observed in both mice strains in the photoreceptor inner segments and GCL. With 10 mg/Kg $NaIO_3$, acas3 was observed only in the photoreceptor inner segment of C57BL/6J retinas, whereas it was observed in RPE and photoreceptors with 20 mg/Kg $NaIO_3$. In DJ-1 KO mice, acas3 was expressed in RPE and photoreceptor degenerating cells and OPL and INL at both concentrations of $NaIO_3$. In C57BL/6J retinas, p-MLKL staining was observed only in GCL with 10 mg/Kg $NaIO_3$, whereas its expression was observed in RPE, ONL, and GCL with 20 mg/Kg $NaIO_3$. In DJ-1 KO mice, p-MLKL was localized in ONL and GCL with 10 and 20mg/Kg $NaIO_3$. Injection of the pan-caspase inhibitor, Z-VAD-Fmk, after 10 mg/Kg $NaIO_3$ injection in DJ-1 KO mice completely inhibited RPE degeneration in DJ-1 KO, thereby, confirming the role of caspase-mediated apoptosis of RPE in the initiation of the degeneration in this mouse model.

Conclusions: Oxidative stress-induced RPE and retinal cell death involve activation of both apoptosis and necroptosis.

CONTROL ID: 3710672

SUBMITTER (NAME ONLY): Edward Ryan Collantes

TITLE: SGMS2 mutation in a large Filipino family with calvarial doughnut lesions with bone fragility and juvenile-onset open angle glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Collantes, J.L. Wiggs, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Flores-Anotado, A. Dumdum, J. Futolan, M. de Guzman, B. Hidalgo, V. Guzman, K. Rivera-Francia, Western Visayas Medical Center, PHILIPPINES|M. Guevarra, University of the East Ramon Magsaysay Memorial Medical Center Inc, Quezon City, PHILIPPINES|

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ABSTRACT BODY:

Purpose: SGMS2 (sphingomyelin synthase 2 (SMS2)) pathogenic variants cause a rare autosomal dominant skeletal disorder with characteristic skull lesions known as Calvarial Doughnut Lesions with Bone Fragility (CDL) (MIM 12655). A recurrent nonsense mutation (c.148 C>T,p.Arg50*) has been found in 4 of 6 reported families and interestingly, affected members of one of these families also exhibit congenital glaucoma with variable expressivity. In this study we report on a large Filipino family with characteristic skull lesions and juvenile onset open angle glaucoma (JOAG).

Methods: Eighteen members of a 4-generation family were recruited. All subjects underwent a comprehensive eye exam and skull radiography, and DNA samples were obtained. Whole exome sequencing (WES) was performed in 5 family members with JOAG. An in-house WES pipeline was used to align sequence reads and complete variant calling and annotation. After confirming the absence of mutations in genes known to cause early-onset glaucoma WES data was filtered to retain rare variants (minor allele frequency <1%) that were protein altering and predicted to be pathogenic. Sanger sequencing was done to confirm segregation of candidate variants.

Results: Six family members were diagnosed with JOAG and presented with a mean age at diagnosis of 25.5 years, 83% blind in at least one eye, mean intraocular pressure of 29.4 mmHg, and glaucomatous optic nerves. No mutations were found in known disease-causing genes and after variant filtering, a known recurrent heterozygous stop gain mutation, SGMS2 c.148C>T(p.Arg50*), was identified in all subjects with JOAG. Ten family members had abnormal skull radiographs, including all 6 JOAG subjects. The SGMS2 p.Arg50* variant was present in all family members with skull abnormalities.

Conclusions: Here we report on the first Filipino family with CDL and confirm segregation of a recurrent SGMS2 variant found in other families with European Caucasian ancestry. Our study also identifies a second CDL family with early-onset glaucoma raising the possibility that SGMS2 genetic variation can contribute to glaucoma pathogenesis. SGMS2 impacts metabolism of ceramide, sphingomyelin and diacyglycerol, all of which could contribute to trabecular meshwork dysfunction and/or retinal ganglion cell degeneration in glaucoma. Further work is needed to confirm a role for SGMS2 in glaucoma development.

CONTROL ID: 3710675

SUBMITTER (NAME ONLY): Santoshi Ramachandran

TITLE: Visual, build-up and motor activity of superior colliculus neurons is correlated with visual suppression and fixation preference in strabismic non-human primates (NHP)

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ramachandran, V.E. Das, Physiological Optics/Vision Science, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Santoshi Ramachandran: Commercial Relationship: Code N (No Commercial Relationship) | Vallabh Das: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Strabismic humans and NHPs often develop the ability to saccade to a target with either eye depending on the targets' spatial location. Fixation preference in strabismus could possibly be accounted for in a competitive decision framework wherein the brain chooses between two retinal errors (since eyes are pointing in different directions) to prepare a saccade. We tested this framework by recording from visuo-motor neurons in the superior colliculus (SC) of strabismic NHPs, a structure critical in target selection and saccade generation.

Methods: Neural recordings from the intermediate/deep SC were obtained while two head-fixed strabismic (~30° XT) NHPs performed a delayed saccade task under binocular viewing conditions. In Exp. 1 (2-target condition), visual targets were presented at two locations corresponding to the neuronal receptive field of either the viewing or deviated eye, and resulted in fixation-switch or no fixation-switch saccades whose amplitude and direction were matched. In Exp 2. (1-target condition), a visual target was placed at a location (single neuronal receptive field) where the animal switched fixation on some trials and did not on other trials. Paired t-tests were performed to compare firing rates of visual, buildup and saccade related response in fixation-switch and no fixation-switch trials.

Results: Exp. 1 (n=25): Robust visual sensory responses were observed when targets were presented at receptive field locations of either the viewing or deviated eye with evidence of only small interocular suppression in both NHPs. Motor responses for fixation-switch and no-fixation switch trials were not significantly different (saccade matched). Mean build-up responses showed no difference in these trials since the cell response corresponds to the 'winning' saccade. Exp. 2 (n=21): Both peak visual and mean build-up responses were reduced for trials in which the cell response did not correspond to the 'winning' eye, suggesting the presence of suppression and that the build-up activity may be used to facilitate eye choice. Data analysis from second NHP is ongoing.

Conclusions: Analysis of neural data from SC visuo-motor cells suggests that this structure plays an important role in eye choice for visual stimuli in strabismus and provides important insight on how visual suppression influences eye choice behavior.

CONTROL ID: 3710676

SUBMITTER (NAME ONLY): Paul Kayne

TITLE: Efficacy and impact of the melanocortin receptor agonists PL8177 and PL9654 in an STZ-rat model of diabetic retinopathy (DR)

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Kayne, P. Dhingra, A. Obr, J. Dodd, C. Spana, Palatin Technologies. Inc., Cranbury, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Paul Kayne: Commercial Relationship(s);Code E (Employment):Palatin Technologies, Inc | Priyanka Dhingra: Commercial Relationship(s);Code E (Employment):Palatin Technologies, Inc. | Alison Obr: Commercial Relationship(s);Code F (Financial Support):Palatin Technologies, Inc. | John Dodd: Commercial Relationship(s);Code E (Employment):Palatin Technologies, Inc. | Carl Spana: Commercial Relationship(s);Code E (Employment):Palatin Technologies, Inc.

ABSTRACT BODY:

Purpose: Anti-inflammatory benefits of the melanocortin system suggest that melanocortin receptor (MCr) agonists have promise in the treatment of inflammatory diseases. The selective MC1r agonist, PL8177 and the MC1r/MC3r/MC4r/MC5r pan-agonist PL9654, were investigated in a streptozotocin (STZ) rat model of DR and their effects on ocular inflammation, retinal cell population composition, and gene and protein expression were determined. The objective was to determine the effectiveness of PL8177 and PL9654 in this model and to characterize its mechanism of action.

Methods: Effect of PL8177 and PL9654 on vision was investigated in a 114-day study. STZ-rats were randomly assigned to 5 separate study arms. On days 4–113, rats received BID subcutaneous administration of vehicle (0.9% NaCl); PL9654 0.05mg/kg, 0.1mg/kg, or 0.5mg/kg; or PL8177 1mg/kg. Visual function was measured by optokinetic tracking every 2 wks from day 43 to day 113. Cataract images were acquired after each optokinetic session. Rats were euthanized on day 114. Right-eye retinas were dissected and snap-frozen; left eyes were enucleated and fixed for histology. Retinal thickness and photoreceptor degeneration/loss were measured.

Results: PL9654 doses of 0.05–0.5mg/kg and PL8177 at 1mg/kg showed significant efficacy in reducing vision loss in STZ-treated rats compared to vehicle. PL9654 0.1 and 0.5mg/kg significantly reduced loss of both visual acuity and contrast vision. At 0.05mg/kg, PL9654 significantly reduced loss of contrast vision. PL8177 1mg/kg significantly reduced loss of visual acuity. Histopathology showed that there was significantly less photoreceptor degeneration with PL9654 0.1mg/kg vs vehicle($P<0.05$). Retinal thickness was also significantly improved for the PL9654($P<0.05$) and PL8177($P<0.05$) groups vs vehicle. There were no adverse events resulting from administration of either PL9654 or PL8177. Changes in the cellular population compositions, gene expression changes and protein level data will be presented and discussed at the conference.

Conclusions: SC BID administration of the melanocortin agonists PL9654 and PL8177 show promise in the treatment of DR by reducing vision loss and photoreceptor degeneration in the STZ-rat model of DR. Single nuclei RNAseq and proteomic data will be interpreted in the context of disease change to identify alterations in immune and cellular states of the rat retinas.

CONTROL ID: 3710677

SUBMITTER (NAME ONLY): Kristen Hagan

TITLE: In vivo recumbent photoreceptor imaging using the first handheld adaptive optics optical coherence tomography probe

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Hagan, J. Park, T. DuBose, S. Soltanian-Zadeh, G. Waterman, A. Dhalla, A.N. Kuo, J. Izatt, S. Farsiu, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|A.N. Kuo, R. McNabb, J. Izatt, S. Farsiu, Department of Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conventional adaptive optics (AO) ophthalmic imaging is largely limited to cooperative adults who are able to sit upright and fixate for extended periods. Our handheld AO optical coherence tomography (HAOOCT) probe enables 3D visualization of photoreceptor cells in upright and recumbent subjects, further extending AO-OCT into clinical settings.

Methods: OpticStudio and SolidWorks were used to design custom optics and mechanics, respectively, for the compact wavefront sensor and lens-based spectral domain HAOOCT system. HAOOCT was designed to achieve 2.26 μm lateral resolution and 4.01 μm axial resolution. The final form factor of HAOOCT is approximately 22 x 18 x 5.2 cm with a total weight of 630 g (Fig. 1). HAOOCT volumes with 1° FOV were acquired with a volume rate of 2.3 Hz. Volumes with overlapping FOVs were registered and averaged. Consented healthy adult volunteers were imaged in both upright and recumbent postures at the Duke Eye Center.

Results: The photoreceptor mosaic was visualized in all volunteers under different experimental setups. The imaging results from two of these subjects are shown in Fig. 2. Subject A was imaged while seated and stabilized with a chin/forehead rest, with HAOOCT mounted on an ophthalmic translation stage. An averaged B-scan (linear scale) and en face maximum intensity projection (MIP) show the photoreceptor mosaic 3-5° from fovea (Fig. 2a-b). Subject B was directed to lay in a fully recumbent position on a reclined chair and imaged with HAOOCT in handheld operation. A single B-scan and en face MIP from an un-registered volume reveal the photoreceptor mosaic (Fig. 2c-d).

Conclusions: We achieved cone photoreceptor visualization in adult volunteers using HAOOCT in both stabilized and handheld configurations. This is the first demonstration of a handheld WFS-based AO ophthalmic system and the first attempt to collect AO-OCT volumes using a handheld system.

CONTROL ID: 3710679

SUBMITTER (NAME ONLY): Pratik Vadlamudi

TITLE: Reducing human capital and human error: a partially automated method of data entry

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lu, E. Webber, L. Niziol, S. Winter, P. Newman-Casey, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|P. Vadlamudi, K. Flaharty, Medical School, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Pratik Vadlamudi: Commercial Relationship: Code N (No Commercial Relationship) | Ming-Chen Lu: Commercial Relationship: Code N (No Commercial Relationship) | Emily Webber: Commercial Relationship: Code N (No Commercial Relationship) | Katie Flaharty: Commercial Relationship: Code N (No Commercial Relationship) | Leslie Niziol: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Winter: Commercial Relationship: Code N (No Commercial Relationship) | Paula Anne Newman-Casey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study evaluated the performance of a semi-automated algorithm to populate a research database with electronic health record (EHR) data, while reducing manual burden and flagging errors.

Methods: We developed a semi-automated algorithm to extract data from structured fields of the University of Michigan EHR for participants enrolled in the Michigan Screening and Intervention for Glaucoma and Eye Health through Telemedicine (MI-SIGHT) Program. Data collected included 76 elements from the technician eye exam such as medical history, visual acuity and refraction, and 196 elements from the physicians' screening results such as assessment of the external and fundus photographs. A randomly selected sample of participants were identified. Data was extracted from the EHR through 1) the semi-automated algorithm, 2) manual extraction, and 3) gold standard double data entry. The algorithm performance and manual data extraction were compared to double data entry and error rates were calculated. Algorithm non-completion rate, or proportion of data elements that still required manual data entry, was measured. Algorithm training continued iteratively until pattern errors could no longer be identified.

Results: Fifty participants and their progress notes from the technician exam and physician screening results were randomly selected for evaluation from the 1288 participants enrolled. Manual data entry took approximately 12 hours, and the semi-automated algorithm took 2 hours for the 50 participants. For technician exams, the algorithm flagged 15.8% of the data (n=585/3700) for manual entry. Reasons for manual entry included typographic errors and non-conventional entries. Of the remaining entries that were entered automatically, the error rate was 0.5% (n=15) for manual extraction errors and 0.1% (n=3) for algorithm errors (p=0.005, McNemar's test). For the physician screening results, 7.0% of data (n=686/9800) was flagged for manual entry. Of the remaining data, the error rate was 0.1% (n=9) for manual extraction errors and 0% for algorithm errors (p=0.003, McNemar's test).

Conclusions: The algorithm showed strong performance in automatic data extraction and substantially reduced manual data entry burden. This type of process could improve both rigor and reproducibility in studies with large samples and numerous data elements. Next steps involve testing the algorithm in a new sample.

CONTROL ID: 3710682

SUBMITTER (NAME ONLY): Matthias Leung

TITLE: Mice lacking the Systemic Retinol Transporter RBPR2 are susceptible to Vitamin A Deficiency and show Retinal Phenotypes

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Leung, V. Dronamraju, R. Radhakrishnan, G.P. Lobo, Department of Ophthalmology and Visual Neurosciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|S. Walterhouse, W. Fitzgibbon, G.P. Lobo, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|A. Kondkar, Glaucoma Research Chair, King Saud University, Riyadh, Riyadh Province, SAUDI ARABIA|M.R. Biswal, Department of Pharmaceutical Sciences, University of South Florida, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The systemic transport of dietary vitamin A/all-trans retinol/ROL bound to RBP4 into peripheral tissues for storage is an important process that continuously provides chromophore precursors to the retina under fasting conditions, which is necessary for visual function. While the blood transport of the lipophilic vitamin A into the eye is facilitated by the membrane receptor STRA6, the systemic transporter for dietary vitamin A remained elusive. Using a mammalian model, we recently identified retinol binding protein receptor 2 (RBPR2), which has high affinity binding for RBP4 and is critical for systemic ROL uptake and transport to the eye.

Methods: A whole body rbpr2$^{-/-}$ null mouse line was generated and maintained with vitamin A sufficient and deficient diets. Morphological, immunohistological, HPLC, and electron microscopy studies were performed on rbpr2$^{-/-}$ mice from 2-8 months of age to evaluate the effects of RBPR2 loss on ocular retinoid content, retinal pathology, and opsin content in photoreceptors. Electroretinography (ERG) analysis was performed to evaluate visual function in rbpr2$^{-/-}$ and control mice. Spectral optical coherence tomography (OCT) analysis was performed to evaluate the retinal layer thickness.

Results: Rbpr2 knockout mice were viable on both vitamin A sufficient and replete diets. Rbpr2 mice on vitamin A sufficient diets, showed lower ocular retinoid levels, but no significant retinal phenotypes. However, when these mice were placed on vitamin A replete diets, they displayed significantly lower ocular retinoid content, decreased opsins, and significant retinal phenotypes. ERG analysis showed significant decreased visual function in rbpr2$^{-/-}$ mice on vitamin A sufficient and replete diets.

Conclusions: Our studies of RBPR2 null mice established the importance of the RBPR2 protein for the systemic availability of dietary vitamin A for proper ocular retinoid homeostasis. Under conditions of vitamin A excess and deficiency, our analyses revealed that RBPR2-mediated systemic vitamin A homeostasis is a regulated process that is important for vitamin A transport to the eye when RBP4-ROL constitutes the only transport mode in the fasting condition/vitamin A deficiency. Our findings identifying RBPR2 as a systemic vitamin A transporter have important implications for disease states associated with impaired blood vitamin A homeostasis and visual function.

CONTROL ID: 3710683

SUBMITTER (NAME ONLY): Omar Mahroo

TITLE: Monthly certifications of vision impairment in England and Wales in 2020 and 2021 compared with pre-pandemic years

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.A. Mahroo, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|O.A. Mahroo, W. Xing, S. Lazarevic, A. Zekite, D. Flanagan, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Omar Mahroo: Commercial Relationship: Code N (No Commercial Relationship) | Wen Xing: Commercial Relationship: Code N (No Commercial Relationship) | Snezana Lazarevic: Commercial Relationship: Code N (No Commercial Relationship) | Antra Zekite: Commercial Relationship: Code N (No Commercial Relationship) | Declan Flanagan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Individuals who meet certain criteria are eligible for a Certificate of Visual Impairment (CVI) in England and Wales. We explored monthly certifications from Jan 2017 to Dec 2021 to investigate any effects of the COVID-19 pandemic.

Methods: CVI forms are sent to the Certifications Office at Moorfields Eye Hospital. Numbers of CVI forms received per month from January 2017 to December 2021 were analysed. Means and standard deviations as well as maximum and minimum numbers of monthly certification forms were calculated for each calendar year. The average for the years 2017, 2018 and 2019 for each calendar month was calculated, and numbers for each calendar month of 2020 and 2021 were expressed as a proportion of this average.

Results: Mean (SD) monthly certification forms received were 2115 (208), 2229 (386), 2245 (187) for the years 2017, 2018 and 2019 respectively. In 2020, the mean (SD) was 1624 (741) certifications; in 2021, the mean (SD) was 2012 (277) certifications. Monthly certifications were consistently greater than 1800 in the years 2017 to 2019, but in 2020, certifications fell drastically in April, May and June (607, 509 and 539 certifications respectively). Monthly certifications were below 1800 also in July and August of 2020 (1231 and 1267 certifications respectively) and in Jan and Feb of 2021 (1580 and 1579 certifications respectively). When expressed as a proportion of the average of the same calendar month in 2017-2019, monthly certifications were below 30% in April, May and June of 2020. For all other months in 2020 and 2021, the proportion remained above 75% of the average for 2017-2019.

Conclusions: We found a marked (>70%) reduction in certification forms received in April, May and June of 2020, coinciding with the first national lockdown. As certifications can enable access to support, this is another manifestation of the consequences of the pandemic for patients with vision loss. A similar magnitude reduction was not seen for subsequent lockdowns.

CONTROL ID: 3710684
SUBMITTER (NAME ONLY): Qingqing (Kinna) Zhao
TITLE: Photopic Negative Response as an Objective Outcome Measure in Dominant Optic Atrophy
SESSION TITLE: Electroretinography: basic mechanisms and disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Q. Zhao, H. Nguyen, M.R. Lalonde, S.G. Coupland, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|Q. Zhao, H. Nguyen, M.R. Lalonde, S.G. Coupland, R. Karanjia, University of Ottawa Eye Institute, Ottawa, Ontario, CANADA|R. Karanjia, Doheny Eye Institute, Los Angeles, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Kjer's dominant optic atrophy (DOA) is an autosomal dominant disorder caused by mutation in the OPA1 gene in chromosome 3. The mutation results in retinal ganglion cell (RGC) degeneration and optic atrophy. The affected patients have varying degrees of visual deficits, including decreased best corrected visual acuity (BCVA), visual field defects, cataracts, and nystagmus. These visual deficits pose challenges to clinical testing. Subjective assessments such as BCVA and visual field tests do not accurately reflect the disease severity due to floor effect. Similarly, the retinal nerve fiber layer (RNFL) thickness, which reflects the structural changes of the retina, also plateaus as the disease progresses.

Photopic negative response (PhNR), recorded via the electroretinogram, can be used to assess the RGC dysfunction in the absence of reliable patient fixation or clear ocular media. The purpose of this study was to validate the use of PhNR as an objective measurement to assess visual function in patients with DOA.
Methods: Data were collected at the University of Ottawa Eye Institute. Ganglion cell complex analysis was performed by Cirrus HD-OCT (Carl Zeiss Meditec). Mean deviations were analyzed by Humphrey Field Analyzer 3 (Carl Zeiss Meditec). PhNR data of control subjects and DOA patients were recorded on Espion E3 (v.6, Diagnosys LLC). Briefly, full field PhNRs were recorded using red (640 nm) flashes on blue (470 nm) rod saturating background. PhNR was performed using three stimulus intensities: 1, 5, and 7 cd•s/m^2. Statistical analysis was performed using SigmaPlot (v.14.5).
Results: Clinical data from 14 eyes of 7 DOA patients with BCVA varying between 20/40 to counting fingers at 2 ft, were compared to control data (n=28). All DOA patients showed visual field mean deviations outside of normal limits, and abnormally reduced RGC layer, inner plexiform layer, and RNFL thickness. PhNR data demonstrated reduced amplitudes across all three stimulus intensities compared to controls (-8.8 ± 6.2 µV vs -32.6 ± 2.2 µV @ 1 cd•s/m^2; -5.1 ± 4.6 µV vs -34.2 ± 2.5 µV @ 5 cd•s/m^2; and -7.5 ± 4.7 µV vs -40.2 ± 3.4 µV @ 7 cd•s/m^2; p = < 0.001).
Conclusions: In combination with the other standard clinical measurements, such as BCVA, visual field and RNFL thickness, the PhNR tests can provide objective measurement of the RGC layer integrity and serve as a biomarker for disease and therapy management.

CONTROL ID: 3710686

SUBMITTER (NAME ONLY): Sandra Freeman

TITLE: Participant experience using novel perimetry tests to monitor glaucoma progression

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Freeman, S. De Arrigunaga, J. Kang, Y. Zhao, A.M. Roldan, M.M. Lin, T. Elze, D. Liebman, D.S. Friedman, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Chang, Genentech Inc, South San Francisco, California, UNITED STATES|D. Chang, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Traditional office-based automated visual field (VF) testing requires expensive machines and poses logistical challenges that limit its use. Novel VF devices could change the paradigm of glaucoma monitoring and dramatically improve access to care if patients can reliably use these devices at home. A positive user experience is crucial for uptake and ongoing use of novel portable VF devices. We compare the patient experience using the IMOvifa virtual reality (VR) VF test (CREWT Medical Systems, Inc., Tokyo, Japan) and tablet-based Melbourne Rapid Fields (MRF) VF test (M&S Technologies, Niles, IL, USA) to that when using the Humphrey Field Analyzer (HFA).

Methods: As part of a pilot observational study, subjects who were either glaucoma suspects or had a prior glaucoma diagnosis performed VF tests on IMOvifa, MRF, and HFA in a random testing order. All subjects were reliable, experienced HFA testers. Participants were trained to use IMOvifa and MRF, then surveyed after completing their first test on each device. The survey used 5-point Likert questions to assess subjects' experiences with the novel devices, how frequently they would be willing to use each one, and to compare each device to the HFA.

Results: We surveyed 56 research subjects with mean age of 62 years (range 30-79). A "very good" overall experience was reported by 75% and 96% of subjects for IMOvifa and MRF, respectively. 68% (95% CI = [56%, 80%]) and 66% (95% CI = [54%, 78%]) of subjects preferred IMOvifa and MRF over HFA, respectively (Table 1). Subjects primarily cited ease of use and comfort as reasons for their preference. Specifically, participants preferred the MRF's portability and IMOvifa's capability to allow both eyes to remain open during testing. 71% (95% CI = [60%, 83%]) and 79% (95% CI = [68%, 89%]) of subjects stated that they would be willing to take IMOvifa and MRF at least once per week, respectively (Table 2).

Conclusions: There was a strong preference for novel VR and tablet-based VF tests over HFA 24-2 SITA Standard, and overall participant experience using these devices was positive. Further research is needed to determine the role of these devices in clinical care.

CONTROL ID: 3710689

SUBMITTER (NAME ONLY): Emanuela Aragona

TITLE: Conjunctival Vessel Density analysis to evaluate the response to treatment with a Sodium Hyaluronate, Xanthan gum and osmoprotectants solution in Dry Eye Disease. A pilot observational study.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Aragona, A. Arrigo, L. Berchicci, E. Miserocchi, F. Bandello, G. Modorati, Ophthalmology, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the conjunctival vessel density (CVD), as a sign of inflammation, before and after treatment with a solution of Sodium Hyaluronate, Xanthan gum and osmoprotectants (HX) in mild-moderate dry eye disease (DED), and to compare it with clinical parameters: matrix metalloprotease 9 (MMP9) test, break-up time (BUT), corneo-conjunctival vital staining, Schirmer test I (STI).

Methods: Images were acquired by Keratograph 5m (OCULUS Optikgeräte GmbH, Wetzlar, Germany) using the R-scan for automatic classification of bulbar redness (BR) and vessel-enhanced images to perform CVD analysis (Fig 1A).

Data collected before (V0) and 4 months-after treatment (V1) with HX artificial tears q.i.d.

Images were exported in TIFF format and loaded in ImageJ software. Images were normalized in terms of grayscale distribution. In order to work in the same conjunctival area, the same ovaloid area was used (Fig 1B). Then, images were binarized by using Otsu threshold. Finally, the ratio of the white pixels, corresponding to conjunctival vessels, with respect to the black pixels of the images, to obtain the CVD (Fig. 1C).

Clinical MMP9 test, BUT, SICCA score, STI were performed.

Adverse events data (burning, blurred vision) were collected.

Continuous variables (mean±standard deviation) were analyzed by using two-tailed T test and chi-square test. Statistical significance was set to $p<0.05$.

Results: We collected data from 12 eyes of 12 patients. None presented adverse events.

MMP9 positivity was 66.7% at V0 and 16.7% at V1 ($p=0.03$); BUT was 4.6±1.4 at V0 and 5±1.3 at V1 ($p=0.0001$); V0 SICCA score was 2.8±1.4, and 1.2±1.1 at V1 ($p<0.0001$); STI was 10.7±6.9 at V0 and 12.9±7.2 at V1 ($p=0.01$). BR score was 0.9±0.3 at V0 and 1±0.5 at V1 ($p=0.001$). CVD was 0.07±0.03 at V0, resulting 0.05±0.02 at V1 ($p<0.0001$) (Figure 2).

Conclusions: The HX formula was effective in improving the anatomical and functional parameters.

CVD seems to offer a more reliable method than BR in evaluating inflammation. In fact, BR score is linked to the area explored, that vary in accordance to ocular discomfort and, for this reason, resulted higher at V1. This bias is overcome calculating CVD in a fixed area. In conclusion, HX formula is effective in treating ocular surface; CVD seems promising as inflammatory marker.

CONTROL ID: 3710690

SUBMITTER (NAME ONLY): Christina Wentz

TITLE: The Effect of Ophthalmic Blue Blocker Lenses and Anti-Reflective Coats on Digital Reading Efficiency and Comfort

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wentz, J. Winters, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Christina Wentz: Commercial Relationship: Code N (No Commercial Relationship) | Janis Winters: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: With increasing time spent on devices, there is rising interest in the use of blue light blocking (BB) lenses to reduce symptoms of digital eye strain. Current research is conflicted about the benefits use of these lenses might have and on what components of eye strain these may be. We conducted an experiment to compare the effects, if any, commercially available BB and/or antireflective (AR) coatings may have relative to a coating-free control on eye movements, reading rate, and subjective assessments of digital eye strain symptoms.

Methods: Twenty-eight emmetropic or contact lens corrected subjects (ages 22-31 years old; 10 male, 18 female) completed pursuit, saccade, and fixation assessments via the RightEye Dynamic Vision test while wearing clear, un-tinted BB, AR, BB/AR, and control (coating-free) lenses in a randomized order. They then completed a 20-minute reading task while wearing each of the lenses and filled out a questionnaire regarding their eye strain symptoms. Analysis of variance tests were used for statistical analysis and a p value of 0.05 was considered significant.

Results: Pursuits, saccades, and fixations were not significantly different between the control and any of the treatment lens options ($p_{pursuits} = 0.39$, $p_{saccades} = 0.91$, and $p_{fixations} = 0.89$). Similarly, there was no significant percent change in the reading rate for any of the treatments relative to the control ($p_{reading} = 0.44$). The subjective eye strain symptom survey found statistically insignificant differences in score for all of the questioned symptoms. These included blurred vision while viewing the text ($p = 0.45$), blurred vision at distance after the task ($p = 0.49$), difficulty/slowness refocusing eyes after the task ($p = 0.96$), irritated or burning eyes ($p = 0.71$), dry eyes ($p = 0.78$), eye strain ($p = 0.94$), headache ($p = 0.65$), tired eyes ($p = 0.56$), sensitivity to bright lights ($p = 0.65$), and discomfort in the eyes ($p = 0.74$).

Conclusions: We find no statistical evidence to support claims that BB lenses with or without AR coat or AR coats alone will improve digital eye strain symptoms. This finding is consistent with other studies using the same symptom questionnaire. Additionally, we find no support for these lenses and coatings to alter eye movements or change reading rate significantly.

CONTROL ID: 3710691

SUBMITTER (NAME ONLY): Kang-Chieh Huang

TITLE: Autophagy Dysfunction Represses mTORC1 Signaling Resulting in Neurodegeneration of Retinal Ganglion Cells in Glaucoma

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Huang, K. VanderWall, S.S. Lavekar, C. Fligor, Biology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|K. Huang, C. Gomes, K. VanderWall, S.S. Lavekar, C. Fligor, J. Harkin, J.S. Meyer, Stark Neurosciences Research Institute, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|Y. Shiga, A. Di Polo, Neuroscience, Universite de Montreal, Montreal, Quebec, CANADA|Y. Shiga, A. Di Polo, Centre Hospitalier de l'Universite de Montreal Centre de Recherche, Montreal, Quebec, CANADA|C. Gomes, J.S. Meyer, Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|J. Harkin, Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of vision loss characterized by the progressive degeneration of retinal ganglion cells (RGCs). Among many underlying causes of the disease, autophagy dysfunction has been associated with the onset of RGC deficits. Here, we hypothesized that an imbalance between autophagy and mTOR signaling resulted in the neurodegeneration of RGCs. Using human pluripotent stem cells (hPSCs), we characterized how a mutation in the autophagy receptor Optineurin (OPTN) contributes to autophagy dysfunction resulting in RGC neurodegeneration through the repression of mTOR, and validated these changes in a mouse glaucoma model.

Methods: hPSCs with an OPTN(E50K) gene mutation and corresponding isogenic controls were differentiated to RGCs following established methods. Changes to autophagic flux as well as mTOR signaling were characterized in hPSC-derived RGCs. To further validate these findings, ocular hypertension was induced in mice by intracameral injection of magnetic microbeads. Retinal protein lysates and cross sections were analyzed at 2 weeks of glaucoma induction.

Results: OPTN(E50K) RGCs exhibited a higher number of OPTN puncta and impaired autophagic-lysosomal degradation. By characterizing the key autophagy modulator mTOR, OPTN(E50K) RGCs demonstrated decreased expression of the mTORC1 effector phospho-S6 and increased expression of the upstream stress sensor AMPK. Pharmacological inhibition of mTOR in otherwise healthy RGCs resulted in neurite retraction similar to RGCs with the OPTN(E50K) mutation, while enhancement of mTOR signaling in OPTN(E50K) RGCs rescued RGC neurodegeneration. In agreement with our findings in hPSC-RGCs, an increase in the expression of autophagy-associated proteins was associated with a decrease in mTOR signaling in the microbead occlusion mouse model.

Conclusions: Our study demonstrates a connection between autophagy disruption and mTORC1 inactivation, which can contribute to neurodegeneration in glaucoma. The delicate balance between autophagy and mTOR signaling demonstrates that RGC neurodegeneration may result from the disruption of multiple signaling pathways. In future studies, an emphasis should be placed upon the targeting of autophagy induction while maintaining cellular homeostasis via mTOR signaling, leading to the investigation of new protective strategies to prevent glaucoma-associated neurodegeneration.

CONTROL ID: 3710692

SUBMITTER (NAME ONLY): Ifat Sher-Rosenthal

TITLE: Chromatic pupilloperimetry for objective diagnosis and monitoring of optic neuritis

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Sher-Rosenthal, A. Rosset, S. Zorani, Y. Rotenstreich, Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|I. Sher-Rosenthal, A. Rosset, S. Zorani, O. Zmira, D. Magalashvili, M. Dolev, A. Achiron, Y. Rotenstreich, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, ISRAEL|O. Zmira, D. Magalashvili, M. Dolev, A. Achiron, Multiple Sclerosis Center, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To characterize rod-, cone- and melanopsin-mediated pupil responses (PLR) for small focal chromatic light stimuli presented in peripheral and central retinal locations in optic neuritis patients.

Methods: Ten acute optic neuritis (ON) patients (mean age ± standard deviation: 32.3 ± 9.29 years) 7 females and 3 males, and 26 age-similar healthy controls (35.4 ± 12.4 years) 15 females and 11 males, were enrolled. The pupil light responses (PLR) for small (0.43°) red and blue light stimuli (peak 485 nm and 625 nm, respectively) presented at 54 locations of a 24-2 visual field were recorded. In addition, the melanopsin-mediated sustained pupil responses (pupil response, recovery, PRP) were evaluated at central and peripheral VF locations. All patients underwent Optical Coherence Tomography imaging, standard perimetry (Humphrey SITA Standard protocol), and their best corrected visual acuity was determined.

Results: Attenuated melanopsin-mediated PLR was recorded in the peripheral VF in ON eyes compared to controls, with ROC AUC = 91.1% (p=0.001). The rod and cone-mediated percentage of pupil contraction (PPC) were lower by more than 2 standard errors (SEs) from the mean of controls in the majority of visual field test targets (mean ± SE: 60% ± 12 % and 55% ± 10 %, respectively) in optic neuritis eyes, even in patients with normal visual acuity. Furthermore, even though normal visual acuity and VEP P100 were recorded in the fellow eyes, substantially lower rod- and cone-mediated PPC values (lower than 2SEs from the mean of controls) were identified in the fellow eyes of all patients (mean ± SE: 33% ± 9 % and 30%± 7 % of test targets, respectively). Peripapillary OCT of both eyes was within normal limits.

Conclusions: Substantially lower rod-, cone- and melanopsin-mediated PLR are recorded in ON and fellow eyes of patients, even in eyes with normal VA. The melanopsin-mediated pupil response to blue light at the peripheral retina may present a novel, highly sensitive surrogate functional biomarker for detection of ON.

CONTROL ID: 3710696

SUBMITTER (NAME ONLY): Minjae Kim

TITLE: Pregabalin, an IOP-reducing CACNA2D1 antagonist, may also preserve optic nerve health by binding to CACNA2D2.

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Kim, T. Hollingsworth, W. Edwards, M.M. Jablonski, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Minjae Kim: Commercial Relationship: Code N (No Commercial Relationship) | TJ Hollingsworth: Commercial Relationship: Code N (No Commercial Relationship) | Will Edwards: Commercial Relationship: Code N (No Commercial Relationship) | Monica Jablonski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: CACNA2D1 is an L-type calcium channel subunit that is expressed by several structures in the eye. Previously, we showed that a topically applied CACNA2D1 antagonist—pregabalin (PRG)—lowered IOP in mice, and that the amplitude of response varied between mice carrying the B and D haplotypes of the gene, originating from C57BL/6 mice (B6) and DBA/2J (D2) mice, respectively. In this study, we aim to show that CACNA2D2, an isoform of CACNA2D1, is expressed in the eye and may be targeted using PRG to modulate optic nerve health.

Methods: Whole eyes from B6 and D2 mice at 1 month of age were immunostained and imaged for CACNA2D1 and CACNA2D2. Systems genetics methods were used to analyze the relationship between optic nerve health and the haplotype of Cacna2d2 using estimates of the number of live axons per optic nerve across the BXD family of mice. Because there is no published crystal structure of CACNA2D2, we used the human N-type voltage gated calcium channel (PDB:7VFU) for homology modeling of both B and D haplotypes of CACNA2D2 (sequence identity: 56%). Molecular docking was performed using Prime software (Schrödinger, Inc., USA).

Results: Immunohistochemical analysis revealed that both CACNA2D1 and CACNA2D2 are expressed in the eye, with CACNA2D2 having its highest expression in the optic nerve. Systems genetics analyses demonstrated a significant reduction in number of live axons per optic nerve in mice with the D haplotype, compared to those with the B haplotype. Finally, molecular docking of PRG to the B haplotype of CACNA2D2 revealed a binding site with a docking score of –10.820 kcal/mol, while that of the D haplotype yielded –5.794 kcal/mol.

Conclusions: Through this study, we confirmed the expression of CACNA2D2 in mouse eyes and using systems genetics analyses demonstrated that it may play a role in modulating optic nerve health. Furthermore, molecular docking of CACNA2D2 revealed PRG's potential binding site and affinity, which differed between the B and D haplotypes. Together, our findings offer promising evidence to support the exploration of PRG being used therapeutically to not only lower IOP, but also to preserve healthy axons in the eye.

CONTROL ID: 3710700

SUBMITTER (NAME ONLY): Urooba Nadeem

TITLE: Effects of Long Duration of High-Fat Diet on Gut Microbiota Composition and Laser-Induced Choroidal Neovascularization

SESSION TITLE: Animal Models of Age Related Macular Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Nadeem, Pathology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|H.A. Barba, B. Xie, M. D'Souza, E. Chang, D. Sulakhe, D. Skondra, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|J. Zhang, J. Xiao, M. Boachie-Mensah, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|E.F. Xie, Rosalind Franklin University of Medicine and Science, Rosalind Franklin University of Medicine and Science, North Chicago, IL, US, academic, North Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Emerging evidence indicates that high-fat diet (HFD)-induced gut dysbiosis exacerbates choroidal neovascularization (CNV), the hallmark lesion of neovascular AMD (nAMD). Previous studies describe the pathogenic effects of short-term (ST) HFD-induced gut dysbiosis on the evolution of nAMD however the impact of long-term (LT) HFD consumption remains unknown. We aim to evaluate and compare the consequences of ST and LT HFD on gut microbiome composition as well as CNV features.

Methods: Seven weeks old male C57BL/6J were fed 23% HFD for 8 weeks (ST-HFD) and 21 weeks (LT-HFD) while control groups were maintained on a regular diet (young-ND and aged-ND, respectively) and then underwent laser induction of CNV. Choroidal flatmounts were immunostained with IB4 isolectin for CNV and IBA-1 for microglia infiltration. 16S rRNA sequencing of fecal DNA from these groups was done on the Illumina MiSeq platform and analyzed by QIIME2.

Results: LT-HFD induced a more prominent effect on gut dysbiosis, reflected by severely suppressed microbial diversity in contrast to the ST-HFD group. Specifically, protective microbes from the phylum (p.) Bacteroidetes/order (o.) Bacteroidales and p.Actinobacteria (o.Bifidobacteriaceae) were further decreased by LT-HFD, while, pathogenic p.Firmicutes (o.Clostridiales) were more prominently increased in the LT-HFD group compared to ST-HFD. The Bacteroidetes to Firmicutes ratio was most affected in the ST-HFD group but somewhat begins to recover in the LT-HFD, as shown in the previous aging-related gut-microbial studies.

LT-HFD caused a larger increase in CNV size compared with the aged ST-ND fed mice (1.62 fold-change, p=0.0049), while the ST-HFD intake compared to ND resulted in a smaller influence on CNV size (1.42fold-increase, p=0.0048). LT-HFD was associated with significantly increased IBA1 activated microglial infiltration within and outside CNV lesion (p=0.003 and p=0.013, respectively), but this was not noted with ST-HFD.

Conclusions: LT-HFD had a more robust effect on gut dysbiosis as well as CNV size and microglial infiltration. Our data indicate that the duration of unhealthy diet intake may influence gut microbial shifts that correlate with nAMD pathogenesis.

CONTROL ID: 3710703

SUBMITTER (NAME ONLY): Mitchell Ross

TITLE: Thermo-responsive and muco-adhesive gels for the treatment of cystinosis

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ross, E. Hicks, H. Sheardown, chemical engineering, McMaster University, Hamilton, Ontario, CANADA|

Commercial Relationships Disclosure: Mitchell Ross: Commercial Relationship: Code N (No Commercial Relationship) | Emily Anne Hicks: Commercial Relationship: Code N (No Commercial Relationship) | Heather Sheardown: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Topical eyedrops remain the primary treatment option of anterior ocular conditions but have been demonstrated have poor efficacy in many cases since less than 5% remains bioavailable after administration. Drug eluting gels applied to the inferior fornix have been developed as alternatives to conventional eyedrops. However, due the high shearing forces and significant globe movement, the retention of these gels is often difficult. To overcome this, degradable thermo-gels with tunable muco-adhesive properties were developed for sustained release of cysteamine for the treatment of ocular cystinosis.

Methods: N-isopropylacrylamide co-polymers were synthetized with varying concentrations of the disulfide co-monomer polydisulfide ethyl ether methacrylate. The polymers were then crosslinked with chitosan (MW 80-200 kDa, DDA = 70%). The muco-adhesive properties of the gels were evaluated by rheologic synergism. The viscosity of the gels (n=3) at 10% (wt/v) was measured either in PBS or 3% (wt/wt) mucin suspensions.

The safety of the cysteamine conjugated thermo-gels was evaluated using 19-week-old female Brown Norway Rats (n=4). Thermo-gels were applied every day for one week. At days 1, 2, 3, and 7 the cornea was assessed utilizing optical coherence tomography imaging system as well as by fluorescence staining to measure corneal disruption. After 7 days, the eyes were harvested, and corneal health was assessed by histology.

Results: By inclusion of varying concentrations of the muco-adhesive disulfide monomer as well as crosslinking with muco-adhesive chitosan, the rheological synergism of the system was found to be highly tuneable from 0.01 to 10 (Pa*s). Importantly, it was found that the inclusion of both components resulted in greater synergy than either component alone. The in vivo histological analysis of corneal morphology and thickness, as shown in Figure 1, demonstrated that the produced thermo-gels did not lead to statistically significant corneal thickening after one week compared to PBS treated rats ($p>0.05$).

Conclusions: The results show that we can produce a wide range of muco-adhesive properties by incorporating different concentrations of muco-adhesive components into the thermo-gels. The cysteamine thermo-gels have been shown to be well tolerated in a rat model, supporting their potential for use as alternatives to conventional, acidic, cysteamine eyedrops which require frequent reapplication on a daily basis.

CONTROL ID: 3710704

SUBMITTER (NAME ONLY): Mirataollah Salabati

TITLE: Refractive Error Change During Diabetic Macular Edema Treatment: A Post Hoc Analysis of the DRCR Protocol T Trial

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Salabati, R. Mahmoudzadeh, M. Starr, J. Hsu, A.C. Ho, C. Regillo, A.E. Kuriyan, Mid Atlantic Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|M. Starr, Department of ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|Q.(. Zhang, J. Sharpe, Biostatistics Consulting Core, Vickie and Jack Farber Vision Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of anti-VEGF therapy and changes in optical coherence tomography (OCT) metrics on the refractive error (RE) in diabetic macular edema (DME).

Methods: A post-hoc analysis of DRCR protocol T. The RE in diopters (D) was measured using standard protocol refraction. Spherical equivalent (SE) data was calculated for study and fellow eyes at baseline, one-year, and two-year visits. The SE change of the eyes with persistent edema was compared to those with resolved edema stratified by lens status. The correlation between RE changes and OCT metrics like baseline fluid and central subfield thickness (CST) was evaluated.

Results: Among 543 patients, a small hyperopic shift was found from baseline to the 1-year follow up in the study eye [0.06 (0.67), p= p=0.015] and the fellow eye [0.07 (0.75), p=0.013]. A small hyperopic shift was also observed from baseline to the 2-year follow-up in the study eye [0.04 (0.82), p=0.022] and the fellow eye [0.12 (0.84), p= 0.001]. There was no significant difference between the SE change of the study and fellow eyes at 1-year and 2-year visits (p= 0.89 and 0.23, respectively). No significant difference in SE shift was found between eyes with and without edema at two years in phakic (0.12 D and 0.08, p=0.87) and pseudophakic eyes (-0.24 and -0.08, p=0.30). In phakic patients, SE change was significantly different in eyes with no edema at 1-year and 2-year visits and baseline (IRF+/SRF-) vs. eyes with baseline (IRF+/SRF+), both at one year [0.19 (0.63) vs. -0.03 (0.85), respectively, p=0.003] and two years follow up [0.16 (0.74) vs. -0.14 (0.98), respectively, p= 0.039]. In pseudophakic patients, no significant difference was noted between SE change of eyes with no edema at 1-year and 2-year visits and baseline (IRF+/SRF-) compared to eyes with baseline (IRF+/SRF+) at one year [-0.01 (0.53) vs. 0.03 (0.55), respectively, p=0.93] and two years [-0.09 (0.63) vs. -0.08 (0.51) , respectively, p=0.77]. The SE shift was not correlated with CST change at the end of the first (r=0.013, p=0.77) nor the second year (r=0.02, p=0.62).

Conclusions: DME patients receiving anti-VEGF therapy have minimal changes in RE. Appropriate refraction may be considered at any point regardless of edema.

CONTROL ID: 3710711

SUBMITTER (NAME ONLY): Patrick Herbert

TITLE: Forecasting Risk of Future Rapid Glaucoma Worsening Using Early Visual Field, Optical Coherence Tomography and Clinical Data

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Herbert, K. Hou, M. Unberath, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|M.V. Boland, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Yohannan, Johns Hopkins University Whiting School of Engineering, Baltimore, Maryland, UNITED STATES|C. Bradley, P.Y. Ramulu, J. Yohannan, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: We assess whether we can forecast future rapid visual field (VF) worsening using deep learning models (DLM) trained on baseline VF, OCT, and clinical data. Additionally, we study the impact of adding additional VF data (beyond baseline) on model performance.

Methods: We included eyes that met the following: 1) followed for glaucoma or suspect status 2) had at least five reliable VFs over time (VF_1, VF_2, VF_3, VF_4, VF_5) 3) had one reliable baseline OCT scan (OCT_1) and one set of baseline clinical measurement: age, gender, BCVA, IOP ($Clinical_1$) at the time of VF_1.

We designed a DLM to detect eyes at risk for future rapid VF worsening (mean deviation (MD) slope <-1 dB/yr across all five VFs). The input to the DLM consisted of spatially oriented total deviation values from VF_1 (+/- VF_2 and VF_3 in some models) and spatially oriented RNFL thickness values from OCT_1 (Figure 1A). We input this VF/OCT stack into a vision transformer feature extractor. The output of the feature extractor was concatenated with $Clinical_1$ and put through a dense linear classifier to make a final prediction for that eyes' risk of future rapid VF worsening (Figure 1B). We used 80% of data for training, 10% for validation, and 10% for testing.

We compared the performance of models with differing inputs by computing area under receiver operating curve (AUC) in the test set. Specifically, we trained models with following inputs: Model (1) VF_1; (2) VF_1 + $Clinical_1$; (3) VF_1 + OCT_1; (4) VF_1 + $Clinical_1$ + OCT_1; (5) VF_1 + VF_2 + $Clinical_1$ + OCT_1; (6) VF_1 + VF_2 + VF_3, + $Clinical_1$ + OCT_1

Results: We included a total of 4,537 unique eyes from 2,963 patients. Mean and (SD) for: age | VF MD at baseline | MD slope, was: 65.9 years (12.4) | -3.4 dB (4.3) | -0.21 dB/yr (1.0). 518 (11.4%) of eyes underwent rapid VF worsening. Model 6 most accurately forecasted rapid worsening with an AUC (95% CI) of 0.85 (0.78, 0.93). Remaining models in descending order of performance and their respective AUC [95% CI] were: Model 5 (0.81 [0.73 to 0.89]), Model 4 (0.75 [0.66, 0.83]), Model 2 [0.75 [0.66, 0.83], Model 3 (0.71 [0.62, 0.80]), Model 1 (0.68 [0.59, 0.77]).

Conclusions: DLMs trained on multimodal data from early visits can forecast future rapid worsening with AUC >0.8. Deployment of such models in clinical practice may allow us to stratify high from low-risk glaucoma patients early in the disease course.

CONTROL ID: 3710713

SUBMITTER (NAME ONLY): Daniel Maruri

TITLE: Subcellular patterning of focal adhesions regulates stiffness-dependent differences in myofibroblast differentiation of corneal keratocytes.

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Maruri, K. Iyer, D. Schmidtke, V. Varner, The Department of Bioengineering, The University of Texas at Dallas, Richardson, Texas, UNITED STATES|M. Petroll, The Department of Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Daniel Maruri: Commercial Relationship: Code N (No Commercial Relationship) | Krithika Iyer: Commercial Relationship: Code N (No Commercial Relationship) | David Schmidtke: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Petroll: Commercial Relationship: Code N (No Commercial Relationship) | Victor Varner: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Following surgery or traumatic injury, corneal wound healing can cause a scarring response that impairs ocular function. This fibrosis is caused in part by myofibroblast differentiation of corneal keratocytes in response to transforming growth factor beta 1 (TGF-β1). Previous studies have shown that the changes in extracellular matrix (ECM) stiffness of can regulate this process, but it remains unclear how keratocytes sense changes in their physical microenvironment. Here, we used a polyacrylamide (PA) gel system to show that the subcellular patterning (and activation of signaling downstream) of focal adhesions underlies stiffness-dependent differences in myofibroblastdifferentiation of corneal keratocytes.

Methods: Soft (1 kPa) and stiff (10 kPa) polyacrylamide (PA) hydrogels were fabricated on glass coverslips, functionalized with type I collagen, plated with primary corneal keratocytes (NRKs), and cultured in defined serum free media with or without exogenous TGF-β1. In some experiments, an inhibitor of focal adhesion kinase (PF-228) was also added to the media. Cells were fixed and stained for F-actin, as well as markers for myofibroblast activation (α-SMA), contractility (pMLC), or focal adhesions (vinculin). We also used traction force microscopy (TFM) to quantify NRK traction stresses.

Results: Treatment with TGF-β1 elicited stiffness-dependent differences in the number, size, and subcellular distribution of FAs in cultured NRKs. On stiff substrata, cells exhibited large FAs distributed throughout the entire cell body, while on soft gels, the FAs were smaller and fewer in number, localized primarily to the distal tips of thin cellular extensions. Larger and increased numbers of FAs correlated with elevated cellular traction stresses. Inhibition of focal adhesion kinase (FAK) disrupted stiffness-dependent differences in contractility and myofibroblast differentiation of cultured NRKs. Further, in the presence of the inhibitor, we no longer observed stiffness-dependent differences in the subcellular patterning of FAs.

Conclusions: Taken together, these data suggest that changes in the subcellular patterning of FAs, as well as the activation of FAK, have important implications for stiffness-dependent myofibroblast differentiation of corneal keratocytes during wound healing.

CONTROL ID: 3710715
SUBMITTER (NAME ONLY): Maxine Joly-Chevrier
TITLE: The Most Influential Articles on Artificial Intelligence in Ophthalmology
SESSION TITLE: Machine Learning and Big Data
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: M. Joly-Chevrier, I. Hardy, Department of Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|A. Nguyen, Faculty of Medicine, McGill University, Montreal, Quebec, CANADA|
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ABSTRACT BODY:
Purpose: Significant advances in artificial intelligence (AI) has led to promising applications in ophthalmology. This study highlights the 100 most cited ophthalmology research papers on AI.
Methods: Ophthalmology research papers published between 1990 and October 2021, were extracted from the Institute for Scientific Information Web of Knowledge platform, using the keywords AI, machine learning (ML), and deep learning (DL). Papers were assessed for eligibility based on title/abstract review, followed by full-text review. The primary outcome measure was the number of times cited. Secondary outcome measures were: publication year, author attributes, journal name, study design and characteristics (ophthalmology subspecialties, pathology examined, AI branches, algorithms, databases, and imaging modalities used).
Results: The 100 publications were cited between 27 and 399 times, with a median of 46 [IQR: 32-74]. All papers were published between 1994 and 2020, with 64% of them published in 2017-2019. They were written by 1 to 30 authors, with a median of 7 [4-9] authors per paper. 482 unique authors wrote between 1 and 13 papers. 46% of corresponding authors were based in the USA and 23% in Europe. The top three journals were: Investigative Ophthalmology & Visual Science (26%), Ophthalmology (14%) and JAMA Ophthalmology (8%). 67 studies were retrospective, 21 prospective and 4 ambidirectional. Out of the 100 publications, 46 focused on retina, 35 on glaucoma and 10 on cornea and external disease. Studies mainly examined glaucoma (37%), age-related macular edema (28%), and diabetic retinopathy (27%). The most used imaging modalities were: fundus photography (42%), optical coherence tomography (OCT, 42%), and visual fields (VFs, 14%). 78 studies were geared towards the development and evaluation of a diagnostic technology. Among the 86 studies specifying their ML algorithms, 78% used supervised learning, 11% unsupervised learning and 12% used a mix of both techniques. 78 studies focused on DL. Among the 95 studies specifying their algorithm approach, convolutional NNs were the most used (51%). Among the 51 studies specifying their database, 65% used private databases and 51% used public databases.
Conclusions: This is the first study to analyze the characteristics of the 100 most-cited ophthalmology papers on AI. The use of AI was predominantly for image recognition to develop and evaluate a new diagnostic technology.

CONTROL ID: 3710717

SUBMITTER (NAME ONLY): Jenson Erapuram

TITLE: Influence of Census Tract Poverty Indicator on Survival in Cases of Conjunctival and Uveal Melanoma diagnosed within the State of Texas

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Erapuram, F. Dihowm, Internal Medicine, Texas Tech University Health Sciences Center El Paso, El Paso, Texas, UNITED STATES|Z.S. Hussain, University of Medicine & Health Sciences, Basseterre, SAINT KITTS AND NEVIS|

Commercial Relationships Disclosure: Jenson Erapuram: Commercial Relationship: Code N (No Commercial Relationship) | Zain Hussain: Commercial Relationship: Code N (No Commercial Relationship) | Fatma Dihowm: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In 2019, the CDC released the National Health Statistics Report highlighting the ultimate impact of poverty on healthcare utilization. Additionally, prior studies have highlighted differential incidences of melanoma stratified by poverty classification within Texas. This retrospective cohort analysis is the first of its kind in characterizing novel survival trends within the class of orbital melanomas in the state of Texas.

Methods: The Texas Cancer Registry (TCR) acted as provision for state-level standardized cancer statistics. 2,585 cases of conjunctival and uveal melanomas diagnosed between January 1, 1995 and December 31, 2018, a 23-year time interval, were extracted. All cases with unknown or arbitrary values of cause of death were eliminated from analysis. Cox proportional hazards modeling was performed to yield hazard ratios (HR) with 95% Confidence Intervals (CI). Kaplan-Meier (KM) curves were curated to visualize survival trends. Statistical significance was achieved at $p<0.05$. All statistical analyses were performed with IBM SPSS Version 26.

Results: N=1966 (79.1%), N=403 (16.2%), and N=116 (4.7%) cases were diagnosed with choroidal, ciliary body, and conjunctival melanomas, respectively. N=606 (24.4%) cases died of cancer-related causes and N=510 (20.5%) cases died due to causes unrelated to cancer. Patients residing in neighborhoods with poverty indices of 10-19.9% and 20-100% demonstrated 24.7%, 43.6%, and 33.0% increased hazards of multi-variable cause-specific, other-cause, and all-cause death, respectively, as compared to patients residing in neighborhoods with poverty indices of 0-5% and 5-9.9%. Within patients residing in poverty indices of 10-19.9% and 20-100%, female patients experienced increased hazards of other-cause death and former tobacco users experienced decreased hazards of cause-specific death as compared to current users (HR=0.619, p=0.019).

Conclusions: To the authors' knowledge, this investigation is the first to characterize the influence of psychosocial parameters, including poverty, gender, and tobacco use on survival in patients diagnosed with conjunctival, choroidal, and ciliary body melanomas within the state of Texas. Reconciliation of poverty and subsequent lack of healthcare utilization and psychological well-being are likely important thought processes when delivering care to those afflicted by ophthalmic cancers.

CONTROL ID: 3710718

SUBMITTER (NAME ONLY): Dimitrios Christaras

TITLE: Peripheral image quality in model pseudophakic eyes measured by a double pass system

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The pseudophakic eye has generally higher peripheral astigmatism compared to the natural eye, leading to worse peripheral image quality. In this work, peripheral astigmatism of the pseudophakic eye is assessed in vitro using an anatomically equivalent eye model with two different types of intraocular lenses (IOL), by using an instrument based on the double pass principle. The purpose of this work is twofold: to measure peripheral astigmatism in the pseudophakic eye and to evaluate the capability of the double pass instrument to assess peripheral image quality in pseudophakic eyes.

Methods: A water-filled artificial eye was used, including a custom meniscus lens acting as cornea, and a black cardboard acting as fundus, which could pivot around a fixed axis, allowing measuring at field angles of up to 30 degrees. The IOL was supported by its haptics in a receptacle behind a diaphragm. Two IOLs were used in this study: a biconvex hydrophobic acrylic IOL with 20D power (Acrysof SA60AT, Alcon) and an inverted meniscus type hydrophobic acrylic IOL with 22D power (ArtIOL, Art55, Voptica) that reportedly has reduced peripheral astigmatism. Peripheral astigmatism was measured using a custom-made double pass instrument featuring a 780nm laser source, a tunable lens (EL-16-40-TC, Optotune) and a retinal camera (DMM37UX273-ML, The Imaging Source). The instrument can record through focus images of the point spread function. By applying the appropriate processing, defocus and astigmatism at each eccentricity can be calculated.

Results: The fundus' position of the artificial eye was set at best focus, i.e. the through focus scan using the double pass system returned 0D for both IOLs. Since defocus depends on retinal curvature, which can vary in the population, only peripheral astigmatism was assessed in this study. At 15 degrees astigmatism was measured to be 1.5D and 0D for the Acrysof IOL and the ArtIOL respectively. At 30 degrees astigmatism was found to be 5.65D and 3.5D for the Acrysof IOL and ArtIOL respectively. In all measurements the axis of astigmatism was at 0 degrees when measuring at horizontal field angles.

Conclusions: A novel double pass instrument for the measurement of peripheral image quality was used to measure peripheral astigmatism at 15 and 30 degrees in two IOLs of different type: a biconvex and an inverted meniscus lens. The meniscus lens produced lower astigmatism at all peripheral locations.

CONTROL ID: 3710719

SUBMITTER (NAME ONLY): Yao Tong

TITLE: Crosstalk among Ferroptosis, Necroptosis, and Pyroptosis during oxidative stress-induced RPE Cell Death

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Tong, Y. Wu, J. Ma, S. Wang, Tulane University, New Orleans, Louisiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a degenerative disorder of the macula, the region of the central retina responsible for the greatest visual acuity. Oxidative stress and aging of retinal pigment epithelial (RPE) cells are the major reason for AMD. 4-Hydroxynonenal (4-HNE) is a major product of lipid peroxidation, which is accumulated in aging cells and could be related to several age-related diseases. The mechanism of RPE cell death under oxidative stress is still controversial. The goal of the current study is to determine RPE cell death mechanisms using 4-HNE and RSL3 treatment models.

Methods: ARPE-19 or human primary RPE cells were treated with 4-HNE or RSL3, cell viability was tested 24 hours later. The effect of apoptosis, necroptosis, pyroptosis, and ferroptosis pathways on cell survival was tested using specific inhibitors. Cellular ATP and ROS levels were measured. PYCARD and RIPK3 expression were used to visualize inflammasomes and necrosomes. Lipid ROS, a ferroptosis marker, was tested using BODIPY reagent. RIPK1 and MLKL knockdown RPE cell lines were established using CRISPR/Cas9 to confirm the roles of the two genes.

Results: 1. 4-HNE-induced RPE cell death can be rescued by ferroptosis inhibitors (Lip-1 and Fer-1) and both upstream and downstream necroptosis inhibitors (RIPK1 inhibitor Nec-1 and MLKL inhibitor NSA, respectively); 2. RSL3-induced RPE ferroptosis can be rescued by Nec-1 but not NSA; 3. Both 4-HNE and RSL3 induce RIPK3 activation in RPE cells which can be inhibited by Lip-1, Fer-1, and Nec-1; 4. Both 4-HNE and RSL3 induce lipid ROS accumulation in RPE cells which can be inhibited by Lip-1, Fer-1, Nec-1 but not NSA; 5. RIPK1 and MLKL knockdown can prevent 4-HNE induced RPE cell death while RIPK1 but not MLKL knockdown can prevent RPE ferroptosis; 6. MCC950, an inflammasome (pyroptosis marker) inhibitor, couldn’t prevent RSL3 induced RPE ferroptosis alone, but the combination of NSA and MCC950 could partially rescue the cells.

Conclusions: Both RSL3 and 4-HNE can induce RPE ferroptosis. Ferroptosis is associated with RIPK3 activation, therefore representing one type of necroptosis. However, 4-HNE but not RSL3-induced RPE cell death can be inhibited by MLKL inhibition. Nec-1 is likely a better inhibitor for RPE ferroptosis compared to NSA, possibly because RIPK1/3 activation can induce inflammasome activation when MLKL is inhibited.

CONTROL ID: 3710720

SUBMITTER (NAME ONLY): Yannis Paulus

TITLE: Biodegradable silicon nanoneedles for sustained treatment of angiogenesis

SESSION TITLE: Drug delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y.M. Paulus, V. Nguyen, Ophthalmology and Visual Sciences, Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|W. Park, C. Lee, School of Mechanical Engineering, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiogenesis is a major cause of vision loss and blindness in numerous ocular diseases, including in the cornea, macular degeneration, and diabetes. To treat angiogenesis, laser photocoagulation, photodynamic therapy, and anti-vascular endothelial growth factor therapy such as bevacizumab (BEV) are often utilized, but these treatments can damage adjacent healthy tissue or require frequent administration and can carry a risk of infection. To improve the treatment efficiency, increase the treatment duration, and reduce these side-effects, the current study describes a novel treatment of ocular angiogenesis using miniature biodegradable silicon nanoneedles (SiNNs) fabricated on a tear-soluble contact lens.

Methods: The SiNNs were encapsulated with BEV (BEV@SiNNs) and used as drug carriers for long-term, sustained drug delivery. The potential treatment effects of BEV@SiNNs were evaluated on a rabbit corneal neovascularization (CNV) model (n = 24) after approval from the University of Michigan IACUC. To generate CNV, a suture was placed on the animal cornea and allowed for CNV development up to one month. BEV@SiNNs were applied on the cornea and monitored by optical coherence tomography (OCT), color photography, and red-free imaging. The treatment outcome was followed up for one-month post-treatment.

Results: The tear-soluble contact lens dissolved within 1 minute. CNV was rapidly reduced within 7 days post-treatment that persisted to at least 28 days (Figure) whereas no CNV reduction occurred with control. Vessel density was 2.9 ± 2.0% for BEV@SiNNs versus 85.8 ± 0.9% for control. SiNNs did not cause cytotoxicity. Histological images showed normal corneal morphology without evidence of cell death or damage to the corneal endothelium cells, corneal thickness, and limbal stem cells.

Conclusions: The SiNNs are an efficient drug delivery vehicle for treatment of ocular angiogenesis.

CONTROL ID: 3710721

SUBMITTER (NAME ONLY): Abigail Moye

TITLE: Ultrastructural analysis of Cep290 mutant cilia in mouse photoreceptors

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Robichaux, West Virginia University, Morgantown, West Virginia, UNITED STATES| A. Moye, M. Robichaux, V. Potter, Z. Zhang, T.G. Wensel, Baylor College of Medicine, Houston, Texas, UNITED STATES|V. Potter, University Hospitals, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: CEP290 (centrosomal protein 290), a large multi-domain containing protein, is a key component of the transition zone in many primary and motile cilia. Mutations in Cep290 cause several ciliopathies, including Meckel Syndrome (MKS) and retinal specific disorders such as Leber Congenital Amaurosis (LCA). The CEP290 protein has been proposed as a component of the “Y-links” structures, which span from the axoneme microtubule doublets to the ciliary membrane in the connecting cilium (CC) of photoreceptor cells. Our goal is to determine the location of CEP290 protein and the structural effects of CEP290 defects at the nanometer scale.

Methods: We use a number of advanced microscopies, including transmission electron microscopy and immuno-electron microscopy, super-resolution and expansion fluorescence microscopy, and cryo-electron microscopy to examine ciliary ultrastructure in WT mice and two Cep290 mutant mouse lines with early-onset retinal degeneration. One is virtually devoid of functional CEP290 (near-null, nn), and the other is a complete knockout (KO).

Results: At post-natal day 10 in both CEP290 mutants, we observe formation of CC, less or no outer segment (OS) discs, and presence of Y-links. Immunogold TEM reveals the ultrastructural location of CEP290 in the area between the microtubules and the ciliary membrane, but not on the Y-links. Immunogold TEM and expansion microscopy also reveal a spiral periodicity in CEP290 staining around the CC. Each mutant displays multiple ciliary protein mislocalization from the CC at P10, preceding photoreceptor degeneration. Each mutant shows slightly different pathogenesis, with extracellular vesicles present instead of OS discs, and more ciliogenesis defects present in the KO.

Conclusions: These results suggest that CEP290 is not required as a structural component of Y-links in the CC. Its location, the formation of EV’s instead of OS discs, and the mislocalization of multiple ciliary proteins, may facilitate a proposed function as a "gate-keeper" for protein trafficking through the CC. CEP290’s localization throughout the length of the CC, an observation unique to photoreceptors and not ubiquitous to all ciliary transition zone proteins, may help explain the retina-specific symptoms of several CEP290 mutations. The additional photoreceptor phenotypes present in the KO mutants hint at the difference between loss of CEP290 vs presence of mutated CEP290 within photoreceptors.

CONTROL ID: 3710722

SUBMITTER (NAME ONLY): Sudeshna Sil Kar

TITLE: OCT-derived SubRPE Compartment Radiomics Features are Associated with the Development of Subfoveal Geographic Atrophy

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sil Kar, A. Madabhushi, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|H. Cetin, J. Abraham, S.K. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Identifying patients who are at high risk for development of subfoveal geographic atrophy (sfGA) in dry age-related macular degeneration (AMD) will be critical to personalized treatment management and potential clinical trial enrichment for eyes at greatest risk. In this study, the role of shape and texture-based radiomic features within the sub-retinal pigment epithelium (subRPE, i.e., space bounded by RPE and Bruch's membrane) on baseline SD-OCT scans is evaluated as potential biomarkers to discriminate between eyes that are at highest risk of sfGA progression.

Methods: This was an IRB-approved retrospective image analysis study of subjects with dry AMD without sfGA with 5-year clinical and SD-OCT follow-up. Based on sfGA status at year five, eyes were categorized as Progressors and Non-progressors. A total of 26 shape-based fractal dimension (FD) and 364 texture-based radiomics features were extracted from the subRPE compartment of the baseline SD-OCT scans. Minimum Redundancy Maximum Relevance (MRMR) feature selection method was employed to identify features from the training set (N=96) and evaluated with 3 different machine-learning classifiers over 500 iterations of 3-fold cross validation. Classifier performance was validated on the test set (N=41).

Results: Random Forest classifier yielded a cross-validated area under the Receiver Operating Characteristics curve (AUC) of 0.89±0.09 and 0.76±0.06 using isolated shape-based FD and isolated texture-based radiomics features, respectively. Mean fractal entropy was identified as the most significant shape-based biomarker with higher values of entropy being associated with greater shape disorder and risk for sfGA progression. The Laws texture features were identified as the most discriminating features with the Progressors having higher feature expression. This suggests higher degree of heterogeneity within the subRPE compartment texture for the Progressors. A combination of shape and texture features yielded a significant improvement in the classifier performance with AUC=0.92±0.02.

Conclusions: In this study, radiomics-based characterization of the subRPE compartment in dry AMD identified multiple potential imaging biomarkers. Future works will involve prospective multi-institutional validation of the fractal and texture features for clinical trial enrichment and assessments for therapeutic response in dry AMD patients.

CONTROL ID: 3710725

SUBMITTER (NAME ONLY): Aaron Coyner

TITLE: Grayscale Retinal Vessel Maps Are Associated with Self-Reported Race: Implications for Artificial Intelligence Models

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.S. Coyner, S. Ostmo, J. Campbell, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Singh, J. Kalpathy-Cramer, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|J. Brown, University of Lincoln, Lincoln, Lincolnshire, UNITED KINGDOM|R.V. Chan, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Artificial intelligence (AI) algorithms can learn and perpetuate racial biases from patterns in medical images if those images contain information relevant to self reported race or ethnicity. Recent studies have shown that convolutional neural networks (CNNs) can be trained to classify images as being from black or white patients from medical images that were not previously thought to contain information relevant to the classification of self-reported race. Herein, we evaluate whether grayscale retinal vessel maps (RVMs) of patients screened for retinopathy of prematurity (ROP) similarly contain the potential for racial bias.

Methods: 4095 retinal fundus images (RFIs) were collected from 245 Black and White infants (as labeled by self-report from parents). A U-Net generated RVMs from RFIs, which were subsequently thresholded, binarized, or skeletonized (Figure). CNNs were then trained to predict self-reported race from color RFIs, raw RVMs, and thresholded, binarized, or skeletonized RVMs. Area under the precision-recall curve (AUC-PR) was evaluated.

Results: CNNs predicted self-reported race from RFIs near perfectly (image-level AUC-PR: 0.999, subject-level AUC-PR: 1.000). Raw RVMs were almost as informative as color RFIs (image-level AUC-PR: 0.938, subject-level AUC-PR: 0.995). Ultimately, CNNs were able to detect whether RFIs or RVMs were from self-reported Black or White babies, regardless of whether images contained color, vessel segmentation brightness differences were nullified, or vessel segmentation widths were normalized.

Conclusions: Both Color RFIs and black and white RVMs contain information relevant to the race of patients. These results suggest that biomarker-based strategies to remove information relevant to race or ethnicity (such as skin or fundus pigmentation) may not be effective, and that the potential for racial bias exists even in images that do not appear to contain relevant information.

CONTROL ID: 3710729

SUBMITTER (NAME ONLY): Russell Quinn

TITLE: Senescent Macrophage Lead to Age Related Macular Degeneration-Like Phenotype in an in vitro 3D RPE/Choroid Model

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Quinn, E. Nguyen, T. Park, C. Zhang, A. Ali, R. Hirday, D. Bose, K. Bharti, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|R.N. Fariss, Biological Imaging Core Facility, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Ferrer, 3-D Tissue Bioprinting Laboratory, National Center for Advancing Translational Sciences, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macrophages are integral to maintenance of choroidal function. This study aims to investigate the role of senescent macrophages in inducing advanced wet age-related macular degeneration (AMD) characterized by choriocapillaris neovascularization and functional atrophy of the retinal pigment epithelium (RPE). Utilizing a 3D bioprinted “choroid” with a confluent capillary network, fibroblasts, primary macrophages and polarized RPE monolayer, we aim to model and investigate the mechanisms behind AMD initiation and progression in this 3D Outer Blood Retinal Barrier (3D-OBRB) system.

Methods: Endothelial cells, choroidal fibroblasts, ocular pericytes, and primary macrophages mixed with a collagen-derived gel were 3D-printed on a degradable scaffold to facilitate development of microvascular networks. iPSC-derived RPEs were seeded on the opposite side of the scaffold 7 days after bioprinting. Primary polarized M1, M2, and mixed ratios of M1+M2 macrophages were included in the hydrogel. Confocal microscopy, trans-epithelial electrical resistance measurements (TER), were used to analyze RPE health and structural integrity of choroidal vasculature.

Results: Single (M1 or M2 only) macrophage treatments resulted in increased capillary growth in the choroid space compared to the non macrophage treated control but, didn’t cause any noticeable pathological effect. Mixed macrophage treatments caused increased vascular growth into the 3D-OBRB sub-RPE space, similar in phenotype of type-I CNV, after 5 weeks, with the 2:1 M1:M2 ratio causing the most severe increase. The RPE monolayer also saw decreased TER at the same time point, with 1:2 M1:M2 macrophage treatment causing the biggest decrease. In all cases, macrophages take on “bloated” foam-cell like morphologies, similar to what is seen in patients with advanced AMD. While our bloated macrophages are ki67-/p16+, we are also investigating said macrophages using gene expression analysis to further demonstrate their senesent state.

Conclusions: While healthy macrophages proved to be beneficial during the initial developmental period, development of senescent macrophages coincides with compromised 3D-OBRB physiology. This 3D tissue model allows for the study of ocular immune populations, and their role in ocular health, via a reductionist in-vitro system.

CONTROL ID: 3710730

SUBMITTER (NAME ONLY): Kevin Emmerich

TITLE: Transcriptomic comparison of two selective retinal cell ablation paradigms in zebrafish reveals shared and cell-specific regenerative patterns

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Emmerich, Human Genetics, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|J.S. Mumm, Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Kevin Emmerich: Commercial Relationship: Code N (No Commercial Relationship) | Jeff Mumm: Commercial Relationship(s);Code P (Patent):Luminomics Inc

ABSTRACT BODY:

Purpose: Humans are unable to regenerate retinal neurons leading to blinding diseases, in contrast zebrafish exhibit remarkable capacity for regenerating lost neurons throughout life. Multiple studies have defined transcriptomic shifts driving zebrafish retinal regeneration following the death of multiple cells types, but to identify disease-relevant therapeutic strategies it is critical to look at the zebrafish response to loss of discrete retinal cell types. Here, we profiled regeneration-associated transcriptomic shifts over a long time course in zebrafish in response to loss of either rod photoreceptors or bipolar interneurons.

Methods: The primary method used was bulk-tissue (whole eyes) microarrays conducted on larval zebrafish samples. Our lab has developed transgenic retinal ablation models to kill specific retinal cells and induce a regenerative response. Groups of larvae were collected following the induced ablation (or non-ablated samples for control) of rods or bipolar cells at multiple timepoints throughout regeneration including 0, 8, 16, 24, 32, 40, 48, 60, 72, 96, 144, and 240 hours into induced regeneration. Pathway analysis tools were used to identify patterns characterizing transcriptomic changes at each timepoint along with a particular interest in comparing differentially expressed genes and pathways between the different cell type patterns.

Results: Throughout our time course we found more cell-type specific transcriptomic changes rather than those shared between the two models. Of the changes that were shared, there was more similarity earlier on following induced cell death (~24h) rather than later (~72h and on). Numerous well-defined pathways were found to be differentially regulated in one model while absent from the other (example: p53 signaling changes more prominent in bipolar cells). We then used the literature to help characterize pathway changes associated with different phases of retinal regeneration including stem cell activation, proliferation, differentiation, and more.

Conclusions: We successfully identified both shared and cell-type specific regeneration patterns, with the majority leaning toward the latter. This supports the theory that further defining these cell-type specific (fate-biased) responses will be critical in developing more therapeutic strategies to induce regeneration in the mammalian retina.

CONTROL ID: 3710732

SUBMITTER (NAME ONLY): Zhiyuan Yu

TITLE: Small molecule agonists of Tyrosine Kinase receptors improve dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Yu, G. Yazdanpanah, C.S. De Paiva, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|T.S. Thompson, K. Burgess, Chemistry, Texas A&M University, College Station, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin3 (NT-3) bind to tyrosine kinase (Trk) receptors, TrkA, TrkB, and TrkC, respectively. This study investigated the efficacy of novel molecule agonists of Trk receptors in an in vivo model of dry eye disease.

Methods: Small molecule agonists for TrkC (C1) or pan-Trk (pan) were synthesized based on structural formula and β-turns. C57BL/6J mice were subjected to desiccating stress (DS) and received bilateral eye drops of C1, pan or vehicle (2x/day). The corneal barrier function was assessed by uptake of a fluorescent dye (n=11-18/ group). The conjunctival goblet cell (GC) density was measured in paraffin-embedded, PAS-stained sections (n=10-14/group). Corneal epithelial lysates were collected for either western blot or RNA extraction. Extracted total RNAs were used for NanoString analysis. Immunofluorescent staining was performed on wholemount corneas using anti-A20 and anti-PTGER4 antibodies.

Results: Compared to naïve mice, desiccated mice treated with vehicle showed corneal barrier disruption (55±11 vs 97.8±38.4 gray levels, $P<0.01$) and goblet cell loss (50±11 vs 37±11 goblet cells/mm, $P<0.01$). Compared to treatment with vehicle, pan and C1- treated mice showed an improvement in corneal barrier function (98±38 vs 59±17 and 72±18 gray levels, respectively, $P<0.01$), and higher conjunctival GC density (37±11 vs 46±10 and 52±13 GC/mm, respectively, $P<0.05$). NanoString results revealed upregulation of specific mRNA transcripts (Ptger4, Tnfaip3 [encoding A20], Il1a and Ptger4, Tlr3, Osal1, respectively) in Pan and C1-treated corneas compared to vehicle-treated corneas (all P-adj<0.05). Western blot results showed that treatment with pan and C1 decreased vehicle-induced NFkB nuclear translocation after DS for one day and increased PTGER4 and A20 protein levels after 5 days of DS in corneal epithelium lysates. These results were confirmed by immunostaining using antibodies for A20 and PTGER4 in wholemount corneas.

Conclusions: Small molecule agonists of Trk receptors improve dry eye disease by decreasing NFkB activation and increasing protein expression of anti-inflammatory molecules A20 and PTGER4. Further studies are needed to investigate whether pan and C1 analogs modulate other pathways involved in dry eye.

CONTROL ID: 3710733

SUBMITTER (NAME ONLY): Samuel Herberg

TITLE: Glaucomatous stressors drive Schlemm's canal cell pathobiology via elevated YAP activity

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Herberg, H. Li, P.S. Ganapathy, Ophthalmology and Visual Sciences, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|M. Kuhn, W.D. Stamer, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dysfunction of the Schlemm's canal (SC) inner wall endothelium and trabecular meshwork is the principal cause of decreased outflow facility in glaucoma. Extracellular matrix (ECM) stiffening and increased transforming growth factor beta2 (TGFβ2) in the aqueous humor are strongly associated with outflow tissue dysfunction. Yes-associated protein (YAP) has emerged as key contributor to glaucoma pathogenesis; YAP1 was recently identified as potential genetic risk factor. However, the precise role of SC cell YAP signaling in response to known glaucomatous stressors is poorly understood. Here, we investigate how ECM stiffness/composition and TGFβ2 regulate YAP activity in human SC cells using biomimetic hydrogels, and whether pharmacologic YAP inhibition increases ex vivo outflow facility.

Methods: ECM hydrogels were fabricated by photocrosslinking functionalized collagen type I, elastin-like polypeptide, and hyaluronic acid. Bioinert alginate was added to facilitate Ca^{2+}-mediated hydrogel stiffening (~3-fold) and alginate lyase-mediated softening. Fibronectin (FN) was used to coat ECM hydrogels (10 μg/cm^2). Donor-derived SC cells were plated on hydrogels and stimulated with TGFβ2 (2.5 ng/ml), Y27632 (10 μM), or latrunculin B (Lat B; 2 μM). Verteporfin (VP; 0.5 μM) was used for YAP inhibition. YAP transcriptional activity, cytoskeletal organization, fibrotic marker levels, and ECM remodeling were quantified. Outflow facility with perfusion of VP (10 μM) was measured in enucleated eyes from C57BL/6J mice using iPerfusion.

Results: ECM stiffening increased YAP activity and F-actin levels in SC cells ($p<0.001$). Nuclear YAP completely translocated to the cytoplasm within 3 h after ECM softening; F-actin levels reached baseline after 24 h ($p<0.0001$). FN coating enhanced SC cell YAP activity and F-actin/ECM remodeling. TGFβ2 increased nuclear YAP ($p<0.001$) contingent on cytoskeletal integrity; Y27632 or Lat B co-treatment interrupted aberrant YAP signaling. VP treatment fully blocked TGFβ2-driven YAP activation in SC cells ($p<0.0001$) and largely restored FN, TGM2, F-actin, αSMA, and pMLC levels ($p<0.001$). Importantly, 6/10 mouse eyes displayed ~15-80% increased outflow facility with VP perfusion.

Conclusions: Our data suggest that YAP modulates SC cell dysfunction in response to known glaucomatous stressors, and that pharmacologic YAP inhibition has promising potential to improve outflow tissue dysfunction.

CONTROL ID: 3710735

SUBMITTER (NAME ONLY): Abhiniti Wagh

TITLE: Ultrastructure of bipolar cell dendritic trees and rod convergence in the simplex retina of L. erinacea

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Wagh, J.G. Fathi, M. Ramon, Y. Yusuf, A. Alazzeh, I. Anastassov, Cell and Molecular Biology (CMB), San Francisco State University, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Abhiniti Wagh: Commercial Relationship: Code N (No Commercial Relationship) | Jessamyn Fathi: Commercial Relationship: Code N (No Commercial Relationship) | Marta Ramon: Commercial Relationship: Code N (No Commercial Relationship) | Yaqoub Yusuf: Commercial Relationship: Code N (No Commercial Relationship) | Aya Alazzeh: Commercial Relationship: Code N (No Commercial Relationship) | Ivan Anastassov: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Visual information processing under scotopic and photopic conditions is generally divided between the rod and cone systems, which transmit information to dedicated bipolar pathways. However, the simplex retina of L. erinacea utilizes rods across the full range of illumination. We know little about what functional and anatomical features of rod pathways in mixed rod-cone retinas are present in skate. Here, we use SB-3DEM to examine the convergence ratio of rods to postsynaptic partners (identified as putative bipolar cells), as well as the dendritic tree architecture of putative bipolar cell types.

Methods: Retinal pieces were embedded in resin blocks, and serial block-face scanning electron microscopy (SB-3DEM) was performed on individual samples from the tapetal retinal region of adult animals. The dataset analyzed here was from the entire cross section of the retina with a width of 82µm, height of 314 µm, and depth of 29 µm. Section thickness was 65nm, and pixel size was 7nm x 7nm.; the dataset has 452 sections. 3-D representations of dendritic processes and synaptic ribbons were obtained through segmentation in Reconstruct software; quantifications were done in Amira 3D software.

Results: We quantified a total of 97 dendritic processes, or tips, in the initial putative bipolar cell examined. In mouse retina, rod bipolar cell dendritic tips are likely sites of contacts with rods and appose a rod synaptic ribbon ~84% of the time (Anastassov et al., 2019). We have so far determined that ~1/5 of the 97 tips identified are likely apposed to a ribbon. Additional measurements on the rest of the dendritic tips, as well as reconstructions of other putative bipolar cells in the dataset, are ongoing. Preliminary observations show that individual bipolar cell processes may be capable of making both invaginating and basal contacts with the same rod terminal.

Conclusions: We show the rod-only skate retina likely has the same high rod-to-bipolar-cell convergence ratio found in mixed rod-cone retinas, supporting prior electrophysiological evidence of high sensitivity. Invaginating putative bipolar cell dendritic tips are likely sites of contact with individual rods, although exact contact probability is yet to be determined. Finally, putative bipolar cells may posses invaginating (normally ON) and basal (normally OFF) contacts within the same cell, suggesting a hybrid dendritic architecture.

CONTROL ID: 3710739

SUBMITTER (NAME ONLY): Tejus Pradeep

TITLE: Association of PPI/H2 Blocker Use and Ocular Toxoplasmosis: Findings from a Large U.S. National Database

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Pradeep, Y. Yu, B.L. VanderBeek, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|C. Conrady, University of Nebraska Stanley M Truhlsen Eye Institute, Omaha, Nebraska, UNITED STATES|

Commercial Relationships Disclosure: Tejus Pradeep: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Conrady: Commercial Relationship: Code N (No Commercial Relationship) | Yinxi Yu: Commercial Relationship: Code N (No Commercial Relationship) | Brian VanderBeek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A previous small case series identified a 50% proton pump inhibitor (PPI)/histamine (H2) blocker usage rate in patients with toxoplasma retinochoroiditis, higher than the rate of 20% described in the general population. A primary defense against T. gondii tachyzoites is acidification of phagolysosomes within an acidic environment. Usage of PPI/H2 blockers can increase gastric pH and weaken host defenses, which we hypothesize may increase susceptibility to infection. Therefore, we conducted a case control study of medical claims data from a national database to determine if PPI/H2 blocker usage is associated with the development of ocular toxoplasmosis.

Methods: A retrospective, matched case control study using data from a medical claims database was performed from 2000-2020. Cases of ocular toxoplasmosis were identified using ICD 9/10 codes. The index date for cases was considered the earliest date of diagnosis of ocular toxoplasmosis. Controls were matched up to 5:1 for age, gender, race, with eligibility date within 3 months from index date of matched cases. Exclusion occurred for being < 18 years old, having congenital toxoplasmosis, having <2 years in the insurance plan prior to the index date and not having at least one visit to an eyecare provider prior to the index date. The primary outcome was defined as having a prescription for PPI or H2 blocker, or a disease that was likely to lead to PPI/H2 blocker use prior to the index date. Multivariate conditional logistic regression analyses were performed controlling for demographic and systemic health variables.

Results: 4069 cases and 19177 controls met our eligibility criteria. 24.3% (989/4069) of ocular toxoplasmosis cases were on PPI/H2 blockers compared to 19.2% (3673/19177) of controls. An adjusted logistic regression model demonstrated a 28% increase in the odds of PPI/H2 blocker use in ocular toxoplasmosis cases compared to matched controls (95% CI: 1.17-1.40, $p < 0.001$).

Conclusions: PPI/H2 blocker exposure was associated with ocular toxoplasmosis, corroborating findings from prior case series suggesting an association between the two. Further research studying the mechanisms of PPI/H2 blocker use, gastric acid suppression and T gondii infectivity may help reduce risk of ocular infection.

CONTROL ID: 3710740

SUBMITTER (NAME ONLY): Collin Chiu

TITLE: Probing the Contribution of Retinal Pigment Epithelium to Eyecup Metabolism

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Chiu, D. Hass, J.B. Hurley, Biochemistry, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Collin Chiu: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Hass: Commercial Relationship: Code N (No Commercial Relationship) | James Hurley: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The eyecup consists of retinal pigment epithelium (RPE), choroid, and sclera. RPE metabolism is assumed to be dominant in eyecup preparations, but this has yet to be proven rigorously. In this study we probe the contribution of retinal pigment epithelial cells to eyecup metabolism. We approach this question by determining metabolic flux in eyecup tissue from control and mice injected with the selective RPE cell toxin sodium iodate ($NaIO_3$).

Methods: We injected C57BL/6J mice with a single intraperitoneal dose of saline or 50 mg/kg $NaIO_3$. Seven days later we sacrificed mice via cervical dislocation and dissected eyecup tissue into Krebs-ringer bicarbonate buffer supplemented with either labeled or unlabeled 5 mM glucose. We quantified extracellular flux of glucose and lactate using spectrophotometric assays and intracellular flux of 1,2-$^{13}C_2$-glucose using gas chromatography-mass spectrometry. We compared glucose flux in saline-injected control eyecups to eyecups from NaIO3-injected mice.

Results: $NaIO_3$ treated eyecups released 42% less lactate from media than controls ($p<0.05$), despite negligible glucose consumption. Surprisingly most glycolytic and TCA cycle metabolite levels were unchanged by $NaIO_3$ injection. $NaIO_3$ treatment did however significantly decrease levels of lactate and the TCA cycle metabolites malate and fumarate. ^{13}C flux from 1,2-$^{13}C_2$-glucose to lactate and malate was also decreased by $NaIO_3$ treatment.

Conclusions: Our results suggest that glycolytic flux and lactate export in the eyecup is partly due to retinal pigment epithelium metabolism. However, metabolite levels and flux were partly maintained, implying that RPE metabolism may not be dominant in the eyecup. The remaining glucose metabolism could be due to contributions from endothelial cells, or microglial cells recruited to the eyecup after $NaIO_3$ treatment. Further analysis is required to fully understand the role of RPE metabolism in the eyecup.

CONTROL ID: 3710743

SUBMITTER (NAME ONLY): Tannin Schmidt

TITLE: Biophysical characterization of recombinant human Proteoglycan 4 (rhPRG4): Effect of Mg^{2+} and high pH

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.A. Schmidt, N.G. Menon, A. Tanguay, A. Deymier, Biomedical Engineering, UConn Health, Farmington, Connecticut, UNITED STATES|L. Zhou, Y. Chen, Biomedical Engineering, University of Connecticut, Storrs, Connecticut, UNITED STATES|M. Han, W. Greene, Institute for Frontier Materials and ARC Centre of Excellence for Electromaterials Science, Deakin University, Melbourne, Victoria, AUSTRALIA|R. Whitehead III, C. Teschke, Molecular and Cell Biology, University of Connecticut, Storrs, Connecticut, UNITED STATES|B. Sullivan, Lubris BioPharma, Naples, Florida, UNITED STATES|G. Jay, Emergency Medicine, Brown University, Providence, Rhode Island, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proteoglycan 4 (PRG4, or lubricin) is a mucin-like glycoprotein present on the ocular surface and in tears, with both lubricating and anti-inflammatory properties. Biological processes occur in solution; therefore, studying proteins' biophysical properties in solution contribute to understanding their function. Here, we biophysically characterize recombinant human PRG4 (rhPRG4), previously shown to be clinically effective in reducing signs and symptoms of dry eye, and determine the effect of the cation Mg^{2+} and high pH on rhPRG4 size in solution.

Methods: rhPRG4 (Lubris BioPharma) at pH7, and in some cases native human PRG4, was assessed in solution for hydrodynamic diameter (Dh, by dynamic light scattering), charge (zeta potential), structure (circular dichroism, CD), density (analytic ultracentrifugation, AUC), and molecular fingerprint (raman spectroscopy). The kinetics of rhPRG4 binding to type 1 Collagen (Col1) was assessed (quartz crystal microbalance). Finally, the effects of 1-5mM $MgCl_2$ or pH9-10 on Dh was assessed.

Results: rhPRG4 had a main (~85%) peak at Dh=~170nm (with a minor at ~30nm, z-avg Dh=~110nm) and a -21mV zeta potential. Native PRG4 Dh and charge were similar to rhPRG4. CD indicated rhPRG4 had a main extended structure peak ~202nm and no discernible tryptophan peak at ~290nm. AUC indicated a dominant species at ~4S. Raman spectroscopy showed the ratio of normalized (to 891cm-1, C-C) peaks at $980cm^{-1}$ and at $550cm^{-1}$, associated with β-sheets and disulfide bonds respectively, was ~2.9. rhPRG4 rapidly bound to Col1, with a t~8sec. $MgCl_2$ caused a decrease of the main Dh peak in a dose dependent manner, reducing to ~140nm at 5mM. Finally, pH9 caused a decrease in the main peak and an emergence of an intermediate peak at ~120nm, and pH10 even more so.

Conclusions: The clinically effective rhPRG4 assessed here had similar size and charge to native PRG4, and quickly adhered to Col1 (which is present on the ocular surface). The size, charge, and density for rhPRG4 are larger than those published for a different version of recombinant human lubricin (ECF843: Dh=~60nm, ~0mV, and a more compact 6.5S major peak), which recently did not produce supportive data in a dry eye clinical trial. Reduced Dh of rhPRG4 caused by Mg^{2+} and pH9-10 may be due to osmotic deswelling of the mucin domain and disulfide bond

reshuffling, respectively, which are likely to affect function as well.

CONTROL ID: 3710744

SUBMITTER (NAME ONLY): Puttur Santhoshkumar

TITLE: Cell-Penetrable Protease-Resistant Amphiphilic Minichaperones for Treating Protein Misfolding Diseases

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Santhoshkumar, G. Shankar, S. MAHALINGAM, K. Sharma, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|S. Srivastava, G. Broitman-Maduro, M. Maduro, University of California Riverside, Riverside, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: An increasing number of eye disorders are associated with protein misfolding, oxidative stress, inflammation, and apoptosis. It is hypothesized that a cell-penetrable, protease-resistant amphiphilic mini chaperone peptide (CPPRAMC) having the core αA-crystallin chaperone region sequence can help treat such disorders. We have tested our hypothesis using cell culture and Caenorhabditis elegans (C. elegans) model systems.

Methods: The CPPRAMC, having all D- amino acids, and the control peptides were synthesized (>95% pure) by GenScript. The anti-aggregation activity of the CPPRAMC was confirmed in vitro by testing the suppression of $A\beta_{1-42}$ (25 μM) oligomerization and fibrillization under TEM. The suppression of mutant myocilin (DsRed-MYOC-Y437H) accumulation in TM cells was confirmed by fluorescence imaging. The ability of CPPRAMC to protect ARPE-19 cells from $A\beta_{1-42}$-induced cytotoxicity was evaluated by performing an EarlyTox cell integrity assay on treated cells. The anti-oxidative property of CPPRAMC was demonstrated in ARPE-19 cells challenged with 7.5 mM sodium iodate for 24 hr. The cellular ROS activity was measured with 2′,7′-Dichloro-fluorescein diacetate. The therapeutic efficacy of the CPPRAMC was also evaluated in C. elegans wild-type (N2) worms subjected to stress and in transgenic (CL4176) worms expressing human $A\beta_{1-42}$. The anti-inflammatory property of CPPRAMC was tested using HEK293 IL-6 reporter cells (Invivogen).

Results: CPPRAMC treatment (5 μM) reduced the accumulation of DsRed-MYOC-Y437H protein in TM cells. Aβ peptide-treated (5 μM) ARPE-19 cells showed 25% apoptosis while cells treated with CPPRAMC (5 μM) + Aβ peptide showed 10% apoptotic cells. Doubling the molar concentration of CPPRAMC reduced the number of dead cells to 5%. CPPRAMC (5 μM) completely suppressed the NaIO3-induced ROS production. CPPRAMC ablates the LPS-induced release of IL-6 in mouse macrophages (Raw264.7) and blocks IL-6 signaling (50 pM) completely in HEK-Blue IL-6 reporter cells when used at 1 μM. CPPRAMC feeding augments the lifespan (46%) and increases the thermotolerance (51%) of wild-type C. elegans. CPPRAMC treatment delays β-amyloid induced paralysis and increases survival (18%) in transgenic CL4176 worms.

Conclusions: The results suggest the beneficial effects of CPPRAMC in treating diseases associated with protein misfolding, oxidative stress, inflammation, and apoptosis that affect vision.

CONTROL ID: 3710745
SUBMITTER (NAME ONLY): Yuebing Li
TITLE: Rho-kinase expression in human ocular fibrotic membranes
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y. Li, S. Zandi, L. Jahnka, V. Enzmann, M.S. Zinkernagel, Ophthalmology, Universitat Bern, Bern, Bern, SWITZERLAND|Y. Li, S. Zandi, L. Jahnka, V. Enzmann, M.S. Zinkernagel, Augenklinik, Inselspital Universitatsspital Bern, Bern, Bern, SWITZERLAND|
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ABSTRACT BODY:

Purpose: Purpose: Proliferative vitreoretinopathy (PVR) is still the most common cause of failure after retinal reattachment surgery due to secondary growth and contraction of cellular membranes within the hyaloid and retina. The epiretinal membrane is a thin sheet of fibrous tissue that develops on the macula. The treatment of choice to date is either surveillance when no retinal detachment has yet occurred or vitreoretinal surgery and removal of those PVR membranes to prevent or treat further complications, such as recurrent retinal detachment. Identification of factors that may interfere with the formation and regulation of PVR membranes could facilitate the development of novel therapeutics. Various groups have shown that the ROCK pathway is involved in PVR pathogenesis; however, the presence of rho-kinase in human PVR membranes has not yet been demonstrated. To compare the ROCK-signaling in two different types of human ocular fibrotic membranes, we aim to study in addition the ROCK pathway in human ERM.

Methods: Methods: Membranes were obtained in the course of vitreoretinal surgery from 6 patient eyes with proliferative vitreoretinopathy (PVR) and 12 eyes with epiretinal membranes (ERM). To show that the Rho/ROCK signalling pathway is involved in these vitreoretinal diseases, immunohistochemistry staining for hematoxylin and eosin, collagen-1, alpha-smooth muscle actin (a-SMA) and Rho-kinase isoforms (ROCK1 and ROCK2) of surgically excised human PVR and ERM membranes were performed. In addition, the human ocular fibrotic membranes were analysed with rtPCR to screen for the Rho-kinase related gene expression levels, expression differences and RNA content.

Results: Results: Different fibrotic markers, such as collagen 1 and a-SMA were detected together with ROCK1 and ROCK2 in PVR and ERM membranes.

Conclusions: Conclusions: The current results indicate that Rho-kinase is expressed in human ocular fibrotic membranes, such as PVR and ERM, and might play a role in its formation.

CONTROL ID: 3710747

SUBMITTER (NAME ONLY): rajeevalochan wudali

TITLE: Ciliary Neurotrophic Factor protects retinal pigment epithelium and photoreceptor cells in sodium iodate induced retinal degeneration model

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. wudali, Y. Hu, C. Romano, Ophthalmology, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

Commercial Relationships Disclosure: rajeevalochan wudali: Commercial Relationship(s);Code E (Employment):Regeneron Pharmaceuticals Inc. | Ying Hu: Commercial Relationship(s);Code E (Employment):Regeneron Pharmaceuticals Inc. | Carl Romano: Commercial Relationship(s);Code E (Employment):Regeneron Pharmaceuticals Inc.

ABSTRACT BODY:

Purpose: Dry age-related macular degeneration is closely related with retinal pigment epithelial (RPE) cell dysfunction and photoreceptor degeneration. Sodium iodate ($NaIO_3$), a chemical oxidizing agent, induces patchy retinal & RPE cell loss in multiple mammalian species. $NaIO_3$ model has been used to test drug candidates for treating retina & RPE degeneration. Neuroprotective effect of ciliary neurotrophic factor (CNTF) has been well demonstrated in retinal ganglion cell and photoreceptor cell damage models. In this study, we evaluated the protective effect of intravitreal (IVT) administration of recombinant human CNTF (rHCNTF) in $NaIO_3$ model in mice.

Methods: 20mg/kg $NaIO_3$ was injected intraperitoneally in 8-10 week old C57BL/6J mice. Mice received IVT injections of 1ml rHCNTF (1.5mg or 2.0mg) or control (buffer or water) in the left eye one day prior and after $NaIO_3$ injection. Optical Coherence Tomography (OCT) and electroretinogram (ERG) were performed at baseline and one-week post $NaIO_3$ injection to evaluate the retinal structural and functional changes. One-week post $NaIO_3$, animals were euthanized. RPE/choroid flat mount was stained with phalloidin to evaluate the damage.

Results: Seven days after $NaIO_3$ injection, subretinal changes and retinal thickness loss (>50um) were observed in both eyes of the control groups (buffer, water) by OCT imaging. In contrast, there were minimal subretinal and retina thickness changes (<10um loss) in rHCNTF injected eyes. ERG showed significant protection of a, b and c wave amplitudes in rHCNTF injected eyes. Interestingly, in the contralateral noninjected eyes of rHCNTF group, there was also less retinal damage by OCT and ERG evaluation. Consistent with the in vivo observations, RPE/choroid flat mounts showed more RPE cell survival, and close to normal morphology in CNTF treated eyes. Contrarily, severe damage and loss of RPE cells were found in the control eyes.

Conclusions: Intravitreal injections of rHCNTF prevented $NaIO_3$ induced structural & functional damages in RPE & retina. These findings demonstrate a protective role of CNTF in RPE and photoreceptor cells after oxidative stress challenge, and support CNTF as a potential therapeutic agent for the treatment of RPE and photoreceptor loss in disease.

CONTROL ID: 3710748

SUBMITTER (NAME ONLY): Conor McConville

TITLE: Machine Learning-Enabled Longitudinal Volumetric Fluid Assessment in the Phase III VISTA Clinical Trial

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. McConville, S. Yordi, L. Lunasco, H. Cetin, G. Kalra, C.J. Mugnaini, K. Wise, C. Calabrise, K. Talcott, S.K. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the feasibility of machine learning enhanced volumetric fluid characterization in diabetic macular edema (DME) and compare the longitudinal fluid dynamics between the treatment groups in the Phase III VISTA DME clinical trial.

Methods: In the Phase III VISTA clinical trial, patients were randomly assigned to receive either 2mg IAI every 4 weeks (2q4), 2mg IAI every 8 weeks following 5 initial monthly doses (2q8), or laser photocoagulation (rescue with IAI was allowed beginning at week 24). Utilizing a machine learning-enhanced fluid feature extraction platform, OCT images taken monthly for each patient were analyzed from Baseline to Week 24, at Week 52, and at Week 100. For each visit, intraretinal fluid (IRF) and subretinal fluid (SRF) metrics were extracted through automated fluid segmentation with manual correction, as needed. IRF/SRF total macular volume, central subfield volume (CSV), and central subfield fluid indices (i.e. percentage of retina occupied by fluid) were analyzed.

Results: Four hundred forty-three patients were included in the study with successful OCT feature extraction, with 148 in the 2q4 group, 148 in the 2q8 group, and 147 in the laser group. At baseline, all groups demonstrated similar IRF and SRF volumetric parameters ($p>0.05$). At Week 100, the pooled IAI group showed significantly less mean panmacular IRF volume than the laser group $0.135\pm0.39mm^3$ vs $0.275\pm0.47mm^3$; $p=0.006$, respectively) and lower CSV IRF fluid index ($0.06\pm0.13\%$ vs $0.12\pm0.18\%$; $p=0.002$), despite 41% of laser patients receiving IAI between weeks 24 and 100. Laser and pooled IAI showed significant improvement in SRF from Baseline to Week 100 (both $p<0.01$).

The 2q4 group showed significantly greater mean change in all IRF parameters at week 100 compared to 2q8, including panmacular IRF volume ($-0.137\pm0.34mm^3$ vs $-0.064\pm0.16mm^3$; $p=0.034$), IRF CSV ($-0.012\pm0.034mm^3$ vs $-0.003\pm0.02mm^3$ respectively; $p=0.006$), and CSV IRF index ($-0.04\pm0.09\%$ vs $-0.01\pm0.07\%$; $p=0.0019$).

Conclusions: Utilizing a machine learning-enhanced extraction platform, longitudinal volumetric fluid assessment was feasible and demonstrated greater reduction in IRF with IAI at week 100 compared to laser photocoagulation. The 2q4 group demonstrated a greater reduction in IRF at week 100 compared to the 2q8 group.

CONTROL ID: 3710750

SUBMITTER (NAME ONLY): Tadas Naujokaitis

TITLE: Optical quality evaluation and vision simulation of a binocular diffractive multifocal intraocular lens system vs. a conventional diffractive multifocal intraocular lens

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Naujokaitis, G. Labuz, G. Auffarth, Dept. of Ophthalmology, Ruprecht Karls Universitat Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|

Commercial Relationships Disclosure: Tadas Naujokaitis: Commercial Relationship: Code N (No Commercial Relationship) | Grzegorz Labuz: Commercial Relationship: Code N (No Commercial Relationship) | Gerd U Auffarth: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon;Code F (Financial Support):Alcon;Code R (Recipient):Alcon;Code R (Recipient):Cristalens Industrie

ABSTRACT BODY:

Purpose: In the binocular diffractive multifocal intraocular lens (IOL) system Artis Symbiose (Cristalens Industrie, France), in addition to the distance focus, one lens features an extended depth of focus profile for intermediate vision (Artis MID) and the other lens for near vision (Artis PLUS). We performed a laboratory study to evaluate the optical quality of the Artis Symbiose IOL system in comparison with a conventional diffractive multifocal IOL AcrySof IQ PanOptix (Alcon, TX, USA), and to simulate binocular vision with the study IOLs.

Methods: The Artis MID and Artis PLUS IOLs were compared with the AcrySof IQ PanOptix IOL using an optical bench setup. Modulation transfer function and phase transfer function were obtained within the defocus range of +0.75D to -4.0D at spectacle plane in polychromatic light at the aperture of 3 mm using a model cornea with positive spherical aberration. Simulated visual acuity (VA) values were derived from the optical transfer function weighted by the neural contrast sensitivity. The United States Air Force (USAF) resolution chart images were acquired and processed to simulate binocular vision.

Results: All the studied IOLs had a predicted VA of 0.2 logMAR or better throughout the range of +1D to -3D. At distance focus, their simulated VA was minimally better than 0.0 logMAR (range -0.03 to -0.01 logMAR). The peak simulated VA values of the Artis MID were at 0D of defocus (-0.02 logMAR) and at -1.5D (0.00 logMAR); of the Artis PLUS, they were at 0D of defocus (-0.01 logMAR) and at -2.5D (0.01 logMAR). The AcrySof IQ PanOptix demonstrated three peaks: at 0D of defocus (-0.02 logMAR), at -1.75D (0.03 logMAR) and at -2.5D (0.02 logMAR). The binocular summation of the USAF chart images in the simulated binocular system indicated comparable results to those of AcrySof IQ PanOptix. However, at a defocus of 1.0D and -1.5D, the combination of Artis MID and Artis PLUS produced a slightly better image quality.

Conclusions: The binocular multifocal IOL system may yield better intermediate VA and wider defocus range in binocular vision compared to monocular implantation of the conventional multifocal IOL. However, more research is needed to better understand the effect of binocular summation in the binocular multifocal IOL system and in bilateral conventional multifocal IOL implantation.

CONTROL ID: 3710753

SUBMITTER (NAME ONLY): Atalie Thompson

TITLE: Assessing the relationship between contrast sensitivity and lower extremity function in the Brain Networks and Mobility Function (B-NET) study

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Thompson, Ophthalmology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|M.E. Miller, Biostatistics, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|A.C. Thompson, J.D. Williamson, C.E. Hugenschmidt, S. Kritchevsky, Geriatrics and Gerontology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|P. Laurienti, Radiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|F.A. Medeiros, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Atalie Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Michael Miller: Commercial Relationship: Code N (No Commercial Relationship) | Jeff Williamson: Commercial Relationship: Code N (No Commercial Relationship) | Christina Hugenschmidt: Commercial Relationship: Code N (No Commercial Relationship) | Felipe Medeiros: Commercial Relationship(s);Code C (Consultant/Contractor):Aeri Pharmaceuticals; Allergan; Annexon; Biogen; Carl Zeiss Meditec; Galimedix; Stuart Therapeutics; Stealth Biotherapeutics; Reichert; Thea Pharmaceuticals;Code F (Financial Support):Allergan; Reichert; Novartis; Google Inc; Heidelberg Engineering; Genentech;Code P (Patent):nGoggle Inc | Paul Laurienti: Commercial Relationship(s);Code C (Consultant/Contractor):Clostra Inc;Code S (non-remunerative):Clostra Inc | Steve Kritchevsky: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the relationship between contrast sensitivity and lower extremity physical function in a population of high-functioning older adults.

Methods: Cross-sectional analysis of 190 older adults in B-NET who completed baseline contrast sensitivity function, corrected distance visual acuity testing, and lower extremity function using the expanded short physical performance battery (eSPPB).

Results: Participant mean age was 76.4 (range 70.3 – 90.7) years with 56% identifying as female. Presenting corrected logMAR visual acuity was good overall with a mean 0.092 +/- 0.10 and median of 0.097 (range 0 – 0.602), which translates to a mean and median Snellen acuity of approximately 20/25 (range 20/20 – 20/80). Mean eSPPB was 2.0 (Range 0.48, 3.26). Log contrast sensitivity accounted for approximately 6.2% of the variance in baseline eSPPB ($p<0.001$) and remained significantly associated with eSPPB after adjusting for age, sex, and presenting visual acuity ($p=0.009$). A 1-standard deviation lower log contrast sensitivity score was associated with a -0.10 adjusted difference in eSPPB. Similarly, participants with a log contrast sensitivity less than 1.55 had a significantly lower eSPPB score than those with better log contrast sensitivity in both unadjusted (Beta = -0.270, 95% CI (-0.45, -0.09), $p=0.003$) and adjusted models (Beta = -0.216, 95% CI (-0.39, -0.038), $p=0.018$).

Conclusions: Impairment in contrast sensitivity is associated with worse performance on tests of lower extremity physical function, independent of corrected distance visual acuity. These findings suggest there may be a subgroup of older adults with poor contrast sensitivity who may be at risk of decline in physical function despite having good visual acuity and who may benefit from targeted screening protocols and interventions to prevent disability.

CONTROL ID: 3710756

SUBMITTER (NAME ONLY): Steffi Daniel

TITLE: Ocular chemoproteomics for determining broad profiles of enzymatic activities

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Daniel, J. Hulleman, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Steffi Daniel: Commercial Relationship: Code N (No Commercial Relationship) | John Hulleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Changes in expression of several enzymes have been reported in age-related and degenerative ocular diseases. However, the current ‘omics approaches (transcriptomics, proteomics) only determine abundance changes, which does not provide true enzyme functionality (e.g., in the case of propeptide processing or the presence of inhibitors). Chemoproteomics (e.g., activity-based protein profiling [ABPP]) is a versatile tool to broadly probe enzyme class activity and is a technique that has not been fully utilized in vision research. Employing ABPP, we performed an unbiased characterization of active serine hydrolases in mouse eyes and primary ocular cultures.

Methods: Neural retina (NR), RPE, and liver from WT C57BL/6 mice were homogenized and probed with a TAMARA-tagged fluorophosphonate (FP) probe that specifically and covalently labels the active-site of functional serine hydrolases. Samples were analyzed by fluorescent imaging after SDS-PAGE. NR, RPE, liver, and serum were also procured from fibulin-3 knockout (F3 KO) mice (a model that we speculated may have a different serine hydrolase activity landscape) and processed similarly. Lastly, samples (apical, basal, and lysates) from primary porcine RPE cells established on transwells were harvested by ABPP after 1 and 6 mo in culture.

Results: ABPP of serine hydrolases with the TAMARA FP probe revealed a number of differential activities between ocular tissues as well as liver in WT animals. Lower amounts of active serine hydrolases were detected in F3 KO animals in all of the tissues compared to WT littermates. Moreover, TAMARA FP probe was able to detect changes in serine hydrolase activity in polarized RPE cultures, highlighting that serine hydrolase activity is concentrated in the apical fraction, with little activity detected basally or in cell lysates.

Conclusions: Our data demonstrate the ability of ABPP to detect tissue-level differences in activity of serine hydrolases. We also identified polarity-specific differences in serine hydrolase activity of RPE cells and changes therein with culture age. We speculate that ABPPs for additional enzyme classes such as MMPs and cysteine proteases will yield important ocular pathobiology information and may serve as potential biomarkers for impending ocular diseases, enabling researchers to identify and monitor the active location of these enzymes, providing an additional dimension to conventional ‘omics approaches.

CONTROL ID: 3710758

SUBMITTER (NAME ONLY): Judith West-Mays

TITLE: Loss of AP-2β in the Developing Corneal Stroma Results in a Shift in Corneal Epithelial Cell Fate

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. West-Mays, E. Moss, A. Taiyab, Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, CANADA|T. Williams, Depts. of Craniofacial Biology and Cell and Developmental Biology, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Activating Protein-2 beta (AP-2β), encoded by Tfap2b, is a transcription factor expressed in the periocular mesenchyme (POM), which gives rise to the developing corneal stroma. We have previously shown that conditional knock out of AP-2β (AP-2β NCC KO) in the POM of mice causes an anterior segment phenotype that includes a closed iridocorneal angle, absent corneal endothelium and reduced corneal epithelial stratification. Our earlier studies have shown that the mutant corneal epithelium lacks Keratin-12 (K12), a corneal epithelial marker, and instead expresses Keratin-15 (K15), a marker of conjunctival and limbal epithelia. The purpose of this study was to expand our investigation and determine if the AP-2β NCC KO corneal epithelium has shifted to a conjunctival cell fate.

Methods: To generate the AP-2β NCC KO model, male mice heterozygous for Tfap2b, Tfap2b$^{+/-}$, and the wnt1-cre transgene, Wnt1Cre$^{+/-}$, were bred with female mice in which the Tfap2b gene was floxed, Tfap2b$^{lox/lox}$. AP-2β expressing offspring from this breeding scheme were used as age-matched controls. Eyes were enucleated from euthanized 6-month-old mice and processed before being embedded in paraffin. H&E staining along with immunohistochemistry for Muc5AC (Abcam), a goblet cell specific marker, were performed.

Results: Similar to our previous findings for 2-3 month old mutants, the corneal epithelium of 6 month old AP-2β NCC KO mice exhibits significantly reduced stratification. Unlike earlier stages, at this later stage the mutant has numerous vesicles in the superficial layer of the corneal epithelium. With respect to Muc5AC staining, the mutants exhibited regions of positive staining along the epithelium that was not observed in the controls.

Conclusions: The present findings of aberrant expression of Muc5AC in the mutant corneal epithelium, along with earlier data showing phenotypic changes in keratin expression, strongly suggest a shift towards conjunctival cell fate. Thus, expression of AP-2β in the developing POM is critical for regulating corneal epithelial cell fate. Further investigation of the corneal epithelial phenotype in AP-2β NCC KO mutants will contribute to our understanding of epithelial cell fate determination and stratification, and the pathogenesis of diseases marked by corneal thinning, neovascularization and opacification.

CONTROL ID: 3710760

SUBMITTER (NAME ONLY): Jeremy Hatcher

TITLE: Lower Income Affordable Care Act Marketplace Subscribers Face Lower Trabecular Bypass Device Surgery Rates Despite Cost Protection

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hatcher, J. Lindsey, J. Mattingly, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|G. Lin, P. Karnam, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Jeremy Hatcher: Commercial Relationship: Code N (No Commercial Relationship) | George Lin: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Lindsey: Commercial Relationship: Code N (No Commercial Relationship) | Preethi Karnam: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Mattingly: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Social determinants of health, especially insurance status, socioeconomic status, and race, have been linked to poor outcomes in patients with glaucoma. The Affordable Care Act (ACA) was passed to address such disparities in access to care, but there is a paucity of literature assessing its efficacy in facilitating access to ophthalmologic care. We evaluated demographic and cost differences between ACA patients who were eligible for trabecular bypass device (TBD) surgery and did or did not receive it.

Methods: This is a retrospective, claims-based cohort study using a novel 2017 to 2019 claims dataset of Affordable Care Act (ACA) marketplace plan subscribers containing deidentified data about medical conditions, procedures, and associated cost (yearly mean n= 3,560,440). Socioeconomic status was inferred from eligibility for cost-sharing reduction subsidies based on the federal poverty limit. ICD-10 and CPT codes identified patients who underwent cataract surgery and were eligible for TBD surgery (n=653) as well as those who went on to receive TBD surgery (n=249).

Results: A statistically significant difference was found in TBD surgery rates between lower income ACA marketplace subscribers with subsidies and higher income patients who were subsidy ineligible (27.6% vs 43.0%, p=0.0035, multiple logistic regression). Lower income patients paid less out-of-pocket TBD cost due to subsidies ($324 vs $2494, p<0.001, Mann-Whitney U test) compared to higher income patients. Actual out-of-pocket costs for TBD surgery were similar to expected costs as advertised on the ACA website.

Conclusions: This investigation of novel ACA claims data highlights a potential disparity in access to TBD surgery for lower income ACA patients. Despite paying much less out-of-pocket, lower income patients receive TBD surgery at lower rates than their higher income peers. Our study design precludes analysis of the individual decisions that contribute to this difference in rates and the role of race. Our investigation examines health equity using a novel ACA dataset and, to our knowledge, is the first to assess eye surgical referral rates and cost experience among the ACA population.

CONTROL ID: 3710761
SUBMITTER (NAME ONLY): Kirsten Stoner
TITLE: Updated Miyake Technique for Anterior Intraocular Imaging
SESSION TITLE: Multidisciplinary Ophthalmic Imaging
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Stoner, K. Pfeffer, M. Hedgeland, S. Camacho Gonzalez, T. Meyer, Device Development, Gyroscope Therapeutics, King of Prussia, Pennsylvania, UNITED STATES|
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ABSTRACT BODY:

Purpose: Recent advancements in treatments for ocular diseases have led to many novel, anterior interfacing medical devices and surgical procedures. This necessitates new methods for visualizing device-tissue interaction and assessing the preclinical performance of these medical devices. One valuable method for visualizing the internal, anterior surface of the eye is the 2004 Miyake-Apple technique. The purpose of this study was to modernize this method using current camera technology.

Methods: Whole human cadaver eyes (LionsGift) were obtained within 72 hours of donor death. A 25-gauge valved Alcon port was inserted to allow for infusion and intraocular illumination of the eye. Rather than slicing the eye in half as previously done in the Miyake-Apple technique, a 8.2mm temporary keratoprosthesis (TKP) was sutured to the posterior of the eye providing an opening for anterior visualization. A custom designed, 3D printed, fixture (Figure 1) held both the eye and a 4K USB web camera utilizing a Sony IMX317 sensor and 20-degree manual focus lens. The eye was secured to the fixture by holding the optic nerve with an alligator clip. A High-Resolution Volk Wide Field Lens was placed into the channel below the sutured TKP. The camera was aligned with the wide field lens and manually focused. Videos and images were then captured utilizing the camera application on a laptop with the USB camera connected.

Results: This custom setup provided high resolution still and video imaging of the intraocular anterior surface of the eye (Figure 2). The wide field lens allowed for visualization from the apex of the cornea to approximately 13mm from the limbus. Anatomic features such as the pupil, intraocular lens, ciliary bodies, pars plana, and choroidal vasculature were clearly visible.

Conclusions: This updated Miyake-Apple technique provides a useful tool for visualizing the anterior surface of the eye. As the globe remains almost fully intact, tissue connectivity is undisturbed which provides a robust anatomic model with visualization for surgical testing. In the future, this model could be used for preclinical assessment of placement and fixation of intraocular lens and drug eluding implants in addition to visualization of intravitreal or suprachoroidal injections and suprachoroidal cannulation.

CONTROL ID: 3710762

SUBMITTER (NAME ONLY): Shihij Takoo

TITLE: Effect of cycloplegia on contrast sensitivity measured by the Ohio Contrast Cards

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Takoo, A. Toole, A. Brown, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Shihij Takoo: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Toole: Commercial Relationship: Code N (No Commercial Relationship) | Angela Brown: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To measure the repeatability of contrast sensitivity measured using the Ohio Contrast Cards (OCC), before and after cycloplegia, in a general pediatric optometric population. The OCC (Precision-Vision, Woodstock IL) present 0.15 cy/deg horizontal square-wave gratings of variable contrast (stepsize=0.15 Log10 units) on cards similar to the Teller Acuity Cards.

Methods: We used the OCC to measure monocular contrast sensitivity (CS) on 41 non-amblyopic children (ages 4-11, mean=7.8, SD=2.1). Each child's CS was measured twice, by different examiners, before their routine, dilated, cycloplegic eye exam. After the exam, when the eyes were still cyclopleged (Tropicamide, Cyclopentolate, or both), CS was measured again. Children who wore glasses were tested with their glasses on before and after the exam, and again after the exam, without their glasses. Refractive errors were obtained by wet retinoscopy. The study was powered to reveal a test-retest difference of one card at corrected $p<0.05$ with power=0.90. We compared the results of the first test, which was pre-cycloplegia and pre-exam, to the results of the post-cycloplegia, post-exam test. For children who wore glasses, we compared the pre- and post- tests with glasses on; otherwise we compared tests with glasses off.

Results: The pre-exam and post-exam results were similar (mean LogCS=2.07, SD=0.14; mean LogCS difference=0.01, SD=0.12). The 95% limits of agreement (±1.96 x SD[difference]) were ±0.24 Log units, and weighted Cohen's K=0.59, 95% CI=0.38–0.80. Under cycloplegia, the uncorrected blur for horizontal gratings at the test distance was +0.08 D to +5.27 D (mean=1.71 D, SD=1.08 D), and uncorrected CS under cycloplegia was not associated with blur (r= -0.01, p=0.94). Mean LogCS, measured across the two pre-exam tests was 2.07 (SD=0.15), and those were also closely similar (mean difference=0.02 Log units, SD=0.12) and highly correlated (r=0.73, $p<0.0001$), and the intra-examiner repeatability was high (weighted K=0.70, 95% CI=0.53–0.87).

Conclusions: The Ohio Contrast Cards show good repeatability in this population when pre-exam pre- cycloplegia tests are compared to post-exam post-cycloplegia tests, indicating that the cards can be used without regard to cycloplegia. There is no significant effect of refractive error on the measurements, showing that the Ohio Contrast Cards is an effective near test used under cycloplegia on a range of refractive errors.

CONTROL ID: 3710764

SUBMITTER (NAME ONLY): Minjuan Bian

TITLE: BDNF/TrkB activation and repolarization increase local translation of axonal targeting reporter mRNA in distal growth cones

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bian, E. Huie, M. Nahmou, J.L. Goldberg, Spencer Center for Vision Research, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Minjuan Bian: Commercial Relationship: Code N (No Commercial Relationship) | Emma Huie: Commercial Relationship: Code N (No Commercial Relationship) | Michael Nahmou: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Goldberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Highly polarized and compartmentalized neurons respond rapidly and precisely to surrounding stimuli at long distances. This capacity has been linked in part to specific RNA localization and local translation. 3' untranslated regions (3'UTRs) regulate RNA localization. In this study, we explored RNA translation and dependence on 3'UTRs in axonal growth cones of hippocampal neurons expressing axonal targeting 3'UTR, dendrite targeting 3'UTR and no 3'UTR in vitro, to explore mechanisms involved in regional growth cone translation.

Methods: We generated constructs carrying photoswitchable fluorescent reporter Dendra^{myr} with axonal targeting GAP43-3'UTR, dendrite targeting Nrgn-3'UTR, and no 3'UTR. Dendra signals in growth cones were recorded in primary hippocampal neuron cultures before and after photoswitching to observe local translation-dependent recovery of Dendra signal, with and without protein synthesis inhibitors. Growth cone protein synthesis was also studied in response to treatment with brain-derived neurotrophic factor (BDNF), forskolin, and KCl-induced depolarization and repolarization.

Results: Neurons expressing axonal targeting Dendra^{myr} 3'GAP43 showed recovery of Dendra signal in distal growth cones 40 minutes after photoswitching; treatment with anisomycin disrupted recovery, demonstrating that recovery was due to local new protein synthesis. No significant recovery was observed in neurons with the expression of Dendra^{myr} 3'Nrgn or Dendra^{myr} controls. Axon-targeted Dendra translation increased with 2 hours treatment with BDNF and was even greater with combination treatment with BDNF and forskolin. KCl-induced depolarization for 2 hours increased local translation, whereas 20 hours of KCl decreased of local Dendra signal after photoswitching. The disruption of local Dendra translation in growth cones after 20 hours incubation with KCl was restored after washing out KCl.

Conclusions: BDNF/TrkB activation increases local translation of axon-targeted mRNA in distal growth cones; cellular repolorization restores long-term depolarization induced disruption of local protein synthesis of reporter Dendra in distal growth cones. Live cell recording distal growth cones in primary neurons expressing axon-targeting Dendra^{myr} 3'GAP43 is a promising platform for screening of candidates that support local translation and promote axon growth.

CONTROL ID: 3710766

SUBMITTER (NAME ONLY): Lindsay Gugerty

TITLE: CCHS Diabetic Retinopathy Screening Project: A Retrospective Review.

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Gugerty, P. Ko, C. Cox-Wong, J.D. Henderer, Christiana Care Health Services Inc, Wilmington, Delaware, UNITED STATES|J.D. Henderer, Temple University Health System Inc, Philadelphia, Pennsylvania, UNITED STATES|L. Gugerty, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Lindsay Gugerty: Commercial Relationship: Code N (No Commercial Relationship) | Paula Ko: Commercial Relationship: Code N (No Commercial Relationship) | Constance Cox-Wong: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Henderer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Non-mydriatic digital retinal imaging can improve patient access to diabetic retinal screening exams. We performed a retrospective review to determine if digital retinal imaging could be utilized in the Christiana Care Health System (CCHS) primary care setting to identify pathology and assist those needing follow-up. This technology could be crucial in maintaining patients' health in a cost-effective way.

Methods: Diabetic patients aged 18 years and older who participated in the Intelligent Retinal Imaging System (IRIS, Pensacola, FL) retinal screening initiative at four primary care clinics in the Christiana Care Health System (Wilmington, DE) from September 2018 to November 2020 were included. Photos were taken by clinic staff using the Volk Pictor Plus Fundus camera. Retinal images were interpreted by CCHS-affiliated ophthalmologists using a modified ICDR system and the results communicated to the primary care clinic via IRIS. IRIS data and the electronic medical record (EMR) was utilized to record the screening result and follow-up recommendations. Outcomes of interest included number of interpretable images, the pathology identified, documentation of referral, and number of patients who completed a follow-up exam.

Results: 613 patients (1226 eyes) underwent the screening exam but there was no documentation of an exam result in the EMR for 50 (8.1%) patients. Of the 411 patients (73%) who had bilateral interpretable images, 323 (78.6%) of patients had no pathology in either eye. 88 patients had a referrable diagnosis which included 53 with diabetic retinopathy ((60.2%) (35 mild, 12 moderate, 2 severe, 4 proliferative), and a mixture of other suspected diseases. For the 238 patients (42.3%) uninterpretable or diseased patients for whom follow-up was recommended, 165 patients (69.3%) had referrals generated by the primary care physician. Of these, 65 (39.4% and 27.3% of the original 238) had a follow-up exam with an optometrist or ophthalmologist documented in the EMR.

Conclusions: Utilizing the IRIS protocol, the majority of patients were able to complete a diabetic screening. However, taking quality photographs remains a limitation. The majority of patients who needed a follow-up referral received one, yet a minority of patients followed through with the exam. We have found several areas to improve: importing IRIS exams into the EMR, generating referrals, and patient follow-up. Our next step is to address these issues.

CONTROL ID: 3710769

SUBMITTER (NAME ONLY): Crystal Colón Ortiz

TITLE: Endothelial-astroglial caspase-9 signaling alters contrast sensitivity in a mouse model of retinal vein occlusion (RVO)

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.K. Colón Ortiz, M. Avrutsky, M. Choi, J. Smart, C.M. Troy, Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|A.M. Neal, Barnard College, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ischemic retinal injuries are a major cause of blindness with limited treatment options. Endothelial caspase-9 (EC Casp9) loss was previously reported to decrease retinal edema and neuronal death in a mouse model of Retinal Vein Occlusion (RVO). But its role on modulating the astroglial response and visual function remained unknown. This study tested the hypothesis that the endothelium and astrocytes share caspase-9 signaling that contributes to contrast sensitivity decline in retinal vein occlusion (RVO).

Methods: We performed RVO in inducible EC-Casp9 (iEC Casp9 WT/KO) and astroglia caspase-9 (iAstro Casp9 WT/KO) adult male and female mice by tail vein injection of Rose Bengal and photocoagulation of major retinal veins. Contrast sensitivity was tested pre RVO and 1-day post-RVO (P-RVO) using Striatech's OptoDrum System at visual acuity ranges 0.05, 0.15, and 0.25 cycles/°. Retinas were collected 1- and 2-days post RVO (P-RVO). Immunohistochemistry against cl-caspase-9, cl-caspase-6, GFAP, Nestin and AQP-4 was followed by blind quantification using thresholding analysis in FIJI. Data was evaluated in injured iEC/iAstro Casp9 WT (n=6-8), iEC/iAstro Casp9 KO (n=4-9), and uninjured groups (iEC/iAstro Casp9 WT, n=3-6, iEC/iAstro Casp9 KO, n=3-6). One-way ANOVA followed by Fisher's LSD test was used for statistical analysis.

Results: Loss of EC-Casp9 led to a decrease in astroglial cl-caspase-9 and a significant decline in downstream effector cl-caspase-6 1- and 2-days P-RVO compared to injured iEC-Casp9 WT ($p=0.02$, $p=0.004$). Injured EC-Casp9 WT/KO did not show differences in GFAP, but a significant decline in AQP-4 expression was noted 1 day P-RVO when compared to uninjured controls ($p=0.01$). Nestin increased significantly at 2 days P-RVO in injured EC-Casp9 WT compared to uninjured controls ($p=0.008$) and injured EC-Casp9 KO ($p=0.02$). Astroglial caspase-9 loss led to a significant decrease in cl-caspase-6 ($p=0.02$) and no changes in GFAP. Knockout of caspase-9 in the endothelium or astrocytes significantly rescued contrast sensitivity decline after vascular injury compared to iEC/iAstro Casp9 WT at low acuity values ($p=0.02$).

Conclusions: Our results demonstrate that EC Caspase-9 contributes to astroglial caspase-6 and Nestin expression after injury. Moreover, that endothelial-astroglial caspase-9 signaling is relevant for contrast sensitivity decline in RVO.

CONTROL ID: 3710770

SUBMITTER (NAME ONLY): Jessica Shantha

TITLE: Systemic and Laboratory Risk Factors for Retinopathy and Detection of Tear Film SARS-CoV-2 RNA

SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Shantha, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|T. Fashina, S. Yeh, University of Nebraska Omaha, Omaha, Nebraska, UNITED STATES|V. Simmons, C. Randleman, L. Ward, M. Regueiro, S. Linderman, R. Ahmed, J. Waggoner, Emory University, Atlanta, Georgia, UNITED STATES|C. Drews-Botsch, The George Washington University Milken Institute of Public Health, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coronavirus-19 (COVID-19) has been associated with ophthalmic manifestations. The relationship between tear film SARS-CoV-2 RNA, timing of illness and eye disease are unknown. We evaluated hospitalized COVID-19 inpatients for retinopathy and tear film viral RNA.

Methods: Hospitalized COVID-19 inpatients were offered enrollment from January-June 2021. Full dilated ophthalmic examination and conjunctival swabs were taken for triplex RT-PCR for SARS-CoV-2 RNA targeting N2, E and RNAse P. Demographic, clinical outcomes and laboratory data were collected. Univariate and multivariate analyses of systemic disease and laboratory risk factors for retinopathy and SARS-CoV-2 RNA detection were assessed.

Results: Sixty patients were prospectively enrolled in this cross-sectional, observational study. The mean age was 58.8 years (Standard deviation [SD] 15.2 years) and 29 (48%) were female. Retinopathy associated with COVID-19 in 12 of 60 patients (20%). Univariate analyses revealed that younger age, greater body mass index (BMI) and extracorporeal membrane (ECMO) requirement were associated with increased odds of COVID-19 retinopathy. The mean age (SD) of patients with COVID-19 retinopathy was 49.0. (11.6) compared to 61.2 (15.1) years in individuals without retinopathy (p=0.01). The mean BMI was 38.8 (9.8) in patients with retinopathy compared to 31.8 (9.0) in those without retinal disease findings (p=0.04). ECMO requirement was observed in 33% of patients with retinopathy compared to 8% in those without retinopathy (p=0.04). Multivariate analyses trended towards increased risk of retinopathy with younger age (aOR 0.95 (95% CI 0.90-1.01, p=0.095) and with increased BMI (aOR. 1.08, 95% CI 1.00-1.18, p=0.056). Fifteen of 60 patients (25%) tested positive in their tear film for SARS-CoV-2 RNA with a trend towards a shorter length of illness and hospitalization in patients who were positive. The N2 gene was particularly sensitive with 18 of 19 eyes (94.7%) showing N2-positivity (with or without E gene detection), including 2 patients in whom the B.117 / B.1.525 alpha or “United Kingdom” variant was detected.

Conclusions: A 20% rate of retinopathy was observed and SARS-CoV-2 RNA within tear film was detected in 25% of hospitalized COVID-19 patients. Continued infection control precautions are required given the risk of viral RNA in tear film, which may also be sensitive for the detection of COVID-19 variants.

CONTROL ID: 3710771

SUBMITTER (NAME ONLY): Tanya Sheth

TITLE: In Vivo Confocal Microscopy Reveals Cellular and Structural Abnormalities in Patients with Definite Ocular Graft-vs-Host Disease (oGVHD)

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sheth, B. Surenkhuu, J. Mun, A. Garcia, D. Hernandez-Castro, A. Pradeep, C. Mun, S. Jain, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate and compare cellular and structural abnormalities in the cornea between patients who develop definite oGVHD after hematopoietic stem cell transplantation (HSCT) and patients who do not develop oGVHD.

Methods: Patients who received HSCT were evaluated in the University of Illinois at Chicago (UIC) Dry Eye and oGVHD Clinic and classified as having definite oGVHD or none oGVHD using the international consensus classification system based on symptom analysis, corneal staining, Schirmer's I test, and conjunctival redness. In vivo confocal microscopy (IVCM) was performed using HRT3 RCM (Heidelberg Engineering, Franklin, MA) to evaluate the corneal epithelium, nerve plexus, and stroma. Abnormalities detected were compared between groups.

Results: Patients with definite oGVHD (n= 100 eyes) had significantly greater abnormalities in the epithelium (21% vs 4.7%; $p < 0.05$) as compared to none oGVHD (n=86 eyes). Epithelial abnormalities included loss of hexagonal shaped cells in a honeycomb pattern with homogenous cell border reflectivity. The number of patients with complete loss of sub basal nerve plexus was significantly greater in definite oGVHD as compared to none oGVHD (20% vs 2%; $p < 0.05$). Sub basal nerve plexus in definite oGVHD patients also showed increased beading of nerves and presence of spindle shaped cells in the nerve plexus area as compared to none oGVHD. The corneal stroma in definite oGVHD and none oGVHD did not show significant differences other than increased reflectivity in definite oGVHD patients.

Conclusions: Patients with definite OGVHD have significant cellular and structural abnormalities in the cornea that may include abnormal epithelium morphology, loss of corneal nerves, and presence of presumed inflammatory cells in the nerve plexus area.

CONTROL ID: 3710778

SUBMITTER (NAME ONLY): Ales Cvekl

TITLE: ROLE OF CHROMATIN AND DNA METHYLATION IN MOUSE LENS DIFFERENTIATION

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Cvekl, W. Chang, Ophthalmology and Visual Sciences, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|Y. Zhao, M. Suzuki, D. Zheng, Genetics, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|Q. Xie, MCD Biology, University of California Santa Cruz, Santa Cruz, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cellular differentiation is marked by temporally and spatially coordinated gene expression regulated at multiple levels, including chromatin landscape dynamics. DNA methylation represents a universal mechanism to control chromatin organization, compaction and its accessibility.Cytosine methylation of CpG dinucleotides regulates binding of methylation-sensitive DNA-binding transcription factors. Earlier studies in mouse lens examined function of DNA methyltransferases Dnmt1, Dnmt3a and Dnmt3b; however, analysis of DNA methylation during lens fiber cell differentiation remains to be determined.

Methods: Using whole genome bisulfite sequencing (WGBS), we investigated dynamics of DNA methylation changes during mouse lens fiber cell and epithelium differentiation between embryos (E14.5) and newborns (P0.5) using microdissected lenses. Embryonic stem (ES) cells and neural progenitor cells (NPCs) data were used for comparisons. To link these data with general chromatin structure and gene expression, our earlier ATAC- and RNA-seq datasets were included. Role of CpG methylation on Pax6 binding was analyzed using lens ChIP-seq data and in vitroanalyses using a set of methylated and unmethylated prototypic Pax6-binding sites.

Results: Major differences in DNA methylation between lens, ES and NPC cells were found. For example, both Pax6and Prox1loci show low and unmethylated regions in lens cells compared to both ES and NPC cells. Within the microdissected lens cells, we identified DNA methylation and “open” chromatin changes by defining differentially methylated and/or accessible regions during mouse lens fiber cell (Path1: epi/E14.5-fib/E14.5-fib/P0.5) and epithelium (Path2: epi/E14.5-epi/P0.5) differentiation. For example, ATAC- and RNA-seq data demonstrate that reduced methylation is directly linked with increased expression of fiber cell abundant genes, including crystallins, intermediate filament proteins Bfsp1 and Bfsp2, and gap junction proteins Gja1 and Gja8. Both in vivoand in vitrodata show that CpG methylation is not detrimental for Pax6 binding to DNA.

Conclusions: Our study has generated the first data on DNA methylation changes between two different mouse lens developmental points and linked these data with chromatin accessibility domains and gene expression. Our data support the model that between E14.5 and P0.5, DNA demethylation modulates gene expression of critical genes required for lens morphogenesis.

CONTROL ID: 3710780
SUBMITTER (NAME ONLY): David Marshak
TITLE: Synaptic inputs to macaque intrinsically-photosensitive ganglion cells
SESSION TITLE: Retinal ganglion cells and central processing
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: D.W. Marshak, A. Bordt, Neurobiology & Anatomy, McGovern Medical School, Houston, Texas, UNITED STATES|S.S. Patterson, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|S.S. Patterson, J. Kuchenbecker, J. Neitz, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|J. Yearick, E. Yang, Biosciences, Rice University, Houston, Texas, UNITED STATES|J. Ogilvie, Biology, Saint Louis University, Saint Louis, Missouri, UNITED STATES|
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ABSTRACT BODY:

Purpose: The goal of this study was to identify the neurons that make synapses onto intrinsically-photosensitive retinal ganglion cells (ipRGCs) with somas located in the inner nuclear layer (INL), also known as the “displaced” type. The working hypothesis was that there were two distinct types of displaced ipRGCs, including one with input from OFF bipolar cells.

Methods: Three pieces of central macaque retina were fixed and stained en bloc with heavy metals. Sets of horizontal sections were acquired using scanning block-face serial electron microscopy. The ipRGCs were readily identified by the large diameters of their somas relative to others in the INL and by the lipofuscin granules they contained. They were analyzed using the Viking Annotation System and SBFSEM-tools. The presynaptic cells were also analyzed and identified morphologically.

Results: The volumes located about 2 mm temporal and 1.25 mm nasal to the center of the fovea each contained one ipRGC with its soma in the INL. Their dendrites had a large diameter and formed very sparse arbors confined entirely to the outermost stratum (S1) of the inner plexiform layer (IPL), and their axons were varicose. The volume located about 1.5 mm inferior to the center of the fovea contained somas of two ipRGCs, one similar to those in the other volumes and one smaller type with distal dendrites that gradually descended into the inner half of the IPL. All four ipRGCs received the majority of their inputs from amacrine cells. These likely included axons of dopaminergic amacrine cells with somas located outside the volumes. The smaller displaced ipRGC received virtually all of its excitatory input from five types of ON bipolar cells, mainly via the distal dendrites. The three larger displaced ipRGCs each received input from three types of OFF bipolar cells: DB1, DB2 and OFF midget (see figure). These would generate robust OFF responses in the larger displaced ipRGCs under a wide variety of conditions.

Conclusions: The larger type of displaced ipRGCs are likely the source of OFF responses recorded recently from human ipRGCs using microelectrode arrays. Input from the OFF pathway may account for the “paradoxical” pupillary responses seen in some patients with congenital stationary night blindness.

CONTROL ID: 3710781

SUBMITTER (NAME ONLY): Elias Mullane

TITLE: Hypercitrullination in a Genetic Model of Spontaneous Retinal Degeneration and Laser Injury Model of Gliosis

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Mullane, S.I. Palko, H. Sun, P. Bargagna-Mohan, R. Mohan, University of Connecticut Health Center, UConn Health, Farmington, CT, US, academic/hospital, Connecticut, UNITED STATES|E. Mullane, R. Mohan, University of Connecticut School of Medicine, Farmington, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: High-power laser models of murine injury have been used to create clinically visible lesions, the study of which has illuminated angiogenesis targets for wet age-related macular degeneration (wet-AMD). We developed a laser injury model featuring subclinical lesions in one quadrant of the retina to elicit retinal gliosis. We also exploited a genetic model of retinal degeneration (JR5558 mouse line), investigating gliosis and the peptidyl arginine deiminase-4 (PAD4)-citrullination axis in both these models.

Methods: A cluster low-power laser protocol (CLPLP) was established where C57Bl6 mice received 9 consecutive pulses of 50 mW for 5 seconds each applying 5 such burns in a cluster to one quadrant of the retina. The conventional laser protocol (CLP; 250 mW 100 msec) was also employed. Non-injured mice and laser injured cohorts were sacrificed along a 7 to 30 day post-injury time course. JR5558 mice were sacrificed at 30 and 60 days of age. Eyes were cryosectioned, antibody stained for glial fibrillary acidic protein (GFAP), citrullination (F95), citrullinated-GFAP and PAD4, then analyzed by epifluorescence microscopy.

Results: In the CLP, fundus imaging reveals bright autofluorescence of the lesion sites at time of injury, remaining visible for extended time periods. In the CLPLP, cluster injury is barely noticeable and rapidly resolved, suggesting the CLPLP models subclinical levels of injury. When retinas from CLPLP were co-stained for GFAP and F95, Muller cell-specific expression was observed at the lesion. PAD4 expression was also observed, however with reduced expression compared to CLP. In the JR5558 mouse line spontaneous lesions revealed striking upregulation of GFAP in Muller cell processes spanning the retina. Remarkably, GFAP citrullination along Muller cell processes starting at the endfeet was observed along with PAD4 expression.

Conclusions: We previously reported that retinal gliosis and hypercitrullination initiates in the endfeet following the CLP, and citrullinated GFAP is also seen in human wet-AMD maculae. We extend this study showing sub-clinical features of retinal pathology created with CLPLP also feature these biomarkers. Furthermore, as the PAD4-hypercitrullination axis is also engaged in the endfeet of JR5558 mice, we propose that Muller glial endfeet are a ‘citrullination bunker’ that initiates and sustains citrullination in retinal degeneration.

CONTROL ID: 3710782

SUBMITTER (NAME ONLY): Robert Mullins

TITLE: Molecular Characterization of Neovascular AMD in Human Eyes using Spatial Transcriptomics and Single Cell RNA Sequencing

SESSION TITLE: Single cell analysis in retinal research in health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.F. Mullins, A.P. Voigt, T.E. Scheetz, N.K. Mullin, M.J. Flamme-Wiese, E.M. Stone, I. Han, B.A. Tucker, University of Iowa Institute for Vision Research, Iowa City, Iowa, UNITED STATES|R.F. Mullins, A.P. Voigt, T.E. Scheetz, N.K. Mullin, M.J. Flamme-Wiese, E.M. Stone, I. Han, B.A. Tucker, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa, UNITED STATES|L. Lin, Department of Neuroscience and Pharmacology, University of Iowa, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neovascular age-related macular degeneration (nvAMD) is a major cause of vision loss. Although very effective treatments exist for nvAMD, these require intervention after the rupture of Bruch's membrane, require multiple treatments, and may be associated with increased risk of atrophy after prolonged treatments. Discovering how neovascular endothelial cells from human eyes differ from non-neovascular cells at the transcriptional level will provide new knowledge about the process of pathologic angiogenesis and may offer opportunities for prevention.

Methods: Three frozen sections were collected from a macula with an extensive type I neovascular membrane (death to freezing interval < 5 hours) and two frozen sections were collected from an age-matched control eye. The spatial transcriptome of each section was evaluated using the Visium platform. Gene expression profiles from each spot were integrated with an independent collection of single-cell expression data comparing the choroid of nvAMD maculas (n = 2), non-neovascular, early AMD maculas (n = 9), and control maculas (n = 9).

Results: Spatial transcriptomics identified three retinal layers, with distinct ganglion cell, interneurons/glia, and photoreceptor cell-associated genes in spots corresponding to ganglion cell layer, inner nuclear layer, and outer nuclear layer, respectively (Figure 1). Twenty four genes were identified with a log fold change of >0.2 between both (a) spots overlapping with neovascular membranes and those in the choroid outside of neovascular membranes and (b) nvAMD single-cells vs controls . These include genes involved in cytoskeleton (TUBA1A, TUBA1B), extracellular matrix (FN1) and stress responses (SOD2, GADD45B).

Conclusions: Spatial transcriptomic analysis of the macula reliably maps transcripts to their cellular sources. Cells from neovascular membranes have altered transcriptomes compared to both the peripheral choroid outside of the CNV lesion and from non-AMD maculas. These two experiments identify several genes enriched in neovascular AMD that may offer insight into pathogenic angiogenesis.

CONTROL ID: 3710785

SUBMITTER (NAME ONLY): Danilo Aleo

TITLE: Stability and Safety of Peptide Based Formulation for the Potential Treatment of Digital Eye Strain Diseases

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Aleo, S. Mangiafico, B. Melilli, M. Saita, F. Spitaleri, M. Cro, R&D, Medivis srl, Tremestieri Etneo, Catania, Italy, ITALY|

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ABSTRACT BODY:

Purpose: Digital Eye Strain Diseases are rapid increasing disorders linked to the growing and more prolonged use of video terminals. To date, the only way to mitigate these disorders is using tear substitute or reducing the exposure to the electronic devices. Focus of our research was the development of an eye drop (MDV 2101) based on a specific peptide (MDV PEPTIDE) able to relieve strain of the ocular muscles. Well demonstrated pharmacological activity of the peptide (MDV PEPTIDE) comprises the attenuation of the eye muscle contraction regulating the release of Acetylcholine and so the binding between the neurotransmitter and their receptors in the muscle.

Methods: MDV 2101 is an isosmotic aqueous solution containing 50 ppm of MDV PEPTIDE in a new and patented Hyaluronic Acid drug delivery system. The stability of the formulation has been executed by means HPLC analysis, Osmolarity and pH changes. The safety of MDV2101 was evaluated by cellular viability using in vitro human corneal cells model (HCE-SkinEthic), through MMT assay.

Results: We found out that the MDV PEPTIDE in the formulation was stable after 24 months at 25°C, pH and osmolality did not exhibit any variation too. The MMT results after 30 min (irritation test) and 24h (cytotoxicity test) of MDV2101 contact time suggested absence of direct toxicity and no epithelial surface damage (viability >98% versus negative control - PBS).

Conclusions: MDV2101, safe and stable under our experimental conditions, thanks to the peculiar mechanism of action of MDV PEPTIDE, may be a helpful candidate to relieve Digital Eye Strain Syndrome symptoms.

CONTROL ID: 3710786

SUBMITTER (NAME ONLY): Kourosh Sabri

TITLE: Current Visual Acuity and Refractive Errors among Indigenous Children in Northern Canada

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sabri, McMaster Children's Hospital, Hamilton, Ontario, CANADA|K. Sabri, Y. Jindani, M. De Melo, McMaster University, Hamilton, Ontario, CANADA|E. Innes, S. Kioke, Weeneebayko Area Health Authority, Moose Factory, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The health inequalities that exist between Indigenous and non-Indigenous Canadians begin in childhood and diverge further from this foundational developmental period. Indigenous children are at high risk for visual impairment (VI) due to limited access to vision care services with a risk of blindness six times greater than non-Indigenous children. These communities consist of a large youth demographic with 28% under the age of fourteen. This study provides data on prevalence and causes of VI in Indigenous children living in remote northern Ontario, Canada.

Methods: This cross-sectional study included 259 Indigenous children aged 8 months to 18 years living in remote northern communities along James Bay, Ontario served by the Weeneebayko Area Health Authority. All children underwent at least one complete eye examination between November 2020 and November 2021, including cycloplegic refraction.

Results: Of the 259 children examined (age range 0.67 to 18 years, mean 10.3, median 9.0 years) the main cause of treatable or avoidable VI was uncorrected refractive error. Of the examined children, 203 (78%) had refractive errors, of which, 156 (77%) did not use correction. Visual acuity (VA) was measured in 518 eyes of 259 subjects and ranged from 20/15 to counting fingers (CF). Of the 203 children with refractive error, 69 (34%) experienced mild VI, (VA worse than 20/40 up to 20/60 in the better-seeing eye), 55 (27%) experienced moderate VI, (VA worse than 20/60 up to 20/200 in the better-seeing eye) and 12 (6%) children experienced severe VI, (VA worse than 20/200 in the better seeing-eye). The overall prevalence of myopia was 33% (85) (range -0.5DS up to -7.0DS of eyes examined, mean -2.3DS, median -2.0DS) and of hyperopia was 29% (76) (range +0.5DS up to +7.0DS of eyes examined, mean +1.8DS, median +1.5DS). Astigmatism was evident in 66% (171) (range -0.5DC up to -5.5DC of eyes examined, mean -2.0DC, median -1.8DC). Of the 259 children, 107 (41%) had never previously received an eye examination.

Conclusions: These findings suggest high rates of uncorrected refractive error, particularly astigmatism, resulting in poor vision among Indigenous children. There is an urgent need to address the gap in the delivery of eye care to Indigenous Canadians.

CONTROL ID: 3710788

SUBMITTER (NAME ONLY): Kyung-No Son

TITLE: Scalable production and testing of overexpressed TMEM97

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Son, D. Shah, S. Lee, M. Ali, V.K. Aakalu, Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: TMEM97 is an important endoplasmic reticular protein involved in cell migration, cancer, cholesterol processing, and neurodegenerative diseases. Histatins are a family of endogenous antimicrobial peptides that have numerous effects in multiple biological systems. Histatin-1 (Hst1) has roles in epithelial wound healing and migration. We recently showed, using biophysical and biological methods including co-immunoprecipitation, and surface plasmon resonance (SPR) that Hst1 is an endogenous ligand for TMEM97. We also determined that presence of TMEM97 was necessary for Hst1 to exert pro-migratory effects in corneal epithelia. Given the growing understanding that TMEM97 is important to ophthalmic biology, we sought to generate a method to scalably produce TMEM97 in an E. coli for future experiments. Commercially sourced TMEM97 is costly and is produced in eukaryotic systems. We validated the function of the E. coli expressed protein utilizing previously tested methods as well as a new orthogonal method [isothermal titration calorimetry (ITC)].

Methods: BL21DE3 cell culture pellets containing His-TEV-TMEM97 was processed and lysate underwent HisTrap affinity and SEC 16/600 SD200 purification. TMEM97 (108-176) was prepared in 10 mM Tris, pH 7.4, 150 mM NaCl, 0.05% Tween-20. All ITC experiments were performed while stirring at 395 rpm using a VP-ITC titration microcalorimeter from MicroCal™, LLC (Northampton, MA). TMEM97 purchased from OriGene and His-TEV-TMEM97 in E.coli were prepared in HBS buffer containing 10 mM HEPES, pH 7.4, 150 mM NaCl, and 0.05% n-dodecyl-β-D-maltoside (DDM). The CM5 sensor surface was first activated by 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC)/N-hydroxy succinimide (NHS) mixture using a Biacore T200 or Biacore 8K instrument (GE Healthcare).

Results: We confirmed that Hst1 bound both commercially sourced and E. coli expressed TMEM97 utilizing. ITC was also performed as an orthogonal analytical method. Utilizing ITC we found that Hst1 bound TMEM97 with high affinity.

Conclusions: This study establishes a scalable research grade method for production of TMEM97, which demonstrates high-affinity binding to Hst1. Furthermore, we were able to demonstrate the binding between Hst1 and TMEM97 using a previously unreported method, ITC. This method will allow future research studies requiring large quantities of TMEM97 to better understand the importance of this protein to ophthalmic cellular function.

CONTROL ID: 3710793

SUBMITTER (NAME ONLY): Ching Yi Wu

TITLE: Defining the phenotype and distribution of resident immune cells surrounding meibomian gland orifices in mice

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Wu, L.E. Downie, H.R. Chinnery, Optometry and Vision Sciences, The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|C. Wu, C. Maldonado-codina, P. Morgan, The University of Manchester, Manchester, Manchester, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Inflammation and keratinisation of the meibomian glands (MGs) and MG orifices (MGOs) are pathophysiological mechanisms involved in MG dysfunction (MGD). However, the normal immune cell (IC) profile of MGOs, which act as an interface between the external environment and internal glandular duct, has not been clearly defined. The aim of this study was to determine the presence, phenotype and distribution of MG orifice-associated immune cells (MOICs) in healthy young and aged mice.

Methods: Flatmounts of the superior and inferior eyelids of young (i.e. 12-15-week old; n=9-12/group) and older (i.e. 21-29-week old; n=5-6/group) $CD11c^{eYFP}$ and Cx3cr1-deficient $Cx3Cr1^{GFP/GFP}$ mice were used. $CD11c^{+}$ dendritic cells (DCs) and $Cx3cr1^{+}$ ICs surrounding MGOs were visualized using four-colour immunofluorescent confocal microscopy. Eyelids were incubated with antibodies targeting MHC-II^{+} ICs, and F-actin to visualise MGOs. MOIC density (cells/mm^2) within a normalized peri-orifice area, relative to the MGO area, were quantified. Two adjacent MGOs in the nasal, central and temporal regions of both superior and inferior eyelids were analysed.

Results: In descending order of average density, $CD11c^{+}$ DCs (abundant), MHC-II^{+} and $Cx3cr1^{+}$ (scarce) ICs were identified at MGOs. More MOICs expressed $CD11c^{+}$ nasally than temporally in young mice (nasal 942±391 vs temporal 680±348 cells/mm^2, p=0.0199), but not in older mice (nasal 932±592 vs temporal 611±446 cells/mm^2 p>0.05). On average, there were more $Cx3cr1^{+}$ IC nasally compared with temporally in older mice (nasal 93±43 cells/mm^2 vs temporal 5±0.2 cells/mm^2, p=0.048). In young mice, there were no regional differences in MHC-II^{+} IC density along the eyelid, but fewer MOICs expressed MHC-II^{+} in young Cx3cr1-deficient mice (186±248 cells/mm^2) compared to $CD11c^{eYFP}$ mice (350±280 cells/mm^2; p=0.0048).

Conclusions: Immune cells that surround mice MGOs are mostly $CD11c^{+}$ and MHC-II^{+}, with few expressing $Cx3cr1^{+}$. There are more $CD11c^{+}$ DCs in MGOs at the nasal eyelid, relative to the temporal region, in young mice. The Cx3cr1 receptor may have a partial role in the presence of MHC-II^{+} ICs around MGOs, as fewer MOICs expressed MHC-II^{+} in young $Cx3Cr1^{GFP/GFP}$ mice. These novel findings provide a basis for further investigations of MOICs and their role in MGD.

CONTROL ID: 3710800

SUBMITTER (NAME ONLY): Bart Leroy

TITLE: Efficacy and safety of sepofarsen, an intravitreal RNA antisense oligonucleotide, for the treatment of CEP290-associated Leber congenital amaurosis (LCA10): a randomized, double-masked, sham-controlled, Phase 3 study (ILLUMINATE)

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: LCA10 is a severe, degenerative inherited retinal disease resulting in childhood blindness, which has no treatment. Sepofarsen, an RNA antisense oligonucleotide designed for LCA10 due to the frequent c.2991+1655A>G variant in the CEP290 gene, produced clinically meaningful improvements in visual acuity in a Phase 1b/2 trial. The aim of the phase 3 trial (ILLUMINATE) was to assess the efficacy and safety of sepofarsen compared to sham in

c.2991+1655A>G-LCA10 participants.
Methods: ILLUMINATE (NCT03913143) was a double-masked, randomized, sham-controlled study performed across 14 sites in Europe, North America and Latin America. Eligible participants were aged ≥ 8 years, carried at least one c.2991+1655A>G in the CEP290 gene and had best-corrected visual acuity (BCVA) ranging from 0.4 (20/50 Snellen equivalent) to 3.0 logMAR (Hand Motion). Participants were randomly assigned (1:1:1) to receive intravitreal injection of sepofarsen 160/80 µg (maintenance dose of 80 µg every 6 months, starting 3 months after the loading dose of 160 µg), 80/40 µg (same regimen but doses of 40µg and 80µg respectively), or sham. The primary endpoint was mean change from baseline in BCVA, in the treatment eye (worse seeing eye), compared with sham at Month 12. Secondary endpoints included full-field stimulus testing threshold (FST; red, blue, white), a mobility course composite score, and safety. Trial recruitment was completed in January 2021.
Results: Between March 29, 2019 and January 6, 2021, 52 participants were screened, of whom 36 were randomized (group allocation masked at the time of abstract submission). At baseline, the mean age was 29.0 (SD 14.5) years, including 12 (SD 33.3%) participants aged 8 to 18 and 24 (66.7%) participants aged >18 years. Sixteen (44.4%) of the participants were homozygous for the target variant whereas 20 (55.6%) were compound heterozygous. Mean baseline BCVA in the treatment eye was 1.25 logMAR (SD 0.66) and mean baseline BCVA in the fellow eye was 1.01 logMAR (SD 0.27).
Conclusions: Sepofarsen, an innovative RNA antisense oligonucleotide, is the most advanced program in development for the treatment of LCA10. Learning from recruitment suggested the commonality of the c.2991+1655A>G variant in LCA10. Updated results will be included as available.

CONTROL ID: 3710801

SUBMITTER (NAME ONLY): Stephen Russell

TITLE: Long-term safety and efficacy of sepofarsen in a Ph1b/2 INSIGHT extension trial in CEP290-associated Leber congenital amaurosis (LCA10)

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Autosomal recessive CEP290-LCA (LCA10) is a severe inherited retinal disease resulting in early vision loss and currently has no treatment. Sepofarsen is an RNA antisense oligonucleotide targeting the most common c.2991+1655A>G disease-causing variant in the CEP290 gene. Long-term safety and efficacy of sepofarsen in the first eye treated (FE) and safety and efficacy in the second eye treated (SE) in this extension trial (Insight; NCT03913130) were evaluated.

Methods: Subjects who completed the Ph1b/2 sepofarsen trial could enroll in the extension trial for continued dosing in the FE and initiation in the SE with the 160/80µg loading/maintenance dose. Frequency and severity of adverse events, and change in best-corrected visual acuity (BCVA) and full-field stimulus testing (FST) threshold were assessed. Baseline was defined as the value measured within the same month of – or last measurement prior to – the first dosing for each eye. Due to covid-19, some participants have missed scheduled injections. As such data up to – or available measurement prior to – 6 months after the last dosing have been included in the analysis for each eye.

Results: At data cut-off in mid-October 2021, 9 subjects (of 11 from the Ph1b/2 trial) aged 15–45 years were followed up to 46 months, 5 of them received at least one intravitreal injection of sepofarsen in the SE. Three subjects developed cataracts in the FE and 2 in the SE, of which 2 recovered following cataract surgery. Time to onset since initial dose was 13 months or later. Between 35-46 months after the 1st injection, long term BCVA improvement was reported in 4/6 FE ranging from -0.20 to -0.54 logMAR and 5/5 FE improved in either blue FST, red FST or both ranging from -0.21 to -2.06 log cd/m2. The SE showed a similar trend as the FE in BCVA (3/5 SE showed a change ranging from -0.06 to -2.50 logMAR) and in blue and red FST (4/4 SE showed improvement ranging from -0.27 to -4.57 log cd/m2).

Conclusions: The longer-term sepofarsen safety profile is consistent with that observed in the Ph1b/2. Meaningful BCVA and FST improvements observed in the Ph1b/2 continued up to 46 months. The responses in the SE were similar to the responses seen in the FE in both visual acuity and retinal sensitivity improvements. A Phase 2/3 (ILLUMINATE; NCT03913143), multiple dose, double-masked, randomized, sham-controlled trial is ongoing.

CONTROL ID: 3710803

SUBMITTER (NAME ONLY): Jennifer Tian

TITLE: Hyaluronic Acid based Therapeutic Bandage Contact Lenses for Corneal Wound Healing

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Tian, L. Liu, M. Ross, H. Sheardown, McMaster University, Hamilton, Ontario, CANADA|

Commercial Relationships Disclosure: Jennifer Tian: Commercial Relationship: Code N (No Commercial Relationship) | Lina Liu: Commercial Relationship: Code N (No Commercial Relationship) | Mitchell Ross: Commercial Relationship: Code N (No Commercial Relationship) | Heather Sheardown: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal scarring resulting from improper healing of the cornea is the third most common cause of blindness worldwide. Current methods for aiding corneal wound healing can be expensive, difficult to source, or have low bioavailability. Plano lenses have been used as bandage contact lenses (BCLs) to reduce pain and prevent the corneal surface from further damage after injury, but they have limited therapeutic effects. By conjugating hyaluronic acid (HA) onto the surface of the contact lens, it is thought that a BCL capable of improving corneal wound healing and minimizing scarring can be produced.

Methods: Model pHEMA-co-TRIS lenses were synthesized using free radical polymerization. Surface acrylation was done in the presence of the catalyst diisopropylethylamine (DIPEA). The small molecules diethylamino ethanethiol (DEAET) and dimethylamino ethanethiol (DMAET) were tethered using a thiol-ene "click" reaction. The successful acrylation and conjugation of the small molecules were confirmed through FTIR. Quantification of HA was performed using radiolabelled HA and subsequent gamma counting. In vitro cell studies using human corneal epithelial cells (HCECs) were conducted to determine cytotoxicity using MTT and LIVE/DEAD.

Results: FTIR showed the successful acrylation and conjugation on the lens surface. DMAET and DEAET modified lenses showed significantly higher ($p < 0.001$) HA binding compared to model pHEMA-co-TRIS controls at all time points shown in Figure 1. The modified lenses improved release kinetics preventing an initial burst release and showed consistent release when unloaded and reloaded with HA. The contact angle was significantly decreased ($p < 0.05$) for the modified model lenses with HA without affecting the equilibrium water content and optical transparency. Finally, the modified model lenses did not exhibit any cytotoxicity in vitro with HCECs.

Conclusions: Our results show that we were able to produce a lens capable of surface binding HA. The lens was able to bind more HA compared to unmodified controls while providing a sustained release of HA and excellent rebinding kinetics. The lenses were well tolerated based on in vitro cell studies.

CONTROL ID: 3710804

SUBMITTER (NAME ONLY): Thomas Meyer

TITLE: Improvements to an Ex Vivo Cadaver Eye Model for Vitreoretinal Testing

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Meyer, S. Camacho Gonzalez, M. Hedgeland, K. Stoner, Device Development, Gyroscope, Philadelphia, Pennsylvania, UNITED STATES|B. Ko, General Manager, Kaleidoscope Innovation, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Porcine eyes are commonly used for training and testing of vitreoretinal surgeries but present limitations due to anatomical differences. While human cadaver eyes work well for exterior work, pupillary visualization is typically too cloudy for vitreoretinal surgery. Our purpose is to describe a method for the preparation of human cadaver eyes that preserves retinal adhesion and allows for clear visualization of the fundus.

Methods: Human eyes that are not eligible for corneal transplants are procured from a partner eye bank. Tissue is stored in Optisol or Life4C storage media. Vials are shipped on ice and refrigerated once received. The globe is placed in a 3D-printed fixture that replicates eye rotation and fixed in position by clamping the optic nerve. A port is inserted and connected to an infusion line which pressurizes the eye with BSS (balanced salt solution) to ~30mmHg. A corneal trephine blade is used to remove the central cornea. Once removed, 0.12 forceps are used to remove the iris and replicate visualization of a dilated eye. Next, the lens is removed through the corneal opening. Finally, a temporary keratoprothesis (TKP) is sutured onto the sclera. The process is summarized in Figure 1.

Results: Eyes prepared by this method allow a clear view of the fundus, with sufficient resolution to identify blood vessels and distinguish the microneedles used in subretinal injections. Our team has performed hundreds of subretinal injections using this model. Figure 2 shows representative visualization through the TKP with a subretinal bleb in the top left quadrant.

Conclusions: Conclusions: A more realistic ex vivo model for vitreoretinal surgery can be achieved with human cadaver eyes by removing the cornea, iris, and crystalline lens, then suturing a TKP to maintain pressure. By shipping eyes in corneal storage media on ice and storing under refrigeration, the retina can remain attached for up to a week post-mortem. This technique can facilitate practice and testing of vitreoretinal surgeries in human eyes.

CONTROL ID: 3710805

SUBMITTER (NAME ONLY): Florence Lorget

TITLE: SPVN06, a novel mutation-independent AAV-based gene therapy, dramatically reduces vision loss in the rd10 mouse model of rod-cone dystrophy

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Lorget, M. Marie, H. Khabou, C. Simon, D. Dalkara, J.A. Sahel, T.D. Leveillard, SparingVision, FRANCE|D. Nuno, P. Vanlandingham, A. Quiambao, R. Farjo, EyeCRO, Oklahoma, UNITED STATES|D. Dalkara, T.D. Leveillard, INSERM, Paris, Île-de-France, FRANCE|J.A. Sahel, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: SPVN06 is a proposed gene therapy for patients experiencing vision loss due to rod-cone dystrophy (RCD), regardless of the causative mutation. In all RCD, photoreceptor degeneration is first observed in rods, and subsequently in cones, in large part due to a lack of trophic support. SPVN06 encodes, in a single AAV, the cDNAs for trophic factor Rod-derived Cone Viability Factor (RdCVF) and thioredoxin enzyme RdCVF-Long (RdCVFL), both isoforms of the NXNL1 gene. RdCVF, secreted by rods, protects cones from degeneration by stimulating aerobic glycolysis. RdCVFL is a potent antioxidant protecting cones from oxidative stress. SPVN06 early nonclinical development included several pharmacology studies in rd10 mice, a fast-progressing model of RCD.

Methods: rd10 mice were born and raised in darkness until transferred to regular cyclic light on postnatal day (P) 31 up to study termination at P48. At P15 or P18, the animals received a bilateral subretinal administration of 1 µL of vehicle or SVPN06 at 1E8 vg/eye. Effect of SPVN06 on retinal function and structure were evaluated by optokinetic (OKT), ffERG, optical coherence tomography (OCT) and histology.

Results: A highly significant protection of the visual function (OKT) was noted at P32 ($p<0.0001$) when the animals received SPVN06 1E8 vg/eye at P18. The level of visual function in SPVN06-treated eyes was similar to wild-type (WT) level versus only ~50% of WT in vehicle-injected eyes. At the later timepoints (P38 and P45), the difference between the 2 groups remained significant, although visual loss continued in both vehicle and SPVN06 treated eyes. H&E staining of the retina at P48 didn't reveal a protection of the ONL, whereas PNA staining at the same timepoint revealed greater density of the cone outer segments and/or their membrane remnants in SPVN06-treated eyes. When injection was conducted at PN15, no protection of the visual function was noted suggesting an optimal timing (P18) for treatment in this model. There were no significant SPVN06-related changes in ffERG or OCT parameters.

Conclusions: SPVN06 dramatically protects retinal degeneration in rd10 mice, a fast-progressing model of RCD, supporting clinical development.

CONTROL ID: 3710809

SUBMITTER (NAME ONLY): Annika Patel

TITLE: Comparison of Virtual Reality Device vs. Standard Automated Perimetry in the Assessment of Superior Visual Field Prior to Functional Upper Eyelid Surgery

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. Patel, W.W. Lee, H. Munshi, T.C. Chang, A.L. Grajewski, D.T. Tse, B.C. Tse, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Insurance coverage (IC) eligibility for functional eyelid surgery requires visual field (VF) exams demonstrating constriction of superior field of vision with improvement after taping the upper eyelids to simulate surgery. Limited access to standard automated perimetry (SAP) machines and the need for a skilled technician produce a bottleneck effect which slows clinic flow. We compared the results of a Superior-64 VF test between a virtual reality (VR) device and SAP in patients with ptosis, brow ptosis, and dermatochalasis.

Methods: Patients undergoing non cosmetic eyelid surgery evaluation had the eyelids in their natural state (unT) and taped (T) assessed by a Superior-64 VF test strategy using VR and SAP in random order. The percentage of grid seen was calculated for both eyelid positions using the devices. Fulfillment of IC criteria for blepharoplasty, defined as a 30% or 12-degree increase in grid seen from unT to T, was assessed for agreement between VR and SAP.

Results: 39 eyes (20 OD, 19 OS) from 20 (15 female, 5 male) patients were tested using SAP and VR (Figure 1). There was significant improvement in the percentage of grid seen from the unT to T state using VR (36% to 75%; $t(38)=-8.94$, $p<0.001$) and SAP (34% to 64%; $t(38)=-7.16$, $p<0.001$). SAP and VR IC results agreed in 29 (74%) eyes (Table 1). A diagnosis of dermatochalasis was significantly associated with meeting IC qualification using SAP ($X2(1, N=39)=4.18$, $p=0.041$) and approached significance using VR ($X2(1, N=39)=3.39$, $p=0.066$). However, this association did not exist for subjects diagnosed with ptosis or brow ptosis. Of subjects with disagreement, there was no association between order of test administration and fulfillment of IC criteria ($X2(1, N=10)=0.28$, $p=0.598$).

Conclusions: VR Superior-64 VF test showed reliable agreement with SAP in meeting IC criteria and may offer a more accessible alternative to SAP in eyelid functional VF evaluation. Patients diagnosed with dermatochalasis have greater ability to demonstrate improvement in VF exam from the unT to T state on both devices than those with ptosis or brow ptosis. Further studies should focus on understanding test-retest variability of superior VF testing and the cause of disagreement between SAP and VR.

CONTROL ID: 3710810

SUBMITTER (NAME ONLY): Patrick Leavey

TITLE: Mistimed NR2f1/2 gene expression in postnatal retinal progenitors induces expression of retinal ganglion cell-specific marker genes

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Leavey, C.P. Santiago, L. Jiang, S. Blackshaw, Neuroscience, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Patrick Leavey: Commercial Relationship: Code N (No Commercial Relationship) | Clayton Santiago: Commercial Relationship: Code N (No Commercial Relationship) | Lizhi Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Seth Blackshaw: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal progenitor cells undergo a transition between transcriptionally distinct early- and late-stage specific states during the course of neurogenesis, which control their ability to generate specific postmitotic cell types. Using integrated scRNA- and scATAC-Seq, we identified NR2F1 and NR2F2 as transcription factors that are strong candidates for maintaining early-stage identity in retina progenitors. In this study, we investigate the effects of misexpressing NR2F1 and NR2F2 in late-stage retinal progenitors.

Methods: We generated single cell RNA sequencing libraries from retinas electroporated ex vivo at P0 with 100ug of either a control GFP-expressing plasmid or individual or a combination of plasmids overexpressing NR2F1 and NR2F2. We then isolated and profiled electroporated cells from 10-15 retinas using scRNA-Seq. We collected between 4500 and 7000 cells per sample and then utilizing the Seurat R package processed the data. We then analyzed expression of known marker genes and conducted differential gene expression analysis to elucidate how NR2F1/2 overexpression impacted cell type population dynamics and gene regulatory networks.

Results: Within these datasets, we identified cell clusters with marker gene expression representing primary RPC, neurogenic RPC, G2/M phase RPC, microglia, amacrine, starburst amacrine, and photoreceptor cells. NR2F1/2 combined overexpression at P0 led to an increased fraction of RPC and amacrine clusters alongside a decrease in the overall fraction of primary RPCs. In addition, we observed ectopic expression of RGC-enriched markers (Ebf3, Elavl3) within the amacrine and neurogenic RPC populations as well as a loss of RPC markers (Pax6). [SB1] Similar effects of NR2F1/2 overexpression were observed at P2 and P5 individually, with additional RGC-specific markers (Rbpms, Calb2, Snca) detected at this age.

Conclusions: Our observation that NR2F1/2 overexpression leads to induction of expression of RGC-specific markers implies that these transcription factors may control temporal patterning of retinal progenitors, and render them competent to generate RGCs. These findings also imply that NR2F1/2 promote the transition from primary to neurogenic progenitors and may promote neurogenic competence.

CONTROL ID: 3710812

SUBMITTER (NAME ONLY): Eric Desjarlais

TITLE: Incidence and Risk of Retinopathy in Patients With and Without Interstitial Cystitis and Pentosan Polysulfate Sodium Use

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Desjarlais, V. Medic, J.E. Kim, Department of Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Eric Desjarlais: Commercial Relationship: Code N (No Commercial Relationship) | Velinka Medic: Commercial Relationship: Code N (No Commercial Relationship) | Judy Kim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pentosan polysulfate sodium (PPS) is an oral medication used for the management of interstitial cystitis (IC). Recent studies have demonstrated an association between prolonged use and pigmentary maculopathy. However, to our knowledge, no studies have investigated or controlled for the potential association between IC and retinopathy. The aim of this study was to investigate the incidence and risk of retinopathy in patients with and without IC and PPS use.

Methods: Data for this retrospective cohort study was sourced from TriNetX, a nationwide, multicenter database. Adult, female patients with IC were matched to non-IC controls with a 1:4 ratio on age, sex, race, and ethnicity. Index dates for patients with IC and their matched controls were determined by the first recorded IC diagnosis. Patients could not have a retinopathy diagnosis before their index date. The IC cohort was subdivided according to duration of PPS use: never, less than five years, at least five years. The outcome measure was any one of six retinopathy diagnoses: exudative or nonexudative age-related macular degeneration, drusen, hereditary retinal dystrophy, toxic maculopathy, or unspecified macular degeneration. Univariate and multivariable Cox proportional hazards models were fitted. The multivariable model adjusted for age, race, ethnicity, smoking, and medical comorbidities. Hazard ratios (HRs) were estimated with the non-IC cohort as the reference category.

Results: The study included 110,300 adult, female patients. There were 22,060 and 88,240 patients with and without IC, respectively. With an average age of 53.92 (SD 16.22) years, 96,110 (87.14%) patients were non-Hispanic white, 8,835 (8.01%) were non-Hispanic black, and 5,355 (4.85%) were Hispanic. Incidence per 100,000 person-years was 173.88 (95% CI 162.96 - 185.53) for patients without IC, 226.63 (95% CI 198.63 - 258.56) for IC without PPS use, 293.02 (95% CI 234.02 - 366.89) for IC with less than five years of PPS use, and 558.91 (409.97- 761.95) for IC with at least five years of PPS use. Adjusted HRs were 1.31 (95% CI 1.13-1.51) for IC without PPS use, 1.70 (95% CI 1.35-2.15) for IC with less than five years of PPS use, and 3.10 (95% CI 2.26-4.27) for IC with at least five years of PPS use.

Conclusions: Patients with IC had greater incidence and risk of retinopathy. Prolonged PPS use further increased incidence and risk of retinopathy.

CONTROL ID: 3710815

SUBMITTER (NAME ONLY): Stephanie Grabitz

TITLE: Glaucoma reduces vision-related quality of life: results from the population-based Gutenberg Health Study

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.D. Grabitz, A. Junglas, E.M. Hoffmann, J.V. Stingl, S. Nickels, N. Pfeiffer, A.K. Schuster, Department of Ophthalmology, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|M. Beutel, Department for Psychosomatic Medicine und Psychotherapy, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|P. Wild, T. Münzel, Department of Cardiology, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|K. Lackner, Institute for Clinical Chemistry and Laboratory Medicine, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|P. Wild, K. Lackner, T. Münzel, German Center for Cardiovascular Research (DZHK), Partner Site Rhine-Main, Mainz, GERMANY|I. Schmidtmann, Institute for Medical Biostatistics, Epidemiology and Informatics (IMBEI), Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|

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ABSTRACT BODY:

Purpose: Glaucoma patients suffer from visual field defects and ultimately blindness due to progressive loss of retinal nerve fibers. It is one of the leading causes of visual impairment in developed countries. The aim of this study is to determine the relationship between glaucoma and vision-related quality of life (VRQoL) and to explore associated factors of VRQoL in participants with glaucoma.

Methods: Participants in the population-based prospective observational cohort study (Gutenberg Health Study) underwent an ophthalmological examination including optic nerve head photography, intraocular pressure (IOP) measurement and a screening visual field exam between 2007-2012. Optic nerve head photographs were graded and classified according to the modified “International Society of Geographical and Environmental Ophthalmology” (ISGEO) glaucoma classification including adjustment for optic disc size. History of glaucoma or ocular hypertension (OHT) was defined as an ongoing prescription of IOP lowering medication or a history of glaucoma surgery. VRQoL was quantified using the German version of the Visual Function Questionnaire-25 and the Rasch-transformed visual functioning scale (VFS) was computed. A priori defined multivariable quantile regression models were carried out to analyze relationships.

Results: A total of 10,075 enrolled participants had both glaucoma grading and VRQoL investigation and were included in the study. Of these, 108 (1.1%) had glaucoma based on the ISGEO classification and 226 (2.2%) had a history of glaucoma or OHT. Glaucoma was associated with a significantly reduced VFS in both, participants with treatment (-8.14 [95% CI, -11.00 - -2,79]; P=0.005) and without treatment (-5.53 [95% CI, -8.31- -2.80]; P <0.001) compared to participants without glaucoma. IOP treatment without an ISGEO glaucoma diagnosis, such as in OHT, was also associated with a reduction on the VFS (-2.71 [95% CI, -5.39 - -0.01]; P=0.046).

Within participants with glaucoma impaired visual acuity of the better seeing eye (-5.62 [95% CI, -9.16 - -3.63] per each 0.1 on the logMAR chart; P=0.020) was associated with lower VFS, whereas history of glaucoma surgery, glaucoma medication use, IOP, size of the visual field defect, and family history of glaucoma were not associated with VFS.

Conclusions: Glaucoma is a common eye disease that reduces VRQoL.

CONTROL ID: 3710818

SUBMITTER (NAME ONLY): Kendall Kohout

TITLE: In vivo and ex vivo characterization of macaque ganglion cells projecting to the superior colliculus

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kohout, S.S. Patterson, A. Walker, J.M. Strazzeri, D.R. Williams, W. Merigan, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|J.M. Strazzeri, W. Merigan, David & Ilene Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|D.R. Williams, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The macaque retina conveys visual information to the brain via ~20 anatomically distinct retinal ganglion cell (RGC) types. Yet only the most common LGN-projecting types have been characterized physiologically. Many of the remaining RGCs project to the superior colliculus (SC), an evolutionarily ancient region implicated in eye movements and, most recently, perceptual decision making. Here we catalog SC-projecting RGC types in the macaque retina and develop an approach to anatomically identify and physiologically characterize them in the living eye.

Methods: Injections of the retrograde tracer rhodamine dextran were aimed at the foveal SC in two macaques. Two stereotaxic-coordinate based injections were made in one macaque, and one MRI-guided injection was made in the second. Rhodamine expression was mapped with a fundus camera, then imaged in detail with adaptive optics scanning light ophthalmoscopy (AOSLO). The second macaque also expressed the genetically-encoded, calcium indicator GCaMP6s in the ganglion cell layer (Fig. 1). In the first macaque, post-mortem ex vivo imaging with a confocal microscope supplemented the in vivo imaging of rhodamine expression.

Results: Each injection labeled a sparse population of SC-projecting RGCs, consistent with earlier reports. We imaged the rhodamine-labeled RGCs in vivo with AOSLO, and some could be coaligned with GCaMP6s-expressing RGCs. The calcium responses of RGCs in rhodamine-labeled regions did not differ from areas without rhodamine expression. We traced the dendritic fields of 64 rhodamine-labeled RGCs that were imaged ex vivo with a confocal microscope, identifying parasol, smooth monostratified, large sparse, broad thorny and narrow thorny RGCs.

Conclusions: A complete account of the retinal input to the SC has been elusive since the rarity of many SC-projecting RGC types makes them difficult to target for physiological investigation. The anatomical approach developed here could address this gap in knowledge, laying the foundation for subsequent in vivo measurements of the response properties of these rare and understudied RGC types.

CONTROL ID: 3710819

SUBMITTER (NAME ONLY): Padmanabhan Pattabiraman

TITLE: Loss of cathepsin K function in trabecular meshwork induces actin polymerization and apoptosis

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.P. Pattabiraman, A. Soundararajan, Ophthalmology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recently we showed that the inactivation of cathepsin K (CTSK), a secretory lysosomal protease, increased the ECM deposition and actin-bundling in the trabecular meshwork (TM) and elevated the intraocular pressure. In this study, we explored the loss-of-function effect of CTSK on the human TM proteome.

Methods: Normal primary human TM (HTM) cells (n=4) in vitro were transfected with either siRNA against CTSK (siCTSK) or scrambled siRNA (siScr) as control. 72h post-transfection, the protein was collected, and mass spectrometry-based quantitative proteomics was performed. Changes in protein levels were screened using criteria- $p \leq 0.05$ and mean $\pm 2\sigma$ of log2 as confidence fold change limits. MetaCore^{TM} was used for the functional pathway enrichment analysis.

Results: We found an increase and decrease in 398 and 132 proteins in TM respectively due to siCTSK. The upregulated proteins were related to– a) TM cell contractility and cell adhesion proteins- actin scaffolding protein tensin 1 (p=0.03), paxillin (p=0.01), docking protein involved in tyrosine kinase-based signaling related to cell adhesion BCAR1/p130cas (p=0.04), tyrosine-phosphorylated growth factor receptor adaptor protein NCK1 (0.04) and NCK2 (p=0.03), serine/threonine-protein kinase D1 (PRKD1) (p=0.001), and Guanine nucleotide exchange factor Vav2 (p=0.04), intracellular signal transducer and transcriptional modulator activated by TGFβ SMAD3 (p=0.04); b) sphingosine kinase 2 (SPHK2) (p=0.0001), which is involved in phosphorylation of the lysosphingolipid sphingosine-1-phosphate; and c) apoptosis-related proteins including caspase 1 (p=0.03), which cleaves and activates caspase 3 (p=0.02), caspase 7 (p=0.01), nuclear factorκB (NFkB) p105 subunit (p=0.05), and a critical apoptosis regulator receptor-interacting serine/threonine-protein kinase 1 (RIPK1) (p=0.03). Interestingly there was a significant decrease in the levels of actin depolymerizing protein phosphatase SSH1 (p=0.03), cell survival or anti-apoptotic protein tank binding kinase 1 (TBK1) (p=0.03), TBK1 adaptor protein 5-azacytidine-induced protein 2 (AZI2) (p=0.01), and as expected CTSK (p=0.04).

Conclusions: These unbiased observations establish the functionality of CTSK in regulating the TM actin cytoskeleton and the maintenance of TM cellularity. We propose that dysregulation of CTSK in TM can cause increased contractility and cell loss leading to elevated IOP and glaucoma.

CONTROL ID: 3710820

SUBMITTER (NAME ONLY): Mathew Dusharm

TITLE: Title: A Novel Test of Low Contrast Reading in Non-Advanced Age-Related Macular Degeneration: A Potential Functional Endpoint for Clinical Trials.

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Dusharm, E. bensinger, K. Dieter, J.D. Rodriguez, M.B. Abelson, G. Wallstrom, R&D, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: The development of effective therapies for nonadvanced age-related macular degeneration (AMD) has been hindered by a lack of sensitive, reversible endpoints to be used in clinical trials. Many clinical reading tests (e.g., MNREAD) use a relatively small number of words (10-20) and yield highly variable estimates of a patient's reading rate (1). Our group developed a novel reading test, Ora Reading Passages™ test, that assessed patients' reading efficiency algorithm under mesopic vision conditions, for naturalistic reading at low and high contrast. This study reports results from a third longitudinal visit for a cohort of non-advanced AMD patients tested in 2017.

Methods: Methods: Nine non-advanced AMD patients with visual acuity of 20/25 or better from the original cohort (2017) and 16 matched controls returned for the third visit. During a single study visit, all participants completed a battery of visual function tests including the Ora Reading Passages™ test. In the Ora Reading Passages™ test, patients viewed four naturalistic reading passages from National Geographic Education (5^{th}-7^{th}) grade-reading levels, presented at low and high contrast levels. Patients were asked to read aloud a passage of text at a comfortable reading pace.

Results: Results: Patients with non-advanced AMD had significant algorithmic efficiency differences for the passages in 'Reading Artifact 05' at both low and high contrast background levels ($p < 0.0077$). 'Reading Silk Road 08' ($p = 0.057$) and Reading Coral 14($p = 0.0611$). Results showed consistent patterns of observable data across our longitudinal study (1).

Conclusions: Conclusions: The Ora Reading Passages™ test, which assesses the algorithmic efficiency of reading in contrast levels (low - high) for mesopic vision conditions, demonstrated significant differences between non-advanced AMD patients and matched controls. These differences have remained relatively consistent over a 3-year longitudinal period. Our results suggest a repeatable test that can serve as a reliable and reversible functional endpoint in future clinical trials for therapies aimed at treating nonadvanced AMD.

CONTROL ID: 3710821

SUBMITTER (NAME ONLY): Christopher Seery

TITLE: Zone 1 Trauma: Wound Dehiscence Compared to Primary Trauma

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Seery, M. Dastjerdi, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular trauma is a significant cause of visual loss. Zone 1 injury is considered favorable prognostically compared to more posterior injuries, however, the same favorable prognosis may not be true for dehiscenced corneal wounds. The goal is to determine if this paradigm holds true for all situations, including wound dehiscence, or just primary traumatic injuries.

Methods: Retrospective chart review of all patients who underwent open globe repair based on CPT codes at University Hospital, Newark, NJ from 1/1/2019 to 12/1/2020. Those with Zone 1 injuries were identified and presenting vision, final visual outcomes, associated ocular pathology, long term complications, and need for further surgeries were reviewed. Zone 1 injuries were defined as all injuries limited to the cornea from limbus to limbus.

Results: 58 eyes were identified- 38 primary trauma and 20 dehisced wounds (11 PKP, 5 clear corneal incisions, 1 laceration, 1 ECCE, 1 RK, 1 tectonic graft). All dehisced wounds were blunt trauma and all primary traumas were projectiles or sharp penetrating injuries. Dehisced wounds had more posterior segment pathology i.e. hemorrhagic choroidal, vitreous hemorrhage, retinal detachment, choroidal effusion (all 20% v 2.63%, 5.26%, 5.26%, and 0% respectively), vitreous prolapse (20% v 2.63%) and uveal prolpase (80% v 36.84%). Dehisced wounds had more traumatic aphakia (40% v 0%) and dislocated lenses (15% v 0%). Primary trauma was more likely to have traumatic cataracts (55.26% v 10%) or no lens changes (44.74% v 25%). 2 dehisced wounds required enucleation, while no primary traumas were enucleated. Cataract/secondary intraocular lens surgery was performed in 34% of the primary traumas (10% in dehisced wounds). Primary traumas achieved 20/40 vision or better 44.74% (10% dehisced wounds). 7.89% patients with wound dehiscence ended NLP (none in primary trauma).

Conclusions: Dehisced wound patients had poorer visual outcomes as well as a higher rate of posterior segment pathology and expulsion of intraocular contents (lens, vitreous, and uvea). More important than the zone of injury is the mechanism. Ruptured globe as defined by Birmingham Eye Trauma Terminology likely portends poorer prognosis while penetrating and lacerating injuries by the same classification system likely a better prognosis, and as such, we believe that the traditional classification of zone of injury being a predictive factor of visual outcome is outdated.

CONTROL ID: 3710823

SUBMITTER (NAME ONLY): David Mathew

TITLE: Aqueous humor lipidomic profile in primary open angle glaucoma patients

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Mathew, I. Livne-Bar, D. Chan, Y. Buys, G.E. Trope, M. Sit, J.M. Sivak, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|D.J. Mathew, J.M. Sivak, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, CANADA|B.A. Flitter, J.G. Flanagan, K. Gronert, Vision Science Program, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify the aqueous humor (AH) profile of lipid mediators in primary open angle glaucoma (POAG) eyes compared to those without glaucoma

Methods: AH samples from eyes with and without glaucoma underwent lipidomic analyses using liquid chromatography-mass spectrometry (LC-MS). Glaucoma samples were obtained from 60-80-year-old POAG patients undergoing a glaucoma surgery with or without cataract surgery. Matched control samples were obtained from patients undergoing routine cataract surgery. Patients with diabetes mellitus, systemic inflammatory disease, uveitis, retinopathy and age-related macular degeneration and those on Aspirin were excluded. From each eye, 100 mL of AH was collected using a 30 Gauge needle mounted on a 1-mL syringe, introduced into the anterior chamber anterior to the limbus, prior to any surgical intraocular entry. The samples were immediately snap frozen on dry ice and stored at -80C until assessment by lipidomic analyses of a panel of 40 polyunsaturated fatty acids (PUFA), metabolites and lipid mediators. All participants signed an informed consent. This study was approved by the University Health Network and Kensington Eye Institute Research and Ethics Boards.

Results: AH was collected from 16 and 18 eyes with and without glaucoma, respectively. The mean age was 68.7±6.4 years for the glaucoma group and 71.0±4.7 years for the control group (p=0.25). The mean preoperative intraocular pressure 14.1±3.1 and 15.2±1.6 mmHg for the glaucoma and control groups, respectively (p=0.24). The cup-to-disc ratios were 0.9±0.1 and 0.3±0.1 for the glaucoma and control groups, respectively (p<0.001). All 16 glaucoma eyes received prostaglandin analogue eye drops prior to surgery; 15 were on beta-blocker eye drops. There were statistically significant differences between glaucomatous and control eyes for arachidonic acid (1328.0±322.0 vs 643.1±130.6, p=0.001), lipoxin A_4 (0.79±0.14 vs 0.32±0.10, p=0.01) and 12-hydoxyeicosapentanoic acid (0.35±0.17 vs undetected, p=0.04). Substantial levels, but no significant differences, were identified for docosahexanoic acid (212.0±46.33 vs 131.1±22.36, p=0.11), eicosapentanoic acid (6.21±1.40 vs 3.76±0.32, p=0.08), prostaglandin E_2 (2.83±1.92 vs undetected, p=0.13) and prostaglandin D_2 (2.43±1.49 vs 0, p=0.09).

Conclusions: Increased levels of lipid mediators are present in glaucomatous eyes. Arachidonic acid metabolites may play a role in glaucoma pathogenesis.

CONTROL ID: 3710824

SUBMITTER (NAME ONLY): George Lau

TITLE: Intraocular lens edge effects on off-axis light source and retinal image quality

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Lau, Medical Affairs, Bausch and Lomb, Bridgewater, New Jersey, UNITED STATES|K. Venkateswaran, Tatvum Research, California, UNITED STATES|N. Tiwari, Tatvum Research, California, UNITED STATES|

Commercial Relationships Disclosure: George Lau: Commercial Relationship(s);Code E (Employment):Bausch and Lomb | Krishnakumar Venkateswaran: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch and Lomb | Nivedan Tiwari: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch and Lomb

ABSTRACT BODY:

Purpose: To assess photic effects caused by interaction between light from off-axis glare source and the edge of various commercially available intraocular lenses.

Methods: An experimental bench was developed to study the effects of off-axis glare source on various intraocular lens edge designs. The lenses were placed in a wet cell behind a model cornea. The lens fixture was designed to suspend the edge of the optic in isolation, so that scattering from edges of the wet cell or the model cornea does not confound the experimental results. A camera was placed behind the cornea and the intraocular lens. The bench setup allows the camera to move axially and be positioned at different angles to the optical axis of the system of the cornea and intraocular lens.

Results: A few commercially available intraocular lenses were tested. Results showed that intraocular lenses with sharp edges have the potential to cause severe glare effects close to the optical axis. Results suggest that even though the sharp edges of the IOL have been shown to reduce posterior capsular opacification (PCO) rates, optimization of lens edge design to reduce light scatter can benefit the patient by reducing PCO and also reduce scattering of light close to the optical axis. Even though there is a high likelihood that the stray light from glare sources will be blocked by the iris, decentered IOL or posterior positioning of the IOL can potentially expose the edge of an IOL to off-axis light entering the cornea.

Conclusions: Intraocular lenses such as enVista and PreVue (Yellow) IOLs (Bausch & Lomb, Inc.) have relatively lower glare, suggesting that these IOLs have an optimal edge geometry leading to low PCO[1], and at the same time reduce off-axis light scattering when compared to other IOLs, such as Alcon's Acrysof IOLs.

1. Packer M, Fry L, Lavery KT, Lehmann R, McDonald J, Nichamin L, Bearie B, Hayashida J, Altmann GE, Khodai O. Safety and effectiveness of a glistening-free single-piece hydrophobic acrylic intraocular lens (enVista). Clin Ophthalmol. 2013;7:1905-12. doi: 10.2147/OPTH.S50499. Epub 2013 Sep 24. PMID: 24109169; PMCID: PMC3792945.

CONTROL ID: 3710831

SUBMITTER (NAME ONLY): Garrett Jones

TITLE: Tear proteomic changes associated with dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Jones, T. Lee, J. Glass, W. Zhi, S. Sharma, A. Sharma, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|L. Ulrich, A. Estes, M. Sezer, S. Sharma, Department of Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|A. Sharma, Department of Population Health Sciences, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The tear film is a protein-rich multilayer fluid that coats the corneal and conjunctival epithelia. Dry eye disease (DED), a multifactorial inflammatory disease of the ocular surface, is characterized by tear film instability. DED diagnostic methods are limited, and there is an urgent need for objective biomarkers. We analyzed human tear fluid to identify potential proteomic biomarkers associated with DED.

Methods: Tear samples were collected via Schirmer strips from 41 DED patients and 41 healthy controls. Proteomic analysis was performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). To ensure proteomic changes did not derive from confounding factors, multivariate regression analysis was performed, adjusting for age, sex, and race. Targeted parallel reaction monitoring (PRM) analysis was used to confirm the changes of 15 selected proteins.

Results: A total of 3288 unique proteins were identified in 82 tear samples. 89 of the 500 proteins detected in at least 50% of the samples were significantly altered in DED patients. 76 of the altered proteins were extracellular exosome proteins, and 28 were glycoproteins. The altered proteins are implicated in retinal homeostasis, cell-cell adhesion, proteolysis, receptor-mediated endocytosis, innate immune response, antibacterial humoral response, phagocytosis, and the complement pathway. The levels of lipocalin-1 (LCN1: 0.12-fold), lactoperoxidase (LPO: 0.15-fold), mesothelin (MSLN: 0.16-fold), heparan sulfate proteoglycan (HSPG2: 0.19-fold), nucleobindin-2 (NUCB2: 0.22-fold), zinc-alpha-2-glycoprotein (AZGP1: 0.33-fold), cystatin-C (CST3: 0.39-fold), polymeric immunoglobulin receptor (PIGR: 0.41-fold), and antileukoproteinase (SLP1: 0.43-fold) were decreased in DED patients, while the levels of serpin B5 (SERPINB5: 3.29-fold), calpain-2 catalytic subunit (CAPN2: 3.27-fold), complement factor H (CFH: 3.18-fold), protein S100-A8 (S100A8: 3.14-fold), and ubiquitin-like modifier-activating enzyme 1 (UBA1: 2.90-fold) were increased.

Conclusions: Using a shotgun approach, we found that the levels of 89 tear proteins were altered in DED patients. Targeted PRM analysis of 15 selected proteins confirmed the changes of 14 proteins in DED patients (9 decreased and 5 increased). These findings demonstrate the potential of tear protein levels as biomarkers for DED, and the pathways involving these proteins may further our understanding of the mechanisms underlying DED.

CONTROL ID: 3710832

SUBMITTER (NAME ONLY): David Wulff

TITLE: 3D printing using a novel bioink with a commercial mSLA printer to fabricate a model contact lens

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Wulff, C. Phan, L.W. Jones, School of Optometry and Vision Science, University of Waterloo Faculty of Science, Waterloo, Ontario, CANADA|D. Wulff, C. Phan, L.W. Jones, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: To develop a cost-effective and scalable 3D printing method and novel bioinks to fabricate contact lenses.

Methods: The bioink formulations consisted of GelMA (gelatin methacrylate), LAP (Lithium phenyl-2,4,6-trimethylbenzoylphosphinate), and a yellow food-grade dye. The dye minimizes unwanted light leakage during the photopolymerization process. A commercial mSLA (masked stereolithography) printer, the Photon Mono X (AnyCubic, Shenzhen), was retrofitted with a custom temperature and humidity control kit. The printing process was performed at 40 ^{O}C and 90% humidity to ensure that the GelMA remained at a liquid state and to prevent the bioink from drying out, respectively. A set of matrix cubes of varying sizes with holes was used as a standard control. Images of the cubes were taken with a camera, top-down and side-review, analyzed with the ImageJ software and compared with the original CAD designs to derive an overall print quality score. Two print variables, exposure time (5 s to 40 s) and yellow dye concentration (1 – 7%), were analyzed in this study.

Results: The best resolution with the highest print scores were obtained at either 5% yellow dye concentration and 30 seconds exposure time, or 3% yellow dye concentration and 20 seconds exposure time. There was an overall optimal range for both print times (20 - 30 s) and yellow dye concentration (3 - 5%). Values above or below this critical value resulted in lower print quality scores of the standard cubes. A prototype contact lens with a 200 μm thickness was able to be 3D printed using the developed print methods and parameters, with a total print time of approximately 20 minutes. Approximately 28 contact lenses can be printed at the same time using the 3D printer. However, the surface and edges of the 3D printed contact lens were still visually very rough.

Conclusions: The current study demonstrated that a low-cost commercial 3D mSLA printer can be used to fabricate model contact lenses using a hydrogel material. Still, further work is necessary to improve the print quality for fabricating ultra-thin devices such as contact lenses. Future work will use this 3D printing method to fabricate contact lenses for drug delivery.

CONTROL ID: 3710833

SUBMITTER (NAME ONLY): Patricia Zulueta

TITLE: Routine ophthalmological examinations in adults with sickle cell disease are low and further adversely affected by the COVID-19 Pandemic

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zulueta, A. Rai, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|C.P. Minniti, Medicine, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|C.P. Minniti, U. Mian, Pediatrics, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|J. Moon, Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|T. Toribio, Ophthalmology and Visual Sciences, Montefiore Medical Center, Bronx, New York, UNITED STATES|U. Mian, Ophthalmology and Visual Sciences, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The American Academy of Ophthalmology (AAO) and the National Heart, Lung, and Blood Institute (NHLBI) suggest sickle cell patients undergo dilated funduscopic exams (DFE) every 1-2 years to screen for sickle cell retinopathy, but there is a paucity of research reporting whether such guidelines are followed in the sickle cell disease (SCD) population. A retrospective study was performed to assess whether adults with SCD at our institution are adhering to the recommendations.

Methods: This study is a chart review of 842 adult patients with sickle cell diagnosis, seen from 3/17 – 3/21 by internists in the Montefiore healthcare system. Data was collected through the Electronic Medical Record (EMR) of patients with a DFE categorized as normal (Retinopathy -, n = 216) or with retinopathy (Retinopathy +, n = 199). A regular DFE was defined as at least one DFE every 2 years. Screening rates were calculated by removing patients with retinopathic disease noted in EMR from total SCD patients. Yearly DFE rates were calculated from March to March, since COVID-19 was declared a global pandemic in March 2020. Two-tailed Student's t-test was used for statistical analysis of continuous data, Fisher's exact test for categorical data, and two-sample proportion test for comparison of yearly exam rates.

Results: The Retinopathy - group was younger ($p<0.001$) and contained less SC genotype ($p<0.001$) compared to Retinopathy +. 40.3% of the Retinopathy - patients were screened regularly (n = 87), whereas 59.7% had irregular screening (n = 129). There was a significant decrease in the total rate of all patients with DFEs, comparing the average rate of 29.8% pre-COVID (3/17-3/20) to 13.6% during COVID (3/20-3/21) ($p<0.001$). Similarly, the screening rate for non-retinopathic patients decreased from an average rate of 18.6% pre-COVID to 6.7% during COVID ($p<0.001$).

Conclusions: The results demonstrate that our rate of routine dilated fundoscopic examination for SCD patients is very low. These low rates were even more adversely affected by the onset of the COVID-19 pandemic, as clinics closed and access to physicians decreased. Screening rates need to be increased by patient involvement and education, easier access to ophthalmologists and novel ways of screening for retinopathy (e.g. annual screening fluorescein angiograms) to reduce risk of blindness in these patients.

CONTROL ID: 3710838

SUBMITTER (NAME ONLY): Sirin Triwutpipatkul

TITLE: Mixed reality headset with obstacle detection software (CU glasses) for improving orientation and mobility in the blind: a pilot study

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Triwutpipatkul, R. Itthipanichpong, B. Khambhiphant, Ophthalmology, Faculty of Medicine , Chulalongkorn University and King Chulalongkorn Memorial Hospital, Pathumwan, Bangkok, THAILAND|

Commercial Relationships Disclosure: Sirin Triwutpipatkul: Commercial Relationship: Code N (No Commercial Relationship) | Rath Itthipanichpong: Commercial Relationship: Code N (No Commercial Relationship) | Bharkbhum Khambhiphant: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To develop a mixed reality (MR) headset with the customized obstacle detection software and voice guided navigation (CU glasses) for avoiding indoor obstacles using a spatial mapping technique and compare its performance with a white cane.

Methods: Ten normal sighted people aged 29-65 years were recruited into this pilot, cross-sectional study. The experiment room was set up with ten soft non-harmful obstacles including 4 face-level, 3 trunk-level and 3 knee-level obstacles. All subjects were blindfolded and trained to use both the CU glasses (CUG) and a white cane (WC) before entering the experiment room. All subjects were randomly assigned to 2 groups (CUG or WC) and walked through the 10 obstacles from entrance (point A) to exit (point B) one by one. After that all subjects were switched the group and walk through the 10 obstacles once again from point B to point A. The number of bumping into obstacles and time from entrance to exit were recorded.

Results: The CUG group had lower number of obstacles hit compared with the WC group

The mean (SD) number of obstacles hit of the CUG group, and the WC group was 0.7 (+/- 0.48) and 1.4 (+/-0.84) respectively. The mean difference (95% CI) of number of obstacles hit between 2 groups was 0.7 (0.12, 1.27), p=0.016. The total time (SD) from start to finish of the CUG group and the WC group was 5.18 (+/-3.42) and 3.21 (+/-2.78) minutes respectively. The mean difference (95% CI) was 1.97 (-4.39, 0.45), p=0.111. All subjects completed the test without any falls or injuries.

Conclusions: The CU glasses can decrease the number of obstacles hit compared with white cane in our indoor experimental environment. Further studies in the blind subjects are needed to assess its full potential as an assistive device for improving orientation and mobility for the blind.

CONTROL ID: 3710840

SUBMITTER (NAME ONLY): Krithika Iyer

TITLE: Treatment with PDGF-BB disrupts the stiffness-dependent myofibroblastic differentiation of corneal keratocytes in response to TGF-β1

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Iyer, D.W. Schmidtke, V. Varner, Bioengineering, The University of Texas at Dallas Erik Jonsson School of Engineering and Computer Science, Richardson, Texas, UNITED STATES|K. Iyer, D.W. Schmidtke, M. Petroll, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: During corneal wound healing, keratocytes located within the stroma are activated into a repair phenotype by the release of soluble growth factors, such as transforming growth factor-beta 1 (TGF-β1) and platelet-derived growth factor-BB (PDGF-BB). This process is often accompanied by an increase in tissue stiffness. Previous studies have shown that the TGF-β1-mediated myofibroblastic differentiation of corneal keratocytes is regulated by changes in stiffness, but it is unclear if the keratocyte response to other growth factors, such as PDGF-BB, is stiffness-dependent. Here, we used a polyacrylamide (PA) gel system to determine if changes in substratum stiffness modulate the proliferation and motility of primary corneal keratocytes cultured in the presence of PDGF-BB. We also investigated how the stiffness-dependent myofibroblastic differentiation of cultured keratocytes is influenced by treatment with both TGF- β1 and PDGF-BB.

Methods: PA substrata with an elastic modulus of either 1 kPa (soft) or 10 kPa (stiff) were fabricated to mimic the mechanical properties of either normal or fibrotic corneal tissue, functionalized with type I collagen, plated with primary rabbit corneal keratocytes (NRKs), and cultured in defined serum-free media in either the presence or absence of TGF- β1 and/or PDGF-BB.

Results: When treated with PDGF-BB, NRKs exhibited a more elongated morphology and a higher rate of proliferation on stiff, as opposed to soft, PA substrata. Using a freeze-injury assay, however, we did not observe stiffness-dependent differences in the PDGF-BB-driven motility of these cells. In the presence of TGF-β1, NRKs cultured on soft PA substrata exhibited low levels of myofibroblastic differentiation, as measured by alpha-SMA immunofluorescence and cellular traction forces. When treated with both TGF-β1 and PDGF-BB, however, increased levels of alpha-SMA immunofluorescence were observed on the soft PA substrata, and we no longer observed stiffness-dependent differences in myofibroblastic differentiation, suggestive of mechanotransductive cross-talk between the signaling pathways downstream of TGF-β1 and PDGF-BB.

Conclusions: Taken together, these data highlight the importance of the combined biochemical and biophysical microenvironment on keratocyte behavior during corneal wound healing.

This work was supported by the NIH grants R01 EY030190 and P30 EY030413.

CONTROL ID: 3710844
SUBMITTER (NAME ONLY): Grace Xiao
TITLE: Assessing resident cataract surgical outcomes using electronic health record data
SESSION TITLE: Vision care training and education
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G. Xiao, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|M. Boland, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Srikumaran, S. Sikder, F. Woreta, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|
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ABSTRACT BODY:
Purpose: To use electronic health record (EHR) data to investigate the relationship between resident experience and cataract surgery outcome measures, including visual acuity and unplanned return to the operating room.
Methods: EHR data were collected from cataract surgeries performed at the Johns Hopkins Wilmer Eye Institute from July 1, 2016 to March 1, 2020, and cases were categorized into resident or attending as primary surgeon. Pre-operative and post-operative visual acuity (VA) were recorded for each surgery, and data on unplanned return to OR were collected.
Results: This study analyzed 14537 cataract surgery cases from July 1, 2016 to March 1, 2020. Out of 337 surgeries that could be attributed to residents with both pre-operative and post-operative VA data, 248 resident cases (73.6%) had better post-operative VA and 170 cases (50.5%) had more than 2 lines improvement in VA. There was no statistical difference in the proportion of cases with better post-operative VA or more than 2 lines improvement between resident and attending cases. The rate of unplanned return to the operating room within 90 days of cataract surgery was not statistically different between resident (1.8%) and attending (1.2%) surgeons.

Attending surgeons had a statistically greater proportion of cases with post-operative VA better than 20/40 but this finding has to be considered in the context that, on average, resident cases started out with poorer baseline visual acuity. Multivariable regression models of VA outcomes versus resident experience that controlled for pre-operative VA, patient age, American Society of Anesthesiologists (ASA) score, and estimated income showed that only pre-operative VA was statistically related to VA outcome.
Conclusions: Resident experience was not related to VA outcomes but pre-operative VA, ASA classification, and attending/resident status were important in predicting post-operative VA. Given the impact of pre-operative VA on post-operative outcomes, VA cutoffs may not provide a high-quality metric to assess resident competency and experience. The use of EHR data can provide an ongoing way to evaluate and monitor resident cataract outcomes.

CONTROL ID: 3710847

SUBMITTER (NAME ONLY): Anil Chekuri

TITLE: AAV mediated delivery of Exon-specific U1 snRNA corrects ELP1 splicing and prevents retinal degeneration in familial dysautonomia

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Chekuri, E. Morini, E. Kirchner, J. Bolduc, S. Slaugenhaupt, Neurology, Massachusetts General Hospital Center for Genomic Medicine, Boston, Massachusetts, UNITED STATES|A.K. Chekuri, L.H. Vandenberghe, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|F. Pagani, International Centre for Genetic Engineering and Biotechnology, Trieste, Friuli-Venezia Giulia, ITALY|

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ABSTRACT BODY:

Purpose: Familial dysautonomia (FD) is an autosomal recessive neurodegenerative disease caused by a splicing mutation in the gene encoding Elongator complex protein 1 (ELP1, also known as IKBKAP). A T-to-C base change in the 5' splice site of ELP1 exon 20 results in exon 20 skipping with tissue specific reduction of ELP1 protein predominantly in the central and peripheral nervous system. In addition to a complex neurological phenotype, FD patients exhibit progressive retinal degeneration that severely affects their quality of life. To rescue retinal degeneration in FD, we have developed a novel splicing-targeted therapeutic approach based on Exon specific U1 small nuclear RNA (ExspeU1 snRNA)). Using a phenotypic mouse model, TgFD9; $Ikbkap^{D20/flox}$, we have tested the therapeutic efficacy of ExspeU1 to correct ELP1 mis-splicing and rescue of retinal degeneration.

Methods: Adeno Associated Vector expressing ExspeU1 was delivered to the retina (AAV2- ExspeU1) by Intravitreal injection. RT-PCR analysis was performed to analyze ELP1 splicing in the retina. Optical Coherence Tomography (OCT) analysis was used to evaluate the thickness of the retinal layers. Retinal whole-mount staining was performed to count the number of retinal ganglion cells (RGCs), and immunohistochemical staining was performed to detect the transduction of AAV2- ExspeU1 in the retina.

Results: To restore ELP1 splicing defect and prevent RGC loss in FD, we have designed a novel splice targeted therapy using ExSpeU1s that permits targeted binding to intronic sequences downstream of the mutant 5' splice site enhancing recruitment of the spliceosomal machinery. In vivo delivery of AAV2- ExspeU1 to the retina showed broader transduction throughout the retina, predominantly in RGCs. Our findings indicated a significant improvement in ELP1 splicing correction in the retina in AAV2- ExspeU1 injected mice (n=6) compared to sham injected mice ($p<0.001$) and support the therapeutic potential of an AAV2- ExspeU1 based treatment to rescue RGC loss in FD.

Conclusions: Our findings demonstrate that delivery of AAV2- ExspeU1 to the retina in FD mice by intravitreal injection corrected the ELP1 splicing defect and therfore it has the potential to rescue the retinal degeneration observed in FD patients. These findings highlight the therapeutic value of AAV2- ExspeU1 delivery to treat retinal degeneration in FD.

CONTROL ID: 3710849

SUBMITTER (NAME ONLY): Ana Ramirez

TITLE: Y-like behavioral responses to contrast-modulated patterns as a specific test of the magnocellular pathway

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ramirez, C. Baker, Ophthalmology, McGill University, Montreal, Quebec, CANADA|L.W. Thompson, A. Rosenberg, Neuroscience, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Ana Ramirez: Commercial Relationship(s);Code P (Patent):Based on these findings the technology transfer office for UW-Madison (WARF) has filed a patent application (pending) with Ari Rosenberg, Curtis Baker and Ana Ramirez listed as inventors. | Lowell Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Ari Rosenberg: Commercial Relationship(s);Code P (Patent):As for first author | Curtis Baker: Commercial Relationship(s);Code P (Patent):As for first author

ABSTRACT BODY:

Purpose: The primate magnocellular pathway originates in parasol retinal ganglion cells, which like Y-cells of the cat, respond nonlinearly to high spatial frequencies (SFs) and temporal frequencies (TFs). However, the contribution of Y-like cells to human visual perception are not well understood.

The contrast-modulated (CM) stimuli used here were composed of high SF contrast-reversing grating carriers that were contrast modulated by a low SF drifting sinewave envelope. Since CM carrier-tuned responses in visual cortex are mediated by Y-cell inputs, we hypothesized that human psychophysical performance for CM stimuli might reflect properties of nonlinear Y-like cells, rather than linear responses to conventional gratings.

Methods: Healthy subjects (N=6) reported the direction of motion of CM envelopes or luminance-modulated (LM) gratings from 2.1-8.5 degrees of eccentricity. SF (for LMs) or carrier SF (for CMs) was varied for different values of TF (LMs) or carrier TF (CMs).

Results: LM performance was low-pass with SF, with the cut-off systematically decreasing with TF. CM performance was bandpass with carrier SF, with best performance at high carrier SFs (1.5-3.0cpd) and TFs (15-20Hz). These observations were confirmed with an ANOVA, showing a significant effect of carrier SF, $p<0.05$, but not carrier TF, $p=0.1$, or their interaction, $p=0.75$. The eccentricity-dependence also differed for LM and CM stimuli. At the highest TF (20Hz), the low-pass LM performance decreased systematically with eccentricity, while CM performance was bandpass with carrier SF, and rather independent of eccentricity. An ANOVA showed a significant main effect for the carrier-SF, $p=<0.05$, but not eccentricity $F(3,2)=0.8$, $p=0.48$, or their interaction, $p=0.56$.

Conclusions: Since nonlinear subunits of Y-like cells respond better at higher TFs than linear mechanisms respond to gratings, the psychophysical performance for CMs is consistent with Y-like cells. The good performance for CM stimuli at carrier SFs that are high for peripheral vision and the relative independence of eccentricity are also consistent with responses of small Y-like nonlinear subunits. These results suggest that our CM behavioral task provides a specific indicator of the functioning of Y-like cells in human vision. This might be relevant to assessing pathologies related to damage in the magnocellular pathway, including glaucoma.

CONTROL ID: 3710853

SUBMITTER (NAME ONLY): Nicholas Iafe

TITLE: Classification and automated detection of retinal arteriovenous crossing morphology in systemic arterial hypertension using infrared scanning laser ophthalmoscopy

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Iafe, H. Hosseini, J. Choi, C. Hoeferlin, I. Chehaibou, S.D. Schwartz, Retina Division, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|A. Hatamizadeh, Computer Science Department, University of California Los Angeles Henry Samueli School of Engineering, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate whether retinal vascular analysis of arteriovenous (AV) crossings in Infrared Scanning Laser Ophthalmoscope (IR-SLO) images using convolutional neural networks (CNN) may contribute to classification and risk stratification of patients with systemic hypertension.

Methods: Medical records and IR-SLO images were reviewed for 152 consecutive patients. Healthy control group images were used to assess normal vasculature. The morphologic characteristics of AV crossings were compared between patients with and without hypertension, evaluating continuity of the central venous light reflex and the presence of venous narrowing. Retinal specialists manually categorized all images by the severity of change; a subset of 99 images was analyzed using a CNN model.

Results: Sixty-three patients (51%) had systemic hypertension. Venous changes at AV crossings were more common in hypertensive patients (44/63, 70%) compared to normotensive patients (19/61, 32%; $P < 0.0001$). Moderate changes were seen in 25 (40%) hypertensive patients compared to 15 (25%) normotensive patients (P=0.002). Severe changes were noted in 19 (30%) hypertensive patients compared to 4 (7%) normotensive patients (P=0.001). Output predictions of the CNN model had a mean Average Precision (mAP) of 81% for image classification.

Conclusions: The presence of morphological changes at AV crossings is correlated with hypertension in this series of patients. The authors propose that IR imaging may be used in the clinical setting to evaluate hypertensive retinal vasculature changes and provide a framework for automated classification and risk stratification.

CONTROL ID: 3710855

SUBMITTER (NAME ONLY): Rachel Fehrman

TITLE: Determining the cellular transduction efficacy of multiple rAAV vectors in the murine retina

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Fehrman, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|R. Fehrman, D.M. Lipinski, Ophthalmology and Visual Science, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D.M. Lipinski, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Rachel Fehrman: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Lipinski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recombinant adeno-associated virus (rAAV) vectors have become promising tools for mediating gene transfer to retinal neurons for the treatment of monogenic inherited retinal diseases. Unfortunately, due to the limited 4.8 kb coding capacity of rAAV and the large size of many therapeutic transgene cassettes, numerous retinal diseases cannot currently be treated using rAAV-mediated gene therapy. To circumvent this limitation, transduction with two or more vectors, each containing separate gene fragments, has been utilized. Although these studies have shown success, in vivo efficiencies remain around 10%. Due to this fact, our study aims to investigate the cellular transduction efficacy when multiple reporter transgenes are delivered to the murine retina.

Methods: Female C57BL/6J mice (N=9) received bilateral intravitreal injections of one, two, or three recombinant AAV (rAAV) vectors packaging a ubiquitously expressing mCherry, green fluorescent protein (GFP), and/or blue fluorescent protein (BFP) transgene cassettes respectively (N=3/group). Dual fluorescence confocal scanning laser ophthalmoscopy (cSLO) was performed 4 weeks post-injection to assess transgene expression in vivo. Retinae were harvested and dissociated allowing quantification of transduction efficiency via flow cytometry.

Results: cSLO imaging revealed dual injection of rAAV2/2[MAX].CBA.GFP and rAAV2/2[MAX].CBA.mCherry (N=6 eyes) resulted in widespread retinal transduction centered on the optic near head. The pattern of GFP and mChery expression was observed to substantial overlap, indicating efficient co-transduction following delivery of multiple vectors. Preliminary flow cytometry analysis of dissociated retinae revealed that up to 62.0% (±9.2%) of GFP+ve cells also co-expressed mCherry, indicating that co-transduction with multiple vectors is only partially efficient. Analysis of triple injected eyes in ongoing.

Conclusions: This study indicates that the ability of multiple rAAV vectors to transduce individual retinal neurons following administration via a single injection is substantially higher than the recombination efficiencies previously reported, suggesting that co-transduction with rAAV vectors containing multiple fragments is not a limiting factor.

CONTROL ID: 3710856

SUBMITTER (NAME ONLY): Carolyn Guan

TITLE: Structure of Astrocytes, Axons, and Lamina Cribrosa Beams in Human Glaucoma

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Guan, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|Y. Ling, T.D. Nguyen, Department of Mechanical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|M. Pease, S. Quillen, T.V. Johnson, H.A. Quigley, Wilmer Ophthalmological Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify the morphology of astrocytes, connective tissue beams, and axonal compartments in post mortem human optic nerve heads (ONH), comparing control to glaucoma, central to peripheral ONH, and by degree of optic nerve damage.

Methods: Serial cross-sections of 16 glaucoma ONH (from 12 donors, median age=79) and 9 control ONH (from 6 donors with no glaucoma history and normal optic nerves, median age=83) were immunolabelled for confocal and second harmonic generation imaging as described in Ling et al. 2019. 63 structural features of lamina cribrosa (LC) were measured, including astrocytic glial fibrillary acidic protein (GFAP) area fraction, actin area fraction, median axonal compartment area, average collagen beam width, and nuclei density. Global and regional differences were compared between controls and glaucoma, and among glaucoma severity groups judged by masked grading of axon loss in nerve cross-sections by two observers.

Results: The area fraction of GFAP and actin in the LC pores was significantly decreased in glaucoma eyes ($P = 0.014$, 0.009, respectively) and these measures declined consistently with increased glaucoma damage (Figure 1). However, the mean area of LC pores was not significantly different in glaucoma eyes. Median axonal compartment area was significantly lower in glaucoma ($P = 0.015$). GFAP area fraction in pores was higher in periphery than center LC in both control and glaucoma ($P = 0.057$, $P = 0.025$, respectively). While in controls the mean collagen beam width was similar in central and peripheral regions, in glaucoma the beam width was significantly lower in peripheral than in central regions ($P = 0.007$).

Conclusions: This cross-sectional, quantitative analysis of LC structure suggests that loss of axons in glaucoma is associated with reductions in astrocyte cytoskeletal components and axonal compartments, as well as progressive beam thinning.

CONTROL ID: 3710859

SUBMITTER (NAME ONLY): Matilda Chan

TITLE: Development of a research pipeline to identify novel treatments for Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.F. Chan, F. Wolfreys, E. Ding, P. Pan, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|M.F. Chan, Francis I Proctor Foundation for Research in Ophthalmology, Francis I Proctor Foundation for Research in Ophthalmology, San Francisco, CA, US, academic/medres, San Francisco, California, UNITED STATES|S. Kuo, M. Kampmann, J.E. Gestwicki, Institute for Neurodegenerative Diseases, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the SLC4A11 gene are associated with Fuchs endothelial corneal dystrophy (FECD). SLC4A11 is expressed by corneal endothelial cells (CECs) and regulates corneal fluid balance and ion homeostasis. SLC4A11 mutations can cause disease through protein misfolding and an unfolded protein response. Prior studies showed that correcting mutant SLC4A11 misfolding can restore CEC functional activity. Thus, a safe and effective chemical corrector for SLC4A11 mutations related to FECD may be identified through an advanced research pipeline consisting of cell-based assays, CRISPR screens, and high content imaging (HCI) technologies. The purpose of this study is to develop a cell-based system for our research pipeline.

Methods: Plasmids suitable for HCI were generated to express doxycycline-inducible (Tet-on) GFP-SLC4A11 wild-type or mutant (G709E) fusion proteins. The plasmids were stably transfected into a HEK293T dCas9-KRAB cell line to allow for CRISPR genetic screens. Confocal microscopy was used to assess the cellular localization of GFP-tagged $SLC4A11^{WT}$ and $SLC4A11^{G709E}$ in the absence or presence of doxycycline and glafenine (positive control compound). The cell culture assay was then miniaturized to 384-well plate format and optimized for high throughput phenotypic screens (HTS). A screening Z' score was determined as a statistical parameter for predicting the success of HTS campaigns.

Results: Confocal microscopy showed that expression of both proteins was doxycycline inducible, but the WT protein was properly trafficked to the plasma membrane while the G709E mutant was retained in puncta. Addition of glafenine partially restored normal trafficking of $SLC4A11^{G709E}$. The doxycycline concentration (2 µg/mL), assay volume (20 µL), treatment time (48 hrs) and number of cells/well (3,000 cells) were successfully optimized. Dose-response curves identified the concentration required for maximal activity (40 µM) and confirmed that the negative control (DMSO) had no measurable effect on fluorescence or cell viability. The calculated Z' score for 40 µM glafenine was 0.32.

Conclusions: We have developed a cell-based assay that is ready for HCI and CRISPR genetic screens for discovering correctors for FECD-associated mutations. More broadly, this assay and workflow can be readily adapted for use in other genetic causes of FECD and other ocular disorders.

CONTROL ID: 3710860

SUBMITTER (NAME ONLY): Manuela Bartoli

TITLE: Anti-senescence properties of the flavone Silymarin in the diabetic retina involve direct inhibition of the histone deacetylase 6 (HDAC6)

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bartoli, M. Thounaojam, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|R. Jadeja, P.M. Martin, Biochemistry and Molecular Biology, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|H. Abouhish, A. Elmasry, Clinical Pharmacology, Faculty of Medicine University of Mansoura, Mansoura, EGYPT|J. Georrge, Bioinformatics, University of North Bengal, Darjeeling, West Bengal, INDIA|R. Devkar, Metabolic Endocrinology Division, Faculty of Science The Maharaja University of Baroda, Vadodara, Gujarat, INDIA|

Commercial Relationships Disclosure: Manuela Bartoli: Commercial Relationship: Code N (No Commercial Relationship) | Hossameldin Abouhish: Commercial Relationship: Code N (No Commercial Relationship) | Ravirajsinh Jadeja: Commercial Relationship: Code N (No Commercial Relationship) | Pamela Martin: Commercial Relationship: Code N (No Commercial Relationship) | Ahlam Elmasry: Commercial Relationship: Code N (No Commercial Relationship) | John Georrge: Commercial Relationship: Code N (No Commercial Relationship) | Ranjitsinh Devkar: Commercial Relationship: Code N (No Commercial Relationship) | Menaka Thounaojam: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously shown that in the diabetic retina histone deacetylase 6 (HDAC6) is one of the initiating factors promoting stress-induced premature senescence (SIPS) in the retinal vasculature. This is a key pathogenic process involved in the onset and progression of diabetic retinal microangiopathy and diabetic retinopathy (DR). Anti-aging and senolytic drugs are thought to be beneficial for neurodegeneration and cardiovascular disease including diabetes. Silymarin (SIL) is a flavone that has been shown to halt senescence in a number of cell types including endothelial cells. Here we have investigated the effects of SIL on retinal vascular SIPS in an experimental model of DR also determining its inhibitory ability towards HDAC6.

Methods: Morphological and biochemical analyses were performed comparing streptozotocin-induced diabetic rats (STZ) with age-matched normoglycemic rats (control) and with STZ-rats that received SIL (200 mg/Kg/day p.o.) starting 2 weeks after the onset of hyperglycemia and continued for all the duration of diabetes (8 weeks). SIPS was shown by immunostaining for S-A-beta GAL and by immunoblotting for p16ink4a and p21waf. HDAC6 expression and activity were measured by immunoblotting and fluorescence enzymatic assay, respectively. Docking studies were done to elucidate at molecular level SIL and HDAC6 interaction.

Results: Our analyses showed that SIL preserved retina cells survival while down-regulating the expression of pro-inflammatory and pro-oxidant factors. SIL also reduced the expression of senescence markers and downregulated the expression and activity of HDAC6. Docking studies-based predictions revealed SIL potential interaction with both the catalytic and zinc-finger ubiquitin-binding domains of HDAC6 demonstrating strong inhibitory activity of SIL towards this deacetylase.

Conclusions: Overall, our studies demonstrate SIL beneficial effects in the diabetic retina by preventing diabetes-induced retinal vascular SISP through its inhibitory activity towards HDAC6. These results also warrant further studies to assess SIL senolytic activity and set the stage to clinical studies evaluating the use of this flavone as potential adjuvant therapy for DR.

CONTROL ID: 3710862

SUBMITTER (NAME ONLY): William Monaco

TITLE: Risk factors for vision loss among nursing home residents: a cross-sectional analysis

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Approximately two percent of older adults currently live in nursing homes and this institutionalized population is at substantial risk for vision loss. It is important that the risks for vision loss be characterized to ensure appropriate vision care is provided for nursing home patients. Our objective was to evaluate the association of age-related eye diseases (AREDs) and multi-morbidities with vision impairment (VI).

Methods: This is a cross-sectional analysis of comprehensive eye examination records for 7927 residents of 74 North Carolina nursing homes who were ≥65 years at time of the initial patient visit. Complete data on outcomes, associated factors, and covariates were included from the standardized Centers for Medicare and Medicaid Services eye exam. We defined VI and blindness respectively as best-corrected visual acuity between 20/40 and 20/200, and 20/200 or worse. Clinical diagnoses of AREDs were defined by the attending clinician. Data were extracted from electronic health records and al analyses were conducted in SAS version 9.4. We used descriptive statistics to summarize the resident characteristics and AREDs and logistic regression analysis to examine independent risk factors for VI.

Results: A total of 7927 initial eye exam records (mean age 83 (SD = 8.5), 68% female) with complete data were included in the analysis. Overall, 34% of the residents had normal vision, 43% had VI, and 23% were blind. The prevalence of vision impaired/blind among participants with AREDs including untreated cataracts, macular degeneration, glaucoma, and diabetic retinopathy were respectively 71%, 76%, 69%, and 63%. Among patients with AREDs, prevalence of blindness ranged from 53% for patients with cataracts to 23% for patients with diabetic retinopathy.

Conclusions: Comprehensive eye examinations showed vision impairment and blindness affected 66% of nursing home residents, overall. This study substantiates the positive impact of comprehensive eye examinations to promote visual, systemic and cognitive health and wellbeing and the need that eye care service be used to inform policy and practice to improve patient functioning and independence. Further analyses are being performed to determine whether or not correction of refractive error could reduce vision impairment or blindness.

CONTROL ID: 3710866

SUBMITTER (NAME ONLY): Isabela Vale

TITLE: Evaluation of dry eye disease after COVID-19 infection

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A prospective observational clinical study was performed to evaluate ocular symptoms related to dry eye disease (DED) in patients infected with COVID-19.

Methods: The staff of an University Hospital in Londrina city, Brazil, who presented respiratory symptoms and underwent nasal swab PCR test for SARS-CoV-2 detection at the outpatient unit during November to December 2020 was assessed by electronic messages and separated in two groups (PCR test negative or control group – CG, and PCR test positive or COVID-19 group - COVG). Sociodemographic data, presence of ocular and systemic comorbidities, place of treatment (home, infirmary or intensive care unit), and the Ocular Surface Disease Index (OSDI) questionnaire, translated and validated to Portuguese for DED evaluation were performed. OSDI contains 3 subsections including visual-related function (category A), ocular symptoms (category B) and environmental triggers (category C). Scores range from 0 to 100 with 0 to 12 representing normal, 13 to 22 mild DED, 23 to 32 moderate DED and 33 severe DED. The data was submitted to statistical analysis.

Results: From 450 electronic messages sent, 113 patients were included. 62(54,85%) had laboratory-confirmed (RT-PCR) Covid-19. The mean age was 36 years, ranging from 21 to 60 years. 83 (73.4%) patients were female. The main systemic comorbidity was smoking (23%), followed by obesity (3.5%) and hypertension (1.76%). The mean OSDI score was 13.85 in the COVG and 5.37 in the CG (p=0.002). The COVG had a mean score of 3.50 related to category A, 1.05 to category B and 2.13 to category C while the CG presented a mean score of 1.41, 0.39 and 0.80 respectively (p = 0.003; p=0.04; p=0.01). Patients who required hospitalization for treatment presented OSDI score proportionally greater than those who were treated at home (25.67) (p=0.052).

Conclusions: OSDI score was higher in the COVG and among patients who required hospitalization for treatment. These results suggest association of COVID infection and DED; and increase of DED according to the severity of respiratory symptoms.

CONTROL ID: 3710868

SUBMITTER (NAME ONLY): Eleonora Micheletti

TITLE: Factors Associated with Enlargement of Choroidal Microvascular Dropout in Glaucoma

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the factors associated with choroidal microvasculature dropout (MvD) enlargement detected by optical coherence tomography angiography (OCT-A) in glaucoma eyes.

Methods: Ninety-one eyes of 68 primary open angle glaucoma (POAG) patients were enrolled. Only eyes with 4 good quality OCT-A and OCT scans of the optic nerve head with 2 years follow-up were included. Area of MvD were analyzed on en-face images at each visit (see Figure). Univariable and multivariable mixed effects models were constructed to identify the factors contributing to MvD area over time.

Results: Peripapillary MvD was detected in 53 (58.2%) eyes at baseline and in an additional 17 (18.7%) eyes during follow-up, whereas MvD was not detected in 21 (23.1 %) eyes during the entire follow-up period. In eyes with MVD at baseline, mean baseline MVD area was 0.15 (0.09, 0.22) mm^2. In eyes with MvD at baseline, mean (95% CI) of rate enlargement of MVD area was 0.05 (0.04, 0.06) mm^2/year. In the univariable model, worse baseline VF MD (coefficient ß =0.27, 95%CI: 0.10, 0.44, P=0.002), greater intraocular pressure (IOP) fluctuations (ß=0.86, 95% CI: 0.24, 1.48, P=0.007), higher peak IOP (ß=0.17, 95% CI: -0.01, 0.35, P=0.067) and greater number of IOP lowering medications (ß =1.36, 95% CI: 0.67, 2.05, P<0.001) were associated with faster MvD area enlargement (Table 1). In the multivariable model, worse baseline VF MD, greater IOP fluctuations, higher peak IOP and greater number of IOP lowering medications remained significantly associated with faster MvD area enlargement (Table 1). No associations were found between mean IOP during follow-up and MvD changes over time. In the 17 eyes that developed MvD during follow-up, long-term IOP fluctuation [95% CI], defined as the standard deviation of IOP measurements during follow-up, was significantly greater (3.5 [2.3, 4.7] mmHg) in eyes with MvD compared to eyes that did not develop MvD (1.9 [1.5, 2.3] mmHg, P=0.012).

Conclusions: IOP fluctuation was associated with MvD enlargement and development. Other factors, including peak IOP, worse baseline VF MD and number of glaucoma medications were significantly associated with MvD area enlargement in glaucomatous eyes. The identification of factors associated with MvD enlargement may improve our understanding of the role of choroidal microvasculature in glaucoma.

CONTROL ID: 3710869

SUBMITTER (NAME ONLY): Michael Fitzpatrick

TITLE: Homeostatic plasticity in retinal illluminance-detection circuits preserves non-image-forming visual behaviors

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Fitzpatrick, C. Lee, D. Kerschensteiner, John F. Hardesty, MD Department of Ophthalmology and Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|M.J. Fitzpatrick, Medical Scientist Training Program, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|C. Lee, Graduate Program in Neuroscience, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|E.D. Herzog, Department of Biology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|E.D. Herzog, D. Kerschensteiner, Hope Center for Neurological Disorders, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: The visual system requires stable encoding of environmental illuminance across a wide dynamic range. Illuminance is encoded within the retina by the M1 subclass of intrinsically photosensitive retinal ganglion cells (M1 ipRGCs). M1 ipRGCs integrate extrinsic signals from photoreceptors with their own intrinsic light responses to drive non-image-forming (NIF) behaviors such as the pupillary light reflex (PLR) and circadian photoentrainment. This integration is vital for illuminance encoding and downstream NIF behaviors; however, it is unknown whether the M1 ipRGC circuit can compensate for perturbations to its synaptic input. In perturbed circuits, homeostatic plasticity can restore neural activity and preserve functional stability. However, it is unclear how and to what extent homeostatic plasticity can restore activity in the highly specialized M1 ipRGC circuit and preserve NIF behaviors at the level of the entire organism.

Methods: To address this question, we used mice in which the type 6 bipolar cell (B6), which provides ~90% of the synaptic input to M1 ipRGCs, was genetically deleted through targeted expression of diphtheria toxin (DTA; B6-DTA mice). We recorded the PLR and circadian rhythms of B6-DTA and control mice under different illuminance regimes to analyze the extent, if any, of homeostatic compensation. Additionally, we performed immunohistochemical assays to confirm B6 deletion and electrophysiological experiments to investigate the B6 to M1 ipRGC synapse.

Results: First, we expand upon previous structural evidence to show that type 6 bipolar (B6) cells functionally provide extrinsic photoreceptor-derived input to M1 ipRGCs. We find preserved PLR magnitude, sensitivity, and kinetics in B6-DTA mice. Using a novel stimulus paradigm to isolate the extrinsic component of the PLR, we found only subtle changes in pupil responses for B6-DTA mice. Furthermore, B6-DTA mice were able to successfully photoentrain their circadian rhythms across a broad range of light levels.

Conclusions: We demonstrate that homeostatic plasticity preserves NIF vision via compensatory rewiring of non-canonical synaptic input to M1 ipRGCs. The mechanisms by which this plasticity is accomplished could reveal fresh insights into both the biology of retinal illuminance-detection circuits as well as novel strategies to preserve visual behaviors after injury.

CONTROL ID: 3710870

SUBMITTER (NAME ONLY): Zhuojun Guo

TITLE: A Comparative Analysis of Alternative Calcium Chelators for the Treatment of Calcific Band Keratopathy

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Guo, R.K. Henry, M. Dastjerdi, Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|R.K. Henry, Rutgers Robert Wood Johnson Medical School New Brunswick, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: K_3EDTA and K_2EDTA are readily available alternatives to Na_2EDTA, the traditional calcium chelator used to treat calcific band keratopathy. In this study we compare clinically relevant biochemical properties of each chelator in terms of pH, osmolarity, and calcium chelation potential.

Methods: 0.2 M Solutions of K_2EDTA (BD) and K_3EDTA (BD, obtained from vacutainer tubes) and Na_2EDTA (0.2M, Sigma Aldrich) were made. The pH of each solution was first measured (Mettler Toledo pH meter) and the theoretical osmolarity calculated with the assumption of full disassociation of EDTA salts. Next, we calculated the calcium chelation potential of each EDTA salt by titrating with 10 µmol of calcium hydroxyapatite or 10 µmol $CaCl_2$ containing Patton-Reeder colorimetric indicator (endpoint indicated by color shift from pink to blue). All titrations were repeated three times to obtain an average and standard deviation. Statistical significance was analyzed using Analysis of Variance (ANOVA) calculations.

Results: The 0.2 M solutions of Na_2EDTA, K_2EDTA, and K_3EDTA have pH values of 4.43, 5.71 and 9.191 and theoretical osmolarities of 600, 600, and 800 mOsm/L, respectively. Calcium chelation ability was similar among all 3 solutions: 0.94-0.98 mol of EDTA was needed to fully chelate 1 mol calcium ions of $CaCl_2$ (P=0.296), 0.100-0.108 mol of EDTA was needed to fully chelate 1 mol calcium ions of the hydroxyapatite aqueous suspension (P=0.296), and 0.992-0.996 mol was needed to chelate 1 mol calcium ions of hydroxyapatite in acidic solution (P=0.178, Table). Compared to the clinical standard 3% Na_2EDTA, approximately 3.3% K_2EDTA and 3.6% K_3EDTA is needed to chelate an equivalent amount of calcium.

Conclusions: Herein we provide clinically relevant biochemical properties of two alternatives to disodium EDTA and demonstrate comparable calcium chelation ability among all 3 solutions. In situations where sterile sources of Na_2EDTA is unavailable, salts of potassium EDTA may provide a convenient and equally effective method of treatment for band keratopathy.

CONTROL ID: 3710872

SUBMITTER (NAME ONLY): Kazuichi Maruyama

TITLE: Management of Vogt-Koyangi-Harada disease with deep learning-based volume image enhancement and quantification of optical coherence tomography

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Maruyama, N. Shiraki, N. Hashida, R. Kawasaki, K. Nishida, Ophthalmology, Osaka Daigaku Daigakuin Igakukei Kenkyuka Igakubu, Suita, Osaka, JAPAN|S. Mei, S. Liu, Z. Mao, Z. Wang, K. Chan, Topcon Advanced Biomedical Imaging Laboratory, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Investigate the relationship between quantitative biomarkers obtained with optical coherence tomography (OCT) and a deep learning analysis and disease recurrence and management.

Methods: A single-medical center retrospective analysis was designed. This study obtained scans of swept-source OCT at a medical center. Thirty-three eyes of 17 patients (7 females, 10 males) with Vogt-Koyanagi-Harada disease (VKH) or sympathetic ophthalmitis (SO) were imaged consecutively between October 2012 and January 2021. Choroidal vessel structure was segmented and visualized in 3D, after which quantitative vessel volume maps are generated. Region-based choroidal vessel volume (CV), choroidal stroma volume (SV), and vessel index (VI) were analyzed for disease severity.

Results: OCT-based CV volume maps disclose regional CV changes in patients with VKH or SO. Two metrics in recurrence VKH, (i) choroidal volume at 1-, 3- and 6-month (p=0.01, 0.04 and 0.03), (ii) CV volume at one months (p=0.03), were higher than well treated VKH.

Conclusions: The deep-learning analysis of OCT images described here provides a 3D visualization of how the choroid may reflect disease severity in VKH patients. Moreover, CV or SV before treatment may become the biomarker for recurrence of VKH.

CONTROL ID: 3710873

SUBMITTER (NAME ONLY): NEERAJ CHAUHAN

TITLE: Protective effect of bis-allylic deuterated docosahexaenoic acid (D-DHA) against Light Induced Retinal Degeneration

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.K. CHAUHAN, V. Ea, W. Bohannan, E. Adewunmi, M.G. Agbaga, Department of Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|H. Park, G. James, J. Brenna, Dell Pediatric Research Institute, The University of Texas at Austin, Austin, Texas, UNITED STATES|M. Shchepinov, K. Schmidt, Retrotope Inc., California, UNITED STATES|N.K. CHAUHAN, V. Ea, W. Bohannan, E. Adewunmi, M.G. Agbaga, Department of Ophthalmology, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Docosahexaenoic acid (DHA) is essential for photoreceptor function and health, therefore retinal DHA depletion is associated with many retinal degenerative diseases such as age-related macular degeneration. However, the multiple cis-double bonds in natural DHA (H-DHA) in the metabolically active retina are highly prone to free radical peroxidation that generates deleterious lipid metabolites that contribute to age-related retinal pathologies. We hypothesize bis-allylic deuterated docosahexaenoic acid DHA (D-DHA) will be more resistant to lipid peroxidation, inhibit light-induced radical lipid peroxidation, and attenuate light-induced retinal degeneration. We therefore determined the protective effect of D-DHA against light-induced oxidative stress in the retina.

Methods: Sprague-Dawley rats were raised on regular lab chow under 25-lux light conditions until 8 weeks of age. The rats were then switched to experimental diets of H-DHA or D-DHA until retinal DHA levels were ~50% or 75%. To determine the protective effect of D-DHA against light stress, we exposed the rats to cool white fluorescent bright light stress (2700-lux for 6 h) and returned them to their normal housing conditions for 1 week after which we determined retinal function by electroretinography (ERG). We examined preservation of retinal structure by H&E staining and further performed immunostaining on retinal sections using 4-Hydroxynonenal (4-HHE) and Carboxyethylpyrrole (CEP) formed from H-DHA under oxidative stress.

Results: We showed that D-DHA replaced H-DHA in the retina in time dependent manner and had no effect on retinal function under no light stress conditions. After light stress, we observed preservation of retinal function as determined by ERG a-wave and b-wave amplitudes in D-DHA fed rats compared to H-DHA fed rats. Histological analyses revealed significant loss of photoreceptor outer nuclear layer in light exposed H-DHA fed rats compared to D-DHA fed rats 1 week after light stress. Our immunohistological data showed high levels of 4-HHE and CEP in H-DHA under oxidative stress compared to D-DHA fed rats.

Conclusions: Deuterium-reinforced DHA preserved retinal structure and function against light-induced retinal degeneration most likely by inhibiting lipid peroxidation. Taken together, our results suggest the dietary D-DHA may be beneficial in attenuating oxidative stress-induced retinal pathologies.

CONTROL ID: 3710874

SUBMITTER (NAME ONLY): Fátima Magaña Guerrero

TITLE: Participation of citrullinated histone a NET associated protein as inflammatory marker of diabetic retinopathy prognosis

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Garfias, Cellular and Tissue Biology Department, Instituto de Oftalmología Fundación Conde de Valenciana IAP, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MX, other/health, Mexico,city, Mexico, city , MEXICO|Y. Garfias, Medicine Faculty, Biochemistry Department, Universidad Nacional Autonoma de Mexico, Ciudad de Mexico, Ciudad de México, MEXICO|J. Rodriguez Loaiza, Retina Department, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|F.S. Magaña Guerrero, P. Sanchez-Cisneros, J. Aguayo-Flores, B. Buentello-Volante, Cellular and Tissue Biology Department, Instituto de Oftalmología Fundación Conde de Valenciana IAP, Mexico city, Mexico, city , MEXICO|L. Islas-Vazquez, Immunology Department, Instituto de Oftalmología Fundación Conde de Valenciana IAP, Mexico city, Mexico, city , MEXICO|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is the major vascular complication of diabetes and is the main cause of blindless worldwide. The development of DR is associated with chronic inflammation of diabetic patients. Neutrophils are inflammatory cells able to release structures formed by extracellular DNA decorated with proteolytic enzymes and proteins with posttranslational modifications such as citrullinated histone 3 (H3Citr) named neutrophil extracellular traps (NETs). The aim of this study is to determine the association between the serum levels of H3Citr and the DR in different clinical stages.

Methods: This is a cross-sectional study. Diabetic (DMT2) patients with and without different stages of RD were included as well as control subjects. Once the informed consent was signed, clinical, ophthalmological, and metabolic evaluations were performed, and a peripheral blood sample was obtained. Activation of Peripheral blood neutrophils (PBN) was achieved by means of flow cytometry, while H3Citr serum levels were evaluated by ELISA. H3Citr and metabolic status correlations were also performed. Finally, PBN-H3Citr was measured by means of western blot and compared among groups.

Results: CD66b is an activation marker for neutrophils. PBN-CD66b+ cells were significantly higher ($p \leq 0.05$) only in the Proliferative DR (PDR) group when compared between the other groups. We observed an increased concentration of H3Citr levels in DMT2 without DR [DMT2-non-DR], respect to the other groups. Regarding the association of H3Citr with the clinical and metabolic conditions, we found a significative positive correlation ($p \leq 0.05$) between serum concentration of H3Citr levels with their clinical and metabolic values such as Body Mass Index (BMI), glycosylated hemoglobin (HgA1b), fasting glucose, cholesterol, Low-Density Lipoproteins (LDL) and triglycerides (TG). Finally, H3Citr expression from PBN obtained from PRD and activated with ionomycin was significantly higher when compared with the other groups.

Conclusions: Taking together these results, suggest that PBN from PRD patients are more prone to be activated and this might reinforce the inflammatory hypothesis of the RD. Interestingly, serum H3Citr is able to predict a systemic inflammatory state among DMT2. This post translationally modified protein is of interest to study DMT2 and its main microvascular complication, the DR.

CONTROL ID: 3710876

SUBMITTER (NAME ONLY): Roy Joseph

TITLE: Role of Fibroblast Growth Factor Receptor 2 (FGFR2) in Corneal Stromal Thinning.

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Joseph, A.K. Boateng, O.P. Srivastava, School of Optometry and Vision Science, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Fibroblast Growth Factor Receptor 2 (FGFR2) is a membrane-spanning tyrosine kinase that mediates signaling of fibroblast growth factors (FGFs). It regulates embryogenesis, angiogenesis, tissue homeostasis and wound repair. It also plays an important role in cell functions such as proliferation, differentiation, apoptosis and migration. Our earlier results showed that FGFR2 was significantly down-regulated in keratocytes of human keratoconus corneal stroma. To determine the functional and mechanistic roles of FGFR2-mediated signaling in keratocytes during corneal development, a stromal specific FGFR2 knockout (KO) mouse was developed.

Methods: FGFR2 KO mouse model was generated by the following methodology: FGFR2 flox mice (Jackson Labs) were crossed with inducible keratocyte specific-Cre mice (Kera-rtTA/tet-O-Cre, Dr. Winston Kao, University of Cincinnati). The pregnant females were fed doxycycline chow (600 mg/kg) to induce corneal stromal-specific FGFR2 KO pups. The flox-, Cre-, and wild-type (wt) mice were used as controls. Corneal thickness were determined using an ultra-high resolution spectral domain optical coherence tomography instrument (SDOCT, Bioptigen). Both males and female mouse were analyzed by OCT at different ages. The topography and pachymetry maps were obtained using an OCT based method. Tunel assay and immunohistochemical analysis were performed to determine the apoptotic cells and collagen 1 expression in KO corneas relative to controls, respectively.

Results: Gene-expression analysis showed that among the two isoforms of FGFR2 (FGFR2-iiib [epithelial-specific] and FGFR2-iiic [mesenchymal specific]), FGFR2-iiic was expressed in the normal corneal stroma. OCT-based analysis of the FGFR2 KO mice (n=20) corneas showed localized stromal thinning compared to control mice (n=20). Some of the mice even developed anterior synechia (iris attached to the anterior cornea), which has been reported in human keratoconus. Immunohistochemical analysis showed relatively lower expression in collagen1 and more apoptotic cells in the FGFR2 KO corneal stroma compared to control mice stroma.

Conclusions: The FGFR2 KO mice showed localized stromal thinning similar to that seen in human keratoconus cornea. This suggested that the stromal-specific conditional FGFR2 KO mouse model would elucidate functional and mechanistic roles of FGFR2 in stromal keratocytes and also serve as a keratoconus animal model

CONTROL ID: 3710877

SUBMITTER (NAME ONLY): Grant Carlisle

TITLE: Full-thickness eyelid laceration repair: human cadaver versus cadaveric pig head as a model for teaching ophthalmology residents

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Carlisle, S. Patel, C. Weller, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Grant Carlisle: Commercial Relationship: Code N (No Commercial Relationship) | Saager Patel: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Weller: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study was to investigate the efficacy of human cadaver and cadaveric pig head as a model to educate ophthalmology residents with the understanding and ability to perform full-thickness eyelid laceration repair at a single institution.

Methods: Ophthalmology residents at Penn State Health Milton S. Hershey Medical Center were anonymously surveyed using a Likert questionnaire inquiring about their comfort and ability to perform a full-thickness eyelid laceration repair. Answers included options 1 (“Incomplete understanding”) - 5 (“Mastery”). The survey was administered pre-intervention (n=9), post-human cadaveric model (n=9), and post-pig cadaveric model (n=8). Prior to working with the model, residents were given a 20-minute tutorial introducing clinical approach to laceration repair as well as a detailed explanation on how to approach the procedure. Wet-labs with either model included one 2-hour session. Survey results were compared using two-tailed Student’s t-test.

Results: Pre-curriculum survey results for full-thickness eyelid laceration repair included the following: “Mean Score Knowledge” PGY2(2.0), PGY3(2.0), PGY4(3.0) and “Mean Score Performance” PGY-2(1.7), PGY-3(2.0), PGY-4(3.3). Thirty-three percent of residents were comfortable with being the primary surgeon during repair. Post-survey results after using a human cadaver model: “Mean Score Knowledge” PGY2(2.7), PGY3(4.3), PGY4(3.3) and “Mean Score Performance” PGY-2(2.0), PGY-3(4.3), PGY-4(3.7). Seventy-eight percent of residents were comfortable being the primary surgeon for repair after training on the human cadaver model. Cadaveric pig head model post-survey results are pending. All training years reported in improvement in knowledge and ability to perform eyelid-laceration repairs after training with a human cadaver.

Conclusions: Human cadavers significantly improved ophthalmology resident’s knowledge and ability to perform full-thickness eyelid laceration. Cadaveric pig heads may be a useful and more affordable model for educating ophthalmology residents with the understanding and ability to perform eyelid-margin involving laceration repair.

CONTROL ID: 3710881
SUBMITTER (NAME ONLY): K V Chalam
TITLE: Evaluation of effect of modified housing on fogging of reusable wide angle panoramic contact lens during vitreoretinal surgery
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Chalam, S. Gupta, Ophthalmology, Loma Linda University, Loma Linda, California, UNITED STATES|
Commercial Relationships Disclosure: K V Chalam: Commercial Relationship: Code N (No Commercial Relationship) | Shailesh Gupta: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To evaluate the effectiveness of modified housing on fogging of reusable wide angle contact lens during vitreoretinal surgery
Methods: Wide angle contact lens provides panoramic view of retina and enables successful vitreoretinal surgery in complex retinal detachments through improved visualization of vitreoretinal periphery upto and beyond ora serrata. However frequent steam sterilization erodes the glue that holds lens elements, allows fogging due to migration of steam in between lens elements and result in poor visualization of the fundus.

In this study, we altered the housing and evaluated its effectiveness. Modified housing has two modes; open mode during sterilization and closed mode after completion of sterilization (Figs 1&2).

The lens system has two lens groups. The first group has a concave posterior surface [Radius of curvature (ROC) = 7.8 mm], for placement on the patient's cornea. This group acts to direct light rays originating from the posterior chamber towards the second lens group II for focusing. The group I lens system collimates the light rays. Group II is located in a spaced–apart relationship with respect to first lens group I. This allows an air space between them. The group II focuses the light rays and provides panoramic visualization of retina.

Housing that holds the two lens systems has a rotational window that is open during steam sterilization and closed during surgery
Results: The lens system provided real and inverted panoramic image of the fundus. The lens system is configured to minimize chromatic aberration and provide improved image as compared to the other lens systems. It provides 160 degrees of fundus view during static viewing and 170 degrees during dynamic view with excellent depth of focus.

Modified housing has facilitated fog free visualization of retina during surgery while allowing effective steam sterilization compliant with standard operating room regulations.
Conclusions: This modified wide angle contact lens provides a real inverted panoramic fog free view of the retina and allow repeated usage without deterioration of image and prolonged the life of wide angle contact lens system. It has added significance in covid era, as stringent sterilization is essential for prevention of disease

CONTROL ID: 3710884

SUBMITTER (NAME ONLY): Shunbin Xu

TITLE: scRNA seq reveals cell-type specific functions of the miR-183/96/182 cluster in shaping the cellular composition of mouse cornea

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Xu, A. Pitchaikannu, N. Gupta, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|K. Gurdziel, Genome Sciences Core, Wayne State University, Detroit, Michigan, UNITED STATES|W. Li, Predoctoral Training Program in Human Genetics, Department of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously we identified that the miR-183/96/182 cluster (miR-183C) regulates corneal resident immune cells (CRICs) and nerves. This study is to uncover its roles in shaping the cellular landscape of the cornea, with a focus on CRICs.

Methods: Corneas anterior to the limbus of naïve, adult, female miR-183C knockout mice (ko) and their wild-type littermates (wt) were dissociated into single cells. Dead cells were removed using a Dead Cell Removal kit and Magnetic Activated Cell Sorting (MACS). To enrich CRIC, CD45+ cells were enriched by MACS. scRNA libraries of total corneal cells or enriched CRICs were prepared using the Next GEM Single Cell 3' Reagent kits v3.1 (10xGENOMICS) before sequencing on an Illumina NovaSeq, followed by alignment and tabulation with Cell Ranger. Analysis were performed in R using Seurat and SingleR packages.

Results: We obtained sc transcriptomes of 8,163 and 7316 total corneal cells of 2-3 months old (mo), and 8,783 and 6,211 corneal cells of 6-8 mo wt and ko mice, respectively; 1,981 (wt) and 2915 (ko) MACS-enriched CRICs of 6-8 mo mice.

In total corneal cells, 11 populations (clusters) were identified, including 4 stromal-keratocyte and/or endothelial, 6 epithelial clusters and 1 CRIC cluster. Mononuclear phagocyte system (MPS), including monocytes, macrophages (Mf) and dendritic cells, were increased in ko vs wt mice, consistent with our previous observation by immunostaining and flow cytometry. Multiple populations changed their representations at both ages and/or at the younger vs the older ages in ko vs wt mice.

In CRICs, 13 clusters were uncovered, 6 of which were CRICs for further analysis. Preliminary data suggest that the number of resident MPS cells and the expression of both classical M1 and M2 signature genes in resident Mf are simultaneously increased of ko vs wt mice. Small subpopulations of CRICs, positive to microglial or T-cell or IL-17 or proliferative cell markers, were also increased in the ko mice.

Further analyses on differentially expressed genes and functional annotation in various cell types between the ko vs wt mice are ongoing to uncover cell type-specific targets and molecular pathways regulated by miR-183C.

Conclusions: scRNA seq provides unprecedented molecular insights into the roles of miR-183C regulating the cellular composition and properties of the cornea.

CONTROL ID: 3710886

SUBMITTER (NAME ONLY): Shuang Liang

TITLE: Antifouling Studies of Lehfilcon A Silicone Hydrogel Contact Lens

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Liang, A. Shows, D. Dunbar, V. Sharma, C.X. Shi, J. Wu, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Shuang Liang: Commercial Relationship(s);Code E (Employment):Alcon | Amanda Shows: Commercial Relationship(s);Code E (Employment):Alcon | Daniel Dunbar: Commercial Relationship(s);Code E (Employment):Alcon | Vinay Sharma: Commercial Relationship(s);Code E (Employment):Alcon | Charlie Shi: Commercial Relationship(s);Code E (Employment):Alcon | James Wu: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: A new silicone hydrogel (SiHy) material, lehfilcon A (TOTAL30®) with surface modification of a 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer, was recently developed. This study was designed to evaluate the in vitro surface biological interactions as well as their impact on tear film stability on the surface of lehfilcon A and other reusable SiHy materials.

Methods: The surface structures of lehfilcon A, comfilcon A, senofilcon A, senofilcon C, and samfilcon A contact lenses were imaged using Atomic Force Microscopy (AFM). After fouling in an artificial tear lipid solution, the distributions of fluorescently labeled non-polar lipids on the entire lenses as well as the cross-sections of these SiHy materials were visualized and quantified in three-dimensional (3D) via confocal laser scanning microscopy (CLSM). The in vitro tear film stability on the fouled lens surface was further assessed using a modified multifunctional topographer method.

Results: Lehfilcon A contact lenses exhibited distinctive surface features and topographies resulting from its densely packed MPC polymer units, which was not seen on other reusable SiHy materials. Fluorescent intensity measurements of 3D CLSM images (Figure 1) showed that lipid deposition on the lens surface was significantly less for lehfilcon A compared to the other reusable SiHy materials ($p<0.05$ for all). Furthermore, lehfilcon A demonstrated a significantly longer surface moisture break up time than other tested contact lenses in the in vitro topography videos (19 s vs. <5 s, $p<0.05$ for all).

Conclusions: The hydrophilic nature of the MPC polymer layer provided an antifouling surface feature for lehfilcon A contact lenses, which delivered greater in vitro tear film stability than other reusable SiHy contact lenses. These exceptional characteristics may help achieve outstanding on-eye performance for this new SiHy contact lens.

CONTROL ID: 3710887

SUBMITTER (NAME ONLY): Jaycob Avaylon

TITLE: Spectral-domain OCT predictors of successful treatment discontinuation in patients with retinal vein occlusion and macular edema

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Avaylon, California Northstate University College of Medicine, Elk Grove, California, UNITED STATES|D. Lent-Schochet, T. Lo, K. Luu, S. Tran, P. Emami-Naeini, A. Moshiri, S.S. Park, G. Yiu, Department of Ophthalmology and Vision Science, University of California Davis, Sacramento, California, UNITED STATES|D. Lent-Schochet, Department of Ophthalmology and Vision Science, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|K. Nava, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify longitudinal SD-OCT biomarkers associated with successful treatment discontinuation and visual outcomes in eyes with central or branch retinal vein occlusion (RVO) and macular edema.

Methods: We retrospectively reviewed 66 eyes with treatment-naïve RVO and ME with 24-month follow-up, and assessed SD-OCT biomarkers including central subfield thickness (CST), intraretinal cyst size, number of intraretinal hyperreflective foci (HF), disorganization of retinal inner layers (DRIL), and outer retinal layer disruptions of the external limiting membrane (ELM), ellipsoid zone (EZ), or interdigitation zone (IZ) at presentation, 3 months, or 6 months after treatment initiation. We employed multivariate regression analyses to identify biomarkers associated with (1) successful treatment discontinuation for at least 6 months without fluid recurrence and (2) visual acuity (VA) at 24-months.

Results: Among 43 eyes with CRVO/HRVO and 23 with BRVO, 47% and 49% of eyes successfully stopped therapy over the 2 years, respectively, with a median time to discontinuation of 5 months (95% CI 2-8) for the CRVO/HRVO group and 5 months (95% CI 3-8) for the BRVO group. SD-OCT biomarkers including CST, cyst size, DRIL, and ELM/EZ/EZ disruptions all improved at 3 months, and remained stable at 6 months. On multivariate regression, lower CST at 6 months ($P = 0.03$) was associated with successful treatment discontinuation, while better BCVA at 6 months ($P = 0.04$) and %DRIL improvement at 3 months ($P = 0.02$) predicted better visual outcomes at 24 months.

Conclusions: Early anatomic response at 6 months is associated with successful treatment discontinuation of RVO with macular edema within 2 years, while early visual gains and DRIL improvements are linked to long-term visual outcomes.

CONTROL ID: 3710888
SUBMITTER (NAME ONLY): Siri Uppuluri
TITLE: Crib-Related Ocular Injuries in Children Ages 0 to 23 Months
SESSION TITLE: Anterior Segment and Trauma Epidemiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Uppuluri, A. Uppuluri, M.A. Zarbin, N. Bhagat, Department of Ophthalmology & Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|
Commercial Relationships Disclosure: Siri Uppuluri: Commercial Relationship: Code N (No Commercial Relationship) | Aditya Uppuluri: Commercial Relationship: Code N (No Commercial Relationship) | Marco Zarbin: Commercial Relationship: Code N (No Commercial Relationship) | Neelakshi Bhagat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The objective of this retrospective, cross-sectional study was to describe the demographics and types of crib-related ocular injuries in children under 2 years of age that occurred between 2000 and 2019, as documented by the National Electronic Injury Surveillance System (NEISS) database.

Methods: The NEISS database was used to identify cases of crib-related ocular injuries in children between the ages of 0 and 23 months from 2000 to 2019. The NEISS reports information on emergency department (ED) visits involving a consumer product from a nationally representative sample of U.S. hospitals. Statistical analysis was performed using IBM SPSS 23.

Results: In total, 551 weighted cases of crib-related ocular injuries were identified. By sex, age, and race, the majority of cases occurred in boys (73.2%), and the plurality of cases occurred at 9 months of age (21.9%) and in Whites (30.8%). There was no significant difference in age by sex ($p = 0.227$). The vast majority of cases were treated and released, rather than admitted (99.1% vs 0.9%), and occurred at home (71.7%). Documented ocular injury types included corneal abrasion (58.4%), foreign body (1.8%), contusion (5.9%), unspecified eye injury (15.1%), subconjunctival hemorrhage (16.1%), and open globe injury (3.6%). When types of ocular injury were stratified by sex, significant differences in prevalence of contusion and subconjunctival hemorrhage were identified, with contusion occurring more commonly in girls (0% vs. 21.9%; $p < 0.001$), and subconjunctival hemorrhage occurring more commonly in boys (22.0% vs 0%; $p < 0.001$). Furthermore, when ocular injury types were stratified by age, with cases divided into either 0-11 months or 12-23 months, contusion (4.8% vs. 7.4%; $p = 0.022$) and corneal abrasion (58.0% vs. 59.0%; $p < 0.001$) were more prevalent in the older age group, while subconjunctival hemorrhage (27.4% vs. 0%; $p < 0.001$) and open globe injury (6.2% vs. 0%; $p < 0.001$) were more common in the younger age group.

Conclusions: In children under 2 years of age, between 2000 to 2019 over 500 cases of crib-related ocular injuries presented to emergency departments in the United States. The majority of injuries occurred in boys, those less than 12 months of age, and at home. The most common ocular injury was corneal abrasion, and the rate of severe ocular injury, open globe injury, was low at 3.6%. The vast majority of cases were triaged in the ED and discharged home.

CONTROL ID: 3710889

SUBMITTER (NAME ONLY): Nathan Agi

TITLE: Sensitivity of tele-ophthalmic diagnosis of diabetic retinopathy when performed by resident physicians

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Agi, R.K. Henry, M. Shah, B. Szirth, N. Bhagat, Ophthalmology, Rutgers The State University of New Jersey, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Nathan Agi: Commercial Relationship: Code N (No Commercial Relationship) | Roger Henry: Commercial Relationship: Code N (No Commercial Relationship) | Megh Shah: Commercial Relationship: Code N (No Commercial Relationship) | Bernard Szirth: Commercial Relationship: Code N (No Commercial Relationship) | Neelakshi Bhagat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: During the Covid-19 era, understanding the benefits and limitations of tele-ophthalmology has become increasingly important. In this study, we aim to assess the accuracy of tele-ophthalmic diagnosis of diabetic retinopathy (DR) and diabetic macular edema (DME) when performed by resident physicians.

Methods: Retrospective study on 16 patients (32 eyes; 28 DR and 4 controls) who presented to a retina clinic at an academic medical center. Automated OCT-B images with 3D topographic maps and fundus photographs of the posterior pole using a Topcon Maestro 3D OCT-1 unit were taken. Images were transmitted remotely to a resident physician who assessed the severity of the DR and DME on the basis of the fundus photographs and OCT. The same images were transmitted to a retina specialist for grading. Primary outcomes included DR and DME grade as defined by the International Clinical Diabetic Retinopathy classification scale. We then tested the concordance between diagnoses rendered via tele-OCT by the resident compared to the retina attending's remote diagnosis and the gold standard retina specialist's clinical examination using Cohen's Kappa statistic (κ).

Results: Agreement between ophthalmology residents and attendings on tele-OCT diagnosis of DR was substantial (78% concordance on presence and 75% on severity), while agreement on identifying and grading edema was moderate (60% concordance on DME presence and 52% concordance on overall DME severity). Detection of DR by residents via tele-retinal imaging is highly sensitive (100% sensitivity), while detection of DME is highly specific (79-95% specificity). Discordance between residents and attendings on DME grading may owe to differences in opinion regarding what constitutes mild edema versus no edema; however, both concordance and predictive accuracy increase when identifying patients with moderate to severe DME.

Conclusions: This study provides proof of principle for the sensitivity and specificity for remote diagnosis of DR via tele-OCT fundus and OCT-B images. This technology may be useful in identifying patients at risk of severe vision loss and enable early detection of patients who need referral for prompt treatment. These findings may be particularly relevant to training programs looking to implement tele-retinal diabetic screening or using tele-OCT where prompt access to a retina specialist may not be possible.

CONTROL ID: 3710891

SUBMITTER (NAME ONLY): Deirdre Harford

TITLE: Examining inner blood retina barrier function in rare neurological conditions

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Harford, J. O'Callaghan, C. Delaney, N. Hudson, R. Connolly, S. Doyle, C. Doherty, M. Cahill, M. Campbell, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The eye is a uniquely accessible organ with very sophisticated imaging systems for evaluation of it's anatomy and vasculature in particular. The tight junction protein claudin-5 which is richly expressed at the inner blood retinal barrier (iBRB) is also expressed at the level of the blood brain barrier(BBB). Developing software which could use ocular vasculature as an indicator of BBB integrity has applications in a number of neurodegenerative disorders and neurological insults. We sought to evaluate the integrity of the in neurological disorders (CSF1R mutation and Visual Snow) using FOVAS (Fluorescent Ocular Vascular Analysis Software), a novel quantitative analysis software tool for FFA studies.

Methods: 3 subjects were recruited, 1 with adult onset leukoencephalopathy with axonal spheroids (ALSP) – (an autosomal dominant CSF1R mutation) and 2 with visual snow syndrome. Fundus fluorescein Angiography (FFA), Optical Coherence Tomography (OCT) and fundal autofluorescence were performed using the Heidelberg SPECTRALIS. Sodium fluorescein (1 mg/mL) was administered and images obtained at 1 minute, 2 minutes, 4 minutes and 5 minutes post injection. FFA and OCT images were obtained with a 30 degree angle of view and 73 line cuts were acquired. Heidleberg Eye Explorer (HEYEX) was used to capture images. FFA analysis and quantification was conducted using FOVAS against a threshold determined from the fluorescein signal of n = 33 normal healthy controls (aged 18 -30).

Results: In the subject with a CSF1R mutation, FFA images showed a significantly increased fluorescein signal in the peri- and para-foveal regions of the macula. In both subjects with visual snow, FFA images showed a significantly increased fluorescein signal in the foveal, peri, para and extra foveal regions suggesting an increased iBRB permeability in this disorder. FOVAS analysis suggests a potential pathology involving tight junctional proteins of the endothelium.

Conclusions: We report increased permeability of the iBRB in a single case of an individual with a condition in involving a dominant acting mutation in the gene CSF1R and in a small case series of patients with Visual Snow syndrome following FOVAS analysis. We conclude that with the development of FOVAS and a robust dataset demonstrating 'normal' inner retinal vascular integrity, we can potentially expedite the study of blood tissue barrier disruption in neurodegenerative diseases.

CONTROL ID: 3710893

SUBMITTER (NAME ONLY): Sourabh Arora

TITLE: Intrasession repeatability of OCTA 4.5mm and 6mm image scans for glaucomatous and non-glaucomatous eyes

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Arora, A. Rao, B. Burkemper, J. Lee, V. Nguyen, B. Xu, B. Wong, B. Song, Department of Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|A. Fard, S. Yu, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|G.M. Richter, Southern California Permanente Medical Group, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Sourabh Arora: Commercial Relationship(s);Code E (Employment):RevHealth Inc., Abbvie Inc. | Arthi Rao: Commercial Relationship: Code N (No Commercial Relationship) | Bruce Burkemper: Commercial Relationship: Code N (No Commercial Relationship) | Jae Lee: Commercial Relationship: Code N (No Commercial Relationship) | Ali Fard: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec | Sophia Yu: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec | Van Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Xu: Commercial Relationship(s);Code F (Financial Support):Heidelberg Engineering;Code C (Consultant/Contractor):Abbvie Inc, Allergan Inc. | Brandon Wong: Commercial Relationship: Code N (No Commercial Relationship) | Grace Richter: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss Meditec | Brian J. Song: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The optimal protocols for using optical coherence tomography angiography (OCTA) for glaucoma patient care is under investigation. We conducted a prospective observational imaging study of glaucoma patients and suspects to determine the OCTA's intrasession repeatability for 4.5x4.5mm and 6x6 image scans.

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Methods: For 46 consecutive patients, two peripapillary 4.5mm and 6mm OCTA scans were obtained on the same day. Images with a signal strength >6, and minimal decentration were analyzed. Inclusion was further determined by 2 graders using a custom quality scale (1-7) for each characteristic: motion artifact, floaters, fadedness, missing data. Vessel Area Density (VAD) and Flux of the annulus around the optic nerve head were obtained using Zeiss quantification software (Cirrus 11.0, Zeiss). Images were evaluated for intrasession repeatability of OCTA metrics using intraclass correlation coefficient (ICC).

Results: From the initial 46 patients, 30 were eligible for inclusion. Their mean age was 47.4±14.6 years with 12 males and 18 females. A total of 180 images from 45 eyes were analyzed.

The mean signal strength of 4.5mm images was 9.7 ± 0.6 and the mean total quality score was 26.4 ± 1.6 (n=180) based on the 2 graders' scores. (Table 1) The ICC for VAD of the annulus was 0.94 (95% CI 0.90-0.97) and 0.95 (95% CI 0.91-0.97) for Flux for the 4.5 mm scans (Table 2). When comparing the ICC for glaucoma patients to glaucoma suspects, for VAD it was 0.94 (95% CI 0.83-0.98) vs 0.89 (95% CI 0.79-0.95), respectively. The ICC for Flux for glaucoma patients and suspects were 0.95 (95% CI 0.85-0.98) vs 0.88 (95% CI 0.77-0.94), respectively.

The mean signal strength of 6mm images was 9.4 ± 0.8 and the mean total quality score was 26.2 ± 1.8 (n=180) based on the 2 graders' scores. The ICC for VAD was 0.94 (95% CI 0.90-0.97) and the ICC for Flux was 0.96 (95% CI 0.93-0.98). For 6mm scans, when comparing glaucoma patients to suspects, the ICC for VAD was 0.96 (95% CI 0.87-0.99) vs 0.89 (95% CI 0.79-0.95), and the ICC for Flux was 0.98 (95% CI 0.93-0.99) vs 0.90 (95% CI 0.80-0.95), respectively.

Conclusions: OCTA 4.5mm and 6mm scans for the same patient taken on the same date demonstrated high repeatability based on ICC for VAD and for Flux. 4.5mm and 6mm images have high repeatability for both glaucoma patients and suspects.

CONTROL ID: 3710894

SUBMITTER (NAME ONLY): Iqbal Ahmad

TITLE: Disease in a Dish Model of Human Glaucomatous Retinal Ganglion Cell Degeneration

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Ahmad, M. Subramani, Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

Commercial Relationships Disclosure: Iqbal Ahmad: Commercial Relationship: Code N (No Commercial Relationship) | Murali Subramani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is a group of multifactorial diseases with a unifying pathology retinal ganglion cells (RGCs) degeneration, leading to irreversible blindness. To test the hypothesis that human RGCs are intrinsically vulnerable in glaucoma we have developed an in vitro disease model using the primary open angle glaucoma (POAG) patient-specific induced pluripotent stem cells (iPSCs) for generating functional RGCs. We have previously demonstrated that RGCs derived from a POAG patient-specific iPSCs with the risk allele of a developmentally relevant gene, SIX6 display developmental and functional abnormalities. Here we have examined the developmental susceptibility of RGCs derived from a POAG patient-specific iPSCs containing mutation in a non-developmental gene, MYOC.

Methods: The model was created using the iPSC technology. Briefly, peripheral blood mononuclear cells (PBMCs) were harvested from patients' and age matched controls' blood samples. PBMCs were reprogrammed using the transduction of Sendai virus, expressing Yamanaka factors (Oct4, Klf4, Sox2, and c-Myc). Multiple MYOC and control iPS clones were generated for the characterization of pluripotency. RGCs were generated by a chemical induction protocol, using small molecules, that recapitulates the mechanism of normal RGC genesis.

Results: A modification of neural induction protocol to generate retinal progenitor cells (RPCs) led to the generation of Rx^+ and Pax^+ cells from both MYOC patient-specific and control iPSCs, however there was a significant decrease in the number of Rx^+ and $Pax6^+$ RPCs in the former versus latter. The neural rosettes (NRs) containing the Rx^+ and $Pax6^+$ RPCs appeared less compact in MYOC patient-specific versus control groups. Examination of select gene expression in RGCs derived from patient-specific RPCs suggested developmental abnormalities. For example, the levels of transcripts of RGC regulators (Atoh7, Brn3b, Isl1), markers (SCNG, Thy1), axon growth and guidance regulators (GAP43, DCC, EPHB3) were significantly decreased in MYOC patient-specific RGCs, compared to controls. The complexity of neurites and length of axons ($SM132^+$ and $Tau1^+$) were also observed decreased in MYOC patient-specific RGCs versus controls.

Conclusions: Our preliminary results suggest that the mutation in MYOC gene may make human RGCs susceptible to developmental abnormalities.

CONTROL ID: 3710898

SUBMITTER (NAME ONLY): Sarah Guo

TITLE: Ophthalmologic findings in children with embryonal tumor with multilayered rosettes (ETMR)

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Guo, M.S. Borchert, M. Chang, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M.S. Borchert, M. Chang, Ophthalmology, Children's Hospital Los Angeles Medical Group, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Sarah Guo: Commercial Relationship: Code N (No Commercial Relationship) | Mark Borchert: Commercial Relationship: Code N (No Commercial Relationship) | Melinda Chang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Embryonal tumor with multilayered rosettes (ETMR) is a rare, newly classified WHO grade IV, highly malignant variant of the primitive neuroectodermal tumor. Ophthalmologic findings associated with this tumor have not been previously described.

Methods: We performed a retrospective, observational review of children diagnosed and treated with ETMR at our tertiary care children’s hospital over the past six years. A total of five patients were identified. Three children had suspected ocular abnormalities and were referred for ophthalmologic evaluation. We reviewed the charts of these three patients and describe the ophthalmologic findings.

Results: Patient 1 was a 2-year-old girl with a tumor located in the right pons extending along the cerebral peduncle who presented with ataxia and esotropia. She was found to have a right abducens palsy and amblyopia of the right eye, and amblyopia treatment was initiated. Patient 2 was a 2-year-old girl with a primary tumor in the right midbrain and pons with extensive leptomeningeal dissemination who presented with right facial weakness, imbalance, intermittent emesis, and nystagmus. She was found to have gaze-evoked right beating and upbeat nystagmus, leading to a preference for left gaze and downgaze. Her therapists were advised not to inhibit the face turn that she adopted to minimize oscillopsia. Patient 3 was diagnosed at 2 weeks old with a posterior fossa tumor involving the roof of the 4th ventricle, superior medullary velum, and surrounding vermis after prenatal testing revealed hydrocephalus. She developed abducens palsy after tumor resection and ventriculoperitoneal shunt placement. Outpatient ophthalmology evaluation was recommended, but the patient did not follow up. The abducens palsy remained persistent at 3 year follow up with oncology despite disease remission.

Conclusions: This case series suggests that ophthalmologic findings are common in children with ETMR and may require treatment and/or inform systemic therapies. It is important for clinicians to assess vision and ocular motility and consider ophthalmology referral in children with ETMR.

CONTROL ID: 3710899

SUBMITTER (NAME ONLY): Deborah Im

TITLE: Potential of aqueous humor as a liquid biopsy for uveal melanoma

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Im, M.E. Kim, P. Kuhn, J. Hicks, J.L. Berry, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|C. Peng, L. Xu, D. Ostrow, V. Yellapantula, M. Bootwalla, J.A. Biegel, X. Gai, J.L. Berry, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tumor biopsy can identify prognostic biomarkers for metastatic uveal melanoma (UM). Aqueous humor (AH) biopsy is less invasive and repeatable, and thus facilitates longitudinal monitoring of disease. We investigated if the AH of UM eyes had sufficient tumor-derived cell free DNA (cfDNA) to perform genetic analysis of the tumor.

Methods: A case series of 37 AH samples from 12 choroidal and 8 ciliary body (CB) tumor patients were studied. From 12 choroidal tumor patients, there were 9 paired pre- and post-radiation, 2 post-radiation only and 1 at enucleation AH samples. One CB tumor biopsy wash sample was collected. AH was analyzed for nucleic acids (Qubit Assay Kits). Whole-genome sequencing was done on DNA samples isolated from the AH samples and cells from tumor wash via 150bp paired-end Illumina sequencing to detect somatic copy number alterations (SCNAs). Hybridization-based capturing and targeted sequencing were subsequently done using a custom gene panel that covers all exonic regions of the BAP1 and GNAQ genes.

Results: Comparing paired pre- and post-radiation AH samples revealed significantly higher nucleic acid concentrations post-radiation. Most significant increases within choroidal and CB groups respectively were seen in miRNA (n=9 pairs, P=0.016 and n=8 pairs, P=0.008). Among post-radiation AH samples, there was a significantly higher concentration of dsDNA (P=0.033), ssDNA (P=0.033) and RNA (P=0.018) in CB compared to choroidal. Highly recurrent UM SCNAs were identified in 0/11 post- choroidal and 5/8 (62.5%) post- CB samples. Of those 5 SCNA-containing post- AH samples that underwent targeted resequencing, BAP1 or GNAQ somatic mutations were detected in 3/5 (60%). The DNA profile of the only available tumor sample was highly concordant with its corresponding post-AH sample (r=0.978).

Conclusions: AH is a source of cfDNA in UM eyes, with a higher yield of nucleic acids post-radiation. This is the first-time that UM SCNAs and mutations were identified in cfDNA isolated from the AH. This suggests that AH can serve as a liquid biopsy for UM.

CONTROL ID: 3710900

SUBMITTER (NAME ONLY): Shi Song Rong

TITLE: A zebrafish model system for studying the ANGPT/TIE2 pathway and glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Rong, A. Larson, J.L. Wiggs, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Shi Song Rong: Commercial Relationship: Code N (No Commercial Relationship) | Anna Larson: Commercial Relationship: Code N (No Commercial Relationship) | Janey Wiggs: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Rodent-based studies have shown that ANGPT1 is indispensable for the development and maintenance of the ocular lymphatic network, which is essential for normal aqueous humor drainage. In humans, ANGPT1 loss-of-function mutations cause primary congenital glaucoma with variable expressivity. In this work, we characterized an angpt1 knock-out zebrafish model allowing for high throughput characterization of potential disease-causing variants as well as investigation of novel gene-based therapeutics targeting the ANGPT/TIE2 signaling pathway.

Methods: Using ABTL zebrafish embryos, angpt1 was disrupted by injection of a splice-site morpholino before 4 cell stage. Microangiography, ocular histology, and visual motor responses (VMR) were compared between morphants and controls at day 5 post-fertilization (5dpf). Phenotype recovery using wild type and mutant human mRNA was also evaluated in the morphants. An adult fish knock-out line was created using CRISPR/Cas9, generating an 11 bp deletion in exon 5 of angpt1. The phenotypic features of the crispant embryos with different genotypes (WT/WT, WT/del, and del/del) were compared.

Results: Morpholino-induced skipping of exon 3 and the exon 5 11bp deletion in crispants was confirmed by next-generation sequencing. Phenotypic characterization of morphants showed abnormal ocular and trunk vasculature compared with controls at 5dpf ($P<0.05$). Additionally, the ventral limbal structures, which anatomically correspond to the aqueous humor outflow pathway in adult zebrafish, the ventral canalicular network, were abnormal in morphants ($P<0.05$). The VMR test showed reduced sensitivity to light in morphants compared to controls ($P_{t\text{-}test}<0.001$). Compared with wild type crispant embryos, homozygous 11bp deletion carriers (crispants) also showed malformation of the vasculature ($P<0.05$), ventral limbal structures ($P=0.019$), and VMR reduction ($P=0.005$). Furthermore, human mRNAs containing c.A62G (p.N21S) and c.C239T (p.S80F), two rare ANGPT1 variants found in human glaucoma cases, failed to rescue the VMR phenotype compared with wild type mRNA ($P<0.05$), suggesting deleterious variant effects.

Conclusions: Loss of angpt1 in zebrafish embryos recapitulates several essential ocular and functional phenotypes from existing animal models. Further work offers opportunities for high throughput evaluation of human ANGPT1 variants as well as exploring novel gene-based therapeutic approaches.

CONTROL ID: 3710902

SUBMITTER (NAME ONLY): Daniel Tso

TITLE: Stimulus-dependent intrinsic optical imaging of the retina of pigmented and albino rats

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Tso, D. Joiner, S. McGillis, R. Miller, Neurosurgery, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize stimulus-driven intrinsic optical signal imaging (R-IOI) in the rat retina, as compared with other, previously studied species (cat, monkey, human, mouse, etc). It is further hypothesized that imaged signals from an albino strain of rat would be larger than those found in a pigmented strain.

Methods: Intrinsic optical signals of anesthetized (K/X) adult rat retina were recorded and imaged in vivo with a cooled CCD camera attached to a custom optical rig with a front-end endoscope/otoscope -- a setup previously used for R-IOI of mice (Begum et al, 2020). Retinal images under near-infrared (700-900nm) illumination were collected at 2Hz for 10-20secs while a brief (300msec) visible (505nm) LED stimulus was delivered to the retina.

Results: Stimulus-driven intrinsic signals were observed in the rat retina, similar to those previously describe in other species (cat, monkey, human, mouse). In comparison to R-IOI of (pigmented) adult C57BL/6J wild-type mouse retina performed under the same stimulated and recording conditions using the same equipment, imaged signals from pigmented Long-Evans adult rats were preliminarily similar in time course, but larger in amplitude (0.24% vs 0.060%). However R-IOI under the same conditions recorded in albino Sprague-Dawley adult rats revealed signals greater in amplitude (0.58% +- 0.16% vs 0.24% +- 0.067%). One major difference is that the retinal return, the amount of NIR illumination reflected back into the camera was also substantially greater in the albino vs pigmented rat -- typically 6-7 times greater.

While the larger retinal return likely contributed to the observed greater signal amplitude in the albino rat, another hypothesis is that a greater contribution of the choriocapillaris is observed in the albino rat. This may be expected due to our previous work demonstrating a dominant hemodynamic component of the R-IOI signal that is driven by rod activity. For comparison, the cat has exhibited the largest signal (1-2%) while the macaque monkey is at 0.25%.

Conclusions: These findings confirm the expectation that R-IOI reveals imaged signals similar to those observed in other species.

Furthermore, the greater signal amplitudes observed in the albino rat coincide with previous evidence of a significant component of the observed R-IOI signal originating from outer retinal sources (rod photoreceptors).

CONTROL ID: 3710903

SUBMITTER (NAME ONLY): Emmanuel Issa Nassrallah

TITLE: Zonular instability and decreased capsulorhexis diameter in post-mortem pseudophakic eyes

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Nassrallah, Oculoplastics, University of Toronto, Toronto, Ontario, CANADA|E.B. Nassrallah, G. Nassrallah, C. Mastromonaco, A.B. Dias, J.J. Mansure, N. Saheb, M.N. Burnier, Pathology, McGill University Health Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Anterior capsular contraction syndrome (ACCS) is characterized by excessive contraction and fibrosis of the anterior lens capsule after phacoemulsification and intraocular lens (IOL) implantation, leading to phimosis of the anterior capsulotomy. Epithelial-to-mesenchymal transition (EMT) of lens epithelial cells and extracellular matrix remodelling (ECMR) are associated with ACCS. Zonular instability (ZI) is correlated with ACCS but it is unclear if zonulopathy (ZP) is caused by lens epithelial changes or if it is an independent risk factor. The aim of this cross-sectional study is to assess the associations of EMT, ECMR, and ZP with progressively smaller capsulorhexis diameter (CD) in post-mortem eyes.

Methods: A total of 104 post-mortem pseudophakic human eyes from the MUHC-McGill University Ocular Pathology & Translational Research Laboratory were examined. Images of the eyes in Miyake-Apple view and region of interest analysis were done using ImageJ to measure capsule area (CA), ciliary ring area (CRA), and CD. Zonular stability was measured using CA over CRA ratio (CCR) and capsule-ciliary ring decentration (CCD). Capsular bags with IOLs were extracted, and EMT and ECMR were quantified via automated immunohistochemistry with anti-SMA (smooth muscle actin) and anti-FN (fibronectin), respectively. Slides were digitized and analyzed via the Positive Pixel Count v9 algorithm. Correlation was assessed via simple linear regression, one-way ANOVA, and two-sample t-test.

Results: There was a statistically significant positive correlation between CCR and CD ($p=0.0106$, $N=104$) but not between CCD and CD ($p=0.44842$, $N=104$). No significant correlation between CD and FN ($p=0.14213$, $N=75$) or SMA ($p=0.41087$, $N=75$) was found. However, when comparing samples with the largest CD with samples of CD <2 standard deviations from the mean, FN staining was reduced in samples with a smaller CD ($p=0.01171$). There was no correlation between CCR or CCD with FN or SMA staining. Cataract-to-death time did not correlate with CCR ($p=0.73958$), CCD ($p=0.14405$), or FN ($p=0.11619$), but did have a positive correlation with SMA ($p<0.0001$).

Conclusions: ZI, as indicated by a low CCR, had the strongest correlation with small CD in post-mortem pseudophakic eyes. Moreover, the degree of ZI does not seem to correlate with EMT or ECMR, suggesting that it may be an independent risk factor for smaller CD and, perhaps, the development of ACCS.

CONTROL ID: 3710904

SUBMITTER (NAME ONLY): William Beltran

TITLE: Long-term follow up of gene therapy for NPHP5-LCA in a canine model shows restoration of photoreceptor function and vision for > 5 years

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.A. Beltran, A. Ripolles-Garcia, V.L. Dufour, Y. Sato, A. Gray, G.D. Aguirre, Clinical Sciences and Advanced Medicine, University of Pennsylvania, School of Veterinary Medicine, Philadelphia, Pennsylvania, UNITED STATES|A.V. Cideciyan, M. Swider, S.G. Jacobson, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|S. Boye, W.W. Hauswirth, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: NPHP5 gene augmentation successfully rescues photoreceptor structure, function, and vision for up to 6 months when delivered at early-stage disease in the canine NPHP5 model of LCA, a severe form of inherited childhood blindness (Aguirre et al. Mol Ther 2021). We now report on the long-term (up to 5.4 years) follow-up of 20 mutant dogs treated unilaterally at more advanced stages of disease including: early/mid (n=3), mid (n=4), late (n=9) and very late (n=4) stages.

Methods: Dogs were subretinally-injected (0.1-0.15 mL) with a scAAV2/5 or scAAV2/8$_{(C\&G+T494V)}$ vector construct (4.74×10^{12} vg/mL) carrying full-length canine or human NPHP5 cDNA under control of a GRK1 promoter. Throughout the course of the study, photoreceptor structure and function were assessed by SD-OCT and ERG. Rod- and cone-mediated visual behavior was evaluated in an obstacle avoidance course under scotopic and photopic illumination.

Results: While progressive ONL thinning was seen by OCT over time, ONL rescue was still detectable in the treated retinal area at the latest post injection (PI) time-point (up to ~ 5 years in early/mid, and mid stage groups; and up to ~ 3 years in the late-stage group). No ONL preservation was seen in untreated areas of injected eyes, nor in BSS or uninjected contralateral eyes beyond the visual streak. ERG showed restoration of both rod- and cone-mediated function in all AAV-NPHP5 injected eyes, with the exception of dogs from the very late-stage group in which only cone-mediated ERG was restored. Vision testing performed in a subset (n=13) of dogs showed persistent recovery in the early/mid- (3 out of 3), mid- (2 out of 2), late- (4 out of 4), and very late- (1 out of 2) stage groups. Vision restoration was independently documented in the single dog from the very late-stage group that refused to enter the obstacle course by using a modification of the protocol.

Conclusions: These results show long-term (3 - 5.4 years) restoration of photoreceptor function and preservation of structure as well as visually-guided behavior following subretinal NPHP5 gene augmentation therapy delivered at patient-relevant advanced stages of disease. A treatment effect was detectable by ERG as early as 4-8 weeks PI. In addition, these results show that cones are receptive to very late-stage intervention even when most rod photoreceptors are lost.

CONTROL ID: 3710905

SUBMITTER (NAME ONLY): Elyse Salpeter

TITLE: Advanced corneal imaging and corneal endothelial cell parameters in rhesus macaques (Macaca mulatta)

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Salpeter, I. Casanova, L. Young, S. Parks, S. Kim, S.M. Thomasy, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California Davis, Davis, California, UNITED STATES|A. Blandino, Department of Statistics, University of California Davis, Davis, California, UNITED STATES|G. Yiu, A. Moshiri, J. Li, S.M. Thomasy, Department of Ophthalmology & Vision Science, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|T. Stout, Department of Ophthalmology, Cullen Eye Institute, Baylor College of Medicine, Houston, Texas, UNITED STATES|J. Rogers, Human Genome Sequencing Center and Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-human primates offer a significant advantage in the study of the pathogenesis and therapeutics for corneal disease because of their ocular similarity to humans. This study aims to define the range of normal central corneal thickness (CCT) and corneal endothelial cell density (ECD) in rhesus macaques (Macaca mulatta) and to determine the effect of age, body weight, and sex on these parameters.

Methods: Ophthalmic examination was performed in 144 rhesus macaques without corneal or anterior chamber lesions. The range of age of the primates examined was 0.2-29.4 years (mean 13.7 ± 7.1 years); 98 were females and 46 were male. The ECD was semi-automatically counted and manually counted using in vivo specular microscopy while CCT was measured via ultrasound pachymetry (USP). Linear regression model and mixed effects linear regression were used to evaluate the main effects of age, body weight, sex, intraocular pressure (IOP) and axial length of the globe (AXL) and refractive error on CCT and ECD. A concordance correlation coefficient (CCC) was calculated to estimate the reliability of semiautomatic versus manual counts. Linear regression with mixed effects linear regression were used to evaluate the main effects of an individual's body weight, age and sex on corneal thickness and corneal endothelial cell density.

Results: Mean ECD was 2717 ± 423 cells/mm^2, similar to the reported range for humans in early adulthood at approximately 2500 cells/mm^2. Mean CCT was 483 ± 39 µm, which was similar to that documented for humans at 534.8 ± 34.7 µm. IOP and sex were statistically significantly associated with CCT, while body weight, age, and AXL were associated with ECD ($p < 0.05$). There was good reliability between semiautomatic and manual ECD counts (CCC=0.79). There was no significant correlation between CCT and ECD (p=0.89).

Conclusions: The rhesus macaque has similar corneal characteristics when compared to humans and can thus serve as an ideal model to study corneal endothelial cell disorders and corneal diseases. This study suggests a normal range of ECD from 2294-3140 cells/mm^2 and 444-522 µm for CCT in rhesus macaques (Macaca mulatta).

CONTROL ID: 3710915

SUBMITTER (NAME ONLY): Xin Xia

TITLE: Impact of Neurofibromatosis type 1 (NF1) heterozygosity on RGC death after optic nerve injury

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Xia, C. Sun, Z. Luo, K. Russano, J.L. Goldberg, Spencer Center for Vision Research, Byers Eye Institute, Stanford University, California, UNITED STATES|S. Shyamsundar, Geisinger Commonwealth School of Medicine, Scranton, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Xin Xia: Commercial Relationship: Code N (No Commercial Relationship) | Catalina Sun: Commercial Relationship: Code N (No Commercial Relationship) | Ziming Luo: Commercial Relationship: Code N (No Commercial Relationship) | Saishravan Shyamsundar: Commercial Relationship: Code N (No Commercial Relationship) | Kristina Russano: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Goldberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Neurofibromatosis type 1 (NF1) due to loss of heterozygosity at the neurofibromin/NF1 locus is associated with optic glioma, degeneration of retinal ganglion cells (RGCs), and vision loss. Understanding the impact of heterozygosity at the NF1 locus remains a major goal when considering neuroprotective or restorative therapies. Previous studies using optic nerve crush injury revealed increased RGC death in NF1-heterozygote mice, illustrating a neurofibromin-dependent intracellular signaling pathway responsible for neuronal survival. But there are several types of neurons and glial cells in the retina and optic nerve. Here we asked whether RGC-specific Nf1 heterozygosity increases RGC death after optic nerve injury.

Methods: Nf1 flox/wt mice aged 4-6 weeks under isoflurane anesthesia were injected intravitreally with AAV2-cre to carry out RGC-specific Nf1 one allele deletion, or AAV2-GFP control viral vectors. Two weeks later, mice underwent optic nerve crush conducted by cross-action forceps 2mm posterior to the globe under direct visualization. Two weeks after optic nerve crush, eyes were harvested and post-fixed with 4% PFA for 1h at room temperature. Retinas were isolated, permeabilized with 2% Triton-X-100 in PBS and stained with an RGC-specific anti-RBPMS antibody, followed by mounting on slides and imaging by confocal laser scanning microscopy. Eight images of each retina were imaged and quantified to measure RGC density. Results are presented as cells/mm^2 for each retina. All experiments were masked.

Results: The survival of RGCs in AAV2-cre-injected eyes was significantly less than that in AAV2-GFP-injected eyes after optic nerve crush (Fig 1.).

Conclusions: RGC-specific Nf1 one allele deletion may exacerbate RGC death after optic nerve injury. Our next step is going to see if astrocyte specific Nf1 heterozygosity using AAV5-GFAP-cre will worsen RGC death after optic nerve injury.

CONTROL ID: 3710919

SUBMITTER (NAME ONLY): Marina Pavlou

TITLE: Reprogramming adult Müller glia in a light-damage model of photoreceptor degeneration.

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pavlou, T. Reh, Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Marina Pavlou: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Reh: Commercial Relationship(s);Code P (Patent):PCT/US2020/030407

ABSTRACT BODY:

Purpose: Patients with degenerative retinal dystrophies suffer from various degrees of blindness as a result of acute or gradual photoreceptor cell death. While gene supplementation therapies attempt to treat affected individuals with monogenic disorders at an early disease stage, there is a clinical demand for universal treatment that can halt or even reverse the effects of degeneration at later stages. We have shown that NMDA-induced ablation of retinal ganglion cells and amacrine cells, together with Ascl1 overexpression in murine Müller glia (MG) induces the MG to generate neurons. This work investigates the potential for glia-to-neuron reprogramming in retinas that suffered photoreceptor ablation, which better mimics the pathology of patients with late-stage retinal degeneration.

Methods: To induce photoreceptor degeneration, adult mice homozygous or heterozygous for the Rpe65 Leu450 were subjected to light-damage by exposing them to ~20,000 lux of white light for 6 hours. To test glia-to-neuron conversion, transgenic mice were used with inducible MG-specific expression of the proneural transcription factor Ascl1 (Glast-CreER/LNL-tTA/TetO-Ascl1-GFP) or Ascl1 in combination with other transcription factors. One week after light-damage, when most photoreceptors in the central retina were ablated, the transgenic mice were injected with tamoxifen to induce the expression of neurogenic factors in MG followed by intravitreal injection of Trichostatin-A (TSA) alone or with γ-secretase inhibitor DAPT. Four weeks later, the number and types of glial-derived neurons was assessed.

Results: Light-damaged retinas showed uniform recombination, confirming that GLAST-controlled gene expression in MG was effective during and after photoreceptor cell death After 4 weeks of Ascl1 expression in MG, approximately 30% of the recombined MG expressed the bipolar/photoreceptor marker Otx2+, similar to the effects previously reported with NMDA-induced retinal injury. The proportions of GFP+Chx10+ (~40%), GFP+Otx2+ (~30%) and GFP+Sox2+ (~65%) populations were similar between eyes that received TSA or TSA+DAPT, suggesting that Notch pathway inhibition with DAPT in this context did not improve the reprogramming outcome.

Conclusions: This work sets the stage for understanding how reprogramming paradigms could translate in models of photoreceptor degeneration, with the aim of regenerating the retina at late disease stages.

CONTROL ID: 3710921

SUBMITTER (NAME ONLY): Baraa Nawash

TITLE: Clinical Characteristics and Treatment Outcomes for Patients with Exudative Age-Related Macular Degeneration with Visual Acuity of 20/40 or Better

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Nawash, J. Ong, J. Chhablani, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Baraa Nawash: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Ong: Commercial Relationship: Code N (No Commercial Relationship) | Jay Chhablani: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Abbvie;Code C (Consultant/Contractor):Salutaris

ABSTRACT BODY:

Purpose: Exudative Age-Related Macular Degeneration (eAMD) is the leading cause of vision loss in the western world. Most of the clinical studies in eAMD include eyes with 20/40 or worse visual acuity (VA). However, a small subset of patients may also present with good VA. Literature lacks knowledge about the clinical characteristics, treatment protocols, and long-term outcomes in this subset. The aim of this study was to describe clinical characteristics and treatment outcomes of anti-VEGF monotherapy in this subset of wet AMD patients with good VA (20/40 or better).

Methods: This was a retrospective chart review study that included patients who had a diagnosis of naive exudative AMD with good VA presenting between 2011 and 2021. Patient charts were from a single hospital system. Eyes with a history of anti-VEGF injections; less than one-year follow-up; history of vitrectomy, and/or any associated ocular disease were excluded. Clinical data were collected for both the eye of interest and the fellow eye including ocular and systemic history, BCVA, imaging findings, and anti-VEGF therapy details.

Results: Fifty-one eyes of 49 patients were included in this study per inclusion criteria. Average age at presentation was 75 ± 8.23 years with 33 (64%) female eyes and 18 (36%) male eyes. All eyes were treated as needed after loading-dose. Average LogMAR at baseline was 0.176 ± 0.11 (Snellen's equivalent 20/30) with a VA at 1 year follow-up of 0.185 ± 0.19 (Snellen's equivalent 20/31) ($p = 0.78$). 3 (6%) patients lost more than 3 Snellen lines after one year. Of the 51 eyes analyzed, 11 fellow eyes concurrently had a confirmed diagnosis of wet AMD with an average LogMAR of 0.181 ± 0.27 (Snellen's equivalent 20/30). An average of 6.14 ± 2.72 injections were administered per patient during the first year of diagnosis with an average maximum treatment-free interval of 3.77 ± 3.03 months

Conclusions: Eyes with good visual acuity with active wet AMD maintained good visual acuity throughout the first year of anti-VEGF monotherapy with a treatment-free interval of approximately 4 months. Further analyses are underway to assess changes in VA and other parameters for area under the curve (AUC) analysis.

CONTROL ID: 3710924

SUBMITTER (NAME ONLY): Alexander Crane

TITLE: Effect of Simulated Cataract on the Accuracy of an Artificial Intelligence Algorithm in Detecting Diabetic Retinopathy in Color Fundus Photos

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Crane, M. Dastjerdi, Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Alexander Crane: Commercial Relationship: Code N (No Commercial Relationship) | Mohammad Dastjerdi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Artificial intelligence (AI) has the potential to augment the clinical utility of ophthalmic imaging. Input data used in training these AI algorithms are often required to meet strict inclusion criteria to maximize accuracy on high quality images. However, in clinical settings, an AI trained on pristine images without ocular co-morbidities may have limited utility. This study aims to evaluate the accuracy of an artificial intelligence algorithm applied to color fundus photos (CFPs) with simulated cataracts in detecting diabetic retinopathy (DR).

Methods: A database of 3662 CFPs (from the Asia Pacific Tele-Ophthalmology Society (APTOS) 2019 data) was used, with 80% of images used for training and 20% for testing. Using transfer learning, a convolutional neural network (Inception-ResNet-v2) was trained to classify the training images as either DR or non-DR. The CNN was then applied to classify the testing images four times, once each with mild simulated cataract, moderate simulated cataract, severe simulated cataract, and no simulated cataract. Cataracts were simulated by applying varying degrees of gaussian blur corresponding with distorting an image to appear as it would to an eye that is 20/40 (mild), 20/100 (moderate) and 20/200 (severe). Accuracy was compared by confusion matrix, including sensitivity (Sn) and specificity (Sp), and receiver operator curves (ROC).

Results: The CNN was able to classify the dataset without any simulated cataract with an accuracy of 97.0%, Sn 95.7%, Sp 98.3%. On the mild cataract dataset, the CNN had an accuracy of 93.1%, Sn 91.8%, Sp 94.3%. For moderate cataract, accuracy was 62.8%, Sn 31.4%, Sp 95.2%. For severe cataract, accuracy was 53.5%, Sn 11.8%, Sp 96.5%.

Conclusions: Artificial intelligence algorithms are often trained on pristine datasets, where variability is controlled to allow for optimum performance. However, real world data often has significant noise. This study shows that the accuracy of an AI algorithm trained to detect DR is significantly diminished when a simulated cataract is superimposed on the image. To prepare AI for clinical use, cataract and other real-world clinical challenges causing poor image quality must be accounted for.

CONTROL ID: 3710930

SUBMITTER (NAME ONLY): Zahra Nafar

TITLE: Area of Schlemm's canal in healthy and glaucoma eyes imaged using swept-source optical coherence tomography

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Nafar, T. Callan, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

Commercial Relationships Disclosure: Zahra Nafar: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Thomas Callan: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc.

ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) of the anterior segment (AS) can provide visualization of small features such as the trabecular meshwork and Schlemm's canal (SC) and become an important tool for diagnosis and treatment of glaucomatous patients. In this study, we evaluate the capability of an AS add-on lens module in visualizing Schlemm's canal and its diagnostic potential by evaluating the cross-sectional area in healthy and glaucomatous eyes.

Methods: A swept-source OCT instrument, PLEX® Elite 9000 (ZEISS, Dublin, CA) with prototype software, was equipped with an AS add-on module. The limbal area was scanned with a High-Definition (HD) Cross scan. An external fixation target was used to perpendicularly scan the limbal region.

HD Cross = 6 mm cross pattern, 5 B-scans with 0.125 mm separation, 1024 A-scans/B-scan and 1536 pixels in depth (3 mm depth) at 100 kHz, with 5 repetitions averaged.

Both eyes of 2 healthy and 2 glaucomatous patients (8 eyes) with ages ranging from 32-67 years old were scanned. Acquisition was done by an expert operator to confirm the presence and consistency of the SC and its location in the scanned area. The area of the SC was then visually evaluated by an expert.

Results: Schlemm's canal was successfully observed in all 8 cases, although it is generally easier to visualize SC in healthy and younger subjects. Consistently the cross-sectional area appears to be smaller in older and glaucomatous eyes (figure 1). However, more data is needed for a clinically significant comparison of cross-sectional area.

Conclusions: PLEX Elite 9000 with AS add-on module provides good quality visualization of Schlemm's canal in both healthy and glaucoma patients. Thus, it has the potential to be used as a diagnostic tool for glaucoma.

CONTROL ID: 3710931

SUBMITTER (NAME ONLY): Mélanie Hébert

TITLE: Outcomes in recurrent rhegmatogenous retinal detachment repair: does initial surgery impact results?

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hébert, J. Garneau, E. You, S. Bourgault, M. Caissie, É. Tourville, A. Dirani, Ophthalmology, Hopital du Saint-Sacrement, Quebec, Quebec, CANADA|

Commercial Relationships Disclosure: Mélanie Hébert: Commercial Relationship: Code N (No Commercial Relationship) | Jerome Garneau: Commercial Relationship: Code N (No Commercial Relationship) | Eunice You: Commercial Relationship: Code N (No Commercial Relationship) | Serge Bourgault: Commercial Relationship: Code N (No Commercial Relationship) | Mathieu Caissie: Commercial Relationship: Code N (No Commercial Relationship) | Éric Tourville: Commercial Relationship: Code N (No Commercial Relationship) | Ali Dirani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: More studies now guide the management of primary rhegmatogenous retinal detachment (RRD), but less is known on managing recurrent RRD (re-RRD). We analyzed outcomes in re-RRD repair using pars plana vitrectomy (PPV) only or PPV with scleral buckle (PPVSB) in a retrospective cohort study.

Methods: Patients operated for re-RRD at the Centre hospitalier universitaire de Québec – Université Laval between 2014 and 2018 were included. Exclusion criteria included: non-RRD etiologies of initial detachment (e.g., traumatic, tractional), initial RRD with proliferative vitreoretinopathy (PVR) grade ≥C2, and patients with silicone oil during first surgery. Procedure choice at first and second surgery was at the surgeon's discretion. Patients were categorized based on surgery sequence of first and second surgery: PPV then PPV (PPV-PPV), PPV then PPVSB (PPV-PPVSB), or PPVSB then PPV (PPVSB-PPV). Primary outcome was recurrent surgery success rate (re-SSR) and secondary outcome was final pinhole visual acuity (PHVA) in logarithm of the minimum angle of resolution (logMAR).

Results: There were 139 patients included. Twelve (9%) underwent PPV-PPV, 51 (37%) underwent PPV-PPVSB, and 76 (55%) underwent PPVSB-PPV. Median [Q1, Q3] age at initial presentation was 64 [59, 72] years. There were 85 (61%) men, 63 (45%) pseudophakic patients, and 24/114 (21%) high myopic patients. Baseline PHVA in logMAR was 0.88 [0.18, 2.30].

Surgery sequence did not significantly alter re-SSR (PPV-PPV: 9, 75% vs. PPV-PPVSB: 38, 75% vs. PPVSB-PPV: 57, 75%; p=1.00). It also did not change the use of silicone oil at second surgery (PPV-PPV: 5, 42% vs. PPV-PPVSB: 18, 35% vs. PPVSB-PPV: 36, 47%; p=0.40). At final follow-up, PHVA was 0.60 [0.18, 1.00] and did not significantly differ by sequence (p=0.16). In multiple regression analyses, main factors influencing re-SSR were pseudophakia (odds ratio (OR) 3.356, p=0.012) and initial macula-off status (OR 0.368, p=0.048), while surgery sequence did not alter re-SSR (p>0.05).

Conclusions: Following re-RRD repair, there were no significant differences in re-SSR and final PHVA based on sequence of surgery. Pseudophakia increased re-SSR, and macula-off status decreased re-SSR. This is likely because pseudophakia allows a closer shave of the vitreous base to reduce the incidence of postoperative PVR and recurrent tears, while macula-off status suggests a more extensive initial detachment.

CONTROL ID: 3710934

SUBMITTER (NAME ONLY): Nigel Zhang

TITLE: Cyclotorsion in Patients in Upright versus Supine Position Undergoing Laser Vision Correction

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Zhang, D. Gu, S. Eichinger, N. Hackett, A. Moore, J. Pecht, P. Bryar, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|N. Maganti, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is variability in the amount and direction of cyclotorsion induced when a person moves from sitting to supine position. For laser vision correction, alignment is measured in the sitting position and surgery is performed in the supine position. In this retrospective study, we examine the amount and direction of cyclotorsion in sitting versus supine position in patients undergoing laser vision correction.

Methods: A retrospective chart review was done at Northwestern Medicine Department of Ophthalmology, Chicago, Illinois, USA of 893 eyes in 515 consecutive patients who underwent LASIK/PRK with successful iris registration. Amount and direction of cyclotorsion between sitting position versus supine position were analyzed. The amount and direction of cyclotorsion of each eye were quantified, and in patients undergoing bilateral procedures, concordance of cyclotorsion between right and left eye was assessed.

Results: 881 (98.6%) of the 893 eyes were found to have cyclotorsion with a mean of 2.88 degrees. 605 (67.8%) excyclotorted and 276 (30.9%) incyclotorted ($p < 0.001$). For a breakdown of degrees of cyclotorsion, see Figure 1. Average cyclotorsion in the right eye was 3.12 degrees and 2.52 in the left ($p < 0.001$). 361 patients underwent bilateral surgeries. 185 (51.2%) had concordant cyclotorsion (eyes rotate in same direction), while 166 (45.9%) had discordant cyclotorsion (eyes rotate in opposite directions).18 patients underwent subsequent retreatment with 14 (77.8%) demonstrating cyclotorsion in the same direction on both surgery days and 4 (22.2%) with cyclotorsion in different directions ($p= 0.001$).

Conclusions: Average cyclotorsion was less than 3 degrees, and when torsion was present about two-thirds of the eyes had excylotorsion. Amount and direction of cyclotorsion in one eye did not always correlate with the same amount and direction of cyclotorsion in the contralateral eye. Understanding that there is variability in cyclotorsion is important in surgeries such as wavefront guided LASIK/PRK where identification of and correction for cyclotorsion can impact visual results.

CONTROL ID: 3710936

SUBMITTER (NAME ONLY): Mahsa Siadati

TITLE: Contrast-enhanced motion-free volumetric retinal structure and angiography reconstruction using optical coherence tomography intensity-based volume registration and averaging process

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Siadati, M. Ju, The University of British Columbia School of Biomedical Engineering, Vancouver, British Columbia, CANADA|Y. Miao, Z. Mammo, M. Ju, The University of British Columbia Department of Ophthalmology & Visual Sciences, Vancouver, British Columbia, CANADA|A. Athwal, D. Ma, Simon Fraser University School of Engineering Science, Burnaby, British Columbia, CANADA|D. Ma, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our research focuses on the development of a robust software-based algorithm to overcome the motion artifacts from the patient's involuntary eye movements on OCT and OCTA retinal images. Acquiring multiple volumes from the same retinal location followed by precise registration and averaging reduces the effects of motion artifacts and improves the contrast, resulting in better visualization of distinctive features and facilitation of retinal diseases diagnosis in clinics.

Methods: In our 3D registration method, prior to the registration, the motion artifacts are detected and eliminated. Following the motion artifact removal, a B-scan-based registration is applied to align the spatial coordinates of all the volumes to the coordinates of a reference volume with minimum motion artifacts. B-scan-based registration is followed by an en face affine registration to correct the rotation angle difference between each volume and the reference volume.

Results: The accuracy and robustness of our proposed method are evaluated on datasets with 3 different field-of-views (FOVs) acquired from 4 custom-built OCT systems. Figure 1 illustrates a small FOV OCT dataset (>100 volumes) obtained using a 1060 nm swept-source OCT system. The final averaged result is a motion-free volume with an increased signal-to-noise ratio (79.43% improvement), allowing for better visualization of retinal capillary, photoreceptor mosaic, and RPE layers. Figure 2 shows a middle FOV OCTA dataset (> 20 volumes) acquired using an 800 nm spectral-domain OCT system. The final OCTA volume data shows a more distinct vasculature network without noticeable motion artifacts in superficial and deep capillary plexus.

Conclusions: We have developed a novel 3D volume registration algorithm that can be utilized for various OCT/OCTA volumes with different spatial resolutions and FOVs. This registration algorithm can be utilized across different OCT platforms to overcome the motion artifacts.

CONTROL ID: 3710938

SUBMITTER (NAME ONLY): Lewis Fry

TITLE: Comparison of CRISPR-Cas13 RNA editing tools for inherited retinal disease

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.E. Fry, M.E. McClements, R.E. MacLaren, Nuffield Department of Clinical Neuroscience, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|L.E. Fry, R.E. MacLaren, Oxford University Hospitals NHS Foundation Trust, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Lewis Fry: Commercial Relationship: Code N (No Commercial Relationship) | Michelle McClements: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Correction of single base mutations in messenger RNA is a potential therapeutic approach for inherited retinal disease. A Cas13 enzyme fused to an adenosine deaminase acting on RNA deaminase domain ($ADAR_{DD}$) can be directed by a guide RNA (gRNA) for the targeted correction of G>A mutations. Here, we compare Cas13 RNA editing tools and the length and design of gRNAs for the correction of premature termination codons (TAG > TGG) in an USH2A gene fragment in a luciferase assay. As USH2A, like many photoreceptor genes, is poorly expressed in common cell lines, the luciferase assay was designed for facile in vitro screening.

Methods: A dual luciferase reporter assay expressing the target mutations was used in HEK293T cells in a 96-well format. Cells were triple transfected with constructs expressing the reporter assay, Cas13-$ADAR_{DD}$ effectors and gRNAs. dPspCas13b, dPspCas13b-Δ984-1090, and the minimal dCas13-bt1, -bt3 and -bt5 orthologues were tested, $ADAR_{DD}$ with E488Q and E488Q/T375G mutations were compared, and 30nt and 50nt gRNAs with a range of distances between a A-C mismatch at the target adenosine and the gRNA scaffold were screened for activity. On-target RNA editing rates were analysed by restoration of firefly luciferase activity and trace decomposition of Sanger sequencing reads of cDNA.

Results: Using dPspCas13b, a screen of 50nt gRNAs with mismatch distances of 18-42nt between the A-C mismatch and the gRNA scaffold demonstrated editing rates of 2-49%. No loss of activity of the best performing guides was seen with the truncated dPspCas13b-Δ984-1090. The minimal dCas13bt orthologues demonstrated lower editing rates of 1-22% with 50nt guides. dPspCas13b constructs with the specific $ADAR_{DD}$(E488Q/T375G) mutation demonstrated a 60% loss of on-target activity relative to constructs with the $ADAR_{DD}$(E488Q) mutation, but off-target editing was undetectable. For both dCas13bt and dPspCas13, 30nt guides were significantly less efficient. Sanger sequencing of corrected transcripts found significantly higher on-target correction than detected by luciferase restoration.

Conclusions: RNA editing with Cas13 efficiently corrects G>A mutations in USH2A gene fragments in vitro. The described luciferase assay allowed efficient comparison of a range of constructs and gRNAs for editing optimisation.

CONTROL ID: 3710940

SUBMITTER (NAME ONLY): Khang Huynh

TITLE: Mapping the origin of two-photon excited fluorescence in macaque retinal layers with adaptive optics fluorescence lifetime ophthalmoscopy

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.T. Huynh, Department of Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|K.T. Huynh, K. Kunala, K. Parkins, Q. Yang, J.J. Hunter, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|A.B. Chadderdon, Departments of Biochemistry and Physics, Monmouth College, Monmouth, Illinois, UNITED STATES|J.J. Hunter, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fluorescence lifetime ophthalmoscopy (FLIO) can distinguish lifetime variations across the normal and diseased fundus, yet the role of individual fluorophores is unclear. Adaptive optics (AO) FLIO enables cellular-scale resolution of unique cell types in distinct retinal layers. Here, we apply in vivo AOFLIO to compare the lifetimes of cellular-scale structures throughout the healthy macaque retina to those of specific retinal fluorophores.

Methods: In 2 male macaques, AOFLIO was performed using two-photon excited fluorescence (730 nm, ~55 fs, 80 MHz, 7 mW) in a scanning light ophthalmoscope (19 1.1x1.3° regions, 5-18° ecc.). The nerve fiber (NF), ganglion cell (GC), and photoreceptor (PR) layers were imaged. At each pixel, phasor analysis, where the cos and sin Fourier transform of the decay trace is computed at the laser pulse rate, yielded a Cartesian coordinate (g,s). Clusters from in vivo data were compared to a phasor fingerprint of common retinal fluorophores NADH, FAD, elastin, all-trans-retinol (ROL), and all-trans-retinal (RAL) in solution measured in the same system.

Results: In the phasor fingerprint, each fluorophore had a unique position. Phasor plots of in vivo data suggested contributions from several fluorophores. The artery wall phasor showed a dominance of elastin not seen in veins (Fig 1). Phasors of NF and GC, dominated by metabolites, oriented along the free/bound NADH axis. Consistent with previous work, the PR phasors separated into rods, M/L cones, and S cones. Rods and M/L cones laid on a ROL/RAL axis (Fig 2); M/L cones had a 48±12% mean relative contribution from ROL, significantly higher than in rods (30±16%) possibly due to increased photopigment bleach (paired t-test, p=.02). After a 2 min 730 nm exposure, the S cone lifetime became longer, which may be indicative of oxidative stress. The optic disc edge clustered separately from PR closer to bound NADH, FAD, and elastin (Fig 2).

Conclusions: The axial and lateral resolution of AOFLIO allows identification of multiple origins of fluorescence in distinct retinal cells and layers. We demonstrated the first in vivo AOFLIO assessment in the inner retina and further characterized the outer retina. Comparing phasor signatures throughout the retina to those of known fluorophores establishes a basis for assessing subcellular molecular pathways that are expected to shift in disease.

CONTROL ID: 3710946

SUBMITTER (NAME ONLY): Stephen Pflugfelder

TITLE: Reduced RXRα signaling increases dry eye disease inducing γδT17 cells in the conjunctiva

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.C. Pflugfelder, J. Alam, G. Yazdanpanah, R. Ratnapriya, C.S. De Paiva, D. Li, R. Guimaraes de Souza, Z. Yu, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|N. Borcherding, Pathology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the mechanism for developing dry eye disease in the Pinkie mouse strain with a loss of function RXRα mutation.

Methods: Measures of dry eye disease were assessed in the cornea and conjunctiva. Expression profiling by single-cell RNA sequencing (scRNA-seq) was performed to compare gene expression in conjunctival immune cells. Conjunctival immune cells were immunophenotyped by flow cytometry and confocal microscopy. Activity of RXRα ligand 9-cis retinoic acid (RA) was evaluated in cultured monocytes and γδT cells.

Results: Compared to wild type (WT) C57BL/6, Pinkie has increased signs of dry eye disease, including corneal barrier disruption, conjunctival cornification and goblet cell loss, and corneal vascularization, opacification, and ulceration with aging. scRNA-seq of conjunctival immune cells identified γδT cells as the predominant IL-17 expressing population in both strains and there is a 4-fold increased percentage of γδT cells in Pinkie. Compared to WT, significantly increased expression of IL-17a and IL-17f in conventional T cells and IL-17f in γδT cells was found in Pinkie. Flow cytometry and immunostaining revealed an increased number of IL-17^{+} γδT cells in Pinkie. Tear concentration of the IL-17 inducer IL-23 is significantly higher in Pinkie. 9-cis RA treatment suppresses stimulated IL-17 production by γδT and stimulatory activity of monocyte supernatant on γδT cell IL-17 production. Compared to WT bone marrow chimeras, Pinkie chimeras have increased IL-17^{+} γδT cells in the conjunctiva after desiccating stress and anti-IL-17 treatment suppresses dry eye induced corneal MMP-9 production/activity and conjunctival goblet cell loss.

Conclusions: These findings indicate that RXRα suppresses generation of dry eye disease inducing γδT17 cells in the conjunctiva and identifies RXRα as a potential therapeutic target in dry eye.

CONTROL ID: 3710948

SUBMITTER (NAME ONLY): Daniel Bastán-Fabián

TITLE: Correlation Analysis between Functional Tests for Dry Eye Disease and OCT-based Tear Film Dynamic Tests in LASIK patients.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Bastán-Fabián, M.E. Quiroga-Garza, J.C. Hernandez-Camarena, J.E. Valdez, Ophthalmology, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To determine whether an association between functional and structural tests of the tear film can be found and to describe if a significant difference between preoperative and postoperative parameters is present.

Methods: We studied 34 eyes of 17 patients undergoing LASIK surgery. OCT tear film (TF) analysis consisted of structural parameters such as tear meniscus height, depth, and area (RTVue-100 Fourier-domain OCT) and functional tests such as Schirmer, Non-Invasive Tear Breakup Time (NIBUT) (Keratograph 5M), and Ocular Surface Discomfort Index (OSDI). Measurements were performed before and 1 month after the procedure. Wilcoxon test was used to compare basal vs postoperative structural and functional TF parameters. Correlation analysis and linear regression were also implemented to model the association between these variables. A p-value of less than .05 was considered of statistical significance.

Results: No significant changes between basal and postoperative measurements were observed in the structural and functional TF variables. The analysis yielded a negative correlation (Rho= -0.349, p= 0.043) between basal tear meniscus height and basal NIBUT. A negative correlation between basal tear meniscus height and 1-month postoperative NIBUT (Rho= -0.409, p=.016) and 1-month postoperative Schirmer test (Rho= -0.360, p= .036) was observed. The linear regression model yielded no significant correlation. Change (delta) in basal vs 1-month postoperative NIBUT was associated with age and spherical equivalent (β=.547, p=.028, and β=-.522, p=.016).

Conclusions: Our analysis did not demonstrate a significant difference between basal vs 1-month measurements in neither structural or functional tests. However, results suggest that Dry Eye Disease can manifest with normal structural TF parameters while yielding altered results in the functional evaluation. More studies are needed in order to determine the presence of significant differences in basal vs longer-term measurements.

CONTROL ID: 3710950

SUBMITTER (NAME ONLY): Juno Cho

TITLE: Medication adherence in the 12-month follow-up period after the Support, Educate, Empower (SEE) glaucoma coaching program

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cho, O. KILLEEN, L. Niziol, P.P. Lee, D.C. Musch, P. Newman-Casey, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|M. Heisler, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, UNITED STATES|K. Resnicow, School of Public Health, University of Michigan, Ann Arbor, Michigan, UNITED STATES|D. Darnley-Fisch, Department of Ophthalmology, Henry Ford Health System, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Motivational Interviewing (MI) has improved medication adherence rates for patients with chronic illnesses. The Support, Educate, Empower (SEE) program, a 7-month MI-based personalized glaucoma coaching program, has previously shown to improve medication adherence by 21-percentage points in a sample of non-adherent glaucoma patients. The goal of this study was to assess adherence in the 12-months following the conclusion of the SEE program intervention.

Methods: Glaucoma patients ≥40 years, taking ≥1 medication, self-reporting poor medication adherence were recruited from the University of Michigan for the SEE pilot study. Participants' medication adherence rates were monitored electronically (AdhereTech, New York, NY) during a 3-month pre-intervention phase (pre-counselling adherence), 7-month intervention phase while they received personalized coaching sessions (counselling adherence), and for an additional 12-months following the conclusion of their coaching sessions (post-counselling adherence). Adherence was summarized with descriptive statistics and compared using paired t-tests.

Results: Medication adherence data were available for 39 participants. Post-counselling adherence rates were censored for 18 participants (56%); 3 participants received glaucoma laser or incisional surgery, 3 had changes made to their glaucoma medication regiment, and 12 stopped using their electronic medication monitors before the full 12-month follow-up period. Average follow-up was 284 days (standard deviation, SD=110, range=41 to 365). The average post-counselling adherence was 66.5% (SD=22.5%), significantly less than the average counselling adherence rate of 81.3% (SD=17.6%, $p<0.0001$) but significantly more than pre-counselling adherence rate of 59.9% (SD=18.5%, $p=0.04$). The decrease in adherence post-counseling was mostly observed in the first 4 months (mean decrease=17.4%, SD=19.5%, $p<0.0001$).

Conclusions: Medication adherence rates significantly decreased among SEE program participants in the 12 months following their last counselling session, although they were still significantly higher than pre-counselling adherence rates. These results suggest that glaucoma patients may need additional counselling sessions to see continued benefit from the program. We suggest that patients should be seen every 3-month for a "booster" counselling session.

CONTROL ID: 3710951

SUBMITTER (NAME ONLY): Deokho Lee

TITLE: Pemafibrate exerts therapeutic effects on retinal damages induced by transient elevation of intraocular pressure via multiple protective pathways

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Lee, Y. Miwa, H. Kunimi, K. Negishi, T. Kurihara, Ophthalmology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|A. Nakai, Ophthalmology, Nihon University School of Medicine, Tokyo, JAPAN|Y. Tomita, Ophthalmology, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, UNITED STATES|K. Tsubota, Tsubota Laboratory, Inc., Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Retinal ischemia-reperfusion injury (I/R) is a general cause of vision loss, and no effective treatment is available for retinal I/R. Pemafibrate, a peroxisome proliferator-activated receptor α (PPARα) modulator, was suggested as a promising therapeutic in ischemic retinopathies. However, its roles have not been clearly unraveled in retinal I/R. In this study, we investigated therapeutic effects of pemafibrate against retinal dysfunction in an experimental model of retinal I/R by transient elevation of intraocular pressure (IOP).

Methods: Adult male mice (5–7 weeks old; C57BL/6) were orally given to pemafibrate (0.5 mg/kg) for 4 days, followed by retinal I/R (IOP: 90–99 mmHg; 40 minutes). Mice were continuously given to pemafibrate (0.5 mg/kg) once every day until the end of experiments, 5 days after retinal I/R. Retinal functional changes were measured using electroretinography (ERG). Then, the retina, liver, and serum samples were used for western blotting (WB), qPCR, immunohistochemistry (IHC, sagittal-sectioning, and flat-mounting), or ELISA analysis.

Results: Retinal dysfunction and retinal ganglion cell (RGC) loss stained by NeuN were prevented by pemafibrate administration (ERG, a-wave and b-wave: 1.7-fold and 1.5-fold increase, $p < 0.05$; IHC, RGC: 1.7-fold increase, $p < 0.001$). Pemafibrate administration increased hepatic PPARα target gene expressions (qPCR, $p < 0.05$) and serum levels of fibroblast growth factor 21 (FGF21; ELISA, 20.3-fold increase, $p < 0.01$), one of the neuroprotective molecules in the eye. Retinal inflammation stained by Isolectin GS-IB4 and pathological gliosis stained by GFAP were reduced by pemafibrate administration (IHC, GS-IB4: 0.26-fold decrease, $p < 0.01$; GFAP: 0.76-fold decrease, $p < 0.05$). Furthermore, pemafibrate administration altered expressions in hypoxia-response genes (qPCR, $p < 0.05$) via hypoxia-inducible factor-1α (HIF-1α; WB, 0.70-fold decrease, $p < 0.01$) pathway and pro-apoptotic and anti-apoptotic genes such as c-Jun, Nrf2, and Ho-1 (qPCR, $p < 0.05$) in the ischemic retina.

Conclusions: Our data suggest possibilities of therapeutic effects of pemafibrate on ischemic retinal degeneration via multiple protective pathways.

CONTROL ID: 3710959

SUBMITTER (NAME ONLY): Rupesh Singh

TITLE: Near infrared photobiomodulation prevents neovascularization in oxygen-induced retinopathy in mouse

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Singh, G. Hoppe, D. Hanna, Z. Miller, P. Freedman, V.L. Bonilha, B. Anand-Apte, J. Sears, Ophthalmic Research, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|V.L. Bonilha, B. Anand-Apte, J. Sears, Department of Molecular Medicine, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the therapeutic effect of near infrared (810 nm) photobiomodulation (PBM) on retinal neovascularization in a mouse model of oxygen-induced retinopathy (OIR).

Methods: Sixteen mouse pups (C57BL/6J) were placed in hyperoxia (75% oxygen) from P7 to P12. Following the switch to normoxia, the pups were treated with 810 nm whole body photobiomodulation (6 J/cm^2) daily for 6 min from P13 to P17. At P17, fluorescein angiography (FA), confocal scanning laser ophthalmoscopy (cSLO) and OCT imaging was performed. Post in-vivo imaging, retinal flatmounts were stained with isolectin GS-IB4-Alexa Fluor-568 and imaged with a Zeiss Axiophot fluorescent microscope. A machine learning based algorithm was used for calculating vascular tufts in isolectin stained flatmount images. The cSLO and volumetric OCT images were evaluated for retinal avascular area in the central 55^o retina. Statistical comparisons were made using non-parametric one tailed t-test with significance at $P < 0.05$, 95% CI.

Results: Photobiomodulation resulted in significantly decreased retinal neovascularization, as observed in flatmount images. FA images were analyzed and quantified for retinal avascular area using central 55^o retina with optic nerve head in center. The avascular area in PBM treated group was decreased compared with OIR non treated controls. The body weight of pups at P17, an indicator of overall health, was significantly increased in PBM treated group compared with control group.

Conclusions: The single wavelength PBM treatment of oxygen-induced retinopathy mouse shows decreased neovascularization and increased body weight. The results suggest PBM as a promising therapeutic for ROP.

CONTROL ID: 3710960

SUBMITTER (NAME ONLY): Christelle GROSS

TITLE: The post-mortem interval influences the properties of human corneal epithelial cells in vitro.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. GROSS, G. Le-Bel, P. Desjardins, C. Couture, L. Germain, S. Guérin, CUO-Recherche, Axe Médecine Régénératrice, Centre de recherche du CHU de Québec, Hôpital du Saint Sacrement; Département d'Opthalmologie, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|C. GROSS, G. Le-Bel, P. Desjardins, S. Cortez-Ghio, C. Couture, L. Germain, S. Guérin, Centre de recherche en organogénèse expérimentale de l'Université Laval/LOEX, Axe Médecine Régénératrice, Centre de recherche du CHU de Québec, Hôpital de l'Enfant-Jésus; Département de chirurgie, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The cornea is crucial for visual acuity as it allow light refraction to the retina and constitutes the first ocular barrier. It ruptures frequently cause infection and in severe cases, lead to the complete loss of vision. In North America, corneal wounds accounts for 37% of visual deficiency. Normal homeostasis of the corneal epithelium is ensured by corneal epithelial stem cells. According to the severity of the trauma, stem cell integrity can be compromised and a corneal transplantation may be required. In order to reduce the need for donor corneas, understanding of corneal wound healing and development of an tissue-engineered human cornea (hTECs) is of prime importance. For transplantation purposes or to conduct research studies, the human corneal epithelial cells (hCECs) used in the hTECs production must be of the highest possible quality. The present study was intended to evaluate the impact of the post-mortem interval (PMI) on the properties of hCECs in vitro.

Methods: hCECs were isolated from the limbal area of donor corneas at different PMI (from 0 to 19 days) and grown as monolayers or on hTECs. The gene expression pattern was determined in ten populations. Growth rate measurements and colony-forming efficiency assays were conducted to evaluate the hCECs proliferative potential whereas the histological integrity of the hTECs was analysed by immunofluorescence. The stem cell population from cultured hCECs with different PMI was evaluated by p63 staining and the PMI impact on the wound closure dynamic studied on both hCECs and hTECs.

Results: Short PMI hCECs have a gene expression pattern distinct from that of long PMI hCECs grown as monolayers, and also displayed an increased number of daily doublings and generated more colonies per seeded cell compared with long PMI hCECs. Immunofluorescence analyses revealed that components of the basement membrane and extracellular matrix were deposited similarly in all hTECs, irrespective of the hCECs PMI. Interestingly, short PMI hCECs have more stem cells than the long PMI cells, which significantly accelerated wound closure in the short PMI group (in both hCECs and hTECs).

Conclusions: These results suggest that hTECs reconstructed using short PMI hCECs have a higher number of limbal stem cells and exhibit a more efficient wound healing response in vitro, making them the best candidates to produce substitutes for clinical studies.

CONTROL ID: 3710962

SUBMITTER (NAME ONLY): Fernando Zvietcovich

TITLE: Multi-meridian wave-based corneal optical coherence elastography in normal and keratoconic patients

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Zvietcovich, J. Birkenfeld, A. Varea, A.M. Gonzalez, A. Curatolo, S. Marcos, Institute of Optics, Consejo Superior de Investigaciones Cientificas, Madrid, Madrid, SPAIN|A. Curatolo, International Centre for Translational Eye Research, Polska Akademia Nauk, Warszawa, Mazowieckie, POLAND|S. Marcos, The Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The detection of pre-clinical keratoconus remains a challenging task. We propose to use wave-based optical coherence elastography to measure full spatial-dependent elasticity of normal and keratoconic corneas. We hypothesize that both advanced and pre-clinical keratoconus corneas can be identified as outliers from a baseline metric.

Methods: A 500 kHz ultrasonic air-coupled transducer co-focused with an optical coherence tomography system was used to generate quasi-harmonic mechanical perturbation at the corneal apex. Lamb wave propagation speed and average thickness were measured within 16 corneal meridians covering 360 degrees during 1s of acquisition. Measurements were conducted in thirty-one human healthy subjects (control group, N = 62 corneas; age: 20-50 yo; corneal astigmatism <2 diopters) and three keratoconic patients (N = 5 corneas; age: 14-50 yo). All measurements were fully non-contact, and followed the approved research protocol adhered to the tenets of the Declaration of Helsinki. Spatial anisotropy of wave speed (SAWS) was calculated from the meridional-dependent wave speed of each cornea. Speed and thickness for each corneal meridian were projected in a thickness-speed map (TSM) for further statistical analysis.

Results: SAWS was statistically significantly higher in advanced (0.353, $p = 1\times10^{-11}$, N = 3) and pre-clinical (0.249, p = 0.04, N = 2) keratoconus corneas when compared to the baseline. Moreover, we found a linear correlation between meridional speed and thickness (RMSE = 0.738, $p = 5.4\times10^{-98}$) in normal corneas when measurements were projected into the TSM (Fig. 1). A 95% confidence level was used as a baseline metric to separate normal (stiffer) from abnormal (softer) corneal elasticity. We found abnormal elasticity in at least 10 out of 16 meridians in advanced keratoconus corneas ($p = 1\times10^{-10}$, N = 3), and in at least in 4 out of 16 meridians in pre-clinical keratoconus corneas ($p = 1.5\times10^{-5}$, N = 2).

Conclusions: Our results show important biomechanical differences in SAWS and TSM between normal and keratoconus corneas, suggesting those as potential biomarkers for progression and severity of keratoconus, following sensitivity and specificity studies on a larger sample of keratoconic (and their contralateral) eyes.

CONTROL ID: 3710964

SUBMITTER (NAME ONLY): Manisha Dagar

TITLE: The role of the Complement pathway in L-ORD pathology caused by mutations in CTRP5.

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Dagar, P. Biswas, S. Pachauri, R. Ayyagari, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, INDIA|A.K. Chekuri, Harvard Medical School, Boston, Massachusetts, UNITED STATES|D. Garland, Harnly LLC, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Late-onset retinal degeneration (L-ORD) is an autosomal dominant disorder caused by mutations in the C1q-tumor necrosis factor-5 (CTRP5/C1QTNF5) gene. The purpose of this study was to understand the pathology of L-ORD by analysis of the proteome of the Retinal Pigment Epithelium-Choroid (RPE-Ch) tissue in mouse models carrying the S163R Ctrp5 mutation. The current study mainly focuses on components of the complement pathway as a function of age.

Methods: The proteomes of the RPE-Ch, which include Bruch's membrane (BrM), were analyzed in wild-type (WT), heterozygous S163R Ctrp5 mutation knock-in (Ki/WT), and homozygous knock-in (Ki/Ki) mice of approximately 5 and 18 months (m) of age. The mass spectral data were analyzed using MaxQuant software for the identification and quantification of the levels of peptides in the RPE-Ch. The proteins identified in the analysis were further experimentally validated in the RPE-Ch tissue of 5 and 18 m old mutant and WT mice by immunohistochemistry (IHC) and western blotting.

Results: Components of the three complement pathways were present in the WT and mutant mouse proteome of RPE-Ch. Five components of the classical pathway were observed to increase over 2 fold ($p<.05$) in WT and mutant mice with age. C4b was increased 2.7 and 3.9 fold with age in WT and Ki/WT, respectively. Both C1qb and C1qc were increased 2 and 3 fold with age in WT and Ki/WT, respectively. CFH, which is involved in the alternative pathway increased 1.4 fold ($p<.05$) with age in the WT mice and was higher in the Ki/WT but it did not reach significance. IHC was used to assess the levels of the components of the alternative complement pathway CFB, CFH, and C3, specifically in BrM. At 18 m of age, the levels of each protein were higher in mutant compared to WT mice. These observations were further validated using western blot analysis. CFB showed an increase by 2.1 fold in Ki/WT and 2.9 fold in Ki/Ki compared to WT. CFH increased by 1.35 fold in Ki/WT and 1.5 fold in Ki/Ki.

Conclusions: Proteome analysis of RPE-Ch revealed an increase in members of the classical complement pathway with age in the WT and L-ORD mouse models. The levels of components of the alternative pathway (CFB, CFH, and C3) were increased in BrM-Ch of mutant mice at 18 m. This study provides insight and support for the potential role of the complement system in L-ORD pathology.

CONTROL ID: 3710967

SUBMITTER (NAME ONLY): Golnoush Mahmoudinezhad

TITLE: Impact of Smoking on Visual Field Progression

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Mahmoudinezhad, T. Nishida, R.N. Weinreb, S. Baxter, M. Eslani, L. Zangwill, S. Moghimi, Hamilton Glaucoma Center, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, San Diego, California, UNITED STATES|J.M. Liebmann, Bernard and Shirlee Brown Glaucoma Research Laboratory, Department of Ophthalmology, Edward S. Harkness Eye Institute, Columbia University Medical Center, New York, New York, UNITED STATES|M.A. Fazio, C.A. Girkin, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the effect of smoking on the rates of progressive visual field damage over time in glaucoma.

Methods: In this longitudinal study, 354 primary open-angle glaucoma (POAG) patients with a minimum of 3 years follow-up and 5 visual fields (VF) tests were enrolled from the Diagnostic Innovations in Glaucoma Study (DIGS) and the African Descent and Glaucoma Evaluation Study (ADAGES). Univariable and multivariable linear mixed models were used to investigate the effects of smoking on the rates of 24-2 VF mean deviation loss after adjusting for confounding factors such as alcohol consumption and Body Mass Index. VF progression was defined using pointwise linear regression (three test locations having a significant regression slope ($p<0.01$) of ≤-1dB per year). Logistic regression was used to identify whether different levels of smoking intensity were associated with VF progression. Kaplan-Meier curve and the log-rank test were used to compare the cumulative risk ratio of progression between different smoking intensity categories.

Results: A total of 511 eyes of 354 patients with glaucoma followed from multicenter glaucoma registries were included over the mean follow-up of 12.4 years. Mean baseline age was 62.3 years; 124 (35%) were African ethnicity. Of the 354 patients, 168 (59.8%) and 149 (42.1%) had reported a history of smoking or alcohol consumption, respectively. 39 (11%) were heavy smokers. In a multivariable model, higher smoking intensity was associated with faster VF loss (coefficient -0.05 (-0.08,-0.01)dB/year per 10 pack-years, P=0.01). Developing VF progression in eyes of heavy smokers (>20 pack-years) was 2.2 times greater than in eyes of non-smokers after adjusting for confounding factors (OR=2.21; 95% CI: 1.02,4.76; P=0.04), Figure 1. A significantly higher proportion of progressing eyes were found in heavy smokers compared to non-smokers by Kaplan-Meier analysis (log-rank test, $P<0.01$), Figure 2.

Conclusions: Heavy smokers are more likely to have VF loss in eyes with glaucoma. The prospective longitudinal design of this study supports the hypothesis that levels of smoking may be associated with glaucoma progression. Additionally, this information can be used for clinically relevant tobacco prevention and intervention messages.

CONTROL ID: 3710969

SUBMITTER (NAME ONLY): Emanuele Crincoli

TITLE: Deep Learning to distinguish Best vitelliform macular dystrophy (BVMD) from adult vitelliform macular degeneration (AVMD)

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Crincoli, Z. Zhao, J. Estrada Walker, C. Mehanna, S. Halouani, A. Miere, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To automatically classify, using a deep learning model, spectral-domain optical coherence tomography (SD-OCT) and blue fundus autofluorescence (FAF) images of Best vitelliform macular dystrophy (BVMD) and adult vitelliform macular degeneration (AVMD).

Methods: Fifty-two BVMD eyes (SD-OCT images and FAF images) and 43 AVMD eyes (SD-OCT images and FAF images) were included. The contrast-based auto local threshold was used to preprocess FAF images. SD-OCT B-scans were binarized and processed using a mean-based auto local thresholding. MatLab deep learning toolbox was used as a framework for the deep learning process. Images were classified using Inception-ResNet-v2 convolutional neural network(CNN). Transfer learning using the ImageNet dataset was performed. Established augmentation techniques were used. Seventy (70)% of the images were used to train the network while 10% was used for validation and 20% for testing. Accuracy, sensitivity, and specificity were assessed using confusion matrices. The area under the receiver operating characteristics (AUROC) curves was determined to evaluate the model performances. The deep learning model's confidence was assessed using binomial logistic regression on the test set.

Results: The accuracy of the classification using FAF images was 96.8%. The model showed a 98.0% sensitivity and 95.4% specificity for the diagnosis of BVMD with an AUROC of 0.980 (CI 0.949 – 1.000). The accuracy of the classification using SD-OCT images was 0.936. The model showed a sensitivity of 94.2%, a specificity of 93.0%, and an AUROC of 0.942 (CI 0.890 – 0.994) for the diagnosis of BVMD. Binomial logistic regression revealed a 92% of correct classification probability.

Conclusions: The study shows good performances of CNN-based automated classification in differentiating the vitelliform stage of BVMD lesions from AVMD based on preprocessed FAF and SD-OCT images. With further developments, this model may help evaluate and distinguish the two clinical entities.

CONTROL ID: 3710980

SUBMITTER (NAME ONLY): Ayesha Badar

TITLE: Outcomes of a Microstent Procedure Combined With Cataract Extraction in Mild/Moderate versus Severe Open Angle Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Badar, R. Enzor, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|Y. Catoira-Boyle, Ophthalmology, Richard L Roudebush VA Medical Center, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Hydrus microstent (Ivantis, Irvine, CA) is a minimally invasive glaucoma surgery (MIGS) that spans approximately 90 degrees of the Schlemm's canal to improve trabecular outflow. Hydrus is FDA-approved to be performed in combination with cataract surgery in patients with mild to moderate open angle glaucoma. We performed this study to evaluate the safety and efficacy of phaco-Hydrus in patients stratified by severity of open angle glaucoma.

Methods: We completed a retrospective chart review of Hydrus microstent combined with phacoemulsification cataract extraction with intraocular lens implantation (phaco-Hydrus) performed in 22 eyes of 21 patients with mild/moderate (n=11) or severe (n=11) primary open angle glaucoma or normal tension glaucoma at a single academic site from 7/2020 to 7/2021. Mean age was 73.29 ± 7.27 years, 62% patients were Caucasian and 29% African American, and 95% were male. The average follow up was 5.95 ± 3.15 months (range 3-12 months). Surgical technique included insertion of the Hydrus microstent into the Schlemm's canal nasally. Data is reported as mean ± standard deviation, and comparisons were made of pre-operative and three-month data using paired Student's t-tests.

Results: At three months postoperatively, the average IOP reduction for all open angle glaucoma patients receiving phaco-Hydrus was -2.55 ± 3.77 mmHg (-24.02 ± 39.00%) (P = 0.0047). The average drop reduction was -0.50 ± 0.91 (P = 0.018). Average IOP reduction for mild to moderate open angle glaucoma was 1.0 ± 3.2 (P = 0.33) and average drop reduction was 0.64 ± 0.81 (P = 0.026). Average IOP reduction for severe open angle glaucoma was 4.09 ± 3.76 (P = 0.0048) and average drop reduction was 0.36 ± 1.03 (P = 0.27). Phaco-Hydrus in patients with severe open angle glaucoma resulted in greater IOP reduction than in mild to moderate glaucoma (P = 0.052). None of the patients required an additional glaucoma surgery during the follow-up period.

Conclusions: The combination of the Hydrus microstent with phacoemulsification cataract surgery results in significant IOP reduction for patients with all stages of open angle glaucoma, including severe. Greater IOP reduction was observed in patients with severe stage compared to mild to moderate stage open angle glaucoma. Phaco-Hydrus may be an effective option for patients with severe open angle glaucoma.

CONTROL ID: 3710981

SUBMITTER (NAME ONLY): Gabriella Hartman

TITLE: APE1/Ref-1 is overexpressed and colocalizes with neovascular tufts and hypoxic regions in the oxygen-induced retinopathy mouse model

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.D. Hartman, A. Muniyandi, M.R. Kelley, T.W. Corson, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Gabriella Hartman: Commercial Relationship: Code N (No Commercial Relationship) | Anbukkarasi Muniyandi: Commercial Relationship: Code N (No Commercial Relationship) | Mark Kelley: Commercial Relationship(s);Code P (Patent):US 16/968,009;Code C (Consultant/Contractor):Ocuphire Pharma;Code C (Consultant/Contractor):Apexian Pharmaceutical | Timothy Corson: Commercial Relationship(s);Code P (Patent):US 16/968,009

ABSTRACT BODY:

Purpose: Current treatments for retinal neovascularization as seen in proliferative diabetic retinopathy (PDR) and retinopathy of prematurity (ROP) include intravitreal injections of anti-vascular endothelial growth factor (VEGF) biologics. However, anti-VEGF biologics are accompanied by tachyphylaxis, high treatment burden, and complications, corroborating an unmet need for novel therapeutic targets. A promising therapeutic target for treatment of PDR and ROP is the redox transcriptional regulatory function of the protein apurinic/apyrimidinic endonuclease 1/reduction-oxidation factor 1 (APE1/Ref-1). Ref-1 activity has been implicated in multiple relevant pathways involved in retinal neovascularization including angiogenesis, inflammation, and stress response. First-generation Ref-1 redox inhibitor APX3330 is already in phase II clinical trials for DR and diabetic macular edema (DME). However, the expression of Ref-1 has yet to be fully characterized in retinal neovascular disease. We aimed to assess Ref-1 expression in the murine oxygen-induced retinopathy (OIR) model to increase understanding of Ref-1's role in retinal neovascularization.

Methods: Neonatal mice and dams were exposed to hyperoxia (75% O_2) or room air for 5 days (P7-P12). Mice were injected with pimonidazole for visualization of hypoxic regions two hours before euthanasia and enucleation at P12, P15, and P17. Retinal flatmounts were coimmunostained for Ref-1, vasculature (isolectin B4), and hypoxia (Hypoxyprobe). Spatial and temporal expression of Ref-1 was analyzed by confocal microscopy.

Results: Ref-1 colocalized with vasculature and hypoxic regions in the OIR model. Mean fluorescent intensity (MFI) of Ref-1 in OIR eyes was higher compared to normoxia control eyes at each time point ($p<0.0001$, two-way ANOVA, Tukey's post hoc test). Ref-1 colocalized with neovascular tufts, and Ref-1 expression was absent in vaso-obliterated areas of the retina.

Conclusions: Previous data revealed that Ref-1 inhibition blocks laser-induced choroidal neovascularization (L-CNV). Here, we revealed that Ref-1 is highly expressed in pathological angiogenic tufts in the murine OIR retina, suggesting that Ref-1 is likewise important for retinal neovascularization, thus providing context for new potential therapeutic use in PDR and/or ROP.

CONTROL ID: 3710986

SUBMITTER (NAME ONLY): Leon Chea

TITLE: Lysine Ubiquitylation in P23H Rhodopsin Protein Degradation

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chea, G. Lee, J. Lin, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|L. Chea, G. Lee, J. Lin, Pathology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|A. Chen, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|P. Chan, Cancer Biology and Genomics, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) is a group of inherited disorders with loss of rod photoreceptors followed later by cone photoreceptors. The most common point mutation of RP in the United States is a proline to histidine amino acid change at position 23 (P23H). Our previous studies indicated that misfolded P23H rhodopsin activates the inositol-requiring enzyme 1 (IRE1) pathway of the unfolded protein response (UPR) and undergoes endoplasmic reticulum associated degradation (ERAD) by unclear mechanisms. Here, we investigate the role of lysine ubiquitination in P23H and wild-type (WT) rhodopsin protein turnover.

Methods: HEK293FT cells were transfected with a pcDNA3.1 plasmid vector expressing WT or P23H human rhodopsin from a cytomegalovirus (CMV) promoter (Invitrogen). A PrimeStar Mutagenesis site-directed primers using in-frame modifications of 5'-AAG-3' to 5'-AGG-3' were used to convert all 11 lysines on human WT and P23H rhodopsin to arginines (K-null). Immunoprecipitation and immunoblots were performed to measure protein levels of rhodopsin and ubiquitin. A cycloheximide chase assay determined $t_{1/2}$ of P23H and K-null P23H rhodopsin. RT-qPCR was performed to measure E3 ubiquitin ligase expression in P23H homozygous ($Rho^{P23H/P23H}$) mouse retinas. HEK293T cells containing I642G mutant allele were treated with DMF or 1NM-PP1 to artificially activate IRE1.

Results: P23H K-null was significantly less ubiquitylated than intact P23H rhodopsin. P23H K-null had significantly increased protein half-life compared to intact P23H rhodopsin in cycloheximide chase assays. Single lysine-to-arginine point mutations did not significantly change P23H rhodopsin ubiquitination. Additionally, a K-null WT rhodopsin also showed reduced ubiquitination of WT rhodopsin. Lastly, we identified 18 E3 ubiquitin ligase genes expressed in HEK293T cells, regardless of IRE1 activation status with 13 genes upregulated in $Rho^{P23H/P23H}$ mouse retinas.

Conclusions: Our findings support that lysine ubiquitylation is an important post-translational modification for WT and P23H rhodopsin protein degradation. Multiple lysine residues are likely ubiquitinylated during rhodopsin protein degradation. Strategies to ubiquitinylate P23H rhodopsin could enhance its clearance by autophagy or proteasome degradation and potentially benefit retinitis pigmentosa patients carrying these mutations.

CONTROL ID: 3710987

SUBMITTER (NAME ONLY): Rina Okazawa

TITLE: Identification of distinct characteristics underlying in various anterior uveitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Okazawa, T. Sato, K. Harimoto, T. Kanda, M. Takeuchi, ophthalmology, Boei Ika Daigakko, Tokorozawa, Saitama, JAPAN|K. Takayama, Sakura street takayama eye clinic, JAPAN|

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ABSTRACT BODY:

Purpose: Anterior uveitis (AU) is the most common form of uveitis and an important condition encountered both in primary care unit and specialist uveitis clinics. There are several known and many possible etiologies for AU, and clinical characteristics in AU differ depending on the cause. In this study, we focused on AU and investigated the detailed epidemiological profile and the clinical finding-related differences.

Methods: Clinical charts of consecutive 275 patients with 335 eyes (mean age 52.5 ±19.1 years, male/female = 124/151) who made a first visit at National Defense Medical College Hospital between January 2010 and March 2020 were retrospectively reviewed. Visual acuity, intraocular pressure (IOP), unilateral/bilateral uveitis at first visit, and diagnosis, were collected from clinical charts. In eyes suspected infectious uveitis, multiplex polymerase chain reaction tests (PCR) using anterior aqueous humor were performed as previous reports, and diagnosed.

Results: Epidemiologically, acute AU was the most frequent (21.8%), followed by viral AU (20.7%) consisting of varicella zoster virus (VZV) at 9.1%, herpes simplex virus (HSV) at 8.0%, and cytomegalovirus (CMV) at 3.6%, scleritis (13.5%), diabetic iritis (7.6%), and Posner-Schlossman (P-S) syndrome (5.5%), although unexplained cases were 17.1%. Unilateral AU was 78.2% of the total, of which 86.7% of acute AU, 96.5% of viral AU (VZV 100%, HSV 100%, and CMV 80%), 75.7% of scleritis, 57.1% of diabetic iritis, and 100% of P-S syndrome. One hundred eleven AU patients (40.4%) were more than 60 years old, which were composed of viral AU at 34.2% (VZV 14.4%, HSV 12.6%, and CMV 7.2%), scleritis at 14.4%, acute AU at 13.3%, P-S syndrome at 6.3%, and diabetic iritis at 4.5%. AU patients with visual disturbance less than 20/30 accounted for 36% of the total, which consisted of 46.7% of acute AU, 50.9% of viral AU (VZV 48%, HSV 54.5%, and CMV 50%), 16.2% of scleritis, 47.6% of diabetic iritis, and 55.6% of Fuchs' uveitis. Comparing acute AU and viral AU, viral AU patients were significantly older and had higher intraocular pressure than acute AU patients.

Conclusions: AU is predominantly unilateral, and the etiology was identified in about 80%. The most frequent disease was acute AU, followed by viral AU, and visual acuity was equally impaired in them. However, it was suggested that viral AU patients were older and had higher IOP than acute AU patients.

CONTROL ID: 3710988

SUBMITTER (NAME ONLY): Rithambara Ramachandran

TITLE: A Feasibility Study For The Use Of Virtual Reality Visual Field Testing For Hospital-Based Ophthalmic Consultations

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ramachandran, V. Paranjpe, L.A. Al-Aswad, Ophthalmology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|L.A. Al-Aswad, Population Health, New York University Grossman School of Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Traditional perimetry is bulky, time-consuming, expensive, requires careful disinfection, and is impractical for use outside the standard outpatient office. The aim of this proof-of-concept prospective study is to demonstrate the feasibility of use of a portable Virtual Reality Visual Field (VRVF) device[1] for hospital-based ophthalmology consultations. Secondary aims are to investigate the clinical utility of the device and to quantitatively compare results to in-office gold standard Humphrey Visual Field (HVF) testing.

Methods: In this ongoing study, all ophthalmology consultations at a single site over the course of a 5-month study period will be included. Patients undergo VRVF testing (BOLT strategy, Stim III) only if the ophthalmology service has been consulted for: blurry vision, unexplained vision loss, rule out papilledema, baseline examination prior to medication initiation or surgical intervention, or suspected neurologic/neuro-ophthalmologic disease. Data collected include patients' attitudes towards testing experience, management decisions made based on testing, diagnoses, and VRVF and HVF parameters.

Results: Of the 45 consultations made over the initial one-month period, 4 patients were eligible for VRVF testing (mean age 57.5 +/- 18.0 years). Average patient usability rating was 5.75 (scale of 1-hardest to 10-easiest), with all participants indicating they would do the test again and none reporting adverse outcomes. 50% of exams were to establish visual field baseline prior to neurosurgical intervention and the remaining were for the workup of PION. In no case did results change management. Follow up HVF was available for 2 participants (4 eyes). Strong correlation between VRVF and HVF was noted for point-by-point comparison ($r=0.93$, $p<0.0001$), mean deviation ($r=0.99$, $p=0.0025$), but not pattern standard deviation ($r=0.31$, $p>0.05$).

Conclusions: Prior VRVF studies have focused on its utility for outpatient glaucoma monitoring. This is the first known study to look at the use of VRVF for hospital-based ophthalmic consultations. Based on our preliminary data, VRVF can be used in the hospital setting in a quick, easy, safe, and reliable manner. However, <10% of total ophthalmic consultations qualified for study participation, suggesting that the technology might be most effectively applied in conjunction with neurology and neurosurgery services. 1. Virtualfield.io

CONTROL ID: 3710991

SUBMITTER (NAME ONLY): Preston Girardot

TITLE: Pentosan Polysulfate Retinopathy in Mice Involves Subtle Changes in Outer Segment Length and RPE Cell Size

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.E. Girardot, X. Zhang, N. Zhang, K.J. Donaldson, M. Chrenek, J.T. Sellers, N. Jain, J.M. Nickerson, J.H. Boatright, Emory Eye Center, Emory University, Atlanta, Georgia, UNITED STATES|P.E. Girardot , J.H. Boatright, Center for Visual and Neurocognitive Research, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|K.J. Donaldson, Neuroscience Institute, Georgia State University, Atlanta, Georgia, UNITED STATES|X. Zhang, N. Zhang, Department of Ophthalmology, Second Xiangya Hospital, Changsha, Hunan, CHINA|

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ABSTRACT BODY:

Purpose: Pentosan Polysulfate Sodium (PPS) is prescribed to treat bladder pain or discomfort. Pearce et al. [2018] reported adults taking this medication presenting with a maculopathy suggestive of a primary retinal pigmented epithelium (RPE) injury. We previously presented that prolonged intraperitoneal injections of PPS cause retinal dysfunction in mice. Here we report observations from a new mouse model.

Methods: 10 male and 10 female age-matched 129S2/SvPasCrl mice were given ad libitum mouse chow, either standard or supplemented with PPS. The daily dosage of PPS from the food was initially 500 mg/kg, later increased to 1000 mg/kg, then finally 2000 mg/kg over 14 months. Mice regularly had retinal function assessed by electroretinography (ERG). Mice were sacrificed after being maintained for 7 months on the highest PPS dose. One eye was fixed by freeze substitution for sagittal paraffin sectioning and histology. The contralateral eye was fixed in Z-Fix for RPE-flatmounting. Flatmounts were imaged using confocal microscopy and images were analyzed using a custom pipeline in CellProfiler.

Results: After 10 months, we observed diminution of mean c-wave amplitudes (10 cd.s/m2 scotopic flash, $p<0.04$, unpaired t-test). By 11 months, we also observed a main drug effect showing diminution of mean scotopic a- and b-wave amplitudes (5 flashes, $p<0.01$ for b-waves, $p<0.03$ for a-waves, two-way repeated measures ANOVA). Post-mortem histology measures showed decreased outer segment thickness superior to the optic nerve head ($p<0.05$, mixed effects analysis). Analysis of the RPE flatmounts revealed increased mean cell area in PPS-treated mice ($p<0.005$, unpaired t-test).

Conclusions: That oral ingestion of PPS results in ERG amplitude reduction, confirms our previous findings from experiments in which delivery was by IP injection, and possibly more closely models the clinical findings. This loss may be related to the decreased outer segment length observed in PPS-treated mice. Increased RPE cell size is known to occur in PPS retinopathy. These observations seem to corroborate the clinical observations suggesting a primary RPE injury.

CONTROL ID: 3710992

SUBMITTER (NAME ONLY): Joseph Lin

TITLE: Injury and disease reconfigure corneal epithelial stem cell differentiation distinct from homeostasis

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.B. Lin, C.W. Pfeifer, F. Shiau, A. Santeford, P.A. Ruzycki, B.S. Clark, A.J. Huang, R.S. Apte, John F. Hardesty, MD Department of Ophthalmology & Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|X. Shen, Q. Liu, Department of Anesthesiology, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: The clear corneal epithelium is crucial for vision and regenerates from limbal stem cells (LSCs) whose differentiation in homeostasis has been resolved transcriptionally by recent single cell RNA sequencing (scRNAseq) studies. Yet, it remains poorly understood how LSC differentiation becomes co-opted after injury to promote wound healing or whether differentiation is perturbed in aging, diabetes, and dry eye disease (DED). In the present work, we evaluate--at the single cell level--corneal epithelium in animal models of these conditions that could impact LSC regeneration of the ocular surface.

Methods: Using scRNAseq, we profiled mouse corneal epithelium in homeostasis, in aging, in streptozotocin-induced diabetes, following debridement of the central cornea, and in aqueous tear-deficient DED resulting from lacrimal gland excision.

Results: In homeostasis, we captured the full sequence of corneal epithelial differentiation from LSC to superficial squamous cell, as well as identify candidate genes and gene networks that characterize key stages of differentiation. In models of aging or diabetes, we found that there were only mild transcriptional changes, with ≤10 dysregulated genes in total across all cell types (adjusted p-value < 0.05, $|\log_2[\text{fold-change}]| \geq 1.5$). However, epithelial debridement or DED induced more dramatic changes to aid the regeneration of the injured ocular surface. First, there was expanded expression of some putative LSC markers to other non-LSC cell types, such as Krt14 and Ifitm3 with $\log_2[\text{fold-change}]$ ranging from 1.5-2.5 (adjusted p-value < 0.05). Second, there was upregulation of epidermal wound healing-associated genes Fabp5 and Rbp1 with $\log_2[\text{fold-change}]$ ranging from 1.5-2.5 (adjusted p-value < 0.05). Finally, we provide markers for new corneal epithelial cell states that appeared after epithelial debridement or in DED. These wound healing-elicited cell states were not apparent in homeostasis (1.7% of cells in control eye vs. 27% after debridement; 0.5% of cells in control eye vs. 11% in DED).

Conclusions: This transcriptional dissection uncovers dramatic reconfiguration of the corneal epithelial stem cell compartment in injury and DED, providing a framework and atlas for future study of these ocular surface stem cells in health and disease.

CONTROL ID: 3710994
SUBMITTER (NAME ONLY): Anupam Mondal
TITLE: Diet, Aging and Retinal Homeostasis
SESSION TITLE: Animal models of human ocular disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A.K. Mondal, D. Brock, J. Gumerson, K. Jiang, J. Nellissery, A. Swaroop, National Eye Institute Neurobiology Neurodegeneration and Repair Laboratory, Bethesda, Maryland, UNITED STATES|E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|
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ABSTRACT BODY:

Purpose: Aging is associated with declining vision and increased risk of age-related ocular diseases. In addition to genetics, extrinsic factors such as dietary habits have been linked to risk of retinal neurodegeneration, as shown by the AREDS1/2 clinical trials. We previously illustrated epigenetic changes as drivers of molecular aging in mouse rod photoreceptors and identified mitochondrial energy metabolism as a key process. However, the precise molecular networks through which aging and diet (nutrients) interact with retinal health remain poorly understood. We hypothesize that aging and lifestyle influence retinal homeostasis through epigenomic changes and altered cellular metabolism. This study employed a multi-omics strategy to characterize the role of nutrition in retinal aging.

Methods: A cohort of 12-month-old male and female C57BL6/J mice were fed (ad libitum) control chow (NIH-31) or one of four special diets: high-fat diet; Mediterranean diet; a custom diet with AREDS2 supplements; or supplementation of vitamins B6, B9 and B12. Supplements were tailored to mimic human allowance. After six-months, each group was subjected to electroretinography (ERG). The retinas were then isolated for Seahorse assays to determine metabolic status or for preparing RNA or DNA for transcriptome or whole genome methylation analyses, respectively.

Results: The control, AREDS and vitamin B groups showed a stable body weight over the treatment course. However, the high-fat and Mediterranean diets displayed remarkable weight gain, with prominent lead by female mice. ERG analysis revealed high variance, in both scotopic and photopic measures, among some of the groups, probably as a result of the ad libitum environment. No significant differences in ERG were detected between the treatments. Retinal extracellular acidification rate (glycolytic activity) and oxygen consumption rate (mitochondrial respiration) were impacted with age but the responses of diet groups and gender remain to be clarified conclusively. Transcriptome and methylation analyses are in progress.

Conclusions: Our study shows that nutritional habits can exert varying responses even in a controlled isogeneic setting. We predict that diet primes the retinal molecular/cellular landscape during aging either in favor or against disease development, with the final outcome being determined by divergent factors. Understanding the nexus between diet, aging, and retinal health is vital for preserving healthy vision.

CONTROL ID: 3710996

SUBMITTER (NAME ONLY): Rahul Dhodapkar

TITLE: Cross-species single-cell transcriptomic analysis reveals factors limiting human Müller glial-derived retinal regeneration

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Dhodapkar, School of Medicine, Yale University, New Haven, Connecticut, UNITED STATES|D. Martell, E. Calapkulu, A. Jin, B.P. Hafler, Ophthalmology and Visual Science, Yale University, New Haven, Connecticut, UNITED STATES|Y. Xing, Gynecology, Dongfang Hospital, Beijing, CHINA|L. Zhang, Neurology, Yale University, New Haven, Connecticut, UNITED STATES|M. Menon, Lydia Becker Institute of Immunology and Inflammation, The University of Manchester, Manchester, Manchester, UNITED KINGDOM|A. Dong, Yale College, Yale University, New Haven, Connecticut, UNITED STATES|B.P. Hafler, Pathology, Yale University, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reactive Müller glial cells in humans do not display the regenerative characteristics of those in zebrafish. We performed the first single-nucleus RNA sequencing of retina from patients with primary open-angle glaucoma (POAG) and controls to characterize the human Müller glial response to injury.

Methods: Nuclei were isolated from trephene punches of the macula taken from postmortem eyes and sequenced. Data was integrated and analyzed after quality control with Seurat v3. Sequencing findings were confirmed by RNAscope and standard immunofluorescence. Human retinal explants were cultured with and without N3B1P3C, an inhibitor of Lats kinase in the Hippo/Yap pathway. Proliferation was measured using AlexaFluor nuclear localization of EdU indicating synthetic nucleotide uptake.

Results: After quality control and data integration, 17,401 nuclei were isolated from 26,471 original droplets, derived from macular samples of 4 patients without retinal disease and 3 patients with POAG. The proportion of retinal ganglion cells in glaucomatous retina was significantly lower than that in healthy retina ($p=0.024$). An activated subpopulation of Müller glia was identified in both healthy and glaucomatous retina by cell clustering. Cross-species analysis comparing zebrafish and humans identified YAP1 activation as a differentiator between zebrafish and human glial activation. Human retinal explants cultured with N3B1P3C demonstrated significant proliferation of GS+ Muller cells ($p=0.044$).

Conclusions: Our data, including the first single-nucleus RNA sequencing of glaucomatous retina in humans, identify an activated subpopulation of human MGCs with transcriptomic signature similar to regenerative MGCs in other species, but limited by molecular brakes such as Hippo/Yap pathway factors. By inhibiting these brakes with a small molecule (N3B1P3C), we induced proliferation of Müller glia in human retinal explants for the first time. Further manipulation of endogenous activation pathways may allow for recruitment of a quiescent stem cell population and vision-restoring therapies.

CONTROL ID: 3711003

SUBMITTER (NAME ONLY): Henry Cousins

TITLE: Genetic Correlations between Corneal Biophysical Parameters and Anthropomorphic Traits

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Cousins, R.B. Altman, Department of Biomedical Data Science, Stanford University School of Medicine, Stanford, California, UNITED STATES|C. Cousins, G. Valluru, S. Ahmad, L.R. Pasquale, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|Y. Liu, Department of Ophthalmology, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although keratoconus has a significant heritable component, the genetic basis of the disease remains poorly understood. Epidemiological evidence suggests a relationship between keratoconus, corneal biophysical parameters, and anthropomorphic measures. To identify potential molecular factors underlying keratoconus, we analyzed genetic correlations between corneal biophysical parameters and anthropomorphic traits.

Methods: We assembled genome-wide association study summary statistics from European-derived participants in the UK Biobank including biophysical parameters (central corneal thickness [CCT], corneal hysteresis [CH], corneal resistance factor [CRF], and 3mm index of keratometry result [3mmK]), and anthropomorphic traits (body mass index [BMI], weight, and height). We calculated global and focal genetic correlations (r_g) between traits using linkage disequilibrium (LD) score regression, applying Bonferroni's correction for multiple hypothesis testing. Finally, we identified genes located within significantly correlated regions and identified patterns of tissue expression and pathway enrichment using gene set enrichment analysis.

Results: We observed significant genetic correlations between height and corneal biophysical parameters, but not keratometry. Global LD score regression revealed significant negative correlations between height and both CH (r_g = -0.12; p = 2.0×10^{-7}) and CRF (r_g = -0.11; p = 6.9×10^{-7}). Focal analysis revealed 68 genomic regions exhibiting significant local genetic covariance between CRF and height, containing 763 protein-coding genes, including 15 with known keratoconus associations in DisGeNet (Table). Gene set enrichment analysis on the list of genes in regions with significant focal r_g revealed enrichment among metabolic pathways with known keratoconus associations, including oxytocin signaling and transient receptor potential (TRP) channel regulation ($p < 0.001$; Figure).

Conclusions: These results suggest that interrogating the shared genetic heritability between CH, CRF and height may inform the genetic architecture for ectatic corneal disease and possibly provide new disease insights for keratoconus.

CONTROL ID: 3711004

SUBMITTER (NAME ONLY): Jessica Kraker

TITLE: Incidence of Retinal Detachment in Type 1 and Type 2 Stickler Syndrome

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kraker, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|M. Hartnett, E. Hwang, Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|L. Schimmenti, Clinical Genomics, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|L. Schimmenti, Biochemistry and Molecular Biology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|M. Amer, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with Stickler syndrome are at increased risk of retinal detachment (RD). The vast majority of Stickler syndrome is due to mutations in COL2A1 and COL11A1, which are responsible for type 1 and type 2 Stickler syndrome, respectively. Few studies have examined patients that had RD prior to presentation, or incident RD, in COL11A1 patients.

Methods: Descriptive retrospective case series of patients with mutations in COL2A1 and COL11A1 presenting to the University of Utah without an incident RD from 2010 to 2020.

Results: 3 of 10 COL2A1 patients who received bilateral prophylactic laser or cryotherapy developed RD. Of these 3 COL2A1 patients with post-prophylaxis RD, all 3 received 360 cryotherapy and developed RD 2 weeks, 3 months, and 2 years after prophylaxis. 2 of 8 COL2A1 patients who did not initially receive prophylaxis developed RD. 0 of 6 COL11A1 subjects who received prophylaxis developed RD and 0 of 5 COL11A1 subjects who did not initially receive prophylaxis developed RD. The average length of follow-up was 5.7 +/- 5.3 years for COL2A1 patients and 7.1 +/- 4.1 years for COL11A1 patients.

Conclusions: In our sample, despite prophylactic treatment, incidence of RD in patients with COL2A1 mutations was higher compared to patients with COL11A1 mutations. We also noted a high rate of RD occurring soon after 360 cryotherapy prophylaxis.

CONTROL ID: 3711006

SUBMITTER (NAME ONLY): Cancan Xue

TITLE: Five-year Incidence of Arterial Hypertension Predicted by Retinal Vessel Analysis: The Tongren Cohort Study

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Xue, D. Chen, Y. Wang, Beijing Tongren Hospital, Beijing, CHINA|C. Xue, C. Zhang, Peking University Third Hospital, Beijing, CHINA|C. Li, J. Zhang, Beihang University, Beijing, CHINA|J. Jonas, Ruprecht Karls Universitat Heidelberg, Heidelberg, GERMANY|

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ABSTRACT BODY:

Purpose: To study the relationship between retinal vessel caliber and tortuosity and the 5-year incidence of hypertension.

Methods: The community-based longitudinal Tongren Cohort Study included individuals undergoing routine health examinations. Using a proved deep learning model called vessel-constraint network, the retinal vessel calibers and tortuosity within a region of 0.5 to1.5 disc diameters from the disc margin were automatically segmented, based on color fundus images.

Results: A total of 9230 individuals(age: 43.6±13.9years) were enrolled, with the 5-year cumulative incidence of hypertension to be 18.8% and severe hypertension to be 7.0%. Narrower retinal arteriolar (odds ratio(OR):0.98; 95%CI:0.97,0.99; P<0.001), wider venular (OR:1.006; 95%CI:1.002,1.01;P=0.005), and smaller arteriole-to-venule caliber ratio (OR:0.72;95%CI:0.63,0.82;P<0.001) were associated with increased hypertension incidence after multivariable adjustment. Compared with individuals with the 5% widest arteriolar or the 5% narrowest venular, those with the 5% narrowest arteriolar or the 5% widest venular had a 17.1-fold or 2.3-fold increased risk for developing hypertension within 5 years. The receiver operating curves(ROC) for retinal vessel calibers to predict hypertension and severe hypertension was 0.79 (95%CI:0.78,0.80) and 0.84 (95%CI:0.82,0.86), respectively. The ROC was higher for women than men(0.81v.s.0.73 for hypertension; 0.87v.s.0.78 for severe hypertension; both P<0.001), and for younger than older participants (0.77v.s.0.72 for hypertension; 0.82v.s.0.76 for severe hypertension; both P<0.05). Baseline venular tortuosity was positively associated with baseline hypertension prevalence (OR:1.57; P=0.01) but not with incident hypertension (P=0.449). Baseline arteriolar tortuosity was associated with neither prevalence nor incidence of hypertension.

Conclusions: Automatically assessed narrower arterioles and wider venules on conventional fundus images indicate an increased risk for incident hypertension within 5 years. Assessment of retinal vessels may help to screen individuals with risk of developing hypertension.

CONTROL ID: 3711007

SUBMITTER (NAME ONLY): William Foos

TITLE: Post-operative outcomes after blepharoplasty in patients with glucocorticoid use within 1 year prior to surgery: A TriNetX Analysis

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare post-operative outcomes up to 1 year in patients after blepharoplasty with and without glucocorticoid use within 1 year prior to surgery.

Methods: A retrospective cohort study was performed using TriNetX (Cambridge, MA, USA): a federated electronic health record database comprised of US healthcare organizations. Patients with upper or lower eyelid blepharoplasty were identified by CPT code and stratified into two cohorts based on glucocorticoid use 1 year prior to surgery. Glucocorticoids included cortisone, prednisone, prednisolone, methylprednisolone, dexamethasone, betamethasone, and hydrocortisone. 1:1 propensity score matching separated two cohorts while controlling for baseline characteristic and comorbidities: age, BMI, gender, primary hypertension, diabetes mellitus, chronic lower respiratory disease, nicotine dependence, heart failure, and alcohol related disorders. Patients with ocular comorbidities were screened out. Primary post-operative outcomes included dry eye syndrome, lagophthalmos, conjunctival edema, dacryoadenitis, orbital and periorbital cellulitis, strabismus, diplopia, orbital hemorrhage, and acute conjunctivitis. 1-year relative risk of post-operative outcomes were compared between the groups; those with a p-value less than 0.05 being statistically significant.

Results: 17,804 patients were included in the analysis with 8,902 patients in each of the blepharoplasty with and without glucocorticoid use cohorts. The cohort receiving glucocorticoids in the past year had a statistically significant increased risk of post-operative dry eye syndrome (RR, 1.25; 95% CI, 1.16-1.36), lagophthalmos (RR, 1.55; 95% CI, 1.13-2.13), and conjunctival edema (RR, 3.9; 95% CI, 1.95-7.81). No significant difference in risk was attributable to either cohort regarding dacryoadenitis, orbital and periorbital cellulitis, strabismus, diplopia, orbital hemorrhage, and acute conjunctivitis.

Conclusions: Pre-surgical glucocorticoid use up to one year may impact post-operative course following blepharoplasty. Patients receiving glucocorticoids up to one year prior were more likely to develop post-operative dry eye syndrome, lagophthalmos, and conjunctival edema. Appropriate patients should be counselled on such risk both before and after blepharoplasty.

CONTROL ID: 3711015

SUBMITTER (NAME ONLY): Andrew Dieu

TITLE: Multimodal Imaging Evaluation of Age-Related Macular Degeneration (AMD) in the AMD Ryan Initiative Study (ARIS)

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: ARIS is a 5-year, multicenter, international, prospective, observational cohort study of participants with early AMD or reticular pseudodrusen (RPD) to identify novel biomarkers of disease progression. The purpose of this abstract is to describe the detailed imaging characteristics of the initially enrolled participants.

Methods: Baseline and 12-month follow up images were evaluated for four cohorts: early AMD, RPD only, RPD and large drusen, and healthy controls. Optical coherence tomography (OCT) images were graded for drusen structure and RPD characteristics. Fundus autofluorescence (FAF) images were graded for hypo and hyperautofluorescence and background pattern. Color fundus photography (CFP) images were graded for drusen size and area, pigmentary changes, RPD, and AMD severity scale.

Results: The cohorts comprised 38 eyes with early AMD, 18 eyes with RPD only, 10 eyes with RPD and large drusen, and 36 healthy control eyes.

In baseline evaluation of the early AMD cohort, OCT showed that drusen were predominantly dome shaped (52.8%) with hyperreflective cores (66.7%). Confluent drusen were observed in 47.2% of eyes. Abnormal FAF was seen in 50% of eyes in this cohort, all with areas of abnormality less than 2 disc areas. There was no significant hypo or hyper FAF in any eyes. CFP findings showed predominantly medium drusen (92.1%) and increased pigmentation in 5.3%. There were no eyes with depigmentation. Baseline AMD severity scale was level 2–4 in 63.2% of eyes. Progression of ≥ 1 step on the AMD scale over 12 months was seen in 17 (44.7%) eyes in the early AMD cohort.

Baseline assessment of the combined RPD cohorts showed global RPD distribution in 88.9% of eyes and superior distribution in 7.4%. Peripapillary RPD was seen in 25.9%. OCT-based staging showed stage 4 RPD in 63%. Baseline AMD scale was level 6 in 32.1% eyes and level 7 in 42.9%. Progression of ≥ 1 steps on the AMD scale over 12 months was seen in 2 (7.1%) eyes in the RPD cohort, with one eye progressing to late AMD. In the RPD subset with large drusen, drusen area ≥ 1 disc area was seen in 70% of eyes at baseline, with no eyes progressing ≥ 1 step on the AMD severity scale.

Conclusions: The 5-year ARIS introduces reproducible methods for detailed documentation of AMD phenotypes. This systematic evaluation will offer insight into the development of outcome variables in future studies of potential AMD treatments.

CONTROL ID: 3711020

SUBMITTER (NAME ONLY): Jian Lian

TITLE: Deep Binary Descriptor-based Identification of Retinal Lesions for Diabetic retinopathy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lian, School of Intelligence Engineering, Shandong Management University, Jinan, Shandong, CHINA|X. Yang, Shandong Normal University, Jinan, Shandong, CHINA|

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ABSTRACT BODY:

Purpose: The detection and classification of retinal lesions play a vital role in screening diabetic retinopathy, one primary cause of visual impairment globally. Extensive research on deep learning has shown their good performance in this area. However, these methods suffer from the image samples' scarcity and diversity of morphological characteristics. This study aims to establish a binary descriptor-based classification instrument for discriminating the retinopathy slices by leveraging deep backbone models capable of resolving complex cases.

Methods: 4 datasets of retinal slices were collected in this study. In total, there are three types of retinal images used as the input for the proposed deep learning-based pipeline, which consists of 3 phases (as shown in Fig. 1):
We added affine transformations to the raw samples.
What fed the original and deformed retinal images into one backbone model.
The generated feature for each slice was fed into a non-linear classifier to discriminate three categories of diabetic cases.
Note that three constraints, including affine transformation in variation, even distributed, and quantization loss minimization was imposed on the features rendered as a binary descriptor. The structure of the proposed approach is shown in Figure 1.

Results: The proposed framework is superior to the state-of-the-art algorithms in accuracy, sensitivity, and precision. The ten-fold cross-validation accuracy of the presented approach on the samples is 98.35%.

Conclusions: The findings indicate that the proposed approach is a potentially helpful instrument for retinal lesion identification. By constraining the output features extracted from the input images it not only can increase the generalization of the deep learning models but also guarantee accuracy.

CONTROL ID: 3711032

SUBMITTER (NAME ONLY): Jacqueline Tan

TITLE: The effect of a novel selenium disulphide-containing topical treatment on ocular signs in individuals with meibomian gland dysfunction

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tan, T. Jia, N. Briggs, F. Stapleton, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|C. Bosworth, M.T. Gleeson, Azura Ophthalmics, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: A novel topical ointment AZR-MD-001, containing selenium disulphide designed to treat meibomian gland hyperkeratinisation, has been shown to improve symptoms and signs of meibomian gland dysfunction (MGD). This study evaluated the effect of biweekly dosing on tear film parameters in a double-masked, vehicle-controlled, randomized, parallel group clinical trial in individuals with MGD.

Methods: Participants with evidence of MGD (Meibomian Gland Secretion score [MGS] ≤12 for 15 glands of the lower lid), and signs and symptoms of dry eye (fluorescein tear break-up time [FBUT] <10 seconds and Ocular Surface Disease Index [OSDI] score >12) in both eyes were enrolled. Participants were randomly assigned to receive either the test AZR-MD-001 1% or control ointment to the lower eyelid margin (NCT04314362). Tear evaporation rate (TER), lipid layer thickness (LLT), non-invasive keratograph tear break-up time (NIKBUT), tear meniscus height (TMH) and FBUT were measured at baseline and after 2, 4, 6 weeks and 3 months of treatment. Differences between active and vehicle were analyzed relative to baseline using ANCOVA.

Results: Twenty-two participants (7 males and 15 females, aged 44.8 ± 17.7 years, average baseline OSDI 37.1 ± 14.2) completed the study. Compared with the vehicle group, a significantly greater improvement (reduction) in TER was observed in the active treatment group at the 2-week visit (mean treatment difference ± standard error: -30.2 ± 14.8$gm^{-2}h$, p=0.044). A corresponding reduction (worsening) in FBUT was also observed in the vehicle group at the 2-week visit compared to the treatment group (1.3 ± 0.6 sec, p=0.037). The number of meibomian glands yielding liquid secretion was significantly higher in the active group at 3 months (1.8 ± 0.9, p = 0.043), whereas the improvement in MGS score didn't quite reach statistical significance (5.6 ± 2.9, p = 0.056). No differences were observed for change from baseline between the two groups for OSDI score, LLT, NIKBUT or TMH at any visit.

Conclusions: Measurable improvements in tear film stability were observed with use of the novel topical ointment containing selenium disulphide. Further work to understand the potential longer-term benefits of the ointment, including any changes to meibomian gland morphology associated with functional improvements, is warranted.

CONTROL ID: 3711033

SUBMITTER (NAME ONLY): Avi Toiv

TITLE: Risk Factors for Enucleation Following Open Globe Injury: A 17-Year Experience

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Toiv, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|A.F. Durrani, Y. Zhou, P.Y. Zhao, D.C. Musch, M. Huvard, D.N. Zacks, Department of Ophthalmology and Visual Sciences, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: At the time of open globe injury, it may be difficult for clinicians to predict which eyes are at highest risk for ultimately requiring enucleation. We performed a 17-year retrospective cohort study to report outcomes and risk factors for enucleation following open globe injury (OGI) to better aid clinicians counseling patients at OGI diagnosis.

Methods: A retrospective cohort study of all patients who presented to the University of Michigan with open globe injury (OGI) and were surgically managed between January 2000 and July 2017 was conducted. At least 30 days of follow-up was required. All eyes that ultimately underwent enucleation following OGI were identified and their clinical course analyzed. The main outcome measured was the rate of enucleation after OGI.

Results: There were 588 eyes meeting inclusion criteria. The mean patient age was 40.75 ± 25.1 (range 1 – 91) and 441/585 (75.2%) patients were male. Average follow up time was 1079.8 ± 1895.7 days. 117/588 eyes (19.9%) required enucleation after OGI, with 95/117 (81.2%) undergoing enucleation less than 30 days from injury. For all eyes, the average presenting logMAR vision was 2.11 ± 1.01 (Snellen equivalent between counting fingers and hand motion). In eyes that underwent enucleation, the mean presenting logMAR vision was 2.91 ± 0.470 (Snellen equivalent between hand motion and light perception). The most common mechanism of injury requiring enucleation was globe rupture, 89/117 (76.1%), with 14/117 (12.0%) eyes having penetrating injuries and 14/117 eyes (12.0%) having perforating injuries. The mean age of patients that underwent enucleation was 45.6 ± 22.5 (range 3 – 91).

Conclusions: Open globe injuries (OGI) are often visually devastating and in a significant number of cases ultimately require enucleation. Despite emergent closure within 24 hours, 19.9% of eyes diagnosed with OGI require enucleation. 81.2% of these eyes required enucleation within 30 days of injury. Eyes that underwent enucleation tended to have worse presenting visual acuity, with mean presenting logMAR vision of 2.91 ± 0.470 (Snellen equivalent between hand motion and light perception), compared to a mean presenting logMAR vision of 2.11 ± 1.01, in all eyes with OGI.

CONTROL ID: 3711036

SUBMITTER (NAME ONLY): Glenn Oh

TITLE: Outcomes of combined pars plana vitrectomy and scleral fixation of intraocular lenses: comparison of Gore-Tex suture versus intrascleral haptic fixation (Yamane) techniques

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Mahmoudzadeh, S.N. Patel, M.A. Khan, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|G.J. Oh, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|T. Tien, B.D. Ayres, B.D. Finklea, Cornea Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study compared clinical outcomes of combined pars plana vitrectomy (PPV) and secondary scleral fixation of an intraocular lens (IOL) using Gore-Tex suture versus the Yamane technique.

Methods: This study was a single-center, retrospective, consecutive case series conducted at Wills Eye Hospital (Philadelphia, PA, USA) between 12/01/2017 and 12/01/2021. Eyes that underwent scleral fixation of a Bausch and Lomb Akreos AO70 or enVista MX60E IOL using Gore-Tex suture or a Tecnis ZA9003 or Zeiss CT LUCIA 602 IOL using the Yamane technique were included. Primary outcome measures were change in visual acuity (VA) and occurrence of intraoperative and postoperative complications with minimum follow-up of 120 days.

Results: Sixty-eight eyes of 64 patients (47% male, mean(± SD) age 72(±12) years) with the main surgical indication of dislocated IOL or retained lens material were included. Mean follow-up was 501 days (median 366 days, range 132-1254 days). Fifty-two eyes (76.5%) underwent Gore-Tex suture fixation and 16 eyes (23.5%) underwent Yamane fixation. Across all eyes, VA improved from 1.34±0.74 (20/437) preoperatively to 0.36±0.37 (20/46) at 3 months and 0.32±0.36 (20/42) at final follow-up ($p<0.001$ for both timepoints). VA improved in statistically significant fashion for each secondary IOL technique (Table 1). No intraoperative complications were noted. Postoperative complications are included in Table 2, and there was no statistically significant difference between groups. In the Gore-Tex group, 2/52 eyes (3.8%) required reoperation for conjunctival erosion with exposed suture (n=1) and for IOL decentration (n=1). In the Yamane group, 2/16 (12.5%) eyes required reoperation for epiretinal membrane formation (n=1) and for retinal detachment (n=1). There were no cases of postoperative endophthalmitis, suture breakage, or haptic breakage in the post-operative follow-up period.

Conclusions: Scleral fixation of IOLs with Gore-Tex suture and intrascleral haptic fixation (Yamane technique) resulted in improvement of VA. No significant difference in post-operative complication profiles was noted. Both techniques appear to be safe and effective for secondary IOL surgery in combination with PPV.

CONTROL ID: 3711037

SUBMITTER (NAME ONLY): James Lai

TITLE: Mechanical Property Comparison of 23-, 25- and 27-gauge Vitrectors Across Vitrectomy Systems

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Patel, Nova Southeastern University College of Allopathic Medicine, Davie, Florida, UNITED STATES|A. Watane, Yale University Eye Center, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|J. Lai, A. Fils, J. Sridhar, N. Yannuzzi, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|N.A. Patel, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of small gauge vitrectomy has improved rates of self-sealing sclerotomies and decreased post-operative pain and inflammation. However, concerns regarding vitrector bending with smaller gauge sizes remains an area of concern. Therefore, the purpose of this study was to investigate the mechanical properties and stiffness of 23-, 25- and 27-gauge vitrectomy vitrectors across three different vitrectomy systems to inform surgical techniques.

Methods: Nine vitrectors (3 each of 23-, 25-, and 27 gauge) from Alcon, DORC and Bausch and Lomb (B/L) were measured. The force required to vertically displace each vitrector by 1mm at the tip and 15mm from the tip was measured using an electronic force gauge (Electroforce 5500 Thermal Analysis Instruments, USA). Measurements were recorded in gramforce (gf). Five measurements were performed at each location and fully elastic deformation was ensured. One way ANOVA and Post-Hoc Tukey analysis were performed to evaluate statistical significance.

Results: Across brands, B/L demonstrated the least stiffness at both the tip and at 15mm for 23-gauge (8.0±0.3 gf, 67.3±1.0 gf), 25-gauge (6.8±0.3 gf, 60.5±0.4 gf) and 27-gauge (3.3±0.1 gf, 33.9±0.5 gf) vitrectors. Within each brand, the 25 gauge vitrector was less stiff than the 23 gauge vitrector and the 27 gauge vitrector was less stiff than the 25 gauge vitrector at both tip and 15mm. These differences were statistically significant for Alcon ($P<0.001$, $P<0.001$), DORC($P<0.001$, $P<0.001$) as well as B/L ($P<0.001$, $P<0.001$).

Conclusions: Based on this study, 25-gauge vitrectors, although larger than 27-gauge vitrectors and less stiff than 23-gauge vitrectors, may offer favorable compromise between stiffness and gauge size. However, surgeon experience, preference, and expertise should be paramount. Knowledge of these mechanical properties may aid surgeons in choosing between gauge size and vitrectomy system to optimize their comfort and efficiency.

CONTROL ID: 3711042

SUBMITTER (NAME ONLY): Terete Borras

TITLE: Exfoliation syndrome (XFS): Production of extracellular aggregates in a human capsulorhexis culture model

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Borras, D. Fleischman, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: XFS in the eye causes the formation of deposits on anterior segment tissues that can lead to the development of exfoliation glaucoma. Clinically, deposits are seen on the lens surface. Our goal was to define human capsulorhexis cultures as an XFS model by determining if lens exfoliation material (XFM) was produced by lens epithelial cells (LE) or deposited externally. To analyze local distribution of XFM components LOXL1, ELN and FBN1 in XFS & normal capsulorhexis tissues and to investigate LOXL1's role in the formation of XFS aggregates.

Methods: Lens-capsules (LC) were harvested in tissue culture (TC) media during capsulorhexis surgery (IRB approved). Four h post-surgery, specimens were stained with trypan blue, transferred to a 2-chamber dish with coverglass bottom (4.2 cm^2), washed, and incubated floating in media overnight. Curled LCs were flattened with craft brushes (LE layer down), incubated with media drops 2 days for attachment, and fed normally for 2-4 weeks. IHC was performed in the same dish with LOXL1, ELN, FBN1, Collagen IV and DDK antibodies. Images were acquired through the chamber coverglass (unmounted) by fluorescence microscopy and analyzed with CellSens. LOXL1 overexpression was achieved by infection with DDK-tagged Ad.LOXL1 (variant G-G).

Results: 83 LCs were processed. LOXL1, ELN, and FBN1 are abundantly secreted by LEs and can raise to the surface through the 14 nm capsule membrane. LCs from XFS patients show patches of aggregates which stain heavily with LOXL1, ELN and FBN1. The XFS cells' morphology exhibit an extracellular ring reminiscence of a pericellular matrix. Interestingly, a similar extracellular ring is observed in LEs transduced with Ad.LOXL1. ELN shows a globular conformation in the aggregate and a fiber shape away from it. Overexpression/secretion of LOXL1 induces LOXL1/FBN1 and LOXL1/ELN deposit-like aggregates. FBN1 forms microfibril bundles in most transduced LCs.

Conclusions: Lens organotypic cultures from capsulorhexis of normal- and XFS- cataractous lenses represent a unique model to identify mechanistic differences between normal and XFS cells. Morphological and functional similarities between XFS- and LOXL1-transduced cells reaffirm the functional relevance of LOXL1 and the prospect of using this gene to manage the disease. This model could also be used to search for potential treatments to disassociate and/or prevent XFM aggregates.

CONTROL ID: 3711043

SUBMITTER (NAME ONLY): Shunya Tatara

TITLE: Difference between fixation target and fixation point during convergence and divergence eye movements recorded using eye tracking

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tatara, F. Maeda, Department of Orthoptics and Visual sciences, Faculty of Medical Technology, Niigata University of Health and Welfare, JAPAN|S. Tatara, T. Handa, Department of Vision Science, Faculty of Sensory and Motor Control, Kitasato University Graduate School of Medical Science, JAPAN|T. Handa, Department of Rehabilitation, Orthoptics and Visual Science Course, School of Allied Health Sciences, Kitasato University, JAPAN|

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ABSTRACT BODY:

Purpose: Convergence and divergence eye movements become asymmetrical movements of both eyes when they are included in saccadic eye movements. The deviation of the fixation point with respect to the fixation target at the time of convergence and divergence eye movements can be quantified using eye tracking. In this study, we aimed to investigate the difference between fixation target and fixation point resulting from the difference in the moving speed of the fixation target.

Methods: We recruited nine university students without abnormalities as our subjects. For the measurement, we used a novel eye tracking device (nac Image Technology, Tokyo, Japan). As the subjects looked into this device with both eyes, the fixation target moved closer and farther from it in a pseudo manner. The subjects repeated convergence and divergence eye movements for 20 s by looking at the fixation target that moved between 0.3 m and 1 m. The sampling rate of the device was 30 Hz, and the movement speeds of the fixation target were 2, 4, 6, 8, and 10 deg/s. We measured the fixation point and calculated the difference from the fixation target. The difference between the fixation point and fixation target at each movement speed of the fixation target was tested using the Friedman test. P-value <0.05 was considered statistically significant.

Results: The differences between the fixation point and fixation target (median [25th–75th percentiles]) were 119.2 [70.6–191.7], 135.8 [101.2–147.6], 147.2 [135.1–173.7], 179.6 [175.4–209.0], and 203.3 [198.7–216.8] mm at 2, 4, 6, 8, and 10 deg/s, respectively. Friedman test revealed that the difference between the fixation point and the fixation target increased as the movement speed of the fixation target increased ($P < 0.001$).

Conclusions: As the movement speed of the fixation target increased, differences between the fixation point and the fixation target in the convergence and divergence eye movements increased, suggesting that the asymmetry of both eyes increased.

CONTROL ID: 3711045

SUBMITTER (NAME ONLY): Alexander Svoronos

TITLE: Complexities in the relationship between aqueous and vitreous VEGF revealed by mathematical models fit to meta-analytic data

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Svoronos, L. Del Priore, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|A.A. Svoronos, NYU Langone Health, New York, New York, UNITED STATES|A.C. Roginiel, Ophthalmology, Northwell Health, New Hyde Park, New York, UNITED STATES|

Commercial Relationships Disclosure: Alexander Svoronos: Commercial Relationship: Code N (No Commercial Relationship) | Aliya Roginiel: Commercial Relationship: Code N (No Commercial Relationship) | Lucian Del Priore: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Many studies measure aqueous VEGF concentration as a proxy for vitreous VEGF concentration. Usually, underlying these studies is the assumption that aqueous VEGF is merely the result of diffusion from the vitreous compartment. Here, we examine the validity of this assumption by implementing it into a mathematical model and assessing how well it fits real data compared to models which implement additional potential mechanisms of intraocular VEGF production and transport.

Methods: This study consists of a meta-analysis of prior studies followed by the generation and fitting of mathematical models to pooled study data. More specifically, a search of studies that simultaneously report both aqueous VEGF and vitreous VEGF concentrations was conducted, and the data was compiled to determine the relationship between the two concentrations and how their corresponding ratio varies with increasing concentration. Several mathematical models, each representing a different potential mechanism of VEGF production or transport, were then generated and fit to the data, and the resulting coefficients of determination (R^2 values) were compared.

Results: As Fig 1 shows, the base model, which only considers the production and subsequent diffusion of vitreous VEGF to the aqueous compartment, where it undergoes clearance, fit the meta-analysis data poorly (average R^2 = 0.162). Models which implemented additional mechanisms on top of the base model performed better (average R^2 values ranging from 0.463 to 0.707), with a model exhibiting supplementary VEGF production in the aqueous compartment or by the ciliary body performing best (average R^2 = 0.707).

Conclusions: The base model is insufficient to explain the relationship between aqueous and vitreous VEGF concentrations. Other mechanisms of VEGF production and/or transport must be present, with a strong candidate being the addition of VEGF production in the aqueous compartment or by the ciliary body.

CONTROL ID: 3711047

SUBMITTER (NAME ONLY): Emily Cole

TITLE: Comparison of smartphone-based fundus imaging and ultra widefield fundus imaging for retinopathy of prematurity screening at Aravind Eye Hospital

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Telemedicine for remote grading of images has been effective in retinopathy of prematurity (ROP) screening in resource-limited settings. Ultra widefield fundus imaging systems can be cost-prohibitive for widespread use. Smartphone-based digital fundus imaging has been described as a low-cost alternative, however the relative effectiveness of this approach has not been fully evaluated. The purpose of this study is to compare ROP diagnosis between the Retcam (Natus Medical Incorporated, Pleasanton CA, USA) and a smart-phone based approach using the MII (Make in India) Retcam adapter.

Methods: 100 paired exams from 95 infants imaged on both the Retcam and MII were acquired during routine image-based ROP screening via telemedicine between August-September 2021 at Aravind Eye Hospital. Images were uploaded to a web-based data management system (iTeleGENx, Chicago, IL, USA) which enabled randomization and matching. A single grader was presented with demographics including birthweight and gestational age, and determined the ROP diagnosis according to the International Classification of Retinopathy of Prematurity. Exams were anonymized and presented in two time periods in random order to prevent recall bias. Sensitivity and specificity calculations were made for TR-ROP, Type 2 or worse, and pre-plus or worse in at least one eye.

Results: Using the Retcam as the gold standard, the sensitivity for type 2 or worse in either eye was 78.6% and specificity was 97.6%. For TR-ROP, the sensitivity was 100% and specificity was 98.9%. The sensitivity for Type 2 or worse on the Retcam and pre-plus or worse on the MII was 85.7% specificity was 90.6%. Table 1 summarizes the diagnosis of ROP on both devices with regards to zone, stage, presence or absence of plus disease, and category of disease.

Conclusions: The MII Retcam demonstrated high sensitivity and specificity for TR-ROP, though did not capture all eyes with type 2 ROP. This may be due to limitations in field of view, image quality, learning curve, or other factors. Our analysis suggests that if pre-plus can be clinically recognized using the MII Retcam, it could be used as a surrogate for the presence of Type 2 or worse disease. Referral criteria using lower field of view cameras should be evaluated, including potential applications of artificial intelligence to these cameras to evaluate vascular severity.

CONTROL ID: 3711050

SUBMITTER (NAME ONLY): Ashley Zhou

TITLE: Socioeconomic Disadvantage and Impact on Visual Outcomes in Patients with Viral Retinitis and Retinal Detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zhou, S. Ong, I. Ahmed, J. Arevalo, C. Cai, J.T. Handa, Wilmer Eye Institute, The Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: While socioeconomic disparities impact clinical care and patient outcomes, their impact on the anatomic and visual outcomes of retinal detachment in patients with viral retinitis is unstudied.

Methods: This case series included 19 eyes in 19 patients from a single academic institution between January 1, 2008 and December 31, 2018. Patient characteristics including age, sex, race, ethnicity, insurance, immunosuppression, viral retinitis, retinal detachment, retinal detachment repair, visual and anatomic outcomes, missed appointments, and Area Deprivation Index [ADI] were collected.

Results: The low-ADI group, indicating less socioeconomic disadvantage, was comprised of twelve patients with national ADIs less than 38, and the high-ADI group of six patients with national ADIs greater than 38. High-ADI patients tended to be younger (average age 38.0 versus 51.3; P=0.056), of female sex (P=0.034), and had more missed appointments (median 11.0 vs 0; P=0.002). A similar number of patients in both the high-ADI and low-ADI groups underwent pars plana vitrectomy alone or pars plana vitrectomy with scleral buckle. Visual acuity was similar in the high-ADI group than in the low-ADI group at baseline, but worse at the final follow-up visit (P=0.004). Post-operative and final visit ocular hypotony were more common in the high-ADI group (P=0.022).

Conclusions: In our series, socioeconomic disadvantage negatively affects the visual outcomes in patients with viral retinitis associated-retinal detachments. These factors should be considered by ophthalmologists when treating these patients.

CONTROL ID: 3711052

SUBMITTER (NAME ONLY): Daoqi Tang

TITLE: Oxidative Stress Induces Apoptosis and Inflammation in in vitro Dry Eye Models Which Can Be Reversed by Antioxidant SkQ1

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Tang, Y. XIONG, C. GAO, B. YANG, H. Fang, ZHUHAI ESSEX BIO-PHARMACEUTICAL CO.,LTD., Zhuhai, Guangdong, CHINA|D. Tang, G. Wan, School of Pharmaceutical Sciences, Sun Yat-Sen University, Guangzhou, Guangdong, CHINA|A. Petrov, N. Perekhvatova, M. Skulachev, Mitotech, SA, Luxembourg City, LUXEMBOURG|Q. Xue, M. Ngiam, Essex Bio-Technology Limited, HONG KONG|

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ABSTRACT BODY:

Purpose: Oxidative stress and inflammation are common phenomena in Dry Eye Disease (DED). However, their roles in the pathogenesis of DED need to be clarified. In our study, we illustrated the relationship between oxidative stress and DED in vitro, with a mitochondria-targeted antioxidant, SkQ1.

Methods: Tert-butyl hydroperoxide (TBHP) was added in cultured human corneal epithelial cell (HCEC) for oxidant damage model. 4 hydroxynonenal (4-HNE) and Malondialdehyde (MDA) were determined as indicated biomarker of oxidant damage. The antioxidant effect of SkQ1 was evaluated. Two dry eye in vitro models were set up by culturing HCEC in hypertonic medium or media with 0.0002% benzalkonium chloride (BAK). Cell statuses were monitored by viability assay (MTT), Reactive Oxygen Species (ROS) assay (FACS and fluorescent staining) and apoptosis assay (FACS), cytokines and matrix metalloproteases were quantified with ELISA.

Results: ROS, 4-HNE and MDA level were increased in TBHP model. SkQ1 effectively eliminated ROS, associated with reduced apoptosis and IL-6, MMP3 production. The relationship between oxidant damage and DED was explored using hyperosmolarity and BAK-induced in vitro models. Excessive mitochondrial ROS was found in both models and happened earlier than cell apoptosis and viability loss. SkQ1 significantly reduced level of mitochondrial ROS, followed by decreased cell apoptosis and reversed cell viability. Upregulation of inflammatory factors production was determined in each model (IL-6, MMP3, MMP9 in hyperosmotic model; IL-1α, IL-6, MMP9 in BAK model), while SkQ1 effectively down-regulates the protein level of these DED-associated cytokines and matrixes.

Conclusions: Our finding indicates that increased mitochondrial ROS level widely occurs in DED models which orchestrates cell apoptotic and inflammatory responses. Antioxidant SkQ1 reverts these cell damages, offering an universal therapeutic potential. 4-HNE and MDA, as widely accepted biomarkers in DED, were significantly upregulated in dry eye patients' tears, suggesting a perspective clinical application of antioxidant agent for DED.

CONTROL ID: 3711055

SUBMITTER (NAME ONLY): Megan Paul

TITLE: Rate of Children Treated for Strabismus and Amblyopia Strongly Correlates with the Prevalence of Pediatric Ophthalmologists in US States

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Paul, T. Frempong, Department of Medical Education, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|T. Frempong, Department of Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Strabismus and amblyopia occur in approximately 3% of US children by age three and, if treated early, can be corrected with excellent results. However, pediatric ophthalmologists (POs) are currently in high demand across the US. Therefore, this ecological study seeks to determine whether the prevalence of POs is associated with the rate of children treated for strabismus and amblyopia in the US.

Methods: The Vision and Eye Health Surveillance System was used to determine each state's rate of treated strabismus and amblyopia. The number of POs by state was determined using the American Association for Pediatric Ophthalmology website while population was taken from the US Census Bureau. A bivariate linear regression compared the prevalence of POs by state to the rate of children treated for strabismus and amblyopia. This was repeated but controlled for health insurance and race by state. A final linear regression compared the economic cost of pediatric vision issues using the Vision Health Initiative and the prevalence of POs in states.

Results: The highest prevalence of POs was in Maryland while the lowest were in Vermont and Wyoming. In the bivariate regression, there was a positive association between the rate of children treated for strabismus and amblyopia and the prevalence of POs ($\beta=2.97$, $p<0.01$). After controlling for health insurance and race, the rate of treated children was still positively associated with the prevalence of POs in each state ($\beta=2.58$, $p<0.01$). Notably, while the prevalence of POs and economic burden of vision issues were not statistically associated ($p=0.196$), Vermont had the highest economic burden of vision issues in children among all states.

Conclusions: This study indicates that the prevalence of POs in a given state is strongly tied to the rate of children being treated for strabismus and amblyopia, even after controlling for health insurance and race. In states where there is a lower prevalence of POs, there are potentially children who are not treated for eye conditions. This is substantiated by the fact that Vermont had one of the lowest rates of POs but the highest economic burden. While more physicians should be encouraged to enter this field, other strategies like telehealth and training technicians in underserved areas may help to mitigate these disparities.

CONTROL ID: 3711056

SUBMITTER (NAME ONLY): Sara Thomasy

TITLE: Effects of long-term application of topical ROCK inhibitor on corneal endothelium and Descemet's membrane of TAZ deficient mice

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.M. Thomasy, S. Park, K. Cosert, M. Mccorkell, N. Echeverria, S.M. Le, C.J. Murphy, B.C. Leonard, Department of Surgical & Radiological Sciences, School of Veterinary Medicine, University of California Davis, Davis, California, UNITED STATES|S.M. Thomasy, C.J. Murphy, Department of Ophthalmology & Vision Science, School of Medicine, University of California Davis, Davis, California, UNITED STATES|V. Raghunathan, The Ocular Surface Institute, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|V. Raghunathan, Departments of Basic Sciences & Biomedical Engineering, University of Houston System, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Wwtr1 gene encodes the transcriptional co-activator with PDZ-binding motif (TAZ), which is a mechanotransducer that can be activated via Rho GTPase activity and actin cytoskeletal tension. Mice deficient in TAZ demonstrate a softer Descemet's membrane (DM) and decreased corneal endothelial cell (CEnC) density. The purpose of this study was to evaluate the impact of Rho-associated protein kinase (ROCK) inhibition on CEnCs and DM in wildtype (WT) and heterozygous TAZ ($Wwtr1^{+/-}$) knockout mice.

Methods: Beginning at 6 months of age, 12 WT and 12 $Wwtr1^{+/-}$ mice were treated with topical netarsudil 0.02% ophthalmic solution (Rhopressa©) or vehicle control twice daily for 6 months. Endothelial cell density (ECD) was monitored using in vivo confocal microscopy. To compare the degree of age-related CEnC loss over time, % ECD change from baseline values were calculated. Following 6 months of treatment, all mice were euthanized and eyes were collected. For the right eyes, elastic modulus of Descemet's membrane (DM) was measured with atomic force microscopy. The left eyes were used for immunofluorescence staining of actin-phalloidin on corneal endothelial wholemounts.

Results: The $Wwtr1^{+/-}$ mice had softer DM than WT mice in control groups; however, treatment with topical netarsudil significantly stiffened DM of $Wwtr1^{+/-}$ mice compared with treated control ($Wwtr1^{+/+}$) mice. There were no statistical differences in % ECD change between netarsudil-treated versus control groups at each timepoint in both WT and $Wwtr1^{+/-}$ mice. While ECD was mildly lower in $Wwtr1^{+/-}$ versus WT mice at baseline, no differences were observed between groups at study termination. Distinct actin-phalloidin staining pattern such as bleb-like appearance was observed in netarsudil-treated groups of both WT and $Wwtr1^{+/-}$ mice consistent with cytoskeletal rearrangement by topical ROCK inhibition.

Conclusions: Topical netarsudil increased DM stiffness in $Wwtr1^{+/-}$ mice to approximate that of WT control mice, suggesting that ROCK inhibition modulates CEnC-matrix interactions. The lack of ECD change is likely due to the mild phenotype displayed by this cohort of $Wwtr1^{+/-}$ mice. Further study with $Wwtr1^{-/-}$ mice with more severe ECD loss is warranted to determine the impact of long-term ROCK inhibition on CEnC loss.

CONTROL ID: 3711061
SUBMITTER (NAME ONLY): David Swain
TITLE: Five-year effects of selective laser trabeculoplasty
SESSION TITLE: IOP and laser therapy
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D.L. Swain, B. Eliassi-Rad, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|D.L. Swain, Anatomy and Neurobiology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: David Swain: Commercial Relationship: Code N (No Commercial Relationship) | Babak Eliassi-Rad: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Studies have shown the efficacy of selective laser trabeculoplasty (SLT) to lower intraocular pressure (IOP) as adjuvant therapy during short-term follow-up; however, few studies have assessed the long-term efficacy of SLT on preventing worsening visual fields and thinning of retinal nerve fiber layer (RNFL) with continued medical therapy. We examined IOP, visual field parameters, and RNFL thickness at 3- and 5-yrs post-SLT.
Methods: A retrospective chart review was performed of 51 eyes of 39 patients with glaucoma treated with SLT at Boston Medical Center between 2012 – 2016 with subsequent follow-up with Humphrey visual field (HVF) and optical coherence tomography (OCT) exams. Outcome measures included IOP, visual acuity, number of glaucoma medications, number of months to subsequent surgical intervention. HVF outcomes included mean deviation (MD) and pattern standard deviation (PSD). OCT outcomes included RNFL mean thickness, and superior and inferior quadrant thickness.
Results: Twenty-five eyes required subsequent surgical intervention to control IOP (mean time to intervention = 33.6 ± 20.0 months) within the follow-up period. In 26 of 51 eyes, IOP was controlled at 5-yrs after SLT. In this group, mean IOP was significantly decreased by 3 mmHg and 3.5 mmHg at 3- and 5-yrs after SLT, respectively. Mean number of glaucoma medications was significantly increased at 5-yrs (2.8 ± 1.6; P = 0.02), compared to pre-SLT (2.1 ± 1.1). Mean HVF MD was significantly higher at 5-yrs (-8.07 ± 7.15 dB) compared to pre-SLT (-5.85 ± 4.04 dB). Mean PSD significantly increased at 3-yrs (5.38 ± 2.94 dB) and 5-yrs (6.76 ± 2.79 dB), compared to pre-SLT (4.78 ± 2.93 dB; P = 0.04 and ≤ 0.01, respectively). Inferior quadrant RFNL thickness decreased significantly at 5-yrs (91.1 ± 20.8 µm), compared to pre-SLT (95.4 ± 23.0 µm).
Conclusions: Overall, 51% of eyes had IOP controlled at 5-yr post-SLT with continued medical therapy; however, mean number of glaucoma medications was significantly higher. Also, there was progression of MD and PSD on HVF and inferior quadrant thinning on OCT at 5-yr follow-up. Our findings suggest that SLT may have some long-term benefit in controlling IOP with continued medical therapy. However, a significant number of patients required subsequent laser/surgical procedure to lower IOP, prevent worsening visual fields, and thinning of RFNL.

CONTROL ID: 3711063

SUBMITTER (NAME ONLY): Dong Won Kim

TITLE: Genetic loss of function of Ptbp1 does not induce glia-to-neuron conversion in retina.

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kim, T.V. Hoang, H. Apple, N. Pannullo, P. Leavey, S. Blackshaw, Neuroscience, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|M. Ozawa, M. Yu, N.S. Peachey, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S. Zheng, University of California Riverside, Riverside, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Direct reprogramming of glia into neurons is a potentially promising approach for the replacement of neurons lost to injury or neurodegenerative disorders. Knockdown of the polypyrimidine tract-binding protein Ptbp1 has been recently reported to induce efficient conversion of retinal Muller glia into functional neurons. However, several major concerns remain to be addressed. First, none of these approaches convincingly demonstrated a reduction of Ptbp1 expression in glial cells in situ. Second, lineage relationships between glia and neurons were inferred through the use of GFAP promoter-based AAV constructs or transgene, which are known to show neuronal expression in some contexts. Third, convincing evidence for direct glia-to-neuron conversion using reliable genetic lineage analysis and/or single-cell RNA-Sequencing (scRNA-Seq)-based trajectory analysis is missing. These concerns need to be addressed before the Ptbp1 knockdown approach can further advance toward clinical applications.

Methods: Here, we use a combination of genetic lineage tracing, scRNA-Seq, and electroretinogram analysis to show that specific deletion of Ptbp1 in adult retinal Muller glia does not lead to any detectable level of neuronal conversion.

Results: Only a few changes in gene expression are observed in Muller glia following Ptbp1 deletion, and glial identity is maintained. These findings highlight the importance of using genetic manipulation and lineage tracing methods in studying cell type conversion.

Conclusions: Our data indicate that the Muller glia-to-neuron conversion reported in previous studies following Ptbp1 knockdown does not reflect the effects of Ptbp1 loss of function.

CONTROL ID: 3711064

SUBMITTER (NAME ONLY): Raymond Wong

TITLE: Generation of a CRISPRi RPE model to study age-related macular degeneration genetics

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Wong, J. Wang, D. Urrutia-Cabrera, S. Mesa Mora, T. Nguyen, S. Hung, A.W. Hewitt, T. Edwards, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|R. Wong, J. Wang, D. Urrutia-Cabrera, S. Mesa Mora, T. Nguyen, S. Hung, T. Edwards, Surgery (Ophthalmology), University of Melbourne, Melbourne, Victoria, AUSTRALIA|J. Lees, O'Brien Institute Department, St Vincent's Institute of Medical Research, Fitzroy, Victoria, AUSTRALIA|J. Lees, Surgery and Medicine, University of Melbourne, Melbourne, Victoria, AUSTRALIA|A.W. Hewitt, University of Tasmania Menzies Institute for Medical Research, Hobart, Tasmania, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a blinding disease characterised by dysfunction of the retinal pigmented epithelium (RPE) which culminates in disruption or loss of the neurosensory retina. Genome-wide association studies have identified >60 genetic risk factors for AMD, however the expression profile and functional role of many of these genes remain elusive in human RPE. Development of a simple-to-use in vitro RPE model would help us study the complex genetics and pathogenesis of AMD.

Methods: To facilitate functional studies of AMD-associated genes, we developed a human RPE model with integrated CRISPR interference (CRISPRi) for gene repression by generating a stable ARPE19 cell line expressing dCas9-KRAB. To demonstrate the potential of this CRISPRi RPE system, we performed transcriptomic analysis of the human retina to prioritise AMD-associated genes and selected TMEM97 as a candidate gene for further knockdown study. Following CRISPRi-mediated knockdown of TMEM97, we analysed cell viability and oxidative stress levels to determine its functional role in ARPE19.

Results: Characterisation of CRISPRi ARPE19 show that the cell line retains stable expression of dCas9-KRAB for at least 2 months. Moreover, the CRISPRi ARPE19 cell line expresses RPE marker ZO-1 and retains the ability to form a polarised monolayer with hexagonal RPE morphology following nicotinamide treatment, supporting the quality of the derived cell line. Our results show that CRISPRi enables significant knockdown of TMEM97 in ARPE19 using specific sgRNAs. In particular, knockdown of TMEM97 in ARPE19 reduces reactive oxygen species (ROS) levels and exerts a protective effect against oxidative stress-induced cell death. This work provides the first functional study of TMEM97 in RPE and supports a potential role of TMEM97 in AMD pathobiology.

Conclusions: Our study demonstrates the potential for using CRISPRi to study AMD-associated genes in RPE, and the CRISPRi RPE platform generated here provide a useful in vitro tool for functional studies of AMD-associated genes.

CONTROL ID: 3711065

SUBMITTER (NAME ONLY): Yanping Li

TITLE: Retinoblastoma Organoids Generated from Patient-derived Induced Pluripotent Stem cells.

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, Y. Wang, W. Wang, X. ZHANG, K. Jin, Z. Jin, Beijing Institute of Ophthalmology, Beijing, Beijing, CHINA|Y. Li, Y. Wang, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|W. Wang, X. ZHANG, K. Jin, Z. Jin, Beijing Tongren Hospital, Beijing, Beijing, CHINA|L. Jin, Aier Eye Hospital Quanzhou, Quanzhou, Fujian, CHINA|

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ABSTRACT BODY:

Purpose: Recently, we (PNAS 2020) and other groups have successfully generated human retinoblastoma (Rb) organoids from pluripotent stem cells with specific mutations of RB1 gene. This study was aimed to establish Rb organoids derived from patient-specific induced pluripotent stem cells (iPSCs) for disease modeling and tumorigenesis study.

Methods: First, we generate iPSCs from an Rb patient with defined heterozygous mutation in RB1 ($RB1^{m1/wt}$). The second allelic mutation was constructed by CRISPR/Cas9 gene editing ($RB1^{m1/m2}$). Established iPSCs were developed into well-layered retinal organoids (ROs) through step-wise differentiation. Live imaging, RNA-Seq and immunostaining were carried out to analyze the Rb organoids.

Results: The $RB1^{m1/m2}$ iPSC-derived ROs displayed apparent tumorigenesis and biological features, consistent with Rb in patients. High-resolution X-ray computer tomography (microCT) scanning confirmed the rosette-like structure and more pores in Rb organoids. The gene enrichment of Rb organoids found by RNA-Seq analysis were highly related to cell cycle. Compared with $RB1^{m1/wt}$ and $RB1^{wt/wt}$ derived ROs, tumor-related markers including SYK, $p16^{INK4a}$, DEK were highly expressed in both the solid tumor and the adjacent tissues in $RB1^{m1/m2}$ derived ROs. We also found the highly expression of photoreceptor precursor markers, CRX and OTX2, in $RB1^{m1/m2}$ derived ROs, in line with Rb derivation from cone-committed cells. Besides, immunostaining showed that ARR3 positive maturing cone precursors are co-localized with proliferative markers Ki67 or PCNA, indicating Rb is originated from maturing cone precursors.

Conclusions: Combined with CRISPR/Cas9 technology and 3D retinal organoids differentiation, we successfully generated Rb organoids and observed tumorigenesis in vitro which derived from $RB1^{m1/m2}$ iPSCs with patient-specific genetic background. Rb organoids generated from iPSC with RB1 compound heterozygous mutation resemble real Rb in structural and molecular aspects.

CONTROL ID: 3711068

SUBMITTER (NAME ONLY): Matthew Shin

TITLE: Prevalence of ocular involvement from comorbid autoimmune disease in patients with Type 1 Diabetes

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shin, T. Winter, S. Orsdemir, Loma Linda University School of Medicine, Loma Linda, California, UNITED STATES|

Commercial Relationships Disclosure: Matthew Shin: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Winter: Commercial Relationship: Code N (No Commercial Relationship) | Sena Orsdemir: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Type 1 Diabetes (T1D) is an autoimmune disease associated with Hashimoto's thyroiditis (HT), Celiac disease (CD) and several other autoimmune diseases, but there is no report exploring the prevalence of eye disease in those with comorbid autoimmunity. This study investigates the frequency of ocular involvement (OI) in patients with T1D and one or more autoimmune diseases.

Methods: Retrospective chart review of patients with T1D, ages 1-100, with one or more autoimmune conditions that may affect the eyes at a tertiary referral center. Co-existing autoimmune diseases involving the eye were specified to include Hashimoto's Thyroiditis, Celiac disease, Systemic Lupus Erythematosus, Graves disease, Multiple Sclerosis, Juvenile Idiopathic Arthritis, Sjogren's syndrome, Ankylosing Spondylitis, Sarcoidosis, and Reactive Arthritis.

Results: 3,880 patients (mean age 36.9 years (median 29), 57.4% female, 47.3% Caucasian) with T1D were identified, of which 331 (8.53%) had one or more comorbid autoimmune condition(s) and OI was present in 13 (3.9%). Similar to other reports in the literature, 186 (4.8%) had HT and 98 (2.5%) had CD. Two autoimmune conditions were present in 302 patients with 8 (2.65%) having OI, 26 patients had three autoimmune conditions with 3 (11.5%) having OI and 3 patients had four autoimmune conditions with 2 (66.7%) having OI. The autoimmune diseases thought to affect the eye included Lupus with uveitis in 1/25 (4%), Graves disease with OI in 3/22 (13.6%), Multiple Sclerosis with OI in 2/9 (22.2%), Juvenile Idiopathic Arthritis with uveitis in 1/7 (14.3%), Sjogrens with OI in 5/6 (88.3%), Ankylosing Spondylitis with OI in 0/5 (0%), Sarcoidosis with OI in 1/3 (33.3%) and Reactive Arthritis with OI in 0/2 (0%).

Conclusions: Ocular involvement from one or more comorbid autoimmune diseases in patients with T1D is uncommon, but becomes more likely with increasing number of comorbid autoimmune diseases. Further clinical studies and reviews will be needed to understand the pathophysiology of this finding.

CONTROL ID: 3711069

SUBMITTER (NAME ONLY): Jeremy Liu

TITLE: Consensus Grading of Persistent Hyper-Transmission Defects on En Face OCT Imaging of Age-Related Macular Degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Liu, R. Laiginhas, P.G. Iyer, M. Shen, Y. Shi, O. Trivizki, L. Wang, E. Vanner, W.J. Feuer, G. Gregori, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|F. Corvi, Eye Clinic, Department of Biomedical and Clinical Sciences "Luigi Sacco", University of Milan, Milan, ITALY|F.L. Ferris, Ophthalmic Research Consultants, Waxhaw, North Carolina, UNITED STATES|T.H. Lim, National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore, SINGAPORE|S.R. Sadda, Doheny Eye Institute, David Geffen, School of Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|N.K. Waheed, New England Eye Center, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: A training exercise was performed using en face optical coherence tomography (OCT) images to study the ability of graders to reliably identify persistent choroidal hyper-transmission defects (hyperTDs), also known as complete retinal pigment epithelium and outer retinal atrophy (cRORA).

Methods: Formal training on how to identify persistent hyperTDs on en face OCT images was provided to 11 graders. Persistent hyperTDs were defined as bright, well-delineated lesions having a greatest linear dimension (GLD) of at least 250 µm. Training consisted of a tutorial session followed by the grading of three pretest exercises, each consisting of three cases. After all the graders scored 100% on the pretest exercises, they evaluated a final test set consisting of 30 en face OCT images from 29 eyes with non-exudative age-related macular degeneration (AMD). These images contained 107 hyperTDs, as determined by a senior author (P.J.R.) and represented a variety of AMD-related atrophic lesions.

Results: A total of 1177 hyperTDs from 30 en face OCT images were reviewed by the graders. The mean sensitivity, PPV, and modified accuracy for all the graders were 99.0%, 99.2%, and 98.2%, respectively. There was a 97% agreement observed between all the graders (AC_1 = 0.97). Internal graders from the Bascom Palmer Eye Institute had a slightly higher agreement compared with the external graders (AC_1 = 0.98 vs. 0.96). The hyperTDs most often incorrectly identified included the following features: (1) hyperTDs containing a hypo-transmission defect (hypoTD) core, (2) single hyperTDs that were incorrectly graded as two separate lesions, and (3) hyperTDs with a borderline GLD close to 250 µm.

Conclusions: The accurate detection of persistent hyperTDs on en face OCT images by graders demonstrates the feasibility of using this OCT biomarker to identify disease progression in eyes with non-exudative AMD. Thus, hyperTDs can represent a clinical trial endpoint in studies designed to test new therapies that may slow disease progression from intermediate AMD to cRORA.

CONTROL ID: 3711070

SUBMITTER (NAME ONLY): Alice Jiang

TITLE: Defining Structure-Function Relationships of Extraocular Motility Disorders Using 18F-FDG PET MRI and CT

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Jiang, C. Hoyt, N. Rasool, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|Y. Li, R. Flavell, Radiology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Positron emission tomography (PET) is a well-established imaging modality to assess tissue metabolism while magnetic resonance imaging (MRI) and computed tomography (CT) are used to provide anatomical information. Combining PET with MRI or CT imaging may provide unique insight into the in vivo pathophysiology of extraocular motility (EOM) in numerous disease processes. The aim of the study was to use 18F-fluorodeoxyglucose (18F-FDG) PET MRI/CT to characterize the structure-function relationships of EOM disorders.

Methods: 18F-FDG PET MRI and CT scans were performed in patients with EOM disorders. The maximum standardized uptake value (SUVmax), a marker of glucose metabolism, was calculated for the lateral, medial, superior, and inferior rectus muscles, as well as the cerebellum. These were compared to SUVmax values of the same structures from control patients without EOM dysfunction.

Results: In our preliminary observations, three orbits with hypoactive motility disorders were compared to five orbits without EOM disorders on 18F-FDG PET MRI and CT imaging. The SUVmax of extraocular muscles in hypoactive motility disorders was significantly less than that of control extraocular muscles, including the superior rectus (mean 2.8 ± SD 1.18 and 6.3 ± 1.20, $p = 0.008$), inferior rectus (3.83 ± 0.91 and 12.73 ± 0.98, $p < 0.00001$), medial rectus (3.37 ± 0.78 and 10.8 ± 2.09, p 0.002) and lateral rectus muscles (3.03 ± 0.55 and 7.98 ± 2.27, $p = 0.015$). There was no significant difference in SUVmax of the cerebellum in both groups (12.33 ± 0.80 and 10.725 ± 0.97, $p = 0.069$) demonstrating equivalent metabolite uptake.

Conclusions: 18F-FDG PET MRI and CT has the ability to illustrate differences in metabolic functioning in hypoactive EOM disorders. The high clinical potential of combining high resolution anatomic structural detail with the metabolic profile of the extraocular muscle will enable improved analysis of extraocular motility and identification of new pathologies.

CONTROL ID: 3711074

SUBMITTER (NAME ONLY): Jason Zhang

TITLE: Multi-Omics Analysis Reveals Effects of High Fat Diet Induced Gut Dysbiosis on RPE/Choroidal Transcriptome and Microbiome-Transcriptome Associations

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The impact of diet and gut dysbiosis on the pathogenesis of retinal disorders has recently been described, but the precise mechanism remains unclear. Previously, our team profiled the retinal transcriptome in the context of high fat diet (HFD) induced gut dysbiosis. Yet, the effect of gut microbial imbalance on the retinal pigment epithelium (RPE) and choroid, key players in retinal diseases, is unknown. Through multi-omics analysis, the purpose of this study is to identify how the RPE/choroid transcriptome is modulated by HFD-induced gut dysbiosis and microbiome-transcriptome associations.

Methods: RPE-choroidal tissue was dissected from C57BL/6 mice on normal diet or fed 23% HFD for 8 weeks (4 mice/group). RNA-seq was performed on NovaSEQ6000. Limma and LYNX were used for functional enrichment analysis of differentially expressed genes (DEGs). 16S rRNA-seq was performed on fecal DNA, and taxonomical microbiome composition was analyzed with QIIME2. Taxonomy was associated with retinal and RPE/choroidal transcriptomic data via Pearson correlation at the genus level within matched mice. The correlation matrix was filtered to contain only significant genera ($p<0.05$) with at least one DEG to highlight relevant host-microbiome associations.

Results: We identified 60 potential DEGs related to HFD ($p<0.05$, $logFC>1$, $logFC<-1$) in the RPE/choroid transcriptome including Serpine1 and Fabp7, players in angiogenesis and fatty acid homeostasis, respectively. Enrichment analysis further highlights a number of key regulatory pathways in angiogenesis and signal transduction. In the choroid, Ppargc1a, a coactivator in angiogenesis and oxidative stress regulation, was found to be tightly correlated with the HFD-associated phylum Firmicutes. Meanwhile, fibronectin and matrix metalloproteinases, both ECM components involved in debris deposition and retinal disease, were strongly associated with the class Clostridia in the retina.

Conclusions: Our study reveals a number of RPE-choroidal genes and pathways modulated by HFD-induced gut dysbiosis. In addition, the genes' implications in various retinal pathologies shed insight into the role of the gut-retina axis in diseases such as AMD. Finally, the strong correlation between specific chorioretinal genes and microbial populations may provide better understanding of the interplay in microbiome-chorioretinal pathways.

CONTROL ID: 3711076

SUBMITTER (NAME ONLY): Yuxun Shi

TITLE: Melatonin Reduces Optic Nerve Crush-Induced Retinal Ganglion Cells Senescence Via the SIRT1-dependent Pathway

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Shi, Y. Xu, J. Huang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Yuxun Shi: Commercial Relationship: Code N (No Commercial Relationship) | Yue Xu: Commercial Relationship: Code N (No Commercial Relationship) | Jingjing Huang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Melatonin, a hormone mainly secreted by pineal gland, is believed to be involved in exerting the protective effects in the aged-related and neurodegenerative diseases through silent information regulator type 1 (SIRT1)-dependent pathway. However，the effect of melatonin on retinal ganglion cells (RGCs) senescence was unknown. Thus, in this study, we aimed to examine the effect of melatonin on RGCs senescence following optic nerve crush (ONC) and explore whether SIRT1 was involved in this process.

Methods: ONC model was established in this study. EX527, an inhibitor of SIRT1, was injected intraperitoneally into mice 30 minutes before ONC and melatonin was administrated abdominally into mice after ONC every day. The immunofluorescence and western blot were used to evaluate the expression of SIRT1, p16 and p53. β-gal staining was employed to detected senescence cells. Hematoxylin & eosin (HE) staining, retina flat-mounts and optical coherence tomography (OCT) were used to evaluate the loss of retina tissue. Pattern electroretinogram (p-ERG) was performed to evaluate the visual function of retina.

Results: Melatonin stimulated the expression of SIRT1 in RGCs 3 days after ONC, which was normally expressed in RGCs of normal C57BL/6J mice and decreased after ONC. Meanwhile, the melatonin therapy restored the decreased RGCs numbers and ganglion cell complex (GCC) thickness ($p<0.001$, 0.01, respectively) 14 days after ONC. Moreover, the treatment of melatonin suppressed the ONC-induced senescence index at day 3 by decreasing the expression of p16, p53 and β-gal positive cells ($p<0.05$). Furthermore, the p-ERG showed that melatonin improved the amplitude of P50 and N95 ($p<0.05$). Besides, administration of EX527 decreased the protective effect of melatonin after ONC, which revealed that SIRT1 was involved in the process of melatonin regulating RGCs senescence after ONC.

Conclusions: Our data suggested that melatonin ameliorated the RGCs senescence via the SIRT1-dependent pathway following ONC, which may provide an important insight for the treatment of RGC senescence.

CONTROL ID: 3711078

SUBMITTER (NAME ONLY): Rajiv Mohan

TITLE: Epigenetic mechanism to induce dedifferentiation of corneal myofibroblast to fibroblast

SESSION TITLE: Corneal stromal biology, wound healing modulators, and regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.R. Mohan, P.K. Balne, N.R. Sinha, A. Hofmann, N. Hauser, R. Tripathi, P. Sinha, S. Gupta, K. Duraisamy, Ophthalmology, University of Missouri System, Columbia, Missouri, UNITED STATES|R.R. Mohan, P.K. Balne, N.R. Sinha, A. Hofmann, R. Tripathi, P. Sinha, S. Gupta, K. Duraisamy, Ophthalmology, Harry S Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Excessive formation and residence of myofibroblasts in stroma following ocular trauma/injury leads to loss of corneal transparency and vision impairment. This study sought to determine if corneal myofibroblasts could be de-differentiated into precursor fibroblasts/keratocytes via epigenetic reprogramming using an established in vitro model.

Methods: Primary human corneal stromal fibroblasts (hCSFs) generated from healthy donor corneas were used to generate human corneal myofibroblasts (hCMFs) by exposing cultures to transforming growth factor beta1 (TGFβ1; 5 µg/mL) for 72 h. Sodium Butyrate (NaB), an epigenetic modifier and histone deacetylase inhibitor, was used to induce epigenetic reprogramming by growing hCMFs in +/- NaB for 72 h. Trypan blue exclusion assay and phage-contrast microscopy were used to examine cytotoxicity and morphologic changes. Quantitative reverse transcription PCR (qRT-PCR) and immunofluorescence were used to study the expression of α-smooth muscle actin (α-SMA), collagen type 3 (Col 3), and fibroblast-specific protein 1 (FSP1). The DNA methylation was quantified by measuring the 5-methylcytosine (5-mC) levels with a commercial assay kit.

Results: TGFβ1 treatment converted >95% hCSFs to hCMFs with significant upregulation of α-SMA protein and gene expression. A dose-dependent cytotoxicity assay with NaB (0-100 mM) in CMFs showed IC_{50} of NaB 20.38 mM. CMFs treated with NaB for 72 h led to the disappearance of typical myofibroblastic morphology and demonstrated a significant reduction in α-SMA, and Col 3, and increase in FSP1 expression compared to control untreated CMFs ($p < 0.05$). A significantly increased DNA methylation was observed in NaB-treated CMFs compared to the control untreated CMFs ($p < 0.05$).

Conclusions: Dedifferentiation of corneal myofibroblasts to precursor fibroblasts seems possible via epigenetic reprogramming with NaB. Further studies are warranted.

CONTROL ID: 3711079

SUBMITTER (NAME ONLY): Javier Nahmias

TITLE: Racial and Gender Differences in the Natural Lens Detected on Dual-Energy (DE) CT

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Nahmias, A.C. Thompson, Ophthalmology, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, UNITED STATES|K. Hiatt, J. Bomar, T.G. West, P.M. Bunch, M. Benayoun, C. Lack, J.R. Sachs, Radiology, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, UNITED STATES|A.C. Thompson, Geriatrics and Gerontology, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is not known whether Dual Energy-Computed Tomography (DE-CT) might be able to detect differences in the crystalline lens that could be related to physiologic differences in lens opacity or incidental cataract formation. This study investigated whether there is a relationship between possible demographic and clinical risk factors for cataract and x-ray attenuation of the crystalline lens on DE-CT of the head.

Methods: Retrospective review of 198 eyes in 103 adult subjects who underwent DE-CT exams of the head. Regions of interest spanning 3-5 mm^2 were placed over the center of the native crystalline lens and the x-ray attenuation of each lens was recorded in Hounsfield Units (HU) at 3 DE-CT energy levels: 40 keV, 70 keV, and 190 keV. Demographic and environmental risk factors for cataract were collected from the medical record. Generalized estimating equations were used to assess the relationship between these risk factors and relative density of the lens at each energy level.

Results: The mean age in the older vs. younger cohort was 81.4 5.7 yrs vs. 22.66 2.93 yrs. 46.6% of subjects were female, 38.8% non-Hispanic white, 22.3% diabetic, and 37.9% never smokers. The mean HU attenuation values were significantly lower for the older vs. younger group (GEE $p=0.022$) at 40 keV, but there was no significant difference at higher energy levels (70 or 190 keV; all $p>0.05$). Mean HU attenuation values were significantly higher for females vs. males (40 keV: 76.4±13.3 vs. 70.7±1.3; 70 keV: 79.0±7.4 vs. 74.2±7.6; 190 keV: 80±7.9 vs. 75.8±9; all $p<=0.01$) and non-whites vs. non-Hispanic whites (40 keV: 77.6±13.1 vs. 70.5±13.2; 70 keV: 80±7.9 vs. 74.1±7.0; 190 keV: 81.0±8.1 vs. 75.5±8.5; all $p<=0.001$) at all 3 energy levels. However, there was no significant association between lens attenuation and either diabetes or smoking status (all $p>0.05$). In multivariable analysis, both female sex (all $p<0.01$) and nonwhite race (all $p<0.01$) but not age-group ($p>0.05$) remained significant independent predictors of lens attenuation at all 3 energy levels.

Conclusions: The crystalline lens of females and non-white subjects had significantly higher attenuation on DE-CT, which may suggest higher density or increased concentration of materials like calcium. These groups may be at greater risk for cataracts independent of other well-known risk factors such as age, diabetes, or smoking status.

CONTROL ID: 3711085

SUBMITTER (NAME ONLY): Stephanie Choi

TITLE: CARES Act Aid to Ophthalmologists and Optometrists During the COVID-19 Pandemic

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Choi, A. Du, S.A. Patil, R. Parikh, NYU Langone Health, New York, New York, UNITED STATES|D. Vail, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|A. Watane, J. Wang, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Congress passed the CARES Act (Coronavirus Aid, Relief, and Economic Security) Provider Relief Fund to help healthcare providers recoup lost revenue during the pandemic. We aimed to determine how much of this federal aid was provided to ophthalmology and optometry practices, and whether the amount of aid received varied based on practice size.

Methods: We used the Centers for Medicare and Medicaid Services (CMS) Physician Compare National Database to identify medical practices that provide eye care. We used practice names to link this database to the Health and Human Services (HHS) Provider Relief Fund (PRF) database to determine how much aid each practice received through the CARES Act.

Results: We identified 2,625 optometry or ophthalmology practices that received funding through the CARES Act Provider Relief Fund that were not hospital-owned or affiliated with multi-specialty practices. Large practices with more than 10 clinicians accounted for only 268 of the 2,625 practices in our sample, but received nearly half of all funding ($182 million). Per-practitioner funding varied based on practice size (p=0.047), but differences in per-practitioner funds were not significant after adjusting for practice specialty (ophthalmology, optometry, or both).
We also found that retina specific practices tended to receive more than their counterparts.

Conclusions: This study demonstrates a relatively uniform distribution of per capita funds when adjusted for ophthalmologists, optometrists, and mixed-practices regardless of practice size. This policy demonstrates how federal aid is distributed to independent ophthalmology practices, and
that smaller practices which are at higher risk may need larger per capita payments to remain viable during times of economic stress.

CONTROL ID: 3711088

SUBMITTER (NAME ONLY): Peter Sonnentag

TITLE: Incidental finding of white dots in the central retinas of two young cynomolgus macaques

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Rasmussen, Y. Krakova, P. Miller, C.B. Kim, J.N. Ver Hoeve, H.D. Wabers, C.J. Murphy, T. Nork, OSOD, Ocular Services on Demand, Madison, Wisconsin, UNITED STATES|R. Chen, Baylor College of Medicine, Houston, Texas, UNITED STATES|C.A. Rasmussen, C.B. Kim, J.N. Ver Hoeve, T. Nork, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|P. Miller, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|C.J. Murphy, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|P. Sonnentag, Toxicology Study Direction, Labcorp Drug Development, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the morphology and functional aspects of an unusual incidental finding in two treatment-naïve cynomolgus macaques.

Methods: Animal #1 was a 2.8 kg, 2.67-year old male of Cambodian origin. Animal #2 was a 3.9 kg, 7.75-year old female of Chinese origin. Both animals underwent clinical ophthalmoscopic examination, color fundus photography, spectral domain optical coherence tomography (OCT), blue (BAF) and infrared (IRFA) fundus autofluorescence, fluorescein angiography (FA), full field electroretinography (ERG), and flash visually evoked potentials (fVEP). Animal #1 also had genomic analysis conducted to assess for known molecular mutations.

Results: Both animals had normal anterior segments including corneas, lenses and vitreous. No cell or flare was noted. Animal #1 had numerous prominent white spots in the macula (Figure 1) and extending peripherally to about 2 disc diameters beyond the nasal margin of the optic disc and the arcade vessels in both eyes. The peripheral retina was unremarkable. FA showed the spots to be window defects, i.e., early hyperfluorescence with late fading but no leakage. The spots were hyper-BAF, hypo-IRAF. OCT showed thickening at the interdigitation zone (IZ) (Figure 2). Animal #2 had fainter spots, but the size and distribution were similar to Animal #1. Except for the fundus findings, both animals were otherwise healthy. Scotopic and photopic ffERG and fVEP were normal. Whole genome sequence analysis of Animal #1 was negative for EFEMP1 (Doyne's), RDH5 (albipunctatus) and RLBP1 (retinitis pigmentosa).

Conclusions: We have not observed similar white spots in the thousands of cynomolgus macaques examined over the past two decades. Thus, the finding is rare in our cohort of animals. There is no obvious human correlate to these spots. They appear to be functionally benign and are not associated with inflammation. The spots were fainter in the older animal, which could indicate fading over time or just be individual variation. Yiu, et al (Sci Rep 2017;7:1513) reported drusenoid lesions in rhesus macaques but the OCT thickening in our animals is in the IZ, not at Bruch's membrane. These findings illustrate the importance of baseline ocular examinations in preclinical toxicity studies.

CONTROL ID: 3711090

SUBMITTER (NAME ONLY): Aditi Gupta

TITLE: Evaluation of Modified Screening Criteria for Retinopathy of Prematurity in India

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gupta, M.A. deCampos-Stairiker, M. Oh, A.S. Coyner, S.R. Ostmo, J. Campbell, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Singh, J. Kalpathy-Cramer, Harvard University, Cambridge, Massachusetts, UNITED STATES|R.V. Chan, University of Illinois System, Urbana, Illinois, UNITED STATES|P. Sparizam, P. Shah, Aravind Eye Hospital, Madurai, Tamil Nadu, INDIA|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of Prematurity (ROP) screening criteria vary around the world based on the population at risk. Screening criteria based on birthweight (BW) and gestational age (GA) can be more broad in low- and middle-income countries like India, where ROP can be more commonly seen in less premature babies than in the US. The purpose of this project was to evaluate the effect of various screening criteria on a large population of premature babies in South India.

Methods: We analyzed two years of data from the Aravind Eye Hospital ROP telescreening program (1/1/19-12/31/20). During that period, participating neonatal care units referred babies for screening who were less than 36 weeks postmenstrual age (PMA), or less than 2000 grams, or who had other risk factors for ROP. We evaluated 3 different screening criteria for sensitivity and specificity for detecting treatment-requiring (TR) ROP: US screening criteria (<31 weeks[w] PMA or < 1500 grams[g] BW), Indian criteria (<36w or <2000g), and intermediate criteria (<34w or <1750g).

Results: The sensitivity / specificity of the 3 sets of guidelines (India, Intermediate, and US) were 100% / 13%, 100% / 40%, and 85% / 67%, respectively, as seen in the table. Of the entire screened population (N = 2714 babies), use of intermediate criteria would reduce screening burden by 38% without missing a case of TR-ROP in this population.

Conclusions: ROP screening criteria evolve as demographics and practices in a region change. Current Indian screening criteria are 100% sensitive, but nonspecific, and US screening criteria are insufficiently sensitive for implementation in this Indian population. An intermediate cutoff produced 100% sensitivity with 38% reduced screening burden and can be considered in the future if 100% sensitivity can be ensured.

CONTROL ID: 3711091

SUBMITTER (NAME ONLY): Zachary Brooke

TITLE: Correlation between Corneal In Vivo Confocal Microscopy and Clinical Findings in Dry Eye Disease

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Brooke, Z. Harbin, S. Sensenbrenner, A. Kheirkhah, Department of Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is discrepancy in reported studies on correlations between in vivo confocal microscopy (IVCM) findings in the cornea and clinical parameters of dry eye disease (DED). The purpose of our study is to evaluate this correlation in our patients.

Methods: This cross-sectional study included 80 eyes of 40 patients with DED which was defined as symptoms of DED plus abnormal tear breakup time (TBUT) or Schirmer test. Patients with previous ocular surgery or contact lens use were excluded. All patients underwent a comprehensive ocular surface evaluation which included Ocular Surface Disease Index (OSDI) questionnaire, corneal fluorescein staining (CFS, NEI grading, 0-15), conjunctival lissamine green staining (LGS, NEI grading, 0-18), TBUT, Schirmer test with anesthesia, and tear osmolarity. In addition, IVCM was performed in the central cornea of both eyes. Three IVCM images of subbasal area were used to measure subbasal nerve fiber length (SNFL) and dendritic cell (DC) density by two independent masked observers. The average values of both observers were used for analysis. Correlations between IVCM parameters and clinical parameters were then investigated.

Results: There were 35 women and 5 men, with a mean age of 61.4±15.1 years (range, 26-86 years). The average values were 53.15 ± 25.4 for OSDI, 6.1 ± 4.3 for CFS, 3.5 ± 3.9 for LGS, 4.9 ± 2.5 seconds for TBUT, 10.6 ± 6.5 mm for Schirmer, and 300.6 ± 27.7 for tear osmolarity. The mean SNFL was 14.69 ± 6.15 mm/mm^2 and mean subbasal DC density was 114.4 ± 64.3 cells/mm^2. Correlation analysis showed that OSDI had significant correlation with CFS (P=0.001, r= 0.60) and Schirmer (P=0.017, r= -0.46). CFS also had significant correlations with LGS (P=0.001, r=0.58), TBUT (P=0.002, r= -0.57), and Schirmer ((P=0.003, r= -0.55). There was also a significant negative correlation between SNFL and age (P=0.028, r= -0.42). However, there were no statistically significant correlations between SNFL or DC density and other clinical parameters. Osmolarity also showed no correlations with any IVCM or clinical parameters.

Conclusions: There are no significant correlations between IVCM parameters and clinical signs or symptoms of DED. Caution should be exercised in clinical use of IVCM for DED evaluation.

CONTROL ID: 3711092

SUBMITTER (NAME ONLY): Ian Dryden

TITLE: PRAME Immunohistochemistry in Conjunctival Melanocytic Lesions

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: PReferentially expressed Antigen in MElanoma (PRAME) immunohistochemistry (IHC) is a valuable diagnostic tool and prognostic marker in the evaluation of cutaneous melanomas. Recently, strong nuclear PRAME IHC labeling was found to help distinguish malignant from benign conjunctival melanocytic lesions (CMLs) (PMIDs: 20805128, 34268800, 34089198). To corroborate these findings, we performed a retrospective study of PRAME IHC staining patterns in previously biopsied CMLs at our institution.

Methods: CMLs were obtained from 16 patients who underwent biopsy of conjunctival lesions. IHC was performed to evaluate for melanocytic differentiation (MelanA, HMB-45, or SOX-10) and nuclear PRAME expression. Patient demographics, lesion characteristics, and PRAME status by IHC were included in the retrospective cohort analysis.

Results: The cohort of 16 patients included 11 females and 5 males, with an average age of 48.8 years (range 3 to 86 years). At the time of the study, all patients were alive and without evidence of metastatic disease. CML diagnoses were categorized as either benign melanosis (5/16), benign nevus (8/16), or malignant melanoma (3/16). Nuclear PRAME immunolabeling was detected in 2 of 3 patients with malignant melanoma (66%) and 0 of 13 histologically benign CMLs. Of the 3 malignant melanoma cases, PRAME nuclear expression was not detected by IHC on both the biopsy and subsequent excision of an invasive melanoma that involved the superior nasal and temporal conjunctiva of an 86-year-old male, harboring BRAF V600E, MSH2 R406X, and TERT promoter mutations.

Conclusions: Our current study is consistent with prior reports, which contend that PRAME IHC can be used as an ancillary marker to help distinguish malignant versus benign CMLs. However, our analysis revealed one patient with a PRAME-negative invasive conjunctival melanoma. Although the findings are promising, additional large-scale studies are needed to determine the specificity and sensitivity of PRAME IHC in the evaluation of suspected conjunctival melanomas.

CONTROL ID: 3711094

SUBMITTER (NAME ONLY): Theresa Akoto

TITLE: Differential response of human corneal and keratoconus fibroblasts to cyclic mechanical stretch

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Akoto, Y. Liu, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|W. Zhi, Y. Liu, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|S. Nicholas, D. Karamichos, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|S. Nicholas, D. Karamichos, Pharmaceutical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Biomechanical factors may contribute to the pathogenesis of keratoconus (KC). We aimed to determine the protein expression alterations of primary human corneal fibroblasts (HCF) and KC fibroblasts (HKC) in response to cyclic mechanical stretch (CMS) to mimic the physiological condition in human corneas.

Methods: HCF (n=3) and HKC (n=3) cells were cultured in 6-well plates with or without of 15% CMS (1 cycle/s for 24-hours) using a computer-controlled Flexcell FX-6000T Tension system. Extracted cellular protein (30µg) was digested with trypsin followed with liquid chromatography-mass spectrometry-based comparative proteomics using label-free spectral counting method. After protein database search, we normalized the peptide spectra matches (PSM) of each protein to the total PSM of each sample expressed as a percentage before comparison to compensate for possible variation due to sample loading. We performed the following comparisons: HKC-CMS vs HKC-no-CMS, HCF-CMS vs HCF-no-CMS, HKC-CMS vs HCF-CMS, and HKC-no-CMS vs HCF-no-CMS. We used two-tailed Student's t-test to identify differentially expressed proteins (DEP) ($p<0.05$). Gene ontology (GO) enrichment analysis was done using the WebGestalt 2013 version.

Results: We identified a total of 5370 proteins in all the samples. On average, 1717 proteins were identified per sample, of which 1241 proteins were detected in ≥6 samples and 696 proteins in all 12 samples. Differential analysis identified 74 and 65 CMS-responsive proteins in HCF and HKC cells respectively. 12 and 6 proteins were induced by CMS in HCF and HKC cells respectively. We identified 79 DEP in HKC-no-CMS vs HCF-no-CMS and 67 DEP in HKC-CMS vs HCF-CMS. GO analysis indicated the involvement of cell cycle regulation and interferon-mediated signaling in HCF response to CMS while HKC responds to CMS with the involvement of DNA damage response, insulin receptor binding, and oxidoreductase activity. KC-specific GO includes protein complex assembly/disassembly, hydrolase activity, and mitochondrial proteins without CMS, but includes wound healing and DNA damage response with CMS.

Conclusions: For the first time, our biomechanical study has identified a differential response of HKC cells to CMS with proteins involved in wound healing, DNA damage response, and oxidoreductase activity, suggesting the potential role of biomechanical stretch in KC development.

CONTROL ID: 3711096

SUBMITTER (NAME ONLY): Marco Nassisi

TITLE: Genotype-phenotype correlation and disease modeling in RPGR-related cone and cone-rod dystrophies.

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Variants in the retinitis pigmentosa GTPase regulator gene (RPGR) and, specifically, in its retinal isoform opening reading frame-15 ($RPGR^{ORF15}$) have been associated with rod-cone (RCD), cone and cone-rod dystrophies (CD and CRD). While RPGR-related RCD is well understood, the characteristics and progression of RPGR-related CD/CRD were less frequently investigated. Here, we report the genotyping and genotype-phenotype correlation of a large cohort of patients with RPGR-related CD/CRD.

Methods: 34 index patients and 2 affected relatives were recruited at the “Quinze-Vingts” Hospital, Paris, France. Genetic screening was performed through direct Sanger sequencing of the $RPGR^{ORF15}$. Phenotypic data were collected retrospectively.

Results: 29 distinct variants in $RPGR^{ORF15}$ were identified, of which 27 were frameshift or nonsense and 24 were located towards the 3’ end of the $RPGR^{ORF15}$ transcript. 20 variants are novel sequence alterations. 15 subjects were affected by CD and 19 were diagnosed with CRD. Mean age at last examination was 43,97 ± 11,24 years. Best corrected visual acuity (BCVA) was 0.97 ± 0.71 LogMAR (20/200 Snellen equivalent). The most important predictors of BCVA seem related to morphologic data, with a significant correlation found for the central retinal thickness (β coeff. -0.523, p=0.003), autofluorescence (β coeff. 0.353, p=0.044) and peripapillary sparing (β coeff. -0.376, p=0.031). When analyzing longitudinal data, progressive decline of BCVA was noted, with more than 60% of the patients reaching a BCVA ≥ 1 LogMar in the best eye during their sixth decade of life.

Conclusions: We confirmed that $RPGR^{ORF15}$ variants associated with CD/CRD phenotypes are mostly located within the 3' end of the transcript (C-terminal part of the protein). Several imaging parameters may be useful as prognostic factors in these patients, although prospective longitudinal studies will be needed to confirm these results. The longitudinal data showed a rapidly progressive disease, possibly locating an optimal window of intervention for future therapies in younger ages.

CONTROL ID: 3711101

SUBMITTER (NAME ONLY): Zachary Harbin

TITLE: A Comparison of Patients' Perspectives on Their Dry Eye Disease Between Spanish- and English-Speaking Patients

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Harbin, L. Vasquez, Z. Brooke, Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|J. Isteitiya, C. Villanueva, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients' perspectives on their disease can significantly affect the disease course and outcome. However, limited data are available on patients' perceptions of their dry eye disease (DED). It also remains unknown whether patient's language plays any role in such perceptions. This study aims to compare patients' perception of DED and the effectiveness of its treatment between Spanish- and English-speaking patients.

Methods: This cross-sectional study included 62 patients with DED in San Antonio, Texas. All patients completed a questionnaire to evaluate their perspectives on their DED including their satisfaction with understanding DED, their opinion on easiness of following doctors' advice, their opinion on the effectiveness of the treatment, their satisfaction with the eye care, and their general outlook on DED. English version was used for English-speaking patients, and Spanish version was used for Spanish-speaking patients. All patients also had a comprehensive ocular surface examination as well as Ocular Surface Disease Index (OSDI) questionnaire. We then compared the patients' perspectives on DED between English- and Spanish-speaking patients.

Results: There were 44 women and 18 men, with an average age of 60.8±13.8 years (range, 27-87 year). There were 18 Spanish-speaking patients and 44 English or bilingual speaking patients. The average OSDI score was 53.4±19.7. Among all, 57% were satisfied with their understanding of DED, 81% found it easy to follow their doctors' advice for DED management, 61% thought that the DED treatment had been helpful, 69% were satisfied with their eye care for DED, and 61% expressed optimism regarding the long-term prospects of their DED. Comparisons between Spanish- and English-speaking patients did not yield significant demographic or clinical differences. However, Spanish-only speaking patients reported a lower understanding of DED compared to English-speaking patients (33.3% vs 65.9%, respectively, P=0.006). There were no significant differences in other DED perspectives between these two groups.

Conclusions: Our data suggests patients speaking only Spanish experience a gap in understanding of their DED. By understanding the ethnic differences in patients' perceptions of their DED, proper measures can be implemented to help guide treatment of this common condition.

CONTROL ID: 3711102

SUBMITTER (NAME ONLY): Jeong Pak

TITLE: Optical Coherence Tomography (OCT) Risk Markers for Progression of Intermediate Age-Related Macular Degeneration (AMD) to Late AMD

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.W. Pak, K. Taylor, S. Whittier, A. Dieu, R. Voland, B.A. Blodi, A. Domalpally, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection of geographic atrophy (GA) is key in preventing progression from intermediate to late AMD. OCT biomarkers provide a novel means of identifying early GA. We aimed to identify the frequency and the predictive role of OCT biomarkers for AMD progression.

Methods: This is a retrospective cohort study performed at the Wisconsin Reading Center. We evaluated OCT and fundus photographs (FP) of 102 eyes of 65 participants at baseline and at 5-years. At baseline, multimodal assessment excluded Complete Retinal Pigment Epithelial Outer Retinal Atrophy (cRORA), late AMD and ungradable images, and 73 eyes of 45 participants with intermediate AMD were evaluated using OCT for presence/number of hyperreflective foci (HRF), largest drusen size, drusen volume, drusen with hyporeflective core, reticular pseudodrusen (RPD) and Incomplete Retinal Pigment Epithelial Outer Retinal Atrophy (iRORA). AMD severity level was graded from FP. At 5-years, cRORA and CNV were assessed from multimodal imaging as a measure of progression to late AMD.

Results: At baseline, HRF were seen in 40 eyes (55%) with a mean of 4 (SD 6.0) per eye. The mean largest drusen size in horizontal width was 0.64 (SD 0.44) mm and the mean drusen volume was 1.06 (SD 0.24) mm^3. Hyporeflective drusen were found in 40 eyes (55%). RPD was present in 20 eyes (27%) with a mean RPD area of 4.1 (SD 10.8) mm^2. iRORA was identified in 24 eyes (33%). Thirteen eyes were the AMD severity levels 1-5 (18%), while 60 eyes were the levels 6-8 (82%). At 5-years, 13% of eyes developed CNV and 37% cRORA. In a multivariate model, iRORA and all drusen characteristics were associated with development of cRORA with an adjusted odds ratio of 4.4 (95% CI 1.2,18).

Conclusions: OCT features of intermediate AMD can be reproducibly graded and serve as precursors for development of endpoints such as cRORA. iRORA and all drusen characteristics are associated with increasing AMD severity and are strong predictors of cRORA. It remains to be studied if some OCT-related features of iRORA may be more predictive of progression than others. Long term studies with larger sample size are required to understand these important harbingers to advance new therapies for AMD.

CONTROL ID: 3711107

SUBMITTER (NAME ONLY): Arthi Rao

TITLE: Evaluation of Peripapillary and Macular Vessel Density following Intraocular Pressure Reduction Using Optical Coherence Tomography Angiography

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rao, C. Huang, J. Lee, B. Burkemper, S. Arora, V. Nguyen, B. Wong, B. Xu, B. Song, Ophthalmology, Keck Hospital of USC, Los Angeles, California, UNITED STATES|R.K. Wang, X. Zhou, University of Washington, Seattle, Washington, UNITED STATES|A. Fard, S. Yu, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|G.M. Richter, Southern California Permanente Medical Group, Pasadena, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The effects of intraocular pressure (IOP) reduction on retinal vessel density (VD) in glaucoma patients undergoing treatment are not fully understood. The purpose of this study is to determine if detectable changes in VD, as measured by optical coherence tomography angiography (OCTA), occur as result of IOP lowering therapy from either a prostaglandin analogue (PGA) or trabeculectomy surgery.

Methods: 6x6mm Spectral Domain OCTA images of the superficial macula and the radial peripapillary capillaries were obtained (Zeiss, Dublin, CA, Cirrus 11.0.0.23113). Images were quality graded then quantified using prototype software. OCTA images of primary open angle glaucoma patients who experienced >20% IOP reduction 3-6 months after treatment with a PGA or trabeculectomy were included. The Wilcoxon Signed Rank Test was used to compare VD change before and after treatment initiation. VD change was compared to the within eye coefficient of repeatability (CRw).

Results: 42 surgically treated eyes (37 patients) and 66 PGA treated eyes (35 patients) underwent OCTA imaging at baseline. After exclusion for image quality and follow-up, 18 surgically treated eyes (17 patients) and 12 PGA eyes (9 patients) were included in the final analysis. The median change in peripapillary VD was -0.0084 (min: -0.0660, max: 0.0578) among trabeculectomy eyes (p=0.958) and -0.0073 (-0.0409, 0.0736) for the PGA eyes (p=0.885) after 3-6 months. Change in macular VD was 0.0121 (-0.0174, 0.0254) for trabeculectomy eyes (p=.230) and -0.0018 (-0.0193, 0.0320) for PGA eyes (p=0.493) during the study period. See Table 1. Based on our prior studies (Lee et al 2021, Vorperian et al 2022 in submission), CRw is 0.087 for peripapillary VD and 0.018 for macular VD.

Conclusions: No significant change in peripapillary and macular VD was seen for either group 3-6 months after IOP reduction. The median differences when compared to the CRw per region are lower, suggesting that the observed differences may be attributable to intersession variability. Further study is needed to determine the utility of macular and peripapillary VD on OCTA as a biomarker for monitoring disease progression and therapeutic efficacy after intervention.

CONTROL ID: 3711108

SUBMITTER (NAME ONLY): Eric Mikula

TITLE: A Finite Element Model to Predict the Effect of Femtosecond Laser Trabeculotomy (FLT) Glaucoma Treatment Parameters

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: FLT is an innovative, non-invasive glaucoma procedure which aims to reduce intraocular pressure (IOP) via the creation of aqueous humor (AH) drainage channels through the trabecular meshwork (TM) and into Schlemm's canal (SC). As of this writing, the optimal physical treatment parameters of drainage channel(s) for FLT are not known. The purpose of this study was to develop a finite element model (FEM) to help predict the optimal drainage channel size (cross-sectional area) for IOP reduction.

Methods: The 3D finite element model of the human eye and the conventional AH outflow pathway used data published in the literature to inform the geometry of the anterior chamber (AC), TM, SC, and collector channels (CC). The major boundary conditions consisted of an AH inflow rate source term (2.5 uL/min) and the episcleral venous pressure, which comprised a pressure condition on the distal boundary of the CC's (9 mmHg). The TM and CC's were modeled as porous material, with given permeabilities, to approximate the resistance to AH outflow found in these tissues in-vivo. The permeability of the TM and CC's was estimated by comparing iterative FEM simulations with IOP data collected from ex-vivo experiments as well as unpublished preliminary clinical data. FLT was modelled by applying a block-like channel of connecting the anterior chamber to SC.

Results: Table 1 shows the finite element model predictions for IOP values following FLT using drainage channels of varying cross-sectional dimension. A channel size of 100 μm x 100 μm was found to achieve approximately (±2%) the maximal achievable IOP reduction (pressure within SC). Beyond this size, no appreciable increase in IOP reduction was achieved. This is in relative agreement with experimental laboratory as well as clinical results which demonstrated similar IOP reduction with channels measuring 200 μm x 500 μm.

Conclusions: The finite element model of FLT developed in this study demonstrates initial predictive power regarding drainage channel geometry and subsequent IOP reduction. Furthermore, the model shows the potential for reducing drainage channel size significantly, thus reducing procured time and overall tissue alteration, without sacrificing IOP performance. Importantly, the model suggests that drainage channel geometry may be chosen to fine-tune IOP reduction, thus optimizing the FLT procedure for a particular patient.

CONTROL ID: 3711114

SUBMITTER (NAME ONLY): Damon Wong

TITLE: Development and Validation of Global Visual Field Prediction using a Gradient Boosted Framework

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate global visual field prediction using a gradient-boosted approach based on optical coherence tomography (OCT) structural measures in primary open angle glaucoma (POAG).

Methods: 721 glaucoma eyes from 506 Asian Chinese participants from a study site in Singapore and 111 glaucoma eyes from 63 Caucasian participants from Bucharest were included in the study. All participants underwent the same study protocol, including OCT imaging and 24-2 visual field testing using standard automated perimetry. Retinal nerve fiber layer (RNFL) thickness measurements and global visual field mean deviation (MD) values were extracted for each study eye. Data from the Singapore site was split using stratified sampling based on glaucoma severity into a training dataset and internal testing dataset using a 80/20 ratio, while an external test dataset was constructed with the Bucharest data. A gradient boosted ensemble tree (GBT) model was trained using 5-fold cross validation with the training data, and evaluated on the internal and external test datasets using mean average errors (MAE). Predictions were compared with a baseline MAE which predicted the mean MD, and with multi-variate linear regression (LR), using Pearson correlation analysis and Wilcoxon signed rank testing. 95% confidence intervals were generated using bootstrapping with 5000 samples.

Results: Participants in the internal dataset had an average age of 66.7±8.1 years and MD of -5.85±5.05 dB, while those in the external dataset had an average age of 63.6±11.7 years and MD of -4.79±5.79 dB. Differences in the mean MD were not significant (P=0.118). Baseline MAE on the internal and external test datasets was 3.80 dB and 4.09 dB respectively. The gradient boosted approach achieved a MAE of 3.01 dB (95%CI: 2.58-3.49) and Pearson correlation of 0.59 (0.47-0.70) on the internal test dataset, and a MAE of 3.04 dB (95% CI: 2.52-3.68) and Pearson correlation of 0.66 (95%CI: 0.44-0.82) on the external test dataset. Results obtained with GBT were significantly better than LR (P<.001) on both datasets.

Conclusions: Global visual field prediction using gradient boosted trees performed better than baseline and linear regression on independent internal and external datasets. The results motivate further evaluation of the approach and its applicability in structure-function studies.

CONTROL ID: 3711120

SUBMITTER (NAME ONLY): Rachel Ka-man Chun

TITLE: Effect of blue-light filtering lens on refractive change in schoolchildren – a randomized controlled study

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the effect of blue-light filtering lens on refractive changes in myopic schoolchildren over 2 years. The current study reports the 1-year interim findings.

Methods: 148 myopic Chinese schoolchildren aged 8-13 years were recruited in a 2-year randomized clinical trial (ClinicalTrials.gov identifier: NCT03538002) and were randomly assigned into blue-light filtering (BF) or single vision (SV) lenses treatment groups. The study outcomes were cycloplegic spherical equivalent (SE) and axial length (AL) measured by open-field auto-refractor and non-contact optical biometer, respectively. Baseline measurements were collected before the lens wear, and subjects were followed-up at a 6-month interval. Only the data of the right eyes were used for analysis. Mixed repeated measures analysis of covariance was applied to compare the within-subject time effect and between-subject treatment effect on SE and AL, controlled with age.

Results: A total of 135 children completed 6- and 12-month follow-ups (65 in BF group vs. 70 in SV group). Subjects in both groups had similar baseline age (mean ±SD; BF vs. SV; 10.0±1.5 vs. 10.2±1.5years), SE (BF vs. SV; -2.70±1.05D vs. -2.62±0.99D), and AL (BF vs. SV; 24.61±0.77mm vs. 24.62±0.77mm). Both SE and AL progressed significantly across time ($p<0.001$), and the interactions with age were both significant ($p<0.001$), in which older children tended to progress slower. The progressions in SE and AL were comparable between BF and SV groups (SE: $p=0.73$; AL: $p=0.73$).

Conclusions: Our findings demonstrated that the 12-month effect of BF lens on myopic progression in schoolchildren was insignificant, which could be due to the partial filtering of blue light. Thus, the contribution of wavelength on myopia development shall not be excluded, and a longer study period is warranted.

CONTROL ID: 3711121

SUBMITTER (NAME ONLY): Rui Wang

TITLE: Gender, Race, and Insurance Status affect Perceived Treatment Burden in Patients Receiving Repeated Intravitreal Injections: findings from the QUALITII Study

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Wang, E.M. Bowie, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|C. McClard, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|S. Laswell, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|E. Lehman, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|C. Regillo, Mid Atlantic Retina, Philadelphia, Pennsylvania, UNITED STATES|N. Saroj, All Eyes Consulting, New York, UNITED STATES|D.A. Eichenbaum, Retina vitreous associates of Florida, Florida, UNITED STATES|A.M. Khanani, Sierra Eye Associates, Nevada, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study characterizes the association of gender, race, and insurance status on burdensome aspects of repeated IVI using a validated patient survey to quantitatively measure patient burden.

Methods: QUALITII is a 50-item validated survey of patients receiving repeated IVI for retinal diseases (McClard et al 2021). The survey introduced the treatment burden score (TBS) composed of 9 items which examines the most salient aspects of burden. In this study, results from the multicenter QUALITII survey were analyzed using multivariate regression to understand how gender, race, and insurance status influenced patient-perceived burden.

Results: Of 1,416 patients surveyed from 4 large urban retinal clinics, 55% were women, 15% were non-White, and 32% had public health insurance only. Women reported more frequent eye pain (53%) and higher mean level of discomfort (2.01) than men (46%, 1.68) (p= 0.009; p=<0.001 respectively). Women reported mean anxiety level of 4.01 and men reported mean anxiety level of 4.51 during treatment (0=very anxious; p=<0.001). Non-White patients reported higher mean anxiety level (3.89) than reported by White patients during treatment (4.30) (p=0.017). A greater proportion of non-White patients reported spending >3 hours for clinic visits (18.9%) compared to proportion of White patients spending >3 hours (6.7%) (p=<0.001). A similar percentage of White and non-White patients required an escort to attend appointments, but non-White patients reported a lower convenience score (3.43) than reported by White patients (4.00) (p=0.002). No significant difference was reported by patients with public insurance compared to private insurance in terms of pain, anxiety, and inconvenience. Median TBS for private insurance (17) and public insurance (15) were equivocal (p=0.11). Median TBS was higher for women (17) than men (14) (p=<0.001) and higher for non-White (17) than White (15) patients (p=0.03).

Conclusions: There are gender and race disparities in perceived treatment burden associated with IVIs. TBS was highest in women and non-White patients. Moreover, the TBS was dictated by higher pain and anxiety score in women while the TBS in non-White patients was driven by higher anxiety and inconvenience of treatment. Insurance status did not have a significant effect on perception of burden.

CONTROL ID: 3711131

SUBMITTER (NAME ONLY): Ranjay Chakraborty

TITLE: Pattern of night-time light exposure before sleep in young adult myopes and emmetropes

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Chakraborty, G. Micic, N. Lovato, L. Lack, Flinders University, Adelaide, South Australia, AUSTRALIA|M.J. Collins, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Several recent studies have demonstrated poor sleep quality in myopes. A recent study found that young myopes have significantly delayed melatonin circadian timing, delayed sleep onset, greater sleep onset latency, and shorter sleep duration compared to emmetropes (Chakraborty et al, PMID: 33030546). To better understand these sleep characteristics in myopes, this study examined the differences in the pattern of night-time light exposure before sleep in myopes and emmetropes.

Methods: 14 emmetropes (mean refractive error, −0.09 ± 0.13 dioptres) and 17 myopes (−4.99 ± 2.18 dioptres) with a mean age of 22.07 ± 2.38 years had objective measures of ambient light exposure collected over 7 days, using a wrist-worn actigraphy device (Actiwatch 2). Measures of visible light illuminance were captured every 30 seconds, 24 hours a day over this period. The average daily light exposure, and light exposure for 1 hour (120 epochs), 3 hours (360 epochs) and 5 hours (600 epochs) before sleep onset, as determined by Actiwatch, were calculated. A linear regression was performed to examine the association between night-time light exposure and sleep onset, sleep latency and the total sleep duration reported in our recent publication (PMID: 33030546). All results are reported as average ± standard error mean.

Results: Compared to emmetropes (507.24 ± 106.65 lux), the average daily light exposure was significantly less in myopes (261.79 ± 52.99 lux, Mann–Whitney rank sum test, p=0.021). The average night-time light exposure across the five-hour duration before sleep was significantly greater in myopes (52.24 ± 8.28 lux) than in emmetropes (25.21 ± 9.47 lux, two-way ANOVA, p=0.014). The average light illuminance between the two groups wasn't significantly different for 1 hour (myopes, 20.81 ± 8.28 lux; emmetropes, 9.31 ± 9.47 lux) and 3 hours (myopes, 45.52 ± 8.28 lux; emmetropes, 29.14 ± 9.86 lux) before sleep onset (both p>0.05). The night-time light exposure was positively associated with delayed sleep onset (r^2 = 0.22, p=0.009), but not with sleep onset latency and sleep duration.

Conclusions: Young adult myopes had greater night-time light exposure compared to emmetropes, which was particularly evident 3 – 5 hours before sleep onset and may contribute to delayed sleep and circadian timing in myopes. These findings in myopes may be related to greater screen time or academic work at night and require further investigation.

CONTROL ID: 3711133

SUBMITTER (NAME ONLY): Prem Patel

TITLE: Electronic Communication Use in Ophthalmology: A Cross-sectional Study Across the United States

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Patel, Ophthalmology, The University of Texas Southwestern Medical Center Medical School, Dallas, Texas, UNITED STATES|S. Hoyek, N.A. Patel, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|H. Al-khersan, K.C. Fan, N. Yannuzzi, J. Sridhar, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize if and how ophthalmologists communicate with patients electronically.

Methods: A survey regarding ophthalmologists' electronic communication habits with patients was distributed online through an electronic mail (e-mail) listserv. Univariate analysis was performed to examine associations between demographic factors and communication with patients though phone calls and email.

Results: Of 92 respondents, the average age was 55.2 years old (range: 32-86). Respondents were predominantly male (70.7%) with >10 years of attending experience (81%). Overall, 37% of respondents choose not to provide any contact information to patients, 13% provide e-mail, 22.8% provide a phone number, and 27.2% provide both modes of contact. Reasons for sharing contact information include checking on post-operative patients (63%) or patients with complications (52.2%). Although most respondents (55.4%) do not discuss guidelines for using their personal e-mail or phone number with patients, the majority express little or no regret sharing their contact information (87%). The majority of respondents (75.2%) endorse reimbursement for extra time talking with patients outside of clinic appointments, however only 6.4% bill their calls. Furthermore, documentation habits for communication encounters in the electronic medical record (EMR) are variable, with 44.6% of physicians documenting most of the time and 30.4% rarely documenting. Among physicians with social media accounts, most allow patients to follow their professional (57.6%), but not personal accounts (14.3%).

Conclusions: Over one-third of attending ophthalmologists do not share email address or phone numbers with patients. Ophthalmologists may share their personal information more frequently for postoperative patients and those with complications. There is widespread support for reimbursements for time spent communicating with patients outside of clinic visits, however, billing and documentation of such encounters are inconsistent.

CONTROL ID: 3711134

SUBMITTER (NAME ONLY): Lisa Lin

TITLE: Dedicated Chalazion Excision Clinic as a Tool for Early Surgical Autonomy in Ophthalmology Residency

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.Y. Lin, G.W. Armstrong, P. Yadav, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmology residency programs aim to improve resident surgical teaching through increased surgical exposure and primary case numbers over a three-year period. Resident run surgical clinics across various surgical specialties have been founded to help develop surgical autonomy and earlier resident surgical experiences. We present the first demonstration of a resident run chalazion clinic in ophthalmology residency with the goal of increasing exposure to orbital procedures for junior residents or post-graduate year 2s (PGY2s).

Methods: The resident run chalazion clinic was founded in July 2020. Retrospective review of ACGME case logs of all residents per academic year before and after establishment of the chalazion clinic was performed in order to assess the number of chalazion excisions performed.

Results: A resident of any class year performed an average of 4.9 excisions prior to the founding of the clinic (91 total), and 14.4 excisions after the founding of the clinic (202 total). The average number of chalazion excision and drainages for each resident increased by 211.1% within the first year of the clinic. Among PGY2s, the average increased from 4.7 excisions per year to 22.3 excisions per year, a 374.5% increase. All juniors residents logged a minimum of 9 cases compared to only 87.5% residents logging a minimum of 3 cases.

Conclusions: To the best of our knowledge, this is the first description of a dedicated chalazion clinic or a resident run minor procedure clinic in ophthalmology. On average, all residents and PGY2s in particular, experienced an increase in the average number of chalazion excisions. While chalazion excisions have low complication rates and are not technically challenging, increased early exposure to and volume of ophthalmic procedures could help improve junior resident’s skills. This model is also beneficial as it offloads other outpatient ophthalmology and oculoplastics clinics, where chalazion excision and drainage may be difficult to add to the schedule or a lower priority for procedural scheduling. This clinic provides a proof of concept of a dedicated minor procedure clinic run by ophthalmology residents. Future directions include integrated future interns (PGY1s) into the clinic to further develop early procedural skills.

CONTROL ID: 3711137

SUBMITTER (NAME ONLY): Dhruv Shah

TITLE: Glaucomatous vs. non-glaucomatous anterior segment features in patients with Lowe oculocerebrorenal syndrome using ultrasound biomicroscopy

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Dortonne, M.M. Manrique, C. Martinez, W. Madigan, M. Jaafar, Department of Ophthalmology, Children's National Hospital, Washington, District of Columbia, UNITED STATES|D.M. Shah, T. Miglani, M.R. Levin, J. Alexander, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: All Lowe oculocerebrorenal syndrome (OCRL) patients develop dense bilateral congenital cataracts, but only 50% develop glaucoma. Carriers of OCRL are at risk for early onset cataracts in the 3rd to 4th decade, but show no increased risk of glaucoma. The cause of the variable glaucoma phenotype in OCRL is unknown, and contrasts sharply with the highly penetrant cataract phenotype. No studies detail the subclinical structural variations in the anterior segment between glaucomatous and non-glaucomatous pediatric OCRL patients. Quantitating these differences may inform why half of OCRL patients develop glaucoma. Ultrasound biomicroscopy (UBM) is a high-resolution imaging technique for noninvasive in-vivo imaging of these anterior segment structures. This prospective case-series compares structural features in UBM images between a pediatric OCRL patient with glaucoma and an OCRL patient without glaucoma.

Methods: We obtained quantitative UBM images of a 1.2-month boy with OCRL who developed glaucoma (diagnosed at age 2 months) to UBM images of a 0.9-month boy with OCRL who did not develop glaucoma after 5 years of follow up (4 eyes, 2 subjects). Iris, lens, angle, and corneal parameters were extracted from images and compared using box plots.

Results: In the setting of OCRL, increased lens reflectivity, steeper corneal curvature (CRC), increased angle opening distance (AOD), thinner central cornea (CCT), and a deeper anterior chamber (ACD) were noted in two eyes of the subject who later developed glaucoma compared to the subject without glaucoma. Mean differences were CRC= -0.95 mm, AOD=+0.49 mm, CCT=-0.04 mm, ACD=+0.32 mm. Angle to angle distance and lens thickness were similar between the subject with glaucoma compared to the subject without glaucoma.

Conclusions: Anterior segment evaluation using quantitative UBM for individuals with OCRL may identify structural risk factors for glaucoma. Future studies will be needed to determine the sensitivity and specificity of UBM features for prediction of glaucoma.

CONTROL ID: 3711139

SUBMITTER (NAME ONLY): Janice Hoi Man Mok

TITLE: The Monitoring of Neovascular Age-related Macular Degeneration with Choroidal Neovascular Membrane using Optical Coherence Tomography Angiography Scan

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mok, W. Lam, Department of Ophthalmology, The University of Hong Kong, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Janice Hoi Man Mok: Commercial Relationship: Code N (No Commercial Relationship) | Wai-Ching Lam: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study investigates the application of Optical Coherence Tomography Angiography (OCTA) in monitoring treatment response of choroidal neovascularization (CNV) in neovascular age-related macular degeneration (nAMD) following intravitreal anti-vascular endothelial growth factor (VEGF) injection.

Methods: In this prospective study, nAMD patients with fluorescein angiographic confirmed CNV who require anti-VEGF injection were included. Subjects received two OCTA scans, namely before and 4-6 weeks after the injection. 34 eyes from 32 subjects were studied between August 2020 and Dec 2021 at Grantham Hospital, Hong Kong. Correlation analysis between the interval changes on the consecutive OCTA scans, including the CNV classification type, vessel area, vessel density, morphology, border, and treatment outcome, including visual acuity (VA), central subretinal thickness (CST), is performed using SPSS Statistics.

Results: The subjects were of mean age 75.7 (63 - 92), a male to female ratio 1:28 to 1, and have a mean visual acuity of 0.232 (0.02 - 0.7). There were 4 eyes with Type 1 CNV, 14 with Type 2, and 7 with Type 4 CNV. CNV was unidentifiable in 9 eyes.

Eyes with type 2 CNV has significantly larger CNV area in outer and choriocapillaris layer, and lower density in choriocapillaris layer. The CNV area (before treatment 3.94 mm2, after treatment 2.76 mm2, P=0.03) and density (before treatment 0.53, after treatment 0.40, P=0.02) in choriocapillaris was significantly reduced in the repeated scan. Statistical analysis revealed significant correlations between the reduction in CNV vessel density in choriocapillaris layer and decreased CST (P=0.001); CNV vessel area in choriocapillaris layer were also significantly correlated to the improvement of VA (P=0.038).

Conclusions: With treatment, the reduction in CST corresponds to reduction in CNV density. This can be attributed to effective anti-angiogenesis and anti-permeability actions by the anti-VEGF treatment. Reduction of CNV area with treatment corresponds to the improvement of visual acuity.

A positive correlation between CNV area and density on OCTA scans and patient's treatment outcome hints at the potential use of OCTA scans to monitor disease progression.

CONTROL ID: 3711142

SUBMITTER (NAME ONLY): Hank Patrick

TITLE: Outcomes of infants with retinopathy of prematurity treated with intravitreal bevacizumab with or without laser ablation

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Patrick, Y. He, A. Wang, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Hank Patrick: Commercial Relationship: Code N (No Commercial Relationship) | Yu-Guang He: Commercial Relationship: Code N (No Commercial Relationship) | Angeline Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a leading cause of blindness in children in the US. It involves development of neovascularization in premature infants and can lead to retinal detachment and blindness. Treatment involves prevention of retinal detachment and has evolved from full-thickness cryotherapy to laser ablation. More recently, physicians have employed anti-VEGF agents, such as intravitreal bevacizumab (IVB), based on the pathophysiology of the disease and evidence from the BEAT-ROP and RAINBOW studies. However, there is a need for data on how these treatments influence the timing of the disease and monitoring recommendations in patients with ROP. This study investigates the outcomes of infants with ROP treated with IVB, including average time to complete revascularization and to subsequent laser therapy.

Methods: A retrospective, hospital-based study. Infants who met threshold for treatment and received IVB between 2018 and 2021 were included (n=20). Patients were monitored from their first ROP screening exam until complete revascularization or laser therapy. Age, weight, and risk factors for treatment were also analyzed.

Results: Patients had an average birth weight of 702 grams and average gestational age at birth of 24.8 weeks. Patients received IVB at an average post-menstrual age (PMA) of 37.1 weeks. 30% (n=6) of patients had disease regression and subsequent complete vascularization and did not require laser treatment. 35% (n=7) required laser for recurrence of ROP. 35% (n=7) required laser treatment for persistent avascular retina. Of those who fully vascularized without laser treatment, close monitoring was stopped at an average PMA of 51.2 weeks, or 18.9 weeks after IVB. Disease recurrence occurred at average PMA of 49.5 weeks, or 13.4 weeks after IVB. Laser for avascular retina occurred at average PMA of 60.9 weeks, or 25.6 weeks after IVB.

Conclusions: This study offers insight into the timing and management of ROP after IVB. Approximately one third of patients will develop recurrence of ROP following injection, and patients need to be followed up to PMA of 60 weeks to monitor for recurrence and to decide on need for laser treatment.

CONTROL ID: 3711145

SUBMITTER (NAME ONLY): Vicente Diaz

TITLE: A comparison study of the effects of ocular scaffolds on human ocular epithelial cells

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Diaz, Ophthalmology, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|Y. Mao, Rutgers The State University of New Jersey, New Brunswick, New Jersey, UNITED STATES|N. protzman, Healthcare Analytics Gallagher, Princeton, New Jersey, UNITED STATES|A. Kuehn, celularity, New Jersey, UNITED STATES|D. Long, celularity, New Jersey, UNITED STATES|A. Gosiewska, Rutgers The State University of New Jersey, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effect of three amniotic scaffolds (Biovance3L Ocular (Biovance3L), AMBIO2®, AmnioGraft®) on human ocular epithelial cell adhesion and proliferation.

Methods: Human corneal epithelial cells (HCEC) and human conjunctival epithelial cells (HConEpiC) were seeded into wells. Adhesion and proliferation were measured at days 1, 4 and 7 on the scaffolds. Extracted conditioned media was used for growth assays.

Results: Biovance3L showed significantly higher epithelial cell viability ($P < 0.001$) and significantly greater epithelial cell adhesion ($P \leq 0.011$) vs other scaffolds. Epithelial cell proliferation rate was
significantly greater on Biovance3L than AmnioGraft® ($P < 0.001$). HCEC migration from cells cultured on Biovance3L and AMBIO2® were comparable ($P = 0.885$) and significantly greater than AmnioGraft® ($P \leq 0.006$). The different scaffolds did not affect the migration of HConEpiC.

Conclusions: Biovance3L had a significant effect on human epithelial cells by supporting greater viability, adhesion, and proliferation compared with other scaffolds. Further research is needed to assess the clinical impact of these findings.

CONTROL ID: 3711146

SUBMITTER (NAME ONLY): Hiroko Iwashita

TITLE: Lubricating effect of three different eyedrops on contact lenses

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Iwashita, T. Itokawa, Y. Okajima, T. Suzuki, Y. Hori, Ophthalmology, Toho Daigaku, Ota-ku, Tokyo, JAPAN|

Commercial Relationships Disclosure: Hiroko Iwashita: Commercial Relationship: Code N (No Commercial Relationship) | Takashi Itokawa: Commercial Relationship: Code N (No Commercial Relationship) | Yukinobu Okajima: Commercial Relationship: Code N (No Commercial Relationship) | Takashi Suzuki: Commercial Relationship: Code N (No Commercial Relationship) | Yuichi Hori: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Many Soft Contact lens (SCL) users medicate several eyedrops to improve discomforts. Friction of both SCL and ocular surface is one of important factor for CL discomfort. This study aimed to detect lubricating effect of three different eyedrops (artificial tears, low surface tension artificial tears, 0.1% hyaluronic acid) by measuring coefficient of friction (CoF).

Methods: The CoF was measured by using developed pendulum friction tester. The weight of the load was set at 17.2 g and estimated the pressure on the CL surface as 1.1 kPa. The maximal sliding velocity was set to 90.0 mm/s. Three daily disposable conventional hydrogel lenses (etafilcon A+ polyvinylpyrrolidone, nelfilcon A, and omafilcon A containing 2-methacryloyloxyethyl phosphorylcholine [MPC]) and four silicone hydrogel lenses (narafilcon A, senofilcon A, delefilcon A, and stenfilcon A) were measured under three different types of lubricants, artificial tears, lubricants containing 2-MPC (MPC solution) and 0.1% hyaluronic acid.

Results: The mean ± SD of CoF of conventional hydrogel were Artificial tear; 0.038 ± 0.01, MPC solution; 0.036 ± 0.005, and 0.1% hyaluronic acid; 0.035 ± 0.005. Those of silicone hydrogel lenses were Artificial tear; 0.036 ± 0.004, MPC solution; 0.035 ± 0.003, and 0.1% hyaluronic acid; 0.036 ± 0.003. There were no significant differences of CoF among three lubricants and there was no significant difference of CoF between hydrogel and silicone hydrogel lenses. ($P > 0.05$).

Conclusions: Conclusions: Low surface tension artificial tears denotes high wettability on SCLs showed similar lubricate effect on SCLs as artificial tear and 0.1% hyaluronic acid. Three different eye drops showed similar lubricant effect on both conventional hydrogel and silicone hydrogel lenses. It was suggested that surface tension and viscosity of 0.1% HA on SCLs would not affect to CoF.

CONTROL ID: 3711147

SUBMITTER (NAME ONLY): Ting Zhou

TITLE: Corneal nerve changes in hyperglycemic mice: association with diabetic neuropathy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Zhou, A. Lee, J.J. Kwok, A.C. Lo, Ophthalmology, The University of Hong Kong, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Diabetic neuropathy represents the third most prevalent neurological disorder. Recent studies demonstrated that diabetic corneal nerve alternations may be a potential surrogate marker to reveal the peripheral nerve status of diabetic patients. Therefore, it is of great importance to investigate the dynamic changes of corneal nerves and its association with intraepidermal nerve damage upon hyperglycemia, which is helpful for further studies on the underlying pathophysiological mechanisms and therapeutic targets of diabetic neuropathy. We tested whether dynamic loss of corneal nerve occurred in the early stage of diabetic neuropathy using in vivo microscopy in a diabetic mouse model.

Methods: 8-week-old Thy-1/YFP mice were injected with 50 mg/kg streptozotocin (STZ) for 5 consecutive days for hyperglycemia induction. Bodyweight and blood glucose levels were recorded weekly. Corneal sensitivity was tested with Cochet-Bonnet esthesiometer weekly. At 4, 8, 12, 16, 20, and 24 weeks after STZ injection, corneal nerves and epidermal nerves from the hind paw and leg skin were visualized with in vivo microscopy. Meanwhile, corneal and epidermal nerve analyses were performed on corneal flat mount and skin from the hind paw and leg, respectively using Imaris and Neuron J software.

Results: Hyperglycemia was successfully induced and led to a loss of corneal nerve fiber. At 4 weeks after STZ injection, the total number of nerve fibers in the central cornea showed a significant loss (23.6±3.7%) while subbasal nerve plexus in the central cornea showed a loss in corneal nerve fiber density (CNFD), corneal nerve fiber length (CNFL) and corneal nerve branch density (CNBD). At 16 weeks after STZ injection, the total number of nerve fibers in the peripheral cornea was significantly decreased (46.2±4.6%). Subbasal nerve plexus in peripheral cornea showed a loss in CNFD, CNFL, and CNBD. At 24 weeks after STZ injection, corneal nerve fibers could be detected except the ones in the stroma. More importantly, these pathological features occurred earlier than changes in epidermal nerve fibers and earlier than cornea functionality (corneal sensitivity test).

Conclusions: Our results show that in vivo microscopy, a non-invasive tool for longitudinal nerve fiber detection, revealed dynamic changes in corneal nerves upon hyperglycemia, suggesting that monitoring of corneal nerve fiber may lead to earlier diagnosis of diabetic neuropathy.

CONTROL ID: 3711149

SUBMITTER (NAME ONLY): Arjun Nanda

TITLE: FIJI-assisted automatic quantitative volumetric analysis of CNV in a laser-induced CNV mouse model

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nanda, The University of Oklahoma College of Medicine, Oklahoma City, Oklahoma, UNITED STATES|D. Pollalis, S. Lee, Ophthalmology, Dean McGee Eye Institute, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|S. Lee, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Arjun Nanda: Commercial Relationship: Code N (No Commercial Relationship) | Dimitrios Pollalis: Commercial Relationship: Code N (No Commercial Relationship) | Sun Young Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Accurate and precise as well as efficient measurements of choroidal neovascularization (CNV) lesions are important in the laser-induced CNV mouse model, one of the major animal models used in developing therapeutic agents for various neovascular retinal diseases. We present the utility of FIJI-assisted automatic quantification of the total volume of CNV.

Methods: Laser-induced CNV was induced in C57BL/6J mice according to the established protocol. Following CNV induction, mice were treated with intravitreal injection of either PBS (n=6-7) or aflibercept (Eylea®) (n=11). One week after treatment, RPE/choroid flat mounts were stained with rhodamine-conjugated Griffonia simplicifolia lectin B4 (GSA). Z-stacks of the entire CNV lesion obtained using laser confocal microscopy were converted to binary stacks using FIJI. Thresholded voxels were quantified using the Voxel-Counter Plugin. Data from volumetric analysis and multiple area analyses from blindly selected, mean, and a maximum of measured areas using FIJI were compared.

Results: FIJI-assisted automatic quantitative volumetric analysis of CNV was useful in detecting experimental outliers in laser-induced CNV genesis and provided accurate and precise measurements of total areas of CNV with a lower coefficient of variance (63%) than in multiple area analyses, including blindly selected, mean, and a maximum of measured areas (76%, 69%, and 67% respectively). A lower coefficient of variance resulted in increased statistical significance (p-value) when comparing CNV lesions in PBS and Eylea treated groups (Figure).

Conclusions: FIJI-assisted automatic quantitative volumetric analysis can be useful for accurate, precise and efficient measurements of total areas of CNV. Further, this approach can be advantageous in determining the efficacy of therapeutic agents in the laser-induced CNV mouse model.

CONTROL ID: 3711154

SUBMITTER (NAME ONLY): Archana Nair

TITLE: Inflammatory Mediators in the Pathophysiology of Diabetic Retinopathy (INSPIRE): Correlation of Inflammatory Markers in Ocular Samples and Serum.

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Nair, J. Fitzpatrick, S. Al-Awamlh, J. Sheng, K. Scavelli, P. Mallory, S. Gangaputra, S.J. Kim, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study aims to establish a correlation of serum inflammatory markers with aqueous samples in patients without diabetic retinopathy. Several cytokines are elevated in the aqueous and vitreous of patients with advanced diabetic retinopathy(DR) and may be future targets for therapy to prevent DR progression. However, the correlation of these ocular inflammatory markers with serum inflammatory markers is unknown. Currently the only serum marker for Diabetes is HbA1c which does not directly reflect the current DR stage.

Methods: This cohort was a cross-sectional study of patients with no diabetic retinopathy who underwent vitrectomy surgery for non-inflammatory conditions. Demographic and clinical data was obtained from chart review. Aqueous humor and serum samples were obtained from all patients concurrently and analyzed for 24 different inflammatory markers. The correlation between serum and ocular cytokines were evaluated using Pearsons correlation.

Results: A total of 70 patients were included in this analysis. 51.4% of the patients were female and 91.4% were Caucasian. 60% of patients were pseudophakic. One patient was treated with Imatinib for metastatic GI Stromal cancer and 4 patients were treated with Latanoprost for elevated IOP. No other patients were on systemic or topical anti-inflammatory medications. 40% of patients underwent surgery for vitreous floaters, 23% for ERM, 20% for Macular Hole, and other non-diabetic indications for vitrectomy. Of the 24 markers evaluated, a total of 6 cytokines were found to have a statistically significant correlation between the aqueous and serum. The following markers had a positive correlation coefficient FIT 3L ($R=0.3017$, $p=0.01$), MCP 3 ($R=0.4072$, $p< 0.001$), MDC ($R=0.3025$, $p=0.01$), IL4 ($R=0.554$, $p=<0.001$). A negative correlation was seen in VEGF ($R=-0.257$, $p=0.032$) and sCD40L ($R=-0.2708$, $p=0.02$).

Conclusions: This study documents the correlation of ocular to serum inflammatory markers in normal eyes. Subsequent longitudinal analyses from this clinical trial studies will evaluate the association between serum and ocular cytokines in various stages of diabetic retinopathy. The data in this study will be invaluable as a baseline for future analysis to evaluate cytokines in diabetic retinopathy.

CONTROL ID: 3711156

SUBMITTER (NAME ONLY): Carly Lam

TITLE: Myopia control in children wearing DIMS spectacle lens: 6 years results

SESSION TITLE: Refractive Error and Social Determinants of Vision Function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.S. Lam, W. Tang, H. Zhang, D.Y. Tse, C. To, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, Hung Hom, CHINA|C.S. Lam, H. Zhang, D.Y. Tse, Centre for Eye and Vision Research (CEVR), Centre, Hong Kong, CHINA|C. To, Research Centre for SHARP Vision, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: To evaluate the changes in refraction and axial length for a period of 6 years in children who completed the two-year clinical trial of Defocus Incorporated Multiple Segment (DIMS) lenses.

Methods: Myopic children who had completed the 2-year randomized clinical trial of DIMS lens were included in this follow-up study. Their cycloplegic refraction and axial length (AL) were measured up to 6 years. Children who changed to other myopia control methods were excluded. Participants were divided into 4 groups - Group 1: wore DIMS spectacles for a total of 6 years (include first two years in RCT); Group 2 wore DIMS spectacles in the first 3.5 years and changed to wear SV spectacles afterward; Group 3: wore SV spectacles in the first 2 years of RCT and switched to wear DIMS spectacles afterward; Group 4: wore SV spectacles in the first 2 years of RCT and switched to wear DIMS spectacles in the 3rd year and then switched to wear SV spectacles lens till end of the 6^{th} year. Changes in spherical equivalent refraction (SER) and AL over the 6 years were analyzed and compared.

Results: 90 children completed the data collection at for a period of 6 years. The children in Group 1 (n=36) wore DIMS lenses throughout the study had -0.92 ± 1.15D of myopia progression and 0.60 ± 0.49mm of axial elongation. The mean annual changes were 0.15D and 0.10mm. Group 2 (n=14) stopped DIMS lens wear after the first 3.5 year and showed more myopia progression (mean differences: 0.2D) and axial elongation (0.07mm) than those in Group 1 between year 3.5 to year 6. Children in both Group 3 (n=22) and Group 4 (n=18) who wore the SV spectacles in the first two years and then switched to wear DIMS lens. Their rate of myopia progression and axial elongation decreased after switching to DIMS lens wear. Children in Group 4 exhibited faster myopic progression when they stopped the DIMS lens wear from year 3.5 to year 6.

Conclusions: DIMS lens maintained the effect on slowing myopia progression and axial growth in myopic children over a period of 6 years. When children stopped DIMS lens wear and wore single vision lenses, their myopia progression was faster than the children who continued with DIMS lens wear.

CONTROL ID: 3711157

SUBMITTER (NAME ONLY): Goutham Pyatla

TITLE: Multi-Allelic Interactions of Glaucoma and Anterior Segment Dysgenesis-Associated Genes in the Pathogenesis of Primary Congenital Glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Pyatla, S. Bera, A. Anthony, A. Mishra, I. Kaur, S. Chakrabarti, Kallam Anji Reddy Molecular Genetics Laboratory, Prof. Brien Holden Eye Research Center, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|L. Moreno-Leon, H. Khanna, Department of Ophthalmology, University of Massachusetts Medical School, Worcester MA, Massachusetts, UNITED STATES|A.K. Mandal, S. Senthil, Jasti V Ramanamma Children's Eye Care Centre, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|A.K. Mandal, S. Senthil, VST Centre for Glaucoma Care, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|R.C. Khanna, Allen Foster Community Eye Health Research Centre, Gullapalli Pratibha Rao International Centre for Advancement of Rural Eye Care, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|R.C. Khanna, School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, New York, UNITED STATES|L. Moreno-Leon, H. Khanna, Iveric Bio, Parsippany, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary congenital glaucoma (PCG) is an autosomal recessive disease that occurs due to developmental defects in the anterior chamber angle and trabecular meshwork. The resulting resistance to aqueous humor outflow raises the intraocular pressure and damages the optic nerve. PCG exhibits considerable genetic heterogeneity, and the known mutation spectrum does not explain the entire genetic basis of this disease. As anterior segment dysgenesis (ASD) and PCG share overlapping phenotypes, we determined the involvement of ASD-associated genes in PCG pathogenesis.

Methods: A large cohort of PCG cases (n=586) and ethnically matched controls (n=1758) were screened by deep sequencing with a customized gene panel comprising of known ASD-associated genes using the Ion Ampliseq chemistry. A combination of GATK and Haploview softwares was used for variant analysis. The identified variants were validated by Sanger sequencing. Pathogenicity of the variants was determined through SIFT, PolyPhen2 and Mutation Taster scores. Ingenuity Pathway Analysis (IPA) was used for network and pathway analyses.

Results: We identified 71 novel and rare pathogenic variants in 123 (20.9%) PCG cases across the ASD genes: FBN1, HMX1, LMX1B, MAF, PITX3, PRDM5, RAX, SIX1, SIX6, SLC4A11, SOX2, TRIM44, VAX1 and WT1. The affected amino-acid residues were conserved across multiple species and the variants were either absent or rarely observed in our controls and global databases. We also identified 52 significantly associated polymorphisms conferring risk to PCG. These genes shared similar molecular functions and were involved in the regulation of Wnt and Hedgehog signaling and cell growth and survival pathways (Akt/PI3K/NfkB). Moreover, we detected co-occurrence of pathogenic variants between ASD and PCG candidate genes in 63 cases (10.75%) indicating potential multi allele interactions and possible dysregulation of multiple pathways in PCG.

Conclusions: Our results expand the mutation spectrum of PCG with the identification of pathogenic variants in ASD genes and suggest their potential involvement in PCG. Our observations on the co-occurrences of pathogenic variants in ASD and PCG candidate genes suggest gene-gene interactions in PCG pathogenesis.

CONTROL ID: 3711163

SUBMITTER (NAME ONLY): Chia Ching Lin

TITLE: Comparison of serum autoantibody against aldehyde dehydrogenase 2 and thyrotropin receptor antibody in patients with Grave's ophthalmopathy

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lin, ophthalmology, Kaohsiung Medical University Chung Ho Memorial Hospital, Kaohsiung, TAIWAN|

Commercial Relationships Disclosure: Chia Ching Lin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Grave's ophthalmopathy (GO) is an autoimmune disorder characterized by orbital inflammation and is associated with Grave's hyperthyroidism. Thyrotropin receptor autoantibody (TRAb) was first identified to be related to Grave's hyperthyroidism and have been demonstrated to be associated with the clinical activity score (CAS) of GO in some studies, while in others its correlation with the severity of GO was controversial. Our previous study has identified an autoantibody against aldehyde dehydrogenase 2 (ALDH2) which has strong correlation with CAS in patients with GO. With the previous literatures that showed TRAb are correlated with the CAS of GO patients, we would expect their titers to be correlated with the titers of anti-ALDH2 antibody. The purpose of this study is to compare the serum titers of anti-ALDH2 antibody and TRAb in patients with GO.

Methods: Fifty patients with active GO were enrolled in this study. The patients' thyroid function status, medical history, surgical history, and serum anti-ALDH2 antibody and TRAb titers were collected. All patients were examined by the same ophthalmologist to determine the levels of the CAS. The correlation coefficients between serum anti-ALDH2 antibody, TRAb, and thyroid function, and the CAS were calculated by Pearson's and Spearman's rho correlation analysis.

Results: There was significant correlation between the titers of anti-ALDH2 antibody and the CAS ($r=0.301$, $p<0.05$) (Figure 1), but not between the titers of anti-ALDH2 antibody and TRAb ($r=0.014$, $P=0.921$). The TRAb level was significantly correlated with T3 and TSH levels ($r=0.406$ and -0.32, $p<0.05$, respectively), but had no significant correlation with the CAS ($r=0.021$, $p=0.884$) (Table 1).

Conclusions: The level of anti-ALDH2 antibody was significantly correlated with the CAS but not the TRAb level and thyroid function, suggesting that it might be more specific to orbital tissue and the disease activity of GO. The TRAb level was significantly associated with thyroid function instead of the clinical activity of GO, indicating its role in Grave's hyperthyroidism rather than ophthalmopathy.

CONTROL ID: 3711170

SUBMITTER (NAME ONLY): Karen Wai

TITLE: Recovery of Vision in Open Globe Injury Patients with Initial No Light Perception Vision

SESSION TITLE: Endophthalmitis & Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.M. Wai, N.A. Sherif, M. Tieger, G.W. Armstrong, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The recovery of vision in open globe injuries (OGI) in patients who present with no light perception (NLP) vision is poorly understood. These patients often undergo primary enucleation or evisceration to mitigate the risk of sympathetic ophthalmia. We conducted a retrospective chart review to identify patient characteristics, OGI features, and surgical events that may predict the recovery of any vision in patients initially presenting with NLP vision to inform clinical management.

Methods: The Massachusetts Eye and Ear (MEE) OGI Database was used to identify patients with NLP vision at presentation from January 1999 to December 2019. The medical records of these patients were analyzed to identify demographic characteristics; zone of injury; time from injury to surgical repair; need for vitrectomy; presence of retinal detachment, vitreous hemorrhage, intraocular foreign body (IOFB), hyphema, amongst 17 other features; and visual acuity (VA) at last follow-up appointment. Logistic regression was used to analyze the relationship between regained vision at the most recent follow-up visit and the above dependent variables (Python 3.10.1). Patients without a documented VA at most recent follow-up were excluded.

Results: A total of 294 OGI cases with NLP at presentation that met inclusion criteria were identified, of which, 119 cases (35.95%) regained better than NLP vision at most recent follow-up. Regained vision ranged from VAs of 20/70 (3.36%) to LP (35.29%). Nine (3.06%%) Zone I, 52 (17.69%) Zone II, 118 (40.14%) Zone III, and 115 (29.12%) Zone unknown injuries were documented. Vitrectomy was positively associated with regained vision (B=2.2, p=0.002), while previous intraocular surgery was negatively associated with regained vision (B=-0.9, p=0.03). Both the presence of an IOFB and OGI repair within ten hours of injury approached statistical significance for association with regained vision (B=-1.5, p=0.08 and B=0.9, p=0.09, respectively).

Conclusions: While OGIs cause severe ocular morbidity, a significant proportion of OGIs with initial NLP vision regained some vision during follow-up care. Previous intraocular surgery was negatively associated with return of vision, while vitrectomy was positively associated. These findings argue for primary closure of OGIs given potential for return of vision rather than primary enucleation, even in the presence of NLP vision at initial presentation.

CONTROL ID: 3711172

SUBMITTER (NAME ONLY): Daniel Tilia

TITLE: Binocular and Accommodative Function of S.T.O.P® contact lenses compared to MiSight

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Tilia, D. Falk, K. Ehrmann, J. Diec, C. Fedtke, R.C. Bakaraju, nthalmic Pty Ltd, Botany, New South Wales, AUSTRALIA|D. Tilia, D. Falk, K. Ehrmann, C. Fedtke, R.C. Bakaraju, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To compare the binocular and accommodative function of Spatio-Temporal Optical Phase (S.T.O.P®) contact lenses (CL) against MiSight® (MS) in myopic young adults. S.T.O.P CL feature rotationally asymmetric power maps, designed with meridionally and azimuthally varying power distributions, combined with a peripheral carrier configured with rotation assisting features The resulting dynamic optical signal on the retina may decelerate the rate of myopia progression and minimise the decay of treatment effect found in options which provide a relatively static optical signal.

Methods: Prospective, randomized, single-masked (participant), cross-over trial where participants aged 18-39 years wore MS and two S.T.O.P designs (F2 and DT), each for a minimum of 5 days at 6 hours/day, daily wear, with CLEARCARE disinfection. Assessments occurred while wearing each design at the end of the wearing cycle. Binocular function assessments comprised phoria at 3m and 40cm (Modified Thorington). Accommodative function measurements comprised monocular accommodative facility (MAF) at 40cm (±2.00D, left eye occluded), and dynamic accommodative response (AR) at 6m, 70cm, and 40cm. Dynamic AR was calculated from autorefraction measurements (Grand Seiko WAM5500, high speed mode: 6 measurements/s) on the left eye (not wearing a CL and occluded under black cardboard placed on the tilted hot mirror), while the right eye (wearing a CL) viewed each target. Customized hardware was used to coordinate measurements, which were recorded for 8s at each distance (144 measurements in total).

Differences between designs were assessed using linear mixed model, a Bonferroni correction was applied where applicable, and significance was set at 5%.

Results: While wearing F2 compared to MS, MAF was higher (12.2±5.9 vs. 10.5±5.3, p=0.007) and AR was lower at 70cm (0.75±0.36 vs 0.95±0.37, p<0.001) and 40cm (1.58±0.55 vs 1.74±0.50, p=0.007). The SD of AR measurements was also lower with F2 compared to MS at 70cm and 40cm (p<0.001), suggesting accommodation was more consistent with F2. There were no differences between designs for phoria at either 3m or 40cm (p>0.2), nor were there any differences between DT and MS for any measurement (p>0.06).

Conclusions: Both S.T.O.P designs were comparable to MS for binocular function. DT was comparable to MS for accommodative function. F2 was better for MAF and required less accommodation compared to MS.

CONTROL ID: 3711176

SUBMITTER (NAME ONLY): Taeyoung Na

TITLE: The novel function of NN2101, an anti-c-kit antibody, as an inhibitor of HIF via c-kit regulation in ocular neovascular disease

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Na, J. Kim, S. Park, Novelty Nobility, Seongnam-si, Gyeonggi-do, KOREA (THE REPUBLIC OF)|S. Park, College of Pharmacy and Research Institute of Pharmaceutical Science and Technology (RIPST), Ajou University, Suwon, Gyeonggi-do, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Taeyoung Na: Commercial Relationship(s);Code P (Patent):Novelty Nobility | Jae-Won Kim: Commercial Relationship(s);Code P (Patent):Novelty Nobility | Sang Gyu Park: Commercial Relationship(s);Code P (Patent):Novelty Nobility

ABSTRACT BODY:

Purpose: Recent preclinical data and post hoc analysis of clinical data suggest the importance of new approaches that inhibit the generation of pathological levels of VEGF while maintaining physiological levels of VEGF in ocular neovascular disease (NV). Here, we investigated the novel function of a fully human monoclonal IgG anti-c-kit antibody (NN2101) in inhibiting hypoxia and pathological angiogenesis while maintaining trophic factor homeostasis.

Methods: HRMEC, RPE, MIO-M1, and Y79 cells were used in vitro to demonstrate the inhibitory effect of NN2101. Proteomic secretome profiling was performed to identify angiogenesis- and inflammation-related proteins in hypoxia-conditioned media. Also, db/db mice were treated every 2 weeks with NN2101 via intravitreal injection for 16 weeks.

Results: Hypoxia-induced expression of c-kit, HIF, and VEGF in Muller glial, photoreceptor, and RPE cells was reduced by NN2101. Interestingly, NN2101 reduced HIF-1α protein stability via the ubiquitin-proteasome pathway. In addition, NN2101 decreased tube formation, migration, and proliferation of hypoxic endothelial cells. Consistently, in vivo Matrigel plug assay showed NN2101 inhibits neovascularization. HRMEC/RPE co-culture exhibited that HIF-1α inhibition by NN2101 effectively blocks VEGF secretion from RPE, similar to Eylea. Also, secretome analysis under hypoxia showed proangiogenic factors, including HIF target genes related to AMD, RVO, and DR were up-regulated, an effect significantly reduced by NN2101 vs Eylea. In muller glial and photoreceptor cells, NN2101 treatment maintained VEGF at basal levels even under the hypoxic conditions, whereas Eylea reduced VEGF to 10% of basal levels. In db/db mice, NN2101 rescued apoptosis in the ganglion cell layer, whereas Eylea-treated mice showed increased apoptotic cell death compared to vehicle control. Analysis of ERG waveforms and immunofluorescence staining demonstrated that the function of photoreceptors, amacrine, and Muller glial cells were significantly improved by NN2101 in the db/db mouse. Also, the number of degenerative capillaries was significantly decreased by NN2101 treatment compared to control.

Conclusions: We demonstrated that c-kit inhibition with NN2101 efficiently suppresses pathological vessels by reducing expression of multiple angiogenic cytokines via destabilization of HIF in the retina.

CONTROL ID: 3711178

SUBMITTER (NAME ONLY): Pourya Hoseini

TITLE: Reducing the size of glaucoma neuroprotective clinical trials through deep learning-based retinal structural predictions

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Hoseini, M. Christopher, E. Walker, J.A. Proudfoot, C. Bowd, R.N. Weinreb, L.M. Zangwill, D.S. Welsbie, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|M.A. Fazio, C.A. Girkin, The University of Alabama at Birmingham School of Medicine, The University of Alabama at Birmingham School of Medicine, Birmingham, AL, US, academic/medsch, Birmingham, Alabama, UNITED STATES|G. De Moraes, J.M. Liebmann, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|A. Schwartzman, Division of Biostatistics, University of California San Diego, La Jolla, California, UNITED STATES|A. Schwartzman, Halicioğlu Data Science Institute, University of California San Diego, University of California San Diego, La Jolla, CA, US, academic, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the efficacy of a deep learning regression method to predict macula ganglion cell-inner plexiform layer (GCIPL) and optic nerve head (ONH) retinal nerve fiber layer (RNFL) thickness for use in glaucoma neuroprotection clinical trials.

Methods: Glaucoma patients with good quality macula and ONH scans were enrolled in two longitudinal studies, the African Descent and Glaucoma Evaluation Study (ADAGES) and the Diagnostic Innovations in Glaucoma Study (DIGS). Spectralis macula posterior pole scans and optic nerve head (ONH) circle scans on 3327 pairs of GCIPL/RNFL scans from 1096 eyes (550 patients) were included. Participants were randomly distributed into training (502 participants) and test (48 participants) sets. Networks had access to GCIPL and RNFL data from one hemiretina of the probe eye and all data from the fellow eye. The models were then trained to predict the GCIPL or RNFL thickness of the remaining probe eye hemiretina (see Figure). Mean absolute error (MAE) and r^2, calculated using each individual bin (“global”) or averaged over the entire hemifield (“mean”), were used to evaluate model performance.

Results: The deep learning model was able to predict superior and inferior GCIPL thicknesses with a global r^2 values of 0.90 and 0.86, r^2 of mean of 0.90 and 0.86, and mean MAE of 3.7 μm and 4.2 μm, respectively (see Table). For superior and inferior RNFL thickness predictions, model performance was slightly lower, with a global r^2 of 0.75 and 0.84, r^2 of mean of 0.81 and 0.82, and mean MAE of 9.3 μm and 8.5 μm, respectively. There was only a modest decrease in model performance when predicting GCIPL and RNFL in more severe disease. Using our predictions, we

estimate that we can reduce patient numbers by 11-fold compared to a conventional trial.
Conclusions: Our deep learning models were able to accurately estimate both macula GCIPL and ONH RNFL hemiretinal thickness. These model predictions may help reduce clinical trial sample size requirements and/or trial duration and facilitate the development of neuroprotective glaucoma therapies.

CONTROL ID: 3711181

SUBMITTER (NAME ONLY): Melinda Toomey

TITLE: Benchmarking glaucoma primary care delivery in Australia

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Toomey, K. Ho, R. Gyawali, F. Stapleton, L. Keay, I. Jalbert, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|K. Ho, Optometry and Vision Science, University of Canberra Faculty of Health, Canberra, Australian Capital Territory, AUSTRALIA|

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ABSTRACT BODY:

Purpose: A national audit of Australian optometry practices estimated the appropriateness of glaucoma primary care against evidence-derived clinical indicators. Benchmarking is a quality improvement activity; however, benchmarks for glaucoma primary care delivery do not exist. We developed benchmarks for glaucoma primary care delivery.

Methods: Normative and realistic benchmarks were developed as more than one comparator improves feedback credibility. A systematic review identified 11 glaucoma audit studies for inclusion. Compliance score averages were extracted to provide normative benchmark ranges. Realistic benchmarks were separately derived from the pre-existing nationally representative dataset using the Achievable Benchmarks of Care (ABC) method. A Bayesian adjustment was used to limit effect of small numbers of eligible patient encounters on practice appropriateness scores. ABCs were calculated from the top ten percent of Bayesian adjusted appropriateness scores. The appropriateness scores for each practice were compared to the developed benchmarks to explore distribution of practices that were at or above benchmarks.

Results: Normative benchmarks were established for 17 clinical indicators. The normative benchmarks for 8 (of 17) indicators were met by more than 80% of practices. Realistic benchmarks were calculated for 34 clinical indicators with 26 indicators having realistic benchmarks set at or above 90% appropriateness. The realistic benchmarks for 14 (of 34) clinical indicators were met by more than 80% of practices. There were 10 clinical indicators where most (>80%) of the optometry practices did not meet either benchmark (Fig). These indicators related to the identification of glaucoma risk factors (migraine history, steroid use, high and low blood pressure status), side effects of glaucoma medication, and physical examinations (applanation tonometry, gonioscopy or van Herick angle assessment, size of optic disc, pattern of neuroretinal rim, visual field assessment).

Conclusions: This study established normative and realistic benchmarks for glaucoma primary care clinical indicators. Most Australian optometry practices provided care at or above the benchmarks. Pockets of sub-optimal care delivery identified should be targeted for quality improvement. The developed benchmarks may be used to provide feedback and monitor the success of such programs.

CONTROL ID: 3711185

SUBMITTER (NAME ONLY): Jing Hou

TITLE: Ginkgo biloba Extracts Showed Myopia Suppressive Effects in a Lens-Induced Myopia Model in Mice

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hou, K. Mori, S. Ikeda, H. Jeong, H. Torii, K. Negishi, T. Kurihara, K. Tsubota, Ophthalmology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|J. Hou, K. Mori, S. Ikeda, H. Jeong, H. Torii, T. Kurihara, Laboratory of Photobiology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|K. Tsubota, Tsubota Laboratory, Inc., Shinjuku-ku, Tokyo Japan, Shinjuku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose:

Screening of food materials for myopia suppressive factors measuring expression of early growth response 1 (Egr-1), a myopia suppressive gene, demonstrated that ginkgo biloba extracts (GBEs) increase Egr-1 activity in a previous study. This study was aimed to assess the suppressive effects of GBEs on myopia using a lens-induced myopia model in mice.

Methods: 3-week-old male C57B6/ J mice were randomly assigned to three groups: mice fed with normal chow and equipped with 0 diopter (D) lenses to their both eyes (control group), mice fed with normal chow and equipped with -30 D lenses to their both eyes (myopia-induced group), and mice fed with 0.0667% GBEs and equipped with -30 D lenses to their both eyes (GBEs group) (n = 8 in each group). Refraction, axial length, and choroidal thickness were measured with an infrared photorefractor and an SD-OCT system before and 3 weeks after feeding.

Results: Compared with the control group, refraction ($p < 0.001$), axial length ($p < 0.05$), and choroidal thickness ($p < 0.001$) showed myopic shifts in the myopia-induced group three weeks after normal feeding. In the GBEs group, change in refraction was significantly suppressed compared with the myopia-induced group (-1.59 ± 3.90 D vs. -9.92 ± 2.49 D, $p < 0.001$). Change in axial length was significantly suppressed compared with the myopia-induced group (0.19 ± 0.04 mm vs. 0.22 ± 0.02 mm, $p<0.05$). Change in choroidal thickness in the GBEs group was significantly suppressed compared with the myopia-induced group (-0.27 ± 0.47 um vs. -1.32 ± 0.56 um, $p < 0.01$).

Conclusions: GBEs showed suppressive effects on myopia in mice.

CONTROL ID: 3711186

SUBMITTER (NAME ONLY): Philippe Morquette

TITLE: A Retinal Representation of Environmental Illumination within the Master Circadian Clock

SESSION TITLE: Retinal ganglion cells and central processing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Morquette, M.H. Do, F.M. Kirby Neurobiology Center, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Philippe Morquette: Commercial Relationship: Code N (No Commercial Relationship) | Michael Tri Do: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mammals sense light primarily with rods, cones, and intrinsically photosensitive retinal ganglion cells (ipRGCs). IpRGCs support a variety of visual processes, one of the most important being synchronization of the circadian clock with the solar day. These neurons provide practically all retinal input to the master clock, the suprachiasmatic nucleus (SCN; located in the hypothalamus). The clock responds to irradiance, the overall intensity of illumination, rather than image detail. We hypothesized that ipRGCs send an effective representation of irradiance to the master clock.

Methods: To preserve natural ipRGC responses and obtain a high level of experimental control, we used an ex vivo, acute brain slice that contained most of the SCN and retained intact connectivity with both retinas (Wong, Graham, and Berson 2007 J Biol Rhythms). We made these explants from adult mice in which ipRGC axons and presynaptic terminals expressed an optical reporter of activity. We imaged this reporter with multiphoton microscopy while delivering visual stimuli to the retinas.

Results: The signals conveyed from ipRGCs to the SCN are complex and dynamic. IpRGC terminals are differentially tuned to light intensity, with distinct subsets activated across the environmental range. The most common terminal is silent when the intensity is below or above its preferred range. Terminals also vary in their response kinetics, with some remaining activated long after the period of illumination. Terminals with different tunings and response kinetics are intermingled within the volume of the SCN. Finally, the retina-SCN explant is robust, with light responses remaining for at least 24 hours after preparation.

Conclusions: IpRGC signals within the SCN appear to support an effective representation of irradiance. By preferring different irradiance ranges, each ipRGC encodes its range at high resolution and the population of ipRGCs collectively encodes a broad range. By silencing outside of their preferred ranges, ipRGCs potentially save energy. By producing persistent responses, ipRGCS smooth temporal contrast to favor the representation of ambient illumination rather than image detail. Moreover, the full spectrum of ipRGC signals appears to be repeated throughout the SCN and is thus broadly available to postsynaptic neurons.

CONTROL ID: 3711187

SUBMITTER (NAME ONLY): Harpal Sandhu

TITLE: Hospitalization for Coronavirus Disease 2019 in Uveitis Patients on Conventional Immunomodulatory or Biologic Therapy: Is IMT Harmful?

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.A. Sandhu, Retina Northwest, Portland, Oregon, UNITED STATES|H.A. Sandhu, Bioengineering, University of Louisville, Louisville, Kentucky, UNITED STATES|L. Park, Z. Steckler, Bing Zhang Department of Statistics, University of Kentucky, Lexington, Kentucky, UNITED STATES|J. Lambert, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|C. Yang, Harvard Medical School, Boston, Massachusetts, UNITED STATES|C. Yang, Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients on systemic immunomodulatory therapy (IMT) for uveitis are at higher risk of infection and infectious complications. While other medical specialties have studied the safety of IMT in non-ocular, autoimmune conditions vis-à-vis coronavirus disease 2019 (COVID-19), little is known about the effects of these drugs in uveitis patients specifically. The objective of this study was to determine if uveitis patients with COVID-19 were at higher risk of hospitalization for this pandemic illness and whether systemic IMT affected this risk.

Methods: Retrospective cohort study of uveitis patients in 2020 in the United States. The Symphony health insurance claims dataset was used. Inclusion criteria were an ICD10 code for COVID-19, a code for any form of non-infectious uveitis or scleritis, and age 18 or greater. Drugs studied included methotrexate, mycophenolate, azathioprine, tacrolimus, cyclosporine, adalimumab, infliximab, tocilizumab, rituximab, and JAK, IL-17, and IL-12/23 inhibitors. The main outcome measure was adjusted odds of hospitalization for COVID-19. Multivariable logistic regression was used to adjust for major risk factors for severe COVID-19 disease, including age, biological sex, cardiac, pulmonary, hepatic, and renal disease, obesity, organ transplant, stroke, and certain cancers.

Results: 3,974,272 patients in the dataset were diagnosed with COVID-19 in 2020. Of these, 6389 (0.16%) had established diagnoses of uveitis or scleritis. Within the uveitis group, mean age was 54 years (SD 16), and 62% were female. 708 (11.1%) of the uveitis patients were hospitalized for COVID-19, significantly greater than the 7.3% rate amongst all adult, COVID-19-positive patients in the dataset ($p < 0.001$) and the CDC estimate of 7.5% for the US population in 2020 ($p < 0.001$). No agent showed a statistically significant effect on hospitalization. The higher rate of hospitalization in uveitis patients was partly, though not completely, explained by higher rates in uveitis-associated autoimmune conditions in the dataset as a whole.

Conclusions: Uveitis patients have a greater risk of hospitalization for COVID-19 compared with the general population. As a whole, conventional IMT and biologics do not increase the risk of COVID-19 hospitalization amongst uveitis patients infected with the virus.

CONTROL ID: 3711188

SUBMITTER (NAME ONLY): Lin Cheng

TITLE: Ethambutol-induced optic atrophy: a mitochondrial fission neuropathy mediated by NO?

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Cheng, H. Shevalye, G. Schmidt, J. Skeie, M.A. Greiner, M.H. Kuehn, Department of Ophthalmology and Visual Sciences, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|L. Cheng, M.H. Kuehn, Center for the Prevention and Treatment of Visual Loss, Veterans Affairs Medical Center, Iowa City, Iowa, UNITED STATES|H. Shevalye, G. Schmidt, J. Skeie, M.A. Greiner, Iowa Lions Eye Bank, Coralville, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ethambutol (EMB) is used in the treatment of tuberculosis (TB) or mycobacterium avium complex infections. A devastating adverse effect of EMB is toxic optic atrophy, which occurs in 1–2.5% of patients. To date, the pathophysiology of EMB-induced optic atrophy is incompletely understood.

Methods: Human iPSC-derived retinal ganglion cells (iPSC-RGC) or retinal organoids were treated with 2, 20, 200, or 2,000 µg/ml EMB. Time and dose-dependent EMB induced changes were observed by confocal microscopy and gene expression changes by RT-PCR. Mitochondrial function in iPSC-RGC was measured using the Seahorse XFe analyzer.

Results: Treatment of retinal organoids with EMB resulted in a time and dose-dependent loss of RGC, but not other retinal neurons. 24 hours of EMB treatment induced the dose-dependent formation of bubbles in the cytosol of iPSC-derived RGC concordant with increased NOS3 synthesis ($P=0.0001$). At higher concentrations significantly elevated expression of the apoptotic mediators BAX, APAF1, CASP3, CASP8, and CASP7 was detected (1.5 to 3-fold). We also detected increased expression of MIEF1 (1.8-fold, $P<0.0001$), suggesting impaired maintenance of mitochondrial DNA. Mitochondrial staining demonstrated decreased mitochondrial length in EMB treated iPSC-RGC (112.1±41.6 µm vs. 212.9±76.3 µm in untreated controls, $P<0.0001$), indicating mitochondrial fragmentation. Functional mitochondrial measurements demonstrated that spare respiratory capacity in iPSC-RGC is increased by 21%, 20% and 27% treated with 2, 20, or 200 µg/ml EMB, respectively ($P<0.05$). Furthermore, cells treated with 200 ug/mL EMB displayed a 24% increase in non-mitochondrial respiration ($P=0.005$).

Conclusions: Our findings suggest that Ethambutol-induced optic atrophy may be caused by nitric oxide stress and dysregulation of mitochondrial dynamics in favor of mitochondrial fission. This, in turn, causes an increase in energy demand that may lead to RGC dysfunction and, eventually, apoptotic cell death.

CONTROL ID: 3711191

SUBMITTER (NAME ONLY): Wenting Zhao

TITLE: Self-attention and mixed loss adversarial networks-based Fundus image segmentation

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Zhao, J. Lian, Shandong Management University, Jinan, Shandong, CHINA|

Commercial Relationships Disclosure: Wenting Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Jian Lian: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Accurate segmentation of the fovea and the arteriovenous vein in the optic disc centre plays a vital role in the diagnostic system for diabetic retinopathy. In recent years, deep learning has shown its powerful performance in medical image analysis. Accordingly, this study presents a fundus image segmentation method based on self-attention and mixed-loss adversarial networks. Extensive experiments were performed on the fovea and the optic disc's central fine arteriovenous vein in two public datasets.

Methods: As shown in Fig. 1, the fundus images were preprocessed by using data augmentation operations such as rotation and symmetry and sent to the generator based on the separable convolutional U-Net. It adopts a self-attention mechanism to adjust the feature weights between the sampling points to guarantee the detection accuracy. Second, we leverage the separable convolutional U-Net to implement the segmentation by adding the adversarial training framework. The generator's outcome is improved by the output of the judge and the loss return.

Results: The proposed method outperforms the state-of-the-art algorithms in accuracy and execution efficiency. In general, the average sensitivity is 95.56%, and the detection performance is 97.21% over the data samples.

Conclusions: The proposed method has low computational complexity while achieving promising accuracy. The segmentation results obtained are close to manual delineation. It is therefore a potential instrument in clinical applications.

CONTROL ID: 3711197

SUBMITTER (NAME ONLY): Srividhya Vilupuru

TITLE: Development and Validation of the Patient Reported Spectacle Independence Questionnaire (PRSIQ)

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vilupuru, E. Thomas, R. Morlock, Surgical Vision, Johnson & Johnson Surgical Vision Inc, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Srividhya Vilupuru: Commercial Relationship(s);Code E (Employment):Johnson & Johnson | Eugenia Thomas: Commercial Relationship(s);Code E (Employment):Johnson & Johnson | Robert Morlock: Commercial Relationship(s);Code C (Consultant/Contractor):Johnson & Johnson

ABSTRACT BODY:

Purpose: Develop and validate a questionnaire that quantitatively determines spectacle independence following bilateral implantation with presbyopia-correcting intraocular lenses.

Methods: The content of the PRSIQ was based on literature reviews as well as clinician and patient input. Draft items were assessed/revised in debriefing interviews for qualitative validation. Two quantitative validation studies were conducted with the initial PRSIQ, and two quantitative validation studies were conducted with the final PRSIQ. Confirmatory factor analyses, including IRT calibration, were performed, as well as reliability estimates and validity analyses of the resulting scores. To estimate effect size, Generalized Estimating Equations (GEEs) were used to account for repeated measures.

Results: Over 50 patients provided direct input in the development of the PRSIQ. Qualitative research demonstrated that patients often considered themselves spectacle independent. Yet, when probed, it was determined some actually wore correction for certain activities.

Quantitative assessments conducted across 4 studies (n=3,208) demonstrated evidence of validity. A higher proportion of patients who achieved spectacle independence had 20/20 or better binocular uncorrected intermediate vision and lower magnitude of residual refraction. Those classified as spectacle independent had higher satisfaction with overall uncorrected vision at all distances. GEE models (n=272) demonstrated a consistent large effect size resulting in significantly greater proportion of participants achieving spectacle independence in the treatment vs. control arm. Test-retest reliability was high (>0.84) overall and in the refractory stable population.

Conclusions: The PRSIQ is a patient-reported measure assessing spectacle independence following cataract surgery. All quantitative analyses conform to predictions and support the use of the PRSIQ as a measure of spectacle independence.

CONTROL ID: 3711198

SUBMITTER (NAME ONLY): Sang Yoon Moon

TITLE: Detection of mutant RP1 protein by HiBiT-tagging of patient derived retinal organoids

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Moon, T.M. Lamey, J.N. De Roach, F.K. Chen, S. McLenachan, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|S. Moon, D. Zhang, S. Chen, F.K. Chen, S. McLenachan, Ocular Tissue Engineering Laboratory, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|T.M. Lamey, J.A. Thompson, T.L. McLaren, J.N. De Roach, Australian Inherited Retinal Disease Registry and DNA Bank, Sir Charles Gairdner Hospital, Nedlands, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Nonsense mutation in the terminal exon of the RP1 gene is a common cause of autosomal dominant retinitis pigmentosa. Production of truncated RP1 proteins has yet to be demonstrated in RP1 patients due to the lack of patient-derived retinal tissue and appropriate antibodies. TO enable detection of truncated RP1 proteins in patient-derived retinal tissues we modified the mutant RP1 locus in patient-derived induced pluripotent stem cells (iPSCs) with the luminescent HiBiT tag.

Methods: Paired nickase CRISPR/Cas9 gene editing was used to insert the HiBiT luminescent tag into iPSCs from an 85-year old female donor with RP1 p.E700X. HiBiT tagged iPSCs were characterised and differentiated into retinal organoids. Retinal organoids were treated with the translational readthrough inducing drug PTC124 and HiBiT-tagged RP1 protein detected by luminescence assays and western blotting.

Results: High efficiency insertion of the HiBiT tag into the RP1 locus was demonstrated in RP1 patient-derived iPSC. Western blotting demonstrated expression of full-length RP1 protein (198kDa) as well as a novel 47kDa band in RP1-HiBiT retinal organoids and adult human retinal tissues. HiBiT blotting of RP1-HiBiT retinal organoids revealed four luminescent bands (22kDa, 47kDa, 90kDa and 100kDa). Treatment with PTC124 reduced expression of the 22kDa and 90kDa bands, increased 47kDa expression and induced expression of a new 120kDa band.

Conclusions: We demonstrate the first direct evidence for production of truncated RP1 protein in retinal cells derived from an RP1 patient. Treatment of patient-derived retinal organoids with PTC124 induced limited translational readthrough of mutant RP1 mRNA, but did not result in production of full-length PR1 protein. We also report but detection of a novel 48kDa RP1 protein isoform in HiBiT retinal organoids and adult human retina.

CONTROL ID: 3711203

SUBMITTER (NAME ONLY): Mahdi Basha

TITLE: Longevity of IOP Control Post Single Bimatoprost Implant Injection in a Phase 3b Study

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Basha, Fraser Eye Care Center, Michigan, UNITED STATES|J. Paauw, Piedmont Eye Center, Virginia, UNITED STATES|S.R. Sarkisian, Oklahoma Eye Surgeons,, Oklahoma, UNITED STATES|M. Kolko, Copenhagen University Hospital, DENMARK|A. Nguyen, S. Mehta, M. Bejanian, R. Craven, Allergan, an AbbVie company, California, UNITED STATES|W. Christie, Scott & Christie and Associates, PC, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Mahdi Basha: Commercial Relationship(s);Code F (Financial Support):Allergan, an AbbVie company | James Paauw: Commercial Relationship: Code N (No Commercial Relationship) | Steven Sarkisian: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan, an AbbVie company;Code F (Financial Support):Allergan, an AbbVie company | Miriam Kolko: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan, an AbbVie company | Ashley Nguyen: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Shraddha Mehta: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Marina Bejanian: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Randy Craven: Commercial Relationship(s);Code E (Employment):AbbVie Inc | William Christie: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan, an AbbVie company

ABSTRACT BODY:

Purpose: Intracameral bimatoprost implant slowly releases bimatoprost to lower intraocular pressure (IOP). Previously reported phase 3 studies of the implant (ARTEMIS) evaluated IOP lowering post single administration only through 15 weeks, because 2 additional implants were administered at 16-week intervals. This analysis used data from a phase 3b clinical trial to evaluate the longevity of IOP control after single administration of the 10-µg bimatoprost implant.

Methods: Ongoing, open-label, multicenter, phase 3b study (NCT03850782) evaluating bimatoprost implant pro re nata in patients with open-angle glaucoma or ocular hypertension inadequately managed with topical IOP-lowering medication for reasons other than efficacy (eg, intolerance or nonadherence). Retreatment criteria were based on clinically meaningful IOP increase (investigator judgement), time from last administration, residual implant size assessment, and safety evaluation. Rescue treatment (IOP-lowering medication or procedure) was allowed. Analysis included Kaplan-Meier estimates of time to rescue/retreatment after the day 1 implant administration in the study eye, and IOP in those participants not rescued/retreated. Data available as of October 20, 2021 were analyzed.

Results: A total of 203 participants administered a 10-µg bimatoprost implant were included in the analysis. Baseline mean (SD) IOP was 25.6 (2.97) mmHg. Mean (SD) IOP and mean (SD) change from baseline (mmHg) in those not rescued/retreated were 17.6 (3.77) and −7.9 (3.90) at week 12 (n=175); 18.3 (4.40) and −6.6 (4.12) at month 6 (n=114); 18.5 (4.17) and −6.1 (4.05) at month 8 (n=74); and 18.5 (3.52) and −5.9 (3.81) at month 12 (n=47). The Kaplan-Meier estimate (95% CI) of the probability of not requiring rescue/retreatment after a single administration of the bimatoprost implant was 97.4% (93.8%, 98.9%) at week 12; 74.6% (67.0%, 80.8%) at month 6; 65.1% (56.5%, 72.4%) at month 8; and 55.5% (46.1%, 63.9%) at month 12.

Conclusions: Based on the available data, the estimated probability of IOP control after a single bimatoprost implant administration was 75% at 6 months and 56% at 12 months. The duration of IOP control is consistent with results of a previous phase 1/2 study (Craven et al. Drugs. 2020;80:167-79). Not all participants included in the present analysis had reached the month 12 visit, and the study is still enrolling. Safety outcomes will be reported at study completion.

CONTROL ID: 3711204

SUBMITTER (NAME ONLY): Grayson Armstrong

TITLE: Physician-to-Physician eConsultations to Ophthalmologists at an Academic Medical Center

SESSION TITLE: Using Technology for Care Delivery and Improvement

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G.W. Armstrong, N.A. Sherif, A.C. Lorch, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|G.W. Armstrong, A.C. Lorch, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Grayson Armstrong: Commercial Relationship(s);Code O (Owner):Ocular Technologies Inc;Code C (Consultant/Contractor):McKinsey & Company;Code C (Consultant/Contractor):Xenon-VR;Code C (Consultant/Contractor):Ophthalytics;Code C (Consultant/Contractor):Kriya Therapeutics | Noha Sherif: Commercial Relationship: Code N (No Commercial Relationship) | Alice Lorch: Commercial Relationship(s);Code C (Consultant/Contractor):Regeneron

ABSTRACT BODY:

Purpose: Despite the known advantages of electronic consultation (eConsult) to patients, providers, and healthcare systems, including increased timely access to specialist consultation, decreased resource waste, and improved care coordination, the role of eConsults in ophthalmology has yet to be explored. We conducted a retrospective chart review to evaluate the feasibility and diagnostic accuracy of a physician-to-physician eConsults ophthalmology program and characterize the types of clinical questions and ophthalmic learning needs of healthcare providers.

Methods: Ophthalmology eConsults were reviewed to identify submission-to-response time, primary diagnoses made by eConsultants, and referral outcomes including symptom resolution, completion of follow-up appointments, and presentation to an emergency department (ED). eConsults underwent thematic review and categorized based on the type of clinical question asked, urgency, and ophthalmic condition addressed. Demographic data on patients and referring providers were also collected.

Results: One hundred ophthalmology eConsults were placed, and 100% were responded to by an ophthalmologist. An average of 1.6 days and a standard deviation (SD) of ±1.9 elapsed from the time an eConsult order was placed to the time the consultation was completed. Of the eConsults, 62% (n=62) were recommended for an in-person evaluation; of these, 48.4% (n=30) presented to an ophthalmologist. For patients who had an in-person follow-up, concordance of diagnoses between eConsultant and in-person evaluation was observed in 93% (n=28) of cases. On average, in person evaluations occurred within 28.9 (SD ±27.4) days of the eConsult response. The most common clinical inquiries were related to appropriate triage and referral (24.4%), management (22%), and diagnosis (19.7%). All eConsults were nonurgent. The most common ophthalmic condition addressed was chalazia/hordeola (14%). Only 5% of patients presented to an ED for the same ophthalmic concern addressed by eConsult.

Conclusions: Ophthalmology eConsultants can diagnose, triage, and manage nonurgent ocular conditions with high accuracy through electronic medical record review. eConsult programs can also facilitate timely access to specialty care.

CONTROL ID: 3711206

SUBMITTER (NAME ONLY): Minghao Jin

TITLE: Benzoic acid-mediated inhibition of retinal necroptosis involves ciliary neurotrophic factor

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jin, C. Lu, S. Li, Neuroscience Center of Excellence, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|M. Jin, Department of Ophthalmology, School of Medicine, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure: Minghao Jin: Commercial Relationship: Code N (No Commercial Relationship) | Chunfeng Lu: Commercial Relationship: Code N (No Commercial Relationship) | Songhua Li: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously showed that ciliary neurotrophic factor (CNTF) suppresses expressions of rod and cone opsins as well as visual cycle enzymes (RPE65 isomerase and lecithin:retinol acyl transferase), thereby reducing the formation of the light sensitive visual pigments that mediate normal vision and photodamage-induced retinal degeneration. The purpose of this study was to test whether benzoic acid, which has been shown to promote CNTF expression in cell culture, and CNTF-deficiency can protect photoreceptors from light damage-induced necroptosis.

Methods: Dark adapted wild-type (129S2/Sv strain) and $Cntf^{-/-}$ mice treated with different doses of sodium benzoate (NaB) were exposed to 15000 lux light to induce retinal photodamage. Expression of the necrosome proteins such as receptor interacting protein kinase 1 (RIPK1), RIPK3, and mixed lineage kinase domain-like protein (MLKL) in the retinas were analyzed by immunoblot and immunohistochemical analyses. Interaction of these necrosome proteins were determined by double-immunostaining and immunoprecipitation assays. Activation of the necrosomes was assessed by detecting phosphorylation of MLKL. Photoreceptor degeneration was evaluated by immunohistochemistry and immunoblot analysis of opsins and cone arrestin.

Results: Intense light exposure induced a significant upregulation of both RIPK expression and MLKL phosphorylation in the WT mouse retinas. Interactions of the necrosome proteins were also enhanced in the WT retinas exposed intense light. Under the same light conditions, NaB treatment inhibited the RIPK upregulation and MLKL activation in a dose-dependent manner in WT retinas. Immunoblot and immunohistochemical analyses showed that intense light exposure caused degeneration of rods and cones in WT mice and NaB-treatment alleviated the light-induced degeneration of photoreceptors in WT. The same intense light exposure induced more greater activation of the necrosomes in the $Cntf^{-/-}$ retinas, as compared to WT mice. NaB-treatment, however, did not significantly inhibit RIPK3 upregulation, MLKL phosphorylation and retinal degeneration in the $Cntf^{-/-}$ mice exposed to the intense light.

Conclusions: 1) activation of the necrosomes contributes to light-induced retinal degeneration in both WT and $Cntf^{-/-}$ mice; 2) NaB inhibited photodamage-induced necrosome activation in the WT, but not in $Cntf^{-/-}$, retinas.

CONTROL ID: 3711210

SUBMITTER (NAME ONLY): Zhiqin Huang

TITLE: Disease modelling and functional characterisation using iPSC derived RPE in RCBTB1-associated retinopathy

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: RCBTB1 has been hypothesized to be involved in biological processes associated with the ubiquitin proteasome system (UPS) and oxidative stress pathways in retinal cells. We sought to expand our understanding of the physiological and pathological role RCBTB1 in retinal cells using an iPSC derived RPE cellular model of RCBTB1-associated retinopathy.

Methods: Expression of RCBTB1 was quantified via qRT-PCR and western blotting in patient derived iPSC-RPE cells (c.[170delG];[707delA]) compared to healthy controls. Co-immunoprecipitation (Co-IP) was conducted in health control iPSC-RPE cells to characterize interactions between RCBTB1 and other proteins including CUL3, UBE2E3 and NFE2L2. Human ubiquitin array analysis in these cells using an R&D Systems Proteome Profiler Human Ubiquitin Array Kit (ARY027, R&D Systems) was performed to measure the ubiquitination level of 49 different proteins. Furthermore, mitochondrial integrity and structure in iPSC-RPE were investigated using transmission electron microscopy.

Results: Reduced RCBTB1 expression level was confirmed in patient derived iPSC-RPE cells compared to healthy controls. Co-IP experiment demonstrated that RCBTB1 interacts with CUL3 and UBE2E3 but not NFE2L2 in iPSC-RPE cells. Analysis of ubiquitin array identified two protein with significant change of ubiquitination level, including PDGFR β (platelet derived growth factor receptor β) and p53. Ultrastructural analysis not only showed a thinner RPE cell layer displaying shorter microvilli, but also showed disrupted cristae formation and architecture of mitochondria in patient derived RPE compared to control, indicating mitochondrial dysfunction and consequent excessive ROS production may play a role in cellular damage in RCBTB1 deficient RPE cells.

Conclusions: We identified RCBTB1 deficiency and its effect on UPS and mitochondria ultrastructure using an iPSC derived RPE cellular model. Furthermore, we identified two potential RCBTB1 interacting proteins, CUL3 and UBE2E3. Our findings shed light on the physiological role RCBTB1 plays in human RPE cells.

CONTROL ID: 3711211

SUBMITTER (NAME ONLY): Sudhir Ranganath

TITLE: Sensing local osmolarity of the tear film on the corneal surface using fluorescent dye-loaded nanoliposomes

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.H. Ranganath, M. Thanuja, Chemical Engineering, Siddaganga Institute of Technology, Tumkur, Karnataka, INDIA|J.A. Bonanno, S.P. Srinivas, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Local hotspots of elevated osmolarity of the tear film, predicted in the tear breakup domains, are implicated in dry eye disease (DED). We have prepared osmosensitive nanoliposomes and characterized for sensing local osmolarity of the tear film by noninvasive fluorescence imaging.

Methods: Nanoliposomes, loaded with fluorescent dyes, calcein (susceptible to self-quenching) and sulforhodamine 101 (SR101), were produced by the thin-film hydration method followed by ultrasonication and repeated extrusion.

Results: Nanoliposomes were spherical, unilamellar, uniform in size and negatively charged (117.9 ± 6.4 nm; polydispersity index [PDI] of 0.15 ± 0.02, -23.7 ± 1.5 mV). They showed negligible dye leakage during storage over 3 days, and underwent minimal changes in size, PDI, and charge. Deliberate swelling and shrinkage of nanoliposomes by exposure to hyposmotic and hyperosmotic media led to rapid de-quenching and quenching of calcein fluorescence. Thus, the ratio of green fluorescence of calcein (F_{Green}) to the red fluorescence of SR101 (F_{Red}) decreased with increasing osmolarity and vice versa; F_{Green}/F_{Red} vs. osmolarity obeyed Boyle-Van't Hoff's law. When nanoliposomes were dispersed in a gelatin film and sucrose solution was introduced at the center, local F_{Green}/F_{Red} altered with osmolarity in response to sucrose gradients. When instilled on contact lenses or ex vivo porcine corneas, nanoliposomes suspension dispersed evenly and showed a decrease in F_{Green}/F_{Red} vs. time when exposed to room air.

Conclusions: Fluorescent nanoliposomes of high osmosensitivity and suitable for sensing local osmolarity on the corneal surface have been prepared and characterized. The measurements of local osmolarity will advance our current understanding of the pathophysiology of DED and possibly establish novel diagnostics to assess the severity of the disease.

CONTROL ID: 3711214

SUBMITTER (NAME ONLY): Janice Ong

TITLE: Optical coherence tomography angiography of arteriovenous relationships in the healthy macula and their derangement in disease

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.X. Ong, G.O. Bou Ghanem, P.L. Nesper, J. Moonjely, A.A. Fawzi, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many retinal diseases differentially affect arteries and veins. We sought to develop a tool to non-invasively analyze arteriolar and venular connectivity of capillary plexuses in the healthy macula using optical coherence tomography angiography (OCTA), and examined clinical applications in eyes with neovascular pathology.

Methods: 20 eyes of 20 healthy controls (age 25.3 ± 2.2 years) were imaged with OCTA, and 3D volumes of the full retinal slab segmented into superficial (SCP), middle (MCP), and deep capillary plexuses (DCP). Large SCP vessels were classified as arterioles or venules by 2 graders. We implemented a custom watershed algorithm to identify arteriolar- and venular-connected capillaries by using the large SCP vessels as seed points for flooding the rest of the vascular network. We calculated A/V ratios of arteriolar- to venular-connected vessels and adjusted flow indices (AFI) for the SCP, MCP, and DCP.

We also analyzed 2 eyes of a patient with proliferative diabetic retinopathy (PDR) and 1 eye of a patient with macular telangiectasia (MacTel) to evaluate utility of this method in visualizing vascular connectivity to pathological neovascularization (NV).

Results: In healthy eyes, MCP A/V ratio was significantly higher than the SCP and the DCP, indicating a higher proportion of arteriolar-connected vessels (all $p < 0.001$). Arteriolar-connected vessel AFIs were higher than venular-connected AFIs in the SCP, but this pattern reversed in the MCP and DCP, which had higher venular-connected AFIs than arteriolar (all $p < 0.001$).

In the PDR eyes, preretinal NV originated from venules, while intra-retinal microvascular abnormalities appeared as dilated capillary loops within the MCP connecting an arteriole and venule. In MacTel, diving SCP venules formed the epicenter of outer retinal NV.

Conclusions: We developed an algorithm for assigning arteriolar and venular connectivity of retinal vessels. Healthy eyes showed increased MCP arteriolar connections but relatively slower arteriolar vs. venular flow velocity in the MCP and DCP, which may contribute to the unique vulnerability of these layers to ischemia in conditions like paracentral acute middle maculopathy (PAMM). In eyes with neovascular pathology, our findings were consistent with histopathologic studies. Further studies are needed to investigate utility of this method in PAMM and other vascular diseases.

CONTROL ID: 3711216

SUBMITTER (NAME ONLY): Akiko Hanyuda

TITLE: Plant-based low carb diet and other risk factors in relation to incident primary open-angle glaucoma characterized by autonomously determined visual field loss patterns

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Hanyuda, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|B. Rosner, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L.R. Pasquale, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|M. Wang, J.L. Wiggs, T. Elze, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Kang, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) manifests as distinct visual field (VF) loss patterns localizing to the nerve fiber layer. We used an autonomous algorithm to classify incident visual field VF loss patterns in POAG and evaluated whether a plant-based low carb diet and other risk factors may be differently associated for POAG with paracentral VF loss versus POAG with peripheral VF loss.

Methods: Participants (n=79,906) from the Nurses' Health Study (NHS), aged ≥40 years and free of glaucoma, were followed from 1980 to 2018. Information on diet, body mass index, smoking, diabetes and other covariates were assessed on biennial questionnaires. Deciles of a plant-based low-carbohydrate-diet (LCD) adherence score were calculated to represent adherence to diets lower in carbohydrate and higher in protein and fat from plant sources. Incident POAG cases with reproducible Humphrey VF loss were confirmed with medical records. The total deviation information of the earliest reliable VF for each eye with POAG was extracted, and a statistical learning method was used to identify optimal solutions for regional vision loss patterns. Each POAG eye was assigned the VF pattern ("archetype") based on the highest weighting coefficient. Multivariable-adjusted hazard ratios (HRs) for POAG of various archetypes and 95% confidence intervals (CIs) were estimated using per-eye Cox proportional hazards models.

Results: We identified 14 archetypes; of these, 9 archetypes represented early loss. For comparison, we combined 2 archetypes showing paracentral VF loss (n=165 eyes with incident POAG) and combined 7 archetypes showing peripheral VF (n=1145 eyes with incident POAG). The associations for body mass index (BMI; kg/m2), cigarette smoking, and diabetes for the two outcomes were not significantly different ($p_{contrast}$≥0.11). However, the association with higher adherence to a plant-based LCD score was stronger for paracentral VF loss (HR=0.79, 95%CI= 0.66, 0.96 per 1 SD increase in diet score) versus peripheral VF loss (HR=1.00, 95%CI=0.98, 1.01), with $p_{contrast}$=0.03.

Conclusions: Compared to POAG with peripheral VF loss, POAG with early paracentral VF loss may have common as well as distinct determinants; higher adherence to a plant-based LCD diet was inversely associated only with paracentral VF loss.

CONTROL ID: 3711220

SUBMITTER (NAME ONLY): Ayumi Ouchi

TITLE: New co-culture system of human iPSC induced retinal organoid and microglia

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ouchi, M. Friedlander, Molecular Medicine, The Scripps Research Institute, La Jolla, California, UNITED STATES|A. Ouchi, N. Ebihara, Ophthalmology, Juntendo Daigaku Igakubu Fuzoku Urayasu Byoin, Urayasu, Chiba, JAPAN|S. Giles, K.T. Eade, M. Friedlander, Lowy Medical Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human iPS cell (hiPSC)-derived retinal organoids would not ordinarily contain microglia because the hiPSC are driven down a neuroectodermal pathway and microglia are derived from yolk sac. In normal development, however, microglia migrate into the retina where the neural environment is essential for the development and maintenance of their mature functional properties. Since microglia are known to play critical roles in maintaining the normal retinal environment, as well as retinal disease, we set out to develop a new 3D in vitro model by co-culturing hiPSC-derived retinal organoids and hiPSC-derived microglia.

Methods: Retinal organoids and microglial progenitor cells were differentiated from a common line of hiPSCs and co-cultured at various numbers of weeks in culture. The localization, morphology, and properties of microglia in the retinal organoids were evaluated by immunostaining and qPCR.

Results: We co-cultured microglial precursor cells with retinal organoids between 20 to 35 weeks old. We observed IBA1-positive microglia in the retina from 2 weeks after the start of co-culture, reaching maximal numbers at 4 to 6 weeks. The mean number of microglia in the retina was 6.0±2.1/mm. At 6 weeks of co-culture, microglia were observed in the outer and inner plexiform, as well as ganglion, cell layers where retinal microglia cells physiologically locate in vivo. While in the retinal organoids, microglia morphology matured from uniformly spherical to small cell bodies with long branching processes. The expression of mature cell type specific microglia markers Tmem119 and P2ry12 was also increased at 6 weeks of co-culture.

Conclusions: We optimized the timing and parameters for successful integration of microglia into retinal organoids. The hiPSC-derived microglial precursor cells co-cultured with hiPSC-derived retinal organoids migrated to their proper anatomical locations and developed a morphological maturity comparable to that observed in vivo. Our results suggested that this co-culture system may be useful for understanding the pathogenesis of retinal diseases involving pathological activity of retinal microglia and for drug discovery.

CONTROL ID: 3711225

SUBMITTER (NAME ONLY): Moaddey Alfarhan

TITLE: Pharmacological Inhibition of Spermine Oxidase Protects Against Neuroinflammation and Oxidative Damage in a Mouse Model of Retinal Excitotoxicity

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Alfarhan, F. Liu, S. Shan, P. Pichavaram, P. Somanath, S. Narayanan, Department of Clinical and Administrative Pharmacy, University of Georgia, Georgia, UNITED STATES|M. Alfarhan, F. Liu, S. Shan, P. Somanath, S. Narayanan, VA Medical Center Augusta Downtown, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neuroinflammation is closely associated with neurodegeneration, and is a major cause of vision impairment in blinding diseases such as diabetic retinopathy (DR). Spermine oxidase (SMOX) is a major enzyme in the polyamine oxidation pathway. Previous findings from our laboratory have shown that treatment with MDL 72527, a selective inhibitor for SMOX, reduced microglial activation and upregulated antioxidant signaling in a mouse model of retinal excitotoxicity. In the present study, using the same model, we investigated the impact of SMOX inhibition on the status of inflammatory cells, cytokine levels, and oxidative damage.

Methods: Mice (8-10 weeks old) received 20 nmoles of NMDA (N-Methyl-D-aspartate) or NMLA (N-Methyl-L-aspartate, control) intravitreally. 40 mg/kg/day of MDL 72527 or vehicle (normal saline) was given to mice through intraperitoneal injections. Retinal cryostat sections were prepared for immunostaining and fresh frozen retinal samples were used for Western blotting or qRT-PCR studies. C8-B4 cells were used for studying the impact of conjugated acrolein in vitro on microglia cells.

Results: Immunostaining of retinal sections showed a significant increase in the number of inflammatory cells of M1 phenotype, positive for CD (Cluster Differentiation) 68 and CD16/32 in excitotoxicity-induced retinas, while MDL 72527 treatment markedly reduced these changes ($N=3-5$, $P<0.05$). SMOX inhibition with MDL 72527 upregulated the number of M2 phenotype cells stained with arginase1 and CD206 ($N=4-6$, $P<0.05$). While retinal excitotoxicity upregulated the level of several inflammatory cytokines, MDL 72527 treatment significantly reduced many of these molecules including IL-1β, TNF-α, CCL3, and IL-21 ($N = 6-8$, $P< 0.05$). Excitotoxicity-induced upregulation in protein-conjugated acrolein (an indicator of SMOX activation and oxidative damage) was also reduced in response to SMOX inhibition ($N=5-6$, $P<0.05$). In-vitro studies using C8-B4 microglia cells showed changes in cellular morphology and an increase in reactive oxygen species formation in response to conjugated acrolein treatment.

Conclusions: Our findings indicate that the inhibition SMOX pathway reduced neuroinflammation and oxidative damage, and suggests its potential as a therapeutic target to treat neurodegenerative diseases of the eye.

CONTROL ID: 3711231

SUBMITTER (NAME ONLY): Mathew Margolis

TITLE: Phase I Study of the Safety of Locally Delivered Allogeneic Mesenchymal Stem Cells for Promoting Corneal Repair: Early Results

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Non-penetrating injuries to the cornea and ocular surface, including non-healing persistent epithelial defects, are a significant cause of combat-related visual loss and morbidity. Mesenchymal Stromal Cells (MSCs) play an important role in tissue repair and maintenance and have been used as a cell-therapy in numerous clinical studies. The purpose of this study was to evaluate the safety and dosing of allogeneic bone marrow-derived MSCs for promoting corneal epithelial repair.

Methods: In the first cohort of our single center, Phase 1, 3 + 3 conventional cohort expansion dose-escalation study, participants with stage 2 or 3 non-healing corneal epithelial defects received a single subconjunctival injection of freshly thawed bone marrow-derived MSCs. Participants met eligibility criteria for clinical trial ID #NCT04626583 and agreed to participate in an IRB approved protocol for Investigational New Drug #18400 (FDA/CBER). MSCs were produced at the University of Illinois Hospital Clinical Stem Cell Laboratory following Good Manufacturing Practice protocols and were stored in cryogenic conditions. Patients received a single subconjunctival injection of 1.0×10^6 (50ul) MSCs along with their standard of care. Primary outcome measures included safety, defined as incidence of treatment emergent adverse events (TAEs) assessed at 28 days, and efficacy, defined as proportion of participants with epithelial defect closure assessed via slit lamp fluorescein staining exam.

Results: The initial cohort of n=3 participants were enrolled. At 28 days no TAEs occurred and all participants had improvement in size of corneal epithelial defects. Complete resolution was seen in one participant by 14 days, and between 28 and 56 days in another participant. The third participant, who is still being followed, had 80% improvement in epithelial defect size at 28 days.

Conclusions: These early results support the safety of locally delivered MSCs for non-healing corneal epithelial defects, while providing some signs of efficacy. Additional cohorts of this dose-escalation study, followed by further double masked, placebo controlled studies of larger size and longer duration are warranted in determining the efficacy of MSC as a treatment modality for corneal epithelial defects.

CONTROL ID: 3711232

SUBMITTER (NAME ONLY): hugo lama

TITLE: Collecting data from a social network as a new method to explore recurrent corneal erosions syndrome

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. lama, J. Bourges, A. Brézin, Universite de Paris, Paris, Île-de-France, FRANCE|H. lama, J. Bourges, A. Brézin, Ophthalmology, Hopital Cochin, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Collecting medical data for clinical research studies needs tremendous perseverance. Yet, patients post a lot of their own personal health data on social media and share their experiences through international virtual support groups. Recurrent epithelial erosion (RCE) induces recurrent pain while reducing patients' quality of life. We report data of RCE patients who belong to an international English-speaking support group hosted by a social network. We aimed at better defining patients' symptomatology and the subjective efficacy of proposed treatments, and subsequently compared our results with literature.

Methods: We designed a 24-question questionnaire consisting in three parts: demographics, clinical data and therapies. The treatments' efficacy to prevent RCE was scored through a semi-quantitative 4-gradescale (from "no effect" to "very efficient"). In May 2021, we posted a 6-month ephemeral hyperlink on the RCE support group forum (Facebook, Meta®) pointing at our questionnaire

Results: The RCE group included 1856 members. We harvested 257 complete responses (13.8%; 222 women and 35 men; average age =42+/-12 y). Responders were mostly North Americans (n=152; 59.1%), and Caucasian (n=214; 83.3%). Fewer than one-third of RCEs were attested by a corneal subspecialist MD (n=70; 27.2%), whereas 91.8% were referred to a health care professional (n=236). The predominant symptom was acute awakening pain (n=198; 77.0%). RCE significantly impaired patients' quality of life (n=176; 68.4%). Daily wearing of an anti-Covid-19 surgical mask may have increased the frequency of episodes (n=41; 16.0%). Among surgical procedures, manual debridement was the most performed (n=56; 21.8%), effective in a third of patients (n=17; 30.3%). PTK was performed in one-fifth of patients (n=52; 20.2%), effective in two-thirds (n=31; 59.6%). 176 patients (68.4%) were treated with hypertonic gel, which, according to the patients was the most efficient medical treatment d (n=103; 58.5%; $p<0.0001$).

Conclusions: To our knowledge, this is the first real-life study involving patients with RCE, and the second collecting data through a social network in ophthalmology. Our results are consistent with previous retrospective or prospective reports based on medical records despite responder selection bias. The use of social networks to collect real life data seems to be promisingly reliable as a medical evaluation tool.

CONTROL ID: 3711236
SUBMITTER (NAME ONLY): Katherine Tien
TITLE:
2022 Amblyopia Smartphone Apps: Do They Help Our Patients?
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Tien, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|G. Wu, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|W. Zhao, University of California Davis, Davis, California, UNITED STATES|A. Elor, R. Jhangiani, A. Parrales, S. Kurniawan, Computational Media, University of California Santa Cruz, Santa Cruz, California, UNITED STATES|
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ABSTRACT BODY:
Purpose:
There are 350,000 eHealth apps.[1] There were 218 Billion app downloads in 2020.[2] Amblyopia is the most common cause of vision impairment in children and young adults, affecting 99.2M worldwide.[3] Amblyopic patients and family members fall into the demographic of mobile app users. What do free apps for amblyopia offer to our patients?
Methods:
We used the search terms “lazy eye,” “amblyopia,” “improve vision,” and “eye exercises” in the Google Play and Apple App stores to compile a list of top 10 free apps. iOS apps do not provide download information.

Inclusion criteria: Free, English language, ≥100,000 downloads in Google Play Store, ≥40 reviews in Apple App Store.
Exclusion criteria: Foreign language, paid apps.
Results: Top 10 apps (most downloads to least) in Google Play Store, Figure 1.
Top 10 apps (most reviews to least) in Apple App Store, Figure 2.

For all Android and iOS apps, vision: 7/20; color vision: 7/20; “fix and follow”: 8/20; OKN stripes: 4/20; color contrast: 5/20; vision games: 6/20; Gabor patch: 4/20; definition/education of amblyopia: 0/20; “dichoptic training: 0/20; AAO reference: 0/20. Amblyopia Va improvement exercises are more common in Android versus iOS apps. Only 1 iOS app has a visual acuity test, versus 6 Android apps. Only 2/10 iOS apps had reviews ≥100.
Conclusions: The free amblyopia apps add to the treatment armamentarium of amblyopia patients. However, additional educational features would be helpful for our amblyopic patients in the future. Eye MDs can continue to play a health education role in digital health solutions.

References:
1. Natanson, E. (2020, July 23). Healthcare apps: A boon, Today and Tomorrow. Forbes. Accessed January 3, 2022. https://www.mobihealthnews.com/news/digital-health-apps-balloon-more-350000-available-market-according-iqvia-report

2. Perez, S. (2021, January 13). App stores saw record 218 billion downloads in 2020, consumer spend of $143 billion. TechCrunch. Accessed January 3, 2022. https://techcrunch.com/2021/01/13/app-stores-saw-record-218-billion-downloads-in-2020-consumer-spend-of-143-billion

3. Fu, Z., et al. (2020). Global prevalence of amblyopia and disease burden projections through 2040: a systematic review and meta-analysis. BJO, 104(8), 1164-1170. https://doi.org/10.1136/bjophthalmol-2019-314759

CONTROL ID: 3711250

SUBMITTER (NAME ONLY): María Rodríguez-Abarca

TITLE: Dichoptic binocular therapy and electronic devices for amblyopia treatment

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Rodríguez-Abarca, S. Padilla-Alanís, A.C. Rodríguez-Martínez, K. Mohamed-Noriega, M.L. Fernández-de Luna, Ophthalmology, Hospital Universitario Dr Jose Eleuterio Gonzalez, Monterrey, Nuevo León, MEXICO|

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ABSTRACT BODY:

Purpose: To determine if binocular dichoptic and monocular occlusive therapies with or without the use of electronic devices are effective for the management of amblyopia in children.

Methods: A prospective randomized doble blinded study was conducted in our institution with 37 amblyopic children, aged from 4 to 10 years. The inclusion criteria were diagnosis of amblyopia anisometropic, strabismic and mixed (both). The exclusion criteria were amblyopia due to deprivation, previous amblyopia treatment, intraocular surgery, neurologic conditions or psychomotor retardation and uncooperative patients for visual acuity assessment. Participants were assigned into 3 groups: the first(1^{st}) group: patch on the fellow eye with near vision activities, the second(2^{nd}) group: patch on the fellow eye with the use of electronic devices and the third(3^{rd}) group: with binocular red-green glasses and electronic devices. The treatment was prescribed for 4 months with 2 consecutive hours daily. Study follow-up visits were scheduled every month during treatment and 2 months after to evaluate amblyopia relapse. With assessment of the best corrected visual acuity (BCVA) using the ETDRS chart and stereopsis using the Titmus test. Friedman test and McNemar test were used for statistical analysis.

Results: A total of 37 amblyopic children (18 boys and 19 girls) were recruited, 18 (47%) with anisometropic, 13 (35%) with strabismic and 6 (16%) with mixed amblyopia; 27 (73%) were classified as moderate and 10 (27%) with severe amblyopia. In the 1^{st} and 2^{nd} group were assigned 13 patients each, and 3^{rd} one 11 patients. A statistically significant improvement was obtained in the BCVA in all three groups (1st one from 0.69 to 0.45 logMAR p=0.024, 2nd one from 0.67 to 0.50 logMAR p=0.050 and 3rd one from 0.63 to 0.40 logMAR p=0.032) compared from baseline up to 16 weeks of treatment, with stabilization of the visual acuity after cessation of the treatment. No improvement in stereopsis was observed in any of the 3 groups.

Conclusions: The binocular red-green glasses group demonstrated improvement of BCVA in the amblyopic eye as well as in the other groups of treatment.

CONTROL ID: 3711252

SUBMITTER (NAME ONLY): Jessica Chen

TITLE: The DMEK Learning Curve in Three Fellows

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Chen, A. Bauer, A. Snyder, M. Straiko, M. Terry, Cornea, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|A. Bauer, A. Snyder, Lions VisionGift, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Jessica Chen: Commercial Relationship: Code N (No Commercial Relationship) | Alex Bauer: Commercial Relationship: Code N (No Commercial Relationship) | Alyssa Snyder: Commercial Relationship: Code N (No Commercial Relationship) | Michael Straiko: Commercial Relationship: Code N (No Commercial Relationship) | Mark Terry: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Descemet Membrane Endothelial Keratoplasty (DMEK) provides excellent visual acuity and decreased tissue rejection compared to other forms of corneal transplantation. However, the thinness and fragility of DMEK tissue makes it more technically challenging with increased risks of failure with poor handling. This study was performed to determine the effect the learning curve has on DMEK outcomes.

Methods: A single-center, retrospective review of 232 DMEK surgeries for Fuchs' Dystrophy completed from start to finish by three corneal fellows was conducted. Using a standardized surgical technique and pre-loaded DMEK tissue, the learning curve for each individual fellow was analyzed by comparing the surgical outcomes from the beginning and the end of fellowship. Consecutive surgeries in groups of 10 were compared to the last 20 consecutive surgeries of the fellowship for tissue unscroll time, rebubble rate, and 6-month endothelial cell loss (ECL). A novice DMEK surgeon was considered proficient when the average outcomes for a group of 10 consecutive surgeries was not statistically different than the last 20 surgeries. Students t-test, Mann-Whitney U test, and a Fisher's exact test was used for statistical analysis.

Results: Fellow 1 (n=83 total DMEKs) had no statistical difference between the first 10 DMEK surgeries and the last 20 DMEK surgeries for rebubble rate (0% vs 15%, P=0.53) tissue unscroll time (5.5 vs 4.5 min, P=0.067), and 6-month ECL (32.2% vs 32.2%, P=0.53). Fellow 2 (n=65) did not have a statistically different rebubble rate (20% vs 10%, P=0.85) or 6-month ECL (22.9% vs 18.4%, P=0.31), however the unscroll time was significantly longer in the first 10 (4.7 vs 2.7 min, P=0.035). The difference resolved by the second 10 DMEKs. Fellow 3 (n=84) had similar 6-month ECLs (29.3% vs 28.1%, P=0.66) in the first 10 DMEKs, however significantly higher rebubble rates (30% vs 0%, P=0.030) and unscroll time (4.1 vs 1.9 min P=0.004). This difference was no longer significant by the second 10 DMEKs in all 3 categories.

Conclusions: By the second 10 surgeries, all three fellows achieved a similar rebubble rate, 6 month ECL, and tissue unscroll time as at the end of their 1 year training. 6 month ECL was the same in all three fellows at the beginning and the end of their training. With adequate supervision and training, DMEK surgery can be taught safely to fellows without significant compromise in patient outcomes.

CONTROL ID: 3711253

SUBMITTER (NAME ONLY): Kuifang Du

TITLE: Retinal nerve fiber layer defect as a prospective biomarker of cerebral stroke in 5 years: findings from the Kailuan Cohort Study

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Du, Q. Wang, W.B. Wei, Y. Wang, Beijing Institute of Ophthalmology, Beijing Tongren Hospital, Capital Medical University, CHINA|K. Du, Beijing Youan Hospital, Capital Medical University, CHINA|J. Jonas, Department of Ophthalmology, Medical Faculty Mannheim of the Ruprecht-Karis-University, GERMANY|S.L. Wu, Cardiology Department, Kailuan General Hospital, CHINA|S.H. Chen, Health Care Center, Kailuan Group, CHINA|

Commercial Relationships Disclosure: Kuifang Du: Commercial Relationship: Code N (No Commercial Relationship) | Qian Wang: Commercial Relationship: Code N (No Commercial Relationship) | Jost Jonas: Commercial Relationship: Code N (No Commercial Relationship) | Shou Wu: Commercial Relationship: Code N (No Commercial Relationship) | Shuo Chen: Commercial Relationship: Code N (No Commercial Relationship) | Wen Wei: Commercial Relationship: Code N (No Commercial Relationship) | Ya Xing Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the predictive value of retinal nerve fiber layer defects (RNFLDs) as a risk factor for an incident stroke in 5 years.

Methods: The Kailuan Cohort Study is a community-based study, performed in Tangshan, China. A total of 14,441 participants (male: 9835 (68.1%); mean age: 53 ± 13 years (range: 21 - 108 years)) have been enrolled since the baseline in 2015,. They underwent a series of ophthalmic and systematic examinations. Using fundus photographs a localized RNFLD was defined as a wedge-shape, not spindle-shaped, defect in the retinal nerve fiber layer, running in direction to and not necessarily reaching the optic disc border. Incident cerebrovascular events including stroke were recorded till December 2019. Cox proportional hazards models were used to assess the relationship between the RNFLD prevalence at baseline and the incidence of stroke in a multivariable model.

Results: Within a follow-up of 5 years (mean: 44 ± 12 months), 291 participants developed a cerebral stroke (2.0% ± 0.1%). After excluding those individuals with glaucoma, optic neuropathy, diffuse RNFL loss, and those with unevaluable fundus photographs, 215 participants with incident stroke were compared with a randomly selected control group (n = 2147). Incident stroke occurred in the 22nd month as mean (95% confidence interval (CI): 20 - 24 months) after enrollment. The RNFLD prevalence at baseline was significantly more frequently observed in the group with incident stroke than in the control group (83/215 (38.6% ± 3.3%) versus 296/2147 (13.8% ± 0.7%); Odds ratio: 3.93; $P < 0.001$). Cox proportional hazards model demonstrated a statistically increased risk of stroke in participants with RNFLDs ($P < 0.001$), with a hazards ratio (HR) of 3.87 (95% CI: 2.45 - 6.13), after controlling of age, sex, and comorbidity of diabetes or hypertension.

Conclusions: This study demonstrated the presence of RNFLDs as a biomarker for an increased risk of future cerebral strokes.

CONTROL ID: 3711255

SUBMITTER (NAME ONLY): Yinga Wu

TITLE: MiRNA-24 represses TGF-β2 induced epithelial-mesenchymal transition (EMT), endothelial-mesenchymal transition (EndMT), and fibrosis program

SESSION TITLE: Subretinal fibrosis – clinical challenges, mechanism, and diagnostic tools

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Wu, Y. Tong, K. Byrnes, Q. Zhou, J. Ma, S. Wang, Tulane University, New Orleans, Louisiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Subretinal fibrosis ccurs in multiple retinal diseases, including wet Age-related macular degeneration (AMD) and proliferative vitreoretinopathy (PVR). We have reported that miR-24 inhibits choroidal neovascularization (CNV) by regulating actin cytoskeleton remodeling. We aim to define the function of miR-24 in subretinal fibrosis. We hypothesize that miR-24 overexpression can repress epithelial-mesenchymal transition (EMT) and endothelial-mesenchymal transition (EndMT), therefore inhibiting fibrosis in AMD and PVR diseases.

Methods: MiR-24 overexpression in RPE and ECs was quantified by RT-qPCR. Fibrosis-related gene expression was measured by Western blot and immunostaining. Novel miR-24 target gene expression was tested by Western blot and confirmed by luciferase assays. Lentiviral-mediated knockdown or overexpression of target genes was used to mimic or rescue this phenotype. The effect of miR-24 on stress fiber formation was visualized by Phalloidin staining and quantified by ratio of G-actin/F-actin. Nuclear translocation of MRTF-A was tested in TGF-β2 treated cells after miR-24 overexpression. In PVR model, miR-24 overexpressing TGF-β2 treated RPE cells were delivered into mouse eye intravitreally. Fundus photography, histologic analysis and a PVR grading scheme were used to monitor PVR progression. Student’s t-test was used for statistical analysis.

Results: MiR-24 overexpression repressed EMT, EndMT-associated gene expression in both RPE and ECs as shown by Western blot and immunostaining. SMAD3, a major protein critical for fibrosis by mediating TGF-β signaling, was identified as a miR-24 target gene and was downregulated by miR-24 overexpression. Knockdown or overexpression of miR-24 target genes partially mimicked or rescued miR-24 overexpression phenotypes. miR-24 also repressed stress fiber formation and increased ratio of G-actin/F-actin, consistent with downregulation of its verified target protein. Overexpression of miR-24 inhibited nuclear translocation of MRTF-A in TGF-β2 treated cells. In the in vivo PVR model, miR-24 overexpression suppressed PVR formation, suggesting that miR-24 could repress fibrosis in vivo.

Conclusions: MiR24 overexpression prevents EMT, EndMT and fibrosis in RPE and EC cells through targeting TGF/SMAD3 and LIMK2/PAK4 pathways. MiR-24 will be investigated as a therapeutic agent for subretinal fibrosis in vivo.

CONTROL ID: 3711256

SUBMITTER (NAME ONLY): Arthur Chang

TITLE: Needs Assessment for the Development of a Patient-Centered Smartphone App for Uveitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Dyer, R. Grecky, D. Bergh, Innovation Center, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|A.Y. Chang, T. Al-Khaled, M. Munro, A. Lobo, P. Bhat, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Arthur Chang: Commercial Relationship: Code N (No Commercial Relationship) | Tala Al-Khaled: Commercial Relationship: Code N (No Commercial Relationship) | Monique Munro: Commercial Relationship: Code N (No Commercial Relationship) | Grace Dyer: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Grecky: Commercial Relationship: Code N (No Commercial Relationship) | Donald Bergh: Commercial Relationship: Code N (No Commercial Relationship) | Ann-Marie Lobo: Commercial Relationship: Code N (No Commercial Relationship) | Pooja Bhat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the unmet needs of inflammatory eye disease patients and their caregivers, with a goal towards developing a patient-centered smartphone application (app) for learning about and managing uveitis.

Methods: Prospective cross-sectional survey of uveitis patients and their caregivers. The data collected included: demographic information, time since diagnosis, educational level, smartphone ownership/use, smartphone type, use of health apps, interest in a uveitis app, current modalities for learning about uveitis, understanding and desired information about uveitis, challenges of being a uveitis patient/caregiver, current challenges in disease management, and the relative importance of a variety of possible app features.

Results: 79 completed surveys were collected from 74 patients and 5 caregivers. Among the respondents, 60% were female, 44.7% were Black or African American, and a majority (80%) of patients were aged between 30-74 years. 66% were uveitis patients or caregivers for less than 5 years, 92% used a smartphone regularly, and 97% expressed interest in a smartphone app for uveitis patients. While 60% of respondents reported having health-related apps on their phones, 58% did not use them regularly, and 85% did not currently use any smartphone apps to manage or learn about uveitis. Important features of a potential smartphone app for patients and caregivers included educational materials about uveitis (96%), accessibility considerations such as text size and text-to-voice features (95%), as well as reminders for appointments (67%), medications (89%) and lab work/blood tests (94%). Challenges faced by patients and caregivers included those related to ocular symptoms, understanding of the disease process, transportation, and the associated psychiatric burden. Patients and caregivers generally reported a moderate understanding of the disease process (55%) but a good understanding of uveitis treatment (81%) and the importance of follow-up testing (90%).

Conclusions: There is an unmet need for a patient-centered smartphone app for uveitis, featuring understandable educational content, reminders for appointments and medications, and a customizable interface to accommodate vision changes. Patients and caregivers who are motivated to seek information about uveitis, including newer patients or those with lower understanding about the disease, could especially benefit from a dedicated uveitis app.

CONTROL ID: 3711257

SUBMITTER (NAME ONLY): Jaime Brown

TITLE: Therapeutic Outcomes of Scleritis Treated with Tumor Necrosis Factor Inhibitors

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Brown, K. Boyd, L. Kopplin, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|A. Thomas, Vitreoretinal Surgery and Uveitis, Tennessee Retina, Nashville, Tennessee, UNITED STATES|K. Armbrust, Department of Ophthalmology, Minneapolis Veterans Affairs Health Care System, Minneapolis, Minnesota, UNITED STATES|K. Armbrust, Department of Ophthalmology and Visual Neurosciences, University of Minnesota, Minneapolis, Minnesota, UNITED STATES|M. Berkenstock, Ocular Immunology Division, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the efficacy of tumor necrosis factor (TNF) inhibitor agents in establishing scleritis quiescence and having a systemic corticosteroid sparing effect within the first year of TNF inhibitor therapy.

Methods: We conducted a multicenter retrospective chart review of patients with scleritis treated with a TNF inhibitor (adalimumab, infliximab, etanercept, golimumab, certolizumab) for at least six months between May 2016 and May 2021. Data on demographics, concurrent systemic diseases, prior therapeutic history, concurrent treatment with systemic corticosteroids, clinician assessment of scleritis activity and reason(s) for TNF inhibitor discontinuation was collected at pre-specified time points. We evaluated for scleritis quiescence and concurrent doses of systemic corticosteroids at 6 and 12 months.

Results: We identified 46 patients (56.5% female) treated for scleritis with TNF inhibitors. Mean ± SD age was 56 ± 13.5 years (range 15-87) when starting a TNF inhibitor. Underlying systemic autoimmune disease was present in 74% of subjects; rheumatoid arthritis was most common. Most patients had received prior immunosuppressive therapy (91%). 43 patients had active scleritis at time of initiation of TNF inhibitor therapy (33 adalimumab, 6 infliximab, 3 certolizumab, 1 etanercept). At 6 months 79% (34/43) of subjects obtained scleritis quiescence with TNF inhibition. At 12 months 77% (30/39) of subjects remained quiescent. Baseline daily corticosteroid use (22.5 ± 21.6 mg) decreased to 5.4 ± 8.4 mg by 6 months ($p<0.001$) and to 2.6 ± 5.9 mg by 12 months ($p<.0001$) of anti-TNF therapy.

Conclusions: TNF inhibitors are an effective scleritis therapy and provide significant systemic corticosteroid sparing effect.

CONTROL ID: 3711260
SUBMITTER (NAME ONLY): Yueh-Hsun Wu
TITLE: Estimating visual acuity without a visual acuity chart
SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: Y. Wu, R. Gage, G.E. Legge, Department of Psychology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|D. Yu, E.C. Watson, L. Waked, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|J.E. Goldstein, M.R. Gobeille, Johns Hopkins Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|M. Kwon, Department of Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|D.K. DeCarlo, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|C. Wang, Measurement and Statistics, University of Washington College of Education, Seattle, Washington, UNITED STATES|
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ABSTRACT BODY:

Purpose: Visual acuity (VA) measurement obtained from a letter acuity chart is assumed to predict the ability to resolve the visual details of objects in real life. Conversely, a person's ability to see object details in daily life could be used to estimate the person's visual acuity. The goal of our project is to determine if a person's Yes/No answers to a series of questions about their vision in daily life can be used to estimate their visual acuity.

Methods: 333 participants from four different testing sites responded to a set of 100 yes/no questions designed to assess people’s acuity for recognizing familiar objects at typical viewing distances. The questions were selected to evaluate acuities ranging from normal to ultra-low vision. A sample question is: "Are you able to count the individual tines on a fork that is sitting on the table in front of you?". Measured VA values were available from all participants and converted to logMAR units. The yes/no responses to the 100 questions were analyzed by a two-parameter (2PL) model based on Item Response Theory. The 2PL model estimated each participant's visual ability (θ) to answer the set of questions and the difficulty and discriminability of each question.

Results: The mean age and VA of the sample were 56.66 years (18 to 93, SD = 20.72) and 0.58 logMAR (-0.3 to 2.0 logMAR, SD = 0.45). The three largest diagnostic categories were glaucoma (17%), macular degeneration (13%), and cataract (9%). The percentage of yes responses answered by each participant was significantly correlated with their VAs ($r = -0.71$, $p < .001$). A strong relationship was also found between each participant's visual ability estimate (θ) from the 2PL model and their VA ($r = -0.72$, $p < .001$). Each participant's VA was predicted by their estimated theta based on the linear relationship between the two variables. The average prediction error, calculated by the absolute difference between the predicted VA and actual VA, was 0.23 logMAR (SD = 0.18). The same linear function was used to infer the acuity limit required for each question. For example, the VA limit of the question above about forks was 0.83 logMAR.

Conclusions: Our results show that a questionnaire can be used for estimating visual acuity worse than 20/40. The item responses provide insights into the real-world visual capabilities of people across a range of acuities and may be a potentially useful tool in telehealth.

CONTROL ID: 3711261

SUBMITTER (NAME ONLY): Eliesa Ing

TITLE: Isolation of trabecular meshwork (TM) RNA and analysis of gene expression following serial bevacizumab injections in rat eyes.

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Ing, W. Cepurna, D.C. Lozano, V. O'Callahan, Y. Yang, F. Chan, K.E. Keller, J.C. Morrison, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mechanism by which repeated intravitreal injections of the anti-VEGF drug beviczimab can produce chronically elevated intraocular pressure (IOP) is poorly understood. Here we describe a novel method for rat TM dissection, RNA isolation, and preliminary findings of TM gene expression after serial beviczimab injections.

Methods: Twelve Brown Norway male retired breeder rats were randomly assigned to receive 3 uniocular, pars plana intravitreal injections of either 0.20 µL bevacizumab (0.005 mg, n=6) or 0.20 µL balanced salt solution plus (BSS+ control, n=6) once per week under isoflurane anesthesia. Fellow eyes were untreated. Awake IOP (10 measurements per eye) was monitored three times per week prior to the start of injections and until the animals were sacrificed. One week after the third injection, animals were sacrificed, followed by immediate enucleation of both experimental and uninjected eyes. Anterior segments were first cut into quarters, and the iris and ciliary body removed with fine jewelers forceps to expose the TM. Using these same forceps, the TM was gently pealed off, revealing the outer wall of Schlemm's canal. TM tissue was placed in Trizol with the aid of a bent 30g needle and RNA was isolated using glycogen as a carrier. After pre-amplification, RT^2 Profiler PCR Arrays (Qiagen) were used to quantitate extracellular matrix and adhesion molecule-related gene expression.

Results: Linear regression indicated that IOP did not change in the experimental (P=.47) or control eyes (P=.48) over the 4 week experiment. We were successfully able to extract RNA from rat TM (n=24) obtained with the above technique (mean=77.6 ng/ml ± 38.1). In PCR arrays, Mmp11 was signficiantly downregulated in the TMs of beviczimab-injected eyes compared to fellow eyes (-2.97 fold, p = 0.046), but not in BSS+-injected eyes. Spp1 was significantly down-regulated in BSS+ eyes (-1.59 fold, p=0.031), but one of the fellow eye samples was unusable.

Conclusions: We can successfully isolate sufficient RNA from rat TM tissue for gene expression analysis. Mmp11 degrades α1-antitrypsin and IGFBP1, but has limited proteolytic activity on classical extracellular matrix molecules. Further work is needed over longer time periods to understand better the chronic effects of anti-VEGF injections on TM gene expression and IOP in this promising model.

CONTROL ID: 3711263

SUBMITTER (NAME ONLY): MILAN RAI

TITLE: Effect of flickering light stimulation on full-field electroretinography in mice

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. RAI, Laboratory of Experimental Optometry (Neuroscience), School of Optometry, The Hong Kong Polytechnic University, HONG KONG|Y. LAKSHMANAN, Centre for Eye and Vision Research (CEVR), 17W Hong Kong Science Park, HONG KONG|H.H. Chan, School of Optometry, The Hong Kong Polytechnic University, HONG KONG|H.H. Chan, Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, HONG KONG|

Commercial Relationships Disclosure: MILAN RAI: Commercial Relationship: Code N (No Commercial Relationship) | Yamunadevi LAKSHMANAN: Commercial Relationship: Code N (No Commercial Relationship) | Henry Chan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Flicker-induced retinal stimulation has been found to increase the retinal blood flow in response to increased metabolic demands of activated retinal neurons, but the influence of flickering light exposure on full-field electroretinogram (ffERG) is still unclear. The purpose of this study was to investigate the physiological changes of retinal response by ffERG after brief flickering light stimulation.

Methods: Nine anaesthetized C57BL/6J mice (10 week-old) were light adapted at 1 cd/m^2 for 10 minutes. After light adaptation, baseline ffERG (pre-flickering) was recorded and then was followed by 60 seconds of resting period to eliminate the aftereffect of light flashes. After resting period, the tested eye was stimulated by 8-Hz flickering light with 0.20 cd.s/m^2 for 60 seconds that was immediately followed by post-flickering ffERG recording. Amplitudes and implicit times of ERG responses measured before and after flickering light stimulation were compared by paired t-test.

Results: Retinal flickering light stimulation induced a significant increase in b-wave amplitude (pre-flickering amplitude=170.50±11.38μV; post-flickering amplitude=187.79±12.37μV; percentage change=10.42%±5.71%, $p<0.001$). However, there was no significant change in b-wave implicit time (pre-flickering implicit time=55.76±3.14ms; post-flickering implicit time=54.33±3.23ms; percentage change=-2.50%±7.18%, $p>0.05$), a-wave amplitude (pre-flickering amplitude=-43.50±7.07μV; post-flickering amplitude=-36.95±6.51μV; percentage change=-11.91%±56.37%, $p>0.05$) and a-wave implicit time (pre-flickering implicit time=22.08±1.11ms; post-flickering implicit time=21.87±1.21ms; percentage change=-1.12%±6.13%, $p>0.05$).

Conclusions: Flickering light stimulation on retina led to a significant increase in ERG responses originating from middle retinal layer, primarily from bipolar cells but did not have significant effect on responses originating from photoreceptors. Further studies are required to understand the mechanism underlying enhanced ERG responses related to flicker-induced hyperemia.

CONTROL ID: 3711264

SUBMITTER (NAME ONLY): M. Ali Khan

TITLE: Retrospective cohort analysis of patients with geographic atrophy (GA) secondary to age-related macular degeneration followed for 3 years in clinical practice.

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Khan, A.C. Ho, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|E. Rahimy, Retina Division, Palo Alto Medical Foundation, Palo Alto, California, UNITED STATES|R. Corley, M. Gallivan, T. Leng, Verana Health, California, UNITED STATES|D. Jones, R. Ribeiro, Apellis Pharmaceuticals Inc, Crestwood, Kentucky, UNITED STATES|T. Leng, Department of Ophthalmology, Stanford University, Stanford, California, UNITED STATES|N.M. Holekamp, Pepose Vision Institute, Chesterfield, Missouri, UNITED STATES|

Commercial Relationships Disclosure: M. Ali Khan: Commercial Relationship(s);Code C (Consultant/Contractor):Genentech, Apellis, Allergan;Code F (Financial Support):Regeneron | Ehsan Rahimy: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Pharmaceuticals | Allen Ho: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Pharmaceuticals | Ryan Corley: Commercial Relationship(s);Code E (Employment):Verana Health | Mark Gallivan: Commercial Relationship(s);Code E (Employment):Verana Health | Daniel Jones: Commercial Relationship(s);Code E (Employment):Apellis Pharmaceuticals | Ramiro Ribeiro: Commercial Relationship(s);Code E (Employment):Apellis Pharmaceuticals | Theodore Leng: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Pharmaceuticals;Code F (Financial Support):Verana Health | Nancy Holekamp: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Pharmaceuticals

ABSTRACT BODY:

Purpose: To report results from a retrospective analysis of clinical data, evaluating disease progression of patients with GA in 1 eye and either GA or choroidal neovascularization (CNV) in the other eye, over 3 years.

Methods: Patients (125,743) with GA in ≥1 eye were identified from the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) from January 2016 to March 2017. Patients were excluded if they had a history of CNV or active CNV in the study eye, a history of any other retinal condition, or <36 months of follow-up. Patients were grouped by fellow eye status: Cohort 1, GA:GA; Cohort 2, GA:CNV (study eye GA, fellow eye CNV). Subgroups were classified by lesion location: nonsubfoveal (NSF) or subfoveal. Main outcomes were study and fellow eye disease progression including visual acuity (VA) over 3 years.

Results: Patients (36,817) met the inclusion criteria: Cohort 1: 21,789 (59.27%); Cohort 2: 14,976 (40.73%). In the GA:GA Cohort, NSF study eyes had a better mean VA at baseline (67.37 letters) than subfoveal eyes (62.33 letters). Mean 3-year VA changes from baseline were comparable for NSF (−10.38) and subfoveal (−9.31 letters) study eyes. Similar trends were observed in the GA:CNV Cohort: NSF study eyes had a better mean VA at baseline (65.80 letters) than subfoveal eyes (46.80 letters). Mean 3-year VA changes from baseline were similar for NSF (−8.53 letters) and subfoveal (−8.26 letters) study eyes. In GA:GA and GA:CNV Cohorts, NSF study eyes with a baseline VA of ≥20/40 lost a mean of −10.33 and −8.19 letters and subfoveal eyes lost a mean of −8.59 and −9.96 letters over 3 years, respectively (Figure). NSF study eyes with a baseline VA of <20/40 and ≥20/100 in GA:GA and GA:CNV Cohorts lost a mean of −12.09 and −11.44 letters vs −13.57 and −12.89 letters, respectively in subfoveal eyes over 3 years (Figure).

Conclusions: GA caused substantial disease burden in this retrospective study of a large real-world database. Eyes with GA lost significant vision over a 3-year period, consistent with trends in the previously reported 2-year analysis. The rate of vision loss was numerically similar regardless of whether lesions were NSF or subfoveal at baseline. Eyes with good vision at baseline lost more letters over 3 years compared to eyes with poor vision.

CONTROL ID: 3711266

SUBMITTER (NAME ONLY): Seen Hang Chan

TITLE: Refractive error in Hong Kong preschool children and its association with near work

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chan, K. Choi, H.H. Chan, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|S. Chan, K. Choi, Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|H.H. Chan, Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Seen Hang Chan: Commercial Relationship: Code N (No Commercial Relationship) | Kai Yip Choi: Commercial Relationship: Code N (No Commercial Relationship) | Henry Chan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This cross-sectional study aimed to investigate the refractive error in Hong Kong preschool children and its association with near work (including digital device usage) among these children.

Methods: A total of 336 preschool children aged between 3 and 7 years from 6 local kindergartens were examined. Eye examinations including habitual visual acuity, photorefraction, and ocular biometric measurements were carried out. Parental questionnaires on environmental and behavioural factors including near work habits were collected. Refractive error, expressed as spherical equivalent power (SE), and axial length (AL) were the main outcome measures. Only data on right eye was presented. SE and AL were compared among groups with different time spent on near work, including reading, drawing, doing homework and using digital devices, including mobile phones and handheld electronic devices.

Results: In total, 9.82% of the children had an SE of at least -0.50 D while 24.70% of the children had an SE more than +0.50 D. The overall mean SE was +0.21±0.73 D, ranging from -4.00 D to +2.50 D. The mean AL was 22.41±0.72 mm, ranging from 20.03 mm to 24.69 mm. SE was negatively correlated with age ($r=-0.13$, $p=0.02$) but no significant difference was found between gender ($p=0.69$). AL was positively correlated with age ($r=0.40$, $p<0.001$) but no significant difference was found between gender ($p=0.23$). AL was also significantly correlated with height after age adjustment ($r=0.14$, $p=0.02$), but not weight ($p=0.90$). Children with less than 2 hours of non-digital near work per day had significantly more hyperopic SE than those with 2 hours or more (+0.29±0.60 vs +0.11±0.84, $p=0.03$), but no significant difference in AL was found ($p=0.09$). Children using digital devices for less than 2 hours per day also had significantly shorter AL than those with 2 hours or more (22.32±0.68 vs 22.50±0.79, $p=0.04$), but no significant difference was found in SE ($p=0.34$).

Conclusions: Longer time spent on near work, including doing homework, reading books and drawing, and on digital devices including mobile phone and handheld electronic devices were associated with more myopic refractive power in Hong Kong preschool children.

CONTROL ID: 3711267

SUBMITTER (NAME ONLY): Hirofumi Yogo

TITLE: Angle kappa measurement with swept-source optical coherence tomography using a vertical cavity surface emitting laser

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yogo, N. Takeno, S. Masegi, Advanced Technology Development Dept., Eye Care Div., Kabushiki Kaisha Nidek, Gamagori, Aichi, JAPAN|

Commercial Relationships Disclosure: Hirofumi Yogo: Commercial Relationship(s);Code E (Employment):NIDEK CO., LTD. | Naoki Takeno: Commercial Relationship(s);Code E (Employment):NIDEK CO., LTD. | Seiji Masegi: Commercial Relationship(s);Code E (Employment):NIDEK CO., LTD.

ABSTRACT BODY:

Purpose: Measurement of angle kappa (κ) is clinically important because a large κ can cause decentrations during intraocular lens (IOL) implantation, leading to decreased vision. However, it is difficult to directly measure κ in clinical practice. Hence, this angle is estimated from the magnitude of displacement of the light reflected from the cornea from the pupil center to the nasal aspect. However, there may be accurate methods to determine κ using optical coherence tomography (OCT). In this investigation, we report the κ measurements from a prototype swept-source (SS) OCT device that simultaneously captures images of the anterior segment and the fundus.

Methods: We captured low-resolution and high-resolution images of healthy eyes with the wavelength sweep frequencies at low-speed and high-speed modes with a SS-OCT. This prototype uses vertical cavity surface emitting laser (VCSEL) technology that can change the wavelength sweep frequency. In low-speed mode, the anterior segment and the fundus were captured in one shot to image the cornea, iris, anterior chamber angle, and fovea. This image serves as a reference image for aligning each segment when constructing the whole eye OCT image. In high-speed mode, the OCT images of the anterior segment and the fundus are captured separately. During anterior segment image capture, we measured the corneal curvature and anterior chamber width as references for calculation of the magnitude of distortion in OCT images captured at low-speed mode. The whole eye OCT image was constructed by aligning the image captured in high-speed mode with the reference image captured in low-speed mode. The whole eye OCT image was used to geometrically establish the pupillary axis (PA). The visual axis (VA) was estimated from the whole eye OCT image considering that the central OCT beam and the ray from the internal fixation lamp to the fundus are coaxial. The angle formed by PA and VA was used to calculate κ.

Results: The κ calculated from the whole eye OCT image was 4.78 deg.

Conclusions: We have developed a SS-OCT that simultaneously acquires images of the anterior segment and fundus and κ measurements. This method for measuring κ is expected to contribute to improving the accuracy of intraocular lens surgery.

CONTROL ID: 3711269

SUBMITTER (NAME ONLY): Isabelle Audo

TITLE: Psychometric validation of patient-reported outcome (PRO) and observer-reported outcome (ObsRO) measures in Retinitis Pigmentosa and Leber Congenital Amaurosis

SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I.S. Audo, Sorbonne Université, INSERM, CNRS, Institut de la Vision, CHNO des Quinze-Vingts, REFERET national rare disease center, Paris, FRANCE|N. Williamson, M. Barclay, J. Sims, K. Boparai, H. Bradley, Adelphi Mill, Bollington, Cheshire, UNITED KINGDOM|F. Patalano, C. Naujoks, C. Spera, J. Banhazi, Novartis Pharma AG, Basel, Basel-Stadt, SWITZERLAND|P. O'Brien, Novartis Ireland Ltd, Dublin, IRELAND|C. Kay, University of Florida, Gainesville, Florida, UNITED STATES|J. Green, Discipline of Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland, CANADA|T. Durham, Foundation Fighting Blindness Inc, Columbia, Maryland, UNITED STATES|M. Fischer, Centre for Ophthalmology, University of Tübingen, Tübingen, GERMANY|M. Fischer, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) and Leber Congenital Amaurosis (LCA) are rare inherited retinal degenerative disorders. There is no RP/LCA-specific measure of visual impairments and impacts on vision-dependent activities of daily living (ADL). The Visual Symptom and Impact Outcomes patient-reported outcome (ViSIO-PRO) and observer-reported outcome (ViSIO-ObsRO) measures were developed through qualitative research with RP/LCA patients, caregivers of child patients and expert clinicians. This study evaluated the psychometric properties of the instruments.

Methods: The 49-item ViSIO-PRO and 27-item ViSIO-ObsRO instruments were completed by 83 adult and adolescent patients and 22 caregivers of child patients aged 3-11 years with RP/LCA, respectively, at baseline and 12-16-day follow-up. Concurrent measures were also administered at BL. Psychometric analyses assessed item (question) properties, dimensionality, scoring, reliability, validity, and score interpretation.

Results: Responses to the ViSIO-PRO and ViSIO-ObsRO items were mainly evenly distributed across response options. Inter-item correlations were mostly moderate-to-strong (>0.30) at baseline within hypothesized domains. Item properties, qualitative data and clinical input supported retention of 35 ViSIO-PRO items and 25 ViSIO-ObsRO items. Confirmatory factor analysis supported a four-factor model (visual function symptoms, mobility, vision-dependent ADL and broader health-related quality of life). A bi-factor model supported calculation of total scores and domain scores. Internal consistency was high for all domain and total scores (Cronbach's alpha>0.70). Test-retest reliability for the total scores was strong between BL and 12-16-day follow-up (Intraclass Correlation Coefficients=0.66-0.98). Convergent validity was supported by strong correlations in a logical pattern with concurrent measures at baseline. There were statistically significant differences in mean ViSIO-PRO and ViSIO-ObsRO scores between known-groups

defined by global impression items at baseline. Distribution-based methods provide initial insights to guide interpretation of scores.
Conclusions: Findings supported item reduction, established the scoring of the ViSIO-PRO and ViSIO-ObsRO instruments, and provided evidence of reliability and validity as outcome measures in RP/LCA.

CONTROL ID: 3711270

SUBMITTER (NAME ONLY): Chu Jian Ma

TITLE: In vivo comparison of intracameral and intravitreal implantation of Miniaturized Injectable Delivery System (MIDS) for timolol maleate

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ma, Y. Zhang, J. Dickson, R. Bhisitkul, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|M. Vyakarnam, Oculinea, California, UNITED STATES|D. Bernards, T. Desai, Bioengineering, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is an unmet need for sustained drug delivery for glaucoma pharmacotherapy. We describe a miniaturized injectable delivery system (MIDS) based on biodegradable polymers engineered for zero-order release of timolol maleate for a minimum of 8 weeks, injected into the intracameral (IC) or intravitreal (IV) space

Methods: MIDS device is a cylindrical implant (unique thin-film semi-permeable polymeric membrane encapsulating a pharmaceutical core) that provides zero-order drug delivery, and fabricated for use with a 23-gauge needle. In vitro pharmacokinetics studies were performed in temperature- and pH-controlled fluid chambers over 20 weeks. MIDS devices were injected into the IC and IV space of New Zealand rabbits. Eyes were examined weekly, with intraocular pressures (IOP) measurements (Tono-Vet, iCare). At sacrifice at 8 weeks post-injection, eyes were enucleated and dissected, and ocular compartment drug concentrations were determined by lipid chromatography-tandem mass spectrometry. Two tailed student’s t-test was used for statistical analysis.

Results: In vitro studies of MIDS devices demonstrated approximate zero-order drug release over 1 to 5 months. Ocular safety was acceptable, without significant intraocular inflammation. At 8-week post injection, in vivo studies demonstrated that IOP in experimental eyes was lowered by 11.1±6.5% (N = 5, p = 0.019) for IC devices and 14.6±3.9% (N = 5, p = 0.020) for IV devices. Analysis of ocular tissues revealed different concentration profiles for IC vs. IV at 8 weeks (in ng/g; except for aqueous in ng/mL): aqueous 28.45±5.44 vs 4.50±2.15, iris 36.67±9.73 vs 32.52±25.30, vitreous 0.28±0.26 vs 37.17±19.03, and ciliary body 14.39±3.59 vs 50.93±18.64. Blood concentration of drug was below the quantitation limit (< 0.4ng/ml) at 8 weeks for both groups

Conclusions: MIDS devices achieved zero-order release of timolol maleate in vitro. Over 8 weeks, implanted eyes' mean IOPs were lowered compared to controls at each weekly timepoint with similar levels of reduction between IC and IV. Target tissue drug concentrations at the ciliary body at 8 weeks exceeded therapeutic levels. Compared to IC, IV injection appeared to result in 4-5 times higher drug levels in the ciliary body. The technology has the potential to be provide continuous IOP-lowering therapy to overcome issues of patient compliance with daily eye drops

CONTROL ID: 3711271

SUBMITTER (NAME ONLY): Carlo Galang

TITLE: Non-adaptive optics imaging of photoreceptor mosaic imaging and parafoveal cone density measurement using high magnification module of Heidelberg Spectralis in patients with age-related macular degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.B. Galang, D. Bartsch, A. Warter, F.P. Kalaw, L. Cheng, W.R. Freeman, Jacobs Retina Center, University of California San Diego, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We wanted to assess the quality of images of photoreceptors and cone density in parafoveal region using the High Magnification Module of Heidelberg Spectralis in patients with age-related macular degeneration.

Methods: We captured 8x8-degree area on primary gaze using the high magnification lens of the Heidelberg Spectralis in high-resolution mode. 10 eyes of 6 subjects with age-related macular degeneration were imaged. A 2mm pupil diameter was achieved by illuminating the fellow eye with a flashlight to eliminate the diffraction from astigmatic errors. We analyzed 200 x 200 μm within 5 degrees from the fixation. Using the image J, we estimated for the cone density and computed for the proportion to the number of cones/mm^2.

Results: Astigmatic errors can be reduced by taking the scans through a pupil of less than 3mm. The mean cone density in our study was 10992 cones/mm^2 (±1460.07) in 6 patients (mean age of 80 years) compared to 14,988 cones/mm2 (±1403.15) in non-AMD eyes (Mendonça et al.) in 8 patients (mean age of 33 years). Our patient population is significantly older, and as expected, analysis of regions in each macula shows more photoreceptor loss in areas of drusen in younger and non-AMD eyes (Mendonça).

Conclusions: We found that elderly patients have reduced number of cone count compared to younger patients. Areas adjoining drusen have particularly lower cone counts. Drusen and age are associated with reduced global and focal macular density. The high magnification SLO using narrow aperture does permit study of regional and focal cone density without adaptive optics.

CONTROL ID: 3711274

SUBMITTER (NAME ONLY): Yeganeh Madadi

TITLE: Identification of Retinal Cell Types Based on Single-Cell Transcriptomics

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Madadi, University of Tehran, Tehran, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)| Y. Madadi, J. Sun, S. Yousefi, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|H. Chen, Pharmacology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|R. Williams, S. Yousefi, Genetics, Genomics and Informatics, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify different retinal cell types from patterns of transcriptome data and to evaluate the model based on data from different batches.

Methods: We developed a deep domain adaptation model to identify retinal cells based on single-cell RNA sequencing (scRNA-seq) data (Fig. 1). The dataset included 44,808 single cells from 39 retinal cell types with 24,658 genes collected from mice in seven different batches (B1 to B7). Our unsupervised model included source classification, adversarial, and target virtual adversarial loss functions in the learning process along with domain adaptation strategy based on conditional maximum mean discrepancy (CMMD) loss function to align the source and target distributions to reduce misclassification error and maximize robustness. We evaluated the proposed model using classification accuracy and confusion matrix based on data from different batches.

Results: The number of cells in each batch ranged from 3226 to 8336 (Fig. 2-B). The accuracy of the model based on different pairs of batches is shown in Fig. 2-C to 2-H. The mean accuracy of the model for correctly classifying 39 different retinal cell types was ~92%. Across seven different batches, the identification accuracies of the model ranged from 74% to nearly 100%. Our results outperformed several state-of-the-art models.

Conclusions: We integrated multiple loss functions to a deep learning-based domain adaptation model to identify retinal cell types from scRNA-seq data and achieved a high level of accuracy in detecting correct retinal cell types. The model was relatively resistant to batch effect and could be used in single-cell studies to detect various cell types from different tissues.

CONTROL ID: 3711275
SUBMITTER (NAME ONLY): Jennie Diec
TITLE: Visual Performance of S.T.O.P® contact lenses compared to MiSight
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: To compare the visual performance of Spatio-Temporal Optical Phase (S.T.O.P®) contact lenses (CL) against MiSight® (MS) in myopic young adults. S.T.O.P CL feature rotationally asymmetric power maps, designed with meridionally and azimuthally varying power distributions, combined with a peripheral carrier configured with rotation assisting features. The resulting dynamic optical signal on the retina may decelerate the rate of myopia progression and minimise the decay of treatment effect found in options which provide a relatively static optical signal.
Methods: Prospective, randomized, single-masked (participant), cross-over trial where participants aged 18-39 years wore MS and two S.T.O.P designs (F2 and DT), each for a minimum of 5 days at 6 hours/day, daily wear, with CLEARCARE disinfection. Following CL wear, visual performance was assessed with subjective questionnaire (0-100 scale) for clarity of vision and ghosting (distance, intermediate, near), driving vision, overall vision satisfaction and comfort. Willingness to purchase was assessed with a binary Yes/No response. High and low contrast visual acuity (HCVA/LCVA) were measured monocularly and binocularly at 6m. HCVA was also measured binocularly at 70, 50 and 40cm. Differences between designs were assessed using linear mixed model, a Bonferroni correction was applied where applicable, and significance was set at 5%.
Results: F2 was better than MS for clarity of vision at intermediate (71±18 vs. 61±24, $p<0.001$) and near (78±16 vs. 64±28, $p<0.001$) while MS was better than DT at near (64±28 vs. 56±26, $p<0.001$). F2 was better for ghosting than MS (79±24 vs. 64±30, $p<0.001$), and the difference was independent of distance ($p=0.13$). There were no differences between designs for driving vision, comfort, overall vision satisfaction, or willingness to purchase ($p>0.06$).
MS was better than F2 and DT for monocular and binocular HCVA at 6m (mean difference [MD]≤ 2 letters; $p\leq0.001$ and ≤0.002, respectively) and binocular HCVA at 50cm (MD≤2 letters, $p\leq0.02$). There was no difference between designs for LCVA ($p>0.07$).
Conclusions: Though MS was significantly better than both S.T.O.P designs for HCVA, the MD was only 2 letters. Overall, both S.T.O.P designs were comparable to MS for visual performance, with F2 outperforming MS in some aspects of subjective visual performance.

CONTROL ID: 3711283

SUBMITTER (NAME ONLY): Lucie Guo

TITLE: Multiplex CRISPR genome regulation in the retina

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: AAV gene therapy in the age of CRISPR-based gene targeting has emerged as a potentially disruptive technology for previously incurable ocular diseases, but its applications are so far limited to monogenic diseases. The capability to perform multiplexed targeting of endogenous genes would open the field of ocular gene therapy to new applications, including polygenic diseases. Recent discovery of alternative CRISPR systems beyond the widely used SpCas9 has expanded the toolkit for genetic manipulation. CRISPR-Cas12a systems enable simultaneous targeting of multiple genomic loci by processing numerous crRNAs from a single transcript, but this capability had not yet been demonstrated in vivo, in part due to relatively low efficiency of Cas12a systems.

Methods: We used structure-guided protein engineering to develop an improved LbCas12a variant, and we tested its in vivo function through AAV-based delivery to retinal ganglion cells as well as subretinal delivery by electroporation in postnatal mice.

Results: Compared to wildtype Cas12a, our improved dCas12a variant has significantly greater efficacy in gene activation, especially at low CRISPR-RNA (crRNA) conditions. It also achieves improved gene repression and gene editing. Additionally, it has similar off-targeting effects compared to its wildtype equivalent. This new Cas12a variant achieved improved AAV-based gene editing in retinal ganglion cells in vivo. Additionally, delivery of the improved dCas12a-activator with a single crRNA array simultaneously activated multiple endogenous targets and directed the differentiation of retinal progenitor cells in retina of postnatal mice.

Conclusions: Our system enables simultaneous modulation at multiple genomic loci, thus paving the way for CRISPR-based modulation of multiple pathways or synergistic targets, such as in the case of non-monogenic diseases which consist of a large proportion of human diseases.

CONTROL ID: 3711284

SUBMITTER (NAME ONLY): Nabill Munshi

TITLE: Incidence and Predictors of SLK in Thyroid Eye Disease

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Munshi, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|D. Rootman, Orbit & Ophthalmic Plastic Surgery, Doheny Eye Institute, Los Angeles, California, UNITED STATES|N. Munshi, Charles Drew University of Medicine and Science, Los Angeles, California, UNITED STATES|R. Goldberg, D. Rootman, Orbit & Ophthalmic Plastic Surgery, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Nabill Munshi: Commercial Relationship: Code N (No Commercial Relationship) | Robert Goldberg: Commercial Relationship(s);Code C (Consultant/Contractor):Horizon Pharmaceuticals | Daniel Rootman: Commercial Relationship(s);Code C (Consultant/Contractor):Horizon Pharmaceuticals

ABSTRACT BODY:

Purpose: Thyroid Eye Disease (TED) is an autoimmune disease that affects 20-25% of patients with Grave's disease. In the course of TED, the eyelids, orbital fat, orbital adnexa, ocular surface and extra ocular muscles have the potential to be affected. TED can be detrimental to patients both physiologically and psychologically, thus severely affecting a patients quality of life. Ocular surface irritation is a common complaint for patients with TED, and it can be multifactorial. One of the lesser studied causes of this discomfort is superior limbic keratoconjunctivitis (SLK). The focus of this study was on understanding SLK incidence in patients diagnosed with TED and what factors may contribute to SLK manifestation.

Methods: Consecutive patients presented to a TED clinic over a 2 year period. A complete thyroid related history and examination was performed following the VISA template. The presence of SLK was determined by the staining of lissamine green of the superior limbus. Other TED markers, such as changes to eyelid position, proptosis and strabismus were recorded. Ocular surface factors were also recorded. All data was extracted and stored in a TED related database. The incidence of SLK was calculated and binary and multivariate statistics were performed to determine potential associated factors.

Results: Sample consisted of 268 patients. The SLK incidence in this cohort was found to be 5%. Bivariate statistical analysis showed no relationship/difference between various demographics, thyroid bloodwork, eyelid position and signs of corneal disease.

Conclusions: Typical demographic, clinical and serum values of TED were not predictive of SLK. A clear relationship between SLK incidence and severity of TED or characteristics of TED was not found. SLK remains an idiosyncratic reaction affecting approximately 5% of patients with TED.

CONTROL ID: 3711285

SUBMITTER (NAME ONLY): Amanda Carpenter

TITLE: Diagnostic efficacy of 24-2C SITA Standard global summary indices

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Carpenter, T. Callan, S. Yu, N. Graves, C. Wu, G.C. Lee, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|I.A. Falkenstein, Glaucoma Specialists of San Francisco, Oakland, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: 24-2C SITA Standard is a prototype visual field (VF) test using the 24-2C test pattern, which added 10 new test locations to the 24-2. In this clinical study, we explored the diagnostic efficacy of global summary indices derived from 24-2C SITA Standard in a preliminary cohort of normal and glaucomatous eyes.

Methods: 24-2C SITA Standard (SS-C) and 24-2C SITA Faster (SFR-C) VFs were acquired on an HFA3 perimeter (ZEISS, Dublin, CA) at each of two visits on one eye of a group of 32 normal and 34 glaucomatous subjects. 24-2 SITA Standard (SS) and 24-2 SITA Faster (SFR) VFs were extracted from 24-2C VFs. The last qualified test for each VF was used for data analyses. The diagnostic performance for the VF global indices of Mean Deviation (MD), Visual Field Index (VFI) and Pattern Standard Deviation (PSD) was assessed using the area under the receiver operator characteristic curve (AROC) and sensitivity. AROCs were compared to those of SS and SS-C.

Results: Mean age was 58.1 (standard deviation, SD: 7.6; range: 44 to 75) years for normal subjects and 71.6 (SD: 9.2; range 53 to 98) years for glaucoma patients. Mean MD_{SS-C} was 0.35 (SD: 1.02; range: -1.63 to 2.45) dB and -8.57 (SD: 8.15; range: -25.29 to 1.39) dB in normal and glaucomatous eyes ($P<0.001$), respectively (see Table 1). The AROC of MD_{SS-C} was 0.95. Compared to MD_{SS-C}, the AROCs for MD_{SS}, MD_{SFR}, and MD_{SFR-C} were 0.94 ($P=0.120$), 0.94 ($P=0.563$), and 0.95 ($P=0.889$), as shown in Table 2. The sensitivities at 95% specificity were 82.0% (MD_{SS}), 71.0% (MD_{SFR}), 85.0% (MD_{SS-C}), and 76.0% (MD_{SFR-C}), respectively. The AROC of VFI_{SS-C} was 0.97. Compared to VFI_{SS-C}, the AROCs for VFI_{SS}, VFI_{SFR}, and VFI_{SFR-C} were 0.96 ($P=0.799$), 0.96 ($P=0.881$), and 0.96 ($P=0.873$), as shown in Table 2. The sensitivities at 95% specificity were 88.0% (VFI_{SS}), 88.0% (VFI_{SFR}), 88.0% (VFI_{SS-C}), and 85.0% (VFI_{SFR-C}), respectively. Similar results were observed for PSD.

Conclusions: The findings in this preliminary cohort suggest that the new 24-2C SITA Standard global summary indices may have similar (non-inferior) diagnostic performance to those of the existing 24-2 and 24-2C SITA strategies. In terms of global summary indices, 24-2C SITA Standard may provide a reasonable clinical alternative to current clinical threshold strategies for the diagnosis of glaucoma.

CONTROL ID: 3711292

SUBMITTER (NAME ONLY): Arijit Chakraborty

TITLE: A multi-day cumulative effect of non-invasive brain stimulation on the visual cortex

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chakraborty, B. Thompson, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|A. Chakraborty, K. Hall, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|B. Thompson, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Non-invasive brain stimulation can induce an acute, transient change in neural excitability when applied to the visual cortex. If sustained, brain stimulation-induced changes in visual cortex excitability could have important implications for the treatment of amblyopia and other brain-based vision disorders. Using a double-blinded study design we investigated whether multiple daily sessions of visual cortex transcranial random noise stimulation (tRNS), a type of non-invasive brain stimulation, have cumulative and lasting effects on visual cortex excitability.

Methods: 53 participants (26 ± 5 years) with normal vision were enrolled. In a preliminary baseline session, phosphene thresholds (the minimum intensity of visual cortex single-pulse transcranial magnetic stimulation required to induce a phosphene percept) were measured. Lower phosphene thresholds indicate greater visual cortex excitability. 34 of 53 adults could reliably detect phosphenes and continued with the study. The participants were then randomly assigned to the treatment (tRNS) or control (sham stimulation) group and completed five consecutive daily tRNS/sham sessions. High-frequency tRNS (1mA, 100-640 Hz) or sham stimulation was applied to the primary visual cortex for 40 mins. Phosphene thresholds were measured pre- and post-tRNS/sham stimulation on each stimulation day, and then every 24h for 3 days after the final stimulation day.

Results: A repeated-measures general linear model conducted on the phosphene threshold data revealed a significant interaction ($p < 0.001$) between Stimulation Type (tRNS vs. sham) and Time (baseline, 5 x stimulation days [post stimulation thresholds], 3 x post-stimulation sessions). tRNS induced a cumulative, daily reduction in phosphene threshold indicating a sustained enhancement of visual cortex excitability. Sham stimulation had no effect. In the tRNS group, phosphene threshold was reduced by 15 ± 3% from baseline on stimulation day 5, an effect that was still statistically significant 24h (9 ± 3.5%, $p < 0.001$) and 48h (4 ± 2%, $p = 0.003$) later. The effect waned when remeasured 72h post-stimulation.

Conclusions: Our results provide the first evidence of a sustained increase in cortical excitability following multi-day non-invasive brain stimulation. This finding warrants further study into the potential of tRNS as a tool to enhance vision rehabilitation in amblyopia and other brain-based visual disorders.

CONTROL ID: 3711294

SUBMITTER (NAME ONLY): Yuhua Rui

TITLE: Imaging retinal microglial cell dynamics in healthy and diseased eyes in vivo with adaptive optics

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Rui, M. Zhang, V. Snyder, R. Raghuraman, S. Yadav, M. Errera, E.A. Rossi, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|Y. Rui, Eye Center of Xiangya Hospital, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|D.M. Lee, E.A. Rossi, Department of Bioengineering, University of Pittsburgh Swanson School of Engineering, Pittsburgh, Pennsylvania, UNITED STATES|E. Gofas, K. Grieve, INSERM, CNRS, Institut de la Vision, Sorbonne Universite, Paris, Île-de-France, FRANCE|E. Gofas, K. Grieve, INSERM-DGOS CIC 1423, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|P. Mecê, DOTA, ONERA, Universite Paris-Saclay, Saint-Aubin, Île-de-France, FRANCE|P. Tiruveedhula, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently showed that a refined sequential detection pattern for multi-offset adaptive optics scanning light ophthalmoscopy (AOSLO) can increase the contrast of weakly scattering inner retinal structures, including presumed microglial cells. However, sequential detection was still time-consuming, preventing dynamics from being monitored over short intervals (< 3 mins). Here we show that fiber-bundle (FB) detection AOSLO overcomes this limitation to reveal microglia and immune cell dynamics in healthy and diseased retinas.

Methods: We designed and implemented a custom 7-fiber optical FB in AOSLO that allows for simultaneous confocal and multi-offset detection. We imaged the nerve fiber layer at several locations at multiple timepoints (from minutes to weeks) in 5 healthy participants and in 3 patients with ocular syphilis or uveitis. Microglia and immune cells were manually segmented for quantification.

Results: Fiber-bundle detection reduced single acquisition time to 10-20 sec, permitting improved imaging over larger areas and monitoring of dynamics over short intervals. Microglia in healthy retinas ranged in size from 7 to 19 μm (mean:13 μm) and appeared in two distinct morphologies including rounded cells and elongated cells with visible processes. Microglia moved slowly in healthy eyes (0.05 μm/sec on average), but their motility was increased in patients with active infections or inflammation up to 0.34 μm/sec. Macrophage-like cells containing granular internal structures were seen in an eye with acute syphilitic posterior placoid chorioretinitis. Images were acquired at multiple time points during treatment, decreases in the quantity and motility of microglia were correlated with improvements of vision and other biomarkers. Microglia activity was apparent in an eye affected by acute retinal vasculitis but absent in another patient’s eye affected by a chronic course of retinal vasculitis that was quiescent at the time of imaging.

Conclusions: FB-AOSLO has revealed the fine-scale structure and dynamics of microglia in the retina during active infection and inflammation in the living eye for the first time. FB-AOSLO offers promise as a powerful tool for detecting and monitoring retinal inflammation and infection in the living eye over short timescales. FB-AOSLO may be useful for distinguishing cases of active infection/inflammation and for evaluating response to treatment.

CONTROL ID: 3711295

SUBMITTER (NAME ONLY): Xiaoran Wang

TITLE: Endoplasmic reticulum stress enhances lens fibrosis through PERK-mediated autophagy

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Wang, S. Huang, Y. Liu, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To investigate the function of endoplasmic reticulum stress in the development of fibrotic cataract and its underlying mechanisms.

Methods: C57BL/6 mice were punctuated with a 26-gauge needle in the central lens capsule as the fibrotic cataract model. Primary rabbit lens epithelial cells (LEC) were exposed to TGF-β2. eIF2α inhibitor ISRIB was used to treat LEC both in vivo and in vitro, ER stress inhibitor 4-PBA, inducer thapsigargin and tunicamycin, IRE1α inhibitor 4μ8C were used to treat LEC in vitro. LECs were transfected with siRNA to knockdown ATF4. Western blot assays and immunofluorescence staining were carried out to measure changes in protein expression such as BIP, eIF2α, IRE1α, LC3-II, p62, FN, α-SMA, etc. mRNA expression was investigated by RT-PCR. Autophagosome was observed by electron microscopy (TEM). Immunostaining and mRFP-GFP-LC3 reporter were applied to indicate autophagy flux. Clinical parameters were measured using slit-lamp bio-microscopy.

Results: ER stress was triggered during fibrotic cataract and TGFβ2-induced EMT of LEC, which in turn enhanced the EMT process. PERK/eIF2α/ATF4 branch of unfolded protein response is selectively required for EMT. Anterior chamber injection of ISRIB in fibrotic cataract mouse model showed significantly improved clinical parameters and limited capsular opacities. Interestingly, we found ISRIB decreased LC3-II, along with impaired the turnover of p62 in a time-dependent manner. Besides, TEM showed abnormally autophagic vacuoles under TGFβ2 stimulation, which was largely abolished by the cotreatment with ISRIB. To further investigate the crosstalk between ER stress and autophagy during fibrotic cataract, autophagic inducer rapamycin and lysosomal inhibitor chloroquine was used. Our results indicated that the suppression of ISRIB on mesenchymal gene expression was attenuated by rapamycin, but augmented by CQ, indicating that the regulation of autophagic flux by ISRIB is implied in the anti-fibrotic process.

Conclusions: Our research for the first time suggests that the activation of ER stress in fibrotic cataract both in vivo and in vitro. PERK/eIF2α/ATF4 branch selectively regulates EMT process in LEC through autophagy. eIF2α inhibitor, ISRIB, is highly effective at suppressing the development of lens subcapsular plaque and keeping the transparency of lens. Thus, ISRIB may be a potential therapeutic target to reduce EMT and fibrotic diseases.

CONTROL ID: 3711298

SUBMITTER (NAME ONLY): Heeyah Song

TITLE: Long-term outcomes of Statin therapy on Vitrectomy: a multicenter electronic medical record cohort study

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Pakhchanian, S. Rosenberg, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|H. Song, E. Flynn, M. Dalal, Ophthalmology, The George Washington University, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine differences in one year postoperative complications following pars plana vitrectomy (PPV) in patients who are on statin therapy.

Methods: A retrospective cohort study was done with data collected from TriNetX (Cambridge, USA), a federated electronic health records network. Patients who underwent PPV were identified by CPT code and separated between those on statin therapy for one-year preceding PPV and those without statin use. This study used propensity score matching to match the two cohorts for age, sex, and other systemic comorbidities. The primary outcomes measured after one year in the postoperative period included: vitreous hemorrhage, choroidal hemorrhage, retinal detachment or break, retinal edema, cystoid macular degeneration, macula puckering, intraoperative complications and disorders of the eye, ischemic optic neuropathy, cataracts, glaucoma, strabismus, corneal edema, dry eye syndrome, central retinal vein and artery occlusion, vitreous opacities, ptosis, lens dislocation, endophthalmitis, and retinal vascular occlusions.

Results: A total of 54,159 patients were identified to have undergone PPV and stratified into statin vs. non-statin use cohorts with 13,592 patients in each cohort after propensity matching. The cohort with prior history of statin therapy had a significantly higher risk of developing vitreous hemorrhage (RR, 1.15; 95% CI 1-1.33), retinal edema (RR, 1.15; 95% CI, 1.02-1.3), macula puckering (RR, 1.21; 95% CI 1.1-1.33), intraoperative complications of the eye (RR, 1.47; 95% CI 1.13-1.91), glaucoma (RR, 1.12; 95% CI 1.02-1.23), vitreous opacities (RR 1.42; 95% CI, 1.19-1.69) and ptosis (RR, 1.42; 95%; CI 1.13-1.79). The statin group had significantly lower risks of developing retinal vascular occlusions (RR, 0.7; 95% CI 0.56-0.89) and lens dislocation (RR, 0.75; 95% CI 0.66-0.86). No other significant differences were found between the cohorts.

Conclusions: Statin is one of the most prescribed medications. This study found an association between statin use with increased risk of developing vitreous hemorrhage, retinal edema and vitreous opacities in the long term post-operative period. This is possibly due to statin's biphasic effect on angiogenesis. Statin use was also associated with lower risks of retinal vascular occlusions and lens dislocation. This study highlights various associations of statin therapy on outcomes after PPV.

CONTROL ID: 3711299

SUBMITTER (NAME ONLY): Tamar Ben-Yosef

TITLE: Autosomal dominant retinitis pigmentosa with reduced penetrance due to an intronic mutation in PRPF31

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ben-Yosef, T. Ali Nasser, S. Zayit-Soudry, Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa, ISRAEL|S. Zayit-Soudry, Department of Ophthalmology, Rambam Health Care Campus, Haifa, ISRAEL|E. Banin, D. Sharon, Hadassah Medical Center Department of Ophthalmology, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: To identify the molecular basis for autosomal dominant retinitis pigmentosa (adRP) with reduced penetrance in an Israeli Muslim Arab family.

Methods: Patients underwent a detailed ophthalmic evaluation, including funduscopic examination, visual field testing, spectral-domain optical coherence tomography, fundus autofluorescence imaging and electroretinography. Genetic analysis was performed by a combination of whole exome sequencing and Sanger sequencing. Pathogenicity of the identified intronic variant was evaluated in silico using several web-based tools; in vitro, using a minigene-based assay; and in vivo, using reverse transcription-PCR analysis of lymphocyte-derived RNA.

Results: Affected individuals had childhood onset of night blindness followed by concentric restriction of the visual field. Ophthalmoscopic findings included narrowed retinal blood vessels and mid-peripheral bone spicule pigmentation. Full-field electroretinography was non-measurable in the third decade of life. In affected individuals we identified a novel heterozygous intronic variant, located at position +5 of PRPF31 intron 11 (c.1146+5G>T). The same variant was also detected in an unaffected family member. The variant was predicted to alter splicing of intron 11 by in silico analysis. In vitro splicing assay and reverse transcription-PCR analysis of lymphocyte-derived RNA revealed that the wt allele yielded both the expected product, harboring exon 11, and a shorter product in which exon 11 was skipped. The mutant allele yielded mainly the shorter product. Skipping of exon 11 is expected to cause a frameshift which yields an aberrant truncated protein (p.Tyr359Serfs*29). These results suggest that some degree of alternative splicing of exon 11 may occur normally, and that the c.1146+5G>T allele further weakens intron 11 donor splice-site and enhances the skipping of intron 11.

Conclusions: We report a novel intronic mutation in PRPF31 underlying adRP. This report expands the spectrum of pathogenic mutations in PRPF31 and further demonstrates the importance of intronic mutations. Moreover, it demonstrates the phenomena of reduced penetrance, previously associated with PRPF31 mutations.

CONTROL ID: 3711300

SUBMITTER (NAME ONLY): Christine Morozova

TITLE: Localization of the Internal Limiting Membrane Flap After Macular Hole Surgery

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Morozova, A. Morozov, D. Kamen, D.S. Boyer, H. Tabandeh, Retina Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|J. Zhang, M. Walsh, Retina Associates, Tucson, Arizona, UNITED STATES|R. Favale, F. Boscia, Department of Neurosciences and Sensory Organs, Universita degli Studi di Bari Aldo Moro, Bari, Puglia, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the status of the internal limiting (ILM) flap following various ILM flap techniques for macular holes (MH).

Methods: Retrospective case series including eyes that underwent pars plana vitrectomy (PPV) and ILM flap for MH. The FLAP techniques included conventional ILM flap (C-ILM), temporal ILM flap (T-ILM), superior wide-base ILM flap transposition (SWIFT), and pedicle ILM flap (P-ILM). Postoperative imaging included ICG fluorescence imaging (ICG-FI) (Spectralis, Heidelberg Engineering Inc., Heidelberg, Germany) and optical coherence tomography (OCT).

Results: 49 eyes of 40 patients, mean age 68.3 years, with mean follow-up of 10.3 months were included in the study. Ten (20%) eyes were highly myopic, 22 (45%) eyes had chronic MH, and 7 (14%) eyes had history of prior MH surgery. The ILM flap technique included C-ILM / T-ILM (22 eyes), SWIFT (25 eyes), and P-ILM (2 eyes).

The MH closed in 46 (94%) eyes. ICG fluorescence attributable to ILM flap was detected in all eyes, however, in 3 eyes the flap borders were not discernable. The ILM flap covered the MH completely in 36 (75%) eyes, partially in 7 (15%) eyes, and provided no coverage in 5 (10%) eyes. In 1 eye it was not possible to ascertain coverage on ICG-FI or OCT. In the 2 eyes with P-ILM the ICG-FI showed a displaced flap with no coverage of the MH.

In cases with closed MH, OCT demonstrated intraretinal ILM fragments in 5 (23%) eye in I-ILM /T-ILM groups, and in none of the eyes in SWIFT or P-ILM group. Imaging with ICG-FI / OCT showed folding of the ILM flap in 14 (64%) eyes in I-ILM / T-ILM group, in 6 (24%) eyes in SWIFT /P-ILM group, and in 1 eye in P-ILM group.

Conclusions: ILM flap techniques are associated with a high MH closure rate and are useful in the management of MHs with high-risk characteristics. Postoperative multimodal imaging including ICG-FI and OCT indicates good coverage of the MH by the ILM flap in the majority of the cases.

CONTROL ID: 3711302

SUBMITTER (NAME ONLY): Vinay Pulimamidi

TITLE: Novel PAX6 variants and their roles in corneal epithelial regulation and homeostasis

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.K. Pulimamidi, S. Maddileti, I. Mariappan, Center for Ocular Regeneration, Prof. Brien Holden Eye Research Center, Hyderabad Eye Research Foundation, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|V.K. Pulimamidi, School of life sciences, University of Hyderabad, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Patients with aniridia associated PAX6 mutations develop corneal and anterior segment defects. This study aims to understand the mechanisms of PAX6 regulation at the limbus and its effects on cornea-specific gene targets.

Methods: Multiple ocular cell lines, primary limbal cultures, human corneo-scleral tissues and hiPSC-derived ocular tissues were evaluated for differential expression of PAX6 variants and their spatial distribution by qRT-PCR, Sanger sequencing, luciferase reporter assays, ChIP-PCR, Immunocytochemistry (ICC), Immunohistochemistry (IHC) and RNA-FISH assays. Statistical analysis was performed using Student's t test.

Results: We report the identification of four novel splice variants of PAX6 in human ocular tissues and are generated by alternative splicing at two major splicing hotspots near Exon 5-6-7 and Exon 12-13 splice junctions. These variants carry in-frame deletions, possibly affecting either the N-terminal paired domain-mediated DNA binding or C-terminal PST domain-mediated transactivation functions. qRT-PCR evaluations revealed that these novel splice variants are driven by the PAX6 pA promoter in all ocular tissues and was highly expressed in the limbal and corneal epithelium. Activation of canonical Wnt signals in limbal cultures induced the expression of novel splice variants. Luciferase reporter assays using recombinant PAX6 isoforms has confirmed negative auto-feedback regulation on PAX6 pA promoter. While PAX6A could activate K3 promoter, it had no effect on K12, TAp63 and dNp63 promoters. However, a paired domain truncated isoform significantly activated the dNp63, K12 and K3 promoters. In situ localization studies using RNA-FISH combined with ICC/IHC has confirmed that the novel variants are co-expressed along with PAX6A transcripts in a sub-set of cells that are predominantly located at the basal and suprabasal layers of limbal and corneal epithelium. These cells are identified as $PAX6^{Low}$, $p63\alpha^{High}$, $BrdU^{+}$ and $K3/K12^{-}$ proliferating and migrating TACs.

Conclusions: The novel PAX6 splice variants alter the relative stoichiometry of wild type transcripts and ensure low levels of PAX6 expression in basal cells. This enables the self-renewal of activated LSC and expansion of TACs, while preventing pre-mature differentiation, thus promoting optimal epithelial stratification during normal corneal development and wound healing.

CONTROL ID: 3711304
SUBMITTER (NAME ONLY): Kique Romero
TITLE: Agreement of macular thickness map in low-cost OCT
SESSION TITLE: OCT Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Romero, H. Bagherinia, S.A. Bello, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Macular Thickness Analysis (MTA) is an important tool for diagnosing and monitoring patients with retinal disease. The robustness of MTA can be limited in low-cost devices due to the quality of the optical coherence tomography (OCT) data. In this study we evaluate the agreement of MTA between repeat scans of the same eye using a low-cost OCT prototype.

Methods: A low-cost OCT prototype system (ZEISS, Dublin, CA) was used to image 42 subjects with a range of ocular pathologies, including age-related macular degeneration (AMD). One eye of each subject was scanned three times. The inner limiting membrane (ILM) and the retinal pigment epithelium (RPE) of each OCT volume were segmented using a prototype segmentation algorithm. Macular thickness (MT) map with 512x512 pixels over an area of 5.78x5.78 mm was created by measuring the difference between the ILM and RPE. Two MT maps (out of the three) were selected based on the segmentation quality determined with a prototype segmentation quality algorithm for this study.

The two MT maps were registered to each other and the ETDRS grid with 9 sectors was placed at the center of each map. The ETDRS grid consists of three concentric circles with radiuses of 0.5, 1.5 and 2.89 mm (Fig 1). Each ETDRS sector value was calculated by averaging the MT values within the sector. Linear regression and Bland-Altman analysis were used to compare the MT maps.

Results: Fig 2 shows the statistical comparison between the ETDRS sectors generated using two MT maps per subject. All sectors show an absolute mean difference less than 2 microns. The 95% lower and higher limits of agreement varied between -18 and 19 microns. R-squared values varied between 0.85 and 0.99.

Conclusions: This study demonstrated the agreement between two MT maps generated from two scans per eye using the low-cost OCT prototype. Our results show good correlation and agreement between two MT maps which is important for diagnosing and monitoring patients using macular thickness analysis.

CONTROL ID: 3711307

SUBMITTER (NAME ONLY): Shaoxue Zeng

TITLE: Jak/STAT signalling mediated glia-neuron interaction following MAPK inhibition

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zeng, T. Zhang, Y. Chen, L. Zhu, M.C. Gillies, Save Sight Institute, The University of Sydney, Sydney, New South Wales, AUSTRALIA|K. Jin, X. Fan, Pharmaceutical Informatics Institute, College of Pharmaceutical Sciences, Zhejiang University, CHINA|

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ABSTRACT BODY:

Purpose: The dysfunction of Müller cells can induce photoreceptor degeneration. We have previously identified a link between Müller cells and photoreceptors through which inhibition of MAPK signalling in Müller cells upregulated the expression of Interphotoreceptor Retinoid-Binding Protein (IRBP), which is a photoreceptor-specific protein, and prevented photoreceptor degeneration. However, the exact signalling transduction remains unclear. We aim to explore the signalling between Müller cells and photoreceptors in response to stresses.

Methods: Retinal tissues from four human eye donors were cultured for 24 hours with PD98059, the ERK1/2 inhibitor, or the same concentration of DMSO as controls. Total RNA was extracted, and its quality was assessed. Next-generation sequencing was performed to explore the transcriptional changes after ERK1/2 inhibition. We then performed QIAGEN Ingenuity Pathway Analysis (IPA) on all the differentially expressed genes ($P<0.05$) to identify canonical pathways that significantly changed after inhibition of MAPK signalling. We also validated the changes of identified signalling pathways after PD98059 treatment in human retinal explants by Western blot. We further treated the human retinal explants with the specific inhibitors of the identified signalling pathway and evaluated the downstream changes compared with the upstream inhibition of MAPK signalling by Western blot.

Results: IPA analysis found JAK/STAT3 signalling pathway, NF-κB Signaling pathway and Interleukin-6 Signaling pathway were significantly inhibited after the inhibition of MAPK in human retinal explants ($P<0.05$). Western blotting further validated that the treatment of PD98059 significantly inhibited the phosphorylation levels of STAT3 (the ratio of phosphorylated STAT3 to total STAT3). The treatment of 5,15-DPP, STAT3 specific inhibitor, on human retinal explants significantly increased the expression of neuroprotective IRBP protein by photoreceptors.

Conclusions: Our findings suggest that JAK/STAT3 pathway is involved in the signalling between Müller cells and photoreceptors in response to stresses. The inhibition of JAK/STAT3 pathway activity may have neuroprotective effects on the retina.

CONTROL ID: 3711309

SUBMITTER (NAME ONLY): Youngyoon Amy Seo

TITLE: Epidermal growth factor-loaded collagen gels to enhance corneal wound healing: Effect of matrix crosslinking chemistry

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Seo, G.M. Rogers, D. Myung, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|D. Myung, Chemical Engineering, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Millions of people suffer from corneal diseases, but less than 2% of patients have access to corneal transplantation due to the shortage of cadaveric donor corneal tissue. Moreover, rapid and complete epithelial wound healing is critical to prevent infection and scarring that can lead to blindness. Biomaterial matrices have been investigated as a way to fill corneal defects and support epithelialization. Loading growth factors into defect-filling hydrogels is a promising approach toward enhancing corneal epithelialization. Here, we incorporate epidermal growth factor (EGF) into in situ-forming collagen gels to study the effect of their controlled release from within defect-stabilizing matrices on epithelial cell adhesion and proliferation.

Methods: EGF was added to a neutralized collagen solution and crosslinked either via N-hydroxysuccinimide chemistry using 8-arm PEG or via UV light using riboflavin as a photosensitizer. We compared the gels' degradation as well as the proliferation, migration, and phenotype of corneal epithelial cells (CECs) seeded on these gels and the epithelial wound healing response in ex vivo organ culture model. Cell viability and cytotoxicity were measured using colorimetric assays. We also executed an in vitro scratch assay which mimics cell migration during wound healing in vivo. The presence of biomarkers that promote epithelial healing were compared across three groups: cells without treatment, collagen gels alone, and EGF encapsulated within PEG- or UV-crosslinked collagen hydrogels.

Results: Encapsulated EGF accelerated in vitro corneal epithelial cell proliferation and migration. Gels loaded with EGF also exhibited a lower degradation rate and accelerated corneal wound healing in our organ culture studies. Immunohistochemical analysis exhibited expression of 4-hydroxynonenal within the epithelium and alpha-smooth muscle actin within the surrounding stroma for 8-arm PEG collagen and UV riboflavin gels with EGF. Immunohistochemical studies demonstrated that both types of EGF-loaded collagen gels fostered tight junction formation and maintained normal epithelial phenotype.

Conclusions: Our study suggests that collagen gels with encapsulated EGF can fill corneal defects and enhance corneal epithelial regeneration. Further work to investigate the effects of EGF-loaded collagen gels in vivo are merited.

CONTROL ID: 3711310

SUBMITTER (NAME ONLY): Ting Zhang

TITLE: Reprogramming of serine and glycine synthesis pathway in the JR5558 mouse model of retinal fibrosis

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Zhang, L. Zhu, S. Lee, S. Zeng, Y. Chen, M. Yam, M.C. Gillies, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|Y. Chen, Sichuan University West China Hospital, Chengdu, Sichuan, CHINA|

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ABSTRACT BODY:

Purpose: Many eyes with neovascular AMD have poor outcomes because they develop subretinal fibrosis which is neither preventable nor treatable. Metabolic reprogramming in the retina is reported as one critical pathogenic process in retinal fibrosis. The JR5558 mouse develops subretinal neovascularization, resulting in local gliosis and photoreceptor death. The subretinal lesions in these mice have several key molecular and pathological features of subretinal fibrosis. The de novo serine/glycine synthesis plays an essential role in the formation of fibrotic scars. We aim to explore the changes of this metabolic pathway in a mouse model of subretinal fibrosis in this study.

Methods: The subretinal lesions in the JR5558 mouse expanded between 4 and 8 weeks of age and became established in size and location around 12 weeks. The changes of four key enzymes in the de novo serine/glycine synthesis (phosphoglycerate dehydrogenase (PHGDH), hydroxymethyltransferase 2 (SHMT2), phosphoserine phosphatase and phosphoserine aminotransferase 1) were evaluated during the time course for the development of subretinal fibrosis. We explored the distribution pattern of these enzymes by immunofluorescent staining in the retina of JR5558 mice compared with the controls, costained with cellular retinaldehyde-binding protein (CRALBP, a Müller cell and retinal pigment epithelium (RPE) marker). We also quantified protein levels of key enzymes in the JR5558 mouse retinas by Western Blot. The C57BL/6 mouse retina was used as a control to compare the expression level of these enzymes in fibrosis mouse retinas.

Results: We found that PHGDH, a key rate-limiting enzyme of de novo serine synthesis, was expressed by Müller cells and RPE in the JR5558 mouse retina. It was strongly expressed in the subretinal lesions. SHMT2, a key mitochondrial enzyme that converts serine to glycine, was expressed by the Müller cells and extensively expressed in the retinal fibrotic lesions. The protein level of PHGDH was significantly upregulated in the JR5558 mouse retinas at 8 weeks of age, the peak stage of the development of subretinal fibrosis, compared with the age-matched C57BL/6 wild type controls.

Conclusions: Our findings suggest that the de novo serine/glycine biosynthesis is activated during the development of the subretinal fibrotic lesions in the JR5558 mouse model, perhaps representing a novel therapeutic target for subretinal fibrosis.

CONTROL ID: 3711311
SUBMITTER (NAME ONLY): Ahmed Hagag
TITLE: Adaptive optics phenotypes of intermediate age-related macular degeneration
SESSION TITLE: AMD Imaging
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: A.M. Hagag, S. Sivaprasad, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|A.M. Hagag, S. Sivaprasad, Institute of Ophthalmology, University College London, UNITED KINGDOM|S. Riedl, U. Schmidt-Erfurth, Medizinische Universitat Wien, Vienna, AUSTRIA|T. Prevost, King's College London, London, UNITED KINGDOM|L. Fritsche, University of Michigan, Ann Arbor, Michigan, UNITED STATES|D. Rueckert, Imperial College London, London, UNITED KINGDOM|H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|H.P. Scholl, Department of Ophthalmology, Universitat Basel, Basel, Basel-Stadt, SWITZERLAND|A.J. Lotery, University of Southampton Faculty of Medicine, Southampton, UNITED KINGDOM|
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ABSTRACT BODY:
Purpose: To describe the microscopic characteristics of known lesions associated with intermediate age-related macular degeneration (AMD) on adaptive optics ophthalmoscopy (AOO) imaging and their correlation to other multimodal imaging methods.
Methods: Patients with intermediate AMD were enrolled in an observational longitudinal multicenter cohort to decipher the natural history of the disease. Participants underwent spectral-domain optical coherence tomography (SD-OCT), infrared scanning laser ophthalmoscopy (IR-SLO), and fundus autofluorescence (FAF) imaging using the Spectralis device (Heidelberg Engineering, Germany). Flood-illumination AOO images were acquired using the commercially available rtx1 camera (Imagine Eyes, France). AO image mosaics were constructed using the montage function on the i2k Retina AO software (DualAlign LLC, USA). En face and/or cross-sectional images across modalities were manually aligned to perform intra- and inter-modality comparisons of retinal lesions.
Results: Heterogeneity of drusen characteristics was observed on AOO. Typical large drusen were characterized by a hyper-reflective rim with central iso-reflectivity. The visibility of the cone photoreceptor mosaic was largely obliterated around and on top of these drusen. On the contrary, cone photoreceptors were visualised in another group of patients with smaller drusen that manifested on AO images as a hyper-reflective rim with internal hypo-reflectivity. Cone visibility on AO correlated with the presence of interdigitation zone on OCT B-scans. Subretinal drusenoid deposits (SDD) typically displayed hypo-reflective circles surrounding areas of iso-reflectivity on AO images. Early stages of the SDD appeared as an ill-defined area of hypo-reflectivity. Several distinct phenotypes of retinal pigment epithelium and outer retinal atrophy were identified on AOO. Variability in the focusing depth can significantly alter the appearance and interpretation of AO images.
Conclusions: We describe various phenotypes of intermediate AMD on adaptive optics ophthalmoscopy, showing distinct patterns, which correlate with known morphologic presentations on multimodal imaging. The significance of the described changes is yet to be determined in large longitudinal cohort studies.

CONTROL ID: 3711312

SUBMITTER (NAME ONLY): Charlotte Ernst

TITLE: Involvement of purines and prostaglandins in hypoxia-induced dilatation of larger and smaller porcine retinal vessels ex vivo

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ernst, T. Bek, Department of Ophthalmology, Aarhus Universitetshospital, DK-8200 Aarhus N, Mid Jutland Region, DENMARK|

Commercial Relationships Disclosure: Charlotte Ernst: Commercial Relationship: Code N (No Commercial Relationship) | Toke Bek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The metabolic pathways leading from hypoxia to retinal vasodilatation involve effects of both purines and prostaglandins, but the interaction between these compounds in the response has not been studied in detail. Therefore, the purpose of the present study was to investigate how effects of purinergic and prostaglandin receptors interact to result in hypoxia-induced dilatation of porcine retinal arterioles, pre-capillary arterioles and capillaries in vitro.

Methods: Porcine superior hemiretinas (n=40) were mounted in a specially designed perfusion chamber, and the diameter of retinal arterioles, pre-capillary arterioles and capillaries were studied during hypoxia with and without the presence of the EP1 receptor antagonist SC-19220, the EP4 receptor antagonist L-161-982, the prostaglandin synthesis inhibitor ibuprofen, and ibuprofen combined with the ecto-nucleotidase inhibitor AOPCP or ATP.

Results: Hypoxia induced vasodilatation of all vascular branching levels ($p<0.01$ for all comparisons). The dilatation of arterioles was inhibited by ibuprofen alone and in combination with the ecto-nucleotidase inhibitor, and by blocking of the EP4 receptor ($p\leq0.04$ for all comparisons). The response in pre-capillary arterioles differed from that of the arterioles by a lack of blocking of the hypoxia-induced dilatation by the EP4 receptor antagonist ($p=0.49$). The response in capillaries differed from that of the pre-capillary arterioles by a blocking effect by all the studied prostaglandin antagonists ($p<0.01$ for all comparisons) on the hypoxia-induced dilatation.

Conclusions: Hypoxia-induced dilatation of retinal vessels is regulated differentially in arterioles, pre-capillary arterioles and capillaries. This may provide the foundation for selective interventions on the diameter of retinal vessels at different branching levels.

CONTROL ID: 3711314

SUBMITTER (NAME ONLY): Chan Hong Min

TITLE: Longitudinal Changes in Outer Nuclear Layer and Choroidal Thickness in Patients using Hydroxychloroquine before Development of Retinopathy

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Min, J. Lee, Y. Yoon, Ophthalmology, Asan Medical Center, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Chan Hong Min: Commercial Relationship: Code N (No Commercial Relationship) | Joo Yong Lee: Commercial Relationship: Code N (No Commercial Relationship) | Young Hee Yoon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Early detection of hydroxychloroquine(HCQ) retinopathy is important. Prior studies have suggested that HCQ primarily damages photoreceptors, with subsequent disruption of retinal pigment epithelium and choroidal thinning. The aim of this study was to determine whether changes of outer retinal layer(ONL) thickness and choroidal thickness might signal impending toxic effects of HCQ before development of retinopathy.

Methods: We included patients who were screened for HCQ retinopathy, and followed for ≥ 12 months. Based on visual field, optical coherence tomography(OCT) and autofluorescence, patients with no retinopathy were collected. During follow-up period, HCQ was continued in 121 patients (continued group), and stopped in 25 patients due to non-retinotoxicity reasons (discontinued group).

Using OCT images, ONL thickness was obtained from fovea, inner ring and outer ring of the Early Treatment of Diabetic Retinopathy Study(ETDRS) grid. Subfoveal choroidal thickness(SFChT) was measured from EDI-OCT. The thicknesses were measured at baseline, and repeated at least 1 year apart. Comparison was made between the baseline OCT and the last OCT available in each group.

Results: At baseline, mean dose/kg were 3.90mg/kg, 4.70mg/kg, and duration of medication 154.2months, 90.5months, in ‘continued’ and ‘discontinued’ group, respectively. There were no significant differences in thicknesses between ‘continued’ and ‘discontinued’; mean ONL thicknesses of foveal(87.9, 88.1um), inner ring(66.5, 64.5um), outer ring(54.2, 51.6um) and mean SFChT(246.6, 229.9um).

Over the follow-up period, 'continued’ group(mean of 37.4months) showed a progressive ONL thinning in outer ETDRS ring(54.2 to 53.0um, p=0.000), and progressive decrease in SFChT(246.6 to 218.7um, p=0.000). ‘Discontinued’ group(mean of 33.3months) also showed a significant ONL thinning in outer ETDRS ring(51.6 to 50.1um, p=0.001), but, interestingly, showed a significant increase in SFChT(229.9 to 239.2um, p=0.024) after cessation of HCQ medication.

Conclusions: ONL thinning was observed progressively in patients taking HCQ prior to development of retinopathy. Although choroidal thickness also decreased while HCQ treatment, thinning was partially recovered following early discontinuation of HCQ. We suggest the measurements of ONL and choroidal thickness might be used for early detection of HCQ retinal toxicity.

CONTROL ID: 3711315

SUBMITTER (NAME ONLY): Li PAN

TITLE: Baicalein Alleviates Microglia-mediated Neuroinflammation and Neurodegeneration in Mouse Retina

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. PAN, C. Do, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|L. PAN, K. Cho, D. Chen, Schepens Eye Research Institute of Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|C. Do, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Excessive microglia activation is considered as a pathological factor that leads to neuroinflammation and neurodegeneration. Baicalein (Ba), a natural occurring flavonoid, displays a wide spectrum of bioactivities including anti-inflammation. In this study, we investigated the effects of Ba on the lipopolysaccharide (LPS)-induced microglia activation in mouse BV2 microglia cell line. We also evaluated the anti-inflammatory and neuroprotective effects of Ba using a retinal ischemia/reperfusion (I/R) mouse model.

Methods: Activation of BV2 cells was induced by 1μg/ml LPS for 6 hours prior to the addition of PBS, vehicle or Ba (10μM). After a total 48-hour incubation, pro-inflammatory cytokine protein and mRNA levels were quantified by cytokine array assays and quantitative polymerase chain reaction (qPCR), respectively. For in vivo studies involving I/R injury, the morphological and transcriptome changes of mouse microglia and retinas were evaluated, either in the presence or absence of Ba (100μM) treatment.

Results: As expected, upregulation of pro-inflammatory cytokines was detected in LPS-primed BV2 cells. Ba effectively suppressed the expression of most cytokines including IL-6, IL-1β, and TNF-α, as compared to the vehicle-treated group which showed a similar expression profile as LPS-stimulated control. Concurrently, Ba significantly suppressed the mRNA expression of Il-6, Il-1β and Tnf-α in LPS-stimulated BV2 cells. After 1 week of I/R injury, mouse retinas displayed an increased population of IBA-1+ microglia/macrophages along with enlarged IBA-1+ cell body and shortened cellular processes, as well as an increased expression of activated microglia markers (e.g. Iba-1, Cox2) and pro-inflammatory cytokines (e.g. Il-1β, Il-1α). Weekly intravitreal administration of Ba retained the morphological and transcriptional features of resting microglia. Ba also effectively reduced the retinal ganglion cells (RGCs) loss by 80% at 4 weeks after I/R injury.

Conclusions: Our results suggest that Ba acts as a negative regulator of activated microglia and immune responses both in vitro and in vivo, effectively alleviating neurodegeneration in retinal I/R injury. This finding indicates that Ba could be a potential therapeutic agent to neurodegenerative retinal diseases.

CONTROL ID: 3711316

SUBMITTER (NAME ONLY): Myrthe Nuijts

TITLE: Prevalence of and risk factors for abnormal ophthalmological findings in children with a newly diagnosed brain tumor: a Dutch prospective nationwide cohort study.

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nuijts, I. Stegeman, G. Porro, M. van Egmond-Ebbeling, S. Imhof, Ophthalmology, Universitair Medisch Centrum Utrecht, Utrecht, Utrecht, NETHERLANDS|I. Stegeman, Otorhinolaryngoloy and Head & Neck Surgery, Universitair Medisch Centrum Utrecht, Utrecht, Utrecht, NETHERLANDS|T. Seeters, Radiology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, Noord-Brabant, NETHERLANDS|C. Bennebroek, Ophthalmology, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|N. Naus, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|A. Schouten-van Meeteren, Neuro-Oncology, Princess Máxima Center for Pediatric Oncology, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Visual impairment is a serious adverse effect in children with a brain tumor. To date, visual impairment is often underestimated and unrecognized, while early detection of visual impairment is important to potentially preserve the visual function. Our aim was to assess the prevalence and type of abnormal ophthalmological findings in children with a newly diagnosed brain tumor and to identify potential oncological and clinical risk factors.

Methods: In this prospective nationwide cohort study, we included children, aged 0-18 years, with a newly diagnosed brain tumor in the Netherlands between May 2019 and August 2021. A comprehensive ophthalmological examination (including orthoptic evaluation, visual acuity, visual fields and fundoscopy) was performed at diagnosis. Multivariable logistic regression analyses were performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of the risk factors.

Results: In total, 170 children were included (43.5% female; median age [interquartile range], 8.3 [3.9 – 13.0] years; 48.2% infratentorial tumors, 35.3% midline tumors and 16.5% cerebral hemispheres tumors). Overall, 101 children (59.4%) presented with visual symptoms at diagnosis. The most common findings on ophthalmological examination were papilledema (50.6%), gaze deficits (31.8%), visual field defects (29.4%), nystagmus (23.5%), strabismus (18.8%) and decreased visual acuity (10.5%). The risk of papilledema was associated with older age in years (OR 1.2, 95% CI 1.1 – 1.3) and hydrocephalus (OR 15.8, 95% CI 5.7 – 43.4). Visual field defects were detected more frequently in children with a tumor located in the cerebral hemisphere (OR 5.3, 95% CI 1.5 – 19.1) or midline (OR 6.0, 95% CI 2.0 - 18.1).

Conclusions: We found a high prevalence of abnormal ophthalmological findings in an unselected cohort of children at brain tumor diagnosis. These findings emphasize the need of standardized ophthalmological surveillance and of awareness of health care providers for ophthalmological abnormalities in this patient group.

CONTROL ID: 3711318

SUBMITTER (NAME ONLY): David Li

TITLE: Sumoylated Pax6 Regulates Lens Stalk Regression During Lens Development

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.W. Li, J. Fu, F. Liu, S. Zheng, Y. Wang, J. Wang, Y. xiao, J. Xiang, Y. Gan, X. Liang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Pax6 is a master regulator governing development of both brain and eye. Our previous studies have shown that SUMO1-mediated sumoylation is an indispensable step towards activation of p32 Pax-6 (Yan et al. 2010. PNAS). However, how does the sumoylated Pax6 regulate lens development is largely unknown. Here, we present evidence to show how sumoylated Pax6 regulates lens stalk regression during lens development.

Methods: CRISPR/Cas9 technology is used to create the mouse model where the conserved amino acid, 90E was deleted so that the conserved sumoylation site was altered. RNAseq analysis was used to analyze the transcriptional activity of the mutated Pax6. In situ hybridization and QRT-PCR were used to confirm mRNA expression of Pax6 and other downstream genes in both wild type and mutant mice. Cycloheximide and MG132 treatments were used to determine the half life of wild type and mutant Pax6 protein. H.E. staining was used to record the lens morphology.

Results: Deletion of the conserved 90E amino acid caused significant changes in the sumoylation pattern of the mutant Pax6, which changes the stability of Pax6. The mutated pax6 displays fundamental changes in regulating expression of the downstream genes. The expression patterns of over 20 genes involved in control of apoptosis in the embryonic lens were altered, leading to inhibition of apoptosis in the lens stalk region of the mutant mouse. As a result, lens stalk regression was halted, causing microphthalmia.

Conclusions: Sumoylated Pax6 regulates apoptotic genes to control lens stalk regression. Supported by National Natural Science Foundation of China (Grants #81970787, #82000876, #81770910) and Natural Science Foundation of Guangdong Province and Guangdong City Joint Program of China (Grant # 2019B1515120014) , and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center.

CONTROL ID: 3711321

SUBMITTER (NAME ONLY): Keiichi Nishikawa

TITLE: Extracellular mitochondria induce cellular damage in photoreceptors and retinal pigment epithelium in diabetic macular edema

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Nishikawa, T. Murakami, K. Ishihara, Y. Dodo, N. Terada, K. Morino, A. Tsujikawa, Opthalmology, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: The damages in photoreceptor-retinal pigment epithelium (RPE) complex are clinically known in DME. We therefore investigated the effects of extracellular microvesicles containing mitochondria on such pathological changes in this translational research.

Methods: 661W cells (mouse cone photoreceptor cell line) were cultured in DMEM containing DME sera, and the cell culture supernatants were applied to a two-step centrifugation in order to obtain extracellular microvesicles as pellets. We performed flow cytometry after staining with Mitobright and PCR was applied to characterize microvesicles derived from 661W cells. The microvesicles were administered to ARPE19 cells (human RPE cell line) and cell death was evaluated by LIVE / DEAD assay. Seven days after the subretinal injection of the microvesicles in C57BL / 6 mice, the RPE flatmount was prepared and immunostained with ZO-1 antibody.

Results: Electron microscopic analyses demonstrated mitochondria with a cristae structure in the vitreous humor of patients with diabetic retinopathy. Flow cytometry revealed mitochondria positive staining in most extracellular microvesicles, and PCR showed a significant increase in mitochondrial DNA in such microvesicles ($P<0.05$). Administration of the microvesicles induced cell death of ARPE19 and 661W cells in a concentration-dependent manner ($P<0.001$ at any concentration), but cell death was significantly suppressed by the single-stranded oligo DNAs C151 and A151 ($P<0.001$ in both comparisons). The aggregation, deformation and enlargement in RPE cells were observed in the RPE flatmounts of the mice administrated with the microvesicles, whereas these changes were reversed by oligo DNAs.

Conclusions: These data suggest that microvesicles containing mitochondrial DNA are involved in photoreceptor-RPE damage in DME.

CONTROL ID: 3711322

SUBMITTER (NAME ONLY): Orwa Nasser

TITLE: Corneal and refractive properties of patients with congenital nystagmus syndrome.

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Nasser, Orasis World Class Eyecare Medical Center, ISRAEL|W. Wahbi, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|

Commercial Relationships Disclosure: Orwa Nasser: Commercial Relationship: Code N (No Commercial Relationship) | Wahbi Wahbi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the corneal and refractive properties of patients with congenital nystagmus syndrome compared to healthy subjects.

Methods: In this comparative cross-sectional observational study, a scheimpflug imaging tomography was conducted on eyes of congenital nystagmus syndrome patients and compared with those of healthy individuals (control group). Corneal astigmatism prevalence, corneal astigmatic power, maximal keratometry, mean keratometry and pachymetry values were obtained and compared between the groups.

Results: 32 eyes of 16 congenital nystagmus syndrome patients and 32 eyes of 16 healthy individuals were included in the study. All nystagmus patients (100%) had astigmatism of at least 1 diopter compared to 11 subjects (34.375%) in the control group ($P<0.001$). The average astigmatic power in the patient's group was 3.383 ± 1.135 diopters compared to 0.8281 ± 0.58.54 diopters in the control group ($P<0.001$). The maximal keratometric power in the patient's group was 44.16 ± 2.444 diopters compared to 42.88 ± 2.052 diopters in the control group ($P=0.027$). The mean keratometric power in the patient's group was 41.98 ± 2.129 diopters compared to 41.40 ± 5.121 diopters in the control group ($P=0.560$). The mean pachymetric value in the patient's group was 557.1 ± 47.15 μm compared to 544.2 ± 29.32 μm in the control group ($P=0.1945$).

Conclusions: All patients with congenital nystagmus syndrome have visually significant astigmatism. Corneal tomography can be used to asses and grade the corneal astigmatism in these patients.

CONTROL ID: 3711323

SUBMITTER (NAME ONLY): Sreesha Kuruvadi

TITLE:

Corneal cold storage breaks down the actin cytoskeleton and tight junctions of the endothelium via oxidative stress

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cold storage of donor corneas is inevitable before endothelial transplantation or preparation of cultured cells for “cell injection therapy”. Here we have examined the effects of hypothermia on endothelial tight junctions (TJs) and its principal regulator, the perijunctional actomyosin ring (PAMR).

Methods: Ex vivo porcine corneas were exposed to hypothermia (HYPO: 4 °C; 1 to 7 days) in Cornisol™ medium with and without pretreatment with a microtubule-stabilizing agent (epothilone B, EpoB; 100 nM), p38 MAP kinase inhibitor (SB-203580, SB; 20 μM), antioxidants (quercetin; 100 μM, or Vitamin E; 1 mM), or iron chelator (deferoxamine; 10 mM) and examined subsequently with and without rewarming (37 °C for 3 h). The damage to microtubules, PAMR, and ZO-1 (a marker of TJs) in the endothelium was assessed by immunocytochemistry. In addition, we imaged paracellular flux of FITC-avidin across endothelial cells grown on biotinylated gelatin to evaluate the functional integrity of TJs.

Results: Exposure to HYPO led to disassembly of microtubules, disruption of PAMR (Figs. A,B), and loss of contiguous distribution of ZO-1 at the cellular periphery (Fig. E,F). These responses were slightly augmented by rewarming after HYPO. However, the damage to PAMR and ZO-1 could be abated by pretreatment with EpoB, SB, antioxidants, or the iron chelator (Figs. C,G). Deliberate oxidative stress to endothelium by exposure to H2O2 and t-butyl hydroperoxide (tBHP) also led to widespread damage to the organization of PAMR and ZO-1 (Figs. D,H) in a p38 MAP kinase-dependent manner. Furthermore, photodynamic treatment with riboflavin or tryptophan + UV-A also caused damage to PAMR and ZO-1, which could be abolished by cotreatment with catalase. In cultured cells, both HYPO and oxidative stress caused a significant increase in the flux of FITC-avidin, indicating a loss in barrier integrity.

Conclusions: Prolonged cold storage of corneas induces destruction of the cytoskeleton in the endothelium via activation of oxidative stress, leading to a breakdown of the barrier function. Thus, the inclusion of microtubule stabilizers, antioxidants, and iron chelators in the storage medium has the potential to overcome the endothelial barrier failure during cold storage of donor corneas.

CONTROL ID: 3711324

SUBMITTER (NAME ONLY): XIAO ZHANG

TITLE: Human pluripotent stem cell-derived retina-resident microglia empower functional retinal organoids

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Equipping the human retinal organoids (hROs) with neuro-immune cells (retinal microglia) to make hROs more representative of real retinas.

Methods: An efficient and simplified method was established to generate high-purity microglia from human pluripotent stem cells (hPSCs), then co-culturing the microglia with hROs to induce the differentiation of retinal microglia. The retinal microglia were characterized by the flow cytometry, ELISA, immunofluorescence staining and RNA sequencing.

Results: We established a simplified approach to differentiate hPSCs into high purity (>90%) microglia (PSC-MG). PSC-MG express microglia-specific markers, release cytokines upon stimulation, and are capable of phagocytizing bacteria. When co-cultured with three-dimensional hROs, PSC-MG migrated into the hROs, tended to differentiate into resident retinal microglia, and simultaneously induced apoptosis in some neural cells and promoted the migration of the photoreceptor precursors.

Conclusions: We developed a simplified and efficient method to generate microglia from human pluripotent stem cells, and we reported the first derivation of retina-resident microglia in vitro, providing a new source of human retinal microglia for developmental and disease studies and regenerative therapeutics.

CONTROL ID: 3711325

SUBMITTER (NAME ONLY): Pratibha Kataria

TITLE: Extraocular muscle and adnexal evaluation in anisomyopia: A high resolution magnetic resonance imaging study

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is no unifying postulate that explains how and why two eyes within the same environment and identical genetic influences develop asymmetrically and produce different refractive errors, sometimes leading to amblyopia and loss of binocularity. This unique pilot study analysed extraocular muscle (EOM) characteristics of the more emmetropic globe acting as an intrinsic control for the more myopic globe in subjects with non-strabismic myopic anisometropia (anisomyopia) of 1D or more by high resolution fast spin echo T2 weighted (T2FSE) surface coil orbital magnetic resonance imaging {(MRI), 3T Siemens Skyra}.

Methods: 5 subjects (10 orbits) of average age 20±7.2 years (3 males) with anisomyopia were imaged with the subject fixating at a central target. 2mm thick contiguous quasi-coronal image planes perpendicular to the orbital axis were analysed for EOM pulley locations, EOM cross sections and LR-SR band length while quasi-sagittal and axial planes were used to measure rectus EOM and optic nerve (ON) length, all by Image J software as per published norms (Figure 1A-E). A comprehensive ophthalmic evaluation was performed in all subjects.

Results: The average refractive error and axial length (AL) in the more myopic eye was -7±3.6D, 26.1±0.4mm versus -1.5±2.4D,24.1±1.7mm in the more emmetropic eye (p=0.02, 0.04).None of the subjects were amblyopic in either eye. The average stereopsis was 520±455 arcseconds (TNO test). 2 subjects with moderate anisomyopia of 2D demonstrated 100 arcseconds stereopsis. There was marked effacement and lengthening of the LR-SR band in the more myopic eye (10.4±0.8mm) versus the more emmetropic eye (8.6±0.6mm, p=0.003). The antero-posterior extent of the LR-SR band was seen in 1.4±0.5 slices in the more myopic eye versus 3.2±0.4 slices in the more emmetropic eye (p=0.0004). The rectus EOM and ON length was similar in both eyes.

Conclusions: Anisomyopia provides a unique biological control to evaluate structural and biomechanical ocular and adnexal differences in the same individual.

CONTROL ID: 3711330

SUBMITTER (NAME ONLY): John Grigg

TITLE: A Phase 1b/2 Study of the Safety and Tolerability of Tinlarebant in Adolescent STGD1 Subjects

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.R. Grigg, R.V. Jamieson, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|F.K. Chen, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|N.L. Mata, Belite Bio, San Diego, California, UNITED STATES|W. Liao, Lin BioScience, Taipei, TAIWAN|T. Chen, National Taiwan University, Taipei, TAIWAN|J.R. Grigg, R.V. Jamieson, Eye Genetics Research Unit, Sydney Children's Hospital Network, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Childhood-onset Stargardt Disease (STGD1) is characterized by accumulation of bisretinoids which cause progressive retinal atrophy leading to rapid visual loss. Because bisretinoid toxins are derived from circulating retinol, reduction of retinol delivery to the eye, via antagonism of serum retinol binding protein 4 (RPB4), has been explored as a means to slow disease progression in STGD1. Tinlarebant, an orally administered, potent and specific non-retinoid antagonist of RPB4, has been developed to determine whether reduction of circulating RPB4-retinol is a safe and effective treatment approach for STGD1.

Methods: The Phase 1b/2 study is a multicenter, single arm, open-label study followed by a 2-year extension to evaluate safety and tolerability and efficacy of Tinlarebant. Eleven subjects aged 12-18 years received oral Tinlarebant (5 mg) daily for a 28-day treatment period. Treatment emergent adverse events (TEAEs), PK/PD, and visual function outcomes were evaluated.

Results: A total of 28 TEAEs were reported and were mild in severity. Seven TEAEs reported by 6 subjects (54.5%) were non-ophthalmic and considered to be non-drug-related; 21 TEAEs reported by 10 subjects (90.9%) were ophthalmic. Delayed dark adaptation (DDA) and xanthopsia (both mild and reversible), reported by 7 subjects (63.6%), were attributed to drug. DDA and xanthopsia were noticed principally on waking and resolved within 10 minutes. All subjects tolerated these AEs. Tinlarebant plasma concentration and RBP4 suppression appeared to be correlated. RBP4 levels declined rapidly within 4 hours of treatment on Day 1. Mean RBP4 level reached 20% of mean baseline on Day 8 of treatment. Suppression was maintained throughout the study. Mean RBP4 level returned to 92.3% of baseline values following 14 days of drug cessation. Visual acuity (VA) was available for all time points in 8 subjects, 7 improved with 3 subjects experiencing a 5-, 10-, and 24-letter improvement, in at least one eye. Where quantitative autofluorescence (qAF) was available qAF was correlated with VA improvements.

Conclusions: Tinlarebant has an acceptable safety profile in adolescent STGD1 subjects. There was a trend for VA improvement. The observed AEs were anticipated based on mode of action. STGD1 subjects from the Phase 1b study are now participating in the 2-year Phase 2 extension study.

CONTROL ID: 3711334

SUBMITTER (NAME ONLY): Jicheng Lin

TITLE: An in situ-crosslinked hydrogel-induced chronic ocular hypertension model with characteristic neurodegeneration

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lin, J. Xue, Z. Liu, Y. Zhuo, Y. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|Q. Xu, C. Zhao, S. A, W. Wang, Charles Institute of Dermatology, School of Medicine, University College Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: A reliable animal model providing chronic ocular hypertension (COH) and characteristic neurodegeneration is essential to recapitulate human glaucoma and understand molecular mechanisms. This study aims to develop an experimental glaucoma model induced by a novel in situ-crosslinked hydrogel and thoroughly evaluate the effectiveness of this model.

Methods: We designed and developed a novel method of inducing persistent IOP elevation in C57BL/6J mice using an injectable hydrogel formulated by hyperbranched macromolecular poly(ethylene glycol) (HB-PEG) and thiolated hyaluronic acid (HA-SH). The hydrogel's characteristics were first assessed to determine its mechanical strength, swelling profile and cytocompatibility. Retinal whole-mount immunostaining was used to determine retinal ganglion cell (RGC) loss and hematoxylin-eosin (HE) staining was used to measure ganglion cell complex (GCC) thickness. All experimental data were analyzed using GraphPad Prism (v9.0; GraphPad Software, CA, USA) and were presented as the mean ± standard error of the mean (SEM). A P value less than 0.05 was regarded as statistically significant.

Results: An appropriate hydrogel formulation was determined to induce chronic IOP elevation and the effectiveness of our model was thoroughly evaluated. We determined that the HB-PEG/HA-SH hydrogel generated under physiological conditions was suitable for intracameral injection. When the concentration ratio of HB-PEG and HA-SH was 1:1 (10 mg/ml each), the highest storage modulus (68 Pa) was observed (Fig. 1A) while minimal swelling (Fig. 1B) and degradation profile (Fig. 1C) was observed. Besides, HTMCs maintained high viability after co-culture with HB-PEG/HA-SH hydrogel (Fig. 1D), indicating the good cytocompatibility of the hydrogel. Injection of the hydrogel (Fig. 2A-B) induced a persistent IOP elevation over 50% above baseline (Fig. 2C), which led to progressive RGC loss (37.12 ± 2.61% and 41.62 ± 4.94% on day 28 in the central and peripheral retinal regions, mean ± SEM, $P<0.001$) (Fig. 2D-E) and GCC thickness reduction (10.03 ± 3.25%, mean ± SEM, $P = 0.0093$) (Fig. 2F-G).

Conclusions: The in-situ forming HB-PEG/HA-SH hydrogel system could be an appropriate strategy for developing a reliable experimental glaucoma model without any confounding factors. We expected this model would be conducive to the development of neuroprotective and neuroregenerative therapies.

CONTROL ID: 3711335

SUBMITTER (NAME ONLY): Jingfei Xue

TITLE: JTE-013 alleviates demyelination and preserves visual function after ischemia/reperfusion by inhibiting sphingosine-1-phosphate receptor 2 (S1PR2)

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Xue, J. Lin, Z. Liu, Q. Zhang, Y. Li, Y. Zhuo, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Myelin sheaths play an important role in neurodegenerative diseases; the conduction of the action potential is impaired without normal myelin sheaths, which could cause visual dysfunction and cognitive impairment. Sphingosine-1-phosphate receptor 2 (S1PR2), a G-protein coupled receptor, was previously reported to be associated with demyelination. We hypothesize that decreased S1PR2 by JTE-013 could reverse the demyelination and protect the survival of retinal ganglion cells (RGCs) and axonal regeneration.

Methods: Adult wild-type male C57Bl/6J mice (5-8 weeks) were purchased to establish the retinal ischemia/reperfusion (I/R) model. The right eye was perfused with sterile 0.9% saline solution for 1 hour to hold the IOP at 70 mmHg. The mice were randomly categorized into three groups in our experiments: blank control group, injured group, and treatment group. The eyes in the treatment group (N=3-7) were intravitreally injected with 3μl JTE-013 immediately after reperfusion, and the eyes in the injured group (N=3-7) with 3μl PBS. The optic nerves were perfusion-fixed and sectioned for immunofluorescent staining. We could detect the change of S1PR2 in the three groups. Then we measured the fluorescence intensity of myelin basic protein (MBP) and SMI32 to evaluate demyelination and axonal degeneration. The retinas were stained with βIII-tubulin and RBPMS to calculate the number of RGCs. Finally, we could observe the myelin sheaths and axons of the optic nerve by transmission electron microscope. One-way ANOVA and unpaired t test was used for statistical analysis.

Results: The expression of S1PR2 significantly increased in the injured ($p<0.05$) groups and the JTE-013 could inhibit the increase of S1PR2 (Figure 1A). The fluorescence intensity of MBP was significantly decreased in the injured ($p<0.01$) group, and JTE-013 could alleviate demyelination ($p<0.001$) (Figure 1B). Meanwhile, inhibiting S1PR2 could increase the number of RGCs ($p<0.001$) and reduce axonal degeneration ($p<0.05$) compared to the injured group (Figure 2). Quantification of G-ration and axons in electron micrographs also showed that JTE-013 could decrease myelin loss and increase the number of axons.

Conclusions: JTE-013 could relieve demyelination by inhibiting S1PR2, protecting RGCs and axons.

CONTROL ID: 3711337

SUBMITTER (NAME ONLY): Shen Yi Lim

TITLE: Assessment of stiffness of posterior eye wall in myopic eyes with an ultrasound-based algorithm using strain elastography

SESSION TITLE: Myopia: Structural Changes from Retina to Sclera

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Lim, K. Ito, Y. Dan, J.D. Yu, S. Saw, Q.V. Hoang, Singapore National Eye Centre, Singapore, Duke-NUS, Singapore, Singapore Eye Research Institute, Singapore, SINGAPORE|J. Mamou, F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|R.H. Silverman, Q.V. Hoang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myopic progression is commonly caused by axial elongation in an eye resulting in the thinning and reduced stiffness of the sclera. There exist limited studies on the stiffness of the posterior eyewall in myopic eyes. Our goal is to examine whether myopic eyes had greater deformability in the posterior eye of a cohort of adults in Singapore.

Methods: Fifty-eight myopic eyes of 29 subjects (ages 37-87) were enrolled.

Ultrasound (US, Quantel Aviso, 20 MHz) B-mode scans were performed in primary gaze across 100 frames to study the posterior of each eye. Manual compression by a handheld ophthalmodynamometer was used at specified intervals to capture the displacement over time and assess the degree of deformability, or strain, of the tissues of the retina-choroid-sclera (RCS) layer in the posterior eye wall.

For each frame, strain elastography was used to measure the relative stiffness (RS) of several regions of interest (ROI) in RCS layer, with orbital fat as the baseline. Softer tissues experience more strain and are expected to be less stiff than harder tissues.

Results: Average RS across 100 frames was compared across eyes for ROIs in RCS layer. At an interval of before-and-after compression, paired t-test showed significant difference between the change in average RS for a ROI ($p=0.01$) and across 2 different ROIs ($p=0.01$ and $p<0.01$) when compared against the baseline orbital fat. Average RS at 2 different intervals of before-and-after compression showed significant difference for an ROI ($p=0.01$) and of 2 different ROIs ($p=0.01$ and $p=0.04$) for paired t-test.

Axial length (AL, measured by IOLMaster) ranged 22.59 to 30.72 mm and spherical error (SE) ranged from 0.7 to -15.7 D. Increase in AL (per 1 mm) showed a decrease in average RS for an RCS layer ROI during compression of -0.283 ($R^2=0.40$, $p<0.01$) and no compression of -0.0139 ($R^2=0.19$, $p=0.04$). During compression, increase in SE (per 1 D) showed an increase in average RS of 0.00783 ($R^2=0.23$, $p=0.02$) for an RCS layer ROI.

Conclusions: Our qualitative and semiquantitative measure of posterior eye wall strain shows promise as an imaging biomarker identifying regions in myopic eyes that are less stiff and more susceptible to deformability that, when combined with other metrics (AL, SE) may help assess at an early stage, the risk of progression of a stable high myopia eye to PM with staphyloma.

CONTROL ID: 3711338

SUBMITTER (NAME ONLY): Amanda Scopelliti

TITLE: GUCY2D-associated autosomal dominant cone-rod dystrophy: Understanding the natural history

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The gene GUCY2D encodes the photoreceptor guanylate cyclase a key phototransduction enzyme involved in the restoration of cytoplasmic cGMP and return to the dark state of the photoreceptor. GUCY2D is associated with inherited retinal diseases including autosomal dominant cone-rod dystrophy (CRD). We performed a retrospective, observational cohort study to describe the natural history and progression of GUCY2D-associated CRD. In addition, the study aimed to investigate structural and functional biomarkers and their correlation with GUCY2D-associated CRD.

Methods: Retrospective analysis was conducted on data from 16 patients with GUCY2D-associated CRD across two sites. Assessments included central macular thickness (CMT) and length of disruption to the ellipsoid zone (EZ) via optical coherence tomography (OCT), electroretinography (ERG) parameters, best corrected visual acuity (BCVA), and fundus autofluorescence.

Results: At first visit, with a mean age of 30 years (range 5 – 70 years), 11 patients had a BCVA below the medical standards for holding an Australian Driver's licence (LogMAR > 0.3 in both eyes), and 1 patient met the Australian definition of legal blindness (LogMAR ≥ 1 in both eyes). Analysis over the observation period (mean = 7 years, range 0 – 17 years) demonstrated a deterioration of LogMAR by -0.019 per year (SE = 0.003, $p < 0.0001$), during which 3 patients crossed the threshold of legal blindness. This study also demonstrated a significant reduction in CMT of -1.3 µm per year (standard error (SE) = 0.4 µm; p = 0.005) and lengthened disruption of the EZ by 42 µm per year (SE = 5 µm, p = <0.0001). Similarly, cone function as measured by ERG was shown to decrease with increasing age; b-wave amplitude of both the light-adapted 30 Hz flicker and fused flicker decreased by 0.83 µV (SE = 0.30 µV, p = 0.005) and 0.21 µV (SE = 0.09 µV, p = 0.02) per year, respectively. Reduction in CMT and increased EZ disruption on OCT were significantly associated with functional changes including poorer BCVA and decreased cone function on ERG.

Conclusions: We have described the natural long-term decline in vision and cone function associated with mutations in GUCY2D. We have also identified a set of functional and structural biomarkers that may be useful as outcome parameters for future therapeutic clinical trials.

CONTROL ID: 3711340

SUBMITTER (NAME ONLY): Bhagya Lakshmi Marella

TITLE: Contrast imbalance and its impact on stereoacuity in keratoconus?

SESSION TITLE: Vision assessment and Clinical applications

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Profound losses in stereoacuity have been documented earlier in bilaterally asymmetric keratoconus. This study determined whether 1) these losses can be explained by imbalances in retinal image contrast between the two eyes, arising from the underlying interocular differences in disease severity (Experiment 1) and 2) correction of the contrast imbalance restores stereoacuity in these subjects to the level of healthy controls (Experiment 2).

Methods: In Experiment 1, the magnitude of contrast imbalance of 50 cases with bilaterally asymmetric keratoconus (11 to 31yrs) with spectacles was determined from the symmetry of interocular rivalry switches of dichoptically-presented orthogonal Gabor patches with 5cpd and 1.5cpd carrier spatial frequency. The stimulus contrast attenuation required in the stronger eye (as judged by greater value of D-index), relative to 100% contrast in the weaker eye, to achieve this symmetry was considered a measure of this contrast imbalance. In Experiment 2, random dot stereoacuity of 40 cases with bilaterally asymmetric keratoconus (16 to 32yrs) was measured at baseline, at the contrast balance point and at 20% below and above the contrast balance point using standard adaptive staircases.

Results: The magnitude of contrast imbalance was positively correlated with increasing interocular difference in D-index ($r=0.74$, $p<0.001$). The magnitude of contrast imbalance was significantly greater for 5cpd than for 1.5cpd stimulus ($p<0.001$). Stereoacuity was positively correlated with the extent of contrast imbalance in these cases ($r=0.47$, $p<0.002$). Contrast balancing improved stereoacuity by a median value of 34.6% (19.0-65.1%), independent of baseline stereoacuity (261.3-1257.3arc sec) or contrast imbalance levels ($r<0.2$, $p>0.26$ for both). Contrast bias towards the weaker eye (239.6-1707.6arc sec) produced a greater loss of stereoacuity than bias toward the stronger eye (181.9-1161.4arc sec) ($p=0.001$).

Conclusions: Contrast imbalance scales with the magnitude of interocular difference in keratoconus severity, more so for higher than lower spatial frequencies. Stereoacuity partially improves with contrast balancing in keratoconus. Results of the contrast biasing experiment indicate that cyclopean viewing may be weighted more towards the input from the stronger eye in keratoconus, independent of its contrast strength.

CONTROL ID: 3711343

SUBMITTER (NAME ONLY): Ling Wang

TITLE: The cAMP Response Element Binding Protein (CREB) Negatively Regulates Pax6 Expression in Lens Epithelial Cells through Its Direct Binding to the Core Promoter of Pax6 Gene

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Wang, Changsha Medical University, Changsha, Hunan, CHINA|L. Wang, J. Fu, Y. Wang, S. Zheng, Y. xiao, J. Wang, J. Xiang, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: CREB is a transcription factor and its most prominent function is to control the synaptic plasticity associated with long-term memory. In our recent studies, we demonstrated that CREB regulates oxidative stress-induced apoptosis and aging in lens by inhibiting αB-crystallin expression but promoting P300-P53-Bak/Bax signaling axis (Wang L et al. 2021. Aging Cell). Whether CREB is capable to regulate lens differentiation remains largely unknown. Here, in the present study, we demonstrate that CREB directly regulates Pax6 and other genes to control differentiation of mouse lens.

Methods: CRISPR/Cas9 Technology was used to create mouse model CREB-S133A. RNAseq analysis was used to compare the transcriptional activity of wild type and mutant CREB-S133A.Gel mobility shifting assays were used to determine binding of CREB to Pax6 gene promoter. ChIP assays were used to confirm the binding of CREB to the Pax6 gene promoter. Reporter gene constructs driven by different promoter and enhancer regions of the Pax6 gene were generated and used to assay the relative strength of different Pax6 gene promoter regions. QRT-PCR and Wes were used to analyze mRNA and protein expression levels.

Results: RNAseq analysis revealed the reverse relationship between CREB and Pax6. EMSA assays demonstrate that CREB directly binds to the promoter region of Pax6. ChIP assay results confirmed that CREB binds to Pax6 promoter in vivo. In mouse lens epithelial cell, overexpression WT-CREB resulted in downregulation of Pax6. Silence of CREB upregulates Pax6. RNAseq analysis also revealed that CREB can regulate a panel of differentiation-related genes.

Conclusions: Through direct control of Pax6 and other downstream differentiation-related genes, CREB regulates lens differentiation. Supported by National Natural Science Foundation of China (Grants #82000842, #81970787, #82000876, #81770910) and Natural Science Foundation of Guangdong Province and Guangdong City Joint Program of China (2019B1515120014) , and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center.

CONTROL ID: 3711345

SUBMITTER (NAME ONLY): Ali Al-Timemy

TITLE: A device-agnostic deep learning model for detecting keratoconus based on anterior elevation corneal maps

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop and validate a deep learning model for detecting keratoconus based on corneal maps from CASIA and Pentacam instruments.

Methods: We collected 3428 corneal maps from CASIA optical coherence tomography (OCT)-based imaging instrument (SS-1000, Tomey, Japan) at Jichi Medical University, Japan, and collected 217 corneal maps from Pentacam Scheimpflug-based imaging instrument (Oculus Optikgerate GmbH) at Al-Amal eye clinic in Baghdad, Iraq. We developed a deep learning framework based on AlexNet architecture to detect keratoconus based on anterior elevation maps in CASIA dataset only. We then evaluated the developed model based on corneal maps in the Pentacam dataset using accuracy, specificity, sensitivity, and area under the receiver operating characteristic curve (AUC) (Fig.1)

Results: The CASIA dataset included corneal maps from 1845 normal eyes and 1583 eyes with keratoconus (annotated based on the CASIA built-in Ectasia Screening Index;ESI). The Pentacam dataset included 114 normal eyes and 103 eyes with keratoconus (annotated based on clinical evaluations through two specialists). The accuracy and AUC of the proposed deep learning model in detecting keratoconus from anterior elevation maps tested on Pentacam dataset was 86.7% and 0.93, respectively (Fig.2). The sensitivity, specificity, and F-score of the model were 0.74, 0.98, and 0.88, respectively.

Conclusions: We developed a device-agnostic deep learning model to detect keratoconus and evaluated it based on corneal maps collected from two different cohorts (Japan and Iraq) based on two different instruments (CASIA and Pentacam). The accuracy of the proposed model in detecting keratoconus from two different instruments was reasonable. This novel approach demonstrates the generalization of the developed deep learning model. This model may augment clinical evaluations of keratoconus in day-to-day ophthalmological care.

CONTROL ID: 3711347

SUBMITTER (NAME ONLY): Zahra Markatia

TITLE: ERGONOMICS OF OPHTHALMIC SURGERY: A PILOT STUDY EVALUATING THE EFFECT OF A POSTURE TRAINER ON INTRAOPERATIVE BACK POSTURE

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ophthalmic surgeons are at an increased risk for musculoskeletal disorders resulting in chronic back and neck pain, which has been linked to disability, productivity loss, and early retirement. Prior studies have correlated these outcomes to work-related routines and equipment specific to ophthalmic exams and surgeries, which may be exacerbated by poor posture. The purpose of this study was to observe the effect that a commercially available posture trainer, Upright Go, can have on the improvement of posture of ophthalmic surgeons.

Methods: Five ophthalmologists-in-training were studied over a period of four weeks during their surgical rotations between September 2020 and June 2021. Participants underwent an “observation” period consisting of two surgical days during which their postural data was tracked via the posture training device and recorded through an associated phone application. The trainees then entered a two-week “training” period, during which the device was calibrated and programmed to vibrate anytime the user slouched past a certain degree specific to the calibration of each user. The final “testing” period consisted of another two surgical days with the vibration setting turned back off while user posture was again tracked. The percentage of time users spent upright intraoperatively pre- and post- training was evaluated.

Results: All five participants demonstrated an increase in the percentage of time spent upright after the training period. Across all participants, the total average percentage spent upright in the observation period was 64.2%, while in the testing period was 89.3%, resulting in an average improvement of 25.1% of time spent in an upright position after the completion of the training period ($p<0.002$). The range of improvement of time spent upright was 16.0% to 33.5%.

Conclusions: This cohort study utilized the Upright Go device to help determine the effect that its training could have on improvement of posture in ophthalmic surgeons. The results indicated a significant increase in the average proportion of time spent with upright posture compared after the training period.

CONTROL ID: 3711348

SUBMITTER (NAME ONLY): Md Rafiqul Islam

TITLE: Detecting Glaucoma From Retinal Fundus Photographs Based on Deep Learning Models

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the accuracy of different deep learning models for detecting glaucoma from fundus photographs.

Methods: We used a dataset with 1707 fundus photographs from 919 normal eyes and 788 eyes with glaucoma. We developed five different deep learning architectures in Google Colaboratory to detect glaucoma based on fundus photographs. We randomly selected 80% of the fundus photographs for development of models and 20% of the fundus photographs for final testing and evaluation of models. We developed a customized convolutional neural network (CNN) with 13 layers and compared it against four of the existing CNN architectures including AlexNet, VGG16, DensNet121, and ResNet50. We used different accuracy metrics to compare the performance of developed models based on the testing subset (Table 1).

Results: Table 1 shows the accuracy of different models in detecting glaucoma based on different CNN architectures using development and testing subsets. The customized CNN architecture achieved an accuracy of 87.2% and 92.6% on testing and development subsets, respectively. Figure 1 shows the receiver operating characteristics (ROC) curves of all CNN architectures. The area under the receiver operating characteristic curve (AUC) of the customized CNN was 81.8% and 96.5% based on testing and development subsets, respectively.

Conclusions: We performed a pilot study to show that it is feasible to detect glaucoma from fundus photographs based on different deep learning architectures. However, two factors are critical in robustly evaluating deep learning models. The datasets would need to be representative of underlying decease characteristics. The model would need to be generalizable. Validating the customized CNN architecture based on larger and independent datasets is desirable and may augment clinical practice in glaucoma assessment.

CONTROL ID: 3711351
SUBMITTER (NAME ONLY): Archayeeta Rakshit
TITLE: Investigation of visual functions in adult anisometropic amblyopia
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
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ABSTRACT BODY:
Purpose: The purpose was to assess visual acuity, binocular vision, higher order executive function (selective and divided attention), and functional ability (fine motor skills and reading speed) in participants with and without anisometropic amblyopia. In addition, to determine if visual acuity and binocular function influence the functional outcome measures. The hypothesise was that as for amblyopic children, adults will also exhibit reduced performance on visual attention and visual search tasks.
Methods: 20 adults with anisometropic amblyopia (mean age= 22±3.9 yr) and 10 adults with normal visual development (26.8±4.4 years; controls) participated. Vision assessment included refraction, visual acuity (monocular and binocular) and binocular function (BF) (Worth 4 Dot and Randot Preschool Stereo test). Fine motor skills and reading speed were tested by Bruninks-Oseretsky Test of Motor Proficiency (BOTMP) and International Reading Speed Texts (IReST) respectively. Visual attention and processing speeds were assessed using the three subtests of the Useful Field of View (UFOV): central processing, divided attention, and selective attention. Visuo-cognitive search proficiency was measured using static and dynamic presentations of the Trail Making Tests (TMTs), parts A and B, with increasing levels of executive function demand. All participants performed these functional tasks binocularly.
Results: Amblyopes showed a mean VA of 0.51(0.25) logMAR in the amblyopic eye. They exhibited slower reading performance (124±40 wpm) and slower completion time in TMT searches (Trail A - 58±24secs, Trail B- 73±28secs) as compared to controls (reading speed:159±34 wpm; TMT: Trail A- 43±4sec, Trail B- 53±8sec) ($p<0.05$). They also performed significantly poorer than control subjects on the fine motor skills subitems (for example, making dots in a circle, transferring pennies and sorting cards) ($p<0.01$). VA in the amblyopic eye was a significant predictor of UFOV performance ($F(2,17)= 2.82$, $p=0.03$). Both VA and BF score were significant predictors of TMT [VA: ($F(2,17)=3.559$, VA: $p=0.048$, BF score: $p=0.03$].
Conclusions: Adults with anisometropic amblyopia exhibited reduced performance on fine motor skills, reading speed, visual attention and visual search compared to control participants. These findings have implications for understanding the impact of amblyopia on everyday function in adults.

CONTROL ID: 3711355

SUBMITTER (NAME ONLY): Xavier Llòria

TITLE: Long-term efficacy and safety of idebenone in patients with LHON in the chronic phase: Results from the LEROS study

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Llòria, L. Tomasso, Chiesi Farmaceutici SpA, Parma, Emilia-Romagna, ITALY|T. Klopstock, Department of Neurology, Ludwig-Maximilians-Universitat Munchen, Munchen, GERMANY|

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ABSTRACT BODY:

Purpose: Leber's hereditary optic neuropathy (LHON) is a rare mitochondrial disorder resulting in severe, bilateral vision loss. Idebenone is approved in Europe for the treatment of LHON, but data in chronic patients is relatively sparse. Here, we report results from LEROS, a Phase 4, externally controlled, open-label interventional study (ClinicalTrials.gov NCT02774005), which included chronic patients (1 to ≤5 years since onset) with LHON treated with idebenone for up to 24 months.

Methods: LEROS included patients with LHON ≥12 years old and with a disease onset ≤5 years prior. Overall, 199 patients were enrolled, 181 of which formed the mITT population (excluded patients without a confirmed primary causative mtDNA mutation). NH data were available from 372 patients. Patients were divided into 2 groups for analysis based on time since onset in the most recent eye: subacute/dynamic (≤1 year) and chronic (>1 year). Outcomes in the idebenone-treated group were compared to retrospective data from the NH cohort, matched based on time since disease onset. Outcome measures (from baseline) were clinically relevant recovery (CRR): improvement from 'off-chart' VA to at least 1.6 logMAR, or a ≥0.2 logMAR improvement if already 'on-chart'; clinically relevant stabilization (CRS): maintenance of VA <1.0 logMAR; and clinically relevant benefit (CRB): reaching a CRR, a CRS, or both.

Results: LEROS met its primary endpoint, showing a significant increase in the proportion of subacute/dynamic eyes with a CRB from baseline following 12 months of treatment, compared to the matched external NH cohort. A secondary endpoint, identical to the primary but in chronic patients, was also successfully met; CRB was observed in 50.3% (72/143) of treated, chronic eyes versus 37.9% (59/153) from the NH cohort (p = 0.0087). CRB was largely driven by CRR, observed in 32.9% (47/143) of treated eyes versus 19.0% (29/153) in the NH cohort (p=0.058). In treated chronic patients, the median best VA at baseline was 1.48 logMAR (n=87) and showed an improvement over the study duration to 1.32 (n= 81), 1.23 (n=70), 1.26 (n=66) and 1.16 (n=55) logMAR at 6, 12, 18 and 24 months, respectively.

Conclusions: LEROS provides evidence of a significant therapeutic benefit of idebenone treatment in patients with LHON in the chronic stage, a group for whom viable treatment options are otherwise severely limited.

CONTROL ID: 3711356

SUBMITTER (NAME ONLY): Néstor Ventura Abreu

TITLE: The discriminative ability of two glaucoma diagnostic calculators in glaucoma suspects and glaucoma patients

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma diagnosis is still based on ophthalmic examination and visual field interpretation. Several structural parameters from the optic nerve and the macular area measured by optical coherence tomography (OCT), and the combination of some of them, have shown noteworthy diagnostic performance. We aimed to validate the discriminative ability of two OCT-based diagnostic calculators (RETICs) and to compare it with that of isolated OCT parameters

Methods: We revised the charts of 76 primary open-angle glaucoma (A), 107 glaucoma suspects (B), and 67 healthy control cases (C). Demographics, visual field, and high-quality OCT disc and macular parameters were included. The reference diagnosis (clinical examination) was compared against the probability of having glaucoma obtained from the two RETICs glaucoma diagnosis calculators (GDC). Both GDC1 and 2 derived from multivariate logistic regressions using either only the numeric (quantitative) data from peripapillary retinal nerve fiber layer (pRNFL), optic disc, and ganglion cell-inner plexiform layer (GCIPL) (GDC2) or along with qualitative data (color scoring of the quantitative data according to a normative database) (GDC1). The sensitivity and specificity of all parameters were analyzed. The Area Under the Receiver Operating Characteristic Curves (AUROCC) were compared in glaucoma suspects and glaucoma patients, for both calculators, and the best OCT parameters

Results: The three best OCT parameters in terms of AUROCC for both A and B were inferior pRNFL (0.931; 0.760), average pRNFL (0.925; 0.745), and minimum GCIPL (0.919; 0.735), showing no statistically significant differences among them. The AUROCC from both GDC1 and 2 were high (0.949 & 0.943, p=0.61) and moderate (0.739 & 0.73, p=0.56) for glaucomatous eyes and glaucoma suspects, respectively; compared to the OCT-derived parameters, the discriminative ability was modestly superior and non-inferior for both calculators in A and B groups, respectively. GDC2 was able to correctly classify 46.9% and 14.7% more cases compared to GDC1

Conclusions: The combination of OCT parameters provided by the RETICs calculators had the highest diagnostic ability to discriminate glaucoma vs control eyes, although it was not as good in glaucoma suspects. GDC2 had the best results, suggesting that adding qualitative structural information does not improve glaucoma diagnosis performance

CONTROL ID: 3711357

SUBMITTER (NAME ONLY): Manuel Hermann

TITLE: Transformation of Subretinal Hyperreflective Material in Exudative Neovascular Age Related Macular Degeneration from Type 2 into Type 1 Appearance under anti-VEGF Therapy

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Subretinal hyperreflective material (SHRM) in eyes with exudative neovascular age-related macular degeneration (AMD) treated with anti-vascular endothelial growth factor (VEGF) may gradually turn from macular neovascularization (MNV) type 2 into type 1 appearance on OCT. We here aimed to study the impact of this transformation on functional and morphological outcomes.

Methods: Data for this post-hoc sub-analysis emerged from a 12-month, randomized, open label, multicenter study comparing the efficacy of Ranibizumab pro re nata versus Aflibercept bimonthly intravitreal injections in treatment-naïve patients newly diagnosed with exudative neovascular AMD (SALT). Imaging comprised fluorescein angiography, color fundus photography and autofluorescence at baseline and month 12, and monthly SDOCT (Spectralis SDOCT, Cirrus HDOCT). 203 eyes of 203 study patients with SHRM on SDOCT at baseline were included. Two certified graders blinded to functional data assigned each eye to one of the following 4 categories: (A) SHRM remains present with type 2 appearance, (B) SHRM partially transformed into type 1 appearance, (C) SHRM completely transformed into type 1 appearance, (D) SHRM disappeared. The area of decreased autofluorescence was additionally evaluated at baseline and month 12.

Results: Analyses of variances (ANOVAs) found a significant effect of the factor SHRM CATEGORY (levels A (n=136), B (n=18), C (n=23), D (n=26)) on the change of BCVA at 3 months compared to baseline ($F[3,196]=6.86;p<0.001$): Post-hoc t-tests were significant ($p<0.05$) for comparisons of SHRM Category A (mean 3.8 ETDRS letters) with B (9.9), C (10.7) and D(10.8). At 12 months ($F[3,196]=4,85;p=0.003$) post-hoc t-tests found a significant difference between SHRM Category A (4.6) only versus C (15.1) and D (10.6), but not B (8.4). For the area of decreased autofluorescence at 12 months, we also found a significant effect ($F[3,170]=4.41;p=0.005$): Post-hoc t-tests showed significant differences between Category A (mean area 1.076 mm^2) versus B (0.079) and C (0.077) but not D (0.385).

Conclusions: Eyes with transformation of SHRM from type 2 into type 1 appearance on the course of therapy had a significantly higher mean improvement of visual acuity 3 and 12 months after initiation of therapy and showed a smaller area of decreased auto-fluorescence after 12 months.

CONTROL ID: 3711365

SUBMITTER (NAME ONLY): Russell Chan

TITLE: Chronic intraocular pressure elevation alters cerebrovascular reactivity in the visual cortex and basal forebrain

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Glaucoma is an eye disease with widespread involvement of the brain. Since visual cortex (VC) may possess lower choline levels in glaucoma, and basal forebrain (BF) has cholinergic projections to VC for modulating cerebral blood flow and visual processing, we postulate that the vascular functions of the VC and BF are involved in glaucoma (PMID: 31242454). Recently, we used a novel whole-brain relative cerebrovascular reactivity (rCVR) mapping technique via resting-state functional MRI (rsfMRI) without gas challenge, and observed rCVR decrease in VC and rCVR increase in BF in patients with increasing glaucoma severity (PMID: 34892116). However, the underlying mechanisms remain to be elucidated. Here, we applied a hydrogel-induced glaucoma mouse model to elevate intraocular pressure (IOP) (PMID: 31176841), mapped whole-brain rCVR using rsfMRI, and measured optomotor responses (OMR). We hypothesize that chronic IOP elevation can lead to rCVR changes in the glaucomatous brain along with visual impairments.

Methods: For the glaucoma model, C57BL/6J mice (male, 15-weeks, n=15) received intracameral injection of cross-linking hydrogel to the right eye to obstruct aqueous outflow and induce chronic IOP elevation. Controls (male, 15-weeks, n=13) were untreated. IOP was measured in both eyes 2-3 times per week for 3 weeks, followed by OMR and rsfMRI experiments at 7 Tesla (Fig. 1A).

Results: Sustained IOP elevation was confirmed in the right eyes of the glaucoma model (Fig. 1B). Over 90% of mouse optic nerve fibers are known to project to the contralateral visual brain; rCVR decreased in the left but not right VC, whereas rCVR increased in the right BF in the glaucoma model but not the controls (Fig. 2A). These rCVR changes were inversely coupled (Fig. 2B). In addition, IOP of the injected eye was inversely correlated with rCVR in the left VC, while positively correlated with rCVR in the right BF (Fig. 2C). OMR revealed a decrease in visual acuity and an increase in visual contrast threshold for the injected eye (Fig. 2D) indicating visual impairment. The decrease in visual acuity was inversely correlated with rCVR in the BF (Fig. 2E).

Conclusions: Mouse rCVR mapping using rsfMRI detects widespread brain changes induced by chronic IOP elevation, and demonstrates vascular involvement in glaucoma both within and beyond the primary visual pathways.

CONTROL ID: 3711366

SUBMITTER (NAME ONLY): Karen Tessmer

TITLE: Donor-host interactions support incorporation, polarization and maturation of human photoreceptors transplanted into a cone-degeneration mouse model

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Retinal degeneration is a leading cause of disability in the industrialized world. Many retinopathies are marked by an irreversible photoreceptor loss, thus photoreceptor transplantation has emerged as a potential treatment strategy. However, conditions allowing donor photoreceptor incorporation and maturation are largely unknown. This study thus aimed to elucidate the regenerative potential of transplanted human photoreceptors in a cone-degeneration only host.

Methods: A hiPSC cone (iPSC-mARR3-GFP) and a hiPSC rod and cone (iPSC-Crx-mCherry) reporter line were used to produce retinal organoids. Reporter-positive photoreceptors at day 200 of differentiation were FAC sorted and transplanted into the subretinal space of adult Cpfl1 (cone photoreceptor function loss 1) mice with vitreal immune suppression. After 3, 10, or 26 weeks, grafts were examined using immunohistochemistry, electron microscopy, next generation sequencing, and multi-electrode array recordings (MEA).

Results: With increased post transplantation time, photoreceptor clusters from both cell lines showed extensive incorporation into the host neural retina, accompanied by considerable interaction with host inner retinal cells. Rod and cone bipolar cells extended neurites into the transplants and Müller glia processes were present throughout grafts, frequently forming a common outer limiting membrane in line with the human cells. Interestingly, increased donor-host interaction correlated with improved graft polarization and maturation. Especially after 26 weeks, properly oriented inner and in several cases well stacked outer segments were observed. Putative synapses between donor cells and host bipolars were detected, while graft function was confirmed by MEA recordings. Transcriptome comparison to age matched retinal organoids further indicated improved human photoreceptor maturation within the murine environment versus the in vitro setting.

Conclusions: This study shows that human photoreceptors can incorporate extensively into the murine host retina and that interaction with host Müller glia and/or bipolars benefits their maturation, polarization and ultimately function. Deciphering the cellular and molecular factors essential for proper donor photoreceptor integration will be of utmost importance to optimize photoreceptor replacement therapy towards clinical application.

CONTROL ID: 3711371

SUBMITTER (NAME ONLY): Juan Tabernero

TITLE: Functional vision testing to study the benefits of the correction of small astigmatism with toric lenses in contact lens neophytes

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop functional visual tests to better understand the potential advantages of a full sphero-cylindrical toric correction for contact lenses (CL) neophytes with low values of astigmatism.

Methods: We used a custom set of video cameras and thin film pressure sensors to monitor and automatically quantified several daily functional activities in terms of time and performance. These activities include i) pouring a liquid into a recipient up to a certain marked level, ii) inserting a key in a lock and turning it, and iii) finding three (digital) files in a computer desktop placed among other files and attach them into an email. Currently, we have tested the procedures in nineteen first year university students. All of them were contact lens neophytes with no previous experience of CL fitting. Subjects were split into two homogenous groups matched by age and refractive error with no statistically significant differences within these variables. Subjects in group one (N=10) had a cylinder value of -0.9 ± 0.3 D and were monocularly fitted with a spherical CL (Precision1, Alcon Laboratories, Inc, Fort Worth, TX). Subjects in group two (N=9) had a similar cylinder, -1.0 ± 0.4 D, and were fitted with a toric CL (Precision1 for Astigmatism). All subjects performed three trials of tasks i) and ii) and a single email test. Data was averaged correspondingly.

Results: On average, subjects in the toric group were able to complete all tasks faster than subjects in the spherical lens group. Pouring the liquid, opening the lock and sending the attachments by email was respectively 28%, 3% and 10% faster in the toric group compared to the spherical group. However, for this pilot study, we only reached statistically significant differences for the first task (pouring the liquid up to a certain level; $p = 0.02$). Interestingly, for those tests with repeated trials (pouring and key lock), subjects in the toric group performed more consistently across trials than subjects in the spherical group. On average, data dispersion was two times smaller in both tests for the toric group.

Conclusions: Toric CL fitting tended to improve some aspects of functional vision compared to a spherical CL fitting in CL neophytes even with low levels of astigmatism. Further studies in a larger population are required to confirm these functional benefits.

CONTROL ID: 3711373

SUBMITTER (NAME ONLY): Thomas Klopstock

TITLE: Long-term efficacy and safety of idebenone in patients with LHON in the subacute/dynamic phase: Results from the LEROS study

SESSION TITLE: Optic Neuropathies - Diagnostic and Therapeutic Approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Klopstock, Department of Neurology, Ludwig-Maximilians-Universitat Munchen, Munchen, GERMANY|L. Tomasso, X. Llòria, Chiesi Farmaceutici SpA, Parma, Emilia-Romagna, ITALY|

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ABSTRACT BODY:

Purpose: Leber's hereditary optic neuropathy (LHON) is a rare mitochondrial disorder resulting in severe, bilateral vision loss. Idebenone is approved in Europe for the treatment of LHON, but controlled data beyond a 6-month treatment duration is lacking. Here, we report results from LEROS, a Phase 4, externally controlled, open-label interventional study (ClinicalTrials.gov NCT02774005), in which visual acuity (VA) outcomes following 24 months of idebenone treatment were compared to an external, matched, natural history (NH) cohort.

Methods: LEROS included patients with LHON ≥12 years old and with a disease onset ≤5 years prior. Overall, 199 patients were enrolled, 181 of which formed the mITT population (excluded patients without a confirmed primary causative mtDNA mutation). NH data were available from 372 patients. Patients were divided into 2 groups for analysis based on time since onset in the most recent eye: subacute/dynamic (≤1 year) and chronic (>1 year). Outcomes in the idebenone-treated group were compared to retrospective data from the NH cohort, matched based on time since disease onset. Outcome measures (from baseline) were clinically relevant recovery (CRR): improvement from 'off-chart' VA to at least 1.6 logMAR, or a ≥0.2 logMAR improvement if already 'on-chart'; clinically relevant stabilization (CRS): maintenance of VA <1.0 logMAR; and clinically relevant benefit (CRB): reaching a CRR, a CRS, or both.

Results: The primary endpoint, the proportion of subacute/dynamic eyes with a CRB from baseline following 12 months of treatment, compared to the matched external NH cohort, was successfully met. CRB was observed in 42.3% (60/142) of treated eyes versus 20.7% (40/193) from the NH cohort (p=0.002). At 24 months, this significant difference was maintained, at 52.9% (64/121) versus 36.0% (27/75) (p=0.0297). In treated subacute/dynamic patients, the median best VA at baseline was 1.28 logMAR (n=109) and showed an initial worsening at 6 months to 1.41 logMAR (n=90). A recovery was then observed to 1.30 (n= 81), 1.20 (n=75) and 1.07 (n=70) logMAR at 12, 18 and 24 months, respectively. No new safety signals were observed for idebenone.

Conclusions: LEROS corroborates the outcomes of previous studies, demonstrating that long-term treatment with idebenone results in prolonged clinical benefit in patients with LHON in the subacute/dynamic phase.

CONTROL ID: 3711374

SUBMITTER (NAME ONLY): Naoya Shigesada

TITLE: Quantifying retinal pigment epithelium (RPE) damage in vivo rat study by fundus autofluorescence (FAF)

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Shigesada, Y. Fujita-Koyama, T. Mochizuki, T. Noto, K. Shibagaki, Santen Seiyaku Nara Kenkyu Kaihatsu Center, Ikoma, Nara, JAPAN|S. Nakada, M. Toshimori, Santen Seiyaku Kabushiki Kaisha, Osaka, JAPAN|A.P. Abraham, Santen Inc, Emeryville, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fundus autofluorescence (FAF) imaging is often used in diagnosis for dry age-related macular degeneration (dAMD). The purpose of this study is to detect the retinal pigment epithelium (RPE) damage using FAF imaging in an animal model and validate the correlation between FAF and other functional evaluation items.

Methods: Thirty or 35 mg/kg sodium iodate ($NaIO_3$) was injected intravenously into Brown Norway rats to induce RPE degeneration. FAF images were obtained on 2, 5, and 8 days after $NaIO_3$ treatment and the RPE degeneration area was quantified. The a, b, and c-wave amplitude of electroretinogram (ERG) were recorded for at least 1 hour after the onset of dark-adaption. In vitreous fluorophotometry (VFP) evaluation, fluorescein was injected intravenously and, after circulating for 2 hours, the fluorescein concentration of vitreous humor was measured by Fluorotron Master to evaluate the outer blood-retinal barrier (BRB) function. The retinal sample was histopathologically observed with hematoxylin and eosin (HE) staining and immunostaining of ZO-1 and RPE65. To examine its effects on the $NaIO_3$ rat model, N-acetyl cysteine (NAC) was administrated intravitreally 30 minutes prior to $NaIO_3$ injection.

Results: Compared to normal rats, $NaIO_3$ rats showed numerous dark spots in the FAF image, indicative of RPE damage. The RPE degeneration area was correlated with reduction of each ERG wave amplitude, dysfunction of outer BRB, and retinal structure changes. In addition, RPE protection by NAC on $NaIO_3$-induced RPE degeneration rat model was confirmed by the quantification of damaged RPE area in the FAF image, and it was consistent with the results of ERG and VFP measurements.

Conclusions: This study demonstrates that FAF is useful to observe the RPE and evaluate the efficacy of RPE protection in vivo rat eye. Using FAF imaging, RPE function of the same sample can be evaluated at several time points. This is an advantage compared to invasive methods such as histopathological examination which is generally used in non-clincial studies.

CONTROL ID: 3711375

SUBMITTER (NAME ONLY): Qingying Jin

TITLE: Glaucomatous progressive retinal nerve fiber layer thinning and its association with patient race

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Jin, Department of Psychology, School of Philosophy and Sociology, Jilin University, Changchun, Jilin, CHINA|Q. Jin, O. Halawa, Y. Li, M. Eslami, S. Kazeminasab, M. Fazli, V. sharma, N. Zebardast, M. Wang, T. Elze, Department of Ophthalmology, Mass. Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate predictors of retinal nerve fiber layer (RNFL) thinning over time and their association with patient race.

Methods: From Mass. Eye and Ear glaucoma service, all patients with at least four reliable (signal strength ≥ 6) Cirrus spectral-domain optical coherence tomography (OCT) peripapillary scans over a minimum period of 2.5 years and an electronically available, questionnaire based self-reported race as either Asian, Black, or White were selected. Patient race, age and sector-specific circumpapillary RNFL thickness (cpRNFLT) at first visit were investigated by multivariable linear regression to predict the slope of cpRNFLT over time. To determine the best parameter combination to predict cpRNFLT slopes, the Akaike Information Criterion (AIC) was applied. A race specific sub-analysis was performed to reveal possible specific race-related impacts.

Results: 3,689 eyes of 1,959 patients (57.3% female) were selected. 159 patients identified as Asian, 395 as Black and 1,408 as White. On average, patients were followed up (mean±std) with 4.99±1.24 visits over 5.15±1.62 years with a mean follow-up interval of 1.32±0.35 years. Entire population results: Fig. 1A compares models to predict cpRNFLT slope over time from baseline. Baseline thickness was the best predictor in all sectors. Race outperformed age except for the temporal sector. In all sectors, the best model over all parameter combinations was the model with all parameters, where higher baseline age and lower baseline thickness were related to faster RNFL thinning over time. Race specific sub-analyses: With the exception of the temporal RNFLT slope (not shown on figures), there was a significant (ANOVA, $p<0.01$) main association between race and all parameters. Black patients are younger at first visit and have thicker baseline RNFL (Fig. 1B,C), but are nevertheless subject to faster RNFL thinning than the other races (Fig.2).

Conclusions: While models based on the entire population identified higher baseline age and thinner baseline RNFL as predictors for faster future RNFL thinning, the race-specific sub-analysis revealed an opposite effect for the group of Black patients alone, who presented at significantly younger ages and with thicker RNFL at their first visits but where still subject to faster RNFL thinning compared to the other races.

CONTROL ID: 3711376

SUBMITTER (NAME ONLY): SEUNGWON AN

TITLE: Therapeutic potential of mesenchymal stem cell-secreted factors on nitrogen mustard-induced corneal injury

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. AN, K. Anwar, X. Shen, M. Ghassemi, A.R. Djalilian, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the therapeutic potential of mesenchymal stem cell (MSC)-conditioned media on NM-mediated corneal damage.

Methods: Nitrogen mustard treatment on cells (human corneal epithelial primary cells, human corneal limbal epithelial cells) and mouse eyes after 2mm-diameter epithelial wound.

Cells and mouse eye were used for LDH toxicity assay, ROS measurements, JC-1 immunostaining, ATP measurement.

Cells are treated and measured metabolic gene changes after nitrogen mustard with or without MSC-CM.

Porcine eye and mouse eye are used for corneal epithelial wound healing.

Results: MSC-CM helps to restore mitochondrial function, resulting in leading cell survival after following NM exposure. MSC-CM decreased intracellular ROS generation after NM exposure and functioned as antioxidant capacity. Moreover, MSC-CM helps epithelial cells migration and proliferation to heal a wound after NM-mediated cell injury. In parallel experiments, both in vivo and ex vivo experiments confirmed that NM exposure on murine and porcine eyes showed that (i) induced apoptosis, (ii) increased corneal epithelial thickness by unpacking cornea structure, and (iii) delayed wound healing. Especially, NM injury of the porcine eye produced extensive damage on the loss of membrane integrity of the surface epithelium and the loss of corneal stromal matrix and it is possibly induced corneal and stromal inflammation and apoptosis. Whereas, MSC-CM enhanced the wound healing process and protected corneal structure compared to the NM exposure group. Moreover, MSC-CM enhanced epithelial cell barrier formation after NM exposure.

Conclusions: Taken together, these studies identified NM-induced corneal injuries damaged on the corneal epithelium, resulting in the loss of epithelium and unpacking cornea structure by disrupting epithelial cell barrier function. However, MSC-CM enhanced epithelial cell barrier formation to protect epithelium-stroma structure after NM exposure. These results suggest that MSC-CM has a therapeutic potential to protect against possible chemical eye injury and it could be helpful in the development of targeted therapies.

CONTROL ID: 3711377

SUBMITTER (NAME ONLY): Miriam Bauwens

TITLE: Deciphering the genetic architecture of inherited retinal diseases (IRD) in the Iranian population by integrated exome sequencing

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bauwens, K. Van Schil, M. De Bruyne, M. Van Heetvelde, Q. Mahieu, T. Rosseel, S. Van Malderen, E. De Baere, Center for Medical Genetics Ghent, Ghent University and Ghent University Hospital, BELGIUM|K. Van Schil, Center for Medical Genetics Antwerp, Universiteit Antwerpen, Antwerpen, BELGIUM|R. Maroofian, Institute of Neurology, Department of Neuromuscular Diseases, University College London, London, London, UNITED KINGDOM|F. Suri, Ophthalmic Epidemiology Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|E. Al-Hajj, Vrije Universiteit Brussel, Brussel, Brussel, BELGIUM|

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ABSTRACT BODY:

Purpose: To uncover the underlying molecular causes of inherited retinal disease (IRD) in 105 unrelated families of Iranian descent, an integrated approach consisting of whole exome sequencing (WES) and autozygosity mapping was used.

Methods: WES was performed in 105 Iranian IRD families, predominantly originating from a consanguineous background (77%). Data-analysis was performed using the in-house Seqplorer tool. Variants were confirmed using Sanger sequencing and families underwent segregation analysis. Copy number variants (CNVs) were assessed via the ExomeDepth algorithm and validated using qPCR. Variants were classified based on ACMG/ACGS guidelines. The AutoMap tool was used to determine runs of homozygosity (ROHs) in unsolved patients. ROHs were inspected for variants in novel candidate genes using Seqplorer and QCI Interpret Translational.

Results: By interrogating known IRD genes (n=290) using a WES-based analysis, we were able to obtain a molecular diagnosis for 85% of the IRD cohort. In total, 103 (likely) disease-associated variants were identified in 42 genes, 58 of which are novel variants (56%). ABCA4, EYS, AIPL1 and CRB1 were the four most implicated genes. Not surprisingly, the majority of causal variants were present homozygously (81%) while compound heterozygous and heterozygous/hemizygous variants were found in 14.5% and 4.5% of solved cases respectively. In addition, the importance of structural variation (SV) in IRD was demonstrated, with CNVs identified in 8% of the cohort, including novel CNVs in CDHR1, CHM and RD3. Homozygous nonsense and missense deleterious variants were found in novel retina-expressed candidate IRD genes, specifically OGDHL, PFKFB2 and QRFPR.

Conclusions: This integrated study using WES and an in-depth analysis of the variants provided insight into the genetic architecture of IRD in Iran, an understudied population. We provided 85% of patients with a molecular diagnosis and expand the molecular spectrum of IRD in Iran by the identification of novel variants in known IRD genes in the majority of patients, emphasizing the power of WES as a first-tier genetic test in consanguineous IRD cohorts. Autozygome-guided exome sequencing revealed several novel candidate genes for IRD in unsolved cases. In the remaining patients, whole genome sequencing has the potential to uncover non-coding variation and complex structural variation.

CONTROL ID: 3711378

SUBMITTER (NAME ONLY): Julien Fars

TITLE: Complementarity of sensitivity and just noticeable difference in the study of Retinitis Pigmentosa and Stargardt disease

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fars, J.J. Kremers, C. Huchzermeyer, Ophthalmology, Universitatsklinikum Erlangen, Erlangen, Bayern, GERMANY|

Commercial Relationships Disclosure: Julien Fars: Commercial Relationship: Code N (No Commercial Relationship) | Jan Kremers: Commercial Relationship: Code N (No Commercial Relationship) | Cord Huchzermeyer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate if sensitivity and just noticeable difference thresholds were modified in patients with retinitis pigmentosa (RP) and Stargardt disease (STGD1).

Methods: We examined 29 normal observers (29±10 years), 19 RP (43±15 years) and 14 STGD1 (43±14 years) using a temporal contrast sensitivity procedure based on the silent substitution paradigm. L-, M-, S-cone and Rod isolating sine-wave modulations were tested with a dedicated LED stimulator at frequencies that stimulate single retino-geniculate pathway in the perifovea without intrusion by other pathways. L- and M-cones at low (parvocellular) and high frequencies (magnocellular), S-cones at low frequencies (koniocellular) and Rods at medium frequencies (rod driven pathway) were analysed. From the temporal contrast sensitivity procedure, two measures were extracted: the sensitivity and the just noticeable differences (JND). The first corresponds to the inverse of the absolute threshold i.e. the contrast at 50% probability of detection. The JND is the difference threshold and is calculated by subtracting the contrast at 75% probability of detection from the contrast at 25%. Then two Bayesian mixed models were produced to detect the influence of subject group (normal subjects and the two patient groups), of the post receptoral pathway and of the age of the observers on either the sensitivity or the JND thresholds.

Results: Sensitivities of RP patients were close to normal. STGD1 patients displayed a large sensitivity decrease for most measurements. JND values of STGD1 patients were close to normal while RP patients had larger values than normal observers, specifically parvocellular and rod mediated pathways.

Conclusions: The two studied perception parameters (sensitivity and JND values) display opposite differences in RP or STGD1 patients. The decreased sensitivity in STGD1 patients can be related to the macular degeneration. RP patients may display a larger uncertainty in stimulus detection because a larger retinal area is affected even though the retinal degeneration is subjacent to the stimulus in the perifovea. The use of JND may allow us to describe early effects of vision loss. Our results exhibit a potential complementarity of the sensitivity and JND methods to describe and follow the development of retinal diseases.

CONTROL ID: 3711381

SUBMITTER (NAME ONLY): Hanako Ikeda

TITLE: Development of new neuroprotective treatment for retinal diseases—a phase 1/2 clinical trial on central retinal artery occlusion with KUS121

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.O. Ikeda, Y. Muraoka, M. Hata, A. Tsujikawa, Ophthalmology, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, Kyoto, JAPAN|M. Hata, Biochemistry and Molecular Medicine, University of Montreal, Montréal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: We have been developing the Kyoto University Substance (KUS) 121 which is an inhibitor of valosin-containing protein ATPase. It has a protective effect on retinal cells in vitro and in animal models of ocular diseases, including retinitis pigmentosa, retinal artery occlusion, and glaucoma. To examine the safety and efficacy of KUS121, we conducted an investigator-initiated clinical trial on patients with central retinal artery occlusion (CRAO).

Methods: Nine patients with CRAO with symptoms lasting between 3 and 48 hours were recruited for the clinical trial (phase 1/2, UMIN000023979). KUS121 was intravitreally injected daily for 3 days. We assessed the safety of the drug and the patients' visual function (visual acuity and visual field) outcomes for 3 months.

Results: Between November 2016 and December 2017, 11 patients with non-arteritic CRAO were assessed, and nine patients were recruited for the study. All the nine patients completed the follow-up. No serious adverse events or side effects were observed. The final best corrected visual acuity (BCVA) was improved compared with that at baseline in all the patients. Seven out of nine (78%) patients showed BCVA equal to or better than 0.05. The average visual field area and scores were also improved.

Conclusions: We confirmed the efficacy and safety of KUS121 in preserving the visual function of patients with CRAO. We are currently preparing for the next phase of clinical trials. Additionally, KUS121 is being developed as a therapeutic agent for other retinal diseases such as age-related macular degeneration.

CONTROL ID: 3711385

SUBMITTER (NAME ONLY): Adam Dubis

TITLE: Structure/Function Correlations in USH2A- associated Usher Syndrome

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Dubis, A.M. Hagag, M. Arikan, Y. Mau, N. Behzad, M. Moosajee, NIHR Biomedical Resource Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|A.M. Dubis, Global Business School for Health, University College London, London, London, UNITED KINGDOM|Y. Mau, Medical School, Queens University Belfast, UNITED KINGDOM|W. Lilaonitkul, Institute of Health Informatics, University College London, London, London, UNITED KINGDOM|W. Lilaonitkul, HDRUK, UNITED KINGDOM|M. Moosajee, Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Usher Syndrome is a leading cause of deaf-blindness, with variants in USH2A being the most prevalent cause. With growing interest in this condition, and potential therapeutics going to trial, further understanding of how structure and function change through the disease course is required. OCT and microperimetry may provide more sensitive markers of progression and need to be further investigated.

Methods: Patients with molecularly confirmed biallelic USH2A variants were recruited at Moorfields Eye Hospital. Subjects were monitored at two time points (12.8 +/- 2 months apart). Heidelberg Spectralis OCT images were acquired. Novel OCT segmentation was developed using UNET with EfficientNet Backbone, based on 2770 double graded images. Micropermetry was performed using MAIA Expert Exam. Custom analysis was developed in Matlab, to evaluate visual sensitivity volume across the macular and by ring (fixation, 2°, 6°, 10°). Comparison between visits used Wilcox Signed Rank test, between devices used Mann-Whitney.

Results: Thirty-five patients were recruited (44 eyes of 23 patients included). Macular sensitivity loss was not significant between visits (p=0.08). Analysis of the individual ring sensitivity was also not significant between exams. Analysis of EZ area showed 5.02% (range:0.02-0.12%) loss across timepoints. EZ thickness compared to MP volume were significantly correlated (fixation- p=0.03; 2°- p=0.04, 6°- p=0.01, 10°- p=0.003). ONL thickness compared to MP volume were significantly correlated 2°- p=0.03, 6°- p=0.01, 10°- p=0.01).

Conclusions: Novel OCT analysis showed better sensitivity for progression than manual measures, or functional analysis. Therefore, more robust analysis should be used, included deep learning trained segmentation models, for future analysis. There was a significant relationship in ONL and EZ thickness with MP sensitivities when compared over specific regions.

CONTROL ID: 3711387

SUBMITTER (NAME ONLY): Hon Shing Ong

TITLE: The immunomodulatory effects of topical extracellular vesicles derived from mesenchymal stem cells (MSC) in a corneal scarring model.

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Corneal scarring is a major cause of blindness worldwide and an important indication for corneal transplantation. With the limitations of corneal grafting, there is a need to explore alternative therapies for corneal scarring. We have previously reported on the optimal dosing frequency and safety of topical delivery of MSC-derived extracellular vesicles (EV) in normal rat corneas. In this study, we investigated the potential therapeutic effects of MSC-EV in a rat corneal scarring model.

Methods: Conditioned media of human embryonic stem cells (ESC)-derived MSC was concentrated and fractionated to obtain enriched EV fractions (80-150nm). Irregular phototherapeutic keratectomy (irr-PTK) was used to induce corneal scarring in Sprague Dawley rats. Topical EV or saline were applied to the injured rat corneas for 6 days or until the epithelium was healed, whichever was earlier. Corneal clarity was assessed using slit-lamp imaging and in-vivo confocal microscopy (IVCM). Stromal reflectivity was quantitatively analyzed. Immunohistochemistry of the excised corneas was performed.

Results: Following irr-PTK, corneas that received topical EV treatment were relatively clearer (with a significantly lower mean corneal haze score) throughout the follow-up period compared to the corneas in the control group with saline treatment ($p=0.002$). Stromal reflectivity imaged using IVCM also showed a significant reduction of haze intensity ($p=0.004$). Corneal vascularisation, quantified by the area of vascularized quadrant, vessel length and diameter, was also significantly lower in EV-treated corneas. Lower expression of CD31 (vascular endothelial marker), LYVE1 (lymphatic marker), fibronectin and Col3a1 (fibrosis markers) were detected in EV treated corneas. EV-treated corneas also displayed a regenerative immune phenotype characterised by a higher infiltration of regenerative M2 over M1 macrophages.

Conclusions: Our findings demonstrated that ESC-derived MSC EV are potential regenerative therapies for corneal injuries, effected through anti-angiogenesis, anti-fibrosis, and immunomodulation.

CONTROL ID: 3711389

SUBMITTER (NAME ONLY): Oussama Habra

TITLE: High resolution optical coherence tomography in patients with age related macular degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Habra, V. Henchoz, C. Dysli, D. Jaggi, S. Wolf, M.S. Zinkernagel, Ophthalmology, Inselspital Universitatsspital Bern, Bern, Bern, SWITZERLAND|

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ABSTRACT BODY:

Purpose: The high-resolution optical coherence tomography (HighRes-OCT) is an improvement of the routinely used spectral-domain OCT (SD-OCT) with increased axial resolution in tissue from 7 to 3 µm and may provide new informations about ultrastructural changes in age related macular degeneration (AMD), especially in iRORA and cRORA (incomplete, complete retinal pigment epithelial, outer retinal atrophy). The aim of this study is to show how increased axial resolution in a novel HighRes-OCT can distinguish structures not detected with conventional OCT in AMD

Methods: The prospective observational pilot study is performed on 50 patients at different AMD stages. An OCT of the macula is performed with the SD-OCT (SPECTRALIS ©, Heidelberg Engineering, Heidelberg, Germany) and the investigational HighRes-OCT (SPECTRALIS ©, Heidelberg Engineering, Heidelberg, Germany). The scan patterns used are 20° x 20° volume scan with 49 sections and 25 ART frames (512 A-scans per B-scan). Two different retina specialists then qualitatively compare the images. The presence of iRORA and cRORA was evaluated according to the consensus definition for atrophy associated with AMD on OCT. The main parameters assessed were the presence or absence of choroidal hypertransmission, zone of attenuation and/or disruption of the retinal pigment epithelium. Furthermore, the hyperreflective foci 94+and the thinning of the outer plexiform layer above atrophy were also investigated.

Results: Our results show that increased axial resolution in HighRes-OCT reveals several features such as better visualization of the Bruch’s membrane complex and the photoreceptor inner segments as well as a better delimitation of the inner plexiform layer than in a SD-OCT image. In geographic atrophy, the hyperreflective foci are clearer and there is a striking thinning of the outer plexiform layer above atrophy compared with conventional OCT in both forms of RORA.

Conclusions: Increased axial resolution OCT provides a higher resolution and yields more information about anatomical features in patients with both, iRORA and cRORA. This new technology can improve the diagnosis precision and will reserve us exciting data.

CONTROL ID: 3711391

SUBMITTER (NAME ONLY): Abraham Olvera-Barrios

TITLE: Time dependence and cumulative exposure of intravitreal anti-VEGF treatment for diabetic macular edema on subsequent development of proliferative diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Olvera-Barrios, T. Heeren, A. Rozenberg, R. Schwartz, A. Warwick, A. Tufail, C.A. Egan, Medical Retina, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A. Olvera-Barrios, T. Heeren, A. Tufail, C.A. Egan, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|A.H. Alsaedi, Imam Muhammad Ibn Saud Islamic University, Riyadh, SAUDI ARABIA|D. Thomas, W. Lilaonitkul, P. Taylor, University College London Institute of Health Informatics, London, UNITED KINGDOM|W. Lilaonitkul, Health Data Research UK, London, UNITED KINGDOM|A. Rudnicka, St George's University of London Population Health Research Institute, London, London, UNITED KINGDOM|A. Warwick, University College London Institute of Cardiovascular Science, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The effect of the timing and cumulative exposure of repeated anti-vascular endothelial growth factor (VEGF) injections for treatment of diabetic macular edema (DME) on the subsequent risk of proliferative diabetic retinopathy (PDR) is unclear. We report associations for PDR development on patients receiving anti-VEGF treatment for DME at point of care and evaluated the application of the novel weighted cumulative exposure (WCE) method to such data.

Methods: Retrospective multicenter electronic medical records-based study from 27 centers across the United Kingdom. We implemented (1) a multivariable Cox model ignoring anti-VEGF exposures as baseline (M_{Cox}), and modelled the complex time-varying nature of repeated anti-VEGF injections using 3 more models as: (2) a time-dependent unweighted cumulative sum of exposures (M_{tdcCox}), (3) as the average anti-VEGF injections over the most recent 6 months (M_{6moCox}), and (4) as a the weighted cumulative sum of past exposures (M_{WCE}). Primary outcome measure was PDR development. All models allowed for baseline diabetic retinopathy (DR) grade, age, sex, ethnicity, type of diabetes and index of multiple deprivation. Model goodness of fit was quantified by Akaike information criterion (AIC).

Results: We included 4439 patients. The unweighted time-dependent multivariable Cox regression (M_{tdcCox} AIC=3454; M_{6moCox} AIC=3452) provided a better model fit than the baseline model (M_{Cox} AIC=3488), and the M_{WCE} had the best fit overall (AIC=3364). Table 1 shows hazard ratios for all models. Severe NPDR showed a more than 5-fold increase in hazards of PDR when compared to mild NPDR ($p<0.0001$) in all models. Every 5-year rise in age was associated with decreased hazards of PDR in all models ($p<0.001$). In M_{WCE}, patients with type 1 diabetes had a 2.02-fold increase in PDR hazards ($p=0.0001$), when compared with type 2 diabetes. The least deprived patients showed a 38 to 42% reduction in PDR hazards when compared to the most deprived patients in all models ($p<0.048$).

Conclusions: Baseline DR features remain the most important predictor for clinical outcomes but, our model highlighted the importance of adjusting for anti-VEGF injection number and timing that is achievable in this novel application of the WCE model to ophthalmology data. WCE models can enhance our interpretation of complex time series data.

CONTROL ID: 3711392

SUBMITTER (NAME ONLY): Marta Zola

TITLE: Late hyperfluorescent plaque in type 1 choroidal neovascularization in age-related macular degeneration and central serous chorioretinopathy

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Zola, E. Bousquet, F.F. Behar-Cohen, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|M. Zola, E. Bousquet, C. Favard, F.F. Behar-Cohen, Ophtalmopole Hopital Cochin, Assistance Publique - Hopitaux de Paris, Paris, Île-de-France, FRANCE|C. Favard, Centre Ophtalmologique de l'Odéon, Paris, FRANCE|A. Gigon, I. Mantel, Department of Ophthalmology, University of Lausanne, Fondation Asile des Aveugles, Lausanne, Vaud, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Type 1 CNV is associated with a late hyperfluorescent plaque (LPHP) that does not increase with time, seen on ICGA (indocyanine angiography). Missing in literature to date, this study evaluates the frequency of LPHP in type 1 CNV in CSCR and AMD and its prognostic value in visual acuity and response to anti-VEGF.

Methods: We retrospectively reviewed the images and medical records of patients from Jules Gonin Eye Hospital in Lausanne, Ophtalmopole Hopital Cochin and Centre Ophtalmologique de l'Odéon in Paris between 2012 and 2021. Inclusion criteria were: type 1 CNV secondary to CSCR and AMD, late ICG cliché (>20mins) and visualisation of CNV on OCTA. Quantitative and qualitative parameters on OCT and best corrected visual acuity were recorded at baseline and after 3 monthly VEGF injections.

Results: 83 eyes of 83 patients were included in the study 35 with CSCR and 48 with AMD. Compared to the AMD group, patients in the CSCR group were younger (61.3 ± 10.4 vs. 80.2 ± 6.8 years, p<0,001), predominantly male (68,6% vs 35,4%; p=0,003) and with a thicker choroid (379 ± 93,3 4 vs 204,2 ± 93,2µm; p<0,001). Type 1 CNV in CSCR showed significantly less LPHP (31,4%) compared to eyes with AMD (77,1%; p<0,001). Patients with LPHP at baseline (n=48) were older (76,1 ± 10,8 years vs. 67 ± 13,2, p=0,002), had a worse baseline BCVA (0,37 ± 0,22 vs 0,27 ± 0,28 LogMAR, p=0,03), compared to eyes without LPHP (n=35). SFCT was higher in the CSCR subgroup (n=35) for eyes with LPHP (n=11) compared to eyes without LPHP (n=24) (434 ± 92,2 vs 346,1 ± 86,4µm respectively; p=0,006). BCVA at baseline did not differ significantly between CNV in CSCR or AMD (0.29 ± 0.28 vs. 0.36 ± 0.23 Logmar, p=0,14). Eyes without LPHP had a significant better BCVA than eyes with LPHP (0,37 ± 0,22 vs 0,27 ± 0,28 LogMAR, p=0,03).

Conclusions: LPHP was significantly less present in chronic CSCR complicated by CNV than in AMD. BCVA was higher in eyes without LPHP at baseline. This shows that leakage of macromolecules from CNV and its accumulation in the RPE imaged by the LPHP differs in eyes with CSCR and AMD. LPHP associated with worse BCVA at baseline in both diseases might suggest a suffering of the RPE. LPHP should not only be considered as a hallmark for choroidal neovascularization but also a sign of RPE dysfunction. Its long-term prognostic value still remains to be explored in larger cohorts.

CONTROL ID: 3711393

SUBMITTER (NAME ONLY): Tina Johansen

TITLE: Manual control and common eye problems in 6- to 16-year-old children

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.R. Johansen, H. Pedersen, R.C. Baraas, E. Svarverud, G. Horgen Vikesdal, H. Schiøtz Thorud, J. Stuart, L.A. Hagen, R. Mork, C. Onshuus Bjørset, T. Langaas, National Center for Optics, Vision and Eye Care, Universitetet i Sorost-Norge, Kongsberg, Buskerud, NORWAY|M. Mon-Williams, R.O. Coats, School of Psychology, University of Leeds Faculty of Medicine and Health, Leeds, West Yorkshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Earlier studies have suggested that poor manual control could detrimentally affect learning in children. The purpose in this study was to investigate the relationship between manual control and common eye problems in children.

Methods: This cross-sectional study included 173 (87 males) children and adolescents aged 6 to 16 years (mean ± SD 10.5 ± 3.4) who participated in a school vision program offered to children in 2nd, 5th and 10th grade in Kongsberg municipality, Norway. Refractive error, visual acuity, binocular vision, ocular biometry measurements and a medical history were obtained for all children. Children who failed (according to predetermined criteria) one or more of these measures were considered to have an uncorrected eye or vision problem and were referred to the university eye clinic. All children completed the Leeds Clinical Kinematic Assessment Tool (CKAT, Flatters et al. 2014;9(2):e88692) — a manual control task where the child made a series of aiming movements and traced two abstract shapes with a handheld stylus on a digital tablet. Welch t-test was used for statistical analysis.

Results: Forty-three (25%) children were classified to have a common uncorrected eye or vision problem. This group had significantly poorer performance in aiming (movement time mean ± SD 1.44 ± 0.26 seconds) compared to those with normal eye and vision status (1.33 ± 0.25 seconds, p=0.018). There was no group difference for tracing (penalised Path Accuracy (pPA) Shape A: 1.37 ± 0.49 vs. 1.51 ± 0.4, p=0.10 and Shape B: 1.32 ± 0.53 vs. 1.39 ± 0.42, p=0.48).

Conclusions: The results suggest that common uncorrected eye and vision problems could affect manual control in children. Because learning benefits from good manual control, uncorrected eye and vision problems may pose an implicit disadvantage for learning.

CONTROL ID: 3711394

SUBMITTER (NAME ONLY): Moussa Zouache

TITLE: Computational Analysis of Diffusion-Limited Regions in the Choriocapillaris and their Effect on Passive Transfers to the Outer Retina.

SESSION TITLE: Myopia: Structural Changes from Retina to Sclera

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.A. Zouache, John A. Moran Eye Center, Department of Ophthalmology & Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|C.A. Klettner, Department of Mechanical Engineering, University College London, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Moussa Zouache: Commercial Relationship: Code N (No Commercial Relationship) | Christian Klettner: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The choriocapillaris fulfills many functions essential to retinal homeostasis. It supports the delivery of metabolism substrates to the photoreceptors, clears metabolic waste products from the subretinal space and may passively regulate the temperature of the back of the eye. Previous experimental and theoretical work have shown that the choriocapillaris comprises diffusion-limited regions, where the passive transport of material is dominantly diffusive. We sought to characterize the salient features of mass transport within these regions and to identify the structural and functional parameters determining their physical characteristics.

Methods: This analysis relied on three-dimensional mathematical models of the choriocapillaris informed by the angioarchitecture of the human choroid as observed through whole mounts stained with Ulex Europaeus Agglutinin I. Blood was modelled as a Newtonian fluid, and analytical and numerical solutions for the blood flow were obtained by solving the Navier-Stokes equation. Mass was modeled as a passive scalar, and its concentration field was determined by solving the advection-diffusion equation. Transfers to the retina were simulated by imposing a Dirichlet boundary condition on the upper surface of the choriocapillaris and studying spatial variations of the Nusselt number.

Results: Diffusion-limited regions represent areas of reduced exchange with the outer retina. Their number is equal to the number of arteries and vein connected to the choriocapillaris, which makes them ubiquitous. The width of these regions is solute-specific and increases with molecular diffusivity. It is mainly determined by the relative arrangement of arteriolar and venular insertions into the choriocapillaris, arterial flow rate and the vascular volume fraction of this capillary bed.

Conclusions: Exchange between the choriocapillaris and outer retina is markedly reduced over diffusion-limited regions. The location and surface area of these regions is determined by both structural and functional parameters, some of them quantifiable using imaging techniques. Their existence and characteristics may partly explain the spatial selectivity of several pathologies associated with degenerative diseases of the retina.

CONTROL ID: 3711395

SUBMITTER (NAME ONLY): Charles Amankwa

TITLE: Hybrid molecule SA-2 improve both mitochondrial respiration and glycolysis in primary human trabecular meshwork cells

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.E. Amankwa, B. Debnath, D.L. Stankowska, S. Acharya, Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|S.R. Gondi, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress (OS) caused by hypoxia/hyperoxia environment results in progressive loss of trabecular meshwork (TM) cells in primary open angle glaucoma (POAG). Our previous report demonstrated; a hybrid nitric oxide (NO) donor-antioxidant molecule SA-2 protect primary human (h) TM cells against t-butyl hydrogen peroxide (TBHP) induced cell death and increased superoxide dismutase enzyme level. Here we investigated the effect of SA-2 on mitochondrial energy metabolism by measuring the respiration status, glycolysis rate and energy production.

Methods: Primary hTM cells obtained from human donor eyes (IRB approved at UNTHSC) were seeded in 24-well culture plates (Seahorse XFe 24 Cell Mito Stress kit, Agilent), and starved for 24h before treatment with SA-2 (1 μM,10μM,100μM, and 1mM). In a separate experiment, the cells were pretreated with TBHP (150μM) for 30 minutes, followed by the addition of SA-2 (10μM,100μM). After 24h, the mitochondrial complex inhibitors and uncoupling reagents (oligomycin, FCCP, rotenone/antimycin A) were added. The plate was analyzed for changes in oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) using the Seahorse XFe24 analyzer following the manufacturer instructions.

Results: The mean OCR was significantly decreased (>70%) followed by increase in the mean ECAR (~3-fold) after treatment with TBHP compared to oligo/FCCP/rot treated cells, hereafter called as negative control. Treatment with SA-2 at 1 μM,10μM,100μM and 1mM concentrations increased both oligomycin/FCCP induced decrease in ATP production and maximal mitochondrial respiration followed by an increase in the mean ECAR compared to negative control. The mean OCR was higher in SA-2 (100μM) +TBHP treated cells followed by an increase in ECAR in SA-2 (10μM or 100μM) +TBHP treated cells than TBHP and negative control treated cells. N =2-3.

Conclusions: Mitochondrial respiration was impaired after TBHP treatment to hTM cells following cell death. While most of the mitochondrial targeting anti-oxidant compounds increase OCR but not ECAR, we found the hybrid NO donor-anti-oxidant compound SA-2 increases ATP production, maximal mitochondrial respiration and increases glycolytic energy production in hTM cells. This finding provides a novel direction for further investigation into the effect of SA-2 and mitochondrial bioenergetics during OS-induced cell death.

CONTROL ID: 3711396

SUBMITTER (NAME ONLY): Sujin Hoshi

TITLE: Adaptive optics scanning laser ophthalmoscopy of photoreceptor structure perturbation by acquired vitelliform lesions

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hoshi, X. Wang, S. Kadomoto, R. Liu, M.S. Ip, S.R. Sadda, Y. Zhang, Doheny Eye Institute, Los Angeles, California, UNITED STATES|S. Hoshi, Department of Ophthalmology, Tsukuba Daigaku Igaku Iryokei, Tsukuba, Ibaraki, JAPAN|S. Kadomoto, Department of Ophthalmology and Visual Sccience, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, Kyoto, JAPAN|M.S. Ip, D. Sarraf, S.R. Sadda, Y. Zhang, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|D. Sarraf, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: An acquired vitelliform lesion (AVL) is a retinal abnormality characterized by the accumulation of yellowish hyperfluorescent material in the subretinal space, but its impact on photoreceptor anatomy is incompletely understood. This study aimed to examine cone photoreceptor structure in eyes with AVL using multi-modal imaging including adaptive optics scanning laser ophthalmoscopy (AOSLO).

Methods: This was a retrospective study of subjects with AVL associated with age-related macular degeneration and adult-onset foveomacular vitelliform dystrophy. Subjects underwent color fundus photography (CFP), en-face infrared reflectance (IR), blue-light reflectance (BR) and autofluorescence (AF) imaging, and spectral-domain volume optical coherence tomography (SD-OCT) of the central macular. AVL was diagnosed based on the characteristic hyper-reflective subretinal material, anterior to the retinal pigment epithelium, with en face and cross-sectional OCT. Photoreceptor structure near the AVL was examined by AOSLO.

Results: AVL was found in a total of 28 eyes of 27 subjects, aged 77.7 ± 6.5 years. All subjects were white non-Hispanic and 14 were female, with mean Snellen visual acuity of 0.25 ± 0.37 (LogMAR, Snellen equivalent:). AOSLO revealed the cone mosaic disruption with apparently decreased cell density and lost or altered (hyper or hypo) reflectivity in the AVL affected areas. (Figure)

Conclusions: AOSLO imaging of cone photoreceptors near AVLs indicate that photoreceptor degeneration may be associated with AVL development. Because AVL represents a high-risk marker for atrophic or neovascular events that lead to significant vision loss, in vivo characterization of photoreceptor status in areas affected by AVL is important for a better understanding of disease pathophysiology and for the development of interventional trials.

CONTROL ID: 3711398

SUBMITTER (NAME ONLY): MANSI GUPTA

TITLE: Presence of diabetic retinopathy as a prognostic factor for diabetic kidney disease progression: A systematic review and meta-analysis.

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. GUPTA, G. TUMKUR CHANDRA, Center for Application Research in India, Carl Zeiss India Pvt Ltd, Bangalore, Karnataka, INDIA|I.R. Rao, S.P. Nagaraju, Department of Nephrology, Kasturba Medical College Manipal, Manipal, Karnataka, INDIA|S.V. Bhandary, Department of Ophthalmology, Kasturba Medical College Manipal, Manipal, Karnataka, INDIA|

Commercial Relationships Disclosure: MANSI GUPTA: Commercial Relationship(s);Code E (Employment):Carl Zeiss India Pvt. Ltd. | GANESH BABU TUMKUR CHANDRA: Commercial Relationship(s);Code E (Employment):Carl Zeiss India Pvt. Ltd. | Indu Rao: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss India Pvt. Ltd. | Shankar Nagaraju: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss India Pvt. Ltd. | Sulatha Bhandary: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss India Pvt. Ltd.

ABSTRACT BODY:

Purpose: This meta-analysis can substantiate the relationship between microvascular changes in retina and severity of diabetic retinopathy (DR) to the risk of progression to end stage renal disease (ESRD) in diabetic kidney disease (DKD) patients.

Methods: Systematic search on PubMed & Embase for articles studying association between DR & chronic kidney disease progression yielded a total of 18,725 articles. Joanna Briggs Institute critical appraisal checklist for cohort studies was used to assess the quality of the selected articles. Higgins & Thompson's I^2 statistic was used to see the degree of heterogeneity. Based on degree of heterogeneity, fixed or random effects model was used to estimate pooled effect using inverse variance method. Results were expressed as hazard ratios and odds ratios with 95% CIs.

Results: After scrutinizing 18017 articles, data from 10 relevant studies (7 prospective and 3 retrospective) were extracted and total of 14,355 patients are included. DR was significantly associated with ESRD with pooled HR of 2.42 (95% CI: 1.70-3.45) [Fig1] and pooled OR of 2.61 (95% CI: 1.76-3.87) [Fig2]. Sensitivity analysis done with biopsy proven DKD and prospective studies yielded similar results with pooled HR 2.76 (1.26-6.04) and OR of 1.79 (1.04-3.09). There was significant association of severity of DR and risk of progression to ESRD with pooled OR for non-proliferative DR: 2.13 (1.82–2.50) and for proliferative DR OR of 3.56 (2.93–4.33).

Conclusions: While association of DR and presence of DKD is already clearly established, this novel meta-analysis substantiates that presence of DR is associated with risk of progression to ESRD. The substantial burden of kidney disease fosters interest in new ways of screening for early disease diagnosis especially via non-invasive imaging. Such an association in clinical workflows can be utilized by an ophthalmologist for early recommendation to patients for possible DKD diagnosis. Since fundoscopy is less invasive and more convenient for the patients than a kidney biopsy, the stage of DR could be useful for prognosticating the clinical course of diabetic nephropathy. Pooled HR of 2.42 & pooled OR of 2.61 with p-value < 0.0001 indicates that presence of DR is predictive of progression of DKD patients to ESRD.

CONTROL ID: 3711401

SUBMITTER (NAME ONLY): Gholamreza Naghibi

TITLE: Piezo2-positive mechanosensory nerve terminals are present in the chamber angle of the human eye

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Naghibi, E. Tamm, University of Regensburg, Institute of Anatomy, Regensburg, Bavaria, GERMANY|

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ABSTRACT BODY:

Purpose: Because of the lack of a specific molecular marker, the question has not been answered conclusively if there are specific proprioceptive sensory nerve endings in the human chamber angle that serve as mechanoreceptors. Piezo2 has been identified as a mechanosensitive ion channel that plays a role in rapidly adapting mechanically activated currents in somatosensory neurons. To clearly identify proprioceptive nerve endings in the human chamber angle, we investigated anterior segments of human eyes for the presence of Piezo2-containing nerve endings.

Methods: Human autopsy eyes (age >80 years) without any obvious ocular pathology were investigated. The anterior eye segment was dissected in quadrants. From each quadrant, wedge-shaped specimens with 1.6 mm width on average, and containing trabecular meshwork and ciliary muscle were cut. The specimens were fixed in 2 % paraformaldehyde for immunohistochemistry or Karnovsky's solution for transmission electron microscopy (TEM). Serial tangential 12-20 µm cryosections were cut and immunostained with antibodies against Piezo2. To distinguish axons from terminal nerve endings, double immunohistochemistry was performed combining Piezo2 antibodies with antibodies against synaptophysin that specifically stains synaptic vesicles in nerve terminals.

Results: Piezo2 immunoreactive axons were identified in iris and ciliary muscle. Piezo2/synaptophysin immunoreactivity was detected almost exclusively in club- or bulb-shaped nerve terminals in the scleral spur (75 %) or, more inwardly, at the apex of the longitudinal portion of the ciliary muscle. The nerve endings were considerably larger (17.7 µm on average) than sympathetic or parasympathetic terminals and resembled Ruffini-like sensory nerve endings as present e.g., in the carotid sinus. TEM confirmed that the nerve endings were identical with putative mechanosensory nerve endings previously identified based on ultrastructural criteria (Tamm et al., IOVS 1994).

Conclusions: We conclusively confirm the presence of mechanosensory nerve terminals that measure stress or strain of the scleral spur extracellular matrix. Such changes are likely induced by ciliary muscle contraction and/or changes in intraocular pressure.

CONTROL ID: 3711405

SUBMITTER (NAME ONLY): Nina Schneider

TITLE: RNA Editing of Israeli Founder Nonsense Mutations causing IRDs using Site-Directed Adenosine Deaminase Acting on RNA

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Schneider, J. Valensi, E. Banin, D. Sharon, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|R. Steinberg, A. Eylon, E. Levanon, S. Ben-Aroya, Bar Ilan University Mina and Everard Goodman Faculty of Life Sciences, Ramat Gan, ISRAEL|

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ABSTRACT BODY:

Purpose: Targeted RNA editing utilizing the ubiquitous human adenosine deaminase acting on RNA (ADAR) enzyme is a possible new genetic therapeutic approach for the treatment of inherited retinal diseases (IRDs). Utilizing guideRNA (gRNA) to recruit the endogenously expressed ADAR enzyme to a mutated RNA and facilitating the deaminization of a specific adenosine to inosine (read as a guanine by the ribosome), allows for the correction of mRNA transcripts in a transient and tunable manner. According to our recent analyses, 40% of single nucleotide variants (SNVs)-causing IRDs are candidates for ADAR-directed editing. Our aim is to design and test gRNAs that induce targeted ADAR editing for 3 common Israeli mutations causing IRDs: TRPM1- p.K294*, FAM161A- p.R523*, and KIZ- p.R76*.

Methods: After determining Israeli IRD candidate mutations, we used a yeast model to identify candidate gRNAs for these mutations by measuring yeast survival and percent editing in next generation sequencing (NGS). Effective gRNA sequences were then assessed for appropriate chemical modifications and produced as single-stranded RNAs. We developed a fluorescence-expressing plasmid reporter system for ADAR editing by inserting a gene cassette harboring a nonsense mutation in between mCherry and EGFP, and subsequently transfected these plasmids into HeLa cells to test the candidate gRNAs. Successful editing of target gene RNA fragments produced by the reporter plasmid is measured through fluorescent microscopy, Sanger sequencing, and NGS.

Results: Our yeast model identified three possible gRNAs, one for each candidate mutation previously mentioned. In this yeast model, the gRNAs targeting mutations in TRPM1, FAM161A, and KIZ showed 9%, 1%, and 0.2% editing respectively of a relevant nucleotide flanking each mutation. Using our reporter system in HeLa cells, we found that the gRNA complementary to the target TRPM1 mutation induced RNA editing levels in our system of up to 55% in Sanger sequencing, 40% in NGS, and the treated cells expressed both mCherry and EGFP. Experiments utilizing the FAM161A and KIZ appropriate gRNAs are in progress.

Conclusions: Targeted RNA editing utilizing the ADAR enzyme could be the next frontier of genetic therapy for IRDs due to its ability to edit SNVs in a tunable manner. Next steps include applying this genetic therapy to the appropriate knock-in mouse models and retinal organoids.

CONTROL ID: 3711406

SUBMITTER (NAME ONLY): Zhenghua Lin

TITLE: Two-years evolution of two-dimensional peripheral refraction in children

SESSION TITLE: Myopia and refractive error development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Lin, P. Artal, Laboratorio de óptica, Universidad de Murcia, Murcia, Murcia, SPAIN|Z. Lin, W. Lan, L. Wen, Z. Luo, Z. Yang, P. Artal, Aier School of Ophthalmology, Central South University, Changsha, Hunan, CHINA|W. Lan, L. Wen, Z. Luo, Z. Yang, Aier School of Optometry and Vision Science, Hubei University Of Science and Technology, Xianning, Hubei, CHINA|

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ABSTRACT BODY:

Purpose: A relative peripheral hyperopia has been suggested as a trigger on myopization in children. However, this is not fully validated yet, due to the lack of longitudinal results following the development process. To address the gap, our aim was to measure high-resolution two-dimensional peripheral refraction maps during two years of myopia progression in a group of children.

Methods: Peripheral refraction maps were measured using a peripheral sensor device (VPR, Voptica SL, Murcia, Spain) in a group of Chinese children (age 9-16 years) under cycloplegia. The maps cover a field from nasal 30° to temporal 30° of every 1°, and from superior 20° to inferior 16° of every 4°. After the study was closed, 214 children's data were available after one year and 152 children's data were available after two years. The participants were classified into three refraction progression groups based on their refractive change for hyperopic, emmetropic, and myopic subjects, separately. The difference of baseline peripheral defocus pattern was compared between each group by using ANOVA test. Central myopia progression as a function of peripheral defocus was investigated by simple linear regression.

Results: After the first year, a significantly different from the baseline refraction pattern was found between the various progression group in emmetropes. Baseline peripheral defocus in the central vertical field (horizontally, within ± 15°) at baseline was found to be significantly correlated with central myopic shift, especially in the superior retina [(S8°-S12°) X (N5°-T5°)]. Emmetropic subjects with more myopic defocus in the superior retina had more myopic progression (for refractive change, $r=0.32$, $p<0.001$; for axial change, $r=0.42$, $p<0.001$) (Figures a&b). In contrast, no obvious difference in baseline refraction pattern was found in the groups of hyperopes and myopes. The same tendency was confirmed after 2 years.

Conclusions: Children having the greater progression of myopia in central refraction over a two-year- period presented an initial relative myopic defocus in the superior retina. This type of relative refraction in the superior retina could be used as a predictor of central myopia. In relation, devices for keeping the superior retina emmetropic in children might be a myopia control strategy.

CONTROL ID: 3711408

SUBMITTER (NAME ONLY): Ya Xing Wang

TITLE: Diabetic Retinopathy and Chronic Kidney Disease: Associations and Comorbidities in a Large Diabetic Population: The Tongren Health Care Study

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Wang, C. Xue, L. Gao, D. Chen, Beijing Tongren Hospital, Beijing, Beijing, CHINA|C. Zhang, Peking University Third Hospital, Beijing, CHINA|J. Jonas, Ruprecht-Karls-Universitat Heidelberg Medizinische Fakultat Mannheim, Mannheim, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate associations between diabetic retinopathy (DR) and chronic kidney disease (CKD) in type 2 diabetes patients.

Methods: In the cross-sectional, community-based Tongren Health Care Study, individuals who attended regular health care check-up examinations from January 2014 to December 2019 were consecutively enrolled. Type 2 diabetes was diagnosed based on fasting plasma glucose concentration of ≥7.0 mmol/L or a medical history, after excluding patients with type 1 diabetes and gestational diabetes. DR was assessed using color fundus photograph. CKD was defined by a reduced estimated glomerular filtration rate (eGFR) of <60ml/min/1.73mm^2 and/or albuminuria.

Results: Out of 62,217 study participants, 5103 (8.2%) had diabetes. Within the diabetic group, the prevalences of DR, reduced eGFR, albuminuria and CKD was 12.8% (95% confidence interval:11.8,13.7), 4.6% (95%CI:4.2,5.1%), 10.1% (95%CI:9.3,10.9%) and 13.3% (95%CI:12.4,14.3%), respectively. DR was present in 21.0% of the individuals with CKD, and CKD was detectable in 20.9% of the DR patients. Reduced eGFR or albuminuria were concurrent with DR in 3.9% and 18.8% of the participants with DR, respectively. The presence of DR and DR severity were significantly associated with the combined occurrence of CKD and albuminuria (P<0.05), but not with reduced eGFR. Factors independently associated (multivariable analysis) with the presence of CKD instead of DR were older age (P<0.001, OR=1.05), a higher body mass index (P<0.001, OR=1.14), a higher serum concentration of triglycerides (P<0.001, OR=1.26), and a lower blood glucose (P<0.001, OR=0.93). Having both diabetes and arterial hypertension was a significant risk factor for the presence of a reduced eGFR as compared with DR (P=0.005, OR=4.47).

Conclusions: Around 1/5 of CKD patients had concurrent DR, and 1/5 of DR patients had concurrent CKD, in this type 2 diabetes population. Those with older age, higher body mass index, combining with hypertension and dyslipidemia had a higher chance of being affected by CKD than by DR, while those with a higher fasting glucose level had a higher chance of being affected by DR than by CKD.

CONTROL ID: 3711409

SUBMITTER (NAME ONLY): Stéphanie Cornelis

TITLE: Personalized recurrence risks in Stargardt disease based on ABCA4 variant severity

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Cornelis, E. Runhart, Z. Corradi, S. Roosing, L. Haer-Wigman, A.T. Vulto-van Silfhout, F.P. Cremers, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|S.S. Cornelis, E. Runhart, Z. Corradi, S. Roosing, F.P. Cremers, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|M. Bauwens, E. De Baere, Center for Medical Genetics Ghent and Department of Biomolecular Medicine, Universiteit Gent Faculteit Geneeskunde en Gezondheidswetenschappen, Gent, BELGIUM|C. Dhaenens, Neuroscience & Cognition, Universite de Lille, Lille, Hauts-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Stargardt disease (STGD1) is the most frequent inherited macular degeneration affecting ~1 in 10,000 persons. STGD1 is caused by bi-allelic pathogenic variants in ABCA4. Due to a complex mechanism in which the combined severity and penetrance of variants determines whether a person is affected by STGD1 and how severely a person is affected, the risks for individuals with STGD1 to pass on STGD1 to the offspring are currently unknown when no genetic data from the other genetic parent of the (future) offspring is available. Knowing the recurrence risks is crucial for individuals with STGD1 who have a desire to have children.

Methods: In this study, based on genetic data from 5,579 published bi-allelic STGD1 patients, we first categorized all known ABCA4 variants into mild, moderately severe or severe categories. This was based on i) existing data from functional and clinical studies, ii) null allele predictions, iii) comparison of variant frequency data in STGD1 individuals versus general population variant data from gnomAD, iv) observed versus expected homozygous variant occurrence in STGD1 individuals and v) the ratio in which variants occur with known mild and severe variants in trans in STGD1 individuals compared to the same ratio of known severe variants. Based on the sum allele frequencies of the variants in the resulting categories, Hardy-Weinberg equations and the STGD1 genotype-phenotype model described previously (Maugeri et al. 1999; PMID 10090887), we estimated the recurrence risks for STGD1 and early onset STGD1. These risk calculations are based on the severity of the variants of the individual with STGD1 when the genetic data of the unaffected partner is unknown.

Results: The recurrence risks for any form of STGD1 for offspring of STGD1 patients range from 0.68-3.1%. The recurrence risks for early onset STGD1 in the offspring range from 0.34-0.79%. The recurrence risks are the highest for STGD1 patients who carry two severe alleles (2.8-3.1%) and are the lowest for STGD1 patients who carry two moderately severe alleles (0.68-0.79%).

Conclusions: These personalized recurrence risk calculations will be of help in the genetic counseling of individuals with STGD1 who have a desire to have children.

CONTROL ID: 3711410

SUBMITTER (NAME ONLY): Vijay Singh

TITLE: Assessment of epithelial restoration using limbal allograft transplantation in rabbit model with persistent corneal epithelial defect

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.K. Singh, A. Kethiri, A. Venuganti, A. Sahoo, M. Salman, S. Basu, V. Singh, Prof Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|V.K. Singh, A. Kethiri, A. Venuganti, A. Sahoo, M. Salman, S. Basu, V. Singh, Centre for Ocular Regeneration (CORE), LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|K. Bokara, Medical Biotechnology Complex, Centre for Cellular and Molecular Biology CSIR, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Defects in corneal limbal epithelium can lead to persistent corneal epithelial defects (PECD), marked by chronic inflammation, neovascularization, scarring and conjunctivalization. A simple, reproducible and sustainable method for generation of animal models with PECD is necessary for assessing the new therapeutic modalities. The purpose of the study is to develop an animal model with PECD and to study epithelial regeneration potential of allogeneic simple limbal epithelial transplantation (allo-SLET) and conjunctival limbal allograft (CLAL).

Methods: Complete corneal and limbal epithelium of the New Zealand White Rabbit (n=10) was mechanically debrided using the Alger brush-II 1.0-mm round-ended burr after 360° Limbal peritomy. Rabbits were observed for corneal haziness, vascularization and epithelial defect using clinical photograph, slit lamp, fluorescein staining and anterior segment optical coherence tomography (AS-OCT) post debridement. At 4-8 week post debridement, allo-SLET without human amniotic membrane (n=5) and CLAL (n=5) was performed in the rabbit eyes with a donor graft obtained from the Dutch-Belted rabbit. The extent of epithelialization was assessed by change in the central corneal epithelial thickness (CCET) using AS-OCT.

Results: All eyes showed epithelial defect up to 4 weeks as evident by the fluorescein staining. In 70% (7/10) of the eyes superficial neovascularization was observed after 4 weeks of which 42% reached the central cornea. Epithelial defect was observed even after 5 weeks of debridement in 70% (7/10) of the eyes. Epithelial migration was observed from the transplanted grafts for up to 3 weeks in both the cases and graft were stable up to 3 months with no sign of epithelial rejection. Allo-SLET treated eye showed significant increase in CCET ($P = 0.0255$, n=5) as compared to CLAL ($P > 0.5$, n=5) at 3 month of transplantation.

Conclusions: Mechanical debridement using alger brush-II 1.0-mm round-ended burr is an effective method for the establishment of persistent corneal epithelial defect in New Zealand white rabbits. Limbal allograft transplantation lead to significant corneal epithelialization in PECD especially in allo-SLET.

CONTROL ID: 3711411

SUBMITTER (NAME ONLY): Francesco Pozzo Giuffrida

TITLE: Morphological outcomes in fellow eyes of patients with exudative AMD after 10 years of follow up: progression rates and OCT risk factors.

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Pozzo Giuffrida, L. de Sanctis, P. Milella, C. Mainetti, D. Galli, L. Dell'Arti, C. Mapelli, M. Nassisi, F. Viola, Ophthalmology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: To determine the 10-year morphological outcomes and progression to exudative AMD in the fellow eyes (FE) of patients with naïve exudative AMD.

Methods: Data from 52 patients with naïve exudative AMD in one eye and at least 10 years of follow-up were retrospectively reviewed. Baseline optical coherence tomography (OCT) features as presence and type of drusen and non-foveal atrophy, central retinal thickness, subfoveal choroidal thickness and presence of intraretinal hyperreflective foci (iHRF) were acquired in the FEs; macular neovascularization (MNV) type was also assessed in the exudative AMD eye. Choroidal vascularity index of the FE was calculated in a region of 1500 µm centered at the fovea. Time and rate of progression of the FEs into exudative AMD were examined by Kaplan-Meier analysis and Cox regression.

Results: Twenty-eight FEs (53.8%) developed exudative AMD within the 10-year follow-up. An earlier progression to exudative AMD was associated with the presence of iHRF (47.625 vs 108.647 months, p=0.014), Subretinal Drusenoid Deposits (SDD) and Cuticular drusen (43.0 and 47.6 vs 90.2 months respectively, p<0.001) at baseline. Cuticular drusen were furthermore associated with a higher risk of developing an exudative MNV (Hazard Ratio [HR] 9.137; 95% confidence interval [CI] 1.643 – 50.818, p=0.023). Type 3 MNVs in the exudative AMD eye significantly associated with early MNV development in the FE (40.51 months; 95% CI 10.921 – 70.222, p=0.041). No other significant associations emerged between baseline features in FE and progression to exudative AMD.

Conclusions: Type 3 MNV in the exudative AMD eye and presence of iHRF, SDD and Cuticular drusen in FEs of patients with exudative AMD may identify eyes at high risk of progression to MNV throughout a 10-year period. Further studies with larger sample sizes will be needed to confirm these findings.

CONTROL ID: 3711415
SUBMITTER (NAME ONLY): julien Adrian
TITLE: Visual field loss and fitness to drive: preliminary results
SESSION TITLE: Mobility, Reading and Driving with Vision Impairment
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J.A. Sahel, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|G. Saillant, FIA, Paris, FRANCE|J.A. Sahel, Institut de la vision, Paris, Île-de-France, FRANCE|P. Chaumet-Riffaud, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|J. Adrian, C. de Montleau, Streetlab, Paris, FRANCE|
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ABSTRACT BODY:

Purpose: Drivers with visual field loss (VFL) such as glaucoma have higher risk of motor vehicle accidents and poorer driving performance when compared to age-matched drivers with no visual field loss. To date, conventional visual field tests have strong limitations in predicting on-road driving performance of VFL drivers. We developed a new screening-test (Driving Visual Field Attentional Test) for drivers with peripheral VFL such as individuals with glaucoma.
The aim of this study was to assess whether or not the Driving Visual Field Attentional Test is able to predict the outcome of an on-road driving test in drivers with VFL.

Methods: Twelve drivers with binocular VFL, aged 65.2 ±9.7, and twenty-four control drivers (matched for age and sex) aged 61.3±11,5, all holders of a driving license and active drivers, were recruited. They were asked to fill in a questionnaire about medical history, driving habits and motor vehicle collisions. They subsequently underwent an ophthalmologic examination including a battery of perimetric tests: Goldmann II-4 and III-1 and Esterman. Finally, they completed the Driving Visual Field Attentional Test, a UFOV test, a MMSE, and performed a practical on-road test under the supervision of expert evaluators. Driving evaluators were not aware of drivers' visual status. The receiver operating characteristic (ROC) curve was used to investigate the ability of the different tests to discriminate between safe and unsafe drivers.

Results: Drivers with VFL detected fewer peripheral targets (p=.002) compared to the control drivers group. Four drivers with VFL failed the driving test. Three drivers with VFL and five controls were found to be "questionable". ROC analysis revealed that the Driving Visual Field Attentional Test was an excellent predictor of failing the road test with an area-under-the-curve (AUC) value of 0.86 (CI: 0.58-1.0, p=0.01). UFOV also reached acceptable predictive power (AUC= 0.72, CI: 0.49-0.95, p=0.06). A cut-off score set at 28 non-responses provided 75% sensitivity (i.e., 75% of people who failed the road test were correctly identified) with a 100% specificity.

Conclusions: Preliminary analyses indicate that Driving Visual Field Attentional Test is a reliable predictor of at-risk driving for patients with visual field loss. Further testing with more subjects will be done to confirm these preliminary results.

CONTROL ID: 3711416

SUBMITTER (NAME ONLY): Martin Sorkhabi

TITLE: Artificial Intelligence model for intraocular inflammation assessment

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Sorkhabi, I. Potapenko, M.C. Kyhn, C.A. Jørgensen, M. Alberti, J. Cabrerizo, Rigshospitalet Glostrup, Glostrup, DENMARK|

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ABSTRACT BODY:

Purpose: Intraocular inflammation in the anterior chamber can occur in ocular infectious, autoimmune conditions and following ocular surgery. In most cases, anterior segment inflammation is assessed through slit lamp examination of the aqueous humor (AH). This technique entails limitations in terms of interobserver agreement, accuracy and precision. The purpose of our study is to present an Artificial Intelligence based Anterior-Segment Optical Tomography (AI-OCT) model for intraocular inflammation assessment and validate it by flow cytometry (FC) analysis of the AH and slit lamp examination

Methods: 16 B-scan AS-OCT imaging (CASIA 2, Tomey Corporation, Nagoya, Japan) and slit lamp examination by Standardization of Uveitis Nomenclature (SUN) were performed immediately before an intraocular surgical procedure in 95 eyes of 70 patients. As the first step of the surgical procedure, >30 µl of AH were aspirated through a paracentesis using a 27G canula. Samples underwent FC analysis within 5 hours after extraction. A cocktail of CD markers (CD3, CD4, CD8, CD16, CD19, CD33, CD45), together with forward and side scatter characteristics, were used to determine the immunologic cellular profile in the AH samples. A gate was constructed to filter out pigmentary cells. OCT radial scans were analysed by the AI-OCT model in five configurations of 1, 2, 4, 8 and 16 radial images. Pearson's R and Spearman's ρ was subsequently calculated to measure FC acquisition correlation with the AI-OCT model and SUN score, respectively

Results: Spearman's ρ rank correlation ($p = 0.0379$, $\rho = 0.2523$) between FC acquisition of AH and the inflammatory score of SUN classification was measured. Pearson's r correlation was measured for each constellation revealing single image scans ($p < 0.001$, $r = 0.7103$, $\sigma = 0.04179$) as the most optimal. Spearman's ρ rank correlation was calculated between inflammatory score of SUN classification and all five AI-OCT system collection-of-image configurations. Sixteen slice configuration achieved the highest Spearman's ρ rank correlation ($p = 0.107$, $\rho = 0.3078$, $\sigma = 0.03639$) of all five collection-of-image configurations

Conclusions: AI-OCT based particle detection shows correlation with FC analysis of AH. These findings suggest that AI-OCT models could represent a quantifiable and objective alternative to slit lamp based examination in patients with intraocular inflammation

CONTROL ID: 3711417

SUBMITTER (NAME ONLY): Jackie Tan

TITLE: Chitosan corneal adhesive: determining the application parameters for optimal adhesion

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tan, L.J. Foster, S.L. Watson, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|L.J. Foster, Chemistry, The University of Alabama in Huntsville, Huntsville, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Jackie Tan: Commercial Relationship: Code N (No Commercial Relationship) | Leslie Foster: Commercial Relationship: Code N (No Commercial Relationship) | Stephanie Watson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine the laser technique and bovine tissue status for optimal adhesion of a novel laser-activated thin-film chitosan-based corneal adhesive.

Methods: Central penetrating corneal linear incisions of 2 mm or 4 mm were created in an ex vivo bovine eye model. Disc-shaped adhesives with an area of 50.2 mm^2 were used and infrared laser of 810 nm, 125 mW, and 1 mm spot diameter was delivered using a manual fiber optic probe to the adhesive. There were 4 test groups; group 1, incisions were closed using either a grid-like (n=20) or concentric (n=20) lasering technique. Group 2, incisions were closed with epithelium-on (n=20) or epithelium-off (n=20). Group 3, using 4 mm incisions, ocular surface temperature was varied to 5.7 °C (n=10), 21.9 °C (n=10) or 33.2 °C (n=10). Group 4, postmortem duration of the bovine tissue was varied to less than 6 hours (n=20) or between 24 to 30 hours (n=20) to close both 2 mm and 4 mm incisions. A custom burst pressure testing chamber was used to assess adhesion strength which was compared using the highest tolerable fluid pressure to cause a wound leak. Data were analyzed using unpaired t-test or one-way ANOVA with statistical significance at $p<0.05$.

Results: The burst pressure of 4 mm incisions was higher when closed using a concentric (205.1 (±16.7) mmHg) technique than the grid-like (86.3 (±14.0) mmHg) lasering technique, $p<0.05$. The burst pressure was higher in 2 mm and 4 mm incisions with the epithelium-on group (224.3 (±20.7) and 205.1 (±65.4) mmHg, respectively) than epithelium-off group (51.7 (±6.5) and 9.8 (±1.5) mmHg, respectively), both $p<0.05$. Burst pressure did not demonstrate any significant difference in groups 3 and 4.

Conclusions: Strongest adhesion was achieved using a concentric lasering technique and with an intact corneal epithelium. Variation of ocular surface temperature and postmortem duration up to 30 hours did not affect adhesion strength.

CONTROL ID: 3711418

SUBMITTER (NAME ONLY): Helen Kuht

TITLE: The Genotypic and Phenotypic Spectrum of Foveal Hypoplasia: A Multi-centre Study on behalf of the Foveal Development Investigators Group (FDIG)

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Foveal hypoplasia (FH) is characterised by the continuation of inner retinal layers posterior to the foveola. Varying degrees of FH represent different stages of arrested foveal development. The Leicester Grading System for FH divides typical FH into four grades and an additional grade for atypical FH. The grading system has been applied to various disorders including albinism, idiopathic infantile nystagmus (with or without FRMD7 variants), and PAX6, SLC38A8 and AHR variants. The grading system is used as a diagnostic and prognostic tool. To date, it is unclear whether variants of certain genes are associated with worse foveal morphology and prognosis. Thus, we aimed to perform a comparative multi-centre study to characterise the genotypic and phenotypic spectrum of FH in the aforementioned aetiologies.

Methods: Patients with known genetic associations with FH and nystagmus (n=575) were identified from 10 centres from 8 countries (75.6%), as part of FDIG, or extracted from publicly available datasets from previously reported literature (24.4%). Genetic diagnosis was achieved using targeted panel-based sequencing or exome sequencing. Due to the rarity of AHR variants, we only included cases reported in the literature (n=2). Optical coherence tomography of the fovea was obtained in all subjects.

Results: The most common genetic aetiology for typical FH was albinism (66.1%), followed by PAX6 (22.8%) and SLC38A8 variants (7.1%). FRMD7 (3.7%) and AHR variants (0.4%) were rare causes of FH. All grades of FH were seen in albinism and PAX6 variants. All SLC38A8 cases demonstrated grade 3 or 4 FH. In AHR variants, only grade 3 FH has been reported. In cases of FH and FRMD7 variants only grade 1 FH was observed.

Conclusions: We characterised the phenotypic and genotypic spectrum of FH. Our data suggests that arrested retinal development occurs earlier in SLC38A8 and AHR variants and much later in FRMD7 variants. The defined time-period of foveal developmental arrest for albinism and PAX6 variants appears to demonstrate more variability. Our findings provide mechanistic insight into disorders associated with FH and have significant prognostic and diagnostic value.

CONTROL ID: 3711420

SUBMITTER (NAME ONLY): Brendan Portengen

TITLE: Maintaining fixation by children in a virtual reality version of pupil perimetry

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The assessment of visual field sensitivities in young children continues to be a challenge. Children often do not sit still, fail to fixate stimuli for longer durations, and have limited verbal capacity to report visibility. We investigated the use of a head-mounted VR display, gaze-contingent flicker pupil perimetry (gcFPP), and three fixation stimulus conditions to determine best practices for optimal fixation and pupil response quality.

Methods: A total of twenty healthy children aged 3-11 years old (mean age and SD 7.2 ± 2.4, 14 male) passively fixated a dot, counted the repeated appearance of an animated character, and watched an animated movie in separate trials of 80s each. We presented large flickering patches at different eccentricities and angles in the periphery to evoke pupillary oscillations (20 locations, 4s per location).

Results: The results showed that gaze precision and accuracy did not differ significantly across the fixation conditions but pupil amplitudes were strongest for the fixation dot ($p < .01$) and count task ($p < .05$) when compared to the animated movie condition. A query revealed that 18 out of 20 children favored the counting task condition.

Conclusions: We recommend the use of the counting task as fixation condition for pupil perimetry because children enjoyed it the most and it achieved strongest pupil responses. The VR set-up appears to be an ideal apparatus for children to allow free range of movement, an engaging visual task, and reliable eye measurements.

CONTROL ID: 3711423

SUBMITTER (NAME ONLY): Ye Eun Han

TITLE: Choroidal Changes in Non-ocular Sarcoidosis

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Han, J. Lee, Ophthalmology, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To investigate choroidal features associated with non-ocular sarcoidosis using optical coherence tomography.

Methods: In this retrospective case-control study, twenty eyes with non-ocular sarcoidosis and 20 age and spherical equivalent-matched healthy controls were evaluated. The subfoveal thickness, area ratio, and choroidal vascularity index (CVI) of the choroid were analyzed. Factors correlated with the choroidal thickness were investigated.

Results: Sattler's layer was significantly thicker in eyes with non-ocular sarcoidosis than in healthy controls, while there were no differences in Haller's layer and total choroid between groups. The area ratio (Sattler's to Haller's layer) was also larger in eyes with non-ocular sarcoidosis than in control. There were no differences in terms of the CVIs of all sublayers between groups. Age was significantly associated with the thickness of Sattler's layer.

Conclusions: A disproportionate enlargement of subfoveal Sattler's layer without vascular or total choroidal thickness changes may be subclinical manifestations of non-ocular sarcoidosis.

CONTROL ID: 3711424

SUBMITTER (NAME ONLY): Zakariya Jarrar

TITLE: Machine learning identification of microbiota associated with age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Jarrar, A. Adebayo, O.A. Mahroo, P.G. Hysi, C.J. Hammond, King's College London, London, London, UNITED KINGDOM|O.A. Mahroo, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To use machine learning to identify gut microbiota associations with age-related macular degeneration.

Methods: Macular OCT scans (Optovue iVue 100, Freemont, CA) taken between 2014-20120 from participants of the TwinsUK cohort were graded for signs of age-related macular degeneration according to the E3 OCT grading system.

Stool samples from TwinsUK participants were collected and DNA extracted and sequenced on an Illumina MiSeq platform. 16S sequences were demultiplexed in QIIME. Amplicon sequence variants (ASVs) were generated using the DADA2 package in R. Chimeras were removed and taxonomy assigned using SILVA 1.3.2. Samples with a sequencing depth of less than 10,000 reads were excluded.

Two different random forest analyses were conducted to select the most important microbiome features that predicted AMD status. The first ordered the microbiome variables based on the Gini classification index and the second used a frequency-corrected ranking approach.

Results: A total of 404 stool samples from 321 AMD participants (mean age ±SD 67.6±7.8, 90% female) and 1,736 stool samples from 1,355 controls (mean age ±SD 61.3±7.6, 91% female) were included in the analysis. Our machine learning analyses identified three microbiota taxa that were likely significant predictors of AMD phenotypic status. Our results indicate that the phylum Firmicutes (RF permutational p-value=0.008) and additionally, two genera: Ruminococcus (RF permutational p-value=0.0005) and Prevotellaceae-NK3B31 are associated with AMD (RF permutational p-value=$1x10^{-05}$).

Conclusions: With the assistance of machine learning, this study suggests that an increased abundance of certain gut microbiome taxa may be associated with an increased probability of having AMD. Further validation is required from other cohorts and further studies are needed to explore any causal relationships between the gut microbiome and AMD.

CONTROL ID: 3711425

SUBMITTER (NAME ONLY): Peter Woodward-Court

TITLE: Generative Adversarial Networks for OCT Counterfactual Visual Explanations in Ophthalmic Imaging

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Woodward-Court, Institute of Health Informatics, University College London, London, London, UNITED KINGDOM|P.A. Keane, D. Alexander, Y. Zhou, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Machine Learning (ML) models have shown above-human performance in the classification of ophthalmic imaging. However, this is often only achieved in limited ways and in unrealistic environments. In addition, many methods use Artificial Neural Networks (ANNs), the workings of which are uninterpretable to human users. These 'black box' models can lead to unintended consequences, including misdiagnosis. As ML models find use in the clinical environment, these errors could be perpetuated at scale and jeopardise patient safety. There is an urgent need for interpretable models, since this will enable users to identify biases, train more accurate models and even find use in machine teaching. Using a new method, counterfactual visual explanations (CVEs), we explore a novel way to allow humans to understand model outputs. This allows clinicians to answer 'What if?' questions like 'How would this OCT showing AMD need to change in order for it to be classified as a healthy scan?'.

Methods: Generative Adversarial Networks (GANs) are a gold standard ML framework for producing synthetic images. We train a state-of-the-art model, StyleGAN, using 1,000 central B-scans from patients with no pathology, and with AMD. In addition, we use a cyclical GAN, cycleGAN, that takes in a healthy scan and outputs a new image with signs of AMD. In an exploratory qualitative investigation, we show our output images to several consultant ophthalmologists for review.

Results: After training, we are able to produce synthetic OCT B-scans at native resolution. We show for the first time that it is possible to create synthetic optical coherence tomography scans of sufficient quality that world leading retinal experts are unable to differentiate between real images and our synthetic ones. We also successfully demonstrate the first example of counterfactual image generation using GANs and provide a framework for further exploration of this method in the literature.

Conclusions: GANs can be used to generate realistic OCT B-scans and generate counterfactual examples. Along with improved interpretability, synthetic images can be produced at scale to help with augmenting datasets and in addition obviate many of the ethical hurdles that currently exist around distributing medical data.

CONTROL ID: 3711428
SUBMITTER (NAME ONLY): Enrique-Josua Fernandez
TITLE: Wide field 2-D rapid scanning peripheral refractor
SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E.J. Fernandez, S. Sager, Z. Lin, P.M. Prieto, P. Artal, Laboratorio de Óptica, Universidad de Murcia, Murcia, Murcia, SPAIN|S. Sager, J. Roca, Voptica SL, Murcia, Murcia, SPAIN|W. Ian, Z. Lin, J. Hao, Z. Yang, P. Artal, Aier School of Ophthalmology, Central South University, Changsha, Hunan, CHINA|W. Ian, J. Hao, Z. Yang, Aier School of Optometry and Vision Science, Hubei University of Science and Technology, Xianning, Hubei, CHINA|
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ABSTRACT BODY:

Purpose: To design, build and validate a new optical instrument to measure ocular refraction and aberrations rapidly in a two-dimensional (2D) wide field. Existing peripheral refractors are constrained to limited meridians, therefore requiring several visual fixations at different points to complete an actual 2D map, making them impractical for clinical use.

Methods: The instrument combined the scanning of 850-nm laser beam with a Hartmann-Shack (H-S) wavefront sensor. A multielement eyepiece was designed for wide field operation. A steering mirror scanned the beam generating a flying spot on the subject's retina. The light backscattered from the retina was de-scanned by the steering mirror and redirected to the H-S relay for optical measurements. The visual fixation stimulus was generated by rotating the steering mirror, forming a flickering disc of 0.5 deg diameter. The stimulus was intermittently presented for 150 ms every 300 ms. During the time off, the beam was sequentially scanned on the retina, and refraction/aberrations were estimated at 98 Hz. Trial lenses were measured at different eccentricities for prior calibration. Accordingly, residual field aberrations of the apparatus were computationally compensated. A group of 10 young normal subjects participated in the first series of measurements.

Results: The instrument estimated the magnitude and orientation of trial lenses within a precision of 5 %. The basic operation mode in real subjects obtained the refraction in 50x50 deg field (88 sampled points, 5 deg step), with a single fixation point, in 3 sec. With 2 fixation points at ±15 deg horizontal, refraction distribution in 80x50 deg field could be obtained. Other protocols included high density, 1 deg step, at any selected meridians. Retinal sampling can be customized and adapted to virtually any clinical need. 2D refraction and aberration maps were obtained in the group of subjects.

Conclusions: The new scanning peripheral refractor permitted the accurate, programmable, and rapid measurements of peripheral optical parameters of the eye. A single fixation point provided data in a field of 50x50 deg in 3 sec. The enhanced capabilities of this instrument, such as wide angle and speed would allow its use in the clinic for the characterization of peripheral optics as a clinical tool in myopia management.

CONTROL ID: 3711429

SUBMITTER (NAME ONLY): Camiel Boon

TITLE: Spontaneous resolution of subretinal fluid in chronic central serous chorioretinopathy: the Fuji sign

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Patients with chronic central serous chorioretinopathy (cCSC) may have spontaneous subretinal fluid (SRF) resolution, but little is known about clinical characteristics that can help to predict which patients will have such a spontaneous resolution. We performed a retrospective clinical study to learn about factors that may predict spontaneous SRF resolution in cCSC patients.

Methods: This retrospective cohort study included 38 treatment-naive cCSC patients in whom spontaneous SRF resolution on optical coherence tomography (OCT) occurred, and 38 gender- and age-matched cCSC patients from the multicenter randomized controlled trials PLACE and SPECTRA, who received treatment after baseline visit. In both groups, clinical characteristics and findings on multimodal imaging were assessed at first presentation. Most importantly, the OCT scan was analyzed for the presence of the Fuji sign, a novel morphological feature on OCT in which SRF has a triangular shape resembling the Japanese Mount Fuji. In addition, the number of focal leakage points on fluorescein angiography (FA) and presence of SRF on OCT in the fellow eye were assessed.

Results: The Fuji sign on OCT occurred significantly more often in the study group compared to the control group (16/38 (42.1%) vs 5/38 (13.2%), respectively; p=0.005). The number of focal leakage points on FA was 0.83 ± 0.72 in the study group and 1.71 ± 1.64 in the control group (p<0.001). SRF on OCT was also present in the fellow eye at baseline visit in 5/38 (13.2%) patients in the study group and in 9/38 (23.7%) patients in the control group.

Conclusions: The Fuji sign on OCT and number of focal leakage points on FA can help to identify which cCSC patients with foveal SRF have a higher chance of spontaneous SRF resolution without treatment.

CONTROL ID: 3711430

SUBMITTER (NAME ONLY): Aveen Kadhum

TITLE: Dose-response relationship and treatment efficiency for patching vs gaming therapy for amblyopia

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To compare the dose-response rate and treatment efficiency between occlusion therapy and dichoptic video gaming using VR goggles in children with amblyopia.

Methods: In this prospective Randomized Clinical Trial (NCT 03767985) newly diagnosed children with amblyopia were recruited. Visual Acuity (VA) was measured using the crowded tumbling E-chart. After informed consent they were randomized to patching therapy: 2 hrs/day; compliance was monitored electronically using the Occlusion Dose Monitor; or dichoptic video game therapy using VR goggles: 1 hr/wk under direct supervision. The dose-response rate and treatment efficiency were calculated for both groups using VA gains and objectively monitored treatment hours. Mann-Whitney U test was used to investigate differences in dose-response and treatment efficiency between the two treatment groups.

Results: Ninety-four children were recruited; 29 subjects refused and 2 were excluded. After refractive adaptation period, 23 subjects (24%) attained interocular VA <0.2 logMAR rendering them ineligible for the RCT; another 7 dropped out. Thirty-three children were included; median age was 5.4 (IQR 4.5-6.7) years. Mean compliance with occlusion therapy was 81±42%. Nine (56%) dropped out of the gaming group compared to 3 (18%) in the occlusion group. Reasons for drop-out in the gaming group were primarily due to young age (i.e. difficulties comprehending the game settings and the game itself) and logistic problems. After 24 weeks of treatment the median dose-response relationship for occlusion therapy was 71.78h/0.1 logMAR VA gain. For the gaming group this was 8.00h/0.1 logMAR VA gain. Median treatment efficiency was 0.08 (-0.19 – 0.68) VA gain/100 h in the occlusion group and 1.25 (0.42 – 2.08) VA gain/100 h in the gaming group ($p<0.001$).

Conclusions: Treatment efficiency and dose-response were significantly more favorable with gaming therapy compared to occlusion therapy after 24 weeks of treatment. However, more than half of the children from the gaming group failed to complete the treatment. Dichoptic video gaming using VR goggles seems to be most applicable in children older than 5.5 years of age with anisometropic amblyopia in whom the amblyopia persists after refractive adaptation.

CONTROL ID: 3711433

SUBMITTER (NAME ONLY): Xiaofan Jiang

TITLE: Flicker electroretinogram peak times in over 1600 adult twins: distribution of times, associations with age and heritability

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cone photoreceptors drive both central and peripheral vision in most lighting conditions encountered during daily activities. Panretinal cone-driven responses can be measured using the light-adapted flicker electroretinogram (ERG). We analysed flicker ERG peak times recorded from over 1600 healthy adult twins to explore the distribution, association with age and heritability.

Methods: Participants were recruited from the TwinsUK cohort and underwent undilated photopic 28.3 Hz flicker ERG recordings (RETeval system with Sensor Strip skin electrodes, LKC technologies, Gaithersburg, MD). The device measured pupil diameter and adjusted stimulus strength to provide retinal illuminance (85 Td s white flicker; 850 Td white background) equivalent to the international standard. ERG peak times were averaged from both eyes. The distribution of responses and relationships with age were explored. Coefficients of intrapair correlation were calculated for monozygotic (MZ) and dizygotic (DZ) pairs as well as formal estimation of heritability by structural equation modelling.

Results: Recordings were obtained from 1594 participants (mean (SD) age 53.2 (16.5) years; 84% female). Mean (SD) peak time was 25.7 (1.3) ms (median 25.4 ms). The distribution deviated significantly from normality (Kolmogorov-Smirnov test $p<0.0001$). Following subtraction of a constant from each peak time, the reciprocal yielded a normal distribution (Kolmogorov-Smirnov $p=1$). Peak times showed significant positive correlation with age (Spearman correlation coefficient 0.54, $p<0.0001$). The increase with age was not linear; an expression by which the rate of change with age increased for older ages described the data mor closely than a simple linear fit. The participants included 675 full twin pairs (444 MZ and 231 DZ pairs). Coefficients of intra-pair correlation were 0.81 and 0.44 for MZ and DZ pairs respectively. Our estimate of heritability was 0.75 (95% CI, 0.70-0.78).

Conclusions: Peak times were not normally distributed, but their transformation to a normal distribution after taking the reciprocal (following subtraction of a constant time) might be consistent with some rate of signal processing being normally distributed. The relationship with age was not linear but showed a greater slope for older age groups. Approximately 75% of the variance in peak times could be attributable to genetic factors.

CONTROL ID: 3711441

SUBMITTER (NAME ONLY): Rob Atkinson

TITLE: Elucidating the Mechanism of PRPF-linked Retinitis Pigmentosa

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Atkinson, C. Yang, M. Georgiou, C. Beh, J. Collin, M. Moya Molina, R. Laws, M. Lako, Bioscience, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|K. Szymanska, C. Johnson, Institute of Medical Research, University of Leeds, Leeds, Leeds, UNITED KINGDOM|S. Mozaffari-Jovin, Max-Planck-Institut fur biophysikalische Chemie, Gottingen, Niedersachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Splicing is essential for most basic cellular processes. It is not known why mutations in the largest and most conserved component of the spliceosome (PRPF8) cause Retinitis Pigmentosa (RP13). We hypothesised that mis-splicing affects those processes critical for vision such as retinal development and cilia function[ML1] . This study investigates using iPSCs derived from four affected individuals and isogenic controls generated using CRISPR/Cas9. Retinal and non-retinal tissues were differentiated and analysed to make clear the tissue specific phenotype and identify similarities to other types of PRPF-linked RP.

Methods: Fibroblasts from one de novo and three familial patients with RP13 were reprogrammed to iPSCs via RNA-based transduction. The missense mutation in PRPF8 was then edited using CRISPR/Cas9 to generate paired isogenic control lines (n = 8). All lines were differentiated in parallel to retinal pigment epithelium (RPE), retinal organoids (RO) and kidney organoids using published protocols. Isogenic pairs were cultured, collected, and processed in parallel for a range of experiments including qPCR, immunofluorescence microscopy, and electron microscopy. Statistical analysis was performed using two-tailed paired t test, results shown as mean ± SEM.

Results: Expression of the mutant PRPF8 transcript was detected by qPCR in RP13 cells but not the RP13-Cas9 controls ($p < .001$ for all cell types). We investigated whether the mutation affects localisation to intranuclear domains enriched with splicing factors, known as nuclear speckles. The colocalization of PRPF8 and nuclear speckle marker SC35 was reduced in RP13 iPSCs, RPE and photoreceptors ($p < 0.05$ for all cell types). In addition, cilia of RP13 RPE were 10% longer ($p < 0.05$) and a fraction of these had swollen axonemes, but cilia frequency was unaffected. To gain insight into possible effects on tissue function we carried out a quantitative ultrastructural analysis. A significantly reduced number of mitochondria were found in RP13 RPE (10 ± 1 vs 17 ± 1, $p < 0.01$) and photoreceptors (57 ± 13 vs 107 ± 11, $p < 0.05$).

Conclusions: These results suggest that retinal and non-retinal tissues exhibit a splicing phenotype in RP13. Retinal cells exhibit ciliary defects and a possible metabolic shift that warrant further investigation. The combined splicing and ciliary phenotype presented resembles that caused by PRPF31 mutations.

CONTROL ID: 3711443

SUBMITTER (NAME ONLY): Sandra Wagner

TITLE: Does reading text with inverted contrast affect the ciliary muscle structure of emmetropic and myopic eyes?

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Wagner, T. Strasser, Institute for Ophthalmic Research Tuebingen, Eberhard Karls University Tuebingen, Tuebingen, GERMANY|T. Strasser, University Eye Hospital Tuebingen, Tuebingen, GERMANY|

Commercial Relationships Disclosure: Sandra Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Torsten Strasser: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previous research found that reading white text on black background increased the choroidal thickness in young adults, possibly inhibiting myopia (Aleman et al., 2018). We have already shown that prolonged reading of conventional text (black-on-white) leads to a thinning of the ciliary muscle (CM) in both emmetropes and myopes (Wagner et al., 2019). We aim to assess whether the contrast polarity of the reading material affects the CM structure and whether this differs between emmetropic and myopic eyes.

Methods: Optical coherence tomography (OCT) is used to image the subjects' CM at baseline and after having read binocularly white text on black background on an ebook reader for a continuous 30-min period at 25cm distance. Before and after the nearwork task, a minimum of 3 OCT images of the right eye's CM is taken while subjects first fixate a far (0D), then a near target (4D) with their left eye, respectively. OCT images are analyzed using custom-developed software to achieve CM thickness (CMT) profiles and selective CMT readings.

Results: Preliminary results with 6 adults (3 myopic, 3 emmetropic; age 19-43) showed that the CMT profiles of myopic eyes decreased after the 30-min reading period, while CMT profiles of emmetropes were rather thicker afterwards, especially for the 4D condition. Analysis of CMT changes (pre-post) likewise showed a thinning in myopic, but a CMT increase in emmetropic eyes in both target conditions (median emm/ my: 0D: -35.29µm/ 38.28µm; 4D: -12.70µm/ 57.19µm; Fig.).

Conclusions: Stimulating predominantly retinal ON pathways by presenting white-on-black text was previously found to produce a thickening of the choroid (Aleman et al., 2018). Our preliminary data suggests that the CM is also affected by the text's contrast polarity, however differing depending on the eye's refractive error. Emmetropic CM becomes rather thicker after reading white-on-black text, being in line with the previous finding of increased choroidal thickness. In contrast, the CM structure of myopic eyes, being thinner after the near task, seems to be unaffected by the contrast polarity, since post-task thinning has equally been measured for black-on-white text previously (Wagner et al., 2019). We further intend to increase the sample size to consolidate the preliminary outcome. A longitudinal dataset would allow to test whether the text polarity only affects the CM prior to myopia onset.

CONTROL ID: 3711445

SUBMITTER (NAME ONLY): David Mackey

TITLE: Evaluating the distribution of laterally corrected foveal avascular zone parameters.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine the distribution and interocular symmetry of foveal avascular zone (FAZ) parameters after correction for lateral magnification, in a large cohort of healthy, young adults.

Methods: Participants underwent a comprehensive ophthalmic examination including axial length measurement and optical coherence tomography angiography (OCTA) imaging of the macula. OCTA images of combined superficial and deep retinal vessel plexuses were processed via a custom software to extract foveal avascular zone area (FAZA) and vessel density in a 300-µm annulus surrounding the foveal avascular zone (FD-300), with and without correction for lateral magnification. Bland-Altman analyses were performed to examine the effect of lateral magnification on FAZA and FD-300, as well as to evaluate the interocular agreement in both parameters.

Results: OCTA images were acquired in 504 adults (261 females [51.8%], 243 males [48.2%]; average [standard deviation] age: 28.2 [0.7]). The mean (SD) of laterally corrected FAZA and FD-300 were 0.22 (0.10) mm^2 and 51.9 (3.2) %, respectively. Relative to raw, uncorrected data, 55.6% of corrected FAZA showed a relative change greater than 5% while all FD-300 changes were within 5%. There was good interocular symmetry (mean OD-OS difference, 95% limits of agreement) in both FAZA (0.006, -0.077 to 0.118 mm^2) and FD-300 (-0.05, -5.39 to 5.30 %).

Conclusions: Clinicians should strongly consider accounting for lateral magnification when evaluating FAZA. If working with a 5% error margin, correcting for lateral magnification is not necessary when evaluating FD-300. Good interocular agreement in FAZA and FD-300 suggests the contralateral eye can be used as control data.

CONTROL ID: 3711446

SUBMITTER (NAME ONLY): Kristina Chern

TITLE: Safety and efficacy of recombinant adeno-associated virus (rAAV) mediated transduction in the anterior chamber of the African Green Monkey (Chlorocebus sabaeus)

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.J. Chern, Cell and Developmental Biology, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|K.J. Chern, G.J. Marcoe, D.M. Lipinski, Ophthalmology, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|K. Isaac, Z. Gumbs, D. Fahie, M. O'Conner, RxGen, New Haven, Connecticut, UNITED STATES|D.M. Lipinski, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Kristina Chern: Commercial Relationship: Code N (No Commercial Relationship) | Gavin Marcoe: Commercial Relationship: Code N (No Commercial Relationship) | Kimica Isaac: Commercial Relationship: Code N (No Commercial Relationship) | Zendorf Gumbs: Commercial Relationship: Code N (No Commercial Relationship) | Dexter Fahie: Commercial Relationship: Code N (No Commercial Relationship) | Melissa O'Conner: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Lipinski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is characterized by progressive retinal ganglion cell loss and optic nerve degeneration, and is a leading cause of blindness worldwide. While pharmacological approaches aimed at lowering intraocular pressure (IOP) are effective at preventing vision loss, patient compliance is extremely poor. As such, there is a need for the development of a long-acting IOP-lowering gene therapy for glaucoma. Herein, we assess the tolerability and tropism of three recombinant adeno-associated virus (rAAV) vectors when injected intracamerally in a non-human primate (NHP) model.

Methods: Six sero-negative African Green Monkeys underwent ophthalmic examinations, including optical coherence tomography (OCT), confocal scanning laser ophthalmoscopy (cSLO), tonometry, pachymetry and slit lamp imaging, to establish pre-injection baseline values. Eyes (N=12) were randomized and injected intracamerally with either a high ($1x10^{12}$vg) or low ($1x10^{11}$vg) dose of rAAV2/2[MAX], 2/6 or 2/9 packaging a ubiquitously expressing green fluorescent protein (GFP) reporter, with the contralateral eye left uninjected as a control. Assessments were repeated 1, 3, 7, 14, 21, 28, 35, 42 and 49 days post-injection at which point eyes were enucleated for histology.

Results: Transient increase in IOP was observed in all rAAV treated eyes immediately following vector injection, with pressures returning to normal by day 7. Slit lamp bimicroscopy revealed increased inflammation as evident by increased cell counts immediately following injection, as well as a secondary phase of inflammation 14-21 days after injection, which both resolved spontaneously without pharmacological intervention. No permanent alteration in retinal volume or appearance was observed in any rAAV treatment eyes via OCT or SLO. Corneal thickness remained constant in 11/12 injected eyes. Specular microscopy at day 42 indicated in all injected groups there were no changes in endothelial health. cSLO imaging at D42 revealed fluorescence signal in several eyes indicative of GFP expression; histology confirmed signal in the lens capsule, iris, and iridocorneal angle.

Conclusions: Together the results indicate that intracameral administration of rAAV appears to be well tolerated in naïve NHPs, leading to transduction of anterior chamber structures and may be relevant for the treatment of glaucoma.

CONTROL ID: 3711447

SUBMITTER (NAME ONLY): Laura Taylor

TITLE: Assessment of scotopic microperimetry as a functional marker in patients with inherited retinal disease.

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.J. Taylor, A.S. Josan, R.E. MacLaren, Nuffield Department of Clinical Neuroscience, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|L.J. Taylor, A.S. Josan, R.E. MacLaren, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|J.K. Jolly, Anglia Ruskin University Vision and Eye Research Institute, Cambridge, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Many inherited retinal degenerations (IRD) present with nyctalopia and peripheral vision loss. Despite this, spatial assessments of scotopic visual function are limited. Scotopic microperimetry combines scotopic two-colour (cyan and red stimuli) perimetry with fundus-controlled microperimetry. By analysing the cyan minus red stimuli sensitivity differences, it enables scotopic central retinal sensitivity mapping and spatial identification of photoreceptor dysfunction. Mesopic microperimetry has become a prominent outcome measure in IRD clinical trials. However, the use of scotopic microperimetry in IRDs is less well established, we sought to determine more about the usefulness of this test.

Methods: Participants underwent 20 minutes dark adaptation before two-colour scotopic microperimetry, on one eye, using the Macular Integrity Assessment System (MAIA; CenterVue, Padova, Italy), 37-point, ultra-wide radial grid, with cyan and red stimuli, respectively. Five participants underwent repeat scotopic testing. The reliability indices and repeatability were analysed.

Results: Thirteen participants with genetically confirmed IRD diagnoses (CHM = 10, USH2A =2 and RHO =1) and good visual acuity (mean VA 83 [SD±5] ETDRS letters) completed microperimetry. Three participants were excluded due to >20% fixation losses. The remaining 10 participants showed good fixation stability with a mean 95% bivariate contour ellipse fixation area of 1.57 (SD±1.71) and 2.56 (SD±3.62) degrees^2 for cyan and red stimuli, respectively. Mean cyan sensitivity (dB) was 5.36 (SD±6.9), mean red sensitivity was 8.41 (SD±7.7), cyan minus red sensitivity was -3.19 (SD±4.9). The individual test point repeatability for cyan stimuli was ±6.42dB, ±4.67dB for red stimuli and ±7.57dB for cyan minus red. Cyan minus red sensitivity plots showed both choroideremia and USH2A-associated retinitis pigmentosa (RP) participants had mixed rod/cone photoreceptor dysfunction. Whereas the Rho-associated RP participant showed diffuse rod specific dysfunction.

Conclusions: Scotopic microperimetry appears a reliable and repeatable marker of scotopic central macular sensitivity. However, to more accurately model the patterns of photoreceptor dysfunction in different IRDs, it may be necessary to consider specific pointwise test-retest variability values when categorising between rod versus cone retinal dysfunction.

CONTROL ID: 3711448

SUBMITTER (NAME ONLY): Brice Vofo

TITLE: Clinical outcome of a modified treat-and-extend protocol in the treatment of neovascular age-related macular degeneration.

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.N. Vofo, Y. Cnaany, I. Chowers, Hadassah Medical Center Department of Ophthalmology, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: To compare the outcomes of neovascular age-related macular degeneration (nvAMD) patients treated with a modified treat and extend protocol (MTAE) to that of those treated with a conventional treat and extend protocol (TAE).

Methods: A retrospective analysis of two consecutive groups of treatment naive nvAMD patients was conducted. The first group began anti-vascular endothelial growth factor (VEGF) therapy between January 2006 and December 2011, and were treated using the conventional TAE protocol. The second group began anti-VEGF treatment between January 2016 and December 2017 and was treated using a MTAE. In the MTAE protocol, visual acuity and dilated fundus exams were performed once in 3 visits, while during the other 2 visits, an OCT assessment was used to guide retreatment. The time spent per encounter, and the visual and anatomical outcomes were compared between the two groups after 36 months of follow-up.

Results: The TAE and MTAE cohorts included 135 eyes (116 patients, 41.4% female, mean age: 76.9±7.8 years) and 119 eyes (94 patients, 55.3% female, mean age 79.8±6.8 years), respectively. Both groups had similar baseline characteristics. At 36 months, the number of injections administered, (7.9±2.9 vs 8.1±2.3 injections, respectively, p=0.55), the number of eyes that gained ≥15 Early Treatment for Diabetic Retinopathy Study (ETDRS) letters 31 (23%) vs 30 (25.2%), respectively (p=0.39) and lost ≥15 EDTRS letters 29 (21.5%) vs 21 (17.7%), respectively, were similar in both groups (p=0.43). Anatomical outcomes per OCT were also similar in both groups. Both waiting time and service time were reduced during OCT-only assessments compared to full assessments (32±20 minutes vs 56±40 minutes, and 9±4 minutes vs 26±10 minutes, respectively, p<0.001 in each case). Saving an average of 41 minutes for each patient encounter.

Conclusions: MTAE and TAE protocols yielded comparable visual and anatomical outcomes. Applying MTAE leads to reduced number of full assessment visits which is associated with shorter time spent in the clinic during the OCT-only assessment visits. MTAE may further streamline anti-VEGF therapy, thereby, reducing patient, caregivers, and staff time allocated to treatment.

CONTROL ID: 3711449

SUBMITTER (NAME ONLY): Maria Llorian-Salvador

TITLE: Regulatory T cells limit age-associated retinal degeneration

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Llorian-Salvador, A.G. de la Fuente, A.W. Stitt, D. Fitzgerald, Queen's University Belfast Wellcome-Wolfson Institute for Experimental Medicine, Belfast, Belfast, UNITED KINGDOM|A.G. de la Fuente, Instituto de Investigacion Sanitaria y Biomedica de Alicante, Alicante, Comunidad Valenciana, SPAIN|M. Llorian-Salvador, Vall d'Hebron Institut de Recerca, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: Age is a major risk factor for many retinal diseases which, together, are estimated to severely impact on the visual function of >1.8 billion people by 2050. The precise pathobiology underpinning age-associated retinal degeneration remains ill-defined although there is broad recognition that low-grade chronic inflammation plays an important role. Regulatory T cells (Treg) have recently emerged as key players in tissue homeostasis, due to their capacity to regulate local immune responses and limit inflammation, as well as their role in metabolic regulation, regeneration, and neuroprotection. However, the role of Treg in retinal homeostasis and age-associated retinal neurodegeneration is yet to be investigated.

Methods: Treg depletion was induced by intraperitoneal diphtheria toxin (DT) administration to Foxp3-DTR mice over 17 days (3 consecutive DT injections and then one DT injection every 4 days). The retinal neurovascular unit was assessed in young (3-4m) and aged (16-23m) Foxp3-DTR mice receiving DT, its vehicle (PBS) and C57BL/6 WT mice receiving DT. Gliosis (GFAP, Iba-1, CD68) and changes in neuronal populations (PKCα/secretagogin, rod/cone bipolar cells; Brn3a, retinal ganglion cells; Cone-arrestin, cone-photoreceptors) were assessed by immunohistochemistry.

Results: We observed a significant decrease Cone-arrestin^{+} and DAPI^{+} cells in the ONL in Treg-depleted aged but not young Foxp3-DTR mice, along with an alteration in the typical laminarity of cone and rod bipolar cells in the INL, further indicating retinal neurodegeneration. Aged Foxp3-DTR mice treated with DT also showed enhanced Müller cell gliosis, especially in the ONL. Interestingly, an increase in Iba-1^{+} cells was found in the ONL of aged Foxp3-DTR treated with DT as well as in the subretinal space of both aged and young Foxp3-DTR, together with RPE dysmorphology. Considering the differences observed between young and aged Treg-depleted mice, we analysed changes in expression in between young and aged Treg. When compared with young Treg, aged Treg showed an upregulation of genes linked to gene ontology terms related to neuronal processes, suggesting that with aging Treg may acquire a neuroprotective role.

Conclusions: Depletion of Foxp3^{+} Tregs exacerbates retinal neurodegeneration, Muller gliosis and microglia infiltration in aged animals compared to young controls. Hence, Treg have a key role in regulating immune homeostasis in age-related retinal pathology.

CONTROL ID: 3711450

SUBMITTER (NAME ONLY): Maurizio Tomaiuolo

TITLE: Open Globe Repairs in the United States 2014-2018: Incidence, risk factors and visual outcomes - An IRIS® Registry (Intelligent Research in Sight) Analysis

SESSION TITLE: Refractive Error and Social Determinants of Vision Function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Tomaiuolo, A. Li, J. Sharpe, Q.(. Zhang, L. Hyman, Vision Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|F. Woreta, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|Y. Yonekawa, Z.A. Syed, D. Ramesh, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|A.C. Lorch, N. Hall, A. Shah, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Shah, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|G. Justin, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Open globe injuries (OGI) are an important cause of visual impairment worldwide. This retrospective cohort analysis evaluates incidence and risk factors associated with open globe repairs (OGR) and visual acuity (VA) outcomes after surgery in the American Academy of Ophthalmology IRIS Registry.

Methods: Patients with OGR were identified by Current Procedural Terminology codes (65275, 65280, 65285, 65286, 65235, 65260, 65265) from 2014 to 2018 in the IRIS Registry. Annual and 5-year incidence rates per 100,000 persons were calculated. Factors associated with OGR and VA <20/40 and VA <20/200 at final follow up (3 to 12 months post OGR) were evaluated using multivariable logistic regression models adjusting for sex, race, ethnicity, US region, concurrent and subsequent surgeries, and baseline VA. Statistical analyses were performed in R.

Results: 15,316 OGR's were identified during the study period; 5-year incidence was 30.1/100,000. Annual incidence ranged from 10.9 to 12.7/100,000. OGR was positively associated with older v younger ages <21 yrs, e.g. > 80 yrs (OR, 4.9 [CI: 4.1-6.0]); male v female (OR, 3.1 [CI: 2.7-3.6]); Black v White race (OR, 1.7 [CI, 1.5-2.1]); Hispanic v Non Hispanic ethnicity (OR, 1.4 [CI, 1.2-1.7]); living in the South (OR, 1.40 [CI, 1.33-1.47]) and West (OR- 1.29 [CI, 1.21-1.36]) (v Midwest) regions and inversely associated with Asian v White race (OR- 0.5 [CI, 0.3-0.8]). Vision impairment final follow up was associated with VA <20/200 at presentation (20/200 v better than 20/40 - OR, 11.6 [CI, 8.0-155.6]); older age e.g. 80+ y (v < 21 y) (OR, 5.8 [CI, 3.2-10.7]); and Black race (v White) (OR, 1.8 [CI, 1.3-2.5]). Risk factors were similar for VA < 20/200 post OGR. Among all OGR patients presenting with VA 20/200 or worse, VA improved to 20/40 or better at follow up in 19% (331/1748) of patients; VA improved to better than 20/40 in only 10% (20/ 192) of Black OSR patients.

Conclusions: Our findings support previously established risk factors associated with OGR of older age and male sex and bring to light racial disparities in risk of OGI and poor visual outcomes that warrant further exploration.

CONTROL ID: 3711451

SUBMITTER (NAME ONLY): Patrícia Barreto

TITLE: Association of genetics and the adherence to the Mediterranean diet: the risk for age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Barreto, C. Farinha, R. Coimbra, M. Cachulo, J.G. Cunha-Vaz, R. Silva, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|P. Barreto, Univ Coimbra, Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, Coimbra, Portugal, Coimbra, PORTUGAL|C. Farinha, M. Cachulo, R. Silva, opthalmology, Centro Hospitalar e Universitario de Coimbra EPE, Coimbra, Coimbra, PORTUGAL|C.C. Hoyng, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|J.B. Melo, I.M. Carreira, Cytogenetics and Genomics Laboratory, Clinical Academic Center of Coimbra (CACC), Faculty of Medicine; University of Coimbra, Coimbra, PORTUGAL|J.B. Melo, I.M. Carreira, Univ Coimbra, Center of Investigation in Environment, Genetics and Oncobiology (CIMAGO), Faculty of Medicine, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To explore the association of the genetic risk score (GRS) for the onset of Age-Related Macular Degeneration (AMD) with the adherence to the Mediterranean diet (MedDiet) – the Coimbra Eye Study (CES).

Methods: 612 subjects (161cases/451 controls) who completed a validated lifestyle and food frequency questionnaire were genotyped in collaboration with the European Eye Epidemiology Consortium. Cases were participants staged 2, 3 or 4 and controls were participants staged 0 (> 60 years-old) or 1 (> 70 years-old), Rotterdam Classification. The adherence to the MedDiet was calculated with mediSCORE (range 0-9) calculated by the sum of nine food group: vegetables, legumes, fruits, cereals, fish, meat, dairy products, fats and alcohol. High adherence to the MedDiet was defined as a mediSCORE equal or >6 (range: 6–9). A GRS was calculated using the 52 single nucleotide polymorphism identified by the International AMD Genomics Consortium. GRS was considered missing if at least one genotype of the major risk variants (CFH rs570618, CFH rs10922109, C2/CFB/SKIV2L rs429608, ARMS2 rs3750846 or C3 rs2230199) was missing. High GRS was classified as greater than or equal to the median. A multivariate logistic regression model with generalized estimating equations for 1216 individual eyes was used to examine the association of AMD, GRS and mediSCORE, controlled by age, sex, smoking and physical exercise.

Results: A higher adherence to the MedDiet was significantly associated with a decreased risk of AMD (OR=0.61, 95%CI 0.39-0.94, p=0.024) and a higher GRS was significantly associated with an increased risk of AMD (OR=2.44, 95%CI 1.66-3.58, p<0.0001). However, no statistical significant interaction was found between the GRS and MedDiet (p=0.284). Despite this, the adherence to the MedDiet was found to be protective for AMD in people with low GRS (OR=0.44, 95%CI 0.21-0.94, p=0.034), while no benefit was observed for people whose GRS was high (OR=0.70, 95%CI 0.40-1.22, p=0.212).

Conclusions: The MedDiet may be protective against the development of AMD, and this protection may depend on the genetic risk. However, it is crucial to carry out further studies on different populations, to clarify the interplay of AMD risk factors, particularly on the MedDiet, in the establishment of the pathophysiology of the disease.

CONTROL ID: 3711452

SUBMITTER (NAME ONLY): Ismael Romero-Castillo

TITLE: Isolation and characterization of EVs from an immortalized human conjunctival epithelium cell line

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Romero-Castillo, L. Garcia-Posadas, Y. Diebold, Instituto de Oftalmobiología Aplicada (IOBA), Universidad de Valladolid - Campus Miguel Delibes, Valladolid, Castilla y León, SPAIN|K. Brennan, UCD School of Biomolecular & Biomedical Science, Conway Institute, University College Dublin, Dublin, Belfield, IRELAND|A. Blanco, Flow Cytometry Core Technology, Conway Institute, University College Dublin, Dublin, Belfield, IRELAND|Y. Diebold, Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Instituto de Salud Carlos III, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: The scarcity of in vitro models is an important drawback to study conjunctiva pathophysiology. The Immortalized Human Conjunctival Epithelial Cell line IM-HConEpiC is commercially available, but has not been widely used in research, yet. The aim of this study is to characterize this cell line and to use it as a source of conjunctival extracellular vesicles (EVs).

Methods: IM-HConEpiC cells were cultured with DMEM/F12 supplemented medium. Total protein was isolated in RIPA buffer and used for Western blot (WB). RNA was isolated in RLT lysis buffer and used for reverse transcription-PCR. Cells grown in slides were fixed and used for immunofluorescence (IF) microscopy. The expression of cytokeratin (CK) 7, CK8+18, CK19, E-cadherin, ZO-1, mucin (MUC) 4, and MUC5AC was analyzed by WB, IF, and/or PCR. IM-HConEpiC cells (passages 7-20) were also used to obtain EVs. Cells were grown to 70% confluence and treated with EVs free-FBS supplemented medium for 48 h. Medium was collected and EVs obtained by differential ultracentrifugation (UC) using two different methods (M): M1, at 4°C, with SW28 rotor, and M2, at 20°C and combination of SW28/SW60Ti rotors. All EVs were resuspended in PBS/trehalose and stored at -80°C for further analysis. The ExoStep Kit (ImmunoStep) was used for the detection and determination of the concentration of EVs by flow cytometry using a Beckman Coulter Navios cytometer. A Beckman Coulter CytoFLEX LX flow cytometer was used to individually characterize the EV content. EVs were morphologically analyzed by atomic force microscopy.

Results: IM-HConEpiC cells expressed CK7, CK8+18, CK19, E-cadherin, ZO-1, MUC4, and MUC5AC, as demonstrated by WB, IF and/or PCR. EVs were isolated from IM-HConEpiC with the two methods. The CytoFLEX results showed that IM-HConEpiC-EVs expressed the EV markers: CD9, CD63, CD81 and CD147 and that the majority of the EV subpopulation was made up of small EVs, with 66.06±2.23% (M1) and 62.63±0.4% (M2) having a similar violet SSC to 80nm Apogee beads.

Conclusions: Cultured IM-HConEpiC cells express typical conjunctival epithelial markers, suggesting that this cell line is a valuable tool for in vitro research. Although the EVs were properly isolated from the conditioned supernatants by UC, an exhaustive analysis is necessary to elucidate the abundance and composition of the different populations.

CONTROL ID: 3711453

SUBMITTER (NAME ONLY): Daniel Jones

TITLE: MOSAIC: A qualitative study of the clinical, humanistic, and financial burden of geographic atrophy (GA) among patients

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: GA, the advanced form of dry age-related macular degeneration (AMD), is a leading cause of blindness in the elderly; however, there is limited research on patient experiences. We conducted a qualitative study of the clinical, financial, and humanistic burden of GA to characterize patient perspectives on living with the disease. The results of this qualitative study guided the design of a global GA patient survey launched in 2021 and are being presented here for the first time.

Methods: Semi-structured interviews were conducted with 28 purposively sampled patients in the US (n=22), UK (n=4), and Australia (n=2). Inclusion criteria were age ≥60 years, a diagnosis of GA in at least 1 eye that did not also have neovascular AMD, and English fluency. Patients were excluded if they had neovascular AMD in both eyes, Stargardt disease, major cognitive impairment, or if they were in an AMD clinical trial or on any investigational agent to treat GA. Consensus-based coding and thematic analysis, using a primarily inductive approach, was conducted using ATLAS.ti. Thematic saturation was assessed in 5 waves and achieved in wave 4.

Results: Mean participant age was 80, and 48% of the sample was female. Major clinical burden concerns among patients included the lack of GA treatment and disease information, poor patient-provider communication, unpredictability of progression, and confusion about the difference between GA and wet AMD or other eye conditions. Major humanistic burden concerns included: impacts on mental health; impacts of visual changes on daily activities (reading, driving, shopping, cooking, cleaning, hygiene, personal care, and hobbies); impacts on social and family life. Patients reported the current or threatened loss of independence was their overriding concern. Key markers of independence included: driving, walking in unfamiliar places, and doing daily activities with little assistance. Patients reported personal injuries and driving accidents due to GA and worried about safety. Financial worries included affording products and services for the vision-impaired, job loss, and needing to hire care.

Conclusions: There is a clear significant unmet need for patients beyond therapy, including GA treatment, disease information, and social and mental health support. Further research is needed to understand the clinical, financial, and humanistic burden of GA on patients.

CONTROL ID: 3711455

SUBMITTER (NAME ONLY): Yanlin Li

TITLE: Cholesterol efflux capacity of high-density lipoprotein (HDL) particles is impaired in age-related macular degeneration patients with high plasma HDL-cholesterol levels

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, Department of Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|Y. Li, L. van der Zee-van Vark, A. Verhoeven, M.T. Mulder, Department of Internal Medicine, Laboratory of Vascular Medicine, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|M. Palumbo, F. Bernini, M. Adorni, F. Zimetti, Department of Food and Drug, Universita degli Studi di Parma, Parma, Emilia-Romagna, ITALY|C.C. Klaver, M. Meester, Department of Ophthalmology and Department of Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Department of Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|P.J. Leenen, Department of Immunology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Epidemiological studies demonstrated an association between elevated plasma high-density lipoprotein-cholesterol (HDL-c) levels and AMD. This is in contrast to the negative association of plasma HDL-c levels with the risk of cardiovascular disease. Apart from the statistical association, little is known with respect to the functional change of HDL in AMD patients. The capacity to mediate cellular cholesterol efflux is one of the major functions of HDL, followed by the transportation of cholesterol by HDL to the liver via a process called reverse cholesterol transport. Genetic studies identified genes associated with AMD, including ABCA1, CETP, LIPC and APOE that are also related to HDL-mediated cholesterol efflux. In accordance, we hypothesized that the cholesterol efflux capacity (CEC) of HDL is impaired in AMD patients, consequently leading to cholesterol accumulation underneath retinal pigment epithelium (RPE) cells, facilitating drusen formation.

Methods: To approach this, HDL was isolated from 30 AMD patients and 30 age-matched controls, and the capacity of HDL to mediate cellular cholesterol efflux from [^{3}H]-cholesterol-loaded ARPE-19 cells was assessed by measuring the percentage of [^{3}H]-cholesterol secreted into the culture medium. Unpaired T test and Mann-Whitney U test were used to assess the difference between patients and controls.

Results: We found no significant differences in CEC between AMD patients and controls when comparing HDL isolated from 1 ml of plasma from each individual. However, HDL from AMD patients with high, but not low plasma HDL-c levels, showed a decreased CEC (11.62%, p=0.027) per HDL particle as compared to healthy controls.

Conclusions: Together, our data suggest that impaired cholesterol efflux capacity of HDL is not causal for AMD pathogenesis but may be a result of other metabolic dysfunctions in AMD patients. Elevated plasma HDL-c levels in AMD patients might compensate for the decreased CEC per HDL particle.

CONTROL ID: 3711456

SUBMITTER (NAME ONLY): Ines Lains

TITLE: Plasma Metabolites Associated with Optical Coherence Tomography (OCT) Features of Age-related Macular Degeneration (AMD)

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I. Lains, A. Nigalye, R. Alvarez, V. Douglas, J.B. Miller, D.G. Vavvas, I.K. Kim, J.W. Miller, D. Husain, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|X. Han, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|J.Q. Gil, J. Providencia, R. Silva, Centro Hospitalar e Universitario de Coimbra EPE, Coimbra, Coimbra, PORTUGAL|J.Q. Gil, J. Providencia, R. Silva, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|R. S Kelly, J. Lasky-Su, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|I. Lains, A. Nigalye, R. Alvarez, V. Douglas, J.W. Miller, D. Husain, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The most widely used classifications of age-related macular degeneration (AMD) are still based on color fundus photographs (CFP). Yet, OCT is the foundation of real-world clinical assessments of patients with AMD and may better subclassify the wide variety of its phenotypes. While it has been proven that AMD patients have a distinct plasma metabolomic profile compared to controls, all studies to date have used the traditional CFP classification systems. This study examined whether plasma metabolomic profiles are associated with OCT features commonly seen in AMD, a potential step forward towards a more comprehensive classification system for AMD.

Methods: Prospective, cross-sectional study, including subjects with AMD and a control group (> 50 years) from Boston, United States and Coimbra, Portugal. All participants were imaged with CFP, used for AMD staging (AREDS classification), and with spectral-domain OCT (Spectralis, Heidelberg). OCT images were graded by two independent graders for the presence of characteristic AMD features (i.e. presence of classic drusen, subretinal drusenoid

deposits, atrophy, among others), according to a predefined protocol. Fasting blood samples were collected for metabolomic profiling (using non-targeted high resolution mass spectrometry by Metabolon, Inc.). Multilevel mixed regression models were used for analysis, adjusting for sex and age. Analyses were first conducted for each cohort (US and Portugal), with subsequent meta-analysis using a fixed-effect inverse variance method.
Results: We included data on 477 subjects (n= 953 eyes), 381 with AMD and 96 controls, and on 718 named endogenous metabolites. Nine metabolite-OCT associations were identified ($p< 0.001$). Most associations were seen with amino acids (n=5). In particular, levels of histidine were associated with the presence of hyperreflective foci, ellipsoid zone disruption and extent of classic drusen. The presence of hyperreflective foci was the OCT feature associated with more metabolites (n= 4).
Conclusions: To our knowledge, we show for the first time that plasma metabolites have associations with specific OCT features seen in AMD. Metabolomics may offer a useful biomarker for an improved classification system for this complex disease with many clinical phenotypes.

CONTROL ID: 3711460

SUBMITTER (NAME ONLY): JAISHREE GANDHI

TITLE: Comprehensive Proteomic Profiling of small extracellular vesicles in a Murine Model of Aspergillus flavus endophthalmitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Fungal endophthalmitis is a relatively uncommon but serious complication of intraocular surgery or trauma and is often associated with poor prognosis. Its incidence has increased in recent years, particularly in tropical countries, with the main aetiology being filamentous fungi, particularly Aspergillus sp. The purpose of this study was to understand the protein cargo of Extracellular Vesicles (EVs) in a murine model of Aspergillus flavus endophthalmitis.

Methods: EVs were isolated by differential ultracentrifugation from C57BL/6 mice eyes challenged with A. flavus at 24-72 hours post-infection (p.i). Isolated EVs were characterized by Dynamic Light Scattering (DLS), ExoCet assay, western blot, and cytokine analysis. Mass spectrometry (LC-MS/MS) quantitative analysis was also performed for comparing the protein profile of these EVs with uninfected mice.

Results: EVs derived from eyes infected with A. flavus ranged from 200-250nm in diameter and the concentration was higher at 24 h p.i. $1.55x10^{10}$ ±554665251, in comparison to EVs from control -$1.24x10^{9}$ ($p = 0.001$). Western blot analysis confirmed the presence of markers: CD9, CD63, and CD81. In addition, IL-6 was significantly elevated at 72 h p.i in EVs from infected eyes ($p=0.02$). Proteomic analysis identified 81 differentially expressed proteins, of which 22 were upregulated and 59 were downregulated. Gene Ontology (GO) functional enrichment analysis of differentially upregulated proteins were enriched for transferase activity, protein complex, and tubulin binding such as CDS-diacylglycerol synthase-1(CDS1), fibrillin 1 (FBN1), microtubule-associated protein-4 (MAP4) and calmodulin-dependent protein kinase-2 (CAMK2G). Among the downregulated proteins, S100 calcium-binding protein (S100A9), annexin A1 (ANXA1), lactotransferrin (LTF), and transferrin (TRF) were associated with transport, negative regulation of apoptotic process, and phagocytosis. Additionally, KEGG pathway analysis revealed that differentially upregulated proteins participate in the glucagon signaling while downregulated proteins participate in metabolic and carbon signaling pathways.

Conclusions: Our findings reveal that EVs cargo in A. flavus endophthalmitis plays a key role in immune regulation and disease progression. Further validation of these proteins can serve as important prognostic markers in patients with fungal endophthalmitis.

CONTROL ID: 3711461

SUBMITTER (NAME ONLY): Tyler Etheridge

TITLE: Intracameral Tissue Plasminogen Activator in Uveitic Cataract Surgery

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Etheridge, M. Larochelle, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|W.F. Hu, University of Rochester David and Ilene Flaum Eye Institute, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tissue plasminogen activator (tPA) has been used as an adjunct to control intraocular inflammation after cataract surgery, with limited data on its use at the time of cataract surgery. We report the operative outcomes of intracameral tPA administered at the time of cataract surgery in eyes with uveitis, which are most at risk for post-operative inflammation.

Methods: A retrospective chart review identified patients with uveitis who received intracameral tPA at the time of cataract surgery between 2015 and 2021. Patients were excluded if they did not have a history of uveitis or if the surgery was not a primary cataract extraction. Surgeries were performed by four surgeons at one institution.

Results: Thirty-six eyes from 31 patients were identified. Mean ± standard deviation age was 36.3 ± 19.9 years. Anterior (66.7%) and idiopathic (41.7%) uveitis were most common. Eyes were absent of active intraocular inflammation for 5.8 ± 4.7 months prior to surgery. >90% had at least one coexisting ocular disease, including cystoid macular edema (50.0%), glaucoma (19.4%), steroid response (13.9%), epiretinal membrane (19.4%), and retinal detachment (5.6%). Anterior or posterior synechiae was present in 97.2% and intraoperative synechiolysis was performed in 94.4%. 52.8% were combined with planned pars plana vitrectomy. Acrylic (100%) single-piece (88.9%) lens placed in the capsular bag (94.4%) was most common. tPA dose of 12.5 µg (50.0%) or 25 µg (50.0%) was injected intracamerally at the surgeon's discretion. Thirty-four cases (94.4%) were uncomplicated. There was one anterior (2.8%) and one posterior capsular (2.8%) tear. LogMAR best corrected visual acuity (BCVA) improved from 1.0 ± 0.7 pre-operatively to 0.7 ± 0.7 post-operatively. 46.2% achieved BCVA ≤0.3 logMAR at 12 months, and only five (19.2%) remained at BCVA ≥1.3 logMAR. Improvement in BCVA was significant across all post-operative time points (p=0.0002). By month 1, 80.0% achieved anterior chamber cell grade of ≤0.5. Two eyes required repeat intracameral tPA injection at week 1 for fibrin formation. Posterior synechiae improved from 8.2 ± 3.8 clock hours pre-operatively to 0.1 ± 0.6 clock hours by month 12. Six eyes (16.7%) experienced hyphema; five (83.3%) resolved spontaneously.

Conclusions: Intracameral tPA administered at the time of cataract surgery in patients with uveitis appears to be effective in controlling acute post-operative inflammation.

CONTROL ID: 3711462

SUBMITTER (NAME ONLY): Imre Lengyel

TITLE: Ectopic calcification in the Bruch's membrane and functional changes in the retina are associated with exon 9 deletion in ENPP1 in a transgenic mice model

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kortvely, Hoffmann-La Roche Limited, Basel, SWITZERLAND|V. MacRae, University of Edinburgh, Edinburgh, UNITED KINGDOM|I. Lengyel, C.N. Brown, J. Augustine, T. Friedel, F. Cunningham, M. Pilgrim, WWIEM, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose:

Under physiological conditions, calcium and phosphate concentrations are tightly regulated, ensuring that calcification is restricted to bones and teeth. However, ectopic calcification in the extracellular space of soft tissues has been associated with ageing disorders including age-related macular degeneration (AMD), pseudoxanthoma elasticum (PXE), and generalized calcification in infancy (GACI). Ectopic calcification is associated with mutations on ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1). Here, we characterised the effects of exon 9 deletion in ENPP1 on ocular calcification and retinal structure and function.

Methods: ENPP1 transgenic mice were generated by breeding mice with loxP sites flanking ENPP1 exon 9 with mice expressing Cre recombinase behind a CAG synthetic germline promoter.. Wild type, heterozygous and knockout animals were maintained for up to 6 months. Animals were regularly assessed by colour fundus photography (CFP), optical coherence tomography (OCT) and electroretinography (ERG). In addition, cadaveric eyes were assessed for calcification using OsteoSense680EX and confocal fluorescent microscopy. $ENPP1^{-/-}$ animals were compared to $ENPP1^{+/-}$ and $ENPP1^{+/+}$ controls.

Results: On CFP we identified visible lesions in the $ENPP1^{-/-}$ animals. No measurable difference could be found in OCT segmentation. Analysis of the ERG traces showed no appreciable changes to scotopic A-wave. However, scotopic B-wave amplitudes were significantly increased with increased implicit time in $ENPP1^{-/-}$ animals(2.5 cd.s/m2: 567.7 µV vs. 442.8 µV, P value: 0.0193; 8.0 cd.s/m2: 685.2 µV vs. 511.2 µV, P value: 0.0037; 25.0 cd.s/m2: 779.8 µV vs. 561.2 µV, P value: 0.0015) . Staining of cadaveric eye tissues with Osteosense showed ectopic calcification in the Bruch's membrane but not in the retina. BrM calcification was more extensive in $ENPP1^{-/-}$ animals compared to $ENPP1^{+/-}$ and $ENPP1^{+/+}$ animals.

Conclusions:

Our preliminary studies indicate that deletion of exon 9 in the ENPP1 results in changes to retinal structure and function. The functional changes in the retina and the associated Bruch's membrane calcification could become a model for studying the effects of calcification and for the development of intervention strategies for diseases like AMD, PXE and GACI.

CONTROL ID: 3711463

SUBMITTER (NAME ONLY): Recivall Salongcay

TITLE: Accuracy of Integrated Artificial Intelligence (AI) Grading at the Point of Care (POC) Using Handheld Retinal Imaging in a Community-Based Diabetic Retinopathy (DR) Screening Program (DRSP)

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To prospectively evaluate handheld retinal images assessed by AI at the time of imaging as compared to standard retinal image graders at a centralized reading center (RC).

Methods: Prospective comparative study of AI assessment of referable DR [(refDR) moderate nonproliferative DR (NPDR) or worse, or any level of diabetic macular edema (DME)] and vision threatening DR [(vtDR) severe NPDR or worse, or any level of center involving DME (ciDME)]. AI assessment of disc and macular images performed at the time of imaging was compared with RC evaluation of validated 5-field handheld retinal images [(5F) disc, macula, temporal, superior and inferior]. RC evaluation of the 5F images followed the international DR/DME classification. Sensitivity and specificity (SN/SP) for ungradable images, refDR and vtDR were calculated.

Results: 1,733 eyes from 869 diabetic (DM) patients were enrolled in the study. Cohort demographic: age 59.5±10.0, 64.7% female, 98.4% type 2, DM duration 6.6±7.2 years. RC distribution of DR severity: no DR 70.5%, mild NPDR 9.3%, moderate NPDR 7.6%, severe NPDR 3.7%, PDR 2.9%, ungradable 6.0%. DME severity: no DME 82.2%, DME 6.2%, ciDME 4.2%, ungradable 7.3%. RefDR was present in 13.8% and vtDR in 7.8% of eyes. Images were ungradable for DR or DME in 7.7% by RC and 20.7% by AI. Table 1 summarizes the SN/SP and operating characteristics of POC AI grading. SN/SP of AI grading compared to RC evaluation was 0.83/0.95 for refDR and 0.96/0.91 for vtDR. 4 eyes with vtDR (3 severe NPDR and 1 proliferative DR) were missed by AI. Comparisons of performance of the POC AI with existing FDA approved algorithms are presented in table 2.

Conclusions: This study demonstrates that POC AI following a defined retinal imaging protocol at the time of imaging has SN/SP for refDR that meets the current acceptable thresholds of 0.80 and 0.95. Integrating AI at the POC could substantially reduce centralized reading center burden and speeds information delivery to the patient, allowing more prompt eye care referral.

CONTROL ID: 3711464

SUBMITTER (NAME ONLY): Josie Carmichael

TITLE: The Influence of Automated Support on Optometrists' Interpretation of Retinal OCT Scans

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Carmichael, E. Costanza, A. Blandford, University College London, London, London, UNITED KINGDOM|J. Carmichael, K. Balaskas, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: One possible barrier to AI deployment in healthcare is over-reliance from users. This, known as automation bias (AB), has not been assessed in ophthalmology but may impact clinical decisions. We tested whether AB was present when optometrists used AI diagnostic support for retinal disease using an online experiment.

Methods: Thirty hospital optometrists (15 more experienced and 15 less experienced) assessed 30 cases. Ten consisted of an OCT scan, basic clinical information, and a fundus image (manual). Ten also displayed AI diagnoses suggestions (AI). Ten additionally displayed an AI-produced OCT segmentation map (segmentation). Participants chose the most probable diagnosis per case and gave their diagnostic confidence. Level of trust in the AI outputs was also reported. Cases were chosen to be matched across conditions and to give 70% accuracy on the AI diagnoses.

Results: Compared to the gold standard clinical diagnoses, 670/900 (74%) responses were correct. There were significantly fewer correct responses for segmentation (204/300, $p<0.001$) and AI (224/300, $p=0.049$) than manual (242/300) and for segmentation compared to AI ($p=0.010$). Agreement with correct AI diagnosis decreased when segmentations were displayed (174/210 vs 199/210, $p<0.001$)(Table 1), with examples suggesting that this may be due to participants paying more attention to segmentation maps over AI diagnoses. There was no significant effect of experience on the number of correct responses across the three conditions ($p=0.24$). More experienced participants were more confident in their diagnoses ($p=0.012$) and trusted the AI less ($p=0.038$). Participants trusted the AI more when segmentation was displayed ($p=0.029$) but AI did not affect diagnostic confidence ($p=0.461$).

Conclusions: Using an imperfect AI system has a significant negative effect on correct diagnoses irrespective of experience. Displaying segmentation maps may increase the likelihood of acceptance if used in practice due to an increased level of trust. If used together in practice, the synchronization of algorithms for segmentation maps and diagnostic suggestions must be improved.

CONTROL ID: 3711465
SUBMITTER (NAME ONLY): Rabia Karani
TITLE: Manhattan Vision Screening and Follow-up Study: Ocular Pathology in Telemedicine Images
SESSION TITLE: Telehealth
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Karani, J.D. Horowitz, W.V. Lin, S. Hirji, I.A. Valenzuela, S. Maruri, D.J. Doobin, T. Sharma, D. Diamond, P. Gorroochurn, L. Park, Q. Wang, N. Harizman, J.M. Liebmann, G.A. Cioffi, L.A. Hark, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: To determine the distribution of ocular pathology found in abnormal retina and optic nerve photos from an inner city vision screening program.

Methods: The goal of this study was to conduct vision screenings using in person and telemedicine modalities to improve vision care for residents of 10 New York City Housing Authority buildings in Upper Manhattan. Screening involved obtaining visual acuity, intraocular pressure, offering refraction services, and obtaining fundus and disc photos using a non-mydriatic hand-held fundus camera. Images were read by two ophthalmologists in the specialties of glaucoma and retina. Participants with abnormal image findings as well as those who had failed their screening and saw the on-site optometrist were referred to an ophthalmologist.

Results: A total of 382 participants were screened to date during the first phase of the study from March 2021-December 2021, with 6 months of screening remaining. Of these 382 participants, 110 were found to have failed screening (VA 20/40 or worse, IOP > 23-29 mmHg) and had an abnormal image (as determined by an ophthalmologist).

Participant ages ranged from 42 to 93 years, with mean 69 and median 70. 35 (32%) identified as male, and 75 (68%) as female. 57 (52%) participants identified as Black/African American, 46 (42%) as Latino/Hispanic, and 7 (6%) as American Indian, Asian, White, or Multiracial. 60 participants (55%) were referred as glaucoma suspects, and 73 (67%) were referred for retina findings. Several had overlapping findings. 26 participants (24.3 %) demonstrated non-proliferative diabetic retinopathy (dot blot hemorrhages, macroaneurysms, cotton wool spots), with 7 of these referred for treatment of edema. 1 (.9%) was found to have retinal neovascularization requiring treatment. 3 (2.7%) demonstrated findings consistent with retinal venous occlusion, with 2 of 3 requiring treatment for edema. 3 (2.7%) were found to have hypertensive retinopathy. 15 (13.6%) had findings of age-related macular degeneration. Regarding optic disc photos, 53 (48.2%) were found to have abnormal cup-to- disc ratio, and 13 (11.8%) were found to have peripapillary atrophy.

Conclusions: This study demonstrates that community-based vision screening using non-mydriatic fundus and disc photography detected significant pathology including diabetic retinopathy, age-related macular degeneration, and glaucoma, among the most common causes for blindness.

CONTROL ID: 3711466

SUBMITTER (NAME ONLY): Mihai State

TITLE: Comparative Analysis of Metrics for MTF at FAR for the Quality Control of IOLs

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. State, H.A. Weeber, C. Canovas, M.D. Jenkins Sanchez, S. Boersma, P. Piers, Implants R&D, Johnson & Johnson Surgical Vision, Groningen, NETHERLANDS|D. Dima, Supply Chain, Johnson & Johnson Surgical Vision, Groningen, NETHERLANDS|R. Melikian, RA, Johnson & Johnson Surgical Vision, Santa Ana, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: For the image quality control of intraocular lenses (IOLs), ISO 11979-2 standard recommends the usage of small (2 to 3 mm) apertures for monofocal designs and both small and large (4 to 5 mm) apertures for multifocal ones. Historically, monofocal and multifocal IOL designs from different manufacturers were characterized by various amounts of pupil dependent optical behavior. JJSV developed IOL designs whose image quality is characterized by progressively higher pupil independence. In this context, for selected monofocal and multifocal designs, the current study evaluates the predictive reliability of 5 mm Modulation Transfer Function (MTF) metric for small apertures.

Methods: A large sample of TECNIS monofocal (ZCB00) and TECNIS Synergy (ZFR00V) IOLs was used for the evaluation of image quality in quality control conditions. Optical bench measurements were performed in an ISO11979-2 model eye 2 (c(4,0) = 0.27 micrometers). MTF at FAR was recorded for both 3 and 5 mm pupils and 546 nm wavelength. For each lens model and figure of merit, statistical evaluations were conducted to assess the measurements capability as well as their reliability to detect failed IOLs. Additionally, a correlation analysis by means of 2D histograms was conducted.

Results: For both lens models and MTF FAR metrics the standard deviations were ≤ 0.02 MTF units. Furthermore, the distance from the average to the specification limit for MTF at FAR with 5 mm was higher than 6.0 deviation units. For both lens models, for the 5 mm FAR metric the critical value corresponds to > 99.9% reliability for detecting failed IOLs with 95% confidence. For both lens models, the correlation analysis between the two MTF metrics evidenced a statistically significant ($p < 0.05$) and positive correlation.

Conclusions: For lens model TECNIS monofocal and TECNIS Synergy, the MTF at FAR with a 5 mm pupil is predictive for and more sensitive to variations than MTF at FAR with 3 mm pupil. Therefore, for specific lens designs, since the 5 mm measurement is a worst-case test condition, the addition of small pupil measurement is not relevant for IOL image quality control. Hence, for specific monofocal and multifocal IOL designs the ISO 11979-2 requirements for image quality control might be considered generic.

CONTROL ID: 3711468

SUBMITTER (NAME ONLY): Kieva Byrne

TITLE: Investigating the impact of degenerating photoreceptors on the behaviour of the retinal vasculature

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Byrne, N. Hudson, M. Campbell, Smurfit Institute of Genetics, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The influence of neuronal activity on the behaviour of the vasculature within the CNS is becoming increasingly recognized. Within the retina, this concept is not yet widely explored and the impacts of neuronal cell types such as photoreceptors on the retinal vasculature remain elusive. In this study we make use of the Rhodopsin knockout (Rho KO) mouse model to analyse the effect of decreasing photoreceptor activity on retinal vascular behaviour. In this model the key rod photoreceptor protein, Rhodopsin is knocked out, resulting in a progressive loss of photoreceptors over the course of 16 weeks, thus effectively allowing us to determine the relationship between the activity of these cells and the vasculature of the retina.

Methods: Transcript analyses were performed by quantitative PCR (qPCR) on Rho KO mice at 3-, 6-, 9- and 16-weeks of age, at AM and PM timepoints, and compared to age-matched wildtype controls at the same timepoints. Samples were screened for key Tight Junction proteins.

For immunohistochemical analyses a combination of retinal cryosections as well as retinal flatmounts were utilized at the same ages mentioned and stained with vascular markers such as IB4 and Claudin 5.

Results: Analyses reveal a changing behaviour within retinal vasculature with progressive photoreceptor loss. In particular, Cldn5 expression levels and patterns are altered in the model, with an apparent loss of normal circadian cycling of the gene as well as an overall decreased level of expression in Rho-/-mice. Additional immunohistochemical analyses reveal further changes to vascular patterning including tortuous vasculature in Rho-/- mice. Isolectin staining also reveals potential regression of blood vessels at late stages in this model.

Conclusions: Insights gained from this investigation indicate that loss of photoreceptor activity is impacting the expression profile of key vascular genes and proteins, most especially the key barrier forming component Claudin-5. This is indicative of a cross-communication between these cells and the retinal vasculature and provides some interesting insights into the factors involved in the complex regulation of the retinal vasculature.

CONTROL ID: 3711473

SUBMITTER (NAME ONLY): Karthikeya R

TITLE: Periventricular white matter changes in concomitant strabismus: A magnetic resonance neuroimaging study

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. R, Z. Chaudhuri, Department of Ophthalmology, Lady Hardinge Medical College, New Delhi, Delhi, INDIA|Z. Chaudhuri, P. Kataria, Vision Research Laboratory, Atal Bihari Vajpayee Institute of Medical Sciences & Dr Ram Manohar Lohia Hospital, New Delhi, Delhi, INDIA|U. Garga, Y. Singh, Department of Radio-diagnosis, Atal Bihari Vajpayee Institute of Medical Sciences & Dr Ram Manohar Lohia Hospital, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Retrospective case-control evaluation of neuroimaging findings acquired over 8 years in 6 distinct pediatric groups (142 subjects) was performed to objectively analyse whether periventricular white matter changes on magnetic resonance imaging (MRI) in esotropic (ET) subjects denoted perinatal insults, as anecdotally reported.

Methods: The study cohort comprised developmentally and neurologically normal ET (Group A, n=26, 5.2±3.3 years, 14 males) exotropic (XT, Group B, n=29, 9.1±4.2 years, 14 males) and orthotropic (Group C, n=19, 7.8±4.5 years, 10 males) subjects, as also, children with established perinatal insult and global developmental delay (GDD) presenting with ET (Group D, n=24, 3.3±3.2 years, 17 males), XT (Group E, n=11, 5.8±6.2 years, 7 males) and orthotropia (Group F, n=33, 4.3±3.9 years, 20 males). Sequential brain MRI analysis (1.5T, Siemens Symphony) evaluated gross changes like ventricular dilatation, encephalomalacia and gyral atrophy as well as subtle periventricular and other non-specific white matter changes.

Results: Structural brain parenchymal changes were ubiquitously seen in all three groups with established GDD though they were significantly less in the orthotropic versus the ET group (p=0.007) and completely absent in the group without GDD irrespective of the presence or type of strabismus. Periventricular white matter changes, while observed in all groups was significantly more in all three GDD groups (Group A versus Group D, ET, p=0.004; Group B versus Group E, XT, p=0.0002; Group C versus Group F, orthotropic, p=0.008). Subjects with orthotropia with no GDD had significantly lesser periventricular changes than those with ET and XT (Group D versus Group F, p=0.006; Group E versus Group F, p=0.02).

Conclusions: ET subjects with GDD demonstrated significantly more encephalomalacia than orthotropic subjects with GDD. Significantly greater extent of periventricular white matter changes was observed in developmentally and neurologically normal ET and XT subjects versus orthotropic subjects (Figure 1a-f). This novel clinico-radiological spectrum generates thoughts on its role in the genesis of concomitant strabismus in neurologically normal children.

CONTROL ID: 3711474

SUBMITTER (NAME ONLY): Michael Tseng

TITLE: Applications of Ripasudil Beyond Descemet Stripping Only: A Case Series

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tseng, R. Feder, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Michael Tseng: Commercial Relationship: Code N (No Commercial Relationship) | Robert Feder: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ripasudil is a rho-kinase inhibitor that is approved in Japan as a twice daily treatment for glaucoma. Ripasudil has gained popularity recently, particularly when used in conjunction with Descemet stripping only (DSO) to hasten visual recovery. Ripasudil has been shown to increase corneal endothelial cell proliferation, intercellular adhesion, and decrease endothelial cell apoptosis. We present 4 cases in which persistent corneal edema following various anterior segment surgeries was successfully treated with ripasudil.

Methods: Retrospective chart review revealed 4 patients who were started on ripasudil due to persistent corneal edema that failed to improve with conventional, non-surgical treatments.

Results: All patients were women. The median age was 73 (mean age was 73, range 66-80. Each patient had symptomatic, persistent corneal edema following anterior segment surgery. All cases achieved improved vision and resolution of edema with the use of ripasudil after 4-6 weeks. One patient had a DSEK that required re-bubbling twice, but had persistent nasal detachment and edema involving the visual axis. Topical Ripasudil 4 times daily was initiated. After 1 month the graft was adherent to the host with resolution of edema. One patient had corneal edema involving the temporal 50% of a penetrating keratoplasty graft following routine cataract surgery which did not improve after intensive topical and oral steroids. The edema cleared after one month on ripasudil. Two patients had persistent edema after cataract surgery. Both patients failed to improve over time with topical steroids or hypertonic sodium chloride ointment. Ripasudil improved the patients' edema and vision after 4-6 weeks of use.

Conclusions: In patients with corneal edema resulting from surgical trauma to the endothelium, who failed to clear over time despite conservative measures, ripasudil was shown to be an effective treatment option that helped prevent the need for endothelial transplantation.

CONTROL ID: 3711475

SUBMITTER (NAME ONLY): Nana Yaa Nsiah

TITLE: The Role of Oxidative Phosphorylation in Müller Glia Survival

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Nsiah, D.M. Inman, Pharmaceutical Science, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|N. Nsiah, D.M. Inman, North Texas Eye Research Institute, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Nana Yaa Nsiah: Commercial Relationship: Code N (No Commercial Relationship) | Denise Inman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The importance of mitochondria to the energy production of Müller glia (MG), the main glial cells of the retina, is controversial. Previous studies showed MG are mainly glycolytic. Others challenge this view because MG are deficient in key glycolytic enzymes. Our goal is to potentially settle this debate by destabilizing the electron transport chain in MG mitochondria and assessing how retinal metabolism may be impacted.

Methods: MG that lack oxidative phosphorylation in vivo through destabilization of Complex IV were generated using $GLAST^{CreERT2}::Cox10^{fl/fl}$ transgenic mice. Mice received daily tamoxifen injections for 5 consecutive days beginning at P30. Confirmation of recombination of the floxed Cox10 locus and enzyme activity was performed using PCR analysis of genomic DNA isolated from the retina and sequential cytochrome c oxidase (COX)/succinate dehydrogenase (SDH) histochemistry, respectively. Cell lysates from primary Müller cells were used for western blotting and total protein analysis. Full-field electroretinography (ERG) was performed to assess MG function from transgenic and wild-type mice in vivo. Scotopic ERGs were recorded (OcuScience® HMsERG, Xenotec Inc., Henderson, NV) in response to six light flash intensities ranging from −3 to 1 log cd x s/m^2 on a dark background. Each stimulus was presented in a series of three. Data were analyzed with GraphPad Prism and ERG b-wave amplitudes were compared using a paired two-tailed Student's t-test. The b-wave amplitude was measured from the trough of the a-wave to the peak of the b-wave.

Results: A 465bp DNA fragment amplified from genomic DNA of mutant mice, with no corresponding fragment from control, confirmed Cox10 locus recombination. Total protein analysis, with normalization to the mitochondrial protein VDAC1, showed lower levels of cytochrome c oxidase protein from mutant mice compared to controls. Scotopic ERG b-wave was not significantly different between mutant and wild-type age-controlled mice at all light intensities. No overt retinal abnormalities were observed in $GLAST^{CreERT2}::Cox10^{fl/fl}$ transgenic mice.

Conclusions: Our results show that cre recombinase induction in $GLAST^{CreERT2}::Cox10^{fl/fl}$ successfully inhibits cytochrome c oxidase activity in MG from adult mice. Our in vivo experiments suggest that oxidative phosphorylation is not necessary for Müller glia energy metabolism under physiological conditions.

CONTROL ID: 3711476

SUBMITTER (NAME ONLY): Rosa María Salmerón-Campillo

TITLE: Novel method of measuring not corrected visual acuity with a smartphone

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Salmerón-Campillo, M. Jaskulski, N. Lopez-Gil, Grupo de Investigación en Ciencias de la Visión (CiViUM), Universidad de Murcia Facultad de Óptica y Optometría, Murcia, SPAIN|M. Jaskulski, Clinical Optics Research Lab (CORL), Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|M. Ogino, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|S. Hunter, V. Hussey, D. Suh, R. Gore, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|D. Piña-Miguelsanz, Visionapp Solutions S.L., SPAIN|

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ABSTRACT BODY:

Purpose: Visual Acuity (VA) is usually measured at a distance of 3-6m (10-20 feet) because it is affected not only by neural (i.e. amblyopia) but mostly by optical (i.e. myopia) factors. VA can be measured using a smartphone, however the size of the device's screen can limit the maximum measurement distance to less than 2 m for low VA's due to the target not fitting on the screen. We study a new method to measure VA interactively with smartphones, at a distance comfortable for the patient, avoiding the optical limitations due to its proximity to the patient.

Methods: Standard clinical measurements of not corrected VA were performed in both eyes of 24 subjects of different ages (35 ± 16 years), using an ETDRS optotype placed 6 m away. These measurements were compared with those obtained with a mobile application (app) used on four different devices. The test used for the measurements with the electronic device consisted of a Landolt C optotype following a four-choice algorithm. Target's size is rescaled automatically by a continuous measurement of the distance device-user by means of the front camera of the device. A blue letter on a black background was used as target so that the measurement made at a distance of 1 or 1.5 m was equivalent to that of a black and white test located at a distance of 3 m or infinity, respectively, due to the longitudinal chromatic aberration of the human eye.

Results: The mean difference between clinical and experimental values of VA for both eyes were 0.013 ± 0.155 and 0.009 ± 0.174 logMAR for the test located at 1m and 1.5 m, respectively. The statistical analysis showed no significant differences between the clinical values and those obtained by the device (p-value 0.443 and 0.461 for measurements at 1 and 1.5 m, respectively). Statistical analysis performed for each eye separately yielded similar results.

Conclusions: The results show that it is possible to measure VA with this novel method, and obtain results on par with the clinical standard (mean difference less than one letter on a line). The method can be used to screen for anomalies limiting patients' VA so that they can be referred to an eye care professional, as well as for a remote follow-up of the evolution of a treatment such as amblyopia.

CONTROL ID: 3711477

SUBMITTER (NAME ONLY): John Taylor

TITLE: Qualitative investigation of information behaviour in individuals with visual impairment to inform virtual digital-assistant design

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Taylor, A. Freitas, D. Mendes Ferreira, C. Dickinson, The University of Manchester, Manchester, Manchester, UNITED KINGDOM|A. Subramanian, City University of London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: People living with visual impairment (VI) can find it difficult to access the right information to help support them with their rehabilitation needs. We used a questionnaire and interviews to investigate the information seeking behaviour of individuals with VI and how they would view the use of a virtual digital assistant to obtain information.

Methods: Qualitative data were collected from UK resident adults who were either visually impaired, a carer or family member of someone with VI, or a professional involved in the support of those with VI. A survey was developed and completed online by 120 participants. In addition, 10 in-depth 1:1 semi-structured interviews were conducted to investigate opinions in more detail. Thematic analysis was used to analyse the findings.

Results: Analysis of information needs identified 7 major themes as important: (1) ocular condition (2) equipment, technology and adaptations (3) daily activities (4) registration (5) finance/employment (6) emotional support (7) support for the carer. Participants used a wide variety of methods to access information across a broad range of sources, and highlighted experience of numerous barriers while accessing information. Participants appeared to be accepting of the potential merits of a dialogue system (virtual digital assistant) aiding in a goal-directed search for a specific piece of information, but often expressed reservations about its abilities in other areas such as dealing with more complex issues and providing emotional support. They described potential advantages including: ease of use (accessible format), control over the timing, quantity and type of information provided, help with navigating and integrating the large array of information sources available, and providing a foundation of basic information to help support those who don’t know what to ask about. Participants also reported that information provided needs to be relevant, targeted, understandable, accurate and trusted.

Conclusions: Participants highlighted potential benefits, limitations and requirements in using a digital virtual assistant. These findings will inform the design of a virtual assistant aimed at improving access to information and support for populations with VI.

CONTROL ID: 3711478

SUBMITTER (NAME ONLY): Pedro Gil Fernández

TITLE: The effect of uncorrected astigmatism on the reading performance of contact lens neophytes

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Gil Fernández, J. Tabernero, Electromagnetismo y Electrónica, Universidad de Murcia, Murcia, Murcia, SPAIN|P. Gil Fernández, A. Farcas, C. Hernandez, A. Benito, J. Tabernero, Laboratorio de Óptica, Universidad de Murcia, Murcia, Murcia, SPAIN|

Commercial Relationships Disclosure: Pedro Gil Fernández: Commercial Relationship: Code N (No Commercial Relationship) | Alexandra Farcas: Commercial Relationship: Code N (No Commercial Relationship) | Celia Hernandez: Commercial Relationship: Code N (No Commercial Relationship) | Antonio Benito: Commercial Relationship: Code N (No Commercial Relationship) | Juan Tabernero: Commercial Relationship(s);Code F (Financial Support):Alcon

ABSTRACT BODY:

Purpose: To compare the effect of toric contact lenses versus spherical soft contact lenses on the reading performance of novel contact lens users with low astigmatism.

Methods: The reading test consisted of two paragraphs of 92 and 97 words divided into six lines (Arial 10 font) shown on a 23.6” screen at a reading distance of 60 cm. Reading performance parameters (reading time, number of fixations, number of regressions and magnitude of saccades) were recorded using an eye-tracking device (GP3 HD, Gazepoint, Vancouver, Canada) at a frequency of 150 Hz. Additionally, contrast sensitivity (CS) was measured with a Visual Adaptative Optics simulator (VAO; Voptica SL, Murcia, Spain) at frequencies of 9 and 15 cpd, respectively. Nineteen first-year university students were recruited. They were all contact lens neophytes, divided into two groups, matched by age and refractive error (no statistically significant differences). Subjects in group one (N=10; age 19 ± 2 years; sphere -2.3 ± 0.7 D; cylinder -0.9 ± 0.3 D) were monocularly fitted with a spherical contact lens (Precision1, Alcon Laboratories, Inc, Fort Worth, TX) while subjects in group two (N=9; age 21 ± 3 years; sphere -2.3 ± 1.3 D; cylinder -1.0 ± 0.4 D) were fitted with a toric lens (Precision1 for Astigmatism).

Results: Saccadic regressions during reading were larger ($p<0.05$) in the group of spherical lenses (mean 22 ± 15) than in the group of toric lenses (mean 14 ± 6). On average, all parameters that characterize reading performance showed a similar tendency, being slightly worse and showing more variability in the spherical group than in the toric group of subjects. For instance, the number of fixations, saccade magnitude and reading time reduced by 10%, 9% and 7%, respectively in the toric group compared to the spherical group. We also observed a significant reduction ($p<0.05$) of the contrast sensitivity threshold at 9 cpd from 9 ± 7% in the spherical group to 4 ± 1% in the toric group and also at 15 cpd, with a 52% reduction of the threshold in the toric group.

Conclusions: A full correction of astigmatism with a toric CL (Precision1 for Astigmatism) improved visual performance in a broad sense, with better CS but also better reading performance. These results may suggest instantaneous visual benefits of fitting toric lenses versus spherical lenses in contact lens neophytes with low astigmatism.

CONTROL ID: 3711479

SUBMITTER (NAME ONLY): Lakshman Subbaraman

TITLE: Clinical performance of a novel toric silicone hydrogel contact lens

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Gustafson, The Eye Doctors Inc, Minnesota, UNITED STATES|S. Whaley, Tallahassee Eye Center, Florida, UNITED STATES|B. Giedd, Maitland Vision Center, Florida, UNITED STATES|L.N. Subbaraman, Alcon Research, LLC, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To obtain on-eye clinical performance data and assess contact lens alignment and fit characteristics of a novel toric silicone hydrogel contact lens (verofilcon A) for astigmatism

Methods: In this prospective, open-label, single-arm, bilateral, multicenter clinical study, eyes of healthy participants were fitted with verofilcon A contact lenses. The study evaluated lens alignment and fit characteristics. Lens alignment was determined in terms of the percentage of lenses with axis orientation within ±5°, ±10°, and ±20° from the intended 90° axis; and lens oscillation with blink on a 4-point scale (none, <3°, 3° to 5°, and >5°). The lens fit characteristics were recorded in terms of lens position and movement. Safety endpoints assessed include adverse events (AEs), device deficiencies, and biomicroscopy findings

Results: A total of 39 subjects (78 eyes; mean (SD) age, 34.1 (10.8) years; female, 66.7%) were exposed to study lenses. The mean (SD) lens settling time was 40.1 (56.8) seconds. At 10 minutes, the proportions of lenses orienting within ±20°, ±10°, and ±5° from the intended axis were 100%, 98.7%, and 89.7%, respectively. The mean (SD) absolute axis orientation at 2 minutes was 2.7 (3.6) degrees. The majority of lenses (98.7%) had less than 5° of oscillation or no oscillation with blink. All lenses studied achieved optimal or acceptable fit (optimal, 88.5%; acceptably tight, 6.4%; and acceptably loose, 5.1%) and optimal or acceptable centration (optimal, 97.4%; and acceptable decentration, 2.6%). There were no AEs, device deficiencies, or clinically relevant changes to biomicroscopic findings

Conclusions: The novel toric verofilcon A contact lens showed optimal alignment and fit without any safety concerns. Owing to the unique material features, advanced surface technology, optimal lens alignment, and fitting characteristics of this lens, it could offer astigmats a better contact lens wearing experience

CONTROL ID: 3711481

SUBMITTER (NAME ONLY): Tobias Wimmer

TITLE: Quantification of the porcine Abca4 V1965X Prime Edit gene correction

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Wimmer, H. Sawinski, U. Anne, K. Stieger, Lab experimental Ophthalmology, Justus Liebig Universitat Giessen Fachbereich Medizin, Justus Liebig Universitat Giessen Fachbereich Medizin, Giessen, Hessen, DE, academic/medsch, Giessen, GERMANY|J. Motlik, PIGMOD Center, Libechov, CZECHIA|

Commercial Relationships Disclosure: Tobias Wimmer: Commercial Relationship(s);Code P (Patent):3650557 | Hannah Sawinski: Commercial Relationship: Code N (No Commercial Relationship) | Urban Anne: Commercial Relationship: Code N (No Commercial Relationship) | Jan Motlik: Commercial Relationship: Code N (No Commercial Relationship) | Knut Stieger: Commercial Relationship(s);Code P (Patent):3650557;Code C (Consultant/Contractor):SpliceBio;Code C (Consultant/Contractor):CoaveTx;Code F (Financial Support):CoaveTx

ABSTRACT BODY:

Purpose: The programmable double-strand break (DSB) inducing endonuclease CRISPR/Cas9 has emerged rapidly over the past years. Non-homologous end joining (NHEJ), microhomology mediated end joining (MMEJ) and homology directed repair (HDR) compete in the repair of the DSB, leading to unwanted insertions/deletions. Inactivation of one of the two catalytic active cleavage domains of the Cas9 molecule generates a nicking Cas9 (nCas9), which cleaves only one DNA strand, recruiting single strand repair molecules instead of DSB repair proteins. The Prime Edit (PE2) system uses a transcriptase fused to an nCas9 in combination with an extended prime edit guide RNA (pegRNA) containing a transcriptase template harboring the desired edit. The PE3 system uses an additional nicking guide RNA (ngRNA) targeting the opposite DNA strand. Employing the PE system, we aim to quantify the correction efficiency of the porcine Abca4 V1965X mutation (insertion of an adenine), using a cellular bioluminescence resonance energy transfer (BRET) based reporter system.

Methods: Porcine Abca4 sequence containing the target mutation was cloned into the BRET reporter plasmid. Overall, 15 different pegRNAs were designed and cloned into a plasmid containing a U6 RNA promotor. HEK293-T cells were transfected with the Prime Edit Cas9, pegRNA (with/without additional nicking guide RNAs) and the BRET reporter. Correction of the target was analyzed by fluorescence microscopy, western blot and a BRET assay.

Results: Prime editing using the PE2 system did not result in a significant correction as shown by western blot, fluorescence microscopy and the BRET assay. Additional nicking of the opposite DNA strand with the PE3 system generated a massive enhancement in correction activity of up to 91 ± 5 % measured with the BRET assay in dependence of pegRNA composition and ngRNA nicking position. Resulting correction measured with the BRET assay could be verified by fluorescence microscopy and western blot.

Conclusions: We showed that the correction of an adenine insertion using the Prime Edit system can be reliably measured and quantified with the cellular BRET assay. Especially the PE3 can be a potential alternative to MMEJ- and HDR-based genome editing approaches, with comparably high correction rates, notably in post-mitotic cells.

CONTROL ID: 3711486

SUBMITTER (NAME ONLY): Pearse Keane

TITLE: Disease activity (DA) monitoring in neovascular age-related macular degeneration (nAMD) with artificial intelligence (AI): a feasibility study

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sahni, Z. Mulyukov, D. Lorand, Novartis Pharmaceuticals AG, SWITZERLAND|P.A. Keane, NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye Hospital, UNITED KINGDOM|S. Liakopoulos, Department of Ophthalmology, Faculty of Medicine and University Hospital Cologne, GERMANY|K. Hatz, Vista Klinik AG Binningen, SWITZERLAND|D. Ting Shu Wei, Yong Loo Lin School of Medicine, National University of Singapore, SINGAPORE|R. Gallego Pinazo, Oftalvist Clinic, Valencia, SPAIN|K. Hatz, Universitat Basel Medizinische Fakultat, Basel, Basel-Stadt, SWITZERLAND|P.A. Keane, UCL Institute of Ophthalmology, London, UNITED KINGDOM|S. Liakopoulos, Department of Ophthalmology, Goethe University, Frankfurt, GERMANY|

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ABSTRACT BODY:

Purpose: DA assessed using optical coherence tomography (OCT) imaging and visual parameters is important for monitoring nAMD. We developed an AI-based DA model to support physicians who treat patients with nAMD with anti-vascular endothelial growth factor (VEGF) agents. We assessed the performance of the DA model in deriving a DA score in an adjudication study.

Methods: Measurements of OCT features and best-corrected visual acuity collected from patients evaluated with Heidelberg spectral domain (SD)-OCT during the phase 3 brolucizumab versus aflibercept HAWK (NCT02307682) & HARRIER (NCT02434328) (H&H) studies were used to develop an AI-based DA model. A retrospective review of selected DA assessments from the H&H dataset was conducted with an independent panel of 10 retina specialists (RS) to further train the model. DA was deemed to be present if the RS indicated treatment was needed and absent if no treatment was indicated. Three categories of DA assessment were defined using model-derived DA score and prediction uncertainty (Table 1).

Results: To train the DA model, 8970 longitudinal DA assessments from a total of 948 patients evaluated with Heidelberg SD-OCT by H&H study investigators were used. This model achieved a cross-validated accuracy of 0.84 (0.87 sensitivity, 0.84 specificity). The RS panel reviewed 486 selected DA assessments from 403 patients. Figure 1 shows the accuracy, sensitivity, and specificity achieved by RS, H&H investigators, and DA model for three categories of DA assessment. The DA model reached 0.94 accuracy and performed as well as RS and H&H investigators for ‘easy’ DA assessments. While the DA model outperformed H&H investigators for both ‘potential label noise’ (accuracy 0.67 vs 0.38) and ‘difficult’ DA assessments (accuracy 0.74 vs 0.58), the DA model underperformed the RS in these categories (mean RS accuracy 0.86 for ‘difficult’ and 0.82 for ‘potential label noise’ assessments).

Conclusions: In this study, we demonstrated encouraging performance of a model in detecting DA in nAMD patients treated with anti-VEGF agents. While further refinements and improvements are planned, these preliminary results suggest the potential of an AI-based DA algorithm in improving the consistency of treatment decisions based on DA assessments.

CONTROL ID: 3711487

SUBMITTER (NAME ONLY): James Willoughby

TITLE: Object detection on medical images with the aid of contrastive gated attention

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Sallo, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|M. Zouache, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|M. Cilkova, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A. Dubis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|W. Lilaonitkul, University College London Institute of Health Informatics, London, UNITED KINGDOM|J. Willoughby, A. Dubis, Joint Library of Ophthalmology Moorfields Eye Hospital and UCL Institute of Ophthalmology, London, London, UNITED KINGDOM|W. Lilaonitkul, Health Data Research UK, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Deep learning enhanced computer aided diagnoses have the potential to help increase the efficiency of image heavy clinical workflows. However, performance of medial deep learning is often limited by (i) lack of large medical training sets due to the high cost of annotations (ii) the heterogeneous, and subtle feature differences in objects of interest. In this work we propose that the inherently structured anatomical topology of a given imaging modality can be leveraged to allow a CNN to learn a more robust embedding by contrasting pairs of normal and abnormal images thereby improving the performance of object detection on pathological features.

Methods: This project leveraged open source Heidelberg Spectralis AMD OCT*, with 600 images expertly annotated for 9 classes of features of interest were. A YOLOv4 network was adapted to contain a novel contrastive induced gated attention module (CIGA) which leverages the anatomical topology to aid detection of pathological objects. The baseline YOLOv4 network was trained on the OCT images and the performance of the CIGA module was assessed by fine-tuning the baseline with the CIGA. The training process was performed with multiple repeats.

*Reza et al, IEEE Transactions on Medical Imaging, 37(4):1024-1034, (2018)

Results: The fine-tuning with the CIGA module produced better overall MAP50 values than the baseline network alone. The CIGA network produced an overall test MAP50 of 0.654(0.023) compared to the baseline performance of 0.635(0.01) and a test mAP50:95 of 0.369(0.007) compared to the baseline performance of 0.355(0.01). Performance was also assessed for the nine classes of pathological feature such as Hyperfluorescent spots where the CIGA achieved an MAP50 of 0.732(0.049) compared to the baseline 0.680(0.021) and PR layer disruption where the CIGA achieved an MAP50 of 0.712(0.095) compared to the baseline performance of 0.635(0.018).

Conclusions: In this work we propose the CIGA network and demonstrate incremental performance gains for the task of object detection in OCT scans. This was achieved by leveraging the structured topological information in the anatomy with the help of gated attention under a contrastive learning framework to enhance the signal of the different pathological objects. This method will improve detection of small biomarkers from imaging, which are traditionally difficult to detect using traditional deep learning methods.

CONTROL ID: 3711488

SUBMITTER (NAME ONLY): wim Quint

TITLE: Post-GWAS screening of candidate genes for refractive error in mutant zebrafish.

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Quint, K. Tadema, N. Kokke, R. willemsen, A. iglesias, Department of Clinical Genetics, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|W. Quint, K. Tadema, N. Kokke, M. Meester, C.C. Klaver, A. iglesias, Department of Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: In the last decade, association studies have focused on dissecting the genetic factors underlying refractive error (RE). These studies resulted in the identification of almost 500 associated loci and potential candidate genes. To explore the genetic mechanisms driving RE development, we made a prioritization of 11 candidate genes based on biological and statistical evidence (i.e., PRSS56, FBN1, TJP2, PDE11A, SHISA6, LAMA2, LRRC4C, KCNQ5, GNB3, RBFOX1, and GRIA4), and generated mutant zebrafish models. In these models, we screened for abnormalities in axial length (AL) and refractive status.

Methods: Published transcriptome databases were assessed to examine whether candidate genes were expressed in human ocular tissues; expression in zebrafish ocular tissue was confirmed by RT-PCR. CRISPR-cas9 was used to generate 11 mutant zebrafish lines. Ocular biometry assessment was performed in lines without large morphological abnormalities and normal breeding rates (n=8). AL was measured at 2 and 4 months (n=20 eyes per group) using Spectral Domain Optical Coherence Tomography which visualized the entire eye; refractive status was measured using a custom eccentric photorefraction setup.

Results: Our database search and expression study in the zebrafish eyes confirmed that all genes were expressed throughout human and zebrafish eyes. Three of the eight studied mutant lines (lama2$^{-/-}$, lrrc4c$^{-/-}$, kcnq5$^{-/-}$) showed a significant ($p<0.01$) increase in AL and corresponding myopic shift in refractive status ($p<0.01$). Two of the three mutants showed the largest increase in AL at 2 months (lrrc4c$^{-/-}$: 140 µm, kcnq5$^{-/-}$: 151 µm) which stabilized at 4 months (lama2$^{-/-}$: 69 µm, lrrc4c$^{-/-}$: 114 µm, kcnq5$^{-/-}$: 92 µm). In line with previous reports in other animal models, the prss56$^{-/-}$ mutant showed a significant reduction in AL (-157 µm, $p<0.001$) and a nanophthalmos-like phenotype at 2 and 4 months. In the other four studied lines (fbn1$^{-/-}$, tjp2$^{-/-}$, pde11a$^{-/-}$, shisa6$^{-/-}$) no significant changes in AL were observed.

Conclusions: Of the eight mutants lines, four showed a change in refractive status. Our study provides functional evidence that these candidate genes selected from GWAS studies induce changes in eye growth and presents new zebrafish eye models for the study of refractive error.

CONTROL ID: 3711489

SUBMITTER (NAME ONLY): Phattharaphong Tantichariyangkul

TITLE: Visual Performance of 2 Trifocal Intraocular Lens Models in Different Illuminance

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tantichariyangkul, B. Khambhiphant, Ophthalmology, King Chulalongkorn Memorial Hospital, Bangkok, THAILAND|

Commercial Relationships Disclosure: Phattharaphong Tantichariyangkul: Commercial Relationship: Code N (No Commercial Relationship) | Bharkbhum Khambhiphant: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the monocular and binocular corrected defocus curves between 2 non-toric trifocal IOL models in 3 different illuminance conditions.

Methods: Patients who underwent phacoemulsification by a single surgeon with bilateral implantation of TFNT00 or ATLISA TRI839 IOLs were enrolled in this study. The main outcome was the comparison of the binocular and the monocular corrected defocus curves plotted from the distance-corrected visual acuity (DCVA) between 2 IOLs within 3 different ambient illuminations of 360, 130, and 30 lux. The uncorrected distance visual acuity (UDVA), distance-corrected intermediate (DCIVA), and near visual acuity (DCNVA) were also measured. Mixed-model analysis of variance (ANOVA) and multilevel mixed-effects linear regression were used to determine the difference of DCVA at each defocus step.

Results: Seventeen patients aged 50 to 77 years with 34 eyes, 9 of whom had bilateral TFNT00 implantation and 8 had bilateral ATLISA TRI839, were enrolled in the study. The average UDVA of TFNT00 and ATLISA TRI839 implanted eyes were 0.003 and 0.029 LogMAR respectively. The monocular corrected defocus curve showed significantly higher visual acuity for TFNT00 at intermediate range (-1.5 D) at 130 and 30 lux, and also (-2.0 D) at 360, 130, and 30 lux (all $p < 0.05$). At near range (-3.0 D), the monocular corrected defocus curve showed significantly higher visual acuity for ATLISA TRI839 at 130 and 30 lux (all $p < 0.05$). There was no significant difference of monocular corrected defocus curve at distant range (+1.0 D to -1.0 D) and at near-intermediate range (-2.5 D) between 2 IOLs. Binocular corrected defocus curves showed no significant difference between 2 IOLs in all illuminance conditions.

Conclusions: Monocular implantation of TFNT00 yielded better intermediate visual acuity scores at all illuminance whereas ATLISA TRI839 performed better at near range in dimmer conditions. There was no significant difference of binocular DCVA between these 2 IOL models.

CONTROL ID: 3711490

SUBMITTER (NAME ONLY): Landon Rohowetz

TITLE: Pars Plana Vitrectomy with Endolaser Panretinal Photocoagulation for Patients with Proliferative Diabetic Retinopathy: A Ten-Year Retrospective Study

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.J. Rohowetz, V. Patel, M. Kalavar, N. Yannuzzi, J. Sridhar, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To review outcomes of patients with proliferative diabetic retinopathy (PDR) who received pars plana vitrectomy (PPV) with endolaser panretinal photocoagulation (PRP).

Methods: Retrospective chart review study that included patients who underwent PPV with endolaser PRP between June 1, 2010 to May 31, 2020.

Results: PPV with PRP was performed in 287 eyes of 250 patients. Two hundred forty-six (85.7%) eyes had preoperative vitreous hemorrhage (VH) and 114 (39.7%) eyes had preoperative retinal detachment (RD). Mean preoperative best-corrected visual acuity (BCVA) was 20/781. Mean postoperative BCVAs were 20/150, 20/142, 20/150, 20/136, and 20/142 at 3 months, 6 months, 12 months, 2 years, and 3 years, respectively ($P < 0.001$). Postoperative complications included VH (18.1%), RD (12.5%), cataract (31.6%), macular hole (2.1%), and endophthalmitis (1.0%). There were negative correlations between age and BCVA at 12 months ($r = -0.27$, $P = 0.002$), 2 years ($r = -0.28$, $P = 0.007$), and 3 years ($r = -0.28$, $P = 0.009$) postoperatively. Individuals with hypertension had worse visual acuity than individuals without hypertension at 3 months ($P = 0.02$), 6 months ($P < 0.001$), and 12 months postoperatively ($P < 0.001$). Individuals with hypertension were also more likely to undergo an additional PPV than individuals without hypertension ($P = 0.002$). Eyes with traction on ultrasound had a greater frequency of postoperative VH ($P < 0.001$), cataract ($P < 0.001$), and need for additional PPV ($P = 0.001$) and PRP ($P < 0.001$) compared to eyes without traction. Patients with type 2 diabetes had superior postoperative BCVA at 2 years ($P = 0.004$) and 3 years ($P = 0.02$) compared to patients with type 1 diabetes. Preoperative PRP, anti-vascular endothelial growth factor, aspirin, warfarin, and clopidogrel therapy were not associated with superior postoperative visual acuity or reduced rates of postoperative complications including VH ($P > 0.05$). There were no relationships between postoperative BCVA and hemoglobin A1c, duration of diabetes, duration of PDR, smoking history, hemodialysis status, or insulin dependence ($P > 0.05$).

Conclusions: PPV with PRP yields significant improvements in visual acuity. Certain factors including diabetes type, hypertension, age, and preoperative exam findings may affect postoperative outcomes.

CONTROL ID: 3711493

SUBMITTER (NAME ONLY): Alfredo Dueñas Rey

TITLE: Identification and characterization of a novel retina-specific lncRNA upstream ABCA4 with a potential role in ABCA4-associated inherited retinal disease

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Dueñas Rey, V. López-Soriano, M. Bouckaert, E. D'haene, M. Bauwens, S. Lefever, E. De Baere, F. Coppieters, Universitair Ziekenhuis Gent Centrum Medische Genetica Gent, Gent, BELGIUM|A. Dueñas Rey, V. López-Soriano, M. Bouckaert, J. Verwilt, E. D'haene, M. Bauwens, S. Lefever, E. De Baere, F. Coppieters, Department of Biomolecular Medicine, Universiteit Gent Faculteit Geneeskunde en Gezondheidswetenschappen, Gent, BELGIUM|Z. Corradi, F.P. Cremers, Radboudumc Department of Human Genetics, Nijmegen, Gelderland, NETHERLANDS|C. Dhaenens, Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, Lille, FRANCE|J. Verwilt, OncoRNALab, Cancer Research Institute Ghent, Ghent, BELGIUM|A.M. Watson, M. Lako, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|K. Ruiz Ceja, S. Banfi, Telethon Institute of Genetics and Medicine, Napoli, Campania, ITALY|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRDs) are a major cause of early-onset vision loss. While mutations in coding regions explain 60% of IRDs, non-coding variants can be a source of missing heritability. A major knowledge-gap lies in the role of long non-coding RNAs (lncRNAs), highly tissue-specific molecules that regulate gene expression at the right time and place. However, little is known about their function in the retina. Here we identified a novel retina-specific lncRNA located upstream ABCA4, the gene implicated in Stargardt (STGD1) disease.

Methods: Expression specificity was determined by re-analysis of published short-read RNAseq data (GTEx, adult human retina, retinal organoids) as well as single-cell data (adult human retina). Long-read sequencing on adult human retina was performed using nanopore sequencing (PCR-cDNA kit, PromethION, ONT). Single-molecule RNA in situ hybridization (RNAScope/BaseScope) was conducted to elucidate cell-type expression. Chromatin interaction profiles (UMI-4C) were generated to evaluate interaction with the ABCA4 promoter. Genomic variation was evaluated in smMIPS data of the ABCA4 locus in 1,054 STGD1 cases.

Results: Short-read RNAseq analysis of ~7,400 transcriptomes of 54 tissues (GTEx) and 152 transcriptomes of adult human retinas revealed a potential novel lncRNA upstream of ABCA4, with expression restricted to the human retina. Long-read sequencing of donor retina identified at least two novel multi-exonic isoforms, for which expression was demonstrated in the outer nuclear layer of adult human retina. The lncRNA is transcribed from an active retinal enhancer interacting with the ABCA4 promoter, suggesting a cis-acting effect on ABCA4. In smMIPS data from 1,054 STGD1 cases we identified 5 heterozygous novel copy number variants overlapping the lncRNA, representing likely pathogenic or modifying alleles. Perturbation knockdown studies in human retinal explants are ongoing to further elucidate its function.

Conclusions: We identified and characterized a novel retina-specific lncRNA, potentially implicated in ABCA4-associated IRD. This study provides novel insight into the role of this lncRNA - an unexplored class of molecule in the

retina field - in gene regulation and IRD pathogenesis, which may ultimately entail therapeutic perspectives.

CONTROL ID: 3711494

SUBMITTER (NAME ONLY): Rebecca King

TITLE: Analysis of Retinogeniculate Synapses in the DBA/2J Mouse Model of Glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. King, Virginia Tech Carilion School of Medicine, Roanoke, Virginia, UNITED STATES|A. Monavarfeshani, M. Fox, Fralin Biomedical Research Institute at VTC, Roanoke, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a degenerative disease of retinal ganglion cells (RGC). More than 30 distinct types of RGCs exist in the mammalian retina, and studies of experimental glaucoma suggest that some types may be more vulnerable to injury from elevated intraocular pressure (IOP). In addition to different morphologies, functional responses, and susceptibility to neurodegeration, RGCs form different types of synapses in retinorecipient nuclei. For example, in the mouse dorsal lateral geniculate nucleus (dLGN), RGC axons generate both simple (single retinal input) and complex (multiple retinal inputs converging on shared regions of relay cell dendrite) retinogeniculate (RG) synapses. At present, it is unclear whether simple and complex RG synapses are generated by distinct RGC types. Here, our goal was to enhance our understanding of RGC vulnerability to injury from elevated IOP by exploring changes to simple and complex RG synapses in the DBA/2J (D2) mouse model of glaucoma.

Methods: To assess RG synapse morphology, we employed serial block-face scanning electron microscopy (SBFSEM), which was performed on dLGN from D2 mice at 6 and 9 months of age. Image analysis and quantification was performed using TrakEM2 in Fiji. Retinal terminals, their axons, and the post-synaptic relay cell dendrites were traced throughout the volume of imaged tissue. At least 50 distinct axons were traced in each data set. Retinal bouton size, complexity, and active zone numbers were quantified and compared to controls.

Results: SBFSEM shows axons with dark axoplasm, a sign of axon degeneration, in the 9-month D2 data set and abnormal membranous organelles in relay cell dendrites in both data sets. In a preliminary analysis of data collected to date, 57% of RG synapses in D2 mice were classified as complex compared to 90% in controls. Additionally, only 11% of complex synapses in D2 mice contained 4 or more retinal terminals while the vast majority (86%) of complex synapses in control mice contained 4 – 14 retinal terminals.

Conclusions: Evidence of axon degeneration suggests the SBFSEM data sets being analyzed are from glaucomatous D2 mice. Currently, our results indicate that glaucomatous D2 mice exhibit changes in relay cell dendrites before axon withdrawal and have significantly fewer complex RG synapses with fewer retinal terminals per complex synapse than controls.

CONTROL ID: 3711495

SUBMITTER (NAME ONLY): Alain Jacot-Guillarmod

TITLE: Normative database of cone photoreceptors in Confocal and Calculated-split Adaptive Optics Scanning Laser Ophthalmoscope images

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Characterizing the photoreceptor mosaic morphology is essential to understand the basis of vision in normal subjects and to detect disease. A novel technique to visualize these cells in vivo is through an Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO). After visualization of these cells, the next challenges is the development of robust, accurate, and automated cell detection strategies. This is followed by the challenge of defining the normal parameters of cone density, thereby allowing more precise and accurate detection of pathological anomalies. This project seeks to identify the correct combination of cell detection strategies to build and annotate a normative database.

Methods: A bespoke BMC Apaeros built AOSLO was used. Images were acquired using 1.5×1.5° FOV at 49 locations in 35 healthy subjects. Images were stabilized and averaged using BMC's proprietary AOImageProcessing software. Two cell detection strategies were used, depending on the eccentricity. For foveal and parafoveal regions (0° to 3°), an original intensity-based image analysis method was developed, which we called Automatic Adaptive Thresholding and Maxima Search (ATMS). To more peripherical regions (4° to 10°), a recently published Deep Learning method was applied (without retraining) (MDRNN, by Davidson et al., 2018).

Results: A normative database of cone density was built in all four cardinal meridians from 0° to 10° eccentricities, currently comprising 35 subjects divided into 3 groups defined as [age range; Male/Female; mean axial length +/- stdev]. Group 1 - 20 to 35; 4/7; 25.09 +/- 1.24; group 2 - 36 to 50; 4/9; 23.91 +/- 1.15; group 3 - 51 to 65; 2/9; 23.67 +/- 0.87. Cone density estimates were consistent with measurements reported in other normative databases (e.g. Chang et al., 2013, Woog et al., 2018).

Conclusions: This normative database of cone density was created using a pipeline based on a combination of cell detection strategies optimized to be effective at different eccentricities, which included an original algorithm for automatic cone count in the fovea. This normative database offers support for the stratified analysis of the relationship between (several) eye phenotypes and cone photoreceptor density. Leveraging our automatic method, the database will incrementally grow through consenting patients at our hospital and through cooperations with other research groups.

CONTROL ID: 3711496

SUBMITTER (NAME ONLY): Ya Ma

TITLE: Mutations in TENM4 and CSMD1 are Associated with High Myopia in a Chinese Cohort

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ma, R. Shen, H. Mou, Z. Jin, Beijing Institute of Ophthalmology, Beijing, Beijing, CHINA|Y. Ma, R. Shen, H. Mou, Z. Jin, Beijing Tongren Hospital, Beijing, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: We previously proposed that TENM4 and CSMD1 are susceptible causative gene for high myopia (PNAS 2017). This study aims to investigate the prevalence of TENM4 and CSMD1 variants in pathologic myopia (PM) in a Chinese cohort.

Methods: One hundred unrelated non-syndromic PM patients were recruited in this study. Patients with fundus changes including posterior staphyloma and myopic maculopathy equal to or more serious than diffuse choroidal atrophy were defined as PM. DNA were subjected to whole-exome sequencing. Variants of TENM4 and CSMD1 were selected and analyzed by multistep bioinformatics analyses.

Results: Pathologic mutations of TENM4 and CSMD1 were detected in 15 (15%) and 8 (8%) unrelated patients respectively. These mutations were rare or absent in the 1000 Genomes Project and Exome Aggregation Consortium. Age and axial length distribution are presented in figures below.

Conclusions: TENM4 and CSMD1 might be responsible for high myopia. This finding provides supportive information for further study of causative gene of high myopia.

CONTROL ID: 3711497

SUBMITTER (NAME ONLY): Samar Al-Swailem

TITLE: Population perceived eye strain due to digital devices usage during COVID-19 pandemic

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Al-Swailem, A.M. Almalki, M. Alblowi, A. Aldosari, R. Khandekar, Research, King Khaled Eye Specialist Hospital, Riyadh, Riyadh, SAUDI ARABIA|A.M. Almalki, A. Aldosari, Ophthalmology, 2.King Abdulaziz Medical City, Jeddah, Saudi Arabia, Jeddah, Jeddah, SAUDI ARABIA|R. Khandekar, Ophthalmology, University of British Columbia, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Lockdowns from the COVID-19 caused a significant increase in the use of digital devices. This increase could result in ocular sequelae such as eyestrain. We used a cross-sectional survey to assess the magnitude severity and determinants of eye strain among Saudi population during the COVID-19 pandemic, lockdown and abuse of digital devices.

Methods: Saudi population of both genders, aged > 15 years old were invited. The questionnaire included demography, eye strain related symptoms, severity, and use of optical aid during covid-19 lockdown. The frequency and severity of eye strain were calculated. Based on the sum of 15 eye strain related sign and symptom, Computer Vision Syndrome (CVS) score was graded as none/ mild moderate and severe CVS. CVS was associated/correlated to determinants. The total score was calculated using a formula score of A X B for each sign and symptom,. The sum of 15 eye strain related sign and symptom score was further graded as <30 = no or mild CVS, 30 to 59 = moderate CVS and more than 60 = severe CVS.

Results: There were 2,009 surveyed participants. Their median age was 20 years. The purpose of using digital devices was work and social purposes for 68.4%, and 61% used the digital devices for more than 6 hours daily. The prevalence of knowledge about CVS and '20-20 rule for using digital devices' was 9.4% and 6.9 respectively. Two hundred and eighty-two (14%) of the study participants were diagnosed with COVID-19, and 223 (11.1%) were quarantined. Three fourth of participants did not use contact lens (CL) or spectacles, 393 (19.6%) were using spectacles, 59 (2.9%) were using CL and 55 (2.7%) were using both Spectacles and CL. The most experienced symptoms of eye strain due to digital devices use were headache, burning, itching, tearing, and redness of eyes. The median of eye strain symptom score was 20 (IQR 10: 32). Based on the symptom score, 'no/ mild' grade of eye strain was perceived by 1,486 (74%), moderate eye strain by 468 (23.3%) and severe eye strain by 55 (2.7%) participants. The daily six hours usage of digital devices was found to have a significant and positive association to the eye strain severity grade during COVID-19 lockdown.

Conclusions: Saudi-population suffered from eye strain during COVID-19 lockdown due to excessive digital devices use. Health care provider should educate general population about healthy measures during daily use of digital devices.

CONTROL ID: 3711498

SUBMITTER (NAME ONLY): Sarah Doyle

TITLE: Innate immune adapter SARM1 drives photoreceptor death in models of retinal degeneration

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Doyle, E. Ozaki, L. Gibbons, N. Neto, C. Greene, M. Carty, M. Monaghan, M. Campbell, A. Bowie, The University of Dublin Trinity College, Dublin, IRELAND|S. Doyle, E. Ozaki, L. Gibbons, Trinity College Institute of Neuroscience, Dublin, IRELAND|

Commercial Relationships Disclosure: Sarah Doyle: Commercial Relationship(s);Code F (Financial Support):Roche | Ema Ozaki: Commercial Relationship: Code N (No Commercial Relationship) | Luke Gibbons: Commercial Relationship: Code N (No Commercial Relationship) | Nuno Neto: Commercial Relationship: Code N (No Commercial Relationship) | Chris Greene: Commercial Relationship: Code N (No Commercial Relationship) | Michael Carty: Commercial Relationship: Code N (No Commercial Relationship) | Michael Monaghan: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Campbell: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Bowie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: SARM1 (sterile alpha and armadillo motif-containing protein) is a highly conserved Toll/IL-1 Receptor (TIR) adaptor with important roles in mediating immune responses. Studies in the CNS have shown that SARM1 plays a role in induction of neuronal axon degeneration in response to a variety of injuries. Activated SARM1 consumes essential metabolite NAD^+ leading to cellular metabolic catastrophe and axon degeneration. Retinal degenerative diseases (RDDs), such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD), are leading causes of incurable blindness and share a common endpoint, the degeneration of specialized neurons; photoreceptor cells. We sought to investigate whether SARM1 serves a pro-degenerative function during photoreceptor cell degeneration in models of RDD.

Methods: Using models of photoreceptor ($Rho^{-/-}$ mice) and RPE (intravenous administration of sodium iodate) degeneration we investigated the role of SARM1 during retinal degeneration, by generation of $Rho^{-/-}Sarm1^{-/-}$ mice and use of $Sarm1^{-/-}$ mice respectively. We performed ocular coherence tomography (OCT), electroretinography (ERG) and histological analysis of retinal tissue sections to characterize the extent of retinal degeneration in these models in the absence of SARM1. We performed fluorescence lifetime imaging microscopy (FLIM) on retinal explant tissue to measure the levels of NADH in the $Rho^{-/-}$model in the presence of absence of SARM1.

Results: In both models Sarm1 deficiency delayed retinal degeneration, preserving photoreceptor cells as assessed by both OCT and hematoxylin & eosin staining of tissue sections. In $Rho^{-/-}$ mice there is reduced NADH levels at 4 weeks of age, this is in contrast to $Rho^{-/-}Sarm1^{-/-}$ mice where NADH pools are maintained. As NADH exists in a relationship with NAD^+ we can infer that SARM1 is cleaving NAD^+ during retinal degeneration in this model. ERG analysis demonstrates preserved function of photoreceptor cones in the RDD models in the $Sarm1^{-/-}$ mice, indicating that the preserved photoreceptor cells are viable and retain light sensitivity for a visual response.

Conclusions: Our present data identifies a previously unappreciated role for SARM1 in photoreceptor cell death but not RPE cell death. SARM1 serves a distinct function in the course of photoreceptor degeneration to its previously described role in other neuronal cell types mediating cell death in addition to axon degeneration.

CONTROL ID: 3711502

SUBMITTER (NAME ONLY): Huibert Simonsz

TITLE: Availability of data for cost-effectiveness comparison of vision screening programmes

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.J. Simonsz, J. Kik, Ophthalmology, Erasmus MC, Rotterdam, NETHERLANDS|H.J. Simonsz, Retina Signal Processing lab, Netherlands Institute for Neuroscience, Amsterdam, NETHERLANDS|E. Heijnsdijk, Public Health, Erasmus MC, Rotterdam, NETHERLANDS|A. Mackey, I. Uhlén, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|G. Carr, Independent Consultant, UNITED KINGDOM|A. Horwood, University of Reading, Reading, Berkshire, UNITED KINGDOM|M. Fronius, Goethe-Universitat Frankfurt am Main, Frankfurt am Main, GERMANY|J. Carlton, School of Health and Related Research, University of Sheffield, Sheffield, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: When the methods and data of vision screening programmes are known in detail, and software is available to calculate their cost-effectiveness, it should be possible to compare their cost-effectiveness. We assessed the current state of data collection and its availability in all countries in Europe.

Methods: In the EUSCREEN Survey (2017-2019) representatives of 42 European countries provided data on demography, existing screening programmes, coverage and attendance, screening tests, follow-up, diagnosis, treatment, benefit and adverse effect of screening. As part of the EUSCREEN Study, software was developed to calculate the cost-effectiveness of screening programmes (miscan.euscreen.org). By sensitivity analysis 6 items essential for cost-effectiveness analysis were identified: prevalence, sensitivity, specificity, coverage, attendance, loss to follow-up. Five others: age at screening, screening test, test threshold, screening professional and costs are determined in the screening protocol or can be calculated with relative ease. In the autumn of 2021, Survey items on data collection, monitoring and evaluation, and the six items essential for cost-effectiveness analysis were updated with an additional questionnaire.

Results: Data was obtained from all countries in Europe and Israel and Turkey, not from Norway and Portugal. For 3 countries, vision screening was reported for a large region instead of a country. The practice of data collection in vision screening was reported in 36% (N=42) of countries; collected data were published in 10%. Procedures for quality assurance in vision screening were reported in 19%, research of screening effectiveness in 43%, whereas cost-effectiveness analysis was performed in 12%. Data on prevalence of amblyopia were reported in 40% of countries, on sensitivity of screening tests in 17%, on their specificity in 19%, on coverage of screening in 45%, on attendance in 21% and on loss to follow-up in 12%.

Conclusions: Data collection in vision screening programmes is deplorable: data essential for cost-effectiveness comparison could not be reported from most countries. It mostly takes place at a local or regional level, for quality assurance or for accountability to commissioners, and the data is often not accessible. The resulting inability to compare cost-effectiveness of vision screening programmes perpetuates their diversity and inefficiency.

CONTROL ID: 3711503

SUBMITTER (NAME ONLY): Sacha Reichman

TITLE: Human iPSC-based retinal cell library for disease modeling and drug discovery

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Reichman, C. Nanteau, M. Clémençon, M. Lechuga, X. Guillonneau, J. Sahel, O. Goureau, S. Gozlan, Institut de la vision, Paris, Île-de-France, FRANCE|S. Reichman, M. Clémençon, S. Gozlan, Sorbonne Universite, Paris, Île-de-France, FRANCE|X. Guillonneau, O. Goureau, INSERM, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The possibility to make a “Disease-in-a-Dish” using patient-derived induced pluripotent stem cells (iPSCs) represent an unexpected opportunity to elaborate useful research tools for drug development. Part of the challenge in cell-based drug discovery is the production of large number of identical cells of interest. In this way, we present here innovative cell-based approaches for large production and banking of specific epithelial, glial or neuronal retinal cells to model retinal dystrophies as retinitis pigmentosa (RP), diabetic retinopathy (DR) or age-related macular degeneration (AMD).

Methods: Defined culture of adherent human iPSC (hiPSCs), floating hiPSC-derived retinal organoids (ROs) and RO-isolated retinal progenitor cells (hiRPCs) were used to produce all retinal cells types. HiPSC-derived retinal pigmented epithelial cells (hiRPE) were produced directly from adherent hiPSC cultures. HiPSCs-derived Muller glial cells (hiMGCs) were selected and expanded from mature ROs. Expandable and multipotent hiRPCs were selected from early ROs using innovative culture conditions and RPC-dedicated medium.

Results: Both hiRPE, hiMGCs and multipotent hiRPCs can be cryopreserved while retaining their proliferation capacity for large-scale productions. The development of a hiRPE-based model of retinitis pigmentosa coupled to high throughput screening (HTS) identified potential repositionable drugs from the FDA-approved compound library. HiMGCs recapitulated inflammatory and angiogenic features of DR in pathological-like culture condition compatible with HTS. Different neuroretinal cells such as photoceptor precursors, ganglion, amacrine and horizontal cells can be easily differentiated from previously expanded hiRPCs. Moreover, specific culture conditions to direct photoreceptor differentiation of hiRPCs allowed the production of large and high enriched cultures of photoceptor precursors (>90%) in 2 weeks without purification step.

Conclusions: Large-scale productions of relevant human retinal cells such as hiRPEs, hiMGCs, hiRPCs and photoreceptor precursors are now available. This retinal cell library offers new biological tools to better understand the different retinal dystrophies and to develop new treatments adapted to each type of the disease.

CONTROL ID: 3711504

SUBMITTER (NAME ONLY): Ruofan Han

TITLE: Retinal expression profile of SpCas9 and EGFP in the CRISPR-Cas9 knockin mouse, NOD.129(Cg)-Gt(ROSA)26Sor$^{tm1.1(CAG-cas9*,-EGFP)Fezh}$/J

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.C. Han, M.E. McClements, P. Charbel Issa, R.E. MacLaren, University of Oxford Nuffield Department of Clinical Neurosciences, Oxford, Oxfordshire, UNITED KINGDOM|R.C. Han, P. Charbel Issa, R.E. MacLaren, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The CRISPR-Cas9 knockin mouse (NOD.129(Cg)-Gt(ROSA)26Sor$^{tm1.1(CAG-cas9*,-EGFP)Fezh}$/J) was originally reported by Platt et al (2014) and is now commercially available from Jax Laboratories, Bar Harbor, Maine. The mouse, which has a CAG-3xFLAG-SpCas9-P2A-EGFP cassette inserted at the Rosa26 locus, theoretically displays ubiquitous Cas9 and EGFP expression in nucleated cells. Previous studies showed Cas9 expression and successful gene knockdown across bone marrow, brain, and lung tissues using AAV and lentiviral-delivered sgRNA (Platt et al., 2014). Our aim was to characterise retinal expression of SpCas9 to determine the suitability of this mouse as a model for optimising retinal gene knockdown.

Methods:

Cas9EGFP homozygotes were killed by cervical dislocation. For Western blot, retinae were dissected and underwent dissociation and magnetic-activated cell sorting (MACS) into CD73+ve (rod photoreceptors) and CD73-ve (remaining retinal cells) populations. Western blot was carried out for FLAG, SpCas9 and α -tubulin. For immunohistochemistry (IHC), eyes were fixed in 4% PFA for 30 minutes, embedded in OCT and frozen. Cryostat sections were stained for SpCas9, FLAG, PKC-a, and calbindin, with secondary Alexa-Fluor goat antibodies, and imaged on a Zeiss LSM710 confocal microscope. In vivo imaging took place using the Heidelberg SLO and OCT.

Results: Western blot showed clear whole retina SpCas9 expression, but weak expression in the CD73+ve extracted cell population (rods). IHC showed Cas9 and EGFP expression in the retinal ganglion cell and inner nuclear layer, but not in the outer nuclear layer or photoreceptor outer segments. Cas9 and EGFP expression did not co-localise with PKC-α or with calbindin, indicating limited horizontal and bipolar cell expression, but showed an expression pattern characteristic of Müller glia.

Conclusions: The NOD.129(Cg)-Gt(ROSA)26Sor$^{tm1.1(CAG-cas9*,-EGFP)Fezh}$/J mouse would be a suitable model for optimising Cas9 knockdown in retinal ganglion cells or Müller cells, but may be a poor model for photoreceptor targets. The apparent lack of both Cas9 and EGFP in this model may reflect variable expressivity from the ROSA26 locus in retinal cell populations.

Reference:
Platt et al. Cell 2014

CONTROL ID: 3711506

SUBMITTER (NAME ONLY): Yingrui Liu

TITLE: Minimal effect of conditional ferroportin KO in the neural retina implicates ferrous iron in retinal iron overload and degeneration

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, G. Su, Department of Ophthalmology, The Second Affiliated Hospital of Jilin University, Changchun, Jilin, CHINA|Y. Liu, B. Baumann, Y. Song, K. Zhang, J.L. Dunaief, F.M. Kirby Center for Molecular Ophthalmology, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|M. Poli, Department of Molecular and Translational Medicine, University of Brescia, Brescia, ITALY|S. Littleton, Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|Z. Kozmik, Institute of Molecular Genetics, Academy of Sciences of the Czech Republic, Akademie ved Ceske republiky, Praha, CZECHIA|

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ABSTRACT BODY:

Purpose: Iron-induced oxidative stress has been implicated in retinal degenerative diseases. Mouse models with systemic, or neural retina-specific knockout (KO) of homologous ferroxidases ceruloplasmin (Cp) and hephaestin (Heph) have retinal iron overload. We previously reported age-dependent iron overload in the retina of Cp/Heph DKO mice by 6mo, and retinal degeneration with features of age-related macular degeneration by 9mo. Because Cp and Heph can facilitate cellular iron export by ferroportin (Fpn), we hypothesized that the impairment of ferroxidase-facilitated, Fpn-mediated iron export from retinal neurons and glia might account for these results.

Methods: To investigate the role of Fpn in retinal iron regulation, we developed mice with neural retina-specific Fpn KO (mRx-Cre+, $Fpn^{flox/flox}$). Mice were aged to 7-10 months of age, and retinal iron levels were analyzed using qPCR and immunolabeling for ferritin light chain (Ft-L). To further test the hypothesis that a combination of elevated ferrous iron plus deletion of Fpn might cause retinal iron accumulation, we developed mice with neural retina-specific Fpn KO and systemic Cp KO. To increase the serum iron level, mice were given an intraperitoneal injection of iron at 3 months of age. Retina iron levels were analyzed using qPCR and immunolabeling for Ft-L.

Results: There was no indication of retinal iron overload in neural retina-specific Fpn KO mice at 7-10 months of age: the mRNA levels of transferrin receptor (Tfrc) measured by qPCR were not altered in retina-specific Fpn KO mice and immunolabeling for Ft-L showed similar intensity in retina-specific Fpn KO mice and controls. Iron injected mice with systemic Cp KO and retina-specific Fpn KO had a significant but small decrease in retinal Tfrc mRNA. There was no effect on Dmt1 mRNA no change in Ft-L immunolabeling, which we have typically observed are less sensitive measures of retinal iron overload than levels of Tfrc mRNA.

Conclusions: These results indicate that impaired Fpn mediated cellular iron export is not sufficient to explain the retinal iron overload observed in Cp/Heph DKO mice. Elevated levels of ferrous iron are likely to contribute in the absence of ferroxidases. Supporting this, injection of ferrous sulfate into the vitreous increased retinal iron levels indicated by significantly decreased Tfrc mRNA followed by rapid retinal degeneration.

CONTROL ID: 3711507

SUBMITTER (NAME ONLY): Mihyun Nam

TITLE: Adeno-associated virus Type 2-mediated Expression of HSPB1 Protects Retinal Ganglion Cells against Ocular hypertension in Mice

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nam, A. Dhillon, R.B. Nahomi, M.B. Pantcheva, R.H. Nagaraj, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the protective effect of adeno-associated virus type 2 (AAV2)-mediated expression of HSPB1 in retinal ganglion cells (RGCs) against ocular hypertension-induced RGC death in mice.

Methods: We constructed an AAV2 vector encoding human HSPB1 with a mini RGC-specific neurofilament light chain promoter PLE345 for specific expression in RGCs. Microbeads were injected into the anterior chamber of mice two weeks before or two weeks after the AAV2-HSPB1 injection. IOP was measured using a tonometer. Retinal flatmounts were fixed and immunostained for RGCs and activated microglia with specific antibodies. Anterograde axonal transportation was assessed by intravitreal injection with Alexa fluor-555 conjugated cholera toxin-B subunit (CTB).

Results: Intravitreal injection of AAV2-HSPB1 resulted in robust expression of HSPB1 in both the soma and axons of RGCs. The IOP was significantly elevated one week after microbeads injection. The microbead-injected mice showed a gradual decrease in RGCs, with a 36% decrease at six weeks post-injection. AAV2-HSPB1 administration one week after microbead injection resulted in significant prevention of RGC loss, with only a 12% decrease at six weeks. The microbead-injected mice showed defective anterograde transportation of CTB along the length of the optic nerve. The AAV2-HSPB1 administration inhibited these axonal defects. In addition, the administration of AAV2-HSPB1 prevented the activation of microglia in microbead-injected mice.

Conclusions: Intravitreal administration of AAV2-HSPB1 resulted in RGC-specific expression of HSPB1. HSPB1 expression protected RGC somas and axons in mice with ocular hypertension. Our results suggest that AAV2-HSPB1 could be advanced as a therapy for neuroprotection in glaucoma.

CONTROL ID: 3711509

SUBMITTER (NAME ONLY): Ashley Park

TITLE: Comparison of erythrocyte flowrates in retinal and nailfold capillaries in human subjects

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Park, S. Chen, V. Chen, O. Saeedi, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Impaired ocular blood flow is associated with major ocular disease, and impaired retinal and peripheral capillary circulation has been observed in glaucoma patients. Nailfold capillaroscopy allows visualization and quantification of peripheral blood flow, while erythrocyte mediated angiography (EMA) permits in vivo determination of retinal capillary blood flow. The purpose of this study is to compare erythrocyte velocities in the retina and the nailfold.

Methods: We conducted a cross-sectional study of five control subjects to determine nailfold and retinal capillary velocities. Nailfold erythrocyte velocities were measured by tracking blood gap displacement in the capillaries across the image frames, and retinal erythrocyte velocities were determined using a MATLAB script as previously described (Tracey et al., Scientific Reports, 2019). Three second and ten second videos of the nailfold were obtained. ARIA in MATLAB was used to obtain diameter measurements.

Results: We analyzed five nailfold capillaries in five control patients. The average nailfold capillary velocity was 0.29 ± 0.08 mm/s and the coefficient of variation for velocity and diameter were 0.012 and 0.03 respectively. The average retinal capillary velocity was 0.94±0.03 mm/s, which was significantly different from nailfold capillaries ($p<0.01$). There was no correlation between retinal and nailfold capillary flowrates (R^2 of 0.286, $p=0.465$).

Conclusions: We found that retinal capillary velocities are significantly higher than nailfold capillary velocities, consistent with high metabolic rates of the retina. Our nailfold capillary velocities were within range of what is reported in literature. We also present high reproducibility rates of our nailfold velocity and diameter measurements.

CONTROL ID: 3711510

SUBMITTER (NAME ONLY): Barbra Hamill

TITLE: Optic disc features in UKBIOBANK (UKBB) and the novel deep learning (DL) algorithm for automated prediction of cup-disc ratio (CDR) from colour fundus (CF) images.

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To provide human grading results which describe features of suspicious glaucomatous disc damage on CF images in UKBB and preliminary results from the DL assisted image interpretation applied to these images.

Methods: Topcon 3D OCT–1000 Mark II system was used to acquire a single CF image of the optic disc and macula on un-dilated eyes. CF images were graded by NetwORCUK (a network comprising Belfast, Liverpool and Moorfields Ophthalmic Reading Centres) to answer pre-determined questions on features of the optic disc. Quality assurance was carried out at a rate of 1 in 20 gradings. CF images in the first batch graded, totaling 33222 participants, were cropped using the 'You Only Look Once' DL model to produce a sub-image of 299x299 pixels centred at the predicted centre of the optic disc before a novel end-to-end DL regression algorithm using an InceptionV3 based network was applied in order to predict CDR.

Results: 68517 participant image sets were analysed by graders for signs of glaucoma; 67985 right eye and 67613 left eye CF images were available. Of these 61,020 right eye and 60,242 left eye CF images were gradable.

CF images, regardless of quality, were included in the AI assisted image interpretation. High level of suspicion for glaucoma, defined as CDR >=0.7 was identified in 481 (0.70%) right eyes and 421 (0.61%) left eyes. There were an additional 299 (0.44%) of right eyes and 237 (0.35%) of left eyes with CDR < 0.7, with suspicious features such as haemorrhage on the disc or notching. In addition, there were 1210 participants with a difference of >=0.2 in CDR between eyes.

Preliminary AI results on the first batch graded using 62398 eyes (31788 right; 30610 left) allowed successful cropping in 54377 eyes (87%), of which 80% were used for training, 10% for validation and 10% for testing. The results on 5444 independent testing images showed the error between the predicted and true measurement of CDR to be <0.05 in 56% (95% CI: 54%, 57%), < 0.1 in 74% (95% CI: 76%, 78%) and <0.2 in 97.6% (95% CI: 97%, 98%) of images.

Conclusions: These data provide human grading for future projects on topics that require optic disc grading in both health and disease. AI assisted image interpretation has shown high accuracy when compared to human grading of the CDR on a large-scale.

CONTROL ID: 3711512

SUBMITTER (NAME ONLY): Carmelina Gordon

TITLE: Poor response to anti-VEGF treatment in macular edema secondary to central retinal vein occlusion and its baseline predictors: a post hoc analysis of COPERNICUS and GALILEO

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Gordon, Specialty Eye Institute, Jackson, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Carmelina Gordon: Commercial Relationship(s);Code F (Financial Support):Alcon, Alimera, Allergan, Genentech, NIH, Novartis, Regeneron Pharmaceuticals, Inc., Santen Pharmaceutical Co., Ltd., and Topco

ABSTRACT BODY:

Purpose: To characterize poor responders to intravitreal aflibercept injection (IAI) following 24-week treatment, evaluate their longer-term visual and anatomic outcomes through week 52, and identify baseline factors associated with poor response in patients with macular edema secondary to central retinal vein occlusion (MEfCRVO).

Methods: Patients with MEfCRVO who received IAI 2 mg every 4 weeks for 24 weeks followed by pro-re-nata (PRN) dosing from Week 24 through Week 52 in COPERNICUS and GALILEO were analyzed post hoc. Poor response at Week 24 was defined by a combination of visual acuity (<58 letters [Snellen <20/80] or ≤5 letters gain from baseline) and anatomic criteria (central subfield thickness [CST] ≥300 µm or presence of intraretinal or subretinal fluid). All other patients were considered responders. Univariate analysis examined baseline factors (sex, ethnicity, race, age, BMI, perfusion status, time since diagnosis, BCVA and CST) associated with poor response at Week 24.

Results: Of 217 eligible IAI-treated patients,18 (8.3%) were poor responders, 184 (84.8%) were responders, and 15 (6.9%) were indeterminate at Week 24. Baseline characteristics were comparable between the two groups with the exception of lower mean BCVA for poor responders vs responders (42.1 vs 52.7; P=0.0145). Poor responders vs responders received more PRN injections through Week 52 (4.2 vs 2.5; P<0.05). Mean difference (95% CI) in absolute BCVA between poor responders vs responders was −23.3 (−30.2, −16.4) letters at Week 24 and −22.3 (−29.8, −14.8) letters at Week 52. A lower proportion of poor responders vs responders had gain of ≥5 letters (61.1% vs 88.6%), ≥10 letters (50.0% vs 81.1%) and ≥15 letters (16.7% vs 66.9%) at Week 52. Mean difference (95% CI) in absolute CST between poor responders vs responders was 77.7 (24.3, 131.1) µm at Week 24 and 40.7 (−12.8, 94.2) µm at Week 52. The odds of having a poor response at Week 24 decreased by 21% for every 5-letter increase in baseline BCVA (P=0.0062).

Conclusions: A small proportion of patients with MEfCRVO had poor response to IAI at Week 24 in COPERNICUS and GALILEO. These patients had smaller BCVA gains at Week 52 despite similar reduction in CST and receiving more PRN injections. Baseline vision was a key predictor of poor response at Week 24.

CONTROL ID: 3711513

SUBMITTER (NAME ONLY): Shaina Kumar

TITLE: Pre-operative Parameters and Post-operative Outcomes for Transscleral Fixated Intraocular Lenses in a Bronx-based population: A Retrospective Review

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kumar, Z. Zhou, BronxCare Health System, Bronx, New York, UNITED STATES|

Commercial Relationships Disclosure: Shaina Kumar: Commercial Relationship: Code N (No Commercial Relationship) | Zimei Zhou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although placement of an intraocular lens (IOL) in the capsular bag is ideal during cataract surgery, complications require ophthalmologists to know alternative methods of IOL implantation. We performed a retrospective chart review to learn about the pre-operative parameters/indications and post-operative outcomes in patients that underwent transscleral-fixated IOL (TSFIOL) implantation at our institution. Our hope is to better understand which patients may be more suitable for TSFIOL's based on these considerations.

Methods: We conducted a retrospective chart review of 30 patients (22 males and 8 females; mean age of 68.6) at our institution that underwent TSFIOL implantation by a posterior segment surgeon. Data was collected from EyeMD (the ophthalmology clinic electronic medical record (EMR)) and Allscripts (hospital EMR), and then separated into 2 main categories: pre-operative parameters/indications for surgery and post-operative outcomes/complications.

Results: Review of pre-operative parameters revealed that 14 patients were aphakic, 7 had a ruptured capsule, 8 had a dislocated IOL, 9 had a traumatic event, 11 had iris damage, 6 had a shallow anterior chamber, and 9 had corneal pathology. Initial preoperative visual acuity (VA) was compared with final VA (3 months post-operatively). The majority displayed an improvement in VA (n = 23), while a minority had a decline (n=2; the remaining were lost to follow up or had no change in VA). We further divided our population into emergent (7 cases) or planned surgeries (22 cases) and compared improvement in VA between the 2 groups. No significant difference was found between the 2 groups in terms of improvement in VA (p=0.748). The overall complication rate was 48.28%, which includes choroidal detachment, hypotony, corneal edema, Irvine Gass syndrome, and elevated intraocular pressure.

Conclusions: Long-term data on functional outcomes after TSFIOL implantation is limited. Overall, 79.31% of patients had unchanged/improved VA. Therefore, the majority had improved VA after TSFIOL implantation. Improvement in VA's among planned and emergency cases was not significantly different. The most common complication in our cohort was ocular hypertension. We hope to include additional patients in our retrospective review to better understand which patients may be more suitable candidates for a TSFIOL.

CONTROL ID: 3711515

SUBMITTER (NAME ONLY): Flavia Plastino

TITLE: UPARANT mitigates human iris angiogenesis through uPAR/LRP-1 interaction in an organotypic ex vivo model

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Plastino, N.A. Pesce, F. Locri, A. Kvanta, H. Andre, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|V. Pavone, Universita degli Studi di Napoli Federico II, Napoli, Campania, ITALY|M. Dal Monte, Universita degli Studi di Pisa, Pisa, Toscana, ITALY|

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ABSTRACT BODY:

Purpose: Rubeosis Iridis (RI) is characterized by an increase in neovascularization and inflammation factors in the iris. During angiogenesis, the urokinase plasminogen activator (uPA) and its receptor (uPAR) play a pivotal role in extracellular matrix remodeling, where uPAR regulates endothelial cell migration and proliferation through assembly with transmembrane receptors. Here, in a context of hypoxia-induced angiogenesis, the antagonist effects of UPARANT onto the uPA/uPAR system were investigated using a novel ex vivo human iris organotypic angiogenesis assay. Additionally, to further elucidate whether UPARANT acts on epithelial or endothelial cells, in vitro assays were performed on human iris epithelial cells (hIEC) versus human retinal endothelial cells (hREC).

Methods: hIEC, hREC and human iris organotypic cultures were kept in normoxia (20% O_2) or exposed to hypoxia-stimulated angiogenesis (1% O_2), and treated with UPARANT and control-vehicle. UPARANT anti-angiogenic effects were analyzed by in vitro wound healing and spheroid sprouting assays, ex vivo human iris sprouting assay, immunofluorescence, quantitative PCR and protein assays (western and dot blots, and co-immunoprecipitation). The effects of UPARANT in human ex vivo iris angiogenesis were focal to endothelial cells.

Results: UPARANT does not affect iris epithelial wound recovery yet reduces sprouting angiogenesis in hREC spheroids and ex vivo human iris organotypic cultures. Western blot analysis demonstrates that UPARANT leads to a decrease of hypoxia-inducible factor (HIF)-1α protein levels, concomitantly with a decrease in phosphorylation levels of protein kinase B (AKT) and cyclic AMP response element-binding protein (CREB) when compared to vehicle treated.

Phospho-protein array illustrated an unidentified antagonism of UPARANT in the interaction of uPAR with the low-density lipoprotein receptor-related protein-1, resulting in inhibition of b-catenin–mediated angiogenesis in this model.

Conclusions: These findings corroborate the role of UPARANT as a multifactor inhibitor of ocular vascular endothelial cells, which could benefit the treatment of RI in patients afflicted with multiple other ocular neovascular diseases.

CONTROL ID: 3711516

SUBMITTER (NAME ONLY): Neringa Jurkute

TITLE: Functional investigation of candidate mis-splicing variants in retinal dystrophy genes using nanopore sequencing from patient blood samples

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Jurkute, M. Michaelides, O.A. Mahroo, A.R. Webster, G. Arno, 1.Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|N. Jurkute, J. Bellingham, L. Varga, M. Michaelides, O.A. Mahroo, A.R. Webster, G. Arno, 2.Institute of Ophthalmology, University College London, London, UNITED KINGDOM|S. Roosing, 3.Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, NETHERLANDS|S. Roosing, 5.Department of Human Genetics, Radboud University Medical Center, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To functionally investigate candidate splice altering variants in inherited retinal dystrophy (IRD) genes including non-coding variants in genes with restricted expression using RT-PCR and nanopore single-molecule sequencing for transcripts from patient blood derived total RNA samples.

Methods: Patients were recruited from the inherited retinal disease clinics at Moorfields Eye Hospital (London, UK) as part of the UK 100,000 genomes project with an additional individual identified at Radboud University Medical Center (Nijmegen, the Netherlands). Ten probands who were identified to carry a candidate pathogenic non-coding or synonymous variant were selected for investigation. RT-PCR was performed on total RNA derived from affected individuals and control blood to amplify fragments flanking the affected intron or whole transcripts where possible. Nanopore sequencing was performed using the Oxford Nanopore Technologies Genomic DNA by Ligation (SQK-LSK109) protocol and sequencing on a flongle flow-cell.

Results: Ten affected individuals diagnosed with IRD were identified to carry candidate variants that were otherwise only classed as variants of uncertain significance. Variants were identified in CDH23, COQ5, NMNAT1, PDSS1, PROM1, PRPF31 and TULP1 following interrogation of whole genome sequencing data and multidisciplinary team investigation. This study demonstrated mis-splicing for nine intronic variants in genes CDH23, COQ5, PDSS1 (N=2), PROM1, PRPF31 (N=3) and TULP1 and a reduced transcript level for an upstream variant in NMNAT1. It was possible to detect transcript alteration for genes that are not expressed in blood (CDH23, PROM1, TULP1) and where standard techniques failed to demonstrate mis-splicing.

Conclusions: This study shows that nanopore sequencing is effective for detecting transcript alterations from blood derived RNA for retinal disease genes, allowing functional characterisation of non-canonical splice and upstream variants, where no mis-splicing was apparent by agarose gel electrophoresis precluding Sanger sequencing analysis. Thus, simple blood samples can be collected for investigation without the need for complicated cloning or induced pluripotent stem cell derived retinal progenitor or organoid experiments. The functional evidence provides the crucial support for interpretation of pathogenicity of these candidate variants.

CONTROL ID: 3711517

SUBMITTER (NAME ONLY): Luke Wiley

TITLE: Characterization of a novel Pde6b-deficient rat model of retinal degeneration and treatment with cGMP-grade AAV vectors.

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Wiley, I. Han, K.M. Sheehan, B.E. Harman, M.J. Riker, E.M. Stone, R.F. Mullins, B.A. Tucker, University of Iowa Institute for Vision Reserach, Iowa City, Iowa, UNITED STATES|L.A. Wiley, I. Han, K.M. Sheehan, B.E. Harman, M.J. Riker, E.M. Stone, R.F. Mullins, B.A. Tucker, Department of Ophthalmology & Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to characterize a novel CRISPR-Cas9-generated rat model of Pde6b-associated retinal degeneration and test the ability of clinical-grade AAV vectors (serotypes 1 and 5) to deliver PDE6B to rat photoreceptor cells and mitigate disease progression.

Methods: Pde6b-null rats were generated on a Sprague-Dawley background via CRISPR-Cas9 genome editing (Cyogen Biosciences). Small guide RNA pairs and in vitro transcribed Cas9 mRNA were co-injected into fertilized eggs for generation of animals. The genotypes of founder animals and subsequent matings were verified via PCR and sequencing analysis. Animals were evaluated at post-natal days 14 (P14), 30, 60 and 90 via optical coherence tomography (OCT), electroretinography (ERG), and immunohistochemistry with histological quantification of outer nuclear layer (ONL) cell density and thickness at each time point. For gene augmentation experiments, Pde6b-null animals received a single subretinal injection (3ml) of either AAV2/1-PDE6B or AAV2/5-PDE6B (total dose of $2x10^9$ vg) into one eye. The fellow eye was used as a vehicle-injected control. A cohort of wild-type animals were also treated with each vector to confirm delivery and lack of overexpression toxicity. ONL measurements were compared in a masked fashion to determine efficacy of gene augmentation.

Results: Compared to wild-type and heterozygous animals, Pde6b-null animals displayed early onset by P14 and rapid photoreceptor degeneration that resulted in blindness (i.e., non-recordable ERG) by P30 and near complete loss of photoreceptors by P60. Delivery of AAV2/1-PDE6B or AAV2/5-PDE6B to wild-type rats showed that AAV2/1-PDE6B drives more full-length human PDE6B protein than AAV2/5-PDE6B. No evidence of overexpression toxicity was detected for either vector. In Pde6b-null rats, eyes that received AAV2/1-PDE6B displayed a delay in photoreceptor cell loss compared to buffer-treated controls and eyes treated with AAV2/5-PDE6B.

Conclusions: These preclinical data will be used to guide development of a gene therapy vector for treatment of PDE6B-associated retinitis pigmentosa. In addition to its utility for evaluating the efficacy of gene augmentation vectors, rapid retinal degeneration resulting in near complete photoreceptor loss by 2 months of age makes the Pde6b-null rat ideal for evaluating autologous stem cell-mediated photoreceptor replacement.

CONTROL ID: 3711518

SUBMITTER (NAME ONLY): Roy Schwartz

TITLE: A deep learning pipeline for the detection and quantification of drusen and reticular pseudodrusen on optical coherence tomography

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Schwartz, H. Khalid, Y. Ouyang, C.A. Egan, A. Tufail, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|R. Schwartz, University College London Institute of Health Informatics, London, UNITED KINGDOM|S. Liakopoulos, Klinikum der Universitat zu Koln Zentrum fur Augenheilkunde, Koln, Nordrhein-Westfalen, GERMANY|C. de Vente, C. González Gonzalo, C. Sánchez, Universiteit van Amsterdam, Amsterdam, Noord-Holland, NETHERLANDS|C. de Vente, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|A.Y. Lee, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: In recent years, reticular pseudodrusen (RPD) have been identified as risk factors for advanced age-related macular degeneration (AMD). Only two studies explored machine learning (ML) techniques for their automatic detection on OCT, neither allowing for accurate lesion quantification. We developed a deep learning pipeline for the detection and quantification of conventional drusen (CD) and RPD in the UK Biobank (UKBB), a large-scale biomedical database and research resource.

Methods: A ML pipeline consisting of several ML models was developed: a. A classification model and an out of distribution model for ungradable scans. b. A classification model to identify scans with drusen of any type (CD or RPD). d. An image segmentation model to independently segment lesions as RPD or CD, allowing their quantification.

Of 2,622 UKBB participants with a self-reported diagnosis of AMD, 1,284 had OCT scans and were included in the study. Manual delineation of features was performed by five experienced graders for the segmentation model. We used 3D Inception-V1 as the architecture for the classification models and a 2D U-Net architecture for the segmentation model.

To measure overlap in segmented areas between the model and graders we used free-response receiver operating characteristic (FROC) curves. In addition, the intraclass correlation coefficient (ICC) for absolute agreement was used to measure agreement in the area of the different lesions between the model and graders and for interrater reliability analysis.

Results: The first classification model classified ungradable scans with an area under the curve (AUC) of 94%. The deep ensemble models achieved an AUC of 87%. The second classification model achieved an AUC of 99.3% for classifying drusen of any type vs. controls. Considering one false positive lesion per image on average, the segmentation model achieved a sensitivity of 85% for drusen and 62% for RPD. The ICC for CD area was 0.79 and for RPD it was 0.66. This exceeded human interrater agreement (0.72 for CD, 0.37 for RPD).

Conclusions: We present a deep learning pipeline for the elimination of ungradable scans, classification of drusen, and segmentation of CD and RPD. To the best of our knowledge, this is the first pipeline enabling the total workflow, and this is the first DL model to allow accurate quantification of these lesions exceeding human performance.

CONTROL ID: 3711519

SUBMITTER (NAME ONLY): Steven Yeh

TITLE: Suprachoroidal triamcinolone acetonide injectable suspension for macular edema associated with uveitis: Integrated analysis of two clinical trials

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yeh, Truhlsen Eye Institute, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|B. Kapik, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Steven Yeh: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch + Lomb, Clearside Biomedical Inc, Allergan, Regenxbio, Adverum | Barry Kapik: Commercial Relationship(s);Code E (Employment):Clearside Biomedical Inc;Code I (Personal Financial Interest):Clearside Biomedical Inc | Thomas Ciulla: Commercial Relationship(s);Code E (Employment):Clearside Biomedical Inc;Code I (Personal Financial Interest):Clearside Biomedical Inc

ABSTRACT BODY:

Purpose: Triamcinolone acetonide injectable suspension, for suprachoroidal use (SCS-TA) provides targeted drug delivery to the choroid and retina while minimizing steroid exposure in nontarget tissues. This integrated analysis evaluated SCS-TA for the treatment of macular edema (ME) secondary to noninfectious uveitis (NIU) across two studies.

Methods: Data from a randomized, double-masked, sham-controlled trial (PEACHTREE) and an open-label trial (AZALEA) were pooled. Only those subjects with ME secondary to NIU defined by a central subfield retinal thickness (CST) ≥300 µm with fluid and a best-corrected visual acuity (BCVA) of ≥5 and ≤70 Early Treatment Diabetic Retinopathy Study (ETDRS) letters in the study eye at baseline were included in the analysis. In both studies, subjects received SCS-TA at baseline and Week 12 and were followed every 4 weeks for 24 weeks. Control subjects received a sham procedure at baseline and Week 12. Outcomes included BCVA, CST, anterior chamber (AC) cells, AC flare, vitreous haze (VH) and adverse events (AEs).

Results: The integrated population included 95 subjects (PEACHTREE 88; AZALEA 7). Increase from baseline in BCVA was greater with SCS-TA vs control with a mean difference of 10.7 letters at Week 24 ($P<0.001$ for all visits). Proportions of subjects achieving a mean ≥15 letters gain were greater with SCS-TA vs control (47.4% vs 16.7% at Week 24; $P<0.001$ for all visits). Reduction in CST was greater and more subjects achieved a CST <300 µm with SCS-TA vs control ($P<0.001$ for all visits). In subjects with baseline inflammation, 72.2%, 71.1% and 72.0% in the SCS-TA group vs 13.6%, 20.0% and 19.0% in the control group achieved resolution of AC cells, flare and VH at Week 24 (all $P<0.01$). Rescue therapy was required by 12.6% and 73.3% of subjects in the SCS-TA and control groups, respectively. AEs were mostly mild and no treatment-related serious AEs were reported. Overall, incidence of elevated intraocular pressure (IOP) was 20% and 15% in the SCS-TA and control groups (7.4% vs 0% at time of procedure; 12.6% vs 15% post-procedure, control IOP events occurred post rescue). Cataract rates were 7.4% and 6.7% for SCS-TA and control respectively.

Conclusions: In this integrated analysis of two Phase 3 clinical trials, SCS-TA was confirmed to be effective and well tolerated in the treatment of ME associated with NIU.

CONTROL ID: 3711520

SUBMITTER (NAME ONLY): Michelle McClements

TITLE: Validation of a rod photoreceptor-specific promoter for CRISPR gene therapy

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. McClements, C.F. Peddle, F. Staurenghi, A. Salman, R.E. MacLaren, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|W. Atkin, H. Steward, E. Archer Goode, C. Gandara, V. Chichagova, Newcells Biotech Ltd, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Cell specific promoters have long been desired and implemented in gene therapy vectors to enable controlled expression of transgenes. With genome editing strategies likely to dominate future gene therapies, cell specific promoters will be particularly necessary to limit unwanted editing possibilities in multiple cell types. We have validated a short PDE6B promoter (154bp) that drives transgene expression specifically in rod photoreceptor cells. This promoter, combined with an SaCas9 transgene, achieved dose-dependent editing of GFP in the Nrl.GFP mouse model, for which GFP expression is restricted to rod photoreceptor cells.

Methods: The PDE6B promoter was amplified from human DNA and reporter expression assessed in HEK293 cells, Y79 cells, retinal organoids and human retinal explants. Nrl.GFP mice were injected with reporter vectors and eyes harvested at 4 weeks post-injection for immunostaining. PDE6B.SaCas9 vectors were prepared with either a non-targeting or GFP targeting guide RNA and injected into Nrl.GFP mice at doses of 1E+08, 5E+08 or 1E+09 genome copies per eye. Expression of GFP was assessed by SLO and SaCas9 expression was confirmed by immunostaining and qPCR. Editing rates were assessed by DNA extraction and subcloning analysis.

Results: The PDE6B promoter enabled reporter expression in Y79 cells, human retinal explants and iPSC-derived retinal organoids. Nrl.GFP injected eyes revealed reporter expression was limited to rod photoreceptor cells with 100% of DsRed positive cells also GFP positive. Of 180 randomly selected GFP positive cells, 55% were also DsRed positive and of 92 cone-arrestin positive cells, none were DsRed positive. A dose dependent increase in SaCas9 expression was achieved that coincided with editing rates 1.67%, 5.00% and 8.33% for the doses of 1E+08, 5E+08 and 1E+09, respectively. SLO assessment of GFP revealed a significant difference in mean grey values from F10 injected eyes compared to paired eyes that received the non-targeting gRNA ($p=0.0248$, $n=10$). The middle dose of 5E+08 achieved the biggest difference with a 36.5% reduction in GFP fluorescence relative to paired injected eyes.

Conclusions: With its small size and rod photoreceptor-specific expression profile, the human PDE6B promoter is a viable option for gene therapy vectors, including CRISPR-based editing strategies where restricted expression profiles with effective editing rates will be desired.

CONTROL ID: 3711521

SUBMITTER (NAME ONLY): Eleni Beli

TITLE: "Mapping in time" the daily rhythmic transcriptome in the diabetic retina

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Beli, H.R. Winter, V. Tiwari, A.W. Stitt, Wellcome Wolfson Institute For Experimental Medicine, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|R.P. Silk, D. Simpson, Institute of Genetics and Cancer, The University of Edinburgh, Edinburgh, Edinburgh, UNITED KINGDOM|R.P. Silk, Wellcome Wolfson Institute For Experimental Medicine, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The eye is an organ attuned to function around the light/dark cycle. Its circadian system fine-tunes this process. Diabetes emerges as a disease that disrupts the overall circadian rhythms. In this study we asked how diabetes affects these daily rhythms in the mouse retina.

Methods: Healthy control and Ins2Akita/J diabetic mice were kept under a physiological 12h:12h light-dark cycle until 4 months of age. Retinas were collected from 4-5 mice every 4 hrs around the day/night cycle. Deep mRNA sequencing was conducted and transcripts were identified. Computational approaches were used for detection of rhythmicity (empirical JTK_Cycle, emp $p<0.05$, FC > 1.2), acrophase prediction (Harmonic Regression with a set period of 24 hrs and normalization set to false), differential rhythmic patterns (DORD analysis BH corrected $p < 0.05$), phase set enrichment analysis (PSEA, BH corrected p-value < 0.01) and upstream regulator predictions (IPA, $p<0.05$).Animal studies were carried out at the institutional animal care facilities at the Indiana University School of Medicine and Queen's University in accordance with institutional and national guidelines for the care and use of laboratory animals (IACUC10604,11167 and PPL2897).

Results: Almost 10% of the retinal transcriptome was identified as rhythmic with a clear 12hr axis of transcriptional activity, peaking at midday and midnight. Although the 12-hour transcriptional axis is retained in the diabetic retina, it was phase advanced by approximately 1-3 hours, however individual genes were phase advanced by up to 10 hours. Phase shifts rather than changes in the amplitude of rhythms of gene expression were more prominent. Interestingly, only mild changes in the circadian rhythms were observed, as those were entrained by the light cycle. However, oxidative phosphorylation and HIF1A and NUPR1 were identified as the major upstream regulators for the phase shifts.

Conclusions: To our knowledge this is the first study mapping the effects of diabetes in the rhythmic output in the retina. Importantly, we identified that much of the daily rhythmicity in the retina is altered and the source of this shift is more related to abnormal metabolic adaptation rather than circadian disruption. This led us to propose that a metabolic shift with an entrained clock within the diabetic retina creates an internal jet lag that contributes to neurodegeneration in diabetic retinopathy.

CONTROL ID: 3711522

SUBMITTER (NAME ONLY): TJ Hollingsworth

TITLE: A chronic proinflammatory retinal microenvironment progresses neurodegeneration in a spontaneous model of inherited retinal dystrophy

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Hollingsworth, X. Wang, W. White, U. Baguda, R. Simpson, M.M. Jablonski, Ophthalmology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|M.M. Jablonski, Pharmaceutical Sciences, The University of Tennessee Health Science Center College of Pharmacy, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal neurodegenerative diseases (NDs) are comprised of numerous disorders which result in loss of varying cell types. These diseases range from glaucoma, which affects retinal ganglion cells, to age-related macular degeneration, a late onset ND affecting cone photoreceptors and the retinal pigment epithelium, to retinitis pigmentosa and Leber congenital amaurosis, two forms of inherited retinal dystrophies (IRDs) which result in primary cell death of the rod photoreceptors (PRs). In the last two decades, groups have uncovered that most NDs are accompanied by increased release of proinflammatory cytokines and proliferation of active microglia which can expedite the disease course. The purpose of this study is to decipher the inflammatory state of the retina of the BXD32 mouse, a novel, spontaneous IRD model.

Methods: We surveyed for IRD phenotypes using funduscopy with fluorescein angiography (F/FA), electroretinography (ERG), optokinetic nystamography (OKN), optical coherence tomography (OCT), and immunohistochemistry (IHC) for GFAP (glial fibrillary acidic protein) as well as TUNEL staining for apoptosis. We also assessed for inflammation using IHC analyses for macrophages (IBA1, ionized calcium binding adaptor molecule 1), TNFα (tumor necrosis factor alpha) and its downstream pathway components NF-κB p65 (nuclear factor kappa B p65), NLRP3 (NOD-, LRR- and pyrin domain-containing protein 3), STAT3 (signal transducer and activator of transcription 3) along with its phosphorylated forms pSTAT3-Y705 and S727, and the pathway antagonist SOCS3 (suppressor of cytokine signaling 3).

Results: F/FA and OCT found vessel attenuation and a rapid degeneration with most PRs lost before 24 weeks. ERG and OKN showed a steady decreasing loss of vision. IHC for GFAP and TUNEL exposed the highly stressed state of the retina with intense GFAP labeling and apoptosis. Co-labeling TUNEL with IBA1 revealed the presence of phagoptosis (phagocytosis of living cells). IHC confirmed heavy upregulation of all inflammatory markers.

Conclusions: The BXD32 mouse exhibits a rapid and early onset retinal degeneration consistent with expectations of an IRD model. The retinas of these mice also maintain a state of steady and increasing proinflammatory signaling with aberrant phagocytosis by macrophages and dramatic increases in proinflammatory cytokine and signaling pathway proteins.

CONTROL ID: 3711525

SUBMITTER (NAME ONLY): Paola Rivera

TITLE: Surgical Time and Postoperative Symptoms Study in Pterygium Excision and Amniotic Membrane Graft using Celularity Triple Layer Dehydrated Amniotic Membrane

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Rivera, L. Barnard, W. Linderman, M. Gill, V. Diaz, Ophthalmology, Yale University, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Paola Rivera: Commercial Relationship: Code N (No Commercial Relationship) | Luke Barnard: Commercial Relationship: Code N (No Commercial Relationship) | Wendy Linderman: Commercial Relationship: Code N (No Commercial Relationship) | Mohsain Gill: Commercial Relationship: Code N (No Commercial Relationship) | Vicente Diaz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate a novel, sutureless, and glueless surgical technique using a triple-layer dehydrated amniotic membrane (TLDAM) for pterygia excisions in terms of surgical time and postoperative pain, epiphora, irritation, and foreign body sensation.

Methods: Twenty eyes of eighteen patients with pterygia underwent pterygia excision with mitomycin C. The conjunctival defect was closed with a sutureless, glueless technique with TLDAM placed directly on the dried scleral bed with the edges of the amniotic membrane tucked under the edges of the conjunctival defect. Surgical times were measured from injection of lidocaine to final placement of bandage contact lens.

Immediately postoperatively, a bandage contact lens was placed, and the eye was patched until postoperative day 1. Subsequently, patients graded self-administered questionnaires to rate pain, foreign body sensation (FBS), irritation, and watering on a scale of 1-5 (1-none; 5-most severe) at postoperative day 1 (POD1) and week 1 (POW1).

Results: Surgical times range from 6:55 to 12:00, with a mean of 8:29. Compared with a previous study of also sutureless and glueless methodology, the difference in surgical time means is 11.9 ($p < 0.0001$). Mean questionnaire scores for each postoperative visit were as follows: POD1 Pain 1.8, FBS 2.3, irritation 1.0, and epiphora 2.6; POW1 Pain 1.5, FBS 1.6, irritation 1.6, and epiphora 1.6. Compared to previous studies, this technique showed statistically significant improved pain at POD1 ($p=.0086$, $p<.0001$, $p<.0001$, $p<.0001$) and POW1 ($p=.0354$, $p=.0002$, $p=.0016$, $p<.0001$). Improvement in foreign body sensation was also noted at POD 1 ($p=.0321$, $p<.0001$). See table for full statistical analysis.

Conclusions: The sutureless, glueless technique using Cellularity TLDAM is a safe and effective surgical technique compared to current standard methods. There appears to be a significant benefit regarding surgical time and postoperative pain, irritation, epiphora, and foreign body sensation compared to previous studies.

CONTROL ID: 3711526

SUBMITTER (NAME ONLY): Jaehyuck Jo

TITLE: Analysis of Intravitreal Bevacizumab Treatment Response in Eyes with Branch Retinal Vein Occlusion via Optical Coherence Tomography Angiography

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Jo, Y. Yoon, Ophthalmology, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Jaehyuck Jo: Commercial Relationship: Code N (No Commercial Relationship) | Young Hee Yoon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Macular edema secondary to branch retinal vein occlusion (ME-BRVO) is a frequent cause of visual loss, especially when it is refractory to anti-VEGF therapy. The purpose of this study is to identify prognostic factors for response to intravitreal bevacizumab in patients with ME-BRVO by analyzing retinal microvascular integrity using optical coherence tomography angiography (OCTA)

Methods: Medical records of ME-BRVO patients who were treated with bevacizumab and followed at least 12 months were reviewed. On OCTA, the foveal avascular zone (FAZ) and vessel density (VD) of the superficial (SCP) and deep capillary plexuses (DCP) were obtained. Poor response was defined as central retinal thickness (CRT) > 300 μm or a decrease in CRT by < 50 μm after three consecutive bevacizumab injections.

Results: Eighty one eyes from 81 patients were included. Among them, 57 eyes were good responder and 23 eyes poor responder. Mean age of good and poor responders was 59.33 ± 10.36 and 66.17 ± 9.78 years ($p = 0.009$). Compared to good responders, poor responders showed larger DCP-FAZ size (SCP/DCP ratio; 0.92 ± 0.11 vs. 0.86 ± 0.17, $p = 0.045$), less DCP-VD at the most ischemic sector (SCP/DCP ratio; 0.99 ± 0.17 vs. 1.10 ± 0.31, $p = 0.046$), and larger FAZ perimeter (2.59 ± 0.75 vs. 4.10 ± 2.54, $p = 0.010$). In multivariate analyses, age, FAZ perimeter, and DCP-VD of the most ischemic sector were significant risk factors ($p = 0.024$, $p = 0.037$ and $p = 0.035$, respectively).

Conclusions: In ME-BRVO patients, poor response to bevacizumab may be predicted when the patient is older, FAZ is more disrupted, or macular ischemia is more severe in DCP than SCP.

CONTROL ID: 3711527

SUBMITTER (NAME ONLY): Ming Zhang

TITLE: Transcriptome analysis of AMD-like pathology in aged BALB/c mice following systemic neonatal murine cytomegalovirus infection

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Zhang, J. Xu, X. Zhang, B. Marshall, Department of Cellular Biology and Anatomy, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our previous studies have shown that systemic neonatal murine cytomegalovirus (MCMV) infection of BALB/c mice spread to the eye with subsequent establishment of latency in choroid/ RPE, and the development of progressive AMD-like pathologies characterized by loss of choroidal capillaries, basal lamina deposits (BLamD), subretinal deposits (SD), degeneration of RPE and photoreceptors and choroidal neovascularization (CNV)-like lesions. In this study, the RNA sequencing (RNA-Seq) analysis was used to determine the molecular genetic changes and pathways affected by ocular MCMV latency.

Methods: MCMV (50 pfu per mouse) or medium as control were injected intra-peritoneally (i.p.) into BALB/c mice at <3 days after birth. At 18 months p.i., MCMV or medium injected mice were euthanized and eyes were collected and prepared for RNA-Sequencing.

Results: Compared to 3 uninfected control eyes, we identified 321 differentially expressed genes (DEGs) in 6 infected eyes (208 downregulated and 113 upregulated, cutoff with |fold change| ≥ 2 and q≤ 0.05). Using the QIAGEN Ingenuity Pathway Analysis (QIAGEN IPA), we identified 17 affected canonical pathways. 10 pathways function in neuroretinal signaling in which the majority of DEGs were downregulated. This was exemplified by the phototransduction pathway in which all 22 differentially expressed genes were downregulated with a p value less than 10^{-27}. 7 upregulated immune response/inflammatory pathways were also detected. Under the QIAGEN IPA, differentially expressed genes were categorized according to related diseases and functions. Many differentially expressed genes were noted in the categories of Ophthalmic Disease, Organismal Injury, Visual System Function, Cell Death and Survival, Inflammatory Responses, Cellular Movement and Immune Cell Trafficking. Genes involved in activation of retinal degeneration, including degeneration of photoreceptors were identified by activation z scores greater than 2. Cell death of retinal cells and epithelial tissues involving both apoptosis and necroptosis, was also activated.

Conclusions: MCMV ocular latency is associated with upregulation of immune and inflammatory responses and downregulation of multiple neuroretinal signaling pathways. Multiple cell death pathways are activated and contribute to the degeneration of photoreceptors, RPE and choroidal capillaries.

CONTROL ID: 3711529

SUBMITTER (NAME ONLY): Alexander Rokohl

TITLE: Novel Point-of-Care Biomarkers of the Dry Anophthalmic Socket Syndrome: Tear Film Osmolarity and Matrix Metalloproteinase 9 Immunoassay

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Rokohl, K. Wall, P.A. Wawer Matos, L.M. Heindl, Department of Ophthalmology, Faculty of Medicine and University Hospital of Cologne, University of Cologne, Cologne, GERMANY|K.R. Pine, School of Optometry and Vision Science, University of Auckland, Auckland, NEW ZEALAND|Y. Guo, Eye Center, Zhejiang University School of Medicine, Hangzhou, Zhejiang, CHINA|W. Adler, Department of Biometry and Epidemiology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, GERMANY|M. Trester, Trester-Institute for Ocular Prosthetics and Artificial Eyes, Cologne, GERMANY|

Commercial Relationships Disclosure: Alexander Rokohl: Commercial Relationship: Code N (No Commercial Relationship) | Katharina Wall: Commercial Relationship: Code N (No Commercial Relationship) | Marc Trester: Commercial Relationship(s);Code O (Owner):Trester-Institute | Philomena Wawer Matos: Commercial Relationship: Code N (No Commercial Relationship) | Yongwei Guo: Commercial Relationship: Code N (No Commercial Relationship) | Werner Adler: Commercial Relationship: Code N (No Commercial Relationship) | Keith Pine: Commercial Relationship: Code N (No Commercial Relationship) | Ludwig Heindl: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare tear film osmolarity (TFO) values and matrix metalloproteinase 9 (MMP-9) levels between anophthalmic sockets and healthy fellow eyes and to assess the use of the MMP-9 and TFO as biomarkers for the Dry Anophthalmic Socket Syndrome (DASS).

Methods: In this prospective single-center study, the anophthalmic sockets and healthy fellow eyes of 98 unilateral anophthalmic patients were assessed using the Ocular Surface Disease Index (OSDI) questionnaire, InflammaDry® MMP-9 point-of-care immunoassay, TFO with TearLab™ Osmolarity System, and clinical conjunctival inflammation. MMP-9 concentration and conjunctival inflammation were graded semi-quantitatively. Differences between anophthalmic sockets and the healthy fellow eyes for OSDI scores, MMP-9, TFO values, clinical conjunctival inflammation, and eyelid abnormalities as well as the correlation between these factors and demographic data were evaluated.

Results: Patients had significantly higher OSDI, MMP-9, and TFO values, as well as higher conjunctival inflammation on the anophthalmic side, compared to the healthy side ($p \leq 0.002$, respectively). For anophthalmic sockets, there was a significant positive correlation between OSDI scores and TFO values ($p=0.007$), between the grade of posterior blepharitis and TFO values ($p=0.026$), between the conjunctival inflammation and MMP-9 values ($p<0.001$), as well as between MMP-9 levels and time since eye loss ($p=0.004$).

Conclusions: Measuring MMP-9 and TFO may be helpful tools as efficient, quantifiable biomarkers, disease course parameters, or predictors for treatment response in the clinical management of patients with DASS or in future therapy studies. Ophthalmologists should consider the updated diagnosis criteria including TFO and the definition for DASS proposed in this study.

CONTROL ID: 3711530

SUBMITTER (NAME ONLY): Richul Oh

TITLE: Predictive Modeling of Long-Term Glaucoma Progression Based on Systemic Data in the Electronic Medical Record

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Oh, T. Kim, E. Lee, Ophthalmology, Seoul National University Bundang Hospital, Seongnam, KOREA (THE REPUBLIC OF)|R. Oh, T. Kim, E. Lee, Ophthalmology, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|H. Kim, Applied Statistics, Yonsei University, Seodaemun-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To determine the baseline systemic features predictive of rapid retinal nerve fiber layer (RNFL) thinning over future 5 years in primary open-angle glaucoma (POAG)

Methods: Database in the electronic medical record (EMR) was searched to include patients diagnosed with POAG between 2009 and 2016, and had been followed up for > 5 years with annual evaluation of RNFL thickness using spectral-domain optical coherence tomography (OCT). Systemic data obtained within 6 months from the time of glaucoma diagnosis were extracted from the EMR and incorporated into the model to predict the rate of progressive RNFL thinning. After training and testing a predictive model using a random forest (RF) method, the model was interpreted by the Shapley additive explanation plots (SHAP) method. The features that can explain the rate of progressive RNFL thinning were identified and interpreted.

Results: Data from 1256 eyes of 696 patients and 1107 eyes of 607 patients were included in the training and test sets, respectively. The R square value for the RF model was 0.88. The prediction model showed that higher serum aspartate aminotransferase, lower blood glucose, higher systolic blood pressure, higher high-density lipoprotein were the four most determinant systemic features predicting faster RNFL thinning over 5 years. Partial interaction plots showed interactions between some systemic features influencing the rate of RNFL thinning; the interactions between aspartate aminotransferase and Alkaline Phosphatase, systemic blood pressure and diastolic blood pressure, high-density lipoprotein and low-density lipoprotein, blood urea nitrogen and creatinine were associated features. Among ophthalmic features, higher global RNFL thickness and higher intraocular pressure were the most important factors predicting rapid RNFL thinning.

Conclusions: Baseline systemic features of POAG patients had predictive value in identifying those at risk of faster progression

CONTROL ID: 3711531

SUBMITTER (NAME ONLY): Avi Caspi

TITLE: Virtual reality game for rehabilitation and monitoring for visual prostheses

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Caspi, Jerusalem College of Technology, Jerusalem, Jerusalem, ISRAEL|A. Caspi, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Avi Caspi: Commercial Relationship(s);Code F (Financial Support):Second Sight Medical Products, Inc;Code C (Consultant/Contractor):Second Sight Medical Products, Inc

ABSTRACT BODY:

Purpose: To demonstrate a training tool based on virtual reality technology that will simulate scenes with increasing for patients implanted with a visual
prosthesis. A virtual reality setup can create scenarios with an unlimited field of view that will enable the recipient to practice the scanning techniques needed to gain maximum benefit from the non-natural restored sight.

Methods: A virtual find-the-dot video game was integrated with the Argus II retinal prosthesis system. The game mimics daily use in which the patient is
required to steer the narrow region of interest (ROI) of the array to the target. A small Inertial Measurement Unit (IMU) was mounted on the glasses in order to track head movements in real-time. In the current setup, the regular video camera was disconnected and the video input was based on the visual content from the projection of the ROI of the array (18° x 11°) on the virtual wall based on real-time head position. A single target was presented on the virtual wall in each trial. The patient used a handheld game to indicate that he/she found the target. When the patient reported that the target was found, the trial is ended and the next trial is initiated with a new target at a different location. The application recorded the sub-area of the array

Results: A feasibility test of an Argus II patient shows that only a subset of the array was used to locate the target. OCT scan confirmed that the area of the array that wasn't used in the virtual game was lifted from the retina.

Conclusions: The usability of a virtual reality environment was shown to efficiently monitor the functionality of a retinal implant during scanning in a controlled
environment. The results indicate an issue with the position of the array that couldn’t be detected in regular use of the device. This methodology based on virtual reality technology can be implemented in both retinal and cortical visual implants that aim to restore sight.

CONTROL ID: 3711532

SUBMITTER (NAME ONLY): Jacob Heng

TITLE: Single-cell transcriptional profiling of the adult murine lacrimal gland in health and disease

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Heng, Ophthalmology and Visual Science, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|J.S. Heng, J. Nathans, Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|B.L. Winer, L.A. Goff, Genetic Medicine, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|L.A. Goff, Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|J. Nathans, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the single-cell transcriptome of the adult murine lacrimal gland in wild-type mice and mouse models of Sjogren's syndrome

Methods: Extraorbital lacrimal glands from adult BALB/cJ male (n=4) and female (n=4) mice, as well as adult NOD.B10.H2b male mice (n=2) and adult MRL-lpr female mice (n=2) were dissected and dissociated for droplet-based single-cell RNA sequencing (sc-RNAseq, 10X Genomics). All mice were 4 months of age at the time of experiment. Cell type annotation and differential gene expression analysis were performed using the Monocle R package. Gene set enrichment analysis (GSEA) was carried out using the Molecular Signatures Database (MSigDB) Hallmark gene sets. Cell type markers and other genes of interest were validated using immunofluorescence.

Results: A total of 102,431 cells were profiled by sc-RNAseq and included all known major cell types in the lacrimal gland. There was notable sexual dimorphism in the expression of the secretoglobins, with most secretoglobins being preferentially expressed in male lacrimal glands. Analysis of the immune cell clusters identified cells of monocyte lineage, plasma cells, B cells, T cells, NK cells, mast cells and a cluster of GM-CSF-producing innate lymphoid cells (ILCs). Cells of monocyte lineage exhibited dynamic transcriptional profiles that included a sub-population of Cd163-positive, Pf4-positive macrophages. GSEA revealed significant upregulation of interferon signaling in NOD.B10.H2b and MRL-lpr lacrimal glands.

Conclusions: sc-RNAseq revealed sexual dimorphism in gene expression and diverse immune cell types in lacrimal glands of wild-type mice and mouse models of Sjogren's syndrome. Interferon signaling appeared to be significantly upregulated in two mouse models of Sjogren's syndrome. The role of novel immune sub-populations, including innate lymphoid cells and Cd163-positive macrophages, in lacrimal gland disease remains to be elucidated and warrants further investigation.

CONTROL ID: 3711533

SUBMITTER (NAME ONLY): Dmitry Romashchenko

TITLE: Objective comparison of two setups for evaluation of positive dysphotopsia from intraocular lenses

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Romashchenko, M.D. Jenkins Sanchez, M. van der Mooren, C. Canovas, R&D, Johnson & Johnson Surgical Vision, Groningen, NETHERLANDS|L. Lundström, Visual Optics, Biomedical and X-ray Physics, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN|

Commercial Relationships Disclosure: Dmitry Romashchenko: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision;Code P (Patent):Johnson & Johnson Surgical Vision | Mark Jenkins Sanchez: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision | Linda Lundström: Commercial Relationship(s);Code C (Consultant/Contractor):Johnson & Johnson Surgical Vision;Code P (Patent):Johnson & Johnson Surgical Vision | Marrie van der Mooren: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision;Code P (Patent):Johnson & Johnson Surgical Vision | Carmen Canovas: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision

ABSTRACT BODY:

Purpose: Positive dyshotopsia (PD) (such as halo, glare, starburst) is one of the main drawbacks of intraocular lenses (IOLs) for presbyopia correction. Adequate assessment of these effects before lens implantation is a valuable tool for both analysis and improvement of currently available IOL designs. This task is non-trivial and can be done by means of different optical setups. In this work we evaluate and compare two see-through setups, designed for simulations of the physical IOL-related visual symptoms.

Methods: Two IOL telescopes, Type 1 (IOL-T1) and Type 2 (IOL-T2) (devices are reported in two separate abstracts), have been objectively compared in their ability to translate visual symptoms from an IOL to an observer. In these systems, an IOL is part of the main ray path, which allows to study PD induced by an actual manufactured IOL. Each setup was evaluated with three different IOL designs: one monofocal, and two multifocals with 2.75 D and 4.00 D add power respectively. All three IOLs had the same base power. A camera was used in place of an observer, and a central glare source was imaged against a black background. The analysis was performed on high dynamic range images obtained from combining several frames (RGB converted to monochrome) with different exposure times. Light scatter data from literature is used as basis for comparison of the level and the field location of the halo of multifocal IOLs.

Results: In both setups, the recorded radial-average scatter function allows to clearly identify the multifocality-related halos and distinguish between the higher- and lower-add IOLs. The scatter levels of monofocal and multifocal IOLs were comparable with earlier reported data (Langeslag et al. JCRS 2014) The location of the IOL-related PD peaks is similar between the two devices and resides below 0.4° in field angle. This is comparable with previously reported theoretical prediction of 0.33° for a 4.00 D add power multifocal IOL (Van der Mooren et al. IOVS2016).

Conclusions: This study compares objectively the PD measured with two see-through setups designed to evaluate actual IOLs. The results show that IOL-T1 and IOL-T2 perform similarly and show data comparable to published pre-clinical data for different IOL designs, allowing objective assessment of PD. Subjective testing with these devices is out of the scope of this work and is reported in two separate studies.

CONTROL ID: 3711535

SUBMITTER (NAME ONLY): Hassan Mansoor

TITLE: Evaluation of the Effect of Topical and Oral Peroxisome Proliferator-activated Receptor α (PPARα) agonist on Corneal Nerve Regeneration in Diabetic Mice.

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Mansoor, Al Shifa Trust Eye Hospital, PAKISTAN|H. Tan, Singapore General Hospital, Singapore, SINGAPORE|I. Lee, M. Lin, H. Ang, G.S. Peh, J.S. Mehta, Y. Liu, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate the potential stimulation effect of topical and oral fenofibrate, a peroxisome proliferator-activated receptor α (PPARα) agonist, on corneal nerve regeneration in diabetes mellitus.

Methods: A total of 108 Ins2Akita mice were divided into 4 groups (n=54 eyes/group): negative control (NC), positive control (PC), topical fenofibrate (TF) and oral fenofibrate (OF) treatment groups. All the mice underwent a 2-weekly clinical evaluation including slit-lamp examination, in vivo confocal microscopy (IVCM), corneal sensitivity, and tear enzyme-linked immunosorbent assay analysis. Mice were euthanized after 6-week and 12-week treatment, and were subjected to immunohistochemistry staining; corneal whole-mount staining, and western blot (WB) analysis.

Results: After 12-weeks of treatment, corneal PPARα protein expression evaluated by WB increased by 2.67-folds and 1.52-folds in the TF and OF groups, respectively. IVCM evaluation showed that the corneal nerve fibre density (CNFD) and corneal nerve fibre length (CNFL) significantly improved in the TF (9.2 to 16.8 fibres/mm^2 (p=0.01) and 3.9 to 6.2 mm/mm^2 (p=0.04), respectively) and OF groups (10.3 to 14.7 fibres/mm^2 (p=0.02) and 3.7 to 5.4 mm/mm^2 (p=0.04), respectively; Figure 1). The area of corneal epitheliopathy reduced in the TF (58.7% to 8.9%; p<0.001) and OF groups (37.4 to 6.8%; p<0.001 Figure 2). Corneal whole mount staining with β3-tubulin demonstrated that corneal nerve parameters decreased in diabetic mice, but they improved with fenofibrate treatment. No significant difference was observed in the corneal sensitivity of different groups. The tear substance P and calcitonin gene-related peptide concentrations significantly increased in the TF (115.07 to 163.4 pg/ml (p=0.03) and 149.22 to 215.92 pg/ml (p=0.02), respectively) and OF groups (112.77 to 116.53 pg/ml (p=0.32) and 156.37 to 247.50 pg/ml (p=0.01), respectively).

Conclusions: Topical and oral fenofibrate potentially promote corneal nerves regeneration and enhance ocular surface health in diabetic corneal neuropathy.

CONTROL ID: 3711537

SUBMITTER (NAME ONLY): Wright Shamp

TITLE: Influence of Age and Race on Axial Elongation in Myopic Children

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Shamp, N.A. Brennan, M.A. Bullimore, X. Cheng, E. Maynes, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: With increasing emphasis on slowing myopia progression and using axial length to monitor eye growth, normative data for axial elongation in myopic children provide valuable clinical information. Percentile growth curves have been presented but are specific to the population tested and often include myopes and non-myopes, limiting their application. We conducted a meta-analysis to model axial elongation in myopic children with emphasis on the influence of age and race.

Methods: A comprehensive electronic systematic search was performed using Ovid Medline, EMBASE, Cochrane Central Register of Controlled Trials and the following terms: (myopia OR myopic) AND (child OR children) AND (progression OR longitudinal OR follow-up OR shift) AND axial. There were 79 studies with 105 untreated subpopulations and 203 evaluations of the mean axial change from baseline that met the inclusion criteria. Log(mean rate of axial elongation) was analyzed using a weighted multivariable linear mixed effects meta-analysis model. All collected covariates were tested for significance (age, race and baseline axial length selected). The model included three levels of random effects to account for all variability.

Results: Only data without missing observations of significant covariates were included in the final model (118 evaluations). The figure plots modeled annual axial elongation (with prediction intervals) by mean age of evaluation and race. Mean axial elongation decreases as age increases (15.0% decrease per year; 95%CI 11.4–18.5%, P <0.0001) and is greater in Asian children (by 27.9%; 95%CI 7.6–52.2%, P <0.01) compared to non-Asians. No other input variables, including baseline axial length, were statistically significant.

Conclusions: This analysis sets benchmark values for assessing axial elongation and monitoring myopia progression. To our knowledge, this is the first weighted random effects meta-analysis of axial elongation in myopic children. Interpretation is limited by use of aggregated data rather than individual subject data. The large prediction intervals should be borne in mind when interpreting individual rates of axial elongation clinically.

CONTROL ID: 3711538

SUBMITTER (NAME ONLY): Sunir Garg

TITLE: Impact of baseline imbalances on the efficacy of pegcetacoplan for the treatment of geographic atrophy (GA): A post hoc analysis of OAKS, DERBY, and FILLY

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To examine the potential impact of baseline imbalances on the 12-month results of OAKS, DERBY, and FILLY.

Methods: This is a post hoc analysis of the OAKS (NCT03525613), DERBY (NCT03525600) and FILLY (NCT02503332) studies. OAKS and DERBY are 24-month, phase 3, randomized studies comparing the efficacy and safety of monthly or every-other-month (EOM) intravitreal pegcetacoplan with sham in patients with GA secondary to age-related macular degeneration. FILLY was a phase 2 study with a similar design. The primary endpoint was change in absolute GA lesion size from baseline to Month 12 in OAKS and DERBY and change in square root transformed lesion size in FILLY. OAKS and FILLY met the primary endpoint while DERBY narrowly missed. In the original, pre-specified analysis, fellow eye CNV (OAKS and DERBY only), time, and baseline lesion size were covariates. To investigate differences in the treatment effect estimate, a systematic covariate analysis was conducted. Eight variables, including 7 baseline characteristics related to GA progression (study eye focality, lesion location, lesion size, pseudodrusen, low-luminance deficit (LLD), intermediate/large drusen number, GA laterality) and region were selected to investigate imbalances between treatment arms within each study. Variables with imbalances

meeting a p<0.2 threshold in any of the studies were included in the common adjusted model and efficacy analyses were repeated.

Results: Four variables with imbalances met the p<0.2 threshold for inclusion in the adjusted model: study eye lesion location (OAKS), study eye intermediate/large drusen number (DERBY, FILLY), study eye LLD (FILLY), and study eye lesion focality (DERBY). Before adjustment, absolute change in GA lesion growth reduction was 22% and 16% (OAKS), 12% and 11% (DERBY), and 31% and 21% (FILLY) for the monthly and EOM arms, respectively, at Month 12. Accounting for imbalanced variables, GA lesion growth reduction was 26% and 18% (OAKS), 16% and 15% (DERBY), and 25% and 18% (FILLY) for the monthly and EOM arms, respectively.

Conclusions: After adjusting for imbalances, results are more consistent across the studies, but this analysis does not fully explain the disparities nor replace the primary analysis. Future studies could consider incorporating additional variables as covariates or pre-specifying a plan for covariate adjustment.

CONTROL ID: 3711539

SUBMITTER (NAME ONLY): Inesa Lelyte

TITLE: Title. Development of human retinal pigment epithelial cells with inducible VEGF expression

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor A (VEGF) is upregulated in neovascular ocular conditions, including diabetic retinopathy (DR). To study the pathological processes in DR and develop novel treatments, VEGF-induced animal models have been established. Intravitreal injections of recombinant VEGF have been shown to mimic many of the complex DR mechanisms. However, the effects are transient due to the short half-life of injected peptides. The aim of this study was to generate an inducible VEGF expression the human retinal pigment epithelium (ARPE-19) cells.

Methods: ARPE-19 cells were transduced with lentivirus (LV) expressing a SparQ^{TM} all-in-one cumate-inducible plasmid (System Biosciences) expressing VEGF-A$_{165}$ at a multiplicity of infection (MOI) of 20. To induce VEGF expression, cumate (30 µg/ml) was added 3d post-transduction. After 48h, VEGF levels were determined in the culture medium by ELISA (R&D Systems) and by qPCR from cell lysates. Cell viability was evaluated by MTT assay; cell motility was measured by scratch assays. Effects of VEGF expression on ARPE19 permeability were performed in Transwell® inserts (Corning Inc.) using conditioned media and quantified using fluorescent permeability standard, 6-carboxyfluorescein (6-CF).

Results: Cumate induction resulted in a 72% increase in VEGF levels as assessed by ELISA (MOI 20: 2005 ± 270 pg/ml vs. Control: 1165 ± 192 pg/ml, $p < 0.05$). qPCR revealed a 2.5-fold increase of VEGF mRNA levels compared with control ($p < 0.01$). MTT assay showed significantly increased number of cells at MOI 20 (115 ± 5%) compared with Control (100 ± 1%, $p < 0.05$), suggesting increased rate of proliferation. Permeability across the RPE monolayer was significantly increased in LV-transduced cells. Treatment of ARPE19 cells with conditioned media resulted in a significant increase in the apparent permeability coefficients (P_{app}) for 6-CF (0.66 ± 0.08 vs. 1.80 ± 0.41 x 10^{5} cm/s, $p < 0.05$). Scratch assays revealed increased motility and presence of tube-like structures in transduced cells, suggesting the presence of VEGF.

Conclusions: Cumate-inducible VEGF expression is a feasible approach for mechanistic studies evaluating the dose-dependent effects of VEGF on ARPE19 in preclinical drug discovery studies. Future work will generate stably expressing cell lines and evaluate the utility of cumate-inducible VEGF-expressing LV in in vivo systems.

CONTROL ID: 3711540

SUBMITTER (NAME ONLY): Isabella Loh

TITLE: Effect of Axial Length on the Quality of ONH Scans Acquired from SS-OCT and SD-OCT in Highly Myopic Eyes

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.Q. Loh, R. Chong, Y. Dan, Q. Wong, J.D. Yu, C.S. Chua, C. Wong, Q.V. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS Medical School, SINGAPORE|Q.V. Hoang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies have suggested that swept-source optical coherence tomography (SS-OCT) may be superior to spectral-domain OCT (SD-OCT) in imaging eyes with pathological myopia. Here, we compare SD-OCT and SS-OCT optic nerve head (ONH) scans in highly myopic (HM) eyes, to determine if one modality is superior to the other in terms of the percentage of usable scans produced (perUSABLE), and if this difference in perUSABLE is correlated with axial length (AL) and the presence of myopic defects, such as staphyloma, peripapillary atrophy and myopic macular degeneration.

Methods: 413 eyes from 212 patients with HM in at least 1 eye (AL 29.1 ± 2.5 mm, range 22.8 to 35.8 mm) were scanned with SD-OCT (Cirrus) and SS-OCT (Triton). Metrics for the quality of each scan were acquired, namely signal strength (SS), centration and motion artifact. Usable scans were defined as having adequate SS (Cirrus: SS≥7; Triton: SS≥30), adequate centration and lack of motion artifact. Paired t-tests and linear regression analysis were performed to compare SD-OCT vs. SS-OCT and evaluate the association between perUSABLE and potential baseline predictor variables (AL, age, gender, lens status, glaucoma diagnosis, myopic macular degeneration presence, peripapillary atrophy presence, disc tilt presence and presence of intrachoroidal cavitations).

Results: On average, ONH RNFL scans resulted in significantly greater likelihood of useable scans in Triton (41.8%p) vs. Cirrus scans (15.0%p, $p<0.001$, paired t-test). Specifically, it was the SS metric that drove this difference. Insufficient SS was found in 1.3%p of Triton scans, but 83.9%p of Cirrus scans ($p<0.001$). After accounting for potential confounders in multivariate analysis in Cirrus scans, every 1 mm of longer AL was associated with a 1.7%p greater likelihood of insufficient SS ($p=0.005$), and presence of MMD with +11.8%p ($p=0.001$). In contrast, in Triton scans, only logMAR VA (worse vision) increased the likelihood of insufficient SS (+1.3%p/ 1.0 LogMAR, $p=0.019$).

Conclusions: SS-OCT appears to be more successful than SD-OCT in providing useable ONH RNFL scans, mainly based on SS differences. In particular, Cirrus SS was affected by longer AL and presence of MMD. Our findings suggest SS-OCT may be more likely to avoid the need for repeated scans to achieve useable ONH RNFL data in HM eyes with MMD.

CONTROL ID: 3711541

SUBMITTER (NAME ONLY): Avril Reddy

TITLE: Dietary cholesterol and inner blood retina barrier permeability drives immune cell recruitment to the retina

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Reddy, N. Hudson, C. Delaney, M. Campbell, Smurfit Institute of Genetics, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: In dry age-related macular degeneration (AMD), immune cells, predominantly macrophages and microglia, migrate to the subretinal space. This is observed in the intermediate stage of disease, prior to retinal pigment epithelial (RPE) atrophy, but the cause of this migration is not clear. Cholesterol, or associated oxidised deposits, accumulate in the subretinal space with age and have been shown to influence microglial migration in vitro. Recently, suppression of claudin-5, the principal tight junction component of the inner blood retinal barrier (iBRB), has been demonstrated to induce a geographic atrophy (GA) like phenotype in mice fed a high cholesterol diet (HCD).

Here, claudin-5 heterozygosity has been induced at the iBRB and mice have been fed HCD for up to 20 weeks, with the aim of elucidating how cholesterol and reduced iBRB integrity may drive the phenotype observed.

Methods: Cldn5 heterozygosity is specifically induced in endothelial cells using the Cre-LoxP system and the endothelial promoter, Tie2. Mice were fed a HCD or normal diet (ND) for up to 20 weeks. Retinal cryosections were examined to determine tight junction composition, cholesterol deposition and immune phenotype, relative to wild-type littermate controls. Serum was extracted from these mice to examine the systemic effect of the HCD.

Results: After 10 weeks of HCD, mice had significantly increased serum levels of cholesterol, as compared to controls fed ND. Filipin and bodipy staining detected an accumulation of cholesterol and lipid deposits in the outer retinal region of these mice. Retinal claudin-5 expression was reduced at the iBRB and increased immunohistochemical signal of macrophage markers, F4/80 and Cd68, suggests an increased presence of macrophages in the retinas of heterozygous mice. Histological analysis also showed greater numbers of cells in the subretinal region that positively stain for Cd68.

Conclusions: These results suggest that the combination of a more permeable iBRB and high dietary cholesterol may influence macrophage recruitment to the retina. Multiple methods of suppressing retinal claudin-5 in mice fed a cholesterol rich diet have now shown to result in RPE atrophy. This study demonstrates another characteristic phenotype of dry AMD, the accumulation of immune cells in the subretinal region, making these animal models an attractive choice for the study of disease progression.

CONTROL ID: 3711542

SUBMITTER (NAME ONLY): Shotaro Shimokawa

TITLE: MyD88 but not Card9 signaling mediates neuroprotective microglial activation in a mouse model of retinitis pigmentosa

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shimokawa, Y. Murakami, J. Funatsu, M. Fukushima, K. Sonoda, Kyushu Daigaku, Fukuoka, Fukuoka, JAPAN|Y. Ikeda, Miyazaki Daigaku, Miyazaki, Miyazaki, JAPAN|

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ABSTRACT BODY:

Purpose: Neuroinflammation is triggered by the recognition of damage-associated molecular patterns (DAMPs) by the pattern recognition receptors (PRRs). Toll-like receptors (TLRs)/MyD88 and C-type lectin receptors (CLRs)/Card9 are two major PRR pathways that mediate inflammatory signaling in tissue injury and repair. In the present study, we investigated the respective functions of MyD88 and Card9 in retinal degeneration and neuroinflammation in a mouse model of retinitis pigmentosa (RP).

Methods: Rd10 mice, a RP model harboring Pde6b mutation, were crossed with Myd88$^{-/-}$ or Card9$^{-/-}$ mice to produce rd10; Myd88$^{-/-}$ or rd10; Card9$^{-/-}$ mice. The retinal phenotype was assessed by TUNEL, HE staining and electroretinogram (ERG). Retinal microglia were immunostained with Iba-1. Retinal mRNA profiles associated with neuroinflammation were analyzed by using nCounter Nano String Neuroinflammation panels. Immunostaining for the differential expressed genes was performed on retinal sections.

Results: Mdy88 deficiency in rd10 mice increased the number of TUNEL-positive cells in the outer nuclear layer (ONL) and exacerbated ONL thinning at P21 ($P < 0.01$, each); whereas Card9 deficiency did not influence the retinal phenotype. Consistently, scotopic ERG showed that b-wave amplitudes were decreased in rd10; Myd88$^{-/-}$ mice compared to rd10 mice ($P=0.002$), while there was no difference between rd10; Card9$^{-/-}$ and rd10 mice. Microglial translocation to the outer retina was significantly decreased in rd10; Myd88$^{-/-}$ compared to rd10 mice($P < 0.01$). Retinal mRNA profiling identified increased expression of Ifitm3 and Serpina3n, activation markers of astrocytic glia, in rd10; Myd88$^{-/-}$ mice. Immunostaining confirmed the upregulation of IFITM3 and SERPINA3N in astrocytes and müller cells in rd10; Myd88$^{-/-}$ mice.

Conclusions: TLRs/MyD88 pathway, but not CLRs/Card9 pathway, is a key mediator of neuroinflammation in rd10 mice, and may provide neuroprotection via promoting microglial translocation and regulating astrocyte/müller cell activation in RP.

CONTROL ID: 3711543

SUBMITTER (NAME ONLY): Nouran Sabbagh

TITLE: White coat adherence in primary open-angle glaucoma

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Sabbagh, Internal Medicine, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S. Poleon, School of Optometry, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|L. Racette, Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Improved adherence to treatment in the days surrounding clinic visits is a phenomenon known as white coat adherence. White coat adherence can lead to clinical measurements that are not representative of those present outside of clinical encounters. In glaucoma, white coat adherence to prescribed hypotensive therapy may lead to artificially low intraocular pressure readings, which may impact clinical evaluation and treatment decisions. The objective of this study was to assess white coat adherence in glaucoma patients.

Methods: In this cohort study, patients with primary open-angle glaucoma were selected from an ongoing longitudinal NIH-funded study if they used hypotensive eyedrops, had a clinic visit during the parent study, and had adherence data during the 56 days evenly bracketing the clinic visit. Adherence within the implementation phase was measured using Medication Event Monitoring System (MEMS) caps. Wilcoxon tests were used to compare mean adherence between the following periods: $Pre_{1\text{-}3}$ (days 1 to 3 preceding the clinic visit) and $Pre_{4\text{-}14}$ (days 4 to 14 preceding the clinic visit; $Post_{1\text{-}3}$ (days 1 to 3 following the clinic visit) and $Post_{4\text{-}14}$ (days 4 to 14 following the clinic visit). Analyses were performed in the full sample, and in patients with optimal (≥80%, n = 48) and suboptimal adherence (<80%, n = 17).

Results: Sixty-five patients were included, of which 47.7% were male. Mean age was 71 ± 8 years. In the six months bracketing the clinic visit, mean adherence was 86.1% ± 17.9. Overall, mean adherence significantly increased from $Pre_{4\text{-}14}$ to $Pre_{1\text{-}3}$ (85.2% to 88.3%) ($p = 0.04$). No significant change was observed after the clinic visit. In patients with optimal adherence, mean adherence significantly increased from $Pre_{4\text{-}14}$ to $Pre_{1\text{-}3}$ (93.8% to 97.7%) ($p = 0.01$), whereas no significant change was observed in patients with suboptimal adherence.

Conclusions: Our results show the presence of white coat adherence in this cohort of patients. However, this effect was not observed in patients with suboptimal adherence. Due to its potential impact on treatment decisions, providers should remain vigilant for white coat adherence and make this a relevant topic in patient-provider discussions.

CONTROL ID: 3711545

SUBMITTER (NAME ONLY): Thomas Carr

TITLE: Clinical applicability of deep learning to predict retinal disease from small OCT datasets

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Carr, D. Broadway, J. Sanderson, School of Pharmacy, University of East Anglia, Norwich, Norfolk, UNITED KINGDOM|T. Carr, S. Sami, Norwich Medical School, University of East Anglia, Norwich, Norfolk, UNITED KINGDOM|D. Broadway, Ophthalmology, Norfolk and Norwich University Hospital, Norwich, Norfolk, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Interpretable staged transfer learning (iSTL), a pipeline for improving image classification with small sample sizes, was trained to carry out classification of optical coherence tomography (OCT) images. Model attention was visualised using SHAP maps, allowing interpretation of its behaviour.

Methods: A disease classification task using the Inception-v4 convolutional neural network architecture and iSTL training pipeline was carried out. Target OCT images are available under licence (Gholami et al). Normal (n=206), macular hole (MH: n=104), diabetic retinopathy (DR; n=109), and central serous retinopathy (CSR; n=104) scans were used. 50 images were used for data augmentation and training, the remainder were used for validation. The model was pre-trained on ImageNet, given randomly initialised output layers; the early layers frozen. The model was then trained on an intermediate bridge dataset (Kermany et al), output layers replaced, and final training carried out on the target dataset. 10 models were trained, the best performing selected for SHAP attention maps visualisation.

Results: SHAP maps showed both image and disease specific features were allocated importance during prediction. High importance areas have a large impact on the model's prediction, low importance areas have less impact. Classifying CSR, high importance was allocated to areas surrounding posterior epithelial detachment and not to areas of subretinal fluid. With DR, retinal microaneurysms and intraretinal oedema were highlighted but subretinal fluid was not. MH scans saw strong regional importance allocated to the vertical edge of full-thickness holes and surrounding intraretinal cysts when present. Normal images typically presented with medium to high importance on the retinal pigment epithelium adjacent to the macula as well as the inner limiting membrane surface. Many images saw moderate attention within areas of the choroid and vitreous that had no apparent clinical importance. When present in the scan field the optic nerve head was not allocated high importance.

Conclusions: Confounding factors are a concern when training deep learning models, particularly with small datasets. The iSTL model appeared to predominantly use clinically applicable features to make predictions. Further work is needed to determine whether some features used to make predictions are confounds or genuine clinical features related to disease biomarkers.

CONTROL ID: 3711546
SUBMITTER (NAME ONLY): Rebecca Deffler
TITLE: Hazard perception in bioptic drivers
SESSION TITLE: Vision Impairment: Impact on Driving and Mobility
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: R.A. Deffler, S. Cooley, T.W. Raasch, B.E. Dougherty, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|
Commercial Relationships Disclosure: Rebecca Deffler: Commercial Relationship: Code N (No Commercial Relationship) | San-San Cooley: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Raasch: Commercial Relationship: Code N (No Commercial Relationship) | Bradley Dougherty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Bioptic telescopic spectacles (BTS) can allow individuals with central vision impairment to obtain driving privileges. Hazard perception is the ability to anticipate potential road hazards to avoid a collision and has been shown to predict collision rates. The purpose of this study was to analyze whether hazard detection is affected by vision loss in bioptic drivers and what role the use of BTS may play.

Methods: ETDRS visual acuity was measured for each eye individually and through the BTS as indicated. Contrast sensitivity testing was performed with the Mars chart. Number of weekly trips and mileage were collected using Driving Habits Questionnaire. Hazard perception testing was conducted using 30 commercially available first-person driving video clips. Subjects signaled when they could first identify a traffic hazard requiring change of speed or direction. Bioptic drivers were tested with and without BTS in alternating blocks. Hazard detection times for each clip were converted to z-scores, converted back to seconds using the average response time across all videos, and then compared among conditions.

Results: Eight visually impaired licensed bioptic drivers and seven normally-sighted control drivers completed the study. There was no significant difference in age (mean±SD = 55±8 years for bioptic drivers vs 52±7 years for controls, P=0.730). Control drivers had significantly better visual acuity (logMAR -0.05±0.04) than visually impaired drivers (logMAR 0.69±0.09, P<0.01), even when these drivers used their bioptic telescope (logMAR 0.13±0.04, P<0.01). Log contrast sensitivity was poorer among bioptic drivers (1.51±0.19 vs 1.80±0.05, P=0.012). There was a trend toward more weekly mileage for bioptic drivers (median of 145 vs 96, P=0.281), but weekly trips were similar (median 9.5 for bioptic vs 10 for control). Standardized mean hazard response times (sec) for each condition were: bioptic with BTS = 5.1±0.9, bioptic w/out BTS = 5.8±1.4, normally-sighted = 3.6±1.9. Hazard response time was improved by about 0.8 sec when bioptic drivers used BTS (P=0.015). Only a low proportion of hazards was missed in all conditions.

Conclusions: Driving hazard response time in bioptic drivers was better with use of bioptic telescopic spectacles on a video-based test, though they still may have reduced response times when compared with normally-sighted drivers. Further work to determine how these findings are related to on-road performance and outcomes is warranted.

CONTROL ID: 3711550

SUBMITTER (NAME ONLY): Maria Toms

TITLE: Use of non-viral episomal vectors as a large gene augmentation strategy for USH2A retinopathy

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: USH2A mutations are a common cause of autosomal recessive retinitis pigmentosa (RP) and Usher syndrome, for which there are currently no approved treatments. Gene augmentation is a promising therapeutic strategy for treating retinal diseases, however conventional adeno-associated virus (AAV) vectors cannot accommodate cDNAs exceeding 4.7kb, such as the 15.6kb-long USH2A coding sequence. We investigated an alternative non-viral strategy using episomal DNA plasmid vectors containing a scaffold/matrix attachment region (S/MAR) and the human USH2A cDNA.

Methods: USH2A-S/MAR vectors were generated by inserting the human USH2A coding sequence into the pS/MAR backbone in five cloning steps. HEK293 cells and USH2A$^{-/-}$ patient-derived dermal fibroblasts were transfected using the Neon transfection system. Wild-type and ush2a^{u507} zebrafish were microinjected with USH2A-S/MAR vector at the single-cell stage of development. Expression of GFP and USH2A protein (usherin) was assessed in both human cell lines and zebrafish using qRT-PCR, immunostaining and Western blot analysis

Results: USH2A-S/MAR vectors were generated, containing a GFP reporter gene and CAG (pS/MAR-CAG-USH2A) or CMV (pS/MAR-CMV-USH2A) promoters, reaching a size of 23kb. The vectors drove persistent transgene expression in patient fibroblasts and zebrafish with usherin detection, and up to 12 months of GFP expression detected in zebrafish retinal photoreceptor cells.

Conclusions: To our knowledge, this is the first reported vector generating expression of full-length usherin in USH2A models. S/MAR DNA plasmid vectors have shown promise as a novel non-viral retinal gene therapy, warranting further translational development.

CONTROL ID: 3711552

SUBMITTER (NAME ONLY): Michael Singer

TITLE: Suprachoroidal triamcinolone acetonide injectable suspension for macular edema associated with uveitis: Effect of disease characteristics on clinical outcomes

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Singer, University of Texas Health Science Center, San Antonio, Texas, UNITED STATES|B. Kapik, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Triamcinolone acetonide injectable suspension, for suprachoroidal use (SCS-TA) provides targeted drug delivery to the choroid/retina while minimizing steroid exposure in nontarget tissues. Efficacy and safety of SCS-TA in the treatment of macular edema (ME) secondary to noninfectious uveitis (NIU) were demonstrated in PEACHTREE. The objective of these post-hoc analyses was to determine whether baseline disease characteristics impact the efficacy of SCS-TA.

Methods: In PEACHTREE, 96 subjects received SCS-TA at baseline and Week 12; best-corrected visual acuity (BCVA) and central subfield thickness (CST; in μm) were evaluated every 4 weeks for 24 weeks. Mean [SEM] change from baseline (CFB) in BCVA (ETDRS letters) and CST (μm) were calculated among SCS-TA-treated subjects by time since ME diagnosis (n=24 ≤71 days, n=22 >71 days) or NIU diagnosis (n=60 ≤177 days, n=36 >177 days), and by disease onset (n=22 sudden, n=74 insidious) or duration (n=18 ≤3 months, n=78 >3 months). Treatment differences were evaluated using an analysis of variance model with a fixed effect for baseline demographic factors.

Results: Significant BCVA gains and CST reductions from baseline were found in all groups at all visits irrespective of time to diagnosis or disease onset/duration (P≤0.05). At Week 24, BCVA gains were 15.5 [1.48] in subjects with ME diagnosis ≤71 days vs 8.0 [3.37] in those with diagnosis >71 days (P=0.024) and 19.6 [3.13] in subjects with NIU duration ≤3 months vs 12.4 (1.55] with NIU >3 months (P=0.048). In subjects with NIU diagnosis ≤177 days vs >177 days and sudden vs insidious disease duration BCVA gains were 15.5 [1.70] vs 10.8 [2.42] and 18.4 [3.09] vs 12.4 [1.56], respectively at Week 24 (P≥0.075). In subjects with more recent vs earlier ME/NIU diagnoses, changes in CST were -164.2 [20.15] vs -115.3 [24.27] and -163.7 [23.28] vs -133.4 [20.15], while those with sudden vs insidious onset and NIU duration ≤3 vs >3 months had CST values of -165.7 [38.50] vs -148.8 [18.25] and -166.3 [45.29] vs -149.3 [17.49], respectively (P≥0.210).

Conclusions: Significant improvements in BCVA and CST were observed regardless of baseline disease characteristics, with trends towards greater improvements in those with more recent diagnosis and shorter disease duration. These findings suggest that treatment should be initiated promptly upon diagnosis.

CONTROL ID: 3711553

SUBMITTER (NAME ONLY): Cameron Hoerig

TITLE: Evaluating chemical-crosslinking induced microstructural changes in the posterior sclera with high-frequency quantitative ultrasound

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hoerig, J. Mamou, Riverside Research, New York, New York, UNITED STATES|J. Aichele, S. Catheline, LabTAU, Lyon, FRANCE|Q.V. Hoang, Singapore Eye Research Institute, Singapore, SINGAPORE|Q.V. Hoang, Ophthalmology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chemical crosslinking (CXL) treatments offer a minimally invasive method of treating corneal ectasia and may also provide a method to halt the progression of myopia by strengthening the posterior sclera. Effective clinical use would require methods to evaluate longitudinal efficacy of CXL. Prior studies revealed the potential of quantitative ultrasound (QUS) to evaluate microstructural changes in the myopic posterior sclera. This study used QUS to monitor changes in sclera microstructure caused by CXL.

Methods: Seven adult ex vivo porcine eyes were procured from a supplier and placed in a -80^{o}C freezer for later use. Prior to data acquisition, eyes were thawed and excess tissue was removed from the posterior pole. Eyes were divided into control (3 eyes) and treated (4 eyes) groups. Control eyes were mounted in the experimental setup and immersed in room temperature phosphate buffered saline whereas treated eyes were immersed in 26mM sodium hydroxymethylglycinate (SHMG), a CXL agent. Eyes were scanned by an 80MHz ultrasound transducer at regular time intervals and the RF echo data were analyzed to compute ten QUS parameters: 5 from backscatter coefficient methods, 4 from envelope statistics, and shear wave speed (SWS) to infer tissue stiffness. Resulting QUS estimates were correlated with immersion time to evaluate the efficacy of QUS to monitor CXL treatment.

Results: Among control eyes, a significant increase in value was measured for spectral intercept (I_0, R^2=0.94, p=0.01), midband fit (R^2=0.91, p=0.01), and effective acoustic concentration (R^2=0.88, p=0.02). When considering treated eyes, positive temporal changes were measured for spectral slope (R^2=0.88, p=0.02) whereas significant decreases were observed for I_0 (R^2=0.86, p=0.02) and effective scatterer diameter (R^2=0.89, p=0.02). SWS estimated by passive elastography showed a significant increase for treated eyes (R^2=0.85, p=0.03) and no significant correlation with immersion time for control eyes (R^2=0.09, p=0.63).

Conclusions: QUS parameters estimated from high frequency ultrasound data are correlated with CXL-induced changes in scleral tissue microstructure. In addition, CXL leads to an increase in tissue stiffness that is measured as an increase in SWS. Results of this study provide preliminary evidence that high frequency QUS may be a useful tool for monitoring CXL treatment in a clinical setting.

CONTROL ID: 3711554

SUBMITTER (NAME ONLY): Matthew Benson

TITLE: Golden-yellow fundus reflex and OCT hyper-reflectivity in RPGR retinopathy

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Benson, A. Agather, D. Blain, R.B. Hufnagel, B.P. Brooks, L. Huryn, W.M. Zein, C.A. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pathogenic variants in RPGR represent a common cause of X-linked retinal degeneration and can cause severe vision loss. While a tapetal-like reflex has been demonstrated in female carriers and less commonly in affected males, a more detailed description of this feature is warranted, including evaluation of corresponding OCT findings and genotype-phenotype correlations. To address this, we report a series of patients with RPGR retinopathy who manifested a golden-yellow fundus reflex and corresponding OCT changes, and highlight the clinical, genetic, and multimodal imaging features.

Methods: We performed a single-center retrospective review of patients with disease-causing RPGR variants from 2014-2021. Clinical data including acuity, full-field electroretinography (ffERG), color fundus images, and OCT images were collected. Of 82 total cases, 66 had both fundus and OCT images available for review. An expert examiner, who was masked to participant demographics, clinical evaluations, and pathogenic RPGR variant, assessed bilateral color fundus photos for the presence of a golden-yellow reflex and paracentral OCT B-scans for an abnormally thick hyper-reflective band in the ellipsoid zone area of the outer retina.

Results: Of the total 66 cases, 12 (18.2%; 10 males and 2 females) had a golden-yellow fundus reflex with each demonstrating corresponding OCT outer retinal hyper-reflectivity on macular scans. Eleven out of these 12 (91.7%) had a cone-rod dystrophy (CRD) pattern of retinal dysfunction on ffERG. In addition, 11 out of the 12 (91.7%) cases had RPGR ORF15 (NM_001034853.2) variants located near the distal end of exon 15. One patient had a CRD and a variant in the middle of exon 15. A female carrier had a normal ffERG with a variant near the distal end of exon 15.

Conclusions: We identified a golden-yellow fundus reflex and corresponding hyper-reflective changes on OCT in nearly one-fifth of patients in our study. Intriguingly, the vast majority of these patients were male, had a CRD pattern of retinal dysfunction, and had RPGR ORF15 variants near the distal end of exon 15. By characterizing these imaging features, we hope to improve both diagnostic accuracy and understanding the pathophysiology in patients with RPGR retinopathy.

CONTROL ID: 3711555

SUBMITTER (NAME ONLY): Yu Fujinami

TITLE: East Asian Patients with Occult Macular Dystrophy Report No.4; Genotype-Phenotype Association

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Two hot spots in the RP1L1 gene including amino acid numbers 45 and 1196-1201 have been recently identified in occult macular dystrophy (OMD). Here, we describe the differential clinical effects of these two hotspots.

Methods: 50 participants from 29 families with OMD caused by pathogenic RP1L1 variants (i.e. Miyake's disease) were enrolled in Japan, South Korea, and China. Patients were classified into two genotype groups; patients with p.R45W variant (group A) and subjects with missense variants located between amino acid 1196 and 1201 (group B). Clinical parameters were statistically compared between these two genotype groups, including age of symptom onset, age at examination, visual acuity in the logarithm of the minimum angle of resolution unit (VA) of one randomly selected eye. The morphological features obtained with spectral-domain optical coherence tomography were also investigated.

Results: There are 31 patients in group A and 19 in group B. The median age of onset/examination was 18.8/43.4 years (range, 2-40/11-80) and 39.4/59.5 years (range, 13-70/34-92) in groups A and B, respectively (P= 0.00013). The median duration of 22.0 years (range, 6-64) and 19.0 years (range, 8-42), in groups A and B, respectively (P= 0.9799). The median VA in the right/left eye of groups A and B was 0.70/0.71 (range, -0.08-1.22/0-1.4) and 0.41/0.44 (range, -0.08-1.0/-0.08-0.82) LogMAR unit, respectively (P= 0.0032). The classical photoreceptor findings showing both blurred ellipsoid zone (EZ) and absence of interdigitation zone (IZ) was identified in 27 (27/31, 87.1%) and 15 (15/19, 78.9%) patients in groups A and B; subtle/early photoreceptor changes of local IZ loss and relatively preserved EZ were found in 3 (3/31, 9.68%) and 3 (3/19, 15.8%) in groups A and B (P=0.6583). Comparison analyses revealed statistically significant differences in terms of age of onset, age at the latest examination, and VA. There were no

significant differences with regards to the duration of the disease.

Conclusions: Different clinical severity derived from the two RP1L1 hotspots were identified; the severer phenotype of early onset and poor VA was related with p.R45W compared to 1196-1201. This genotype-phenotype association can be helpful for genetic counselling of patients regarding the visual severity.

CONTROL ID: 3711556

SUBMITTER (NAME ONLY): Zeinab Ghassabi

TITLE: Dehazing of Visible-light OCT B-scans using deep neural model improves visualization and quantification of retinal sub-layers.

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Multiple sublayers of retina can be visualized with visible light (vis-) OCT.However, image quality can be compromised due to patient movement, cataracts, small pupil size, and light scattering causing haziness and variability in signal to noise ratio in individual A-scans and in entire B-scans.The purpose of this study was to examine the effect of conventional and deep neural network dehazing techniques on the visibility and quantitative assessment of retinal sub-layers on vis-OCT images.

Methods: 9 healthy and 5 glaucoma subjects were scanned 3 times during one session.Scanning was done on the superior nasal side of para-foveal region,1.5 mm from the fovea with a 3D speckle reduction raster scanning protocol(3x3x1.6 mm with 8192x16x1024 samplings) using a prototype vis-OCT system.16 A-scan lines were averaged to reduce speckle noise.Gray-scale image dehazing guided by depth information and pretrained Dehazenet deep model following deep convolutional neural network with residual learning(DnCNN) were applied on original B-scans.Quality improvement were evaluated using quality index(QI) and contrast to noise ratio(CNR) on dehazed B-scans.For each subject, the dehazed B-scan of Dehazenet and DnCNN from a fixed location adjacent to the fovea were selected.The distances between each of 3 bright inner plexiform layers(IPL) and retinal pigment epithelium(RPE) sublayers were segmented manually for thickness measurements using a 8 A-scan averaged profile(Fig.).Coefficient of variations (CVs) were calculated to assess the measurement repeatability of the sublayers on original and dehazed B-scans.

Results: Healthy and glaucoma subjects were age 45.67±11.7and 59.60±13.4($p=0.07$,t-test),visual field mean deviation(MD)-1.55 to1.20 dB,and from -26.42 to -7.70dB($p= 0.003$,Wilcoxon),global mean circumpapillary retinal nerve fiber layer(RNFL)thickness 96.33±12.20 and 59.80±9.09mm($p<0.001$,Wilcoxon),respectively.Dehazed B-scans obtained by deep models have statistically significant better QI and CNR(Table1).Overall intra-subject CVs showed significantly improved reproducibility on all measured sub-layers of dehazed B-scans compared to original scans for all subjects(Tables 2,3).

Conclusions: Vis-OCT image quality can be improved using deep neural network dehazing model resulting in higher reproducible thickness measurements of retinal sublayers within subjects in dehazed B-scans.

CONTROL ID: 3711558

SUBMITTER (NAME ONLY): Elliott Sohn

TITLE: MMP9 associated with choroidal neovascularization in AMD is expressed in human immune cells

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.H. Sohn, C. Jiao, A.P. Voigt, T.E. Scheetz, R.F. Mullins, Institute for Vision Research, University of Iowa, Iowa City, Iowa, UNITED STATES|E.H. Sohn, C. Jiao, T.E. Scheetz, R.F. Mullins, Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Immune-mediated mechanisms play an important role in AMD pathogenesis and choroidal neovascularization (CNV), which may explain why many with exudative AMD are incomplete responders to anti-VEGF therapy. The MMP9 gene encodes matrix metallopeptidase 9, aka type IV collagenase, associated with degradation of the extracellular matrix that is implicated in angiogenesis and fibrosis. We recently confirmed that MMP9 increases risk only for exudative AMD. We sought to determine the cell-specific localization of MMP9 gene expression and the levels of MMP9 expressed by human cells.

Methods: Data from single cell RNA sequencing enriched for CD31+ expressing cells of the human posterior segment were analyzed for MMP9 gene expression. THP-1 monocyte cells were differentiated into M0 polarized macrophages with PMA and M2 macrophages with PMA/interleukin(IL)-4/IL-13. THP-1 cells were differentiated into immature dendritic cells (iDCs) with IL-4/GM-CSF, and into mature DCs (mDCs) with IL-4/GM-CSF/TNF-alpha/ionomycin. ELISA for MMP9 was performed on the conditioned media of M0, M2, iDCs and mDCs followed by normalization of the total cell numbers. Zymography was used to detect active and latent forms of MMP9. Immunostaining was performed with CD86 and CD206 to label mDCs and M2 macrophages, respectively.

Results: scRNA-seq of human donor eyes with AMD enriched with CD31+ cells reveal that MMP9 expression is highest in a choroidal DC-like cluster that includes DCs and macrophages with very low to no expression in other cell types or regions of the posterior eye. DCs (mature>immature) expressed higher levels of MMP9 compared to M0 and M2 macrophages (see figure). The band intensity of MMP9 from zymography showed similarly high signal for DCs relative to macrophages. Verification of mature DCs and M2 macrophages was confirmed with immunolabeling.

Conclusions: MMP9 plays a role in CNV through immune cells found in the choroid. Protein expression of MMP9 from dendritic and macrophage cells confirm the plausible mechanism of its role in AMD. Elucidating the disease mechanisms associated with MMP9 is of importance to reveal new targets for therapeutic intervention, the next milestone in exudative AMD.

CONTROL ID: 3711561

SUBMITTER (NAME ONLY): Seth Buscho

TITLE: Longitudinal Visualization of Retinal Vascular Changes with OCT Angiography in a Mouse Model of Tauopathy

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Buscho, E. Palacios, J. Luisi, F. Xia, S. Shi, M. Motamedi, W. Zhang, H. Liu, Ophthalmology and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|J. Luisi, Department of Pharmacology and Toxicology, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|W. Zhang, Departments of Neuroscience, Cell Biology and Anatomy, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tauopathies are a family of debilitating neurodegenerative disorders which include Alzheimer's disease, frontotemporal dementia, and more than 20 others. Since the retina is an extension of the CNS, it has attracted significant attention for its use as a biomarker for neurodegenerative diseases. Our previous study has found retinal vascular inflammation and leakage at the very early stage of tauopathic mouse model. Here, we aimed to non-invasively assess the temporal alterations of retinal vasculature and evaluate its potential as the biomarker for the early diagnosis of tauopathy.

Methods: P301S transgenic mice overexpressing human tau with a P301S mutation and age-matched WT littermate mice were used. The alterations of retinal vasculature down to the capillary level were examined by non-invasive imaging technique optical coherence tomography angiography (OCTA) at 3, 6 and 11 months of age. Retinal vasculature of superficial vascular plexus (SVP), intermediate capillary plexus (ICP) and deep capillary plexus (DCP) was analyzed using Angiotool for vessel density, number of branch points and total vessel length.

Results: At the early stage of tauopathy, although retinal vascular features were not greatly altered in the SVP, significant decreases of vessel density, number of brunch points and total vessel length were observed in the ICP and DCP of P301S retinas at 3 months of age. At 6 months of age, moderate decreases in vessel density and length were detected in the SVP of P301S retinas, but they were more significantly decreased in the ICP and DCP of P301S retinas. With aging, vessel density, branch points, and total vessel length in all three vascular plexuses were dramatically decreased in 11-month-old P301S mice compared to age-matched WT mice.

Conclusions: Our results demonstrate that retinal vascular features progressively change during the progression of tauopathy. Vessels in the ICP and DCP may be more susceptible to dysfunction/degeneration than vessels in the SVP. Since changes in retinal vasculature often precede tau pathology in the brain, noninvasive identification of retinal vasculature alterations with OCTA may be a useful biomarker for the early diagnosis of tauopathy.

CONTROL ID: 3711564

SUBMITTER (NAME ONLY): Anna Tichenor

TITLE: Regional Comparison of MUC1 Expression in the Bulbar Conjunctiva of Dry Eye and Normal Subjects

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Tichenor, M. Choi, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Anna Tichenor: Commercial Relationship: Code N (No Commercial Relationship) | Moonjung Choi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To utilize a novel capillary electrophoresis nano-immunoassay system to evaluate and compare regional conjunctival protein expression of ocular surface mucin MUC1 in normal and dry eye subjects.

Methods: Adults with and without signs and symptoms of dry eye disease were recruited. Impression cytology was performed by placing a semicircle of filter paper on the bulbar conjunctiva to collect epithelial cells and membrane associated mucin MUC1 protein. Cells were collected from the temporal, superior, inferior, and nasal bulbar conjunctiva of both eyes, and the lid wiper area of the upper eyelids. After protein extraction using RIPA buffer, two samples from both eyes of a single individual were pooled into one protein sample and expression was analyzed using Jess, a capillary electrophoresis nano-immunoassay system. The chemiluminescence intensity of each single antigen binding signal was calculated using the Compass Simple Western software 6.1 following normalization to the total protein amount. Statistical analyses were conducted using GraphPad Prime 9.

Results: Seven dry eye and seven normal subjects were enrolled. Identifiable antibody binding signals for MUC1 were seen in all samples around 280 kDa as expected. In normal samples, MUC1 protein expression from the nasal bulbar conjunctiva was significantly greater than the superior ($p=0.004$), inferior ($p=0.005$), and eyelid margin ($p=0.008$). While not statistically significant, the MUC1 binding signal intensity was also higher in the temporal bulbar conjunctiva. In the dry eye samples, MUC1 expression was highest in the superior bulbar conjunctiva compared to the inferior ($p=0.01$) and nasal ($p=0.001$) regions. When comparing MUC1 expression between dry eye and normal subjects, MUC1 expression was lower in the nasal ($p<0.0001$) and temporal ($p=0.01$) regions of the dry eye samples.

Conclusions: The Jess system provides numerous advantages over a traditional Western blot especially when analyzing high molecular weight proteins like ocular surface mucins with small sample aliquots. The increased expression of MUC1 in the temporal and nasal bulbar conjunctiva of healthy subjects suggests a functional need for increased lubrication in these areas not normally protected by the eyelids. In addition, the decreased MUC1 expression in dry eye samples, especially temporally and nasally, is consistent with results from previous studies in dry eye patients.

CONTROL ID: 3711566

SUBMITTER (NAME ONLY): Hui Wang

TITLE: Relationship between retinal layer thicknesses of the macula and depression

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Wang, Institute for Psychology and Behavior, Jilin University of Finance and Economics, Changchun, CHINA|H. Wang, A. Witte, Y. Li, M. Wang, K. Wirkner, C. Engel, M. Loeffler, T. Kirsten, R. Steffi, F.G. Rauscher, T. Elze, Leipzig Research Centre for Civilization Diseases (LIFE), Leipzig University, Leipzig, GERMANY|J. Girbardt, K. Wirkner, C. Engel, M. Loeffler, F.G. Rauscher, Institute for Medical Informatics, Statistics, and Epidemiology (IMISE), Leipzig University, Leipzig, GERMANY|J. Girbardt, A. Witte, M. Schroeter, A. Villringer, Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, GERMANY|A. Zülke, M. Luppa, R. Steffi, Institute of Social Medicine, Occupational Health and Public Health (ISAP), Leipzig University, Leipzig, GERMANY|Y. Li, M. Wang, T. Elze, Schepens Eye Research Institute, Harvard Medical School, Boston, Massachusetts, UNITED STATES|T. Kirsten, Medical Informatics Center - Department of Medical Data Science, Leipzig University Medical Center, Leipzig, Saxony, GERMANY|M. Schroeter, A. Villringer, Clinic of Cognitive Neurology, Leipzig University Medical Center, Leipzig, GERMANY|

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ABSTRACT BODY:

Purpose: To study the relationship between depression and thickness of macular layers.

Methods: From the population-based, age- and sex-stratified LIFE-Adult-Study, reliable (quality ≥20 dB) macular spectral-domain optical coherence tomography (OCT) volume scans (97 B-scans at 512 A-scans) from participants with healthy eyes were selected and segmented into ten retinal layers (Fig. 1A). Each of the 49,664 A-scans of each layer was statistically associated with two measures of depression: First, a lifetime diagnosis of depression as reported by participants in the anamnestic interview (logistic regression; outcome: depression diagnosis, regressors: layer thickness with age as covariate); second, depressive symptoms as evaluated using the Center for Epidemiologic Studies Depression Scale (CES-D), a questionnaire assessing depressive symptoms during the past week (partial Pearson correlation between thickness and CES-D score adjusted for age). P-values were adjusted for multiple comparisons by the false-discovery method.

Results: 11,124 eyes of 6,471 participants were included (mean age: 55.5 years, 53.1% female). Participants who reported physician-diagnosed depression (n=705) had a significantly higher CES-D score (t-test, $p<10^{-15}$, see Fig. 1B). Concerning physician-diagnosed depression, retinal thickness of the ten layers was not significantly related to existing depression diagnosis for any of the examined retinal locations. Regarding current depressive symptoms, the heat maps in Fig. 2 show the partial (age-adjusted) correlations between CES-D and thickness for each of the ten layers. There were significantly correlated locations on each retinal layer, except for IZ and RPE layers, ranging from less than 1% of the retinal area for OPL to over 60% for EZ+OS. While for EZ+OS and the ONL, higher depression scores were associated with a thinner retina over widespread areas, for other layers, particularly GCL and the IPL, specific, localized spatial patterns of associations were found with more pronounced thinning at a ring around the fovea.

Conclusions: In 8 out of 10 retinal layers we found significant correlations between macular layer thickness and depressive symptoms, assessed using the CES-D. Anamnestic physician-diagnosed depression was not significantly associated with thickness.

CONTROL ID: 3711569

SUBMITTER (NAME ONLY): Pam Heutinck

TITLE: Diagnosis and identification of the genetic defect in a large Dutch cohort of children with retinal dystrophy: the RD5000 consortium

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Heutinck, M. Meester, M. Vermeer, A.A. Thiadens, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|L.I. van den Born, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|M. Meester, Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Ophthalmology/Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|V.J. Verhoeven, Clinical Genetics, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Gene-based therapies for numerous inherited retinal degenerations (IRD) are on the horizon, and current experience with RPE65 gene therapy suggests that treatment given early in life may be most beneficial. We aimed to identify and register all children in the Netherlands with IRD, and determined the genetic cause and risk profile of patients most suitable for future therapies.

Methods: Clinical and genetic data from IRD patients (N=767, 62% male) aged 0-20 years were collected from medical charts from the 5 centers participating in the national RD5000 study group in the Netherlands over a mean follow-up period of 5.95 ± 4.0 years. Patients were stratified in 2 groups: progressive retinal dystrophies and stable retinal dysfunction disorders. Outcome measures were prevalence of diagnosis, causal genes, mean best-corrected visual acuity (BCVA) in LogMAR at age categories 0-5 years, 5-10 years, 10- 15 years and 15 -20 years. Wilcoxon signed Rank Test was used to analyze differences between groups.

Results: Mean age at diagnosis was 6.75 ± 5.0 yrs. Among patients with a progressive retinal dystrophy, retinitis pigmentosa (RP) and Leber congenital amaurosis (LCA) (together N=249; 52%) and X-linked retinoschisis (XLRS; N=63; 13%) were most prevalent. Within the stable retinal dysfunction group, achromatopsia (N= 62; 53%) and congenital stationary night blindness (CSNB; N=49; 41%) were most prevalent. Almost half of the patients (367/767; 48%) were genetically solved. Most frequently reported disease-causing genes for progressive retinal dystrophies were CEP290 (N=33) and RPE65 (N=15) and RS1 (N=29); most frequent disease-causing genes for stable retinal dysfunctions were CNGB3 (N=22) and CACNA1F (N=15). For RP and LCA cases (122 eyes), mean BCVA was 0.73 ± 0.52 at 0-5 years compared to 0.59 ± 0.49 at 5-10 years (p=0.002), 0.40 ± 0.40 at 10-15 years (p=0.014), and 0.32 ± 0.35 at 15-20 years (p=0.028).

Conclusions: In the Netherlands, CEP290 and RS1 are the most frequently identified genetic causes of progressive retinal dystrophies in children, and CNGB3 and CACNA1F the most frequently identified causes of stable retinal dysfunction disorders. The Dutch national RD consortium will be an important source for selection of patients most suitable for future gene-based therapies.

CONTROL ID: 3711570

SUBMITTER (NAME ONLY): Manon SZCZEPAN

TITLE: CCR2+ monocytes critically contribute to subretinal fibrosis at the chronic stage of the disease.

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. SZCZEPAN, M. Llorian-Salvador, M. Chen, H. Xu, Queen's University Belfast School of Medicine Dentistry and Biomedical Sciences, Belfast, Belfast, UNITED KINGDOM|M. Mack, Department of Internal Medicine II – Nephrology, Universitatsklinikum Regensburg Klinik und Poliklinik Innere Medizin II, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Subretinal macular fibrosis occurs in up to 50% of neovascular age-related macular degeneration (nAMD) eyes and is a major cause of anti-VEGF resistance in nAMD. Currently, there are no medications to prevent or treat macular fibrosis secondary to nAMD. The aim of this study was to investigate the role of CC-chemokine receptor 2 (CCR2) expressing monocytes in the development of the fibrovascular phenotype of nAMD.

Methods: Subretinal fibrosis was induced in C57BL/6J mice using the two-stage laser-induced protocol previously described by Little et al (2020). The dynamics of the fibrotic lesion and infiltrating macrophages were assessed by immunofluorescence staining of collagen-1, F4/80 and CCR2, respectively at days 0, 1, 3, 6 and 10 post-second laser. Circulating $CCR2^{+}$ monocytes were depleted using the CCR2 depleting antibody, MC-21, from day 1 to day 5 (acute stage depletion) or from day 5 to day 10 (chronic stage depletion). The level of depletion was confirmed by flow cytometry. Vascular and fibrotic components of the fibrovascular membrane were examined at day 10 post-second laser by immunofluorescence staining of isolectin B4 and collagen-1, respectively.

Results: The fibrotic lesion size reaches its peak 3 days after the second laser. $CCR2^{+}F4/80^{+}$ macrophages were detected in and around the fibrotic lesion and their number increased from day 3 to 10 post-second laser. Depletion of $CCR2^{+}$ monocytes at the acute stage of disease did not affect the size of subretinal fibrosis. However, depletion of $CCR2^{+}$ monocytes at the chronic stage of the disease significantly reduced the vascular and fibrotic components of the fibrovascular membrane.

Conclusions: Our results suggest that $CCR2^{+}$ monocytes play a critical role in the development of the fibrovascular phenotype of nAMD during the chronic stage of inflammation. The underlying mechanism of $CCR2^{+}$monocytes in promoting subretinal fibrosis warrants further investigation.

CONTROL ID: 3711571

SUBMITTER (NAME ONLY): Weilin Song

TITLE: A unified model of hyperoxia of prematurity: systemic HIF stabilization protects developing vasculature of the eye and brain

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Song, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|D. Hanna, A. Benos, G. Hoppe, J. Sears, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|T. DeSilva, Neuroscience, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have demonstrated that a 2-step murine model of phase 1 hyperoxia followed by phase 2 relative hypoxia can induce hypomyelination of the corpus callosum (CC), gliosis, and impaired maturation of pre-myelinating oligodendrocytes consistent with periventricular leukomalacia (PVL). In this investigation, we test whether stabilization of hypoxia inducible factor (HIF) in phase 1, which has been previously shown to prevent oxygen-induced retinopathy, is protective against white matter injury observed in a model of oxygen-induced PVL.

Methods: C57BL/6 pups were placed in 80% oxygen from postnatal day 4 (P4) until P8 and returned to normoxia until P11. Myelination, glial fibrillary associated protein, and capillary density within the CC were quantified using immunofluorescent microscopy and western blotting. Numbers of oligodendrocytes were counted within the CC. Each of these parameters were compared to pups treated with both direct and remote (liver) HIF-1 stabilization in the wild type and hepatic HIF-1 knockout mouse subjected to the oxygen-induced PVL model.

Results: Hyperoxia caused a 3-fold reduction in myelination, a 30% increase in gliosis, a 40% decrease in capillary density, and 50% reduction in oligodendrocytes within the CC. Pharmacological HIF stabilization during hyperoxia resulted in lower HIF-1 levels in hypoxic phase 2 and increased white matter capillary density. While inducing hepatic HIF-1 by DMOG increased CC myelination by 150% compared to hyperoxia alone, direct brain HIF-1 stabilization by Roxadustat suppressed myelination even further than hyperoxia alone (by 50%). The therapeutic effect of remote hepatic stabilization was ablated in the hepatic HIF-1 KO.

Conclusions: PVL can be induced by a 2-step mechanism of oxygen-induced vaso-obliteration that leads to untimely HIF upregulation in phase 2 in synchrony with the oxygen-induced retinopathy model. In this model, remote HIF stabilization during phase 1 results in increased capillary density, decreased evidence of hypoxia within the CNS, and promotion of white matter myelination. These findings support the hypothesis that a unified model of hyperoxia of prematurity results in dysregulation of vasculature development in the eye and brain.

CONTROL ID: 3711578

SUBMITTER (NAME ONLY): Natalia Mussi

TITLE: Chronic hyperglycemic stress drives mitochondrial adaptation in human corneal epithelial cells

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Mussi, Ophthalmology, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|W.L. Stuard, J. Sanches, D.M. Robertson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Delayed corneal epithelial wound healing is a common complication of diabetes. Our laboratory has found that primary cultured diabetic human corneal epithelial cells show varying levels of mitochondrial depolarization and morphological changes compared to non-diabetic controls. In this study, we characterized mitochondrial and metabolic activity in corneal epithelial cells subject to acute and chronic hyperglycemic stress.

Methods: Telomerase-immortalized human corneal epithelial (hTCEpi) cells were cultured in a defined serum-free keratinocyte growth media containing 6 mM D-glucose. To simulate hyperglycemia, cells were supplemented with additional glucose up to a final concentration of 25 mM. Mannitol was used as an osmotic control. Cells were cultured for 24 hours, 3, 5, 7, 9 or 14 days. Mitochondrial morphology and polarization were assessed using JC-1 and visualized using laser scanning confocal microscopy. Metabolic activity was quantified in real time using a Seahorse metabolic flux analyzer. Oxygen consumption rate (OCR, mitochondrial respiration) and extracellular acidification rate (ECAR, glycolysis) were analyzed using a Seahorse XFp Cell Mito Stress Test kit. Beta oxidation of fatty acids were further measured using a Substrate Oxidation Test kit.

Results: Using JC-1, only cells cultured in high glucose for 14 days showed a loss of polarization and mitochondrial fragmentation. Metabolic activity was unchanged in cells cultured in high glucose for 24 hours. By day 3, cells showed a measurable drop in spare respiratory capacity that remained decreased through day 14. By day 5, glycolysis (ECAR) began to decrease and remained low through day 9. At days 7 and 9, OCR was increased, shifting cells towards a more respiratory phenotype. By day 14, consistent with JC-1 staining, OCR decreased and ECAR increased to normoglycemic levels.

Conclusions: Chronic, not acute, exposure to high glucose negatively impacts mitochondrial structure and function. The decline in mitochondrial activity was associated with a recovery of glycolysis, indicative of metabolic adaptation. The ability of corneal epithelial cells subject to chronic hyperglycemia to rely on glycolysis as the primary energy source would account, in part, for the delayed wound healing seen in diabetes.

CONTROL ID: 3711579

SUBMITTER (NAME ONLY): Colleen McDowell

TITLE: Molecular pathology of the glaucomatous optic nerve head

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.M. McDowell, E.K. Geiduschek, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optic nerve head (ONH) shows the earliest signs of damage during glaucoma. An imbalance of extracellular matrix (ECM) protein formation and degradation in the human lamina cribrosa (LC) region leads to retinal ganglion cell (RGC) axon damage and eventual apoptosis. ONH astrocytes, LC cells, and microglia have been implicated in glaucomatous ONH damage, with early microglia activation releasing damage associated molecular patterns (DAMPs) that can activate toll-like receptor 4 (TLR4). Current literature shows significant crosstalk between TLR4 and TGFß2 signaling in the development of fibrogenesis and TGFß2 is known to be increased in the glaucomatous ONH. From this, we hypothesize that endogenous DAMPS activate TLR4 and augment TGFß2 signaling, increasing ECM production and pathogenic paracrine signaling between cells of the ONH.

Methods: Normal and glaucomatous human donor eyes were received from the Lions Eye Banks of WI, fixed, cryo-embedded, and processed for immunohistochemistry. Primary ONH LC cells were isolated from fresh normal human donor eyes, cultured, and characterized by western blot and ICC. Immortalized microglia were purchased from ATCC (CRL-3304). Cells were treated with a TLR4 selective inhibitor TAK-242 in the presence or absence of TGFβ2, LPS, or cFN for 48 hours and changes to protein production was assessed by western blot and immunocytochemistry.

Results: The ECM protein fibronectin (FN), as well as the endogenous DAMP fibronectin extra domain A (FN-EDA) were elevated in the LC region of glaucomatous (N=3) human donor eyes compared to normal controls (N=3). Primary human LC cells expressed alpha-SMA and were negative for astrocytic marker GFAP. Treatment with TGFβ2 elevated FN expression and the TLR4 inhibitor, TAK-242, blocked TGFβ2 induced FN expression ($p<0.05$). Immortalized microglia (ATCC CRL-3304) exposed to the TLR4 activator LPS in the presence or absence of TGFβ2 increased FN and Laminin protein expression by western blot and ICC.

Conclusions: These data suggest that multiple cell types within the ONH show significant crosstalk between TLR4 and TGFβ2 signaling during the development of fibrogenesis in the LC region.

CONTROL ID: 3711580

SUBMITTER (NAME ONLY): Amitha Domalpally

TITLE: Influence of Race on Training Data Quality for Artificial Intelligence (AI) Algorithms

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Domalpally, R. Channa, A-EYE Unit, Dept of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|A. Domalpally, R. Voland, R. Slater, E. Corkery, P. Vargo, B. Kuhtz, J. Reimers, B.A. Blodi, Wisconsin Reading Center, Dept of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) severity level is evaluated from stereoscopic 7-field color photographs by masked graders at the Wisconsin Reading Center and used as a reference standard for training and validation of AI algorithms. Training data quality influenced by race is understudied relative to standards established for White subjects. Retinal pigmentation is greater in individuals with darker skin tones, and the reduced contrast may affect the detection of DR features by graders. We explored the effect of race-related fundus pigmentation on the grader's ability to document DR.

Methods: All images were acquired by a certified photographer at a single site using the same camera. and evaluated for DR by two experienced graders masked to all demographics. Following our standard protocol for quality assessment, graders determined a confidence score (CS) of high or low (borderline and ungradable) for each image. Graders were permitted to use digital enhancement tools for better visualization. The Red, Green, and Blue (RGB) channel values were also obtained for a representative image of each subject.

Results: Of 183 subjects, 37 (20.2%) were identified as White, 11 (6%) Black and 135 (73.8%) Other with Hispanic ethnicity. DR prevalence was 10.4% in the full cohort (366 eyes), mostly with mild-moderate non-proliferative DR. DR prevalence across the 3 racial/ethnic groups was 12.2%, 0% and 12.2% respectively. CS was high in 93%, 77% and 82%, borderline in 5%, 23% and 16% and ungradable in 1.4%, 0% and 1.5% respectively. There was significant difference between high and low CS across the three groups ($p = 0.029$) and also for the red channel of RGB values: 129 (95% CI 95,105), 85 (77,104), and 94(88,99) ($p < 0.001$).

Conclusions: Grader confidence for evaluating DR features was lower in pigmented retinas which could affect data accuracy from images obtained from darker skinned individuals. It is possible that DR was under called in Black population due to difficulty in detecting early features. This bias can transfer into AI models via training data. Photographer education in image capture techniques and grader training in racially diverse datasets is needed to obtain high quality, categorically delineated data.

CONTROL ID: 3711581

SUBMITTER (NAME ONLY): Bhavya Gorimanipalli

TITLE: Immune profile in patients with COVID-19 associated rhino-orbital-cerebral mucormycosis

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Nair, S. Mahajan, S. Sethu, A. Ghosh, GROW Research Laboratory, Narayana Nethralaya Foundation, Bangalore, INDIA|B. Gorimanipalli, R. Shetty, S. Ananthakrishna, A. Kiran, M. Goswami, V. Hemanth Vasanthapuram, R. Rao, G. Kundu, A. Krishna Murthy, G. Dudeja, R. Gupta, Narayana Nethralaya, Bangalore, Karnataka, INDIA|S. Sethu, A. Ghosh, Immunoprofiling Consortium for COVID-19, Indian Council of Medical Research, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Rhino-orbital-cerebral mucormycosis (ROCM) is a prevalent manifestation of mucormycosis affecting COVID19 patients with significant morbidity and mortality. Despite sharing a similar set of risk factors, only a subset of patients is affected by ROCM . Hence, we have performed immune-profiling in patients with active COVID19-associated ROCM (Ca-ROCM) to determine their anti-fungal immunity status

Methods: Study includes subjects (i) with COVID19 and ROCM (C^+R^+, n=13), (ii) with COVID19 and no ROCM (C^+R^-, n=9) and (iii) without COVID19 history and no ROCM (C^-R^-, n=7). Proportions of ~50 immune cells subsets (immunophenotyping) and 60 secreted factors (multiplex ELISA) were determined in the peripheral blood of the study subjects using flow cytometry. The COVID subjects included in the study were of non-severe form in C^+R^+ and C^+R^- group

Results: A significant reduction in the natural killer (NK cells), dendritic cells and lymphocytes along with a significant increase in neutrophils was observed in C^+R^+ group compared to the other groups. A significant increase in sIL-1Rs, sTNFRs, sICAM1, IL-6, IL-8, MMP, MPO, NGAL, PDGF-AA/BB, HGF and VEGF, along with significant reduction in angiogenin and IFNα was also observed in C^+R^+ group. Area under the curve and logistic regression analysis demonstrated that proportion of NK cells, Angiogenin and sIL-1R levels were unique in patients with ROCM

Conclusions: The distinct immune profile in patients with Ca-ROCM can be explored as an additional factor in stratifying COVID-19 patients with increased risk of ROCM thereby reducing the morbidity and mortality burden of Ca-ROCM.

CONTROL ID: 3711582

SUBMITTER (NAME ONLY): Eric Thee

TITLE: Automated drusen quantification for the prediction of late age-related macular degeneration

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.F. Thee, B. Liefers, D.T. Luttikhuizen, C.C. Klaver, Ophthalmology, Epidemiology, Erasmus MC, Rotterdam, NETHERLANDS|B. Liefers, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|C.C. Klaver, Ophthalmology, Radboudumc, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Prediction of age-related macular degeneration (AMD-)progression based on early imaging biomarkers is currently imprecise, but important for risk-based management and patient selection for clinical trials. Here, we evaluated the impact of drusen on AMD progression based on automated drusen area quantification.

Methods: In total, 7964 participants aged 55+ from the population-based Rotterdam Study were followed up for AMD progression during a study period up to 15 years. Drusen areas within the early treatment diabetic retinopathy (ETDRS) grid on fundus photographs were automatically segmented with a deep learning algorithm at baseline, and were evaluated for their log correlation with consensus annotation by human graders. Associations between drusen area and incident late AMD were determined with cox proportional hazards models, adjusted for age and sex. Optimism-corrected area under the operating receiving curves (AUCs) were constructed for late AMD.

Results: Drusen area quantifications by the deep learning model were highly correlated with consensus annotation by experienced graders ($r = 0.81$, $p < 2.8e\text{-}10$). During a mean follow-up of 6.7 years (SD 1.8), 107 participants developed incident late AMD. A 1 mm^2 increase in deep learning-based drusen area in the ETRDRS grid was associated with a 4.9 times increased risk of incident late AMD (HR 4.9, 95%CI 3.3– 7.2). The prediction model based on automated drusen area quantification reached an AUC of 0.89 (95%CI 0.83-0.95).

Conclusions: The deep learning model was on par with consensus annotation by human graders, and can be used as a quick and objective method for AMD end stage risk prediction. Automated quantification of early and intermediate AMD imaging biomarkers will enhance the investigation of causal relationships and patient selection for clinical trials.

CONTROL ID: 3711584

SUBMITTER (NAME ONLY): Jeffrey Bair

TITLE: D and E series Specialized Pro-Resolving Mediators Inhibit Capsaicin-induced Calcium Influx in Rat Trigeminal Ganglionic Neurons

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bair, A.E. Ross, D.A. Dartt, J. Ciolino, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|C.N. Serhan, Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesia, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: E-series resolvins (Rv), derived from the n-fatty acid, eicosapentaenoic acid (EPA), and the D-series Rvs, protectins, and maresins all derived from the n-fatty acid docosahexaenoic acid (DHA), comprise three categories of specialized pro-resolving mediators (SPMs) that actively resolve inflammation in disease. The purpose of this study was to determine if one or more of these SPM families can attenuate the capsaicin-evoked activity of rat trigeminal ganglion neurons indicating a decrease in corneal pain.

Methods: Rat trigeminal ganglia (TG) were extracted and dissociated first in a solution of papain in HBSS for 20 minutes before transferred to a solution of collagenase and dispase for a further 20 minutes. The dissociated cells were then separated using a percoll density gradient. The TG neurons were isolated and plated onto poly-L-lysine and laminin coated glass-bottom dishes and left to grow overnight. The following day, cells were washed with Krebs Ringer Buffer (KRB) and loaded with the calcium-sensitive fluorescent dye fura2. An increase in intracellular [Ca^{2+}] indicated activation of the neuron and pain in the nerve endings. Thirty minutes prior to the experiment cells were treated with one of the following: RvD1, RvD2, RvD3, RvD4, RvD5, or RvE1 at concentrations between 10^{-11}M and 10^{-8}M. The cells were then stimulated with capsaicin (10^{-7}M) and intracellular [Ca^{2+}] were recorded over time.

Results: Pre-treatment with RvD1 10^{-8}M reduced the magnitude of the capsaicin-induced calcium influx by an average of 36.03% (N=7 p=0.013). RvD2 10^{-11}, 10^{-10}, 10^{-9}, and 10^{-8}M reduced the magnitude of the response by an average of 49.29%, 49.57%, 35.64% and 63.58% respectively (N=7, p= 0.001, 0.002, 0.001, and 0.001 respectively). RvD3 10^{-8}M inhibited the response by an average of 25.05% (N=4, p =0.003). RvD5 10^{-9}M inhibited the response by an average of 59.93% (N=4, p= 0.003). RvE1 10^{-10}M significantly reduced intracellular Ca^{2+} influx following capsaicin administration by an average of 19.32% (N=4, p=0.042).

Conclusions: The SPMs RvD1, RvD2, RvD3, RvD5, and RvE1 significantly decrease capsaicin-evoked intracellular [Ca^{2+}] influx in rat TG, with RvD2 being the most potent SPM treatment could decrease ocular surface pain.

CONTROL ID: 3711586

SUBMITTER (NAME ONLY): Ji He

TITLE: Measurement of the Refractive Index of the Crystalline Lens in the Human Eye in vivo by Using an Optical Coherence Tomography Equipped Ray-Tracing Scheimpflug Imaging System

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. He, Vision Science, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Ji He: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Measurement of the refractive index of the crystalline lens in the human eye in vivo has been a challenge for a long time. The anterior segment optical coherence topography (AS-OCT) and Scheimpflug imaging (SI) technique have been used to access the refractive index in vivo, but need assumption of the lens thickness. Theoretically, a combination of the AS-OCT and the SI could solve the lens refractive index and lens thickness simultaneously. The purpose of this study was to measure the refractive index of the human eye in vivo by using an AS-OCT equipped ray-tracing SI system (RTSI).

Methods: An AS-OCT was constructed to be combined with a RTSI, and mounted on a slit lamp platform together. Both AS-OCT and RTSI shared the same vertically scanning light illumination (about 850nm). The right eyes of five subjects (24 to 62 yr old) were tested. The images were processed to trace the light ray from the cornea to the lens and to accurately solve the lens refractive index and the lens thickness by using a self developed MatLab program. The derived lens refractive index represents the equivalent refractive index in the optical axis direction.

Results: During the image processing, the refractive index of aqueous was first obtained. For the five subjects, the mean aqueous refractive index was 1.3312±0.0013. The mean refractive index of the lens at the center was 1.4032±0.0177, with a range of 0.0366, which was more than 10 times of that for the aqueous (0.0034). The lens refractive index decreased as the distance from the lens center increased, and the rate of reduction in the lens refractive index varied from subject to subject. The mean central lens thickness was 3.93±0.49mm with a range of 1.10mm.

Conclusions: A combination of AS-OCT with RTSI accurately measures the refractive index of the ocular media in the human eye in vivo, and the measurement of the refractive index of the aqueous provides a useful validation of this method. The lens refractive index changes from one eye to another, and reduces from the lens center to the periphery. The rate of the reduction of lens refractive index estimates the gradient refractive index of the lens. With the lens refractive index measured, accurate estimate of the posterior lens shape is achieved.

CONTROL ID: 3711588

SUBMITTER (NAME ONLY): Amber-Lee Curran

TITLE: Light-Adapted Electroretinographic (ERG) Responses to Full-Field Stimuli in Children Treated for Retinopathy of Prematurity (ROP)

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Curran, D. Vanderveen, I. Mantagos, C. Wu, J.D. Akula, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|D. Vanderveen, I. Mantagos, C. Wu, A.B. Fulton, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J.D. Akula, Northeastern University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Amber-Lee Curran: Commercial Relationship: Code N (No Commercial Relationship) | Deborah Vanderveen: Commercial Relationship: Code N (No Commercial Relationship) | Iason Mantagos: Commercial Relationship: Code N (No Commercial Relationship) | Carolyn Wu: Commercial Relationship: Code N (No Commercial Relationship) | James Akula: Commercial Relationship: Code N (No Commercial Relationship) | Anne Fulton: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare cone-mediated ERG responses to full-field stimuli in children with severe ROP treated with either intravitreal bevacizumab (IVB) or laser photocoagulation.

Methods: Light-adapted responses to a range of red flash intensities were recorded. Cone photoreceptor sensitivity and saturated amplitude were calculated from the a-wave. Post-receptor activity (represented by the b-wave) and inner retinal function (represented by the oscillatory potentials (OPs)) were also analyzed. All response parameters were expressed relative to the mean of the IVB group. Linear mixed effects (LME) modeling was used to determine significant differences between groups. We studied children treated with IVB (n=20; 37 eyes) or laser (n=10; 17 eyes). Twelve patients (22 eyes) receiving IVB required additional laser treatment. Among these groups there was little difference in gestational age, birthweight, or age at ERG test. The gestational age at birth was median 25 (range 21–31) weeks and birthweight was median 572.5 (range 410–1750) g. Corrected age at ERG was median 47.4 (range 8–1,334) weeks. None had retinal detachment.

Results: The first LME model detected a significant difference in function at the various retinal depths ($P < 0.05$). Inner retinal function, represented by the OPs, was higher in laser-treated eyes. Photoreceptor and post-receptor function were similar across the groups. The second LME model detected no significant difference between IVB patients who required subsequent laser and those who did not.

Conclusions: These cone-mediated ERG data identify significant difference between IVB and laser-treated ROP retinas. Specifically, laser may confer relative preservation of the inner retina.

CONTROL ID: 3711589

SUBMITTER (NAME ONLY): Sander Kneepkens

TITLE: The effect of home confinements on myopic risk profile in European adolescents: The Generation R Study.

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kneepkens, W. Tideman, J. Polling, C.C. Klaver, Ophthalmology & Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|S. Kneepkens, generation R, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C. Enthoven, Child and Adolescent Psychiatry, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Ophthalmology, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|W. Tideman, Ophthalmology, Martini Ziekenhuis, Groningen, Groningen, NETHERLANDS|J. Polling, Optometry/Orthoptics, Hoge school Utrecht, Utrecht, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To battle the spreading of the COVID-19 virus, all over the world measures like home confinement and nation-wide lockdowns have been implemented at regular intervals. These measures have shown an increase in myopic incidence particularly in China, which applied a very strict lockdown and home confinement. The Netherlands used a so called “intelligent lockdown” which allowed children to go outside. We evaluated the association between COVID restrictions and myopia risk factors in an European cohort of adolescents.

Methods: A total of 1101 participants (mean age 16.3 ± 3.65 yrs) of the population-based prospective birth-cohort study Generation R filled in a questionnaire about their behavior before, during, and after lockdown in the Netherlands. These participants had undergone cycloplegic refractive error measurement at 13 years of age. We evaluated time spent outdoors, time spent online (handheld or other devices), time spent on near work (education and non-educational) from March-October 2020 in myopic (spherical equivalent <-0.5D) and non-myopic children. We used a repeated measures ANOVA to compare differences between these time periods, and logistic regression corrected for age, gender, and ethnicity to evaluate differences between myopic and non myopic children.

Results: During and after lockdown the children spent signicantly more time online (+113 and +59min/day) on both hand held (+64 and +10 min/day) and other devices (+49 and +7 min/day), and on educational nearwork (+73 and +63min/day). Non-educational near work increased only significantly during lockdown (+176 min/day). Time spent outside did not change significantly and was ±2 hours/day. Children of non-European descent spent more time online (235min/day vs 260 min/day, P= 0.004) and on non-educational near work (452 min/day vs 559 min/day, p=0.0002). We found no significant difference in behavior between myopic and non-myopic children.

Conclusions: The Dutch lockdown for COVID increased digitized near work in adolescents, but did not affect outdoor exposure. Children without myopia did not do better than those already myopic. Based on these results, we expect that the COVID pandemic will also lead to an increase in myopia prevalence and progression in European children, but to a lesser extent than in Asia.

CONTROL ID: 3711591

SUBMITTER (NAME ONLY): Yu-Yen Chen

TITLE: The risk of psoriasis in patients with uveitis: A population-based cohort study

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, Department of Ophthalmology, Taichung Veterans General Hospital, TAIWAN|M. Hung, Department of Medical Education, Taichung Veterans General Hospital, TAIWAN|

Commercial Relationships Disclosure: Yu-Yen Chen: Commercial Relationship: Code N (No Commercial Relationship) | Man-Chen Hung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate whether the risk of subsequent psoriasis and psoriatic arthritis development is increased in patients with uveitis.

Methods: In Taiwan's national health insurance research database, we identified 195,125 patients with new-onset uveitis between 2001 and 2013. We randomly selected 390,250 individuals without uveitis who were matched 2:1 to uveitis cases based on age, sex and year of enrolment. The characteristics of the two groups were compared. Using multivariate Cox regression, hazard ratios (HRs) for psoriasis or psoriatic arthritis corresponding to uveitis were computed after adjustment for age, sex, insurance cost and comorbidities. In subgroup analyses, separate HRs for mild psoriasis, severe psoriasis and psoriatic arthritis were calculated.

Results: The mean age of the study cohort was 50.2 ± 17.2 years. Hypertension, diabetes, hyperlipidaemia and obesity were more prevalent in the uveitis group (all $p < 0.0001$). The hazard of psoriasis or psoriatic arthritis development was significantly greater in the uveitis group than in the non-uveitis group ($p < 0.0001$); this increased risk persisted after adjustment for confounders [adjusted HR = 1.41; 95% confidence interval (CI), 1.33–1.48]. Adjusted HRs showed an increasing trend from mild psoriasis (1.35; 95% CI, 1.28–1.44) to severe psoriasis (1.59; 95% CI, 1.30–1.94) and psoriatic arthritis (1.97; 95% CI, 1.60–2.42).

Conclusions: This nationwide population-based cohort study revealed that patients with uveitis have an increased risk of subsequent psoriasis or psoriatic arthritis development.

CONTROL ID: 3711592

SUBMITTER (NAME ONLY): Venkata Chavali

TITLE: Stem cell transplantation for treatment of retinal ganglion cell loss in Glaucoma

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.R. Chavali, V. Vrathasha, J. He, Y. Liu, S.S. Nikonov, B.A. Bell, K.E. Uyhazi, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Venkata Chavali: Commercial Relationship(s);Code P (Patent):University Of Pennsylvania | Vrathasha Vrathasha: Commercial Relationship: Code N (No Commercial Relationship) | Jie He: Commercial Relationship: Code N (No Commercial Relationship) | Yingrui Liu: Commercial Relationship: Code N (No Commercial Relationship) | Sergei Nikonov: Commercial Relationship: Code N (No Commercial Relationship) | Brent Bell: Commercial Relationship: Code N (No Commercial Relationship) | Katherine Uyhazi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is an optic neuropathy characterized by progressive death of retinal ganglion cells (RGCs) leading to permanent visual field loss. Existing treatments for glaucoma target lowering the intraocular pressure, laser trabeculoplasty, and surgical interventions. There are no treatments available once RGC death has occurred in the advanced stages of this disease. We investigated induced pluripotent stem cell derived RGC replacement as a therapy to treat for ganglion cell loss in glaucoma.

Methods: Human induced pluripotent stem cells (hiPSCs) were differentiated in vitro using a standardized two-step protocol in 36 days. iPSC-RGCs were characterized for RGC markers by FACS sorting with RGC specific antibodies. Mature iPSC-RGCs were labeled by transduction with AAV2.7m8 SNCG-eGFP. Purified and labeled iPSC-RGCs transplanted intravitreally (5×10^5 cells/2ul) into wild type 4-month-old C57BL/6J mice using a 33-guage needle (n=10). Survival of the transplanted hiPSC-RGCs was assessed at 2, 4 and 6-weeks post-transplantation using Micron III and confocal scanning laser ophthalmoscopy (cSLO). Histological studies were performed 2 and 5 months post-transplantation on retinal flatmounts, retinal and optic nerve sections to study localization and integration of the transplanted hiPSC-RGCs. Functional integration was assessed by electrophysiologic responses to full field photopic stimuli in voltage and current clamp modes under whole cell configuration.

Results: hiPSC differentiation in vitro generates pure populations of iPSC-RGCs. Purified iPSC-RGCs are positive for RGC markers BRN3, SNCG, CD90, and RBPMS. iPSC-RGCs transduced with AAV2.7m8 express eGFP as early as 48-hour post-transduction. eGFP+ve hiPSC-RGCs were detected within the ganglion cell layer of the murine retina as early as 2-weeks post injection and seen as punctate hyperfluorescent foci in the cSLO and color fundus imaging. We detected hiPSC-RGCs integrated in the mouse retina with extensive arborization in 6 weeks following intravitreal injections. hiPSC-RGCs stained positive for BRN3 and RBPMS markers and produced spontaneous firing in response to depolarizing stimuli indicating that the integrated iPSC-RGCs are functional.

Conclusions: Our studies will provide key strategies to enhance the efficiency of stem cell replacement therapy and advance potential treatments for neurodegenerative diseases including glaucoma and optic neuritis.

CONTROL ID: 3711594

SUBMITTER (NAME ONLY): Samuel Minaker

TITLE: Surgical Outcomes of Rhegmatogenous Retinal Detachment in Patients 30 Years of Age or Younger at Three Months, One Year and Five Years Follow Up

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Minaker, S. Abdel-Hadi, M. Parker, M. MacCumber, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Samuel Minaker: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Abdel-Hadi: Commercial Relationship: Code N (No Commercial Relationship) | Makena Parker: Commercial Relationship: Code N (No Commercial Relationship) | Mathew MacCumber: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to investigate the associations with and surgical outcomes of rhegmatogenous retinal detachments in young adults with three months, one and five years of follow up.

Methods: A retrospective consecutive case series of patients 30 years of age or younger who underwent surgical repair for RRD between 2014 and 2021 at a single practice (12 offices).

Results: 101 patients (109 eyes) were included with at least 3 months of follow up. 67 patients (74 eyes) and 17 patients (19 eyes) were followed for at least 1 year and 5 years respectively. The most common association was myopia 66 eyes (60.1%) followed by trauma 8 eyes (7.3%) and prior ocular surgery 7 eyes (6.4%). Median pre-op Snellen visual acuity was 20/40. The macula was attached in 31 eyes. Five eyes (4.6%) presented with giant retinal tear detachments. The most common method of surgery was Scleral buckle alone (SB) in 71 eyes followed by Vit buckle in 29 eyes and PPV alone in 8 eyes. Single surgery anatomical success was 88.7% for SB, 89.7% for SB/PPV and 75% for PPV. The median final post-operative Snellen visual acuity was 20/30. 12 Patients presented with bilateral retinal detachments and the most common treatment was sequential surgery in 8 patients followed by 4 patients who underwent surgery with laser barricade in the fellow eye. 14 eyes developed a retinal tear or detachment in the fellow eye with a mean interval of 8 months from presentation, the longest interval was 3 years and 11 months. Of the 17 patients that were followed for at least 5 years, 3 patients (17.6%) developed a retinal tear or detachment in the fellow eye. After initial anatomical success 4 eyes (3.6%) developed redetachment with the most common cause being proliferative vitreoretinopathy. The longest interval of redetachment from initial repair was 9 months.

Conclusions: The most common association of rhegmatogenous retinal detachment in this study was myopia. Scleral buckle was the most common surgical intervention. Outcomes were generally favorable. Surgeons and patients should be aware of the risk of bilateral retinal detachment as well as the risk of retinal tear and detachment in the fellow eye. Patients require long term surveillance in both eyes.

CONTROL ID: 3711597

SUBMITTER (NAME ONLY): Mashidur Rana

TITLE: Diphenyleneiodonium (DPI) treatment moderates the severity of herpes stromal keratitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Rana, M. Setia, A. Chakraborty, P.K. Suvas, S. Suvas, Opthalmology Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Mashidur Rana: Commercial Relationship: Code N (No Commercial Relationship) | Mizumi Setia: Commercial Relationship: Code N (No Commercial Relationship) | Anish Chakraborty: Commercial Relationship: Code N (No Commercial Relationship) | Pratima Suvas: Commercial Relationship: Code N (No Commercial Relationship) | Susmit Suvas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In this study, we measured the intracellular level of ROS in neutrophils and CD4 T cells in HSK lesions and determined the outcome of manipulating ROS level on HSK severity.

Methods: C57BL/6J (B6) mice were infected with HSV-1 after mild scratching of the corneas. Multi-colored flow cytometry (FCM) was carried out to enumerate the ROS producing cells' frequency in infected mice. qRT-PCR assay measured the transcripts of antioxidant genes and NOX isoforms in uninfected and infected corneas. A slit lamp was used to grade the corneal opacity and angiogenesis in infected corneas of gp91-/-, vehicle and DPI treated groups of B6 mice.

Results: The flow cytometry data showed that approximately 90% of ROS generating leukocytes in HSK lesions were neutrophils. Antioxidant enzymes play an essential role in regulating intracellular ROS levels. Our results showed significant downregulation in antioxidant genes SOD1, GSS, and NQO1 but an upregulation in Hmox1, SOD2, SOD3, and GSR in infected corneas at 10- and 15-day post-infection (DPOI) as compared to uninfected corneas. ROS generation is regulated by flavoenzymes, including NADPH oxidase 2 (NOX2). qRT-PCR studies showed a two to six-fold increase in the expression of NOX2 subunits in infected corneas at 5- and 12-DPOI than uninfected corneas. FCM experiments showed NOX2 (gp91) protein predominance in neutrophils and monocytes in infected corneas at 15-DPOI. The corneal HSV-1 infection of gp91-/- and B6 mice showed no significant difference in the intracellular level of ROS in HSK lesions, suggesting NOX2 does not regulate ROS formation in HSK lesions. To ascertain the functional significance of ROS in regulating HSK, HSV-1 infected mice received a subcutaneous injection of DPI (1mg/Kg /day), a flavoenzyme inhibitor, from 7- through 15-DPOI. Our results showed significantly reduced corneal opacity and angiogenesis in DPI than vehicle-treated mice. Intriguingly, DPI treatment caused an increased level of ROS in neutrophils. An increased ROS level can cause cell death by apoptosis. However, FCM experiments revealed no significant difference in the frequency of apoptotic neutrophils from treated and vehicle groups, indicating the decreased frequency of neutrophils in the DPI treated group is not due to apoptosis.

Conclusions: Together, our results suggest that manipulating ROS level in HSK lesions can play an important role of regulating the severity of HSK.

CONTROL ID: 3711598

SUBMITTER (NAME ONLY): Shuo JIA

TITLE: Digital Light Processing Bioprinting of Poly-NAGA-GelMA-Hybrid Keratoprosthesis

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. JIA, J. CHAN, Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, Hong Kong, HONG KONG|W. LU, Orthopaedics and traumatology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|Z. ZHANG, W. LIU, School of materials science and engineering, Tianjin University, Tianjin, Tianjin, CHINA|

Commercial Relationships Disclosure: Shuo JIA: Commercial Relationship: Code N (No Commercial Relationship) | Zhuodan ZHANG: Commercial Relationship: Code N (No Commercial Relationship) | William Weijia LU: Commercial Relationship: Code N (No Commercial Relationship) | Wenguang LIU: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Cheuk-Hung CHAN: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To explore the feasibility of reconstructing and fabricating personalized biosynthetic keratoprosthesis using digital light processing (DLP) 3D bioprinting technique and N-acryloyl glycinamide/gelatin methacrylate-hybrid (PNG) bioink.

Methods: Cornea-mimicking constructs based on synthetically cross-linked PNG bioink were produced by DLP 3D bioprinting. Its characteristics in terms of hydrophilicity, water content, nutrient permeability, stability, optical and mechanical properties were then tested for suitability as corneal replacement tissue. Cytocompatibility was evaluated with human corneal epithelial, stromal, and endothelial cell lines. In-vitro immune response was analyzed with human peripheral blood mononuclear cells by illumina RNA sequencing. In-vivo performance was assessed using an anterior lamellar keratoplasty (ALK) and intrastromal keratoplasty (ISK) model in New Zealand white rabbits.

Results: DLP-bioprinting allows individualization of physical dimensions including thickness and curvature of the PNG keratoprosthesis. The material is superhydrophilic (contact angle 47°), has pre-specified water content (78%), good glucose permeabilization (diffusion coefficient: 2.11*10-6 cm2/s), high stability in PBS, bionic light transmittance (over 90%) and refractive index (≈1.375), and good structural strength (Young's modulus≈0.2MPa). In-vitro evaluation displays that it supports the adhesion and viability (above 90%, over 7 days of cultivation) of corneal epithelial, stromal, and endothelial cells, while maintaining the phenotype and function of keratocytes (positive for Keratocan, CD34 and ALDH1A1). RNA sequencing results indicate that it activates type 2 immunity in macrophage, facilitates tissue regeneration and suppresses inflammation. In-vivo assessment in rabbits showed excellent surgical handling characteristics, and no adverse effects on the host corneal stroma, endothelium or other ocular tissues, although epithelialization was not achieved with the ALK model. Postoperative IOP, corneal sensitivity, and tear formation remains unaffected during the 1-month follow-up.

Conclusions: Our DLP-bioprinted PNG keratoprosthesis is a novel, safe, and effective corneal graft alternative with personalisable physical dimensions which can potentially achieve better clinical outcome and address the current worldwide shortage of donor corneas.

CONTROL ID: 3711600

SUBMITTER (NAME ONLY): Lynn Ebner

TITLE: Single-cell RNA sequencing of the hypoxic retina identifies an oxygen-dependent isoform switch in RNA-binding proteins and a cone-specific motor protein

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.J. Ebner, D. Karademir, F. Peters, C. Grimm, Laboratory for Retinal Cell Biology, Universitat Zurich, Zurich, ZH, SWITZERLAND|L.J. Ebner, D. Karademir, C. Grimm, Center for Integrative Human Physiology, Universitat Zurich, Zurich, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Age-dependent processes like extenuated vascular density as well as reduced choroidal blood flow limit oxygen supply to the outer retina. Together with the formation of drusen and thickening of Bruch's membrane this might lead to hypoxic conditions in the ageing retina, linking age-dependent changes to hypoxia. To understand the cellular response of specific retinal cell types upon hypoxic conditions, we performed droplet-based single-cell RNA sequencing (scRNAseq) of mouse retina tissue after hypoxic exposure.

Methods: Droplet-based single-cell RNA sequencing of hypoxic (7% O_2 for 6h) and normoxic male and female mouse retinas (N=2) was performed using the 10X Genomics platform. Data analysis focused on differential gene expression of hypoxic and normoxic cells in each cluster. In-situ hybridization targeting Kif4 was used to confirm the exclusive expression in cone photoreceptors. qPCR was performed to identify Rbm3 and Cirbp isoforms.

Results: 21 retinal cell types and one RPE cluster were identified among the 9410 normoxic and 9033 hypoxic cells in the analysis. Known hypoxic markers including Bnip3, Higd1a and Egln1 were significantly upregulated in various hypoxic clusters, confirming a general response to hypoxia. Interestingly, RNA-binding proteins Rbm3 and Cirbp were differentially expressed across clusters. Remarkably, both genes underwent an isoform switch in hypoxia leading to the preferential expression of short variants. Focusing on photoreceptor-specific responses, we identified a kinesin motor protein (Kif4) to be induced specifically in cones upon hypoxic exposure. In-situ hybridization confirmed the observed cone specific expression.

Conclusions: Our results identified an oxygen-dependent isoform switch in RNA-binding proteins Rbm3 and Cirbp, suggesting functional consequences that might contribute to the pathological impact of reduced tissue oxygenation. Additionally, we identified a hypoxia-induced upregulation of a cone-specific motor protein, Kif4, which needs to be further characterized. Possible functions include axonal transport, cargo-delivery to the cone outer segment and enrichment of transmembrane receptors or channels. Identifying the cargo of this cone-specific kinesin might open the possibility for a new therapeutic target.

CONTROL ID: 3711601

SUBMITTER (NAME ONLY): Michel Guillon

TITLE: Letter Contrast Sensitivity Validation

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Guillon, P. Pepe, Ocular Technology Group International, London, London, UNITED KINGDOM|M. Guillon, School of Heath Sciences, Aston University, Birmingham, UNITED KINGDOM|J. Hull, R. Suryakumar, Alcon Inc., Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Michel Guillon: Commercial Relationship(s);Code O (Owner):Optometric Technology Group Ltd, Optometric Technology Group (Jersey) Ltd, ThermaMEDx LLC;Code C (Consultant/Contractor):Alcon Inc, CooperVision, Novartis, Horus Pharma, International Ltd | Pasquale Pepe: Commercial Relationship(s);Code C (Consultant/Contractor):Optometric Technology Group Jersey Ltd | Jessie Hull: Commercial Relationship(s);Code E (Employment):Alcon Inc. | Rajaraman Suryakumar: Commercial Relationship(s);Code E (Employment):Alcon Inc.

ABSTRACT BODY:

Purpose: Contrast sensitivity measurement with sinusoidal patterns (SinCS) is known to have significant variability and influenced by learning effects. Letter contrast sensitivity (LetCS) using a familiar testing process may be better suited in such a case. The purpose of the study was to validate LetCS produced by an iPad application driving a standard 4K screen compared with SinCS produced by two commercial systems (M&S Technologies (M&S) and Vector Vision (VV) by measuring their repeatability.

Methods: The study was a single arm, prospective, repeated measure study. The study population (n=20), a young presbyopic phakic population (43.6 ±2.8 years; range 40 to 49years) attended an initial enrolment / test familiarisation visit and two test visits. CS was measured under photopic (85cd/m2) and mesopic (3cd/m2) conditions, at five spatial frequencies (SF) 1.5, 3, 6, 12 and 18cpd. Repeatability was established by comparing the mean and 95% CI of the difference between the measurements made at the two test visits and the variance between the measurements.

Results: i. Under photopic conditions test variance was lower at all SF for LetCS (Test-retest difference: mean -0.03 to -0.01logCS; 95%CI 0.05 to 0.07logCS) than for SinCS M&S (Test-retest difference: mean -0.14 to -0.04logCs; 95%CI 0.16 to 0.37logCS) ($p \leq 0.001$) and VV (Test-retest difference: mean -0.07 to +0.01logCS; 95%CI 0.12 to 0.18logCS) ($p = 0.020$ to <0.001). ii. under mesopic conditions test variance was lower at all SF for LetCS (Test-retest difference: mean -0.05 to -0.03logCS; 95%CI 0.11 to 0.16logCS) than SinCS M&S (Test-retest difference: mean -0.11 to -0.04logCs; 95%CI 0.21 to 0.34logCS) (p 0.011 to <0.001) and all SF for VV (Test-retest difference: mean -0.08 to -0.01logCS; 95%CI 0.14 to 0.35logCS) ($p = 0.004$ to 0.001) other than 6cpd ($p=0.973$).

Conclusions: Letter contrast sensitivity was shown to be highly repeatable and exhibited significantly lower variance than sinusoidal pattern contrast sensitivity. The implications are that letter contrast sensitivity, needing minimal training, could be well suited for use in clinical studies and its lower variance than sinusoidal contrast sensitivity results in the need for a smaller sample size to achieve the same statistical power than sinusoidal contrast sensitivity.

CONTROL ID: 3711603

SUBMITTER (NAME ONLY): Sitara Hirji

TITLE: Manhattan Vision Screening and Follow-up Study: Epidemiologic characteristics of individuals referred to ophthalmology

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hirji, W.V. Lin, N. Harizman, R. Karani, I.A. Valenzuela, D.J. Doobin, J.D. Horowitz, L. Park, Q. Wang, S. Maruri, D. Diamond, P. Gorroochurn, J.M. Liebmann, G.A. Cioffi, L.A. Hark, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Higher rates of undetected eye disease have previously been identified in older individuals, minority populations, and those with low income and education level. Community-based vision screening may target at-risk populations in urban environments such as Manhattan. This study evaluates the social determinants of health of individuals who failed vision screening and received a referral to ophthalmology in the Manhattan Vision Screening and Follow-up Study.

Methods: We performed a retrospective analysis of preliminary data collected from the Manhattan Vision Screening and Follow-up Study. A total of 382 individuals aged 40 and older and living in affordable housing developments in upper Manhattan were enrolled and screened. Visual acuity, intraocular pressure, and fundus photography are measured. Participants with visual acuity equal to or worse than 20/40, or IOP 23 to 29 mmHg, or unreadable fundus images fail the screening and are scheduled with the on-site optometrist who also refers to ophthalmology. Those with an abnormal image or IOP greater than or equal to 30 mmHg are referred directly to ophthalmology.

Results: Of the 382 individuals enrolled and screened, 256 participants were ultimately referred to ophthalmology, among them 109 after optometry evaluation (Figure 1). Of this population, average age was 70.6 years old, 70.1% female, 50.7% Black/African American, 42.3% Hispanic/Latino, 79.6% unmarried, 67.1% completed less than college education, 39.8% did not speak English as a primary language, 66.3% had Medicare or Medicaid insurance, 87.5% were unemployed, 17.4% were active smokers, and 77.6% had not had an eye exam within the previous year. The most common reasons for referral to ophthalmology were glaucoma suspect (49.2%), retinal abnormality (42.2%), and cataract (14.8%).

Conclusions: This study identified African American and Hispanic race, single marital status, low education level, federal insurance, and unemployment as common epidemiologic characteristics of individuals who needed referral to ophthalmology. Identifying social determinants of health that prevent detection of eye disease may help providers target at-risk populations, and improve access to and utilization of eye care services.

CONTROL ID: 3711609

SUBMITTER (NAME ONLY): Lucia Dominguez

TITLE: Confocal laser microscopy and Fluorescence lifetime Imaging microscopy of Retinal pigment epithelium of mice.

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Dominguez, R.M. Torres, J.I. Etchart, J. Adur, Bioengineering, Instituto de Investigación y Desarrollo en Bioingeniería y Bioinformática (IBB), Oro Verde, Entre Rios, ARGENTINA|

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ABSTRACT BODY:

Purpose: An ex-vivo experiment was designed for developing and employing an imaging technique performed with a scanning laser confocal microscope for measuring fluorescent lifetime of endogenous fluorophores of the retinal mice.

Methods: The enucleated eyes of BALBC/c mice are used. They are placed on a slide and observed with a confocal laser scanning microscope, LSM 880 – Carl Zeiss, by a transscleral approach.

This microscope is composed of continuous wave lasers from 405 nm to 613 nm which are used to analyze the intensity and location of the fluorescence signal for each wavelength, and a fluorescence lifetime imaging microscopy (FLIM) system, which is fitted by micropulse lasers of 405 and 440 nm, synchronized with a photomultiplier, and a time correlated single photon counting (TCSPC) device. That system works by exciting fluorophores and measuring their fluorescence lifetime.

Results: We obtained images of a monolayer of autofluorescent hexagonal cells with large nuclei compatible with the retinal pigment epithelium (RPE) using a 488 nm wavelength laser, as is shown in Fig. 1. The mean cell diameter is 5.3 mm and the nucleus diameter is 2.7 mm.

The fluorescence lifetimes measured were 0.8 ns and 2.2 ns, with an excitation wavelength of 405 nm and an emission wavelength range of 465-515 nm, compatible with melanin granules and Flavin adenine dinucleotide (FAD) free, as is observed in Fig. 2.

Conclusions: During the development of this setup for capturing images of the retina ex-vivo it was possible to penetrate sclera and chroroid with the scanning laser until reaching the RPE in the enucleated eyes. Images were taken and the fluorescence lifetime of the endogenous fluorophores was measured.

The next step is to perform in-vivo experiments with anesthetized animals and mouse holders.

CONTROL ID: 3711610

SUBMITTER (NAME ONLY): Stefan Steiner

TITLE: Birefringence of the retinal nerve fiber layer is reduced in early glaucoma eyes analyzed by polarization-sensitive OCT

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Steiner, F. Schwarzhans, S. Desissaire, H. Resch, G. Fischer, M. Pircher, C.K. Hitzenberger, C. Vass, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To study the circumpapillary birefringence (BIR) of the retinal nerve fiber layer (NFL) in healthy and early glaucoma eyes using polarization-sensitive optical coherence tomography (PS-OCT). The NFL is birefringent, which is caused by intracellular parallel microtubules within the NFL. The number of these microtubules is thought to be reduced as an early sign of glaucoma damage.

Methods: This is a prospective cross-sectional study where we compared circular PS-OCT B-scans in 49 early glaucoma (age: 64 ± 10 years) vs. 49 age-matched healthy eyes (age: 61 ± 9 years). The circular scans (diameter: 3.5 mm) were extracted from volume scans and centered on the optic disc (OD). The BIR value at each virtual A-scan position was the quotient of the retardation (RET) measured at the IS/OS junction divided by the NFL-thickness (NFLT). Early glaucoma was defined by glaucomatous appearance of the OD and repeated pathologic visual field tests with a mean deviation (MD) better than -6 dB. Main outcome parameters were BIR, NFLT, and RET.

Results: Glaucoma eyes showed statistically significantly reduced NFLT (69±13 µm vs. 99±12 µm, $p<0.001$), RET (6.5 ±1.6° vs. 10.5 ±1.9°, $p<0.001$) and BIR (0.108 ±0.008°/µm vs. 0.112 ±0.009°/µm, $p=0.0033$) compared to healthy eyes. Figure 1 shows plots in temporal (T), superior (S), nasal (N), inferior (I) order for NFLT (A), RET (B) and BIR (C). Surprisingly the BIR showed no double-hump pattern as usually observed for NFLT and RET, instead it appeared to have a single dip at the temporal region. This was confirmed in averaged maps shown in Figure 2, whereas: column A-D-G= healthy eyes, B-E-H= glaucoma eyes with superior visual field (VF) impairment (n=27), C-F-I= glaucoma eyes with inferior VF impairment (n=19) and row A-B-C= NFLT, D-E-F= RET, G-H-I=BIR. Glaucoma eyes with both visual field hemispheres affected (n=3) were excluded from the averaged maps.

Conclusions: We report a reduced BIR of the NFL in early perimetric glaucoma, which may be interpreted as a sign of a loss of intracellular microtubules and might contribute to a better understanding of early glaucoma development. Early reduction of BIR in glaucoma models has been shown before in non-human primates. Nevertheless, to establish whether BIR is altered in preperimetric human glaucoma prior to the reduction of NFLT, prospective longitudinal studies are needed.

CONTROL ID: 3711611

SUBMITTER (NAME ONLY): Kim Worley

TITLE: ClinGen Variant Curation for X-linked Inherited Retinal Disease Genes

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As part of the Clinical Genome Resource (ClinGen), the X-linked Inherited Retinal Diseases Variant Curation Expert Panel (XLIRD VCEP) was established in 2020 to address the need for consistent variant interpretation in inherited retinal disease (IRD) genes with an X-linked inheritance pattern, which account for ~15% of IRD reported in large cohorts.

Methods: The XLIRD VCEP implements the ClinGen variant curation practices that have been recognized by the U.S. FDA to assess individual variants in seven X-linked genes (CACNA1F, CHM, NPD, OFD1, RPGR, RP2 and RS1). By combining expertise in phenotypes and molecular mechanisms of the IRD from clinical and laboratory experts, a set of variant curation rules customized to each gene is specified to assess the pathogenicity of the variants. All reported variants in the seven genes are systematically scored, following the rules and categorized into five classes, including pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign, according to ACMG/AMP guidelines.

Results: We established the XLIRD VCEP, with membership and curation protocols available on the ClinGen website (https://clinicalgenome.org/). Starting with RPGR, in which variants account for 9% of rod-cone and cone-rod dystrophies, gene-specific curation rules are generated. Performance of various computational prediction tools are evaluated, and proper allele frequencies in population databases are selected to determine the pathogenicity of the variant. To facilitate the curation process, in addition to published variants, private variant data from genetic testing laboratories are also collected. Pilot curation exercises being performed will be evaluated to refine the initial rules, which will then be applied to curate variants in the RPGR gene. This process will be repeated for the other XLIRD

genes, and the curations reviewed iteratively to refine the processes further.

Conclusions: Systematic and consistent curation of variants from FDA-recognized gene-specific guidelines supported by sharing genomic data and expertise will evaluate the current classification of variants and decrease the numbers of VUS within these XLIRD genes. This will improve the specificity and accuracy of the molecular diagnoses of patients with variants in these genes and increase the value of genetic testing as a diagnostic tool and guide for patient eligibility for genetic therapies for these IRD.

CONTROL ID: 3711613

SUBMITTER (NAME ONLY): Muralidharan Arumugam Ramachandran

TITLE: Intermittent exposure to bright light can prevent form-deprivation myopia in a monkey model

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Arumugam Ramachandran, L. Yong Chong, D. Milea, R. Najjar, Visual Neuroscience, Singapore Eye Research Institute, Singapore, SINGAPORE|M. Arumugam Ramachandran, D. Milea, Ophthalmology and Visual Sciences Academic Clinical Programme, Duke-NUS Medical School, Singapore, SINGAPORE|R.K. Tan, Bioengineering & Devices, Singapore Eye Research Institute, Singapore, SINGAPORE|V. BARATHI, Translational Pre-Clinical Animal Model, Singapore Eye Research Institute, Singapore, SINGAPORE|V. BARATHI, R. Najjar, Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, SINGAPORE|L. Hung, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|B. Tan, L. Schmetterer, School of Chemical and Biomedical Engineering, Nanyang Technological University, Singapore, Singapore, SINGAPORE|L. Schmetterer, Ocular Imaging, Singapore Eye Research Institute, Singapore, SINGAPORE|J. Kok Yen, Duke-NUS Medical School, Singapore, SINGAPORE|J. Kok Yen, Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore, Singapore, SINGAPORE|S. Saw, Saw Swee Hock School of Public Health, National University of Singapore, Singapore, SINGAPORE|S. Saw, Myopia, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To evaluate the impact of intermittent bright light exposure on ocular growth and refractive error development in a monkey model of form-deprivation myopia.

Methods: Eight infant macaques (21±4 days old) were housed for 210 days under a 12/12h light/dark cycle using standard fluorescent light (SL, 140 lux, 4000K). Macaques were assigned into 2 groups. Animals in group 1 (n=5, 2 rhesus, 3 cynomolgus) were raised under SL, whereas animals in group 2 (n=3, 2 rhesus, 1 cynomolgus) were exposed to an additional 4h/day of intermittent bright light (IBL). IBL consisted of 1h of high intensity LED light (11,066 lux, 4000K) delivered every 2h of SL. Form-deprivation myopia (FDM) was induced monocularly over 154 days using a custom-built 3D-printed helmet fitted with a plano lens and occlusion foil (20/300 VA) covering the form deprived (FD) eye. The fellow (control) eye was covered with a plano lens. Axial length (AL), refractive error and choroidal thickness were assessed fortnightly. Results are expressed as average inter-ocular difference (IOD= FD - control eye) ±SD. Outcome measures were compared between eyes on day 154 (D154) using a paired t-test and between groups using a Mann-Whitney U-test on areas under the outcome measures' curves (AUC) across form-deprivation (D0 to D154).

Results: By the end of form-deprivation (D154), FD eyes exposed to SL had increased AL (IOD = +0.25±0.17 mm; P=0.03) and myopic refraction (IOD= -3.80±0.89 D; P<0.001), and thinner choroids (IOD= -11.8±5.72 µm; P=0.009) compared to control eyes. On the other hand, FD eyes exposed to IBL showed no changes in AL (IOD= +0.02±0.03 mm), refraction (IOD= +0.08±0.14 D) or choroidal thickness (IOD= -1.0±2.64 µm) (all P>0.05). Overall, across the form deprivation period, FD eyes exposed to IBL displayed reduced/abolished IOD in axial elongation, myopic refraction and choroidal thinning compared to the eyes exposed to SL (all P<0.05; Fig.1A-C).

Conclusions: Our preliminary findings suggest that 4h/day of IBL can prevent the development of FDM in infant macaques. Data from 5 additional animals are being collected and analyzed and will be presented at ARVO 2022.

CONTROL ID: 3711618

SUBMITTER (NAME ONLY): Huijun Yuan

TITLE: Depletion of GSDMD by AAV-Mediated Crispr/SaCas9 Rescues Hyperoxia-induced Cell Death in Vitro

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yuan, S. Chen, M.R. Duncan, P. Chen, M. Benny, A. Schmidt, K. Young, S. Wu, Division of Neonatology, Bachelor Children's Research Institute, Department of Pediatric, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gasdermin D (GSDMD) is a key executor of inflammasome-mediated pyroptotic cell death and inflammation. Previously we demonstrated that global knockout of the GSDMD gene in vivo prevents hyperoxia-induced retinopathy in a neonatal murine model. Here we investigated if depletion of GSDMD expression with single strand AAV9 vector-mediated Crispr/SaCas9 gene editing rescues hyperoxia-induced cell death in murine retinal ganglion cell-5 (RGC-5) and primary retinal microvascular endothelial cells (RMVECs) in vitro.

Methods: Three editing vectors (AAV9-SagRNA-SaCas9-HA) each containing a guide RNA (SagRNA) targeting GSDMD exons 2, 3 or 4 were constructed with a HA tag fused to SaCas9 C-terminal plus a control vector with a scrambled SagRNA. Each of these vectors was transduced into RGC-5 and RMVECs with the helper adenovirus 5. Immunofluorescence and Western blotting for the HA tag were used to confirm transduction. Western blot was used to examine the efficiency of depletion of GSDMD expression. To examine the effects of these vectors on preventing hyperoxia-induced cell death, transduced RGC-5 and RMVECs were incubated in room air (21% O_2) or hyperoxia (95% O_2) for 64 h. Cell survival was detected by cell counting and pyroptotic cell death was assessed by LDH assays.

Results: All GSDMD gene-editing vectors as well as the control vector were effectively transduced in RGC-5 and RMVECs, as evidenced by immunofluorescence and Western blotting. Western blots showed that GSDMD expression was drastically decreased in RGC-5 and RMVECs by the vector containing the guide RNA targeting exon 4. Moreover, DNA sequencing revealed that this vector effectively edited a GSDMD genomic mutation. We found this vector significantly attenuated hyperoxia-reduced cell survival by 40% in RGC-5 compared to controls ($p<0.001$). Similarly, depletion of GSDMD in RMVECs significantly increased cell numbers under hyperoxia compared to controls by 4-fold ($p<0.005$). Furthermore, LDH assay showed that hyperoxia-induced cell death in RMVECs transduced with this vector was significantly decreased by 3-fold compared to controls ($p<0.001$).

Conclusions: Depletion of GSDMD expression by AAV9-mediated Crispr/SaCa9 gene editing markedly rescued hyperoxia-induced cell death in RGC-5 and RMVECs. Thus, this strategy has potential as a novel treatment to prevent oxygen-induced retinopathy in neonatal rodent models as well as in premature infants.

CONTROL ID: 3711619

SUBMITTER (NAME ONLY): Jack Sullivan

TITLE: RNA Structure-Function Properties of Enhanced Hammerhead Ribozymes with High Catalytic Efficiency

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Sullivan, J. Myers, Research Service, VA Western NY Healthcare System, Buffalo, New York, UNITED STATES|J.M. Sullivan, J. Myers, Ophthalmology (Ross Eye Institute), University at Buffalo-SUNY, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Investigate RNA structure/function properties of Enhanced hammerhead ribozymes (EhhRz) to ascertain underlying molecular biophysical properties of log-order kinetic improvements.

Methods: EhhRz-266 attacks full length human rhodopsin mRNA at CUC↓266, a rare position accessible for annealing and cleavage. Minimal substrate RHO-266 RNA is 15 or 14 nt long with 5' FAM and 3' BHQ1 (IDT); cleavage at CUC↓ 266 and product release results in liberation of quenched fluorescence which is quantified optically in real time in a qRT/PCR machine. EhhRzs are transcribed (T7pol) from PCR templates or synthetized (IDT). Mutations in substrate or/and EhhRz assess structure-function relationships in reactions initiated by mixing EhhRz with substrate RNA (100 nM: 1 uM) in buffer (10 mM Tris-HCl, pH 7.5) at 0.5 mM Mg2+ and optically measured at 37°C. Data are analyzed in Origin.

Results: Variation of Stem-II tetraloops (n=24) had marked impact on kinetic turnover activity relative to wild type (GAAA) with both 15-mer (ANOVA, p = 0) and 14-mer (ANOVA, p=0) substrates. Optimal tetraloops are from a class with unique 3D structure. Changes in the 5' end of the EhhRz, base pairing with the 3' end of the substrate, have marked impact on turnover rates at the A7 position (ANOVA, p=0), severe impact at the G6 position (ANOVA, p=0), and less marked impact at the A5 position (ANOVA, p=4.44E-16). Length and composition of Stem-II has a marked impact on turnover rate (ANOVA, p=1.11E-16). The number of G residues at the 5' end of the EhhRz has a marked impact on turnover rate (ANOVA, p=0). Addition of a structured stem at the 5' end of the EhhRz is inhibitory (ANOVA, p=0). Variation of the NUH↓ cleavage site impacts turnover (ANOVA, p=0).

Conclusions: Kinetic efficiency (Vmax/Km) of EhhRzs is on scale of protein RNaseA. EhhRz upstream antisense flank (bound to substrate mRNA) interacts with Stem-II tetraloop to promote catalysis. The optimum Stem-II length (4bp) infers critical distance-dependent interactions. Variation in rate with upstream composition suggests specific nucleotide interactions with Stem-II-tetraloop. Variation in rate with tetraloop infers that these interactions can be highly varied (topological) and dynamic. Outcomes are relevant to establishment of design rules for EhhRzs as nucleic acid therapeutics for arbitrary target mRNAs.

CONTROL ID: 3711620

SUBMITTER (NAME ONLY): Naman Gupta

TITLE: Topical application of anti-miR-183/96/182 cluster causes transient, reversible corneal nerve reduction and demonstrates therapeutic potential against bacterial keratitis

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Gupta, S.A. McClellan, D. Bessert, L.D. Hazlett, S. Xu, Ophthalmology, Visual and anatomical sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously we identified that the miR-183/96/182 cluster (miR-183C) modulates corneal response to Pseudomonas aeruginosa (PA) infection by regulating corneal nerve function and innate immunity[1-3].Local application of anti-miR-183C in a prophylactic regimen causes a transient, reversible reduction of corneal nerve density and protects against PA keratitis[4]. This study is to test whether topical application of anti-miR-183C alone in a therapeutic regimen has similar effects on corneal nerves and PA keratitis.

Methods: 8 weeks old, female C57BL/6 mice were used. Under anesthesia, the cornea of the left eye was scarified by three 1-mm incisions using a 25 5/8-gauge needle. 5.0×10^6 CFU PA (strain 19660; ATCC) in 5 µl was topically delivered. Six or 24 hours after infection and twice daily thereafter, 5 µl of anti-miR-183C or negative-control oligoribonucleotides (NC ORN) in sterile saline (8 µM/each) was topically applied to the infected cornea for 5 days. To test the effect of anti-miR-183C alone on corneal nerves, anti-miR-183C or NC ORNs were topically applied to the cornea 24 hours after a mock infection and twice daily thereafter. At 5 days post (mock) infection (dpi), immunofluorescence (IF) of flat-mounted corneas with bIII-tubulin antibody was done and corneal nerve density was determined.

Results: Topical application of anti-miR-183C resulted in a significant reduction of corneal nerve density. To test whether anti-miR-183C-induced reduction of corneal nerves causes permanent changes to corneal nerves, after the last topical application, another group of anti-miR-treated mice were held for another week without any treatment. Our result showed that their nerve density was fully recovered. Preliminary data on PA-infected corneas showed that topical application of anti-miR-183C significantly reduced the severity of the disease at 3 dpi ($p<0.05$); at 5 dpi, anti-miR-183C treated eyes had slightly decreased severity, however, didn't pass the statistical threshold ($p=0.09$).

Conclusions: Topical application of anti-miR-183C causes transient and reversible corneal nerve density reduction and has a therapeutic potential against PA keratitis. Further studies to optimize the treatment regimen and uncover the molecular mechanisms of the therapeutic effect are warranted.

CONTROL ID: 3711623

SUBMITTER (NAME ONLY): Paul Missel

TITLE: Surgical Retina Instrument Reach Modeling for Highly Myopic Eyes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Missel, L. Yin, R. Grueebler, B. Pultar, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The prevalence of high myopia (spherical refraction [SR] > -6D or an axial length > 26 mm) with a maximum recorded length of 37 mm is projected to increase from 2.7% to 9.8% by 2054. Retinal surgery requires instruments of sufficient length to reach the retina. To assist in the selection of appropriate instruments, modeling was conducted to estimate the length of instruments required for highly myopic eyes.

Methods: A geometric model for a myopic eye was constructed as a guide to determine the length of an instrument required to reach the position of the retina furthest from the point of insertion. The anterior portion of the model included only the cornea, with anterior radius of 7.77 mm drawn to a white-to-white distance of 11.69 mm, and the anterior sclera of radius 13.12 mm extending from this point to a length of 3.5 mm, representing the point of instrument insertion at the pars plana. The posterior portion was comprised of the retinal surface from the posterior pole to +/- 11 mm from the optical axis, parameterized to allow the retinal shape and location to scale with mean SR, according to the model. Matlab code was written to determine the distance to the location on the retina furthest away from the point of insertion.

Results: For the model eye, when axial length increased from 23.6 to 37.3 mm, maximum required instrument reach increased from 23.3 to 33.7 mm.

Conclusions: An instrument with a maximum reach of 34 mm is sufficient to treat an eye with axial length up to 37 mm.

CONTROL ID: 3711624

SUBMITTER (NAME ONLY): WAI KIT CHU

TITLE: Genetic Association of ANGPT2 with Primary Open-Angle Glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. CHU, J. He, T. Ng, S. Lu, P. Tam, P.P. Chan, C. Tham, C.C. Pang, L. Chen, Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|T. Ng, Joint Shantou International Eye Center of Shantou University and The Chinese University of Hong Kong, Shantou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To determine the association of the ANGPT2 gene with primary open-angle glaucoma (POAG) in Chinese.

Methods: Six single-nucleotide polymorphisms (SNPs) in ANGPT2 (rs2515487, rs2922869, rs13255574, rs4455855, rs13269021, and rs11775442) were genotyped in a total of 2,601 study subjects from two cohorts. One is a Hong Kong Chinese cohort of 484 high tension glaucoma (HTG) and 537 normal tension glaucoma (NTG) patients, and 496 non-glaucoma control subjects. Another cohort is a Shantou Chinese cohort of 403 HTG and 135 NTG patients, and 543 non-glaucoma control subjects. Subgroup analysis by sex was conducted. Outcomes from different cohorts were combined for a meta-analysis.

Results: SNP rs11775442 showed a nominal association with NTG in the Hong Kong cohort ($P = 0.0498$, OR = 1.24, 95% CI: 1.00-1.55) after adjusting for age and sex. Other SNPs were not significantly associated with NTG, HTG and POAG in individual cohort or in the combined analyses ($P > 0.05$). In the subgroup analysis by sex, SNP rs13269021 in the Shantou cohort was significantly associated with NTG in males ($P = 0.0081$, OR = 1.67, 95% CI: 1.14-2.43; Table 3) but not in females ($P = 0.874$).

Conclusions: For the first time, we identified a sex-specific association of ANGPT2 locus (rs13269021) with NTG in the Shantou cohort, indicating ANGPT2 may have a role in the genetic mechanism of NTG in Chinese males. Further studies are needed to verify the association between ANGPT2 and NTG.

CONTROL ID: 3711625

SUBMITTER (NAME ONLY): Yun Yu

TITLE: In Vitro and In Vivo Characterizations of GB-401, A Sustained Release Intravitreal Implant Containing A Beta-Adrenergic Antagonist Prodrug for Primary Open Angle Glaucoma (POAG)

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yu, J. Chisholm, D. McKenzie, D. Lucena Domingues, D. Cardona, T. Young, Q. Lu, M. Yang, Graybug Vision Inc., Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intraocular pressure (IOP) fluctuation is a major risk factor for glaucoma progression and vision loss and is associated with either non-adherence to or poor topical anti-glaucoma drug penetration in patients with POAG. GB-401 is a biodegradable implant formulation containing a beta-adrenergic antagonist prodrug that has the potential to enable sustained IOP reduction with twice-a-year intravitreal (IVT) injections. This study includes in vitro characterization of GB-401 and in vivo evaluation for pharmacokinetics (PK) and ocular toxicity.

Methods: The prodrug was synthesized by conjugating hydrophobic linkers to the parent beta-adrenergic antagonist and loaded in an injectable biodegradable implant. The drug loading, implant injectability and release kinetics were assessed in vitro. Intraocular pharmacokinetics were evaluated in Dutch-belted rabbits at two dose levels. Ocular tissues and blood samples were collected at various timepoints and analyzed for drug concentrations. A repeat-dose GLP toxicity study in minipigs is in progress to evaluate the ocular safety of GB-401.

Results: GB-401 achieved high drug loading and sustained drug release kinetics owing to the modified physiochemical properties of the prodrug. The linkers of the prodrug degrade by hydrolysis, allowing full conversion to the active beta-adrenergic antagonist. The prodrug was previously shown to effectively reduce IOP in an ocular hypertensive rat model (Hoang et al., ARVO 2019). Sustained drug release from GB-401 lasted approximately 120 days in vitro under sink condition. Significant drug levels were achieved in target tissues (iris-ciliary body) from day 3 (180-fold of K_i) and through 4 months (100-fold of K_i), with a maximum concentration >4,000-fold greater than the K_i, whereas no drug was detected in plasma at any timepoint. The implant formulation was well tolerated in the completed PK study in rabbits, as well as the ongoing toxicity study in minipigs, with no signs of ocular toxicity.

Conclusions: GB-401 is an injectable implant formulation containing a beta-adrenergic antagonist prodrug that has the potential to enable a long-term treatment paradigm with sustained IOP reduction achieved via twice-a-year IVT injections in patients with POAG. A Phase 1/2a first-in-human study is planned.

CONTROL ID: 3711626

SUBMITTER (NAME ONLY): Monica Ravenstijn

TITLE: Myopic choroidal neovascularization: a long-term follow-up of anti-VEGF treatment in a large European cohort.

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ravenstijn, Rotterdams Oogheelkundig Instituut, Rotterdam, Zuid Holland, NETHERLANDS|C.C. Klaver, Dept. of Ophthalmology / Dept. of Epidemiology, Erasmus MC, Rotterdam, NETHERLANDS|C.C. Klaver, S. Yzer, Dept. of Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

Commercial Relationships Disclosure: Monica Ravenstijn: Commercial Relationship(s);Code R (Recipient):Bayer | Caroline Klaver: Commercial Relationship(s);Code C (Consultant/Contractor):Bayer; Thea Pharma;Code R (Recipient):Thea Pharma | Suzanne Yzer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intravitreal anti-vascular endothelial growth factor (VEGF) improves the visual prognosis in myopic choroidal neovascularization at short term, but visual acuity (VA), recurrence rate, and second eye involvement at long-term remain unclear. We performed a longitudinal clinical study with real-world data to learn about the long-term outcomes of anti-VEGF in a large European cohort.

Methods: Up to 12 years of longitudinal data from a tertiary hospital in the Netherlands (2008 – 2018) were analyzed. Patients with high myopia (spherical equivalent (SE) ≤-6D), an active CNV lesion, European descent and no history of anti-VEGF treatment were monitored. A total of 98 eyes (mean SE -14 ± 4D) of 87 patients (mean age 57±14 years) were included. Course of VA during follow-up, recurrence rate and second eye involvement were analyzed as outcomes. Change in VA during follow-up was compared using paired t-tests. Cox proportional hazard models tested the effect of the presence of chorioretinal atrophy (CRA) and lacquer cracks on mCNV recurrence or second eye involvement.

Results: VA significantly improved after a median of 2 anti-VEGF injections ($P<0.001$). At 4 years, the improvement in VA disappeared ($P=0.6$) and continued to deteriorate (Figure 1). The average decrease of VA was 0.05 LogMar per year. The cumulative incidence of recurrent mCNV was 52% at 5 years after the first episode. VA in eyes with recurrent mCNV decreased at a similar rate ($P=0.5$). Diffuse CRA (HR 10.6 95% CI 2.2-51.3, $P=0.003$) and patchy CRA (HR 5.2 95% CI 1.2-22.0, $P =0.027$) were significant predictors for mCNV recurrence. In 22 (25%) patients, the fellow eye developed mCNV after an average of 5.7 years. Age ≤ 40 years at first onset of mCNV significantly increased the risk of bilateral mCNV (HR 4.5, 95% CI 1.4–13.9, $P=0.008$). CRA and lacquer cracks in the fellow eye at baseline did not add significantly to the risk of mCNV in that eye.

Conclusions: This large mCNV study revealed that VA improvement after IVB injections was not maintained at long-term. Recurrences occurred frequently but did not alter the already poor visual prognosis. We advise to closely monitor patients with mCNV since recurrences occur in more than 50%, and pay particular attention to patients younger than 40 years as they are at high risk of second eye involvement.

CONTROL ID: 3711627

SUBMITTER (NAME ONLY): Thomas Cronin

TITLE: Remote Assessment of Anterior Chamber Depth Using Novel Stereoscopic Digital Slit Lamp Images

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Cronin, Geisinger Commonwealth School of Medicine, Scranton, Pennsylvania, UNITED STATES|A. Gupta, J. Olson, H. Ingraham, Ophthalmology, Geisinger Medical Center, Danville, Pennsylvania, UNITED STATES|G.W. Armstrong, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Thomas Cronin: Commercial Relationship: Code N (No Commercial Relationship) | Ankur Gupta: Commercial Relationship: Code N (No Commercial Relationship) | Grayson Armstrong: Commercial Relationship(s);Code O (Owner):Ocular Technologies Inc;Code C (Consultant/Contractor):McKinsey & Company;Code C (Consultant/Contractor):Xenon-VR;Code C (Consultant/Contractor):Ophthalytics;Code C (Consultant/Contractor):Kriya Therapeutics;Code S (non-remunerative):American Medical Association | Joanna Olson: Commercial Relationship: Code N (No Commercial Relationship) | Herbert Ingraham: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Anterior chamber (AC) depth is a frequently assessed component of the ophthalmic examination, as shallow AC is correlated with risk of acute and chronic angle closure glaucoma or risk of angle closure due to pharmacologic dilation. AC depth can be assessed through gonioscopy or the Von Herick slit lamp evaluation. Telemedicine has recently been employed to enable screening, diagnosis, and management of ophthalmic conditions. In order to evaluate the utility of telemedicine to assess AC depth, we implemented a novel modified slit lamp capable of transmitting stereoscopic images of patients' eyes to remote reviewers. We hypothesized that AC depth assessment using digital stereoscopic slit lamp images would correlate with in-person ophthalmologist assessment of the AC depth.

Methods: We prospectively captured five standardized images of patient eyes (n = 5) using a stereoscopic slit lamp camera. One in-person physician and five remote physicians graded the depth of the AC and graded it on a binary scale as either shallow or deep.

Results: There was 76% agreement (kappa = 0.766) in remote grading of AC depth. The agreement between the in-person and remote graders numbers 1-3 was 100% (kappa =1.0), 50% (kappa = 0.5) for remote grader 4, and 83% (kappa = 0.83) for remote grader 5.

Conclusions: Remote telemedical assessment of the depth of patients' AC using stereoscopic images appears to be feasible according to the results of our small prospective pilot study. Telemedicine may therefore be able to improve access to high quality eye care for patients at risk for shallow AC and associated ophthalmic conditions. Larger future studies are needed to validate the results of this pilot study.

CONTROL ID: 3711628
SUBMITTER (NAME ONLY): Urvi Gupta
TITLE: Lipocalin-2 homodimer variant: Role in dry age-related macular degeneration
SESSION TITLE: Pathobiology of AMD
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: U. Gupta, S. Ghosh, P. SHANG, H. Liu, A. Strizhakova, S.L. Hose, D. Sinha, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.S. Zigler, D. Sinha, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|
Commercial Relationships Disclosure: Urvi Gupta: Commercial Relationship: Code N (No Commercial Relationship) | Sayan Ghosh: Commercial Relationship: Code N (No Commercial Relationship) | PENG SHANG: Commercial Relationship: Code N (No Commercial Relationship) | Haitao Liu: Commercial Relationship: Code N (No Commercial Relationship) | Anastasiia Strizhakova: Commercial Relationship: Code N (No Commercial Relationship) | Stacey Hose: Commercial Relationship: Code N (No Commercial Relationship) | J. Zigler: Commercial Relationship: Code N (No Commercial Relationship) | Debasish Sinha: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly. We have shown that a pro-inflammatory adipokine, Lipocalin-2 (LCN-2), is upregulated in retinal pigment epithelium (RPE) cells in both a mouse model with a dry AMD-like phenotype and in early/dry human AMD donor samples, but only after chronic inflammation has been established. Many elegant studies have shown that LCN-2 exists as either a monomer or a homodimer variant. While the monomer is a potent iron chelator and has anti-microbial effects, the homodimer variant, which has a longer half-life, is unable to chelate iron and has been linked to the onset of several diseases. However, it is not known whether the homodimer variant is also upregulated in AMD nor if it is associated with disease progression. In this study, we evaluated the level of LCN-2 homodimer in AMD and investigated its possible role in inducing retinal degeneration.

Methods: Western blotting (WB) was performed on the RPE cell lysates under reducing and non-reducing conditions to evaluate the levels of the LCN-2 homodimer and monomer variants in our mouse model and human dry AMD donor samples. The levels of the LCN-2 variants were evaluated in spent medium from WT RPE explants overexpressing LCN-2 (RSM-LCN-2). To determine if the homodimer variant can induce retinal degeneration, NOD-SCID mice were injected with RSM-LCN-2, and effects on retinal structure (SD-OCT) and function (electroretinography) were assessed.

Results: WB analysis revealed an increased LCN-2 homodimer:monomer ratio in the RPE lysates from our mouse model and human AMD donors. The presence of the homodimer was confirmed by WB under reducing and non-reducing conditions. RSM-LCN-2 also showed elevated levels of the homodimer variant. Sub-retinal injection of RSM-LCN-2 in NOD-SCID mice, induced significant alterations in retinal structure and function.

Conclusions: Our data suggests that LCN-2 homodimer is the pathogenic form of the adipokine and is involved in AMD pathogenesis. Further, targeting/neutralizing the homodimer variant could be helpful in delaying the onset of retinal degeneration as seen in dry AMD, a multifactorial disease for which there are no treatment options at the present time.

CONTROL ID: 3711629

SUBMITTER (NAME ONLY): Vinay Sharma

TITLE: Surface softness characterization of a novel biomimetic silicone hydrogel contact lens using an atomic force microscopy indentation method

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Sharma, C.X. Shi, J. Wu, Alcon Research Institute, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Vinay Sharma: Commercial Relationship(s);Code E (Employment):Alcon | Charlie Shi: Commercial Relationship(s);Code E (Employment):Alcon | James Wu: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: An atomic force microscopy (AFM) indentation method was employed to measure the surface softness of a novel reusable biomimetic silicone hydrogel (lehfilcon A) contact lens with surface modification of a cross-linkable bioinspired 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer. The purpose of the study was to measure and compare the surface softness of the lehfilcon A contact lens, the cornea, and other reusable SiHy contact lenses including comfilcon A, senofilcon A, senofilcon C, and samfilcon A.

Methods: An AFM nanoindentation method was developed to test corneas and contact lenses in fully hydrated conditions. The AFM probe used for the indentation experiments had a design (tip size, geometry and spring constant) especially suited to characterize soft materials and biological tissues, and it allowed precise contact-point determination as well as accounted for the fluid-load support effect. Indentation force-curves (FC) were generated for the cornea and contact lens samples at a fixed force, chosen to generate a contact pressure within the physiological range of the upper eyelid pressure on the human ocular surface. These FC were then analyzed to calculate the surface modulus values to conclude relative comparisons in the surface softness.

Results: The improved sensitivity and accuracy of the indentation method allowed precise measurement of the extremely low surface softness for the cornea and lehfilcon A contact lens. The surface modulus of the lehfilcon A contact lens (46±7 kPa) was similar to that of the cornea sample (55±31 kPa), but significantly lower than those of the comfilcon A (231±51 kPa), senofilcon C (251±47 kPa), senofilcon A (257±36 kPa), and samfilcon A (266±39 kPa) contact lenses ($p<0.05$ for all).

Conclusions: A new AFM indentation method with increased sensitivity and accuracy was developed to measure the surface modulus of a novel biomimetic MPC surface-modified SiHy contact lens as well as the cornea and other reusable SiHy contact lenses. The results indicated that the surface of the lehfilcon A contact lens was as soft as the cornea surface and was significantly softer than the comfilcon A, senofilcon A, senofilcon C, and samfilcon A contact lenses. The surface softness of a contact lens might affect the mechanical contact stress on ocular tissues thus its impact on eye comfort.

CONTROL ID: 3711633

SUBMITTER (NAME ONLY): Nicole Scripsema

TITLE: Aflibercept and High-Dose Aflibercept: Real-world outcomes at 48 months

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.K. Scripsema, A. Atkuru, A. Wagner, K.G. Kapoor, Ophthalmology, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|N.K. Scripsema, A. Wagner, K.G. Kapoor, Wagner Kapoor Research Institute, Norfolk, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Nicole Scripsema: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan | Abhijith Atkuru: Commercial Relationship: Code N (No Commercial Relationship) | Alan Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Kapil Kapoor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the efficacy of high-dose aflibercept and aflibercept for neovascular age-related macular degeneration.

Methods: This retrospective review included age-matched neovascular age-related macular degeneration (nAMD) patients treated with aflibercept (2mg/0.05ml) and high-dose (HD) aflibercept (3mg/0.075ml). Our current clinical practice patterns are to treat nAMD eyes initially with bevacizumab and transition to aflibercept and HD aflibercept when clinically necessary. Visual acuity, central retinal thickness (CRT), qualitative optical coherence tomography (OCT) data was compared from baseline to 48 months for eyes requiring treatment with aflibercept and HD aflibercept.

Results: A total of 200 eyes of 177 patients were included. Mean visual acuity was similar at baseline for HD aflibercept (logMAR 0.50 ± 0.46 20/63) and aflibercept groups (logMAR 0.51 ± 0.39 (20/64), p=0.20). Mean visual acuity was stable over 48 months in both HD aflibercept (logMAR 0.46 ± 0.37 (20/57), p=0.27) and aflibercept groups (logMAR 0.56 ± 0.48 (20/72), p=0.46). The HD aflibercept group started with a thicker mean CRT (313.7 ± 102.8 µm versus 276.5 ± 68.8 µm, p<0.01) and required more injections than the aflibercept group (34.8 ± 12.5 vs 27.3 ± 9.7 injections respectively, p<0.01). HD aflibercept eyes were also less likely to be extended (27% versus 45%, respectively, p<0.01). Of the 100 eyes who had an incomplete response to monthly bevacizumab and monthly aflibercept, 97% achieved a dry macula with monthly HD aflibercept. Central retinal thickness also improved in HD aflibercept (313.7 ± 102.8 µm to 264.7 ± 52.26 µm, p<0.001) and aflibercept groups (276.5 ± 68.8 µm to 231.0 ± 54.8 µm, p<0.001) over 48 months.

Conclusions: Aflibercept and HD aflibercept are effective at maintaining visual acuity and central retinal thickness in eyes with nAMD over 48 months. Eyes with a suboptimal response to monthly bevacizumab and monthly aflibercept were able to achieve comparable visual acuity and OCT outcomes with high-dose aflibercept. Further studies are necessary to elucidate the real-world applications of standard dose and HD aflibercept.

CONTROL ID: 3711635

SUBMITTER (NAME ONLY): Katie Bales

TITLE: Exercise promotes BDNF and specific TrkB isoform expression in retinal astrocytes and protects against retinal degeneration

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bales, M.T. Pardue, J.H. Boatright, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|A. Chacko, M.T. Pardue, Georgia Institute of Technology College of Engineering, Atlanta, Georgia, UNITED STATES|J.M. Nickerson, J.H. Boatright, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our labs have demonstrated exercise as a promising intervention in animal models of retinal degeneration (RD). Exercise-induced retinal protection was accompanied by increased levels of brain derived neurotrophic factor (BDNF) and required intact signaling via its high-affinity receptor, TrkB. In the brain, imbalances in astrocytic expression of BDNF and specific TrkB isoform expression, particularly increased TrkB.T1, contribute to neurodegeneration severity. Here, we explore the role of retinal astrocytes in exercise-induced retinal neuroprotection using a light-induced retinal degeneration model (LIRD) that exhibits phenotypes found in patients with RD.

Methods: Adult male BALB/c mice were assigned to active(A)-dim, inactive(I)-dim, inactive(I)-LIRD and active(A)-LIRD groups (n=36 per group). Active mice were treadmill exercised (1hr/d, 10m/min) for two wks, then LIRD was induced (5000 lux/4hrs). Inactive groups were on a static treadmill for the same schedule. At week three, retinal function was assessed using ERG. Retinal flat mounts were stained for astrocytes (GFAP) and density, branching and dendritic arborization were quantified. Magnetic activated cell sorting (ACSA-2) and ddPCR was used to isolate retinal astrocytes and quantify gene expression of BDNF and various TrkB isoforms. Data were analyzed using 2-way ANOVA.

Results: A-LIRD a- and b-wave mean amplitudes were 2.5x and 1.9x greater than I-LIRD means respectively ($p<0.001$), indicating that exercise significantly preserved retinal function. Flat mounts from A-LIRD mice had 50% more astrocytes ($p<0.0001$), 44% more branching ($p<0.0001$,) and 69% more arborization ($p<0.05$). Isolated retinal astrocytes from A-LIRD mice had increased TrkB.FL expression ($p=0.006$), I-LIRD mice had increased TrkB.T1 expression ($p=0.014$) and active groups had increased BDNF expression compared to inactive ($p=0.025$).

Conclusions: Our results indicate exercise influences retinal astrocyte morphology and gene expression. Retinal astrocytes from A-LIRD groups showed increased expression of BDNF and TrkB.FL, the TrkB isoform associated with cell survival. These results suggest exercise can alter retinal astrocyte morphology and restore BDNF-TrkB signaling during RD, providing insight for exercise-based therapies for RD.

CONTROL ID: 3711636

SUBMITTER (NAME ONLY): Tatiana Nevinitsina

TITLE: Effect of ophthalmic mitochondrial reactive oxygen species scavenger Visomitin® on visual acuity of patients diagnosed with Leber hereditary optic neuropathy: findings of an observational clinical study.

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Nevinitsina, N. Sheremet, N. Andreeva, N. Zhorzholadze, I. Ronzina, FGBNU Naucno-issledovatel'skij institut glaznyh boleznej, Moscow, Moscow, RUSSIAN FEDERATION|K. Lyamzaev, M. Skulachev, E. Karger, Moskovskij gosudarstvennyj universitet imeni M V Lomonosova Naucno-issledovatel'skij institut fiziko-himiceskoj biologii imeni A N Belozerskogo, Moscow, Moscow, RUSSIAN FEDERATION|T. Krylova, P. Tsygankova, FSBI Research Center for Medical Genetics, Moscow, RUSSIAN FEDERATION|A. Petrov, Mitotech S.A., Luxembourg, LUXEMBOURG|

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ABSTRACT BODY:

Purpose: This observational clinical study was designed to assess the effects of mitochondrial reactive oxygen species (mtROS) scavenger Visomitin (SkQ1 ophthalmic solution) in Leber hereditary optic neuropathy (LHON) patients relative to data demonstrated by prior natural history studies of disease progression and to identify potential primary endpoints for a future double-blind, randomized, placebo-controlled study.

Methods: This was an uncontrolled, open-label, observational study, comprising 6 visits over the course of 30 months. 43 subjects diagnosed with mitochondrial optic neuropathy who were prescribed Visomitin (0.155ug/mL SkQ1 Ophthalmic Solution) for Dry Eye Disease were observed. 26 patients (24 men and 2 women) had genetically confirmed LHON-related mutations in mtDNA. There was no designated primary endpoint. Best Corrected Visual Acuity was assessed using Freiburg Vision Test for low vision.

Results: All 26 subjects with LHON-related mtDNA mutations completed the initial 12-month observation period. Average BCVA of LHON patients significantly improved by 0.37 logMAR ($p=2x10^{-8}$) relative to baseline after 12 months. After 30 months of treatment BCVA change from baseline was 0.42 logMAR ($p=1x10^{-10}$). According to the International Consensus, BCVA improvement of 2 lines (0.2 logMAR) is considered clinically relevant in LHON patients. Studies of natural history of LHON patients carrying the m.11778G>A mutation suggest that over a comparable time frame, BCVA improvement of 0.3 logMAR or more occurs in 18% of patients, and the deterioration of BCVA of the same value (0.3) occurs in 14%. In this study, among patients with m.11778G>A mutation treated with Visomitin an improvement by 0.3 logMAR and more was observed in 56% of patients by the end of the study, while deterioration by 0.3 LogMAR or more was not observed.

Conclusions: Visomitin ophthalmic solution, a drug designed for protection of ocular tissue from oxidative stress at mitochondrial level, demonstrated statistically significant improvement of BCVA relative to baseline in LHON patients. These improvements compare favorably when considering the typical natural history of disease progression. These findings warrant design of a double-masked, randomized, placebo-controlled study of Visomitin efficacy in LHON patients.

CONTROL ID: 3711639

SUBMITTER (NAME ONLY): Johnathon Sturgis

TITLE: Characterizing the effects of mitochondrial DNA mutations on retinal health in the Polg^{D257A} mouse.

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sturgis, C. Milliner, P. Freedman, R. Singh, I.S. Samuels, V.L. Bonilha, Ophthalmic Research, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|J. Sturgis, V.L. Bonilha, Lerner College of Medicine, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, UNITED STATES|I.S. Samuels, Research, Louis Stokes VA Medical Center, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Johnathon Sturgis: Commercial Relationship: Code N (No Commercial Relationship) | Caroline Milliner: Commercial Relationship: Code N (No Commercial Relationship) | Paul Freedman: Commercial Relationship: Code N (No Commercial Relationship) | Rupesh Singh: Commercial Relationship: Code N (No Commercial Relationship) | Ivy Samuels: Commercial Relationship: Code N (No Commercial Relationship) | Vera Bonilha: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mitochondrial DNA (mtDNA) mutations that promote mitochondrial dysfunction have been implicated in age-related retinal diseases. This study used a novel pre-clinical model to test the hypothesis that impaired mitochondrial function due to mtDNA damage results in age-related retinal and retinal pigment epithelium (RPE) degeneration.

Methods: 3-, 6-, 9-, and 12-month-old Polg^{D257A} mutant and wild-type (WT) mice were imaged using optical coherence tomography (OCT) and confocal scanning laser ophthalmoscopy (cSLO)(N=4). In addition, photoreceptor and RPE functions were assessed using electroretinogram (ERG). Histological and immunohistological evaluation of the retinas of Polg^{D257A} mutant and control mice were also performed in cryosections. Cryosections (8 um) were incubated with commercially available antibodies specific to retinal cells and mitochondria. Sections were analyzed using a Leica TCS-SP8. A Student's t-test was used for all statistical analyses.

Results: OCT image analysis revealed a decrease in the size of several retinal cell layers starting at 6 months of age. Most notably, the RPE and photoreceptor (PR) layers were significantly decreased compared to WT mice and accounted for nearly 57% of the total retinal degeneration observed. Analysis of SLO images detected a significant decrease in blue auto fluorescence at 6 months of age. ERG testing displayed a drastic reduction in a-wave, b-wave, and light-adapted response at 12 months of age. Finally, retinal tissue collected for immunofluorescence showed decreases in COX4 and Ezrin proteins compared to WT. Together, this data indicates that mtDNA mutations result in both degenerative and physiological effects in the mouse retina. The degeneration is associated with decreased total retina and RPE thickness, impaired electrophysiological activity from multiple neural retina cell types, and reduced essential proteins implicated in retinal metabolism and integrity.

Conclusions: Polg^{D257A} mutant mice that accumulate mtDNA mutations due to an error-prone exonuclease domain in Polymerase gamma, exhibit an age-related retinal pathology.

CONTROL ID: 3711640

SUBMITTER (NAME ONLY): TIANXI WANG

TITLE: SOCS3 regulated retinal angiogenesis via modulating myeloid lineage cell recruitment

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. WANG, E. Lam, D.I. Tsirukis, Y. Tomita, S. Kaneko, Y. Sun, Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a major cause of blindness in children. The incidence of ROP continues to increase and there is an urgent need to understand the molecular mechanism of ROP development. Immune cells are a source of cytokines and growth factors that may interact with endothelial cells and contribute to retinopathy. We reported that myeloid cells regulated choroidal neovascularization via suppressor of cytokine signaling 3 (SOCS3). However, the role of myeloid cells in ROP is still unknown. We aimed to study the role of myeloid cells and SOCS3 in ROP.

Methods: Socs3 myeloid-specific knockout mice (Socs3 cKO) were generated by breeding Socs3 flox/flox (Socs3 f/f) mice with LysM-Cre mice. Socs3 myeloid-specific overexpression mice (Socs3 cOE) were generated by breeding Socs3 OE flox/flox (Socs3 OE) mice with LysM-Cre mice. Oxygen induced retinopathy (OIR) mouse model was generated by exposing newborn mice to 75% oxygen from postnatal day (P)7 to P12 and to room air from P12 to P17. CD45 positive cells were isolated from retinas with OIR (age-matched normal retina as control) using flow cytometry for single cell RNA sequencing (10x genomics). Retinas were stained with endothelial cell marker Isolectin B4 (Invitrogen) and flat mounted for phenotypical analysis. Results were presented as mean ± SEM and compared using the unpaired nonparametric Mann-Whitney test. Statistical analyses were performed with GraphPad Prism.

Results: Using single cell RNA sequencing data, we applied t-Distributed Stochastic Neighbor Embedding (t-SNE) method to analyze the immune cell profile at steady state and during OIR. All clusters were assigned based on cell markers, which mainly included microglia, macrophages, neutrophils, B cells, T cells, and CD45-positive endothelial cells. A few clusters were identified that only appeared in OIR retinas including subtypes of microglia and macrophages as well as potential myeloid lineage derived endothelial cells. In addition, metabolism, inflammation, and cell proliferation related pathways were ranked on the top based on the pathway analysis using differential expressed genes (DEGs) in clusters that are different from OIR retinas compared with normal retinas.

Conclusions: SOCS3 regulated retinal angiogenesis via modulating myeloid lineage cell recruitment. Manipulating SOCS3 expression in myeloid cells may provide a new way to cure neovascularization in retinas.

CONTROL ID: 3711641

SUBMITTER (NAME ONLY): Rohit Dhakal

TITLE: Does the spectral composition of an ambient light vary between indoors and outdoors “in myopia perspective”?

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Dhakal, P.K. Verkicharla, Myopia Research Lab, Prof. Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|R. Dhakal, B. Huntjens, R. Shah, J. Lawrenson, Centre for Applied Vision Research, School of Health Sciences, City University of London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Considering that differences in the characteristics of ambient light between indoor and outdoor environment may impact myopia development in children, this study investigated the spectral composition of ambient light in different a) outdoor/indoor locations, b) times of a day, and c) seasons.

Methods: The spectral power distribution (SPD) was recorded using a hand-held spectrometer in three outdoor (‘open playground’, ‘under shade of tree’, and ‘canopy’) and three indoor locations (‘room with multiple windows’, ‘closed room’, and ‘closed corridor)’ at five different time points (3-hour intervals between 6:30 and 18:00 clock-hours) on two days, each during summer and monsoon seasons. The pattern and the distribution of SPD across the spectrum, namely the short (380-500 nm), middle (505-565 nm) and long wavelengths (625-780 nm) were further assessed to understand the percentage composition in different locations.

Results: The overall median SPD (IQR [25th-75th percentile] W/nm/m2) across three outdoor locations (0.11 [0.09,0.12]) was 157 times higher than indoor locations (0.0007 [0.0001,0.001]). A considerable locational, diurnal and seasonal variation was observed in the distribution of median SPD value, with the highest value recorded in the ‘open playground’ (0.27 [0.21,0.28]) followed by ‘under shade of tree’ (0.083[0.074,0.09]), ‘canopy’ (0.014[0.012,0.015]), and ‘room with multiple windows’ (0.023[0.015,0.028]). While the spectral power of short, middle, long, and blue wavelengths was significantly lower in indoor compared to outdoor locations, the pattern and the relative percentage composition of short, middle and long wavelengths were similar in both the outdoor and indoor locations.

Conclusions: Irrespective of variation in SPD values with location, time, day and season, outdoor locations exhibited significantly higher SPD than indoor locations. The relative percentage composition of short, middle and long wavelengths of light are similar across all the locations. From a myopia perspective, our findings indicate a possibly greater importance of the spectral power of ambient light rather than its spectral composition, as the latter was similar across outdoor and indoor locations. This finding warrants further research to understand its causal association with myopia.

CONTROL ID: 3711643

SUBMITTER (NAME ONLY): Olivia Roby

TITLE: Sex matters in eye and brain metabolism: targeted metabolomics reveals tissue-specific sex difference in metabolism in fasted vs. fed state

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Roby, S. Meghashr, R. Xu, Y. Wang, J. Du, biochemistry, West Virginia University Eye Institute, Morgantown, West Virginia, UNITED STATES|O. Roby, S. Meghashr, R. Xu, Y. Wang, J. Du, Ophthalmology, West Virginia University Eye Institute, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Metabolism plays critical roles in neuronal health and diseases. Sex is an important biological variable, but how sex influences metabolism in the eye and brain remains unclear. This study aims to address the sex difference in metabolites from mouse eye tissues, brain, and plasma in fed and fasted state using targeted metabolomics.

Methods: Three-month-old C57B6/J mice were ad libitum fed or deprived of food for 18 hours. Mouse eye tissues (retina, eyecup, and lens), brain, and plasma were harvested for targeted metabolomics. The steady-state metabolites were analyzed with liquid chromatography mass spectrometry and gas chromatography mass spectrometry. The data were analyzed with both multivariate Partial least squares-discriminant analysis (PLS-DA) and univariate Volcano Plot analysis ($P<0.05$ and fold change >1.3).

Results: Multivariate PLS-DA separated male and female groups in all tissues under either fed or fasted state in scores plots, demonstrating there is sex difference in the metabolome. Volcano Plot analysis showed that 8-47 metabolites were different between males and females under the fed state. The lens and retina had the largest number of changes but the plasma had the least. However, under the fasted state, the changed metabolites were reduced to 5-28, and the profiles of changed metabolites were mostly different from the fasted group. Intriguingly, ATP was reduced in the fasted eye cup, lens and brain, but its level was unchanged in the fasted retina. These results suggest that different sexes have different metabolic flexibility. Remarkably, the CoA precursor, Pantothenate, was the only metabolite that was significantly increased in all the female tissues. The fasting further increased Pantothenate in the female eye cup and lens. We also found tissue-specific changes between sexes. Hypoxanthine was retina-specific, succinate was eye cup specific, and cystine, ascorbic acid, adenine, UTP and UDP-Glucosamine were specific to the lens.

Conclusions: Sex influences eye and brain metabolism. Different sexes have tissue-specific and metabolic state-specific changes in metabolome. Our findings support that sex should be considered as a biological variable in the design of metabolomics studies.

CONTROL ID: 3711644

SUBMITTER (NAME ONLY): Eunice Kim

TITLE: Discontinuation, switching, and other long-term real-world treatment patterns among patients with diabetic macular edema initiating anti-VEGF: 6-year follow-up using the IRIS® Registry

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kim, V. Garmo, D. Tabano, Genentech Inc, South San Francisco, California, UNITED STATES|B. Kuo, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|T. Leng, M. Hatfield, A. LaPrise, Verana Health, San Francisco, California, UNITED STATES|R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study aimed to characterize long-term treatment patterns among patients with diabetic macular edema (DME) from a large ophthalmology registry.

Methods: A retrospective analysis was performed among treatment-naïve DME patients (no prior anti-vascular endothelial growth factor (anti-VEGF) intravitreal therapy [IVT] in the past 12 months) initiating IVT from 1/1/2015-12/31/2019 using de-identified electronic medical records (IRIS® Registry). Anti-VEGF agent utilization patterns, including agent type, switches (defined as ≥3 consecutive injections of a different anti-VEGF agent from the original agent), and discontinuations (defined as no anti-VEGF IVT for ≥12 months). Results were stratified by baseline visual acuity (VA) and initial anti-VEGF agent including on-label (ranibizumab and aflibercept) and off-label agent (bevacizumab).

Results: Of 190,345 eyes (147,687 patients), 147,336 eyes (77%) received only 1 anti-VEGF agent over a mean follow-up of 2.3 years, with bevacizumab being the most commonly used agent (53% of eyes). Bevacizumab use decreased by a mean of 5.6% each year and on-label agent use increased by a mean of 6.9% each year (Figure 1). 15% of eyes switched anti-VEGF agents after a mean of 53 weeks, of which 74% switched from bevacizumab to an on-label agent. 52% of eyes discontinued anti-VEGF treatment after a mean of 24 weeks, of which 33% reinitiated after a mean of 91 weeks. Rates of discontinuation, switching, and reinitiation were mostly similar regardless of baseline VA, though discontinuation with no reinitiation of IVT during follow-up was highest in patients with VA ≤20/200 at baseline (Figure 2).

Conclusions: Although a majority of patients with DME discontinue IVT therapy after a mean of 6 months, a third reinitiated. 58% patients initially received bevacizumab, but its use decreased over time with an increased use of on-label agents. Reasons for switching and discontinuation should be further explored.

CONTROL ID: 3711645

SUBMITTER (NAME ONLY): Rong Xu

TITLE: Rod photoreceptor-specific deletion of MPC1 impairs visual function with age-dependent retinal degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Xu, J. Huang, Y. Wang, S. Zhu, Biochemstry, West Virginia University, Morgantown, West Virginia, UNITED STATES|J.B. Hurley, Biochemistry, University of Washington, Seattle, Washington, UNITED STATES|R. Xu, J. Huang, Y. Wang, S. Zhu, J. Du, ophthalmology, West Virginia University, Morgantown, West Virginia, UNITED STATES|J.B. Hurley, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mitochondrial pyruvate carrier (MPC) transports pyruvate from glycolysis into mitochondria. We recently reported pan-retinal deletion of MPC1 (a major component of MPC) disrupts retinal metabolism and causes retinal degeneration. In this study, we aim to understand the role of MPC in rod photoreceptors

Methods: MPC1 flox/flox mice were crossed with rod photoreceptor cre mice to generate mice with rod-specific deletion of MPC1 ($RMPC1^{-/-}$). We measured visual function by electroretinogram (ERG), retinal thickness by optical coherence tomography (OCT) and H&E, protein expression by immunohistochemistry, ultrastructure by electron microscope (EM), and retinal metabolites by targeted metabolomics and metabolic flux analysis

Results: Immunostaining with a customized antibody confirms the specific deletion of MPC1 in rod photoreceptors in $RMPC^{-/-}$ mice. Scotopic a-wave and b-wave decrease in $RMPC1^{-/-}$ mice starting at postnatal 30 days (P30), and further decline at P60. However, $RMPC1^{-/-}$ mice show a late-onset photoreceptor degeneration after P90. Photoreceptor inner segments are partially damaged in EM but the expression of mitochondrial complexes is normal. Pyruvate and aspartate accumulate, but citrate, glutamate and glutamine remain at normal amounts in $RMPC1^{-/-}$ retinas, suggesting metabolic compensation by other cells and/or nutrients. Consistently, the expression of GFAP and glutamine synthetase is upregulated in Müller glial cells. To study whether an alternative fuel could rescue the phenotype, we fed the mice with a ketogenic diet for 2 months starting at P21. The ketogenic diet significantly improves scotopic ERGs in $RMPC1^{-/-}$ mice in the first month but there is no protection after two months.

Conclusions: Mitochondrial pyruvate transport in photoreceptors is essential for visual function and photoreceptor viability. Although mitochondria have the flexibility to use a variety of nutrients, pyruvate, mostly from glycolysis, is indispensable for normal rod function and survival.

CONTROL ID: 3711646

SUBMITTER (NAME ONLY): Xavier Sánchez-Sáez

TITLE: The loss of visual motion perception in Parkinson's disease could be explained by the degeneration of starburst amacrine cells and the impairment of their synaptic contacts with dopaminergic cells

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Sánchez-Sáez, I. Ortuño-Lizarán, C. Sánchez-Castillo, O. Kutsyr, H. Albertos-Arranz, V. Maneu, P. Lax, N. Cuenca, Universitat d'Alacant, Alacant, Comunitat Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: Besides the motor deficits, Parkinson’s disease (PD) patients display visual disturbances in the early stages of the disease. One of these symptoms is the impairment of motion perception. Hence, we sought to evaluate if the main cell type involved in motion perception, the starburst amacrine cells, are degenerated in PD and if so, whether this degeneration is related to the degeneration of the dopaminergic system.

Methods: Human eyes from control and PD donors were available for this study. Tyrosine hydroxylase-positive cell density (dopaminergic amacrine cells), choline acetyltransferase-positive cell density (starburst amacrine cell) was evaluated by immunohistochemistry and confocal microscopy in whole-mount retinas. We also quantified the dopaminergic synaptic contacts with starburst amacrine cells using vesicular monoamine transporter-2 (VMAT2) antibodies.

Results: We found a significant decrease in the number of dopaminergic amacrine cells in PD retinas. Moreover, there is a decrease in the density of starburst amacrine cells in the two plexuses where they are located. Importantly, this work describes for the first time that dopaminergic amacrine cells contact with starburst amacrine cells in healthy control retinas and that these connections decrease in PD.

Conclusions: This work shows that there is a degeneration of starburst amacrine cells and their synaptic connections with dopaminergic cells which may explain the motion perception alterations in PD. Hence, these alterations can be used as a biomarker of the pathology using functional tests for motion perception.

CONTROL ID: 3711647
SUBMITTER (NAME ONLY): Jennyfer Zapata
TITLE: Effective intracameral injection in the mouse model
SESSION TITLE: Drug delivery
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: J. Zapata, A. Abid, M. Djallali, M. Piché, C. Boutopoulos, I. Brunette, Ophthalmology, Hopital Maisonneuve-Rosemont Centre de Recherche, Montreal, Quebec, CANADA|A. Abid, Institute of Biomedical Engineering, Universite de Montreal, Montreal, Quebec, CANADA|I. Brunette, Ophthalmology, Hopital Maisonneuve-Rosemont Centre Universitaire d'Ophtalmologie, Montreal, Quebec, CANADA|C. Boutopoulos, Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|J. Zapata, M. Meunier, Engineering Physics, Polytechnique Montreal, Montreal, Quebec, CANADA|
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ABSTRACT BODY:

Purpose: Intraocular injection is a standard route of administration for the treatment of several eye diseases, including AMD, intraocular inflammation, infection, and gene therapy. In human subjects, intracameral injection is rapid and easy to perform, with minimal discomfort for the patient. However, in the murine model these injections are more challenging due to dimension and anatomy of the eye. Our goal was to develop a semi-automated procedure for safe intracameral injection improving precision and reproducibility in the mouse model.

Methods: A 3D printed plate was developed to safely stabilize the body and immobilize the head of the animal. A color camera and an optical coherent tomography (OCT) system were adapted for injection real-time monitoring. Needles were mounted on a Hamilton syringe fixed on a 4-axis motorized manipulator for precise positioning. In vivo experiments were performed under general anesthesia (IP ketamine 60mg/Kg and Medetomidine 1mg/Kg), while animal's temperature was maintained at 37C. A perforated Tegaderm was applied to the periocular region to recline lashes and partially protrude the globe. Microneedles of various sizes (31-35G) and laser-tailored tip profiles (30 to 14°) as well as different puncture site orientations and speeds of injection were tested. Intracameral injections consisted of 0.4 µL of either BSS or OCT contrast agent. Recorded videos were used to estimate the best injection conditions.

Results: Adult C57Bl/6 mice (20 ex vivo, 6 in vivo) were used. Most successful injections were performed with a custom tri-surface 14° 35G laser-sharpened needle (Fig. 1a). Injections at the iridocorneal angle, tangential to the limbus resulted in effective piercings with less distortion of the globe. By using acute bevel angles facing the endothelium, less damage to the iris and lens, and less bleeding and leaking were reported (Fig. 1b-c). Implementation of a semi-automatic system with real-time monitoring ensued in reproducible results (Fig. 1d).

Conclusions: Implementation of a semi-automatic system under real-time OCT monitoring using tailored needle tip profiles allowed successful and safer intracameral injection in mice. Such setup is suggested to increase precision and reproducibility in murine models.

CONTROL ID: 3711648

SUBMITTER (NAME ONLY): Umar Bello

TITLE: Efficacy of Non-invasive Brain Stimulation on Vision: A Systematic Review and Meta-analysis

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U.M. Bello, J. Wang, B. Thompson, A.M. Cheong, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|U.M. Bello, A.S. Park, K.W. Tan, W.S. Cheung, B. Thompson, A.M. Cheong, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Multiple studies have explored the use of non-invasive brain stimulation (NIBS) to enhance visual function. These studies vary in sample size, outcome measures and NIBS methodology. We conducted a systematic review and meta-analyses to assess the effect of NIBS on visual function in human participants with normal vision.

Methods: We followed the PRISMA guidelines, and a review protocol was registered with PROSPERO before study commencement (CRD42021255882). We searched Embase, Medline, PsychInfo, PubMed and Web of Science using relevant keywords. The search covered the period from database inception until 4th February 2021. Comprehensive meta-analysis (CMA) software was used for quantitative analysis.

Results: Twenty-four studies were included in the meta-analyses. A single session of visual cortex transcranial electrical stimulation (tES; Hedges's g: 0.56, 95% CI: 0.23-0.90, p=0.001) and anodal transcranial direct current stimulation (tDCS; Hedges's g: 0.66, 95% CI: 0.27-1.04, p=0.001) reduced visual crowding. Other pooled analyses showing significant effects included impaired motion perception following cathodal tDCS of the middle temporal area (Hedges's g: 0.46, 95% CI: 0.006-0.92, p=0.047), improved contrast sensitivity (Hedges's g: 0.23, 95% CI: 0.02-0.44, p=0.03), and increased visual evoked potential amplitude (Hedges's g: 0.38, 95% CI: 0.11-0.66, p=0.006) following visual cortex tES. The effects of visual cortex anodal tDCS on visual acuity, motion perception, and contrast sensitivity were not statistically significant.

Conclusions: There are significant effects of visual cortex NIBS on crowding, motion perception, contrast sensitivity and visual evoked potential amplitude among normally sighted individuals.

CONTROL ID: 3711651

SUBMITTER (NAME ONLY): Jiaxiong Lu

TITLE: Spata7 is Required for Maintenance of the Retinal Connecting Cilium

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lu, K. Xiong, X. Qian, J. Choi, Y. Shim, J. Burnett, G. Mardon, R. Chen, MHG, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: SPATA7, an early onset LCA3 retinal disease gene, encodes a putative scaffold protein that is essential for the proper assembly of connecting cilium (CC) complex in the photoreceptor cells. Previous studies show that SPATA7 interacts with other photoreceptor-specific ciliary proteins, such as RPGR and RPGRIP1, and maintains the integrity of CC integrity. However, although it is clear that Spata7 is required for the early formation of the CC, whether it is also required for the maintenance of the CC is not clear. This study aims to elucidate the function of Spata7 in the adult retina.

Methods: To investigate Spata7 function in the retina at the adult stage, loss of function mutation is induced in the adult retina upon tamoxifen induction of the inducible Spata7 knockout mouse (Spata7flox/-; UbcCreERT2/+). The phenotype of the mutant mice retina is characterized through a combination of histology, immunohistochemistry, and electroretinogram (ERG).

Results: Spata7 is also essential for maintaining the integrity of the mature retinal CC. Loss of Spata7 in adults causes phenotypes similar to those seen in germline mutant mice, including photoreceptor cell degeneration, defective ERG responses, etc. Close examination of CC reveals that significantly shortened NPHP1 length can be detected when Spata7 is deleted. Consistently, mislocalization of Rhodopsin protein is observed in the outer nuclease layer, which leads to ER stress-mediated apoptosis.

Conclusions: Our results indicate that Spata7 is not only required for the establishment but also for the maintenance of the CC of the photoreceptors. In addition, the approach used in this study will facilitate achieving a mechanistic understanding of CC architecture and function.

CONTROL ID: 3711652

SUBMITTER (NAME ONLY): Quan Hoang

TITLE: Novel Super Resolution Magnetic Resonance Imaging Processing Pipeline for Whole Eye Imaging with Short Scan Times in High Myopic Eyes

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q.V. Hoang, R. Najjar, D. Milea, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS Medical School, SINGAPORE|Q.V. Hoang, S. Chang, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|L. Yannuzzi, K. Freund, Vitreous Retina Macula Consultants of New York, New York, NY, New York, UNITED STATES|J. Grinband, Radiology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To produce a high resolution (250μm isotropic), 3-D images of human highly myopic eyes while minimizing eye movements via a novel super-resolution MRI (srMRI)acquisition and processing pipeline with significantly lowered scan times.

Methods: Twenty-two eyes of 11 emmetropic subjects, 25 eyes of 14 subjects with myopia (with vision > 20/40 in >1 eye) with no prior eye medical history or surgeries aside from cataracts underwent IOLMaster biometry and srMRI imaging (3T, 8-channel head coil). A fat-suppressed, axial T2-weighted volumetric scanning sequence with four 90-second scans was acquired using various slice orientations resulting in 4 non-overlapping voxels. Images underwent registration, thresholding, upsampled with tri-linear interpolation producing isotropic voxels (FSL and Matlab). The coronal and axial acquisitions were then co-registered, averaged together and re-registered to achieve a resolution of 0.25 x 0.25 x 0.25 mm. The axial length from the anterior lens surface to the ILM was then calculated. Moreover, in order to quantify motion artifacts, we measured the frequency of blinks and saccades, two measures that indicate that the subject was unable to maintain fixation with eye tracking data over 25 minutes (EyeBrain, NeuroLite, 5-min-blocks with 1-min washout x 5 gazes) that was collected from 11 myopic subjects correctable to 20/20. Ages ranged from 22.5 to 84.7 years old, 60% female with axial lengths ranging from 22.4 to 33.2 mm.

Results: In terms of eye-tracking data, over the course of the 25-minute-long study, there was a steady increase the total time the eyes were closed to approximately 12 sec (40%) of each block. The frequency of saccades similarly increased from ~0.01 to ~0.12 saccades per sec. Both results indicate that MR imaging of the globe would benefit from reduced scan time. Comparing the axial lengths measured by SR-MRI with estimates by IOLMaster, the resulting slope was 1.037 ($p = 4 \times 10^{-29}$), which was not significantly different from a slope of 1 ($p = 0.28$). The residuals were heteroscedastic increasing exponentially with axial length ($p = 2 \times 10^{-5}$) with a rate constant of 5.8 mm.

Conclusions: A novel super-resolution magnetic resonance imaging acquisition and processing pipeline were used to acquire high resolution images of the whole eye with significantly lowered scan times, which is key in reducing motion artifacts.

CONTROL ID: 3711656

SUBMITTER (NAME ONLY): Ossi Kaikkonen

TITLE: ERG-based thermal dosimetry for subthreshold retinal laser therapy in anaesthetized pigs

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Kaikkonen, T. Turunen, A. Koskelainen, Department of Neutoscience and Biomedical Engineering, Aalto-yliopisto Perustieteiden korkeakoulu, Espoo, FINLAND|M. Amirkavei, A. Meller, J. Åhlgren, University of Helsinki Laboratory Animal Center, FINLAND|

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ABSTRACT BODY:

Purpose: Subthreshold retinal laser therapies (SLT) have vast clinical evidence in the treatment of various retinal disorders, including diabetic macular edema and central serous chorioretinopathy, and also early evidence for age-related macular degeneration. SLTs aim to trigger the heat shock response (HSR), a cellular response to combat stress, in the retinal pigment epithelium (RPE) through laser-induced hyperthermia without causing cell death. However, the therapeutic temperature window for triggering HSR but avoiding apoptosis is narrow, and the same laser exposure produces differing temperature elevations in different patients. Hence, SLT protocols without thermal dosimetry may lead to suboptimal treatment efficacy or safety profile. Here we present a focal electroretinogram (fERG) based method to provide thermal dosimetry for long-pulse SLT to enable personalized treatments.

Methods: Thirty-six laser treatments were delivered to 8 eyes in 4 anaesthetized pigs with 5 mm laser spot diameter and 60 s laser pulse duration. Each treatment was preceded by a laser power calibration protocol, where retinal temperature elevation per unit laser power was determined with a fERG-based method. The obtained value was used to estimate the laser power needed to reach a target temperature between 43.6 and 48.6°C. The treated areas were investigated for visible lesions with fundus imaging and fluorescein angiography. The threshold temperature for lesion generation and the accuracy of the thermal dosimetry were determined by fitting a probit model between the target temperature and damage classification data.

Results: The kinetics of the fERG response was found to accelerate linearly with temperature up to 43°C. At temperatures above 45°C the kinetics of the fERG signal started to decelerate accompanied by a drop in signal amplitude. The fERG-based thermal dosimetry method produced a standard relative error of 7% of the laser-induced temperature elevation. The steady-state threshold temperature for generating a lesion was determined to be 48.0°C for 60 second laser exposures.

Conclusions: fERG responses can be used to estimate laser-induced changes in retinal temperature and to estimate the laser power needed to reach a desired retinal temperature with high accuracy. We conclude that fERG-based retinal temperature determination can enhance the safety and efficacy of SLT with large spot size and long pulse duration.

CONTROL ID: 3711658

SUBMITTER (NAME ONLY): Daan Panneman

TITLE: Cost-effective identification of causal variants in 113 genes underlying retinitis pigmentosa and Leber congenital amaurosis

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Panneman, R.J. Hitti-Malin, E.G. Boonen, L.K. Holtes, M. Guimaraes Ramos, A. Tracewska, M. van de Vorst, C. Gilissen, A. Hoischen, F.P. Cremers, S. Roosing, Department of Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|D. Panneman, R.J. Hitti-Malin, F.P. Cremers, S. Roosing, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|B. de Koning, Department of Clinical Genetics, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|C. Gilissen, A. Hoischen, Radboudumc Radboud Institute for Molecular Life Sciences, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The identification of genetic variants underlying retinitis pigmentosa (RP) and Leber congenital amaurosis (LCA) is challenging as 108 genes are involved. Whole exome sequencing is often used in diagnostic facilities to identify causal variants explaining these phenotypes, but the costs are still prohibiting global applicability. An efficient and cost-effective targeted sequencing method is therefore needed.

Methods: We sequenced the exons and splice sites, and pseudo-exons due to pathogenic deep-intronic variants of 113 genes, and the RP17 autosomal dominant RP locus, using 16,812 smMIPs designed by Molecular Loop Biosciences. Sequencing libraries for 2,000 probands and control cases were prepared in series of 384 samples and analyzed using Illumina NovaSeq 6000. Single nucleotide variants (SNVs) were annotated with an in-house pipeline and prioritized for ≤1.0% allele frequency. Variants with a Franklin-ACMG classification of class 3, 4, or 5 variants were selected for further interpretation.

Results: Across five sequencing runs an average read count per nucleotide of 662x was achieved. All 19 SNVs and 22 copy number variants (CNVs) in control cases were reliably detected. All prioritized variants were evaluated in the first 480 probands. 248 RP and LCA probands (53%) were solved in the initial data analysis encompassing homozygous CNVs, homozygous and compound heterozygous SNVs in genes associated with autosomal recessive phenotypes, and heterozygous variants in genes associated with autosomal dominant or X-linked phenotypes. The 5 most frequently mutated genes were USH2A (12.5%), ABCA4 (11.3%), EYS (10.9%), CRB1 (4.9%), and RPGR (4.1%).

Conclusions: We showed that the smMIPs panel utilized in this study can be used to effectively sequence RP and LCA genes and loci. While the initial solve rate for this cohort of partially prescreened RP/LCA cases is 53%, further analysis will include the analysis of duplications and heterozygous deletions as well as an in-depth analysis of potential splice-site altering variants, adding to this diagnostic yield. We encourage professionals from low- and middle-income countries to contact us for potential patient inclusion.

CONTROL ID: 3711665

SUBMITTER (NAME ONLY): Joel Quinn

TITLE: The role of immune checkpoint ligands in retinal immune homeostasis and inflammation

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Quinn, A. Salman, M.E. McClements, R.E. MacLaren, K. Xue, Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|C. Dendrou, Wellcome Centre for Human Genetics, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|R.E. MacLaren, K. Xue, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Joel Quinn: Commercial Relationship: Code N (No Commercial Relationship) | Ahmed Salman: Commercial Relationship: Code N (No Commercial Relationship) | Michelle McClements: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship) | Calliope Dendrou: Commercial Relationship: Code N (No Commercial Relationship) | Kanmin Xue: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The blood-retinal barrier is maintained by both physical barriers (e.g. intercellular tight junctions) and immunomodulatory molecular signals. Infiltrating leukocytes express various immune checkpoint receptors which regulate activation and effector activity upon engagement with their cognate ligand. We characterized the retinal immunosuppressive milieu under physiological and uveitic states with a focus on immune checkpoint ligand expression by retinal cells.

Methods: Experimental autoimmune uveitis (EAU) was induced in 6-10 week-old female C57BL/6J mice by immunization with 400 µg human IRBP1-20 emulsified with 2.5 mg/mL complete Freund's adjuvant. Age and sex-matched naïve mice were used as controls. Using immunohistochemistry and confocal microscopy (n=4), and cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq), we profiled the expression of a panel of known immune checkpoint molecules in normal and inflamed retinae.

Results: Immunostaining of mouse retinae revealed expression of HVEM (BTLA ligand), CD200 (CD200R ligand) and PD-L1 (PD-1 ligand), but not PVR (TIGIT ligand) during both homeostasis and inflammation (Figure 1). HVEM was expressed in ganglion cell and bipolar cell bodies, and in the photoreceptor layer. CD200 expression was found to be predominantly axonal in the inner plexiform layer, and in the outer plexiform layer at a lower level. PD-L1 expression in healthy retina was seen in the outer plexiform layer and, to a lesser extent, in the ganglion cell and photoreceptor layers. Interestingly, PD-L1 did not colocalize with Iba1+ microglia, and expression levels appeared reduced in EAU. In contrast, expression levels of the other checkpoint ligands appeared similar in the inflamed retina. CITE-seq was performed to validate these findings at the single-cell level in both retinal and immune cells, revealing distinct immunomodulatory gene expression profiles.

Conclusions: Distinct expression patterns of immune checkpoint ligands by different retinal cell types contribute to immunosuppressive homeostasis within the eye. CITE-seq provides the first simultaneous single-cell gene expression profiling and immunophenotyping of healthy versus inflamed retina.

CONTROL ID: 3711667

SUBMITTER (NAME ONLY): Daire Hurley

TITLE: Virtual triaging in an Ophthalmic Emergency Department during the Covid-19 pandemic

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hurley, S. Neary, Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|

Commercial Relationships Disclosure: Daire Hurley: Commercial Relationship: Code N (No Commercial Relationship) | Simon Neary: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this audit was to assess the effect of new guidelines on phone triage referrals to an Irish eye emergency department (EED) during the Covid-19 Pandemic. We intended to maximise virtual reviews of non-urgent conditions to reduce footfall within the department.

Methods: A retrospective phone triage referral and clinical note audit was performed to assess outcomes of phone triaging in October. Guidelines for phone triage were formulated with particular regard to what conditions should be seen in EED, treated over the phone or sent straight to outpatients clinic or minor procedures. A prospective phone triage referral and case note audit to assess outcomes after introduction of the guidelines in November

Results: A total of 1,700 patients were referred to the eye emergency department, 861 in October and 839 in November. A total of 617 patients were triaged to EED in November, compared to 692 prior to implementation of guidelines ($p < 0.05$). The number of patients referred straight to outpatients (74 in November vs 51 in October) ($p < 0.05$) and treated over the phone (131 vs 104) ($p < 0.05$) was also significantly reduced. Ultimately, the number of conditions wrongly triaged to EED, as per the guidelines implemented, was significantly reduced (91 vs 240) ($p < 0.05$).

Conclusions: This audit addressed the need to reduce footfall during the Covid-19 pandemic, identified suitable avenues of referrals for certain conditions and demonstrated that these guidelines significantly reduced the number of patients presenting to EED with conditions amenable to phone review or clinic follow-up.

CONTROL ID: 3711668

SUBMITTER (NAME ONLY): Ruth van Nispen

TITLE: Evaluation of measurement properties of an online nurse-assisted eye-screening tool for home healthcare patients

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. van Nispen, E. Elsman, O. Lee, G. van Rens, H.P. van der Aa, Ophthalmology, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|H.P. van der Aa, Lighthouse Guild, New York, New York, UNITED STATES|R. Wisse, Ophthalmology, Universitair Medisch Centrum Utrecht, Utrecht, Utrecht, NETHERLANDS|J. Keunen, Ophthalmology, Radboud UMC, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Reliability and agreement of an online nurse-assisted eye-screening tool versus manifest tests was investigated in a home healthcare setting.

Methods: Near and distance visual acuity and macular function (Amsler) was tested in patients (mean age 83 years, range 65-97) from home healthcare organizations in the Netherlands. The online Conformité Européenne (CE)-marked eye-screening tool (Easee B.V.) was administered by nurses at the participants' homes using a tablet or laptop and a smartphone as a remote control. Manifest tests were administered within two weeks by a researcher. Bland-Altman's limits of agreement were computed, comparing online and manifest tests. Reliability was analyzed with intraclass correlation coefficients (ICC) and (weighted) kappa. Non-inferiority was set at a difference of less than ±0.15 logMAR.

Results: Forty patients (80 eyes) were included. Between the eye-screening tool and manifest test the following mean differences were found: distance visual acuity 0.02 logMAR, near visual acuity measured with tumbling-E optotypes 0.07 logMAR and 0.03 logMAR with the triangle-circle optotypes. For distance visual acuity 75% of the individual data points were within the non-inferiority threshold. For near visual acuity, 53% and 55% were within the non-inferiority threshold for the tumbling-E and triangle-circle optotypes, respectively. Good reliability between the tests was found for distance visual acuity (ICC=0.78), and moderate for the near visual acuity tests (ICC=0.74 and ICC=0.67) and for detecting macular problems (kappa=0.48).

Conclusions: Nurse-assisted eye-screening seems promising with this online tool in an elderly home healthcare population. Agreement and reliability of the tool was satisfactory. As a next step, acceptability of the tool by the various stakeholders and also cost-effectiveness of eye-screening in home healthcare will be investigated to confirm public support.

CONTROL ID: 3711673

SUBMITTER (NAME ONLY): Lajos Csincsik

TITLE: Phenotyping people with Down syndrome using ultra-widefield retinal imaging

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Csincsik, T. Peto, I. Lengyel, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|M.J. Walpert, T. Holland, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: People with Down syndrome (pwDS) have a high prevalence of early-onset Alzheimer's disease (AD). With the two-fold increase in life expectancy for pwDS, identifying early biomarkers for AD is needed. Previously we have shown that phenotyping using ultra-widefield retinal imaging (UWFI) has the potential to identify peripheral retinal biomarkers for AD in the general population (PMC8377778). Phenotyping peripheral retina in pwDS using this imaging modality has not been reported, therefore we present the feasibility of UWFI in pwDS.

Methods: Our cohort comprises of 24 pwDS with no or early signs of clinical dementia. UWFI was performed using the OPTOS P200DTx laser scanning ophthalmoscope. The peripheral retina was graded by a masked, experienced grader (LC) and ten percent of the images were adjudicated by a senior ophthalmologist (TP). Based on their cognitive scores pwDS were divided into two groups, those without (DSnD, CAMCOG>80) and those with (DSD, CAMCOG<80) clinical dementia.

Results: There was no significant age (DSD 37.09±7.84 vs DSnD 36.43±5.56; p=.849) or sex (males DSD 9[81.8%] vs DSnD 4[57.1%] p=.255) difference between DSD and DSnD groups. All patients required operator assistance to keep their eyes open for acquiring a sufficient quality image. Images could not be taken in 4 cases due to touch phobia and/or lack of compliance, and in 1 case the eyelids obscured the majority of the retina, resulting in 39 gradable images of 20 patients. Peripheral hard drusen were detected on the majority of the images (34 [87.2%]), with 56.7% in DSnD and 43.3% in DSD groups. Most of the images had only a few (<5) hard drusen (24/34). Other peripheral pathologies included: pigmentary changes (8 [20.5%]; DSnD 75%, DSD 25%), haemorrhages (4 [10.3%]; DSnD 25%, DSD 75%). Vitreoretinal degeneration (1), white without pressure (1), RPE atrophy (1) and retinal hole (1) were only detected in DSnD.

Conclusions: This study proved that UWFI is feasible in pwDS. We generated gradable images despite the need for operator assistance. The use of this imaging modality opens up the possibility of detailed phenotyping of pwDS in the peripheral retina where we found a variety of retinal phenotypes, some with high prevalence.

CONTROL ID: 3711674

SUBMITTER (NAME ONLY): Rob van der Linden

TITLE: The impact of season and sunlight on depression in adults with visual impairment

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. van der Linden, H.P. van der Aa, R.M. van Nispen, Ophthalmology, Amsterdam UMC, Amsterdam, Noord-Holland, NETHERLANDS|

Commercial Relationships Disclosure: Rob van der Linden: Commercial Relationship: Code N (No Commercial Relationship) | Hilde van der Aa: Commercial Relationship: Code N (No Commercial Relationship) | Ruth van Nispen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Depression is a common mental health problem in people with visual impairment. Exposure to light might influence the onset of depression in this population The aim of this study was to determine if seasonal variation and sunlight are associated with depression in adults with visual impairment, and if effects differ between: 1) adults who are blind vs. adults who have low vision; 2) adults with different eye diseases and; 3) adults who are sensitive to bright light vs. those who are not.

Methods: This study consisted of a quantitative analysis of pre-existing data from seven baseline measurements of studies conducted between 2009-2018. People with visual impairment, aged 18 and above, who were recruited from outpatient low vision rehabilitation organizations in the Netherlands were included. Self-reported data on experienced depressive symptoms was combined with information on season and the amount of sunlight that people were exposed to, retrieved from the Royal Netherlands Meteorological Institute. Logistic regression analyses were performed to analyse the data.

Results: Participants (N=1925) experienced most depressive symptoms in winter (32,8%), followed by summer (27,4%) spring (26,2%), and fall (24,2%). There was a significant difference between the odds to experience depressive symptoms in fall compared to winter (Odds ratio (OR)=0,656, p=0,004). The amount of sunlight was significantly associated with experienced depressive symptoms (OR=0.995, p=0,004). No significant interaction effects were found.

Conclusions: The results of this study support the hypothesis that seasonal variation and the amount of sunlight are associated with depression in people with visual impairment. [HvdA1] It may be interesting to compare these results with people without visual impairment and look at possibilities for treatment[HvdA2] in future research.

CONTROL ID: 3711675

SUBMITTER (NAME ONLY): Anaïs Françon

TITLE: The impact of exposure condition and light composition in phototoxicity in a rat model

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Françon, F.F. Behar-Cohen, A. Torriglia, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|A. Françon, Universite de Paris, Paris, Île-de-France, FRANCE|F.F. Behar-Cohen, Hopital Cochin, Paris, Île-de-France, FRANCE|A. Torriglia, INSERM, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The current phototoxicity threshold for rodents is set at a retinal dose of 11J/cm^2. It corresponds to the threshold for blue light at 445nm, as the blue component is assumed to be the only responsible for phototoxicity. The other parts of the spectrum such as green or red wavelengths are considered as non-toxic for the retina. In addition, phototoxicity thresholds are defined using acute exposure to light. We previously showed that the phototoxicity threshold for rodents could be overestimated by a factor 50. Here, we aim to evaluate the impact of light exposure on the retinal pigmented epithelium (RPE), the use of acute exposure instead of chronic exposure to assess the phototoxicity threshold and finally the effect of each part of the spectrum on the retina.

Methods: Male Wistar rats were exposed to light-emitting diodes (LED) displaying different wavelengths. We used acute or chronic exposure for 15 days, twice a day and various retinal doses. Light-induced damages were evaluated by immunostaining and TUNEL staining on retina sections or flat mounts of RPE. Protein quantification by western blot on retina samples was also performed.

Results: Exposure to blue and white LED at retinal doses below 11J/cm^2 triggers damages of the RPE with modification of the cell structure and size, and accumulation of albumin and rhodopsin aggregates. We observe that for retinal doses of blue and white LED that were safe in acute exposure, a chronic exposure to these doses induces a significant photoreceptor loss and macrophages invasion of the retina. Finally, addition of a red component to a white LED decreases photoreceptor cell death and modifies the retinal stress response. Meanwhile, decomposition of the white light into blue and green lights highlights the negative impact of the green component that induces photoreceptor loss and an increased expression of several stress markers.

Conclusions: Taken together, these results suggest that light induces damages in the neural retina and the RPE at retinal doses below the current phototoxicity threshold. Moreover, the overestimation of the phototoxicity threshold could be greater than of a factor 50 as chronic exposure should be used to define the threshold. Finally, the protective effect of the red component and the negative impact of the green component underline the importance of each part of the spectrum to evaluate the phototoxicity of a light source.

CONTROL ID: 3711677

SUBMITTER (NAME ONLY): Shizuka Koh

TITLE: Long-Term Follow-Up of Biomechanical Changes in Very Asymmetric Ectasia

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Koh, R. Inoue, Innovative Visual Science, Osaka Daigaku, Suita, Osaka, JAPAN|S. Koh, S. Maeno, N. Maeda, K. Nishida, Ophthalmology, Osaka Daigaku, Suita, Osaka, JAPAN|R. Inoue, SEED CO., LTD., Tokyo, JAPAN|R. Ambrósio, Ophthalmology, Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro, RJ, BRAZIL|R. Ambrósio, Instituto de Olhos Renato Ambrósio/Visare Personal Laser, Rio de Janeiro, BRAZIL|V. Jhanji, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate chronological corneal biomechanical changes in fellow eyes with normal topography from patients with very asymmetric ectasia (VAE) for 3 years.

Methods: The clinical records of patients with VAE were retrospectively reviewed. Patients with VAE were defined as having clinical ectasia in one eye and a fellow eye with normal topography. Corneal biomechanical assessment with high-speed dynamic Scheimpflug-based corneal imaging was performed at baseline and at each follow-up visit in each eye. The deformation amplitude ratio within 2 mm, integrated radius, Ambrósio relational thickness to the horizontal profile, stiffness parameter at the first applanation (SPA1), Corvis Biomechanical Index (CBI), stress–strain index (SSI), and tomographic/biomechanical index were used to investigate the chronological changes in biomechanical parameters. Linear mixed-effects models were used to evaluate changes in biomechanical and clinical parameters over time.

Results: Thirty patients (17 men, 13 women) with VAE met the study criteria. The patients' age at baseline examination was 46.4 ± 14.4 years. Significant changes in SPA1, CBI, and SSI ($p = 0.048$, $p = 0.012$, and $p=0.011$, respectively) were observed during the 3-year period, and only SSI showed a decreasing trend over time. There were no significant changes in other corneal biomechanical parameters and clinical parameters during the 3-year period. A significant association between the SSI and age at initial biomechanical assessment. ($p<0.001$)

Conclusions: Based on corneal biomechanical evaluation over a 3-year period, possible corneal softening in such eyes was observed, highlighting the characteristics of progressive ectatic corneal disorder even in a subclinical status. Future studies using a longer follow-up period are required.

CONTROL ID: 3711679

SUBMITTER (NAME ONLY): Jackie Shane

TITLE: Prob-eye-otics: Cytokine Producing Therapeutic Ocular Commensals

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.L. Shane, Y. Rigas, R.M. Shanks, A. St. Leger, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Jackie Shane: Commercial Relationship: Code N (No Commercial Relationship) | Yannis Rigas: Commercial Relationship: Code N (No Commercial Relationship) | Robert Shanks: Commercial Relationship: Code N (No Commercial Relationship) | Anthony St. Leger: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: HSV-1 can infect the ocular surface and induce the inflammatory disease, herpes stromal keratitis (HSK), which can result in corneal scarring and blindness. Immune regulating cytokines like IL-10 can suppress inflammation and reduce immunopathology. We hypothesize that delivering IL-10 using a genetically modified ocular commensal, Corynebacterium mastitidis (C. mast), will reduce immunopathology associated with HSK.

Methods: For cytokine release from C. mast, functional native secretion signals were identified by creating a phosphatase transposon library. Secretion from positive isolates was quantified using a PNPP assay and the most efficient secretion signal was fused to mIL-10 and transposed into the C. mast genome. mIL-10 production from positive transformant supernatants was analyzed by ELISA, and supernatants were added to T cell cultures to evaluate immune cell proliferation and cytokine production by flow cytometry and ELISA. To assess fitness, transformants were grown 1:1 with WT C. mast (AS1) for 6 hours then plated on agar with and without antibiotic to quantify the survival of the mutant. The ability of transposon mutants to colonize the eye was measured by applying $5x10^5$ and $2.5x10^6$ CFU to the eye every other day for a total of three applications. After 1 week, eyes were swabbed and plated on media containing selecting antibiotics and in vivo immune responses were measured by flow cytometry.

Results: The three best mIL-10 producing isolates caused reduced proliferation ($p<.005$) and INF-γ production ($p<0.01$) in T cells but did not significantly affect IL-17 production. mIL-10 producing isolates were also able to survive alongside AS1 in vitro but only 2 mutants were able to colonize the mouse eye. In vivo immunity was similar between AS1 and the colonizing mIL-10 isolates.

Conclusions: We have demonstrated the potential of genetically engineering ocular bacteria to produce and secrete functional murine IL-10. mIL-10 from C. mast regulates T cell responses by suppressing proliferation and IFN-γ production. Conversely, mIL-10 from C. mast does not affect IL-17, which prevents C. mast from becoming a pathobiont. Together these data suggest that the host should well-control mIL-10 C. mast, and the bacterium may be able to limit HSK in vivo. Overall, this study illustrates the first steps in engineering an ocular bacterium that can control excessive inflammation at the ocular surface.

CONTROL ID: 3711681

SUBMITTER (NAME ONLY): Daphne Vergouwen

TITLE: An in-depth protein analysis of scleritis using mass spectrometry

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Vergouwen, J. Ten Berge, A. Rothova, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|D. Vergouwen, M. Schreurs, Immunology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C. Guzel, T. Luider, Neurology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|T. van den Bosch, R. Verdijk, Pathology, section Ophthalmic Pathology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Scleritis is a severe inflammatory ocular disorder with unknown pathogenesis. We investigated sclera affected by non-infectious scleritis as well as healthy sclera for differentially expressed proteins using a mass spectrometry-based proteomics approach.

Methods: We collected scleral samples of eyes enucleated due to severe scleritis (n=3), and control scleral tissues (n=5), all exenterated eyes for eyelid carcinomas without scleral invasion. Clinical data of patients were retrospectively gathered from medical files. Scleral samples were microscopically scraped from tissue slides, and loaded on the LC-MS mass spectrometer after trypsin digestion. In addition, all samples were stained for immuno-histopathological evaluation. Results were analyzed using the proteomics software Scaffold (Proteome Software), and considering the Benjamini-Hochberg method for multiple testing a P-value lower than 0,00016 was considered significant.

Results: Mass spectrometry identified 629 proteins within the healthy and diseased scleral tissues, whereof collagen type I was the most abundantly expressed protein. Collagen type II to XII were also present. Fillagrin-2 was found to be significantly upregulated (P=0.0001) in scleritis, a protein that plays a crucial role in epidermal barrier function. Elongation factor 2 and vinculin were other proteins upregulated in scleritis compared to healthy scleral tissue, however they were not significantly different in this small sample set.

Conclusions: Using this highly powerful and innovative technique, we found that fillagrin-2 was upregulated in scleral samples from patients with non-infectious scleritis. Further research, ideally including more scleritis cases, is needed to validate our findings, and identify the role of fillagrin-2 in the pathogenesis of scleritis.

CONTROL ID: 3711682

SUBMITTER (NAME ONLY): Brian Goldhagen

TITLE: Pilot Study of Artificial Intelligence to Complement the Teleretinal Screening Program in a Multi-Center Veterans Affairs Setting

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.E. Goldhagen, N.Z. Gregori, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|B.E. Goldhagen, J. Fabian, K. Zann, M. Johnson, N.Z. Gregori, VA Miami Healthcare System, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Veterans Healthcare Administration (VHA) has led the nation's most successful screening program for the detection of diabetic eye disease to date and the demand for such screening continues to increase. While Artificial intelligence (AI) has strived to revolutionize the field of Ophthalmology, actual real-world data has been less than promising, particularly within the VHA setting. We hypothesize that a novel AI-based algorithm created specifically to enhance, rather than replace, the existing standard image analysis by experienced optometrists may be utilized to improve efficiency and patient safety.

Methods: A proof-of-concept AI algorithm based on machine-learning was developed to prescreen patients within the VHA without reducing their quality of care. The algorithm analyzes images for individual image quality, image set completeness, evidence of diabetic retinopathy, and the presence of other ocular pathology. To validate this algorithm, fundus photographs of 100 consecutive Veterans within VISN 8 within a single month (2/2017) were assessed by the algorithm and also reviewed by the optometrists experienced at teleretinal screening. The conclusions of both readings were compared.

Results: 1004 images from 100 patients (~10 images/set) at 17 imaging sites within VISN 8 were included in this study. Quality metrics succeeded in being at least as stringent as the reads of the experienced reviewers. 33% of all patients were found to have image sets of adequate quality (vs. 85% by reviewers). None of the 4 patient image sets that were deemed "abnormal" for retinopathy by the experienced optometrists was passable as "normal" by the algorithm. Of the 33 adequate quality patient image sets, the algorithm detected a total of 14 image sets as "normal." There was a zero false negative rate, supporting the safety of the algorithm. The remaining 19 image sets were subsequently reviewed by a retina specialist. One set, which was previously deemed normal by optometry reviewers, was actually "abnormal" due to the presence of mild nonproliferative diabetic retinopathy.

Conclusions: In this pilot study, the AI algorithm was able to provide adequate screening of fundus images obtained for diabetic screening with a zero false negative rate. Our algorithm serves as an example of a means of increasing efficiency and safety while not sacrificing the quality of care to patients.

CONTROL ID: 3711684

SUBMITTER (NAME ONLY): Stephen Yoon

TITLE: Differentially expressed tear proteins in Sjögren syndrome keratoconjunctivitis sicca

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Yoon, E. Serrano, Z. Yu, S.C. Pflugfelder, C.S. De Paiva, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if there are significant differences in the concentrations of tear proteins in Sjögren syndrome keratoconjunctivitis sicca (SS KCS) compared to healthy controls.

Methods: Tear samples were collected with unmarked Schirmer strips from 15 SS KCS patients and 21 healthy controls. Tear protein was eluted and the concentration measured. Inflammatory mediators were assayed with a Raybiotech L-507 glass slide array and normalized by strip wetting length. All patients underwent an ocular surface exam to evaluate tear-break-up time (TBUT), corneal fluorescein staining, and conjunctival staining. Symptom assessment questionnaire in dry eye (SANDE) scores were collected for all patients.

Results: 57 of the 507 tear proteins analyzed were significantly upregulated in SS patients compared to controls (Table 1). Spearman correlations showed that all 57 upregulated tear proteins were significantly inversely correlated with TBUT and positively correlated with corneal fluorescein staining, conjunctival staining and SANDE scores.

Conclusions: These findings indicate that hundreds of factors can be assayed in tear proteins collected from a Schirmer strip. The results suggest tear protein concentrations are altered in SS KCS compared to controls. The upregulated tear proteins correlated with clinical measures of dry eye symptoms and disease severity. Tear protein concentrations could serve as important biomarkers for studying pathogenesis and in clinical diagnosis and management of SS KCS.

CONTROL ID: 3711687

SUBMITTER (NAME ONLY): Fionn O'Leary

TITLE: Circadian regulation of the inner blood retinal barrier: a paradigm for dry age-related macular degeneration development

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. O'Leary, N. Hudson, J. O'Callaghan, M. Campbell, Smurfit Institute of Genetics Trinity College, Dublin, IRELAND|F. O'Leary, M. Cahill, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is divided into an atrophic (dry) and neovascular (wet) form. The disease aetiology is yet to be fully elucidated and no effective treatment exists for the end stage of dry AMD, known as geographic atrophy. We have shown that the inner blood retinal barrier (iBRB) cycles in a circadian manner in young healthy adult controls. The tight junction protein claudin-5 which cycles in a circadian manner, is thought to be central to the maintenance of iBRB integrity. We performed a case control study to determine the circadian effect on iBRB kinesis in AMD.

Methods: Participants with dry AMD (n=19) and age matched controls (n=12) were recruited. The Munich Chronotype Questionnaire was used to establish participant chronotype. Participants were assessed using optical coherence tomography (OCT) and fundus fluorescein angiography (FFA). Mid phase fluorescein signal in the macula was quantified using novel Fluorescent Ocular Vascular Analysis Software and analysed as per the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. Fluorescein signal was compared between the morning and the evening for each participant, a proxy for circadian effect on iBRB integrity. Recruitment of participants is ongoing.

Results: There was an increased fluorescein signal throughout all areas of the macula in the evening compared to the morning in young healthy controls (n=30, P =.033). The evening versus morning fluorescein signal differential was reduced and therefore not significant in AMD participants (P =.78). The fluorescein signal appears to persist in the macula longer in AMD participants compared to young healthy controls.

Conclusions: These findings suggest that the iBRB is highly dynamic, with increased fluorescein permeability in the evening compared to the morning in young healthy controls. The circadian associated fluorescein signal differential present in young healthy controls appears attenuated in age matched controls, with no significant difference present in AMD subjects. This suggests that the circadian dependant regulation of iBRB kinesis decreases with ageing and may be arrested in AMD. We suggest that this disruption may be due to decreased or dysfunctional claudin-5 resulting in a more open, "leakier" iBRB, which may be one of the early initiating factors in AMD pathogenesis.

CONTROL ID: 3711688

SUBMITTER (NAME ONLY): Lucy Mudie

TITLE: Evaluation of the SUN Classification Criteria for the Uveitides in an Academic Uveitis Practice

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mudie, A.K. Reddy, J.L. Patnaik, P. Pecen, E. Kim, K. Cole, A. Palestine, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|P. Pecen, Carolina Eye Associates, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the ability of the new Standardization of Uveitis Nomenclature (SUN) classification criteria for uveitides to classify patients in an academic uveitis practice.

Methods: A retrospective review of electronic medical records was conducted for all patients attending the uveitis service at the University of Colorado Hospital between January 1, 2013 and December 31, 2020. Patients with scleritis, ocular cicatricial pemphigoid and peripheral ulcerative keratitis were excluded. We attempted to classify each patients' uveitis using the SUN classification criteria. We recorded whether classification was possible as well as their clinical diagnosis by a uveitis specialist.

Results: Of the 1143 patients with uveitis, 50.0% (572/1143) had a disease that was not listed in the SUN classification system, and so no attempt to classify these patients was possible. Of the remaining 571 patients, 522 (91.4%) were able to be classified by SUN and in 94.3% (492/522) of cases their SUN classification matched their clinical diagnosis by a uveitis specialist.

Conclusions: A significant percentage of patients at an academic uveitis practice had a disease for which no SUN classification criteria existed. In cases where classification by SUN could be attempted, the system performed well and agreed with their clinical diagnosis in most cases.

CONTROL ID: 3711689

SUBMITTER (NAME ONLY): Dinesh Singh

TITLE: OCU410, a Potential Therapeutic for Dry-AMD, Suppresses Inflammatory Cytokine Gene Expression in Retinal Epithelial Cells

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.K. Singh, S.S. Kattala, A.K. Upadhyay, Ocugen Inc, Malvern, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this study, we evaluated role of OCU410 (human RORA) in controlling inflammation, a causative factor for dry age-related macular degeneration (dry-AMD) pathogenesis, in an in vitro assay. While there is no approved therapy for dry-AMD, most therapeutics in clinical trials target the complement system (cell death pathway), inflammation, or oxidative stress. However, these therapies target only one pathway. OCU410 is an orphan nuclear receptor, a transcription factor, that may target multiple pathways, particularly in suppressing inflammatory cytokine gene expression, which can potentially limit damage to the retina due to dry-AMD.

Methods: To assess the effects of OCU410, we created an inflammatory model system using LPS in human immortalized retinal epithelial cells (hTERT-RPE1). Inflammatory cytokine genes for inflammatory cytokines (e.g., IL1b, IL6, CXCL8, etc.) were measured by quantitative reverse transcriptase real time polymerase chain reaction (qRT-PCR). LPS-induced expression of Gluc luciferase was compared in the presence and absence of OCU410 using a robust CXCL8 promoter driven secretory Gaussia Luciferase (GLuc). Secretory Alkaline Phosphatase (SEAP) driven by constitutive strong CMV promoter was used as the internal control for signal normalization. This promoter reporter luciferase system was used to access the direct role of RORA on CXCL8 promoter. In silico analysis also shows that human CXCL8 has a consensus RORA binding site within 1.5kb of the CXCL8 start site.

Results: LPS stimulated the expression of inflammatory cytokines IL1b, CXCL8, and IL6 in a dose dependent manner in hTERT-RPE1 cells treated with OCU410. The expression of inflammatory cytokines in response to LPS was inversely related to the expression of RORA. Furthermore, the GLuc/SEAP luciferase assay on CXCL8 promoter reporter assay demonstrates that the suppression of luciferase activity is mediated through RORA binding on the CXCL8 promoter.

Conclusions: Dry-AMD is characterized by expression of inflammatory cytokines. OCU410 transduction leads to the expression of nuclear hormone receptor RORA upon viral transduction which suppresses inflammatory cytokine gene expression, including CXCL8, in an LPS-induced inflammation model in hTERT-RPE1 cells. Thus, OCU410's ability to inhibit multiple inflammatory cytokines strengthens its potential as a gene therapy molecule for dry-AMD.

CONTROL ID: 3711694

SUBMITTER (NAME ONLY): Alexa Gray

TITLE: Surgical Procedure and Applicability of the Orbit Subretinal Delivery System (SDS)™ in the Normal Adult Canine Eye

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.P. Gray, Y. Sato, W.A. Beltran, University of Pennsylvania School of Veterinary Medicine, Philadelphia, Pennsylvania, UNITED STATES|T. Meyer, K. Stoner, Gyroscope Therapeutics, King of Prussia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To optimize the surgical procedure and test the applicability of the Gyroscope Therapeutics Orbit SDS™ in normal adult canine retinas. This suprachoroidal approach to subretinal delivery eliminates the need for a vitrectomy and avoids the formation of a retinotomy.

Methods: Right eyes of four adult mongrel dogs (age: ~ 129 weeks; axial globe length: 22 ± 1.3 mm) underwent subretinal injection of an AAV2/5-GRK1-GFP vector with the Orbit SDS™. A 3 mm wide scleral incision located 8 mm posterior to the limbus in the supero-temporal quadrant was performed. The flexible cannula of the device was then introduced into the suprachroidal space and its progression towards the central tapetal fundus monitored under direct visualization through a digital operating microscope with intraoperative OCT. The microneedle was advanced into the subretinal space. A ~10 µL injection of BSS enabled formation of a subretinal bleb which was further expanded by injection of 100 µL of the viral vector solution. cSLO/OCT imaging and OCT angiography (OCTA) were performed with a Spectralis HRA/OCT2 unit at 5 and 9 weeks post injection to monitor GFP expression and integrity of the retinal layers.

Results: All 4 dogs (4 eyes) had successful subretinal injections in the tapetal fundus, and retinas reattached within 48 hours. No adverse effects nor signs of ocular discomfort were seen. cSLO (BAF mode) showed GFP expression that had expanded beyond the bleb borders identified during surgery. A focal dark spot was seen funduscopically in the tapetal area that corresponded to the site of entry of the microneedle. En face OCTA imaging of the choriocapillaris confirmed this was the site of puncture. No evidence of choroidal neovascularization was seen in any of the 4 eyes. OCTA segmentation at the level of the nerve fiber layer confirmed in 1 out of 4 eyes perforation of the neuroretina with the microneedle that had been suspected at the time of surgery.

Conclusions: Preliminary results show that the off label veterinary use of the Orbit SDS™ is a viable surgical approach for subretinal injections in healthy adult canine retinas. The presence of tapetal cells in the canine choroid caused some resistance but did not impair advancement of the microneedle into the SRS. Further histologic examination of the choroid and neuroretina will examine structural integrity of these tissues.

CONTROL ID: 3711695

SUBMITTER (NAME ONLY): Zhiyi Cao

TITLE: Targeting Galectin-8 to reduce the severity of Pseudomonas keratitis in a mouse Model

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Cao, N.A. Panjwani, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|M. Hassan, Centre for analysis and synthesis, department of Chemistry, Lunds Universitet, Lund, SWEDEN|U. Nilsson, Centre for analysis and synthesis, department of Chemistry, Lunds Universitet, Lund, SWEDEN|N.A. Panjwani, Developmental, molecular and chemical biology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies in our Laboratory have demonstrated that a carbohydrate-binding protein, galectin-8 (Gal-8), plays an important role in the pathogenesis of Pseudomonas Aeruginosa (PA) keratitis. Using a mouse model of PA keratitis, we have shown that: (i) Gal-8 KO mice are resistant to PA keratitis, and that (ii) Gal-8 modulates innate immune response by dampening the TLR4 and inflammasome pathways. These data suggest that inhibiting Gal-8 may improve the outcome of the disease. Therefore, in an effort to find effective strategies to control the disease, the goal of the current study was to test the therapeutic potential of inhibitors of Gal-8 in PA keratitis

Methods: Two groups of Wild type mice (7 – 10 weeks old) were anesthetized, the central corneas of mice were scarified with three parallel 1-mm incisions and a 5 µL drop containing 2000 CFU of bacterial strain PA 6077 was applied to the eye. Immediately prior to infection, control group received a subconjunctival injection of vehicle (10 µL of PBS + DMSO) and the experimental group received a subconjunctival injection of Gal-8 inhibitor, 19a (Hassan et al. Eur J Med Chem, 223:113664, 2021) (10 µL, 5 mg/mL in vehicle). The severity of bacterial keratitis was graded on post-infection day 1, and then corneas were harvested for bacterial enumeration. The experiment was repeated four times. Also, varying concentrations of the inhibitor were tested.

Results: Galectin inhibitor, 19a, at 5 mg/ml concentration, substantially reduced opacity score (Vehicle: 2.7±0.12; 19a: 1.9±0.16; n=40, $p<0.0002$) and the bacterial load (Vehicle: $1.6x10^6$; 19a: $0.6x10^6$ n=40) compared to vehicle.

Conclusions: Targeting Gal-8 is an attractive strategy for the development of novel treatment for blinding immunopathology resulting from bacterial keratitis and possibly other ocular disorders, such as corneal graft rejection and dry eye disease.

CONTROL ID: 3711700

SUBMITTER (NAME ONLY): Ketil Fjaervoll

TITLE: Purinergic Type 2Y 2 and -6 Receptors (P2Y2R and P2Y6R) are Functional in Rat Conjunctival Goblet Cells

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Fjaervoll, H. Fjaervoll, M. Yang, J. Bair, T. Utheim, D.A. Dartt, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|K. Fjaervoll, H. Fjaervoll, The Medical Student Research Program, Universitetet i Oslo, Oslo, Oslo, NORWAY|T. Utheim, Department of Medical Biochemistry, Oslo Universitetssykehus, Oslo, Oslo, NORWAY|

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ABSTRACT BODY:

Purpose: P2Y receptors (P2YRs) are G protein-coupled receptors activated by nucleotides and are of significance in fluid and mucous secretion in the conjunctiva. Endogenous nucleotides such as UDP are specific to P2Y6R and P2Y14R, while UDP-glucose is specific to P2Y14R, but not P2Y6R. In addition, selective P2Y2 receptor agonists, such as MRS 2768, were developed for treatment of dry eye. The purpose of this study is to elucidate which P2YRs that are functional in rat conjunctival goblet cells (CGCs) by determining their effect on the intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$).

Methods: Conjunctiva from male Sprague-Dawley rats was minced and placed in six-well plates for culture of CGCs. To measure function, first passage CGCs were incubated with the Ca^{2+} specific ratiometric dye Fura2-AM and $[Ca^{2+}]_i$ measured after cells were stimulated with the P2YR selective agonists: UTP (P2Y2R, P2Y4R and P2Y6R), UDP (P2Y6R and P2Y14R), UDP-glucose (P2Y14R) or an agonist specific to P2Y2R (MRS 2768). To investigate $[Ca^{2+}]_i$ response after knockdown of P2Y2R or P2Y6R, cells were treated with siRNA or scsiRNA specific to each receptor or vehicle before incubation with agonist. Calcium experiments were done in duplicate or triplicate and all experiments were performed on CGCs from at least three rats.

Results: Stimulation with UTP 10^{-4} M increased $[Ca^{2+}]_i$ to 897 ± 44 nM, while $[Ca^{2+}]_i$ responses were 817 nM ± 103, 102 ± 26 nM and 262.2 nM ± 60 for UDP 10^{-3} M, UDP-glucose 10^{-7} M and MRS2768 10^{-10} M, respectively. After knockdown of the P2Y2R and P2Y6R, $[Ca^{2+}]_i$ responses were significantly lower after stimulation with UTP 10^{-4} M, MRS 2768 10^{-6} M or UDP 10^{-5} M/UDP 10^{-4} M, respectively.

Conclusions: We conclude that P2Y2R and P2Y6R, but not P2Y14R, are the major P2YRs responsible for conjunctival goblet cell function.

CONTROL ID: 3711703

SUBMITTER (NAME ONLY): Catherine Culp

TITLE: Risk of Corneal Graft Rejection in COVID-19 Vaccinated Patients in the 120-day postoperative period: A Multi-Healthcare System Analysis

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Culp, W.F. Foos, D. Belyea, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|H. Pakhchanian, C. Chan, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare corneal transplant failure in patients who have been vaccinated against COVID-19 to a control group of patients who have received an influenza vaccination.

Methods: A retrospective cohort study was conducted using TriNetX, a federated electronic health records research network comprising data from more than 50 health organizations in the United States. Patients who underwent corneal transplantation and either COVID-19 vaccination or Influenza A vaccination were identified by CPT and medication codes and separated into cohorts based which vaccination they had received. COVID-19 vaccination was defined as receiving either 2 doses of Moderna or Pfizer COVID-19 Vaccine or 1 dose of J&J's COVID-19 Vaccine. Cohorts were matched for age, gender, body mass index, and medical comorbidities (essential hypertension, diabetes mellitus, chronic lower respiratory diseases, heart failure, nicotine dependence, and alcohol related disorders). The primary outcome was corneal graft failure at 120 days after corneal transplantation surgery. The relative risk for this outcome was compared between each cohort before and after 1:1 propensity score matching.

Results: A study population of 784 corneal transplant patients who received COVID-19 vaccination and a control population of 1661 patients who received Influenza A vaccination were identified. After propensity matching, 715 matched patients from each cohort were compared. The incidence of corneal transplant failure rate was 1.8% for the COVID-19 vaccine cohort and 1.6% for the Influenza A cohort. While the rate of corneal transplant failure was slightly lower in COVID-19 vaccine recipients in comparison to Influenza vaccine recipients (RR=0.92%, CI 0.42-2.01), this result was not statistically significant (p 0.84).

Conclusions: While there have been several case reports of corneal graft failure after COVID-19 or COVID-19 vaccination, there appears to be no statistically significant impact of the COVID-19 vaccine on corneal transplant failure in this retrospective cohort study. Additionally, corneal graft rejection in vaccinated patients was rare in our study.

CONTROL ID: 3711704

SUBMITTER (NAME ONLY): Fatema Ghasia

TITLE: Fixation Eye Movement Abnormalities, Stereopsis and Inter-ocular suppresion in Amblyopia.

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.F. Ghasia, C. Dulaney, J. Murray, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|F.F. Ghasia, Director of Visual Neurosciences and Ocular Motility Lab, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Fatema Ghasia: Commercial Relationship: Code N (No Commercial Relationship) | Cody Dulaney: Commercial Relationship: Code N (No Commercial Relationship) | Jordan Murray: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Amblyopic patients are known to have fixation instability, which arises from alteration of physiologic fixation eye movements (FEMs) and nystagmus. The purpose of the study is to examine the association between amblyopia type and FEM abnormalities on stereopsis and inter-ocular suppression.

Methods: We recruited 34 amblyopes (anisometropic=14, strabismic=12,mixed=8) and 7 controls. Eye movements were recorded using infrared video-oculography during a) Fellow eye viewing(FEV), b) Amblyopic eye viewing(AEV) c) Both eye viewing(BEV), and d) Dichoptic viewing(DcV) at varying FE contrasts. Subjects were classified as having either no nystagmus(n=15), fusion maldevelopment nystagmus (FMN)(n=7), and patients with nystagmus without any structural anomalies that do not meet the criteria of FMN and infantile nystagmus(n=12). An adaptive staircase method was used to measure visual acuities during FEV, AEV and BEV and inter-ocular suppression using Dichoptic Motion Coherence(DMC). The threshold of inter-ocular suppression was determined by the number of dots required to correctly identify the motion coherence at a given FE contrast and area under the curve was computed. Stereoacuity was measured with the Titmus fly test.

Results: Increased fixation instability was associated with greater stereopsis and inter-ocular suppression deficits. Stereopsis deficits were greatest in patients with FMN (Controls: 1.6±0, None:2.1±0.25,Nystagmus no FMN:3.1±0.92, FMN:3.3±0.92,ANOVAp<0.005) and patients with mixed amblyopia(Controls: 1.6±0,Anisometropic:2.1±0.25,Strabismic: 3.1±0.92, Mixed:3.3±0.92,ANOVAp<0.005). AUC for DMC thresholds was greater in amblyopia than controls while controlling for visual acuity deficits. (Controls:415.6± 275.9, Amblyopia:1094.3±884, #ofdots x contrast level, p <0.04). The suppression deficits were dependent on AE visual acuity deficit (p=0.003 and p=0.014) with no significance noted as a function of amblyopia type or FEM abnormalities (p=0.87, p=0.74 respectively).

Conclusions: Neurophysiologic studies have shown that horizontal binocular connections in MT/MST are critical for emergence of stereopsis. Lack of binocular connections in MT/MST drives the development of FMN. We have found that the presence of FMN was associated with greater stereopsis deficits whereas the extent of suppression is primarily driven by severity of amblyopia.

CONTROL ID: 3711706

SUBMITTER (NAME ONLY): Franklin Caval-Holme

TITLE: Subcellular Origins of Extensive Spatial Integration by Ganglion Cell Photoreceptors

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mammals detect light for visual perception, but also for regulation of physiology, cognition, mood, and development. Many of these ‘non-image’ visual functions exhibit extensive integration of light over visual space. Intrinsically photosensitive retinal ganglion cells (ipRGCs), which capture photons with a receptor called melanopsin, are indispensable for many non-image visual functions. Melanopsin is distributed throughout ipRGCs, including in the axon. We hypothesized that phototransduction in axons allows ipRGCs to integrate light over an exceptionally large area.

Methods: We performed electrophysiological recordings from ipRGCs in retinas isolated from transgenic reporter mice. We first determined if ipRGCs detect selective illumination of the distal axon, >1 mm from the soma and dendrites. Next, to measure the axonal contribution to overall photosensitivity, we compared responses elicited by illumination restricted to the soma and dendrites (local) to those elicited by illumination of the entire cell (global). Recording from ipRGCs in the central and peripheral retina permitted a natural comparison of axonal photosensitivity in cells with short and long axons, respectively. Antagonists of synaptic transmission were added to the extracellular medium to isolate melanopsin’s contribution to the light response.

Results: Our observations were consistent with axonal photosensitivity. IpRGCs exhibited excitatory currents and spiking responses to illumination of the distal axon, but not to illumination of an equidistant location on the retina that did not include the axon. Peripheral ipRGCs (1.4-1.8 mm from the optic disk) were ~30% more sensitive to global than local illumination, while central ipRGCs (≤ 0.3 mm from the optic disk) were equally sensitive.

Conclusions: Melanopsin phototransduction within the axons of ipRGCs generates electrical responses to photon absorption far from the cell’s soma and dendrites. The first steps of non-image vision produce greater spatial integration than previously understood.

CONTROL ID: 3711709

SUBMITTER (NAME ONLY): Jonathan Eintracht

TITLE: Shared morphological and molecular pathways in microphthalmia using patient-derived iPSC-optic vesicles

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Eintracht, P. Harding, N. Owen, M. Moosajee, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|M. Moosajee, The Francis Crick Institute, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Eye morphogenesis is tightly regulated by a highly conserved genetic network that when disrupted, can result in severe ocular malformation on a spectrum known as microphthalmia, anophthalmia and coloboma (MAC). While over 90 genes are associated with MAC, little is known about disease mechanisms shared between patients with differing genetic diagnoses. This study aimed to identify aberrations to pathways involved in early eye development shared between different causes of microphthalmia. Due to low genetic diagnostic rates, studying shared pathways will critically reveal new candidate genes for future diagnostics.

Methods: Patient-specific (PAX6-associated microphthalmia p.(Asn124Lys) and an unsolved microphthalmia patient) and healthy control iPSC-derived optic vesicles were generated using two clones from each line to model ocular development until day 35. Data on gene and protein expression were generated through RNA-seq, qRT-PCR and immunohistochemistry. Apoptosis, cell proliferation and vesicle diameter were quantified using ImageJ.

Results: At day 35, vesicle diameter was significantly reduced in both microphthalmia models compared to healthy controls. TUNEL staining revealed a significant increase in apoptotic cells in patient vesicles compared to healthy controls while PH3 staining revealed decreased cell proliferation. Using RNA-seq, we detected upregulation of pro-apoptotic genes in microphthalmia optic vesicles. Dysregulation of Notch signalling modulated through an ASCL1 negative feedback loop between the DLL ligand and HES effector families was also common between microphthalmia samples. This resulted in differential expression of Notch target genes such as MITF and HDAC1. Additionally, the increased production of extracellular matrix (ECM) components such as collagen and laminin, resulting in ECM abnormalities, was detected in microphthalmia optic vesicles.

Conclusions: Our study identified reduced size and proliferation, and increased apoptosis in microphthalmia patient-derived optic vesicles possibly contributing to the small eye phenotype. Disruptions to Notch signalling may contribute to a global increase of ECM production and further dysregulation of key early ocular developmental genes. Additionally, abnormally high production of ECM in microphthalmia patients may overly restrict optic vesicle growth, resulting in ocular malformations.

CONTROL ID: 3711711

SUBMITTER (NAME ONLY): Daniel Kulman

TITLE: Comparative analysis in outcomes follow pars plana vitrectomy in patients on beta blockers vs those who are not on beta blockers in the 1-year postoperative period: a multicenter electronic medical record cohort study.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kulman, S. Dang, M. Dalal, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|H. Pakhchanian, R. Raiker, S. Akosman, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare differences in outcomes following pars plana vitrectomy (PPV) for retinal detachment (RD) in the postoperative period between individuals on beta blockers (BB) and those who are not using BB.

Methods: A retrospective cohort study was conducted using TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple large health organizations in the United States. Patients who underwent PPV for RD were identified by CPT code and stratified into BB use and non-BB use. Cohorts were matched for age, gender, and medical comorbidities (essential hypertension, diabetes mellitus, cerebrovascular disease, heart failure, nicotine dependence, alcohol related disorders, and body mass index). The primary outcomes were: Vitreous hemorrhage, choroidal hemorrhage, RD or RD with retinal break, iridocyclitis, retinal edema, cystoid macular edema, macular pucker, toxic maculopathy, intraoperative/postoperative complications, ischemic optic neuropathy, glaucoma, cataract strabismus, hemorrhage of orbit, corneal edema, dry eye syndrome, central retinal vein occlusion (CRVO,) central retinal artery occlusion (CRAO.) One-year outcomes were compared between the cohorts after propensity score matching using logistic regression and greedy nearest-neighbor matching algorithm.

Results: A total of 17,388 patients were included in analysis with 8,694 in each of the BB use and non-BB use cohorts after propensity matching.

The BB cohort had a significant greater risk of developing vitreous hemorrhage (RR, 1.16; 95% CI, 1.1-1.22), and cystoid macular degeneration (RR, 1.11; 95% CI, 1.0-1.22). No significant difference was seen in rate of development of choroidal hemorrhage, RD or RD with retinal break, Iridocyclitis, retinal edema, macular pucker, toxic maculopathy, intraoperative/postoperative complications, ischemic optic neuropathy, glaucoma, cataract, strabismus, hemorrhage of orbit, corneal edema, dry eye syndrome, CRVO and CRAO between the BB and non-BB use cohorts.

Conclusions: Betablocker use is an important consideration when discussing risks during preoperative counseling and evaluating for postoperative complications following PPV for RD. Patients using betablockers were more likely to develop vitreous hemorrhage and cystoid macular edema.

CONTROL ID: 3711712

SUBMITTER (NAME ONLY): Hanagh Winter

TITLE: Circadian rhythms in diabetic retinal endothelial cells

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Winter, A. Margariti, A.W. Stitt, E. Beli, Wellcome Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diabetes has been reported to disrupt circadian rhythms with circadian disruption emerging as an important factor in the disease prognosis and treatment success. Endothelial cells are central in the progression of diabetic retinopathy and have a robust circadian clock with rhythms in diverse cellular processes. Thus, we asked whether diabetes alters the expression of circadian genes in these cells and if so, which aspects of the diabetic microenvironment drive these changes.

Methods: Induced pluripotent stem cell derived endothelial cells (iPS-ECs) from healthy and diabetic patients were sequenced and differential analysis was performed, identifying genes related to circadian rhythms. Primary human retinal endothelial cells (hRECs) were cultured in vitro in hyperglycaemia or normoglycaemia for 7 days. Cultures were then synchronised with 50% serum shock and repeated samples collected every 2 hours over 25 hours in either hypoxia or atmospheric oxygen levels. Circadian gene expression was measured with RT-PCR.

Results: iPS-ECs from diabetic patients have 4.03-fold higher Bmal-2 mRNA expression and 5.7-fold less Dec2. Hypoxia, and not hyperglycaemia, affects circadian gene expression in synchronised hRECs. In hypoxia, Bmal1 expression is increased at all time points and phase advanced. The opposite is true of its negative regulator, Per2, which is instead reduced in hypoxia with weakened rhythmicity. Hyperglycaemia alone slightly increases the rhythmicity of Per2 oscillation. Circadian rhythmicity in gene expression persists in all treatments for both Bmal1 and Per2 but is lost in Cry1 expression when cells are treated with hypoxia (normoxia $p=0.02$ vs hypoxia $p=0.18$), as analysed using JTK_Cycle.

Conclusions: Diabetes can alter the expression and rhythmicity of the circadian molecular clock in endothelial cells. In separately testing some elements of the diabetic microenvironment, we have shown that hypoxia alone drives major changes in key core loop genes of the molecular clock. More, hypoxia alters the positive and negative arms of this molecular clock in different ways, with potential implications for the period of the clock and transcription of clock-controlled genes, many of which are immediately relevant to diabetic retinopathy including VEGF. Bmal1, a master transcription factor, appears to have bolstered expression in hypoxia while its negative regulator, Per2, is reduced.

CONTROL ID: 3711713

SUBMITTER (NAME ONLY): Bennie Jeng

TITLE: PEARL Phase 2 Study of OC-02 Nasal Spray for the Treatment of Dry Eye Disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.H. Jeng, Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|A. Gibson, P. Shah, L. hendrix, Oyster Point Pharma, Princeton, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye is a multifactorial disease characterized by a persistently unstable and/or deficient tear film causing discomfort and/or visual impairment, accompanied by variable degrees of ocular surface epitheliopathy, inflammation and neurosensory abnormalities. OC-02 (simpinicline), a novel compound delivered via nasal spray, is a nicotinic acetylcholine receptor agonist that pharmacologically activates the trigeminal parasympathetic pathway to stimulate the lacrimal functional unit to reestablish the natural tear film. This Phase 2 study (PEARL) evaluated the efficacy and safety of OC-02 in the treatment of signs and symptoms of dry eye disease.

Methods: A total of 182 subjects were randomized 1:1:1:1 with OC-02 1.1 mg/mL (n=41), OC-02 5.5 mg/mL (n=41), OC-02 11.1 mg/mL (n=41), or vehicle control (VC, n=42) nasal spray over two visits. Outcome measures were pre- to post-treatment in anesthetized categorical Schirmer's Test Score (STS) outcomes (percentage of ≥10mm) at Visit 1 and Eye Dryness Score (EDS, 0-100 scale) under controlled adverse environment (CAE) exposure at Visit 2.

Results: Subjects treated with 5.5 mg/mL and 11.1 mg/mL OC-02 nasal spray showed statistically significant improvement compared with VC as indicated by a percentage gain in STS ≥10 mm from baseline at Visit 1. The 5.5 mg/mL, 11.1 mg/mL, and VC groups were: 73%, 76%, and 7% ($p<0.0001$), respectively (fig. 1). Correspondingly, improvements in EDS at Visit 2 from pre- to 5 minutes post-treatment in CAE were -16.5 ($p = 0.0067$), -19.0 ($p= 0.0006$), and -6.8, respectively. Of the treated groups, significant improvement in the percentage of eyes was seen with 11.1 mg/mL in baseline EDS <60mm and 5.5 mg/mL and 11.1 mg/mL in baseline EDS >60mm (Fig.2). Most common adverse events reported in >5% of treated subjects was coughing, throat irritation, sneezing, and instillation site irritation.

Conclusions: Compared to VC, OC-02 nasal spray demonstrated improvement in both signs and symptoms of dry eye disease and was safe and well-tolerated under conditions of the study.

CONTROL ID: 3711716

SUBMITTER (NAME ONLY): Jasmine Geathers

TITLE: Sodium Iodate increases focal vimentin expression and other RPE lesions in a dose-dependent manner in the neural retina of mice.

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Geathers, S. Grillo, J. Liao, A.J. Barber, J. Sundstrom, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular degeneration is one of the leading causes of blindness in people over the age of 50; the most common being age-related macular degeneration. The pathology can include hyperreflective foci (HRF) detected by spectral-domain optical coherence tomography (SD-OCT) in association with sub-retinal pigment epithelium (RPE) drusen and hyper-pigmentation. Sodium iodate (SI) rapidly induces retinal degeneration in mice that involves RPE pathology modeling some of the characteristics of macular degeneration. The purpose of this study was to determine whether the sodium iodate-induced pathology includes elevated expression of vimentin in the RPE, as well as HRF and other pigmentary changes.

Methods: Twenty C57BL/6J young adult male mice were injected with SI dissolved in PBS at 15, 30, 45, or 60 mg/kg. SD-OCT (Bioptigen) images were acquired pre-injection, and 1, 3, 5, and 7 days post-injection Retinal thickness was measured using Bioptigen software and HRF were counted manually. Frozen vertical retinal cross-sections (12 µm thick) of eyes were processed for H&E staining and IHC. Tissue from each group was also processed for electron microscopy (EM).

Results: HRFs were detected by SD-OCT in the retinas of mice given 30, 45, and 60 mg/kg SI, but not those given 15 mg/kg SI. HRFs were visible as early as post-injection day 1, and became more distinct by day 7. The higher doses of SI caused retinal thickness to be significantly decrease by day 5 post-injection compared to control ($p>0.001$). H&E images showed that the 15mg/kg dose had no apparent effect compared to the control, whereas sections from mice treated with 30, 45, and 60mg/kg contained pigmented lesions in the neural retina. The pigmented lesions in the IS/OS layer and the ONL were also detected by EM. Vimentin expression was increased in the RPE layer of the retina in a dose-dependent manner, detected by IHC.

Conclusions: The results suggest that SI induces HRF and pigment migration into the neural retina of mice. Furthermore, the SI-induced expression of vimentin in the RPE layer suggests a change in phenotype consistent with endothelial to mesenchymal transition (EMT). Overall, the results suggest a causal link between HRF, hyperpigmentation and EMT of RPE cells.

CONTROL ID: 3711718

SUBMITTER (NAME ONLY): Joy Sarkar

TITLE: Flt-1 and KDR knockdown affects receptor tyrosine phosphorylation and VEGF-mediated neurite growth in PC12 neuronal cells

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sarkar, D. Lara, E. Katz, Q. Zhou, Y. Luo, E. Ivakhnitskaia, M. Sun, V.H. Guaiquil, M. Rosenblatt, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: In angiogenesis, activation of Flt-1/KDR by ligand binding leads to phosphorylation at intracellular tyrosine residues and activation of downstream signaling cascades. Nevertheless, details of these processes in corneal nerve repair are unclear. VEGF-B has previously been shown to have potent effects in the peripheral nervous system (PNS) possibly due to the existence of receptor heterodimers. The purpose of this study was to investigate Flt-1/KDR tyrosine phosphorylation at specific residues in neuronal cells and characterize similarities and differences with endothelial cells as well as investigate the effects of Flt-1/KDR knockdown on phosphorylation and VEGF-mediated neuronal growth.

Methods: Rat neuronal (PC12), mouse aortic endothelial (MVEC), mouse venous endothelial (MVEC) and human umbilical venous endothelial (HUVEC) cell lines were used. “Receptor Control Group” of cells were acutely stimulated either with VEGF-A or VEGF-B (50 ng/µL) or “vehicle” (PBS; control group). “Receptor Knockdown Group” of cells were treated with siRNA specifically directed against Flt-1 or KDR as per manufacturer’s instructions and then acutely stimulated with VEGF-A or B as described earlier. After treatment, cells were used as follows: (i) One group was fixed in 4% paraformaldehyde and processed for TUBB3 immunostaining and neurite length was visualized using fluorescence microscopy (ii) the second group was harvested in cell lysis buffer (containing anti-protease / anti-phosphatase cocktail), lysed and processed for immunoblotting (IB; LI-COR® Systems) with anti-Flt-1, anti-KDR, anti-phospho-Flt-1 (Tyr1213, Tyr1333), anti-phospho-KDR (Tyr951, Tyr1054, Tyr1175, Tyr1214) antibodies to evaluate receptor tyrosine phosphorylation at specific residues.

Results: Differences in tyrosine phosphorylation at specific residues were observed for Flt1 and KDR in neuronal versus endothelial cells. siRNA-mediated knockdown of Flt1 and KDR caused decreased tyrosine phosphorylation at specific residues in neuronal and endothelial cells. VEGF-A and -B treatment increased neurite outgrowth and branching in PC12 neuronal cells. siRNA knockdown of Flt1 or KDR caused reduction in neurite length and number.

Conclusions: Differences in Flt-1/KDR tyrosine phosphorylation at specific residues may regulate downstream signaling events and influence corneal nerve regeneration.

CONTROL ID: 3711719

SUBMITTER (NAME ONLY): Pratap Naha

TITLE: Binding affinity: A measure of potency for OCU200, a potential therapeutic for the treatment of wet-AMD and DME

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.C. Naha, S. Neupane, A.K. Upadhyay, R&D, Ocugen, Inc, Malvern, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Potency assays for biologicals are complex in nature, and reproducibility, response range, and accuracy depend on various factors such as nature of molecule, mechanism of action, target location, and concentration. Accurate and reproducible potency determination is vital for controlling product quality during manufacture and release. OCU200, a novel fusion biological consisting of human transferrin and tumstatin, is being developed for treatment of DME and wet age-related macular degeneration (wet-AMD). Transferrin facilitates targeting and delivery of OCU200 to the target choroidal endothelial cells through endo/transcytosis. To this end, we developed an enzyme-linked immunosorbent assay (ELISA)-based binding assay and biolayer interferometry (BLI) method to determine binding affinity as a measure of in vitro potency for OCU200.

Methods: In the ELISA, biotinylated transferrin receptor was coated on a streptavidin-coated 96-well plate and varying concentrations of OCU200 were added. A detection antibody (anti-tumstatin-HRP) was applied to measure signal using a UV-visible spectrophotometer, and data was analyzed to determine the dissociation constant. Parallelly, a BLI method was developed to determine the molecular interaction between OCU200 and transferrin receptor. BLI analyzes the interference pattern of white light reflected from two surfaces: the layer of immobilized transferrin receptor on a fiber optic sensor and on the internal reflection surface. Interactions between OCU200 and immobilized transferrin receptor on the biosensor cause a shift in the refracted wavelengths. The shift in the refracted wavelength was measured in real-time, allowing determination of precise and accurate association and dissociation rates.

Results: Dose dependent binding of OCU200 with transferrin receptor was observed in both ELISA and BLI assays. In the ELISA, the dissociation constant was found to be 3.7 ± 0.1 nM. Binding parameters in BLI, i.e. affinity constants (K_D) found to be 0.38 ± 0.01 nM, the association rate (K_{on}) found to be 3.67E+05 (1/Ms), and dissociation rate (K_{off}) found to be 1.43E-04 (1/Ms).

Conclusions: OCU200 binds to the transferrin receptor in a dose dependent manner, supporting our hypothesis that transferrin targets OCU200 to the choroid and retina mediated through the transferrin receptor. Binding affinity with receptor can be used a measure of potency for OCU200.

CONTROL ID: 3711722

SUBMITTER (NAME ONLY): Devin Cohen

TITLE: Adherence to dual-energy x-ray absorptiometry scan recommendations and fracture risk in non-infectious uveitis patients

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Cohen, B.L. VanderBeek, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|N.J. Butler, Ophthalmology, VA Boston Health Care System Jamaica Plain Campus, Boston, Massachusetts, UNITED STATES|Y. Yu, Center for Preventive Ophthalmology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|J.H. Kempen, L. Sobrin, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J.H. Kempen, Ophthalmology, Addis Ababa University, Addis Ababa, Addis Ababa, ETHIOPIA|

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ABSTRACT BODY:

Purpose: Non-infectious uveitis (NIU) patients are often exposed to high-dose systemic corticosteroids (CS), yet little is known about the risk of osteoporosis/bone fracture in these patients or their adherence to recommended screening protocols. This study assessed the rate of dual-energy x-ray absorptiometry (DXA) monitoring of CS-exposed NIU patients. It also compared the risk of osteoporosis/bone fractures with cohorts of rheumatoid arthritis (RA) patients and normal controls.

Methods: Using data from a commercial and Medicare Advantage claims database, cohorts were created from NIU and RA patients given a cumulative dose of ≥900mg of oral prednisone (or bioequivalent dose of alternative corticosteroids (CS)). Patients were included in the analysis if they had at least 2 years of data prior to the date of reaching the minimum cumulative dose of oral CS, did not have a history of a DXA scan in the previous 18 months, and were ≥18 years old. NIU patients were excluded if they had any diagnosis of infectious uveitis or uveitis associated with systemic inflammatory disease at any time. RA patients were excluded if they were diagnosed with any form of uveitis. Patients were allowed to re-enter the analysis after DXA scan testing if the above criteria were again met. Cox proportional hazard regression estimated the hazard ratio of receiving DXA screening. A separate cohort analysis was conducted to compare the risk of osteoporosis/bone fractures in NIU patients versus matched normal controls, independent of CS use.

Results: 77,630 observations of NIU patients were compared with 80,862 observations of RA patients. During the follow-up period, 17,825 and 24,639 DXA scans were performed in NIU and RA patients, respectively. The adjusted hazard ratio (aHR) of NIU patients to have a DXA scan was 0.64 (95%CI:0.63-0.65; $p<0.001$) with respect to RA patients. After propensity score matching, the aHR of getting osteoporosis or a bone fracture of NIU patients was 0.95 (95%CI:0.93-0.98; $p<0.001$) compared to normal controls.

Conclusions: NIU patients are 36% less likely to receive a DXA scan after high-dose CS exposure compared with RA patients. No elevated risk of osteoporosis for NIU patients was found compared to normal controls.

CONTROL ID: 3711723

SUBMITTER (NAME ONLY): Giuseppe Giannaccare

TITLE: A dual polymer lubricant eye drop containing also osmoprotectants improves ocular discomfort symptoms and tear film stability in patients with dry eye disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Giannaccare, M. Borselli, G. Carnovale Scalzo, V. Scorcia, Universita degli Studi Magna Graecia di Catanzaro, Catanzaro, Calabria , ITALY|

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ABSTRACT BODY:

Purpose: To investigate changes of objective signs and ocular discomfort symptoms in patients affected by dry eye disease (DED) treated with a new commercially available tear substitute.

Methods: A pilot study including 15 patients (6 males, 9 females; mean age 58.4±14.8 years) with mild-moderate DED was conducted. The patients were treated with a new commercially available tear substitute containing two natural polymers (sodium hyaluronate and xantham gum) and osmoprotectants (glycine and betaine). Patients were instructed to instill the study product 4 times daily for 2 months. Non-invasive ocular surface examination was carried out before (T0) and after treatment (T1) by means of Keratograph (Oculus, Germany) for the measurement of: i) tear meniscus height (TMH); ii) non-invasive break-up time (NIBUT); iii) infrared meibography of upper and lower eyelids (Pult scale); iv) ocular redness. During each visit, discomfort symptoms were scored by means of standardized patient evaluation of eye dryness (SPEED) questionnaire. The Wilcoxon test was used to compare changes of ocular parameters from T0 to T1. A P value equal or less than 0.05 was considered statistically significant.

Results: All patients instilled regularly the eye drop reporting a good profile of tolerability. Compared to T0, SPEED score decreased significantly (from 16.0±3.8 to 7.0±3.2; $P<0.001$), while NIBUT value improved significantly at T1 (from 6.3±1.1 to 9.3±3.1 s; $P=0.05$). Furthermore, TMH and Pult score also improved after treatment, but to a lesser extent (respectively, from 0.244±0.028 to 0.332±0.080 mm, $P=0.08$ and from 1.3±0.5 to 1.5±0.6, $P=0.3$). Redness score did not change significantly during the study period ($P=0.2$).

Conclusions: This novel tear substitute containing sodium hyluronate, xantham gum and osmoprotectants improved significantly ocular discomfort symptoms as well as tear film stability in patients with DED. A longer period of treatment could be useful to detect improvement in the other parameters.

CONTROL ID: 3711724
SUBMITTER (NAME ONLY): James Edmonds
TITLE: Expert in the Loop Training to Optimize Clinician Time
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Edmonds, R. Chan, D. Yi, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|
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ABSTRACT BODY:

Purpose: One of the limiting factors to the broad adoption of medical computer vision is the high cost of annotation. In this work, we introduce the Expert In The Loop (EITL) framework to reduce annotator time requirements with minimal sacrifices to deep model performance.

Methods: We built a cloud native platform based on CVAT (an open source image annotation software) that allows clinicians (i.e. the expert) to annotate medical images (step 1). Upon annotation of subsets of images, a crude deep learning model can be trained. This model can be used to run inference on the unlabeled images (step 2). We then ask the expert to accept or reject the network predictions (step 3), then we retrain our network on our original expert-labeled images and the accepted network-labeled images (step 4). We can repeat steps 2-4 as needed until its accuracy reaches a suitable level.

To validate this pipeline we decided to tackle Optic Disc (OD) segmentation and Vessel Segmentation on Fundus photographs. We use the publicly available Drishti-GS dataset for OD segmentation and High-Resolution Fundus (HRF) dataset for the vessel segmentation. For training, we use supplied ground truth annotation for the baseline network but manually label two images for the EITL experiments. Labeling time for the full dataset has been extrapolated from the annotation time. All reported IoU values are on the Drishti-GS test set and HRF image index 11-15 (fifteen total images for normal, DR, and glaucoma) for each respective dataset. To expedite labeling, the expert in this case is not a clinician but a computer science researcher. We train on a standard U-Net with a combination of cross-entropy and IoU loss.

Results: A full list of network performance can be found in Table 1. For OD segmentation and vessel segmentation, annotating the two images took 79 seconds and saved the expert 32 minutes of time, and 52 minutes, saving the expert over 12 hours, respectively. We see that our network was able to match the performance of an exhaustively annotated dataset after only collecting labels for 2 images.

Conclusions: This study shows that we can employ expert time more efficiently in medical computer vision. By keeping an Expert In The Loop while training we can expand our datasets across more domains while not sacrificing model performance. In the future, we hope to expand our experiments to include model performance where the expert also annotates the most problematic cases.

CONTROL ID: 3711725

SUBMITTER (NAME ONLY): Gavin Braithwaite

TITLE: A temporary hydrogel vitreous substitute in support of retinal detachment repairs

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.G. Vavvas, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES| G. Braithwaite, M. Xheka, M. Deshnica, V. Holmes, Cambridge Polymer Group Inc, Woburn, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Gavin Braithwaite: Commercial Relationship: Code N (No Commercial Relationship) | Mimoza Xheka: Commercial Relationship: Code N (No Commercial Relationship) | Marsela Deshnica: Commercial Relationship: Code N (No Commercial Relationship) | Veronica Holmes: Commercial Relationship: Code N (No Commercial Relationship) | Demetrios Vavvas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal detachment is a common problem impacting almost 50,000 people annually in the US. If not immediately treated, loss of vision can result but the current state of the art, using synthetic “tamponades”, has serious drawbacks. We hypothesize that a refractive-index match hydrogel with tailored swelling pressure and degradation time will allow normal eye function during healing without significant behavioral changes or secondary surgeries.

Methods: Eighteen (18) male and 18 female New Zealand White rabbits received full baseline ophthalmic exams. Following vitrectomy and subretinal injection of 0.9% NaCl to create a large inferotemporal RD, 24 animals received hydrogel and 12 animals received normal saline as controls. ERG, and OCT were measured at 1, 7, 14, 28, 49 and 84 days post-vitrectomy. IOP, slit-lamp and gross exams were performed at 1 week intervals. Eyes were collected at 14, 28, 49 and 84 days and histology was determined at each time point for one control and one test article. In addition a chromatographic analysis technique developed here was used to determine the evolution and clearance of the hydrogel components as it degraded at each timepoint.

Results: There was no significant increase in intraocular pressure during the length of the study. Chromatographic tracking of the hydrogel components demonstrate that the gel is degrading in vivo over 2-3 weeks, and that the components clear from the eye over time. By the end of the study only trace levels of both components are detected. In addition, histology indicates only minimal differences between the control and test articles. The healing process was also tracked to allow comparison between the control (bleb only) and the test article.

Conclusions: The development of a new hydrogel with tunable properties is demonstrated that can be designed to degrade over a period consistent with the healing process. The gel possesses properties similar to the native tissue and therefore works well as a temporary vitreous replacement. By designing a degradable hydrogel one can leverage the natural fluid flow of the eye to refill the eye after healing has occurred and avoid the need to permanently implant synthetic materials in this space. The preliminary data indicates that the material is well tolerated and the healing process in the presence of the gel is at least as good as the unsupported surgery.

CONTROL ID: 3711727

SUBMITTER (NAME ONLY): Olivier Mauduit

TITLE: Analysis of chronic lacrimal gland inflammation using Visium spatial gene expression

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Mauduit, V. DELCROIX, A. Srivastava, T. Umazume, H.P. Makarenkova, Scripps Research Institute Department of Molecular and Experimental Medicine, La Jolla, California, UNITED STATES|D.A. Dartt, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Olivier Mauduit: Commercial Relationship: Code N (No Commercial Relationship) | Vanessa DELCROIX: Commercial Relationship: Code N (No Commercial Relationship) | Amrita Srivastava: Commercial Relationship: Code N (No Commercial Relationship) | Takeshi Umazume: Commercial Relationship: Code N (No Commercial Relationship) | Darlene Dartt: Commercial Relationship: Code N (No Commercial Relationship) | Helen Makarenkova: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Chronic inflammation of the lacrimal gland (LG) is a leading cause of aqueous deficiency dry eye. It results in eye irritation, pain and may lead to severe ocular surface disorders. Visium technology makes it possible to measure the topography of gene expression. Here, we propose to underly the potentials of Visium to compare healthy and chronically inflamed LGs.

Methods: We used the 10X Genomics Visium spatial expression solution on 10µm LG cryosections of 4.5 months old BALB/cJ (control) and NOD.B10Sn-H2b/J (diseased) mice. Each sample was sequenced at a minimal depth of 280 million reads. Raw data was processed with Space Ranger (v1.3.1) to obtain spatial maps of gene expression. Data was normalized and integrated with Seurat (v4.0) to perform clustering and expression analysis.

Results: After integration of data from BALBc and NOD mice, 7 clusters (C0-6) were identified. Overall, we noted in each cluster, an upregulation of immunoglobulins (Ig) and a downregulation of exocrine gland-secreting peptides and secretoglobins (SCGB) in NOD mice. C0 and C1 represented secretory units containing mostly acinar and myoepithelial cells expressing SCGB, which play a barrier function in secretory organs. C2 was characterized by the expression of Ig typical of B cells. In C3, we detected genes expressed by activated lymphocytes and macrophages. In BALBc, it represented 5% of all spots, while in NOD it reached 15% and colocalized with immune infiltrates. C3 is enriched in glycoproteins belonging to the major histocompatibility complex protein family. C4 and C5 were enriched in genes found in ductal cells. C4 likely contained cells releasing mucins and participating in ion exchange. C5 corresponded to excretory ducts. C6 was enriched in fibroblast and macrophage markers.

Conclusions:

We successfully identified the major cellular components of healthy and chronically inflamed LG: secretory units, major ducts and immune cells. Contrary to RNA-seq, Visium indicates which cellular compartment contributes to gene expression changes observed during disease development. Despite the relatively low spatial resolution of this approach, each compartment can be compared between control and diseased LG to evidence local or structure-specific transcriptomic alterations. For example, the downregulation of secreted peptides by the acinar compartment can be related to LG dysfunction and could be involved in immunoregulatory processes.

CONTROL ID: 3711729

SUBMITTER (NAME ONLY): Vanessa DELCROIX

TITLE: The lacrimal gland epithelium activates inflammasome signaling during acute and chronic inflammation

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. DELCROIX, O. Mauduit, A. Srivastava, T. Umazume, H.P. Makarenkova, Scripps Research Institute Department of Molecular and Experimental Medicine, La Jolla, California, UNITED STATES|M. Yang, D.A. Dartt, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|V. Shestopalov, University of Miami School of Medicine, Miami, Florida, UNITED STATES|C.S. De Paiva, Baylor College of Medicine Department of Ophthalmology, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The lacrimal gland (LG) is the exocrine tubuloacinar gland that secretes tears. LG chronic inflammation induced by autoimmune disease or aging impairs tear secretion and causes dry eye disease. Current treatments alleviate symptoms but do not restore LG function, which could be improved by better understanding the mechanisms promoting inflammation. As aberrant inflammasome activation was shown in autoimmunity and age-related diseases, we analyzed the inflammasome pathway in inflammation models and investigated potential modulators.

Methods: We used immunodetection and the R26-CAG-ASC-citrine mouse to detect inflammasomes, a fluorescent reporter of inflammasome complex activation. Acute LG injury was induced by IL-1a injection, and we used RT-qPCR and published RNA-seq data (GSE99093) for gene expression analysis. Chronic inflammation was studied in diabetes-free NOD.B10.H2b (NOD) mice compared to BALBc mice, and their LG transcriptome was analyzed by RNA-seq at 2, 4, and 6 months old. Sequencing data were processed with Rosalind software platform.

Results: The number of ASC specks in LG epithelium was increased by acute or chronic inflammation. Several types of inflammasome sensors were upregulated in inflamed LGs, including Nlrp3, Aim2, and Ifi204. This was associated with an upregulation of the inflammasome effectors Casp1 and Casp4, along with the downstream pro-inflammatory interleukin genes Il1b and Il18, thus suggesting that they are functional. Inflammasome activation following IL-1a-injury preceded epithelial cell death and immune infiltration. We also found that the lipid metabolism pathway genes were upregulated after IL-1a-injury, during the switch from the primary inflammatory response to the tissue repair process. By contrast, Srebf1 and genes involved in fatty acid synthesis were downregulated during chronic inflammation, whereas the expression of lipid transporters and genes promoting the generation of cholesterol was increased.

Conclusions: Epithelial cells can sense tissue injury and may contribute to the development of chronic inflammation by activating the inflammasome signaling pathway. During inflammation, various types of inflammasomes are activated in the LG, thereby illustrating the complexity of the inflammatory response. Altered lipid metabolism might trigger epithelial cell damage that sustains inflammasome activation, promoting LG chronic inflammation.

CONTROL ID: 3711730

SUBMITTER (NAME ONLY): Jessica Tran

TITLE: Genetic correlations between smoking- and glaucoma-related traits

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.H. Tran, L.R. Pasquale, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|P.G. Hysi, Ophthalmology, King's College London, London, London, UNITED KINGDOM|K.V. Stuart, A.P. Khawaja, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|C. Cousins, J. Wang, J.L. Wiggs, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|P.G. Hysi, Twin Research & Genetic Epidemiology, King's College London, London, London, UNITED KINGDOM|R. Do, S. Bafna, Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai Department of Genetics and Genomic Sciences, New York, New York, UNITED STATES|J. Kang, Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|S. MacGregor, Statistical Genetics, QIMR Berghofer Medical Research Institute, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: We assessed global cross-trait genetic correlations between glaucoma- and smoking-related traits to gain insights into the pathogenesis of primary open-angle glaucoma (POAG).

Methods: We gathered publicly available genome-wide association study summary statistics from participants of European-ancestry regarding the following glaucoma-related traits: intraocular pressure (IOP; n=139,555), macula retinal nerve fiber layer (mRNFL; n=31,434) thickness, macula ganglion cell-inner plexiform layer (mGCIPL; n=31,434) thickness, vertical cup-disc ratio (vCDR; n=23,899), artificial intelligence-determined vertical cup-disc ratio (AI-vCDR; n=111,724) and POAG (n=216,257). We gathered similar data for the following smoking-related traits: smoking initiation (n=1,232,971; defined as ever having been a regular smoker) and cigarettes smoked per day (CPD; n=337,334). We estimated genetic correlations (r_g) between traits using linkage disequilibrium score regression and tested for causal associations using two-sample Mendelian randomization (MR). The threshold of significance was Bonferroni-corrected for multiple comparisons.

Results: There were positive global genetic correlations between POAG and IOP (r_g=0.68; p<1E-100), vCDR (r_g=0.51; p=4.15E-20) and AI-vCDR (r_g=0.56; p=3.57E-50). There was no global genetic correlation between POAG and mRNFL (r_g=-0.082; p=0.07) or mGCIPL (r_g=-0.03; p=0.55). There were also global genetic correlations between IOP and AI-vCDR (r_g=0.28; p=1.29E-31) and vCDR (r_g=0.19; p=2.16E-6). There were nominal non-significant inverse global genetic correlations between smoking initiation and POAG (r_g=-0.05, p=0.05), IOP (r_g=-0.06, p=0.01), mGCIPL (r_g= -0.07, p=0.03) and AI-vCDR (r_g=-0.04, p=0.03). CPD and IOP also exhibited nominal inverse correlations (r_g=-0.06, p=0.04). Inverse variance weighted MR analyses revealed a significant association between smoking initiation and IOP (-0.18mmHg per standard deviation increase in the smoking initiation instrument, 95% confidence interval: -0.30 to -0.06, p=3.0E-4). A similar significant association was observed with MR-PRESSO, but not with other MR methods.

Conclusions: While shared genetic correlation between smoking- and glaucoma-related traits were nominal, MR analyses demonstrate a possible causal link between smoking initiation and IOP. Further efforts could define shared loci between IOP and smoking initiation that might lead to new drug targets for glaucoma.

CONTROL ID: 3711731

SUBMITTER (NAME ONLY): Matthew Geiger

TITLE: Sex-Based Disparities after Cataract Surgery based on Operative Complications and Visual Acuity Outcomes

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. Geiger, A.M. Lynch, A. Palestine, N.C. Grove, K.L. Christopher, R. Davidson, M. Taravella, N. Mandava, J.L. Patnaik, Department of Ophthalmology, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|M.D. Geiger, Medical Student, University of Toledo College of Medicine and Life Sciences, Toledo, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate sex differences in the frequency of intra- and post-operative complications and visual outcomes following cataract surgery.

Methods: A retrospective chart review (2014 to 2019) was conducted on the medical records of patients who had phacoemulsification cataract surgery at the Sue Anschutz-Rodgers Eye Center, University of Colorado School of Medicine. Data collected included the patient's health history, ocular comorbidities, operative and post-operative complications, and the post-operative best corrected visual acuity (BCVA). The data were analyzed using univariate and multivariable logistic regression with generalized estimating equations to account for the correlation of some patients having two eyes included in the study.

Results: A total of 12,549 eyes from 7,650 patients were included in the study. Ocular comorbidities were different by sex, with males having significantly higher percentages of traumatic cataracts, intraocular injections, prior ocular surgery, mature cataracts, and planned pars plana vitrectomy (PPV). Conversely, females had significantly higher rates of pseudoexfoliation. In multivariable analysis, males had 1.7 higher odds of posterior capsular rupture (PCR) (95% CI:1.0-2.7, p=0.0398) and 1.6 higher odds of vitreous loss (95% CI:1.1-2.5, p=0.0211). Post-operatively, males had a significantly increased risk of retinal detachment, but in multivariable analysis this was no longer significant, and were significantly less likely to undergo Nd:YAG laser capsulotomy for posterior capsule opacification (OR=0.8, 95% CI=0.7-0.9, p=0.002). The best corrected visual acuity (BCVA) was slightly worse for males pre-operatively (mean logMAR 0.376 (Snellen equivalent 20/47) vs. 0.340 (Snellen equivalent 20/44) for females, p=0.002); but post-operatively, both sexes exhibited similar visual acuity of Snellen equivalent 20/25 (p=0.2096) with exclusion of traumatic cataracts, combined surgeries with PPV, and complicated surgeries.

Conclusions: Our study found significant differences by sex in patient presentation and outcomes following cataract surgery. These findings underscore the importance of incorporating sex into studies that investigate cataract surgery outcomes.

CONTROL ID: 3711732

SUBMITTER (NAME ONLY): Aiswaryah Radhakrishnan

TITLE: Cognitive visual functions among diabetic and healthy individuals with diabetic family history

SESSION TITLE: Vision assessment and Clinical applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Radhakrishnan, S. Rout, Department of Optometry, SRM Institute of Science and Technology, SRM Medical College Hospital and Research Centre, Kancheepuram, Tamil Nadu, INDIA|

Commercial Relationships Disclosure: Aiswaryah Radhakrishnan: Commercial Relationship: Code N (No Commercial Relationship) | Suchismita Rout: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetes Mellitus is a multisystemic disorder having systemic, ocular and cognitive complications. We studied the changes in visual attention, spatio-visual memory and visual search among diabetic individuals and healthy individuals with family history of diabetes.

Methods: Diabetic and healthy individuals with diabetic family history (N=92, Mean age 45±8.8 years) were included after obtaining informed consent. None of the subjects had any ocular diseases and had best corrected visual acuity of 6/9 or better. Visual attention and processing time (APT) was measured using a Stroop task with congruent and incongruent stimuli, with subjects keying in code for the print color. For Spatio-visual memory, subjects were presented targets sequentially at random locations and the maximum number of blocks the subjects could recall in correct sequence was measured. The difference in processing time for congruent and incongruent stimuli was calculated. Visual search time (VST) was measured as choice reaction time. The time taken for the subject to identify an upright orange colored “T” among 15 distractors was collected. All measurements were performed using PsyToolKit on a calibrated monitor in a normal room setting with the subjects viewing the targets binocularly.

Results: All the visual cognitive parameters were degraded in diabetics compared to healthy individuals. The processing time was significantly higher ($p<0.0001$) for incongruent stimuli ($RTInCon_{DM}$: 1593±198msec; $RTInCon_{HI}$: 1429±112msec) than congruent stimuli ($RTCon_{DM}$: 1312±176msec; $RTCon_{HI}$: 1305±105msec) for both group of subjects. The mean APT longer for diabetics (DM: 281±152msec, HI: 124±91msec; $p<0.0001$) than for healthy individuals. The VST was significantly ($p=0.03$) delayed for diabetic individuals (3156±389msec) than for healthy individuals (3017±316msec). The mean span for spatio-visual memory in diabetic individuals was (3.6±0.8) which was significantly lesser than that for healthy individuals (5±1.3). The reaction time (irrespective of the task) and span of memory was significantly correlated with the age of the patient ($r_{RT}=0.64$, $r_{span}=-0.67$, $p<0.001$).

Conclusions: Diabetics with normal had impaired cognitive functions, when compared to healthy individuals with diabetic family history. Our results imply that cognitive visual impairment can manifest earlier than ocular complications and should be routinely assessed.

CONTROL ID: 3711733

SUBMITTER (NAME ONLY): George Sanchez

TITLE: Diagnosis and Management of Zoster Sine Herpete: A Case Report and Survey of the Zoster Eye Disease Study Group

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Sanchez, D.M. Miller, C. Phan, H. Zheng, M.E. Zegans, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, UNITED STATES|G. Tsougranis, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|B.H. Jeng, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|E. Cohen, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To present a case of zoster sine herpete (ZSH) manifesting with retinal phlebitis and to examine and compare differences in ZSH diagnosis and treatment patterns among investigators in the Zoster Eye Disease Study Group (ZEDS) in the United States, Canada, and New Zealand.

Methods: Case report, along with a survey of physicians associated with the ZEDS Group in September 2021. Survey participation was voluntary, and participants were surveyed regarding their findings on initial exam, method of diagnosis, treatment undertaken, and overall clinical course.

Results: We report the case of a 55-year-old woman who initially presented with acute anterior uveitis and was diagnosed with ZSH via positive VZV PCR results. The patient also developed iris transillumination defects and retinal phlebitis in her right eye prior to valacyclovir. Her clinical course stabilized after starting oral valacyclovir. At the eight-month follow-up visit, the patient remained on valacyclovir and topical steroid treatment. A total of 28 responses to the survey were collected. Of the 28 respondents, 11 (39.3%) indicated that they had diagnosed ZSH. Methods of diagnosis varied, however clinical exam findings (70%), VZV DNA identification via PCR 14 (50%), and resolution of symptoms following treatment 14 (50%) were most common. Of the 11 respondents who had diagnosed ZSH, three (27.3%) obtained fluorescein angiography and only two (18.2%) diagnosed retinal phlebitis in the setting of ZSH. Oral antivirals were used in all 28 cases (100%) with valacyclovir as most popular with 25 total cases (89.3%). No intravenous or intravitreal treatments were reported. Three (27.3%) of the respondents who had diagnosed ZSH were unable to discontinue antiviral treatment.

Conclusions: Our survey of ZEDS investigators indicates that the majority of ZSH cases are diagnosed via clinical findings and detection of VZV DNA by PCR. Oral antivirals are overwhelmingly the therapy of choice. However, antiviral treatment could not be discontinued in 27.3% of cases. While posterior segment complications were reported in 18.2% of cases, keratitis and uveitis were most common.

CONTROL ID: 3711734

SUBMITTER (NAME ONLY): Michael Tri Do

TITLE: Evolutionary Conservation of Photosensory Mechanisms in the Primate Melanopsin Neuron

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Do, A. Liu, E.S. Milner, P. Morquette, H. Blume, M.C. Brown, G.S. Bryman, A.J. Emanuel, Neurology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M.H. Do, A. Liu, E.S. Milner, P. Morquette, H. Blume, M.C. Brown, G.S. Bryman, A.J. Emanuel, F.M. Kirby Neurobiology Center, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|P.D. Gamlin, University of Alabama at Birmingham, Alabama, UNITED STATES|Y. Peng, University of California Los Angeles, Los Angeles, California, UNITED STATES|J.R. Sanes, Harvard University, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mammals sense light for diverse purposes—including perception and the regulation of development, physiology, behavior, mood, and cognition—that require intrinsically photosensitive retinal ganglion cells (ipRGCs). These ocular neurons capture photons with a receptor called melanopsin and send information widely throughout the brain. IpRGCs are evolutionarily conserved, providing an opportunity to compare cell types across ecological niche; indeed, few other retinal output neurons appear to be shared between rodents and primates. Present knowledge indicates that rodent and primate ipRGCs diverge fundamentally in their photosensory mechanisms. However, studies of the latter are few, in large part because their live identification is challenging. We pursue the idea that comparison of rodent and primate ipRGCs will clarify our understanding of how cells are tailored to their tasks.

Methods: We developed an acute, ex vivo method of identifying macaque ipRGCs based on immunotagging of melanopsin's extracellular domain. We performed patch-clamp electrophysiological recordings from macaque ipRGCs, as well as from mouse ipRGCs that expressed macaque melanopsin in lieu of their own. We delivered a suite of visual stimuli and analyzed responses using biophysical methods. To focus on cell-autonomous mechanisms, we added antagonists of synaptic transmission to the extracellular medium.

Results: Our experiments indicate that N-terminal immunotagging is innocuous for melanopsin function. Using this approach, we observed deep conservation between macaque and mouse ipRGCs, from molecular mechanisms that broaden wavelength sensitivity and response lifetime to cellular mechanisms that generate dynamic range for encoding a breadth of environmental light levels. We found one divergence: While the electrical discharges of mouse ipRGCs are irregular, those of macaque ipRGCs are precisely timed.

Conclusions: It appears that many ipRGC mechanisms for sensing environmental illumination are effective enough to stand across the ~70-million-year separation of mice and macaques. Live immunotagging offers a way to identify cell types for functional analysis, and may be especially useful in the study of species that are unamenable to genetic manipulation.

CONTROL ID: 3711735

SUBMITTER (NAME ONLY): Finny Monickaraj

TITLE: Chemokine CXCL1 mediates through Neutrophil and Monocyte recruitment in Blood-Retinal Barrier Alteration in Diabetic Retinopathy

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Monickaraj, G. Acosta, A. Cabrera, A. Das, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|F. Monickaraj, A. Das, New Mexico VA Health Care System, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our previous transcriptomic studies on retinal endothelial cells under hyperglycemic conditions have shown the significant upregulation of the chemokine CXCL1. The purpose of this present study is to show the effect of CXCL1 on recruitment of neutrophils and monocytes in the alteration of blood retinal barrier in an in vivo model of diabetic retinopathy.

Methods: The experiment design included the following groups: A) Streptozotocin induced diabetic mice (3 months) vs. diabetic mice treated with neutrophil depleting Ly6G-1A8 antibody (50ug) for 15 days (n=10); B) Wildtype C57BL/6 J mice intravitreally (IVT) injected with recombinant CXCL1 (100 ng/eye) vs. animals pretreated with Ly6G-1A8 antibody (50ug) followed by IVT with recombinant CXCL1 (n=10). Flow cytometry analysis for immune cell infiltration (neutrophils and monocytes) in the retinas. qPCR analysis was used to determine mRNA expression of chemokines and its receptors, proteases and adhesion molecules. Western Blot analysis was used to evaluate the expression of albumin to detect retinal vascular permeability. ELISA was used to measure serum levels of CXCL1 levels in patients with human diabetic retinopathy.

Results: Retinas of both diabetic and intravitreally CXCL1 injected mice showed increased neutrophils ($p = 0.01$) and monocytes ($p = 0.01$) and mRNA expression of proinflammatory chemokines (Ang2, CCL2, CCL5, CCL7, VEGF), chemokine receptors (CCR2, CCR5, CXCR2), proteases (Cathepsin-B,K,L,S, MMP2 and MMP9) and adhesion molecules (ICAM1 and VCAM1). The Ly6G-1A8 antibody treatment had significantly decreased infiltration of both neutrophils and monocytes ($p=0.05$) and decreased expression of these chemokines and proteases. Likewise, western blot analysis confirmed increased extravasation of albumin in retinas of diabetic mice and CXCL1 injected mice ($p=0.01$) and the Ly6G-1A8 antibody treatment significantly reduced the extravasation ($p=0.01$). Also, the CXCL1 level was significantly increased in the serum samples of diabetic retinopathy patients compared to non-diabetic subjects ($p=0.001$).

Conclusions: Overall, we have shown evidence that neutrophil infiltration triggered by CXCL1 plays an important role in the alteration of the BRB in diabetes. A combination therapy of a CXCL1 inhibitor and the anti-VEGF drugs may be a potential therapeutic approach in the management for diabetic macular edema.

CONTROL ID: 3711736

SUBMITTER (NAME ONLY): Marwa Daghsni

TITLE: Investigating the chromatin landscape of retinal ganglion cells during mouse retinogenesis

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Daghsni, F. Bian, F. lu, J.M. Gross, T. Kuwajima, I. Al Diri, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|S. Liu, Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|D. Kostka, Developmental Biology, Computational & Systems, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a retinal degenerative disease that leads to a progressive loss of retinal ganglion cells (RGCs) and optic nerve degeneration. Atoh7/Math5 is a transcription factor required for RGC competence. In humans, an enhancer deletion was associated with nonsyndromic congenital retinal nonattachment (NCRNA), where patients lack of RGCs and show an aplasia of the optic nerve. Our work aims at utilization a genomic approach to characterize the enhancer structure of Atoh7 and other factors contributing to retinal ganglion cell formation.

Methods: We performed single cell (sc) ATAC-Seq analysis on wild type mouse developing retina at E14.5 to define RGCs regulatory landscape in detail. We investigated the genomic occupancy of PAX6, a transcriptional factor important for RGC genesis at E14.5, using a genomic technique called CUT and RUN. We analyzed transcriptional defects resulting from deleting the Atoh7 enhancer landscape using bulk and sc-RNA-seq at E14.5. We performed anterograde labeling to investigate defects in RGC axons in Atoh7 enhancer deficient mice.

Results: sc-ATAC-Seq analysis captured the cellular heterogeneity and progression from proliferation to differentiation underlying retinal development at E14.5 and revealed the landscape dynamics of Atoh7 enhancer. Genomic profiling of PAX6 uncovers occupancy on cis-regulatory elements nearby genes important for retinal proliferation and RGC differentiation, including Atoh7. Mice harboring CRISPR/Cas9 mediated deletion of an Atoh7 enhancer leads to a profound reduction in Atoh7 expression but did not alter the RGCs formation. RNA-Seq analysis of the KO-mice at E14.5 revealed changes in transcriptional programs related to RGC differentiation and axon formation. Importantly, deletion of Atoh7 enhancer disrupts eye-specific targeting of RGC axons in the dorsal lateral geniculate nucleus (dLGN).

Conclusions: Sc-ATAC analysis reconstructed retinal differentiation trajectories known to exist at E14.5. Genomic occupancy of PAX6 revealed how PAX6 coordinates a complex retinal gene regulatory network important for retinal proliferation and differentiation. Our RNA-Seq analysis of mouse lacking Atoh7 enhancer revealed requirement of this regulatory element to proper axonogenesis. We propose that high levels of Atoh7 expression is required for proper circuit organization of the eye-specific targeting of visual system but is dispensable for RGC formation.

CONTROL ID: 3711737

SUBMITTER (NAME ONLY): Sophia Zagora

TITLE: Improving paediatric uveitis visual outcomes and quality of life.

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zagora, T. Karaconji, P.J. McCluskey, J.R. Grigg, Ophthalmology, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|S. Zagora, T. Karaconji, J.R. Grigg, Ophthalmology, Children's Hospital at Westmead, Westmead, New South Wales, AUSTRALIA|D. Singh-Grewal, J. Chaitow, Paediatric Rheumatology, Children's Hospital at Westmead, Westmead, New South Wales, AUSTRALIA|D. Singh-Grewal, Department of Medicine, University of Sydney, Sydney, New South Wales, AUSTRALIA|P.J. McCluskey, Ophthalmology, Sydney Hospital and Sydney Eye Hospital, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To investigate visual outcomes and perceived quality of life of paediatric patients with uveitis treated in a multidisciplinary clinic involving Ophthalmologists and Rheumatologists at a tertiary children's hospital.

Methods: Review of all paediatric uveitis patients presenting to the Children’s Hospital Westmead, Sydney Eye Hospital and Save Sight Institute from 2005-2020. Inclusion criteria includes less than 18 years age of diagnosis, any form of diagnosis of uveitis based on SUN criteria, follow up at least 3 months, WGA paediatric glaucoma guidelines for OHT and glaucoma, ocular morbidities and treatment of the uveitis. Completion of 3 validated instruments for children to assess (1) functional visual ability (FVA) with the Cardiff Visual Ability Questionnaire for Children (CVAQC), (2) VR QoL with the Impact of Vision Impairment for Children (IVI-C), and (3) HR QoL with the Pediatric Quality of Life Inventory (PedsQL) version 4.0.

Results: There were 111 patients (207 eyes) diagnosed with paediatric uveitis 2005-2020. There were 61 female and 48 male patients. The most common aetiological diagnoses was JIA-U (n =65, 59%) followed by Idiopathic uveitis (n = 33, 29.6%) with 84% being anterior uveitis and 16% being non-anterior uveitis. Fifty-three patients were on Methotrexate/Mycophenolate, 30 patients on Adalimumab, 3 patients Infliximab, 3 patients on Tocilizumab and 2 patients Tofacitinib. The mean duration of inflammation prior to commencement of a biological agent was 22.0 months (range: 1-48 months). Over 50% eyes diagnosed with uveitis developed raised IOP at some point, 43/207 eyes (21%) had glaucoma surgery. Mean VA significantly improved after 6 weeks of biological therapy and then was maintained over 12 months. Scores for FVA, VR QoL, and HR QoL were reduced in children with paediatric uveitis. Patients and family members reported improved quality of life being able to be seen by all treating doctors at the same multidisciplinary clinic.

Conclusions: Paediatric uveitis has a marked effect on FVA and QoL. Control of intraocular inflammation is essential in paediatric uveitis. Rapid taper of any steroids crucial as ocular hypertension /glaucoma and cataract is dose and duration dependent. Commencing a step ladder of systemic therapy quickly if steroid treatment not working. Biological therapy reduced intraocular inflammation with maintained visual acuity. Multidisciplinary clinics are gold standard treatment.

CONTROL ID: 3711740

SUBMITTER (NAME ONLY): Kayleigh Slater

TITLE: $CysLT_1$ antagonist, 1,4-dihydroxy quininib, alters the secretion of inflammatory mediators from primary uveal melanoma explants and reduces ATP5B expression in a metastatic xenograft model.

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Slater, C. Jahangir, A. Rahman, W. Gallagher, B.N. Kennedy, Conway Institute, School of Biomolecular and Biomedical Science, University College Dublin, Dublin, IRELAND|R. Bosch, A. Villanueva, Xenopat, S.L., Barcelona, SPAIN|F. O'Connell, J. O'Sullivan, Department of Surgery, Trinity Translational Medicine Institute, The University of Dublin Trinity College, Dublin, IRELAND|J. Piulats, Medical Oncology Department, Catalan Institute of Cancer, SPAIN|S.E. Coupland, Liverpool Ocular Oncology Research Group, Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, Merseyside, UNITED KINGDOM|V. O'Neill, N. Horgan, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|J. Piulats, IDIBELL Bellvitge Biomedical Research Institute, SPAIN|

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ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is a rare, but often lethal, ocular cancer which metastasises to the liver in up to 50% of patients. There are no effective therapies available to treat metastatic UM and as few as 8% of patients survive beyond two years. We previously identified that high expression of $CysLT_1$ is associated with poor UM patient outcomes in a UK cohort, and that $CysLT_1$ antagonists alter the tumorigenic properties of UM cell lines in vitro. This preclinical in vivo and ex vivo research further evaluates the clinical relevance and therapeutic potential of CysLT receptors in UM.

Methods: Immunohistochemical staining was conducted on an independent, primary UM patient cohort from Spain (n=68) to analyse expression of CysLT receptors and their relationship to matched survival data. Primary UM tumours (n=11) were grown as explant cultures and treated with 20 μM 1,4-dihydroxy quininib or vehicle. Following 72 hours of treatment, tumour conditioned media was analysed by ELISA and the secretion of factors was correlated to clinical data. An orthotopic cell line-derived xenograft model of metastatic UM was generated in female athymic Nude-Foxn1nu mice using OMM2.5 metastatic UM cells. 1,4-dihydroxy quininib was administered intraperitoneally at a dose of 25 mg/kg every 3 days, for 3 weeks (n=8). Upon sacrifice, tumour weight was compared to vehicle (n=9) and Dacarbazine (80 mg/kg)(n=8) treated mice and tumours were assessed by immunohistochemistry and digital pathology analysis.

Results: We confirmed that high expression of $CysLT_1$ in primary UM is significantly associated with reduced survival in an independent, validation cohort (p=0.01). Treatment of ex vivo explants derived with 1,4-dihydroxy quininib significantly alters the secretion of IL-13, IL-2 and TNF-α. In an orthotopic xenograft model of metastatic UM, treatment with 1,4-dihydroxy quininib did not significantly decrease tumour weight versus vehicle (p=0.81) but did significantly decreases ATP5B (p=0.03), a marker of oxidative phosphorylation, versus vehicle, mimicking our published in vitro data.

Conclusions: These preclinical data strengthen the importance of CysLT signalling in UM. Our findings suggest that high expression of $CysLT_1$ in UM could act as a biomarker for poor prognosis and that antagonism of $CysLT_1$ may be of therapeutic interest in UM.

CONTROL ID: 3711741

SUBMITTER (NAME ONLY): Imran Bhutto

TITLE: Ex vivo analysis of mast cell degranulation in human donor choroids

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.A. Bhutto, T. Niizawa, A. Pado, E. McDonnell, G.A. Lutty, M.M. Edwards, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously demonstrated that mast cells are increased in number and there is increased mast degranulation in submacular choroids in all stages of age-related macular degeneration (AMD). We also recently reported ex vivo and in vivo rat models in which a snake venom-like compound, 48/80, stimulates degranulation of choroidal mast cells. Moreover, both oral and topical administration of ketotifen (KTF), a known mast cell stabilizer, reduced mast cell degranulation in the rat model. This study was designed to determine whether human choroid explants can be used as an ex vivo model to study mast cell degranulation and screen potential therapies. In addition, this study investigated the ability of C-reactive protein (CRP), which is elevated in AMD, to stimulate mast cell degranulation.

Methods: Human donor eyes (N=4) were received on wet ice within 30 hrs postmortem. Retinas were isolated from the choroid/RPE complex. The RPE/choroid complex adjacent to the submacula was dissected into pieces. The choroid pieces incubated for 3 hrs at 37°C in either Dulbeccos modified Eagle's media (DMEM) (control), 48/80 (300µg/ml), 48/80 + KTF (300µg/ml), or hCRP (2, 4, and 10 ng/ml). The RPE were then removed with 1% EDTA. Choroids were then fixed in 2% PFA in cacodylate buffer at 4°C overnight and stained for non-specific esterase (NSE) activity. Pigments were bleached with 30% hydrogen peroxide and NSE-stained choroids were imaged. Mast cells were counted using Image J. The percent of degranulated mast cells was calculated in 20x images (4 random fields per piece).

Results: 48/80 stimulated mast cell degranulation in human choroid explants. Moreover, this stimulation was significantly reduced by KTF. CRP also increased mast cell degranulation in a dose-dependent manner, reaching significance at 4 and 10ng/ml. At the 10 ng/ml CRP dose, 43.5% of mast cells were degranulated compared to 15% in the control.

Conclusions: Similar to previous observations in rats, KTF can prevent 48/80-induced mast cell degranulation in human donor eyes. CRP, at physiological concentrations, significantly stimulates mast cell degranulation ex vivo. The ability to study mast cell degranulation ex vivo in human donor choroids may prove useful in testing therapies.

CONTROL ID: 3711742

SUBMITTER (NAME ONLY): Gairik Kundu

TITLE: Understanding ocular surface pain based on discordance between symptoms and signs:associating clinical features,imaging,AI and tear molecular profiles.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Various ocular surface conditions including dry eye disease can present with pain.However,it is challenging to establish etiology and prescribe right treatments due to discordance between patient symptoms and signs.To understand basis of such discordance,we stratified subjects with ocular surface pain based on concordance between severity of signs and symptoms and evaluated corneal structural features and tear molecular factors.We also analysed the various confocal nerve parameters along with systemic and orthoptic parameters in these patients presenting with ocular surface pain using a random forest artificial intelligence(AI) model.

Methods: 300 eyes of 151 patients underwent slit lamp examination,ocular surface disease index (OSDI) scoring,dry eye evaluation and ocular surface staining.Subjects were stratified into -group 1-with no symptoms and clinical signs;group 2-with no symptoms but with signs;group 3-with similar severity of symptoms and signs;and group 4- with symptom severity higher than that of signs.In vivo confocal imaging (IVCM)evaluation was performed in all study subjects.We also evaluated presence or absence of orthoptic issues and connective tissue disorders and in the first step the area under curve (AUC),accuracy,recall,precision and F1-score of the AI model were evaluated.Tear fluid was also collected using Schirmer’s strips and evaluated for soluble factors related to inflammation by multiplex ELISA.

Results: The AI achieved an AUC of 0.736,accuracy of 86%,F1-score of 85.9%,precision of 85.6% and recall of 86.3%.Top 5 parameters used for classification by AI were microneuromas,immature and mature dendritic cells,presence of orthoptic issues and nerve fractal dimension parameter.Patients with higher grade of symptoms and signs showed increased corneal dendritic cells(cDC) density which was more pronounced in subjects with discordant symptoms to signs(group 4).Significantly higher proportion of microneuroma-like structures and cDC were seen in group 4.Higher levels of IL-17A were found in group with more discomfort.

Conclusions: Correlating ocular surface pain and the disparity between signs and symptoms with IVCM and tear molecular factors can help clinicians improve diagnosis and provide targeted treatment for pain and coupled with AI can improve the diagnoses and help better customise treatment of ocular surface pain.

CONTROL ID: 3711744

SUBMITTER (NAME ONLY): Roberto dell'Omo

TITLE: Prevalence of vitreoschisis in eyes with primary rhegmatogenous retinal detachment repaired with pars plana vitrectomy.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. dell'Omo, M. Affatato, G. Rapino, M. Filippelli, Medicine and Health Sciences, Universita degli Studi del Molise, Campobasso, Molise, ITALY|C. Costagliola, Universita degli Studi di Napoli Federico II Scuola di Medicina e Chirurgia, Napoli, Campania, ITALY|N. Gianfrancesco, D. Trivisonno, F. Petti, P. Polisena, Ophthalmology, Antonio Cardarelli Hospital, Campobasso, ITALY|

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ABSTRACT BODY:

Purpose: To investigate the prevalence of vitreoschisis and the effect of its removal on anatomical outcomes in eyes undergoing pars plana vitrectomy (PPV) for primary rhegmatogenous retinal detachment (RRD) repair.

Methods: Prospective analysis and comparison of preoperative imaging and intraoperative findings in eyes with primary RRD. Before operation, the vitreous status was assessed by means of ophthalmoscopy, ultrasound and optical coherence tomography . Intraoperatively, the presence of vitreoschisis was visualized with the aid of desamethasone; the vitreous cortex remnants were removed with a flex loop as much as possible from the vascular arcades to the periphery. All the operations were performed by a single surgeon.

Main outcome measures were the prevalence of intraoperative vitreoschisis and the rate of post-operative complications at 6 month follow-up (development of macular epiretinal membrane and redetachment)

Results: Eighty-four eyes from 84 patients were enrolled into the study. The primary anatomical success rate was 92.9 %. Intraoperatively, vitreoschisis was found in 40 (47.6%) eyes and extended from the major vascular arcades to the ora serrata in all cases. Age and axial length were independent risk factors associated with the presence of vitreoschisis. Successful removal of vitreoschisis from the detached retina was accomplished in 32 eyes (80%). Redetachments occurred in 6 eyes in which vitreoschisis was not identified or removal was not feasible at the time of operation. The postoperative development of a macular epiretinal membrane causing significant wrinkling and alteration of the foveal profile was found in 7 eyes (8.3%).

Conclusions: The prevalence of vitreoschisis in eyes with primary RRD is almost 50%. The identification and removal of vitreoschisis may have a significant impact on the anatomical success rate in eyes undergoing PPV for primary RRD.

CONTROL ID: 3711746

SUBMITTER (NAME ONLY): Anania Woldetensaye

TITLE: Racial and Socioeconomic-Based Disparities in Anti-Vascular Endothelial Growth Factor Treatment and Visual Outcomes in Patients with Branch Retinal Vein Occlusions

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Socioeconomic status (SES) and minority racial status are associated with disparities in healthcare quality and disease outcomes.[1] The objective of this project is to assess differences in anti-vascular endothelial growth factor (anti-VEGF) treatment and visual acuity (VA) outcomes of branch retinal vein occlusions (BRVO) across the dimensions of race and SES.

Methods: A retrospective chart review was conducted of all patients with BRVO and cystoid macular edema (CME) treated with anti-VEGF injections at Wake Forest Baptist Health from 2013 to present. Patients were excluded if they had other visually significant visual pathology. Baseline patient characteristics including VA, age, gender, insurance status, phakic status, were recorded. The national percentile of area deprivation index (ADI) was recorded. Anti-VEGF injection type and number of treatments, and final VA outcomes were collected.

Results: 99 eyes of 96 patients were included. 79 patients belonged in the bottom half and 20 belonged in the top half national percentile of ADI. 79 patients identified their race as White and 20 patients identified their race as non-White. The mean presenting logMAR VA of patients in the top 50^{th} and bottom 50^{th} percentile ADI was 0.44 and 0.66 respectively (p=0.06); presenting vision was 0.60 for White patients and 0.71 for non-White patients (p=0.24). The mean final logMAR VA of patients in the top 50^{th} and bottom 50^{th} percentile ADI was 0.27 and 0.47 respectively (p=0.03); final VA was 0.43 for White patients and 0.50 for non-White patients (p=0.27). The number of anti-VEGF injections per year of follow up for patients in the top 50^{th} and bottom 50^{th} percentile ADI was 3.2 and 1.5 respectively, and was 2.5 for White patients and 1.4 for non-White patients. The mean duration of follow up for White patients was 5.2 years and 4.3 years for non-White patients (p=0.16) while it was 4.7 years for the top 50^{th} percentile and 6.6 years for the bottom 50^{th} percentile ADI (p=0.03).

Conclusions: Final VA was worse in patients with lower SES, but did not differ between white and non-White patients. The number of anti-VEGF injections was different between White and non-White patients and across measures of ADI. These results may help increase awareness of barriers to ophthalmic care associated with SES and race.

CONTROL ID: 3711748

SUBMITTER (NAME ONLY): William Domm

TITLE: Microbiological Evaluation of an Investigational Multi-Purpose Solution Against Acanthamoeba Trophozoites and Cysts

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Domm, H. Wheeler, T. Bassage, M. Byrnes, D. McGrath, K. Millard, Research and Development, Lens Care, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Biguanides have been shown to have amoebicidal activity against Acanthamoeba species. The addition of biguanides in a multi-purpose solution (MPS) may improve protection from Acanthamoeba Keratitis (AK) associated with contact lens wear (CLW). Testing of Acanthamoeba trophozoites and cysts in an investigational triple disinfectant MPS containing Alexidine, a biguanide, Polyaminopropyl Biguanide (PAPB), and Polyquaternium-1 (PQ-1) was conducted to determine Acanthamoeba disinfection efficacy and to further mitigate risk by assessing the potential for encystment.

Methods: A. castellanii (A.c, ATCC 50370) or A. polyphaga (A.p, ATCC 30461) trophozoites or cysts were used to prepare an inoculum of $1x10^7$ organisms/ml. For stand-alone disinfection 10 ml of the MPS (3 lots) was inoculated and incubated for 4 hours. For a regimen test, 6 types of contact lenses were inoculated on each surface and allowed to adsorb for 5 minutes. Each lens (N=4) was rubbed for 10 seconds and rinsed for 5 seconds per side. The treated lens was placed in a lens case well with 3 ml MPS (3 lots) and soaked for 4 hours. Recovery of Acanthamoeba was performed by placing test solution (stand-alone) or lens and soak solution (regimen), separately, into neutralizer broth for 10 minutes. Aliquots were serially diluted in a 96-well microtitre plate containing ¼ strength Ringer's solution. E. coli was added to each well, incubated for 14 days at 26-30^{o}C, and inspected microscopically for recovery. Acanthamoeba recovery values were determined using the Spearman-Karber method and Log_{10} Reduction (LR) was calculated. Encystment was conducted with A.c trophozoites as directed in ISO 19045.

Results: Stand-alone disinfection showed a mean LR of 3.8 and 3.7 for A.c and A.p trophozoites respectively and a mean LR of 3.6 and 1.8 for A.c and A.p cysts respectively after 4 hours of disinfection. Regimen disinfection recovery was <0.5 log for A.c and A.p trophozoites, <1.0 log for A.c cysts, and <0.5 log A.p cysts in all 6 lens types tested. No encystment of A.c was detected after incubation in the MPS for 20-24 hours.

Conclusions: The investigational MPS containing biguanides and polyquaternium-1 showed robust effectiveness of Acanthamoeba trophozoites and cysts in stand-alone, regimen, and encystment testing. Together, these results support that the investigational MPS may reduce the risk of AK associated with CLW.

CONTROL ID: 3711749

SUBMITTER (NAME ONLY): Julia Zeng

TITLE: Clinical Characteristics of Dry Eye Patients Diagnosed During Cataract Surgery Evaluation

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zeng, D. Cui, G. Li, P. Mathews, S. VanCourt, E.K. Akpek, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the incidence and clinical characteristics of patients diagnosed with dry eye during evaluation for cataract surgery.

Methods: Dry eye patients evaluated by an ophthalmologist between 3/2015 and 7/2021 were identified using international classification of disease codes. A total of 600 of the 1630 identified dry eye patients, randomly selected by a computer software (Microsoft Excel), had their medical records reviewed. Patients diagnosed with dry eye during cataract surgery evaluation were identified, and an equal number of primary dry eye patients were selected as controls. Electronic medical records were reviewed to obtain information regarding demographics, objective dry eye parameters at baseline, dry eye treatments, and dry eye symptoms.

Results: Twenty-six patients (4.3% of total reviewed) received a dry eye diagnosis during cataract surgery evaluation, and an additional 26 patients were selected as controls. More patients from the cataract evaluation group were men (42.3% vs 23.1%, P=.139) and self-identified as racial/ethnic minorities (34.6% vs 19.2%; P=.184), however these differences were not statistically significant (both P>.05). Objective dry eye parameters demonstrated no statistically significant difference (all P>.05) between groups for mean conjunctival lissamine green staining (cataract 2.4 vs control 2.8) and corneal fluorescein staining (cataract 2.1 vs. control 2.2). Fifteen (57.7%) cataract patients and 25 (96.2%) of controls had symptoms of dry eye at presentation (P<.001). Prior to presentation, fewer cataract evaluation patients had used any over-the-counter treatments (53.8% vs 84.6%; P=.016) or prescription treatment (15.4% vs 50.0%; P=.008)

Conclusions: The prevalence of dry eye diagnosed during cataract surgery evaluation is rare, however these represent a greater proportion of asymptomatic patients with no prior dry eye treatment. Objective dry eye parameters and demographic between groups are not statistically significant, however larger studies are warranted to evaluate for clinically and statistically significant differences.

CONTROL ID: 3711750

SUBMITTER (NAME ONLY): John Fingert

TITLE: Novel risk factor gene for POAG identified with GWAS of Ocular Hypertension Treatment Study

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To identify and characterize genes associated with primary open angle glaucoma (POAG) in the Ocular Hypertension Treatment Study (OHTS).

Methods: We conducted a genome-wide association study of 1,057 OHTS participants, of whom 374 developed POAG and 683 did not develop POAG after 20 years of follow-up. Participants were typed at 905,636 SNPs that were imputed to 10 million SNPs. We compared allele frequencies with a chi-square test and a genome-wide threshold for statistical significance was set at $p < 5 \times 10^{-8}$. We further evaluated the association with gamma amino butyric acid type A receptor subunit gamma 2 (GABRG2) identified in the OHTS participants by 1) comparing probability for POAG between GABRG2 risk allele carriers and non-carriers using Kaplan-Meier survival analysis; 2) testing a second cohort of POAG patients (n=922) and controls (n=419) for the association with GABRG2; and 3) analyzing human donor eyes with homozygous GABRG2 high-risk alleles (n=4) and homozygous low-risk alleles (n=4) with immunohistochemistry.

Results: We identified a chromosome 5 locus that was highly associated with POAG in the OHTS ($p = 1.9 \times 10^{-8}$). Kaplan-Meier analyses also showed one allele of this risk factor is associated with a 16% increased probability of POAG after 20 years, while two alleles are associated with a 25% increased probability for POAG ($p = 3 .0 \times 10^{-9}$). The chromosome 5 association with glaucoma was confirmed in an independent cohort of POAG patients and controls from Iowa ($p = 3.8 \times 10^{-2}$). GABRG2 is the nearest gene in this chromosome 5 locus. Immunohistochemical analysis of human donor eyes with an antibody directed against GABRG2 demonstrated greatly increased labeling of retinal ganglion cells in eyes with homozygous risk alleles when compared to eyes with no risk alleles.

Conclusions: We have identified a new POAG risk factor locus, GABRG2, that has a significant influence on risk for glaucoma. GABRG2 has a role in gamma amino butyric acid (GABA) signaling / GABAergic activity, which may be an important biological pathway contributing to retinal ganglion cell death in glaucoma.

CONTROL ID: 3711751

SUBMITTER (NAME ONLY): Lindsay Chun

TITLE: Utility of 3-0 Prolene ripcord with Baerveldt-350 to partially occlude tube lumen and minimize hypotony-associated complications when ligature dissolves

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.Y. Chun, M. Qiu, Ophthalmology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Lindsay Chun: Commercial Relationship: Code N (No Commercial Relationship) | Mary Qiu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To retrospectively review a single surgeon's (MQ) experience of using a 3-0 Prolene ripcord in the lumen of Baerveldt 350 Glaucoma Implants (BGI-350) and review of the clinical outcomes of this technique.

Methods: Retrospective chart review was performed on adult patients who received BGI-350s with performed by a single surgeon (MQ) at a single academic center between 10/1/2019 and 6/30/2021. All patients had removable 3-0 prolene ripcords intraoperatively placed in the lumens of BGI-350s. Demographic characteristics, ocular examination findings, and ripcord management outcomes were collected at preoperative and postoperative time points. Outcome variables included intraocular pressure (IOP), number of IOP-lowering medications, and anterior chamber (AC) inflammation at 2 time points: the soonest scheduled visit after the ligature suture dissolved and the postoperative day (POD) of ripcord removal.

Results: 29 eyes of 27 adult patients who received BGI-350s were included in this study. 17/29 [PM1] (58.6%) eyes had prompt ripcord removal at the soonest scheduled visit following ligature dissolution (mean POD 47, IOP 13.1 mmHg on 3.6 meds). The other 13/29 eyes (44.8%) had delayed or no ripcord removal. Among this cohort, 9/13 eyes (69.2%) had low pressure without complications at the time of ligature dissolution (mean POD 47.6, IOP 7.6 mmHg on 3.3 meds). 8 of these eyes (only one of whom had transient AC shallowing) underwent medication de-escalation and subsequent delayed ripcord removal (mean POD 59.9, IOP 14.9mmHg on 2.6 meds). 1 eye had persistent IOP 9 on 0 meds, so the ripcord was trimmed and left in place permanently to prevent hypotony. Furthermore, ripcord removal was delayed due to excessive AC inflammation upon ligature dissolution requiring sustained steroids in 2/13 eyes (15.4%), and due to logistical delays in 2/13 eyes (15.4%) (mean POD 60.1, IOP 13.1 mmHg, 3.2 meds). 0 patients developed choroidal effusions, suprachoroidal hemorrhage, or infections associated with an exposed segment of ripcord in the inferior fornix.

Conclusions: The intraoperative placement of 3-0 Prolene ripcords to partially occlude the lumen of BGI-350s may serve as a useful strategy to safely optimize and sustain postoperative IOP control, prevent hypotony, allow for improved patient outcomes.

CONTROL ID: 3711752

SUBMITTER (NAME ONLY): Jamel Corredores Dieb

TITLE: Uveitis in children: the role of biological agents in its management

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Corredores Dieb, R. AMER, Hadassah Medical Center Department of Ophthalmology, Jerusalem, Jerusalem, ISRAEL|

Commercial Relationships Disclosure: Jamel Corredores Dieb: Commercial Relationship: Code N (No Commercial Relationship) | RADGONDE AMER: Commercial Relationship(s);Code R (Recipient):Abbvie

ABSTRACT BODY:

Purpose: To determine the efficacy and long-term effects of biological agents in the management of chronic pediatric uveitis

Methods: Retrospective review of medical charts of patients of a single academic referral center.

Results: Included were 48 patients (80 eyes), of whom 33 were females (68.7%). Mean age at time of diagnosis of uveitis was 7.3±4.0 years. At baseline (time when biologic therapy was initiated), all patients had active uveitis: 28 had anterior uveitis (58%), 12 had intermediate uveitis (25%) and 8 had posterior or panuveitis (17%). Uveitis was bilateral in 32 (66.6%) patients. Mean total follow-up was 4.9±2.8 years and mean follow-up after baseline was 39±31.5 months. Complete control of ocular inflammation was achieved with the first biologic medication in 86.2% (n=69) of eyes. 7 patients (14.5%) required to switch to another biologic agent. The most commonly used biologic agent was adalimumab in 43 patients (89.5%). Mean logMAR BCVA at baseline was 0.23 ±0.44 (range 2 to -0.1 logMAR), it was 0.15±0.39 at 12 months of follow- up and remained stable at 24 months, with a mean logMAR BCVA of 0.18±0.41. At baseline, mean dose of prednisone was 13.7±13.4 mg/day and it significantly decreased to 4.4±2.8 mg/day and 2.8±2.8 mg/day at 12 and 24 months of follow-up, consecutively. At baseline, 66.6% (n=32) of patients were dependent on oral corticosteroids and this decreased to 30.2% (n=13) at 12 months and to 21.8% (n=7) at 24 months. At baseline, 34 (42.5%) eyes used topical steroids, at a mean dose of 1.04±1.77 drops/day and this decreased at 12 months to 4 eyes (6.3%), at a mean dose of 0.14±0.47 drops/day and remained stable at 24 months. After starting biologic therapy, 19 eyes (23.7%) experienced flare, at an average time of 10.34±11.76 months (range 5 to 24 months), of which; 14 eyes (73.6%) were treated with adalimumab and 5 eyes (26.4%) with infliximab. Rate of treatment failure was 10.4% (5 patients), 2 treated with adalimumab and 3 with infliximab.

Conclusions: Uveitis was effectively controlled in 86.25% of children. The use of biologic agents enabled stabilization of visual acuity and significantly exerted oral and topical corticosteroid-sparing effect.

CONTROL ID: 3711753

SUBMITTER (NAME ONLY): Teele Palumaa

TITLE: Late chronotype is positively associated with myopia and hyperopia

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Palumaa, E. Abner, N. Taba, M. Teder-Laving, T. Esko, Estonian Genome Centre, Tartu Ulikool, Tartu, Tartumaa, ESTONIA|T. Palumaa, Eye Clinic, AS Ida-Tallinna Keskhaigla, Tallinn, Harjumaa, ESTONIA|N. Taba, Institute of Molecular and Cell Biology, Tartu Ulikool, Tartu, Tartumaa, ESTONIA|T. Esko, Broad Institute, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Teele Palumaa: Commercial Relationship: Code N (No Commercial Relationship) | Erik Abner: Commercial Relationship: Code N (No Commercial Relationship) | Nele Taba: Commercial Relationship: Code N (No Commercial Relationship) | Maris Teder-Laving: Commercial Relationship: Code N (No Commercial Relationship) | Tõnu Esko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Increasing evidence suggests that circadian rhythms modulate the development of refractive errors. This retrospective, observational cross-sectional study aimed to uncover the associations between circadian rhythms and refractive errors by analysing the chronotype or morning-evening preference of people with myopia and hyperopia.

Methods: 23,112 participants of the Estonian Biobank who had completed the Munich Chronotype Questionnaire (MCTQ) before the age of 70 were included in the analysis (35% male, aged between 17-69, median age 39 years). Chronotype was defined as the mid-point of sleep on non-working days adjusted for sleep deficit on workdays (MSFsc). The participants' electronic health records were enquired for the diagnoses of myopia and hyperopia (ICD-10 codes H52.1 and H52.0, respectively). The dataset was filtered for participants who had been diagnosed with both refractive errors. Only those who had received one of these diagnoses on at least two separate occasions were considered as having the corresponding refractive error. A logistic regression model was fitted with the outcome as myopia or hyperopia; and MSFsc, age, sex, and time people reported to spend outdoors as covariates.

Results: 4,951 participants with myopia and 2,865 with hyperopia were identified in the study population. The median MSFsc for those diagnosed with myopia was 3.9 (interquartile range, IQR 3.2–4.7), for those with hyperopia 3.3 (IQR 2.6–3.9) and those without myopia or hyperopia 3.7 (IQR 3.0–4.4). After adjusting for age, sex and time people reported spending outdoors, those with higher MSFsc (later chronotype) were more likely to be myopes (OR = 1.16, 95% CI 1.12–1.19, p = 1.53E-18). Interestingly, higher MSFsc was also positively associated with hyperopia (OR = 1.07, 95% CI 1.02–1.12, p = 0.004).

Conclusions: We demonstrate that later chronotype is positively associated with myopia and hyperopia. With access to the genomic information of the Estonian Biobank participants, further genomic analyses will reveal the potential molecular basis for these associations.

CONTROL ID: 3711754

SUBMITTER (NAME ONLY): Kaiyue Teng

TITLE: Characterisation of phosphorylation sites of PERP and their function in regulation of apoptosis in uveal melanoma

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Teng, L.I. Paraoan, Department of Eye and Vision Science, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Liverpool, UNITED KINGDOM|I. Prior, Department of Molecular Physiology and Cell Signalling, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Liverpool, UNITED KINGDOM|

Commercial Relationships Disclosure: Kaiyue Teng: Commercial Relationship: Code N (No Commercial Relationship) | Ian Prior: Commercial Relationship: Code N (No Commercial Relationship) | Luminita Paraoan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: PERP (p53 apoptosis effector related to PMP-22) is an apoptosis-specific p53 effector downregulated in uveal melanoma. This study aimed to investigate post translational modifications of PERP and evaluate their effect on PERP regulation in relation to induction of apoptosis.

Methods: Possible phosphorylation sites were predicted by in silico analysis and halo-tag system was used to generate Halo-PERP, Halo-PERP S46A and Halo-PERP S192A constructs. Halo-tagged proteins were pulled-down from transfected human melanoma mel202 cell lysate and analysed by immunoblotting alongside caspase 3 protein forms. Flow cytometry was used to evaluate apoptosis levels in transfected mel202 cells.

Results: Phosphorylation of serine residues of PERP was identified by specific immunoblotting. Two possible phospho-serine sites, S46 and S192, were identified by in silico analysis. Western blotting showed phosphorylated bands were maintained on PERP S192A-transfected mel202 cell lysates pull-downs and not on PERP S46A-transfectants. However, the apoptosis level determined by flow cytometry was lower in Halo-PERP S192A-expressing cells compared with Halo-PERP and Halo-PERP S46A-expressing cells, consistent also with the respective expression levels of caspase 3.

Conclusions: PERP is phosphorylated on S46 residue. However, this mutant does not appear to be involved in regulation of apoptosis. Instead, given its location in the extracellular loop, it is likely to be involved in the stability of the desmosome complex and therefore possibly linked to migratory properties of uveal melanoma cells. Intriguingly, PERP S192A mutant associates with decreased apoptosis suggesting its involvement in the p53 related apoptosis through a different mechanism.

CONTROL ID: 3711756

SUBMITTER (NAME ONLY): Ruti Sella

TITLE: The association between pupil diameter and apparent chord mu length value

SESSION TITLE: Cataract surgery 1

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sella, K. Shouchane-Blum, O. Reitblat, I. Bahar, Ophthalmology, Rabin Medical Center, Petah Tikva, ISRAEL|R. Sella, K. Shouchane-Blum, O. Reitblat, I. Bahar, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|

Commercial Relationships Disclosure: Ruti Sella: Commercial Relationship: Code N (No Commercial Relationship) | Karny Shouchane-Blum: Commercial Relationship: Code N (No Commercial Relationship) | Olga Reitblat: Commercial Relationship: Code N (No Commercial Relationship) | Irit Bahar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Chord mu length represents the distance between the pupil center and the visual axis. It is considered a new reference marker for evaluation before implantation of diffractive multifocal intraocular lenses (IOLs). Previous studies suggested that multifocal IOLs should be well considered in patients with an apparent chord mu length greater than 0.6, as it may be associated with a higher incidence of halos and glare. This value can be measured by a routine biometry prior cataract surgery, using the IOL Master 700 device (Carl Zeiss Meditec, AG). Pupil diameter can vary in different patients and measure differently for the same patient at different light conditions. The purpose of this study was to evaluate the correlation between apparent chord mu length and pupil diameter.

Methods: This prospective study evaluated patients scheduled for an elective cataract surgery at a single tertiary medical center between 2021-2022. Pupil diameter and Chord mu length, in photopic condition, before and after pupil dilatation (by administering a drop of mydramide 0.5% and a drop of cyclophentolate 1%, twice, 10 minutes apart), were measured using the IOL master 700. Exclusion criteria were visual acuity worse than 20/100 and pseudophakia. Wilcoxon signed-rank was used to compare the change in chord mu length.

Results: Forty-nine eyes of 49 patients were included. Mean ± SD pupil diameter, before and after pupil dilatation was 3.11 mm ± 0.83 and 6.66 mm ± 1.14 ($p<0.001$), respectively. Chord mu length increased from 0.322 mm ± 0.22 to 0.44 mm ± 0.25 ($p=0.001$), respectively.

Conclusions: Chord mu length significantly increases after pharmacological pupillary dilatation. This should be taken into consideration in preoperative planning, especially when the apparent chord mu value is taken into account for patient selection in cases of a planned multifocal IOL.

CONTROL ID: 3711757

SUBMITTER (NAME ONLY): David Boyer

TITLE: The safety of APX3330, an oral drug candidate for the treatment of diabetic eye disease, in the ongoing masked 24-week ZETA-1 Phase 2 clinical trial

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.S. Boyer, Ophthalmology, Retina Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|M. Brigell, A. Kolli, K. Rahmani, A. Lazar, M. Sooch, R. Patel, E. Lazar, J.S. Pepose, M.R. Kelley, Ocuphire Pharma, Inc., Farmington Hills, Michigan, UNITED STATES|

Commercial Relationships Disclosure: David Boyer: Commercial Relationship(s);Code S (non-remunerative):Ocuphire Pharma Inc.;Code I (Personal Financial Interest):Allegro;Code I (Personal Financial Interest):DigiSight;Code C (Consultant/Contractor):4D Molecular Therapeutics;Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Achillon Pharma;Code C (Consultant/Contractor):Acucela;Code C (Consultant/Contractor):Adverum Biotechnologies | Mitch Brigell: Commercial Relationship(s);Code C (Consultant/Contractor):Ocuphire Pharma Inc. | Ajay Kolli: Commercial Relationship(s);Code C (Consultant/Contractor):Ocuphire Pharma Inc. | Kavon Rahmani: Commercial Relationship(s);Code C (Consultant/Contractor):Ocuphire Pharma Inc. | Audrey Lazar: Commercial Relationship: Code N (No Commercial Relationship) | Mina Sooch: Commercial Relationship(s);Code E (Employment):Ocuphire Pharma Inc. | Ronil Patel: Commercial Relationship(s);Code E (Employment):Ocuphire Pharma Inc. | Eliot Lazar: Commercial Relationship(s);Code C (Consultant/Contractor):Ocuphire Pharma Inc. | Jay Pepose: Commercial Relationship(s);Code C (Consultant/Contractor):Ocuphire Pharma Inc. | Mark Kelley: Commercial Relationship(s);Code C (Consultant/Contractor):Ocuphire Pharma Inc.

ABSTRACT BODY:

Purpose: APX3330 is a novel, small molecule inhibitor of Ref-1, a transcriptional regulator of key angiogenic (VEGF) and inflammatory signaling pathways relevant to diabetic retinopathy (DR), diabetic macular edema (DME), and neovascular age-related macular degeneration (AMD). In over 300 subjects in 11 prior Phase 1 and Phase 2 clinical trials, oral APX3330 demonstrated a favorable safety and tolerability profile with doses up to 600mg over multiple months in healthy subjects, hepatitis patients, and solid tumor patients. The most common related adverse events (AEs) were mild diarrhea or soft stool (4% with APX3330, 2% with placebo) and mild rash or pruritis (4% with APX3330, 1% with placebo). This abstract reports the masked safety and tolerability of APX3330 in the ongoing 24-week ZETA-1 Phase 2 clinical trial.

Methods: The ZETA-1 trial is a randomized, placebo-controlled, double-masked, multi-center study designed to evaluate the efficacy and safety of oral APX3330 600mg daily dose over 24 weeks in DR patients. Safety data for 35 masked subjects who have been randomized to APX3330 or placebo has been evaluated and summarized, which represents over 1,500 total subject exposure days.

Results: In both trial arms, there have been 28 AEs reported in 16 (46%) of subjects. No adverse events have been thought to be related to the oral study medication, aside from two episodes of diarrhea in the same subject. Five serious AEs have been reported, all designated unrelated to study medication (2 cellulitis, 1 abnormal involuntary movement; before dosing 1 CAD and 1 osteomyelitis). Only 2 subjects have withdrawn from the trial due to non-serious AEs (vasovagal near syncope and worsening diabetic macular edema). With oral administration, no significant organ toxicity (liver, heart, kidney, brain, lung), no vital sign abnormalities (blood pressure and heart rate), and no rash were observed.

Conclusions: Similar to prior trials in healthy subjects, cancer patients, and hepatitis patients, oral administration of APX3330 and placebo have demonstrated a favorable ophthalmic and systemic safety and tolerability profile. Addition safety data from the ongoing ZETA-1 trial will be evaluated to further characterize the efficacy and safety of APX3330 for the oral treatment of diabetic eye diseases.

CONTROL ID: 3711760

SUBMITTER (NAME ONLY): Michael Belkin

TITLE: GLAUrious, a multicentre, randomised, controlled non-inferiority study of direct selective laser trabeculoplasty in open angle glaucoma

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Belkin, Eye Research Institute, Tel Aviv University, Tel Aviv, ISRAEL|M. Belkin, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|

Commercial Relationships Disclosure: Michael Belkin: Commercial Relationship(s);Code C (Consultant/Contractor):Belkin Vision;Code I (Personal Financial Interest):Belkin Vision;Code P (Patent):Belkin Vision;Code C (Consultant/Contractor):NovaSight;Code I (Personal Financial Interest):NovaSight;Code P (Patent):NovaSight;Code P (Patent):SpringVision;Code C (Consultant/Contractor):SpringVision

ABSTRACT BODY:

Purpose: Effective first-line treatment of open-angle glaucoma (OAG) is currently limited by non-adherence to daily topical hypotensive medication and by lack of access to selective laser trabeculoplasty (SLT). A worldwide need therefore exists for evidence-based, cost-effective, and widely accessible treatment options for OAG, with convenient modes of administration to maximise adherence to treatment and improve long-term outcomes. Direct selective laser trabeculoplasty (DSLT) is a novel, automated, non-contact procedure in which SLT-like laser beams are delivered to the limbus to reduce intraocular pressure (IOP) in patients with OAG, that can be administered within seconds, without the use of a gonioscope and the need for the specialised training required for traditional SLT. GLAUrious (NCT03750201) is a confirmatory clinical trial to assess the safety and efficacy of DSLT, compared with conventional SLT, in patients with OAG.

Methods: In this evaluator-masked, randomised, controlled, non-inferiority study, patients aged ≥40 years with ocular hypertension or OAG, including exfoliative or pigmentary glaucoma, and untreated/washout IOP 22–35 mmHg were recruited between November 2018 and April 2021 at 13 ophthalmology centres in the United Kingdom, Italy, Israel, and the Republic of Georgia. Eligible patients were randomised 1:1 to receive DSLT or SLT. The primary outcome was between-group difference in mean IOP change from baseline to 6 months. Secondary 6-month outcomes were: proportion of patients with ≥20% reduction in unmedicated IOP from baseline; change in mean number of topical hypotensive medications from screening. Rates of adverse events in each treatment group were also evaluated.

Results: A total of 192 patients were randomised to receive treatment, 98 with DSLT and 94 with SLT. Baseline patient and eye characteristics were similar between treatment groups. Primary and secondary endpoints for non-inferiority of DSLT, compared with SLT, at 6-month follow-up will be presented.

Conclusions: The results of the GLAUrious study are expected to support use of DSLT as a widespread, convenient modality that can provide fast, effective laser treatment for OAG across a broad range of clinical settings.

CONTROL ID: 3711761

SUBMITTER (NAME ONLY): Leyla Mirzaee

TITLE: Age-Dependent Perception of Ocular Pain and its Differential Impact on Quality of Life Dimensions

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Mirzaee, M. Posarelli, P. Hamrah, Ophtalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Leyla Mirzaee: Commercial Relationship: Code N (No Commercial Relationship) | Matteo Posarelli: Commercial Relationship: Code N (No Commercial Relationship) | Pedram Hamrah: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular discomfort and pain are one of the most common reasons for ophthalmic consultations. This study aims to assess the age-dependent patient perception of ocular pain and to measure its impact on different health-related quality of life (QoL) dimensions.

Methods: A prospective, single-center, cohort study was conducted with (N= 285) patients with and without corneal and ocular surface pain who completed the multi-dimensional ocular pain assessment survey (OPAS) at an initial and one follow-up visit. The calculation comprises N=127 patients diagnosed with corneal or ocular surface pain who completed at least one item of the pain scales on the OPAS questionnaire. The OPAS comprises somatic (vision-related), social and psychological dimensions of QoL through six items. The age groups were determined as group 1 which includes patients aged 18-40, group 2 comprises ages 41-60 and group 3 considers age 61-80. For the statistical analysis, IBM SPSS Statistics for Windows was used.

Results: The mean age of study patients was 48.42 (± 16.19), ranging from 18 to 80 years. The level of eye pain intensity when it is most was 2 (IQR 0-4) (in the past 24 hours) and 3 (IQR 1-5) in the past 2 weeks. The interference of pain on QoL dimension (0-10 scale) among all ages was 5 (IQR 1-8) for reading/computer use, 4 (IQR 1-8) for driving/TV watching, 2 (IQR 0-6) for general activity, 4 (IQR 0.75-7) for mood, 2 (IQR 0-6) for sleep, and 3 (IQR 0-7) for enjoying life/relationship with other people. The interference of pain on all QoL dimensions was statistically significant: reading/computer ($R= 0.473$; $p< 0.001$), driving/TV watching ($R= 0.459$; $p< 0.001$), general activity ($R= 0.461$; $p< 0.001$), mood ($R= 0.498$; $p< 0.001$), sleep ($R= 0.477$; $p< 0.001$), enjoying life/relationship ($R= 0.477$, $p< 0.001$). Furthermore, the effect of age on pain perception increased in patients of groups 2 and 3, as compared to age group 1. The pain interference on the vision-related dimensions of QoL in age groups 2 and 3 was lower compared to age group 1. Age group 1 was most affected by the psychological (mood) and social dimensions (life relation) of QoL.

Conclusions: The current study demonstrates that ocular pain interferes with all QoL dimensions, particularly with the vision-related QoL dimensions. Older patients report stronger levels of eye pain than younger patients, althouh this has a lower impact on their QoL.

CONTROL ID: 3711762

SUBMITTER (NAME ONLY): Marco Ruggeri

TITLE: Longitudinal changes in thickness of the aging human lens measured with OCT

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Ruggeri, Y. Chang, L. Rohman, B. Maceo Heilman, F. Cabot, S.H. Yoo, A. Ho, J. Parel, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Ruggeri, Y. Chang, L. Rohman, B. Maceo Heilman, F. Manns, Department of Biomedical Engineering, College of Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|I. Cabeza, Aragón Institute of Engineering Research (i3A), Universidad de Zaragoza, Zaragoza, Aragón, SPAIN|F. Cabot, S.H. Yoo, Ann Bates Leach Eye Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|A. Ho, J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Marco Ruggeri: Commercial Relationship(s);Code P (Patent):US patent 8,425,037 | Yu-Cherng Chang: Commercial Relationship: Code N (No Commercial Relationship) | Iulen Cabeza: Commercial Relationship: Code N (No Commercial Relationship) | Leana Rohman: Commercial Relationship: Code N (No Commercial Relationship) | Bianca Maceo Heilman: Commercial Relationship: Code N (No Commercial Relationship) | Florence Cabot: Commercial Relationship: Code N (No Commercial Relationship) | Sonia Yoo: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Ho: Commercial Relationship: Code N (No Commercial Relationship) | Jean-Marie Parel: Commercial Relationship(s);Code P (Patent):US patent 8,425,037 | Fabrice Manns: Commercial Relationship(s);Code P (Patent):US patent 8,425,037

ABSTRACT BODY:

Purpose: Continuous growth of the lens in adulthood produces age-related increase in lens thickness and curvature which impact the lens power. Previous studies on biometry of the aging lens are cross-sectional. In this study, we quantify the longitudinal changes in thickness of the aging human lens using OCT.

Methods: This retrospective study evaluates lens biometry data from 10 eyes of 5 subjects (Age at the initial visit: 21, 26, 30, 34 and 42 years) acquired with a custom-built OCT system at variable intervals between sessions (6.5 months on average) over about 10 years. The system combines a fixation target with adjustable vergence and a SD-OCT system that enables imaging from the anterior corneal surface to the posterior crystalline lens (Ruggeri et al, Biomed Opt Exp 2012). Each OCT dataset consists of at least three images of the lens sequentially acquired across the horizontal meridian of the eye without repositioning the system. All images were acquired with the fixation target adjusted to a vergence of 0 D (distance). For each eye and time point, three consecutive OCT images extracted from the same dataset were processed to manually select the lens surface boundaries and calculate the lens thickness. The processing relies on peak detection of the average reflectivity profile of the lens over the 0.5 mm zone. The lens thickness was obtained from the optical path length assuming a uniform refractive index for the lens (n = 1.415). The average lens thickness across the three measurements was then calculated. Linear regression was used to describe the change in average lens thickness with age. All eyes were included in the analysis.

Results: As expected, the lens increases in thickness with age (Figure A) in all subjects (Age 21: R^2=0.704, P=0.002; Age 26: R^2=0.9996, P=0.039; Age 30, R^2=0.939, P<0.001; Age 34: R^2=0.973, P<0.001 and Age 42, R^2=0.960, P=0.001) of on average 28 µm/year (range 21 to 42 µm/year) (Figure B), which is consistent with findings from cross-sectional studies using Scheimpflug imaging (Dubbelman et al, Optom Vis Sci 2001). The increase in lens thickness was on average greater in the two oldest subjects (36 vs 21 µm/year), suggesting the lens grows faster in incipient presbyopia (Figure A).

Conclusions: We used OCT to quantify the longitudinal increase in crystalline lens thickness over 10 years in 5 adult subjects. The preliminary data suggest a faster growth of the lens in incipient presbyopia.

CONTROL ID: 3711764

SUBMITTER (NAME ONLY): Ali Djalilian

TITLE: In-Situ Repair of Corneal Stroma using A Light-Curable Hydrogel from Porcine Corneal Extracellular Matrix

SESSION TITLE: Corneal stromal biology, wound healing modulators, and regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.R. Djalilian, G. Yazdanpanah, X. Shen, T.T. Nguyen, K. Anwar, M. Rosenblatt, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|O. Jeon, T. Shokuhfar, E. Alsberg, Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|Y. Jiang, M. Pachenari, Y. Pan, Department of Mechanical and Industrial Engineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: A Light-curable COrnea Matrix (LC-COMatrix) derived from decellularized corneal extracellular matrix was fabricated. LC-COMatrix application to repair corneal stromal defects was evaluated ex-vivo and in vivo.

Methods: The LC-COMatrix was produced from porcine cornea by decellularization, digestion, and methacrylation. The in-situ cross-linking was achieved by combination of LC-COMatrix with a photo-initiating cocktail and curing with visible light (520 nm). The biodegradation, swelling behavior, viscosity, and rheological gelation kinetics of LC-COMatrix were studied. The adhesion-strength, burst-pressure (BP) following perforation repair, and tissue adhesiveness of LC-COMatrix were assessed ex-vivo using human corneas as substrate and compared to fibrin glue (FG) and 20% gelatin methacrylate (GelMA). The potential of LC-COMatrix to repair corneal stromal defects and full-thickness perforations was examined in a rabbit model.

Results: LC-COMatrix has proper swelling behavior, biodegradation, and viscosity for user-friendly corneal repair applications. The storage modulus of LC-COMatrix is 7.8±0.5kPA and is higher than FG (4.8±0.3kPa) and GelMA (5.1±3.2kPa). The adhesion-strength of LC-COMatrix is 21.8±2.3kPa which is significantly higher than that of GelMA (11.1±3.8kPa, $p<0.0001$) and FG (4.9±2.3 kPa, $p<0.0001$). The BP of a 2 mm perforation made by punch-biopsy and repaired with LC-COMatrix is 327±175 mmHg, while this value for GelMA is 151±48 mmHg ($p=0.007$) and for FG is 11±4 mmHg ($p<0.0001$). LC-COMatrix consistently repaired a human corneal stromal defect (10 mm diameter, 300 μm depth) and remained stable for 30 days with a smooth surface and comparable transparency to native human corneas. However, the FG degraded by day 15. In the corneal defects repaired with GelMA, the hydrogel shrank to the center of the corneal stromal defect during follow-up. Moreover, LC-COMatrix successfully integrated and repaired 3-mm lamellar defect in rabbit corneas which the epithelium regenerated, and the defect area remained transparent at 28 days follow-up. Additionally, the corneal macro-perforation (1-mm) in rabbit cornea was repaired with LC-COMatrix with healed epithelium and no subsequent leakage for 28 days.

Conclusions: LC-COMatrix is a natural ready-to-apply bio-integrating adhesive that is representative of the native corneal matrix with potential applications in corneal and ocular surgeries.

CONTROL ID: 3711767

SUBMITTER (NAME ONLY): Benjamin Soares

TITLE: Comparison of giant vacuole type and size in the inner wall endothelium of Schlemm's canal in human eyes perfused at 7 and 15 mmHg using serial block-face scanning electron microscopy

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Soares, D.L. Swain, T.D. Le, S. Yasmin, B. Fernandes, I. Dasgupta, T. Valerio, I. Zhao, H. Gong, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|D.L. Swain, H. Gong, Anatomy and Neurobiology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study investigated differences in the types and size of giant vacuoles (GVs) at 7 mmHg (physiological pressure in enucleated eyes) and an elevated pressure of 15 mmHg in the inner wall endothelium of Schlemm's canal (SC), using serial block-face scanning electron microscopy (SBF-SEM) and subsequent three-dimensional (3D) reconstruction of GVs.

Methods: Four normal human eyes from four donors were perfused, two at 7 mmHg and two at 15 mmHg, with fluorescent tracers to label the segmental outflow pattern followed by perfusion-fixation. Three radial wedges of tissue including SC from high-, low-, and non-flow areas of each eye based on tracer distribution was processed for SBF-SEM. A similar number of images was analyzed at 7 mmHg (9586) and 15 mmHg (9802). GVs were counted and typed (Type I: no basal opening or I-pore, Type II: basal opening, no I-pore, Type III: I-pore, no basal opening, and Type IV: basal opening and I-pore). A subset of GVs was randomly selected for 3D reconstruction to measure GV volume. For the reconstructed type II GVs, thickness of cellular lining around GVs was measured.

Results: There was a greater number of GVs at 15 mmHg (3302) compared to 7 mmHg (1312). Type IV GVs were more abundant in the high-flow than non-flow areas at both pressures ($P<0.01$). GVs with I-pores were significantly larger than GVs without I-pores in all flow-type areas at both pressures ($P<0.01$). For GV volume across all flow-type areas, GVs with I-pores were not significantly different between pressures. However, GVs without I-pores were significantly larger in volume at elevated pressure ($P<0.01$). Type II GVs had thinner cellular lining at 15 mmHg ($P<0.01$).

Conclusions: SBF-SEM and 3D reconstruction allowed for accurate identification of GV types and size. Comparing both pressures, the volume of GVs with I-pores were similar, while the volume of GVs without I-pores were larger at elevated pressures. This may indicate a threshold size of GVs for pore formation. GVs with I-pores were significantly larger than GVs without I-pores in all flow-type areas at both pressures suggesting that larger size of GVs is a contributing factor for GV-associated I-pores. More Type IV GVs observed in the high-flow areas at both pressures suggest increasing this type of GV may increase the total high-flow area.

CONTROL ID: 3711768

SUBMITTER (NAME ONLY): Connor Ross

TITLE: Conversion Rates from Non-exudative to Exudative Age-Related Macular Degeneration: An AAO IRIS Registry Analysis

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Ross, D. Gong, N. Hall, T. Elze, L. Sobrin, J.W. Miller, A. Lorch, J.B. Miller, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|C. Ross, D. Gong, N. Hall, T. Elze, L. Sobrin, J.W. Miller, A. Lorch, J.B. Miller, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study examined conversion rates from non-exudative (dry) to exudative (wet) age-related macular degeneration across different patient populations using real-world data from the AAO IRIS Registry (Intelligent Research in Sight).

Methods: A retrospective cohort analysis was conducted using the IRIS Registry spanning 2016-2019. A total of 2,664,789 patients with dry AMD in at least one eye were included in this study. Observed patient characteristics including age, sex, race, geographic region, and smoking status; dry and wet AMD stage; and conversion time from dry to wet AMD. Descriptive statistics and hazard ratios (HRs) from a Cox proportional hazard model were conducted across these characteristics.

Results: Overall conversion rates from dry to wet AMD were 2.0, 6.1, and 6.7% for early, intermediate, and advanced stages respectively ($p<0.001$). Among those converting to wet AMD, there was decreased risk for males relative to females (HR 0.89, 95% CI [0.88, 0.89]) and Asians (HR 0.52, 95% CI [0.50, 0.54]) or Blacks/African-Americans (HR 0.39, 95% CI [0.37, 0.40]) relative to whites. Relative to patients with bilateral dry AMD, those with wet AMD in one eye and dry in the other eye (HR 5.65, 95% CI [5.56, 5.75] and those with unilateral dry AMD (HR 3.60, 95% CI [3.57, 3.63] had a higher risk of conversion for the eye with dry AMD. Relative to patients with early dry AMD, those with intermediate dry AMD (HR 2.46, 95% CI [2.41, 2.51] and advanced dry AMD (HR 2.69, 95% CI [2.61, 2.77]) had a higher risk of conversion. Among patients with dry AMD in one eye and wet AMD in the other eye, compared with having active choroidal neovascularization in one eye, those with wet AMD with inactive choroidal neovascularization (HR 0.60, 95% CI [0.56, 0.64]) and wet AMD with inactive scar (HR 0.58, 95% CI [0.53, 0.62]) in one eye had a lower risk of conversion to wet AMD in the fellow eye.

Conclusions: In this cohort analysis of the IRIS Registry, females, whites, and smokers had higher risk of conversion from dry to wet AMD. Patients with one eye with wet AMD and one eye with dry AMD and patients with unilateral dry AMD were more likely to convert than patients with bilateral dry AMD. More advanced stages of dry AMD and active choroidal neovascularization in the fellow eye were associated with higher risk of conversion.

CONTROL ID: 3711769

SUBMITTER (NAME ONLY): Nihaal Mehta

TITLE: Association between Progression and Systemic Beta Blocker Use Among Patients with Intermediate Age-Related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Mehta, I. Marin, Z. Gill, J.L. Patnaik, M. Mathias, N. Manoharan, A. Palestine, A.M. Lynch, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Beta-adrenergic blockade has been shown in non-human models to have anti-VEGF effects including choroidal neovascularization (CNV) regression. However, previous clinical studies of age-related macular degeneration (AMD) patients have shown conflicting results in the association between beta blocker (BB) use and clinically significant changes in neovascularization or AMD progression. We performed a novel analysis utilizing prospective data to investigate this question.

Methods: We analyzed intermediate AMD (iAMD) patients recruited into the University of Colorado AMD Registry. Grading of AMD stage was performed by two vitreoretinal specialists using multimodal imaging. At enrollment, baseline information was collected including the use of systemic BB medications. We compared the proportion of iAMD patients who were on a systemic BB at enrollment who did progress to advanced AMD with those who did not progress. We also compared the subset of converters to neovascular AMD and geographic atrophy (GA) and performed Kaplan-Meier (K-M) failure analyses to assess the risk of progression by BB use.

Results: 340 iAMD patients were included with a mean age of 75.5 (SD 11.6) and mean follow-up was 33.7 months. Eighty (23.5%) patients were using a systemic BB at time of enrollment. In total, 17.9% of patients converted to advanced AMD, 39 to NV and 24 to GA. There was no significant difference in the proportion of non-converters who were using a BB (24.0%), and those who did convert and were using a BB (21.3%) ($p = 0.652$) (Table 1). Conversion to neovascular AMD or GA was also not associated with decreased BB use (25.6% and 16.7%, $p = 0.741$ and 0.411, respectively). In K-M analysis, BB use was not associated with risk of conversion to advanced AMD ($p = 0.517$) (Figure 1) or to neovascular AMD ($p = 0.863$).

Conclusions: In this prospective AMD cohort, BB use at time of enrollment was not associated with risk of progression from intermediate to advanced AMD.

CONTROL ID: 3711770

SUBMITTER (NAME ONLY): Debarshi Mustafi

TITLE: The diversity of genetic testing platforms for inherited retinal diseases

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Mustafi, J.R. Chao, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|D. Mustafi, Ophthalmology, Seattle Children's Hospital, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate genetic testing platforms used to aid in the diagnosis of inherited retinal degenerations (IRDs). As clinical trials for other IRDs progress to treatment, genetic testing will be essential to properly identify patients who may benefit from intervention.

Methods: Data collected regarding targeted genetic panel testing for IRDs offered by different labs were investigated for inclusion of coding and non-coding variants in disease genes. Both large IRD panels and smaller, more focused disease specific panels were included in the analysis. The list of genes assayed by each IRD panel as well as inclusion of any non-coding variants was documented. The genomic location and name of each disease gene was documented across each panel. If non-coding variants were tested it was documented for the gene in question. This curated list was then compared to examine overlapping and unique genes across testing platforms.

Results: Across the three comprehensive IRD panel tests investigated, 404 unique genes are represented, of which 258 genes are tested by all three panels. The top 20 genes known to cause over 70% of all IRDs were represented in the 258 common genes tested by all three panels. In addition, 138 non-coding variants are assayed across the three platforms in 50 unique genes. Focused disease specific panels exhibited significant variability across the 5 testing platforms studied.

Conclusions: Ordering genetic testing for IRDs is not straightforward, as evidenced by the multitude of panels available to providers. It is important that there is coverage of both coding and non-coding regions in IRD genes to offer a diagnosis in these patients. This work details the diversity of testing platforms currently available to clinicians and provides a thorough explanation of genes tested in the different IRD panels. More importantly, this analysis highlights the commonalities and differences that separate these tests. In a time of increased importance for clinical genetic testing of IRD patients, knowledge of the proper test to order is paramount.

CONTROL ID: 3711771

SUBMITTER (NAME ONLY): Jason Slakter

TITLE: Efficacy and Safety of OPT-302 in combination with Ranibizumab for Polypoidal Choroidal Vasculopathy

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor-C and D (VEGF-C/-D) are angiogenic mediators which may contribute to treatment escape with VEGF-A suppression of retinal disease. The aim of this investigation was to assess combination therapy of OPT-302 (anti-VEGF-C/-D) with ranibizumab (anti-VEGF-A) for the treatment of polypoidal choroidal vasculopathy (PCV).

Methods: Prespecified subgroup analysis of a Phase 2b, randomized, sham-controlled study of OPT-302 administered to treat neovascular age-related macular degeneration (NCT03345082). Participants in the subgroup analysis had PCV identified in the study eye by masked readers at a central reading center. Polyps were identified and defined using multimodal imaging, including fundus photography (subretinal orange nodules), fluorescein angiography (typical primarily occult multifocal lesions) and spectral domain optical coherence tomography (notched, sharply peaked or multi-lobular pigment epithelial detachments with or without a ring of hyperreflectivity along the inner border). Eyes were randomized to receive 6-monthly intravitreal injections of either ranibizumab (0.5 mg) + OPT-302 (0.5 mg or 2 mg) or ranibizumab + sham. Outcomes measures included best-corrected Early Treatment Diabetic Retinopathy Study visual acuity (BCVA), anatomic changes, and safety / tolerability.

Results: Sixty-six participants with PCV were included. OPT-302 with ranibizumab was well tolerated, consistent with the full study population, with no clinically significant safety findings. The mean BCVA change from baseline to week 24 showed a dose response in participants with PCV, who gained 13.5 letters in the 2 mg OPT-302 combination group (n = 22), 10.9 letters in the 0.5 mg OPT-302 combination group (n = 24) and 6.9 letters in the ranibizumab control group (n = 20). The +6.7 letters comparative superiority of 2 mg OPT-302 combination therapy over ranibizumab (p = 0.0253) was accompanied by a greater proportion of participants gaining ≥ 10 or ≥ 15 letters, fewer losing ≥ 5 letters and fewer with retinal fluid at week 24.

Conclusions: OPT-302 combination therapy was well tolerated, with greater improvements in BCVA and less retinal fluid compared to ranibizumab monotherapy in participants with symptomatic macular PCV. Larger studies of dual inhibition of VEGF-C/-D and VEGF-A for the treatment of PCV are warranted.

CONTROL ID: 3711772

SUBMITTER (NAME ONLY): Tiana Toribio

TITLE: Quantification of Unused Pharmaceuticals for Retrobulbar Blocks in Retina Surgeries at a Tertiary Care Hospital

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Toribio, U. Mian, J. Tauber, Montefiore Medical Center, Bronx, New York, UNITED STATES|A. Rai, J. Tauber, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify the impact of unused medications for the administration of retrobulbar blocks during retinal surgeries.

Methods: This prospective observational study of 8 consecutive cases performed by a single vitreoretinal surgeon was performed at Montefiore Medical Center, Bronx, NY in December 2021. Standard retrobular injection medications (single dose vials of 10mL of 0.75% bupivacaine and 5mL of 2% lidocaine) used for preparation of 1:1 10mL retrobulbar block were weighed (ounces) a. prior to opening, b. after medications were drawn up, c. a representative empty bottle was weighed. The quantity of the prepared block that was administered was noted. The quantity of medication that was ultimately used and left unused was quantified by weight and percent. Using the medication purchasing costs, the costs of the unused medications were calculated.

The environmental emissions and impacts from unused medications were calculated using the purchaser price model in the economic input-output life cycle assessment (EIO-LCA) model and the US Environmental Protection Agency's tool for the reduction and assessment of chemical and other environmental impacts (TRACI; version 2.1).

Results: On average, 0.29 oz of 0.75% bupivacaine (74.05%) and 0.11oz of 2% lidocaine (55.79%) were unused per case. On average, 5mL of the prepared 10mL were administered as a retrobulbar block. Costs and environmental emissions of unused medications are shown in Table 1 for a single case, for 100 cases and for 150 cases. Average cost of unused medications per case was $1.29, equating to 0.016 kg CO_2 emissions for pharmaceutical preparation manufacturing. For this surgeon at our institution (estimated 150 surgeries/year) approximately $193.61 for every $294 spent are wasted.

Conclusions: The cost and carbon footprint of unused medications from retrobulbar blocks from a single surgeon are relatively small but meaningful. There are an estimated 300,000 retinal surgeries performed annually in the US (Charles S. Retinal Physician, 2017), so the impact of this waste may be amplified when considered on a larger scale.

CONTROL ID: 3711773

SUBMITTER (NAME ONLY): Zhongdi Chu

TITLE: Automated machine learning for diagnosis of geographic atrophy and subfoveal involvement using real-world fundus autofluorescence and infrared reflectance images

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Chu, M. Mbagwu, D. Borka, A. Ramakrishnan, K. Khapare, C. Candano, A.Z. Torres, H. Kalvaria, M.T. Roe, T. Leng, Verana Health, California, UNITED STATES|M. Mbagwu, T. Leng, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|D. Borka, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a machine learning(ML) aided pipeline to automatically confirm geographic atrophy(GA) using real-world fundus autofluorescence(FAF) and infrared reflectance(IR) images linked to the IRIS Registry

Methods: The American Academy of Ophthalmology IRIS® Registry(Intelligent Research in Sight)is the nation's first comprehensive eye disease clinical database, with over 70% of US ophthalmologists contributing. A ML aided pipeline was developed for the IRIS Registry, using a de-identified clinicoimaging dataset with images contributed by 2 large retina practices, patients with a dry age-related macular degeneration(AMD) diagnosis were identified from 2006 to 2019. ML models were developed to assess FAF and IR image quality using features of signal, contrast, noise and sharpness. FAF images with a predicted quality score lower than 0.4[range: 0-1] were excluded. For patients with multiple images at the same encounters, or multiple encounters, the image with the highest quality score was selected. Lastly, training and testing sets were selected using patient-level stratified sampling(age, sex, and race) and labeled by a trained grader. Two deep learning models were developed to classify patients into three categories: no GA, GA without subfoveal involvement, and GA with subfoveal involvement. The models were trained on the training sets with an 80:20 split for training and validation. The trained models were then deployed on the entire cohort

Results: In total, 15,023 FAF and 16,470 IR images from 4,372 eyes of 2,248 patients were identified. After removing low quality images(1,931 FAF images) and multiple images from the same visit(6,825 FAF images, 8,285 IR images), 6,267 pairs of FAF and IR images from 3,372 eyes of 1,872 patients were included. A training set of 442 patients and a testing set of patients(one pair of FAF and IR images per patient) were selected from the cohort. A modified VGG network was developed for GA diagnosis. The model achieved an accuracy of 0.96, 0.96 and 0.94 for training, validation and testing, respectively. The second model for subfoveal involvement is under development

Conclusions: The proposed pipeline demonstrated satisfactory performance confirming GA in AMD eyes using images collected in routine practice. It could potentially be useful in screening patients for GA trials and future GA treatments

CONTROL ID: 3711775

SUBMITTER (NAME ONLY): Gary Hin-Fai Yam

TITLE: Human corneal stromal stem cells express microRNA-29a in exosomes – a robust cell selection for stem cell therapy of corneal scarring

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Yam, M. Santra, J.A. Sahel, J. Funderburgh, V. Jhanji, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|G. Yam, J.A. Sahel, V. Jhanji, University of Pittsburgh McGowan Institute for Regenerative Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal blindness due to scarring is treated with cornea transplantation. However, there exists a global challenge of donor material shortage. Preclinical and clinical studies have shown that cell therapies using corneal stromal stem cells (CSSC) suppress scar formation. However, not every CSSC batches achieve stromal regenerative effects. MicroRNA-29 is a “master fibro-regulatory miRNA”, with pivotal roles in regulating tissue fibrosis. Our group identified an upregulated expression of hsa-miR-29a in extracellular vesicles (EV) produced by human CSSC with good healing effects. This work examined miR-29a expression among CSSC batches, and the anti-scarring potency of cells was assessed with a mouse model of corneal injury. We aimed to design a quantitative tool to screen CSSC with healing potency for clinical applications.

Methods: EV fractions from conditioned media of human CSSC cultures (from n=13 donors) were harvested for small RNAs using miRNeasy protocol (Qiagen). The abundance of miR-29a and 16 (housekeeping EV-miRNA) was analyzed with Taqman RT-PCR assay (Thermo Fisher). Corneal stromal wound was induced by Algerbrush burring in Swiss-webster mice (n=18) and treated with human CSSC ($5x10^4$ cells) in fibrin gel. Corneas were examined by Spectral Domain OCT every 4 days and harvested at day 14 for scar evaluation and fibrosis marker expression analysis by qPCR and immunohistochemistry.

Results: The normalized levels of miR-29a expression were upregulated in EV fractions of HC540 and 641 and were low in HC572 and 618 ($P<0.05$, Mann-Whitney U test). On injured mouse corneas, topical treatment using HC540 and 641 (high miR-29a levels) nearly prevented corneal scarring, maintained normal corneal thickness, and lower expression levels of fibrosis genes (mouse collagen III, fibronectin, α-smooth muscle actin, and Thy-1). In contrast, treatment with HC618 and 572 (low miR-29a levels) resulted in thicker corneas with intense scarring, and upregulated fibrosis gene expression, similar to wound controls.

Conclusions: We demonstrated that EV-miR-29a expression could distinguish CSSC with anti-scarring quality, providing a tool to select suitable CSSC for clinical applications.

CONTROL ID: 3711776

SUBMITTER (NAME ONLY): Jianhua Wang

TITLE: Multi-center repeatability of macular capillary perfusion density using optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, A. Simms, H. Jiang, Ophthalmology, Bascom Palmer Eye Institute, Florida, UNITED STATES|S. Sadaghiani, G.K. Aguirre, J.A. Detre, Neurology, University of Pennsylvania Perelman School of Medicine, Pennsylvania, UNITED STATES|Y. Jiang, J.I. Morgan, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Pennsylvania, UNITED STATES|H. Jiang, Neurology, University of Miami Miller School of Medicine, Florida, UNITED STATES|P.M. Pattany, Radiology, University of Miami Miller School of Medicine, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the test-retest repeatability in quantifying macular capillary perfusion density (CPD) using optical coherence tomography angiography (OCTA) in a multi-center setting.

Methods: OCTA data was obtained in self-reported healthy subjects from Bascom Palmer Eye Institute at the University of Miami (UM, N = 18) and the University of Pennsylvania (UPenn, N = 25). OCTA was repeated at an interval of one week for assessment of repeatability (precision) in the same subjects. Analysis of OCTA-derived capillary perfusion density (OCTA-CPD) focused on the macula. Image processing procedures and fractal analysis developed in our lab were used to process OCTA data. Fractal analysis was performed on the skeletonized vascular images to yield vessel densities by box-counting in an annulus to fractal dimension (Dbox) yielding OCTA-CPD. Large vessel and microvessel network densities (D_{box}) as CPD of annuli (0.5-2.5 mm in diameter from 3 mm scans and 0.5 – 5.0 mm from 6 mm scans) in the total retinal vascular network (RVN), superficial (SVP), and deeper vascular plexuses (DVP) were analyzed. Repeatability was assessed by 3 measures: standard deviation (SD), coefficient of variation (CV) of repeated measures, and intraclass correlation coefficient (ICC).

Results: SD, CV, and ICC are listed in table 1. Both sites (UPENN and UM) had similar results. The CV% was about 0.5% which presents high measurement repeatability. However, the ICC was lower than expected, possibly due to the narrow CPD ranges in this healthy cohort. The ICC for the 3 mm scans was higher than that for the 6 mm scans from both sites.

Conclusions: While data collection and analysis are ongoing, our preliminary data showed high repeatability in both research sites, according to the CV. Scans with the 3 mm setting appear to be more repeatable.

CONTROL ID: 3711779

SUBMITTER (NAME ONLY): Daniela Rodrigues-Braz

TITLE: Therapeutic potential of combination treatment of mineralocorticoid receptor antagonist and glucocorticoids in a rat model of corneal neovascularization

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Corneal neovascularization (CN) is a major cause of vision loss worldwide. Steroids are widely used to treat CN, but the results are highly variable. Glucocorticoids act through binding to both glucocorticoid (GR) and mineralocorticoid receptors (MR). MR overactivation contributes to retinal and choroidal neovascularization, and endothelial MR invalidation reduces CN in mice. In a rat model of CN induced by limbal deficiency, MR antagonism also inhibits CN and upregulates GR expression tilting the GR/MR balance in favor of GR pathway. We thus aimed to evaluate the additive effects of MR antagonism combined with glucocorticoids for CN.

Methods: CN was induced in one eye of Lewis rats by a 360° circumstance total corneal de-epithelialization and limbal cell scratching. Rats were injected with systemic MR antagonist (MRA) spironolactone (SPL, 25mg/kg/day) or vehicle for 14 days alone or in combination with subconjunctival injection of dexamethasone (DEX, 4 mg/ml) at day 3 and 7 or triamcinolone acetonide (TA, 4 mg/ml) at day 3. Corneal morphology and thickness were assessed in vivo at day 3, 7 and 14 using Micron III optical coherence tomography (OCT). Corneal re-epithelialization was evaluated by fluorescein staining under slit lamp at day 3 and 7. Fluorescein (FA) and indocyanine green angiographies (ICG) were performed at day 14 to evaluate the surface of CN. Peripheral cornea and tissues adjacent to limbus were dissected at day 3, 7 and 14 for quantitative PCR and at day 3 and 7 for transcriptomic analysis.

Results: SPL combined with TA showed a greater anti-angiogenic and anti-inflammatory effect compared to SPL alone and improved the corneal re-epithelialization delayed by TA. The effect of combination treatment of SPL and DEX was not different from SPL alone. The transcriptomic analysis identified a greater number of differentially expressed genes in the combined treatment of SPL and TA than SPL or TA alone. Gene set enrichment analysis showed pathways involved in corneal wound healing and differentiation, infectious responses, inflammatory and immune responses, myogenesis, hypoxia, angiogenesis and neuroprotection, suggesting synergetic effects.

Conclusions: The combined treatment of MRA and TA has additive effects on CN and could be a potential therapeutic option for CN.

CONTROL ID: 3711780

SUBMITTER (NAME ONLY): Emmanuel Kobia-Acquah

TITLE: Prevalence of childhood myopia in Africa: a systematic review and meta-analysis

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kobia-Acquah, I. Flitcroft, G. Lingham, J. Loughman, Centre for Eye Research Ireland, Technological University Dublin, Dublin, Dublin, IRELAND|P. Akowuah, School of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myopia is a growing public health problem due to its association with sight-threatening conditions. In Africa, the problem is exacerbated by lack of ophthalmic services and spectacle coverage, such that uncorrected refractive error is the leading cause of vision impairment. This study was designed to provide contemporary and future estimates of childhood myopia prevalence in Africa.

Methods: A systematic online literature search (PubMed, Google Scholar, Cochrane Library, Africa Journals Online, Scopus) was conducted for articles on myopia (≤-0.50D or VA≤6/9.5 correctable with minus lenses) from 2001-2021 in Africa. Meta-analysis [OpenMeta (analyst)] was performed to estimate the prevalence of childhood myopia and high myopia. Freeman-Tukey double arcsine transformation was used to minimize the effects of high/low prevalence on the overall pooled estimates. Myopia prevalence from subgroup analysis for urban and rural settings were used as baseline for generating a prediction model using linear regression (SPSS V28).

Results: Forty studies from 19 (of 54) African countries were included in the meta-analysis (N=735400). Overall prevalence of childhood myopia and high myopia was 4.7% (95% CI: 3.8%–5.8%) and 0.4% (95% CI: 0.2%–0.8%), respectively (Fig 1). Prevalence of myopia from 2011-2020 was approximately double that from 2001-2010 for all studies combined and between 2 and 2.5 times higher for ages 5-11 and 12-18 years, for males and females and urban and rural settings, separately. Childhood myopia prevalence is expected to increase in urban settings to 11.1% by 2030, 14.4% by 2040, and 17.7% by the year 2050, marginally higher than expected in the overall population (16.4% by 2050) and noticeably higher than in rural settings (8.4% by 2050) (Fig 2).

Conclusions: Prevalence of childhood myopia has approximately doubled since 2010, with a further 3-fold increase predicted by 2050. This trend has potentially serious implications despite the comparatively low myopia prevalence in Africa. Provision of myopia control treatments is desirable, but implementing basic myopia prevention programs, enhancing spectacle coverage and ophthalmic services as well as generating more data to better understand the changing myopia epidemiology in Africa merit greater attention.

CONTROL ID: 3711782

SUBMITTER (NAME ONLY): Abbie Jensen

TITLE: Zebrafish models of Stargardt Disease reveal RPE and cone photoreceptor defects that suggest mechanisms of disease

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.M. Jensen, Molecular and Cell Biology Graduate Program, University of Massachusetts Amherst, University of Massachusetts Amherst, Amherst, MA, US, academic, Amherst, Massachusetts, UNITED STATES|A.M. Jensen, J. Willoughby, Biology, University of Massachusetts Amherst, Amherst, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Juvenile onset macular degeneration, Stargardt (STGD) disease, affects nearly 1:8,000 people and age-related macular degeneration (AMD) is the leading cause of vision loss in people over the age of 50. Both diseases arise primarily from the loss of cone photoreceptors. Recent advances in genome engineering technology and the cone-rich retina of the zebrafish model organism provides the powerful and unique opportunity to create macular degeneration disease models for developing new therapies to slow, prevent, or reverse cone photoreceptor degeneration and prolong vision.

Methods: STGD disease is most commonly caused by mutations in ABCA4. Using CRISPR/Cas9, we created double null mutants for the two zebrafish abca4 homologs (abca4a and abca4b) that also include transgenic fluorescent reporters for retinal pigmented epithelium (RPE) and UV cones. We examined aged retinas labeled with cone subtype specific markers and visualized lipofuscin.

Results: Our analyses of aged (17 month) abca4 double mutants reveals all cone outer segment (COS) subtypes are dysmorphic: green COSs appear longer and thinner, crumpled with ragged outlines; UV COS appear longer and thinner; red COSs are much longer; and blue COSs are distinctly dysmorphic. Rod outer segments appear normal in the mutants. RPE phagocytosis of all COS subtypes is altered, with fewer green, red, and blue phagosomes, but more UV phagosomes present in RPE cell bodies (while none are in wildtype (wt) RPE). abca4 double mutant RPE is dystrophic; showing loss of microvillar alignment and gaps/holes. COS quantification reveals reduced numbers and phagosome quantification (per COS) shows diminished RPE phagocytosis.

Lipofuscin accumulation is observed in STGD disease, but its causal relationship to degeneration is unclear. To examine lipofuscin in the zebrafish Stgd mutants, we used 4-channel laser scanning confocal (LSC) and Fluorescence lifetime imaging microscopy (FLIM). Few, if any, structures in the wt retina are consistent with fluorescence profiles expected for lipofuscin but in the abca4 double mutant, there are several large and bright structures in both the 'lipofuscin' confocal channel and FLIM.

Conclusions: This zebrafish Stgd model provides the unique opportunity to begin to identify and understand the cellular and molecular processes that contribute to cone degeneration in STGD and perhaps to AMD.

CONTROL ID: 3711783

SUBMITTER (NAME ONLY): Jenae Stutzman

TITLE: Clinical outcomes of infants with type 2 and low grade retinopathy of prematurity after discharge from the neonatal intensive care unit

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Stutzman, C. Fonteh, A.M. Lynch, Ophthalmic Epidemiology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|E. McCourt, M. Mathias, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a leading cause of childhood blindness. Infants with ROP receive intense surveillance of their ROP status while they are in the neonatal intensive care unit (NICU). There is, however, a paucity of research regarding the outcomes and treatment of infants with unresolved ROP following discharge from the NICU. Thus, the purpose of our study was to focus on infants who were classified as having unresolved type 2 or low grade ROP at discharge and determine the number of infants who required ROP treatment following discharge.

Methods: This descriptive study was conducted at an academic eye center. Using an ROP registry (2006-2021), we identified infants with type 2 (defined as ROP without plus disease that is stage 1-2 in zone 1, or stage 3 in zone 2) and low grade ROP (defined as ROP not qualifying as type 1 or type 2 ROP) at the time of NICU discharge. We examined the infants' medical records to determine the clinical follow-up and to specifically identify the number of infants who required ROP treatment after discharge.

Results: Our analysis included 114 (21%) infants with type 2 ROP and 433 (79%) infants with low grade ROP whose ROP had not resolved before discharge from the NICU. 337 infants (61.6%) were followed through resolution as an outpatient at our institution. Three (0.9%) of these infants required treatment after discharge. One infant, who was ventilator dependent throughout their first year, received laser treatment for delayed vascularization at 81 weeks post-menopausal age (PMA). Another converted from type 2 to type 1 ROP shortly after discharge, requiring laser treatment at 40 weeks PMA. The third infant received laser treatment for arrested vascularization and signs of reactivity in zone 3 at 68 weeks PMA.

Conclusions: Among infants with type 2 and low grade ROP, we found less than 1% required laser treatment after discharge from the hospital. The majority of infants received outpatient care at our institution. While the percentage of infants who required treatment after discharge was encouragingly low, adequate follow-up remains essential to preventing negative outcomes.

CONTROL ID: 3711784

SUBMITTER (NAME ONLY): Salma Ferdous

TITLE: Spatial single cell atlas of the mouse retina using MERFISH

SESSION TITLE: Single cell analysis in retinal research in health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Ferdous, J. Choi, J. Li, R. Chen, Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: With the advance in single-cell omics technologies in the last decade, studies have identified more than 100 different subtypes of retinal cells in the mouse retina. One of the major drawbacks in the current technologies is that they require the dissociation of the tissue, resulting in the loss of spatial information. The purpose of this study is to establish the first single cell spatial atlas of the mouse retina using spatial transcriptome technology.

Methods: To generate the spatial atlas of the mouse retina, we performed single cell spatial transcriptomics analysis on the wild type C57Bl/6J mouse retina using multiplexed error-robust fluorescence in situ hybridization (MERFISH). Based on single cell RNA-seq (scRNA-seq) data from the mouse retina, probes against a panel of 368 cell subtype marker genes were designed and synthesized. To achieve accurate cell segmentation in the highly packed retina, a set of oligo-conjugated antibodies specific to a cell membrane protein was co-stained with MEFISH probes. Deep-learning segmentation algorithms were then used to identify cell boundaries and assign transcripts to single cells. Using single-cell analysis tools such as scVI, tangram, and Giotto, cell type annotation and further downstream spatial analysis were performed.

Results: Six MERFISH experiments each containing 4-9 tissue sections were performed to generate spatial transcriptomic profiles of ~200,000 cells in total. By leveraging scRNA-seq data through data co-embedding, all major cell types and 120 cell subtypes in the retina have been identified. Investigation of the C57Bl/6J single cell spatial atlas revealed that a group of 8 amacrine cell subtypes are mis-localized in the ganglion cell layer, including the previously reported starburst amacrine cells. Spatial proximity analysis has further identified cell subtype pairs that exhibit spatial interaction, such as bipolar cell subtypes 1A and 1B (BC1A and BC1B). Lastly, co-embedding with scRNA-seq data was used to impute gene expression of MERFISH cells, generating spatial expression pattern of the entire transcriptome.

Conclusions: In short, we have generated the first comprehensive spatial single cell reference map of the mouse retina, an essential step toward gaining a comprehensive understanding of the mechanism of retinal function.

CONTROL ID: 3711786

SUBMITTER (NAME ONLY): Virginia Calder

TITLE: Comparison of topical Nomacopan, a dual Complement and leukotriene LTB4 inhibitor, with dexamethasone in downregulating experimental allergic conjunctival disease (EAC)

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.L. Calder, M. Eskandarpour, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Nunn, W. Weston-Davies, Akari Therapeutics Plc, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Allergic eye disease can lead to corneal cicatrisation and vision loss. Topical or systemic dexamethasone and/or cyclosporin A is often required. Topical administration of Nomacopan, a bifunctional recombinant biologic, was shown to effectively attenuate ocular surface inflammation in a model of experimental allergic conjunctival disease (EAC)[1]. The aim of this study was to compare the anti-inflammatory effects of Nomacopan with topical dexamethasone.

Methods: EAC was induced by immunizing 8-10 week old female C57Bl/6J mice (n=8 per group) with ovalbumin (OVA; 1mg)[2] followed, on day 21, with once daily challenges with topical OVA (250ug/mL) for 12 days. Ocular surface inflammation was readily detectable by Day 5 of OVA challenge. Topical Nomacopan at various concentrations (0.063%-0.5%) or dexamethasone (0.1%) was applied twice daily in both eyes from Day 6. Placebo-treated and unchallenged groups were used as controls. All eyes were examined daily and clinical scores assessed from Day 7 post OVA challenge. Animals were euthanised and eyes harvested for histology, flow cytometry and intracellular cytokine expression.

Results: Nomacopan (0.25, 0.5%), but not dexamethasone, significantly downregulated EAC on Day 7 whereas, on Day 10, all three treatments were equally effective when compared to placebo in decreasing EAC clinical scores [p=0.001]. Lower concentrations of Nomacopan were ineffective. Histological findings matched the clinical scores. Conjunctival $CD4^+$T cells were elevated in all treatment groups compared to unchallenged animals. Percentages of conjunctival IL-9^+cells and IL-4^+GATA3^+ $CD4^+$T cells (Th2) were increased in all OVA challenged groups and were significantly inhibited by Nomacopan treatment, but not by dexamethasone. In contrast, IL-4^+IL-9^+CD4^+T cells were significantly decreased [P<0.001] by all three treatments.

Conclusions: Topical Nomacopan suppressed inflammation in EAC by downregulating Th2 and Th9 cells, whereas dexamethasone only decreased Th9 cells, suggesting Nomacopan as an additional treatment option for allergic eye disease.

[1]Eskandarpour ME et al. Allergy. 2021 Oct 6. doi: 10.1111/all.15128

[2] Adahome Sd et al. JCI Insight. 2016 Aug 4;1(12):e87001

CONTROL ID: 3711787

SUBMITTER (NAME ONLY): Cris Martin Jacoba

TITLE: Comparisons of Handheld Retinal Imaging Devices with Ultrawide Field (UWF) and Early Treatment Diabetic Retinopathy Study (ETDRS) Photographs for Determining Diabetic Retinopathy (DR) Severity

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.P. Jacoba, J.K. Sun, L.P. Aiello, P.S. Silva, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|C.P. Jacoba, J.K. Sun, L.P. Aiello, P.S. Silva, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|R. Salongcay, T. Peto, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|L. Aquino, C. Salva, University of the Philippines Manila Philippine Eye Research Institute, Manila, Metro Manila, PHILIPPINES|

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ABSTRACT BODY:

Purpose: To compare DR severity identified on handheld retinal imaging with UWF and ETDRS photographs.

Methods: Mydriatic images of 225 eyes in 116 diabetic patients were taken with the Aurora (AU) handheld retinal imager and compared with stereoscopic UWF images and standard 7-field ETDRS photos taken at the same visit. Monoscopic 5-field imaging protocol was used for handheld images (centered on macula, optic nerve, and steered superior, inferior, and temporal). Images were evaluated for DR severity by certified graders using the International Classification for DR. Exact and within 1-step agreement between the two imaging modalities were determined, simple and weighted kappa statistics (K/Kw) were calculated. Grading discrepancies were adjudicated to determine the lesions and the sources of error.

Results: Distribution of DR severity by AU/ETDRS photos/UWF images (%): no DR 41.3/33.3/36.0, mild nonproliferative DR (NPDR) 18.7/20.4/17.8, moderate 10.2/14.2/10.7, severe in 16.4/11.6/15.1, proliferative DR (PDR) 13.3/20.4/20.4. All eyes were gradable by all modalities. Agreement between ETDRS and AU images was exact 65.8%, within 1-step 93.8%, k= 0.55 kw=0.75. Agreement between ETDRS and UWF was exact 70.6%, within 1-step 98.7%, k= 0.62 kw=0.81. Agreement between UWF and AU was exact agreement 68.0%, within 1-step 92.9%, k= 0.58 kw=0.76. Table 1 shows the cross-tabulation of DR severity by UWF and AU. Discrepancy of ≥2-steps between UWF and AU was observed in 16 eyes [8(50%) not in AU field, 6(37.5%) poor AU image quality, 2(12.5%) AU grader error) and the lesion causing the discrepancy was intraretinal microvascular abnormalities 5(31.2%), hemorrhages or microaneurysms 4 (25.0%), vitreous/preretinal hemorrhage 4(25.0%, figure 1), new vessels 3(18.8%)]. Using a referral threshold of moderate NPDR, 3(6.5%) eyes with PDR will be missed by AU due to limited field, while for a threshold of severe NPDR, 10(21.7%) eyes with PDR would be missed by AU due to image quality and field discrepancies.

Conclusions: Mydriatic 5-field handheld images using AU had moderate to strong agreement with UWF and ETDRS imaging. However, depending on the referral threshold, substantial levels of vision-threatening disease may be missed, suggesting that lower thresholds of referral are warranted if handheld devices are to be used.

CONTROL ID: 3711788

SUBMITTER (NAME ONLY): Kaoru Fujinami

TITLE: Full-Field Scotopic Thresholds for Color Stimuli in Severe Patients with Retinitis Pigmentosa

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Full-field stimulus thresholds (FST) are essential in assessing visual function, especially in patients with severe visual impairment. We describe the distribution of luminance thresholds in subjects with retinitis pigmentosa (RP), aiming to establish a deep phenotyping system.

Methods: Cases with RP who have severe visual acuity decline (counting finger or worse) were enrolled. Comprehensive clinical examinations were performed, including full-field electroretinograms (ffERGs) recorded according to the ISCEV standard. Full-field color stimuli were generated by the Diagnosys Profile ganzfeld ColorDome (Diagnosys, LLC, MA, USA) which utilizes narrow-band LEDs of 448 nm (blue), 530nm (green), and 627 nm (red). FST was performed according to the previously published method (Klein, Birch 2009). The dark-adapted color FST was performed after 40 minutes dark adaptation in the following order: (i) blue; (ii) red; and (iii) white stimulus. The FST data obtained in RP patients were compared with those of seven healthy participants (median age 29, range 23 to 45 years) with no ocular diseases.

Results: The median age of disease onset/age at examination of 28 eyes from 14 cases with RP was 9.0 (range, 0 to 40)/64.0 (36 to 75). The median visual acuity of 28 eyes was 2.7(range, 1.98 to 3.00) LogMAR unit. The full-field ERGs were undetectable both in dark-adapted and light adapted conditions in all 14 RP cases. The median value of thresholds for blue/red/white FST was 7.06(range, -33.1 to 21.8)/10.00(-6.5 to 18.9)/9.37(-25.5 to 24.7) dB. The median value of thresholds for blue/red/white FST was -59.9/-35.8/-54.0 dB in the seven healthy subjects. FST revealed a significant different range of thresholds for each colour stimulus between severe RP patients and healthy subjects.

Conclusions: Distribution of luminance thresholds was demonstrated in 14 cases with severe RP, which was significantly higher than that of healthy participants. Quantitative assessment for patients with severe visual impairment was available with FST, in keeping with previous reports (Roman AJ et al. Prog Retin Eye Res. 2021; Klein et al. Doc Ophthalmol. 2019). Further data from additional affected participants are required to validate the clinical investigation in patients with severe visual impairment.

CONTROL ID: 3711791

SUBMITTER (NAME ONLY): Joys Annika David

TITLE: TLR3 and TLR4 regulate complement-induced AMD cellular phenotype in iPSC-derived retinal pigment epithelium

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.G. David, C. Zhang, A. Fausey, R. Sharma, M. Farnoodian, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alternate complement signaling via NF-kB activation is known to regulate subRPE drusen and intracellular lipid deposition in iPSC-derived RPE (iRPE) models of age-related macular degeneration (AMD). Although toll-like receptor (TLR) stimulation is known to culminate in NF-kB activation, whether it is responsible for triggering complement-induced AMD phenotype is less clear. Here, we explore the role of TLR3 and TLR4 in complement-induced cellular responses in AMD pathogenesis.

Methods: Mature iRPE were pretreated with TLR3 or TLR4 inhibitors followed by treatment with either no serum, complement competent human serum (CC-HS) with activated anaphylatoxins, or complement incompetent human serum (CI-HS) with inhibited anaphylatoxin activity as previously described (Sharma et al., 2021). ELISA assays were performed on apical and basal media of cells to quantify cytokine IL-8. Target TLRs were located using immunofluorescent staining and intracellular lipid was detected by BODIPY dye. Additionally, iRPE were treated with TLR3 activator Poly (I:C) and stained for BODIPY and ubiquitin ligase TRIM3 known to mediate polyubiquitination of TLR3. Cells were visualized by fluorescence microscopy.

Results: Inhibitors for TLR3 and TLR4 decreased complement-induced lipid deposition exhibited by reduced BODIPY levels. TLR 4 inhibitor decreased human complement-induced IL-8 secretion in apical media and TLR3 inhibitor decreased IL-8 secretion in basal media. No significant difference in IL-8 secretion was found between CC-HS controls and TLR 4 inhibited cells in basal media or TLR3 inhibited cells in apical media. In iRPE treated with Poly (I:C) at concentrations of 10, 50, and 100 ug/ml, BODIPY and TRIM3 levels increased in a concentration-dependent manner.

Conclusions: In iRPE, complement-induced lipid deposition and activation of NF-kB leading to elevated IL-8 secretion characteristic of inflammation and AMD are mediated by TLR 3 and TLR 4. The regulatory role of these receptors in AMD pathogenesis reflects a possible upstream presence of aberrant RNA and viruses or bacterial endotoxins that trigger the activation of TLR3 and TLR4 respectively.

CONTROL ID: 3711796

SUBMITTER (NAME ONLY): Daphne Zou

TITLE: Vascular physiology-informed machine learning to identify similar subgroups of glaucoma patients across studies: Indianapolis Glaucoma Progression Study, Thessaloniki Eye Study, and Singapore Epidemiology of Eye Disease Study

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Intraocular pressure (IOP) and blood pressure (BP) are two risk factors in the development and progression of open angle glaucoma (OAG). However, various population-based studies differ for the role that the IOP-BP association has in OAG. To address this, we present a novel approach based on a physiology-informed mathematical model and machine learning (ML) applied to 3 studies conducted in different continents.

Methods: We considered: the Indianapolis Glaucoma Progression Study (IGPS) of 115 OAG eyes; the Singapore Epidemiology of Eye Disease Study (SEED) of 19,625 eyes (283 OAG); and the Thessaloniki Eye Study (TES) of 3,136 eyes (140 OAG). For each study, a validated mathematical model (Guidoboni et al 2014, IOVS) was used to generate 8 hemodynamic variables based on measurements of 4 patient-specific inputs (systolic and diastolic BP, heart rate, IOP). These combined variables form a 12-dimensional physiology-enhanced dataset. An unsupervised ML clustering algorithm, Fuzzy C-Means (FCM), was applied to the 3 enhanced datasets, partitioning eyes into groups with similar hemodynamics.

Results: The FCM algorithm produced 3 clusters on the 12-D data. Fig.1 shows the clustering result from the IGPS study (only OAG eyes) projected onto the IOP-MAP plane (MAP=mean arterial pressure=(2/3)DBP+(1/3)SBP). A wedge-like shape with a tilted boundary between cluster 1 (green) and cluster 3 (blue) is observed, indicating a non-trivial interplay between IOP and MAP. Clustering only the OAG eyes in SEED yielded similar wedge-shaped clusters (Fig. 2a), but with all eyes considered (healthy+OAG) the resulting clusters were vertically stacked (Fig. 2b), indicating they differ only by MAP. A similar phenomenon occurred in TES (Figs. 2c and 2d).

Conclusions: The physiology-informed ML approach revealed a wedge-shaped pattern among OAG eyes that is consistent across studies and continents. When OAG eyes are pooled together with healthy eyes in population-based studies, such as TES and SEED, this pattern is masked by the overwhelming presence of healthy eyes. The pattern

identifies OAG eyes with similar disease biomarkers and may enable individualized OAG management and treatment across populations.

CONTROL ID: 3711797

SUBMITTER (NAME ONLY): Daniel Balikov

TITLE: Synthetic Matrices with Customizable Cell-Matrix Interfaces Enhance Retinal Organoid Culture

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Stem cell-derived retinal organoids have uncovered the dynamics of retinal tissue development and pathology caused by inherited retinal degeneration, some of which have suggested potential therapeutics. Yet, the consistency of neuro-retinal architecture is not uniform in suspension cultures as they lack a robust physical scaffold. Therefore, if a physical scaffold that was easy to employ were available, then vitro retinal organoid models may more faithfully recapitulate features of the structure and neuro-retinal maturation found in vivo. Hence, we generated a reproducible and broadly employable synthetic extracellular matrix that improved in vitro retinal organoid generation and maturation.

Methods: A Rx-GFP mouse embryonic stem cell line was used to create retinal organoids. On day three of differentiation, organoids were embedded in polyethylene glycol (PEG) hydrogels containing reactive groups that could be quickly crosslinked with cell-binding and enzymatically sensitive crosslinking peptides that controlled cella adhesion and gel stiffness, respectively. Samples were fixed, stained, and imaged in seven-day intervals until day 32 of differentiation. Evaluation for the presence of retinal progenitor cells, retinal ganglion cells, and cone photoreceptors were done by IHC staining for Chx10, Brn3a, and Thrb2, respectively.

Results: Hydrogels containing less than 5% (weight percent) PEG or more than 7% PEG were either too fragile for handling or unable to be synthesized due to solubility limits, respectively. Compared to suspension culture, the spheroid shape was better maintained in the hydrogel model, producing an even laminar structure of neural retina. The 5% PEG hydrogel had more robust Chx10, Brn3a, and Thrb2 staining compared to the 7% PEG hydrogel and sustaining it through the entire differentiation course. Finally, replacement of standard RGD cell-matrix binding peptides with laminin or basement membrane-binding peptides further enhanced neural retina differentiation.

Conclusions: The creating and screening for a synthetic matrix that embeds retinal organoids improves the efficacy of in vitro retinal stem cell culture. This work can expand to human stem cell-based retinal organoids as well as disease model stem cell lines that not only better understand but also screen for potential therapeutics for retinal diseases with complex genomic heterogeneity.

CONTROL ID: 3711798

SUBMITTER (NAME ONLY): Gennadiy Moiseyev

TITLE: A novel non-retinoid visual cycle inhibitor RPE65-61 protects the retinal photoreceptors from light-induced degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The visual cycle regenerates visual pigments chromophore, 11-cis-retinal, and eliminates its toxic byproducts from the retina, supporting visual function and retinal neuron survival. Unfortunately, during the visual cycle, when 11-cis-retinal is being regenerated in the retina, toxic byproducts, such as all-trans-retinal and bis-retinoid such as N-retinylidene-N-retinylethanolamine (A2E), are produced, which contributes to the pathogenesis of dry form of age-related macular degeneration (AMD) and Stargardt's disease (STGD). To prevent all-trans-retinal mediated retinal degeneration, slowing down the retinoid flow by inhibiting the visual cycle with a small molecule was proposed. The present study describes RPE65-61, a novel, non-retinoid compound, as an inhibitor of RPE65 intended to modulate the excessive activity of the visual cycle to protect the retina from degenerative diseases.

Methods: To determine the inhibition mode of the RPE65-61, we used an adenoviral vector to express chicken RPE65 in 293A cells, and the chicken RPE65 was used in a liposome-based isomerase assay. One hour after the systemic administration of RPE65-61 or vehicle, mice were placed in a light box with white fluorescent tube lights (10,000 lux for 3 hr). The mice were returned to regular housing for five days, and then the light-induced retinal damage (LIRD) was assessed using histology and ERG. Retinoid profiles recovery after the photobleach was assayed using HPLC.

Results: RPE65-61 selectively inhibited retinoid isomerase activity of RPE65 via an uncompetitive mechanism, with IC_{50} of 80 nM. Systemic treatment of mice with RPE65-61 resulted in slower chromophore regeneration after the photobleach and protected the retina from LIRD. Furthermore, RPE65-61 down-regulated the cyclic GMP-AMP synthase stimulator of the interferon genes pathway, decreased the inflammatory factor, attenuated retinal apoptosis caused by LIRD, which led to the preservation of the retinal function.

Conclusions: RPE65-61 potently and selectively inhibited conversion of all-trans-retinyl ester to 11-cis-retinol catalyzed by RPE65. Mice injected with RPE65-61 exhibited delayed chromophore regeneration after photobleach and conferred protection of retina against LIRD. Taken together, these results suggest that RPE65-61 may be used to slow down the visual cycle and to prevent the accumulation of A2E in STGD and AMD.

CONTROL ID: 3711799

SUBMITTER (NAME ONLY): John Han

TITLE: GLUT1 is Required for the Anabolic Metabolism of Photoreceptor Cells

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glucose supports catabolic and anabolic metabolism in the neural retina. It is transported into the retina by the outer (RPE) and inner blood-retinal barrier (BRB) via the glucose transporters GLUT1, encoded by Slc2a1. GLUT1 is highly expressed by Muller glia and photoreceptor cells in the outer retina, while the neurons express GLUT3 in the inner retina. To understand how glucose supports the metabolism and function of the retina, we generated and characterized mouse models with the deletion of the glucose transporter GLUT1 in the neural retina and photoreceptors.

Methods: Mice carrying floxed alleles for Slc2a1 (The Jackson Laboratory, #031871) were crossed with transgenic mice expressing Cre recombinase in the retina (129.B6C3-Tg(Crx-cre)1Tfur), rods Pde6gCre-ERT2 (Tsang lab) and cones (Tg(Opn1mw-cre)1Asw) to generate RetinaΔGlut1, RodΔGlut1, ConeΔGlut1 and GLUT1$^{Flox/Flox}$ (control). Structure and function were assessed by optical coherence tomography (OCT), confocal scanning laser ophthalmoscopy (cSLO) and electroretinograms (ERGs). Immunofluorescence (IF), in-situ hybridization, qPCR, and GC/MS were used to determine changes in the retinas.

Results: In-situ hybridization, IF, and western blot were done to confirm the deletion of GLUT1 in the neural retinas. RetinaΔGlut1 mice showed loss of GLUT1 as early as P3, but exhibited normal retinal lamination at 1 month of age. We found that Slc2a1 and Slc2a3 are the highest expressed glucose transporters in the neural retina. In-situ hybridization of Slc2a1 showed expression in both inner and outer retinal layers, but Slc2a3 was only seen in the inner retinal layers. Scotopic ERGs from RetinaΔGlut1 and RodΔGlut1 were reduced. Photopic ERGs were reduced in RetinaΔGlut1, but not in ConeΔGlut1. OCT scans of RetinaΔGlut1 and RodΔGlut1 only showed ONL thinning and OS shortening. TUNEL positive cells were detected only in the ONL. There were no changes in cone density in RetinaΔGlut1 and ConeΔGlut1. Rhodopsin transcript and protein were severely reduced when normalized to OS length and ONL thickness, consistent with nutrient deprivation. Metabolic measurements confirmed decreased aerobic glycolysis.

Conclusions: GLUT1 expression in the neural retina is required for visual function and the viability of rods, but not cone photoreceptors. Glucose uptake via GLUT1 is necessary for OS renewal. Genetic deletion of GLUT1 does not cause cell death in the inner retina.

CONTROL ID: 3711800

SUBMITTER (NAME ONLY): Lukas Goerdt

TITLE: Proliferation of intraretinal vessels and disease progression in Macular Telangiectasia Type 2 (MacTel)

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the natural progression of vascular and neurodegenerative alterations using multimodal retinal imaging in patients with MacTel.

Methods: In this retrospective, longitudinal analysis, patients underwent annual ophthalmic examinations including color fundus photography (CFP), fluorescein angiography (FLA), optical coherence tomography (OCT) and OCT-angiography (OCTA). Only treatment-naïve eyes lacking any signs of neovascular membranes/ activity were included, and reviewed for ≥20 months. Eyes were analyzed for the progression of vascular and neurodegenerative changes, including vascular proliferation, perivascular leakage, pigment accumulation, and progression of ellipsoid zone (EZ) loss.

Results: 97 eyes from 57 patients (mean age 63.1 years (range: 39-83); 35 females) were included and followed over a mean period of 22.3 months (range: 20.5-38.2). On OCTA, a proliferation of retinal vessels was observed in 36 eyes (37%). Proliferating vessels were primarily found at the level of the deep retinal plexus and within the temporal parafovea. Seven eyes showed a proliferation of vessels at the level of the outer retina/choriocapillaris layer, possibly involving both choriocapillaris and displaced deep plexus vessels. The latter finding was associated with the development of retinal-choroidal anastomoses in all cases.

In all eyes, the proliferation of intraretinal vessels (PIV) was associated with a focal increase in reflectivity on OCT and increased leakage on FLA. A de novo development of subretinal/sub-RPE neovascular membranes was observed in a single eye only. The progression of EZ-loss did not differ between eyes with or without PIV (0.0017 mm^2/month versus 0.0015 mm^2/month; p=0.09). Eyes with PIV showed a significantly higher frequency of perivascular pigment accumulation compared to eyes without PIV (10/36 (28%) vs 4/61 (7%); chi-square test X^2 (1, N=97) = 8.3, p = 0.004).

Conclusions: The proliferation of intraretinal vessels appears to represent a common finding in MacTel, and can be observed in eyes previously classified as “non-proliferative”. Our results thus indicate the need to reevaluate our current understanding and classification of MacTel into “proliferative” and “non-proliferative” disease stages.

CONTROL ID: 3711801

SUBMITTER (NAME ONLY): Sujoy Bhattacharya

TITLE: Modeling of mitochondrial bioenergetics and autophagy impairment in MELAS-mutant iPSC-derived retinal pigment epithelial cells

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mitochondrial dysfunction and mitochondrial DNA (mtDNA) damage in the retinal pigment epithelium (RPE) have been implicated in the pathogenesis of macular degeneration. Elimination of dysfunctional mitochondria through mitochondrial autophagy (mitophagy) is an important quality control mechanism in the RPE. In this study, we model the impact of a prototypical systemic mitochondrial defect, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS), in RPE health and homeostasis as a model for impaired mitochondrial bioenergetics.

Methods: We used iPSCs derived from skin biopsies of MELAS patients (m.3243A>G tRNA leu mutation) with different levels of mtDNA heteroplasmy and differentiated them into RPE cells. Mitochondrial depletion of ARPE-19 cells (p^0 cells) was also performed using 50ng/mL ethidium bromide (EtBr) and 50mg/ml uridine. Cell fusion of the human platelets with the p^0 cells performed using PEG-SMEM mixture to generate platelet:RPE “cybrids”. Confocal microscopy, FLowSight Imaging cytometry, and Seahorse XF Mito Stress test were used to analyze mitochondrial function. Western blotting was used to analyze expression of autophagy and mitophagy proteins.

Results: We found that MELAS iPSC-derived RPE cells exhibited key characteristics of native RPE. We observed heteroplasmy-dependent impairment of mitochondrial bioenergetics and reliance on glycolysis for generating energy in the MELAS iPSC-derived RPE. The degree of heteroplasmy was directly associated with increased STAT3 activation, reduced AMPKα activation, and decreased autophagic activity. In addition, impaired autophagy was associated with aberrant lysosomal function, and failure of mitochondrial recycling. The mitochondria-depleted p^0 cells replicated the effects on autophagy impairment and aberrant STAT3/AMPKα signaling and showed reduced mitochondrial respiration, demonstrating phenotypic similarities between p^0 and MELAS iPSC-derived RPE cells.

Conclusions: Our studies demonstrate that the iPSC-derived RPE lines from MELAS patients are useful tools for identifying molecular, cellular, and functional features that contribute to age-related RPE degeneration. We propose that heteroplasmic mitochondrial disease models can be used for the assessment of mitochondrial and cellular dynamics and provide a new experimental model for the RPE in aging and macular degeneration.

CONTROL ID: 3711804

SUBMITTER (NAME ONLY): Eva Sobas Abad

TITLE: Stress and sleep deprivation-related biomarkers in tear fluid in Retinitis Pigmentosa. Pilot study

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Sobas Abad, M. Mateo-Olivares, C. García-Vazquez, R. Usategui-Martín, J. Pastor, A. Enriquez-De-Salamanca, S. Pastor, Ophthalmology, IOBA, Valladolid, Valladolid, SPAIN|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) patients commonly experience sleep-related problems and susceptibility towards stress which may be detected by specific biomarkers in tears. We investigated the association between the grade of severity of RP (by clinical assessment), and biochemical stress (by analyzing proposed biomarkers in tears) and determine the impact of psychological factors and sleep disturbances among RP patients

Methods: Seventy-eight RP patients were recruited. The study encompassed administration of State-Trait Anxiety Inventory (STAI), Epworth Sleepiness Scale (ESS) and Pittsburg Sleep Quality Index (PSQI) questionnaires, a complete ophthalmological examination for severity grading of RP and collection of tear samples. The activity of biomarkers (Figure.1) was estimated by 20 Plex-Luminex and statistical analysis was performed to determine associations between perceived stress, sleep quality, sleepiness, and biomarkers activity. To complete the assessment, sampling in healthy controls is being analyzed to compare

Results: At the time of evaluation, 52 (67%) of patients had a severe RP (33 (63.5%- males) and 19 (36.5%) females) with a mean age 53.83 ± 13.17 yrs, and 26 (33%) a mild-moderate grade (14 (53.8%) males) and 12 (46.2%) females) with a mean age 47.12 ± 12.94 yrs (Table.1). The severity of RP tends to be highest in older patients (p=0.036). Fifty-eight (58,9%) patients reported severe-anxiety and 18 (23.,1%) high-anxiety
status measured by STAI. Forty-six (59%) of patients obtained pathological values in PSQI and 43 (55.1%) in EES. Patients with severe and mild-moderate RP (n=38 and 20, respectively) did not show significant differences when sleep quality, and perceived anxiety scores were compared. We found high tear concentrations of EGF, GRO, IL-1Ra, IL-8, and MCP-1. Differences were not significant by age, grade of severity, stress status, and gender between groups, but patients with more severe disease, poor sleep quality, and higher scores of anxiety status showed higher concentrations

Conclusions: Pro-inflammatory cytokines seem to be elevated in tear fluid from RP patients. Present findings reveal that tear fluid biomarkers could be appropriated for the objective assessment of sleep deprivation and stress in RP patients in a non-invasive way

CONTROL ID: 3711807

SUBMITTER (NAME ONLY): Benton Chuter

TITLE: Use of a deep learning image quality model to evaluate impact of clinically relevant forms of degradation on the glaucoma gradability of fundus images

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.G. Chuter, J. Huynh, M. Christopher, C. Bowd, R. Fan, M.H. Goldbaum, A. Belghith, C.A. Girkin, M.A. Fazio, R.N. Weinreb, L.M. Zangwill, Hamilton Glaucoma Center, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|J. Huynh, Department of Computer Science and Engineering, University of California San Diego, La Jolla, California, UNITED STATES|R. Fan, College of Electronics and Information Engineering,, Tongji University, Shanghai, CHINA|M.A. Fazio, Department of Biomedical Engineering, The University of Alabama at Birmingham College of Arts and Sciences, Birmingham, Alabama, UNITED STATES|C.G. DeMoraes, J.M. Liebmann, Bernard and Shirlee Brown Glaucoma Research Laboratory, Harkness Eye Institue, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Poor image quality can adversely affect the ability of DL algorithms to detect glaucoma. This study evaluates the effect of several common types of image degradation on a DL model that automates quality assessment of fundus photographs.

Methods: 2,815 fundus images from the Diagnostic Innovations in Glaucoma Study and African Descent and Glaucoma Evaluation Study were used to develop a DL model to automate quality assessment. This model was tested on 11,350 photographs from the Ocular Hypertension Treatment Study. Several ablative operations were separately implemented to degrade high-quality images (QS=0) into low quality ones (QS≥0.1). Gaussian blur, brightness (bias) increases and decreases, contrast enhancement factor (gain) decreases, and Gaussian-distributed additive noise were applied. In order to determine the range of degradation values, images were degraded until quality scores peaked at a maximum quality value. For each type of ablation, the maximum degree of degradation was set as the value for which the resulting quality score first surpassed 95% of this peak poor quality value. Within this range, each image was incrementally degraded to create 100 progressively ablated photographs for that ablation form.

Results: While all degradations consistently yielded poor quality scores (Figure 1), each type of ablation yielded different degradation-QS profiles. Noise was the strongest determinant of quality, followed by contrast and focus. The model was more limited in recognizing the extent of degradation for both increased and decreased brightness (max

QS = 0.45 and 0.76, respectively). The model appeared especially sensitive to the Gaussian noise ablation type; random distribution variance of 0.0075 and 0.0125 proved sufficient to degrade an image to a poor quality score.
Conclusions: A DL model to assess fundus photography quality can offer insights into factors influencing DL models for detection of eye disease. Evaluation of the performance of a glaucomatous optic neuropathy model on variably degraded datasets in conjunction with grading by human experts may validate or refute these insights.

CONTROL ID: 3711809

SUBMITTER (NAME ONLY): Monica Le

TITLE: Impact of COVID-19 Vaccine on Intravitreal Injection During the SARS-CoV-2 Pandemic

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Le, B. Gundlach, J.C. Strawbridge, S. Ashrafzadeh, I. Tsui, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: During the COVID-19 pandemic lockdown, ophthalmology injection clinic volume at the Veteran Affairs (VA) Greater Los Angeles decreased by 50% and it rebounded back to pre-COVID clinic volumes immediately after. The COVID-19 vaccines were introduced for individuals 16 years and older under emergency use authorization by the FDA in December of 2020. The focus of this study is to examine non-ophthalmic characteristics of patients in intravitreal injection clinic during the COVID-19 vaccine era.

Methods: Retrospective chart review study of patients who received intravitreal injections during 7-week period in 2021 (COVID-19 vaccine era) was compared to 2019 (baseline pre-pandemic), and 2020 (peak COVID-19). Electronic medical records were used to obtain patients' demographics, ophthalmic conditions, non-ophthalmic conditions, and COVID-19 vaccine records.

Results: During the 7-week period in 2021, 88.5 % of patients receiving intravitreal injections were vaccinated (n= 263). Of the vaccinated patients, 83.6% received the Pfizer vaccine, 3.8% Moderna, and 1.1% J&J. Of those receiving either the Pfizer or Moderna vaccine, 1.7% were partially vaccinated while all others were fully vaccinated. Patients with a higher BMI were more likely to follow up after vaccination compared to baseline (p=0.019). Hispanic patients were more likely to follow up after vaccination compared to peak COVID-19 period (p=0.026). Cancer patients were more likely to follow up following vaccine compared to baseline (p=0.0001), but no difference compared to peak COVID-19 period. Transplant patients were more likely to follow up following vaccination compared to peak COVID-19 period (p=0.0001), but no difference compared to baseline (p=0.656). Patients with COPD were less likely to follow up even with vaccine (p=0.0001).

Conclusions: The availability of the COVID-19 vaccines impacted intravitreal injection follow up at the VA Los Angeles ophthalmology injection clinic. Most patients receiving intravitreal injection clinic were fully vaccinated. Immunocompromised patients and those with higher BMI were more likely to follow up after the availability of COVID-19 vaccination. Patients with COPD were less likely to follow up even with the availability of vaccines.

CONTROL ID: 3711810

SUBMITTER (NAME ONLY): Maria Gelmi

TITLE: MITF: a progression marker in uveal melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gelmi, M. Marinkovic, T. Vu, P. van der Velden, G. Luyten, M.J. Jager, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: In uveal melanoma (UM), heavy tumour pigmentation has been associated with a bad prognosis. Microphthalmia-associated transcription factor (MITF) is located on chromosome 3 and it is the master regulator of melanin synthesis and melanocyte development. In cutaneous melanoma, the role of MITF is not completely clear but loss of MITF is associated with epithelial-to-mesenchymal transition (EMT), an increase in stem cell markers and inflammation. In UM, MITF loss is associated with loss of expression of BAP1, which is a negative prognostic marker. We explored the role of MITF in two cohorts of enucleated UM patients: a cohort of 64 UM patients enucleated at the Leiden University Medical Centre (LUMC) and the The Cancer Genome Atlas (TCGA) cohort (n = 80).

Methods: We analysed the relation between MITF expression in UM and clinical-pathological and genetic features and carried out survival analyses on both cohorts. Next, we tested whether MITF expression was related to pigmentation, inflammation and EMT markers in both cohorts and performed a differential expression and gene set enrichment analysis (GSEA) between MITF-low and MITF-high UM in the LUMC cohort.

Results: In the LUMC cohort, MITF expression was lower in dark UM than in light tumours ($p = 0.004$). Moreover, MITF expression was lower in UM with monosomy 3 ($p < 0.001$) and in UM with a high expression of PRAME ($p = 0.01$). However, MITF expression was not significantly related to survival ($p = 0.22$). These results were confirmed in the TCGA cohort. In differential expression analysis, MITF-low UM showed upregulation of the inhibitory receptor TIM-3 and of several genes (such as CXCL16 and HCP5) that have been shown to increase cell proliferation and migration in other cancer types, and in GSEA, MITF-low tumours showed an upregulation of hallmark pathways involved in inflammation.

Conclusions: Since monosomy 3, PRAME expression and inflammation are features of poor prognosis in UM, we propose that MITF loss in UM is related to tumour progression and may have a direct link with the inflammatory state. Further studies are needed to understand if the role of MITF is independent of its relation with chromosome 3 and BAP1 status.

CONTROL ID: 3711811

SUBMITTER (NAME ONLY): Marta Jiménez-García

TITLE: How to define keratoconus progression?

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jiménez-García, S. Ní Dhubhghaill, C. Koppen, J.J. Rozema, Ophthalmology, Universitair Ziekenhuis Antwerpen, Edegem, Antwerp, BELGIUM|M. Jiménez-García, S. Ní Dhubhghaill, C. Koppen, J.J. Rozema, Translational Neurosciences, Universiteit Antwerpen Faculteit geneeskunde en gezondheidswetenschappen, Wilrijk, BELGIUM|E.O. Kreps, Ophthalmology, Universitair Ziekenhuis Gent, Gent, Oost-Vlaanderen, BELGIUM|E.O. Kreps, Universiteit Gent Faculteit Geneeskunde en Gezondheidswetenschappen, Gent, BELGIUM|

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ABSTRACT BODY:

Purpose: Although corneal crosslinking (CXL) was a major breakthrough in keratoconus (KC) management, there has been debate about its efficiency. Cochrane reviews have only found limited, low quality evidence and there is no consensus on which KC cases need CXL, nor on how to establish progression. This is complicated further by noise in the measurements. Some progression criteria may better reflect our clinical knowledge of KC evolution, such as the % of progressive KC based on clinical changes, hence, this study aimed to verify the performance of diverse criteria.

Methods: The retrospective REDCAKE study included data from 743 KC patients measured longitudinally with Pentacam (Oculus, DE). Habitual progression criteria based on (combinations of) the maximum keratometry (K_{MAX}), astigmatism (A_F), and minimum pachymetry (P_{MIN}), or based on ABCD Progression Display were analyzed. For each criterion and cut-off, we calculated the eyes flagged progressive at some point (R_{PROG}), the individual consistency C_{IND} (% of examinations after detection of progression that would still be considered progressive), and the population consistency C_{POP} (% of eyes with C_{IND} > 66%). Finally, we studied more monotonic and consistent variables, such as the front steep keratometry (K_{2F}), the keratometry in a 3 mm area around K_{MAX} ($K_{ZONAL3mm}$), and the mean radius of the back surface (R_{mB}).

Results: Use of a single criterion (e.g. $\triangle K_{MAX}$ >1D) led to rather high values of R_{PROG}, unless the cut-off exceeded the measurement noise. When two criteria were required, (K_{MAX} AND A_F) led to worse C_{POP} and higher variability than (K_{MAX} AND P_{MIN}); alternative criteria ($K_{ZONAL3mm}$ AND R_{mB}) and (K_{2F} AND R_{mB}) obtained the best C_{POP} and the lowest variability (Fig 1; all $p < 0.0001$). ABC, as defined by its authors, obtained a very high R_{PROG} of 74.2%. Using wider 95% confidence intervals (95CI) and requiring two of ABC over the 95CI reduced R_{PROG} to a more realistic 27.9%.

Conclusions: Clinical observation of contact lens parameters, visual acuity, incidence of scarring or corneal transplants suggest 20–35% of KC cases are progressive. This clinical R_{PROG} value should be considered when defining KC progression to avoid overtreatment. By using combinations of alternative variables and wider 95CI for ABC, the R_{PROG} can be brought closer to clinical observations; furthermore, these approaches obtained better longitudinal consistency than current definitions.

CONTROL ID: 3711814

SUBMITTER (NAME ONLY): Flavia Chiosi

TITLE: OCT ANGIOGRAPHY INDICES AND CHOROIDAL VASCULARITY INDEX IN HEREDITARY TRANSTHYRETIN AMYLOIDOSIS

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Chiosi, G. Manzi, O. GALLO, E. Paolillo, Ophthalmology, AORN Ospedali dei Colli, Napoli, Campania, ITALY|G. LIMONGELLI, M. CAIAZZA, Inherited and Rare Cardiovascular Disease, Universita degli Studi della Campania Luigi Vanvitelli, NAPOLI, Campania, ITALY|G. PALMIERO, Cardiology, Ospedale Monaldi, Napoli, Campania, ITALY|M. Rinaldi, Ophthalmology, Universita degli Studi della Campania Luigi Vanvitelli, Napoli, Campania, ITALY|C. COSTAGLIOLA, Ophthalmology, Universita degli Studi di Napoli Federico II, Napoli, Campania, ITALY|

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ABSTRACT BODY:

Purpose: Retinal angiopathy is a known ocular manifestation of hereditary transthyretin amyloidosis (ATTR). We performed a retrospective, observational clinical study to determine whether vessel density (VD) indices as measured by optical coherence tomography angiography (OCTA) and choroidal vascularity index (CVI) provided insights into retinal and choroidal vascular changes in patients affected by ATTR.

Methods: Twenty-six patients with genetic diagnosis of wild-type ATTR were enrolled to undergo structural optical coherence tomography (OCT) and OCTA. An age-gender-matched control group of twenty-four healthy subjects was selected for statistical comparisons. Swept-source OCT and OCT angiography data from TOPCON DRI OCT Triton were exported using Topcon IMAGENET 6.0 software, and 3D datasets were analysed to determine retinal, choroidal thickness and VD. Images were binarized using the ImageJ software, and total choroid area (TCA), luminal area (LA) and stromal area (SA) were acquired to measure the CVI. Statistical analysis was conducted using MedCalc version 11.5.1 (Medcalc software, Mariakerke, Belgium).

Results: Mean VD was significantly reduced in the superficial capillary plexus (SCP), deep capillary plexus (DCP) and choriocapillaris (CC) in all five Early Treatment Diabetic Retinopathy Study (ETDRS) sectors in the ATTR group compared to controls (P =. 006)

Retinal thickness did not statistically differ between the two groups, while a significantly reduced chororidal thickness was recorded in ATTR patients (P = .008).

The mean CVI was lower in the ATTR group compared to controls (P = .006).

Conclusions: VD resulted reduced at the level of SCP, DCP and CC in ATTR patients, along with choroidal thickness and CVI compared to healthy control.

OCT-A indices and CVI may serve as a noninvasive biomarker to quantitatively evaluate retinal and choroidal vascular involvement in ATTR patients and the possible correlation with systemic parameters.

CONTROL ID: 3711817

SUBMITTER (NAME ONLY): Alicja Strzalkowska

TITLE: Intraocular Pressure Measurement in Childhood Glaucoma under Standardized General Anaesthesia - the Prospective EyeBIS Study

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Strzalkowska, J. Buse, N. Pirlich, J. Stingl, A. Schuster, J. Rezapour, F. Wagner, E.M. Hoffmann, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|

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ABSTRACT BODY:

Purpose: To compare intraocular pressure (IOP) measurements using iCare® PRO rebound tonometry (iCare) and Perkins applanation tonometry (Perkins) in childhood glaucoma suspects and healthy children under protocol-defined general anaesthesia (GA).

Methods: A prospective clinical, case-control study of children who underwent an ophthalmologic examination under GA according to our Childhood Glaucoma Center protocol between April 2019 and March 2021. IOP was taken three times (T1-T3) according to the depth of GA, measured with bispectral index (BIS), which is a continuous form of complex processed electroencephalogram (EEG). IOP measurment was taken three times, alternating, starting with iCare: T1 iCare-Perkins, T2 iCare-Perkins, T3 iCare-Perkins, see Figure 1. Central corneal thickness (CCT) was measured before IOP measurement. Correlation between iCare and Perkins was analysed at each measurement point. CCT was taken into account.

Results: 150 eyes of 75 children were included: 53 glaucoma suspects and 22 healthy controls. Children were 45.45 ± 29.76 months old [mean ± SD]. 54.05% of all children were female. Glaucoma suspects: IOP measured with iCare was 26.8±11.2, 23.2±11.4, 21.7±10.3mmHg and Perkins 18.2±7.7, 16.0±7.1, 16.1±7.4mmHg [mean ± SD] at T1, T2, T3, see Figure 2.

Healthy controls: 14.3±4.7; 10.5±2.5; 10.1±3.0mmHg and 10.2±3.1; 7.4±3.0; 6.9±2.5mmHg, respectively [mean ± SD]. The correlation between iCare and Perkins was good: the intraclass correlation coefficient (r) between the two methods was 0.629 ($p<0.001$). The mean IOP is statistically significantly higher with iCare than with Perkins ($p<0.001$) in both groups. The mean difference (iCare and Perkins) was 6.0±6.1mmHg.

Correlation between IOP and CCT was not statistically significant in both groups.

Conclusions: The IOP were higher in glaucoma subjects than in the healthy ones. iCare leads to higher IOP compared to Perkins in standardized anaesthesia in children. The IOP changes during the course of anesthesia and should be measured at the beginning of anaesthesia according to our protocol, because at this point the IOP is the highest. In our study, IOP was independent of CCT.

CONTROL ID: 3711818

SUBMITTER (NAME ONLY): Aoife Hunter

TITLE: Higher Macular Pigment Levels are Associated with Better Contrast Sensitivity and Photostress Recovery Time in Patients with Open-Angle Glaucoma Supplemented with Carotenoids

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Hunter, E. Loskutova, G. Lingham, J.S. Butler, J. Loughman, Technological University Dublin, Dublin, IRELAND|C.J. O'Brien, Department of Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: To investigate the relationship between macular pigment optical volume (MPOV) and contrast sensitivity (CS), microperimetric pointwise sensitivity (PWS) and photostress recovery time (PRT) during 18 months of carotenoid supplementation in patients with open-angle glaucoma (OAG).

Methods: MPOV was measured (central 6°) in one eye using fundus autofluorescence (Spectralis HRA + OCT) in 54 patients with OAG, randomised to receive treatment (10 mg lutein, 10 mg meso-zeaxanthin, 2 mg zeaxanthin, n = 37 [mean age: 66.2 years, range: 48 – 86]) or placebo (n = 17 [mean age: 61.8 years, range: 36 – 76]) supplementation. CS was measured at 1.5, 3, 6, 12 and 18 cycles per degree under photopic (85 cd/m^2) and mesopic (3 cd/m^2) conditions, each with and without glare (Functional Vision Analyzer). Area under log contrast sensitivity function (AULCSF) was calculated for each test condition. PWS at 19 visual field locations (central 10°, MAIA 2) and PRT (MDD-2 Macular Adaptometer) were also measured. All tests were conducted at six monthly intervals from baseline to 18 months. Linear mixed-effects models were used to assess relationships between each visual function measure (response variables: AULCSF, PWS and PRT) and MPOV (fixed effect) over time. Treatment, time and adaptation condition (AULCSF) were included as fixed effects and participant as a random effect to adjust for such factors in the model.

Results: Positive significant relationships were observed between AULCSF (all adaptation conditions) and both MPOV (Beta coefficient [β] = 0.013, P = 0.028, fig. 1a) and time (β = 0.035, P = 0.011). PRT had a significant inverse association with MPOV (β = -0.924, P = 0.045, fig. 1b) and a significant positive association with time (β = 3.78, P=0.019). PWS was not significantly related to MPOV (β = -0.077, P = 0.203, fig. 1c) or time (β = 0.036, P = 0.819).

Conclusions: Patients with OAG and higher MPOV exhibited better CS under mesopic and photopic conditions both with and without glare. PRT was faster in those exhibiting higher MPOV over the supplementation period. Visual function may be improved in glaucoma by increasing MPOV through carotenoid supplementation, but further work is required to determine its longer-term effects on visual function.

CONTROL ID: 3711819

SUBMITTER (NAME ONLY): Erika Shaw

TITLE: Characterization of a primary porcine RPE ‘drusen in a dish’ cell culture model

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shaw, Cell Biology, Neurobiology, and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|E. Shaw, D.M. Lipinski, Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D.M. Lipinski, University of Oxford Nuffield Laboratory of Ophthalmology, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Erika Shaw: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Lipinski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly and is estimated to affect approximately 8.7% of all individuals between the ages of 45 and 85. In the early or 'dry' form of the disease, protein and lipid deposits, termed drusen, develop between the retinal pigment epithelium (RPE) and the selectively permeable barrier separating the RPE and retina from the choroidal circulation, called Bruch’s membrane, particularly within the macular region of the eye. Apart from aged non-human primates, drusen development is not easily replicated using animal models, however several studies have demonstrated that primary RPE cells, cultured in monolayers accumulate drusen-like deposits. Herein, we assess the accumulation of ‘drusen’ longitudinally in primary porcine RPE cultures and characterize the protein and lipid content of individual drusen to establish their similarity to drusen recovered from human donor eyes with diagnosed AMD.

Methods: Fresh (< 6 hours post mortem) porcine eyes were obtained from a local abattoir and disinfected through immersion in PVP prep solution. On ice, the cornea, lens, vitreous body and retina were removed mechanically before the primary RPE was isolated via enzymatic dissociation using serial incubations in 0.25% trypsin in L-15 media at 37°C. Cells were incubated in 1% DNase I for 2 minutes, purified via centrifugation on a 40% Percoll cushion with 0.01 M Na_2PO_4 and 0.15 M NaCl (pH 7.4), and plated directly on polyethylene terephthalate (PET) transwell membranes. RPE cultures were maintained for up to 26 weeks without passaging. Transwell inserts were fixed in 4% PFA and cryosectioned or flat mounted. Drusen components, size, and quantity were analyzed via immunofluorescence microscopy.

Results: Freshly isolated RPE take approximately 5 – 6 days to fully anchor to the membrane, after which cells no longer slough off with feeding. Throughout the 26 week aging period, approximately 60% of the cultures show no signs of infection. As young as 22 weeks post isolation, primary RPE cultures developed deposits with drusen-like characteristics such as lipid accumulation indicated by Nile Red and positive immunofluorescent staining for known drusen components such as ApoE, vitronectin, and TIMP3.

Conclusions: Through this study, we further verify the efficacy and reproducibility of primary RPE culture as a method of ex vivo modeling of drusen-formation.

CONTROL ID: 3711821

SUBMITTER (NAME ONLY): Danielle McLaughlin

TITLE: Visual Field Testing in a Telehealth Setting: Remote Perimetry Using a Head-Mounted Device in Normal Eyes

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. McLaughlin, H. Munshi, E. Savatovsky, E. Vanner, T.C. Chang, A.L. Grajewski, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the feasibility of remote visual field (VF) testing using a virtual reality visual field (VRVF) device with and without assistance.

Methods: Individuals without ocular disease (age ≥ 60) completed a standard automated perimetry (SAP) 24-2 SITA Standard on a Humphrey Field Analyzer and a VRVF (V_0) exam in random order on the same day in clinic with assistance. Participants were taught how to operate the VRVF equipment and given a device to take home. The following day, participants were telehealth-assisted to establish a remote testing environment, confirm proper use, and complete a VRVF exam (V_1). Participants tested remotely and without assistance once a week for 3 weeks (V_{2-4}). A pointwise mean absolute difference and SD between light sensitivity threshold values (LSTV) were calculated (V_0 vs SAP and V_{1-4} vs V_0). Using a normal perimetric database for SAP ages 60-69, the number of points below normal (OD) was graphed. Data input was validated by a second party. Reliability indices were analyzed.

Results: 7 participants (14 eyes) were enrolled and completed reliable VRVF exams in clinic and remotely as determined by mean reliability indices (fixation losses ≤ 0.15, false positives ≤ 0.05, false negatives ≤ 0.06). The mean absolute difference and SD of LSTV between exams appear in Table 1. Excluding an outlier (P2 V_4) and missing data (P7 V_4), the absolute mean difference between V_0 and V_{1-4} generally decreased as the study progressed. Figure 1 displays the number of LSTV below normal (OD), which decreased with weekly, remote self-testing (V_{2-4}) and was greater in those who took V_0 first (x_{V0}=14.5) than SAP first (x_{V0}=1.6).

Conclusions: Variability of LSTV from V_0 and number of points below normal reduced with weekly testing, implying that experience with testing improves results. Initial exposure to SAP may be useful for VRVF testing and could confound comparisons between V_0 and V_{1-4}. VRVF was generally reliable in a telehealth setting for individuals with normal eyes. Further research is needed to assess viability in a glaucoma patient population.

CONTROL ID: 3711822

SUBMITTER (NAME ONLY): Andrey Dmitriev

TITLE: O_2 consumption in the outer and inner mouse retina.

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.V. Dmitriev, A.A. Dmitriev, R.A. Linsenmeier, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|R.A. Linsenmeier, Neurobiology, Northwestern University, Evanston, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Andrey Dmitriev: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Dmitriev: Commercial Relationship: Code N (No Commercial Relationship) | Robert Linsenmeier: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Light stimulation decreases oxygen consumption (QO_2) in the photoreceptors, but there is indirect evidence that it increases QO_2 in proximal retina, at least during flickering light. However, in the intact eye, the presence of the retinal circulation makes it difficult to isolate QO_2 of the inner retina from the O_2 supply. Here vascular interference was eliminated by making microelectrode recordings in the isolated retina, permitting us to test the hypothesis that QO_2 changes during flicker in opposite directions in the outer retina (OR) and inner retina (IR).

Methods: Double-barreled O_2-sensitive microelectrodes were used to measure local PO_2 in isolated mouse (C57Bl/6J) retinae. Simultaneously recorded local ERGs assisted in verifying the electrode position. Steady and diffuse white square wave flickering (1 Hz) light of scotopic and photopic intensities was applied. Previous recordings of retinal electrical activity and light-induced K^+ changes demonstrated that 1 Hz stimulation is optimal to evoke metabolic changes in the IR.

Results: Spatial profiles of PO_2 across the retina could be fitted with a 5-layer diffusion model in which the OR was represented, as in vivo, by non-consuming layers for the outer segments and outer nuclear layer (1^{st} and 3^{rd} layers), and a consuming layer for the inner segments (2^{nd} layer). The IR is divided into two more layers, in which the 4^{th} layer represented the OPL through INL and had a QO_2 designated Q4, and a 5^{th} layer, with a QO_2 of Q5, describing the GCL/NFL. In 75% of the profiles, Q5 was negligible, Q5/Q4 =0. The weighted average of QO_2 across the inner retina (Q_{IR}) in many cases was comparable or even larger than the weighted average of QO_2 across the outer layers (Q_{OR}). Flickering light applied while the electrode was stationary at different retinal depths showed that the PO_2 slowly increased over more than 3 min in the OR, reflecting lower Q_{OR}. However, flicker decreased PO_2 in the IR with a faster time course, stabilizing in less than 40 sec, reflecting an increase in Q_{IR}.

Conclusions: Retinal QO_2 can be described by a five-layer model that separates QO_2 in the OR and IR. Using microelectrodes allows a spatial analysis that is not possible with Warburg-type measurements, and we show directly the increase in Q_{IR} underlying neurovascular coupling.

CONTROL ID: 3711823

SUBMITTER (NAME ONLY): Leslie Hyman

TITLE: Thyroid Eye Disease: A USA (Wills Eye Hospital) and India (LV Prasad) Comparison

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Hyman, J. Sharpe, Q.(. Zhang, K. Alessi, E. Peskin, Vickie and Jack Farber Vision Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|S. Ramesh, A. Watson, Oculoplastic and Orbital Surgery, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|S. Ramesh, Center for Eye and Facial Plastic Surgery, Somerset, New Jersey, UNITED STATES|M.N. Naik, Ophthalmic Plastic Surgery Service, L V Prasad Eye Institute, INDIA|M. Moster, Neuro-Ophthalmology, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|A. Das, L V Prasad Eye Institute, INDIA|L. Hyman, Ophthalmology, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thyroid eye disease (TED) is an autoimmune process with possible vision-threatening manifestations. Little is known about the variability of TED characteristics in different ethnic populations. This pilot study aimed to compare demographic and clinical characteristics of TED and its impact on quality of life among patients at LV Prasad (LVP), Hyderabad, India and Wills Eye Hospital (WEH), Philadelphia, USA and to explore feasibility for a larger longitudinal study.

Methods: TED patients ages ≥18yrs, with active disease (onset ≤18m or Clinical Activity Score (CAS) ≥4) were recruited between 3/2021 -10/2021 at each center. Demographic, medical history, smoking and quality of life data were collected, a comprehensive orbital and ocular evaluation performed, and external eye photographs taken using standard protocols. Data between the WEH and LVP groups were compared using $\chi 2$, Fisher's exact tests, t-tests, or Wilcoxon rank sum tests.

Results: Sixty patients (30/center) were enrolled. WEH and LVP patients did not differ significantly by age (50.7 yrs. vs 45.6 yrs., respectively; p=0.13) or smoking status: % smokers (23% vs 13%; p=0.51). Significant differences between groups were seen by sex (% female: WEH: 86.7% vs LVP: 46.7%; p<0.001) and associated thyroid state (% Graves Disease: WEH: 93% vs LVP: 3%: p<0.0001; and % history of hyperthyroidism: WEH: 80% vs LVP: 50%: p=0.01). Clinical features (corneal and optic nerve status, exophthalmometry), quality of life measures and symptoms of retrobulbar ache and pain with eye movements did not differ significantly between groups (all p> 0.05). However, all (30/30) WEH patients vs. 11% of LVP patients exhibited CAS ≥4. WEH patients also were more symptomatic, e.g. higher CAS scores (mean (SD) 4.17 (1.7) for WEH vs 1.8 (1.7) for LVP), had higher frequencies of chemosis and conjunctival injection and more reported subjective symptoms of ocular irritation and blurry vision (all p values <0.0001).

Conclusions: Significant differences observed in the WEH and LVP patients by sex, underlying thyroid state, clinical activity, signs and some symptoms raise questions about possible variations in underlying pathogenesis, clinical disease expression or other unknown factors that may influence TED and its course in different ethnic populations. A larger study with longitudinal follow up is needed to further elucidate these novel observations.

CONTROL ID: 3711825

SUBMITTER (NAME ONLY): Ian Patterson

TITLE: Safety and efficacy of resident performed GATT (gonioscopy-assisted transluminal trabeculotomy)

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Patterson, M. Qiu, Ophthalmology, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Ian Patterson: Commercial Relationship: Code N (No Commercial Relationship) | Mary Qiu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A variety of literature exists assessing the safety and efficacy of resident-performed laser and traditional glaucoma surgery. In contrast, there is no available literature studying outcomes of resident-performed microinvasive glaucoma surgery (MIGS) due to the novelty of these surgeries. The purpose of our study is to observe the effectiveness and safety of resident performed GATT. Herein, we describe a single surgeon's experience teaching residents GATT.

Methods: Retrospective chart review of patients undergoing resident-performed GATT at an academic medical center from 12/18/19 to 9/30/2021. A resident must have performed more than 50% of the GATT. Patients required at least 90 days of follow-up for inclusion in IOP analysis. Cases of NVG were excluded.

Results: There were 49 eyes from 40 patients (24 POAG, 9 mixed mechanism, 6 chronic angle closure, 5 steroid induced, 2 low tension, 1 trauma, 1 pigmentary, and 1 secondary glaucoma due to ghost cell). Phaco-GATT was performed on 40 eyes. GATT-alone was performed on 9 eyes. Mean follow-up for phaco-GATT was 251 days (range 27-579), and for GATT alone was 369 days (range 48-643). In the phaco-GATT group, 35/40 reached follow-up >90 days. In the GATT alone group, 8/9 eyes reached follow-up >90 days. Both mean IOP and mean number of medications were reduced from baseline at 3, 6, and 12 months postoperatively in both surgical groups (except for mean medications at 12 months in the GATT-alone group), however some timepoints did not reach statistical significance, likely due to small sample size. Complications included 5 hyphemas at postoperative week one (12%), 2 hyphemas at postoperative month one (6%) (all hyphemas <0.5mm in height), 1 Descemet's detachment that resolved with air bubble (2%), 1 choroidal effusion (2%), and 1 cystoid macular edema (2%). GATT-alone took an average of 39 minutes (range 23-77 minutes). Phaco-GATT took an average of 67 minutes (range 31-156 minutes).

Conclusions: GATT is being performed more readily both in the community and at academic centers. As such, physicians in training will be learning how to perform this surgery more readily. Our study has shown that trainees have a similar success and complication rate to that reported in the literature, although operating times may be longer than expected for attending-performed cases.

CONTROL ID: 3711826

SUBMITTER (NAME ONLY): Heather Chandler

TITLE: MG53 Maintains Limbal Epithelial Cells to Promote Corneal Regeneration

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.L. Chandler, Q. jiang, T. Tan, H. Zhu, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Heather Chandler: Commercial Relationship: Code N (No Commercial Relationship) | qiwei jiang: Commercial Relationship: Code N (No Commercial Relationship) | Tao Tan: Commercial Relationship(s);Code E (Employment):TRIM-edicine | Hua Zhu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal wound healing is a complex and coordinated process involving injury repair to the epithelial layer and stimulation of limbal epithelial cell (LEC) migration and proliferation for tissue regeneration. Prevention of excessive stromal myofibroblast activation and vascular ingrowth is imperative to avoid fibrosis and angiogenesis, which can compromise corneal transparency. We hypothesize that MG53 constitutes an active component of corneal healing and regeneration by maintaining the health of LEC.

Methods: An alkaline-induced injury was introduced to the corneas of wildtype (WT) and MG53 knockout (mg53-/-) mice (n=6); healing was monitored for 14 days. Tissue from mice that overexpress MG53 or their littermate controls (n=6) were evaluated for expression of the LEC marker ΔNp63α. Cultured murine LEC were treated with Alexa-647-labeled recombinant human (rh)MG53 to determine protein uptake (n=4). Further, in the presence or absence of rhMG53, LEC underwent a colony formation assay (n=6), a microglass bead injury model followed by an LDH assay to evaluate viability (n=6), and a scratch assay to evaluate migration and proliferation (n=4).

Results: Mice with ablation of MG53 showed reduced expression of ΔNp63α. Further, following injury, the mg53-/- corneas exhibited hallmarks of limbal stem cell deficiency with compromised corneal epithelial regeneration, increased goblet cell infiltration, and pronounced stromal fibrosis and vascularization, compared to WT littermates. Mice with sustained elevation of systemic MG53 circulation show enhanced ΔNp63α expression within the limbus and increased tissue regenerative capacity with enhanced LEC function. Cultured LEC treated with rhMG53 internalized the protein and, when compared to controls, had significantly increased viability following injury ($p<0.001$), more colony forming units ($p<0.01$), and improved migration and proliferation ($p<0.01$).

Conclusions: We demonstrate that the protein MG53 is important in modulating LEC function associated with corneal injury-repair. Based on our data, we conclude that MG53 constitutes an active component of corneal injury-repair and regeneration by maintaining the health of LECs, as well as controlling the stromal fibrotic response.

CONTROL ID: 3711827

SUBMITTER (NAME ONLY): Valentina Sarao

TITLE: A comparison between two white LED confocal imaging systems for detection of diabetic retinopathy.

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Sarao, D. Veritti, P. Lanzetta, Dept of Ophthalmology, Universita degli Studi di Udine, Udine, Friuli-Venezia Giulia, ITALY|V. Sarao, P. Lanzetta, Istituto Europeo di Microchirurgia Oculare-IEMO, Udine, ITALY|

Commercial Relationships Disclosure: Valentina Sarao: Commercial Relationship(s);Code C (Consultant/Contractor):Centervue;Code C (Consultant/Contractor):Roche | Daniele Veritti: Commercial Relationship(s);Code C (Consultant/Contractor):Bayer;Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Roche | Paolo Lanzetta: Commercial Relationship(s);Code C (Consultant/Contractor):Aerie;Code C (Consultant/Contractor):Apellis;Code C (Consultant/Contractor):Bayer;Code C (Consultant/Contractor):Biogen;Code C (Consultant/Contractor):Centervue;Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Roche

ABSTRACT BODY:

Purpose: To evaluate the performance of two different white-light emitting diode (LED) confocal imaging systems in diabetic retinopathy (DR) grading.

Methods: In this prospective, instrument validation study, participants with type 1 or type 2 diabetes were scanned consecutively with two different white LED confocal scanners: Eidon and DRSplus (Centervue, Padova, Italy). Two-field retinal photographs were captured for each eye using Eidon (60 degrees, macula-centred and disc-centred fields) and DRSplus (45 degrees, macula-centred and disc-centred fields). Retinal images were randomly submitted to a certified retinal expert for grading in accordance with the DR grading system used in the UK National Health service (NHS). All case were also graded as referable DR (RDR) or not RDR.

Results: One hundred and fifty-five eyes of 78 diabetic patients were included in the analysis. Mean (± standard deviation) age of enrolled patients was 59.2 (± 5.3) years. Images from 5 eyes (3.2%) were classified as ungradable using DRSplus, 3 of these cases were judged as not gradable using Eidon. Among all gradable exams, the level of DR identified on images acquired using DRSplus agreed with those obtained with Eidon in 94% of cases. Cohen's kappa coefficient (κ) was 0.88. There was a 100% agreement when considering RDR.

Conclusions: An excellent agreement between Eidon and DRSplus was reported in determining the DR severity and RDR.

CONTROL ID: 3711828

SUBMITTER (NAME ONLY): Junji Morokuma

TITLE: Role of the adenylate cyclase/cyclic AMP pathway in oxytocin-induced lacrimal myoepithelial cells contraction

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Morokuma, M. Bowman, A. Garriz, M.V. Mariano, G.P. Hatzipetrou, D.Z. Zoukhri, Department of Comprehensive Care, Tufts University School of Dental Medicine, Boston, Massachusetts, UNITED STATES|D.Z. Zoukhri, Department of Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Junji Morokuma: Commercial Relationship: Code N (No Commercial Relationship) | Maytal Bowman: Commercial Relationship: Code N (No Commercial Relationship) | Angela Garriz: Commercial Relationship: Code N (No Commercial Relationship) | Michael Mariano: Commercial Relationship: Code N (No Commercial Relationship) | Georgios Hatzipetrou: Commercial Relationship: Code N (No Commercial Relationship) | Driss Zoukhri: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Lacrimal gland myoepithelial cells (MEC) play a key role in lacrimal fluid secretion. We recently reported that when MEC are stimulated with oxytocin (OXT), the phospholipase C/calcium pathway is activated, causing these cells to contract. In other tissues, OXT is also known to activate adenylate cyclase to generate the secondary messenger cyclic adenosine monophosphate (cAMP). In this study we aimed to investigate the involvement of cAMP and its downstream effectors in OXT-mediated lacrimal gland MEC contraction.

Methods: Lacrimal gland MEC were isolated and propagated from α-smooth muscle actin (SMA)-GFP mice, in which MEC express GFP making them easily identifiable. RNA and protein samples were prepared to analyze the mRNA and protein expression of adenylate cyclase coupling G proteins (Gαs, Gαo, and Gαi) by RT-PCR and Western blotting, respectively. To increase intracellular cAMP concentration, the following agents were used: forskolin (FKN, a direct activator of adenylate cyclase), 3-isobutyl-1-methylxanthine (IBMX, an inhibitor of the phosphodiesterase that hydrolyzes cAMP), or dibutyryl-cAMP (db-cAMP). In addition, selective inhibitors were used to investigate the role of protein kinase A (PKA) and exchange protein activated by cAMP (EPAC) in OXT-induced MEC contraction. MEC contraction was monitored in real time and changes in cell size were quantified using Fiji software.

Results: The adenylate cyclase coupling G proteins, Gαs, Gαo, and Gαi, are expressed in lacrimal gland MEC at both the mRNA and protein levels. FKN, IBMX and db-cAMP significantly stimulated MEC contraction, and preincubation of cells with either myr-PKI (PKA inhibitor) or ESI09 (EPAC inhibitor) resulted in almost complete inhibition of OXT- and FKN-stimulated MEC contraction.

Conclusions: We conclude that cAMP agonists modulate lacrimal gland MEC contraction via PKA and EPAC and also play a role in oxytocin-induced MEC contraction.

CONTROL ID: 3711829
SUBMITTER (NAME ONLY): Mariana DuPont
TITLE: Retinal vessel changes during early-stage diabetic retinopathy
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M.D. DuPont, M.B. Grant, The University of Alabama at Birmingham Department of Ophthalmology and Visual Sciences, Birmingham, Alabama, UNITED STATES|R.N. Mames, R. Moorthy, Retina Center, Florida, UNITED STATES|K. Kichler, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|
Commercial Relationships Disclosure: Mariana DuPont: Commercial Relationship: Code N (No Commercial Relationship) | Kara Kichler: Commercial Relationship: Code N (No Commercial Relationship) | Robert Mames: Commercial Relationship: Code N (No Commercial Relationship) | Robert Moorthy: Commercial Relationship: Code N (No Commercial Relationship) | Maria Grant: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Current evaluation of DR relies heavily on grading of secondary vascular effects, such as microaneurysms and hemorrhages, by clinical examination instead of by evaluation of actual vascular changes. VESsel GENeration (VESGEN) is a 2D automated microvascular mapping and quantification software that provides an interactive interface that has been used to map and quantify vascular changes in DR (Parsons-Wingerter, 2010); however, a limitation of the previous study was the lack of comparisons of DR subjects with age-matched controls.
Methods: Type 2 diabetics (n=8; 15 eyes) with an HgA1C of 6.2 to 10.5 and age-matched non-diabetic controls with HgA1C < 5.4 (n=8; 15 eyes) and age range from 25 to 52 years underwent retinal fluorescein angiography (FA). The diabetic cohort was grouped based on their DR level using modified ETDRS criteria and compared to controls. Vessel generations were determined and grouped based on vessel branching and dimeter into large (G1-3), medium (G4-5), and small (G≥6) vessels by VESGEN and output data from FA binary input images were analyzed using GraphPad
Results: Unexpectedly, no age-related changes were observed in arterial and venous tortuosity, density, or a total number of vessels in the controls. Diabetic subjects (mild and moderate) showed significantly less vessel length ($p=0.0047$) and branchpoint density ($p=0.0059$) compared to controls among total vessels (macro and microvessels, arterial and venous). Tortuosity of the total arterial and venous macrovessels (G1-5) were not significantly different in retinas of the controls, mild DR, or moderate DR subjects. However total tortuosity of the arterial but not venous microvessels (G≥6) were significantly increased in both mild ($p=0.0012$) and moderate ($p=0.006$) DR when compared to controls. The total number of arterial but not venous microvessels (G≥6) were increased in both mild ($p=0.001$) and moderate ($p=0.006$) DR when compared to controls. The vessel density of both arterial and venous microvessels in the retina of the mild DR ($p=0.024$ and $p<0.0001$, respectively) and moderate DR ($p=0.001$ and $p<0.0001$, respectively) subjects were statistically significantly increased compared to controls.
Conclusions: This study suggests that in microvessels (>G-5), vascular changes begin at mild DR. VESGEN with FA imaging may serve as an additional clinical tool for monitoring the small changes in progression of DR.

CONTROL ID: 3711831

SUBMITTER (NAME ONLY): Yukun Zhou

TITLE: Exploring Retinal Vascular Morphology via A Deep Learning Pipeline

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhou, D. Alexander, Centre for Medical Image Computing, University College London, London, UNITED KINGDOM|Y. Zhou, S. Wagner, M. Chia, P. Woodward-Court, P.A. Keane, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|P. Woodward-Court, Institute of Health Informatics, University College London, London, UNITED KINGDOM|S. Wagner, M. Chia, P.A. Keane, Institute of Ophthalmology, University College London, London, UNITED KINGDOM|D. Alexander, Department of Computer Science, University College London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Yukun Zhou: Commercial Relationship: Code N (No Commercial Relationship) | Siegfried Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Mark Chia: Commercial Relationship: Code N (No Commercial Relationship) | Peter Woodward-Court: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Alexander: Commercial Relationship: Code N (No Commercial Relationship) | Pearse Keane: Commercial Relationship(s);Code C (Consultant/Contractor):DeepMind, Roche, Novartis, Apellis, BitFount;Code O (Owner):Big Picture Medical;Code R (Recipient):Heidelberg Engineering, Topcon, Allergan, Bayer

ABSTRACT BODY:

Purpose: Retinal vascular morphology provides valuable information for both ophthalmic disease and systemic disease (termed 'oculomics'), e.g., atherosclerosis and diabetes mellitus, in a rapid and non-invasive way. To help recognise high risk cases of ophthalmic and systemic disease through observing the changes of retinal vascular morphology, we propose a deep learning pipeline to automatically analyse the vascular morphology (AutoMorph) which measures 12 kinds of metrics, such as vessel calibre and tortuosity.

Methods: AutoMorph consists of four functional modules: image pre-processing, image quality grading, anatomical segmentation, including binary vessel, artery/vein, and optic disc/cup segmentation, and vascular morphology feature measurement. Image quality grading and anatomical segmentation use the most recent deep learning techniques and are trained on 12 public datasets, such as DRIVE, STARE, and CHASEDB1. We employ model ensemble strategy to achieve robust results and analyse the prediction confidence to rectify false gradable cases in image quality grading. We quantitatively validate module performance on 6 external publicly available datasets including EyePACS image quality dataset (EyePACS-Q), DDR, AV-WIDE, DR-HAGIS, IOSTAR-AV, and IDRID datasets.

Results: The EfficientNet-b4 architecture used in the image grading module achieves comparable performance to the state-of-the-art method in EyePACS-Q, with an F1-score of 0.86. The confidence analysis reduces 76% of false gradable images. The binary vessel segmentation module achieves an F1-score of 0.73 on AV-WIDE and 0.78 on DR-HAGIS. The artery/vein module scores 0.66 on IOSTAR-AV, and optic disc/cup module achieves 0.94 in disc segmentation in IDRID. These results verify that AutoMorph performs well in external validation, being quantitatively on par or even better than some recent work in internal validation.

Conclusions: AutoMorph performs well even when the external validation data shows significant difference to the training data, e.g., validation on ultra-wide field retinal photography. The fully automatic pipeline integrates recent technical work to facilitate 'oculomics' research.

CONTROL ID: 3711832

SUBMITTER (NAME ONLY): Ruth Kelly

TITLE: The effect of L-NAME on outflow facility in whole porcine eyes.

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Kelly, F.S. McDonnell, W.D. Stamer, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|D.R. Overby, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: N(ω)-nitro-L-arginine methyl ester (L-NAME), a nitric oxide synthase (NOS) inhibitor, has previously been shown to decrease outflow facility in human anterior segments and murine eyes, but not in enucleated whole globes of porcine eyes. The aim of the present study was to test the effects of L-NAME on outflow facility in enucleated whole globes of porcine eyes.

Methods: Paired porcine eyes (n=5) were used within 24 hours of death. Eyes were perfused at constant pressure of 15 mmHg. Following a 1 hour baseline, one eye of each pair was exchanged with 50 μM of L-NAME in Dulbecco's Phosphate-Buffered Saline with 1 mg/mL D-glucose (DBG), and then perfused for 3 hours, while the contralateral control eye was perfused with DBG for 3 hr.

Results: Over the course of the perfusion, control porcine eyes displayed a “washout” rate of 5.2 [-23.1, 33.6] % increase in outflow facility (mean [CI], p = 0.6354, one sample t-test to theoretical mean of 0, n=5). In contrast, outflow facility in contralateral eyes that were treated with L-NAME significantly decreased by 12.2 [-23.0, -1.3] % over time of perfusion (mean [CI], p = 0.0361, n=5), with a net decrease of 17% compared to control (p = 0.1101, paired t-test, n=5).

Conclusions: Results showing that L-NAME significantly decreases outflow in porcine eyes are consistent with those observed previously in mouse and human eyes and suggests that basal levels of endogenous NO production by endothelial cells of Schlemm’s canal is an important mediator of outflow resistance, and thus IOP.

CONTROL ID: 3711834

SUBMITTER (NAME ONLY): Winston Ong

TITLE: KPI-287 Demonstrates Superior Efficacy Over Axitinib in a VEGF-induced Retinal Leakage Model

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Ong, P. Baciu, E. Enlow, Kala Pharmaceuticals, Inc., Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Winston Ong: Commercial Relationship(s);Code E (Employment):Kala Pharmaceuticals, Inc. | Peter Baciu: Commercial Relationship(s);Code E (Employment):Kala Pharmaceuticals, Inc. | Elizabeth Enlow: Commercial Relationship(s);Code E (Employment):Kala Pharmaceuticals, Inc.

ABSTRACT BODY:

Purpose: Anti-VEGF therapeutics that provide both reliability of administration and durability of action are critical for patients suffering from neovascular disease. Small molecule pan-VEGFR inhibitors hold great promise to meet this unmet medical need. However, the ability to deliver small molecule VEGFR2 inhibitors to posterior ocular tissues is hindered by unfavorable solubilities and dosing limitations. These shortcomings are addressed by KPI-287, an investigational NCE that potently inhibits VEGFR family members with a superior pharmacokinetic/pharmacodynamic (PK/PD) profile relative to compounds currently undergoing clinical trials.

Methods: In vitro kinase pharmacological profiles of KPI-287 and axitinib were evaluated against a panel of 97 kinases distributed across the kinome (Eurofins DiscoveRx, USA). IC_{50} for VEGFR-2 and PDGFR-β were determined in HUVEC and NIH3T3 cell lines, respectively (ProQinase, Germany). PK/PD profiles of both compounds were evaluated in Dutch-belted rabbits following topical administration and intravitreal (IVT) challenge with rhVGEF.

Results: Both KPI-287 and axitinib demonstrate comparable inhibitory profile against VEGFR and PDGFR kinases (FLT1, KDR, FLT4, PDGFR-α and PDGFR-β). However, the two compounds exhibited differing secondary pharmacology, with KPI-287 showing activity at EGFR, ALK and TGFβ1. Despite the similar activities at VEGR subtypes, KPI-287 showed superior in vivo efficacy compared to axitinib in the rabbit rhVEGF challenge model despite more frequent dosing of axitinib. The superior efficacy of KPI-287 correlated with a greater solubility and higher tissue levels achieved in the retina and choroid of Dutch-belted rabbits compared to those for axitinib. PK/PD profiling of KPI-287 demonstrated that efficacy can be achieved at retinal concentration >250 nM, supporting administration of KPI-287 by intravitreal and suprachoroidal routes.

Conclusions: Relative to axitinib, the most potent VEGFR2 inhibitor currently in the clinic for the treatment of wet AMD, KPI-287 demonstrated comparable in vitro potency and superior efficacy in the rabbit VEGF challenge model. The favorable efficacy profile was associated with greater solubility and ability to achieve higher tissue levels. These data support the development of KPI-287 for the treatment of choroidal neovascular disease using IVT and suprachoroidal routes of delivery.

CONTROL ID: 3711838

SUBMITTER (NAME ONLY): Preetam Kumar

TITLE: Suprathreshold contrast perception remains unimpaired in keratoconus despite loss of contrast sensitivity

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Kumar, S.R. Bharadwaj, Brien Holden Institute of Optometry and Vision Sciences, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|P. Kumar, C. Hull, P. Campbell, Division of Optometry and Visual Science, School of Health Sciences, Northampton Square, London EC1V 0HB, UK, City University of London, UNITED KINGDOM|P.K. Vaddavalli, The Cornea Institute, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S.R. Bharadwaj, Prof. Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Threshold-level spatial vision (e.g., contrast sensitivity, logMAR visual acuity) is known to be deteriorated in keratoconus. However, suprathreshold spatial visual performance in this disease condition remains largely unknown. This study assessed the suprathreshold contrast perception in keratoconus using the well-known contrast constancy paradigm. The study hypothesized that suprathreshold contrast matches for keratoconus will show deficiencies that may be predicted from the pattern of loss in their contrast sensitivity function (CSF).

Methods: Apparent contrast matches were determined at 10% and 50% stimulus contrast in 10 unilateral keratoconic cases (24 – 29yrs) and 10 age-similar controls using an adaptive staircase procedure with 8 reversals. Contrast matches were determined between a “standard” Gabor grating, with spatial frequency corresponding to the peak of the subject’s CSF, and “test” gratings with frequencies at one-third, one-half, twice or thrice that of the standard grating.

Results: Contrast sensitivity of keratoconic cases showed significant deterioration (mean±1SD area under CSF: 1.25±0.37log units), relative to controls (2.23±0.24log units) ($p<0.001$). For both cases and controls, the matching contrasts of test gratings for both suprathreshold contrast levels were within ±20% of the standard grating contrast for spatial frequencies greater than the peak CSF ($p=0.12$ for both). In comparison, the contrast matches of test gratings were significantly higher (~40 – 60%) for spatial frequencies lower than the peak CSF ($p<0.05$ for both frequencies).

Conclusions: Suprathreshold contrast perception appears to remain unaltered in keratoconus for spatial frequencies higher than the peak of the CSF, even though contrast sensitivity is significantly deteriorated. Suprathreshold contrast losses may however be perceived in both keratoconics and controls for spatial frequencies lower than the peak of the CSF.

CONTROL ID: 3711839

SUBMITTER (NAME ONLY): Sunny Kwok

TITLE: IOP-related Mechanical Deformation is Concentrated in the Anterior Optic Nerve Head and Peripapillary Sclera

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kwok, J. Liu, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|Y. Ma, J. Liu, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|X. Pan, Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Sunny Kwok: Commercial Relationship: Code N (No Commercial Relationship) | Yanhui Ma: Commercial Relationship: Code N (No Commercial Relationship) | Xueliang Pan: Commercial Relationship: Code N (No Commercial Relationship) | Jun Liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To apply a 3D ultrasound elastography technique to map and evaluate the through-depth and regional variation of tissue deformation in the optic nerve head (ONH) and the surrounding peripapillary sclera (PPS) during intraocular pressure (IOP) elevation.

Methods: Inflation tests were performed in 15 normal human donor (20-78 years old) globes while IOP was raised from 15 to 30 mmHg. A 3D volume of the posterior eye centered at the ONH (10 mm × 10 mm) was scanned at each pressure step using a 50MHz ultrasound probe (MS700, Vevo2100, VisualSonics). A correlation-based 3D speckle tracking algorithm was used to compute tissue displacements. Radial, circumferential, meridional and shear strains in spherical coordinates were obtained. ONH and PPS were manually segmented on 3D ultrasound images and divided into equal anterior and posterior layers. Average strains at 30 mmHg were calculated for each region and compared using linear mixed models with unconstrained covariance matrix to account for associations of different regions of the same eye.

Results: Strain maps (Figure 1) showed higher magnitudes of radial (ε_{rr}) and out-of-plane shear ($\varepsilon_{\varphi r}$) strains in the anterior ONH and PPS. Quantitative analysis showed that ε_{rr} and $\varepsilon_{\varphi r}$ were significantly greater in the anterior PPS than posterior PPS (-4.80±0.84% vs -1.42±0.74% and 1.53±0.43% vs 0.76±0.21%, p's<0.001; Figure 2). Similarly, ε_{rr} and $\varepsilon_{\varphi r}$ were significantly greater in the anterior ONH than posterior ONH (-4.15±0.83% vs -0.10±0.61% and 2.45±0.93% vs 1.30±0.42%, p's<0.001). Anterior ONH had larger shear but smaller radial strain compared to anterior PPS (p=0.0003 and 0.0001).

Conclusions: Despite a small total thickness, the ONH and PPS exhibited significant depth-dependent variation in IOP-related mechanical deformation. Radial and shear strains were largely concentrated in the anterior region, possibly underlying glaucomatous damage such as tissue tear and disc hemorrhage in this region.

CONTROL ID: 3711840

SUBMITTER (NAME ONLY): Quintin Richardson

TITLE: Diagnostic accuracy of an iPad application for detection of visual field defects

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q. Richardson, C. Moe, D. Wittberg, K. O'Brien, J.D. Keenan, Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|R. Kumar, B. Ramgopal, M. Rackenchath, S. A V, S. Nagaraj, Narayana Nethralaya, Bangalore, Karnataka, INDIA|R. Kumar, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|R. Stamper, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Quintin Richardson: Commercial Relationship: Code N (No Commercial Relationship) | Rajesh S. Kumar: Commercial Relationship: Code N (No Commercial Relationship) | B Ramgopal: Commercial Relationship: Code N (No Commercial Relationship) | Mahalakshmi V Rackenchath: Commercial Relationship: Code N (No Commercial Relationship) | Sathi Devi A V: Commercial Relationship: Code N (No Commercial Relationship) | Sriharsha Nagaraj: Commercial Relationship: Code N (No Commercial Relationship) | Caitlin A Moe: Commercial Relationship: Code N (No Commercial Relationship) | Dionna M Wittberg: Commercial Relationship: Code N (No Commercial Relationship) | Kieran S O'Brien: Commercial Relationship: Code N (No Commercial Relationship) | Robert L Stamper: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Keenan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the diagnostic accuracy of iPad perimetry using the visualFields Easy (VFE) application for glaucoma screening.

Methods: This was a prospective, cross-sectional study that enrolled patients undergoing their first Humphrey Field Analyzer (HFA) visual field test at the glaucoma clinic at a tertiary eye hospital in India between October 2014 and September 2015. Patients were excluded if they had undergone intraocular surgery within 2 weeks of enrollment. Participants received 24-2 SITA Standard HFA testing followed by iPad perimetry with the visualFields Easy application. The diagnostic accuracy of iPad perimetry was assessed for visual field defects relative to HFA results and for glaucoma relative to ophthalmologist diagnosis.

Results: iPad perimetry showed an area under the receiver operating characteristic (AUROC) curve of 0.67 (0.61-0.74) for visual field defect detection. This is in contrast with 0.86 (0.81-0.91) using 24-2 HVF. For detection of any glaucoma, VFE had an AUROC of 0.66 (0.58-0.73) while HVF had 0.89 (0.84-0.93). Sensitivities for glaucoma detection were 66.7% (48.7-78.5) and 80.2% (69.6-90.1) for VFE and HVF, respectively.

Conclusions: Our findings suggest that iPAD perimetry using the VFE application is inferior to 24-2 Standard HVF testing in detecting any visual field defects and glaucoma. The limited sensitivity of VFE minimizes its utility as an optimal tool for a glaucoma screening.

CONTROL ID: 3711841

SUBMITTER (NAME ONLY): Ailis Moran

TITLE: Elucidating Intrinsic and Extrinsic Regulators of Outer Segment Phagocytosis in Zebrafish

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Regulated, cyclical peaks of outer segment phagocytosis (OSP), by the retinal pigmented epithelium (RPE), maintain healthy photoreceptors. Defective OSP is implicated in inherited and age-related blindness˙ However, the mechanisms instigating OSP in photoreceptors, particularly in cones, remains poorly characterised, leaving a knowledge gap in retinal biology and disease. This study investigates extrinsic environmental and intrinsic molecular regulators of OSP in zebrafish.

Methods: Real-time PCR was carried out on cDNA generated from 15 dpf zebrafish eyes collected under normal light-dark (14h:10h) or following 1 day under dark-dark conditions. For TEM analysis of shed OS, phagosomes were manually counted, and the density calculated as phagosomes per µm of RPE (n=3). Proteomic profiling of sibling eyes collected at ZT 4, ZT 9 and ZT 17 was performed by mass spectrometry (MS) (n=3).

Results: Real-time PCR identified candidate OSP regulators including cerkl, mertka and abcf1 to maximise expression prior to one or both OSP peaks under a regular light-dark cycle (n=3). Dark:dark environmental conditions revealed the number of RPE phagosomes at circadian time (CT) 4 (0.12 phagosomes/um RPE) was significantly ($p=0.003$) reduced compared to the peak number (0.18 phagosomes/um RPE) at ZT 4 under a normal light dark cycle, suggesting an absence of circadian regulation. Preliminary data (n=2) suggests that the absence of light alters the transcription profiles of several known OSP regulators. Potential novel regulators of OSP were uncovered using proteome profiling of the zebrafish retina at ZT 4, ZT 9 and ZT 17 and these are being validated by immunostaining.

Conclusions: The data provides a model for insights into the regulators of OSP in a cone-rich retina. In summary, the results shown here identify transcript and proteomic profiles of known and putative OSP regulators, revealing highly upregulated expression levels at time-points correlating to both dawn and dusk peaks of OSP. Exposure to light:dark transition is necessary to fully initiate the burst of OSP at peaks in the zebrafish retina, and may be involved in controlling expression profiles of molecular regulators. This data also holds biomedical significance as defective OSP may be part of the disease pathway for many retinal and macular degenerations.

CONTROL ID: 3711842

SUBMITTER (NAME ONLY): Eberhart Zrenner

TITLE: Effects of Intra-orbital Mechanical Forces on Subretinal Implant ALPHA: Assessment of Cable Movement by Dynamic Computer Tomography during Gaze Changes as a Possible Cause for Subretinal Implant Movements

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Zrenner, H. Faber, C. Kernstock, L. Kuehlewein, K. Stingl, Center for Ophthalmology, University of Tuebingen, Tuebingen, GERMANY|

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ABSTRACT BODY:

Purpose: The aim was to assess the effect of eye movements on intraorbital cables of retinal implants using dynamic computer tomography (CT) scan series during gaze changes that can cause mechanical forces leading to movements of subretinal electronic arrays in patients.

Methods: In 27 datasets of patients with Retina Implant Alpha IMS (Retina Implant AG, Reutlingen, Germany) the displacements of the microchip were investigated relative to the optic disc and major blood vessels. Additionally, three techniques for intra-orbital cable routing were analyzed (straight cable route, para-bulbar loop and encircling band). The bending radius of the intra-orbital cable was measured as indicator for mechanical stress; additionally, gaze restrictions were analyzed.

Results: Chip position remained stable in 12/27 cases (44%) whereas in 15/27 (56%), displacement occurred. The mean ± SD displacement in those 15 eyes was 0.66 ± 0.35 mm (range, 0.24–1.67 mm); similar data were obtained in 8 patients who had received Alpha AMS implants. CT-investigation of average bending radius variation of intra-orbital cables was 87% for straight cable route, 11% for para-bulbar loop routing and 16% for encircling band technique. The analysis of eye motility showed a restriction in the up-gaze and gaze to the temporal side directly after surgery in 8/9 Implant Alpha AMS patients. The degree of motility restriction decreased continuously with recovery during the observation time.

Conclusions: In patients with Retina Implant Alpha, firstly, the majority shows slow implant displacements in the subretinal space (mean ± SD 0.66 ± 0.35 mm), developing without major sequelae; secondly, arcuate routes with large bending radius of intra-orbital cables significantly reduce cable movement and thereby mitigate mechanical forces; thirdly, short intra-orbital cable lengths are mainly restricting up-gaze and gaze to the temporal side. There are several mechanical forces, related to eye movements and cable properties, including breaks, that need careful consideration of engineering techniques, selection of cable routes and surgical procedures.

CONTROL ID: 3711843

SUBMITTER (NAME ONLY): Preeya Mehta

TITLE: Incidence and Risk Factors for the Development of Treatment-Warranted Diabetic Macular Edema at 5 Years Following Initial Diagnosis of Type 2 Diabetes

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Mehta, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|W.S. Gange, J. Lopez, B. Xu, S. Seabury, B. Toy, USC Roski Eye Institute, Department of Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|K. Lung, S. Seabury, Keck-Shaeffer Initiative for Population Health Policy, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the incidence and risk factors for developing treatment-warranted diabetic macular edema (TW-DME) within 5 years after diagnosis of type 2 diabetes (DM2). This may aid identification of patients at increased risk of vision loss who may benefit from additional interventions.

Methods: We performed a retrospective longitudinal cohort study using the Optum's de-identified Clinformatics® Data Mart Database from 2007 to 2015. Individuals 18 years of age and older with a diagnosis of DM2 and continuous insurance enrollment of 6 years (1 pre, 5 post-diagnosis) were identified. The cumulative incidence of TW-DME within 5 years was determined using medical claims data. Associations between TW-DME and sociodemographic and clinical factors were tested with multivariable logistic regression. Statistical significance was evaluated with a p-value of 0.05.

Results: Of 72,067 patients newly diagnosed with DM2, 540 (0.75%) patients had developed TW-DME at 5 years after DM2 diagnosis. Patients who developed TW-DME were more likely to be of older age at diagnosis (age 65-74, OR 1.58, p=0.009) and to have other systemic complications of DM2, including renal disease (OR 2.59, p<0.001), neurological disease (OR 2.40, p<0.001), and peripheral circulatory disorders (OR 2.15, p=0.007). In addition, insulin use (OR 4.11, p<0.001) was more common, and max A1c was higher (9.7 ± 2.5 vs 7.6 ± 2.0, p<0.01) in those developing TW-DME. Young age at diagnosis (age 18-34, OR 0.36, p=0.005), Medicare insurance (OR 0.47, p<0.001), morbid obesity (OR 0.62, p=0.001), smoking (OR 0.77, p=0.046), and dyslipidemia (OR 0.80, p=0.034) were identified as protective factors. African-Americans and Hispanics had a higher incidence of TW-DME, 0.84% and 0.79% respectively, while Asians had a lower incidence of 0.64%.

Conclusions: Patients with a history of A1c > 9%, insulin use, renal disease, neurologic disease, and peripheral circulatory disease, and advanced age at diagnosis are at a higher risk for early development of TW-DME. These patients may require additional and earlier screening after diagnosis of DM2.

CONTROL ID: 3711844

SUBMITTER (NAME ONLY): Harry Quigley

TITLE: Astrocytes of the optic nerve head in pig and human eyes have no aquaporin channels

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.A. Quigley, C. Keuthan, M. Pease, E. Kimball, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been proposed that glaucoma's optic nerve (ON) injury is related to glymphatic pathway fluid movement and thus would be dependent on astrocytic aquaporin (AQP) channels [1]. We have reported that AQPs are absent in the astrocytic lamina of rodent optic nerve head (ONH) [2]. This study quantified regional AQP channel expression in astrocytes of the porcine and human retina, ONH and myelinated ON (MON).

Methods: In pig and human post mortem eyes, we immunolabeled sections containing retina, ONH and MON against AQP1, 4, and 9, myelin basic protein, glial fibrillary acidic protein (GFAP) and α-dystroglycan (αDG). AQP label was quantified in each region [2] and quantitative gene expression data were analyzed in retina, ONH and MON tissues separately by qPCR in pig eyes. Human eyes were confirmed to have no retinal or ON disease histologically and by pre-mortem history.

Results: Pig and human eyes had abundant AQP4 in Müller cells, retinal astrocytes, and MON astrocytes, but minimal expression in the ONH lamina cribrosa. AQP1, 9 were present in retina, but not in ONH. Immunolabeling of GFAP and αDG were present and had similar staining patterns in ONH and MON. Quantitative AQP4 labeling was at background level in ONH, but substantial in MON (ONH vs MON, $p \leq 0.01$). AQP4 mRNA expression was minimal in ONH, but significantly higher in MON ($p=0.0001$). GFAP mRNA expression was uniform in ONH and MON.

Conclusions: The absence of AQP4 channels in ONH astrocytes is evolutionarily conserved in all mammals studied. Aqp4 knockout mice have no beneficial or detrimental outcomes in experimental glaucoma. The regionally specific lack of AQP channels in ONH astrocytes is likely to be a protective mechanism against swelling in the narrow ONH region. The glymphatic pathway is unlikely to play a role at the site of damage in glaucoma.

CONTROL ID: 3711846

SUBMITTER (NAME ONLY): Yudong Tao

TITLE: Variance reduction for visual field testing algorithms through optimization of initial estimation

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Tao, M. Khodeiry, R. Ma, X. Mendoza, X. Liu, K. Alawa, R.K. Lee, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|Y. Tao, R. Ma, M. Shyu, Electrical and Computer Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Variance of the probability mass function (PMF) for sensitivity estimation is an important measure for visual field (VF) testing algorithms, as a smaller variance indicates that the algorithm is more confident that the PMF represents the true sensitivity. We developed and tested a variance reduction technique to optimize the initial sensitivity estimation, thereby improving the overall performance of visual field testing algorithms.

Methods: The Zippy Estimation by Sequential Testing (ZEST) algorithm was simulated on our visual field dataset with 504 normal and 784 glaucomatous visual fields with a 24-2 testing pattern. Visual fields were divided into multiple VF regions and fixed the testing locations of the first batch of light stimuli to be inside the nasal and arcuate region. After obtaining the sensitivity estimations from these testing locations, a gradient boosting decision tree classifier was used to determine whether the visual field is from a normal or abnormal group. Then, the initial PMFs of the remaining locations were set to be the empirical distribution obtained from a normal or abnormal group based on prediction outcomes. Finally, these locations were tested with the adjusted initial PMFs.

Results: By adopting the proposed variance reduction approach, ZEST becomes 4.57% faster and 4.17% more accurate ($p<0.01$). Meanwhile, the gradient boosting decision tree classifier achieves a 97% average classification accuracy.

Conclusions: Our results indicate that using a carefully designed testing sequence can effectively reduce the variance in sensitivity estimation and greatly improve the quality of visual field tests, leading to shortened testing time, higher testing accuracy, and improved patient’s satisfaction.

CONTROL ID: 3711847

SUBMITTER (NAME ONLY): Clara Llorens Quintana

TITLE: Anterior topographic limbal demarcation with ultrawide-field OCT

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Llorens Quintana, Y. Li, D. Huang, Casey Eye Institute, Department of Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S. Chen, J. Lin, J.G. Fujimoto, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an automatic method to find the external limbal transitions points between the cornea and the sclera based on anterior topography obtained from ultrawide-field anterior segment optical coherence (OCT) images.

Methods: An ultrahigh-speed (325 kHz) ultrawide-field swept-source OCT prototype was used to obtain corneo-scleral (CS) images of the left and right eyes from four subjects. The imaging depth range is 15.5 mm with an axial resolution of 12.2 µm (in air). The scan pattern consisted of 16 radial scans of 20 mm width. This scan pattern was centered on the pupil and repeated three times consecutively in each acquisition. The CS profile, segmented from the OCT cross-sectional images, was corrected for the field distortion inherent to the OCT scans. For each meridian, the second central moment of the OCT signal was projected to obtain a radial profile on which the anterior CS junction [DH1] and pupil can be identified by sharp transitions. The anterior corneal surface inside the CS junction was fitted with a 4^{th} degree polynomial and the anterior conjunctival surface over the sclera outside the CS junction was fit with a 2^{nd} degree polynomial. The external limbus was identified as the point where these best-fit corneal and scleral surfaces intersected. The external [DH2] limbal positions from the 16 meridians were combined and modelled with a best-fit ellipse.

Results: The average ± standard deviation radial distance from the pupil center to the limbal transition was 6.16 ± 0.24 mm. Further, the limbus was modeled with an ellipse which average ± standard deviation minor and major axes of 11.87 ± 0.70 mm and 13.01 ± 0.48 mm, respectively.

Conclusions: Ultra-fast swept-source OCT provides high-resolution CS images. Using the central moment of the OCT signal, the CS transition and the pupil can be identified automatically. The external limbus defined by the shape of the anterior surface is different to the WTW distance and therefore an automatic method, as the one proposed, would be more suitable to define the external limbus which is needed for scleral lens fitting.

CONTROL ID: 3711849

SUBMITTER (NAME ONLY): Nathan Giauque

TITLE: Separately Imaging Zeaxanthin and Meso-zeaxanthin in the Human Fovea with Polarized Resonance Raman Microscopy

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Giauque, F. Chang, Z. Wan, B. Li, P.S. Bernstein, Department of Ophthalmology and Visual Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Zeaxanthin and meso-zeaxanthin are the dominant carotenoids in the human fovea. These two carotenoids are stereoisomers, sharing the same molecular formula but differing from each other only in the orientation of the hydroxyl group at the C3' of the β-ionone ring. Conventional resonance Raman microscopy cannot distinguish zeaxanthin from meso-zeaxanthin. Here, we investigated whether zeaxanthin and meso-zeaxanthin can be separately measured using polarized resonance Raman microscopy.

Methods: Our XploRA Plus confocal resonance Raman microscope is equipped with three polarized laser modes (vertical, horizontal, and circular) and three polarized Raman detection modes (vertical, horizontal, and non-polarized), generating nine polarized test conditions. To determine the optimal condition for the separation of zeaxanthin and meso-zeaxanthin, 100 μM zeaxanthin and 100 μM meso-zeaxanthin solutions in methanol were mixed with ratios of 1:0, 3:1, 2:1, 1:1, 1:2, 1:3, and 0:1, respectively, and tested at nine polarized conditions with excitation of a 473 nm laser. Using the optimized condition, we further measured the carotenoid in the fovea of an 87-year-old female donor eye. A total zeaxanthin map was created by mapping the intensity of the V1 peak at 1528 cm^{-1}. Separate maps of zeaxanthin and meso-zeaxanthin were generated by LabSpec6 software's Classical Least Squares(CLS) fitting algorithm.

Results: The compositions of zeaxanthin and meso-zeaxanthin in the mixed carotenoid solutions measured under two polarized conditions: horizontal laser vs vertical Raman (H-V), and circular laser vs vertical Raman (C-V), were significantly correlated to the known ratios of the mixed carotenoid solutions. The Raman signals of carotenoids under C-V condition were stronger than the H-V condition, serving as the optimized condition to measure carotenoids in the human fovea. The retinal distribution of total zeaxanthins exhibits a circle with a dot at its center. Further analysis revealed that zeaxanthin was localized mainly at the central dot area, whereas the meso-zeaxanthin was allocated on the circle.

Conclusions: This demonstrates that zeaxanthin and meso-zeaxanthin can be separately measured under polarized Raman conditions, which might offer new knowledge to understand the physiological role of macular carotenoids in the prevention of retinal disease.

CONTROL ID: 3711850

SUBMITTER (NAME ONLY): Shuhong Jiang

TITLE: Visual and retinal function changes in a mouse model of Alzheimer Disease

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Jiang, K. Chang, K. Cho, A. Lennikov, W. Tai, A. Ashok, D. Chen, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is emerging that there are early changes of visual function in association with Alzheimer's disease (AD). In this work, we propose to test the potential changes and when the changes start to appear in the retinas o AD mice, using the triple transgenic mouse model (3×Tg-AD).

Methods: We carried out a longitudinal study in AD (3×Tg-AD) mice at 2, 4, 6, 12 months of ages. Age and sex-matched wild-type mice were used as controls. Visual acuity and contrast sensitivity were assessed by optomotor response (OMR). Retina functional changes were evaluated by electroretinography (ERG) to record the ganglion cell dominated positive scotopic threshold response (pSTR) that were elicited with the dimmest flashes (0.0001765 cd/m^2). Outer retinal layer functions were recorded by ERG maximum scotopic response (Xenon lamp, 2cd. cd/m^2), light-adapted photopic (Xenon light, 600 cd/m^2), S cone test (green light, 13 cd.s/m^2), and M cone test (blue light, 13 cd.s/m^2).

Results: Significantly reduced visual contrast sensitivity (CS) was detected in 3xTG-AD mice at as early as 2 months (2M) of age compared to age-matched wild-type control mice. Notably, female AD mice showed better CS than male mice when examined at 2M of age. Starting from 6M old, there was significant reduction of visual acuity (VA) in 3xTG-AD mice comparing with age-matched WT control mice. The ERG pSTR amplitude in 3xTg-AD mice was also significantly reduced at 4M of age comparing to WT, and this difference persisted throughout the later ages examined (4M, 99.308+/-7.194 vs 107.307+/-6.986, $p < 0.01$; 12M, 56.39+/-15.56 vs 78.77+/-16.89, $p < 0.05$ by two-way ANOVA). 3xTg-AD mice also revealed a significantly higher scotopic b-wave amplitude and light-adapted photopic response than WT mice starting from 6M of age. The a-wave amplitude and S cone test or M cone test in AD mice were not significantly different from the WT at all time points.

Conclusions: Our results suggest visual function deficit at a very early-stage of AD. Sex differences in the spatial frequency threshold should be considered. The pattern of neuronal dysfunction in AD mice occurs primarily in the inner retina and probably progresses to encompass the outer retina with age.

CONTROL ID: 3711853

SUBMITTER (NAME ONLY): Palak Gupta

TITLE: Effects of subthalamic deep brain stimulation (DBS) on binocular coordination of saccades and strabismus angle in Parkinson's disease (PD)

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Gupta, A. Shaikh, Biomedical Engineering, Case Western Reserve University Case School of Engineering, Cleveland, Ohio, UNITED STATES|P. Gupta, S.B. Beylergil, J. Jacobs, A. Shaikh, Daroff Dell 'Osso Ocular Motility Lab, Louis Stokes VA Medical Center, Cleveland, Ohio, UNITED STATES|J. Murray, F.F. Ghasia, Ophthalmology, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vergence insufficiency, impaired saccades contribute to depth perception deficits, poor navigation, and increased fall risk in PD patients. 1/3rd of PD patients also have strabismus and disabling double vision. DBS is becoming increasingly common for improving general motor symptoms of PD. In this study we examined the effects of bilateral STN DBS on the binocular coordination of saccades in PD.

Methods: We measured binocular eye positions during gaze-holding and saccades using high-resolution video-oculography (Eyelink1000™) in twenty PD patients and seven healthy controls. Saccades were quantified by placing LED targets at 150 cm distance on an isovergence circle with angle of ±10° and ±20°. Subsequently, clustering was performed to analyze gaze-holding performance. Saccades were identified and analyzed using the Engbert algorithm.

Results: Binocular coordination in PD was significantly better with DBS switched ON, as compared to OFF ($p<0.05$). Supervised clustering was applied to gaze fixation data in order to assess performance. Controls had a mean of maximal deviation (Horizontal: 1.9±0.56°, Vertical: 1.94±0.6°) significantly different from PD DBS OFF (Horizontal: 3.08±2.98°, Vertical: 1.54± 1.40°), but not from PD DBS ON (Horizontal: 1.71± 1.28°, Vertical: 1.27± 1.4°). This was also reflected in saccade tasks with fusion maintenance. Post saccade drift variance in controls (Mean:0.01±0.03°; $p<0.05$) was found to be different from PD with DBS OFF (Mean:0.19±0.76°). Meanwhile, there was no difference in post saccade drift variance between controls and PD DBS ON (Mean:0.01±0.02°). The difference in latency of controls (Mean:0.244±0.029msec), PD DBS ON (Mean:0.50±0.47msec) and PD DBS OFF (Mean:0.32±0.11msec) approaches statistical significance ($p=0.09$).

Conclusions: Objective analysis of gaze-holding and saccadic eye movements suggest that saccadic abnormalities and strabismus are prevalent, significant, and interrelated in PD. The results suggest that STN-DBS affects the neural pathway common to both vergence and saccades, possibly by acting on the STN–substantia nigra pars reticulata–superior colliculi pathway. These findings provide novel insights into the pathophysiology of Parkinson's disease and may yield better treatment strategies for strabismus, including using STN DBS.

CONTROL ID: 3711854

SUBMITTER (NAME ONLY): Megan Straiko

TITLE: Simplifying DMEK with a Double Scroll Graft: How to Achieve It and How to Avoid Excessive Tissue Damage

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Straiko, K. Can, K.D. Tran, Research, Lions VisionGift, Portland, Oregon, UNITED STATES|K. Odell, M. Hikes, Tissue Processing, Lions VisionGift, Portland, Oregon, UNITED STATES|P.B. Veldman, Ophthalmology and Visual Sciences, University of Chicago, Chicago, Illinois, UNITED STATES|A. Blitzer, Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine tissue quality resulting from manipulation to form double scroll (DS) DMEK grafts during and after graft preparation.

Methods: DS during preparation: Grafts prepared from 10 pairs of donor corneas (age 39-66) were floated in BSS and allowed to spontaneously scroll. Controlled bursts of BSS were used to promote DS formation in one member of each pair. Grafts were subsequently stained with Calcein-AM, imaged, and analyzed for endothelial cell loss (ECL) by FIJI segmentation. Cell loss from manipulated and unmanipulated mate grafts was compared using unpaired Student's t-test. Double scrolling preloaded grafts: Grafts from 18 pairs of donor corneas (split into 'young' (age 48-64) and 'old' (age 66-80) cohorts) were prepared and loaded into a Straiko modified Jones tube. One member of each pair was induced to DS by applying repeated push-pull action on a BSS-filled syringe attached to the injector tube. Manipulated and unmanipulated mate grafts were analyzed and compared as described above.

Results: An eye bank processing technician was able to successfully form a DS during graft preparation in 9/10 attempts. There was no difference in ECL in manipulated compared to unmanipulated mate grafts (15.2%±3.3% vs 15.2%±4.4%, P=0.99). For preloaded DMEK grafts, the old cohort could form a DS in 9/9 attempts while the young cohort could only form DS in 6/9 attempts. The additional tissue manipulation resulted in a significant difference in ECL in the old cohort (manipulated: 17.4%±3.5% vs unmanipulated: 13.0%±4.2%, P=0.03), but not the young cohort (15.5%±4.4% vs 13.0%±4.5%, P=0.24).

Conclusions: DS DMEK grafts can be successfully formed during or after graft preparation. In older donor grafts, additional manipulation required to form a DS results in increased ECL; but this cell loss is within the acceptable range for transplant tissue. In younger donor grafts, additional manipulation using either technique does not result in increased ECL. For older donor grafts, surgeons should weigh the advantage of an easily opened DS against the risk of higher ECL. These two techniques may encourage the use of younger donor grafts, as neither technique produced an increase in ECL in younger donors. These techniques may also prove useful with both young and old donor tissue in more complex surgical cases, as they yield easily opened DS grafts that may reduce the difficulty of DMEK surgery.

CONTROL ID: 3711857

SUBMITTER (NAME ONLY): Ji Won Bang

TITLE: Cerebrospinal fluid dynamics and its coupling with global brain activity are altered in early glaucoma patients

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Glaucoma is a widespread neurodegenerative disease affecting the retinal ganglion cells, optic nerve, distal visual pathways and beyond. Recent studies suggest that cerebrospinal fluid (CSF) plays a role in clearing wastes from the brain and that CSF dynamics may be altered in neurodegenerative diseases. Since CSF dynamics can be facilitated by the global brain activity, in the present study, we investigated how the dynamics of CSF and its coupling with global brain activity may be altered in glaucoma using functional magnetic resonance imaging (fMRI).

Methods: 19 early glaucoma patients (62.3±1.7 yrs) (mean±SEM), 19 advanced glaucoma patients (64.7±2.4 yrs), and 19 healthy subjects (59±2.4 yrs) underwent anatomical MRI and resting-state fMRI with eyes closed. Age did not differ across groups (P=0.188). We extracted the CSF signal time profiles from the fourth ventricle (Fig. 1A) and the global brain activity [blood-oxygenation-level-dependent signal time profiles] from the entire gray matter (Fig. 1B). Following previous literature (Han F, et al. PLOS Biol 2021;19), the coupling between the CSF signals and the global brain activity (CSF-BOLD coupling) was examined via cross correlation at the 4s time lag, where more negative values indicate stronger coupling. We also associated these correlations with the volumes of the anterior visual pathway in anatomical MRI.

Results: A significant group difference was observed in the power (i.e., strength) of the low frequency (0.01-0.03Hz) in the CSF signals (P=0.013; Fig.1C). Specifically, early glaucoma patients showed significantly greater power than advanced glaucoma patients (Bonferroni P=0.010). The power of the global brain activity showed similar trends but did not reach significance (P=0.390; Fig.1D).

The CSF-BOLD coupling at the 4s lag differed significantly across groups (P=0.007; Fig. 1E). Early glaucoma patients had significantly stronger coupling than advanced glaucoma patients (Bonferroni P=0.025) and healthy controls (Bonferroni P=0.013).

Further, CSF-BOLD coupling was correlated with the volumes of optic nerve (right: R=-0.342, P=0.009; left: R=-0.344, P=0.009, Fig. 2D,E) and optic chiasm (R=0.264, P=0.047, Fig. 2F).

Conclusions: Our observations of the altered CSF dynamics and CSF-BOLD coupling provide physiological evidence to support the recent hypothesis of widespread brain involvements in the early stage of glaucoma.

CONTROL ID: 3711858

SUBMITTER (NAME ONLY): Christopher Bowd

TITLE: Primary Open-Angle Glaucoma Detection with Vision Transformer: Improved Generalization Across Independent Fundus Photograph Datasets

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To compare the accuracy and generalizability of Vision Transformer, a new deep learning (DL) technique, to a traditional convolutional neural network, ResNet-50, for detecting primary open-angle glaucoma (POAG) using Ocular Hypertension Treatment Study (OHTS) fundus photographs and 5 external datasets.

Methods: 66,715 photographs of 1,636 participants in the OHTS were used to compare the best-performing Vision Transformer model (Data-efficient image Transformer, DeiT) to ResNet-50 for detecting the OHTS Endpoint Committee determinations of POAG attributable to optic disc changes (ENPOAGDISC), visual field changes (ENPOAGVF), or both (ENPOAGANY) and OHTS Optic Disc Reading Center (RCPOAGDISC) and Visual Field Reading Center (RCPOAGVF) determinations. The accuracy of Vision Transformer and Resnet-50 DL models also were compared in 5 external international test datasets of fundus images labeled as glaucoma or healthy: 1) Diagnostic Innovations in Glaucoma Study (DIGS) and African Descent and Glaucoma Evaluation Study (ADAGES, United States) datasets, 2) the ACRIMA (Spain) dataset, (3) the Large-Scale Attention-based Glaucoma (LAG, China) dataset, (4) the Retinal IMage database for Optic Nerve Evaluation (RIM-ONE, Spain) dataset, (5) The Online Retinal Fundus Image Dataset for Glaucoma Analysis and Research (ORIGA, Singapore) dataset. Areas under receiver operator characteristic curves (AUROC) were used to measure model accuracy.

Results: The Vision Transformer models demonstrated similar performance to the ResNet-50 on the OHTS test sets for all 5 ground truth POAG labels (Figure: panel a). The diagnostic accuracy of Vision Transformer was consistently

higher than Resnet-50 on the independent external fundus photograph datasets (Figure: panels b-f). For example, the DeiT model AUROC for ENPOAGANY was between 0.08 and 0.20 higher than the ResNet-50 model AUROC.
Conclusions: Vision Transformer has the potential to serve as a critical tool to reduce biases and improve the generalizability of DL models for the detection of glaucoma from fundus photograps.

CONTROL ID: 3711859

SUBMITTER (NAME ONLY): Edoardo Midena

TITLE: Artificial Intelligence Based Quantification of Major OCT Biomarkers in the Diagnosis and Follow-up of Diabetic Macular Edema.

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To validate the role of an artificial-intelligence (AI) based quantification of most relevant OCT biomarkers in assessing disease activity and treatment response in eyes affected by center-involved diabetic macular edema (DME).

Methods: After adequately training the deep learning algorithm using normal and diabetic OCT images, a specific tool for automatically detect and quantify: intraretinal and subretinal fluids (IRF and SRF), hyperreflective retinal foci (HRF), the integrity of external limiting membrane (ELM) and ellipsoid zone (EZ), and the area of retinal exudates (AHE) was developed, trained and then validated versus two blinded experienced examiners. Three-hundred eyes affected by center-involved DME were consecutively enrolled to validate the automatic tool, and 100 DME treated eyes were used to quantify each parameter over time (at least three follow-up examinations). Fluid volumes (IRF and SRF) and AHE were measured for three concentric circles with diameters of 1, 3 and 6 mm (fovea, paracentral ring and pericentral ring). HRF were measured in the central 3 mm, whereas the integrity of ELM/EZ was quantified in the central 1 mm. ICC was calculated for each parameter between the two human examiners, and versus the automated tool.

Results: The agreement for any OCT biomarkers detection and quantification, at any time point, between operators was complete (ICC: 1.0), as versus the AI tool (ICC: 0.99). In all DME eyes most intraretinal fluid per square millimeter was present at the fovea, followed by the paracentral ring and pericentral ring ($p<0.0001$). And this was also the case for subretinal fluid ($p<0.0001$). In the follow-up eyes, at every time point, this observation was confirmed. HRF significantly decreased after treatment ($p<0.001$), recovey of ELM/EZ integrity was reached ($p<0.005$) and the area of hard exudates slowly reduced in all rings ($p<0.005$).

Conclusions: Accurate, repeatable location and quantification of major OCT biomarkers of DME, namely: individual macular fluids (IRF and SRF), HRF, integrity of ELM/EZ, and area of hard exudates, are currently mandatory to adequately diagnose and prognosticate treatment response over time. A fully validated AI based tool, as reported, allows the clinicians to routinely identify and quantify the most relevant OCT biomarkers offering an objective way of planning and following DME eyes.

CONTROL ID: 3711862

SUBMITTER (NAME ONLY): Hao Zhang

TITLE: Balanced-detection visible-light optical coherence tomography in humans at 125 kHz

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Zhang, I. Rubinoff, D.A. Miller, R. Kuranov, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The recently developed visible-light OCT (vis-OCT) enabled an axial resolution of 1.3 μm, enhanced tissue scattering contrast, and introduced new functional imaging capabilities. These capabilities are increasingly desirable in the clinic. However, its clinical translation is limited by supercontinuum light sources with high relative-intensity noise (RIN), which degrades image quality and limits imaging speed. Therefore, we seek to develop a high-speed vis-OCT by eliminating RIN.

Methods: We developed a vis-OCT, which uses two subpixel calibrated spectrometers in a Mach-Zehnder interferometer (MZI) to achieve balanced detection and RIN cancelation. We first coupled a supercontinuum light source (NKT Photonics, 78 MHz repetition rate) into a 10:90 fiber coupler. We delivered 10% of the light to the eye (200 μW) and 90% of the light to a transmission-based reference arm. Light backscattered from the eye was transmitted to a second 50:50 fiber coupler and was simultaneously detected by two well-calibrated spectrometers (Blizzard, Opticent Health).

Results: Compared with the previous vis-OCT influenced by RIN, balanced detection achieved nearly shot-noise-limited imaging in humans, reduced the noise floor by 20.5 dB, increased the peak signal to the noise floor ratio from 16.1 dB to 31.8 dB, and increased the contrast to noise ratio from -9.7 dB to 3.8 dB (Figs. 1a&1b). We performed all imaging at a 125 kHz A-line rate with a field-of-view up to 10 mm × 4 mm (1024 A-lines × 256 B-scans) as shown in Fig. 1c, the fastest ever for ophthalmic vis-OCT.

Conclusions: We developed the first subpixel-calibrated balanced detection MZI for significant RIN suppression in retinal vis-OCT. RIN suppression enabled the highest speed vis-OCT imaging at 125 kHz and the largest field-of-view in humans.

CONTROL ID: 3711863

SUBMITTER (NAME ONLY): Sailee Lavekar

TITLE: Modeling blood-brain barrier phenotypes in glaucoma with human pluripotent stem cells.

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is a neurodegenerative disease that affects the retina, resulting in the degeneration of retinal ganglion cells (RGCs) and subsequent loss of vision. While RGCs are the primary cell type affected in the disease state, previous studies have demonstrated that blood brain barrier (BBB) properties may be compromised in glaucoma. However, the factors responsible for BBB disruption have remained elusive and thus, the goal of the study was to explore how changes in paracrine signaling within the BBB may be responsible for certain aspects of glaucoma using human pluripotent stem cell (hPSC)-derived cells.

Methods: To model aspects of barrier dysfunction in glaucoma, hPSCs with a glaucoma-specific Optineurin (E50K) mutation, as well as isogenic controls, were directed to differentiate into cells of the BBB, including RGCs, astrocytes, and microvascular endothelial cells (MVECs). Subsequently, MVECs were seeded into the top of an established in vitro barrier transwell model, while RGCs and astrocytes grown in the bottom. The ability to recapitulate characteristic properties of the BBB were then tested, including trans-endothelial electrical resistance (TEER), permeability and rhodamine transport. Further, RNA sequencing and ELISA identified factors responsible for changes observed.

Results: The establishment of the barrier model with RGCs, astrocytes, and MVECs resulted in a significant enhancement of barrier properties compared to MVECs grown alone. However, when the barrier model was assembled with cells with the glaucoma OPTN(E50K) mutation, barrier integrity was compromised, including reduced TEER and increased barrier permeability along with reduced efflux transporter activity and/or localization. An increased expression of certain secreted factors were identified from OPTN(E50K) astrocytes, and addition of exogenous factors applied to healthy cultures resulted in barrier dysfunction similar to the glaucoma barrier model.

Conclusions: The results of this study will expand our understanding of the mechanisms by which glaucoma affects the BBB. Overall, the in vitro glaucoma barrier model demonstrated characteristic functional deficits, mimicking some aspects of the phenotypes observed during the progression of glaucomatous neurodegeneration, with strong implications for the use of this model for disease modeling and drug development to rescue neurodegenerative phenotypes.

CONTROL ID: 3711866

SUBMITTER (NAME ONLY): Souvick Mukherjee

TITLE: Automated detection of Drusenoid Pigment Epithelial Detachments (DPEDs) on OCT's in patients with Age related Macular Degeneration (AMD)

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mukherjee, T. de silva, C. Duic, A. Thavikulwat, K. Hess, H. Wiley, T.D. Keenan, E.Y. Chew, C. Cukras, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: DPEDs in AMD appear as large yellowish mounds on stereoscopic examination. DPEDs are an important risk factor for progression to late AMD and vision loss. Spectral Domain OCT (SD-OCT) is an important imaging modality in the evaluation of retinal diseases. Automated detection of DPEDs on SD-OCT may help understand the pathophysiology of AMD progression and be useful for clinical trial screening.

Methods: 131 patients (294 eyes) enrolled in a longitudinal study of dark adaptation (NCT01352975) with a range of AMD severities from no AMD to eyes with advanced atrophic disease were imaged using both color fundus imaging (Topcon) and SD-OCT imaging (Heidelberg, Germany). Color fundus images were graded by the Wisconsin Reading Center and assigned AMD severity scores (AMDSC) of 0-10.

SD-OCT imaging consisted of a volumetric macular scan (30°x25°, 496×768×121 voxels). A 3D-UNet trained to segment the Retinal Pigment Epithelium (RPE) and Bruch's membrane (BM) layers was used to contour all 294 macular volumes. The $6x6mm^2$ region representing the grid centered around the fovea was considered for calculating the mean ± std of the maximum width (W) and maximum elevation (H) between the RPE and BM layers in eyes with DPEDs. The layer contours were screened to identify measures satisfying the requirements of distinct elevations (>50μm) in the RPE Drusen Complex region with minimum diameter (>433μm), defining a DPED.

Results: Out of 76 eyes with no AMD (AMDSC 0-1), 111 with early AMD (AMDSC 2-5), 96 with intermediate AMD (AMDSC 6-8), and 11 with Geographic Atrophy (GA) (AMDSC 9-10)- 12/329 (eyes/B-scans) in the intermediate AMD group (W=1168.48±598.19μm, H=143.85±56.62μm) and 4/81 (eyes/BScans) in the GA group (W=715.92±279.52μm, H=113.53±40.28μm) met the DPED criteria. These occurred in 1/27 (eyes/BScans) AMDSC-6, 10/269 AMDSC-7, 1/33 AMDSC-8, and 4/81 AMDSC-10, with no DPEDs identified in eyes with AMDSC 0-5.

Conclusions: Segmentation of RPE and BM layers by a 3D-UNet can subsequently be used for automated and objective detection of DPEDs on B-scans within the macular volume. Eyes with DPEDs are of special interest with some studies targeting this phenotype. By automating this process using OCTs, more quantitative and reproducible DPED detections are possible leading to more efficient clinical trial designs.

CONTROL ID: 3711872

SUBMITTER (NAME ONLY): WonKyung Cho

TITLE: Ocular surface mast cells delay regression of pathological corneal blood vessels

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Cho, E. Elbasiony, Y. Guan, A. Singh, S. Mittal, S. Chauhan, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal angiogenesis, induced by various ocular insults, compromises corneal transparency. Our previous studies have shown that activation of ocular surface mast cells directly promote the development of new blood vessels. Here we investigated whether mast cells contribute to the stability of inflammatory blood vessels and impede vessel regression.

Methods: Neovascularization was induced by placing a single figure-8 intrastromal suture in the cornea using 11-0 nylon. On day 9, the suture was removed upon establishment of mature blood vessels. Corneas were harvested and stained with avidin^{+} (mast cells) and CD31^{+} (vascular endothelial cells) for immunohistochemistry (IHC) analysis. Real-time vessel regression was followed by capturing slit-lamp pictures. To investigate the direct effect of mast cells on vessel regression, suture was placed in mast cell deficient cKit$^{w\text{-}sh}$ and their wildtype (WT) C57BL/6 controls. To evaluate the effect of pharmacological blockade of mast cells on the reversion of mature blood vessels, corneas were treated one day prior to suture removal with mast cell inhibitor, cromolyn (2% in PBS). Slit lamp images were analyzed using ImageJ software. Corneas were harvested on day of suture removal and 2 days post-suture removal and expression of angiogenic factor, VEGF, was quantified to assess vessel regression at the molecular level.

Results: IHC analysis demonstrated an abundance of mast cells surrounding the new corneal blood vessels on day 9 post-suture. By 48 hours following suture removal, a significant 51.3% (± 0.67%) regression of blood vessels were observed in cKit$^{w\text{-}sh}$ mice, compared to 11.5% (± 2.15%) regression in WT controls ($p=0.002$). Established vessels completely regressed in cKit$^{w\text{-}sh}$ mice by day 7 post-suture removal. Moreover, cromolyn treatment promoted faster regression of inflammatory blood vessels, as demonstrated by complete regression of pathological vessels by 24 hours post-suture removal, compared to PBS treatment resulting in no significant change in the inflammatory vessels. Furthermore, molecular analysis of vessel regression showed a 59% lower expression of VEGF in the cromolyn-treated corneas, relative to PBS-treated groups ($p=0.03$).

Conclusions: Our data demonstrate that deficiency of ocular surface mast cell function results in faster regression of pathologic corneal blood vessels, suggesting mast cells promote the stability of inflammatory vessels.

CONTROL ID: 3711875

SUBMITTER (NAME ONLY): Olivia Farah Rezek

TITLE: In vitro modelling of autosomal dominant TGFBI corneal dystrophies and development of a targeted therapeutic approach

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Rezek, B. Sanchez-Pintado, M.E. Cheetham, A.E. Davidson, A.J. Hardcastle, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|S. Tuft, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: TGFBI corneal dystrophies are autosomal dominant inherited diseases with distinctive phenotype-genotype correlations, characterised by the accumulation of TGFBI protein (TGFBIp) positive deposits in the sub-epithelial, Bowman and/or stromal layers of the cornea. Current surgical treatments do not target the underlying genetic cause of the disease, with disease symptoms frequently reoccurring. In order to generate disease models, patient derived induced pluripotent stem cells (iPSCs) were differentiated towards corneal epithelial-like cells to study the pathophysiology of TGFBI corneal dystrophies, and explore the use of targeted antisense oligonucleotides (ASOs) as a potential therapy.

Methods: Fibroblasts obtained from patients harbouring heterozygous hotspot mutations c.370C>T, p.R124C or c.371G>A, p.R124H were reprogrammed to iPSCs by nucleofection with the pluripotency factors Oct3/4, Kfl4, Sox2, L-Myc, Lin28 and mir302/367. iPSCs were differentiated towards a corneal epithelial-like cell lineage, in parallel with control iPSC, and characterised for expression of epithelial markers using quantitative reverse transcriptase PCR and immunocytochemistry. ASOs were designed to reduce expression of TGFBI mutant alleles and treatment effects were explored by reverse transcriptase (RT)-PCR, Sanger sequencing and quantitative RT-PCR.

Results: Immunofluorescence confirmed the expression of the stem cell markers Oct4, Nanog, SSEA4 and Tra-1-81 in all iPSC lines. Characterisation of the iPSC derived model confirmed a corneal epithelial-like phenotype with endogenous expression of markers KRT3, KRT14, P63, ABCG2 and E-cadherin at transcript and protein level. Following ASO treatment, a reduction of TGFBI transcript levels was observed by RT-PCR. Sanger sequencing demonstrated a specific reduction of the mutant allele in comparison to the wild type allele.

Conclusions: We have established a patient iPSC derived in vitro model to investigate the molecular mechanisms of TGFBI corneal dystrophies and test therapeutic approaches in an appropriate genomic and cellular context. Preliminary investigations indicate that ASO treatment targeting mutations at position p.R124 may be effective in reducing the expression of the mutant allele. Further investigations are required to further characterise the molecular mechanisms of disease and the effect of ASOs on TGFBIp.

CONTROL ID: 3711876

SUBMITTER (NAME ONLY): Yilin Guan

TITLE: Ocular surface mast cells promote nerve damage and trigeminal ganglion inflammation following corneal injury

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Guan, W. Cho, E. Elbasiony, A. Singh, S. Mittal, S. Chauhan, Department of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nerve damage following injury has been associated with impaired wound healing. We have previously shown that corneal injury leads to increased activation of ocular surface mast cells. Here, we investigated whether mast cells interact with corneal nerve and contribute to nerve degeneration and neuroinflammation.

Methods: Corneal injury was induced by mechanical removal of the epithelium (3 mm) and one-third of the anterior stroma in C57BL/6 mice using an Algebrush II. To evaluate the proximity of mast cells and damaged nerves, corneas were harvested 6 hours post-injury and stained with β-tubulin III (corneal nerves), and avidin (mast cells), for immunohistochemistry (IHC) analysis. Trigeminal ganglions (TGs) were harvested post-injury and lysates were prepared to measure levels of tryptase (mast cell activation marker), CD11b and Substance P (SubP), using colorimetric assay and PCR analysis. To assess direct interaction between mast cells and inflamed corneal nerves, primary TGs were co-cultured with bone marrow-derived mast cells for 24h. Brightfield images were captured, and neurite length was quantified using ImageJ software. TGs harvested from co-cultures were assessed for expression of nerve activation marker SubP and CGRP. To assess the in vivo effect of mast cell activation on nerve damage, injured corneas were treated with mast cell inhibitor cromolyn (2% in PBS) and hyperactivation of nerves were measured using eye wipe test.

Results: IHC analysis demonstrated that ocular surface mast cells infiltrated into the injured cornea in close proximity to the damaged corneal nerves. Corneal injury resulted in a significant activation of TG mast cells and inflammation, as indicated by increased levels of tryptase ($p=0.003$), CD11b ($p<0.001$) and SubP ($p=0.009$). Co-culturing of TGs with mast cells resulted in an approximate 13-fold upregulation in CGRP ($p<0.001$), and ~1.5-fold increase in SubP ($p=0.008$), compared to TGs cultured alone. Moreover, mast cells resulted in significant neuronal degeneration, as indicated by 50% decrease in neurite length compared to control TG cultures ($p<0.001$). Pharmacological inhibition of ocular surface mast cell activation resulted in a significant decline in TG inflammation and hyperalgesia, as shown by decreased eye wipes ($p=0.005$).

Conclusions: Ocular surface mast cells exacerbate nerve degeneration and promote inflammation in the trigeminal ganglion.

CONTROL ID: 3711879

SUBMITTER (NAME ONLY): Maria Vähätupa

TITLE: Comparison of the laser-induced choroidal neovascularization model pathology in C57BL/6J mice from different vendors

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The mouse laser-induced choroidal neovascularization (CNV) model is the most popular experimental model to mimic the wet form of age-related macular degeneration (AMD). In this study we aimed to compare the differences in CNV pathology between C57BL/6J mice from different vendors.

Methods: 8-week-old male C57BL/6JRj mice from Janvier Labs (France) and C57BL/6JRccHsd from Envigo (Netherlands) were used in the study. CNV was induced by using a 532 nm laser and the development was monitored in vivo by fluorescein angiography (FA) and spectral domain optical coherence tomography (SD-OCT) on days 0, 3, 7 and 14. The lesions were qualitatively graded from FA images for vascular leakage (non-leaky or leaky). FA scans were analysed by a proprietary algorithm, where the neural network was trained to recognize and quantify CNV lesions using transfer learning approach. Choroidal flat mounts (D7 n = 5-6/group or D14 n = 6/group) were immunolabelled with isolectin B_4, anti-iba1 and anti-collagen I antibodies, scanned using Leica THUNDER 3D microscope and manually analysed using FIJI/ImageJ (NIH). The data were statistically analysed with Mixed-effects model (FA) or Mann-Whitney U test (histology).

Results: There was no difference in the CNV grading (% of leaky lesions) in Janvier mice compared to Envigo (p=0.96). While absolute values of FA leakage area were overall lower in Janvier mice in all time points, this study was not sufficiently powered to detect that difference (area in mm^2, mean ± SD, Janvier vs. Envigo: 0.04±0.042 vs. 0.056±0.054 on D3; 0.014±0.028 vs. 0.043±0.092 on D7; 0.008±0.015 vs. 0.035±0.067 on D14). Isolectin area was larger in Envigo mice lesions on D7 ($p < 0.05$) and on D14 ($p < 0.0001$) as compared to Janvier mice. Iba1 area was bigger in Envigo mice as compared to Janvier mice on D7 ($p < 0.001$). There was a trend towards bigger Collagen I area in Envigo animals compared to Janvier mice on D7 ($p = 0.077$).

Conclusions: Envigo C57BL/6JRccHsd mice show more severe CNV pathology than Janvier C57BL/6JRj mice. These data suggest strain-specific differences in neovascular and fibrotic processes after laser CNV induction. These

differences should be considered when selecting animal strains for IND-enabling studies in wet AMD.

CONTROL ID: 3711880

SUBMITTER (NAME ONLY): Bledi Petriti

TITLE: Reduced systemic mitochondrial function is associated with faster rates of visual field progression in primary open angle glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Patients with primary open angle glaucoma (POAG) deteriorate despite intraocular pressure (IOP) reduction, suggesting other factors confer susceptibility. Evidence from our group and others implicates systemic mitochondrial (mt) function in glaucoma pathogenesis. We wanted to establish whether systemic mt function is associated with the rate of visual field (VF) progression in patients with POAG treated with IOP-lowering

Methods: Mt function parameters (Basal, ATP-linked, Maximal, Reserve), expressed as oxygen consumption rate (OCR) pmol/min/100,000 cells (XFe24 Analyzer), were measured in lymphocytes of 168 treated white-European POAG patients. Inclusion criteria: ≥6 reliable VFs and ≥3 years follow up. Exclusion criteria: secondary and narrow angle glaucoma, systemic conditions / drugs potentially affecting mt function. Both eyes of the same patient were included if eligible. Mixed-effect linear models were used to investigate the association between VF Mean Deviation (MD) rate of change and mt function, after adjusting for baseline age, central corneal thickness (CCT) and IOP during the observation period; separate IOP models for mean, peak, % reduction and standard deviation (SD) were generated

Results: A total of 211 eyes were included. Mean (±SD) age, IOP, and CCT were 72.6 (±10.0) years, 14.9 (±2.8) mmHg and 538 (±41) μm, respectively. Mean (±SD) rate of VF MD progression was -0.61 (±0.53) dB. In all models and for each measure of OCR, lower mt function was highly significantly associated with faster rates of VF progression. Table 1 shows results of the 'SD IOP' multivariable model; IOP mean, peak and % reduction were not significantly associated with VF progression. Figure 1a shows Basal OCR and SD IOP were significantly associated with MD rate of progression. Fig. 1b shows the relationship between basal OCR and VF progression rate. The model total marginal R^2 was 0.084. Semi-partial R^2 (proportion 'variance accounted for') was 0.020 and 0.074 for SD IOP and Basal OCR, respectively

Conclusions: Systemic (lymphocyte) mt function is highly significantly associated with the rate of VF loss in POAG patients treated with IOP lowering. Our findings suggest that measurement of mt function may help identify patients at high risk of more rapid progression. Mt function may be a new target for glaucoma treatment

CONTROL ID: 3711882

SUBMITTER (NAME ONLY): Julia-Sophia Bellingrath

TITLE: Development of a functional assay for the assessment of two common CRB1 mutations

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Pathogenic variants in the Crumbs homolog 1 (CRB1) gene are associated with autosomal recessive, early-onset retinal degeneration. The most common pathogenic CRB1 variant c.2843G>A, pCys948Arg occurs in the first nucleotide of exon 9, and is widely classified as a missense mutation. The single nucleotide variant (SNV) c.2842+5G>A is a common CRB1 splice site variant which is positioned in the splice donor site of intron 8. A dual luciferase assay utilising an out-of-frame CRB1 intron-exon hybrid was designed, validated and used to functionally evaluate these two common CRB1 mutations.

Methods: The out-of-frame CRB1 exon-intron hybrid sequence was inserted into the SGDLuc3.0 backbone between the Renilla and firefly luciferases. Correct splicing, which would result in an in-frame sequence and correlate with firefly luminescence was predicted in-silico. Site-directed mutagenesis introduced the above-mentioned SNVs into the wild-type plasmid. Luciferase assays measuring Renilla and firefly luminescence were performed on transfected HEK293T cells. Splice products were analysed with Sanger sequencing.

Results: A 7.4-fold increase (SD ± 3.1) in firefly luminesce from baseline Renilla expression was detected in cells transfected with the intron-exon hybrid sequence. Correct splicing of the hCRB1.IE.8.9 hybrid sequence was confirmed with Sanger sequencing. The plasmid containing the SNV c.2842+5G>A resulted in a loss of firefly luciferase luminescence. Sanger sequencing confirmed a read-through of splice donor site. Firefly luminesce fold increase from the plasmid containing the SNV c.2843G>A was significantly reduced (3.31 (SD ± 0.46)) compared to the wild-type plasmid (6.16 (SD ± 1.74)). Sanger sequencing the splice products confirmed a read-through of the splice acceptor site 60% of splice products, while 36% of splice products exhibited correct splicing.

Conclusions: Due to the location of the most common CRB1 pathogenic variant at the first nucleotide of exon 9, it is plausible that this SNV might affect splicing in addition to causing a missense change. The data generated from the dual luciferase assay is the first to implicate the c.2843G>A SNV as a splice site mutation. A common splice site mutation, c.2842+5G>A, was validated to cause a splice defect in this assay. In future experiments, this dual luciferase assay could be used to screen guide RNA in CRISPR-Cas based therapies.

CONTROL ID: 3711883

SUBMITTER (NAME ONLY): Hannah Nonarath

TITLE: Investigating the pathophysiology of USH3A in a zebrafish model

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.J. Nonarath, B.A. Link, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|A. Dinculescu, Ophthalmology Research, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in CLRN1 cause Usher syndrome type 3A (USH3A), a recessive inherited disorder leading to combined hearing and vision loss. In this study, we created and characterized a novel zebrafish model lacking clrn1 to investigate the pathophysiology of USH3A.

Methods: CRISPR/Cas9 was used to delete 90% of the zebrafish clrn1 coding sequence. High-intensity light (3500 lux) exposure experiments were performed in 5-7dpf larvae, along with phalloidin and TUNEL staining. In 4 to 20-month adults, we assessed the retinal structure and the cone photoreceptor mosaic using spectral-domain optical coherence tomography. We also analyzed photoreceptor morphology using hematoxylin and eosin staining, and cell death and regeneration using staining for activated caspase-3, and BrdU incorporation assays.

Results: High-intensity light treated clrn1 mutant zebrafish presented with a significant increase in the number of TUNEL positive photoreceptor nuclei and regions of absent or disrupted phalloidin staining, indicating that the absence of Clarin1 sensitizes photoreceptors to stress. In adult clrn1 mutant zebrafish raised under normal lighting, we observed progressive alterations of the photoreceptor mosaic from 4 to 20-months of age, suggesting a loss of photoreceptor integrity. Histological analysis of clrn1 mutant zebrafish retinas showed gross changes at 20 months compared to wildtype. Specifically, we observed a significant thinning of the outer nuclear layer (ONL) in the central retina, an indication of photoreceptor cell death. At the time points investigated, we did not observe a significant increase in activated-caspase 3 staining. However, there was a small but significant increase in BrdU incorporation at 4-months, suggesting regeneration and therefore loss of photoreceptors at an early age. BrdU incorporation decreased with age, potentially as a consequence of losing regenerative potential in older adults.

Conclusions: The clrn1 mutant zebrafish represents the first model of USH3 disease that displays photoreceptor disorganization and degeneration. Collectively, our data indicates that the loss of Clarin1 function in zebrafish induces a slow, progressive retinal degeneration. We will utilize this model, along with cell-specific clrn1 re-expression and RNAseq analysis, to investigate the mechanisms promoting retinal degeneration in USH3A.

CONTROL ID: 3711884

SUBMITTER (NAME ONLY): Chhavi Saini

TITLE: HSP-Specific T Cell Counts in Boston Keratoprosthesis Type I Patients

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Saini, J. Devlin, E.I. Paschalis, J. Chodosh, D. Chen, L.Q. Shen, Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|K. Cho, L. Pan, S. Jiang, E.I. Paschalis, D. Chen, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L. Pan, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Prior animal studies have shown that T cell specific for heat shock proteins (HSPs) play an important role in glaucomatous neurodegeneration. Given the high incidence of glaucoma in patients with Boston keratoprosthesis type I (KPro), we investigated the levels of HSP specific $CD4^+$ T-lymphocytes in the peripheral blood of patients with KPro.

Methods: Adult patients with KPro and healthy control subjects were prospectively enrolled. Patients with any autoimmune or immunodeficiency diseases were excluded. Peripheral blood monocytes (PBMC) were isolated from the blood of each participant and stimulated with HSP-27 or another member of the small HSP family, α-crystallin. Both interferon gamma+ helper T cells (Th1) and transforming growth factor beta+ regulatory T cells (Treg) were quantified by flow cytometry and presented as percentage of total PBMC counts. Retinal nerve fiber layer thickness (RNFLT) was measured for all. Ophthalmic data were collected for the KPro eye for KPro patients and worse eye (based on RNFLT) for controls.

Results: KPro patients (n=6) with an average of 9.2±5.0 years from their first KPro surgery and healthy controls (n=13) were similar in age, gender, body mass index and intraocular pressure (IOP) ($p>0.22$ for all; Table 1), although all KPro patients were treated for IOP. Best corrected visual acuity, cup to disc ratio and average RNFLT were worse for KPro patients (0.4±0.3 LogMAR, 0.7±0.3 and 63.5±33.5 μm, respectively) compared to controls (0.05±0.09 LogMAR, 0.3±0.1 and 95.1±11.7 μm respectively; $p\leq0.002$ for all). Total unstimulated Th1 and Treg cell counts were similar in KPro (2.6±6.5% and 0.8±0.9%) and controls (3.3±1.9% and 1.7±1.7%, $p>0.25$ for both; Figure 1A). After stimulation with HSPs, Th1 cells specific for HSP-27 and α-crystallin were more abundant in KPro patients than controls (10.1±6.6% vs 2.5±2.2%, $p=0.001$; 8.9±3.1% vs 2.4±0.8%, $p<0.001$ respectively; Figure 1B), whereas Treg cells specific for HSP-27 and α-crystallin did not differ between the groups (2.2±1.4% vs 0.9±1.7%, $p=0.10$; 1.0±0.3% vs 0.6±0.8%, $p=0.42$, respectively; Figure 1B).

Conclusions: Although our findings are preliminary and larger cohorts of patients are being recruited to validate the results, the data suggest robust systemic HSP-specific Th1 responses were induced in patients with KPro. The elevated level of these T-cells may contribute to the prevalent and severe glaucomatous neurodegeneration in these patients.

CONTROL ID: 3711885

SUBMITTER (NAME ONLY): Hongwei Ma

TITLE: Programing Human iPSC Differentiation into a Cone-rich Cell Population by Targeting Multiple Regulatory Pathways

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Ma, F. Yang, C.M. Primeaux, L.R. York, X. Ding, Department of Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: The progressive death of cones ultimately causes loss of vision in patients with retinal degenerative diseases, and there is currently no treatment available. Differentiation of human-induced pluripotent stem cells (hiPSCs) into a cone-rich cell population represents a potential therapy for cone/retinal degeneration. COCO is a multifunctional antagonist of the WNT, TGF-β, and BMP pathways and has been shown to promote cone differentiation from hiPSCs. NRL and NR2E3 are key transcription factors for photoreceptor differentiation. Thyroid hormone is known to orchestrate cone development. This work investigated the potential of differentiating hiPSCs into a cone-rich cell population by targeting these different regulatory pathways.

Methods: Wild-type iPS(IMR90)-4 cells and mutant iPS(IMR90)-4 cells with deletion of NRL or NR2E3 were used. NRL or NR2E3 knockout cell lines were generated using Synthego Gene Knockout Kit V2 and confirmed by Sanger sequencing. Embryonic bodies generated from the wild-type and mutant cells were cultured in a retinal induction medium containing COCO (30 ng/ml) for 4 weeks. Neuronal retinal vesicles formed were then transferred into bioreactors (Synthecon) and cultured in the COCO differentiation medium containing triiodothyronine (T3, 5 nM) for another 2-3 months, followed by evaluation of the expression of photoreceptor genes and differentiation of cones using qRT-PCR and immunofluorescence labeling.

Results: Treatment with COCO enhanced differentiation of IMR90-4 cells into cones and increased expression of the photoreceptor precursor genes (PAX6, CRX, and RXR) and the cone-specific genes (OPN1SW, ARR3, and GNAT2). Deletion of NRL or NR2E3 further enhanced the gene expression and cone differentiation. COCO plus thyroid hormone induced differentiation of IMR90-4 cells into M-cones and increased expression of OPN1MW, compared with cells treated with COCO only.

Conclusions: COCO induces differentiation of IMR90-4 cells into retinal/photoreceptor precursors and cone photoreceptors. Deletion of NRL or NR2E3 promotes cone differentiation. Thyroid hormone promotes differentiation of M-cones from IMR90-4 cells. These findings highlight the potential of differentiation of hiPSCs into a cone-rich cell population by targeting multiple regulatory pathways.

CONTROL ID: 3711886
SUBMITTER (NAME ONLY): Brian VanderBeek
TITLE: Visit Adherence and Visual Acuity in SCORE2
SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy
SESSION TYPE: Paper Session
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ABSTRACT BODY:

Purpose: The impact of missed appointments for anti-vascular endothelial growth factor (anti-VEGF) injection treatment for macular edema due to retinal vein occlusion (MERVO) on visual acuity (VA) is unknown. We performed a secondary analysis of Study of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2) data to evaluate the association between patients' adherence to clinical trial visits and VA in patients with central retinal vein occlusion (CRVO) or hemiretinal vein occlusion (HRVO).

Methods: The SCORE2 protocol included a visit every 4 weeks (every 28-35 days) during the first year. Visit adherence was measured as: number of missed visits, average (avg days) and longest (max days) visit interval, average (avg missed days) and longest (max missed days) unintended visit interval. Avg and max missed days were categorized as on time (0 days), late (>0-60 days), and very late (>60 days). Primary outcome was change in Early Treatment Diabetic Retinopathy Study (ETDRS) VA between baseline study visit and last attended visit during Year 1, using multivariate linear regression models controlling for baseline VA, baseline central subfield thickness, age, gender, race, ethnicity, study eye disease type, prior anti-VEGF in study eye, disease duration at baseline, history of diabetes, coronary artery disease or hypertension, whether or not patient was re-randomized at Month 6, and total number of injections.

Results: Of the 362 patients enrolled in SCORE2, 358 were included in the study. Only 48 patients missed a visit during the initial year of follow up, and only 12 missed more than 1 visit. After adjustment, for each visit missed, patients lost 3.0 letters (95%CI: -6.2, 0.2) of vision (p=0.07). On average, the 48 patients who missed at least 1 visit lost 9.4 letters (95%CI: -14.4, -4.3, p<0.001) of vision after adjustment. Average days and maximal interval between visit were not associated with changes in VA (p>0.22) for both comparisons). However, when a visit was missed, the average missed days between missed visits and the max missed interval were both associated with loss of VA (both variables: 0 days missed as reference, late [1-60 days] -10.8 letters [95%CI: -16.9, -4.7], very late [>60 days] -7.3 letters [95%CI: -14.5, -0.2]; p=0.003 for both). See Table 1 for additional results.

Conclusions: Visit adherence is associated with VA outcomes during Year 1 in SCORE2 participants.

CONTROL ID: 3711888

SUBMITTER (NAME ONLY): Omer Trivizki

TITLE: The Symmetry of Macular Fundus Features in Age-Related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Trivizki, L. Wang, P.G. Iyer, Y. Shi, G. Gregori, W.J. Feuer, P.J. Rosenfeld, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES| O. Trivizki, D. Rabinovich, Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: The symmetry of macular fundus features in the two eyes of the same patient with age-related macular degeneration (AMD) was investigated using swept-source optical coherence tomography (SS-OCT).

Methods: AMD patients were enrolled in a prospective SS-OCT natural history study from April 2016 to June 2021. SS-OCT imaging was performed at the time of their first visit. Two graders diagnosed the presence of drusen, geographic atrophy (GA), and exudative AMD (eAMD) in each eye. Medical records were reviewed to assess prior exudation. Validated algorithms were used to measure the area and volume of drusen. To assess asymmetry, one eye of each patient was randomly selected as the index eye and compared with the fellow eye. The kappa statistic (κ) was used to assess the symmetry of diagnosis. The intraclass correlation coefficient (ICC) was used to assess the symmetry of the drusen area and volume.

Results: A total of 1310 patients with AMD were included. The average age was 78 years old (range, 50-102) with 60% women. Of the 1310 subjects, 54% (701) presented with symmetric disease; 20% with bilateral drusen, 11% with bilateral GA, and 22% with bilateral eAMD. Only 0.5% of subjects had both GA and eAMD in both eyes. Of the randomly selected index eyes, 825 (47%) were right eyes. Overall, limited interocular agreement was observed between index and fellow eyes (54%; $\kappa = 0.29$). Kappa coefficients were poor (<0.4) for index eyes diagnosed with drusen ($\kappa = 0.27$), eAMD ($\kappa = 0.17$), and mixed disease ($\kappa = 0.03$). There was moderate agreement between index and fellow eyes for GA ($\kappa = 0.50$). Of the 265 patients with bilateral drusen, the symmetry of drusen area measurements had moderate ICC values of 0.70, 0.71 and 0.70 in the 3 mm and 5 mm diameter circles centered on the fovea and in the total scan area, respectively. The ICC for the drusen volume was slightly lower with ICC values of 0.65, 0.66 and 0.64 respectively.

Conclusions: Interocular symmetry was poor for eyes with drusen, eAMD, and mixed, but moderate for GA. While the diagnosis of drusen was not appreciably symmetric between eyes, the drusen area and volume measurements were moderately symmetric in patients with bilateral drusen.

CONTROL ID: 3711889

SUBMITTER (NAME ONLY): Aastha Singh

TITLE: Mesenchymal stem cells-derived interleukin-11 inhibits activation and proliferation of T cells

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Singh, S. Mittal, W. Cho, Y. Guan, E. Elbasiony, S. Chauhan, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uncontrolled T cell activation can result pathological conditions including autoimmunity and graft rejections. Our group has previously shown that mesenchymal stem cells (MSCs) inhibit activation of innate immune cells including neutrophils and macrophages. Here, we investigate whether MSCs regulate T cell responses by secreting interleukin-11 (IL-11).

Methods: Human bone-marrow derived MSCs (hMSCs) were purchased and phenotypically characterized for their expression of CD45- CD34- CD73+ CD90+. CD4+ CD25- T cells (purity: >95%) were magnetically sorted from human peripheral blood mononuclear cells for the MSC-T cell co-culture assays. Expression and secretion of IL-11 by hMSCs were evaluated using real-time PCR and ELISA, respectively. Expression of IL-11 receptor was confirmed in activated CD4+ CD25- T cells using flow cytometry. CD4+ CD25- T cells stimulated with anti-CD3/CD28 beads (1:1 ratio) were co-cultured with MSCs at 1:1 ratio for 24 hours (for early activation) and 66 hours (for proliferation) in the presence and absence of hIL-11 neutralizing antibody (20 µg/ml). Early T cell activation was assessed by evaluating expression of CD40L and CD69 (Median Fluorescence intensity; MFI) using flow cytometry. For proliferation, CD4+ CD25- T cells were stained with CFSE prior to co-culture and their proliferation was quantified by measuring CFSE dilution via flow cytometry.

Results: hMSCs constitutively express high levels of IL-11 at both mRNA and protein levels. Naïve CD4+ CD25- T cells showed the expression of IL-11 receptor, which was upregulated by 2-fold following CD3/CD28 stimulation. hMSCs significantly suppressed early activation of naive T cells, as indicated by an approximate 70% reduction in expression of both CD69 (p=0.025) and CD40L (p=0.011). This MSC mediated reduction in early T cell activation was not observed following the neutralization of IL-11. Furthermore, our CFSE dilution assay demonstrated that hMSCs significantly prevented the proliferation of CD4+ CD25-T cells (p=0.006); however, this MSC-mediated suppression of proliferation was abrogated following IL-11 neutralization.

Conclusions: IL-11 secretion by human mesenchymal stem cells is critical for inhibition of early T cell activation and proliferation.

CONTROL ID: 3711890

SUBMITTER (NAME ONLY): Jeremy Nortey

TITLE: Identifying Small-fiber Neuropathy of the Corneal Sub-Basal Nerve Plexus in Sjögren Syndrome Using In-Vivo Confocal Microscopy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Nortey, E. Gebreegaziabher, J.D. Keenan, T. Lietman, J.A. Gonzales, Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|J. Nortey, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Jeremy Nortey: Commercial Relationship: Code N (No Commercial Relationship) | Elisabeth Gebreegaziabher: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Keenan: Commercial Relationship: Code N (No Commercial Relationship) | Tom Lietman: Commercial Relationship: Code N (No Commercial Relationship) | John Gonzales: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Small fiber neuropathy is known to be associated with Sjögren Syndrome (SS) and in-vivo corneal confocal microscopy can identify features of a small fiber neuropathy. Here we performed a descriptive study to identify features of a short fiber neuropathy of the corneal sub-basal nerve plexus using in-vivo confocal microscopy in participants from the Sjögren's International Collaborative Clinical Alliance (SICCA) returning for up to 15-year follow-up compared to healthy controls.

Methods: We recruited 14 participants from the SICCA, the largest SS cohort in the world and funded by the National Institutes of Health, and 22 healthy controls. Eleven participants met SS classification based on updated 2016 American College of Rheumatology/European League Against Rheumatism criteria. All participants underwent slit-lamp examination and in vivo confocal microscopy of the central cornea's sub-basal nerve plexus centered about the central vortex to create a 30-image montage. Each image was analyzed with automated software (ACCmetrics, Manchester, United Kingdom) to produce seven nerve metrics. We performed t-tests to make comparisons of nerve metrics between SS (from SICCA cohort) and healthy controls (recruited from outside SICCA cohort) as well as SS and non-SS (both from SICCA cohort).

Results: Most nerve metrics were significantly lower in SS participants compared to healthy controls. Mean corneal nerve fiber density was found to be 3.5 mm/mm^2 in SS participants compared to 10.6 mm/mm^2 in healthy controls (95% CI: 0.48 to 6.46, $p<0.001$). Mean corneal nerve branch density was 2.7 main fiber branch points/mm^2 in SS participants compared to 15.2 in healthy controls (95% CI: -0.5 to 6.0, $p=0.001$). Mean corneal nerve fiber length was 4.3 mm/mm^2 in SS participants compared to 9.9 in healthy controls (95% CI: 2.6 to 6.1, $p<0.001$). When we compared SS (n=10) and non-SS (n=4) returning SICCA participants, mean nerve metrics were generally higher in those classified as non-SS, though these findings did not achieve statistical significance.

Conclusions: SS exhibits lower corneal nerve metrics compared to healthy controls. These findings suggest that a short fiber neuropathy can distinguish SS from healthy controls and may serve as a potential novel biomarker in identifying SS.

CONTROL ID: 3711891

SUBMITTER (NAME ONLY): Liping Tang

TITLE: A PCO Predictive In Vitro Model to Examine the Role of Fibronectin and IOL Surface Property on PCO formation

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Tang, J. Roy, A. Jaitli, A. Chatila, Bioengineering, The University of Texas at Arlington, Arlington, Texas, UNITED STATES|

Commercial Relationships Disclosure: Liping Tang: Commercial Relationship(s);Code C (Consultant/Contractor):Progenitec Inc;Code S (non-remunerative):Progenitec | Joyita Roy: Commercial Relationship: Code N (No Commercial Relationship) | Arjun Jaitli: Commercial Relationship(s);Code E (Employment):Alcon | Amjad Chatila: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: The occurrence of posterior capsule opacification (PCO) is due to the residual lens epithelial cells to infiltrate at the interface between lens capsule (LCs) and IOLs. IOL material adhesiveness is believed to affect cell infiltration and PCO formation. Extracellular matrix (ECM) proteins, particularly fibronectin (FN), have been suggested to play an important role in PCO formation. While many studies have examined the interaction of FN with IOLs, the role of adsorbed FN on influencing PCO is yet to be investigated. Using a PCO predictive in vitro model based on IOL:LC adhesive force, we investigated the influence of FN adsorption and IOL surface hydrophilicity on cell infiltration and PCO formation at IOL:LC interface.

Methods: To mimic cell infiltration at IOL:LC interface, an in vitro model was established with simulated LC and a custom-designed micro-force tester. By adding various amounts of FNs onto the simulated LCs prior to placing commercially available IOLs, including acrylic foldable, PMMA, and silicone IOLs, the influence of FNs on adhesion force between IOLs and LCs was examined. In addition, such influence on cell infiltration at the interface was examined by analyzing the amount of dye infiltration in a macromolecular dye imaging system. Finally, the influence of surface hydrophilicity on IOL:LC adhesive force and cell infiltration was examined using acrylic foldable IOLs coated with hydrophilic polymer- Di(ethylene glycol) (Diglyme).

Results: We observed that IOLs show different adhesiveness with LCs in the following order: acrylic foldable>silicone>PMMA. FN plays a significant role in increasing the adhesion force of acrylic foldables, but not PMMA & Silicone IOLs. As expected, FN significantly reduced dye penetration at the interface between acrylic foldable IOLs (~50% reduction) and LCs. However, Diglyme coating significantly reduced the IOL:LC adhesive forces while increased dye penetration compared to acrylic foldable controls. The presence of FN had an insignificant influence on the adhesive forces and dye penetration.

Conclusions: The results support the overall hypothesis that FN adsorption may increase the IOL:LC adhesive force and reduce cell infiltration at the interface (Fig. 1). By increasing surface hydrophilicity, Diglyme coating significantly reduced IOL:LC adhesive force and increase dye infiltration while demolished the influence of FN.

CONTROL ID: 3711892

SUBMITTER (NAME ONLY): Darlene Miller

TITLE: Survey of Archaeal Signatures in Contaminated Lens Case Ecosystems

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Miller, J. Maestre-Mesa, H.W. Flynn, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Darlene Miller: Commercial Relationship: Code N (No Commercial Relationship) | Jorge Maestre-Mesa: Commercial Relationship: Code N (No Commercial Relationship) | Harry Flynn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Archaea are prokaryotic members of the Third domain. Although usually missing or ignored in human microbiome studies, they are emerging as intimate and influential immune/disease modulators of the human microbiome in collaboration but distinct from bacteria and or other microbiota. To date, there are 5, but still increasing number of phyla; Crenarchaeota, Euryarchaeota, Korarchaeota, Nanoarchaeota and Thaumarchaeota. They have been recovered from mucosal surfaces including the gastrointestinal tract (GIT), nose, lung, vagina, and also skin. Our purpose was to investigate and document the presence and diversity of archaeal signatures in contact lens case ecosystems collected from the ocular surface of patients presenting with microbial keratitis.

Methods: We used whole genome sequencing (WGS) to document and compare the prevalence and diversity of archaeal signatures in 30 contact lens systems (CTLS) of 15 patients presenting with bacteria keratitis (BK), n=6, Acanthamoeba keratitis (AK), n=6, microbial keratitis (MK), n=2 and or fungal keratitis (FK), (n=1).

Results: A total of 3 phyla, 55 genera and 86 species were detected during the WGS survey. At least one archaeal signature was found in all patients' contact lens cases, but relative abundance for all ecosystems was low (<1%, 9244 tags). Two of the five phyla were detected in 96.7% (n=29/30) of CLTS. These included Euryarcheota (n=78.3%, n=7240 tags, 96.7% of CTLS) and Crenarchaeota, 21.7%, n=2003 tags, also 96.7% of cases. Thaumarchaeota was detected in only 1 patient (6.7%) in 3.3% of cases. Archaeal signatures (tags) were more frequently detected in cases of patients with AK (n=5648, 61.09%) than in cases of patients with BK (n=3527, 38.15%, p<0.0001), FK, n=28, 0.30%, p<0.0001), and or microbial keratitis, n=41, 0.44%, p<0.0001). Methane-producing species (n=39/77, 50.6%) were the dominant members detected among the Euryarchaeota phyla.

Conclusions: Archaea may be present on the ocular mucosa surface. The role these unique prokaryotes may play in ocular surface immune defense or disease disorders is unknown.

CONTROL ID: 3711893

SUBMITTER (NAME ONLY): Grant Higgins

TITLE: Ultrasonic vitrectomy device-tissue interaction characterization

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Higgins, A. Papour, Surgical R&D, Bausch and Lomb, Saint Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Grant Higgins: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch & Lomb;Code E (Employment):EASI | Asael Papour: Commercial Relationship(s);Code E (Employment):Bausch & Lomb

ABSTRACT BODY:

Purpose: Electrical signatures of ultrasonic vitrectomy devices during tissue interaction have not been fully characterized and are not well understood as a theoretical model does not exist. Electrical measurements in BSS and pig vitreous show the ultrasonic energy-tissue interaction behavior and reveal high sensitivity of the ultrasonic probe to tissue type and sub-type. This is a first demonstration of ultrasonic vitrectomy tissue detection capability that may detect tissue type in real-time during surgery.

Methods: Measurements: Electrical data of Vitesse 25 gauge vitrectomy probe, driven by Stellaris Elite^{TM} (Bausch & Lomb, LLC) was measured using voltage and current probes on a mixed signal oscilloscope (Tektronix MSO 4054) with 1MS/s high resolution acquistion rate. The vitrectomy probe was operated in BSS and two forms of pig vitreous with 60 um stroke and 100 mmHg vacuum. Vitreous was harvested from a fresh pig eye and separated into two samples; viscous liquid (water and hyluronan) and thick gel-like (with collagen matrix).

Results: Vitesse shows an average power increase of 70% when operated in thick gel-like vitreous (Vit Base) compared to BSS with a 36% increase in voltage, a 16% increase in current, and a 20% increase in impedance. When operated in the viscous liquid (thin vitreous), Vitesse shows an average power increase of 47% when compared to BSS with a 23% increase in voltage, an 18% increase in current, and a 6% increase in impedance. A two sample unpaired t-test of the electrical parameters in tissue vs BSS with a significance level of 0.01 show extremely high statistical significance ($p < 0.001$).

Conclusions: There is a substantial difference in the electrical characteristics required to operate on posterior tissue types and BSS. With all four electrical parameters showing statistically significant results, this displays proof of concept that ultrasonic devices may be able to sense changes in tissue interaction during surgery in real-time.

CONTROL ID: 3711894

SUBMITTER (NAME ONLY): Clemens Strohmaier

TITLE: OCT-A analysis of filtration bleb vascularization after Santen preserflo microshunt implantation

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Strohmaier, M. Kallab, S. Beka, A. Reisinger, M. bolz, Ophthalmology, Johannes Kepler Universitat Linz, Linz, AUSTRIA|A.S. Huang, Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate filtration bleb vascularization after ab-externo implantation of the Santen Preserflo microshunt using anterior segment OCT-angiography

Methods: 9 patients underwent Preserflo microshunt implantation according to the standard protocol recommended by Santen. The pre- and postoperative drug regimen was according to department standards. At 1 week, 2 weeks, 1 months, 2 months, 3 months and 6 months postoperatively, OCT-A images of the filtration bleb were acquired using a Zeiss Plex Elite 9000 angio-OCT. A 20D add-on lens enabled anterior segment imaging with the device. A 3x3 mm rectangle (posterior pole scale, equals approx. 6x6 mm on the anterior surface) was imaged. Vascularization was assessed by calculating the perfusion density using algorithms provided by Zeiss (ARI network)

Results: Perfusion density in the filtration bleb was 30.82, 26.33, 29.09, 29.06 and 25.09 respectively (1w, 2w, 1m, 2m, 3m, 6m) (p=0,432). IOP decreased from 21,85 ± 6,80 mmHg to 7,69 ± 1,77 mmHg, 8,54 ± 1,98 mmHg, 10,84 ± 2,71 mmHg, 11,92 ± 4,21 mmHg, 11,08 ± 4,66 mmHg and 13,40 ± 8,99 mmHg.

Conclusions: The present study demonstrates that the perfusion density algorithm on the Zeiss Plex Elite can be used to monitor filtration bleb vascularization longitudinally. Larger cohorts are needed to gain insight in the relationship between bleb vascularization and surgical outcome

CONTROL ID: 3711895

SUBMITTER (NAME ONLY): Hyeonhee Roh

TITLE: Electrically-evoked Responses of ON and OFF Ganglion Cells in Retinal Degeneration 8 (rd8) Mice

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Roh, Y. Otgondemberel, M. Im, Brain Science Institute, Korea Institute of Science and Technology, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|H. Roh, Division of Electrical Engineering, Korea University, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|M. Im, Division of Bio-Medical Science & Technology, University of Science and Technology, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Hyeonhee Roh: Commercial Relationship: Code N (No Commercial Relationship) | Yanjinsuren Otgondemberel: Commercial Relationship: Code N (No Commercial Relationship) | Maesoon Im: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Microelectronic retinal prostheses have been implanted to restore the vision of individuals blinded by outer retinal degenerative diseases but showed considerable performance variations across users. Given that retinitis pigmentosa has the numerous genotypes which have distinct phenotypes, there is a possibility of different characteristics in electrically-evoked responses across those genotypes. However, the past prosthetic researches have typically used retinal degeneration 1 (rd1) and 10 (rd10) models which have Pde6b gene mutation. To extend our understanding to another type of degenerate retinas, we studied electric responses of retinal ganglion cells (RGCs) in rd8 mice which have Crb1 gene mutation for the first time.

Methods: We used cell-attached patch clamping method to record spikes from RGCs in the wild-type (wt, C57BL/6J; n = 6 and n = 7 for ON and OFF RGCs, respectively) and rd8 mice (C57BL/6N; n = 7 and n = 9 for ON and OFF RGCs, respectively). First, ON and OFF RGCs were identified by their responses to 1-sec-long stationary white spot flash on a gray background. Second, an electric stimulus (4 ms duration, -100 μA) was applied to evoke network-mediated responses. Similar to our previous works, the electrically-elicited spiking responses were divided into two parts: first burst and delayed response.

Results: Both peak firing rate and spike count of delayed responses arising in rd8 RGCs were considerably lower compared to those of wt RGCs. For example, in the wt mice, the peak firing rates of ON and OFF RGCs were 277.4±122.4 and 361.5±209.5 Hz; however, those were decreased in the rd8 mice to 162.7±149.4 and 260.1±177.3 Hz, respectively. Also, the average spike counts of both ON and OFF types were smaller in rd8 than wt: 49.1±26.3 vs. 17.1±13.4 (wt vs. rd8 for ON RGCs), and 12.2±9.6 vs. 8.3±4.4 (wt vs. rd8 for OFF RGCs), respectively.

Conclusions: In summary, we characterized the electrically-evoked responses of ON and OFF RGCs in rd8 mice. In addition to our recent publication regarding network-mediated responses of rd10 mice, systematic comparison of results from rd8 vs. rd10 will enhance our understanding of electrically-elicited responses of RGCs in different forms of retinal degeneration. These researches are likely to contribute in reduction of performance variations across prosthetic users.

CONTROL ID: 3711897

SUBMITTER (NAME ONLY): Monica Hu

TITLE: Report of a rare mild phenotype of retinitis pigmentosa in a family with distal USH2A mutations predicted to result in truncated protein

SESSION TITLE: Inherited Retinal Disease Genetics I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Hu, S. Rehman, L.E. Fry, M.E. McClements, R.E. MacLaren, K. Xue, University of Oxford Nuffield Laboratory of Ophthalmology, Oxford, Oxfordshire, UNITED KINGDOM|S. Rehman, R.E. MacLaren, K. Xue, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mutations in USH2A, encoding usherin, are the most common cause for non-syndromic autosomal recessive retinitis pigmentosa (RP) and Usher syndrome type 2. Here we report two siblings with extremely mild forms of retinitis pigmentosa without hearing impairment, each confirmed to be compound heterozygous for an USH2A c.6590C>T missense variant and an exon 70 deletion.

Methods: Each patient underwent clinical examination, microperimetry, OCT, fundus autofluorescence (FAF) imaging, and genetic testing by targeted next generation sequencing.

Results: Two sisters, aged 50 and 48 years, presented with slow, progressive peripheral visual field loss and nyctalopia beginning in their 30s. They were otherwise clinically well, had no hearing deficit on audiology testing, and no family history of any vision problems. Cancer-related retinopathy had been excluded. Visual acuities were 6/5 OD 6/6 OS in the elder and 6/6 OU in the younger, both retaining sufficient visual fields for driving. FAF in both patients showed a hyperautofluorescent ring surrounding the macula bilaterally. OCT demonstrated well-preserved retina within the ringed areas, but ellipsoid zone loss outside the ring. Genetic testing of the older sister initially found a heterozygous missense variant of uncertain significance, USH2A c.6590C>T (Thr2197Ile). Multiplex ligand-dependent probe amplification (MLPA) analysis revealed heterozygosity for an exon 70 deletion, predicted to result in a frameshift. Genetic testing of the younger sister showed identical mutations. Further segregation analysis confirmed bi-allelic inheritance.

Conclusions: Compound heterozygosity of a missense mutation and a 3’ exon deletion in USH2A is associated with a very mild form of RP with preserved central vision and hearing. USH2A c.6590C>T was previously reported as a variant of uncertain significance with conflicting evidence of pathogenicity. Deletion of the penultimate exon 70 is predicted to cause read-through of the terminal splice site into terminal exon 72 before reaching a stop codon. While this transcript may evade nonsense-mediated decay, disruption of the C-terminus may affect the PDZ-binding motif (PBD) and its interaction with harmonin. While there remains some uncertainty regarding the pathogenicity of c.6590C>T variant, the mild phenotypes observed would be compatible with partially retained protein function.

CONTROL ID: 3711898

SUBMITTER (NAME ONLY): Hong Jiang

TITLE: Retinal capillary function in patients with multiple sclerosis: 2-year follow-up

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Jiang, A. Simms, G. Gregori, J. Wang, Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Florida, UNITED STATES|H. Jiang, S. Delgado, J. Hernandez, Neurology, University of Miami Miller School of Medicine, Florida, UNITED STATES|

Commercial Relationships Disclosure: Hong Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Ava-Gaye Simms: Commercial Relationship: Code N (No Commercial Relationship) | Silvia Delgado: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Hernandez: Commercial Relationship: Code N (No Commercial Relationship) | Giovanni Gregori: Commercial Relationship: Code N (No Commercial Relationship) | Jianhua Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the retinal capillary function (the efficiency of blood flow transferring capacity of retinal capillary network) in patients with multiple sclerosis: 2-year follow-up.

Methods: A total of 22 patients (22 eyes) with RRMS were followed for a period of 27 ± 6 months. One eye of each subject was imaged at baseline and at follow-up. Retinal blood flow (RBF) was measured using a Retinal Function Imager and retinal capillary density (RCD, expressed as fractal dimension Dbox) was measured using optical coherence tomography angiography. The efficiency of blood flow transferring capacity of retinal capillary network retinal capillary function (RCF) was defined as the ratio of RBF to RCD.

Results: RCF was 1.36 ± 0.26 nl/s/Dbox (mean ± SD) at baseline and significantly increased to 1.61 ± 0.36 nl/s/Dbox after training (P = 0.03), reflecting an increase of 19%. There were 15 study subjects without clinical and radiological disease activity during the follow-up period, while there were 8 subjects with disease activity. Further analysis showed that the significant increase of RCF (i.e. change 0.33 nl/s/Dbox' P = 0.042) occurred only in the subgroup without disease activity. The change in the subgroup with active disease was 0.08 nl/s/Dbox (P = 0.50).

Conclusions: This is the first prospective study to demonstrate an increased RCF in MS patients with stable disease at 2-year follow-up, suggesting a possible recovery of RCF which may be associated to an enhanced blood flow to the retina in these patients.

CONTROL ID: 3711901

SUBMITTER (NAME ONLY): Mohamed Abdel-Rahman

TITLE: Germline MBD4 variants in uveal melanoma patients

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Abdel-Rahman, F.H. Davidorf, C.M. Cebulla, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|M.H. Abdel-Rahman, Division of Human Genetics, The Ohio State University, Columbus, Ohio, UNITED STATES|P. Johansson, N. Hayward, Oncogenomics Group, QIMR Berghofer Medical Research Institute, Herston, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: There is variable data regarding the frequency of germline MBD4 variants in patients with uveal melanoma (UM). The frequencies of pathogenic/likely pathogenic (P/LP) variants range from ~0.7% (8/1099) in a French cohort to 0.23% (1/432) in a Finnish cohort with no loss of function variants detected in the Finnish cohort. This casts doubt on the association of germline MBD4 variants and UM predisposition. Therefore, the goal of this study was to evaluate the frequency of MBD4 variants in a cohort of UM patients with strong personal and/or family history of cancer.

Methods: Germline variants in MBD4 were assessed in 182 UM patients with strong personal and/or family history of cancer including 27 patients with familial UM. Screening was carried out by next generation sequencing of individual or pooled samples (8 samples/pool) and all detected variants were confirmed by Sanger sequencing. Mutation burden was available in one patient that was included in The Cancer Genome Atlas (TCGA) project.

Results: Three patients (1.65%), all females, had germline P/LP variants in MBD4, which was significantly higher than in the European, Non-Finnish, general non-cancer population (Fisher's exact 2-tailed p =0.001, RR 95% CI: 15.96 (5.1-50.4)). The ages of these patients were 41, 58, and 71 years. The 41-year-old female had multiple family members affected with breast and colon cancer. She was recurrence free at 91 months after enucleation of her large monosomy 3 (M3) tumor, with very high mutation burden. The 58-year-old female died shortly after diagnosis and treatment of her UM from an unrelated cause. She reported a family history of throat cancer in her father and unknown cancers in her maternal and paternal cousins. The 71 year-old-female, had a history of two additional relatives on the same side of the family with UM. Germline DNA was available on one of them and he tested negative for the MBD4 pathogenic variant.

Conclusions: Our results support a role for MBD4 P/LP variants in predisposition to UM, likely through modifying the effect of other cancer predisposition genes. Further studies of the clinical phenotype of subjects with germline pathogenic variants are warranted.

CONTROL ID: 3711902

SUBMITTER (NAME ONLY): Jose David Rios

TITLE: Specialized Pro-Resolving Lipid Mediators, Maresin 1 (MaR1) and Neuroprotectin D1 (NPD1) Reduce Gliosis in Retina and Optic Nerve after Blast Exposure

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rios, P. Edsall, D. Golden, J. Butler, A. Szczesniak, T.J. Pearson, H. Crespocruz, Pain and Sensory Trauma Care, US Army Institute of Surgical Research, Fort Sam Houston, Texas, UNITED STATES|C.N. Serhan, Anesthesiology, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|C.N. Serhan, Oral Medicine, Infection, & Immunity, Harvard Medical School, Boston, Massachusetts, UNITED STATES|R.D. Glickman, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure: Jose David Rios: Commercial Relationship: Code N (No Commercial Relationship) | Peter Edsall: Commercial Relationship: Code N (No Commercial Relationship) | Dallas Golden: Commercial Relationship: Code N (No Commercial Relationship) | Jacinque Butler: Commercial Relationship: Code N (No Commercial Relationship) | Anthony Szczesniak: Commercial Relationship: Code N (No Commercial Relationship) | Trent Pearson: Commercial Relationship: Code N (No Commercial Relationship) | Harling Crespocruz: Commercial Relationship: Code N (No Commercial Relationship) | Charles Serhan: Commercial Relationship: Code N (No Commercial Relationship) | Randolph Glickman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate specialized pro-resolving lipid mediator (SPMs) as neuroprotective interventions to ameliorate neuroinflammation caused by blast exposure. We hypothesized that early administration of the SPMs, NPD1 or MaR1, will mitigate neuroinflammation, preserving retinal and optic nerve tissues after blast exposure in a blast-induced eye injury model.

Methods: A compressed-air driven shock tube was used to expose anesthetized adult male Long-Evans rats to shock waves simulating an open-field blast exposure. Blast waves of peak overpressure of 133 ± 4 kPa and a positive phase duration of 3.34 ± 0.05 ms were used. Approximately 30 minutes after blast exposure, rats were treated with either 1.0 µg/kg MaR-1, 0.1 µg/kg NPD1 or vehicle (0.9% saline) delivered via tail vein injection and treated daily thereafter until day 7. Unexposed rats were included as controls. Rats were euthanized at 9, 23, and 33 days after blast exposure. The retina and optic nerve tissue were subjected to immunohistochemistry and Western Blots analyses for glial fibrillary acidic protein (GFAP) and for ionized calcium-binding adaptor 1 (Iba1) as indicators of gliosis. Tissues were evaluated for relative levels of positive signals compared to the unexposed controls.

Results: An increase in GFAP-immunostaining was detected throughout the Müller cell processes traversing the inner plexiform layer and in retinal ganglion cells of vehicle blast-exposed rats compared to controls. Immunolabeling of Iba-1 showed an increase in microglia reactivity in the retinas and optic nerve at 9, 23, and 33 days post blast of vehicle-treated blast rats compared to controls. Western Blot analysis showed a ~1.5-fold increase in GFAP protein levels in optic nerve homogenates from vehicle-treated blast exposed rats as compared to the control group. MaR1 and NPD1 treatment reduced GFAP upregulation and mitigated microglial reactivity in the retina and optic nerve up to 33 days after blast injury.

Conclusions: Blast wave exposure resulting in retinal damage, manifested by increased expression of proteins involved in gliosis, was reduced by either MaR-1 and/or NPD1 intervention. Thus the treatments of MaR1 or NPD1 suggest an effective strategy to reduce or halt retina and optic nerve glia cell activation due to blast wave exposures.

CONTROL ID: 3711903

SUBMITTER (NAME ONLY): Menaka Thounaojam

TITLE: Altered bile acids-gut microbiome axis in oxygen-induced retinopathy: potential implications for retinopathy of prematurity

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Thounaojam, A. Oxenrider, T. Bui, M. Bartoli, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|R. Jadeja, P.M. Martin, Biochemistry and Molecular Biology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies by our group and others have shown a significant role of bile acids (BA) in various retinal diseases. Gut microbiota has been shown to profoundly affect BA metabolism and systemic composition due to bacterial bile salt hydrolases (BSH). Dysregulated BA-gut microbiome axis (BGA) contributes to various pathologic conditions, including diabetic retinopathy. In addition, exogenous administration of the BA ursodeoxycholic acid (UDCA) has been shown to balance gut microbiota and, from our studies, to ameliorate oxygen-induced retinopathy (OIR), an experimental model of retinopathy of prematurity (ROP). Here, we have investigated whether OIR in mice alters the BGA and whether treatment with UDCA could normalize it.

Methods: Seven days-old mice pups (P7) were subjected to OIR. A group of OIR mice was treated with 50 mg/kg/day of UDCA administered ip. from postnatal days 7 to 17 (P7–P17). Age-matched fully untreated (RA) mice were used as control. BA and microbiome composition was assessed in cecal samples of mice at P17 in all experimental groups, using LC-MS/MS and 16S sequencing, respectively. Spearman's rank correlation coefficient was assessed to determine the specific association of altered BA profile with relative microbiome composition. In addition, levels of BSH activity and systemic insulin-like growth factor 1 (IGF-1) were analyzed in all experimental groups.

Results: BA composition in cecal samples of OIR mice at P17 showed increased levels of unconjugated BA in OIR mice and decreased glycine and taurine conjugated BA, indicating dysregulated BA metabolism. In addition, microbiome composition in OIR mice was significantly disrupted with higher levels of Proteobacteria and lower composition of BSH-producing phyla such as Firmicutes and Bacteroidetes compared to control mice (RA). Furthermore, Spearman's rank correlation coefficient analysis confirmed a significantly dysregulated BGA in OIR. Finally, UDCA treatment of OIR mice corrected the BA-gut microbiome dysregulation. These changes were further associated with a significant decrease in serum IGF-1 levels and increased cecal BSH enzymatic activity in OIR+UDCA mice compared to OIR mice.

Conclusions: Our experimental data evidence a potential correlation between dysregulated BGA and ROP and suggest UDCA as an effective therapy to correct BA-gut microbiome dysregulation in ROP.

CONTROL ID: 3711906

SUBMITTER (NAME ONLY): Michael James Gilhooley

TITLE: Isolation of retinal ganglion cells for single cell transcriptomics in a model of dominant optic atrophy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gilhooley, N. Owen, M. Moosajee, P. Yu-Wai-Man, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|P. Yu-Wai-Man, Mitochondrial Biology Unit, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|M. Gilhooley, M. Moosajee, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Melanopsin-expressing intrinsically photosensitive retinal ganglion cells (ipRGCs) survive late in dominant optic atrophy (DOA), long after other RGC sub-types (and vision) have been lost: the underlaying mechanism is unclear. Our purpose here was to optimise a pathway for the preparation and enrichment of single RGC suspensions from an experimental mouse model of DOA and wildtype retinas. This will facilitate single cell RNA sequencing (scRNAseq) approaches to determine if differentially upregulated neuroprotective genes or pathways in ipRGCs are the source of this resistance.

Methods: Retinas of C57/BL6J (P21) mice of both sexes were compared: four groups underwent papain enzyme treatment for 20, 30, 40 or 45 minutes respectively while a final group underwent mechanical disruption [N=3 mice (n=6 retinas) / group]. Fluorescence Assisted Cell Sorting (FACS) on the resulting single cell suspensions was used to enrich the samples for viable RGCs [CD90(thy1.2)$^{+}$,CD48^{-},CD57^{-},CD15^{-},DAPI^{-}]. This was validated by FACS-post-sort-purity-check, RGC marker (SNCG) immunocytochemistry (ICC) & RT-qPCR for RGC specific genes (Thy1, Brn3a, Sncg). This optimised protocol was used to isolate RGCs from both Opa1$^{+/TTAG_del}$ mice and littermate (wildtype) controls (5 months old, N=18 mice per group) for subsequent scRNAseq analysis.

Results: Viability post papain digestion was (mean±SEM) 60.8±2.4%, 54.4±4.3%, 60.2±5.9%, 59.3±3.3% at 20,30,40,45 minutes respectively with no difference between timepoints (one- way ANOVA $F_{(1.28, 2.56)}$=1.84 p=0.30)). Mechanical dissociation led to lower viability (10.41±2.90%; t-test p<0.0001 vs. papain (30m) group). Following FACS processing, papain (30m) suspensions showed RGC enrichment of 78.0±6.6% on post-sort-purity-check and viability of 96.5±3.2% maintained (90.1±1.8%) 5 hours later. ICC showed 75.2±10.6% of cells in the RGC enriched sample staining for SNCG, compared to 13.1±3.1% in the remaining suspension (t-test p<0.0001); across the same comparison, expression of RGC specific genes demonstrated logfold increases by RT-qPCR of: Thy1 25.3±0.9, Brn3a 61.4±0.8, Sncg 7.5±0.9.

Conclusions: This optimised protocol has allowed for enrichment of RGCs from wildtype and DOA model retina for use in scRNAseq. Such investigations will contribute to a greater understanding of the disease resistance of ipRGCs, potentially opening the way for novel neuroprotective therapies for DOA.

CONTROL ID: 3711907

SUBMITTER (NAME ONLY): C Ethier

TITLE: A Novel Image-Based Method to Determine Iris Biomechanics in Angle-Closure Glaucoma

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.R. Ethier, B. Safa, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|C.R. Ethier, M. Bahrani Fard, Mechanical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Established risk factors for primary angle-closure glaucoma (PACG) include anatomical deficits (e.g., anterior chamber crowding), age, and genetic background, yet only a small percentage of people classified as high-risk progress to PACG (ZAP trial), indicating that current risk factors are incomplete. Here we consider iridial biomechanical properties as a risk factor, and specifically describe an imaging-based technique to determine such factors in vivo.

Methods: We repurposed an existing public biometric database [Konnison+, 2019 Int Conf Biometrics; 163 near-infrared videos from 42 subjects] depicting both eyes during the pupillary light reflex (PLR). Pupil size was determined in darkness and at maximal constriction by segmenting the pupillary margin, and iridial surface features were automatically tracked to determine iridial deformations. Deformations were fit using engineering inverse finite element modeling (iFEM), thereby determining T_s, the magnitude of the sphincter muscle traction; and E and v, the modulus and Poisson ratio of the stroma.

Results: Pupillary segmentation was reliable, repeatable in a test-retest paradigm, and symmetric between eyes in this ostensibly normal cohort (Figure). Stromal feature tracking was less reliable. iFEM fitting of pupillary contraction showed a strong linear correlation between T_s and E, with a mean T_s:E value of 5 (range 4-13, depending on assumed sphincter muscle size).

Conclusions: Our methodology to estimate iris biomechanical properties from near-infrared videos is fast and inexpensive and may aid in understanding additional risk factors for PACG, complementing OCT anatomic measurements. Our estimate of sphincter muscle stiffness is greater than previous estimates [Pant+, IOVS 2018; Panda+, IOVS 2021], possibly due to different patient populations in our study (European descent) vs. previous studies (Asian), of interest due to differential incidence rates of PACG in these populations. Better methods for determining sphincter muscle size in vivo and iridial feature tracking are needed to improve the methodology.

CONTROL ID: 3711909

SUBMITTER (NAME ONLY): Hoang Mai LE

TITLE: Quantitative analysis of choriocapillaris flow using swept-source optical coherence tomography angiography in eyes with angioid streaks

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. LE, A. Miere, S. Halouani, E. Souied, Ophthalmology, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|E. Borrelli, G. QUERQUES, Universita Vita Salute San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: The purpose of the study is to quantitatively analyze the choriocapillaris alterations using SS-OCTA in eyes presenting with angioid streaks and to compare these alterations with control eyes.

Methods: Macular 6x6 mm SS-OCTA scans were retrospectively analyzed in eyes with angoid streaks and in control eyes. The choriocapillaris en face slabs (structure and flow) were extracted from the SS-OCTA device after a manual segmentation. En face choriocapillaris flow images were compensated with en face choriocapillaris structure images, followed by Phansalkar local thresholding method using both using a window radius 4 and 8 pixels, respectively. Quantitative analysis was performed in the 4 peripheral 1X1mm corners of the OCTA 6x6mm image in order to include equidistant and comparable regions in all eyes outside of the area of MNV, if present. The percentage of flow deficits (FD%), the number and size of the flow deficits and the total area of FDs were then computed for comparison.

Results: 54 eyes of 31 patients were included in the analysis: 27 eyes diagnosed with angioid streaks (14 patients) and 27 controls (17 patients). Macular neovascularization was associated in 21 of the eyes with angioid streaks. Analysis of the 4, 1X1mm peripheral corners of the 6X6mm OCTA image showed that eyes with angiod streaks had a higher FD% compared to the control group (47.62+/-8.06 versus 38.90+/-6.38 using radius 4 pixels ($p<0.001$); 48.37+/-7.65 versus 39.66+/-6.51 using radius 8 pixels ($p<0.001$).The average size of FDs as well as the total area size of the FDs were significantly higher in eyes with angioid streaks compared to control eyes ($p<0.001$)

Conclusions: Angioid streaks eyes present a reduced choriocapillaris flow compared to control eyes using SS-OCTA. A reduced choriocapillaris perfusion may contribute, among other factors, to development of neovascularization and atrophy in patients with angioid streaks.

CONTROL ID: 3711911

SUBMITTER (NAME ONLY): Jamie Shaffer

TITLE: Evaluating access to laser therapy by driving distance using Medicare data and Geographic Information Systems mapping

SESSION TITLE: Health Economics and Health Care Delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Shaffer, A.Y. Lee, C.S. Lee, Ophthalmology, University of Washington Department of Medicine, Seattle, Washington, UNITED STATES|D.D. Miller, Ophthalmology, Mayo Clinic, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To address concerns about regional variation in access to eye care, several states allow optometrists to perform laser procedures previously limited to ophthalmologists, including selective laser trabeculoplasty (SLT) and Nd:YAG laser procedures. We evaluated access to care for residents of three such states by comparing driving distances to optometrists versus ophthalmologists.

Methods: Medicare Fee For Service Data was obtained from the Centers for Medicare & Medicaid Services for 2016 to 2020 for Oklahoma, Kentucky, and Louisiana. Nine digit zip codes for the offices where YAG and SLT were performed were geocoded into GPS coordinates using GEODATA from Melissa (Rancho Santa Margarita, CA) matched by the year of service. Using TomTom historical traffic data, isochrones for 10, 20, and 30 minute driving times were generated for each office location. Population weighted centroids at the census block level from the US Census 2020 data were then used to measure the proportion of the population within 30 minutes of an optometrist or ophthalmologist performing YAG and SLT procedures.

Results: Isochrones for optometrists and ophthalmologists show that optometrists cover an area similar to that covered by ophthalmologists for SLT (Figure 1) and YAG (Figure 2) laser procedures. For SLT, the percent of population covered within 30 minutes of driving time by optometrists was 73.40% (95% CI 73.38 - 73.42), compared to 84.05% (95% CI: 84.03 - 84.07) for ophthalmologists. For YAG, the percent of population covered by optometrists was 84.77% (95% CI 84.75 - 84.79), compared to 85.25% (95% CI: 85.23 - 85.27) for ophthalmologists. For both laser procedures, the percent of the population covered exclusively by optometrists was 5.63% (95% CI 5.62 - 5.64), compared to 6.06% (95% CI: 6.05 - 6.07) by ophthalmologists. The odds ratio for coverage by optometry was 0.92 (95% CI: 0.92 to 0.93).

Conclusions: Despite expansion of laser privileges to optometrists in Oklahoma, Kentucky, and Louisiana, ophthalmologists continue to serve a statistically significant higher percentage of the population for both laser procedures. The expansion of laser privileges to optometrists has not resulted in a statistically significant increase in access to laser procedures.

CONTROL ID: 3711913

SUBMITTER (NAME ONLY): Kelly Mulfaul

TITLE: Relative abundance of FH and FHR-4 in genotyped human donor eyes: significance for AMD pathogenesis

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mulfaul, M.M. Collins, L.M. Affatigato, E.M. Stone, B.A. Tucker, R.F. Mullins, University of Iowa Institute for Vision Research, Iowa, UNITED STATES|K. Mulfaul, M.M. Collins, L.M. Affatigato, E.M. Stone, B.A. Tucker, R.F. Mullins, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a leading cause of vision loss globally. A single nucleotide polymorphism Y402H in Complement factor H, a key negative regulator of complement activation, has been shown to increase an individual's risk of developing AMD. The CFH gene is located on chromosome 1 in the regulator of complement activation gene cluster. Factor H related proteins 1-5 are encoded downstream of CFH. In contrast to FH, FHR-4 acts to promote complement activation and has been suggested to compete with FH for ligand binding. Recently FHR-4 levels have been shown to be elevated systemically in the plasma and serum of AMD patients, however the abundance of FHR-4 protein in RPE choroid tissue from genotyped AMD donors and age-matched controls has not been assessed.

Methods: We studied FH and FHR-4 protein expression in genotyped human donor eyes by both western blot and immunohistochemistry. Western blots were performed on serially extracted aqueous soluble (circulating) and detergent soluble (tissue bound) protein fractions from 2 YY control, 2 YY AMD, 2 HH control and 2 HH AMD donors. Macular tissue sections from 4 YY control, 4 YY AMD, 3 HH control and 3 HH AMD donors were incubated with goat-anti-FH and mouse anti-FHR-4 antibodies.

Results: We found that serum FH protein levels were similar in all donors whereas FHR-4 was elevated in AMD donor serum, consistent with previous reports. We next assessed the relative abundance of FH and FHR-4 in choroid and detected FH protein in both soluble and insoluble RPE/choroid fractions, whereas low levels of FHR-4 were observed only in the soluble fraction. Immunohistochemically we observed robust labeling for FH in all samples, most notably in extracellular domains surrounding the choriocapillaris. In contrast, labeling for FHR-4 protein was variable and relatively weak.

Conclusions: Individuals homozygous for Y402H polymorphism who have increased risk of developing AMD have elevated levels of FHR-4 in their serum, however, no alterations are observed in the local choroidal concentrations of FHR-4. FH, but not FHR4, was found in the detergent soluble, ECM bound protein fraction. Thus, FH is the most abundant member of the FH/FHR family in the choroid, highlighting its importance in AMD pathogenesis.

CONTROL ID: 3711914

SUBMITTER (NAME ONLY): Carlos Muller Morales

TITLE: Clinical outcomes, short-term survival and complications of Lucia Keratoprosthesis

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Muller Morales, K.M. Arteaga-Rivera, D. Jimenez-Collado, A. Ramírez-Miranda, A. Navas, E.O. Graue-Hernandez, Córnea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To report visual outcomes, survival rate and short-term complications in patients treated with Lucia KPRO.

Methods: All eligible patients were included. Suitable patients for keratoprosthsis surgery were those who weren't candidates for conventional PKP, including severe bilateral limbal stem cell disease, history of repeat corneal graft failure, ocular surface chemical burns or immune mediated ocular surface disease. Analyzed variables include diagnosis prior to transplantation, age, gender, BCVA, IOP, and postop complications. Descriptive analysis was performed using Excel (Microsoft, Redmond, WA) and statistical analysis was performed using StatPlus (StatPlus, Version 6, AnalystSoft Inc., Walnut, CA). Chisquare test was used to analyze categorical data. Normality test was performed to determine if a data is normally distributed.Preop and postop LogMAR VA were determined to be normally distributed. Then, paired two-tailed t-test was used to compare VA. Statistical significance was set at $p < 0.05$. Log-rank test was performed on Kaplan-Meier survival curves for maintenance of VA and device retention.

Results: 20 eyes of 19 patients were included . Mean age 53.85±17.25 yo. Average follow up 95.3±69.89 days. Previous transplants were performed in 13 eyes (65%), in 7 eyes (35%) KPRO implant was the primary procedure. Mean preop VA 2.40±0.38 logMAR, immediate postop VA was 1.08±0.67 logMAR and 0.98±0.99 logMAR at end of follow up (6 mo) having a statistically significant improvement ($p<0.05$). Most frequent complication was ocular hypertension in the immediate postoperative 25%, retroprothesic membrane formation 5%, sterile vitretiis 10% and corneal thinning around the optic 10%. 11 eyes (55%) had prior diagnosis of glaucoma and 1 eye had corneal dehiscence secondary to trauma. 5 patients required a second surgical intervention to address complications: 2 amniotic membrane grafts, 1 vitrectomy and cyclodestructive procedure for uncontrolled IOP, 1 antibiotic/steroid intravitreal inyections for sterile vitreiitis, and 1 KPRO re-suturing for dehiscence. Device retention throughout the follow-up period was 100%.

Conclusions: First short-term study reporting Lucia KPRO outcomes. All patients improved VA and 100% retention rate. Results are comparable with type I Boston KPRO with the undoubtable advantage of reaching a higher quantity of patients because of its costs, especially in our population.

CONTROL ID: 3711915

SUBMITTER (NAME ONLY): Jordan Bell

TITLE: Validation of SD-OCT Derived Automated Machine Learning-Augmented Volumetric Fluid Quantification

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Bell, J. Whitney, H. Cetin, N. Cardwell, T.K. Le, S.K. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|J.M. Bell, Lerner College of Medicine, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accurate detection and quantification of fluid in SD-OCT images can assist with treatment decisions and prognostic evaluations in exudative retinal diseases. This study evaluated the performance of a fully-automated, machine learning (ML)-augmented OCT segmentation platform in quantifying macular fluid volumes in wet age-related macular degeneration (AMD) and diabetic macular edema (DME).

Methods: A total of 120 volumetric SD-OCT scans (60 wet AMD and 60 DME) from both Cirrus and Spectralis devices (1:1 ratio for both diseases) were included. A previously developed ML segmentation platform provided fully-automated segmentation of intraretinal fluid (IRF) and subretinal fluid (SRF). Two trained readers (R1 & R2) independently reviewed and corrected the baseline ML segmentation (semi-automated segmentation) while two senior readers collaborated to create a gold-standard (GS) semi-automated segmentation for reference. Central macular fluid volumes (i.e., central 2 mm foveal-centered zone) from ML, R1, and R2 were compared to GS volumes. Agreement was assessed using intraclass correlation coefficients (ICC) and Bland-Altman plots.

Results: In DME, ML achieved an ICC of 0.976 for IRF compared to reader values of 0.992 for both R1 and R2. In wet AMD, ML achieved an ICC of 0.895 for IRF compared to values of 0.971 and 0.970 for R1 and R2, respectively. For SRF volumes in wet AMD, ML achieved an ICC of 0.988 compared to reader values of 0.997 for both R1 and R2. Bland-Altman plots with mean volume differences and 95% limits of agreement are shown in figure 1.

Conclusions: The ML automated platform demonstrated excellent agreement with the gold-standard achieving performance comparable to the readers in IRF quantification in DME and SRF quantification in wet AMD validating its potential use in future disease characterization. The fully-automated segmentation platform allows for quick and accurate measurements of fluid volumes in SD-OCT scans of DME and wet AMD from two widely used OCT devices.

CONTROL ID: 3711916

SUBMITTER (NAME ONLY): Lucas Janeschitz-Kriegl

TITLE: Worldwide multicenter ocular imaging study (EyeConic) to identify patients eligible for cone-based optogenetics therapy

SESSION TITLE: Retinal Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Janeschitz-Kriegl, G. Calzetti, B. György, H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|L. Janeschitz-Kriegl, B. György, H.P. Scholl, Department of Ophthalmology, Universitatsspital Basel, Basel, BS, SWITZERLAND|G. Calzetti, Department of Ophthalmology, University Hospital Parma, Parma, ITALY|Z. Nagy, V. Szabo, Department of Ophthalmology, Semmelweis Egyetem, Budapest, Budapest, HUNGARY|J.A. Sahel, B. Rosin, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|M. Michaelides, M. Georgiou, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|K. Stingl, University Eye Hospital, Center for Ophthalmology, University of Tuebingen, Tuebingen, GERMANY|J. Zi-Bing, Beijing Institute of Ophthalmology, Beijing, Beijing, CHINA|E. Banin, Department of Ophthalmology, Hebrew University of Jerusalem, Jerusalem, Jerusalem, ISRAEL|B.L. Lam, P. Rosa, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J.L. Duncan, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We are developing a cone-based optogenetic vision restoration approach that aims to resensitize dormant cone photoreceptors in patients with low vision. In a subset of patients with inherited retinal dystrophies (IRDs), cones lose their light-sensitive outer segments but remain alive in a dormant stage. This creates an opportunity to resensitize them through targeted optogenetic tools. However, the true proportion of low vision patients harboring dormant, non-functional cones, is currently unknown. The worldwide multicenter retrospective study (EyeConic) aims to estimate the proportion of low vision patients with remaining cone cell bodies for the first time.

Methods: We have enrolled 276 eyes of 174 patients with generalized IRDs (study patients) from 7 centers, 15 patients with Stargardt macular dystrophy (STGD) and 15 healthy individuals. Eyes of patients with generalized IRDs and best-corrected visual acuity (BCVA) less than 20/400 were included. We developed a machine-learning-based algorithm to segment total retina in study participants based on macular optical coherence tomography (OCT) scans and calculated the volume of the central foveolar hypercylinder (350 µm diameter). This value is used as a proxy for the remaining cone mass and is expressed as normalized z scores of healthy outer nuclear layer volume.

Results: Foveal hypercylinder volumes of study patients followed a normal distribution and were highly variable ranging from complete atrophy to normal volumes. We found that 31% and 39% of study patients had foveolar hypercylinder volumes within 2 and 3 z scores (indicating 2 and 3 standard deviations from the normal), respectively. There was no correlation between foveolar hypercylinder volume of study patients and BCVA (r=0.04). The highest z-scores were observed in patients harboring biallelic mutations in CEP78, IFT140, CEP290, CRX and TULP1.

Conclusions: A substantial number of patients with generalized IRDs show a foveal hypercylinder volume that is within the range of a healthy cone volume. Such structure-function dissociation provides an opportunity for cone-based optogenetic vision restoration. A significant fraction of patients with low vision are thus candidates for cone-

based optogenetics therapy.

CONTROL ID: 3711917

SUBMITTER (NAME ONLY): Brian Lee

TITLE: Long-term effects of panretinal photocoagulation (PRP) vs intravitreal ranibizumab (IVR) on OCT-measured choroidal thickness, and retinal thickness and integrity

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.L. Josic, Jaeb Center for Health Research, Tampa, Florida, UNITED STATES|B. Lee, M.G. nittala, A.N. Karamat, F. Corvi, G. Singh, S.R. Sadda, M.S. Ip, Doheny Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate PRP vs IVR effects on choroidal thickness, and retinal thickness and integrity in eyes with proliferative diabetic retinopathy (PDR) requiring treatment.

Methods: This is a post hoc analysis of Protocol S participants randomized to PRP or IVR to treat PDR. The data source is the DRCR Retina Network, but the content and conclusions presented herein are solely the responsibility of the authors and have not been reviewed or approved by the network. Zeiss Cirrus map and Heidelberg Spectralis raster line OCT images at baseline, 2 and 5 years were evaluated. Choroidal thickness (between Bruch's membrane and the choroid-sclera junction) was manually measured at a single point using calipers in the devices' software at the fovea, and the superior and inferior outer ring center points. The images were evaluated for foveal central subfield (FCS) thickness, total retinal volume (TRV), disorganization of retinal inner layers (DRIL), external limiting membrane (ELM) integrity and ellipsoid zone (EZ) integrity.

Results: Choroidal thickness was graded in 159 of 177 PRP and 143 of 166 IVR eyes at baseline, 135 PRP and 119 IVR at 2 years, and 67 PRP and 62 IVR at 5 years. Mean change from baseline choroidal thickness at the fovea (-3 vs -6 and -8 vs -11 um), superiorly (-4 vs -6 and -15 vs -11 um), and inferiorly (-13 vs -14 and -27 vs -19 um) for PRP vs IVR at 2 and 5 years were not significantly different between treatments (all p>.05). The decreases compared to baseline were significant in both groups superiorly at 5 years (both p=.03), and inferiorly at 2 and 5 years (both p = .003 at 2 years; p<.001 for PRP and p=.003 for IVR at 5 years). Mean change from baseline FCS (8 vs -39 and -4 vs -39 μm) and TRV (-.03 vs -.79 and -.39 vs -1.07 mm3) for PRP vs IVR at 2 and 5 years were significantly different between treatments (p<.001 and p=.04 for FCS; p<.001 and p=.01 for TRV). Rates of DRIL (52% vs 39% and 58% vs 56%), ELM (58% vs 64% and 52% vs 46%), and EZ (53% vs 58% and 52% vs 49%) for PRP vs IVR at 2 and 5 years were similar.

Conclusions: In this randomized cohort, we did not find differences in choroidal thickness changes between PRP and IVR from baseline to 2 or 5 years. Both study arms had significant decreases in superior and inferior choroidal thickness at 5 years. IVR had greater FCS thickness and TRV reductions than PRP.

CONTROL ID: 3711918
SUBMITTER (NAME ONLY): Axel Kattar
TITLE: Encapsulation of epalrestat in niosomes
SESSION TITLE: Drug delivery
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Kattar, C. Alvarez-Lorenzo, A. Concheiro, Pharmaceutical Technology, Universidade de Santiago de Compostela, Santiago de Compostela, Galicia, SPAIN|
Commercial Relationships Disclosure: Axel Kattar: Commercial Relationship: Code N (No Commercial Relationship) | Carmen Alvarez-Lorenzo: Commercial Relationship: Code N (No Commercial Relationship) | Angel Concheiro: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The increase of diabetic patients leads to an increase of ocular diabetic diseases as diabetic retinopathy. This occurs when the retina degrades due to osmotic pressure and oxidative stress caused by the polyol pathway, activated in high glycemic conditions. This pathway is blocked by epalrestat, a drug already used in the context of diabetic neuropathy, but the epalrestat molecule is very hydrophobic. It is hypothesized that the formation of a niosomal complex as a carrier for epalrestat will display physicochemical properties and have an encapsulation efficiency that points towards the molecule being able to reach the posterior segment of the eye, which is the therapeutic site.

Methods: Formulation of the niosomes was done using different molar ratios of surfactant:helper lipid:charge modifier/Tween80:cholesterol:DOTMA. The reagents were dissolved in ethanol, dried with a rotavapor, then hydrated with MilliQ water. The flask was ultrasonicated, and then sonified with a probe sonifier. Dialysis was performed to remove unencapsulated drug. The niosomes formed were characterized in terms of size, polydispersity, surface charge and morphology using DLS, zeta-potential and TEM. Quantification of epalrestat in subsequent experiments was done by HPLC. The encapsulation efficiency and release profile were measured by dialysis, in 14 000 kDa cellulose tubing.

Results: Loaded niosomes were formed with the physicochemical properties and encapsulation efficiency as described below. The morphology was spherical.

T60CD0ef: 84 nm, 0.541 PDI, -23.34 ± 5.341 mV zeta-potential, 99.86 ± 0.24% encapsulation efficiency.

T60CD5ef: 69 nm, 0.460 PDI, +17.27 ± 10.29 mV zeta-potential, 99.75 ± 0.35% encapsulation efficiency.

T60CD10ef: 75nm, 0.279 PDI, +40.39 ± 10.29 mV zeta-potential, 99.64 ± 0.13% encapsulation efficiency.

The release profile showed better release with lower DOTMA percentage, up until 10 days, when the niosomes with 5% DOTMA released more than niosomes without charge modifier. (Image 1)

Conclusions: The hypothesis was confirmed and niosomal particles were prepared using a robust protocol. To confirm the viability of such particles tissue permeation experiments will be performed. The effect of surface charge on the ability of epalrestat to escape the niosomes should be explored in more detail.

CONTROL ID: 3711919

SUBMITTER (NAME ONLY): Lori Sullivan

TITLE: A rare variant in ZBED1, a gene from the pseudoautosomal region of the X and Y chromosomes, is a likely cause of dominant retinitis pigmentosa in several large families.

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.S. Sullivan, E. Cadena, S. Bowne, S.P. Daiger, Human Genetics Center, The University of Texas Health Science Center at Houston School of Public Health, Houston, Texas, UNITED STATES|R. Ayyagari, Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|D.G. Birch, K. Jones, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|K. Branham, Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan, UNITED STATES|D. Koboldt, The Institute for Genomic Medicine, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|K.M. Bujakowska, E. Galdikaite-Braziene, E. Place, E.A. Pierce, Massachusetts Eye and Ear Infirmary, Harvard University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Lori Sullivan: Commercial Relationship(s);Code C (Consultant/Contractor):Applied Genetic Technologies Corporation, 4D Molecular Therapeutics | Elizabeth Cadena: Commercial Relationship: Code N (No Commercial Relationship) | Sara Bowne: Commercial Relationship: Code N (No Commercial Relationship) | Kinga Bujakowska: Commercial Relationship: Code N (No Commercial Relationship) | Egle Galdikaite-Braziene: Commercial Relationship: Code N (No Commercial Relationship) | Emily Place: Commercial Relationship: Code N (No Commercial Relationship) | Eric Pierce: Commercial Relationship: Code N (No Commercial Relationship) | Radha Ayyagari: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Koboldt: Commercial Relationship: Code N (No Commercial Relationship) | David Birch: Commercial Relationship: Code N (No Commercial Relationship) | Kaylie Jones: Commercial Relationship: Code N (No Commercial Relationship) | Kari Branham: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Daiger: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To identify the cause of autosomal dominant retinitis pigmentosa (adRP) in a cohort of families without mutations in known adRP genes and consequently to characterize a novel, dominant-acting mutation in ZBED1, a gene in the pseudoautosomal region 1 (PAR1) of the X and Y chromosomes.

Methods: Families from the University of Texas and the Ocular Genomics Institute (OGI) cohorts were screened using whole-exome NGS. Following identification of a novel ZBED1 variant in two families, UTAD076 and UTAD1013, a second cohort from the Ocular Genomics Institute (OGI) at Harvard was screened for the variant. Genealogies were established by interviews of family members; additional samples were collected and sequenced. Haplotypes segregating with the mutation were determined using STR and SNV polymorphisms and LOD scores were calculated in two large families from the University of Texas. Blood samples were obtained from an affected/unaffected sib pair and were used to create iPSCs. Whole genome sequencing was performed in both families to rule out additional, co-segregating pathogenic variants.

Results: A novel variant in ZBED1 (c.754T>A, p.Tyr252Asn) was the only segregating, potentially pathogenic, coding variant identified by exome sequencing in two large adRP families. We subsequently identified an additional two patients in the OGI cohort carrying the same heterozygous variant. One patient overlapped with the UTAD1013 family but the other could not be definitively placed in either family. Using the variant as a marker, LOD scores of 3.6 (UTAD1013) and 4.5 (UTAD076) were calculated. The location of the gene in the pseudoautosomal region confounds haplotype analysis, but genealogies suggest an Irish founder.

Conclusions: A novel, dominant-acting gene mutation in a pseudoautosomal gene is the likely cause of retinitis pigmentosa in two large Irish-American families. The phenotype in both families is similar, with relatively late onset in females and earlier onset in males. Genes in the PAR1 escape X-inactivation but still have lower total expression in females. The ZBED1 gene is thought to function as a transcription factor and is ubiquitously expressed. In retina, ZBED1 is expressed in both rod and cone photoreceptors with even higher expression in bipolar and amacrine cells.

CONTROL ID: 3711922

SUBMITTER (NAME ONLY): Babak Safa

TITLE: The Effects of Negative Periocular Pressure on Biomechanics of the Optic Nerve Head (ONH) and Cornea: A Computational Modeling Study

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Safa, C.R. Ethier, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|J. Berdahl, Equinox Ophthalmic, Inc, North Dakota, UNITED STATES|

Commercial Relationships Disclosure: Babak Safa: Commercial Relationship: Code N (No Commercial Relationship) | John Berdahl: Commercial Relationship(s);Code O (Owner):Equinox Ophthalmic, Inc;Code P (Patent):Equinox Ophthalmic, Inc | C Ethier: Commercial Relationship(s);Code C (Consultant/Contractor):Equinox Ophthalmic, Inc

ABSTRACT BODY:

Purpose: Decreasing intraocular pressure (IOP) is the only approved treatment for glaucoma. The Multi-Pressure Dial system (MPD; Equinox Ophthalmic) is a medical device consisting of goggles connected to a programmable vacuum pump that delivers a negative periocular pressure (NPP; Swan+, 2020 Transl Vis Sci Technol). Experimental data show that IOP is reduced during goggle wear, yet the effects on ONH and corneal biomechanics are unknown. Our objective was to evaluate the effect of NPP on ONH and corneal biomechanics by using finite element (FE) modeling.

Methods: An axisymmetric FE model of the eye was developed based on the existing model from Sigal et al. (IOVS 2005; Fig. 1A). At baseline, we imposed the following pressures: IOP = 15.8 mmHg, NPP = 0, retrolaminar pressure (RLTP) = 8 mmHg. During goggle wear (NPP = -7.9 mmHg), we imposed a lowered IOP = 11.5 mmHg (based on experimental data Swan+, 2020), and unchanged RLTP. IOP was uniformly applied on the interior surface of the corneoscleral shell; NPP was applied uniformly from the apex to ~2.5 mm posterior to the limbus and then decreased linearly to zero at the edge of the peripapillary sclera (ppSC). Tissues were modelled as incompressible neo-Hookean materials, with the ppSc including circumferential collagen fibers. To validate our model, we compared the computed compliance of the corneoscleral shell to literature data.

Results: Our model had a predicted ocular compliance of 3.1 μL/mmHg, in agreement with literature values of 1.4-3.9 μL/mmHg (McEwen&Helen, 1965 Ophthalmologica). Application of NPP increased the average first principal Lagrangian strain (Ξ, a measure of tissue stretching) at the corneal apex by 27.3%, and at the limbus by 23.4%. Importantly, NPP decreased ONH strain by 54.5% (Fig. 1B).

Conclusions: Imposing a negative periocular pressure is predicted to increase corneal and limbal strains but reduce the mechanical strain in the ONH. ONH strain reduction occurs because the effects of IOP lowering seem to outweigh the effects of globe expansion, which in theory should be beneficial for glaucoma patients.

CONTROL ID: 3711924

SUBMITTER (NAME ONLY): Kanza Aziz

TITLE: In-State versus Out-of-State Ophthalmic Telemedicine Utilization during the COVID-19 Pandemic

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Aziz, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|J.Y. Moon, A. Devgan, A. Lorch, D.S. Friedman, J.B. Miller, G.W. Armstrong, Ophthalmology, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Kanza Aziz: Commercial Relationship: Code N (No Commercial Relationship) | Jade Moon: Commercial Relationship: Code N (No Commercial Relationship) | Anjali Devgan: Commercial Relationship: Code N (No Commercial Relationship) | Alice Lorch: Commercial Relationship(s);Code C (Consultant/Contractor):Regeneron | David Friedman: Commercial Relationship(s);Code F (Financial Support):Zeiss Meditec;Code F (Financial Support):Genentech Inc;Code C (Consultant/Contractor):W.L. Gore and Associates;Code C (Consultant/Contractor):Bausch and Lomb;Code C (Consultant/Contractor):Thea Pharmaceuticals;Code C (Consultant/Contractor):Life Biosciences | John Miller: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon;Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Carl Zeiss;Code C (Consultant/Contractor):Sunovion;Code C (Consultant/Contractor):Genentech | Grayson Armstrong: Commercial Relationship(s);Code O (Owner):Ocular Technologies Inc;Code C (Consultant/Contractor):McKinsey & Company ;Code C (Consultant/Contractor):Xenon-VR;Code C (Consultant/Contractor):Ophthalytics;Code C (Consultant/Contractor):Kriya Therapeutics;Code S (non-remunerative):American Medical Association

ABSTRACT BODY:

Purpose:

During the COVID-19 pandemic, regulatory changes in the United States allowed physicians to practice telemedicine across state lines. Data on the use of interstate ophthalmic telemedicine during the pandemic are limited. We aimed to evaluate the geographic characteristics and interstate utilization of telemedical care as compared to in-person care at a tertiary eye care center during the pandemic.

Methods:

In this single-center, retrospective, cross-sectional study at Massachusetts Eye and Ear (MEE) from January 1 to December 31, 2020, clinical encounters were reviewed to extract patient and visit characteristics. In-person versus telemedical visit types were identified based on institutional categories and billing codes. Residential zip codes were used to estimate geographic characteristics of patients including distance from MEE and in-state versus out-of-state status. Pearson chi-squared tests were used to compare telemedical and in-person care groups.

Results:

A total of 1911 telemedical patients (2262 encounters) and 65763 in-person patients (147211 encounters) were included. The median (interquartile range; IQR) age of telemedicine patients was 61 (43-72) years, 62% of which were female. The median (IQR) age of in-person patients was 63 (49-72) years, 58% of which were female. Telemedicine patients included 14.7% (n=281) out-of-state patients, as compared to 12.0% (n=7876) out-of-state in-person patients ($p<0.001$). Regarding distance, 42.5% of telemedicine patients and 47.5% of in-person patients lived <10 miles ($p<0.001$), 41.9% and 41.3% lived 10-50 miles ($p=0.611$), 8.8% and 7.0% lived 51-100 miles ($p=0.002$), 3.9% and 2.5% lived 101-250 miles ($p<0.001$), and 3.0% and 1.8% lived >250 miles ($p<0.001$) away from MEE, respectively.

Conclusions:

A significantly greater proportion of telemedical care, as compared to in-person care, was provided to out-of-state patients at a large eye care center during the pandemic. Moreover, a significantly greater proportion of telemedical care was utilized by patients living further away from the eye center. Proposals to revert to pre-pandemic policies requiring in-state telemedicine could set back forward progress made during the pandemic, including negative impacts on access to care and continuity of care for established patients. Expanded telemedicine licensure and scope could help advance the efficiency and deployment gains seen during the pandemic.

CONTROL ID: 3711925

SUBMITTER (NAME ONLY): Michael Schwartz

TITLE: A novel Visual Navigation Challenge Mobility Course to assess functional vision in patients with CEP290-associated Leber Congenital Amaurosis (LCA10)

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schwartz, A. Girach, ProQR Therapeutics NV, Leiden, NETHERLANDS|B.L. Lam, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|K. Stingl, Eberhard Karls Universitat Tubingen Mathematisch-Naturwissenschaftliche Fakultat, Tubingen, Baden-Württemberg, GERMANY|C.J. Boon, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|C.C. Hoyng, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|L.I. van den Born, Hogeschool Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS|H. Dollfus, Universite de Strasbourg, Strasbourg, Grand Est, FRANCE|I.S. Audo, INSERM, Paris, Île-de-France, FRANCE|C. Sundstrom, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: LCA10 is a severe, inherited retinal disease (IRD) resulting in early blindness, with no treatments available. Current validated endpoints to assess vision may show some limitations in individuals with profound visual impairment. To address this need, new endpoints such as a mobility course (MC), are being assessed. The aim of the study was to assess the novel Ora MC as an efficacy endpoint to evaluate functional vision in individuals with a phenotype representative of LCA10.

Methods: This was a prospective non interventional study testing the Ora MC composite score (MCCS) based on participants' ability to navigate through two sets of MCs of decreasing difficulty: The Low-Contrast Visual Navigation Challenge® (LCVNC) and the High-Contrast Visual Navigation Challenge® (HCVNC), each with eight increasing luminance levels (range 0.35 to 500 lux). Participants navigated both MCs 3 times during each of 3 separate visits assessing each individual eye and both eyes. The MCCS was derived from the most difficult course a participant was able to navigate, and the scores were provided by a masked central reading center (a more difficult MC passed meant a better MCCS). Visual assessments including best corrected visual acuity (BCVA), were performed at the same visit in all participants.

Results: 48 participants (mean age 27.3, range 6-57, 23 females) with LCA10 (n=39) or other LCA or IRD with phenotype representative of LCA10 (n=9) underwent complete assessments and were included in the final analysis. Mean BCVA was 1.14, range 0 to 4. The test-retest reliability of the MCCS, as assessed by the intra-class coefficient, was high (ICC 0.97, 95% CI: 0.93 – 0.99), demonstrating the high reproducibility of this tool as an endpoint for clinical trials. There was a high negative correlation between the MCCS and BCVA, as demonstrated by a Pearson correlation coefficient of -0.75 (95% CI: -0.84, -0.56) for the better eye, -0.75 (95% CI: -0.85, -0.59) for the worse eye and -0.73 (95% CI: -0.83, -0.54) for both eyes.

Conclusions: Ora MCCS was highly reproducible and had a strong negative correlation with BCVA, showing that a decrease in logMAR values was correlated with an increased MCCS and vice-versa. This novel tool can be used as an efficacy endpoint to assess functional vision in clinical trials in individuals with a phenotype representative of LCA10.

CONTROL ID: 3711927

SUBMITTER (NAME ONLY): Emily Sechrest

TITLE: Characterization of cone structure and function in a mouse model for blue cone monochromacy patients with a C203R mutation

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Sechrest, W. Deng, Ophthalmology and Visual Sciences, West Virginia University, Morgantown, West Virginia, UNITED STATES|X. Ma, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|W. Deng, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|

Commercial Relationships Disclosure: Emily Sechrest: Commercial Relationship: Code N (No Commercial Relationship) | Xiajie Ma: Commercial Relationship: Code N (No Commercial Relationship) | Wen-Tao Deng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Blue cone monochromacy (BCM) is a severe vision disorder caused by severely reduced or absence of function in L- and M-cones. Presence of a C203R missense mutation in a single OPN1LW/MW hybrid gene or in multiple OPN1LW/MW genes is the most common cause of BCM. In this study, we seek to dissect the disease mechanism of a C203R mutation through characterizing the structure and function of cone photoreceptors in a knock-in mouse model carrying a corresponding mutation.

Methods: Opn1mw^{C198R} (OPN1L/MW^{C203R} equivalent) knock-in mice were generated using CRISPR/Cas9 genome editing technology and were bred into an Opn1sw$^{-/-}$ background to eliminate interference from endogenous S-opsin. Retinal whole mounts of Opn1mw^{C198R} mice were labeled with peanut agglutinin (PNA) to assess cone viability at 1, 3, 6, and 9 months of age. Quantitative RT-PCR was used to evaluate mRNA levels of Opn1mw^{C198R} at P5, P15, and P30. In tandem, cross-sections from Opn1mw^{C198R} retinas were examined by immunohistochemistry (IHC) using antibodies against L/M-opsin, PDE6α', and GNAT2. Finally, M-cone mediated retinal function was analyzed at P30 by electroretinography (ERG). Age-matched C57BL/6J mice were used as controls.

Results: Ventral and dorsal regions of Opn1mw^{C198R} retina display significantly reduced cone viability by 3 months and cones continue to degenerate with age. By 6 months, Opn1mw^{C198R} cones in the dorsal and ventral regions of the retina are reduced by 60.0% and 43.9%, respectively, compared to those at 1 month of age ($P < 0.05$). While qRT-PCR shows that Opn1mw mRNA is comparable between WT and mutant at P5, mutant mRNA levels drop 44% by P30 ($P<0.05$). Surprisingly, OPN1MW^{C198R} protein was not detected by IHC at P5, P15, or P30. GNAT2 staining appeared brighter at P5 compared to WT, but was mislocalized to the cone cell body and inner segment. Furthermore, GNAT2 staining dissipates by P15 and P30, suggesting cone outer segments are absent or significantly shortened in Opn1mw^{C198R} mice. Moreover, ERG demonstrates that Opn1mw^{C198R} eyes have no M-cone mediated retinal function at P30.

Conclusions: Cone structure and function in Opn1mw^{C198R} mice appear to phenocopy BCM patients with C203R mutations, demonstrating that this model can be adequately used for characterization of the disease mechanism behind a C203R mutation and in development of therapy.

CONTROL ID: 3711928

SUBMITTER (NAME ONLY): Luka Lapajne

TITLE: TRPV4 involvement in inflammation and tissue damage in corneal epithelium

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lapajne, M. Lakk, D. Krizaj, Department of Ophthalmology and Visual Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|L. Lapajne, M. Hawlina, Eye Hospital, University Medical Centre Ljubljana, Ljubljana, SLOVENIA|

Commercial Relationships Disclosure: Luka Lapajne: Commercial Relationship: Code N (No Commercial Relationship) | Monika Lakk: Commercial Relationship: Code N (No Commercial Relationship) | Marko Hawlina: Commercial Relationship: Code N (No Commercial Relationship) | David Krizaj: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal epithelium is subjected to biological, chemical, and physical stressors from the environment, many of which are known activators or modulators of TRPV4 channel. TRPV4 signaling has been linked to nociception and release of inflammatory molecules which might contribute to tissue damage but the role of TRPV4 in corneal epithelial pathophysiology is not understood well. Here, we investigate the involvement of TRPV4 in ultraviolet light-mediated injury, G-protein receptor-dependent signaling and cytokine release.

Methods: Corneas from C57BL/6 and TRPV4$^{-/-}$ mice were enzymatically detached from the stroma and used for in situ experiments. They were subjected to assorted agonists and antagonists as well as to UVB radiation, mimicking UVB damage inflicted to the cornea. For cytokine release assay, epithelial cells were dissociated, subjected to the UV stimuli or the selective TRPV4 agonist GSK1016790A and supernatants were evaluated by chemiluminescence reaction. Optical imaging assessed the properties of Ca^{2+} homeostasis under different experimental conditions.

Results: UVB radiation reversibly elevated $[Ca^{2+}]_i$ in mouse corneal epithelial cells, an effect that was slightly attenuated by TRPV4 ablation or inhibition. UV-evoked increases in $[Ca^{2+}]_i$ principally reflected release of calcium from the pool stored intracellularly within the endoplasmic reticulum. Pharmacological activation of the protease-activated receptor-2 (PAR-2) sensitized TRPV4 for agonist activation. UVB radiation and TRPV4 activation evoked stimulus-specific release of proinflammatory cytokines and inflammatory substances, effects that were antagonized by pharmacological blockade of TRPV4.

Conclusions: Our data suggest that corneal epithelial cells respond to harmful UVB radiation with parallel and additive activation of TRPV4 channels and release of calcium from intracellular stores. It is possible that substances residing in tears contribute to PAR-2-mediated TRPV4 regulation in corneal epithelial cells under pathological conditions. In addition, the corneal milieu is likely to be influenced by TRPV4- and/or UVB-dependent release of cytokines and inflammatory substances, with potential effects on transparency, would healing and nociception. Overall, this study identifies TRPV4 as a potential target of ocular surface inflammation and tissue damage.

CONTROL ID: 3711930

SUBMITTER (NAME ONLY): Miltiadis Tsilimbaris

TITLE: Comparison of macular atrophy progression in nAMD eyes and non-nAMD fellow eyes

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Tsilimbaris, S. Blazaki, E. Blavakis, A. Stavrakakis, Ophthalmological Clinic, University Hospital of Heraklion, Panepistemio Kretes Iatrike Schole, Heraklion, Crete, GREECE|G. Bontzos, G. Smoustopoulos, M. Kabanarou, T. Xirou, Ophthalmology, Korgialenio-Benakio General Hospital, Athens, GREECE|E. Dimitriou, E. Chatziralli, 2nd Department of Ophthalmology, Attikon Hospital, Ethniko kai Kapodistriako Panepistemio Athenon Iatrike Schole, Athens, Attica, GREECE|G. Chlouverakis, Department of Biostatistics, Panepistemio Kretes Iatrike Schole, Heraklion, Crete, GREECE|

ABSTRACT BODY:

Purpose: To evaluate the evolution of MA in patients with neovascular AMD (nAMD) treated with anti-vascular endothelial growth factor (anti-VEGF) agents, compared with their fellow eyes exhibiting dry AMD.

Methods: This retrospective study included 124 patients from three centers with neovascular AMD treated with anti-VEGF intravitreal injections in one eye and dry AMD in the fellow eye. We analyzed data from two groups of patients: 91 patients without MA at baseline in order to study time to first MA development in treated and fellow eyes, and 47 patients with a total of 4 years of follow-up in order to study time course and growth rate of MA in treated and fellow eyes. MA was evaluated using NIR images, while all available OCT images were used to confirm that the atrophic area fulfilled the criteria proposed by the Classification of Atrophy Meetings (CAM) group.

Results: MA first detection in treated eyes (TE) increased in significant levels from year 2 to year 6 in comparison with fellow eyes (FE). Presence of MA during the 4-year of follow up was recorded in 50% of TE and in 18% of FE. Repeated measures ANOVA revealed significant time, eye and time eye interaction effects. MA in treated eyes exhibited a steady significant increase up to year 6, whereas in the FE the significant increase is halted at year 4. The annual increase in the TE was 0.275 mm/y [0.10 mm/y for year 1, 0.23 mm/y for year 2, 0.37 mm/y for year 3, and 0.49 mm/y for year 4]. The respective annual increase for the FE was 0.110 mm/y; [0.09 mm/y for year 1, 0.14 mm/y for year 2, 0.11 mm/y for year 3 and 0.10 mm/y for year 4].

Conclusions: In this study we documented a significant difference in MA incidence and progression in eyes with nAMD treated with anti-VEGF agents compared to fellow eyes exhibiting dry AMD. Treated nAMD eyes tend to develop more often MA; moreover, MA progresses in a faster rate in these eyes compared to fellow dry AMD eyes.

CONTROL ID: 3711931

SUBMITTER (NAME ONLY): Anshuman Singh

TITLE: Role of Fibroblast growth factor 21 in hyperglycemia-associated retinopathy

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Singh, Y. Tomita, E. Bull, W. Allen, Z. Fu, L.E. Smith, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|S. Talukdar, Merck Research Laboratories Boston, Boston, Massachusetts, UNITED STATES|A. Hellström, Goteborgs universitet Institutionen for neurovetenskap och fysiologi, Goteborg, SWEDEN|

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ABSTRACT BODY:

Purpose: Early postnatal hyperglycemia (phase I retinopathy of prematurity (ROP)) is a significant risk factor for proliferative retinopathy of prematurity (phase II ROP), a leading cause of blindness in children. Abnormalities of glucose and lipid metabolism affect development and progression of retinal vascular growth (Phase I ROP). Fibroblast growth factor 21 (FGF21), a metabolic regulator of lipid and glucose usage, may improve Phase I ROP metabolism. FGF21 effects on lipid metabolism in retina were addressed in hyperglycemia-associated retinopathy (HAR) in C57BL/6J mice with delayed vascular growth, a model of phase I ROP.

Methods: Hyperglycemia-associated retinopathy (phase I ROP) was induced with intraperitoneal (i.p.) injection of streptozotocin administered from postnatal day (P) 1 to 9. At P10, retinal vessel growth was evaluated in FGF21 vs. vehicle-treated mice (i.p. from P7 to P9) (n=14-16). Co-treatment of HAR mice with FGF21 plus intravitreal siRNA Acaca (de novo fatty acid synthesis enzyme) (n=8-9), or i.p. etomoxir (CPT1A inhibitor) (n=8-9) vs. controls was also conducted. Lipid and proteins were assessed in retina of FGF21- vs. vehicle-treated mice (n=5 each). A transcriptome array was assessed in retina of FGF21- vs vehicle-treated mice (Affymetrix (Santa Clara, CA).

Results: In the phase I ROP mouse model with hyperglycemia-induced delayed retinal vascular development, FGF21 administration increased retinal vascularization (with increased deep vascular coverage ($P=0.0007$)). Inhibition of CPT1A greatly decreased ($P<0.01$) FGF21 protection of hyperglycemia-induced delayed retinal vascular growth. Mild changes were observed in phospholipids between FGF21- vs. vehicle-treated HAR mice. Proteomics analysis showed an increased level of antioxidant enzymes in HAR mice treated with FGF21. Transcriptome analysis suggests the involvement of transforming growth factor beta (TGF-β), Integrin and p53 signaling pathways with FGF21 prevention of hyperglycemia associated phase I ROP.

Conclusions: FGF21 promotes normal vascularization during hyperglycemia associated vessel growth delay in phase I ROP, associated with regulation of retinal lipid metabolism. Preventing vessel growth cessation in phase I ROP prevents phase II ROP.

CONTROL ID: 3711932

SUBMITTER (NAME ONLY): Annika Balraj

TITLE: Selective oligodendrocyte ablation alters optic nerve conduction and retinal ganglion cell layer density

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Balraj, R. Miller, Anatomy, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Annika Balraj: Commercial Relationship: Code N (No Commercial Relationship) | Robert Miller: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Successful signal propagation along axons is important for the survival of neural networks. In the optic nerve, oligodendrocytes produce the myelin sheath which provides insulation for retinal ganglion cell (RGC) axons. Optic neuritis (the demyelination and inflammation of the optic nerve) results in visual deficits and thinning of retinal nerve fiber and ganglion cell layers. Demyelination can induce functional deficits; however, the impact of demyelination on upstream network connectivity is not well understood. This study evaluates the effect of local optic nerve demyelination on axonal conduction and retinal connectivity.

Methods: In the MBP-iCP9 transgenic mouse, the myelin basic protein (MBP) promoter drives expression of an inducible caspase 9 (iCP9) sequence and a DsRed reporter. Eye injection of the chemical inducer of dimerization (CID) results in the selective apoptosis of MBP+ oligodendrocytes and subsequent demyelination. MBP-iCP9 mice were injected at P14 with either CID or vehicle for three consecutive days. After two weeks, immunohistochemistry was used to quantify oligodendrocyte loss and retinal layer density and identify RGC subtypes. Optic nerve compound action potentials (CAPs) were measured using extracellular recordings. Axon populations were identified as axons with similar conduction speeds. Within-nerve controls used tetrodotoxin to isolate and remove the stimulus artifact during analysis.

Results: CID-treated nerves had a significant loss of DsRed+ CC1+ oligodendrocytes ($n>5$, $p=0.04$). Average CAP area (a measure of functional axons) was reduced in CID-treated mice ($n<5$). CID-treated nerves retained the fastest-conducting axon populations but lost slow-conducting axons. Average ganglion cell layer density was significantly lower in CID-treated retinas ($n>4$, $p=0.03$), while inner and outer nuclear layer density were unaffected ($p>0.05$). Analysis of the ganglion cell layer found a significant loss of RBPMS+ ($p=0.03$) and Brn3a+ ($p=0.02$) cells in CID-treated retinas and a non-significant reduction of ChAT+ amacrine cells ($p=0.06$).

Conclusions: These results suggest that partial demyelination of the optic nerve can induce a significant conduction deficit and disrupt retinal connectivity through the loss of alpha-RGCs. This provides valuable insight into the regulatory role of myelination in the maintenance of upstream neural networks.

CONTROL ID: 3711933

SUBMITTER (NAME ONLY): Omar Shareef

TITLE: Validating the Usefulness of a Random Forests Classifier as an Alternative to SCORTEN in Predicting Mortality for Individuals with SJS/TEN

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Shareef, J.T. Kwan, S. Lau, H.N. Saeed, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|O. Shareef, Harvard College, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The SCORTEN scoring system was developed in 2000 as a severity-of-illness score for Stevens Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) and has since been used for predicting mortality for individuals with SJS/TEN. Survivors of SJS/TEN can develop blinding ocular surface disease, and a higher SCORTEN score can be a predictor of worse ocular complications. However, certain predictors required for the SCORTEN scale can be difficult to assess accurately, particularly total body surface area (TBSA) involvement. An alternative method that uses laboratory results can serve as a simpler way to predict mortality and severity of ocular disease and can be easily implemented into existing electronic health record (EHR) systems.

Methods: A random forests classifier (RFC) model to predict mortality was trained on laboratory data from 156 patients. The test dataset included 36 patients. Missing values in the training data were handled using k-nearest neighbors imputation and categorical data were split using one-hot encoding. Cross-validation was used to determine that an RFC was the most robust in predictive power. Several RFCs were trained on the data using the full set of predictors (n=97). The top five predictors were found from the most accurate model and a final RFC was trained using only this subset of predictors on an upsampled dataset.

Results: On the testing data, the accuracy and the area under the receiver operating characteristic curve (AUROC) for the SCORTEN model were 0.833 and 0.688, respectively. For the RFC model, the accuracy and AUROC were 0.889 and 0.842, respectively. The differences in both accuracy ($p = 0.32$) and AUROC ($p = 0.488$) were not statistically significant. The five predictors used to train this algorithm in order of importance were: Bilirubin (total), PT, RBC, WBC, and NRBC.

Conclusions: The similar performance between the SCORTEN and RFC models indicates that the RFC model can be utilized as an alternative to SCORTEN and may be more easily calculated. The RFC model does not share any of the predictors used by the SCORTEN model including TBSA involvement, which can be notoriously difficult to calculate. This alternative model can be easily implemented in existing EHR systems by simply pulling from lab tests and may serve as a useful tool in predicting ocular morbidity.

CONTROL ID: 3711936

SUBMITTER (NAME ONLY): Syed Zaidi

TITLE: Retinal ganglion cell specific deletion of arginase-2 preserves visual function after optic nerve crush

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.A. Zaidi, Z. Xu, T. Lemtalsi, R.B. Caldwell, Vascular Biology Center, Augusta University, Augusta, Georgia, UNITED STATES|S.A. Zaidi, Z. Xu, T. Lemtalsi, R. Caldwell, R.B. Caldwell, James and Jean Culver Vision Discovery Institute, Augusta University, Augusta, Georgia, UNITED STATES|A. Fouda, Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, UNITED STATES|R. Caldwell, Pharmacology and Toxicology, Augusta University, Augusta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Syed Zaidi: Commercial Relationship: Code N (No Commercial Relationship) | zhimin Xu: Commercial Relationship: Code N (No Commercial Relationship) | Tahira Lemtalsi: Commercial Relationship: Code N (No Commercial Relationship) | Abdelrahman Fouda: Commercial Relationship: Code N (No Commercial Relationship) | R. William Caldwell: Commercial Relationship: Code N (No Commercial Relationship) | Ruth Caldwell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have shown that global deletion of the mitochondrial arginase isoform arginase 2 (A2) limits retinal ganglion cell (RGC) death in various models of retinal neurodegeneration. Herein, we examined the mechanisms of this neuroprotection and show that neuron-specific deletion of A2 is sufficient to prevent optic nerve crush (ONC)-induced neurodegeneration.

Methods: Wild type (WT), $A2^{-/-}$ global knockout (A2KO), and Calbindin2-specific ($Calb2\text{-}cre^{+}$ $A2^{f/f}$) KO mice on the C57BL/6J background were subjected to ONC. Stress-activated calcium signaling and mitochondrial dysfunction were assessed by changes in activation status of p38 MAPK, calcium/calmodulin-dependent protein kinase II (CAMKII), and the mitochondrial fission marker dynamin-related protein 1 (Drp1), respectively at 6 and 24 h post ONC. Survival of RGC was quantified with NeuN immunostaining of retina flat-mounts at day 14 and TUNEL labeling of retina sections at day 5 post ONC. Pattern ERGs, spectral domain-optical coherence tomography (SD-OCT), and OptoMotry responses (OMR) were measured at day 21 post ONC. Axonal sprouting was determined by anterograde transport of Cholera Toxin B (CTB).

Results: Early increases in A2 expression, phosphorylation of stress-activated proteins p38 and CAMKII, and the mitochondrial fission protein DRP-1 at ^{616}Ser, (n=4-7; $p<0.05$) were detected in WT retinas, and this was abrogated by deletion of A2. IHC showed increased A2 and phospho p38 immunoreactivities within RGC of WT mice. Further, the number of NeuN positive RGC was significantly reduced in $A2^{f/f}$ mice post ONC (39% of sham controls). This RGC loss was reduced in Calb2 A2 KO mice ($p=0.07$; n=5). Calb2 A2 KO mice also showed fewer TUNEL positive RGC neurons compared to $A2^{f/f}$ ($p=0.02$; n=4). PERG and visual acuity were decreased in $A2^{f/f}$ mice and improved in Calb2 A2 KO mice (n=4-7; $p<0.05$). OCT and CTB analysis of retinal thickness and axonal sprouting, respectively, showed improved responses in the Calb2 A2 KO mice after ONC as compared with the $A2^{f/f}$ (n=4-7; $p<0.05$).

Conclusions: Our data indicate that A2 is neurotoxic in RGCs after injury, and deletion of A2 in Calb2 expressing RGCs limits ONC-induced retinal neurodegeneration and thereby improves visual function. Based on our preliminary findings, stress-activated Calcium signaling via CaMKII/p38 and mitochondrial dysfunction are probable mechanisms involved in A2-mediated RGC cell death.

CONTROL ID: 3711938

SUBMITTER (NAME ONLY): Marilyn Marquez

TITLE: Near-infrared imaging of the optic disc obtained during macular OCT as a screening tool for glaucomatous optic neuropathy.

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Marquez, L.J. Haddock, J.A. Fortun, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Marilyn Marquez: Commercial Relationship: Code N (No Commercial Relationship) | Luis Haddock: Commercial Relationship: Code N (No Commercial Relationship) | Jorge Fortun: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the utility of near-infrared imaging (NIR) of the optic disc, obtained as part of routine optical coherence tomography (OCT) of the macula during evaluation in a retina clinic, as a screening to tool to identify eyes with possible glaucomatous optic neuropathy.

Methods: A series of consecutive patients seen in the retina clinic underwent optic nerve-head OCT with RNFL analysis, in addition to routine macular OCT. The NIR images of the optic disc acquired during the macular OCT were evaluated by two different masked graders (both retina specialists) to determine whether the images were suspicious for glaucomatous optic neuropathy and would warrant further evaluation or referral to a glaucoma specialist. An unmasked glaucoma specialist then evaluated the optic disc RNFL analysis of each eye to determine whether there was a glaucomatous optic nerve damage or a suspicion of glaucomatous optic neuropathy

Results: Of 216 eyes (108 patients) who had imaging in the retina clinic, 15 % of those eyes were unable to be assessed by the IR image. From the eyes that were able to be assessed, 14% of the images had a discrepancy between the results of the unmasked grader and the masked graders, and 86% of images had a coincidence between the masked and unmasked grader.

Conclusions: NIR obtained as part of routine OCT of the macula during evaluation in a retina clinic, can serve as a useful screening tool to identify eyes with possible glaucomatous optic neuropathy.

CONTROL ID: 3711939

SUBMITTER (NAME ONLY): Chenna Sugali

TITLE: SMAD4-β-catenin nuclear complex inhibits TGFβ2-induced pathological changes in the trabecular meshwork.

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.K. Sugali, N. Rayana, J. Dai, W. Mao, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Chenna Sugali: Commercial Relationship: Code N (No Commercial Relationship) | Naga pradeep Rayana: Commercial Relationship: Code N (No Commercial Relationship) | Jiannong Dai: Commercial Relationship: Code N (No Commercial Relationship) | Weiming Mao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is the primary risk factor of primary open-angle glaucoma (POAG). TGFβ2 and Wnt signaling pathways are associated with POAG. Excessive TGFβ2 induces pathological changes in the trabecular meshwork (TM). Also, TGFβ2 elevates IOP in mouse and human eyes. In contrast, inhibition of Wnt signaling contributes to POAG. We reported that an elevation of sFRP1 and Dkk1, the Wnt inhibitors, in the POAG TM and/or aqueous humor. Overexpression of either sFRP1 or Dkk1 elevates IOP in mouse and/or human eyes. There is also a cross-inhibition between TGFβ2 and Wnt signaling pathways. Here, we determine the mechanism of this cross-inhibition and if the activation of the canonical Wnt signaling inhibits TGFβ2 signaling and its related pathological changes in the TM.

Methods: HTM cells were treated with or without TGFβ2, Wnt3a, and/or GSK3β inhibitors. Cytosolic and nuclear fractions were co-immunoprecipitated (Co-IP). Some of the nuclear fractions were used for electrophoretic mobility shift assay (EMSA). Förster resonance energy transfer and fluorescent live imaging (FRET-FLIM) was used to study protein-protein interaction using pHTM cells transduced with Ad5-SMAD4-GFP with or without Ad5-β-catenin-mCherry. Human donor eyes were used for perfusion cultures.

Results: We treated pHTM cells with TGFβ2 with or without Wnt3a/GSK3β inhibitors and found that in single or in combination, they promoted SMAD4 and β-catenin nuclear translocation. Co-immunoprecipitation assays showed that Smad4 was associated with β-catenin in pHTM cells. FRET-FLIM assays showed a shortening of the fluorescent lifetime of Smad4-GFP in the presence of β-catenin-mCherry in pHTM cells, indicating a direct binding between the two proteins. EMSA assays showed that the Smad4-β-catenin complex did not interfere with DNA binding. Western immunoblotting and immunofluorescence studies showed that the activation of Wnt signaling using Wnt3a or GSK3β inhibitors inhibited TGFβ2-induced TGFβ signaling as well as ECM proteins in pHTM cells. Topical application of CHIR inhibited TGFβ2-induced ocular hypertension in perfusion culture human eyes.

Conclusions: The activation of either signaling pathways promotes the nuclear translocation of both β-catenin and Smad4 and they form a complex in the nucleus via direct binding. Also, the activation of Wnt signaling inhibits TGFβ2-induced pathological changes in the TM.

CONTROL ID: 3711941

SUBMITTER (NAME ONLY): Manuel Sedano Montoya

TITLE: Cumulative dissipated energy during phacoemulsification: a comparison between surgeons with different training experience

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Sedano Montoya, E. Fernandez Muñoz, A. Medina Andrade, R. Gonzalez Salinas, Segmento Anterior, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|N. Ramos-Betancourt, Coordinadora de investigación clínica, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|N. Ramos-Betancourt, Córnea y cirugía refractiva, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|G. Ordóñez Ranz, Córnea y cirugía refractiva, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: Cumulative Dissipated Energy (CDE) is the amount of ultrasound energy used during phacoemulsification (PHACO). We carried out a cross-sectional study to prove that the higher the number of PHACOS, the less CDE was used by the ophthalmic surgeon.

Methods: We conducted a cross-sectional, data was obtained from a training residency program from August 2020 to November 2020. Patients undergoing surgery with LOCS III nuclear opalescence, grades 2 and 3 (NO2 and NO3), were consecutively included. Exclusion criteria included patients with one functional eye, zonular weakness, congenital and traumatic cataracts. Three groups were created: group 1, less than 80 surgeries performed, group 2 between 80 and 160 surgeries, and group 3 more than 160 surgeries.All patients were operated on the same PHACO platform, the Alcon Centurion system. Statistical analysis was performed with SPSS (Ver. 22. IBM Corp. Armonk, USA). The CDE between the groups was compared with the Bonferroni post hoc analysis.

Results: One hundred and thirty-five eyes of 135 patients were included, 45 eyes per group, 54.1% (n = 73) were right eyes. The median CDE was 11.5, 10.4, and 7.4 in groups 1, 2, and 3, respectively. The interquartile range, the minimum and maximum values of CDE per group are shown in Table 1. When comparing the three groups, it was found that the surgeon with more experience used less CDE ($p = 0.014$). (Figure 1) When comparing groups, there were no significant differences between group 1 vs. group 2 ($p=0.61$) or when comparing group 2 vs. group 3 ($p = 0.2$). Nevertheless, there was a significant difference when comparing group 1 with group 3 ($p=0.006$).

Conclusions: The final amount of CDE may be helpful to measure surgical progress in trainee residents, as it may be directly related to the efficacy of the surgical technique and could be a reliable parameter to predict future outcomes of postoperative inflammation. More than 160 surgeries are required to achieve CDE reduction compared to more experienced surgeons. Most training centers consider this parameter and provide residents with the number of surgeries required to achieve a benchmark for the PHACO learning curve. The CDE is an important variable to evaluate the progress of an ophthalmologist in training, so it would be a valuable parameter to evaluate the progress that he has during his surgical training.

CONTROL ID: 3711942

SUBMITTER (NAME ONLY): Kevin Zhang

TITLE: Intercellular material transfer following retinal ganglion cell transplantation

SESSION TITLE: Gene and Cell Therapy for Retinal Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.Y. Zhang, E.A. Aguzzi, A. Nagalingam, C. Keuthan, X. Chang, D.J. Zack, T.V. Johnson, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Notable transplantation studies demonstrated intercellular transfer of cytoplasmic material including fluorescent labels between donor and host photoreceptors (PR). This phenomenon, material transfer (MT), confounds cell tracking analyses. We examined whether MT is PR-specific by conducting rigorous assessments for MT after retinal ganglion cell (RGC) transplantation.

Methods: Organotypic retinal explants from B6 ACTb-EGFP mice were cocultured with tdTomato$^+$ (tdT$^+$) human embryonic stem cell derived RGCs (hRGCs) on the vitreous surface for 1 week. We assessed MT by inspecting for tdT labeling and human-specific lineage markers colocalized to host GFP$^+$ retinal cells. We compared the incidence of MT in retinas with intact and enzymatically disrupted internal limiting membrane (ILM) using Pronase. We also assessed MT rates following in vivo intravitreal hRGC transplantation.

Results: 3D reconstructions of tiled confocal retinal flatmounts revealed tdT$^+$GFP$^+$ cells in the host inner nuclear layer (INL) with distinct Müller glial (MG) morphology. Immunostaining confirmed GFAP and tdT colocalization throughout the soma and radial processes in 85% of the atypical cells sampled (n=20). tdT$^+$GFP$^+$ cells were in contact with tdT$^+$ hRGCs and retained a nuclear heterochromatin structure that was specific to mouse INL cells and distinct from hRGCs. We assessed recipient retinas for human-specific donor-derived nuclear antigen (HuNu) and mitochondrial antigen (HuMito), and found 92.7% of tdT$^+$GFP$^+$ MG were HuNu$^+$ (n=68) and 72.7% were HuMito$^+$ (n=11). Fluorescence activated cell sorting of tdT$^+$GFP$^+$ cells demonstrated greater expression of human-specific RGC transcripts, including BRN3B, RBPMS, and TUBB3, compared to tdT$^-$GFP$^+$ cells. We found 6.7% of BSS (n=15) and 35.5% of Pronase-treated (n=31) retinal explants exhibited tdT$^+$GFP$^+$ cells (p=0.037). Following in vivo transplantation, we observed tdT$^+$GFP$^+$ MG within the host INL exclusively in retinas with ILM disruption (0% in BSS-treated, n=32; 9.7% in Pronase-treated, n=31; p=0.071).

Conclusions: We identified that hRGC xenografts into mouse retinas transferred donor-derived material, including cytoplasmic, nuclear, and organelle proteins and mRNA. The primary recipient cell type is MG, and MT is dependent on ILM disruption. We demonstrated that retinal MT is not unique to PRs and must be emphasized when interpreting hRGC transplantation results.

CONTROL ID: 3711944
SUBMITTER (NAME ONLY): Ella Gehrke
TITLE: Cone rescue with low titer subretinal gene replacement in the Rs1 mouse
SESSION TITLE: Photoreceptors and disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Gehrke, J. Thompson, Y. Hsu, A. Mahoney, A.V. Drack, Department of Ophthalmology and Visual Sciences, Institute for Vision Research, The University of Iowa, Iowa City, Iowa, UNITED STATES|
Commercial Relationships Disclosure: Ella Gehrke: Commercial Relationship: Code N (No Commercial Relationship) | Jacob Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Ying Hsu: Commercial Relationship: Code N (No Commercial Relationship) | Angela Mahoney: Commercial Relationship: Code N (No Commercial Relationship) | Arlene Drack: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the efficacy of retinoschisin (Rs1) gene rescue in a mouse model (Rs1-KO) of juvenile X-linked retinoschisis (JXLR) through administration of low dose AAV2/4 – RS1 with an Ef1α promoter.
Methods: An AAV2/4-RS1-Ef1α promoter vector was delivered by subretinal 2 ul injections of 2E9/ml in Rs1-KO mice (N=7). Injections occurred on postnatal days 18-26. Full field Electroretinogram (ERG), Optical coherence tomography (OCT), and a visually guided swim assay (VGSA), were chosen as endpoints to assess efficacy. ERGs were completed at one, two-, and five-months post injection (PI). OCTs were completed at 3 weeks, 2 months, and 4 months PI using a masked retinoschisis severity score. Mice underwent a VGSA performed in light and dark conditions to assess functional vision at six months of age. Experimental eyes were compared to untreated fellow eyes as well as eyes of untreated Rs1-KO mice (N=13).
Results: ERG: At one-month PI, treated eyes showed significantly higher b-wave amplitudes ($p=0.0187$) than untreated eyes on light adapted 3.0 cone ERG, which persisted until 5 months PI ($p=0.0029$). For the 5 Hz flicker, a pure cone response, treated eyes showed higher amplitude at one and two months than untreated eyes ($p=0.0014$ and $p=0.0002$), but lost significance by 5 months PI. Dark adapted rod amplitudes were not significantly different between treated and untreated eyes at any time point; however, the b/a ratio of the standard combined response was significantly higher in treated eyes than untreated eyes at 1- and 2-months PI ($p=0.0092$, $p=0.0063$). OCT: Treated Rs1-KO eyes had less severe retinoschisis at 3 weeks and 2 months PI ($p=0.022$, $p<0.0001$) compared to untreated eyes, but significance was lost at 5 months PI. VGSA: at five months after treatment, treated mice had a significantly faster time to platform than untreated mice under light adapted (cone) conditions ($p=0.0024$) but not in dark adapted (rod) conditions ($p=0.755$).
Conclusions: Subretinal gene therapy delivering 2E9/ml AAV2/4-RS1-EF1α promoter resulted in improved cone ERG, reduced retinoschisis observed by OCT, and functional vision measured by VGSA, but no effect in rod ERG or rod mediated visual function. Patients with JXLR lose central cone function over time; our study suggests cones may be rescued separately from rods using subretinal gene therapy.

CONTROL ID: 3711945

SUBMITTER (NAME ONLY): Robert Hufnagel

TITLE: A gene-centric nomenclature and classification system for inherited retinal disorders

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.B. Hufnagel, National Eye Institute, Bethesda, Maryland, UNITED STATES|J. Goldstein, W. Hankey, K. Lee, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|P.I. Sergouniotis, The University of Manchester Faculty of Biology Medicine and Health, Manchester, Manchester, UNITED KINGDOM|G. Arno, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The Clinical Genome Resource (ClinGen) has established a Retina Gene Curation Expert Panel (GCEP) to evaluate the clinical validity of more than 200 genes implicated in inherited retinal disorders (IRD). The ClinGen clinical validity framework requires (1) defining the disease entity for gene curation, and (2) finding an appropriate standardized term (Mondo identifier). IRD nomenclature includes a variety of pathologic, morphologic, gene locus, and eponymous terms. These challenges are exacerbated by variable expressivity, locus heterogeneity, and allelic disorders among IRDs. Thus, the Retina GCEP has sought to revise the Mondo ontology and terminology for IRDs to capture the phenotypic spectrum in a standardized nomenclature.

Methods: The Retina GCEP is using the ClinGen gene-disease clinical validity framework (version 8.0) to evaluate the clinical validity of over 200 IRD-implicated genes. The group follows ClinGen guidance (clinicalgenome.org). Subsequently, a Mondo ID is used to label the disease entity (mondo.monarchinitiative.org).

Results: To date, the ClinGen Retina GCEP has finalized the clinical validity of over 30 gene-IRD relationships. For many genes currently under review, identification and systematic merging or splitting of multiple overlapping retinal phenotypes into unified disease terms is required to capture the phenotypic spectrum for causal genotypes and observed inheritance patterns. To name these disease entities, the Retina GCEP proposes a gene-first nomenclature system with the gene first followed by a disease descriptor (e.g. TSPAN12-related vitreoretinopathy). For genes associated with IRD with multiple inheritance patterns, or distinct genotype-phenotype relationships, the disease entities can be split (e.g. RPE65-related dominant retinopathy, and RPE65-related recessive retinopathy). Disease terms are periodically updated in the Mondo disease ontology database. Historical names of the lumped disease entities are included as synonyms for improved search purposes.

Conclusions: Due to the significant locus heterogeneity and the broad, overlapping spectrum of clinical presentations linked to many genes implicated in IRD, a unified nomenclature system is optimal for capturing the spectrum of IRD gene:disease relationships. We anticipate that these efforts will clarify clinical indications for gene augmentation and similar gene-based therapies as they emerge.

CONTROL ID: 3711946

SUBMITTER (NAME ONLY): Leila Eppenberger

TITLE: First Clinic Experiences of Transscleral Optical Imaging to Study Retinal Pigment Epithelium and Photoreceptor Cells

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.S. Eppenberger, S. Mohanna, O. Pfaeffli, M.A. Thiel, M.K. Schmid, Eye Clinic, Luzerner Kantonsspital, Luzern, Luzern, SWITZERLAND|L.S. Eppenberger, Health Sciences and Technology, Eidgenossische Technische Hochschule Zurich, Zurich, Zürich, SWITZERLAND|L.M. Bachmann, M.A. Thiel, M.K. Schmid, Faculty of Medicine, Universitat Zurich, Zurich, ZH, SWITZERLAND|L.M. Bachmann, Medignition AG, Zurich, Zurich, SWITZERLAND|

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ABSTRACT BODY:

Purpose: In vivo cellular imaging with transscleral optical imaging (TOI) (Cellularis®, prototype Version 2.0) allows studying retinal structure and function. We currently conduct a prospective clinical validation study assessing retinal pigment epithelium (RPE) and photoreceptor (PR) cells with the TOI in subjects referred to the tertiary care eye clinic. Here we report on our observations of using this new technology.

Methods: Adult subjects (>18 years of age) with visual acuity <0.3logMAR and absence of pregnancy and epilepsy qualify for inclusion. Participants undergo full clinical examination including Optical Coherence Tomography (OCT) scanning followed by TOI imaging. If possible both eyes of a participant are imaged in 5 macular zones of 2mm x 2mm (Figure 1). Both RPE and PR layer images are acquired.

Results: By the end of 2021, we analyzed 206 eyes of 116 of participants (54% women; 46% men; mean age 59±18 years). RPE and PR images were acquired in at least 1 zone for all 206 eyes (Figure 2). For 75% (n=154) of the eyes, RPE and PR images were acquired in all 5 zones. Alignment and acquisition time was on average 1 minute per zone. When comparing the group of eyes where all 5 zones could be imaged to those where this was not the case, the proportion of participants with e.g. myopia ≤-2D or cataract was significantly higher (64% vs. 90%, $p<0.001$). However, especially with cataract, it depended on the type; image acquisition was easily feasible with myopic cataract for example. In subjects with darker colored eyes examination was easier than in those with light eyes (51% vs. 29%, $p=0.008$). Other factors, including insufficiently dilated pupils, higher degrees of astigmatism jeopardized complete image acquisition and quality. No adverse events were observed, only two subjects complained about slight discomfort during the examination.

Conclusions: Due to its good handling properties and quality of the presentation of RPE and PR cells, TOI has the potential to become a significant tool in the evaluation of retinal diseases.

CONTROL ID: 3711947

SUBMITTER (NAME ONLY): Sunit Dutta

TITLE: An Effective and Versatile Zebrafish Model Using CRISPR Interference to Investigate Gene Functions Regulating Eye Development.

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dutta, G. Shi, B.P. Brooks, OGVFB, National Eye Institute, Bethesda, Maryland, UNITED STATES|G. Shi, L. Dong, Genetic Engineering, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Sunit Dutta: Commercial Relationship: Code N (No Commercial Relationship) | Guangpu Shi: Commercial Relationship: Code N (No Commercial Relationship) | Lijin Dong: Commercial Relationship: Code N (No Commercial Relationship) | Brian Brooks: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Antisense Morpholinos ologoneucleotides (MO) has been routinely used in genetic functional studies in zebrafish embryos. However, it's well known that MO activate p53-associated genes to induce apoptosis. This study was aimed to generate transgenic zebrafish models using CRISPR Interference (CRISPR-i) to interrogate gene functions during eye development.

Methods: Zebrafish-codon-optimized dCas9 was generated from a zebrafish-codon-optimized Cas9 through mutagenesis of D10A and H840A in HNH and RuvC domains respectively. The dCas9 was linked to a synthesized zebrafish- codon-optimized Krab domain and reporter. Using Gateway cloning technology, we generated the following three TolII plasmid systems, Ubi-dCas9-Krab-GFP, Ubi-GFP, and Hsp70-dCas9-Krab-GFP and coinjected these recombinant plasmids and transposes mRNA into zebrafish embryos and screened for founder fish by reporter expression and genotyping. We studied the eye phenotypes in these transgenic embryos expressing dcas9-Krab-GFP by injecting chemically modified-sgRNAs specific for the genes important for eye morphogenesis.

Results: With repeated experiments, we verified that there was no detectable cutting activity of both HNH and RuvC domains of zebrafish-codon-optimized dCas9, and further verified the repressive activity of the synthesized zebrafish-codon-optimized dCas9-Krab system in cultured HEK293 cells using sgRNAs targeting Pax6 and Otx2. rx3 sgRNA injected transgenic embryos expressing dcas9-Krab-GFP developed microphthalmia and/or coloboma at as early as 24 hour post fertilization (hpf) compared to uninjected control transgenic embryos. The microphthalmia and colobama persisted through the observations after 48 hours post fertilization (hpf).

Conclusions: Our experiments indicated that CRISPR-i can be used as a transgenic system in zebrafish and this system is of great value in the investigation of gene functions in ocular morphorgenesis, given the ease of use, versatility for the targets and the short period of time (~24 hrs) needed for induction of ocular phenotypes. This system will allow more rapid ascertainment of phenotypes associated with gene expression screens and paves the way for generating a model system to knock down gene expression in a spatiotemporally regulatable manner.

CONTROL ID: 3711948

SUBMITTER (NAME ONLY): Claudia Thieme

TITLE: Assessment of filtering bleb morphology after Gel-Stent-Implantation (XEN^{TM}) with anterior segement OCT

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Thieme, R. Burk, Ophthalmology, Universitat Bielefeld, Bielefeld, Nordrhein-Westfalen, GERMANY|

Commercial Relationships Disclosure: Claudia Thieme: Commercial Relationship: Code N (No Commercial Relationship) | Reinhard Burk: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The success of a filtrating operation depends on the maintenance of the filtering bleb (FB). The purpose of this study is to illustrate the persistance of the FB after Gel-Stent-Implantation (XEN^{TM}) in different types of open angle glaucoma by anterior segment OCT (asOCT).

Methods: 78 eyes of 78 patients (32 women, 46 men, age 69 ± 12 years, perimetry: median MD 7,9dB, Min. -11,7dB Max. 20,9dB; median sLV: 6dB, Min. 1,7dB Max.11,5dB) have been examined by asOCT (HRA OCT II Spectralis), at timepoints T1: 97 days (± 53 days) and T2: 699 days (± 242 days): primary open-angle glaucoma (pOAG) (n=50), secondary open-angle glaucoma (sOAG) with pseudoexfoliation (PEX) (n=20) and sOAG with pigmentdispersion (n=8). The FB was morphologically classified as microcystic (m), mixed (mx) and absent (a). The correlation between FB, intraocular pressure (IOP) and medical therapy (TX) was analyzed with IBM SPSS Statistics Version 21.

Results: At T1 bleb classification was: n=61 (m), n=8 (g), n=9 (a), at T2 the bleb classification was: n=31 (m), n=24 (g), n=23 (a). Surgery resulted in a significant IOP reduction from preoperative (21 ± 8 mmHg) to postoperative IOP at T1 (15 ± 5 mmHg) and T2 (14 ± 4 mmHg) ($p<0.01$), the difference between IOP-T1 and IOP-T2 is not significant ($p>0.01$). The number of medications was preoperative 3 (±1) and significantly reduced compared to TX-T1: 0,5 (±1) and T2: 1 (±1) ($p<0.01$). The need for bleb revision was as follows: no revision n=45, 1 revision n=23 (pOAG n=15, sOAG with PEX n=6, sOAG with pigmentdispersion n=2), two revisions n=7 (pOAG n=6, sOAG with PEX n=1) and 4 revisions n=3 (pOAG n=2, sOAG with PEX, n=1). The revisions included a second stent implantation (n=20), third stent implantation (n=1), needling (n=11), viscocanalostomy (n=1), cyclophotocoagulation (n=2), cyclocryocoagulation (n=1), tenoncyst exzision (n=1).

Conclusions: FB classification reveals a microcystic structure. FB-revisions are not dependent on glaucoma classification. Further studies with longer follow-up time and larger patient cohorts are necessary to evaluate the effect of glaucoma type and FB persistance.

CONTROL ID: 3711949

SUBMITTER (NAME ONLY): Fu-Yen Chang

TITLE: Effects of Carotenoid Supplementation on the Lipid Profile of the Serum of a Transgenic Mouse

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Chang, A. Ranganathan, B. Li, P.S. Bernstein, Department of Ophthalmology and Visual Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Fu-Yen Chang: Commercial Relationship: Code N (No Commercial Relationship) | Arunkumar Ranganathan: Commercial Relationship: Code N (No Commercial Relationship) | Binxing Li: Commercial Relationship: Code N (No Commercial Relationship) | Paul Bernstein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Lipoproteins deliver lipids and macular carotenoids to the eye. The lipid contents of lipoproteins in the circulation are associated with the risk of the progression of age-related macular degeneration (AMD). We investigated the effects of carotenoid supplementation on the serum lipid profile of a transgenic mouse line that takes up carotenoids.

Methods: BCO2 knockout mice with expression of RPE-Cre ($Bco2^{-/-}$ Transgenic) were kept on vitamin A deficient chow for one month to increase the bioavailability of carotenoids. They were then divided into four groups (3 mice/group) and fed with zeaxanthin, lutein, β-carotene, and the control chow (no carotenoid) for one month. The contents of HDL, LDL, and triglycerides (TG) in the serum of these mice were analyzed using a CURO L7 Lipid Analyzer. Briefly, 35 µL of serum from each animal was loaded on a lipid profile test strip for a 3-minute measurement. T-test was used for statistical analysis, and $p<0.05$ was considered statistically significant.

Results: Supplementation with zeaxanthin, lutein, and β-carotene significantly increased the HDL cholesterol in the serum of the $Bco2^{-/-}$ transgenic mice, and the contents of HDL cholesterol in the mice fed with carotenoids were increased about twofold relative to the control. Zeaxanthin significantly reduced ~ 50% of the serum TG, whereas no significant alteration was detected from lutein or β-carotene supplementation. Interestingly, the contents of LDL cholesterol were not detectable because they were below the detection limit.

Conclusions: Our data show that supplementation with zeaxanthin, lutein, and β-carotene can increase serum HDL cholesterol in mice, while zeaxanthin may reduce serum TG. Our finding demonstrates that carotenoid supplementation might alter the lipid profile in the circulation, offering new insights into AMD prevention using carotenoids.

CONTROL ID: 3711950

SUBMITTER (NAME ONLY): David Portney

TITLE: The impact of Laser Assisted in Situ Keratomileusis (LASIK) on Major League Baseball batting performance

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.S. Portney, C. Hood, Ophthalmology & Visual Sciences, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|D.A. Portney, Orthopedic Surgery, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|R. Parikh, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many professional athletes undergo laser assisted in situ keratomileusis (LASIK) during their careers, though no study has shown improved performance following the surgery. The objective of this study is to determine how LASIK impacts Major League Baseball (MLB) player batting performance.

Methods: MLB players who underwent LASIK during their careers and had greater than 130 at-bats in the seasons before and after surgery were identified via public records. Seasonal changes in individual player batting performance were measured with batting average (BA), slugging percentage (SLG), on-base plus slugging percentage (OPS), and wins above replacement (WAR). Batting statistics were compared across seasons for individual players.

Results: Thirty-seven unique MLB players with mid-career LASIK were identified. In the season prior to LASIK, players experienced an average change of -0.014 in BA ($p = 0.024$), -0.023 in SLG ($p = 0.073$), -0.032 in OPS ($p = 0.089$), and -1.09 in WAR ($p = 0.004$). In the season after LASIK, players experienced an average change of 0.009 in BA ($p = 0.109$), 0.017 in SLG ($p = 0.221$), 0.018 in OPS ($p = 0.343$), and 0.68 in WAR ($p = 0.088$). 66% percent of players experienced an increase in BA, 63% an increase in SLG, 55% an increase in OPS, and 55% an increase in WAR. Each of the batting statistics followed a similar trend across the four seasons, where the mean drops in the season prior to LASIK before rebounding back towards the baseline for the two seasons after LASIK.

Conclusions: Our study demonstrated that professional baseball players have a significant drop in batting performance in the season prior to LASIK, likely motivating some to seek surgery. While performance improved on average after LASIK, the change was not statistically significant, and may be related to regression to the mean. Ophthalmologists and athletes should have an individualized informed discussion regarding the potential risks and benefits of refractive surgery and have tempered expectations for the magnitude of performance benefit from the procedure.

CONTROL ID: 3711951

SUBMITTER (NAME ONLY): Xiao Lin

TITLE: Effects of ROS mediated hyaluronan fragmentation on corneal epithelial wound healing

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Lin, I. Moreno, L. Nguyen, H. Cementwala, T.F. Gesteira, V.J. Coulson-Thomas, University of Houston College of Optometry, Houston, Texas, UNITED STATES|T.F. Gesteira, Optimvia, LLC, Texas, UNITED STATES|

Commercial Relationships Disclosure: Xiao Lin: Commercial Relationship: Code N (No Commercial Relationship) | Isabel Moreno: Commercial Relationship: Code N (No Commercial Relationship) | Lawrence Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Huzefa Cementwala: Commercial Relationship: Code N (No Commercial Relationship) | Tarsis Gesteira: Commercial Relationship: Code N (No Commercial Relationship) | Vivien Coulson-Thomas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Hyaluronan (HA) is a key component of the corneal limbal extracellular matrix and is upregulated after injury, playing an important role in corneal wound healing. Excess reactive oxygen species (ROS) are toxic to cells and HA is susceptible to oxidation by ROS, yet the precise chemical structures of oxidized HA (oxHA) and their physiological properties remain unknown. The aim of this study was to characterize the molecular weight and structure of oxHA generated using different ROS, and to compare the effects of oxHA and unoxidized HA of different molecular weights on cellular responses of corneal epithelial cells that are related to wound healing.

Methods: High molecular weight HA (HMWHA - 2670kDa) was oxidized using increasing molar ratios of hydrogen peroxide (H_2O_2) and hypochlorous acid (HOCl). Thereafter, the oxHA was purified using chromatography by Sephadex PD 10 columns. The size of oxHA was characterized by agarose gel electrophoresis and gel filtration high-pressure liquid chromatography. The structure of the oxHA was characterized by ^{1}H and ^{13}C NMR at 500 MHz. Human corneal epithelial cells (HTCEs) were treated with oxHA, or size-matched unoxidized HA, and cell viability, proliferation, and migration assayed.

Results: Smaller HA fragments were generated with increasing molar ratios of both H_2O_2 and HOCl. Chlorinated HA was detected after treatment with HOCl, according to ^{1}H NMR spectra. HMWHA significantly promoted corneal epithelial cell viability when compared to LMWHA, ULMWHA and oxHA. LMWHA and oxHA promoted cell migration, while HMWHA and ULMWHA did not.

Conclusions: HA fragmentation by ROS alters its physiological activity on corneal epithelial cells.

CONTROL ID: 3711952

SUBMITTER (NAME ONLY): Jonathan Soucy

TITLE: Multipolar migration and the SDF1-CXCR4 axis direct human retinal ganglion cell integration in mice

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Soucy, M.H. Phay, P.Y. Baranov, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Soucy, M.H. Phay, P.Y. Baranov, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Jonathan Soucy: Commercial Relationship: Code N (No Commercial Relationship) | Monichan Phay: Commercial Relationship: Code N (No Commercial Relationship) | Petr Baranov: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma leads to the loss of retinal ganglion cells (RGCs). Cell transplantation has been proposed to restore RGCs; however, current attempts show limited donor RGC integration. We previously used stromal cell-derived factor-1 (SDF1) to direct mouse RGCs into the retina, but the migration mechanisms have not yet been studied.

Methods: To improve clinical relevance, human RGCs were differentiated from Brn3b-tdTomato hESC in organoid cultures. RGCs were isolated by magnetic microbeads against CD90.2 at day 38-46 of differentiation. We studied RGC migration kinetics and modes in response to SDF1 gradient in vitro and in vivo using transwell setup and subretinal transplantation, respectively. For loss-of-function studies, we have applied: 1) small-molecule inhibitor of CXCR4 receptor on RGCs – AMD3100; 2) somal translocation inhibitor – CK666; 3) multipolar migration inhibitor – roscovitine.

Results: Expression of CXCR4 on hESC-derived RGCs was confirmed by transcript- and proteomics, with ~83% of RGCs being CXCR4+. AMD3100, an SDF1 antagonist, treatment decreased the RGC recruitment in response to SDF1 from 42.2±10.5% to 12.7±1.8% (n=3; $p<0.01$) in vitro. Time-lapse studies in vitro show that inhibiting somal translocation decreases migration speed from 5.64±2.18 to 4.69±2.01μm/s (n=3, $p<0.01$), whereas inhibiting multipolar migration decreases speed to 3.20±1.52μm/s (n=3, $p<0.01$) in vitro – demonstrating hESC-RGCs migration via both modalities.

The short-term transplantation studies confirmed our previous observations that an SDF1 gradient significantly improves the migration and integration of human RGCs within three days after subretinal delivery. Blocking CXCR4 in donor RGCs also led to decrease in transplantation outcome: transplantation score (TS) of 3.3±0.3 (n=3, m=15) vs 1.3 (n=1, m=6).

Lastly, transplantation experiments with inhibitors suggest that multipolar migration is the major contributor to donor RGC migration in the retina, with donor RGCs migrating via multipolar migration having a TS of 3.2 (n=1, m=6) and RGCs migrating via somal translocation having a TS of 2.8 (n=1, m=5).

Conclusions: Establishing an SDF1 gradient across the host retina enhances donor hESC-RGCs integration primarily through multipolar migration, and SDF1 acts through the CXCR4 receptor – suggesting the possibility that RGCs selected for these features before transplantation will improve donor cell integration.

CONTROL ID: 3711953

SUBMITTER (NAME ONLY): Thomas Swain

TITLE: Associations of rod-mediated dark adaptation measures in older adults without AMD or with early or intermediate AMD, baseline results from the ALSTAR2 study

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. McGwin, Department of Epidemiology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|T.A. Swain, G. McGwin, M. Clark, C.A. Curcio, C. Owsley, Department of Ophthalmology and Visual Sciences, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Thomas Swain: Commercial Relationship: Code N (No Commercial Relationship) | Gerald McGwin: Commercial Relationship: Code N (No Commercial Relationship) | Mark Clark: Commercial Relationship: Code N (No Commercial Relationship) | Christine Curcio: Commercial Relationship(s);Code I (Personal Financial Interest):MacRegen;Code C (Consultant/Contractor):Genentech/ Hoffman LaRoche;Code C (Consultant/Contractor):Regeneron | Cynthia Owsley: Commercial Relationship(s);Code P (Patent):MacuLogix

ABSTRACT BODY:

Purpose: The slope of the second component of rod-mediated dark adaptation (RMDA), rod-intercept time (RIT), and, more recently, the area under the dark adaptation curve (AUC) are metrics used in characterizing RMDA. Associations among all 3 measures have yet to be examined by AMD status and severity in the same persons.

Methods: RMDA testing at 5° eccentricity was completed in the ALSTAR2 baseline visit using the AdaptDx (83% equivalent bleach). Testing terminated once RIT was calculated by the AdaptDx or stopped at 45 minutes in cases where sensitivity did not recover. The slope of the second component was obtained from a linear model fit for all data points > 2.5 log sensitivity. AUC was calculated using the trapezoidal rule for all sensitivities < 3 log units for the full test time, and with test data truncated at 20, 12, and 6 minutes. The AREDS 9-step classification was used to determine AMD status and severity. Spearman correlations were used to associate the measures.

Results: Among 481 participants (mean age 71.8 years, 60% female, 91% white), there were 239 normal, 139 early AMD, and 103 intermediate AMD eyes. Slope of the second component, RIT, and all AUC measures were significantly associated among participants. Slope of the second component was more strongly associated with RIT (r_s=0.65) than the AUC measures (r_s=0.44 or less) (Table). As AUC measures were based on increasingly shorter test times, correlations with RIT and slope decreased. Compared to early and intermediate AMD, RIT and AUC associations were lower among normal eyes. The slope and AUC measures were not associated among normal eyes. The strongest associations of RIT with slope and the full AUC measure were among those with intermediate AMD (r_s =0.75 and 0.94 respectively).

Conclusions: All RMDA measures are associated with each other when examined among all participants. As AUC decreases at shorter test times, it becomes less correlated with RIT. This suggests that reductions in test time, specifically < 12 minutes, for faster screening do not produce measures that are good substitutes for RIT. The lack of association between the slope and AUC among normal eyes suggests that AUC is insufficient in conveying RMDA results for older adults without AMD. Slope and AUC based on 12 minutes or more are acceptable surrogates of RIT among those with early and intermediate AMD.

CONTROL ID: 3711958

SUBMITTER (NAME ONLY): Bo Tian

TITLE: Transduction of self-complementary AAV in the Trabecular Meshwork and Anterior Chamber in mouse

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tian, S. sun, W. Su, A. Makhlouf, H. Lin, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|R. He, P.W. Tai, J. Xie, G. Gao, Horae Gene Therapy Center, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|S. sun, Tianjin Key Laboratory of Retinal Functions and Diseases, Tianjin International Joint Research and Development Centre of Ophthalmology and Vision Science, Eye Institute and School of Optometry, Tianjin Medical University Eye Hospital, Tianjin, CHINA|W. Su, Ophthalmology, Tianjin Medical University General Hospital, Tianjin, CHINA|

Commercial Relationships Disclosure: Bo Tian: Commercial Relationship: Code N (No Commercial Relationship) | shuo sun: Commercial Relationship: Code N (No Commercial Relationship) | Wenqi Su: Commercial Relationship: Code N (No Commercial Relationship) | Abed Makhlouf: Commercial Relationship: Code N (No Commercial Relationship) | Ran He: Commercial Relationship: Code N (No Commercial Relationship) | Phillip Tai: Commercial Relationship: Code N (No Commercial Relationship) | Jun Xie: Commercial Relationship: Code N (No Commercial Relationship) | Guangping Gao: Commercial Relationship: Code N (No Commercial Relationship) | Haijiang Lin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Adeno-Associated Virus (AAV)-based gene therapies have been developed for various anterior segment diseases involved cornea, trabecular meshwork and iris. Intracameral injection is the appropriate procedure to deliver AAV to transduce anterior segment. Self-complementary AAV (scAAV) can bypass the rate-limiting step of second-strand synthesis and has shown to mediate a rapid onset and higher level of transgene expression compared to the parent vector. However, the transduction profile of different scAAV serotypes following intracameral injection has not been established. This study aims to evaluate transduction of scAAV2, 3b, 6, 8 and 9 in anterior segment tissues.

Methods: EGFP gene was packaged in conventionally used AAV serotypes 2, 3b, 6, 8 and 9, with the chimeric CMV–chicken ß–actin (CBA) promoter. In 8-week old C57BL/6J mice, 1.0µl scAAV-CBA-EGFP solution for one serotype was injected into the anterior chamber of right eye for each mouse (n=6). The formulation buffer injected eyes serve as the negative control (n=6). Four weeks post injection, the intracameral injected eyes were enucleated and subjected to immunohistochemistry. The anterior segment including cornea, anterior chamber angle, ciliary body and iris was imaged and evaluated for the transduction efficiency and tropism using EGFP as a surrogate marker. EGFP-positive cells/structures in the anterior segment was analyzed for distribution and EGFP-signal was quantitated.

Results: The self-complementary AAVs resulted in the transduction of corneal endothelium, corneal keratocyte, trabecular meshwork and ciliary body but with varied distribution, transduction efficiency and cell specificity. The inflammatory cells infiltration was observed in different levels for serotypes studied.

Conclusions: Our results provides the dataset applicable to the development of AAV-based therapy, targeting the ocular diseases involved the anterior segment. In addition, this data generated from this study may also be applied to the appropriate AAV vector selection for the gene therapy for glaucoma and corneal diseases, which can be targeted by intracameral administration.

CONTROL ID: 3711960

SUBMITTER (NAME ONLY): Fabrice Manns

TITLE: Relation between lens equivalent index and lens gradient parameters and their age-dependence

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Manns, M. Ruggeri, J. Parel, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|F. Manns, A. Ho, M. Ruggeri, J. Parel, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Fabrice Manns: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Ho: Commercial Relationship: Code N (No Commercial Relationship) | Marco Ruggeri: Commercial Relationship: Code N (No Commercial Relationship) | Jean-Marie Parel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Eye models generally represent the lens as a homogenous thick lens with an equivalent index calculated to match the known lens power. Studies have found that the equivalent index decreases with age. In parallel, lens growth is associated with the progressive formation of a central plateau in the refractive index gradient profile. The purpose of this study is to determine the relation between lens gradient parameters and equivalent index and evaluate the impact of the plateau formation on lens optics.

Methods: A paraxial model of the lens with gradient was developed. The gradient is characterized by the axial variation of the index, n(z), and radius of curvature of isoindicial surfaces, R(z). n(z) was a power function with three parameters: surface and equatorial indices and power coefficient (p). The surface (1.371) and equatorial (1.418) indices were independent of age. The power coefficient was age-dependent. A linear variation was assumed for R(z) in the anterior and posterior lens. An expression of lens power in terms of gradient parameters was derived by integrating the incremental gradient power over the thickness of the lens. Comparison with the formula for the equivalent lens power produced a relation between gradient parameters and equivalent index. The model was used to predict the age-dependence of p corresponding to equivalent index data from three studies: 1.441-0.00039*Age (Dubbleman et al, Vis Res 2001), 1.4506-0.00035*Age (Atchison et al, J Vis, 2008) and 1.4483-0.0007*Age (Chang et al, Biom Opt Exp, 2018). The calculated value of p was compared with values obtained from MRI (Kasthurirangan et al, IOVS 2008) and OCT (De Castro et al, J Mod Opt 2011).

Results: Power coefficient (p) and equivalent index (neq) are related by p = (neq - 1.371) / (neq - 1.418). At age 20, p ranged from 2.8 to 4.1, consistent with MRI and OCT data (Figure 1). With all three datasets, the decrease in neq with age is correlated with an increase in p, consistent with the formation of a refractive index plateau.

Conclusions: The model produces results that are consistent with experimental data. The formation of a central refractive index plateau is associated with a decrease in lens equivalent index.

CONTROL ID: 3711961

SUBMITTER (NAME ONLY): VIJAY KALASKAR

TITLE: Evaluation of ampyrone (4-aminoantipyrine), an activator of the intra-melanosomal domain of human tyrosinase, as a potential therapeutic agent for oculocutaneous albinism type 1B

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.K. KALASKAR, M. Dolinska, S. Dutta, I.F. Onojafe, R. alur, D. Shukla, R. Kee, M.M. Campos, M. Abu-Asab, T. Cogliati, Y. SERGEEV, B.P. Brooks, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|N. Coussens, Molecular Pharmacology Laboratories, Applied and Developmental Research Directorate, Frederick National Laboratory for Cancer Research, Frederick, Maryland, UNITED STATES|Y. Jittayasothorn, Laboratory of Immunology, Immunoregulation Section, National Eye Institute, Bethesda, Maryland, UNITED STATES|

ABSTRACT BODY:

Purpose: To evaluate the role of 4-aminoantipyrine (ampyrone) in improving pigmentation in a mouse model of oculocutaneous albinism type 1B (OCA1B).

Methods: We used high-throughput screening (HTS) to identify potential activators and inhibitors of the intra-melanosomal domain of human tyrosinase (hTyr). Activators were investigated by in vitro enzymology. C57BL/6J-Tyr $^{c\text{-}h/c\text{-}h}$ mice (a model of OCA1B) were intraperitoneally (i.p.) injected with three doses of ampyrone for thirty days and evaluated for increased melanin pigmentation in the fur and eyes using clinical/biochemical methods and light/electron microscopy.

Results: High-throughput screening of ~34,000 unique compounds identified 115 candidate inhibitors and 9 candidate activators of hTyr enzymatic activity. Among the activators, ampyrone increased the in vitro catalytic efficiency of the OCA1B-related hTyr variant P406L by ~40%, suggesting a partial recovery of function. Treating OCA1B mice with ampyrone up to 48 mg/kg/day i.p. for 30 days resulted in a mild improvement of melanin deposition in fur, as determined by spectrophotometric analysis. However, data on changes in pigmentation of iris and retinal pigment epithelium upon treatment were inconclusive.

Conclusions: Our data support the use of HTS for the identification of candidate compounds to modulate tyrosinase activity. The limited effect of ampyrone on pigmentation, especially in eye tissues, suggests the need to expand the pool of candidate activators through alternative screening strategies and to combine in vitro with in vivo testing for the identification of promising candidates.

CONTROL ID: 3711962

SUBMITTER (NAME ONLY): Jade Vargas

TITLE: The scramblase anoctamin-6 has a role in diurnal phosphatidylserine exposure of photoreceptor outer segment tips

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Vargas, S.C. Finnemann, Fordham University, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Jade Vargas: Commercial Relationship: Code N (No Commercial Relationship) | Silvia Finnemann: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the mammalian retina, daily renewal of light-sensitive photoreceptor outer segments involves coordinated shedding of distal outer segment tips and their engulfment by adjacent retinal pigment epithelial (RPE) cells. Exposure of the anionic membrane lipid phosphatidylserine (PS) at the outer leaflet of photoreceptor outer segment tips promotes shedding and subsequent phagocytosis by RPE cells. The mechanisms underlying this PS exposure remain to be understood. Anoctamin-6 (also known as TMEM16F) is a calcium-activated lipid scramblase that can promote PS exposure. Here we investigated whether anoctamin-6 has a role in PS exposure by photoreceptor outer segments in mouse retina in vivo.

Methods: ano6$^{+/-}$ mice were extensively backcrossed to 129T2/SvEmsJ (WT129) and then bred to yield ano6$^{-/-}$ mice. For experiments, ano6$^{-/-}$ and control WT129 mice were housed in strict 12 h light/dark cycles and sacrificed at 4-5 months of age at time points relative to light onset. Retinas were immediately dissected and incubated photoreceptor side up with PS detection reagent pSIVA (polarity-sensitive indicator of viability and apoptosis). X-y image stacks were obtained using a Leica TSP8 laser scanning confocal microscopy system. Maximum projections were analyzed using ImageJ. Data sets of n≥4 were analyzed using two-tailed Student's t-test.

Results: Anoctamin-6 knockout mice (ano6$^{-/-}$) are not viable in C57BL6/J genetic background. We found that ano6$^{-/-}$ mice in 129 background are viable and have no obvious gross abnormalities up to 6 months of age. Moreover, ano6$^{-/-}$ mice breed with fecundity similar to WT129 mice. Ano6 protein was detected in WT129 but not ano6$^{-/-}$ retina. ano6$^{-/-}$ retina behaved similarly to WT129 tissue in dissections. In WT129 mice, outer segment PS tips elongate and change in frequency in a characteristic diurnal rhythm. Here, we found that at light onset, when outer segment PS tip length in WT129 peaks, PS tip length in ano6$^{-/-}$ was significantly less than in WT129 ($p<0.05$). One hour after light onset, the peak of frequency of outer segment PS tips in WT129 retina, PS tip frequency in ano6$^{-/-}$ was significantly less than in WT129 ($p<0.05$).

Conclusions: Lack of anoctamin-6 leads to loss of rhythmic outer segment PS tip elongation and change in frequency. To our knowledge, anoctamin-6 is the first scramblase to be linked to PS exposure of photoreceptor outer segment tips.

CONTROL ID: 3711963

SUBMITTER (NAME ONLY): Kyle Kim

TITLE: Mass Spectrometry Identification of Wild-type and P23H Rhodopsin Protein Interactome

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kim, L. Safarta, E. Lee, J. Lin, Pathology, Stanford University School of Medicine, Stanford, California, UNITED STATES|K. Kim, L. Safarta, E. Lee, J. Lin, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|W. Chiang, Developmental Neurobiology Unit, Okinawa Institute of Science and Technology Graduate University, Okinawa, JAPAN|J. Coppinger, School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons in Ireland, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: P23H rho is a common genetic cause of retinitis pigmentosa and encodes for misfolded P23H rhodopsin protein. The mechanisms by which rods recognize and target misfolded rhodopsin for degradation are not well understood. Here, we performed mass spectrometry on P23H rhodopsin immunopurified from $rho^{P23H/P23H}$ mice retinas to identify interacting proteins and compare with wild-type (WT) rhodopsin from $rho^{+/+}$ mice.

Methods: Monoclonal anti-rhodopsin antibody 1D4 (Santa Cruz Biotechnologies) was used to immunoprecipitate 5mg of WT or P23H rhodopsin protein and its interacting proteins from retinal protein lysates of postnatal day 15 $rho^{+/+}$ (24 retinas) or $rho^{P23H/P23H}$ (40 retinas) mice. Liquid chromatography with tandem mass spectrometry (LC-MS-MS) was performed on 3 independent samples of WT or P23H rhodopsin protein (LTQ-Orbitrap mass spectrometer, Thermo Finnigan, Waltman, MA). As a negative control, LC-MS-MS was also performed on immunoprecipitates from mouse embryonic fibroblasts. Spectral counts from WT, P23H, and MEF LC-MS-MS experiments were collected and analyzed by Gene Ontology (GO), Kyoto-Encyclopedia of Genes and Genomes (KEGG), Reactome, and CytoScape.

Results: We found 276 proteins that bound to WT rhodopsin, and 286 proteins bound to P23H rhodopsin of which 173 proteins were unique to P23H rhodopsin. GO, KEGG, and Reactome analysis identified enrichment of multiple unique pathways such as ER-associated protein degradation and ubiquitinoylation in the P23H rhodopsin interactome compared to WT. By contrast, phototransduction and visual perception terms were less enriched for P23H rhodopsin. GO-cellular compartment analysis showed decrease in outer segment, cilium, and inner segment proteins but increase in axonal/synapse proteins in the P23H interactome.

Conclusions: Proteomic analysis reveals numerous differences between P23H and WT rhodopsin protein interactome. The P23H rhodopsin interactome is enriched in translational and post-translational quality control processes. The P23H rhodopsin interactome differs throughout all regions of the rod photoreceptor cell. These proteomic and subcellular changes could correspond to mechanisms rods use to eliminate misfolded rhodopsin. These molecular alterations may contribute to pathogenesis of retinitis pigmentosa caused by P23H rhodopsin.

CONTROL ID: 3711964

SUBMITTER (NAME ONLY): Phuoc-Hanh Le

TITLE: Geographic atrophy measured by machine learning and manual segmentation on optical coherence tomography in non-neovascular age-related macular degeneration

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Le, S. Sharma, K. Baynes, T.K. Le, K. Sarici, L. Lunasco, G. Kalra, K. Wise, C. Calabrise, N. LaMunyon, C.J. Mugnaini, J. Friedl, D. Burton, J.P. Ehlers, S.K. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-neovascular age-related macular degeneration (NNAMD) is associated with loss of ellipsoid zone (EZ) on optical coherence tomography (OCT). Geographic atrophy (GA) in NNAMD can be identified and measured using sub-RPE (retinal pigment epithelium) illumination area (IA) on commercially available software. In this study we compare sub-RPE IA changes using a commercial software program to changes in EZ loss on OCT identified by machine learning analysis with manual correction in patients with NNAMD with GA.

Methods: This is a retrospective review of patients diagnosed with NNAMD and GA with growth. IA was measured by the Advanced RPE Analysis feature of FORUM Viewer (Carl Zeiss Meditec, Inc.) which measures the area (mm^2) exhibiting sub-RPE hyper-reflectance within a 2.5-mm radius from the fovea on OCT due to loss of outer retina. IA was manually corrected where needed. OCTs were also analyzed by machine learning algorithms followed by manual correction of layer segmentation using custom software. EZ loss was measured by the percentage of the 6x6-mm scan where EZ thickness was zero µm. Correlation was calculated using Pearson correlation coefficient.

Results: 60 eyes of 60 patients were included in the study with a mean follow-up length of 5.1 years. At baseline, mean age was 79 and mean IA was 3.0 mm^2. Mean EZ loss measured 1.67 mm^2 after machine learning analysis and 5.3 mm^2 after manual correction. IA strongly correlated to EZ loss measured by machine learning ($r = .85$) and manual correction ($r = .93$) on 60 OCTs. Area where EZ measured 10 or less microns was 3.4 mm^2 after machine learning and 6.1 mm^2 after manual correction. Mean annual growth of IA was 1.15 mm^2/yr while mean annual change in EZ loss on manually corrected OCTs was 1.4 mm^2/yr.

Conclusions: EZ measurements on OCT can be used to estimate GA in NNAMD. IA correlates strongly to EZ loss measured by machine learning and manual segmentation. GA area measures smaller than area of EZ loss and can take several years of growth to reach the area of EZ loss. IA and OCT layer segmentation should be compared to measurements of GA on fundus autofluorescence to determine their potential as outcomes measures in clinical research.

CONTROL ID: 3711966
SUBMITTER (NAME ONLY): Matthew Schulgit
TITLE: Nocardia scleritis masked as post-operative inflammation
SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Schulgit, K. Baynes, A. Hamdan, D. Mammo, S.K. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|M. Schulgit, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|
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ABSTRACT BODY:

Purpose: Nocardia scleritis is rare and can mimic other infectious species, needing specific medication which delays resolution. Early identification is integral to avoid permanent damage. This report describes two patients presenting with Nocardia scleritis that masked as post-surgical inflammation and were exacerbated by local steroids.
Methods: A retrospective chart review of patients with Nocardia scleritis. Demographics, clinical history, and outcomes were reviewed.
Results: Two cases were identified:

Case 1: A 71-year-old female s/p conjunctival biopsy with cryotherapy presented with eye pain, blurred vision. Oral corticosteroid and moxifloxacin initially resolved discomfort. Periocular steroids were delivered during corticosteroid taper. After several weeks, symptoms and visual acuity worsened leading to referral. Upon evaluation, visual acuity was counting fingers with scleral necrosis and ovoid dense hypopyon. Right eye anterior chamber paracentesis elucidated Nocardia, prompting initiation of systemic, topical, and intravitreal antibiotics (bactrim, topical linezolid and amikacin, and intravitreal amikacin). Clinical symptoms and exam significantly improved with antibiotic course with resolution of scleritis. Visual acuity remains poor due to cataract formation 4 months after diagnosis.

Case 2: A 62-year-old female presented for evaluation of chronic postoperative inflammation after a trabeculotomy with mitomycin 3 months prior. Postoperative course was complicated by persistent scleral and anterior chamber inflammation. A systemic workup revealed a positive HLA B27 antigen. Corticosteroids including systemic, IV, and periocular steroids were administered to control postoperative inflammation. Upon presentation, the visual acuity was hand motions with multiple ovoid hypopyons. Aqueous paracentesis revealed Nocardia species. Multiple intravitreal amikacin antibiotics were administered. Despite aggressive intravitreal and systemic antibiotics, the eye worsened and was enucleated.
Conclusions: Clinical presentation of Nocardia scleritis can be masked and exacerbated by local steroids. In cases of post-operative scleral inflammation, caution is advised prior to the use of local steroid injections. The indolent nature of Nocardia infection can lead to diagnostic delay. As surgical trauma can precede infection, early consideration of Nocardia is important when postoperative patients present with scleritic symptoms.

CONTROL ID: 3711967

SUBMITTER (NAME ONLY): Megan McDonald

TITLE: Assessment Photographic Resolution of Toxoplasmosis lesions treated with Intravitreal Clindamycin

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. McDonald, R. Bergstrom, C.Y. Lowder, K. Baynes, S. Sharma, S.K. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the time to effectiveness of intravitreal clindamycin in patients with toxoplasmosis chorioretinitis.

Methods: This is a retrospective review of patients with toxoplasmosis chorioretinitis who had fundus imaging. All patients received intravitreal clindamycin (1mg) as therapy. For this analysis, a masked physician qualitatively marked the first sign of improvement based on fundus appearance. The time from injection to first sign of improvement was calculated for each individual, and averaged amongst the patients. The time to inactivity was calculated as well. Those who were lost to follow-up were excluded.

Results: 19 patients were identified with 276 fundus photos reviewed. 5 patients were treated with clindamycin monotherapy, 2 patients were given oral Bactrim only, and 12 patients were given oral Bactrim and clindamycin therapy. On average, patients showed observed first improvement 20.67 days after their injection (range 7 to 42 days). The fastest time to response was 7 days after treatment with intravitreal clindamycin. 5 patients time to response was within 8-15 days. The average time to complete inactivity was found to be 9.37 weeks (1-35 weeks). The average time to respond for those on oral Bactrim and intravitreal clindamycin was 18.71 days (3 days to 47 days). Average number of injections to signs of improvement was 1.44. Two patients worsened despite intravitreal injections. 6 patients resolved with intravitreal clindamycin only. 5 patients had optic nerve or macular lesions and were treated with oral Bactrim and intravitreal clindamycin.

Conclusions: In this series, intravitreal clindamycin shows a photographic response lesion improvement on average of 3 weeks after injection. Compared to oral regimens that can take from 4 weeks to several months to reduce activity, intravitreal clindamycin potentially works faster. Intravitreal clindamycin can be considered a first line of therapy for active toxoplasmic chorioretinitis especially in those with macular and nerve threatening disease.

CONTROL ID: 3711968

SUBMITTER (NAME ONLY): M Isabel Casanova

TITLE: Topical netarsudil for the treatment of canine corneal endothelial degeneration

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Casanova, N. Echeverria, M.A. Bowman, K.L. Good, B.C. Leonard, C.J. Murphy, S.M. Thomasy, Department of Surgical and Radiological Sciences, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|M.A. Mayes, Veterinary Medical Teaching Hospital, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|K.L. Good, B.C. Leonard, C.J. Murphy, S.M. Thomasy, Department of Ophthalmology & Vision Science, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We evaluated the tolerability and efficacy of the topical rho-kinase inhibitor netarsudil in the treatment of canine corneal endothelial degeneration (CED).

Methods: Eighteen eyes of 14 client-owned dogs with CED were enrolled in a prospective, randomized, placebo-controlled clinical trial. The patients received topical netarsudil 0.02% (Rhopressa©, Aerie Pharmaceuticals) or vehicle control twice daily for the initial 4 months, then all patients received netarsudil for the final four months. Ophthalmic examination with measurement of Schirmer tear test I (STT), intraocular pressure (IOP), anterior segment photography, ultrasonic pachymetry (USP), Fourier-domain optical coherence tomography (FD-OCT), and in-vivo confocal microscopy was performed prior to and at 1, 2, 4, 6 and 8 months throughout treatment. The effect of treatment on corneal thickness, corneal stromal thickness, percentage of cornea affected by edema, and endothelial cell density (ECD) was evaluated by repeated measures ANOVA.

Results: Seven dogs (9 eyes) received placebo during the first 4 months, while 7 dogs (9 eyes) received netarsudil for 8 months. During netarsudil treatment, conjunctival hyperemia (n = 13), reticulated intraepithelial bullae (n = 1), and corneal stromal hemorrhage (n = 1) were identified were identified at one or more timepoints; one patient with stromal hemorrhage required temporary cessation of netarsudil for 1 month. Five eyes treated with netarsudil had decreased tear production at one or more timepoints during the study and required immunomodulatory treatment. No significant differences in corneal thickness, corneal stromal thickness, ECD, and percentage of the cornea affected by edema were observed between treatment groups or over time ($p>0.05$).

Conclusions: Netarsudil is generally well-tolerated in dogs with endothelial degeneration but may result in dry eye thus tear production should be closely monitored. While improvement was not observed in canine CED patients treated with topical netarsudil, interim analysis suggests stable disease after 4 or 8 months of treatment. Enrollment of more patients is required to fully evaluate the efficacy of netarsudil for canine CED.

CONTROL ID: 3711974

SUBMITTER (NAME ONLY): E Eugenie Hartmann

TITLE: Instrument-Based Vision Screening: Integration into Primary Care with Referral and Follow-Up at Vision Center

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Hartmann, Vision Center and Research Institute, Akron Children's Hospital, Akron, Ohio, UNITED STATES|I. Boydstun, R.W. Hertle, Vision Center, Akron Children's Hospital, Akron, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the relationship between screening outcomes using the SPOT Vision Screener at 3-, 4- and 5-year-old Well Child Checks (WCC) in general pediatric offices and comprehensive eye examination follow-up in the Vision Center specialty care clinics at Akron Children’s Hospital.

Methods: Staff and providers in pediatric offices were systematically trained on the use of the SPOT Vision Screener. This instruction included the importance of identifying amblyogenic risk factors in the preschool age group as well as hands on demonstration and practice with the device. Two primary care clinics were selected as initial sites for launching this project. Electronic charting was designed to automatically order and report instrument-based vision screening for all 3-,4- and 5-year-old WCCs. Results from SPOT screening were compared with findings from comprehensive eye examinations during the first four months of this new protocol.

Results: Of the 177 referrals resulting from 724 WCCs that included instrument-based vision screening, 87 patients (49% of referrals) presented for comprehensive eye examinations in the Vision Center. The SPOT results for one of these patients did not detect any abnormality, however, the provider had observed exotropia OD, which resulted in an accurate referral. Of the remaining 86 referrals based on the SPOT, 82 (95%) were identified as having astigmatism (unilateral, bilateral or with other potential conditions). A summary of the SPOT results by condition compared with the number of patients who were prescribed refractive error correction is shown in Table 1. Only 4 patients were identified by the SPOT as having a potential condition other than astigmatism. Patients identified with potential bilateral astigmatism only were twice as likely to be prescribed glasses based on the findings from their eye examination as patients identified with potential unilateral astigmatism only.

Conclusions: Understanding the effectiveness of instrument-based vision screening in pediatric offices requires tracking referrals, as well as outcomes of eye examinations. The preponderance of referrals we observed for astigmatism was not surprising based on the inherent design of these devices. Correlation of refractive errors obtained by our eye-care providers along with their treatment protocols will provide greater understanding of the strength and weaknesses of these devices.

CONTROL ID: 3711976

SUBMITTER (NAME ONLY): Shikha Pachauri

TITLE: Single-nucleus multi-modal analysis of MFRP associated retinal degeneration

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Pachauri, P. Biswas, M. Dagar, A. Berry, B. Kurmanov, R. Ayyagari, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|A.K. Chekuri, Harvard Medical School, Boston, Massachusetts, UNITED STATES|D. Garland, Harnly LLC, Bethesda, Maryland, UNITED STATES|K. Dang, R. Lancione, S. Preissl, A. Wang, Center for Epigenomics, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the RPE expressed gene Mfrp (membrane-type frizzled related protein) results in early-onset retinal degeneration (RD) in human and mice. The goal of this study is to identify the cell type-specific transcriptional and gene-regulatory events in the retina that lead to RD using Mfrp gene knock-out (KO) mice.

Methods: Retina + RPE tissue from Mfrp$^{-/-}$ and Wild type (WT) mice at 28 days and 2.5 months were analyzed via single nucleus (sn) RNA-seq and ATAC-seq (n=3) followed by experimental validation.

Results: Cluster analysis of the snRNA-seq data (~140,000 nuclei) revealed >30 clusters encompassing known retinal cell-types. To identify the transcriptional changes associated with RD, we performed differential expression analysis (WT vs. Mfrp$^{-/-}$) with a focus on RPE cells, Rods, and Cones. Notably, more than 50 significantly differentially expressed genes (DEGs) ($p < 0.05$, Wilcoxon Rank-Sum) in RPE cells, rods, and cones are involved in Mfrp related RD. Among these, ~21 genes are differentially expressed in RPE cells, and about 35 are differentially expressed in rods and cones. In photoreceptors, a majority of DEGs are observed at 28 days, the exception being rhodopsin - which was significantly down-regulated at 2.5 months ($P< 0.05$) in rods. These DEGs include transcription factors, structural proteins, and members of visual transduction. In RPE cells, we observed more DEGs at 2.5 months than at 28 days. These DEGs with $P\leq 0.02$ by snRNA-seq are involved in visual transduction and phagocytosis pathways and include Rdh10, Rpe6, Lrp2, Cralbp, Mertk, Igtav which were validated by qRT-PCR ($P< 0.05$). Genes involved in lipid metabolism (Hmgcs2 $P< 0.05$ and Slc16a1 $P< 0.05$) and glucose transport (Slc2a1 $P< 0.05$) are also downregulated in RPE cells at 2.5 months by qRT-PCR. Lastly, our snRNA-seq analysis revealed downregulation of genes associated with PI3K-AKT pathway in RPE cells at 2.5 months. We further validated that AMPK and mTOR pathways show altered activation in Mfrp$^{-/-}$ mice.

Conclusions: The snRNA-seq data revealed that RPE cells show progressive changes in regulation of key pathways with age while photoreceptors show more prominent alterations in transcriptional regulation at 28 days in Mfrp$^{-/-}$ mice. Analysis of changes in additional cell types as well as analysis of snATAC-seq data is in progress to understand the mechanism underlying Mfrp related RD pathology.

CONTROL ID: 3711977

SUBMITTER (NAME ONLY): Nathan Jensen

TITLE: An improved method for OCT-based, murine laser-induced choroidal neovascularization lesion quantification

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Jensen, N. Lambert-Cheatham, G.D. Hartman, A. Muniyandi, B. Park, K. Sishtla, T.W. Corson, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|N. Jensen, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: The laser-induced choroidal neovascularization (L-CNV) murine model provides quantifiable data to evaluate efficacy of therapeutic treatments and genetic effects. We previously validated lesion quantification from optical coherence tomography (OCT) images as a reliable assessment of CNV lesion size. However, the existing method is time consuming, and the subjective nature of defining lesion borders led to variability between evaluators. We therefore investigated if OCT lesion quantification could be simplified, streamlined, and made more reliable among evaluators.

Methods: The rate-limiting step in analysis is defining the borders of a given lesion. We developed a workflow where the lesion borders are specified using the multi-point tool in ImageJ. The lesion borders were pinpointed to the pixel coordinates in the x-plane and y-plane. These coordinates were imported to a custom Excel template and converted to μm, adjusting for the different degrees of scaling in the OCT x and y planes. Volume was calculated as previously described. This streamlined method was compared against the prior method to evaluate reliability and quantification time per lesion. To evaluate the interrater reliability, 10 OCT images of lesions were scored by 6 trained evaluators and superimposed to assess consistency.

Results: The new process demonstrated improved time efficiency and precise quantification of OCT lesion volume. The time to calculate the volume of a lesion previously was 2 minutes, 56.9±16.4 seconds (mean±SD). The new method averaged 22.0±1.9 seconds, or ~8 times faster (paired t-test, $p<0.0001$, $n=5$). Subjectively, evaluators noted that the new method allowed for greater reliability in lesion border identification. Some lesions had near unanimous agreement with only minor differences between volume measurements while others had larger differences. The largest discrepancy between evaluators was the determination of the superior-most coordinates. Expert consensus demonstrated the importance of identifying the lesion as an ellipsoid shape and avoiding edema or a bleb as the superior coordinate of the lesion.

Conclusions: A new method of evaluating L-CNV lesion size greatly reduced analysis time, and subjectively allowed for more precise lesion border identification. Inter-evaluator discrepancies exist but may be minimized by group discussion and training.

CONTROL ID: 3711980

SUBMITTER (NAME ONLY): Lana Pollock

TITLE: Role of Müller cell retinoic acid signaling in blood-retinal barrier maintenance

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Anand-Apte, Cell Biology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|L. Pollock, J. Xie, B. Anand-Apte, Ophthalmic Research, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Lana Pollock: Commercial Relationship: Code N (No Commercial Relationship) | Jing Xie: Commercial Relationship: Code N (No Commercial Relationship) | Bela Anand-Apte: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The blood-retinal barrier (BRB) mediates movement of molecules from the blood to the inner retina, protecting the neural retina from potentially harmful molecules and maintaining retinal homeostasis. We previously demonstrated that retinoic acid (RA) signaling is necessary for BRB integrity in the zebrafish model. RA signaling is known to induce expression of RA-metabolizing enzyme Cyp26a1 in a sensitive feedback mechanism. The purpose of this study was to investigate the cellular mechanisms by which RA maintains the BRB by examining the expression patterns of cyp26a1 in the retina.

Methods: To visualize the BRB in vivo, we utilized the transgenic Tg(l-fabp:DBP-EGFP) zebrafish model that expresses vitamin D binding protein (a member of the albumin gene family) tagged to GFP. This model displays the integrity of the BRB with GFP-tagged protein localized within the retinal vasculature by 3 days post-fertilization. Breakdown of the BRB is visualized as “leaking” of GFP outside the vasculature. To disrupt RA signaling, zebrafish embryos, larvae, and adults were treated with varying concentrations of DEAB and BMS493, antagonists of retinal dehydrogenase and the RA receptor, respectively. To visualize the Müller cells and endothelial cells, gfap:GFP and kdrl:GFP transgenic fish were used, respectively. RNAScope analysis was used to detect and quantify the expression of cyp26a1 in retinas of zebrafish at different developmental stages.

Results: Treatment with DEAB or BMS493 resulted in a non-functional disrupted BRB in up to 95% of embryos and adults. In the retina, cyp26a1 was primarily detected in the Müller cells starting at 3 dpf, and treatment with pharmacological RA signaling inhibitors significantly decreased Müller cell cyp26a1 expression.

Conclusions: The gene encoding RA-metabolizing enzyme Cyp26a1 is primarily expressed in the Müller cells of the retina, indicating that Müller cells may play a critical role in RA-mediated BRB maintenance.

CONTROL ID: 3711981

SUBMITTER (NAME ONLY): Avinash Soundararajan

TITLE: Clusterin modulates IOP homeostasis by regulating the actin cytoskeleton and attenuating profibrotic responses in TM

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Soundararajan, P.P. Pattabiraman, Ophthalmology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Avinash Soundararajan: Commercial Relationship: Code N (No Commercial Relationship) | Padmanabhan Pattabiraman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Clusterin is a secretory chaperone protein known to regulate cell-matrix interactions. Altered cytoskeletal rearrangement and excessive extracellular matrix (ECM) deposition in the trabecular meshwork (TM) outflow pathway results in increased AH outflow resistance and elevated IOP. This study evaluated the role and mechanism of clusterin in regulating IOP.

Methods: Immunoblotting (IB) was used to analyze the effect of– a) adenovirus-mediated clusterin expression (AdCLU) on proteins related to actin organization, ECM and fibrosis; b) effect of recombinant clusterin (rhCLU) on TGFβ2-mediated ECM changes in TM. Immunofluorescence (IF) and live-cell imaging using SiR-actin was used to analyze the effect of clusterin on ECM and actin fibers, respectively. The effect of clusterin on TGFβ2-mediated IOP elevation was studied using human anterior segment perfusion cultures by perfusing with TGFβ2 followed by rhCLU in the presence of TGFβ2. Students t-test was used for statistical analyses with significance of $p<0.05$.

Results: The IB analysis showed AdCLU significantly reduced- a) actin-cytoskeleton associated proteins- PRK2(p=0.0006), LIMK1(p=0.04); b) Integrins- INTαV(p=0.04), INTβ5(p=0.01); c) tight junction protein Zo-1(p=0.007) d) ECM- COL1A(p=0.04), FN(p=0.03), ELN(p=0.005), and secretory FN(p=0.002); e) pro-fibrotic proteins- TGFβ2(p=0.03), TSP-1(p=0.005), and secretory PAI-1(p=0.007) and TSP-1(p=0.05). rhCLU treatment significantly reduced pro-fibrotic effect of TGFβ2, evidenced by significant reduction in COL1A(p=0.002) and TSP1(p=0.01), and secretory TSP1(p=0.01) and PAI-1(p=0.02). IF showed reduced COL1A and FN distribution in AdCLU. Live cell imaging showed reduction in F-actin distribution with rhCLU, which was initially increased by TGFβ2 treatment. Perfusion of TGFβ2 in the human anterior segment increased IOP significantly (n=5, p=0.006) by the third day which was significantly reduced on day eight (p=0.008) due to rhCLU perfusion.

Conclusions: For the first time, we show importance of clusterin in lowering actin-based tension and attenuating profibrotic ECM accumulation in TM, possibly facilitating the increase in AH outflow and, thereby regulating IOP homeostasis. Further understanding of the functional role of clusterin and its binding partners in mediating cell-matrix interactions in TM will pave way for novel therapeutic approaches for lowering elevated IOP.

CONTROL ID: 3711983

SUBMITTER (NAME ONLY): Martha Neuringer

TITLE: Toward a gene-edited nonhuman primate model of Usher syndrome 1B

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Neuringer, J. Ryu, J.D. Hennebold, J.P. Statz, W. Chan, C. Ramsey, F. Burch, L. Renner, C.B. Hannah, Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, Oregon, UNITED STATES|M. Neuringer, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|B. Kempton, E.V. Porsov, J.V. Brigande, Oregon Hearing Research Center, Oregon Health & Science University, Portland, Oregon, UNITED STATES|B. Burwitz, Vaccine and Gene Therapy Institute, Oregon Health & Science University, Beaverton, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Martha Neuringer: Commercial Relationship(s);Code F (Financial Support):Sana Biotechnology | Junghyun Ryu: Commercial Relationship: Code N (No Commercial Relationship) | Jon Hennebold: Commercial Relationship: Code N (No Commercial Relationship) | John Statz: Commercial Relationship: Code N (No Commercial Relationship) | William Chan: Commercial Relationship: Code N (No Commercial Relationship) | Cathy Ramsey: Commercial Relationship: Code N (No Commercial Relationship) | Fernanda Burch: Commercial Relationship: Code N (No Commercial Relationship) | Beth Kempton: Commercial Relationship: Code N (No Commercial Relationship) | Edward Porsov: Commercial Relationship: Code N (No Commercial Relationship) | Lauren Renner: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Burwitz: Commercial Relationship: Code N (No Commercial Relationship) | Carol Hannah: Commercial Relationship: Code N (No Commercial Relationship) | John Brigande: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Better translational models are urgently needed for many retinal degenerative diseases to facilitate understanding pathogenetic processes and test potential therapies. Usher syndrome presents a particularly compelling need for such models, due to the devastating nature of the disease and the lack of rodent models showing retinal degeneration. Usher 1B is a primary target due to its rapid onset and prevalence among Usher subtypes. Nonhuman primates best mirror human retina anatomy and function by having a macula and fovea, as well as photoreceptor calyceal processes that are a major site of dysfunction in Usher syndrome but are absent in rodents.

Methods: We used CRISPR-Cas9 editing to create rhesus monkey embryos with mutations in exon 3 of MYO7A. Custom guide RNAs and Cas9 mRNA or protein were injected into zygotes 16 hours after in vitro insemination. Trophectoderm biopsies from day 8 blastocysts were genotyped, and those with desired mutations were selected for transfer to surrogate dams. Infant PBMCs, skin and cheek cells were sequenced to confirm infant genotype. Infant audition was assessed by auditory brainstem responses (ABR) and distortion product otoacoustic emissions (DPOAE). Retinal structure and function were evaluated by multimodal retinal imaging and ERG.

Results: In the first live infant, genotyping of skin and buccal cells and single-cell sequencing of PBMCs showed a mosaic pattern with half of cells possessing a homozygous single base insertion in exon 3 resulting in a premature stop codon, while half were homozygous for wild type MYO7A. ABR and DPOAE responses were attenuated at one month of age but were normal in subsequent tests through 2 years of age, and normal retinal structure and function were present at all ages. A second infant born in November 2021 showed a compound heterozygote pattern with 1bp and 63bp deletions in exon 3. Auditory testing at 4 weeks of age showed no detectable ABR or DPOAE responses. Retinal imaging at 6 weeks detected no significant abnormalities. Development of the auditory and retinal phenotypes will be followed longitudinally.

Conclusions: This study showed the ability to induce mutations in the MYO7A gene in rhesus macaques, resulting in absence of auditory function in early infancy. Continued confirmation of an USH1B phenotype will set the stage for studies of gene therapy in this first gene-edited nonhuman primate model of Usher syndrome.

CONTROL ID: 3711984

SUBMITTER (NAME ONLY): Ranran French

TITLE: Beliefs about object motion in the world affect depth perception during self-motion

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.L. French, University of Rochester Medical Center, Rochester, New York, UNITED STATES|G.C. DeAngelis, Brain and Cognitive Sciences, University of Rochester School of Arts and Sciences, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: Ranran French: Commercial Relationship: Code N (No Commercial Relationship) | Gregory DeAngelis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is crucial for animals to accurately judge the depth of moving objects. During observer translation, the relative image motion between stationary objects at different distances, known as motion parallax (MP), provides important depth information. However, when an object also moves relative to the scene, the computation of depth from MP is complicated by the object's independent motion. Previously, we demonstrated that humans show systematic depth biases during self-motion that depend on object motion in the world. Here, we propose and compare two distinct perceptual mechanisms by which object motion may induce depth biases.

Methods: Naïve human subjects viewed a virtual 3D scene consisting of a ground plane and stationary background objects, while lateral self-motion was simulated by optic flow. A target object, lying above the ground plane, could be either stationary or moving laterally at different velocities. In a dual report task, the subjects were asked to judge the depth of the target object relative to the plane of fixation, as well as whether they thought the object was moving independently relative to the scene.

Results: We constructed Bayesian ideal observer models for two proposed perceptual mechanisms: (incomplete) flow parsing (FP) and causal inference (CI). In the FP model, some fraction of image motion resulting from object motion can be attributed to self-motion, but the model assumes that a moving object is always present. In the CI model, the ideal observer can probabilistically attribute image motion to two separate causes: scene-relative object motion and self-motion. Both models predict systematic depth biases that depend on object motion relative to the scene, but only the CI model captures biases that depend on subjects' belief about object motion. By the Akaike information criterion, the CI model provides a consistently better fit than the FP model across 6 subjects.

Conclusions: We demonstrate that both incomplete flow parsing and causal inference are feasible explanations for the substantial depth biases that are induced by scene-relative object motion. However, the component of depth bias that depends on a subject's belief about object motion is consistent with involvement of a causal inference process that adjudicates whether image motion is caused by a combination of object motion and self-motion.

CONTROL ID: 3711985

SUBMITTER (NAME ONLY): Ciara O'Byrne

TITLE: Determinants of non-attendance in asynchronous telemedicine ophthalmology clinics

SESSION TITLE: Using Technology for Care Delivery and Improvement

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. O'Byrne, S. Wagner, L. Raja, R. Struyven, M. Cortina-Borja, P.A. Keane, J. Huemer, K. Balaskas, D. Sim, J. Rahi, A. Solebo, S. Kang, Medical Retina, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|C. O'Byrne, School of Medicine, The University of Dublin Trinity College, Dublin, IRELAND|

Commercial Relationships Disclosure: Ciara O'Byrne: Commercial Relationship: Code N (No Commercial Relationship) | Siegfried Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Laxmi Raja: Commercial Relationship: Code N (No Commercial Relationship) | Robbert Struyven: Commercial Relationship: Code N (No Commercial Relationship) | Mario Cortina-Borja: Commercial Relationship: Code N (No Commercial Relationship) | Pearse Keane: Commercial Relationship(s);Code F (Financial Support):Allergen, Bayer, Heidelberg Engineering, Novartis, Roche, Topcon;Code C (Consultant/Contractor):Apellis, DeepMind;Code I (Personal Financial Interest):Big Picture Medical | Josef Huemer: Commercial Relationship: Code N (No Commercial Relationship) | Konstantinos Balaskas: Commercial Relationship: Code N (No Commercial Relationship) | Dawn Sim: Commercial Relationship: Code N (No Commercial Relationship) | Jugnoo Rahi: Commercial Relationship: Code N (No Commercial Relationship) | Ameenat Lola Solebo: Commercial Relationship: Code N (No Commercial Relationship) | Swan Kang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ophthalmic services are facing unprecedented pressures. Telemedicine has emerged as a potential solution to increase healthcare accessibility to a greater number of patients. This has been particularly emphasised by the COVID-19 pandemic, where digital health facilitated the provision of ophthalmic services in the face of strained resources, widespread service cancellations and social distancing restrictions. Thus, telemedicine has proven itself to be an invaluable resource. However, greater reliance on digital technology may further exacerbate healthcare inequalities faced by certain populations. The purpose of our study was to determine factors associated with non-attendance at asynchronous tele-ophthalmic clinics.

Methods: This was a retrospective cohort study that reviewed all patients newly referred to Moorfields Eye Hospital (MEH) in London, United Kingdom, between January 1st 2019 and October 31st 2021. Electronic healthcare records were used to extract sociodemographic information, clinical variables and appointment details. The primary outcome measure was attendance at asynchronous clinics. 'Asynchronous' is the approach in which the patient attends for in-person assessment and/or imaging by technician with subsequent review of results by a clinician. Multivariable logistic regression modelling was used to examine attendance status against sociodemographic, clinical and operational exposure variables.

Results: A total of 8878 eligible patients (median age 57±20 years, 52% female) attended asynchronous clinics across all MEH sites in the defined time period. Non-attendance was 11.7%. All asynchronous clinics were either medical retina (n=2740) or glaucoma (n=6138). Medical retina patients had 61% less odds ($p<0.001$) of attending their appointment compared to those attending the glaucoma service. Patients with diabetes (adjusted OR 2.16, CI 1.70-2.75) and registered sight impairment (OR 1.53, CI 0.35-6.60) were more likely to attend. Male sex (OR 0.78, CI 0.68-0.89) and greater levels of socioeconomic deprivation (OR 0.92, CI 0.90-0.95) were associated with increased rates of non-attendance.

Conclusions: Male sex and socioeconomic deprivation are associated with greater rates of non-attendance at asynchronous teleophthalmic clinics. Further study into the identified factors associated with poor attendance may determine potential solutions and improve healthcare provision in these populations.

CONTROL ID: 3711986

SUBMITTER (NAME ONLY): Praveen Balne

TITLE: H_2S induces dose-dependent changes in inflammatory and apoptotic responses in human corneal stromal fibroblasts in vitro

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.K. Balne, N.R. Sinha, R. Tripathi, P. Sinha, R.R. Mohan, Ophthalmology, Harry S Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|P.K. Balne, N.R. Sinha, R. Tripathi, A. Houmes, L.A. Suleiman, P. Sinha, R.R. Mohan, Ophthalmology, University of Missouri System, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Earlier we optimized an in vitro model for studying hydrogen sulfide (H_2S) toxicity to the human cornea. This study examined if H_2S toxicity to corneal stromal fibroblasts is due to (a) changes in inflammatory and apoptotic parameters and (b) whether the effects are concentration-dependent using an established in vitro model.

Methods: Healthy donor human corneas (n=30) were obtained from the eye bank and used to generate primary human corneal stromal fibroblasts (hCSFs) following our standard protocol. Sodium hydrosulfide (NaSH) was used as a source of H_2S. Primary hCSFs were exposed to different concentrations of NaSH (1 mM - 10 mM) for 24h. The changes in inflammatory and apoptotic parameters were assessed using quantitative real-time PCR, mitochondrial membrane potential ($\Delta\Psi m$), and TUNNEL assays.

Results: H_2S toxicity to hCSFs is dose-dependent. Exposure to lower concentrations (1 - 4 mM) of NaSH showed alteration of inflammatory genes IL-1α, IL-1β, and TNF-α ($p \leq 0.05$). However, higher concentrations (5 - 10 mM) of NaSH exposure leads to alterations in inflammatory genes IL-1α, IL-1β, and TNF-α as well as apoptotic genes caspase 8 and FADD and showed loss of mitochondrial membrane potential and significantly increased TUNEL positive cells as compared to the non-H_2S exposed hCSFs ($p \leq 0.05$).

Conclusions: H_2S causes dose-dependent toxicity and changes in inflammatory and apoptotic mediaters in hCSFs in vitro. Onging studies will provide additional mechanistic information.

CONTROL ID: 3711987

SUBMITTER (NAME ONLY): Jingyun Wang

TITLE: Comparison of OCT Eccentric Fixation in Children with Non-residual vs Residual Strabismic Amblyopia

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Wang, SUNY College of Optometry, New York, New York, UNITED STATES|S. Lehman, D. Hendricks, J. Jin, Nemours Children's Hospital Delaware, Wilmington, Delaware, UNITED STATES|

Commercial Relationships Disclosure: Jingyun Wang: Commercial Relationship: Code N (No Commercial Relationship) | Sharon Lehman: Commercial Relationship: Code N (No Commercial Relationship) | Dorothy Hendricks: Commercial Relationship: Code N (No Commercial Relationship) | Jing Jin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previously, eccentric fixation was reported in children with residual amblyopia who had an interocular difference [IOD] of visual acuity ≥0.2 logMAR after treatment (glasses, patching, atropine). Using OCT, we measured eccentric fixation (called OCT fixation shift) in children with residual amblyopia (Jin et al, 2020). We found that OCT fixation shift is significantly higher in amblyopic eyes than in fellow eyes and control eyes, especially in children with strabismic amblyopia where 78% of had measurable OCT eccentric fixation. We ask how common OCT fixation shift is present in children without residual strabismic amblyopia (IOD of visual acuity improved to <0.2 logMAR with treatments). Here, we report OCT fixation shift in strabismic amblyopic children without residual amblyopia and compare it with those with residual amblyopia.

Methods: Children aged 4 to 16 years (mean±SD = 9.7±3.3 years) with non-residual strabismic amblyopia (n=23), with residual strabismic amblyopia (n=28), and normal controls (n=75) were studied. Spectral-domain OCT was used to estimate fixation shift. We asked the child to focus on the internal blue dot fixation target of the OCT. OCT fixation shift, i.e. the distance between the foveal center and the fixation point, was measured, adjusted for axial length, and converted into visual degrees. OCT fixation shifts in the amblyopic eye in two amblyopic groups and the right eye of the control group were compared by ANOVA.

Results: OCT fixation shift was 0.17±0.29° for control eyes, 1.54±1.48° for residual amblyopic eyes, and 0.43 ± 0.44° for non-residual amblyopic eyes ($F=34.2$, $P<0.001$). Fixation shift between the non-residual amblyopic group and control group did not differ ($P=0.31$), and fixation shift for the non-residual amblyopic group was significantly lower than the residual amblyopic eyes ($P<0.001$). Fifteen (65%) in the non-residual group had the measurable fixation shift, which is not significantly different from that (78%) in the residual group (chi-squared=0.56, p=0.45).

Conclusions: Eccentric fixation, assessed by OCT fixation shift, is measurable in about 2/3 of children with strabismic amblyopia (both residual and non-residual). Although the occurrence of OCT fixation shift shows similar frequency in both groups, the magnitude of OCT fixation shift is less in children without residual strabismic amblyopia than those with residual strabismic amblyopia.

CONTROL ID: 3711989

SUBMITTER (NAME ONLY): Ethan Willis

TITLE: COVID-19 impact on delayed clinical visits in diabetic retinopathy patients

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Willis, The University of Tennessee at Chattanooga College of Arts and Sciences, Chattanooga, Tennessee, UNITED STATES|E. Willis, A. Brock, D. Reichstein, Tennessee Retina, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Ethan Willis: Commercial Relationship: Code N (No Commercial Relationship) | Anderson Brock: Commercial Relationship: Code N (No Commercial Relationship) | David Reichstein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The COVID-19 pandemic created an unprecedented setback for diabetic retinopathy (DR) patients receiving routine anti-vascular endothelial growth factor (VEGF) injections. In this retrospective clinical study, we assessed visual and anatomical outcomes of “late follow-up" appointments cancelled or rescheduled during an 11-week quarantine period from March 15th- June 1st, 2020, due to the urgency to limit non-emergent clinical visits. This study tested the hypothesis that strict frequency of treatment is a requisite for successful therapy.

Methods: To meet “late follow-up" requirements, all study patients had appointments scheduled within the quarantine period that were delayed past their previous physician recommended interval, beyond June 1st, 2020. Of the 7042 delayed patients, 5137 returned for examination. 2764 were injection patients, of which 616 were delayed beyond the quarantine period. These 616 patients were subsequently categorized by diagnosis. We then analyzed the electronic medical record (EMR) for 300 eyes with treatment-requiring diabetic retinopathy to establish baseline anatomical and visual status prior to the delayed clinical visit. The EMR of the follow-up appointment was subsequently viewed for comparison. Best-corrected visual acuity (BCVA) and retinal examination findings were recorded from both visits. All eyes received at least 1 anti-VEGF injection prior to March 15th, 2020.

Results: 300 eyes were delayed beyond their previously scheduled interval an average of 14.04 weeks. Upon return, 37 eyes (12.3%) had improved BCVA, 169 (56.3%) remained stable, and 94 (31.4%) had worsened. Of the 300 eyes, there was an average of 2.2 lines lost (p=0.03). 29 delayed eyes (9.7%) returned with improved macular edema, 121 (40.3%) remained stable, and 143 (47.7%) had worsened upon examination. Due to vitreous hemorrhage, edema progression in 7 eyes (2.3%) was unknown. 290 eyes (96.7%) remained with non-proliferative DR, while 10 (3.3%) progressed to proliferative DR. 23 (7.6%) returned with new or worsened vitreous hemorrhages. No patients developed a retinal tear or detachment during this period.

Conclusions: COVID-19 had a severe impact on routine clinical visits. Prolonged frequency of anti-VEGF treatment for DR is associated with increased risk for BCVA decline and negative anatomical outcomes. Effective therapy requires strict compliance with intravitreal injections and routine clinical appointments.

CONTROL ID: 3711990

SUBMITTER (NAME ONLY): Said Arevalo-Alquichire

TITLE: Encapsulated RUNX1 inhibitor (Ro24-7429) reduces angiogenesis in retinal endothelial cells

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Arevalo-Alquichire, J. Arboleda-Velasquez, L.A. Kim, Schepens Eye Research Institute of Massachusetts Eye and Ear, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, MA, US, academic/medres, Boston, Massachusetts, UNITED STATES|S. Arevalo-Alquichire, J. Arboleda-Velasquez, L.A. Kim, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Overexpression of runt-related transcription factor 1 (RUNX1) has been recently linked to aberrant angiogenesis in proliferative diabetic retinopathy and choroidal neovascularization. Topical delivery of small-molecule inhibitors of RUNX1 such as Ro24-7429 could lead to a novel and non-invasive treatment for a wide variety of angiogenic diseases of the eye. This study evaluated the in vitro effect of a nanoemulsion loaded with Ro24-7429 on migration and proliferation of human retinal endothelial cells (HRECs).

Methods: Ro24-7429 dispersed in the oil phase was homogenized and subsequently sonicated to fabricate an oil in water nano-emulsion. Dynamic light scattering (DLS) measured the drop size of the nanoemulsion. In vitro cytotoxicity and proliferation assays of unloaded (eNanoV), loaded (eNanoRo24) nanoemulsions, and Ro24-7429 in DMSO were used to test several concentrations. Scratch wound assay was performed for the evaluation of cell migration. Immunofluorescence staining (IF) for RUNX1 and delta-like four (DLL4) was carried on to assess the tip and stalk morphology of HRECs.

Results: We confirmed that the nano-emulsion constitutes lower than 200 nm in drop size. eNanoV and eNanoRo24 were not toxic for the HRECs even at the highest concentration tested of 8% v/v at 48h. A significant reduction (P-value<0.5) of proliferation and migration were observed after treatment. eNanoRo24 had higher reduction of proliferation than Ro24-7429 in DMSO. IF described a reduction of RUNX1 as well as DLL4 on treated HRECs. DLL4 is a protein-related to the tip phenotype of endothelial cells in sprouting angiogenesis.

Conclusions: eNanoRo24 reduced the proliferation and migration of HRECs in vitro. We did not observe any toxicity with application of eNanoRo24 in HRECs. Also, eNanoRo24 may improve the activity of the Ro24-7429. The inhibition of migration may be mediated by a change in the tip/stalk morphology. The reduction of both migration and proliferation strongly suggests that eNanoRo24 modulates the activity of endothelial cells and the angiogenic process, thus demonstrating the therapeutic potential of this drug delivery system.

CONTROL ID: 3711991
SUBMITTER (NAME ONLY): Susan Su
TITLE: Comparison of 24-2C SITA Standard and 24-2C SITA Faster
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Su, T. Callan, S. Yu, N. Graves, C. Wu, G.C. Lee, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|I.A. Falkenstein, Glaucoma Specialists of San Francisco, Oakland, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|
Commercial Relationships Disclosure: Susan Su: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Thomas Callan: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Sophia Yu: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Nolleisha Graves: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Charles Wu: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Iryna Falkenstein: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Todd Severin: Commercial Relationship(s);Code C (Consultant/Contractor):East Bay Eye Center | Gary Lee: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc.

ABSTRACT BODY:

Purpose: The recent 24-2C SITA Faster visual field (VF) test increases sensitivity of central field defects by adding 10 test locations from the 10-2 pattern to the end of the 24-2 test. However, some clinicians prefer to test glaucoma patients with the SITA Standard strategy. The purpose of this ongoing clinical study was to compare the 24-2C SITA Standard to the 24-2C SITA Faster in healthy and glaucomatous eyes.
Methods: 24-2C SITA Standard (SS) and 24-2C SITA Faster (SFR), as well as 10-2 SS, and 10-2 SITA Fast VFs were acquired on an HFA3 Model 860 perimeter (ZEISS, Dublin, CA) at each of two visits on one eye for healthy and glaucomatous subjects. 24-2 SS VFs were extracted from 24-2C SS as a reference for disease severity. Data from last qualified visit were used for analyses; 10-2 VFs were not used for these analyses.

Bland-Altman and scatter plots were used to assess agreement for the Mean Deviation (MD), Visual Field Index (VFI), and Pattern Standard Deviation (PSD) global parameters. The sum of any total deviation (TD) and pattern deviation (PD) points flagged for the VFs were totaled and compared using paired equivalence t-tests ($\alpha = 0.05$). Limits of equivalence were chosen as 5% of total test points.
Results: Mean age was 57.3 (standard deviation, SD: 7.6; range: 44.3 to 74.7) years for 28 healthy eyes and 71.3 (SD: 9.0; range 54.0 to 97.9) years for 28 glaucoma eyes. Mean 24-2 SS MD was 0.38 (SD: 1.17; range: -1.89 to 2.62) dB and -7.92 (SD: 7.72; range: -23.42 to 1.63) dB in healthy and glaucoma eyes, respectively.

MD, VFI, and PSD values were similar between both strategies across all eyes, with linear correlations ranging from 0.98 to 0.99 (See Fig. 1). For healthy eyes, mean difference (SD) for TD was -0.9 (SD: 3.9) points and 1.1 (5.1) points for PD while glaucoma mean difference was -0.1 (8.8) for TD and 1.2 (5.9) points for PD (see Table 1).
Conclusions: 24-2C SITA Standard showed comparable sensitivity to detect visual field defects as 24-2C SITA Faster in this study, with mean differences between the number of any flagged TD and PD points ranging from -0.9 to 1.2 defects. Thus, the 24-2C test pattern with the reference SITA Standard strategy may offer clinicians a similar ability to detect central visual field loss as SITA Faster without the need to run a supplementary SITA 10-2.

CONTROL ID: 3711992
SUBMITTER (NAME ONLY): Jennifer Fogt
TITLE: Oculomotor characteristics of video game players
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Fogt, N.F. Fogt, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Fogt, A. Emerson, O. James, W. Kraemer, N.F. Fogt, Human Performance Collaborative, The Ohio State University, Columbus, Ohio, UNITED STATES|W. Kraemer, Department of Human Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|O. James, College of Medicine, School of Heath and Rehabilitation Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|
Commercial Relationships Disclosure: Jennifer Fogt: Commercial Relationship(s);Code F (Financial Support):Nevakar, Eyenovia, Alcon, Innovega, Contamac;Code C (Consultant/Contractor):Alcon, Contamac | Angela Emerson: Commercial Relationship: Code N (No Commercial Relationship) | Onate James: Commercial Relationship: Code N (No Commercial Relationship) | William Kraemer: Commercial Relationship: Code N (No Commercial Relationship) | Nick Fogt: Commercial Relationship(s);Code C (Consultant/Contractor):Oak Ridge Institute for Science and Education

ABSTRACT BODY:

Purpose: This study was conducted to assess differences in oculomotor characteristics of high and low skill level video game players as it has been suggested that the efficiency saccadic eye movements is enhanced with video game play.

Methods: Forty-six collegiate video game players (41 male, 5 female) participated in a combine event in which the game Overwatch was played competitively. Participants consented to complete various tests and questionnaires before and after playing in the competition, including oculomotor testing using a RightEye Vision System, and answering questions about their playtime (hours per week) and skill level in the game. Dynamic visual acuity reaction time, dynamic visual acuity speed, reaction time processing speed, overall reaction time, reaction time saccadic latency, horizontal saccade efficiency, and vertical saccade efficiency from the RightEye was compared for the high skill (Diamond level or higher) and low skill players with a student t test. Oculomotor data were also compared to playtime using linear regression. calculated. Visual acuity and ocular health was assessed at all visits.

Results: Twelve participants were classified as high skilled and 34 were low skilled players in Overwatch. There were no statistical differences ($P>0.05$) when comparing distance visual acuity reaction time, reaction time processing speed, overall reaction time, reaction time saccadic latency, or horizontal saccade efficiency for the high and low skill levels. Dynamic visual acuity speed was 81.5mph in the high skill group and 82.0 in the low skill group, which was significantly different ($P=0.01$). These values are at or close to the maximum tested velocity (82mph). Vertical saccade efficiency, the distance of the eye from the ideal path, was 8.1mm in the high skill group and 6.58mm in the low skill group, ($P=0.047$). Regression analyses found no significant correlations between any of the oculomotor tests and the amount of playtime per week.

Conclusions: Most of the oculomotor skills tested in this study were not related to skill level or the amount of playtime per week in these college video game players.

CONTROL ID: 3711995

SUBMITTER (NAME ONLY): Gary Foulks

TITLE: Eyelid Application of NCX 4251 for Treatment of Signs and Symptoms of Dry Eye Disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Foulks, Retired/Consultant, North Carolina, UNITED STATES|A.C. Kothe, Silver Pharma Consulting, Texas, UNITED STATES|S. Mallick, J.L. Boyer, Nicox Ophthalmics, Inc., North Carolina, UNITED STATES|E. Nowicki, Statistics and Data Corporation, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: An unmet medical need exists for treatments for blepharitis, as well as for additional treatments for dry eye disease (DED) which is reported in some 70 to 80% of patients with blepharitis. We performed a post hoc analysis of a prospective, randomized, double-masked phase 2 clinical trial that evaluated the safety and efficacy of NCX 4251 (fluticasone propionate ophthalmic suspension) 0.1% for the treatment of acute exacerbations of blepharitis.

Methods: A total of 224 subjects with a documented history of blepharitis and exhibiting an acute exacerbation of blepharitis in both eyes (based on minimum scores for eyelid redness, eyelid debris and eyelid discomfort at the Screening and Baseline Visits) were randomized in a 1:1 ratio to NCX 4251 or its vehicle. Subjects performed current standard of care (i.e., daily lid scrubs with dilute baby shampoo) and administered NCX 4251 or its vehicle once daily for 14 days, followed by an additional 14 days of lid scrubs only. Signs and symptoms of blepharitis and DED, as well as safety parameters were assessed. A post hoc analysis was performed on a subgroup of subjects (123 of the 224 subjects) with baseline scores ≥2.0 on a scale of 0 (none) to 4 (severe) for inferior cornea fluorescein staining.

Results: The analysis demonstrated a statistically significant difference between NCX 4251 versus vehicle for change from baseline in eye dryness score as assessed on a Visual Analog Scale (VAS) at Day 8 (earliest timepoint assessed; $p=0.0085$), Day 11 ($p=0.0020$) and Day 15 ($p<0.0016$). Statistically significant differences versus vehicle were also observed in other symptoms of dry eye disease (photophobia, blurred vision, burning/stinging, foreign body sensation, ocular itching, pain) at all timepoints during treatment (Day 8, Day 11 and Day 15). In some symptoms statistically significant treatment effects persisted up to two weeks after the end of treatment. At Day 15, the difference in reduction from baseline in inferior cornea fluorescein staining reached a p-value of 0.0524. NCX 4251 was well tolerated. There were no serious or treatment-related adverse events.

Conclusions: NCX 4251 Ophthalmic Suspension, 0.1% was effective, safe and well tolerated. NCX 4251 has the potential to provide a safe and efficacious short-term treatment for DED. The encouraging findings from this post hoc analysis must be confirmed in larger prospective clinical trials.

CONTROL ID: 3711996

SUBMITTER (NAME ONLY): Olivia Rodts-Palenik

TITLE: Safety and efficacy of the topically administered Rho-kinase inhibitor ripasudil (Glanatec®) in canine ADAMTS10-open-angle glaucoma (ADAMTS10-OAG)

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Rodts-Palenik, C. Harman, A. Cabble, J.P. Steibel, A.M. Komaromy, Michigan State University, East Lansing, Michigan, UNITED STATES|K. Kato, Kumi Animal Hospital, Misato-City, JAPAN|

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ABSTRACT BODY:

Purpose: To assess safety and efficacy of topically administered 0.4% ripasudil ophthalmic solution (Glanatec®; Kowa Pharmaceuticals), a topical Rho-kinase inhibitor, in dogs with ADAMTS10-open-angle glaucoma (ADAMTS10-OAG).

Methods: Eleven three-year old Beagle dogs with ADAMTS10-OAG (five males and six females) were used. The four-week study included a baseline period (week 1), q24h administration (week 2), q12h administration (week 3), and washout period (week 4). Left and right eyes were randomly assigned to receive either balanced salt solution (BSS) sham or ripasudil treatment. Efficacy assessments consisted of diurnal intraocular pressure (IOP) and pupil diameter measurements. Safety was assessed by diurnal conjunctival hyperemia, routine eye examinations, central corneal thickness, and gonioscopy. The linear Gaussian model was used to evaluate the differences in least square means of quantitative outcome measures between eyes that received BSS and ripasudil.

Results: There were no significant differences in mean IOPs between ripasudil- and BSS-treated eyes (baseline period: ripasudil 27.9 ± 1.5 mmHg vs. BSS 27.0 ± 1.5 mmHg; q24h-treatment: ripasudil 28.8 ± 1.7 mmHg vs. BSS 27.7 ± 1.7 mmHg; q12h-treatment: ripasudil 30.8 ± 2.8 mmHg vs. BSS 29.7 ± 2.8 mmHg; washout period: 34.7 ± 2.7 mmHg vs. BSS 32.9 ± 2.6 mmHg). There was also no effect on diurnal pupil diameter. Mild to moderate conjunctival hyperemia developed in both ripasudil- and BSS-treated eyes during the treatment periods (weeks 2 & 3). No other adverse effects were observed.

Conclusions: Due to lack of efficacy, these results do not support future use of ripasudil ophthalmic solution as treatment for canine glaucoma.

CONTROL ID: 3711997

SUBMITTER (NAME ONLY): Mishal Rao

TITLE: Aldose reductase inhibition promotes retinal ganglion cell survival after optic nerve injury

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Huang, K. Chang, Graduate Institute of Medicine, Kaohsiung Medical University College of Medicine, Kaohsiung, TAIWAN|X. Xia, J.L. Goldberg, Spencer Center for Vision Research, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|Y. Huang, Division of Neurosurgery, Department of Surgery, Kaohsiung Medical University Chung Ho Memorial Hospital, Kaohsiung, TAIWAN|M. Rao, C. Meadows, C. Liu, H. Cheng, T. Kuwajima, K. Chang, Department of Ophthalmology, Louis J. Fox Center for Vision Restoration, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|M. Zhou, Y. Cheng, Department of Computational and Systems Biology, Hillman Cancer Institute, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optic nerve trauma induces retinal microglia (RMG) activation and causes irreversible retinal ganglion cells (RGC) loss in mammals. Since aldose reductase (AR) is an inflammatory response mediator and is highly expressed in RMG, we investigated the effects of AR inhibition on RMG activation, RGC survival, and axon regeneration in an optic nerve crush (ONC) model.

Methods: BV2 microglia were utilized to study the effects of AR inhibition on cytokine secretion, cell migration, and microglia-retinal organoid co-culture with LPS exposure. Adult animals underwent ONC (OS) or sham (OD) and were treated with AR inhibitor- Sorbinil or DMSO by intraperitoneal injection. Total protein of ONs and retinae was collected for Western blot probing with Iba-1, AR, GFAP, and GAPDH. Cryosections of ONs and retinae were stained with Iba1, Cleaved Caspase 3, GFAP, and DAPI. RGC survival and regenerating axons were observed 1 and 2 weeks post-ONC (pONC). Flatmount retinae were stained with RBPMS for RGC counting. Regenerative axons were visualized by CTB-555. RGC function was detected by pattern ERG. The study was conducted in compliance with ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and approved by IACUC at University of Pittsburgh. All experiments were performed in independent triplicate and considered significant if $P < 0.05$.

Results: In-vitro, results show that Sorbinil attenuates LPS-induced BV2 activation, migration, and retinal organoid apoptosis in the BV2-organoid co-culture. In-vivo, we observed that Iba-1 and AR protein expression was elevated by ONC and attenuated by Sorbinil in the retina and ON. However, GFAP protein expression was only altered in the retina and reduced by Sorbinil. Detected by cryosection staining, Iba-1+ cells and GFAP+ cells were elevated by ONC and attenuated by Sorbinil. In addition, Sorbinil reduced apoptotic marker expression in the ONC retina. Although experiments of 2 weeks pONC display no change, we did observe that Sorbinil promoted RGC survival, restored RGC function and displayed a trend towards delaying axon degeneration 1 week pONC.

Conclusions: This is the first study to explore the effects of AR inhibition on RMG and RGC in the ONC model. AR inhibition promotes RGC survival, restores RGC function and delays axon degeneration by attenuating RMG activation, which provides a potential therapeutic strategy against ocular inflammatory diseases.

CONTROL ID: 3711999

SUBMITTER (NAME ONLY): Anne Marie Berry

TITLE: Single Nucleus Multi-modal Analysis of the Aging Mouse Retina

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Berry, P. Biswas, S. Pachauri, M. Dagar, R. Ayyagari, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|K. Dang, R. Lancione, S. Preissl, A. Wang, Center for Epigenomics, University of California San Diego, La Jolla, California, UNITED STATES|D. Garland, Harnly LLC, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify cell type-specific and age-related changes in gene expression and gene regulation in the mouse retina.

Methods: Retina and RPE tissue were isolated from 2.5 month-old (n=3) and 21 month-old (n=3) mice and analyzed via single-nucleus RNA-seq and single-nucleus ATAC-seq.

Results: Cluster analysis of the snRNA-seq data (~62,000 nuclei) revealed >30 clusters encompassing known retinal cell-types such as photoreceptors, horizontal cells, RPE, and RGCs. To identify differences in gene expression in the retina between young and old mice, we performed differential expression (2.5 months vs. 21 months) for each cell cluster. Overall, we identified several age-related gene expression patterns across retinal cells. To further investigate these changes, we compared age-related retinal genes to those that have previously been reported in the brain. Strikingly, 168 genes that were identified in retinal tissue were also reported in the brain. 67 of these genes followed the same trends of being up or down regulated with age in both the mouse retina and brain tissue, although there was variation in expression among cell types in both tissues. Among the 67 genes in common between the retina and brain, 10 are known to be associated with retinal disease. Notably, Ahi1, Son, Ubb, Cst3, and Gngt2 were all significantly up-regulated ($p < 0.01$, Wilcoxon Rank-Sum) with aging in the retina via snRNA-seq. These findings were further confirmed by qRT-PCR. Ahi1 was up-regulated in RGCs, (p=8.92E-09) and Gngt2 was up-regulated in cones (p=5.49E-94). Son and Cst3 were both up regulated in all cell types with age with p-values ranging from 1.32E-84-0.015 and 3.12E-132-1, respectively. Ubb was up regulated in all cell types except for rods (P = 1.25E-75 to 1). Out of these 5 genes, only Cst3 did not show the same pattern of expression in the retina and brain.

Conclusions: In the retina, horizontal cells, RPE, and RGC cells showed most of the age-related differences. Several genes that matched the aging pattern in both mouse brain and retina are found to have a significant role in apoptosis and regulation of the apoptotic pathway. Analysis of additional genes/pathways and cell types as well as snATAC-seq data is in progress. This study provides key insight into genes that show altered regulation with age in retinal tissue and contribute to aging.

CONTROL ID: 3712000

SUBMITTER (NAME ONLY): Perry Thompson

TITLE: Subjective Improvement and Complications following Neodymium-doped Yttrium Aluminum Garnet Vitreolysis

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Thompson, J. Olson, Ophthalmology, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|S. Roston, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|D. Mammo, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to identify complications and subjective rates of improvement in a patient population that received Neodymium-doped Yttrium Aluminum Garnet (Nd:YAG) vitreolysis for symptomatic vitreous floaters.

Methods: All patients who underwent Nd:YAG vitreolysis for symptomatic floaters were retrospectively identified from January 1, 2015 to October 31st, 2019 at the University of Minnesota Medical Center. Primary outcomes were adverse events and patient reported subjective symptomatic changes following treatment. Secondary outcomes included visual acuity and intraocular pressure (IOP) before and after treatment. A standardized questionnaire was used to rate floater symptoms on a scale of 1 to 10 after treatments were completed (1=unnoticeable, 10=unbearable). Patients were also asked if they would choose to have another laser treatment for floaters if symptoms return. The paired t-test was used to compare pre- and post-procedure visual acuities, IOP, and questionnaire ratings ($P<0.05$).

Results: 129 treatments in 80 eyes of 62 patients were identified. Twelve (15%) eyes were referred for possible pars plana vitrectomy. Six (7.50%) eyes were lost to follow-up since their last treatment. Three (3.75%) eyes experienced adverse events consisting of a transient IOP increase, posterior subcapsular cataract formation, mild vitreous hemorrhage, and an episode of vasovagal syncope. No complications were visually significant. 53 (85%) patients indicated that they would repeat the laser treatment if symptoms return. Pre- and post-treatment visual acuity was not statistically different. Pre- and post-treatment IOP was statistically different, with lower IOP after treatment. Symptomatic improvement was found to be statistically significant ($p<0.0001$) (Table 1).

Conclusions: Our findings demonstrate high rates of subjective symptomatic improvement with rare complications necessitating regular peri-operative follow-up. None of the encountered complications were visually significant. These results increase the available evidence that Nd:YAG vitreolysis for floaters is a reasonable treatment option for persistently symptomatic syneresis. Future prospective and larger sample size studies are needed to define the incidence of complication with Nd:YAG vitreolysis and the effect on IOP.

CONTROL ID: 3712001

SUBMITTER (NAME ONLY): Karl Stonecipher

TITLE: Optimal pupil size for near-vision improvement without distance-vision loss in the GEMINI studies of AGN-190584 for presbyopia

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.G. Stonecipher, Ophthalmology, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|M. Hom, Canyon City Eyecare, California, UNITED STATES|D.H. Chang, Empire Eye and Laser Center, Bakersfield, California, UNITED STATES|W. Christie, Scott and Christie Associates, Pennsylvania, UNITED STATES|J. Yuan, H. Liu, M.R. Robinson, Allergan, an AbbVie company, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: When pupil size reduces, defocus blur and peripheral aberration decrease to improve vision, while diffraction blur increases and retinal illumination decreases to reduce vision. Since reduced pupil size might have a different impact on distance and near vision for people with presbyopia, this exploratory analysis investigated an optimal range of pupil size that improves near vision while minimally impacting distance vision, based on pooled data from individuals who received AGN-190584 for presbyopia in the GEMINI studies.

Methods: The randomized, double-masked, multicenter, vehicle-controlled, phase 3 GEMINI 1 and GEMINI 2 studies (N=750 total) evaluated safety and efficacy of AGN-190584 (once daily ophthalmic formulation of pilocarpine HCl 1.25% optimized in a proprietary vehicle [now FDA-approved as Vuity™]) in individuals with presbyopia. At 8 prespecified timepoints on Day 30, distance corrected near visual acuity (DCNVA) at 40 cm, corrected distance visual acuity (CDVA) at 4 m, and pupil diameter for the nondominant eye (per Neuroptics' pupillometer) were assessed in mesopic conditions (10-11 lux at target). Analyses were conducted on pupil size when individuals gained ≥3 lines in DCNVA or lost >5 letters in CDVA from baseline on Day 30, by pupil diameter (using measurements at all 8 timepoints).

Results: At day 30 in individuals who received AGN-190584, a trend suggesting a negative correlation between the change in DCNVA from baseline and pupil size was noted; smaller pupil sizes produced greater DCNVA improvement, with 50.6% (n=40/79), 24.0% (n=116/483), 16.6% (n=63/379), and 12.4% (n=73/588) of individuals gaining ≥3 lines for pupil sizes ≤1.5 mm, >2 to ≤2.5 mm, >3 to ≤3.5 mm, and >4 mm, respectively. However, when the pupil size was ≤2 mm, mesopic CDVA appeared to become compromised, with 4.4% (n=11/250) and 10.7% (n=6/56) of individuals losing >5 letters in CDVA for pupil sizes >1.5 to ≤2.0 mm and ≤1.5 mm, compared with 2.1% (n=7/335), 1.7% (n=5/296), and 4.1% (n=20/483) for pupil sizes >2.0 to ≤2.5 mm, >3.0 to ≤3.5 mm, and >4 mm, respectively.

Conclusions: An optimum pupil size should consider both NVA and DVA as a smaller pupil size benefits NVA, while too small a pupil size can compromise DVA. Our study findings suggest that the optimum pupil size should be between 2.0 and 2.5 mm.

CONTROL ID: 3712003

SUBMITTER (NAME ONLY): Maximilian Binter

TITLE: A novel method for isolation of murine trabecular meshwork cells.

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Binter, F. Langer, P. Luedtke, C. Framme, M. Heider, J. Tode, H. Fuchs, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Glaucoma is one of the leading causes of blindness worldwide. The outflow pathway, especially fibrosing trabecular meshwork (TM), plays an essential role in this disease, and the availability of TM cells is crucial for in vitro research. To date, extracting TM cells from mice is complex and relies on injecting magnetic microbeads in the anterior chamber of living mice with subsequent isolation. Therefore, a cost-effective and animal experiment-reducing strategy for the extraction of mouse TM cells is required.

Methods: After Enucleation, eyes were cut in half anterior-to-posteriorly. Lens and posterior segment were removed, Iris and the attached ciliary body were gently pulled backwards and disconnected from the remaining tissue to expose the TM. Cuts anterior and posterior the TM allowed for removal of the TM region. Tissue was cultured facing down in a 6-well filled with Eagle`s Minimum Essential Medium supplemented with 10% FBS. Phagocytotic properties were assessed using fluorescent microbeads, and Immunocytochemistry (ICC) analysis was performed for different markers present in TM cells.

Results: An outgrowth of cells could be observed after 4-7 days. These cells were able to phagocytize fluorescent microbeads and were positive in ICC for collagen IV, fibronectin 1, vimentin and α-smooth muscle actin. Also, typical cross-linked actin networks (CLANs) were expressed after one-week TGFB2 exposure. As previously reported for TM cells, treatment of the isolated cells with 100 nM Dexamethasone for one week led to increased Myocilin expression.

Conclusions: The isolated cells show phagocytotic properties and specific expression of markers reported in TM cells. Therefore, our presented dissection-based method is an inexpensive, reproducible method for isolating TM cells in mice.

CONTROL ID: 3712004

SUBMITTER (NAME ONLY): Raffael Liegl

TITLE: Quantitative Autofluorescence in patients with central serous chorioretinopathy

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Liegl, I. Stasik, B. Lahme, F.G. Holz, C. Weber, Ophthalmology, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: To evaluate characteristics of fundus autofluorescence in patients with central serous chorioretinopathy (CSC). CSC belongs to the spectrum of pachychoroid disease. These are associated with a thickened choroid and a dysfunctional RPE. Quantitative fundus autofluorescence (qAF) is a scanning laser device that is able to measure autofluorescence signals quantitavely. In acute CSC autofluorescence is typically decreased while in chronic forms an increased signal can be found.

This study was performed to quantify the alterations in qAF signals in patients with CSC and in their fellow-eye in comparison with a healthy control group.

Methods: Patients clinically diagnosed with CSC were recruited prospectively. All patients received a full clinical examination including best corrected visual acuity (BCVA), EDI-OCT and qAF. EDI-OCT was acquired using a Spectralis OCT (Heidelberg Engineering) and choroidal thickness was measured in each eye at four different localizations. QAF images were taken with a confocal scanning laser ophthalmoscope (Heidelberg Engineering). QAF values were subsequently assessed using a Delori-grid and mean values of the inner eight ring (IN8) and the middle ring (MID) were collected. Data was collected in an Microsoft Excel spreadsheet and statistical analyses were performed using SPSS statistics.

Results: In total, 66 eyes from 33 patients suffering from CSC were included. Among these 45 eyes had a manifest CSC while 21 fellow eyes did not show signs of CSC. QAF values between these two groups did not show significant differences neither in the IN8 ring ($p=0.46$) nor in the MID ring ($p=0.23$). Mean qAF units in the CSC eyes were 194 (IN8) and 224 (MID) and 182 (IN8) and 205 (MID) for the fellow eyes. We compared our CSC group to a healthy cohort comprising of 18 eyes from 12 patients. QAF units differed significantly compared to both CSC manifest and fellow eyes.

Conclusions: QAF is a useful technology to assess alterations of the RPE. Our data show that patients with CSC have increased qAF values in comparison to healthy controls. In fellow-eyes of CSC patients, qAF signals do not differ significantly from manifest CSC eyes. This finding suggests that RPE alterations might be present not only in the manifest CSC eyes, but also in their fellow-eyes, even though these are clinically unremarkable.

CONTROL ID: 3712005

SUBMITTER (NAME ONLY): Constance Weber

TITLE: Real-world outcomes following Paul Glaucoma Implant (PGI) surgery

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Weber, R. Liegl, F.G. Holz, K. Mercieca, Ophthalmology, Universitatsklinikum Bonn, Bonn, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Glaucoma is one of the leading causes of irreversible blindness worldwide. Drainage devices are among the most popular surgical procedures to lower intraocular pressure (IOP) in order to prevent glaucoma progression. The Paul Glaucoma Implant (PGI) is an innovative device with a smaller size and internal diameter compared to more “traditional” tubes such as the Ahmed and Baerveldt. It was developed to overcome typical drawbacks of these tubes, including early failure in the former and post-operative hypotony and delayed function in the latter. In theory, a smaller tube should also result in reduced corneal endothelial cell loss over time. This large descriptive case series shows the one-year results of the very first patient cohort receiving a PGI in Germany.

Methods: A prospective database of patients undergoing PGI implantation at the University Eye Hospital in Bonn was created in a Microsoft Excel spreadsheet. Data of preoperative and follow-up visits have been collected until now and the database is continuously updated at every visit. Major outcomes were IOP, number of glaucoma medication, best corrected visual acuity (BCVA), visual field results, corneal endothelial cell count and complications. Statistics were obtained with SPSS statistics for Windows.

Results: A total of 60 eyes from 58 patients were included. The mean review period was 8 months (range from 1-13 months). The mean IOP at baseline was 26 mmHg. The PGI led to a mean IOP reduction of 64%. The mean IOP was 9 mmHg at 6 weeks, 11 mmHg at 3 months and 12 mmHg at 6 months postoperatively. Complication rates were low, with 5% (n=3) of patients having a temporary hyphema postoperatively whilst another 5% (n=3) developed a numerical hypotony postoperatively that resolved without an additional intervention. Only 3 % (n=2) needed topical glaucoma medication at six months postoperatively.

Conclusions: The PGI is a safe and effective new glaucoma drainage device that reduces IOP effectively with a low complication rate. Thus, it represents an innovative new treatment modality. Further studies are necessary to evaluate its long-term effect.

CONTROL ID: 3712006

SUBMITTER (NAME ONLY): gerami seitzman

TITLE: A Metagenomic Deep Sequencing Analysis of Infectious Conjunctivitis in Burkina Faso, Africa.

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. seitzman, K. ruder, C. Chen, L. Zhong, E. Colby, E. Lebas, M. Deiner, A. Hinterworth, T. Lietman, T. Doan, Francis I Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|M. Bountogo, A. Sié, B. Coulibaly, Ophthalmology, Nouna Health Research Center, BURKINA FASO|

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ABSTRACT BODY:

Purpose: Burkina Faso, in West Africa, is one of many countries that experience frequent seasonal outbreaks of presumed infectious conjunctivitis of unknown etiology. This study leverages the hypothesis free diagnostic tool of metagenomic deep sequencing (MDS) to determine the local causes of infectious conjunctivitis

Methods: Inclusion criteria required acute conjunctivitis symptoms for less than 14 days. Sterile polyester applicators (Puritan) were used to swab the lower conjunctival fornix of each eye. All swabs were immediately placed in DNA/RNA-Shield (Zymo Research). Details of sequencing, library preparation, and bioinformatics analyses have been previously described.

Results: Samples were obtained from 19 participants. 47% were female. The average age was 9 years. Both eyes were affected in 15/19 cases (79%). The predominant ocular presenting symptom was purulent discharge, present in 17/19 (89%) cases. MDS identified a virus as the causative pathogen 53% (10/19) of cases. Bacterial pathogens were identified in 16% (3/19) of cases. A mixed bacterial and viral infection was noted in 2/19 (11%). Of the 10 viral etiologies identified, an adenoviral species was identified in 2 cases. This represents 20% of all viral pathogens and 11% of all cases. Other viruses identified as pathogenic include rhinovirus, influenza A and herpes viridae including herpes simplex virus (HSV), varicella zoster virus (VZV), Epstein Barr virus (EBV) and cytomegalovirus (CMV). The five bacteria identified as causative etiologies were Streptococcus pneumonia, Corynebacterium mastiditis, Moraxella catarrhalais, Neisseria meningititis, and Hemophilus influenza

Conclusions: Causative pathogens of patients presenting with acute, mostly purulent, clinically presumed infectious conjunctivitis in Burkina Faso are surprising. Adenoviridae were isolated in only two cases (11%). Bacterial pathogens only were identified in three cases. This study suggests that clinicians' clinical suspicions of causative etiologies for infectious conjunctivitis may not be accurate. Similarly, classic teaching for what clinical findings predict which pathogen (viral vs bacterial) may need to be critically re-evaluated. Local surveillance with pathogen identification of seasonal and epidemic conjunctivitis outbreaks is necessary to determine definitive etiologies determine appropriate treatment strategies and inform region-specific public health initiatives.

CONTROL ID: 3712007

SUBMITTER (NAME ONLY): Matthew Tarchick

TITLE: Developmental Progression of X-Linked Retinoschisis in Mouse Rods

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: X-linked Retinoschisis (XLRS) is an early onset degenerative retinal disease that causes cystic lesions in the middle layers of the retina, a loss of visual acuity, and decreased contrast sensitivity. XLRS is caused by mutations in Retinoschisin 1 (RS1) which encodes the secreted protein retinoschisin (RS1). Rs1-mutant mouse models develop key hallmarks of XLRS including intraretinal schisis and reduced ERG b-waves. The disease phenotype is present at early ages leading to the question of whether retinal development is ever normal. Here we explore the early ERG properties of Rs1 mutant mice, using an ex vivo system and pharmacological blockade to isolate ERG components generated by photoreceptors, depolarizing bipolar cells (DBCs) and Müller glial cells (MGCs).

Methods: We recorded light evoked responses from WT and two Rs1-mutant strains $Rs1^{KO}$, $Rs1^{C59S}$ at P13, an age where Rs1 mutants have developed intraretinal schisis. After dark adaptation, mice were sacrificed and retinae were isolated and mounted on a custom ERG chamber. ERGs were evoked by 1-4 ms pulses from a LED band-passed at 505±20 nm in triplicate. Photon intensity was varied from 5-50,000 photons/um^{-2}. ERGs were recorded while retinae perfused by normal Ringers, Ringers contains barium chloride (100 µM) and then also LAP-4 (14 µM). Response components reflecting MGCs and DBCs were estimated by waveform subtraction.

Results: In comparison to WT, ERGs of Rs1 mutant mice had comparable b-waves, and a tendency toward larger a-waves, while MGC responses were only larger in $Rs1^{C59S}$ mice.

Conclusions: These results indicate that Rs1 mutations have less impact on the rod pathway at P13 than at later ages. Ongoing studies will determine the ERG phenotype at still younger ages.

CONTROL ID: 3712008

SUBMITTER (NAME ONLY): Pascale Charpentier

TITLE: Comparison of integrin protein expression in native and cultured corneal endothelium.

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Charpentier, S. Proulx, Ophtalmology and ORL-CCF, Universite Laval, Quebec, Quebec, CANADA|P. Charpentier, S. Proulx, Axe médecine régénératrice, Centre de recherche du CHU de Quebec-Universite Laval, Quebec, Quebec, CANADA|M. Theriault, Hopital Maisonneuve-Rosemont, Montreal, Quebec, CANADA|J.R. Casey, Ophtalmology and Visual Sciences, University of Alberta, Edmonton, Alberta, CANADA|J.R. Casey, Biochemistry, University of Alberta, Edmonton, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: Although many integrins have been previously identified in native corneal endothelium, integrin expression between native and cultured cells remains incomplete. The goal of this study is to compare the integrin expression profile of native corneal endothelium and of cultured corneal endothelial cells (CECs), using both primary cultures and an immortalized cell line.

Methods: Human CECs were isolated from healthy eye bank corneas (n=1) and cultured on plastic until first passage. Immortalized CECs (HCEnC21T; P26) and primary cultures of CECs were seeded on glass coverslips at an initial seeding density of 10,000 cells per cm^2 and cultured for 7 days before fixation (90% acetone). Fixed cells, and fixed native cornea (n=1), were immunostained against integrins subunits (α1, α2, α4, α5, α6, α10, α11, αv, β1, β4 and β5), and photographed (Zeiss LSM-800 confocal microscope).

Results: Collagen-binding integrin subunit α1 was expressed in CEnC21T cells, whereas α1 and α2 were present in primary cultures of CECs and native corneal endothelium. Subunits α10 and α11 were absent from CEnC21T, native CECs and native endothelium. Laminin-binding integrin subunits α6 and β4 were absent from cultured CECs, in both the cell line and the primary cultures, but were expressed in native endothelium. For the RGD-binding integrin subunits, α4, α5, αv and β5 were absent in cultured CECs (in both the cell line and the primary cultures), whereas native corneal endothelium expressed the four of them. Integrin subunit β1, which can pair with a variety of different α subchains to form 12 different known integrins, was expressed in cultured CECs as well as in native corneal endothelium.

Conclusions: The integrin expression profile of cultured CECs was different from the profile of native corneal endothelium, namely the loss of α4, α5, α6, αv, β4 and β5 with cultured CECs, demonstrating that cell culture conditions affect integrin expression. While much has been learned about integrins, additional knowledge on the roles of integrins in the adhesion of CECs is needed, as loss of adhesion may be implicated in corneal diseases.

CONTROL ID: 3712009

SUBMITTER (NAME ONLY): Braedon Murdock

TITLE: Doxycycline Use and Risk of Post-operative Complications Following Keratorefractive Surgery

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Doxycycline is a known treatment for meibomian gland disease (MGD), which is a major risk factor for the development of dry eye syndrome (DES) and recurrent corneal erosion (RCE). The degree to which pre-existing corneal conditions pose a risk for complications after keratorefractive surgery (KRS) is as yet undetermined. This study compared differences in outcomes in the 1-year postoperative period following KRS between patients with and without a 1-year history of doxycycline use.

Methods: A retrospective cohort study was conducted using TriNetX, a real-time, national, federated research network. Patients who underwent KRS were identified by Current Procedural Terminology (CPT) code and stratified into two cohorts based on their history of doxycycline use. Each subject was then matched to a control via 1:1 propensity score matching based on age, gender, BMI, and medical comorbidities such as essential hypertension, diabetes mellitus, and chronic lower respiratory diseases. The primary endpoint of the study was the comparative 1-year postoperative incidence of the following outcomes: DES, RCE, secondary corneal edema, corneal scar or opacity, corneal ectasia, acute conjunctivitis, diffuse lamellar keratitis, corneal neovascularization, vitreous degeneration, ischemic optic neuropathy, vitreous hemorrhage, retinal detachment or break, retinal edema, and cystoid macular degeneration.

Results: A total of 2,056 patients were included in the analysis with 1,028 patients in each cohort after propensity matching. The doxycycline cohort had a statistically significant higher risk of developing DES (RR 1.46, 95% CI 1.2-1.78; RD 6.32%, 95% CI 3.1-9.55) and RCE (RR 2.8, 95% CI 1.37-5.73; RD 1.75%, 95% CI 0.59-2.91) within 1 year of undergoing KRS compared to matched controls. No significant differences were detected between the two cohorts for the other 1-year postoperative outcomes.

Conclusions: Dry eye syndrome and RCE are commonly seen in the postoperative period of KRS and can impact the quality of life in patients. In this study, patients with a history of doxycycline use were significantly more likely to develop DES and RCE following KRS. All other assessed clinical outcomes revealed no significant difference. The severity of pre-existing corneal conditions should be considered when evaluating patients for KRS and discussing outcomes with patients both pre- and post-operatively.

CONTROL ID: 3712010

SUBMITTER (NAME ONLY): Sarah Singh

TITLE: Comparing distance-center and near-center multifocal soft contact lenses for myopia control

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Singh, E. Tian, Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies have shown that multifocal soft contact lenses (MFSCLs) are effective in slowing myopia progression. While distance-center (DC) lenses are used more commonly and have been investigated in multi-center clinical trials, near-center (NC) lenses have not, despite having more commercially available and daily disposable options. This retrospective study was designed to compare the myopia controlling effect of DC and NC lenses.

Methods: A retrospective analysis of patient data from the UC Berkeley Myopia Control Clinic, captured between 2013 and 2019, was performed to compare rates of myopia progression between patients using NC and DC MFSCLs. Participants had between -0.25D and -6.00D spherical equivalent refraction at baseline and were patients in the clinic for at least 4 months. We included participants that had < 1.50D of anisometropia and < -1.75D of cylinder at any axis. Patients were excluded if they were concurrently using another method of myopia control, such as topical atropine. Additional exclusion criteria were a strabismus observed during a visit in clinic, history of amblyopia, or pathology such as retinopathy of prematurity. Myopia progression rates were estimated using linear regression of autorefraction measurements.

Results: 56 DC and 24 NC subjects were analyzed. There was no significant difference between the right and left eyes, so only right eye data is reported. At baseline, mean [SD] age was 10.9 [2.6] for the DC group and 11.3 [2.2] for the NC group. 32 [54.1%] were female in the DC group, and 13 [54.2%] in the NC group. After treatment, the estimated monthly progression rates were -0.032 D/month (95% CI, -0.054 to -0.0095, SD 0.082) for the DC group and -0.054 D/month (95% CI, -0.090 to -0.018, SD 0.017) for the NC group. There was no significant difference ($p = 0.2859$) between monthly progression rates between the two groups, which can be extrapolated to annual progression rates of (-0.032 x 12) = 0.38 D/year for the DC group and (-0.054x12) = 0.65 D/year for the NC group.

Conclusions: NC and DC MFSCLs slow myopia progression at a similar rate. With more commercially available and daily disposable options, near center lenses could be considered to slow progression in young myopic patients. While the exact mechanism of how MFSCLs slow myopia progression is unknown, these results suggest that competing hyperopic and myopic defocus across the entire retina is important.

CONTROL ID: 3712015

SUBMITTER (NAME ONLY): Antonio Yaghy

TITLE: A new method for calculating macular neovascularization vessel density in patients with neovascular age-related macular degeneration: A comparison

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Yaghy, N.K. Waheed, OCT Lab, New England Eye Center, Boston, Massachusetts, UNITED STATES|A.Y. Alibhai, Boston Image Reading Center, Boston, Massachusetts, UNITED STATES|M.C. Liang, N.K. Waheed, Retina, New England Eye Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular neovascularization (MNV) vessel density (VD) has been traditionally measured by manually delineating the borders of the MNV lesion on en face OCTA and processing with software for automatic thresholding, skeletonization, and VD calculation. This area-dependent method might be inaccurate as the MNV lesion size changes with treatment (Figure 1). We propose a new, quicker, area-independent method to measure MNV VD that gives comparable results to the traditional method.

Methods: A retrospective analysis was performed to measure the VD of 30 MNV lesions using en face OCTA images across four quarterly visits (N=120) using both methods. The new method consisted of drawing a fixed pattern around the MNV lesion only once, registering both the pattern and image for subsequent visits, and finally calculating the respective VD. (Figure 2) Ten OCTA volumetric scans of MNV lesions were selected from three different OCTA machines (Angiovue®, Cirrus5000®, and PLEX® Elite). For optimal MNV lesion display, different OCT slabs were selected for all images belonging to each of the OCTA machines: choriocapillaris slab for Angiovue®, RPE-RPE fit slab for Cirrus5000®, and custom global slab for PLEX® Elite. The OCTA Analysis Toolbox software was used for manual delineation of the MNV lesion, skeletonization, and VD calculation.

Results: Median area-independent MNV VD was significantly lower than area-dependent MNV VD for all visits and across all devices ($p \leq 0.005$) except for visit 3 ($p=0.052$) and visit 4 ($p=0.052$). Spearman's rank-order correlation showed a strong relationship between MNV VD measured using both methods ($\rho > 0.5$) in all cases across all visits except the Angiovue cases at 3 months follow-up ($\rho = 0.3$). On Bland-Altman analysis, all measured values for all three OCTA devices fell between the upper and lower limits of agreement.

Conclusions: Area-independent MNV VD measurements were reliable and comparable to results obtained via the more traditional, area-dependent VD measurement. Moreover, these measurements were easier and less time-consuming to perform as the fixed pattern used to delineate the MNV lesion at initial visit is registered for subsequent visits.

CONTROL ID: 3712017
SUBMITTER (NAME ONLY): Jelle Vehof
TITLE: The work-related burden of dry eye disease
SESSION TITLE: Dry Eye, Clinical
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: To investigate the relationship between dry eye disease (DED) and work functioning, unemployment, absenteeism, and worry about job loss in a general population.

Methods: 89,215 subjects (18–96 years, 59.5% female) from the Dutch population-based Lifelines cohort were included. DED was assessed using the validated Women's Health study (WHS) questionnaire (either a clinical diagnosis of dry eye or both dryness and irritation symptoms often or constantly present). Unemployment, absenteeism, and worry were assessed with single-item questions. Work functioning was assessed in 36,399 working participants using the validated work role functioning questionnaire (WRFQ) 2.0. The relationships between DED and work functioning, unemployment, absenteeism, and worry about job loss were assessed with logistic regression models, corrected for age, sex, body mass index (BMI), income, education, smoking, and 48 comorbidities associated with dry eye.

Results: 9.1% of participants were defined as having DED: 8.5% had a previous clinical diagnosis of dry eye and 1.9% had highly symptomatic dry eye. Participants with DED had impaired overall work functioning compared to those without DED (49.4% vs 41.1%, OR 1.24, 95% CI 1.14-1.35, P=0.002, corrected for everything). Absenteeism was only slightly increased in DED participants (OR 1.10, 95% CI 1.01-1.20, P=0.04). DED carried a similar risk of impaired work functioning as rheumatoid arthritis and COPD. For participants with highly symptomatic dry eye (often or constant symptoms) impaired work functioning was even higher (60.3%) and at the level of obstructive sleep apnea syndrome and depression. The impaired work functioning scores seen with increasing symptom load were greater for undiagnosed subjects than for diagnosed subjects (interaction term 'clinical diagnosis * dry eye symptoms' P=0.002). After correction for comorbidities, DED was not associated with unemployment (OR 1.07, 95% CI 0.94-1.21, P=0.32), but remained tied to increased worry about job loss (OR 1.23, 95% CI 1.10-1.36, P<0.0005).

Conclusions: In this large population-based study, DED was particularly linked to a substantially impaired work functioning, and less to unemployment and absenteeism. The impact of DED on work functioning is comparable to that of other severe chronic disorders, and undiagnosed subjects may be more affected. This highlights the importance of recognizing DED as a severe disorder and providing a diagnosis.

CONTROL ID: 3712018

SUBMITTER (NAME ONLY): Fiona Waters

TITLE: Educate. Participate. Innovate: Training and empowering patients living with rare, degenerative retinal diseases as active stakeholders in medicines research, development, and policy.

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Waters, Retina International, IRELAND|

Commercial Relationships Disclosure: Fiona Waters: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is an increasing demand for patient involvement in medical innovation at research, industry, and policy levels. Retina International (RI) has observed an unmet need amongst its community, where the knowledge and skills to effectively engage in an advisory or advocacy capacity are not developed. As the demand for patient expertise increases, so must our panel of informed patient advocates.

Methods: RI developed a 3-month training programme. 11 globally representative trainees, consisting of 9 patient representatives and 2 PhD candidates were selected following application. The curriculum was co-created with subject matter experts (SMEs) and patients. Three learning streams were designed: 1) Education: Genetic Testing, Patient Registries, PROMs, Clinical Trials, and Regulation & HTA; 2) Participation: Ethics, Advisory Boards, and Health Futurism; and 3) Innovation: Rare Disease Policy, Data Generation, and the Student Project, where trainees were tasked with generating data via surveys and designing their own advocacy strategies. A blended learning approach consisting of independent e-learning, interactive seminars led by an SME, and skills development workshops was used.

Results: Analysis of the programme is underway. 9 of 11 participants completed the programme on schedule. Preliminary findings highlight increased understanding of the scope, processes, and role of patients in medicines R&D for retinal diseases, and the policy actions that support them. The breadth and depth of topics covered, as well as the side-by-side learning of patients and researchers was of high value to both groups. The student project was also reported as a practical, confidence-building experience. As a result of the skills developed, 5 graduates have enrolled in RIs 2022 policy action taskforces to date.

Conclusions: This pilot has demonstrated the potential impact of a tailored and education programme, that develops advisory and advocacy skills in retina patients. Results of this programme by way of increased engagement of graduates with RI projects is already evident. This engagement is predicted to yield broader representation of effective retina patient experts at a global and national level, leading to patient-centred innovations in medicines R&D and health policy.

CONTROL ID: 3712019

SUBMITTER (NAME ONLY): Jasmin Rezapour

TITLE: Multi-Modal deep learning classifier for glaucoma diagnosis using wide optic nerve head cube scans in eyes with and without high myopia

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rezapour, A. Belghith, C. Bowd, M. Christopher, R.N. Weinreb, L. Zangwill, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|J. Rezapour, Ophthalmology, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|J. Jonas, Ophthalmology, Ruprecht Karls Universitat Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To evaluate the diagnostic accuracy of a multi-modality deep learning (DL) classifier using wide optical coherence tomography (OCT) optic nerve head (ONH) cube scans in eyes with and without axial high myopia.

Methods: This cross-sectional study included 371 primary open-angle glaucoma (POAG) eyes (mean (95% CI) visual field MD -3.78dB (-4.16, -3.41)) and 86 healthy eyes without axial high myopia (axial length (AL) <26 mm) and 92 POAG eyes (mean (95% CI) visual field MD -4.05dB (-4.85, -3.26)) and 44 healthy eyes with axial high myopia (AL≥26mm) from the Diagnostic Innovations in Glaucoma Study (DIGS). We used OCT cube scans of 30deg x 25deg (8.7 x 7.3mm) centered on the ONH, which was formed by 121 horizontal B-scans. The multi-modal DL classifier combines the output features of 3 individual VGG16 models applied on the Spectralis ONH cube scans as follows: 1) texture-based enface image, 2) circumpapillary retinal nerve fiber layer (cpRNFL) thickness map image and 3) scanning laser ophthalmoscope (SLO) image. Area under the receiver operating curves (AUROC) adjusted for both eyes, AL, age, Bruch's membrane opening area and image quality were used to compare different approaches.

Results: Adjusted AUROCs were 0.91 (95% CI = 0.87, 0.95) for the multi-modal DL model, and significantly higher (p-value ≤0.05 for all comparisons) than individual VGG16 model: 0.83 (0.79, 0.86) for texture based en-face image, 0.84 (0.81, 0.87) for cpRNFL thickness map, and 0.68 (0.61, 0.74) for SLO image. A subset analysis of high myopic eyes with AL ≥26mm showed significant higher diagnostic accuracy (AUROCs (95% CI)) of multi-modality DL model 0.89 (0.86, 0.92) compared to texture based en-face image 0.83 (0.78, 0.85), cpRNFL 0.85 (0.81, 0.86) and SLO image 0.69 (0.63, 0.76) with p-value ≤ 0.05 for all comparisons.

Conclusions: Combining the cpRNFL thickness map with texture based en-face images showed higher ability to discriminate between healthy and glaucoma in high myopic eyes than thickness maps alone. While more work is needed, it is likely that texture based en-face images have a role in differentiating high myopic eyes with glaucoma from those without glaucoma.

CONTROL ID: 3712022

SUBMITTER (NAME ONLY): Ana Villaplana Velasco

TITLE: Decreased retinal vascular complexity is an early biomarker for myocardial infarction during the next 5 years after ophthalmic examination

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Villaplana Velasco, J. Englemann, K. Rawlik, O. Canela-Xandri, T. MacGillivray, K. Rannikmae, A. Tenesa, M. Bernabeu, E. PAIRO-CASTINEIRA, The University of Edinburgh College of Medicine and Veterinary Medicine, Edinburgh, Edinburgh, UNITED KINGDOM|M. Rama Krishnan Mookiah, E. Trucco, University of Dundee, Dundee, Dundee, UNITED KINGDOM|

ABSTRACT BODY:

Purpose: There is increasing evidence that retinal vascular complexity (D_f) might offer earlier insights into myocardial infarction (MI) progression. Our recent study indicates that D_f predictive power is as important as systolic blood pressure and body-mass index in predicting MI risk. We present here a study analysing D_f utility period on predicting MI over the past 8 years succeeding the ophthalmic examination.

Methods: We used a subset of 516 incident MI cases and 516 random and age-matched controls from UK Biobank (UKB) that had good quality images from both eyes. We obtained D_f from this imaging subset with VAMPIRE 3.1 software and calculated a polygenic risk score for coronary artery disease (PRS_{CAD}) for each participant using the summary statistics from the CArdioGRAM consortium and PRSice2 software. We developed a MI predictive model combining sex, body-mass index, SBP, smoking, both eyes D_f, PRS_{CAD} and a random forest algorithm. Predicted MI risk obtained through internal cross-validation was next used to separate individuals at high and low MI risk(high MI-risk>0.5 and low MI-risk=<0.5). We investigated potential survival rate differences between these by completing Kaplan-Meier curves and a Log-rank test. We assessed D_f utility period by comparing in time windows of three years the MI risk accuracy of our model with the one from a reproduction of an established risk model named SCORE, based only on epidemiological variables

Results: There is a significant survival rate difference(Log-rank Test P-value<10^{50}) between high vs low MI risk groups. Longitudinal analysis on the timeline of these MI events suggest that our model yields the greatest accuracy during the first 5 years since the ophthalmic examination($Accuracy_{0\text{-}2}$=0.749, $Accuracy_{3\text{-}5}$=0.787, and $Accuracy_{6\text{-}8}$ =0.732). Time-matched comparisons between our MI risk predictions and SCORE-based estimations shows that our approach achieves a higher accuracy during the first 5 years(Accuracy-$SCORE_{0\text{-}2}$=0.697, Accuracy-$SCORE_{3\text{-}5}$= 0.734). Afterwards, the accuracy between both MI risk models is similar(Accuracy- $SCORE_{6\text{-}8}$=0.708).

Conclusions: This study discloses a promising holistic strategy that can prevent MI incidence and triage those with an elevated hazard. Our project highlights the value of easily accessible vascular imaging phenotypes and their promising application in personalised medicine.

CONTROL ID: 3712025

SUBMITTER (NAME ONLY): Charles Blizzard

TITLE: Safety and Pharmacodynamic Assessment of Repeated Intracameral Travoprost Implant Administration in Beagle Dogs

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.D. Blizzard, C. Patel, J. Hartman, S. Serell, K. Yeh, A. Vanslette, P.K. Jarrett, M. Goldstein, R. Gurses-Ozden, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Charles Blizzard: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Chintan Patel: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Jeremy Hartman: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Sean Serell: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Kevin Yeh: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Andrew Vanslette: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Peter Jarrett: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Michael Goldstein: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Rabia Gurses-Ozden: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix

ABSTRACT BODY:

Purpose: Hydrogel-based, intracameral travoprost implant (OTX-TIC) is designed to deliver sustained-release travoprost to the anterior chamber for the treatment of glaucoma and is currently in a Phase 2 clinical trial. The purpose of this study was to evaluate the safety, tolerability and pharmacodynamic (PD) profile of repeated OTX-TIC administrations in a canine model.

Methods: Normotensive female beagle dogs received either one placebo vehicle implant (Group 1), one 26 µg OTX-TIC (Group 2), two 26 µg OTX-TIC (Group 3) or one 13 µg OTX-TIC (Group 4) implant injected intracamerally into the right eye (n = 8/group). Groups 1, 2 and 3 were dosed on Days 1 and 127, and Group 4 was dosed on Days 1, 57, 113, and 169. Group 2 represented an intended clinical dose and Group 3 provided a 2X dose multiple and 2X implant safety factor for travoprost drug and implant biomaterial. Group 4 used a shorter persisting hydrogel with a daily travoprost dose comparable to Group 2. Intraocular pressure (IOP), endothelial cell count and corneal thickness were collected. Ocular exams were performed with slit lamp and graded using a modified Hackett-McDonald Scoring System which included conjunctival hyperemia (0 = normal to 3 = severe) and pupillary reflex (0 = normal to 3 = miotic pupil).

Results: OTX-TIC was well-tolerated following repeated administration through 30 weeks. No signs of intraocular inflammation (aqueous cell or flare, vitreous cell) were observed in any eyes of all groups during the study. Mean reduction in IOP (standard deviation) compared to baseline was 7.7% (10.2), 25.7% (13.4), 25.3% (16.2), and 31.0% (12.0) for Groups 1, 2, 3 and 4, respectively throughout the study period. Conjunctival hyperemia and miosis, both known PD responses to travoprost in dogs, were observed in OTX-TIC treated eyes for 30 weeks. Mean conjunctival hyperemia scores and pupillary reflex scores were higher in OTX-TIC treated eyes (Groups 2, 3 and 4) compared to placebo vehicle (Group 1) at all study timepoints.

Conclusions: Multiple, repeated OTX-TIC administrations were generally safe and well-tolerated with no signs of inflammation observed and produced a clinically meaningful reduction in IOP through 30 weeks in beagles. OTX-TIC is currently being investigated in a Phase 2 clinical trial in the US.

CONTROL ID: 3712026

SUBMITTER (NAME ONLY): Vahid Mohammadzadeh

TITLE: Detection of Glaucoma Progression on Longitudinal Series of Macular Optical Coherence Tomography Angiography Maps with a Deep Learning Model

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Mohammadzadeh, S. Moghimi, T. Nishida, A. Kamalipour, M. Christopher, L. Zangwill, R.N. Weinreb, Ophthalmology, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|Y. Liang, P. Xie, T. Javidi, Department of Electrical and Computer Engineering, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To design a deep learning (DL) model for detection of glaucoma progression with longitudinal series of macular optical coherence tomography angiography (OCTA) images.

Methods: Two-hundred and two eyes of 134 patients with open angle glaucoma were included. Eligible eyes were required to have 4 visits and 2 years of follow up of OCTA. Glaucoma progression was defined as having 24-2 visual field (VF) mean deviation (MD) rates of < 0 and P value < 0.05 during the follow-up. The data were split with 80% in the training dataset and 20% in the testing dataset. The baseline and final macular OCTA images were aligned according to the center of fovea avascular zone automatically, by checking the correlation of the two images on vector space (Figure 1). To improve the generalizability of the model, data augmentation such as random cropping and resizing were used to increase the training data. For the classification model, a customized convolutional neural network (CNN) with a multi-layer perceptron (MLP) classifier was used. The baseline and final images for each eye were concatenated along the color channel and then sent into the CNN for classification. The cross entropy was used as the loss function for training and a weight of 0.13 was assigned to the non-progressing samples and 0.87 for progressing samples. The performance of the model was evaluated using the area under receiver operating characteristics (AUC), sensitivity, specificity and accuracy. As a comparison method, a logistic regression model was performed to evaluate the performance of whole image vessel density (wiVD) loss on detection of glaucoma progression.

Results: The average (range) follow-up time was 3.5 (2.4-5.5) years and average (standard deviation) baseline VF MD was –3.4 (±5.0) dB. Twenty-eight (14%) eyes demonstrated glaucoma progression. The AUC for detection of progression from macular OCTA images of the DL model was 0.81and for the logistic regression model 0.66 (Figure 2). The sensitivity, specificity and accuracy of the DL model on the testing dataset was 67%, 83% and 80%, respectively.

Conclusions: The optimized DL model detected glaucoma progression based on longitudinal macular OCTA images with high performance. Implementation of this DL model, after external validation, could enhance detection of glaucoma progression.

CONTROL ID: 3712028

SUBMITTER (NAME ONLY): Anna Potenski

TITLE: Elucidating endothelial caspase-9 signaling pathways in retinal vein occlusion.

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Potenski, Molecular Pharmacology and Therapeutics, Columbia University, New York, New York, UNITED STATES|C.M. Troy, M. Choi, J. Smart, Pathology, Columbia University, New York, New York, UNITED STATES|C.M. Troy, Neurology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-apoptotic induction of endothelial caspase-9 by retinal vein occlusion (RVO) sets off a signaling pathway causing edema, BRB breakdown, and eventual neuronal loss, however the exact mechanism of this pathway is still unknown. Previous studies by our lab have shown that knocking out endothelial caspase-9 diminishes the amount of edema and neuronal damage after RVO, suggesting that the endothelial caspase-9 is motivating the signaling pathway. Since this large induction of caspase-9 seems to be non-apoptotic which is atypical of the normal function, we are determining if the upstream activation of caspase-9 by Apaf-1 is the driving force behind the non-apoptotic signaling. These experiments will be carried out using inducible endothelial cell Apaf-1 knock out mice (Apaf-1 iECKO) and WT littermates who are injured with retinal vein occlusions.

Methods: 2-month-old Apaf-1 iECKO and WT littermate mice will undergo the RVO procedure previously described in Avrutsky, et al. Live imaging readouts will be used to track the pathology of the animals and compare to previous data from the caspase-9 iECKO mice. Immunohistochemistry and western blotting will be used to determine the presence of a known downstream target caspase-7, other caspases, and proteins known to be associated with other cell death pathways. TUNEL staining will be used to measure the amount of cell death present after injury in knockout and wild type littermates.

Results: Apaf-1 iECKO mice show less edema after injury than Apaf-1 WT littermates measured using total retinal thickness. They also do not show the same level of thinning 8 days post injury suggesting that there is more neuronal death in the WT animals than the KOs. Apaf-1 iECKOs have lower expression of caspase-9 and direct target caspase-7 as well as less TUNEL staining, indicating less neuronal death.

Conclusions: The activation of caspase-9 specifically in endothelial cells seems to be different than its canonical function however we see that Apaf-1 iECKO is protective in many of the same ways that caspase-9 iECKO is. This suggests that although endothelial caspase-9 is not leading to cell death within the endothelial cells, it is still being activated by Apaf-1. This suggests that the activation of caspase-9 is not driving the non-apoptotic function in endothelial cells and may instead be due to the downstream signaling.

CONTROL ID: 3712029

SUBMITTER (NAME ONLY): Qinqin Zhang

TITLE: Capillary velocimetry on human retina---a preliminary study

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q. Zhang, X. Zhou, R.K. Wang, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the capillary blood flow velocity on human retina with various pathologies in vivo based on commercial OCTA device with modified scanning protocols

Methods: A 1060 nm SS OCTA engine (PLEX® Elite 9000, ZEISS, Dublin, CA) with 200 kHz A-line rate and motion tracking mechanism was utilized in our study. New scanning protocol with 200 A-linesx200 B-scans covering ~ 2mmx2mm with 10 repetitions was designed and implemented on the device for capillary velocimetry estimation. The time interval between the adjacent B scans was ~1ms that gives a distinguishable velocity range from 0 mm/s to ~0.5mm/s according to the theorical analysis. The mean frequency (MF) of signal was calculated by eigen-decomposition (ED) approach representing the mean velocity of blood flow within the scanned tissue volume. Depth-resolved retinal and choroidal layers were segmented to investigate the speed variations in different plexus, including the superficial retinal layer (SRL), deep retinal layer (DRL), and choriocapillaris (CC) layers. Color images were utilized to demonstrate the flow speed with red-ish color indicating the fast flow, and blue-ish color indicating the slow flow. To keep the consistency, a fixed display range ([0, 700 Hz]) was applied to all the color images, which was only determined by the time interval of the scanning protocol.

Results: Ten normal eyes (mean age 27.7±3.3), twelve NPDR eyes (mean age 57.2±5.9) and twenty PDR eyes (mean age 56.2±16.6) were recruited in this preliminary study. The MF has shown the capability of differentiating the flow speed at capillary level (Fig.1) in human retina. Overall, the capillaries in retinal layers (SRL&DRL) showed a larger mean MF compared with the flow in CC layer both in normal and DR eyes. A significantly deceased flow speed was observed in PDR eyes by one-anova test among the three groups. However, the ages were not age-matched among the three groups which may introduce bias in the flow speed comparison. Age-matched normal eyes are required for further comparison.

Conclusions: The modified scanning protocol in PLEX Elite with a time interval of ~ 1ms has the capability to differentiate the blood flow speed of capillaries in human eyes with various ocular pathologies using the ED-based capillary velocimetry approach. The results showed the velocimetry may play a role not only in the investigations of ocular disease but also in developing endpoints for therapeutic clinical trials.

CONTROL ID: 3712030

SUBMITTER (NAME ONLY): Alexandra Miere

TITLE: Deep learning-based classification of diabetic retinopathy with or without macular ischemia using optical coherence tomography angiography images

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Miere, C. Pallonne, M. Filali Ansary, E. Souied, Ophthalmology, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|J. Excoffier, S. Kerr, M. Ortala, Kaduceo SAS, FRANCE|

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ABSTRACT BODY:

Purpose: To evaluate a deep learning classifier for the automated classification of optical coherence tomography angiography images from diabetic retinopathy (DR) eyes with and without macular ischemia (MI).

Methods: In this study, 241 3x3 mm superficial vascular complex (SVC) OCTA images of DR patients with and without MI, as well as healthy controls were used to train a multi-layer deep convolutional neural network (DenseNet121) to differentiate between healthy versus DR with and without MI. A two-class (DR versus healthy controls) and a three-class classification system (DR without MI, DR with MI, and healthy control) were implemented. In order to evaluate classification performances overall in the dataset, a 5-fold cross-validation method was used. Visualization of the output of the DL classifier on OCTA images was performed using two different methods: Smoothed Saliency Maps and GradCAM++.

Results: The accuracy of the binary classification (DR versus healthy controls) was 90.87%, along with a sensitivity of 88.96% and a precision of 96.48%. The three-class classification (DR with MI, without MI, and controls) showed an accuracy of 85.89%. Healthy controls and DR with MI obtained the highest sensitivity, of 94.25% and 93.98%, respectively.

Conclusions: This study describes the use of a deep learning-based model to automatically classify DR with/without MI on central 3x3mm OCTA images. Thus, this model may be a useful screening tool and help improve the clinical management of DR patients.

CONTROL ID: 3712031

SUBMITTER (NAME ONLY): Kiran Bora

TITLE: Genetic deficiency of RORα leads to retinal bipolar cell dysfunction in aging mice

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bora, C. Liu, F. Yemanyi, A.K. Blomfield, M. Maurya, Y. Sun, J. Akula, J. Chen, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinoic acid receptor-related orphan receptor alpha (RORα) is a lipid-sensing nuclear receptor and transcription factor expressed in many retinal cell types including photoreceptors, ganglion cells and bipolar cells. It plays a crucial role in regulating expression of target genes involved in diverse physiological processes in the eye, such as those in lens and photoreceptor development. Genetic variations of RORα have been linked to development of age-related macular degeneration. In this study, we investigated the role of RORα in retinal bipolar cell function during aging using mice with spontaneous RORα deletion mutation ($RORα^{sg/sg}$).

Methods: $RORα^{sg/sg}$ and age-matched wild-type (WT) mice were assessed at various time points during aging for functional and phenotypical analysis. The distribution of RORα in retina was analyzed using single cell RNA sequencing (scRNA seq) database and its localization was monitored by immunohistochemistry, along with evaluation of changes in bipolar cell morphology using PKCα, a rod bipolar cell selective marker. Further, visual function was assessed by scotopic full-field electroretinography (ERG), and retinal expression of genes involved in signal transmission through bipolar cells was determined in $RORα^{sg/sg}$ and WT mice.

Results: RORα expression was found in retinal bipolar cells in scRNA seq analysis and its localization was confirmed in retinal sections. Compared with WT, $RORα^{sg/sg}$ mice showed substantial impairment of visual function with significant attenuation (P=0.0002) of b-wave ERG amplitude at 5 month, with greater reduction (P=0.04) at 12 month, suggestive of bipolar cell dysfunction. However, ERG a-waves, which originate in photoreceptors, were comparatively normal. $RORa^{sg/sg}$ mice revealed significant degeneration and progressive loss of bipolar cells upon aging, with notable loss of rod bipolar cells at 5 months followed by more conspicuous loss and severely disrupted morphology upon aging (9 months and >12 months old), with respect to WT. Furthermore, $RORa^{sg/sg}$ retinal tissues revealed significant dysregulation of genes involved in glutamate and calcium signaling.

Conclusions: These findings suggest that RORα deficiency results in progressive, age-related rod bipolar cell degeneration with associated visual dysfunction, indicating a crucial role of RORα in regulating rod bipolar cell integrity and function in aging eyes.

CONTROL ID: 3712034

SUBMITTER (NAME ONLY): Katherine Lee

TITLE: Impact of Glare Strength on Contrast Sensitivity in Pseudophakes

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Lee, Clinical Operations, Johnson & Johnson Vision, Inc., Irvine, California, UNITED STATES|C. Sefton, Self, California, UNITED STATES|

Commercial Relationships Disclosure: Katherine Lee: Commercial Relationship(s);Code E (Employment):Johnson and Johnson Vision, Inc. | Cameron Sefton: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Vision, Inc.

ABSTRACT BODY:

Purpose: Evaluation of contrast sensitivity (CS) in clinical trials of intraocular lenses (IOLs) has long been used as a supplemental measure of image quality. Factors such as IOL design and lighting/glare conditions are known to degrade image quality and reduce CS. While general parameters for CS testing are outlined in ANSI/ISO standards, glare strength (illuminance) is not. ANSI/ISO recommend a level of glare that reduces mean mesopic CS by 0.1 log units at 6 cpd, determined through a pilot study of young, healthy adults. In a previous pilot study, researchers demonstrated that the manufacturer's standard glare (150 lux) on the Clinical Trial Suite (CTS, M&S Technologies) as well as two attenuated settings (69 and 110 lux) sufficiently reduced the mean CS at 6 cpd by at least 0.1 log units. This study was conducted to compare the effect of the lower glare level on CS for pseudophakic subjects.

Methods: This was a prospective, non-interventional, multi-center clinical study in adults previously implanted with a TECNIS 1-piece monofocal IOL, Model ZCB00 (at least two months postoperative). Subjects with BCDVA worse than 20/20, posterior capsular opacification, or other adverse ocular/lens findings were not eligible for enrollment. Monocular mesopic CS at 6 cpd with and without standard and attenuated glare (150 and 69 lux, before 1.5 ND filter) was measured using the M&S CTS.

Results: Monocular data from 88 subjects were evaluated. Mean (SD) mesopic CS without glare was 1.669 (0.288) log units. Under standard and attenuated glare conditions, mean mesopic CS was 1.393 (0.308) and 1.519 (0.324) log units, respectively. This represented a 0.28 and 0.15 log unit decrease in mean mesopic CS under standard and attenuated glare, respectively. This study showed that two different glare levels can both satisfy ANSI/ISO criteria for CS testing. Testing under approximately 50% lower glare illuminance resulted in a near 50% gain in mesopic CS at 6 cpd in monofocal patients.

Conclusions: ANSI/ISO criteria for CS testing can be met with standard and attenuated glare conditions, based on this study. These findings suggest that CS is highly dependent on glare illuminance, and CS loss due to glare in pseudophakic patients should be carefully interpreted.

CONTROL ID: 3712036

SUBMITTER (NAME ONLY): Claudia Lasalle

TITLE: A Comparison of Symptoms at Diagnosis in Sequential Neovascular Age-related Macular Degeneration

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lasalle, O. Onwuka, J. Saddemi, F.S. AKKAN AYDOGMUS, D.J. Ramsey, Ophthalmology, Lahey Hospital and Medical Center, Peabody, Massachusetts, UNITED STATES|J. Saddemi, Department of Ophthalmology, Cooper University Health Care, Camden, New Jersey, UNITED STATES|C. Lasalle, O. Onwuka, D.J. Ramsey, Department of Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|F.S. AKKAN AYDOGMUS, Department of Ophthalmology, Ankara Sehir Hastanesi, Cankaya, Ankara, TURKEY|

Commercial Relationships Disclosure: Claudia Lasalle: Commercial Relationship: Code N (No Commercial Relationship) | Oluchukwu Onwuka: Commercial Relationship: Code N (No Commercial Relationship) | Jackson Saddemi: Commercial Relationship: Code N (No Commercial Relationship) | Fatma AKKAN AYDOGMUS: Commercial Relationship: Code N (No Commercial Relationship) | David Ramsey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this study is to determine if there is a difference in the rate at which symptoms are reported at diagnosis in the first versus second eye to develop neovascular age-related macular degeneration (nAMD).

Methods: A retrospective chart review identified patients who developed nAMD sequentially (defined as a >30-day gap in diagnosis of each eye). Demographic and clinical characteristics were abstracted from the medical record. Symptoms relatable to nAMD included reduced central vision, visual distortion, increased difficulty adapting to low light levels, needing more light to read or to perform close work, increased difficulty reading printed words, decreased intensity of colors, difficulty recognizing faces, and/or a well-defined blurry spot or blind spot in the central field of vision. In cases where patients could not determine, or did not specify which eye was affected, symptoms were attributed to both eyes. For comparison, patients with sequential nAMD were matched to those who had unilateral nAMD, controlling for age, gender, vision, observation period, and treatment agent.

Results: 47 patients with sequential nAMD were matched with 47 patients with unilateral nAMD. Both groups were equally likely to present with symptoms at the time of diagnosis of their first eye (60% vs. 55%, X^2=0.369, p=0.543), but very few patients reported symptoms in their fellow eyes (6.4% vs. 0%, X^2=1.044; p= 0.307). Among patients who went on to develop bilateral nAMD, fewer symptoms were reported at diagnosis of the second eye compared with the first eye (34% vs. 60%, X^2=6.153, p=0.0131). For comparison, at an equivalent time after the diagnosis of nAMD in unilateral nAMD patients, few patients reported symptoms in their fellow eyes (4.3% vs. 34%, X^2=17.1716; p<0.001). And both groups of patients rarely reported symptoms in their fellow eyes at the preceding visit (6.5% vs. 4.3%, X^2 =0.212; p=0.646).

Conclusions: Patients with nAMD more commonly present with symptoms at the diagnosis of their first eye. Despite being taught to monitor and report symptoms concerning for nAMD, fewer patients reported symptoms at the time that their second eye was diagnosed with nAMD. This underscores the importance of regular examinations to monitor the fellow eyes of patients with unilateral nAMD to permit early detection of treatable disease.

CONTROL ID: 3712037
SUBMITTER (NAME ONLY): Geertje van der Sterre
TITLE: Intergenerational utility in parents of children with amblyopia
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: G. van der Sterre, E. van de Graaf, H.J. Simonsz, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|H. van der Meulen-Schot, E. Abma-Bustraan, Ophthalmology, Reinier de Graaf Gasthuis, Delft, Zuid-Holland, NETHERLANDS|
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ABSTRACT BODY:
Purpose: We measured the loss of disease-related quality of life in parents whose child was treated for amblyopia.
Methods: Eligible were the parents of children age three to six who were first treated for amblyopia with occlusion therapy.
Interviews took on average 20 minutes and were conducted by telephone after 6 weeks of occlusion therapy.

Parents were asked how many years of their life they would be willing to give up (Time Trade-Off) in exchange for a completely cured amblyopia with their child. Answers were obtained using a staircase forced choice procedure. Options were 1 day, 1 week, 1 month, 3 months, 6 months, 1, 2, 5, 10, 20, 30 years.

Secondly, they were asked how much risk of unilateral blindness they are willing to take (Standard Gamble) in exchange for a completely cured amblyopia with their child. This question asked participants to imagine they could give their child good vision in both eyes, by themselves undergoing a hypothetical procedure that would accomplish this, but also carried the risk of blinding one of their own eyes.
Results: So far, we have been able to interview 19 parents.

For TTO, widely differing options over the entire range from 0 to 30 years were chosen. The average was 4.8 years, median 5 years, standard deviation 6.8 years.

For SG, 5 out of 12 parents presented with this question were willing to risk the sight in one eye (10% and 1%), 4 opted for risks of 0.01% or 0.005%, 3 for no risk.

No correlation existed between these scores and the clinical variables of the child. However, parents who had amblyopia themselves were willing to take a higher risk in SG, and parents who had a family member with amblyopia were willing to sacrifice more life years with TTO.
Conclusions: It is surprising to see how much of their life or vision parents are willing to give up for a healthy child. These results may seem trivial as most parents wish the best for their child anyway. However, parents and not their children vote and thereby decide on the availability of screening programs and amblyopia treatment. Hence, intergenerational utility should be included as a component in their cost-effectiveness analysis.

CONTROL ID: 3712038

SUBMITTER (NAME ONLY): Michaela Dunn

TITLE: Detecting glaucomatous loss in the photopic full-field electroretinogram (ERG): influence of chromatic contrast, flash duration and flicker frequency

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Dunn, G. Cull, J. Reynaud, D. Jennings, T. Holthausen, B. Fortune, Discoveries in Sight Research Laboratories, Devers Eye Institute, Legacy Health, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Michaela Dunn: Commercial Relationship: Code N (No Commercial Relationship) | Grant Cull: Commercial Relationship: Code N (No Commercial Relationship) | Juan Reynaud: Commercial Relationship: Code N (No Commercial Relationship) | Dawn Jennings: Commercial Relationship: Code N (No Commercial Relationship) | Trinity Holthausen: Commercial Relationship: Code N (No Commercial Relationship) | Brad Fortune: Commercial Relationship(s);Code F (Financial Support):Heidelberg Engineering, GmbH, Perfuse Therapeutics, Inc.;Code C (Consultant/Contractor):Perfuse Therapeutics, Inc., Perceive Biotherapeutics, Inc.

ABSTRACT BODY:

Purpose: The ERG photopic negative response (PhNR) is reduced in glaucoma; generally detected best using a red stimulus flash on a blue background (R/B). Longer duration flashes separate the ERG "on" (increment) and "off" (decrement) responses, which also combine to shape flicker responses in a manner that depends on stimulus frequency, and possibly also sensitivity to glaucoma. Here we compare brief (4.5 ms) R/B flashes, long (200 ms) R/B and white-on-white (W/W) flashes, and varied W/W flicker frequencies for their ability to detect early functional loss in a non-human primate (NHP) model of experimental glaucoma (EG).

Methods: Photopic ERGs were recorded (UTAS BigShot, LKC, Gaithersburg, MD) at an early stage of unilateral EG (defined by OCT structural changes, PMID: 27564522) in 6 anesthetized adult rhesus monkeys (Macaca mulatta, 5F/1M ages 4.7-16.5 y) with dilated pupils after 10 min adaptation to 30 cd/m^2 blue light, then scotopic ERGs after 20 min dark adaptation. All photopic stimuli were 560 cd/m^2, including 4.5 ms R/B, 200 ms R/B and W/W flashes, and 4.5 ms W/W flicker at 5, 10, 20, 30.3, 40, and 50 Hz; scotopic W flashes ranged -3.6 to 2.4 log cd-s/m^2. Amplitude and implicit time (IT) of a-wave, b-wave and d-wave peaks were measured, along with PhNR amplitude 65 ms after flash onset and 80 ms after long flash offset. Flicker amplitude and IT were measured by peak-trough and harmonics by Fourier analysis (latter not shown). ANOVA and paired t-tests were used for statistical analysis.

Results: Peripapillary retinal nerve fiber layer thickness in EG and fellow control (FC) eyes was 86.0 ± 11.3 and 101.2 ± 7.4 µm, respectively. Significant ERG differences between EG and FC eyes were found only for the PhNR amplitude of the R/B brief flash ($p = 0.031$) and the “on” PhNR of the R/B long flash ($p = 0.042$, Table/Fig). D-wave latency ($p < 0.0001$) and IT ($p = 0.003$) were delayed by 10-15 ms for R/B relative to W/W long flashes, but did not differ between EG and FC eyes.

Conclusions: At this early stage of NHP EG, full-field ERG changes were limited to reduction of the PhNR for brief R/B and the “on” PhNR of long R/B flashes. Thus, R/B stimuli were better than W/W for detecting early functional loss and separating “off” responses offered no benefit. The chromaticity-dependent timing of the d-wave has some precedent but requires further investigation.

CONTROL ID: 3712039

SUBMITTER (NAME ONLY): Ali Salehi

TITLE: Deep learning-based fovea localization in low-cost OCT using macular thickness and corresponding principal curvatures

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Salehi, H. Bagherinia, S.A. Bello, L. Ramirez, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular Thickness Analysis (MTA) is a widely used tool for diagnosing and monitoring patients with ocular pathologies. The robustness of MTA is directly connected to the location of the fovea, which is used to place the ETDRS grid on the macular thickness (MT) map. The fovea localization based on OCT data becomes problematic when the OCT data is generated by a low-cost OCT system due to low contrast in the data. We developed a deep learning-based algorithm to localize the fovea using MT maps for low-cost OCT.

Methods: Scans from one or both eyes of 562 subjects (with one or more scans) were used for training and validation. In each case, the resulting OCT volumes over 6×6 mm using PLEX® Elite 9000 (ZEISS, Dublin, CA) and CIRRUS™ HD-OCT 5000 with/without AngioPlex® OCT Angiography (ZEISS, Dublin, CA) were segmented to delineate the inner limiting membrane (ILM) and the retinal pigment epithelium (RPE). The prototype segmentation was used to generate MT maps with 512x512 pixels over an area of 5.78×5.78 mm. The principal curvature maps (min and max) were calculated using the MT map (Figure 1). One grader manually selected the center of fovea used as the ground truth. This resulted in 1020 samples, from which 816 are used for training and 204 for the first test set (i.e., high-quality set). Additionally, 492 samples (extracted from multiple scans, one or both eyes of 82 subjects) from a prototype low-cost device formed a second test set. No samples from this low-cost device are used for training. The MT map and corresponding curvatures maps were input to a MobileNetV2, trained to estimate a single point. Various geometric and photometric augmentations were used during the training to increase the model's generalization.

Results: The difference between ground truth and estimation was 65±71 microns for the first test set of 204 samples from the same devices as training data. Error on test data from the low-cost device was 100±138 microns (see Figure 1-d). Figure 2-a shows the error distribution on low-cost OCT data and other mentioned devices. Figure 2-b shows the model's accuracy for various error thresholds. Processing time was 40 ms on an Intel Xeon CPU and 15 ms using a GTX 1080Ti GPU.

Conclusions: The result showed the effectiveness and robustness of the method to locate the fovea from MT maps obtained using low-cost OCT data.

CONTROL ID: 3712040

SUBMITTER (NAME ONLY): Bruno Ferreira

TITLE: PARAFOVEAL OCT-ANGIOGRAPHY BIOMARKERS AND MICROPERIMETRY FEATURES IN BEHÇET'S RETINAL VASCULITIS

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Occlusive retinal vasculitis is the most common ocular manifestation of Behçet's Disease (BD). In such cases, OCT-angiography (OCT-A) evaluates the retinal vascular plexus and microperimetry can assess macular sensitivity. We performed a cross-sectional structural and functional study of the parafoveal retina in Behçet's uveitis (BU) patients, comparing them to age- and sex-matched non-ocular BD (NOBD) and healthy subjects (HS).

Methods: Of 151 potentially eligible patients that met the International Criteria for Behçet's Disease (2014), 45 presented ocular involvement. We enrolled 75 eyes from 14 patients with BU (mean age 40.6 ± 11.7 years), 13 with NOBD (41.2 ± 8.7), and 13 HS (39.9 ± 11.1) in this study. Thirty-one patients were ineligible by refusal, inability to acquire OCT-A images, or neuro/retinopathies. All BU patients had inactive retinal vasculitis evaluated on fluorescein angiography. We analyzed foveal avascular zone (FAZ) area and vessel density (VD) in superficial vascular plexus (SVP), intermediate capillary plexus (ICP), and deep capillary plexus (DCP) with Spectralis® (Heidelberg Engineering, Heidelberg, Germany) (Figure 1A). They were measured using ImageJ (NIH, Maryland, USA) (Figure 1B). The MP-3 microperimeter (Nidek, Tokyo, Japan) evaluated macular sensitivity (MS). In addition, we also compared the groups' retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and full-thickness retina (FTR). This study had Institutional Ethics Committee approval.

Results: Variance analysis showed reduction ($p < 0.05$) in parafoveal VD in DCP in BU patients (Figure 1C), especially in the nasal quadrant (~ 20%) (Figure 1D). There was thinning in nasal (< 25.5%) and inferior (< 17%) GCL thickness, as well as in superior (< 6.8%), nasal (< 13.8%), and inferior (< 7.9%) FTR (Figure 2A). FAZ area and VD in the SVP and ICP did not differ between the groups (Figure 2B). MS was generalized reduced with a predilection to the nasal quadrant (~ 40%) (Figure 2C). Non-perfusion areas (34.8%) and microvascular abnormalities (78.2%) were observed in all plexuses and were more visible in the DCP (Figure 2D-F).

Conclusions: In patients with BU, vasculitis primarily affects the DCP, structural and functional macular changes are more critical in the nasal quadrant, MS loss may occur even if there is no structural damage, and qualitative vascular findings seem to be a promising diagnostic biomarker.

CONTROL ID: 3712042

SUBMITTER (NAME ONLY): Leon von der Emde

TITLE: Histologic cell shape descriptors for the retinal pigment epithelium in age-related macular degeneration

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Phenotypic alterations of retinal pigment epithelium (RPE) cells are central in age-related macular degeneration (AMD). Shape descriptors for individual RPE cells based on RPEs cytoskeleton may help to delineate healthy from AMD affected cells, even in early stages of disease. Here, we quantified differences in RPE morphology between donors with unaffected macula and with AMD.

Methods: Twenty-two human RPE flatmounts (7 AMD, mean age 85 ± 3 yrs (early: 3, geographic atrophy: 1; neovascular: 3;); 15 unaffected (≤51 yrs, n = 8; >80 yrs, n = 7)) were imaged at different locations (fovea, perifovea, near periphery) using a laser scanning confocal fluorescence microscope (exc. 488 nm; emission: 490-695 nm; z-stack: 390 nm steps). Hypoautofluorescent gaps between adjacent RPE cells were formed by the absence of lipofuscin/melanolipofuscin granules between the F-actin cytoskeletons. These gaps were manually marked with computer-assistance and considered borders between cells. Shape descriptors including form factor (measure for circularity), area, solidity, convexity, and roundness for each cell were calculated using customized software. Total autofluorescence (AF) per cell was defined as the integrated density of intensity from all pixels within the cell. Statistical analysis was performed using an ensemble classifier based on logistic regression.

Results: Comparing young vs healthy aged eyes, there was a trend to increased area and reduced form factor. In AMD eyes, RPE shape was significantly altered at all locations with area, solidity and form factor being the most discriminatory descriptors. In samples from healthy donors, with increasing distance to the fovea, area, solidity, and convexity increased, while form factor decreased. Finally, reduced RPE cell AF in AMD was significantly associated

with decreased roundness and solidity of the RPE.

Conclusions: Morphological RPE cell alterations in presence of AMD can be accurately quantified using cell shape descriptors. Enlarged and deformed cells in AMD are assumed to be indicative of structurally and functionally impaired RPE cells. The results of this study may help guide the interpretation of RPE morphology in in vivo studies utilizing high-resolution single cell imaging, e.g., adaptive optics scanning laser ophthalmoscopes or transscleral optic phase imaging.

CONTROL ID: 3712043

SUBMITTER (NAME ONLY): Sara Mokhtar

TITLE: A higher level of glycemia, lower adherence to a healthy diet, lower cardiorespiratory fitness, smoking, and higher systolic blood pressure are cross-sectionally associated with lower retinal sensitivity in a population-based study – The Maastricht Study

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mokhtar, F. van der Heide, M. Said, A. Kroon, P. Dagnelie, S. Eussen, C. van der Kallen, M. van Greevenbroek, N. Schaper, M. Schram, C. Stehouwer, Universiteit Maastricht Cardiovascular Research Institute Maastricht, Maastricht, Limburg, NETHERLANDS|S. Mokhtar, T. Berendschot, C.A. Webers, Maastricht University, MHeNS School of Mental Health and Neuroscience, Maastricht, Limburg, NETHERLANDS|F. van der Heide, M. Said, A. Kroon, P. Dagnelie, C. van der Kallen, M. van Greevenbroek, C. Stehouwer, Department of Internal Medicine, Maastricht University Medical Centre+, Maastricht, Limburg, NETHERLANDS|A. Khanna, Department of Ophthalmology, Sharp sight eye hospital, INDIA|S. Eussen, CAPHRI Care and Public Health Research Institute, Universiteit Maastricht Care and Public Health Research Institute, Maastricht, Limburg, NETHERLANDS|T. Berendschot, J. Schouten, C.A. Webers, University Eye Clinic Maastricht, Maastricht University Medical Centre+, Maastricht, Limburg, NETHERLANDS|J. Schouten, Department of Ophthalmology, Canisius Wilhelmina Ziekenhuis, Nijmegen, Gelderland, NETHERLANDS|H. Savelberg, NUTRIM School for Nutrition and Translational Research in Metabolism, maastricht University, Maastricht, Limburg, NETHERLANDS|H. Savelberg, Department of Nutrition and Movement Sciences, Maastricht University, Maastricht, Limburg, NETHERLANDS|N. Schaper, Department of Social Medicine, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|M. Schram, Heart and Vascular Centre, Maastricht University Medical Centre+, Maastricht, Limburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy is preceded by subtle functional neurodegenerative changes, including reduced light sensitivity "lower retinal sensitivity". It is not yet understood if potentially modifiable risk factors may be determinants of retinal sensitivity (RS). Using cross-sectional data from a cohort study, we investigated whether those risk factors were associated with RS.

Methods: We used data from The Maastricht Study, up to 5,255 participants, 50.5% men, age 59.7±8.7 years, and 22.6% with type 2 diabetes (T2D). We determined HbA1c (mmol/mol) and total cholesterol (mmol/L) in fasting plasma samples. We assessed dietary intake and alcohol consumption with a validated food frequency questionnaire, and smoking status via a questionnaire. We measured cardiorespiratory fitness, defined as the maximum power output adjusted for body mass. We measured 24-hour ambulatory blood pressure (mm Hg). We assessed waist circumference (cm) and physical activity (hours/day). We estimated the RS using Heidelberg Edge Perimeter and defined RS as the mean (peri)macular RS of both eyes. We used linear regression analyses with adjustment for potential confounders and tested for interaction by sex and T2D.

Results: After full adjustment, greater HbA1c, lower healthy diet score and cardiorespiratory fitness, and current versus never smoking were significantly associated with lower RS, per SD-β[95% CI], -0.05[-0.08; -0.02], -0.06[-0.09; -0.03], -0.05[-0.08; -0.01], and -0.14[-0.22; -0.06], respectively; greater 24-hour ambulatory systolic blood pressure was

significantly associated with lower RS in individuals with, but not in individuals without, T2D -0.06[-0.12; -0.04]. In contrast, greater total cholesterol was significantly associated with greater RS 0.05[0.02; 0.08]. Alcohol consumption, antihypertensive medication use, lower physical activity, and greater waist circumference were not associated with RS. Sex did not modify the associations.

Conclusions: In this study, higher levels of glycemia or systolic blood pressure, lower adherence to a healthy diet, or cardiorespiratory fitness, and smoking were associated with a lower RS. Hence, early-stage prevention of these factors may contribute to the prevention of loss of RS and, ultimately, diabetic retinopathy.

CONTROL ID: 3712044

SUBMITTER (NAME ONLY): Brian Kevany

TITLE: AAV204, a Novel AAV Capsid, Demonstrates Superior Macular Transduction Following Para-Retinal Administration in Non-human Primates

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kevany, S. Kerns, L. Padegimas, Abeona Therapeutics Inc, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To achieve the highest transduction levels, AAV administration to the eye has traditionally been performed by subretinal injection between the neural retina and underlying retinal pigmented epithelium. While this method provides the benefit of positioning the vector directly next to its cellular target, it requires retinal detachment, an operating room, and a trained retinal surgeon. A therapy that is administered directly into the vitreous of the eye could provide a safer and more feasible approach. Previously, we characterized a novel AAV capsid, AAV204, which facilitates transduction of both the inner and outer retina after intravitreal administration in mice and non-human primates. We hypothesized that using this capsid with a modified intravitreal injection, termed para-retinal injection, may produce more robust transduction levels, particularly in the macula and optic nerve.

Methods: Para-retinal administration was performed by layering the virus on top of the retina between the vitreous and the inner limiting membrane, thus not creating a subretinal detachment. 100 µL of viral suspension (1×10^{11} total vector genomes) of AAV204.CBh.GFP or AAV8.CBh.GFP were administered to four non-human primate eyes. GFP expression was monitored using scanning laser ophthalmoscopy (SLO). 28 days post-injection, eyes were collected, processed, and analyzed by immunohistochemistry.

Results: SLO imaging of AAV204.CBh.GFP dosed eyes showed intense GFP expression in the macula, papillomacular bundle, and retinal nerve fibers. Immunohistochemistry imaging confirmed SLO analysis results, revealing high levels of GFP expression in the macula and foveal pit, as well as retinal ganglion cells and the associated retinal nerve fibers extending to the optic nerve. Alternatively, AAV8.CBh.GFP-injected animals showed little to no GFP expression in the macula or optic nerve. Of note, the dose used in this study was at least 10-fold lower compared to intravitreal AAV injections commonly used in the field.

Conclusions: These results suggest that para-retinal injection of AAV vectors, and more specifically using our novel AAV204 capsid, may be an efficient route of administration for drugs that target the macula or optic nerve/retinal ganglion cell layer.

CONTROL ID: 3712045

SUBMITTER (NAME ONLY): Mark Draelos

TITLE: Head orientation-independent optical coherence tomography with a robotically-aligned scanner

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Draelos, P. Ortiz, A. Narawane, A.N. Kuo, J.A. Izatt, Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|R.P. McNabb, A.N. Kuo, J.A. Izatt, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Standard-of-care optical coherence tomography (OCT) systems are manually-aligned tabletop instruments that require strict patient cooperation and careful head stabilization with chinrests. These requirements limit imaging of pediatric patients, who are frequently unwilling or unable to cooperate, and of bedbound or hospitalized patients, who cannot use a tabletop OCT system. Compensation for variation in both position and orientation of the patient's head is necessary for successful imaging under such circumstances.

Methods: We extend our previous robotically-aligned OCT (RAOCT) scanner to support face tracking without assumptions on head orientation (Fig. 1). Two scanner-integrated depth cameras replaced previous fixed-mount cameras, and we generated an artificial frontal face view for subject tracking from their composite face surface maps. Our control software then maneuvered the robot to position the scanner's pupil pivot at the subject's pupil and to match the subject's head orientation. We evaluated this approach through IRB-approved imaging of human subjects in varied head orientations. Subjects were either freestanding or seated upright facing the system and were asked to orient their head with non-zero pitch and yaw. An operator then triggered the system to perform semi-automatic alignment and imaging of the desired eye, after which the system returned to its starting configuration. We conducted imaging in this fashion for multiple positions and head orientations for each subject.

Results: The RAOCT system successfully obtained motion-stabilized OCT images in widely varying subject positions and head orientations (Fig. 2a). For each subject, OCT volumes obtained with different positions and orientations captured the target retinal anatomy (Fig. 2b). The time to first images after initiation of alignment was routinely under 30 seconds.

Conclusions: Robotically-aligned OCT with scanner-integrated head tracking enables reliable imaging of subjects with arbitrary head orientations. This approach promises to facilitate imaging of pediatric and hospitalized patients.

CONTROL ID: 3712048

SUBMITTER (NAME ONLY): Jennifer Noel

TITLE: Stereopure oligonucleotide treatment results in durable rescue of disease phenotype in a P23H hRHO pig model of human autosomal dominant retinitis pigmentosa (adRP)

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Yang, Q. Pan, F. Liu, Y. Yin, R. Looby, C. Vargeese, M. Byrne, Wave Life Sciences, Cambridge, Massachusetts, UNITED STATES|J.M. Noel, A. Jalligampala, O.N. Jacobs, J. Prestigiacomo, M.A. McCall, Ophthalmology and Visual Sciences, University of Louisville, Louisville, Kentucky, UNITED STATES|M.A. McCall, Anatomical Sciences and Neurobiology, University of Louisville, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: AdRP is an inherited retinal disease that affects ~400,000 people worldwide. In the United States, ~2500 people have a proline to histidine substitution at codon 23 (P23H) in rhodopsin (RHO). It is believed that misfolded mutant Rho protein contributes to rod photoreceptor (rod) death. Wave Life Sciences has previously reported that stereopure antisense oligonucleotides (ASOs) bind to RNA via complementary base pairing that promotes RNase H–mediated degradation of mutant RNA. Here we evalutated the efficacy of stereopure ASOs targeting P23H hRHO mRNA injected into the vitreous of transgenic P23H hRHO (TgP23H hRHO) pigs on retinal structure and function.

Methods: Four neonatal TgP23H hRHO pigs received bilateral intravitreal (IVT) injections (50 uL) of ASOs targeting the P23H hRHO mutation at 10 µg (n=2) or 25 µg (n=2). Controls included: TgP23H hRHO eyes injected with PBS (n=1), or non-targeting ASO (n=3; 25 µg), and uninjected age-matched WT and TgP23H hRHO eyes. Presence of ASO in retina (retinal exposure), aqueous, vitreous and RPE were assessed by hybridization ELISA. We conducted regular ocular exams, fundus imaging, full-field ERGs and OCTs to assess tolerability and efficacy of ASOs on retina structure and function. Animals were euthanized at 8 (n=5) or 16 (n=3) weeks post injection (wpi). Morphological assessments were conducted in immunohistochemically labeled frozen sections.

Results: PK analysis found dose and time dependent retinal exposure (25 µg dose: 5 and 2 µg/g at 8 and 16 wpi, respectively; 10 µg dose: 0.7 and 0.2 µg/g at 8 and 16 wpi, respectively). ASOs did not induce inflammation and rejuvenated rod structure and function in treated retinas. Naïve and PBS injected TgP23H hRHO pigs had no scotopic ERG b-wave (flash intensity; 0.01 $cd*s/m^2$). At 16 wpi, all Tg retinas treated with 25 µg of targeting ASO had scoptopic b-waves of whose amplitudes were ~40% of WT. Rod morphology and rhodopsin expression were preserved compared to untreated Tg littermates.

Conclusions: InTgP23H hRHO pigs, a single IVT injection of an ASO targeting P23H hRHO is well tolerated, preserves rod morphology and rhodopsin expression, and rejuvenates rod function for at least four months after administration. This represents a strong resolution of rod photoreceptor degeneration.

CONTROL ID: 3712049

SUBMITTER (NAME ONLY): Sheetal Uppal

TITLE: An amphipathic helix directs membrane binding and function of RPE65 retinol isomerase

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Uppal, E. Poliakov, S. Gentleman, T. Redmond, NEI, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: RPE65 association with RPE smooth endoplasmic reticulum (sER) is required to regenerate 11-cis retinal. How RPE65 binds to sER is unclear as it lacks transmembrane motifs, but a crystallographically unresolved “missing loop” (ML) at residues 107-125 is proposed to be involved. This contains a highly conserved PDPCK motif. Our previous studies reveal that C112 in the missing loop region is palmitoylated and partly important for RPE65-membrane binding and visual cycle function. To elucidate the mechanism of RPE65-membrane binding, we targeted the functional significance of the crystallographically unresolved region in RPE65 membrane binding.

Methods: Secondary structure analyses of the ML were studied using web-based servers (I-TASSER and HELIQUEST). Circular dichroism (CD) spectroscopy and gel filtration chromatography (GFC) was performed using synthethic peptides corresponding to the ML of RPE65. Extensive mutational analyses, palmitoylation detection, subcellular fractionation, and isomerase assays were done. We made a GFP-RPE65$^{107\text{-}125}$ construct for immunofluorescence (IF) studies. We predicted the orientation of RPE65 containing the modelled ML and employed molecular dynamic (MD) simulations to study binding.

Results: In silico analysis of the ML predicts this region to form an amphipathic alpha (α)-helical (AH) structure. CD and GFC analyses of unpalmitoylated synthetic peptide confirmed the capacity of the disordered loop to fold into α-helices upon association with lipid-like molecules, while the palmitoylated synthetic peptide was always α-helical. Mutagenesis revealed that most of the residues forming the AH significantly affect the palmitoylation level of RPE65 and membrane association of RPE65. Moreover, we found that mutation of almost all residues in the hydrophobic face and some charged/polar residues in the hydrophilic face have severe (>50% reduction) to total loss of RPE65 isomerase activity. IF studies reveal that this sequence functions as a membrane sensor and a membrane targeting motif. MD simulations clearly show AH-membrane insertion, strongly validating our experimental findings.

Conclusions: We conclude that the AH plays a major role in the regulation of RPE65 palmitoylation and sER membrane interaction and, thus, the catalytic function of RPE65. Taking all these findings into consideration, we propose a hypothetical working model for RPE65-membrane binding.

CONTROL ID: 3712055

SUBMITTER (NAME ONLY): Valeria Sanchez-Huerta

TITLE: Results of a Phase 1b clinical trial of KPI-012, a novel secretome therapy, in patients with Persistent Corneal Epithelial Defect (PCED)

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: PCED results from the failure of rapid epithelialization and closure within 10-14 days after a corneal injury, even with standard supportive treatment. If left untreated, PCEDs can result in stromal scarring, perforations, secondary infections, ulcerations, and vision loss. KPI-012 topical ophthalmic solution is a novel, bone marrow derived mesenchymal stem cell (MSC) secretome with a multifactorial mechanism of action that has the potential to treat PCED of various etiologies. In preclinical studies KPI-012 has demonstrated the ability to accelerate corneal wound healing and reduce scarring, inflammation, and angiogenesis. The purpose of this Phase 1b trial was to evaluate the safety and efficacy of twice daily (BID) KPI-012 for the treatment of PCED.

Methods: A prospective, single-arm, Phase 1b trial enrolled 12 subjects at two independent sites in Mexico. The initial safety cohort consisted of 3 subjects with low vision and no active corneal disease. KPI-012 was administered BID for 1 week and subjects were followed for 1 week. The efficacy cohort consisted of 9 subjects with PCED of various etiologies. In this cohort, KPI-012 was administered BID for up to 8 weeks and followed for up to 18 weeks. The key efficacy endpoint was complete healing of corneal defects evaluated by corneal staining. Other efficacy endpoints included reduction in defect size, visual acuity, corneal neovascularization, and opacity. The safety measures included tolerability/pain, intraocular pressure, vital signs, and adverse events.

Results: In the efficacy cohort, 6 of the 8 subjects had complete healing of their PCED. There was one early withdrawal unrelated to the KPI-012 treatment in the efficacy cohort. Among the 6 completely healed subjects, four achieved complete healing after one week of treatment, one after two weeks, and one after four weeks of treatment. Improvement in PCED was observed in one subject but complete healing was not achieved. All subjects with complete PCED resolution remained healed through end of their follow-up periods. KPI-012 was well-tolerated with favorable safety profile in both the safety and efficacy cohorts.

Conclusions: KPI-012 topical solution administered twice daily for up to 8 weeks appeared safe, well-tolerated, and effective in the treatment of PCED with various etiologies.

CONTROL ID: 3712059

SUBMITTER (NAME ONLY): Jahan Alam

TITLE: Single cell transcriptional profiling of murine conjunctival immune cells reveals distinct populations expressing homeostatic and regulatory genes.

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Alam, G. Yazdanpanah, R. Ratnapriya, C.S. De Paiva, D. Li, S.C. Pflugfelder, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|N. Borcherding, Department of Pathology & Immunology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify distinct populations expressing homeostatic and regulatory genes and specific identity markers based on gene expression profiles.

Methods: Female C57BL/6J (B6) mice aged 6–8 weeks were allowed to house in 50–75% relative humidity before the experiments. The CD45+ cells were sorted from the conjunctiva of B6 mice using the Aria-II cell sorter. Single-cell gene expression libraries was prepared using the Chromium Single Cell Gene Expression 3v3.1 kit and sequenced on the NovaSeq 6000 Sequencing System using the S2 v1.0 Flowcell. Raw sequence reads in the FASTQ format were aligned to the mouse reference genome using Cell Ranger Count v6.0.1 and analyzed with Seurat v3.1. Cell-cell interactions were analyzed by Cell Chat and Gene pathway analysis using Qiagen IPA. Immunofluorescence staining in whole-mount conjunctival tissue samples was visualized using laser scanning confocal microscope.

Results: Sixteen distinct clusters were identified, including myeloid cells (neutrophils, monocytes, macrophages), dendritic cells (DC), and lymphoid cells (B, T, gdT, ILC2, and NK) lineages. Novel neutrophil [lipocalin (Lcn2) high and low), MHCIIlow macrophage (MP), and Retnla DC2 clusters were identified. Approximately half of the cells map to myeloid and dendritic cell populations with differential expression profiles that include genes with homeostatic and regulatory functions. Serpinb2 (MHCIIlo macrophage), Apoe (monocyte), Cd209a (macrophage), Cst3 (cDC1), and IL4i1 in migratory DC (mDC). Suppressed inflammatory and activated anti-inflammatory/regulatory pathways were observed in certain myeloid and DC populations. Confocal immunolocalization of identity markers showed cDC2 and mDC located on or within the conjunctival epithelium. Monocyte, macrophage, cDC1 and IL-13/IL-5+ ILC2 were located below the conjunctival epithelium and goblet cells.

Conclusions: This study provides valuable information that can be used for more specific cell identification and cell-specific gene expression profiles that can be compared with those in ocular surface inflammatory diseases, such as dry eye where there is recruitment and activation of immune cells. It provides biomarkers that can be used to determine factors, such as diet and microbiome, that maintain the production of the homeostatic and regulatory factors by the conjunctival immune cells.

CONTROL ID: 3712060

SUBMITTER (NAME ONLY): Ke Ning

TITLE: IFT88 Mediates Cilia-Associated Wound Repair in Retinal Pigment Epithelium

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kowal, Y. Sun, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|R. Bansal, N. Berbari, Department of Biology, Indiana University-Purdue University Indianapolis School of Public and Environmental Affairs, Indianapolis, Indiana, UNITED STATES|D. Vollrath, Department of Genetics, Stanford University School of Medicine, Stanford, California, UNITED STATES|K. Ning, M.B. Bhuckory, T. Kowal, M. Chen, D.V. Palanker, V.B. Mahajan, Y. Hu, Y. Sun, Spencer Center for Vision Research, Byers Eye Institute, School of Medicine, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary cilia are microtubule-based organelles that transduce extracellular cues into intracellular signals critical for diverse processes including proliferation and tissue repair. Defective ciliary function results in multisystemic diseases known as ciliopathies in humans. Many ciliopathies in the eye, such as Bardet-Biedl Syndrome, share a common feature of atrophy of the retinal pigment epithelium (RPE). Mutation in genes involved in cilia formation, including IFT88 or BBS4 which cause Bardet-Biedl Syndrome, result in loss of or shortened cilia. However, the roles for RPE cilia in vivo remain unknown. This study investigates the role of primary cilia in the proliferative and reparative responses of mouse RPE after targeted laser-injury.

Methods: RPE flatmount from Bbs4$^{-/-}$ mutant mice and wildtype controls from pups on the day of birth (P0), were obtained and immunostained for cilia markers. Transgenic mice were generated with RPE-selective loss of primary cilia (RPE-cKO mice) by crossing IFT88$^{flox/flox}$ mice and BEST1-cre mice. Using a laser-induced injury model in vivo, primary cilia formation was assessed by ciliary markers on RPE flatmounts in response to injury using fluorescence microscopy. Anti-Ki67 antibody was used as a proliferative cell marker. The re-epithelialization was analyzed for wound size measurement with anti ZO-1 antibody and phalloidin. Statistical analyses were performed using Student's t-test or One-way ANOVA, $p<0.05$ was considered statistically significant.

Results: Ciliation in Bbs4 mutant RPE cells is disrupted early during eye development. RPE cilium were reassembled after laser injury, followed by rapid disassembly when repair is completed (n=4 mice). Consequently, faster repair is observed with loss of cilia in RPE-cKO mice than control eyes. Additionally, the removal of cilia by RPE-cKO mice improved wound healing by enhancing cellular proliferation in mouse RPE (n=6-10 eyes, Student's t-test, $P<0.05$).

Conclusions: This study supports a novel role for primary cilia in RPE repair and provides insights into potential cilia-based therapeutic targets for RPE degenerative diseases.

CONTROL ID: 3712063

SUBMITTER (NAME ONLY): Matthew Conley

TITLE: Assessing the Relationship of Exfoliation Syndrome and Abdominal Aortic Aneurysm: A Large Database Study

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Conley, A. Patil, C. Paulson, S.C. Taylor, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|M.E. Conley, A. Patil, C.J. Pompoco, C. Paulson, S.C. Taylor, C.J. Swiston, J. Herrick, K. Curtin, B.M. Wirostko, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|R. Ritch, New York Eye and Ear Infirmary, Mount Sinai Health System, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Controversy exists concerning the possible association of exfoliation syndrome and abdominal aortic aneurysms due to conflicting evidence in prior studies. A retrospective, electronic medical records (EMR) study was performed using the statewide Utah Population Database (UPDB) to investigate the relationship of exfoliation syndrome and exfoliation glaucoma (XFS/XFG) in abdominal aortic aneurysm (AAA) patients.

Methods: A population-based, retrospective study was undertaken using the Utah Population Database (UPDB). Patients ages ≥40y identified with an AAA diagnosis from 1996-2015, based on International Classification of Diseases (ICD) version 9/10 codes, were included (n=7167). An XFS/XFG outcome in AAA patients and in 5:1 sex- and age-matched controls (n=35,923) was determined from a patient population identified with XFS/XFG (n=3,582) based on ICD 9/10 codes. A hazards model with a competing risk of death was used to determine the risk of XFS/XFG in AAA patients compared with controls. A chart review was conducted to confirm a clinical diagnosis of AAA in XFS/XFG patients.

Results: Of AAA patients, 20 (0.3%) developed XFS/XFG, while in controls, 118 (0.3%) developed XFS/XFG. We found no increased risk of XFS/XFG in AAA patients compared with controls (HR=0.99, 95%CI 0.6-1.6). Of the XFS/XFG patient cohort, 9 patients had a clinical diagnosis of AAA (0.3%) upon chart review. Of chart-review patients confirmed to have both conditions, 50% were male and, on average, had: AAA presentation at age 76y; initial AAA size, 3.9 cm; and XFS/XFG presentation age, 77y.

Conclusions: Exfoliation syndrome is a multifactorial, age-related systemic disorder with genetic and environmental influences associated with various clinical comorbidities. Although prior studies have shown a relationship between XFS and AAA, these findings, from a large UPDB investigation, do not support an association between AAA and the development of XFS/XFG.

CONTROL ID: 3712064

SUBMITTER (NAME ONLY): Amanda Travis

TITLE: Disrupting the ciliary gradient of active Arl3 affects rod photoreceptor nuclear migration

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.M. Travis, S. Manocha, J.R. Willer, J.N. Pearring, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human mutations in the small GTPase Arl3 cause a variety of inherited retinal dystrophies that can present as either autosomal recessive or autosomal dominant; however, the underlying pathobiological mechanism of these mutations remains unexplored. Transgenic expression of constitutively active Arl3-Q71L in wild type mouse rods was shown to cause rod nuclei to be displaced to the inner nuclear layer. We hypothesized that dominant mutations in Arl3 would cause a rod nuclear migration defect leading to a possibly divergent disease mechanism.

Methods: FLAG-tagged Arl3 constructs with either autosomal dominant or well characterized GTPase cycle mutations were exogenously expressed in mouse rod photoreceptors via in vivo electroporation. Positively expressing eyes were collected at P21 and then sectioned and immunostained with FLAG antibodies and Hoechst to visualize the location of Arl3-overexpressing rod nuclei. The 3D location of each nucleus within the nuclear layers was then graphed as a function of distance from the outer plexiform layer. In addition, the GTPase activity of each mutant was studied by overexpression in AD293 cells using GST-effector pulldowns and in vivo crosslinking with the cell membrane permeable crosslinker DSS.

Results: Expression of the autosomal dominant mutations D67V and Y90C resulted in nuclei positioned more basally within the outer nuclear layer or even mislocalized to the inner nuclear layer, similar to the GTP-locked Q71L. We found that while Arl3-D67V behaves as a constitutively active mutant, Arl3-Y90C behaves as a fast-cycling mutant. Fast cycling Arl3-Y90C has increased binding to the guanine exchange factor, Arl13B, as well as aberrant GEF-independent Arl3 activity. Finally, we show that the Y90C-dependent nuclear migration defect can be rescued by the overexpression of Arl3 effectors or the ciliary cargo of Arl3 effectors, the disruption of Y90C-Arl13B binding, or the disruption of GTP binding to Y90C.

Conclusions: Our results are consistent with the hypothesis that dominant mutations in Arl3 cause a defect in the migration of rod photoreceptor nuclei by disrupting the ciliary Arl3-GTP gradient. We found that either removing Arl3-GTP or restoring the ciliary Arl3-GTP gradient is sufficient to rescue the nuclear migration defect. Further studies will be necessary to find the ciliary signal underlying this phenotype.

CONTROL ID: 3712068

SUBMITTER (NAME ONLY): Bing-Yi Wang

TITLE: Long-term integration of the retina with 3D implants: structure and function

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Wang, Physics, Stanford University, Stanford, California, UNITED STATES|M.B. Bhuckory, D.V. Palanker, Opthalmology, Stanford University, Stanford, California, UNITED STATES|Z. Chen, EE, Stanford University, Stanford, California, UNITED STATES|A. Shin, Material Science and Engineering, Stanford University, Stanford, California, UNITED STATES|L. Galambos, T. Kamins, D.V. Palanker, Hansen Experimental Physics Laboratory, Stanford University, Stanford, California, UNITED STATES|K. Mathieson, Institute of Photonics, University of Strathclyde, Glasgow, Glasgow, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: For high-resolution prosthetic vision, pixels should be small, and crosstalk should be low. However, shallow penetration of the electric field with planar bipolar pixels prevents sufficient neural stimulation within the safe charge injection limit for pixels under 40μm. To overcome such limitation, we developed 3D arrays with deeper penetrating field and investigated the functional integration of these structures with the retina in vivo.

Methods: 3D implants were constructed by polymerizing honeycomb-shaped 25μm tall walls on planar photovoltaic arrays of 40μm and 20μm pixels, with a common return electrode on the edge of each device. Following subretinal implantation in rats with degenerated retinae (RCS rats), visually evoked potentials (VEPs) were measured in response to pulsed NIR (880nm) activation of the implants. Stimulation threshold was measured with full-field illumination, while visual acuity was assessed using alternating gratings, utilizing current steering-based field confinement. To verify the long-term effects, the VEP performance was followed up for at least 32 weeks post-op.

Results: Bipolar, horizontal and glial cells migrated into the honeycomb-shaped wells of both sizes. The full-field stimulation threshold with 3D implants was around 0.06mW/mm^2 with 10ms pulses - the same as with their flat counterparts, independent of the pixel size. The threshold remained nearly constant over the follow-up period. The VEP amplitude at high irradiances (2-5mW/mm^2) usually exceeded 100μV on the day of implantation, dropped drastically to a few tens of μV after a week, and gradually recovered to the initial level, if not greater, in approximately 15 weeks. Grating acuity matched the row pitch with 40μm pixels. With 20μm pixels, the prosthetic acuity matched the natural resolution of rats: 27.9 +/- 2.8μm.

Conclusions: Retinal integration with 3D implants did not adversely affect its electrical excitability. The stimulation threshold and visual acuity with 3D arrays were not different from those measured with flat arrays, utilizing current steering-based field confinement. If successful in human patients with atrophic macular degeneration, 3D honeycomb-shaped implants with 20μm pixels may enable prosthetic visual acuity as high as 20/80.

CONTROL ID: 3712069

SUBMITTER (NAME ONLY): Tatevik Takhmazyan

TITLE: Comparing the Visual Acuity of Zebrafish Using Analog and Digital Systems

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Takhmazyan, College of Osteopathic Medicine of the Pacific, Western University of Health Sciences, Pomona, California, UNITED STATES|D. Cameron, College of Optometry, Western University of Health Sciences, Pomona, California, UNITED STATES|

Commercial Relationships Disclosure: Tatevik Takhmazyan: Commercial Relationship: Code N (No Commercial Relationship) | D Joshua Cameron: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Danio rerio (zebrafish) are often used as a model to study visual physiology. Previous methodologies utilize an analog system to assess binocular and monocular visual acuities using the optokinetic response (OKR); however, an analog device presents with disadvantages, such as being multi-step, inefficient, and containing paper components prone to water damage. Thus, we have developed a digital system to observe the optokinetic response in zebrafish and effectively measure visual acuity.

Methods: Adult zebrafish were maintained under standard conditions and visual acuity was measured using an analog OKR device. Similarly, visual acuity was measured using a new digital OKR device. Acuity measurements were measured using high contrast, black-and-white stripes as well as colored stripes. A comparison between the measured visual acuities was completed using a paired t-test.

Results: The average analog visual acuity obtained using black-and-white stripes was 0.74 cycles per degree (cpd), while the average digital visual acuity was 0.48 cpd, as demonstrated in Figure 1. The analog system yielded significantly higher visual acuity in comparison to the digital system ($p<0.05$, $n=10$; Student's T-test). Likewise, visual acuity using red, blue and green produced similar results—the analog system had an overall higher visual acuity threshold in comparison to the digital system. Despite these differences, the analog and digital systems show a similar trend in visual acuity measurements, as seen in Figure 2.

Conclusions: Here, we demonstrate that visual acuity trends are consistent among analog and digital systems in both black-and-white and colored stimuli. Thus, an improved digital model can be beneficial for quickly evaluating visual response in adult zebrafish and facilitating disease-related research.

CONTROL ID: 3712070

SUBMITTER (NAME ONLY): Ming-Chen Lu

TITLE: Prediction of Visual Acuity in Patients with Microbial Keratitis

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lu, L. Niziol, L. Kang, M.A. Woodward, Department of Ophthalmology & Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|D. Ballouz, A. Thibodeau, M.A. Woodward, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|K. Singh, Department of Learning Health Sciences, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To predict visual acuity (VA) in patients with microbial keratitis (MK), at 90-day after diagnosis and at presentation, from data at the initial clinical ophthalmic encounter.

Methods: Patients with MK were identified in the University of Michigan electronic health record between August 2012 and February 2021. VA was extracted for the affected eye in MK patients with a unilateral infection, or for the better seeing eye in patients with bilateral infections, at the time of diagnosis and at day 90 (final). Random forest (RF) models were used to predict initial and final VA (iVA and fVA) that were <20/40. Predictors included age, gender, iVA (for the 90-day prediction model), and information documented in the clinical notes at presentation but excluding the assessment and plan. Model diagnostics are reported with 95% confidence intervals (CI) for area under the curve (AUC), misclassification, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results: 1791 MK patients were identified. Patients averaged 48.0 years old (standard deviation, SD=20.3) with 1734 (96.8%) unilateral infections and 57 (3.2%) bilateral infections. LogMAR iVA was on average 0.85 (Snellen equivalent=20/142; SD=1.25) in the affected or better eye and was <20/40 in 43.0% of patients. fVA was <20/40 in 26.6% of patients. The RF model for predicting fVA of <20/40 had an AUC of 0.95 (CI, 0.94- 0.97) and a misclassification rate of 11% (8-13%). The sensitivity, specificity, PPV, and NPV were 91% (86-95%), 89% (86- 91%), 73% (65-79%), and 97% (95-98%), respectively. Older age, worse presenting VA, and more mentions of “hypopyon,” “PKP,” and “OS” in the clinical note were found to be associated with 90-day VA <20/40. The RF model for predicting iVA of <20/40 had an AUC of 0.88 (CI, 0.85-0.91) and a misclassification rate of 17% (14- 20%). The sensitivity, specificity, PPV, and NPV were 77% (71- 82%), 88% (84-91%), 83% (78- 88%), and 83% (79-87%), respectively. Older age, less mentions of the term “quiet” in the clinical note, and more mentions of “hypopyon,” “OD,” and “BID” were associated with iVA of <20/40.

Conclusions: RF models showed strong performance in predicting fVA and iVA. The model identified morphologic features, past ocular surgery, and indirect measure of medication use as key risk factors associated with poor VA outcomes. Predicting fVA can inform clinicians when risk stratifying patients with MK.

CONTROL ID: 3712073

SUBMITTER (NAME ONLY): Syed Ali

TITLE: Ultra-wide field fluorescein angiography using wireless hand-held retinal camera in pediatric retinal conditions

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ali, I. Kozak, ophthalmology, moorfields eye hospital centre abu dhabi, Abu Dhabi, AD, UNITED ARAB EMIRATES|

Commercial Relationships Disclosure: Syed Ali: Commercial Relationship: Code N (No Commercial Relationship) | Igor Kozak: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ultra-wide field retinal imaging has become a useful tool for diagnosing and monitoring pediatric retinal diseases especially those affecting the retinal periphery. Recently, wireless retinal camera system has been used for ultra-wide field imaging mostly in pediatric population. This study investigated its additional feature, fundus fluorescein angiography (FFA) in diagnosing, treatment and follow-up monitoring of pediatric retinal conditions.

Methods: In this pilot, consecutive case series, the eyes with various retinal diseases were imaged at three sites: Moorfields Eye Hospital Abu Dhabi, Danat Al Emarat Hospital for Women and Children an d Kanad Hospital in al Ain, United Arab Emirates. PanoCam wireless hand-held retinal camera with built-in LED screen (Visunex, San Ramon, CA, U.S.A.) was used. Photos were taken of the posterior pole, including the optic nerve and macula and extended to 130° to include superior, inferior, nasal, and temporal retinal fields. Full control of illumination and image sharpness was achieved by finger control and focusing on working area and not on the screen. Weight calculate dose of fluorescein dye was injected intravenously and individual frames were captures. Images with significant artifacts were removed.

Results: Ultra-wide field fundus image acquisition and analysis was carried out in a total of 42 eyes of 21 children during the period from January and December 2020. Eight patient (16 eyes) had ultra-wide field FFA. All examination were uneventful. Patients were aged between 0 - 50 months, with mean age of 4.7 months. Of all 21 children, 11 were male and 10 were female. The diagnoses included retinopathy of prematurity, Coat’s disease, familiar exudative vitreoretinopathy, retinoschisis and others. Case management between different sites was made easy by sharing on Cloud.

Conclusions: By providing high quality fundus fluorescein angiograms the wireless hand-held retinal camera system is a suitable platform for diagnosis, treatment and follow-up monitoring of pediatric retinal diseases.

CONTROL ID: 3712075

SUBMITTER (NAME ONLY): Kwame Baffour-Awuah

TITLE: Investigating central visual field loss and its effects on how patients read the ETDRS chart

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Baffour-Awuah, L.J. Taylor, A.S. Josan, J.K. Jolly, R. Ahmed, R.E. MacLaren, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|K. Baffour-Awuah, L.J. Taylor, A.S. Josan, R. Ahmed, R.E. MacLaren, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|J.K. Jolly, Anglia Ruskin University Vision and Eye Research Institute, Cambridge, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Choroideremia is an inherited retinal degeneration in which asymmetric retinal deterioration occurs with greater temporal preservation. This correlates with higher retinal sensitivity nasal to central fixation, which we have previously documented. A key question is whether visual acuity (VA) in constricted visual fields measured with the Early Treatment Diabetic Retinopathy Study (ETDRS) chart is impacted by a neglecting of letters temporally compared to nasally. To investigate this further, we assessed whether choroideremia patients made errors more on the temporal than nasal side of the ETDRS chart in each eye under test conditions.

Methods: Monocular VA for right (RE) and left (LE) eyes was measured with a standard ETDRS chart at 4 metres. Letter columns were labelled from nasal (N) to temporal (T) visual field: N2, N1, C (central), T1 and T2 (Figure 2). Total errors per column in the chart were counted until 1 row below the “threshold” row (lowest row with no more than two errors). The distribution of column errors for each group was analysed with the X^2 test.

Results: Sixty eyes from 30 choroideremia patients (median age 44.9 years [IQR 39.1-58.9]) and 86 eyes from 43 healthy controls (median age 20 years [IQR 20-21]) were examined. Median VA was 72 for patients and 93 for controls. Results showed greater errors in T2 compared to N2 in the RE of choroideremia patients (p=0.045). However, there was no significant difference in the LE of patients (p=0.26), or in either eye in controls (RE p=0.77, LE p=0.32).

Conclusions: Choroideremia patients seem less able to read the right compared to the left side of the EDTRS chart with the right but not left eye. Since the left side is read first with each row, this may represent difficulties in tracking saccades in the right eye since the more sensitive temporal retina is not aligned with any letters along the row being read. Conversely, this surviving temporal retina in the left eye may provide a clearer view of the entire row, which may facilitate correct identification of subsequent letters. The ETDRS chart may not therefore be optimal for patients with asymetrically constricted visual fields so alternative approaches, such as reading rows backwards, may provide more consistent results.

CONTROL ID: 3712076

SUBMITTER (NAME ONLY): Gopal Jayakar

TITLE: Evaluating Hydroxychloroquine Induced Retinopathy with different OCT Imaging Instruments

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.K. Jayakar, T. de silva, C.A. Cukras, Unit on Clinical Investigation of Retinal Disease, National Eye Institute, Bethesda, Maryland, UNITED STATES|R. Membreno, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure: Gopal Jayakar: Commercial Relationship: Code N (No Commercial Relationship) | Tharindu de silva: Commercial Relationship: Code N (No Commercial Relationship) | Raul Membreno: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Cukras: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Quantitative metrics derived from OCT images could help detect hydroxychloroquine (HCQ) toxicity, which can be especially challenging in early (mild) disease. This project aims to investigate the generalizability of OCT metrics from different OCT instruments in their ability to discriminate early toxicity cases from unaffected eyes.

Methods: Participants enrolled in a case-control study (NCT01145196) underwent multimodal screening tests including SD-OCT imaging using both the Spectralis (Heidelberg Engineering, Heidelberg, Germany) (30^{o}x25^{o}, 60 µm spacing) and Cirrus (Carl Zeiss Meditec, Inc., Dublin, CA, USA) (6mmx6mm, 48 µm spacing) and were classified into unaffected or affected eyes. Forty-four participants (mean age 55, 91% female) included participants without any evidence of toxicity (99 eyes) and those with mild HCQ toxicity (14 eyes), defined as ≤100 µm Ellipsoid Zone loss on the foveal B-scan. Quantitative metrics computed from OCT images included total retina thickness (TRT), outer retina thickness (ORT) and minimum intensity (MinI) in both the TR and OR. OCT metrics were averaged across Early Treatment Diabetic Retinopathy (ETDRS) sectors. Bland-Altman plots assessed the agreement of metrics computed from the two instrumentation. The area under the receiver operating characteristic curves (AUC) were used to evaluate the ability of each metric from each OCT platform to discriminate between eyes with and without HCQ toxicity.

Results: Bland Altman analysis demonstrated minimal differences between the instruments for TRT (0.015 mm, 95% CI -0.019 mm to 0.039 mm) and ORT (0.005 mm, 95% CI -0.013 mm to 0.022 mm) measurements. However, minimum intensity measures had comparatively less agreement between instruments (t-test for TR p=0.0008, OR p=0.04861). For both instruments, ORT and TRT afforded excellent ability to discriminate between unaffected and mildly affected eyes with highest AUC values for ORT> 0.98 in the inner ETDRS subfields. OR MinI metrics from both instruments demonstrated good discrimination in the inner subfields (Heidelberg 0.95, Cirrus 0.91) but with larger differences between the instruments.

Conclusions: OCT metrics such as ORT, TRT and MinI derived from both instruments demonstrated successful generalizability in discriminating early/mild HCQ toxicity eyes from unaffected eyes. This bolsters the potential utility of OCT metrics to aid HCQ screening.

CONTROL ID: 3712077

SUBMITTER (NAME ONLY): Supraja Varadarajan

TITLE: Probing the role of retinorecipient target cells in visual circuit regeneration

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Varadarajan, O. Dhande, P. Le, A. Huberman, Neurobiology, Stanford University School of Medicine, Stanford, California, UNITED STATES|A. Huberman, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cells (RGC) are vulnerable to damage in diseases and injuries that cause blindness and cannot repair themselves. One promising approach is to reapply developmental mechanisms that form visual circuits, to promote repair. During development, target-derived cues and neural activity are required in both, the RGCs and target cells, to connect RGC axons with their synaptic partners in the brain. While many studies have identified events occurring in the RGCs to promote repair, far less is known about the role of target cells in RGC axon regeneration. Here we are testing a novel idea that post-synaptic target cells in the retinofugal pathway can be leveraged to promote regeneration of visual circuits.

Methods: We performed a distal injury to sever the optic tract of adult mice anterior to the pre-tectum. We increased neural activity broadly in the distal optic pathway using a chemogenetic approach; injury-only animals served as controls. To identify the specific contribution of target cells, we used synaptotagmin17::cre (Syt17::Cre) mice to precisely activate cells in the nucleus of the optic tract (NOT), a subcortical visual target. We used the rabies viral tracing system to identify inputs to cre-labeled cells in the NOT. We assessed RGC degeneration through immunohistochemistry, and axon regeneration through intravitreal injection of fluorophore-conjugated cholera-toxin subunit β.

Results: We observed significant regeneration of RGC axons ($p=0.0007$, Mann-Whitney, $n=10$) in the group that received increased neural activity, with significant regeneration within pre-tectum targets. We confirmed that cre-labeled cells in the NOT are bonafide retinorecipient cells. We also observed significant regeneration of RGC axons ($p=0.03$, Mann Whitney, $n=7$) in Syt17::Cre mice in which only the retinorecipient target cells were activated.

Conclusions: Our data shows that increasing electrical activity of neurons in the distal optic pathway can promote regeneration of RGC axons, and that specific activation of retinorecipient targets is sufficient to promote RGC axon regeneration in a distal injury model. These results suggest that target-derived cues are important to promote robust, accurate rewiring of injured visual circuits. These experiments will address the role of post-synaptic cells in CNS repair and have widespread relevance for treating blinding diseases, stroke and traumatic brain injury.

CONTROL ID: 3712078

SUBMITTER (NAME ONLY): Jennifer Haensel

TITLE: Associations Between Distance Visual Acuity and Cycloplegic Refractive Error in Children Aged 5 to 9 Years

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.X. Haensel, T.L. Roberts, Spencer Center for Vision Research at Byers Eye Institute, Stanford University School of Medicine, California, UNITED STATES|A. Chen, S.A. Cotter, S. Han, K. Huang, R. Patel, D.V. Retnasothie, Marshall B Ketchum University, California, UNITED STATES|I. Lorenzana FCOVD FAAO, Advanced Vision Center, Illinois, UNITED STATES|A.E. Aldrich, Snowy Range Vision Center, Wyoming, UNITED STATES|L. Jordan, College of Optometry, The Ohio State University, Ohio, UNITED STATES|A. Raghuram, Boston Children's Hospital, Massachusetts, UNITED STATES|A. Raghuram, Harvard Medical School, Massachusetts, UNITED STATES|V. Manh, Seattle Children's Hospital, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Distance visual acuity (VA) testing is commonly performed in children to screen for significant refractive error; however, the diagnostic value of distance VA remains unclear. We examined associations between VA and different types of cycloplegic refractive error in children.

Methods: Unaided distance VA (logMAR) was assessed monocularly in 234 children using single-surround ATS-HOTV (5-6 years) or eETDRS (7-9 years) protocols. Better-eye VA was used for analyses. Cycloplegic refractive error was determined using the Grand Seiko WR-5100K autorefractor. Refractive error was classified as emmetropia (EMM; -0.75D< sphere (sph) <+0.75D & cylinder (cyl) <0.75D), simple myopia (SM; sph≤-0.75D & cyl<0.75D), simple hyperopia (SH; sph≥+0.75D & cyl<0.75D), compound myopic/hyperopic astigmatism (CMA/CHA; both meridians myopic/hyperopic & cyl≥0.75D), simple myopic/hyperopic astigmatism (SMA/SHA; one myopic/hyperopic & one emmetropic meridian), or mixed astigmatism (MA; one hyperopic & one myopic meridian). Receiver operating characteristic (ROC) analysis was conducted to identify optimal logMAR VA thresholds for the detection of each refractive error type (if N>10) using the Youden Index.

Results: VA ranged from -0.3 to 1.2 logMAR (median=0.0, IQR=0.3), SE from -3.15D to +10.45D (mean=+1.00D, SD=1.79D), and astigmatism from 0.03D to 4.24D (mean=0.75D, SD=0.75D). Refractive error distribution was SH (N=90), EMM (N=52), SHA (N=27), CHA (N=26), SM (N=16), SMA (N=13), CMA (N=7), and MA (N=3). Analyses found low optimal logMAR VA thresholds across refractive error types (SM=0.15, SMA=0.05, SH=-0.25, SHA=-0.05, CHA=0.05), with high sensitivity (SM=94%, SMA=85%, SH=100%, SHA=85%, CHA=81%) but low specificity (SMA=63%, SH=1%, SHA=39%, CHA=66%) except for SM (79%). Analyses were repeated with clinically significant hyperopia (sph≥+2.00D; SH: N=13, CHA: N=13), also yielding low optimal thresholds (SH=-0.25, CHA=0.05), high sensitivity (SH=100%, CHA=92%), and low specificity (SH=2%, CHA=55%). ROC analysis on any clinically significant refractive error type showed a low optimal logMAR threshold (0.05) with 78% sensitivity and 87% specificity.

Conclusions: Distance VA had poor diagnostic value in the detection of clinically significant refractive error in children 5 to 9 years of age. Optimal logMAR VA thresholds based on the Youden Index were not informative in discriminating refractive error type.

CONTROL ID: 3712080

SUBMITTER (NAME ONLY): Mohammed Nasar Ibrahim

TITLE: Quantification of choroidal Haller's sublayer vasculature in 3D based on wide-field SS-OCT scans using 3D tensor voting and geometric modeling

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ibrahim, J.A. Sahel, J. Chhablani, K.K. Vupparaboina, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|S. Singh, Nilima Sinha Medical College & Hospital, INDIA|A. Samanta, Texas Tech University Health Sciences Center, Lubbock, Texas, UNITED STATES|A. Selvam, V. Sant, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|M. Rasheed, University of Waterloo, Waterloo, Ontario, CANADA|S. Jana, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|S.B. BASHAR, Manzoor Alam Optician, Kolkatta, West Bengal, INDIA|

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ABSTRACT BODY:

Purpose: The choroid is the dense vascular layer present posterior to the outer retina, serving various metabolic functions such as supplying oxygen and nutrients to the retina layers. Studies indicate that choroidal structural changes are related to several vision-threatening posterior segment disorders. Clinicians hypothesize that early manifestations of retinal diseases may be localized to specific regions of choroidal vasculature. However, studies so far were based on gross choroidal biomarkers including the thickness, volume, and vascularity index but not based on finer vasculature quantification. In this regard, to enable early diagnosis, clinicians seek to have biomarkers at the level of blood vessels in 3D. In response, we proposed and validated an end-to-end methodology to quantify choroidal Haller's sublayer vasculature in 3D using wide-field SS-OCT volumes.

Methods: This is a retrospective study performed using healthy and diseased wide-field SS-OCT volume scans taken from the Carl Zeiss Plex Elite 9000 device. We proposed an end-to-end algorithm to quantify Haller's sublayer vasculature. Firstly, we employ previously validated 3D residual U-Net, binarization based on exponential and non-linear enhancement, and 3D smoothing to segment the vasculature. Secondly, we employ TEASAR, 3D tensor voting, and geometrical modeling to estimate centerline (CL) and cross-sectional (CS) radius (Figure 1(a)). The accuracy of CL and CS estimates was validated based on subjective grading, performed on both synthetic and choroidal (of one healthy and two diseased eyes) vasculature. In each session (total 3 sessions), the grader graded CS at 5 randomly picked CL points (Figure 1(b)) to measure various parameters (Figure 1(c)).

Results: For each of the four parameters under consideration, we achieved an average grading score above 92%, demonstrating the efficacy of the proposed methodology. 3D heatmaps depicting relative CS radius as well as histograms of the representative healthy and diseased eyes facilitate quantitative visualization of the vasculature (Figure 2).

Conclusions: The proposed methodology is accurately quantifying choroidal Haller's sublayer vasculature in 3D.

CONTROL ID: 3712082
SUBMITTER (NAME ONLY): Keshav Narain
TITLE: Visual Evoked Potential (VEP) Latency and Vitamin B12 Level Association: Pilot Study to Determine if Electrical Response Patterns of the Retina and Optic Nerve are Indicative of B12 Deficiency
SESSION TITLE: Neurodegeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Narain, J. Revashetti, S. Limaye, South Bay Retina, California, UNITED STATES|
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ABSTRACT BODY:
Purpose: Vitamin B12 is a water-soluble essential micronutrient required for the development, myelination, and function of the nervous system. Absorption of vitamin B12 occurs via the GI tract and is impaired with age and certain medication. Deficiency in serum vitamin B12 is more common over age 60 and is known to impact optic nerve function and testing.

Serum B12 levels are considered normal above 250 pg/mL. 3% of men and 8% of women were found to have suboptimal B12 intake in the 2013-2016 National Health and Nutrition Examination Survey. Vitamin B12 deficiency is known to directly impact optic nerve function.

Our working hypothesis was that lower levels of B12 would be more likely to demonstrate abnormalities in optic nerve function, resulting in misdiagnosis of glaucoma or other conditions.
Methods: We retrospectively examined the impact of low, suboptimal, and normal B12 levels on optic nerve function using perimetry, visual evoked potential, and pattern electroretinography within a population of patients at increased risk for glaucoma.
Results: We found no correlation between the level of B12 (above 300mg) and electrophysiologic parameters. Due to small numbers, it was not possible to draw conclusions regarding the correlation between various parameters. Of the patients with sub-optimal B12, a majority had concurrent diagnoses of glaucoma or other optic nerve diseases.
Conclusions: Our data is limited and demonstrates that vitamin B12 deficiency may impact optic nerve function in a way that resembles more common diagnoses such as glaucoma. Our numbers were insufficient to define any correlation between latency, amplitude, phase, or other electrophysiologic parameters. We propose a further study to include larger numbers of patients with a randomization strategy to identify electrophysiologic parameters that may be specifically affected by various ranges of B12 deficiency.

Patients with characteristics of optic nerve disease including glaucomas should be evaluated for B12 deficiency. Not only could the deficiency result in worsening optic nerve function, but it may also influence the ability of the tissue to regenerate and heal. Neurogenesis, like other cytoproliferative events, requires B12. Suboptimal levels of B12 can both impair the diagnosis and also the treatment of glaucoma.

CONTROL ID: 3712083

SUBMITTER (NAME ONLY): Chanon Thanitcul

TITLE: Accuracy of Intraocular Lens Formulas in Combined Phacovitrectomy

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Thanitcul, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|A. Awidi, Y.J. Daoud, J.G. Ladas, D. Srikumaran, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is currently inconclusive how the newer generation intraocular lens (IOL) power formulas perform on eyes undergoing combined phacovitrectomy. We performed a retrospective, clinical study to assess the refractive accuracy of 4 newer generation formulas in eyes which underwent combined phacovitrectomy.

Methods: Preoperative optical biometry and postoperative outcomes were obtained from 61 eyes which underwent combined phacovitrectomy from 2017 to 2020 at the Johns Hopkins Wilmer Eye Institute. Inclusion criteria were postoperative best corrected visual acuity of 20/40 or better within 6 months and IOL implantation in the capsular bag. Exclusion criteria include eyes with any history of ocular surgeries, intraoperative complications, or evidence of corneal pathology. The Barrett Universal II, Kane, EVO v2.0, and Hill-RBF v3.0 were compared for their accuracy in predicting postoperative spherical equivalents (SE). Correlations between biometric parameters and errors were also assessed. A Wilcoxon rank sum test and Pearson's correlation coefficient were used for statistical analyses.

Results: Errors ranged from -2.36 to 2.97 diopters (D), mean absolute errors (MAE) ranged from 0.47 to 0.50 D, and median absolute errors (MedAE) ranged from 0.28 to 0.34 D. The Barrett formula had the lowest mean error (-0.035), MAE (0.469) and MedAE (0.275). The Barrett formula also had the highest percentage of eyes with predicted error within ±0.25 D (49.2%) and ±0.5 D (72.1%). Based on the MedAE, however, the Barrett formula had a comparable accuracy to other formulas (p ranged from 0.46-0.75). No other pairwise comparisons resulted in statistically significant differences. The anterior chamber depth (ACD) was found to have a weak negative correlation with error for all formulas. (correlation coefficients: -0.29 to -0.32, p: 0.011 to 0.026) The axial length (AL), mean keratometry (Km), and IOL power did not have a statistically significant correlation with error for all formulas.

Conclusions: All 4 newer generation formulas had a comparable accuracy in predicting refractive outcomes in eyes undergoing combined phacovitrectomy. Because the ACD had a statistically significant correlation with error in all formulas, this may serve as a target for improving the accuracy of newer formulas.

CONTROL ID: 3712085

SUBMITTER (NAME ONLY): Rachel Kuchtey

TITLE: Investigation of fibrillin-1 and LOXL1 in ocular health and disease

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.W. Kuchtey, L. wareham, H. Wu, J. Kuchtey, ophthalmology and visual sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|R.W. Kuchtey, molecular physiology and biophysics, Vanderbilt University, Nashville, Tennessee, UNITED STATES|E. Krystofiak, Y. Wu, C. Reinhart-King, E. Pokidysheva, S. Budko, Vanderbilt University, Nashville, Tennessee, UNITED STATES|V. Raghunathan, Basic sciences, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lysyl oxidase-like 1 (LOXL1) and fibrillin-1 (FBN1) are abundant proteins in exfoliation material (XFM), a hallmark of exfoliation syndrome (XFS). LOXL1 is associated with XFS and many mutations in FBN1 cause Marfan syndrome (MFS). LOXL1 and fibrillin-1 also co-exist in normal lens zonules. Zonule weakness is a common ocular feature shared by XFS and MFS. Here we sought to uncover their involvement in ocular health and disease.

Methods: $Loxl1^{-/-}$ and $Fbn1^{C1039G/+}$ mice on a 129 background were gifts from Drs. Tiansen Li and Hal Dietz and were used to create a double mutant (dbm) line, $Fbn1^{C1039G/+}/Loxl1^{-/-}$. Survival and systemic phenotypes were monitored and anterior segment morphology was measured by SD-OCT. Immunohistochemistry (IHC), transmission electron microscopy (TEM), atomic force microscopy (AFM) and biochemistry approaches were employed.

Results: $Fbn1^{C1039G/+}$ mice survive more than 1 year, consistent with being a mild MFS mouse model. Likewise, $Loxl1^{-/-}$ mice survive beyond 1 year of age. However, dbm mice do not survive beyond 3 months of age due to aorta dilation. Dbm mice also exhibited more pelvic floor organ prolapse. SD-OCT demonstrated thin central corneal thickness (CCT) and increased anterior chamber depth (ACD) in both $Fbn1^{C1039G/+}$ and $Loxl1^{-/-}$ mice. Thinning of CCT and deepening of ACD were more pronounced in dbm mice with normal axial length, indicating compromised zonules, which was confirmed by IHC for MAGP-1. Compared to wt, $Loxl1^{-/-}$ mice had fewer and abnormally formed elastic fibers, and enlarged and less defined collagen fibrils in their peripapillary sclera (PPS) revealed by TEM. Interestingly, by AFM we observed lower Young's modulus of cornea in all 3 lines compared to wt. Conversely, $Loxl1^{-/-}$ mice demonstrated higher Young's modulus of PPS than wt did. To investigate such differential biomechanical effects due to LOXL1 absence in the cornea and sclera, we used acetic acid collagen extraction which revealed differential collagen solubility and post-translational modification. Lastly, we also observed the differential influence of aging on collagen crosslinking in cornea and sclera.

Conclusions: The phenotypic and mechanistic investigations of our mouse models demonstrated their potential as an invaluable resource for further understanding and treatment of ocular and systemic manifestations of connective tissue disease.

CONTROL ID: 3712088

SUBMITTER (NAME ONLY): Ajoy Vincent

TITLE: Microperimetry and optical coherence tomography measures over 2 years in the RUSH2A study: annual rates of change from mixed effects modeling

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vincent, Ophthalmology and vision sciences, The Hospital for Sick Children, Toronto, Ontario, CANADA|A. Vincent, Ophthalmology and vision sciences, University of Toronto, Toronto, Ontario, CANADA|E.M. Lad, Duke University, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Ajoy Vincent: Commercial Relationship: Code N (No Commercial Relationship) | Eleonora Lad: Commercial Relationship(s);Code F (Financial Support):Jaeb Center for Health Research, Novartis, Iveric Bio, 4DMT

ABSTRACT BODY:

Purpose: Mean retinal sensitivity (MS) from microperimetry (MP), and ellipsoid zone (EZ) area and central subfield thickness (CST) from optical coherence tomography (OCT) are quantitative measures that provide insight to functional and structural function in inherited retinal degenerations (IRDs). There are few available estimates for their rates of change in IRDs. Here we provide estimates of change over 2 years from the Rate of Progression in USH2A-related Retinal Degeneration (RUSH2A) study based on these measures using mixed effects models.

Methods: In this prospective multicenter study, participants with visual acuity ≥20/80, stable fixation, and kinetic visual field of ≥10° in the study eye had MP and OCT testing at baseline, 1, and 2 years. MP was performed only in centers that had available equipment, while OCT was performed in all participants. Summary measures were MS from MP, and EZ area and CST from OCT. CST values were excluded when intraretinal cystoid spaces were detected. Mixed effects models were used to estimate the annual rates of change and percentage rates of change using log transformed data with 95% confidence intervals (CI). Models were applied to all eyes and to a restricted group of eyes with baseline levels above specific thresholds: >2 dB for MS and >1 mm^2 for OCT EZ area to mitigate floor effects. A model down-weighting outlier rates of change was also applied.

Results: 102 eyes were included. The average decline in MS [N=85] was 0.42 (0.27, 0.57) dB/year (Table 1) or 8.8 (6.2, 11.3)%/year (Table 2) in the entire cohort, and 0.51 (0.32, 0.69) dB/year or 8.8 (6.1, 11.5) %/year in the restricted cohort [N=69]. The average decline in EZ area for the entire cohort [N=100] was 0.11 (0.02, 0.20) mm^2/year or 1.2 (-1.1, 3.6) %/year vs 0.15 (0.03, 0.27) mm^2/year or 0.8 (-1.0, 2.6) %/year in the restricted cohort [N=72]. The decline in CST was 2.05 (1.07, 3.02) µm/year or 0.8 (0.4, 1.2) %/year in the entire cohort [N=63] when no cystoid spaces were detected. Down-weighting outliers reduced the estimated decline of MS and EZ, but not CST, compared to the unadjusted model.

Conclusions: Based on 2 years of follow-up in RUSH2A, estimates of the annual rates of decline in MP and OCT measures were affected by the baseline values of the eyes included in the analysis. Down-weighting outliers reduced the estimated decline of MS and EZ, but not CST.

CONTROL ID: 3712090

SUBMITTER (NAME ONLY): Yao Xue

TITLE: Dual patch-clamp recording of synaptic transmission between morphologically and physiologically characterized cone bipolar cell types and a diffused ganglion cell in wholemount mouse retina

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Xue, S. Lee, J. Zhou, Yale University Department of Ophthalmology and Visual Science, New Haven, Connecticut, UNITED STATES|Y. Xue, Yale University Graduate School of Arts and Sciences, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Yao Xue: Commercial Relationship: Code N (No Commercial Relationship) | Seunghoon Lee: Commercial Relationship: Code N (No Commercial Relationship) | Jimmy Zhou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While bipolar cells have been successfully studied with imaging, connectomic, and transcriptomic methods in recent years, the output synaptic physiology and functional circuitry of bipolar cell types remain poorly understood, except in the case of rod bipolar cells. This study is to characterize the physiology and synaptic transmission of identified cone bipolar cell (CBC) types in the mouse retina.

Methods: Patch-clamp recordings were made with two-photon microscopy from various morphological types of CBCs in the wholemount mouse retina. Receptive field properties were characterized using visual stimuli of various sizes and patterns. Dual patch-clamp recording was used to characterized synaptic transmission from CBC types to an ON-OFF small-field ganglion cell (tentatively termed XGC), which was brightly labelled in a transgenic line used.

Results: Receptive-field properties, baseline synaptic inputs, and major voltage-gated currents were characterized for 12 out of the 14 known morphological types of CBCs in the wholemount mouse retina. A catalog was generated to correlate physiological properties with morphological types of CBCs. Almost every CBC type showed distinctive physiological characteristics that distinguished one type from other types of CBCs. When the physiological and morphological features were analyzed together, all CBC types could be unambiguously defined. Dual patch-clamp recordings were then made from pairs of physiologically and morphological identified CBC types and XGCs in the whole-mount retina. Two distinctive kinetic patterns of signal transmission were found, suggesting differential temporal encoding of spatial visual integration. The results revealed an intriguing synaptic organization involving both chemical and electric synapses.

Conclusions: This study correlated distinct receptive-field and intrinsic physiological properties with morphologically identified CBC types and revealed new patterns of synaptic transmission from CBC types to XGCs, which may enhance spatiotemporal encoding of visual information.

CONTROL ID: 3712091

SUBMITTER (NAME ONLY): Jeremy Kulwin

TITLE: Assessment of Bifoveality in Adults with Retinal Polarization Scanning

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.K. Kulwin, J.M. Holmes, The University of Arizona Department of Ophthalmology and Vision Science, Tucson, Arizona, UNITED STATES|

Commercial Relationships Disclosure: Jeremy Kulwin: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Holmes: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Simultaneous binocular retinal polarization scanning has been successfully used to distinguish bifoveal fixation from monofixation as a means of screening for amblyopia in children. Although device performance is known to be degraded by spectacles and relies on accommodation (originally designed for screening children), we evaluated the ability of retinal polarization scanning to distinguish bifoveal fixation from monofixation in adults.

Methods: We studied 36 adults, ages 18 to 85y, presenting to an adult strabismus referral clinic. The gold standard for bifoveality was defined as at least 60 seconds of arc (arcsec) on the Randot Preschool stereoacuity test (StereoOptical, Chicago IL) performed at 40cm. Sensory monofixation was defined as 200 arcsec or worse, and indeterminate as 100 arcsec. To minimize potential confounding from poor VA, only subjects with 20/40 or better VA in each eye were included. Retinal polarization scanning was performed using the blinqPro (Rebion, Boston, MA), yielding a binocularity score from 0% to 100%. Analogous to children, we defined bifoveality by retinal polarization as a blinqPro binocularity score of 60% or better. Testing was performed through spectacles if worn. We compared assessments of bifoveality versus monofixation using kappa statistics.

Results: Of 36 adults, 7 (19%) were classified as bifoveal based on Randot Preschool near stereoacuity testing, 8 (22%) as indeterminate and 21 (58%) as monofixational. Only 3 (8%) of subjects were classified as bifoveal by the blinqPro. Agreement in bifoveality, between Randot Preschool and blinqPro was poor (kappa = -0.07, 95% CI -0.20 to 0.06, excluding subjects indeterminate on stereoacuity testing). No adults identified as bifoveal on Randot Preschool testing were identified as bifoveal on blinqPro testing.

Conclusions: In contrast to application of the blinq to children, where it is very useful in screening for amblyopia, the current device does not reliably distinguish bifoveality from monofixation in adults. The blinq manufacturers had already identified limitations in detecting bifoveality in adults; inadequate accommodation, attempting to scan through spectacles where coatings and reflections interfere with the signal, and image degradation from less than clear media. Further modification of methods to identify bifoveality are needed for adults.

CONTROL ID: 3712092

SUBMITTER (NAME ONLY): Monica Jablonski

TITLE: Spontaneous Polygenetic AMD Preclinical Models Selected from the BXD Family of Mice

SESSION TITLE: Animal Models of Age Related Macular Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.M. Jablonski, X. Wang, R.N. Simpson, T. Hollingsworth, Ophthalmology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|A. Swaroop, E.Y. Chew, National Eye Institute, Bethesda, Maryland, UNITED STATES|D. Ashbrook, R. Williams, Genetics, Genomics & Informatics, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Modeling of complex, polygenetic and environmentally-modulated diseases such as age-related macular degeneration (AMD) presents the need for a nuanced approach to accurately mimic the disease that is found in humans. To tackle this problem, we mined the BXD family of recombinant inbred lines of mice for polygenetic models of AMD using a systems genetics approach. Our goal is to provide the vision community with one or more spontaneous polygenetic pre-clinical models of AMD.

Methods: Based on the literature, we identified 27 genes associated with human AMD, 11 of which have polymorphisms in the BXD family of mice that are predicted to change the function of the gene product in a similar manner to that predicted in humans. We chose 6 strains of mice with various combinations of the 11 genes with the goal of selecting mice with various presentations of AMD. BXD strains and C57B/6J controls are being aged from 6 to 18 months and are evaluated clinically every three months. Optical coherence tomography (OCT), full field electroretinogram (ERG), funduscopy/fluorescein angiography (FA) and optokinetic nystagmus (OKN) measurements are used to document any pathophysiology. Histological and ultrastructural analyses are being performed upon euthanasia at 18 months.

Results: Here we present preliminary data from our two most promising polygenetic AMD mouse strains. BXD34 presents with functional deficits documented as lessened ERG amplitudes along with reductions in visual acuity and contrast senstitivity by 9 months of age. Subretinal deposits are evident by OCT analyses and ultrastructural analyses reveals marked basal linear and basal laminar deposits. Moreover, there are numerous vesicles filled with debris present in the cytoplasm of the retinal pigment epithelium (RPE). In contrast, BXD38 presents with no functional deficits up to 9 months of age despite the presence of subretinal deposits that were detected using OCT. These strains are continuing to be aged and phenotyped.

Conclusions: Currently, BXD34 exhibits the most similarities to an atrophic AMD-like phenotype by exhibiting drusen-like deposits and both anatomical and physiological declines in retinal health. BXD38 presents with more mild functional deficits coupled with the presence of subretinal deposits. These strains are continuing to be evaluated up to 18 months of age at which time ultrastructural and immunohistochemical analyses will performed.

CONTROL ID: 3712093

SUBMITTER (NAME ONLY): Narendra Pandala

TITLE: Development of chemically crosslinked PEG-PAA hydrogels suitable for engineering of the vascularized outer retina

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pandala, M. LaScola, E. Lavik, University of Maryland Baltimore County, Baltimore, Maryland, UNITED STATES|K. Mulfaul, E.M. Stone, R.F. Mullins, B.A. Tucker, The University of Iowa Hospitals and Clinics Department of Pathology, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To engineer a micorphysiologic system that more accurately recapitulates the vascularized outer retina suitable for evaluating AMD pathology and development of novel therapeutics.

Methods: A hydrogel library based on poly (ethylene glycol) (PEG), poly-L-lysine (PLL) and poly(allylamine) (PAA) was generated using succinimide and free amine reaction chemistry. Cellular compatibility was evaluated using a rat endothelial cell line and human iPSC-derived choroidal endothelial cells generated via directed differentiation and CD31 magnetic bead immunopanning. Cell health and identity was evaluated using a series of live dead assays and immunofluorescence staining.

Results: A library of 12 synthetic, chemically crosslinked, hydrogels with tunable mechanical and degradation properties were developed. Hydrogels with a lower amine content were found to have superior endothelial cell compatibility. We hypothesize that this is due to the cell surface disrobing characteristics of the polycations presents in the gels. Hydrogels with a higher polycation concentration showed relatively poor endothelial cell compatibility. Gels with optimal compatibility were found to promote endothelial cell spreading, migration, and capillary network-like formation.

Conclusions: In this study novel hydrogels with unique mechanical and degradation properties were generated via chemical crosslinking of PEG, PLL and PAA. Low amine hydrogels were found to be superior for promoting endothelial cell spreading, migration and vascular tube formation. To create in vitro models that more accurately recapitulate the choriocapillaris, optimized hydrogels will be used as a bioink for screen-based printing of rat and human vascular endothelial cells.

CONTROL ID: 3712094

SUBMITTER (NAME ONLY): Yongling Zhu

TITLE: Genetic dissection of a new amacrine cell type shaping object motion sensitivity in the mouse retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhu, S.H. DeVries, A. Jo, S. Deniz, S. Cherian, J. Xu, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|Y. Zhu, S.H. DeVries, A. Jo, S. Deniz, S. Cherian, J. Xu, Neuroscience, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Amacrine cells (ACs) are the most abundant inhibitory interneurons in the retina yet remain the least understood retinal cell class. The great diversity of ACs has been a major obstacle to access individual cell types for systematic studies. The development of genetic tools that allow for cell type-specific targeting and manipulation would be an important step towards the characterization of AC types. In this study, we aim to use new mouse intersectional genetic tools combined with functional imaging and electrophysiology recording to morphologically and functionally dissect AC circuits.

Methods: We created intersectional strategies by using a combination of Cre and tTA expression to discover new AC types and to target these cells with increased specificity. After that, we focused on a new AC type for functional analysis. We characterized its light response properties by imaging Ca^{2+} responses at the sites of neurotransmitter release, and then identify its post-synaptic RGCs with intersectional ChR2 activation. Finally, we developed a chemogenetic mouse line to inactivate the AC and examine its functional roles in different circuits.

Results: With Slc32a1-iCreER/ CaMK2a-tTA intersectional strategy combined with temporally controlled Cre induction, we discovered a narrow-field AC subtype (named CK2-AC1) in the mouse retina and achieved single AC type targeting. Two-photon Ca^{2+} imaging revealed that CK2-AC1 received synaptic inputs from OFF bipolar cells and responded strongly to local motion but not to global motion. Optogenetic stimulation showed that CK2-AC1 provided glycinergic inputs to several RGC types stratified in the middle of the IPL, such as HD1-RGC and HD2-RGC. Chemogentic inactivation experiments further demonstrated that CK2-AC1 provided suppression to several RGC types during local stimulation and shape the object motion sensitivity (OMS) of these RGCs.

Conclusions: This study introduced a workflow based on Cre/tTA intersectional strategies for systematically analyzing AC types and examining their circuit roles in visual processing. With this workflow, we discovered a new AC type and revealed its functional roles in the OMS circuits. We propose that CK2-AC1, together with other ACs in the OMS circuits, controls the objective motion sensitive signals RGC send to the brain.

CONTROL ID: 3712095

SUBMITTER (NAME ONLY): Assylbek Zhylkibayev

TITLE: Modeling the Ocular Tissue Exposure to Chemical Warfare Agent Arsenicals in Mice

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Gorbatyuk, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|R.K. Srivastava, M. Athar, Department of Dermatology, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|A. Zhylkibayev, Department of Optometry and Vision Science, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal tissue damage is often associated with exposure to arsenicals, which are highly toxic chemical warfare agents (CWAs), including lewisite (LEW). However, the difficulties associated with accessing the posterior ocular tissues in CWA-affected individuals and the technical challenges of using CWAs in laboratory settings make it necessary to use relatively less toxic arsenicals in eye research. Similar to LEW, phenylarsine oxide (PAO) activates a pro-inflammatory response, oxidative stress, and a cell death program in the lung, liver, and skin tissues. We hypothesized that arsenical exposure results in corneal injury and retinal tissue damage.

Methods: Human corneal epithelial cells (HCEC), keratocytes (HCK), and retinal endothelial cells (HREC) were incubated with 200 nM PAO for 6, 12, and 24 h. Cytokine expression was detected using qRT-PCR. Direct ocular exposure of C57BL/6 mice to PAO was conducted at doses of 5 and 50 µg for 3 min using the patch method. Cytokine gene expression, retinal functional, and histological analyses of PAO-treated mice were performed 1 day and 14 days after exposure using qRT-PCR and ERG, respectively.

Results: Treating human corneal and retinal cells with PAO resulted in a significant elevation of Il-1β (HREC 2.7-fold; HCEC 2-fold), Cox2 (HCK 3.7-fold; HREC 15.5-fold; HCEC 4.6-fold), and Ifn α (HCK 349.3-fold; HREC 11.5-fold; HCEC 33.7-fold). Similar to the in vitro results, the in vivo findings showed that there was a marked increase in cytokine gene expression in both the corneal and retinal tissues of exposed mice. Mice treated with 5 µg PAO per eye showed significant increases in Il-6 (cornea 13-fold; retina 106-fold), Il-1β (cornea 7-fold; retina 22-fold), and Cox2 (cornea 11-fold; retina 109-fold). Mice exposed to 50 µg PAO per eye showed a remarkable elevation of Il-6 (cornea 1,337-fold; retina 134-fold), Il-1β (cornea 1,213-fold; retina 2,705-fold), and Cox2 (cornea 82-fold; retina 80-fold) mRNA. In addition, PAO exposure resulted in diminished scotopic a- and b-wave ERG amplitudes at 2 weeks after exposure.

Conclusions: These findings establish a foundation for future mechanistic ocular toxicity studies of arsenical exposed populations, demonstrating that not only the corneal tissue, but also the retina may be damaged depending on the severity of exposure.

CONTROL ID: 3712099

SUBMITTER (NAME ONLY): Karin Lypka

TITLE: Comparison of Manual and Automated Retinal Flow Deficit Measurements in Proliferative Diabetic Retinopathy using Swept-Source OCT Imaging

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.R. Lypka, M. Shen, H. Al-khersan, W.J. Feuer, G. Gregori, P.J. Rosenfeld, Department Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|Q. Zhang, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|J. Russell, Institute for Vision Research and Department of Ophthalmology and Visual Sciences, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|M. Zou, Columbia University, New York, New York, UNITED STATES|R.K. Wang, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Manual measurements of retinal flow deficits (RFDs) in eyes with proliferative diabetic retinopathy (PDR) imaged with widefield swept-source OCT (SS-OCT) were compared with measurements from an automated algorithm.

Methods: In a retrospective review of patients enrolled in a prospective SS-OCT (PLEX® Elite 9000, Carl Zeiss Meditec, Dublin CA) imaging study, a consecutive case series of eyes with PDR were imaged using a foveal-centered 12x12mm scan pattern underwent manual segmentation of areas with RFDs. Total retinal vasculature slabs were used for analysis of RFDs. A previously published algorithm was used to assess RFDs by converting a 2-dimensional en face SS-OCTA image to a vessel binary image using MATLAB. The areas of RFDs identified using the manual and automated methods were compared.

Results: A total of 19 eyes with PDR from 15 patients over 62 visits were compared. All scans were evaluated. The average RFD area measurements were not significantly different between manual (16.72 ± 17.27 mm^2) and algorithm (17.64 ± 15.33 mm^2) (p=0.15). 75% of the manual and algorithm measurements were within 5 mm^2 of each other, with total measurements ranging from 0-80 mm^2. There was also no significant difference between areas of RFDs detected only by the manual approach (5.14 ± 3.94 mm^2) compared with the algorithm approach (6.06 ± 3.91 mm^2; p=0.15). Examples of the scans and RFD outlines are shown in Fig. 1.

Conclusions: On average, the two techniques yielded similar results for total RFD area measurements with no disparity in areas detected by only one technique. This suggests that the automated approach might be useful for grading and monitoring RFDs in eyes with PDR.

CONTROL ID: 3712100

SUBMITTER (NAME ONLY): S Scott Whitmore

TITLE: Simulating the altered photoreceptor cell topography of progressive retinal dystrophies using OCT images and public data

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Whitmore, A.P. DeLuca, J.L. Andorf, J.L. Cheng, M. Motlagh, C.R. Fortenbach, D. Critser, E.M. Stone, I. Han, University of Iowa Institute for Vision Research, Iowa City, Iowa, UNITED STATES|S. Whitmore, A.P. DeLuca, J.L. Andorf, J.L. Cheng, M. Motlagh, C.R. Fortenbach, D. Critser, E.M. Stone, I. Han, Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The topography of rod and cone photoreceptor cells shapes the patterns of outer retinal loss observed in progressive cone-rod and rod-cone dystrophies. To better understand these diseases, we modeled the OCTs observed in progressive photoreceptor degenerations by simulating differential survival of rod and cone cells.

Methods: We assumed that the thickness of the outer retina is proportional to the topographic composition of living rod and cone photoreceptor cells. Consequently, the death of rods or cones will reduce the thickness of the outer retina proportionally to the baseline composition of these cells. By definition, 100% of rods and 100% of cones survive in eyes unaffected by disease. Using this framework, we imaged the maculas of an unaffected control using a Heidelberg Spectralis OCT, segmented the retinal layers using the Iowa Reference Algorithms, and located the fovea and the optic nerve within these volumes. We registered these volumes to published densities of photoreceptor cells (Curcio et al. J Comp Neurol 1990), interpolated the cell densities at every A-scan, and computed the expected proportion of rod and cone photoreceptor cells at every A-scan. To simulate the death of photoreceptor cells, we reduced the thicknesses of the outer retinal layers as a function of the contribution of rods and cones, reconstructed the segmentation, and resampled the voxels within each layer.

Results: When more cones are lost than rods, our model reproduces the basic pattern of a cone-rod dystrophy, such as autosomal recessive Stargardt disease. When more rods are lost than cones, our model reproduces the basic pattern of a rod-cone dystrophy, such as USH2A-associated retinitis pigmentosa. Users can explore the interactive model at https://observablehq.com/@barefootbiology/simulating-rod-and-cone-loss.

Conclusions: Clinicians can infer the approximate proportions of surviving rods and cones by comparing the simulated output to B-scans of actual patients. Computational biologists can use the model to communicate with clinicians by translating mathematical models of cell survival into the visual idiom of the clinic.

CONTROL ID: 3712102

SUBMITTER (NAME ONLY): Yanhui Ma

TITLE: Multi-dimensional quantification of diabetic retinopathy early detection

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ma, A. Letson, M. Ohr, C.J. Roberts, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|C.J. Roberts, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To extract vascular features in the superficial (SVC) and deep (DVC) vascular complex using optical coherence tomography angiography (OCTA), and to compare them among subjects with mild to moderate diabetic retinopathy without macular edema (DR), diabetics without retinopathy (DnoR), and normal controls (NRL)

Methods: En face OCTA images of the SVC and DVC were generated after scanning the 3 × 3 mm^2 macular regions. Twenty subjects were imaged, including 5 NRL, 10 DnoR, and 5 DR, and only the right eye was included in the analysis. The quantification defines the region of interests (ROIs) as 45° equal-area sectors namely NS, SN, ST, TS, TI, IT, IN, and NI (N = nasal, S = superior, T = temporal, I = inferior), in addition to the whole circular zone centered at the macula. The microvascular morphologic features were analyzed using fractal dimension (FD) and vascular orientation pattern curve (Ma et al, Sci Rep, 2021). FD is a metric to characterize global vessel anatomical complexity. Vascular orientation pattern captures local variations in the vessel orientation ranging from 0 to 180°, and the area under the curve indicates the vessel area density (VAD). An analysis of variance (ANOVA) and post hoc Tukey's test was performed to detect the difference in FD and VAD in each ROI among the three groups.

Results: For the whole macular zone, significant differences in FD and VAD were observed between NRL and DR (Fig1). Different sectoral ROIs exhibited different abilities to differentiate DR from the other two groups. Sector ST showed no difference among the three groups in FD nor VAD, although n is too low to be conclusive; whereas sector IN showed significant difference not only between NRL and DR, but also between DnoR and NRL in VAD (p=0.0060 for SVC; p=0.0225 for DVC), and between DnoR and DR in FD (p=0.0033 for SVC; p=0.0401 for DVC). In addition, the vascular orientation pattern in DR shows greater difference from NRL or DnoR in sector IN than in the whole macular zone (Fig2).

Conclusions: Retinal vascular features were extracted from OCTA images for multi-dimensional quantification using layer- and sector-based ROIs. DR-associated microvascular deterioration is not uniform in all sectors. Sector IN detected the microvascular difference between DnoR and DR, and its sectoral analysis holds promise for DR detection at the earliest stage.

CONTROL ID: 3712103

SUBMITTER (NAME ONLY): Bethany Higgins

TITLE: Evaluating an OCT-based grading of age-related macular degeneration severity from The Northern Ireland Sensory Aging studies using measurement of dark adaptation

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.E. Higgins, G. Montesano, D.P. Crabb, Optometry and Vision Sciences, City University of London, London, London, UNITED KINGDOM|G. Montesano, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|T. Naskas, K. Graham, U. Chakravarthy, F. Kee, D. Wright, R.E. Hogg, Queen's University Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Studies suggest delayed rod-mediated dark adaptation (DA) is a diagnostic indicator of age-related macular degeneration (AMD). We assessed if DA differences (estimated by rod-intercept time [RIT]) are more discernible between AMD severity grades using an OCT-based criteria (including subretinal drusenoid deposit [SDD] presence) over a Colour Fundus Photography (CFP)-based classification.

Methods: Data was acquired from two related cross-sectional population based studies - Northern Ireland Sensory Aging studies (NISA;NISA-2). Participants with RIT data (AdaptDx [Maculogix,USA]) and both CFP (Canon CX-1 Digital Fundus Camera [Canon,USA]) and spectral domain OCT (SD-OCT;Heidelberg Spectralis SD-OCT [Heidelberg Engineering, Germany]) images were used. SDD presence was identified and images graded by Beckman and OCT-based classifications. Age-corrected time-to-event analysis assessed the magnitude of differences in RIT and plotted using Kaplan Meier curves (Fig 1).

Results: 459 eyes (mean [standard deviation; SD] age 66[8] years) were stratified into Beckman0-3 and then OCT0-2. Uncorrected mean(SD) RIT for Beckman groups was 7.5(5.3), 8.0(4.3), 7.3(4.7) and 15.6(11.9) mins, respectively. Uncorrected mean(SD) RIT for OCT groups appeared more distinct between gradings: 7.4(5.5), 10.0(7.2) and 15.3(21.0) mins respectively. After age-correcting, eyes in B3 had statistically significantly worse average RITs compared to the other groups (B0-2; p=<0.005 all) but there were no differences in RIT between the other Beckman groups. Eyes in OCT2 had worse RITs compared to controls (OCT0) (p=<0.001) and eyes in OCT1 (p=0.009). No statistically significant difference was found between OCT0 and OCT1 (p=0.195). SDD presence significantly worsened RIT within OCT2 (p=0.002) but not within OCT1 (p=0.285). In OCT0 the presence of SDDs gave better RIT values(p=0.012).

Conclusions: There is some evidence of differences in RIT being more apparent between AMD severity grades using an OCT-based rather than a CFP-based classification, but differences were less clear once corrected for age. OCT classifications including SDDs, may be useful for clinical trials in AMD. A highlight of our enriched population study is a uniquely large SDD sample (n=109) not regularly reported in recent DA research.

CONTROL ID: 3712104

SUBMITTER (NAME ONLY): Saber Kazeminasab

TITLE: A Python collection of tools for analyzing visual fields

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kazeminasab, M. Eslami, Y. Li, M. Fazli, V. Sharma, M. Wang, T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|N. Zebardast, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Artificial intelligence (AI) methods have become an indispensable part of ophthalmology in recent years. A variety of AI methods are available to analyze visual fields (VFs) and to detect or predict vision loss progression. Nearly all of the recent deep learning VF models have been implemented in the Python language, which provides numerous readily available algorithms and techniques for this purpose. At the same time, the vast majority of VF analytic tools have been implemented in the R language. Here, we aim to bridge this gap by providing a Python-wrapped package to make numerous previously developed R libraries and functions for VF analysis available in the Python language.

Methods: In a first step, we analyzed existing R libraries for visual fields, most notably the vfprogression [1] and the visualFields [2] libraries for overlaps as well as distinct functionality. Based on this, we conceptualized a Python package combining the functionality of the existing R libraries and harmonizing their data structures. Finally, with help of the wrapper library rpy2, we translated this functionality and the according data structures into Python.

Results: The developed Python package is available as open-source software at the GitHub repository: https://github.com/mohaEs/PyVisualField. In the same repository, we demonstrate the capabilities of the new Python package in the categories of presenting data, plotting, scoring and progression as well as normalization analysis. For each category, we provide function descriptions and examples and the function output in Jupyter notebooks. Fig. 1 shows examples of demonstration from the functionality from the original vfprogression R library and, analogously, Fig. 2 shows examples from the visualFields R library.

Conclusions: To make the considerable VF analysis functionality of existing R libraries available to the Python AI community, we developed a Python package and demonstrate its functionality to support ophthalmic researchers in VF statistical analysis, plotting, and progression prediction.

[1] Elze, T., Li, D., Wall, M., Choi, E. U., vfprogression: Visual Field (VF) Progression Analysis and Plotting Methods, available at: https://cran.r-project.org/package=vfprogression.

[2] Marin-Franch, I. Swanson, W.H., Wall, M., Turpin, A., Artes, P.H., Huchzermeyer, C., Montesano, G., Dul, M., W, visualFields: Statistical Methods for Visual Fields, available at: https://cran.r-project.org/package=visualFields

CONTROL ID: 3712105

SUBMITTER (NAME ONLY): Marin Gantner

TITLE: The serine biosynthetic enzyme, PHGDH, is essential for retinal health

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Gantner, R. Fallon, C. Bates, M. Friedlander, Lowy Medical Research Institute, California, UNITED STATES|Y. Ideguchi, M. Friedlander, The Scripps Research Institute, La Jolla, California, UNITED STATES|M. Handzlik, C. Metallo, Salk Institute for Biological Studies, La Jolla, California, UNITED STATES|M. Wallace, Dublin City University, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Macular telangiectasia type II (MacTel) is a late onset macular disease leading to progressive vision loss. Previous work determined that low circulating levels of serine in MacTel patients is associated with retinal dysfunction. Whole exome sequencing studies found that rare variants in PHGDH, the rate limiting enzyme in serine synthesis, account for a significant fraction of the disease. The purpose of this study was to determine the potential impact of reduced PHGDH function on retinal health.

Methods: To test the rate of serine and glycine biosynthesis in the retina, as well as uptake of these amino acids from the circulation, we used heavy carbon (C^{13}) labeled glucose, serine or glycine coupled with mass spectrometry. To determine the consequences of reduced PHGDH activity on retinal health we used mice heterozygous for PHGDH and monitored their retinal function and metabolite levels.

Results: We determined that the neural retina and RPE/choroid exhibit high de novo serine synthesis, comparable to that in the brain. Additionally, a large portion of retinal serine originates in the circulation. Mice with reduced PHGDH function have altered circulating, retinal and RPE metabolite levels. Electroretinogram (ERG) measurements in mice indicate visual impairment with reduced PHGDH activity.

Conclusions: The high rate of serine biosynthesis, as well as uptake from the circulation, suggests that the serine pool in the retina is highly dynamic. Variants in PHGDH that impair enzyme function, as observed in a subset MacTel patients, are sufficient to generate metabolite defects and drive retinal dysfunction.

CONTROL ID: 3712107

SUBMITTER (NAME ONLY): Kathryn Pepple

TITLE: Systemic Administration of Acazicolcept (ALPN-101), a Dual ICOS/CD28 Antagonist, Suppresses Ocular Inflammation in Rat Experimental Autoimmune Uveitis

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: T cell costimulation has been implicated in the pathogenesis of autoimmune uveitis. Acazicolcept (ALPN-101) is an Fc fusion protein of the human inducible T cell costimulator ligand (ICOSL) and a variant immunoglobulin domain (vIgD™) designed to inhibit the CD28 and ICOS T cell costimulatory pathways. Here we evaluate the efficacy of systemic administration of acazicolcept in experimental autoimmune uveitis (EAU).

Methods: EAU was induced on Study Day 0 (SD0) in female Lewis rats using IRBP peptide R16 in complete Freund's adjuvant. Rats were treated with acazicolcept (100 mg/kg), an Fc control protein (50 mg/kg), or triamcinolone acetonide (0.8 mg/kg) once by subcutaneous injection on SD7. Masked clinical scores, body weights, and ocular histologies were assessed through SD14. Aqueous and intraocular contents collected on SD14 were analyzed by multiplex cytokine analysis and flow cytometry.

Results: Compared to Fc control, acazicolcept significantly reduced the number of eye-infiltrating CD45+ cells and IL-17A+ and IFNγ+ CD3+ T cells and tended to decrease intraocular aqueous cytokines including leptin, IL-1β, RANTES, IFNγ, IL-17A, VEGF, CXCL5, and IP-10, as effectively as steroid treatment (though not always statistically significantly). From SD10-13, Fc control-treated rats demonstrated a significantly higher average masked clinical score than the steroid or acazicolcept-treated groups (AUC, $p<0.01$). Histology scores of eyes from steroid- (4.7 ± 4.9, $p<0.05$) or acazicolcept-treated rats (4.2 ± 5.2, $p<0.05$) were also significantly lower than Fc-treated rats (19.1 ± 10.39) on SD14. Steroid-treated animals lost a significant amount of body weight during treatment between SD7-14, as compared to acazicolcept- ($p=0.0003$) or Fc control-treated ($p=0.0071$) animals.

Conclusions: Systemic treatment with acazicolcept significantly suppresses EAU in rats, as evidenced by reduced clinical and histological scores, and correlated with reduced eye-infiltrating IL-17A+ and IFNγ+ T cells. Acazicolcept was well-tolerated without the weight loss induced by steroid treatment. Due to species- and disease-related differences, the dose regimen used in this study is not predictive of the effective dose in humans. However, these data suggest acazicolcept may be a safe and effective alternative to corticosteroids for use in treatment of autoimmune uveitis.

CONTROL ID: 3712109

SUBMITTER (NAME ONLY): Scott Plafker

TITLE: Carbohydrate restriction preserves visual acuity and motor function in a mouse model of autoimmune demyelination

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Ocular pathologies are understudied sequelae of multiple sclerosis (MS) and other autoimmune diseases. Current treatments are expensive, highly immunosuppressive drugs that increase infections and cause other adverse effects but are only partially efficacious. The goal of this study was to test the hypothesis that a well-formulated ketogenic diet (WF-KD) can reduce optic neuritis and preserve vision in a mouse model of MS called experimental autoimmune encephalomyelitis (EAE).

Methods: Male and female C57BL/6J mice were fed the WF-KD (77.1% fat, 22.4% protein, 0.5% carbohydrate) or a nutrient-matched control diet (10.4% fat, 20.4% protein, 69.3% carbohydrate) and 2 weeks later immunized with a myelin oligodendrocyte glycoprotein peptide antigen to induce EAE. Motor deficits, visual acuity, as well as glucose and ketone levels in blood were measured longitudinally. Post-mortem, retinal ganglion cells (RGCs) were quantified and splenocytes were immuno-profiled. Circulating cytokines and fatty acid content were also analyzed.

Results: Unlike obesogenic western diets containing pro-inflammatory fats and high carbohydrate content, EAE mice fed a WF-KD did not gain weight. The WF-KD conferred resistance to EAE motor deficits and preserved RGCs and visual acuity. Analysis of plasma showed that the WF-KD decreased circulating C-reactive protein and proinflammatory cytokines, reduced pro-inflammatory omega-6 fatty acids (e.g., arachidonic acid), and increased anti-inflammatory omega-3 fatty acids.

Conclusions: These findings demonstrate that a diet enriched in healthy fats and restricted for carbohydrates promotes a systemic anti-inflammatory milieu that mitigates autoimmune-induced visual and motor deficits, further supporting ongoing clinical trials testing this dietary strategy to treat MS patients.

CONTROL ID: 3712110

SUBMITTER (NAME ONLY): Mason Seely

TITLE: Associations between oxygen supplementation and choroid thickness in preterm infants

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The choroid plays a crucial role in the health and function of the outer retinal layers, yet little is known about the impact of perinatal systemic health factors on its development. There is some evidence that suggest hyperoxia is associated with a thinner choroid in preterm infants. We hypothesize that higher oxygen support during the intensive care period is associated with a thinner subfoveal choroid in preterm infants.

Methods: Preterm infants were imaged using handheld swept-source optical coherence tomography (SS-OCT) as a part of the prospective, observational, IRB approved BabySTEPS (STudy of Eye imaging in Premature infantS) clinical study. Choroidal thickness (SFCT) was measured across the central 1mm at 36±1 weeks postmenstrual age (PMA) and averaged between eyes. Highest, mean, and lowest oxygen saturation (SpO2) and fraction of inspired oxygen (FiO2) values in a 24 hour interval on day of ROP screening at 31±1 and 36±1 weeks PMA were recorded and correlated with SFCT at 36±1 weeks PMA. For statistical analysis, FiO2 and SpO2 were categorized with low FiO2 binned as room air equivalent “FiO2=21%” or requiring extra support “FiO2>21%.”

Results: Mean (+/- standard deviation) SFCT was 199.4 ± 64.7 μm from 53 eyes (27 infants) at 36 weeks PMA. After univariable analysis, infants with higher FiO2 need (lowest value in 24 hours; FiO2=21% vs FiO2>21%) at 31 and 36 weeks PMA had a thinner choroid at 36 weeks (31 weeks: 205.9±12.5 vs 126.4±2.6 μm; 36 weeks:201.3±12.8 vs 162.2±3.7 μm, p=0.003 for all). SpO2 and other FiO2 measures at 31 and 36 weeks PMA were not associated with SFCT or could not be correlated due to limited sample size. Higher FiO2 need (lowest value) remained significant in the multivariable analysis at both 31 weeks and 36 weeks PMA (p=0.001 and p=0.002 respectively).

Conclusions: Preterm infants requiring higher levels of oxygen support, reflected by increased FiO2 needs at both 31 and 36 weeks PMA, had thinner subfoveal choroid measurements at 36 weeks. Understanding how higher FiO2 exposures effect the developing choroid and influence choroidal thickness measurements could help explain poorer visual outcomes in preterm infants with a thinner choroid. Further investigations are necessary.

CONTROL ID: 3712113

SUBMITTER (NAME ONLY): Shanjida Khan

TITLE: Measurement of true Henle's fiber layer and outer nuclear layer thickness using volumetric directional optical coherence tomography

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Khan, S. Ni, T. Nguyen, B. Lujan, O. Tan, D. Huang, Y. Jian, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|S. Khan, S. Ni, D. Huang, Y. Jian, Biomedical Engineering, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|R. Ng, School of Engineering Science, Simon Fraser University, Burnaby, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Progressive photoreceptor loss and resultant thinning of the outer nuclear layer (ONL) is an important feature of age-related macular degeneration (AMD). However, ONL thickness measurements cannot be obtained clinically in standard optical coherence tomography (OCT) because of the oblique-orientation of the Henle's fiber layer (HFL). This observational study uses a novel volumetric directional OCT (VD-OCT) prototype, and a custom spoke-circular scanning pattern to clearly differentiate the two layers over the entire macular area with a single OCT volume.

Methods: Previously, we discovered that imaging the retina at an oblique angle can provide better contrast to differentiate the HFL and ONL. However, measuring the thickness of ONL and HFL over the entire macular required acquisition of OCT volumes at several different pupil entry positions, which is only possible with high level of patient cooperation and complex image processing. In this study, we built a novel OCT prototype that incorporates two sets of optical scanners in the sample arm to synchronously scan the imaging beam on both the pupil and retina. By synchronization of the two scanners, we can precisely control the OCT beam entry positions and maintain optimum beam incident angles on the retina to generate sufficient optical contrast for the HFL over the entire macular area.

Results: Five healthy adult volunteers were imaged upon dilation with the VD-OCT prototype for about five minutes in this study. The thickness of the true ONL can be assessed objectively on the cross-sectional scans acquired from the VD-OCT prototype (Fig. 1(a-c)). The volumetric ONL thickness heat maps can be calculated and plotted as demonstrated in Fig. 1(d) (spoke-circular scanning pattern) and Fig. 1(e) (regular spoke scanning pattern). The global and local ONL thickness variations are apparent in comparison with the heat maps: HFL became hyper-reflective in the macular region with the spoke-circular scanning pattern.

Conclusions: VD-OCT was used to visualize the otherwise invisible HFL with the aid of synchronous imaging beam scanning at both the retina and pupil planes. The VD-OCT prototype provides sufficient contrast to delineate the directionally reflective HFL tissue over the macular volume. True ONL thickness can be measured for the characterization of photoreceptor loss and its consequent thinning of the tissue.

CONTROL ID: 3712115
SUBMITTER (NAME ONLY): Anjali Herekar
TITLE: Characterization of Corneal Endothelium in Glaucomatous Eyes
SESSION TITLE: Corneal Imaging and Corneal Nerves
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Herekar, V. Hussey, K.Y. Lin, O.L. Lee, School of Medicine, University of California Irvine, Irvine, California, UNITED STATES|Y. Shi, University of California Irvine, Irvine, California, UNITED STATES|K.Y. Lin, O.L. Lee, Y. Shi, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: The corneal endothelium plays an important role in maintaining corneal health and transparency. Glaucoma is a widely prevalent disease which can be managed medically, surgically, and/or with laser treatment, yet the effects of glaucoma treatments on the corneal endothelium is unknown. We performed a retrospective, observational clinical study to describe the characteristics of the corneal endothelium of glaucomatous eyes by specular microscopy. Our goal was to compare the health of the corneal endothelium of glaucomatous eyes treated with various treatment modalities.

Methods: The central cornea of 121 eyes consisting of normal control and glaucoma-affected eyes were imaged using the Konan NSP-9900 specular microscope. Any eyes with corneal pathology (other than dry eye disease), keratoplasty, or cataract or glaucoma surgery within the past 6 months were excluded. Glaucomatous eyes were divided into those treated by topical medication only, or those who received two or more treatment types: glaucoma drops, laser, or incisional surgery. The Konan CellChek software was used to perform analysis of endothelial cell density (ECD).

Results: The mean ECD was significantly decreased in glaucomatous eyes compared to normal control eyes ($p<0.001$). Glaucomatous eyes treated with topical medication had lower average ECD compared to controls. A one-way ANOVA performed comparing the ECD of control, medically treated, and eyes that received 2 or more treatment types showed a statistically significant difference between groups ($p<0.0005$). Glaucomatous eyes that had undergone 2 or more treatment types (laser, surgery, and medication) had a significantly decreased ECD compared to those which received medication alone ($p<0.05$).

Conclusions: Eyes with glaucoma, particularly those receiving 2 or more treatments, have a lower corneal ECD than controls. Lower ECD suggests that corneal endothelial cell loss is associated with glaucoma treatment and/or the disease process itself. Eyes that had undergone multiple treatments had significantly lower ECD than eyes treated with medication alone, indicating that cell loss in the corneal endothelium likely increases with additional glaucoma treatments. Further studies are needed to explore the underlying mechanism for this decrease in corneal endothelial cell density in patients with glaucoma, and to characterize which treatments have the most impact on the health of the corneal endothelium.

CONTROL ID: 3712116

SUBMITTER (NAME ONLY): Anbukkarasi Muniyandi

TITLE: APE1/Ref-1 is highly expressed in murine laser-induced choroidal neovascularization and human neovascular age-related macular degeneration

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Muniyandi, G.D. Hartman, M.R. Kelley, T.W. Corson, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|X. Qi, M. Boulton, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|K. Day, Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Apurinic/apyrimidinic endonuclease 1/reduction-oxidation factor 1 (APE1/Ref-1) is both a DNA repair enzyme and a redox (reduction-oxidation) signaling protein. We have identified Ref-1 as a potential therapeutic target for neovascular age-related macular degeneration (nvAMD) and other neovascular eye diseases; Ref-1 inhibitor APX3330 is currently in Phase II trials for diabetic retinopathy. Ref-1's redox-sensitive transcription activation modulates angiogenesis and inflammation as it stimulates transcription factors including HIF1-α, NF-κB, and STAT3. We previously showed that inhibiting Ref-1's redox function reduces angiogenesis in vitro and in murine laser-induced choroidal neovascularization (L-CNV). This study aimed to analyze Ref-1 expression during the progression of L-CNV in mice and in human nvAMD and control eyes.

Methods: L-CNV was induced in 7-week old, wild-type female C57BL/6J mouse eyes to simulate features of nvAMD, and eyes harvested at 1, 3, 5, 7, 10, and 14 days after laser treatment. De-identified paraffin sections of human nvAMD and age-matched control patients were acquired from the National Disease Research Interchange (NDRI). Ref-1 expression was analyzed by confocal microscopy on immunostained retinal and choroidal flat-mounts and frozen cryosections from mouse eyes, and on human nvAMD vs control sections.

Results: In L-CNV, Ref-1 was highly expressed in and around the lesions, especially soon after the laser treatment on days 1, 3, and 5. The higher expression of Ref-1 was seen in the ganglion cell layer, inner and outer nuclear layers, inner and outer segments of photoreceptors in the retina and in the retinal pigment epithelium (RPE)/choroid. Expression was lower in lesions at later time points on days 7, 10, and 14. The human eye immunostaining showed that Ref-1 is predominantly highly expressed in the RPE layer in nvAMD compared to healthy eyes.

Conclusions: High expression of Ref-1 in L-CNV mice eyes at different time points and in the eyes of human nvAMD patients further supports a functional role of Ref-1 in CNV. Overall, this study provides further insight into the importance of Ref-1 for nvAMD pathogenesis and highlights the potential of this novel drug target for nvAMD.

CONTROL ID: 3712119

SUBMITTER (NAME ONLY): Thomas Ach

TITLE: The impact of lens autofluorescence and opacification on fundus autofluorescence imaging.

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ach, G. Rennen, M. Sassmannshausen, F.G. Holz, L.A. von der Emde, Department of Ophthalmology, University Hospital Bonn, GERMANY|M. Pfau, National Eye Institute, National Institutes of Health, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Thomas Ach: Commercial Relationship(s);Code C (Consultant/Contractor):Roche, Novartis, Heidelberg Engineering;Code R (Recipient):Novartis, Nidek;Code I (Personal Financial Interest):Macregen | Geena Rennen: Commercial Relationship: Code N (No Commercial Relationship) | Maximilian Pfau: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Pharmaceuticals | Marlene Sassmannshausen: Commercial Relationship(s);Code F (Financial Support): Heidelberg Engineering, CenterVue, Carl Zeiss MedicTec | Frank Holz: Commercial Relationship(s);Code C (Consultant/Contractor):Acucela, Apellis, Bayer, Boehringer-Ingelheim, Bioeq/Formycon, Roche/Genentech, Geuder, Graybug, Gyroscope, Heidelberg Engineering, IvericBio, Kanghong, LinBioscience, Novartis, Oxurion, Pixium Vision, Oxurion, Stealth BioTherapeutics, Zeiss;Code F (Financial Support):Acucela, Allergan, Apellis, Bayer, Bioeq/Formycon, CenterVue, Ellex, Roche/Genentech, Geuder, Heidelberg Engineering, IvericBio, Kanghong, NightStarX, Novartis, Optos, Pixium Vision, Zeiss | Leon von der Emde: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Quantitative and qualitative fundus autofluorescence (FAF) analysis strongly depends on the clearness of the optical media. Especially the lens status is crucial in FAF imaging since the aging lens has both light blocking and AF properties that impact and distort image analysis. Here, we report both lens opacification and lens autofluorescence (LAF) to aid the development of a lens correction factor for adequate FAF analysis.

Methods: Seventy-four subjects (18-95 years, mean of 9.2 +/- 4.1 per decade, 28 females) received quantitative LAF (using laser scanning ophthalmoscope), Scheimpflug, as well as blue FAF, green FAF, and infrared (IR) imaging. LAF values were determined following the protocol as recently proposed (PMID: 28973367). The Pentacam nucleus staging (PNS) score was extracted from Scheimpflug images to estimate lens opacification. Mean opinion scores (MOS) of FAF and IR image quality (focus, illumination, symmetry, zoom, centering) were compiled by two medical readers. Linear regression analyses between PNS/LAF and age were calculated, and the coefficient of determination (r^2) was reported. Finally, a Pearson's correlation coefficient (r) between PNS/LAF and the respective MOS was determined.

Results: Mean LAF for the third and seventh life decade were 4.2 +/- 2.1 and 13.5 +/- 7.2 [a.u]. Both PNS and LAF showed a significant age-dependent increase ($p < 0.01$) with an r^2 of 0.28/0.38. LAF was associated with a significantly reduced MOS ($p=0.04$) only for blue FAF with an r of 0.2. Similarly, PNS was associated with a reduced MOS ($p= 0.02$) for blue FAF with an r of 0.3.

Conclusions: Age only explained a limited fraction of the variability in both lenticular autofluorescence and opacification. Retinal image quality, especially in the shorter wavelengths, deteriorated slightly with lenticular remodeling. These results question the current practice of simple age-based opacification correction in quantitative FAF imaging. Individualized measures of lens remodeling have the potential to characterize the influence of the optical media more precisely. We propose LAF and PNS as novel methods to correct for lenticular autofluorescence and opacification.

CONTROL ID: 3712123

SUBMITTER (NAME ONLY): Kiyoko Gocho

TITLE: Pilot investigation of multimodal and multiscale retinal imaging technology developed by a trans-European multidisciplinary consortium

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Gocho, K. Grieve, M. Paques, Clinical Investigation Center 1423, Inserm, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|N. Lefaudeux, Imagine eyes, Orsay, FRANCE|C. Valdes, J. Andilla, P. Loza-Alvarez, Barcelona Institute of Science and Technology, Institut de Ciencies Fotoniques, Barcelona, SPAIN|M.F. Shirazi, F. Schwarzhans, M. Pircher, Center for Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|K. Ntatsis, L. Sanchez Brea, D. Andrade De Jesus, Biomedical Imaging Group Rotterdam, Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|M.W. Torm, C. Eckmann-Hansen, A. Amini, Department of Ophthalmology & University of Copenhagen, Rigshospitalet, Kobenhavn, DENMARK|

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ABSTRACT BODY:

Purpose: Adaptive optics (AO) has enabled visualizing cellular structure in the retina, yet its clinical usability has been hampered by small field-of-view and bulkiness of instrumentation. We developed a compact imaging system with a multiscale optical architecture that delivers large views of the retina as well as highly-magnified AO-corrected images. This study explored imaging performance in human eyes.

Methods: The prototype included three imaging modalities: confocal scanning laser ophthalmoscopy (SLO) based on 786 nm super-luminescent diode scanned at 8 kHz, optical coherence tomography (OCT) based on a 1050 nm swept-source at 200 kHz, and OCT angiography (OCTA). Each modality could be operated with a field-of-view of either 40 x 30 deg or 4 x 3 deg. In the latter case, ocular wavefront aberrations were corrected by AO operating in closed loop at 13 Hz. During OCT/OCTA examinations, head and eye movements were compensated by automated pupil and retinal tracking at 100 Hz. The ability to visualize microscopic retinal structure was experimented in 35 healthy volunteers and 39 patients affected by various fundus pathologies, including diabetic retinopathy, age-related macular degeneration and inherited retinal dystrophies.

Results: The overall dimensions of the system were 49 x 50 x 50 cm. Large-field SLO and OCT provided quick overviews of the retina while both AOSLO and AOOCT enabled the visualization of parafoveal cone cells, nerve fiber bundles, capillaries, and microscopic lesions. Multiple-averaged AOOCT B-scans revealed Müller-cell-like structures. AOOCTA could image capillaries and choriocapillaris with minimal shadowing artifacts. In pathological cases, AOSLO showed the distribution and lateral extent of microscopic lesions like micro-aneurisms, micro-exudates, atrophic region borders, pigment clusters, and photoreceptor losses. AOOCT scans completed these observations with information on depth location and axial extent of these alterations.

Conclusions: The multimodal multiscale imaging architecture enabled in-depth retinal examinations through a straightforward process: 1) acquire an overview image, 2) identify regions of interest, 3) examine these regions with near-histology 3-D resolution. When confirmed by further investigations, this technology should offer new possibilities for retinal phenotyping and clinical research in new therapies.

CONTROL ID: 3712124

SUBMITTER (NAME ONLY): Shyam Chaurasia

TITLE: Ossabaw Mini Pigs-fed on a Western Diet Exhibits Degenerative Changes in the Retina

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Chaurasia, T.B. Connor, B. Ahmad, Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|S.S. Chaurasia, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|R. Lim, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Shyam Chaurasia: Commercial Relationship: Code N (No Commercial Relationship) | Rayne Lim: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Connor: Commercial Relationship: Code N (No Commercial Relationship) | Baseer Ahmad: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously established that Ossabaw mini pigs exposed to the western diet develop the metabolic syndrome (MetS) and acquire type 2 diabetes (T2DM), resembling the human phenotype. In this study, we sought to elucidate the structural and histological characteristics of the Ossabaw pig retina.

Methods: Six-month-old Ossabaw pigs were fed on a western diet for six weeks. At the end of the study, blood profiling was performed to confirm type 2 diabetes and metabolic syndrome. The retina was dissected and cryosectioned for light microscopy and immunohistochemistry. Retinal sections were immunostained using specific antibodies for ganglion cells, synapses, bipolar cells, and retinal photoreceptors and imaged on a confocal microscope.

Results: The Ossabaw mini pigs had elevated fasting blood glucose concentrations and dyslipidemia. Ossabaw pig retinas showed disrupted cellular architecture across neural layers, with numerous large vacuoles seen in the inner nuclear layer's cell bodies and the ganglion cell layer. The immunostained retina showed degenerative neuronal cells and loss of synapses that are vital to retinal function.

Conclusions: The present study described the early degenerative and neuronal changes in the retina caused by the western diet-induced metabolic abnormalities in the Ossabaw mini pigs.

CONTROL ID: 3712125

SUBMITTER (NAME ONLY): Mehdi Lemdani

TITLE: Pain following cataract surgery is impacted by objective and patient perceived surgical duration

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lemdani, H. Choudhry, A. Patel, M. Jaffry, M. Dastjerdi, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous research suggesting some agreement between patients' perceived duration (PSD) of cataract surgery (CS) and objective duration (OSD) also explored the pain perception. We performed retrospective data analysis to explore the relationship between a patient's perception of pain following CS.

Methods: Retrospective data analysis was carried out on data published in the Dryad database and collected CS cases between 17 May 2011 and 22 July 2011 in the Department of Ophthalmology of Hôpital Cochin, a teaching university hospital located in Paris, France. Multivariate regression analysis was also run to assess significant associations of various factors, including age, gender, operative duration, and complication rate, with both objective and patient percieved duration of cataract surgery.

Results: 356 total cases were collected between 17 May 2011 and 22 July 2011 in the Department of Ophthalmology of Hôpital Cochin. 151 patients were male and 205 were female. In males, OSD and PSD significantly predicted the pain level perceived, with each minute in objective and percieved surgery duration corresponding with increases in log odds of .082 (95% CI .022 to .141, p=.007) and .064 (95% CI .012 to .115, p=.016). In females, only PSD significantly predicted pain, with each minute corresponding to .49 increase in experienced pain level (95% CI .008 to .090, p=.020). Age groups were stratified into <60, >=60 and <69, >=69 and <79, and >=79. In the youngest age stratification for each minute of OSD there was a predicted increase of 0.64 in experienced level of pain (95% CI 0.16 to 1.12, p=0.009*). However for every minute in PSD, there was a predicted decrease of 0.25 in the experienced pain level (95% CI -0.49 to -0.01, p=0.039). In ages >=60 and <69 and >=69 and <79 , each minute of PSD corresponded to an increase of .10 (95% CI 0.02 to 0.18, p=.019) and 0.06 (95% CI 0 to 0.11, p=.036) in experienced pain level. In the oldest age group, only an increase in OSD significantly predicted patient perceived pain, where each minute corresponded to an increase of 0.12 in experienced pain level (95% CI 0.04 to 0.20, p=.003).

Conclusions: These findings suggest variation in OSD and PSD impact on pain across age groups and gender. However, our study also suggests that OSD and PSD are more likely to predict patient perceived pain than other factors such as postoperative complications.

CONTROL ID: 3712128

SUBMITTER (NAME ONLY): Yukihiro Shiga

TITLE: Light-evoked RGC calcium dynamics are altered in glaucoma: live imaging evidence of abnormal calcium clearance

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The mechanisms underlying retinal ganglion cell (RGC) vulnerability and dysfunction in glaucoma are poorly understood. Here, we used two-photon laser scanning microscopy to investigate alterations in real-time light-evoked RGC calcium (Ca^{2+}) responses during ocular hypertension (OHT) damage.

Methods: Transgenic mice carrying the Ca^{2+} indicator GCaMP6f (Thy1.GCaMP6f) received an intracameral injection of magnetic microbeads to induce OHT. Two weeks following induction, prior to cell loss, retinae were two-photon imaged through the sclera of anesthetized mice or acutely dissected for ex vivo imaging. Next, ROIs were drawn on response movies using ImageJ or using suite2p to extract RGC signals and custom code (Rstudio/MATLAB) used to compute: i) rise time, ii) decay time, iii) amplitude, and iv) ON-OFF index, which indicates ON-OFF preference. For ex vivo recordings, computational methods (PCA/UMAP) were used to divide sham data into 7 functionally defined RGC types. Student's t-test or ANOVA methods were applied to detect significant differences (significance: $P \leq 0.05$).

Results: In vivo and ex vivo RGC Ca^{2+} transients were significantly altered and showed abnormalities consistent with a change in Ca^{2+} clearance in the mouse glaucoma model. Specifically, trans-scleral imaging showed a several-fold increase in Ca^{2+} decay time in ON RGC (sham: 0.93 ± 0.09 sec, OHT: 3.53 ± 0.57 sec, N=7-8 mice/group, n=74-89 cells/group, $p<0.01$) and Ca^{2+} rise time in OFF RGC (sham: 2.92± 0.42 sec, OHT: 6.60 ± 1.19 sec, N=4 mice/group, n=8-14 cells/group, $p<0.05$) leading to sustained Ca^{2+} accumulation. Data obtained with explant imaging were consistent and showed an increase in mean Ca^{2+} decay time for OHT RGC (sham: 0.97± 0.058 sec, OHT: 1.85± 0.197 sec, N>5 mice/group, n>400 RGC/group, $p<0.05$). We also observed a decrease in the proportion of OFF-RGCs as seen by a shift in the mean of the ON-OFF index (Sham: -0.05 ± .015 ON-OFF index, OHT: +0.03 ± .012 ON-OFF index).

Conclusions: Our study reveals major alterations in light-evoked RGC Ca^{2+} dynamics under OHT conditions, notably abnormal Ca^{2+} clearance. These findings suggest significant defects in the mechanisms that regulate Ca^{2+} efflux which can lead to RGC dysfunction and increased vulnerability in glaucoma.

CONTROL ID: 3712131

SUBMITTER (NAME ONLY): EZEQUIEL SALIDO

TITLE: Interphotoreceptor matrix proteoglycans IMPG1 and IMPG2 undergoes intramolecular proteolysis and reveal localization interdependency

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. SALIDO, C. Coulter, B. Mitchell, Biochemistry, and Ophthalmology and Visual Sciences, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The interphotoreceptor matrix (IPM) is a specialized extracellular matrix that surrounds the photoreceptors inner and outer segments. Two major constitutes of the IPM are the interphotoreceptor matrix proteoglycan 1 and 2 (IMPG1 and IMPG2). Both proteoglycans possess SEA domains (Sperm protein, Enterokinase and Agrin) which are linked to self-cleave intramolecular proteolysis in proteoglycans. Mutations in the SEA domains of IMPG1 and IMPG2 are associated with vision loss. This work studies the possible proteolysis of IMPG1 and IMPG2 and its relevance to vision physiology

Methods: We used protein alignment computational tools, and classical Wester blot and immunohistochemistry techniques

Results: The amino acid sequence alignment of IMPG1 and IMPG2 against established proteolytic sequences predicted that one of the two SEA domains on both proteins are likely to undergo proteolysis. Western blot analysis of IMPG1 confirmed protein proteolysis independently of IMPG2 presence. On the other hand, western blot and immunohistochemical analysis confirmed IMPG2 proteolysis involving the generation of two IMPG2 subunits, a membrane attached and a free extracellular peptide. These experiments revealed that the extracellular portion of IMPG2 migrates from the IPM inner segment to the IPM outer segment by a mechanism dependent on IMPG1.

Conclusions: Overall, this work demonstrates that IMPG1 and IMPG2 proteolyzed as part of their maturation process and revealed the IPM outer segment localization of the extracellular portion of IMPG2.

CONTROL ID: 3712137

SUBMITTER (NAME ONLY): Hasan Usmani

TITLE: Electrophysiological evidence for GABA-mediated feed-forward transmission as a major cone signal ON pathway in the outer retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Usmani, M.M. Giarmarco, M. Neitz, J. Neitz, J.A. Kuchenbecker, University of Washington, Seattle, Washington, UNITED STATES|S.S. Patterson, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Small bistratified ganglion cells are proposed to carry S-ON signals required for color vision. However, to the contrary, the ON signals from cones to bipolar cells including S-cone bipolar cell input to small bistratified cells are interrupted in patients with mutations in the gene encoding mGluR6 yet they have normal color vision and cone vision is little disturbed in general (Dryja et al. 2005, PNAS, 102, p. 4884). This suggests that there is a second principle ON pathway whereby signals including those involved in conscious color vision are relayed to bipolar cells. To begin testing the hypothesis that it's based on GABA mediated feedforward via horizontal cells, we have used an ex vivo ERG system in mice which allows recording of signals transretinally in the presence and absence of GABA antagonists.

Methods: Pieces of mouse retina from defined locations were placed in an ex vivo ERG chamber and perfused with Ames' solution at 37°C. ERG responses were recorded transretinally to on-off stimuli. Light arriving from the photoreceptor side was from a Gooch & Housego OL 490 Agile Light Source that has an incorporated diffraction grating and Digital Light Processor; it was controlled by custom ERG hardware and software to deliver programmable spectral output capable of producing cone isolating stimuli and narrowband lights for measuring spectral sensitivity functions.

Results: High signal-to-noise ratio responses could be recorded for several hours from a single preparation. We compared responses before and after application of the glutamate agonist, L-AP4, and GABA antagonists, gabazine and TPMPA; recordings before and after washout of the drugs were reproducible. ERG waveforms in the presence of gabazine and TPMPA could be subtracted from the control to reveal a GABA mediated waveform or "GABAwave". This was compared to responses mediated by glutamate signaling that were obtained by subtracting the waveform after application of L-AP4 from the control ERG.

Conclusions: The ERG ON waveform attributable to GABA signaling had a faster onset than the ON response mediated by the G-protein-coupled receptor mGluR6 which was blocked by application of L-AP4, demonstrating the outer retina as the source of the GABAwave. The GABAwave constituted a major component of the ERG b-wave indicating that GABA mediated feedforward is a major ON signaling pathway in the outer retina.

CONTROL ID: 3712138

SUBMITTER (NAME ONLY): Alessandro Rabiolo

TITLE: Intraocular pressure fluctuation and rates of visual field progression in primary open-angle glaucoma: an exploratory analysis from the United Kingdom Glaucoma Treatment Study (UKGTS).

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rabiolo, G. Montesano, D.F. Garway-Heath, NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, London, UNITED KINGDOM|G. Montesano, D.P. Crabb, Optometry and Visual Sciences, City University of London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The role of intraocular pressure (IOP) fluctuation in glaucoma progression remains controversial. We investigate whether IOP fluctuation is independently associated with the rate of visual field (VF) progression.

Methods: Participants from the UKGTS with ≥5 VFs were included. Associations between IOP metrics and the mean deviation (MD) rate of progression (RoP) were tested with mixed models. The variables of interest were mean ocular pulse amplitude (OPA), and standard deviation (SD) of diurnal IOP (diurnal fluctuation) and of IOP at all visits (long-term fluctuation). The effect of correlated IOP metrics (Fig1) and multicollinearity were controlled with a principal component analysis of peak and mean IOP during the trial, and baseline (untreated) IOP. The first principal component (PC1) was included as a model covariate. Interactions between variables of interest and time from baseline modelled the variables' effect on the RoP. Analyses were conducted separately in the two arms.

Results: 213 patients in the placebo arm (mean±SD age: 66.5±10.3 years) and 217 patients in the treatment arm (mean±SD age: 65.2±10.4 years) were included. The median [IQR] of mean IOP, diurnal and long-term fluctuation were, respectively, 18.4 [16.0-21.9], 1.4 [0.9-2.0] and 2.1 [1.6-2.9] mmHg in the placebo arm, and 15.2 [13.2-17.1], 1.3 [0.8-1.7] and 1.9 [1.4-2.6] mmHg in the treatment arm. Mean±SD RoP were -0.32±0.65 and 0.03±0.58 dB/year in the placebo and treatment group, respectively. In the univariable analysis, diurnal and long-term IOP fluctuations were significantly associated with RoP in the placebo arm ($p<0.001$), and long-term fluctuation in the treatment arm ($p=0.047$). PC1, combining information of baseline, mean and peak IOPs, were significantly associated with RoP in the placebo ($p=0.029$) but not in the treatment arm ($p=0.95$). In the multivariable model, diurnal (placebo estimate: 0.047 dB/year, $p=0.60$; treatment estimate: 0.046 dB/year, $p=0.63$) and long-term IOP fluctuations (placebo estimate: -0.124 dB/year, $p=0.16$; treatment estimate: -0.119 dB/year, $p=0.63$) were not significantly associated with the RoP (Fig2). OPA was also not associated with RoP ($p\geq0.11$).

Conclusions: This study confirms that IOP fluctuation is not an independent factor for glaucoma progression and other aspects of IOP may be more informative.

CONTROL ID: 3712141

SUBMITTER (NAME ONLY): Grant Cull

TITLE: Pharmacodynamic response of optic nerve head (ONH) tissue blood flow measured by laser speckle flowgraphy (LSFG) after administration of PER-001, an endothelin receptor antagonist

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Cull, J. Reynaud, K. Ly, M. Dunn, D. Jennings, T. Holthausen, H. Lockwood, S.K. Gardiner, L. Wang, B. Fortune, Discoveries in Sight Laboratories, Devers Eye Institute, Legacy Health, Portland, Oregon, UNITED STATES|C. Jadach, J. Wilk, Department of Comparative Medicine, Legacy Research Institute, Legacy Health, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reduction of ocular blood flow in glaucoma is thought to be related to upregulation of the endothelin system. Our purpose here was to determine the time course and dose dependency of ONH tissue blood flow in response to a single administration of PER-001.

Methods: LSFG (Softcare Co., Ltd.) was used to measure ONH tissue blood flow (as previously described in detail, PMID: 23737471) in 6 anesthetized adult rhesus monkeys (Macaca mulatta, 4F/2M ages 7-12 y) with unilateral experimental glaucoma (EG). Three LSFG scans were obtained for each eye and averaged at each time point, starting 30 min prior to bilateral intravitreal administration of 50 µL of PER-001 or vehicle, and thereafter every 15-30 min for 6 hr. The dose of PER-001 was varied in random order between 0.001, 0.01, 0.1 mg or vehicle for each subject. The effects of dose, time after administration and eye (EG vs fellow control, FC) were assessed using repeated measures ANOVA, mixed-effects models and generalized estimating equations to include effects of an array of vital signs.

Results: At the beginning of the series of 4 weekly PER-001 assays, ONH neuroretinal minimum rim width in EG and FC eyes, respectively was 155 ± 74 vs 291 ± 39 µm ($p=0.005$); peripapillary retinal nerve fiber layer thickness was 77 ± 21 vs 100 ± 8.5 µm ($p=0.04$); and mean blur rate (MBR) from LSFG was 12.3 ± 3.0 vs 14.2 ± 4.9 ($p = 0.18$); thus, representing a moderate stage of EG damage. Following administration of PER-001 (Figs.1,2), LSFG MBR increased significantly in EG eyes with time after injection ($p<0.0001$), indicating increased flow; there was a significant time-dose interaction ($p<0.0001$) and effect of dose ($p=0.0006$). Whereas, in FC eyes, only the effect of time after injection was significant ($p<0.0001$). The effect of PER-001 on ONH blood flow was relatively greater in EG eyes such that blood flow increased to a level comparable to FC eyes after ~4 hr, for the mid and high dose. This pattern held after controlling for end-tidal CO_2, the only vital sign significantly associated with MBR.

Conclusions: ONH tissue blood flow increased in a dose-dependent manner after administration of PER-001. The effect was more prominent in EG compared to FC eyes, consistent with the hypothesis that upregulation of the endothelin system contributes to reduction of blood flow in glaucoma.

CONTROL ID: 3712142

SUBMITTER (NAME ONLY): Brad Fortune

TITLE: Pharmacodynamic response of optic nerve head (ONH) vasculature measured by OCT-angiography (OCTA) after administration of the endothelin receptor antagonist PER-001

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Fortune, G. Cull, K. Ly, M. Dunn, D. Jennings, T. Holthausen, H. Lockwood, S.K. Gardiner, L. Wang, J. Reynaud, Discoveries in Sight Research Laboratories, Devers Eye Institute, Legacy Health, Portland, Oregon, UNITED STATES|C. Jadach, J. Wilk, Department of Comparative Medicine, Legacy Research Institute, Legacy Health, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reduction of ocular blood flow in glaucoma is thought to be related to upregulation of the endothelin system. The purpose of this study was to characterize the effect of PER-001 on the macro and microvasculature of the ONH in glaucomatous and control eyes.

Methods: OCTA (Spectralis, Heidelberg Engineering GmbH) was used to quantify the ONH vasculature in 6 anesthetized adult rhesus monkeys (Macaca mulatta, 4F/2M ages 7-12 y) with unilateral experimental glaucoma (EG, PMID: 27564522). OCTA scans were 15 x 15 deg (768 x 768 A-lines) centered on the ONH and registered to the original baseline in real time during acquisition. ONH rim was defined by Bruch's membrane opening laterally and posteriorly and by the internal limiting membrane anteriorly; the integral of all voxels within these boundaries (scaled for lateral magnification of the rhesus eye) defined ONH rim volume, while the same voxels weighted by the OCTA signal defined the ONH rim vascular volume. Large vessels and microvascular-capillaries were also analyzed separately. OCTA scans were recorded for each eye, starting 15-30 min prior to bilateral intravitreal administration of 50 µL of PER-001 or vehicle, and thereafter every 30 min for 6 hr. Statistical analysis included repeated measures ANOVA, linear regression and t-tests.

Results: At the point PER-001 assays were conducted, ONH neuroretinal minimum rim width in EG vs fellow control (FC) eyes, respectively, was 155 ± 74 vs 291 ± 39 µm (p=0.005); peripapillary retinal nerve fiber layer thickness was 77 ± 21 vs 100 ± 8.5 µm (p=0.04); thus, representing a moderate stage of EG damage. Following administration of PER-001, ONH volume increased significantly more in EG than FC eyes, which was explained almost entirely by an increase in total vascular volume, including an increase for both large vessel and microvascular-capillary volume (Figs. 1,2). Subtle effects of vehicle alone were far exceeded by those of PER-001.

Conclusions: Administration of PER-001 elicited an increase of ONH vascular volume, including dilatory effects on both large vessels and ONH tissue microvasculature. These effects were stronger in EG compared to control eyes and consistent with the hypothesis that upregulation of the endothelin system contributes to vascular compromise in glaucoma. Further studies of PER-001 in glaucoma are warranted.

CONTROL ID: 3712145

SUBMITTER (NAME ONLY): WILLIAM SPENCER

TITLE: The WAVE complex is an essential component of the actin network that initiates photoreceptor disc membrane morphogenesis

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.J. SPENCER, N.F. Schneider, N.P. Skiba, V.Y. Arshavsky, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The vertebrate photoreceptor cell's outer segment is a highly modified primary cilium filled with hundreds of disc-shaped membranes known as "discs" which serve to efficiently capture light. To cope with light stress of disc membranes, photoreceptor cells constantly renew them. This is accomplished by the daily formation of new discs at the outer segment base and the engulfment of old discs from outer segment tips by the retinal pigment epithelium (RPE). The formation of each new disc begins at the base of the outer segment where Arp2/3 driven actin polymerization pushes out the ciliary membrane to form a membrane evagination. To drive actin polymerization, the Arp2/3 complex is known to require the activity of a nucleation promoting factor. Here, we sought to identify the nucleation promoting factor working with Arp2/3 during disc formation. Defects in disc morphogenesis underlie many blinding retinal diseases and understanding the basic molecular mechanism of the process lays the foundation for the development of future therapies.

Methods: We conducted a series of proteomic experiments to identify proteins potentially interacting with Arp2/3 at the site of disc formation. We identified protein isoforms representing all five members of the WAVE regulatory complex, including the nucleation promoting factor, Wasf3. We next analyzed the retinas of Wasf3$^{-/-}$ mice by Western blotting, light microscopy and electron microscopy.

Results: We found that the WAVE complex serves as the nucleation promoting factor for Arp2/3 at the site of disc formation. We identified the major protein isoforms of the WAVE complex present in rod outer segments, and showed that the absence of one of them, Wasf3, results in the complete loss of actin at the site of disc morphogenesis. Without the action of actin to initiate disc formation, the membranes delivered to the outer segment in Wasf3$^{-/-}$ mice grossly overgrow and their photoreceptors degenerate having disorganized membrane whorls emanating from their cilia rather than normal outer segments.

Conclusions: These data establish the WAVE complex as an essential component for photoreceptor disc morphogenesis and vertebrate vision.

CONTROL ID: 3712146

SUBMITTER (NAME ONLY): Hanna Dumanska

TITLE: Protein kinase C regulates hypoxia-induced effects on NMDA receptor-mediated retinocollicular neurotransmission

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Dumanska, N. Veselovsky, Department of Neuronal Network Physiology, Institut Fiziologii imeni O O Bogomolca Nacional'na akademia nauk Ukraini, Kiiv, Kiiv, UKRAINE|

Commercial Relationships Disclosure: Hanna Dumanska: Commercial Relationship: Code N (No Commercial Relationship) | Nickilai Veselovsky: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Hypoxia is the main factor in the pathogenesis of numerous retinal and optic nerve diseases. The retinocollicular projections are part of a fundamental set of structures in visual attention. We have previously reported that hypoxia-induced pathological long-term potentiation (LTP) of NMDA retinocollicular transmission is associated with a decrease of the current decay time. Such a decrease reflects an increase in NR2A/NR2B ratio and subsequent decrease of calcium influx and is a protective cellular mechanism in response to hypoxic injury. In this study, we tested the hypothesis that the protein kinase C (PKC) pathway is involved in hypoxia-induced LTP of NMDA retinocollicular transmission as well as in changes in NMDAR subunits ratio.

Methods: We developed the in vitro model of the visual retinocollicular pathway - a coculture of dissociated retinal cells and superficial superior colliculus (SSC) neurons. Using paired patch-clamp technique, we recorded pharmacologically isolated evoked NMDA postsynaptic currents in SSC neurons by generation action potentials in presynaptic retinal ganglion cells. Spontaneous postsynaptic currents we recorded in absence of presynaptic stimulation. The method of fast local superfusion was used for the application of hypoxic solutions on the pairs of neurons. We tested effect of chelerythrine chloride (ChC, 5 μM) - an inhibitor of PKC. The decay time constants were determined from a single exponential fit of the decay phase of currents.

Results: The presence of ChC completely blocked LTP of NMDA transmission induced by hypoxia. The ChC also abolished the hypoxia-induced increase of spontaneous NMDA currents amplitudes but did not affect the increased occurrence frequency. Moreover, we observed that ChC blocked the decrease of the decay time of evoked and spontaneous currents (for example control 48.2 ± 4.6ms; hypoxia 13.5 ± 5.4ms; hypoxia in presence of ChC 45.8 ± 5.5 ms; reoxygenation in presence of ChC 46.2± 4.8ms; reoxygenation 43.8 ± 5.6ms).

Conclusions: The results obtained are consistent with our hypothesis. Inhibition of PKC pathway completely blocked LTP of NMDA retinocollicular transmission and lead to the offset of associated changes in NMDA receptor subunits. The revealed electrophysiological basis of plasticity and protective mechanism in response to hypoxic injury might be targeted to prevent lesions of the retinocollicular pathway.

CONTROL ID: 3712148
SUBMITTER (NAME ONLY): Erin Tomiyama
TITLE: Compounding of low-concentration atropine for myopia control
SESSION TITLE: Myopia epidemiology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Tomiyama, M.A. Bullimore, K. Richdale, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|
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ABSTRACT BODY:

Purpose: Low-concentration atropine is commonly prescribed to slow myopia progression in children but is not FDA-approved for that indication and is only available in the US from compounding pharmacies. The purpose of this study was to ascertain the most common procedures used to compound low concentration atropine.
Methods: US compounding pharmacies were identified via a survey of myopia management doctors in practice and at optometry schools, via social media, conferences, email, and web search. Based on this screen, a total of 28 pharmacies were contacted via telephone and asked a standard set of questions about their pharmacy practices regarding the preparation and storage of their compounded atropine product.
Results: Twenty-six pharmacies across 19 US States provided answers to at least three questions. The most frequently reported bottle size was 5 ml (IQR: 3.5-10). For storage, 7 of 18 pharmacies (39%) recommended refrigeration and 11 (61%) stated room temperature was sufficient. The median beyond use date provided was 60 days (IQR: 45-180).

For preparation, 14 pharmacies (54%) used commercially available 1% atropine solution, 9 (34%) used powdered atropine, 2 (8%) used either, and 1 (4%) stated their approach was proprietary. For the added inactive ingredients, 10 pharmacies (42%) used commercially available artificial tears only, 6 (25%) added saline only, 6 (25%) used more than one ingredient, and 2 (8%) were proprietary. Only two pharmacies mentioned adding Boric acid and one mentioned “pH adjusted” saline.
Conclusions: There were a wide variety of methods used to compound low-concentration atropine, which may alter the pH and affect its stability and potency. Whether these differences ultimately affect the efficacy and safety of low-concentration atropine is not known. Further research is needed to assess how these variations may affect the outcomes of myopia management.

CONTROL ID: 3712149

SUBMITTER (NAME ONLY): Oliver Liu

TITLE: Extra-retinal localization of retinol binding protein 3 (RBP3) suggests novel functions beyond the visual cycle

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Most studies of retinol binding protein 3 (RBP3) have focused on its role in the vitamin A cycle or transport of lipids in the retina. RPB3 is the major protein component of the interphotoreceptor matrix (IPM) and plays a role in maintaining the health and integrity of the retina. However, studies have detected RPB3 in other compartments of the eye, and this study seeks to further explore its presence in the humors of the eye as a step in determining extra-retinal function.

Methods: Intact human globes were used with postmortem times from 3-12 hrs. Aqueous was obtained by inserting a 30-gauge syringe through the cornea into the anterior chamber. Vitreous was obtained via a syringe after removing the anterior structures by a circumferential incision at the level of the ciliary body. 7 vitreous and 7 aqueous samples were collected from 14 different individuals without history of ocular disease. To challenge human sample data, aqueous and soluble IPM fractions were collected from wildtype (WT) and RBP3-/- adult albino Sprague Dawley rats reared under cyclic dim light. Aqueous was collected by the same methods as human eyes. To collect IPM, retinas were detached under chilled PBS and gently agitated. The extract was centrifuged to remove cell fragments. Western blot analysis used rabbit monoclonals directed against human and rat RPB3s.

Results: RBP3 (124 kDa) was easily detected in human aqueous and vitreous. Minor immunoreactive bands were detected, particularly in vitreous, at 100, 75 and 60 kDa. Intensity of bands did not correlate with postmortem interval. In the aqueous, RBP3 was 65% less concentrated vs. vitreous and typically lacked lower bands. Western blot analysis showed an immunospecific full-length 140 kDa band in the WT IPM which was not seen in RBP3-/- animals. Minor bands were not detected. In the aqueous, RBP3 was detected by Western blot and appeared to be the most prominent protein overall, although its level corresponded to ~2% of that in the IPM.

Conclusions: RBP3 is not restricted to the IPM but is a prominent component of the aqueous and vitreous. Our data indicates that there is a gradient in RBP3's concentration, with levels decreasing from the IPM to vitreous, with the lowest in aqueous. These distribution patterns across species suggest extra-retinal roles and merit further investigation of RBP3's expression and function throughout the eye.

CONTROL ID: 3712150

SUBMITTER (NAME ONLY): J Crawford Downs

TITLE: Biomechanics of the Laminar Load-bearing and Neural Tissues with Body Position Change

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Downs, C.A. Girkin, A. Karimi, Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S.M. Rahmati, School of Biological Sciences, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|R. Razaghi, Heel of Scene, Ltd, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: The laminar region of the eye is continuously exposed to intraocular pressure (IOP) and cerebrospinal fluid pressure (CSFP) on its anterior and posterior surfaces, respectively. Body position-dependent changes in IOP and CSFP also changes translaminar pressure (TLP=IOP-CSFP), which has been hypothesized as a risk factor in glaucoma. However, there have been few studies of the resultant stresses and strains within the lamina cribrosa beams (LC) and interspersed laminar neural tissues (NT) with TLP change. This study aimed to calculate the influence of postural change (sitting vs. supine) on the resultant stresses and strains in the optic nerve head (ONH), LC, and NT, under simultaneously applied IOP and CSFP.

Methods: Three eye-specific posterior eye finite element models were constructed, including the LC/NT microstructure, and cable elements representing anisotropic collagen fibers embedded in the peripapillary sclera and pia via a fully coupled, mesh-free, penalty-based cable-in-solid algorithm. The FE models were then subjected to three combinations of IOP and CSFP loadings consistent with postural changes; results were then interpreted in relation to the postural role in the resultant ONH, LC, and NT deformations, stresses, and strains.

Results: Moving from sitting to supine body position caused a larger tensile, compressive, and shear stresses and strains in the ONH (Figure). IOP was the dominant ($p<0.05$) factor in the resultant stresses and strains in the LC and NT compared to CSFP. IOP also was the dominant factor ($p<0.05$) driving deformation of the anterior and posterior scleral canal openings as well as anterior and posterior laminar insertions (~ 3 times larger than CSFP) while CSFP played a pivotal role in controlling posterior laminar deformation. The cable elements representing the collagen fibers in the peripapillary sclera experienced a larger axial force in the supine compared to the sitting position, with IOP being the dominant factor compared to CSFP.

Conclusions: Postural changes in the stresses and strains in the LC and interspersed laminar NT could improve our understanding the pathogenenic mechanisms of glaucoma, the ocular effects of idiopathic intracranial hypertension, and visual impairment in astronauts in long-duration spaceflight.

CONTROL ID: 3712151

SUBMITTER (NAME ONLY): Abdullah Amini

TITLE: Multimodal assessment of retinal blood flow characteristics in conditions with macular edema or stromal hyperreflectivity

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Amini, O.N. Klefter, B.A. Sander, M. Larsen, Department of Ophthalmology, Rigshospitalet, Copenhagen, DENMARK|A. Amini, M. Larsen, Faculty of Health and Medical Sciences, Kobenhavns Universitet, Copenhagen, DENMARK|

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ABSTRACT BODY:

Purpose: To examine the contribution of retinal venous congestion in selected retinal diseases where it is suspected of being a unifying pathogenic factor.

Methods: In cases of unilateral retinal vascular disease, comparison of vessel and blood flow characteristics between the affected and unaffected eye was made using noninvasive assessment of linear capillary blood flow velocity by motion contrast fundus photography, retinal blood oxygen saturation by spectrophotometry, retinal hyperreflectivity and thickness by optical coherence tomography (OCT), capillary perfusion by OCT angiography and fluorescein angiography, and disc vessel pulsation by infrared videography.

Results: In 9 patients with unilateral central retinal vein occlusion (CRVO), diabetic retinopathy (DR) or paracentral acute middle maculopathy (PAMM), retinal arterial oxygen saturation in the affected eye was elevated by 1.9% in CRVO, reduced by 4.2% and 4.4% in DR and PAMM, respectively, while venous oxygen saturation was reduced by 15.9%, 15.4% and 2.2% in CRVO, DR and PAMM, respectively. Mean arterial capillary perfusion velocity in affected eye were reduced by 67%, 83% and 15% in CRVO, DR and PAMM, respectively, while venous capillary perfusion velocities were reduced by 76%, 22% and 21% lower in CRVO, DR and PAMM, respectively. Intravenous reflectivity patterns were blurred in most of the affected eyes. Venous pulsation was absent in 7 out of 9 affected eyes, but only in 3 out of 9 unaffected eyes.

Conclusions: Intra-patient comparison of retinal vessels and blood flow contrasting findings, in agreement with the assumption that flow reduction secondary to venous congestion is a unifying characteristic of unilateral CRVO, DR and PAMM.

CONTROL ID: 3712152

SUBMITTER (NAME ONLY): Maureen McCall

TITLE: Characterization of a Humanized Mouse Model of P23H Rhodopsin Autosomal Dominant Retinitis Pigmentosa (adRP)

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. McCall, O.N. Jacobs, Ophthalmology & Visual Sciences, University of Louisville, Louisville, Kentucky, UNITED STATES|M.A. McCall, Anatomical Sciences & Neurobiology, University of Louisville, University of Louisville, Louisville, KY, US, academic, Louisville, Kentucky, UNITED STATES|N. Hasan, Ophthalmology & Visual Sciences, University of Louisville Health Sciences Center, Louisville, Kentucky, UNITED STATES|N. Hasan, Biochemistry & Molecular Genetics, University of Louisville Health Sciences Center, Louisville, Kentucky, UNITED STATES|J. Smith, D. Jantz, V. Bartsevich, K. Viles, Precision Biosciences Inc, Durham, North Carolina, UNITED STATES|D. Cowley, TransViragen Inc, Research Triangle Park, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gene editing is a powerful tool to eliminate expression of mutant proteins. Before any editing approach goes to the clinic, targeted and "off target" editing must be evaluated, preferably in the same animal in situ. The P23H mutation in rhodopsin (RHO) is a common cause of human adRP and a frequent target for gene editing approaches. To evaluate genome editing of an ARCUS meganuclease, RHO1-2, we created humanized mice that harbor WT and mutant P23H hRHO near the P23H mRho locus. One line harbors two humanized WT hRHO alleles (hRHO KI Hz), the other, two humanized P23H hRHO alleles (P23H hRHO KI Hz). When crossed the progeny harbor one WT and one P23H hRHO allele (hRHO KI/P23H hRho KI). We To characterized retinal structure and function in all three mouse lines to define the optimal time frame for evaluation of RHO1-2 gene editing.

Methods: We compared dark and light adapted full field electroretinogram (ffERG) responses in all three genotypes to C57Bl6/J mice. Responses were evoked using a standard ISCEV protocol. b-wave amplitudes at all flash intensities were compared across genotype x age. Morphological assessments were conducted in immunohistochemically labeled frozen sections. Outer nuclear layer (ONL) thickness - DAPI labeled somata and rod morphology - rhodopsin and REEP6.

Results: Retinal structure/function in hRHO KI Hz is similar to C57Bl6/J through P65. At P40, P23H hRHO KI Hz retina has no scotopic ERG and the ONL is a single layer of nuclei with clumped chromatin, emblematic of cones. hRHO KI/P23H hRho KI retinal structure shows time dependent ONL thinning. At P20, hRHO KI/P23H hRho KI retina is similar to hRHO KI Hz. At P30 and P60, hRHO KI/P23H hRho KI ONL thins significantly, albeit not as severe as P23H hRHO KI Hz. hRHO KI/P23H hRho KI scotopic b-wave amplitudes are reduced compared to hRHO KI (~ 60% at P20 and 50% at P75). Across all genotypes, photopic b-wave amplitudes are similar through P70. We continue to track changes in retinal structure and function in older mice.

Conclusions: hRHO KI/P23H hRho KI retina has a broad window for genome editing. Early treatment (first postnatal week) will determine maximum editing capability and late treatment will define efficacy in late stage disease. P23H hRHO/hRHO mice are a valuable resource for in situ evaluation of targeted and "off target" editing of P23H and WT hRHO alleles.

CONTROL ID: 3712153

SUBMITTER (NAME ONLY): Catarina Castro

TITLE: Corneal biomechanical index as a biomarker of subclinical and clinically definite corneal edema in eyes with Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Castro, N. Silva, P. Sousa, M. Neves, M. Gomes, L. Oliveira, Ophthalmology, Centro Hospitalar Universitário do Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: To evaluate the corneal biomechanics using Corvis ST® in different stages of Fuchs Endothelial Corneal Dystrophy (FECD), and to compare with healthy subjects.

Methods: Cross-sectional retrospective study that included FECD eyes without edema (n=54, Group 1), with subclinical edema (n=47, Group 2), and with clinically definite edema (n=17, Group 3), and healthy controls (n=53). All eyes were submitted to Scheimpflug tomography and Corvis ST® in the same day. The exclusion criteria were history of previous corneal transplantation, other corneal diseases, high refractive error and ocular hypertension or glaucoma. All biomechanical corneal parameters provided by the updated version of Corvis ST® were analyzed. For statistical purpose, study groups were compared with the use of ANOVA (parametric) and Kruskall-wallis (nonparametric) tests followed by post-hoc analysis.

Results: Comparing with controls, all FECD groups had lower time at highest concavity (HC, all p=0.001); Groups 1 and 2 had higher deflection amplitude at HC (p=0.018 and p=0.044), but also higher peak distance (p<0.001 and p=0.022); Group 1 had higher time at second applanation (A2, p=0.003); Group 2 had lower time at first applanation (A1, p0.001), and stress-strain index (p=0.027); Group 3 had higher deflection length at A1 (p=0.012); Groups 2 and 3 had higher corvis biomechanical index (CBI, p=0.013 and p=0.04). Comparing with Group 1, Group 3 had higher deflection length at A1 (p=0.047), and lower integrated radius (p=0.04).

Conclusions: FECD eyes in all severity stages had different corneal biomechanical behavior compared with controls. Overall, FECD corneas without edema or with subclinical edema were more deformable than controls, while FECD corneas with clinically definite edema were less deformable compared with those without edema and controls. CBI was higher in FECD corneas with subclinical and clinically definite edema.

CONTROL ID: 3712154

SUBMITTER (NAME ONLY): Bryan Gopal

TITLE: Automatic retinal layer segmentation of visible-light optical coherence tomography images using deep learning

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.D. Gopal, Department of Computer Science, Stanford University, Stanford, California, UNITED STATES|A. Norcia, Wu Tsai Neurosciences Institute, Stanford University, Stanford, California, UNITED STATES|T. Zhang, J.L. Goldberg, A. Dubra, B. Soetikno, Spencer Center for Vision Research, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|H. Zhang, Department of Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visible-light optical coherence tomography (vis-OCT) is an emerging imaging modality that can provide retinal imaging with an axial resolution of ~1.2 microns. Accurate retinal layer segmentation has yet to be established for vis-OCT. In this study, we built an end-to-end, deep learning-based segmentation algorithm to obtain boundaries for 12 retinal layers in human vis-OCT images.

Methods: The dataset consisted of 96 Vis-OCT B-scan images of the macula from human participants collected using the Aurora X2 vis-OCT system (Opticent Health, Evanston IL). Fourteen areas of the retina (12 layers + 2 backgrounds) were manually annotated. The images were resized to a height of 512 pixels and divided into strips of 32 pixels in width for training. The images were augmented with linear contrast, scaling, rotation, and translation. The final augmented dataset was split into training, validation, and test sets at a ratio of 60:20:20, respectively. A four-level U-net was then constructed with 5x3 pixel kernel sizes. The deep learning model was trained for 60 epochs with an Adam optimizer.

Results: Fig. 1A shows an example vis-OCT image from the testing dataset. The image was used as an input to the deep learning model, which produced as a segmented image with 14 labels as output. The boundaries of each layer segmentation were determined and plotted in Fig. 1B. The combined average dice coefficient for the segmented layers was 0.90 +/- 0.06 (max: 0.98, min: 0.76).

Conclusions: We successfully created an automatic retinal layer segmentation algorithm that utilized an end-to-end deep learning approach for vis-OCT images. We characterized the accuracy of the modelmodel's accuracy on our testing dataset and demonstrated its utility in investigating the sub-laminae of the inner plexiform layer. This study serves as the foundation for future work on automatic segmentation of vis-OCT images.

CONTROL ID: 3712155

SUBMITTER (NAME ONLY): Charlotte Crist

TITLE: Expected Visual Field Outcomes Following Boston Keratoprosthesis Type I and II in Eyes without Glaucoma

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Crist, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|C.H. Dohlman, J. Chodosh, T.C. Chen, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if the aperture of the Boston keratoprosthesis (Kpro) type I and II device causes visual field defects on standard white-on-white perimetry in eyes without glaucoma. It is critical to know what should be expected for baseline visual field testing in Kpro eyes without glaucoma, in order to accurately assess for any progressive restriction in peripheral vision, which may herald the onset of glaucoma, one of the leading causes of irreversible blindness in Kpro patients.

Methods: We performed a retrospective chart review and analyzed the Humphrey visual field 24-2 testing (HVF Swedish Interactive Threshold Algorithm standard 24-2 test, Humphrey visual field analyzer Carl Zeiss Meditec, Inc., Dublin, CA) of patients aged 18 and older who had undergone Boston Kpro I or II surgery from January 1, 1990 to June 1, 2021 and who did not have glaucoma at the time of visual field testing. Patients were included if their central vision was 20/40 or better with correction. Patient were excluded if they had poor reliability indices (i.e. more than 33% fixation losses, false positives, and/or false negatives) or if they had any other non-glaucomatous disease that could independently affect their HVF test results.

Results: Out of 414 Kpro I eyes (of 389 patients) and 90 Kpro II eyes (of 78 patients) analyzed, 9 patients (4 Kpro I and 5 Kpro II) met the inclusion and exclusion criteria. We analyzed 36 HVFs of these 9 patients: 14 HVFs of 4 Kpro I patients and 22 HVFs of 5 Kpro II patients. Of the 14 Kpro I HVFs, 9 (64.3%) were full fields, 3 (21.4%) had a rim artifact, and 2 (14.3%) had a borderline superior nasal step. Of the 22 Kpro II HVFs, 10 (45.5%) of the Kpro II HVFs were full fields, 9 (40.9%) had a rim artifact, 2 (9.1%) had a rim artifact with borderline inferior nasal step, and 1 (4.5%) had a significant lid artifact. Seven of 9 patients had at least one full field, with the last two patients having a rim artifact and a rim artifact with a borderline inferior step.

Conclusions: Kpro I and II devices do not significantly affect peripheral vision on HVF SITA standard 24-2 testing in eyes without glaucoma. The most common artifact in Kpro patients was the rim artifact, affecting only the outermost testing points.

CONTROL ID: 3712156

SUBMITTER (NAME ONLY): Eric Furfine

TITLE: Variants of IGT-427 are long-acting, bispecific antibodies for the treatment of degenerative retinal diseases

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Furfine, J. Slocum, S. Capehart, T. Brown, M. Weir, A. Jackson, S. Summers, C. Prananta, Mosaic Biosciences, Boulder, Colorado, UNITED STATES|M. Choo, K. Kim, S. Han, Ingenia Therapeutics, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor (VEGF) inhibitors are standard of care first-line treatment for diabetic macular edema (DME) and wet type age-related macular degeneration (wAMD) although moderate frequency of intraocular administration and the substantial inadequately responding population limit the utility of these treatments. Variants of IGT-427 were designed to address both limitations of the current therapies. The dual function of VEGF inhibition and Tie2 activation is designed to improve the quality of the retinal vasculature and the longer vitreous half-life designed to reduce the frequency of administration compared to the current standard of care. This study set out to evaluate variant's biological and biophysical characteristics.

Methods: The binding affinity was assessed by SPR analysis and the potency in regulating target signaling pathways was assessed in mammalian cell-based assays. Laser-induced choroidal neovascularization (CNV) model in rabbits was employed to examine its in vivo mode of action. In addition, its vitreous pharmacokinetics was measured in a rabbit model.

Results: IGT-427, a bispecific antibody, simultaneously suppressed VEGF signaling and activated Tie2 signaling pathways in heterologous CHO cells and vascular endothelial cells. IGT-427 bound human Tie-2 with Kd < 1 nM in a bivalent interaction, analogous to the cellular surface interaction, and bound human VEGF with a Kd < 10 pM. It displayed comparable high affinities toward rabbit orthologs. Intravitreal IGT-427 reduced vascular leakage in the rabbit CNV model. Engineered variants of IGT-427 were site-specifically PEGyated to increase the apparent molecular weight of the bispecific antibody by > 3-fold. While these variants had slightly reduced apparent affinity for Tie-2 and VEGF, they were similar in activity blocking VEGF and activating Tie-2 in cell-based assays. The extended ocular half-life in rabbit eyes compared to unmodified IGT-427 and Aflibercept will be presented.

Conclusions: IGT-427 has potential as best-in-class therapeutics with superior efficacy compared to agents that only inhibit VEGF, have more potent agonist activity on Tie-2 compared to Ang2 inhibiting agents, and have reduced frequency of intravitreal administration.

CONTROL ID: 3712158

SUBMITTER (NAME ONLY): Gilles Thuret

TITLE: Characterization of elementary lesions of Fuchs endothelial corneal dystrophy and attempt at classification: analysis of 500 Descemet's membranes.

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Thuret, H. VAITINADAPOULE, Z. HE, J. THOMAS, S. POINARD, F. MASCARELLI, P. GAIN, Lab biology, engineering and imaging of Corneal Graft, BiiGC, University Jean Monnet, Saint-Etienne, FRANCE|G. Thuret, S. POINARD, P. GAIN, Ophthalmology, University Hospital, Saint-Etienne, FRANCE|F. MASCARELLI, Centre de Recherche des Cordeliers, UMR S1138, Université Paris Descartes, Paris, FRANCE|N. Koizumi, N. Okumura, Department of Biomedical Engineering, Doshisha University, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: Fuchs' endothelial corneal dystrophy (FECD) is characterized by progressive changes in Descemet's membrane (DM). Its pathophysiology is only partially elucidated and involves certain genetic backgrounds, an abnormal response to oxidative stress, abnormal production of extracellular matrix and endothelial apoptosis. However, despite these similarities, there is heterogeneity in the clinical course. Objectives: To describe and characterize the different lesions of DM to determine whether there are subgroups of FECD

Methods: Study on operative residues, approved by an ethics committee. DMs of approximately 8 mm in diameter were obtained by Descemetorhexis from patients undergoing endothelial transplantation in one of 23 participating French and French-speaking centers (French Fuchs Study group). They were stored either in water to remove residual cells and allow analysis of the MD surface or fixed in 0.4% paraformaldehyde to allow analysis of residual cells. MDs were flat-mounted on glass slide, dehydrated, and then observed by brightfield and phase-contrast light microscopy with manual classification and image analysis.

Results: DM were procured from 500 patients (63% female) aged 71+/-11 years. 65% of the MD were in perfect condition, in one piece, allowing analysis of its entire surface without loss of information. Several elementary lesions were described: 1/ Guttae (constant) of different shapes, diameter, and with differences in organization (between central and peripheral areas but also from one patient to another), in particular radial alignments; 2/ fibrillar and curly structures (inconstant) more or less covering the most central Guttae; 3/ intra- or extracellular pigment (inconstant); 4/ other reliefs "imprinted" in the DM (constant); 5/ several populations of residual cells of normal or dystrophic appearance. Some associations were more frequent than others, allowing to define subgroups of FECD.

Conclusions: This unique and large collection allows, for the first time to our knowledge, to describe with great precision all lesions constituting DM at the stage when patients are transplanted in France. It highlights an unsuspected diversity of the histology of FECD. This first study will be followed by a prospective study to establish correlations between elementary lesions, possible subgroups, clinical characteristics and genetic background

CONTROL ID: 3712159

SUBMITTER (NAME ONLY): Sharad Mittal

TITLE: Alkylating agent activates mast cells to secrete inflammatory and chemotactic mediators

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mittal, W. Cho, A. Singh, Y. Guan, E. Elbasiony, S. Chauhan, Department of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vesicant injuries have been associated with chronic corneal pathology, including persistent inflammation and neovascularization. We and others have shown non-IgE-mediated activation of mast cells upon tissue injury leads to piecemeal release of inflammatory mediators. Here, we investigated the effect of alkylating agent exposure on mast cell activation and secretion of various inflammatory and chemotactic factors.

Methods: Human mast cells (LAD2) were maintained in culture medium containing hSCF (100 ng/ml). To assess the direct effect of alkylating agents, mast cells were exposed directly to 10 μM of nitrogen mustard (NM) for 2 hours. To delineate whether NM-exposed human corneal epithelial cells (HCEC) activate mast cells, HCECs were pretreated with 10 μM of NM for 2 hours and the harvested supernatant were added to LAD2 cultures for additional 2h. To evaluate the continuous effect of NM exposure, mast cells were washed and incubated for another 6h in fresh media. Mast cell activation was evaluated by measuring level of β-hexosaminidase in the culture supernatant. Expression of inflammatory (TNFα, VEGF) and chemotactic factor (IL-8) were quantified in mustard-exposed mast cells. To evaluate the efficacy of mast cell inhibitor-cromolyn, NM-exposed mast cells were treated with 0.2% cromolyn.

Results: Direct nitrogen mustard exposure of mast cells resulted in a 2-fold increase in levels of β-hexosaminidase, compared to media alone ($p<0.001$). Supernatants harvested from NM-exposed corneal epithelial cells also resulted in mast cell activation as evaluated by a significant upregulation of β-hexosaminidase levels (6-fold; $p<0.001$). Cromolyn treatment substantially suppressed the observed NM-induced mast cell activation ($p=0.009$, $p=0.01$, respectively). A significant increase in inflammatory factors TNFα (3-fold; $p=0.029$) and VEGF ($p=0.005$), and chemotactic factor IL-8 (>10-fold; $p<0.001$) was observed in mast cells following NM exposure. Moreover, inhibition of mast cells by cromolyn treatment significantly abrogated expression of both inflammatory and chemotactic factors ($p<0.05$).

Conclusions: Our data demonstrate that direct exposure of nitrogen mustard and NM-exposed corneal epithelial cells activate mast cells to secrete inflammatory and chemotactic molecules, suggesting blockade of mast cells as a potential therapeutic strategy in attenuating alkylating agent-induced ocular inflammation and tissue damage.

CONTROL ID: 3712161

SUBMITTER (NAME ONLY): Mizumi Setia

TITLE: Non-hemostatic role of Factor X in corneal herpes simplex virus-1 (HSV-1) infection

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The focus of current study is to explore the non-hemostatic role of Factor X (FX), clotting factor, in HSV-1 infected mice.

Methods: The corneal HSV-1(McKrae) infection was carried out on anesthetized C57BL/6J (B6) mice after mild corneal scratching. qRT-PCR assay was performed on uninfected and HSV-1 infected corneas to measure the expression of FX, protease activated receptors (PARs), and Tissue factor (TF). FX protein level was determined by ELISA. Immunohistochemistry (IHC) staining for FX, PAR-1, and PAR-2 molecules was carried out on frozen corneal sections. The cellular expression of FX, PAR-1, and PAR-2 was investigated using flow cytometry (FCM). Viral plaque assay measured the amount of infectious virus in infected tissue.

Results: qRT-PCR analysis showed an average 38-fold increase in FX transcript in infected corneas at 13DPOI than 5DPOI. ELISA results also showed higher levels of FX protein at 13DPOI compared to 5DPOI. Furthermore, qRT-PCR analysis of separated corneal epithelium and stroma showed the higher expression of FX in stroma than in epithelium. IHC staining revealed FX localization in the anterior stroma of infected corneal sections at 15DPOI. The flow cytometry data showed the significantly higher expression of FX (both membrane-bound and intracellular levels) in myeloid (CD11b+) than CD4 T cells in infected corneas. Tissue factor (TF) converts FX to an active FXa product. Intriguingly, qRT-PCR results depicted significant downregulation in TF transcripts in infected than uninfected corneas. FXa exerts its effect by binding to PARs. Our results showed no significant change in PAR-1 and PAR-2 mRNA levels in infected than uninfected corneas. To evaluate the role of FX in regulating HSV-1 induced inflammation, oral Rivaroxaban (10mg/kg/day) treatment was given to HSV-1 infected mice. We observed an increased encephalitis incidence in drug than vehicle-treated groups of mice. Viral plaque assay showed the presence of infectious virus in the brainstem of the drug than vehicle-treated groups of infected mice at 10DPOI, suggesting the role of FXa in regulating HSV-1 clearance. The ongoing experiments are ascertaining the outcome of manipulating factor X signaling in HSK lesions.

Conclusions: Together, our results showed that FX expression in HSV-1 infected corneas is localized in myeloid cells and systemic inhibition of FXa signaling increased the incidence of HSV-1 induced encephalitis.

CONTROL ID: 3712162

SUBMITTER (NAME ONLY): Alexandra Kling

TITLE: Unusual properties of novel ganglion cell and amacrine cell types in macaque and human retina

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The primate retina contains ~20 anatomically identified retinal ganglion cell (RGC) types and >10 polyaxonal amacrine cell (PAC) types. However, only 7 RGC types and 1 PAC type have been studied functionally in detail. Our goal is to understand the diversity of visual processing in the RGC and PAC types of the macaque and human retina.

Methods: Large-scale multi-electrode recordings were performed from the peripheral retina. The spike-triggered average of each cell was calculated from responses to flickering checkerboards and used to summarize its spatial, temporal and chromatic properties. Cell types were identified by clustering their functional properties. Substantial errors due to spike sorting were ruled out by stereotypical properties of cells across the electrode array, refractory periods, spatiotemporal structure of electrical footprints, and mosaic organization of receptive fields (RFs) within each type.

Results: In every recording, the well-known ON & OFF parasol, ON & OFF midget, ON & OFF smooth monostratified, and small bistratified RGCs, and A1 PACs, were identified. In 12 macaque retina recordings, at least 15 new RGC and 12 new PAC types with distinct RF properties were identified (Fig. 1A). Each new cell type was observed in several retinas. Most of the novel cell types exhibited one or more unusual properties: 1) inhomogeneous spatial RFs composed of multiple spots or branches; 2) spatially segregated ON and OFF inputs, driven by L/M cones or S cones, not in a center-surround arrangement (Fig. 1B); and 3) sparse spiking in response to checkerboards and naturalistic movies. In 4 human retina recordings, ~20 putative homologs of macaque RGC and PAC types were identified (Fig. 1B). One human PAC type exhibited double the spatial density of its macaque homolog, and one had no obvious homolog.

Conclusions: Most novel RGC and PAC types in the primate retina exhibited unusual spatial and spectral RF properties and firing patterns, suggesting specific functions in visual processing. While most human cell types appear to have macaque homologs, a few cells and properties may be unique to the human retina.

CONTROL ID: 3712163

SUBMITTER (NAME ONLY): Abdus Samad Ansari

TITLE: Associations between dietary Selenium, thyroid medications and glaucoma-related endophenotypes

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Selenium is an essential trace element, which once ingested is incorporated into antioxidant enzymes that prevent cellular damage. However, clinical studies have identified excess selenium levels in plasma and aqueous in patients with glaucoma. Given reported benefits of selenium supplementation in thyroid-associated ophthalmopathy, we aimed to evaluate whether dietary selenium, iodine, and prescribed medication for thyroid dysfunction were associated with glaucoma-related endophenotypes in the general population.

Methods: Participants from the TwinsUK registry were recruited. Firstly, energy-adjusted selenium and iodine intake from 1,977 individuals was estimated through a validated food frequency questionnaire(FFQ). Secondly, self-reported prescribed thyroid medication use was recorded for 1,234 twins. Endophenotypes evaluated included intraocular pressure (IOP), retinal nerve fibre layer (RNFL) thickness and vertical cup to disc ratio (VDCR) adjusted for disc area. Linear mixed models investigated associations of individual nutrients and endophenotype after stratifying intake into quartiles. Logistic regression modelling evaluated use of thyroid hormone medication and IOP > 21mmHg, VCDR > 0.7 and RNFL< 90µm. All models were adjusted for age, sex, spherical equivalent (SE) and family structure.

Results: Mean(SD) age was 62.1(12.25). Mean endophenotype values were IOP: 13.3mmhg(2.82), VCDR: 0.4(0.14) and RNFL: 95.1µm(10.10). Dietary iodine was not associated with any endophenotypes. Multivariate regression models evaluating lowest versus highest quartiles of dietary intake of selenium identified an effect of high selenium intake on VCDR (β=0.02,p=0.04) and a trend towards a thinner RNFL(β=-1.28, p=0.068). IOP was not associated with selenium uptake(β=0.23, p=0.279). The use of oral thyroid hormone medication was associated with a greater risk of having an RNFL thickness less than 90µm (odds ratio (OR):1.67,p=0.001), and non-significant odds ratios of having an IOP>21mmHg (OR:1.30,p=0.80) or a VCDR >0.7(OR:1.26,p=0.83).

Conclusions: In a healthy population, higher levels of dietary selenium appear to be related to a larger VCDR and oral thyroid medication is associated with a greater risk of having a thin RNFL. Larger longitudinal studies are required to replicate these results and determine whether hypothyroid patients and individuals with high selenium intakes are at greater risk of glaucoma.

CONTROL ID: 3712165

SUBMITTER (NAME ONLY): anita barikian

TITLE: Characteristics and outcomes of patients with nAMD managed in US routine clinical practice

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. barikian, East Florida Eye Institute, Stuart, Florida, UNITED STATES|J. Badhwar Kumar, Florida Retina Institute, Orlando, Florida, UNITED STATES|A. McCullough, F.Q. Silva, S. Sherman, H. Moini, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the management of nAMD, visual outcomes at 1 year, factors predicting sufficient treatment, and the impact of treatment sufficiency on visual outcomes in routine clinical practice.

Methods: This retrospective analysis of the Intelligent Research in Sight (IRIS)® registry included treatment-naïve eyes diagnosed with nAMD between Jan 2013 and Dec 2019 with best-corrected visual acuity (BCVA) ≥20/400, anti-VEGF treatment within 3 months of diagnosis, and 1 year of follow-up. Eyes were considered sufficiently or insufficiently treated if they received ≥7 or <7 anti-VEGF injections in Year 1, respectively. Logistic regression identified factors associated with visual outcomes and treatment sufficiency, and the impact of treatment sufficiency on BCVA.

Results: Of 295,561 eligible eyes, 206,517 eyes were treated and 88,990 eyes were not actively treated. Of 184,258 treated patient-eyes, 109,696 (59.5%) received sufficient and 74,562 (40.5%) insufficient treatment. Baseline characteristics were largely comparable across treated groups; mean baseline BCVA was ~61 letters. Mean number of injections was 8.9 vs 4.0 with sufficient vs insufficient treatment, respectively. Asian, African American, Hispanic; Medicaid insured; or non-retina specialist treated patients were less likely to receive sufficient treatment (all P<0.001). Mean BCVA change from baseline at 1 year was significantly greater with sufficient vs insufficient treatment (3.5 vs –0.3 letters; P<0.0001), with larger gains in eyes with baseline BCVA of 20/100-20/200 (10.2 vs 3.1 letters) and <20/200-≥20/400 (19.9 vs 8.9 letters). Sufficiently treated eyes had higher odds of gaining ≥15-letters (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.6, 1.7) and lower odds of losing ≥15-letters (OR, 0.7; 95% CI, 0.6, 0.7) compared to insufficiently treated eyes. Older age, Medicaid insured, and/or better BCVA were associated with worse visual outcomes in both sufficiently and insufficiently treated eyes (all P<0.05).

Conclusions: A substantial number of eyes diagnosed with nAMD were insufficiently treated over 1 year, with worse visual outcomes compared with sufficiently treated eyes. Patient race, ethnicity, insurance type, and treating physician speciality impacted nAMD management. Such findings can identify gaps in care leading to suboptimal outcomes during management of nAMD.

CONTROL ID: 3712167

SUBMITTER (NAME ONLY): Inès De Hoon

TITLE: Influence of size and charge of carbon quantum dots on corneal penetration

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. De Hoon, M. Wels, B. Vanmeerhaege, S. De Smedt, F. Sauvage, General biochemistry and physical pharmacy, Universiteit Gent, Gent, BELGIUM|I. De Hoon, A. Barras, S. Szunerits, Nanobiointerfaces, Universite de Lille, Lille, Hauts-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Corneal blindness is the fourth leading cause of blindness. Currently, corneal transplantation is the only remaining therapeutic option as pharmacotherapy remains limited. As the cornea has several physiological and anatomical barriers, direct delivery of therapeutics into the eye remains highly challenging. This work will study corneal penetration of carbon quantum dots (CQDs) as a function of size and charge. Highly positively charged spermidine-derived CQDs, have shown to allow the opening of the tight junctions of the corneal epithelium, the major barrier for drug delivery into the anterior segment of the eye.

Methods: Synthesis of CQDs was achieved in a microwave reactor from solutions of glucosamine hydrochloride and capping agent at different temperatures. CQDs with hydrodynamic diameter varying between 1-389 nm were obtained. Zeta potential varied between -24 and +32 mV. The influence of size, surface properties and composition of CQDs on corneal permeation and the ability to reach deeper layers in the eye was investigated. CQDs were topically instilled on a bovine ex vivo eye model. Confocal microscopy imaging of the cornea was performed to determine the presence of CQDs in the corneal epithelium and endothelium.

Results: Negatively charged CQDs synthesized from glucosamine hydrochloride and b-alanine show poor penetration into the corneal epithelium. Positively charged CQDs prepared from glucosamine hydrochloride and ethylenediamine as a passivating agent penetrated through the tight junctions of the corneal epithelium. The same was observed for positively charged formed using spermidine as capping agent at 200°C. Decreasing the reaction temperature results in positively charged CQDs of very small size(1.5±0.55nm) shown to reach even the corneal endothelium.

Conclusions: We have shown that CQDs could cross the corneal epithelium and the corneal endothelium. We found that size is the most critical factor for permeation into the cornea. The corneal epithelium is a major barrier for the penetration of nanostructures > 20 nm, while particles < 10 nm could cross the endothelium. Also, the charge influences penetration efficacy. It was observed that positively charged particles could more easily penetrate the epithelium and reach the subsequent layers of the cornea. In contrast, negatively charged particles can barely cross the epithelium. This can be explained by the negative charge of the corneal epithelium.

CONTROL ID: 3712168

SUBMITTER (NAME ONLY): Irina De la Huerta

TITLE: The Angiogenic Effects of Rod Photoreceptors in Response to Hyperglycemia

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. De la Huerta, J. Penn, Department of Ophthalmology and Visual Science, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|J. Nunez, J. Polloway, Y. Chen, V. Reddy, D. Zaminski, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of rod photoreceptors, the most numerous cells in the retina, in proliferative diabetic retinopathy is unknown. This study aims to investigate if, upon exposure to elevated glucose, rod photoreceptors produce pro-angiogenic mediators and can trigger the retinal vascular endothelial cell angiogenic responses of proliferation, migration and branching.

Methods: Primary cultures of mouse rod photoreceptors and retinal microvascular endothelial cells (RMECs) were generated and used for all experiments. The mediators produced by rod photoreceptors exposed to physiologically relevant levels of high glucose were analyzed by multiplex ELISA. Angiogenic responses of RMECs treated with photoreceptor-produced mediators, or with control stimuli, were evaluated by proliferation, migration, and tube formation assays. Transcriptomic shifts in RMECs stimulated with photoreceptor-produced mediators were assessed by qRT-PCR.

Results: Rod photoreceptors treated with 25 mM D-glucose (high glucose) produced higher concentrations of VEGF (2.5-fold increase, $p<0.05$), TNF-α (2.4-fold increase, $p<0.05$), and IL-6 (2-fold increase, $p<0.05$) compared to rod photoreceptors treated with 5 mM D-glucose (normal glucose), or with 25 mM L-glucose (osmotic control). Conditioned media produced by photoreceptors treated with high glucose elicited a 2.5-fold increase in RMEC proliferation ($p<0.001$) and a 2-fold decrease in the time required for scratch closure by migrating RMEC ($p<0.001$). Photoreceptor-produced mediators had proangiogenic effects on RMEC branching and maximum RMEC tube lengths increased 1.9-fold after incubation with media from photoreceptors treated with high glucose ($p<0.001$). Conditioned culture medium produced by photoreceptors in high glucose conditions induced the expression of matrix metalloprotease 9 (MMP-9) (10-fold increase, $p<0.001$) and of MMP-2 (2.3-fold increase, $p<0.001$) in RMEC.

Conclusions: Rod photoreceptors under elevated glucose conditions produce mediators that increase RMEC proliferation, migration, and branching and induce a proangiogenic transcriptomic shift in endothelial cells.

CONTROL ID: 3712173

SUBMITTER (NAME ONLY): Kyle Marra

TITLE: Application of deep learning to quantify vascular tortuosity in mouse models of oxygen-induced retinopathy

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.V. Marra, G. Wei, E. Aguilar, Y. Ideguchi, M. Friedlander, Molecular Medicine, The Scripps Research Institute, La Jolla, California, UNITED STATES|K.V. Marra, School of Medicine, University of California San Diego, La Jolla, California, UNITED STATES|J.S. Chen, J. Miller, S. Prenner, E. Nudleman, Shiley Eye Institute, Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|H. Robles-Holmes, K. Ly, College of Optometry, Pacific University, Forest Grove, Oregon, UNITED STATES|D. Erdogmus, Department of Electrical Engineering, Northeastern University, Boston, Massachusetts, UNITED STATES|P. Campbell, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Increased retinal vascular tortuosity has been quantified in retinal images of humans with retinopathy of prematurity (ROP). The oxygen-induced retinopathy (OIR) model of ischemic retinopathy mimics hallmark features of ROP, including initial ischemia followed by neovascularization. The purpose of this proof-of-concept study was to develop a semi-automatic deep learning algorithm that can be used to investigate whether there is a correlation between retinal vascular tortuosity and disease activity in OIR mice, analogous to what is observed in infants with ROP. Application of this algorithm to images of OIR retinas aimed to characterize vascular tortuosity as a novel outcome measurement in the OIR model.

Methods: OIR was induced in C57BL/6J mice via hyperbaric oxygen exposure from postnatal day 7 (P7) to P12. Retinal flat-mounts of P17 OIR mice were manually segmented for superficial vessels by 4 graders and validated using a subset of images. The optic disc of each image was manually demarcated prior to algorithm input. Using a previously pre-trained DL algorithm for calculating tortuosity index (TI) in retinopathy of prematurity (iROP-Assist), each segmentation and its corresponding disc center was used to generate a TI. Statistical significance between groups was defined as $p \leq 0.05$ and determined using a Student's T-Test.

Results: 50 flat-mount images representing normoxic (NOX) mice and 50 flat-mount images representing untreated P17 OIR mice were included in this analysis. The median tortuosity index for NOX and OIR images was 1.01 [IQR 0.0] and 1.04 [IQR 0.02] respectively (Figure 1), which represented a statistically significant difference ($p < 0.01$). Examples of paired real and segmented NOX and OIR images are shown in Figure 2.

Conclusions: The tortuosity index of retinal vasculature can be semi-automatically calculated for retinal images of OIR mice using a deep learning algorithm. Application of this algorithm to compare the TI for NOX and OIR mice at P17 demonstrated significantly greater tortuosity in OIR mice. Future studies may employ this tool to rapidly assess the effects of therapeutic interventions on the TI of the OIR phenotype.

CONTROL ID: 3712175

SUBMITTER (NAME ONLY): Sylvia Smith

TITLE: Sigma 1 receptor (SIG1R) modulates Cullin3 (CUL3) in retinal cone photoreceptor cells.

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal degenerative diseases frequently involve photoreceptor cell (PRC) death. We have observed dramatic rescue of cone PRCs in the rd10 mouse model of retinopathy when administered (+)-pentazocine ((+)-PTZ), a high affinity SIG1R ligand. The molecular mechanisms of SIG1R-mediated neuroprotection are under investigation. We previously reported that NRF2 may be central to SIG1R-mediated PRC rescue in rd10 mice. CUL3 is a component of the NRF2-KEAP1 pathway and facilitates NRF2 ubiquitination. CUL3 is critical to caspase-8 ubiquitination which regulates cellular apoptosis. Here, we asked whether SIG1R co-localizes with CUL3 and whether its activation alters CUL3 expression.

Methods: 661W cone cells were treated with (+)-PTZ. We used qRT-PCR to investigate Cul3 gene expression, immunoblotting to detect protein levels, CellROX assay to assess oxidative stress and reactive oxygen species (ROS) levels. Small interfering RNA (siRNA), targeting Sig1R or Cul3, was transfected into cells using lipofectamine RNAiMAX reagent to knockdown protein expression. Proximity ligation assay (PLA), co-immuno-EM and co-immunoprecipitation (co-IP) were used to detect the extent to which SIG1R co-localizes and interacts with CUL3.

Results: Treatment of 661W cells with (+)-PTZ [20 μM] significantly increased the expression of Cul3. With increasing concentrations of (+)-PTZ, CUL3 protein levels increased in a dose-dependent manner (~5 fold [3 μM], ~13 fold [10 μM], 18 fold [20 μM] & 18 fold [50 μM]). After silencing SIG1R using siRNA, Cul3 expression decreased dramatically. In Müller cells isolated from $Sig1R^{-/-}$ mice, we observed a significant decrease of CUL3, similar to that observed in 661W cells. In Cul3-siRNA-transfected 661W cells, cellular ROS levels increased significantly. Using PLA and EM immunogold labeling we observed co-localization of SIG1R and CUL3 in 661W cells. The proteins were co-localized in mouse retina tissue as well. Co-IP verified the interaction of SIG1R with CUL3.

Conclusions: Our data provide first evidence that SIG1R co-localizes/interacts with CUL3, a key player in the NRF2-KEAP1 antioxidant pathway. Furthermore, activation of SIG1R modulates Cul3 expression, which may be relevant to its retinal neuroprotective properties. Future studies will investigate comprehensively the role of CUL3 in SIG1R-mediated cone PRC rescue.

CONTROL ID: 3712176

SUBMITTER (NAME ONLY): Isadora José

TITLE: ASSESSMENT OF SAFETY IN THE CORNEAL DONATION PROCESS DURING THE COVID-19 PANDEMIC

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.C. José, A.M. Casella, A. Pelaquim, B.I. Santos, R.C. Feijó, A.P. Oguido, Universidade Estadual de Londrina, Londrina, PR, BRAZIL|

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ABSTRACT BODY:

Purpose: To evaluate the impact of the covid-19 pandemic and the safety of the corneal donation process in an Eye Bank in Southern Brazil.

Methods: This is a cross-sectional, observational, retrospective study involving 771 potential corneal donors and their respective RT-PCR COVID-19 results. The tests were performed by collecting secretions from the oropharynx and nasopharynx and processed in a laboratory at the University Hospital of Londrina-PR, from March 2020 to November 2021. The individuals were submitted to a complementary check list to the traditional one for clinical and epidemiological screening of potential corneal donors against coronavirus (SARS-Cov2). Patients not tested for COVID-19 in this first step were excluded using the main clinical screening criteria already routinely used. The criteria used for further validation of potential donors were: donor who had COVID-19 with complete remission of symptoms for more than 28 days, donor with no clinical suspicion, and no suspected or confirmed contact of COVID-19. Donors diagnosed with COVID-19, donor with COVID-19 suspected by clinical and epidemiological evaluation, contacts of suspected or confirmed COVID-19 less than 14 days ago, and donor with clinical suspicion less than 28 days ago but negative molecular test were discarded in this evaluation.

Results: Among the 771 potential corneal donors, 710 individuals performed the RT-PCR test. A total of 689 (97.04%) individuals tested negative for COVID-19. The average age of suitable donors was 52.52 ± 18.10 years, 289 (41.9%) were female and 400 (58.1%) were male. However, 21 (2.96%) individuals tested positive for COVID-19 and were discarded, even after the complementary screening implemented due to the coronavirus pandemic. Among the positives, 9 (1.2%) cases were female and 12 (1.6%) were male; the average age was 55.10 ± 23.10.

Conclusions: Despite the complementary exclusion criteria for potential organ and tissue donors in the pandemic, the use of RT-PCR for COVID-19 proved to be essential to maintain safety in the corneal donation process.

CONTROL ID: 3712178

SUBMITTER (NAME ONLY): Sobha Sivaprasad

TITLE: A Phase I/IIa trial examining the safety and efficacy of BI-X in patients with diabetic macular ischemia and diabetic retinopathy: The HORNBILL study

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Diabetic macular ischemia (DMI) is a complication of diabetic retinopathy (DR) that can result in irreversible vision loss. There is no approved treatment for DMI. The non-randomized, open-label, single rising dose (SRD)/multiple dosing (MD) HORNBILL study (NCT04424290) is investigating the safety and efficacy of intravitreal BI-X, an anti-ischemia modulator, in patients with DMI.

Methods: Patients with DR treated with pan-retinal photocoagulation who have evidence of DMI are eligible for inclusion in both parts of the study, defined (using optical coherence tomography angiography) in the completed SRD part as any degree of disruption in retinal vascularity within the superficial and/or deep retinal plexus, and in the ongoing MD part as a foveal avascular zone (FAZ) size of ≥0.5 mm^2. The SRD part comprised three dosing cohorts (0.5, 1.0, and 2.5 mg of BI-X), and the primary endpoint was the number of dose-limiting events; secondary endpoints were the number of drug-related adverse events (AEs) and number of ocular AEs. The primary MD endpoint is the number of patients with drug-related AEs; secondary endpoints include change from baseline of best-corrected visual acuity (BCVA), FAZ size, and central retinal thickness.

Results: The SRD part enrolled 12 patients. Half of the patients were female, and the mean age was 61.8 years. The mean time since reported onset of DMI was 4.8 years, and mean BCVA was 30.8 letters. In total, 8 AEs were reported; 5 were ocular (conjunctival hemorrhage, ocular hyperemia, procedural pain, temporary intraocular pressure increase, vitreous detachment), all of which were deemed procedure-related other than hyperemia and vitreous detachment. There were no dose-limiting events, or drug-related AEs reported. Preliminary signs of efficacy were observed; BCVA improved by 5.3 and 4.0 letters in the 1.0 mg and 2.5 mg groups, respectively. The maximum feasible dose in the SRD part was 2.5 mg, which is now being used in the ongoing MD cohort, into which two patients have been enrolled.

Conclusions: Single doses of BI-X were well tolerated by patients with DMI, with no dose-limiting events or drug-related AEs reported. The ongoing single-masked, randomized, MD study will further examine the efficacy of BI-X in patients with DMI.

CONTROL ID: 3712179

SUBMITTER (NAME ONLY): Hao Zhou

TITLE: Depth-resolved visualization and quantification of hyper-reflective foci on OCT scans using optical attenuation coefficients

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Depth-resolved visualization and quantification of hyper-reflective foci in the entire 3D OCT scan corresponding to intraretinal pigment migration and pigmentation along the retinal pigment epithelium (RPE) were achieved using an OAC-based algorithm.

Methods: Subjects with intraretinal hyper-reflective foci and increased reflectivity along the RPE were imaged using a SS-OCT (PLEX® Elite 9000; ZEISS, Dublin, CA) 6×6 mm macular scan pattern. Inner limiting membrane (ILM), RPE, and Bruch's membrane (BM) were segmented using the manufacturer's software. OCT scans were converted to images contrasted by OACs in linear space (Fig. 1A, B). Hyper-reflective foci judged by OACs within a slab from the ILM to 10 μm above the RPE were labeled in green as intraretinal pigmentary deposits. The RPE was color-coded from yellow to red to demonstrate OAC values in which foci of increased reflectivity were highlighted in red. The total pigment burden was segmented from the en face sum projection of an OAC slab from the ILM to BM using an adaptive thresholding method. En face areas of hyper-reflective foci identified by the algorithm were compared with manual segmentations.

Results: A total of 49 eyes from 42 patients were recruited. Visualization of these hyper-reflective lesions was successfully accomplished, and intraretinal hyper-reflective foci were distinguished from increased reflectivity along the RPE (Fig. 1D, E). Hyper-reflective lesions from 24 eyes were manually segmented by identifying intraretinal lesions on B-scans and choroidal hypo-transmission defects on sub-RPE slabs extending 64 to 400 μm below BM. A significant correlation was found in area measurements of the total pigment burden between automated and manual segmentations ($P<0.001$, Fig. 1C).

Conclusions: An automated algorithm based on OACs was able to visualize, localize and quantify hyper-reflective foci in the retina and along the RPE, and the automated quantifications were successfully validated against manual segmentations.

CONTROL ID: 3712180

SUBMITTER (NAME ONLY): Victoria Silveira

TITLE: Optic Nerve Head Changes After Intraocular Pressure Lowering Glaucoma Surgeries Detected with Swept-Source Optical Coherence Tomography

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.D. Silveira, R.L. Lindenmeyer, H.M. Pakter, D. Lavinsky, F. Lavinsky, Ophthalmology, Hospital de Clinicas de Porto Alegre, Porto Alegre, RS, BRAZIL|A. Skaat, Ophthalmology, Sheba Medical Center, Tel Hashomer, Tel Aviv, ISRAEL|H.M. Pakter, E. Picetti, Ophthalmology, Hospital Conceicao, Porto Alegre, Rio Grande do Sul, BRAZIL|P.D. Mello, Ophthalmology, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|F. Lavinsky, School of Medicine, Universidade do Vale do Rio dos Sinos, Sao Leopoldo, RS, BRAZIL|V.D. Silveira, D. Lavinsky, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, BRAZIL|

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ABSTRACT BODY:

Purpose: The aim of this study is to detect optic nerve head (ONH) changes with swept-source optical coherence tomography (SS-OCT) evaluated with the hypotenuse of the ONH cupping (HOC) after intraocular pressure (IOP) lowering procedures.

Methods: Subjects with progressing glaucoma presenting typical ONH and SS-OCT findings that were referred to IOP-lowering glaucoma procedures were included. Patients underwent 24-2 perimetry (SITA standard; Humphrey Field Analyzer; Zeiss) and SS-OCT (DRI-Triton; Topcon) using the wide-field 9mmx12mm raster scan. IOP and SS-OCT scans were obtained at the preoperative period (pre-op), up to 7 days (PO1) and between 30 to 90 days post-operatively (PO2). A B-scan at the center of optic disc and an average of five central B-scans were used to calculate the ONH parameters. HOC was calculated using the Pythagorean theorem: $hypotenuse^2 = leg1^2 + leg2^2$ using the length and depth of the cupping as the legs of a right triangle (figure 1). We also evaluated the change of the BMO-to-BMO extension. Statistical analysis was performed using Generalized estimating equations (GEE).

Results: Fifteen eyes (12 subjects) qualified for the study and underwent the 3 visits. The average age was 70±11.04 years. At the baseline, the average circumpapillary retinal nerve fiber layer (cRNFL) was 60.13±23.21 µm and the visual field (VF) mean deviation (MD) was -13.29±8.5 DB. The mean IOP on each visit (pre-op, PO1 and PO2) were: 20.5±4.99; 11±4.95 and 15.7±5.04, respectively ($p<0.01$). Average HOC decreased significantly after the IOP-lowering procedures ($p=0.001$), markedly between pre-op to PO1. The average components of HOC, depth and lenght, and the BMO-to-BMO extension also decreased significantly (table 1). There was no significant change from PO1 to PO2 in all parameters.

Conclusions: HOC evaluated with SS-OCT significantly decreased after IOP-lowering surgeries to treat progressing glaucoma. This biomarker may be useful to evaluate short-term ONH changes. Notwithstanding, a longer follow-up is needed to determine the persistence of these changes.

CONTROL ID: 3712182

SUBMITTER (NAME ONLY): Stephanie Grillo

TITLE: Extracellular vesicles from ARPE-19 cells expressing R345W-Fibulin-3 can induce epithelial-mesenchymal transition in recipient cells via a TGF-beta pathway

SESSION TITLE: Subretinal fibrosis – clinical challenges, mechanism, and diagnostic tools

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.L. Grillo, M. Zhou, Y. zhao, S. Weber, A.J. Barber, J. Sundstrom, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|M. Ford, MS Bioworks, Michigan, UNITED STATES|H. Chen, X. Liu, H. Wang, M. Swulius, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of the current study was to investigate the size, cargo, and function of extracellular vesicles (EVs) derived from healthy ARPE-19 cells expressing wild-type (WT)-Fibulin-3 (WT-RPE-EV) compared to diseased ARPE-19 cells expressing the R345W-Fibulin-3 mutation (R345W-RPE-EV).

Methods: ARPE-19 cells were infected with luciferase-tagged WT-Fibulin-3 or luciferase-tagged R345W-Fibulin-3 using lentiviruses. EVs were isolated from the media of ARPE-19 cells by conventional ultracentrifugation or density gradient ultracentrifugation. The amount and size distribution of EVs was determined by Nanoparticle Tracking Analysis (NTA). EV protein concentrations were quantified using the DC^{TM} Protein Assay (Bio-Rad). Transmission and cryogenic electron microscopy (EM) were used to image the morphology of the EVs. EV markers were validated using western blot analysis. EV cargo was analyzed by unbiased proteomics using LC-MS/MS with subsequent pathway analysis (Advaita). The EV-associated transforming growth factor-beta 1 (TGF-β1) protein was measured by enzyme-linked immunosorbent assay. EV uptake was investigated by using PKH67-labeled vesicles and was analyzed by confocal imaging. Migration ability was evaluated in ARPE-19 cells using scratch assays in the presence or absence of EVs. mRNA expression levels of endothelial-mesenchymal transition (EMT) markers were measured in ARPE-19 cells after EV treatment, by RT-PCR.

Results: NTA analysis showed that the particle size distributions of R345W-RPE-EV were smaller than those of the WT-RPE-EV, however, there was no difference between EV protein concentrations. Similarly, EM revealed spherical and concave-appearing EVs with two subpopulations of diameters: 30 nm and over 100 nm. Pathway analysis revealed that primary cilia and sonic hedgehog pathways were found to be 3- to 5-fold more abundant in WT-RPE-EV. In contrast, EMT drivers, lysosome components, and ribosome components were found to be 3- to 7-fold more abundant in R345W-RPE-EV. We also found higher levels of TGF-β1 associated with R345W-RPE-EVs compared to WT-RPE-EVs ($p<0.001$). Incubation with R345W-RPE-EVs caused enhanced migration and elevated EMT marker expression in ARPE-19 cells.

Conclusions: These results suggest that R345W-RPE-EVs potentially induce EMT in RPE cells, which may be significant to RPE disease progression.

CONTROL ID: 3712184

SUBMITTER (NAME ONLY): Kenkichi Baba

TITLE: Re-entrainment of retinal circadian clock rescues retinal function after the environmental circadian disruption

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Baba, I. Roberts, H. Duong, G. Tosini, Pharmacology/Toxicology, Morehouse School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The circadian clock plays important roles in the regulation of retinal functions. Previous studies have indicated that removal of the clock gene, Bmal1, from the retina alters photosensitivity, spectral identity and cone viability. We have previously reported that environmental circadian disruption (ECD) also affected circadian clocks in retina and retinal pigment epithelium (RPE). ECD also affected retinal function by altering peripheral retinal circuitry. In this study we investigated whether the re-exposure to stable light cycle is able to re-entrain circadian clocks in the eye and rescue retinal function after ECD.

Methods: PER2::LUC and C57BL/6 mice were placed in a light tight isolated chamber and expose to ECD light cycles by advancing the time of light-on at 6 hours/week for 4 weeks. For control group, mice were exposed to a 12/12 Light/Dark (LD) cycle without any shifts. After the end of ECD cycle, mice were re-exposed to a 12/12 LD cycle for two to four weeks. Then after two or four weeks, PER2::LUC mice (3-4 mo. old) were sacrificed and the retina and the RPE were isolated and cultured for bioluminescence measurement. C57BL/6 mice (3-4 mo. old) were also subjected to both scotopic and photic electroretinogram (ERG).

Results: The circadian rhythm in PER2::LUC bioluminescence revealed that re-exposure of stable light cycle for two weeks re-entrained circadian clock in the retina and RPE. Two weeks of re-exposure to a 12/12 LD cycle did not rescue the amplitude of scotopic b-wave after ECD, but after four weeks of re-exposure to a 12/12 LD the amplitude of scotopic b-waves did not show any difference with respect to control group.

Conclusions: Our data indicates that two weeks of exposure to a 12/12 LD after ECD re-entrains circadian clocks in retina and RPE and the re-entrainment ocular clock rescues the retinal functioning. Thus, our results suggest that ECD induced visual impairment can be reversed by the stable light cycle.

CONTROL ID: 3712186

SUBMITTER (NAME ONLY): Korina Steinbergs

TITLE: A digital morphometric comparison of nucleolar features in BAP1-mutant versus BAP1-wildtype uveal melanomas

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Steinbergs, I. Dryden, J. Lin, Pathology, Stanford University School of Medicine, Stanford, California, UNITED STATES|K. Steinbergs, I. Dryden, J. Lin, Pathology, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveal melanomas (UM) are the most common primary intraocular malignancy in adults. Using gene expression profiling (GEP), UMs can be prognostically categorized as either Class 1 (low risk) or Class 2 (high risk) tumors. Most high risk metastatic UMs harbor a deactivating mutation BRCA1 associated protein-1 (BAP1) gene. A BAP1 mutation leads to loss of nuclear BAP1 expression which strongly correlates with a Class 2 GEP. Recent investigations have shown that the digital morphometry of tumor nuclei correlates with BAP-1 status. Here, we performed a retrospective cohort analysis between BAP1 status and nucleolar features, a relationship that remains unexplored.

Methods: 10 H&E stained slides composed of 5 BAP1-mutant and 5 BAP1-wildtype UMs were scanned by Phillips IntelliSite Scanner and uploaded as whole slide images to the Phillips Intellisite Suite for morphometric analysis. The longest nucleolar diameter (in μm) and nucleolar organizing region (NOR) number was determined for 200 consecutive tumor nuclei in one high-powered field for a total of 2,000 tumor cells. A Student t-test was performed to determine possible statistical differences between mean nucleolar diameter and NOR number in BAP1-mutant and BAP1-wildtype UM groups.

Results: The BAP1-mutant group had a mean nucleolar diameter of 2.43 μm (range 1–9.1) and mean NOR number of 1.4 (range 1–5). The BAP1-wildtype group had a mean nucleolar diameter of 2.15 μm (range 0.5–6) and mean NOR number of 2 (range 1–6). A strong statistical difference between mean nucleolar diameter (P = 7.65E-24) and mean NOR number (P = 4.68E-47) was observed between BAP1-mutant and BAP1-wildtype UM groups.

Conclusions: BAP1-mutant UMs have larger nucleoli and fewer NORs than BAP1-wildtype UMs. This finding supports previous research regarding the prognostic relevance of nucleolar size and number of NORs in Class 1 and Class 2 UMs but suggests that BAP1 alteration may account for these observations. With use of advanced whole slide image analytical techniques, further investigation of this phenomenon should be pursued to determine if standard H&E stained slides can be used to predict GEP Class in UM.

CONTROL ID: 3712187

SUBMITTER (NAME ONLY): Tina Felfeli

TITLE: Effect of Sample Collection and Storage on Biological Stability of Cytokines in Human Aqueous Humor and Vitreous Samples

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cytokines are inherently prone to proteolytic degradation and thus conclusions drawn from collection and storing of the ocular samples could potentially result in misled clinical decisions. This study aimed to determine the effects of sample collection and storage duration on the levels of various cytokines in the human aqueous humor and vitreous samples.

Methods: Samples were obtained from 27 human eyes that underwent pars plana vitrectomy for various diagnoses. Undiluted samples (0.1-0.3ml) were aliquoted into 3 tubes and stored at -80^{O}C for analysis within 1-week, 3-month and 9-month duration since collection. All 27 cytokine analytes were analyzed with the Bioplex Pro-Human cytokine 27-plex assay kit. An ANOVA was run to assess the impact of storage time and sampling location for each biomarker. Cytokine profiles were embedded using principal component analysis (PCA) to view the proximity between timepoints for each sample. A p-value less than the Bonferroni corrected threshold of 0.05 was considered significant.

Results: Four of the 27 biomarkers were significantly impacted by storage duration at both 3- and 9-month timepoints (Interleukin 2 [IL-2], IL-10, IL-12, and Platelet-derived growth factor [PDGF-BB]), whereas 11 were significantly influenced by sampling location of anterior chamber versus vitreous within the same eyes (Granulocyte-macrophage colony-stimulating factor [GM-CSF], IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-12, IL-15, PDGF-BB, and vascular endothelial growth factor [VEGF]). Amongst biomarkers where sample duration was significant, the relative abundance tended to decrease with time. For biomarkers where sampling location of anterior chamber versus vitreous was significant, cytokine concentrations tended to be higher in aqueous humor, with the exception of IL-7. Neither sampling location offered a significant advantage of mitigating deterioration in storage. Separability of patient-specific cytokine profiles at all 3 timepoints in the PCA remained relatively the same over time.

Conclusions: Although there is degradation amongst specific cytokine analytes over 9 months of sample storage, sampling between aqueous humour and vitreous specimens within the same eyes shows much more variation than individual sample deterioration. In all cases, the overall patient-specific cytokine profiles remained relatively the same over time.

CONTROL ID: 3712189

SUBMITTER (NAME ONLY): Dhirendra Singh

TITLE: Topical instillation of Metformin Prevents Oxidative Stress-Induced Eye Lens Opacity Through Induction of AMPK-Nrf2-Mediated Antioxidant Pathway

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.P. Singh, B. Chhunchha, R.R. krueger, Ophthalmology and Visual Sciences, University of Nebraska Medical Center College of Medicine, Omaha, Nebraska, UNITED STATES|E. Kubo, Department of Ophthalmology, Kanazawa Medical University, Kanazawa, JAPAN|

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ABSTRACT BODY:

Purpose: Oxidative stress amplification due to dysregulation of antioxidant pathway with advancing age is a major cause of aging diseases. Metformin (Met), an antidiabetic, has been found to be a potent inducer of Nrf2 (NFE2-related factor 2) antioxidant pathway. Using C57BL/6 mice as a model system, herein we showed that topical application of Met in the eye internalizes in lenses and prevents lens opacity ex-vivo through activation of AMPK-Nrf2/antioxidant-mediated defense pathway.

Methods: 18-month-old mice (n=18) were used for study and anaesthetized with an oxygen-isoflurane pump before Met topical application. Buffered saline (n=6) or 5mM/5µl (n=6) of Met in buffered saline (pH7.4) or Met blocker, atropine (3.5mM) followed by Met (n=6) was instilled once daily in the eyes for 7 days and lenses were collected. To assess Met penetration, lenses were isolated and lens extract was processed and analyzed by Acquity UPLC with Waters triple-quad Xevo TQS. Also, total RNA and protein were isolated and processed for qPCR and Western analyses to assess levels of Nrf2 and its target genes, like Prdx6 and phaseII enzymes expression using specific probes. In another set of ex-vivo experiments, the isolated lenses were exposed to 0-100µM of H_2O_2 for variable times to assess lens opacity. The lenses were photographed (Nikon SMZ 745T) and lens opacity was determined using densitometry. H2DCF-DA dye measured reactive oxygen species (ROS) levels. Two-tailed Student's t-test and one–way ANOVA were used for statistical analysis.

Results: Data analyses revealed that Met could internalize in the lenses, and the lenses displayed upregulation and activation of AMPK. These lenses showed significantly increased expression of Nrf2 and its target antioxidant genes mRNA and protein like Prdx6 and PhaseII enzymes ($p<0.001$) with dramatic reduction in ROS levels compared to untreated lenses. Untreated lenses developed H_2O_2-induced lens opacity ex-vivo, while treated showed significantly less opacity; 81% at 48h and 68% at 120h of H_2O_2 exposure.

Conclusions: All together, our results demonstrate that topically applied Met internalizes in eye lenses and prevents oxidative stress-evoked the lens opacity through activation of AMPK-Nrf2- antioxidant defense pathway, thus raise the possibility of Met-based interventions to delay/prevent aging-related cataract.

CONTROL ID: 3712191

SUBMITTER (NAME ONLY): Geunyoung Yoon

TITLE: Development of a Portable Scanning Wavefront Sensor with Open-View Central Fixation for Use in Children

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Yoon, C. Degre Kendrick, D. Pusti, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|C. Huang, Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|Y. Wu, Flaum Eye Institute, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is of interest to determine how aberrations across the wide visual field and eye shape change over time in children. The study aims to demonstrate the following features of a scanning Shack-Hartmann wavefront sensor (WFS): (1) compact size, (2) natural open-view central fixation, (3) invisible laser and (4) rapid scanning speed.

Methods: We have designed an innovative scanning mechanism with compact motorized stages to achieve scanning along horizontal, vertical, and diagonal meridians. Scanning the horizontal meridian uses the rotary stage only, while scanning in the vertical direction is achieved by translating the x-z linear stage and tilting the hot mirror. Diagonal scanning involves both operations. A high sensitivity CCD sensor ensured each scan was completed within a blink interval, and an invisible 980 nm laser minimized visual distractions. An open-view design allows participants to maintain their central fixation while minimizing instrumental myopia and providing accommodation control without cycloplegia. The accuracy of the WFS was tested by comparing an optical ray-tracing simulation in Zemax to horizontal scan measurements from a model eye. The model eye consisted of a 25 mm focal length doublet with a diffuser at its focal point. Optical ray tracing was performed at 0 to 30° degrees in 5° steps and compared with the measured aberrations.

Results: Zernike coefficients from the Zemax simulation for vertical astigmatism (z5) and horizontal coma (z8) were plotted against data from wavefront measurements collected with the sensor and the model eye. The r^2 values from linear regression were 0.9835 (z5) and 0.9805 (z8), representing a good correlation. As expected, z5 and z8 increased in magnitude with eccentricity, while z12 remained stable at 0.008 ± 0.006 μm (mean ± stdev) across the horizontal meridian. A single scan, up to ±30°, was completed in less than 3 seconds.

Conclusions: We have demonstrated a new version of a compact scanning WFS covering up to ±30°, ±35°, and ±20° along horizontal, diagonal, and vertical meridians, respectively. The WFS can be easily transported to measure the children's eye's aberrations across the visual field in a clinical or school setting.

CONTROL ID: 3712192

SUBMITTER (NAME ONLY): Colin Xu

TITLE: Anti-Vascular Endothelial Growth Factor Treatment Patterns and Outcomes in Retinal Vein Occlusion in Routine Clinical Practice

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Xu, E. Kim, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|C. Xu, E. Kim, C. Carvalho Soares Valentim, K. Seth, J. Muste, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize retinal vein occlusion (RVO)-related macular edema (ME) treatment patterns and its impact on 12 and 24-month best visual acuity (BVA) and central subfield thickness (CST).

Methods: A retrospective cohort study of patients diagnosed with RVO in a tertiary ophthalmic center was performed. Patients who developed RVO-related ME and received their first anti-vascular endothelial growth factor (anti-VEGF) injection between 2003-2020 were included. Treatment patterns analyzed included steady-state anti-VEGF injection interval, time between diagnosis and treatment of ME, and steroid usage. Linear regression analyzed the relationship between treatment patterns and 12 and 24-month BVA and CST, adjusting for sociodemographic factors and systemic comorbidities.

Results: Analysis included 215 eyes with branch RVO (BRVO) and 185 eyes with central RVO (CRVO) or hemiretinal RVO (HRVO). 50.2% of BRVO patients received anti-VEGF injections ≤q8 weeks, 25.6% received injections q8-12 weeks, and 24.2% received injections >q12 weeks. 44.3% of CRVO/HRVO patients received anti-VEGF injections ≤q8 weeks, 31.9% received injections q8-12 weeks, and 23.8% received injections >q12 weeks. There was no significant difference in BVA and CST at baseline, 12, or 24 months in all injection interval subgroups in BRVO and CRVO/HRVO patients. 8.4% of BRVO and 9.2% of CRVO/HRVO patients were treated with steroids. In BRVO patients, steroid usage was associated with a 6.61 (95% CI=0.27-12.96, p<0.01) letter loss in BVA at 12 months and a CST increase of 58.32 (95% CI=9.66-106.97, p=0.02) and 68.47 (95% CI=12.42-123.51, p=0.02) μm at 12 and 24 months, respectively (Tables 1 and 2). Delay between diagnosis and treatment of ME was 35.8±130.5 days in BRVO patients and 10.7±34.2 days in CRVO/HRVO patients. In BRVO patients, every day of delay was associated with a 0.03 (95% CI=0.01-0.05, p=0.01) letter loss of BVA at 24 months. CST was found to be increased by 0.18 (95% CI=0.04-0.31, p=0.01) and 0.79 (95% CI=0.22-1.36, p=0.01) μm for every delayed day at 24 months in BRVO and CRVO/HRVO patients, respectively.

Conclusions: Treatment delay and steroid usage were associated with worse improvements in long term BVA and CST. Steady-state anti-VEGF injection interval was not found to be significant predictor of patient outcomes.

CONTROL ID: 3712193

SUBMITTER (NAME ONLY): Omkar Thaware

TITLE: Application of optical coherence elastography for corneal stiffness measurement.

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.C. Thaware, E. Pavlatos, S. Ni, Y. Li, Y. Jian, D. Huang, Casey eye institute, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine corneal elastic modulus with optical coherence elastography (OCE). The OCE technology is eventually aimed to determine efficacy of a novel corneal collagen crosslinking (CXL) protocol by measuring corneal elastic modulus.

Methods: Ex-vivo experiments on three enucleated adult rabbit eyes were performed. A custom benchtop 100 kHz, 5-μm axial resolution swept-source optical coherence tomography (SS-OCT) system operating at 1060 nm wavelength was built. Corneoscleral discs were mounted on an artificial anterior chamber with closed-loop intracameral pressure control using a micro-infusion pump and pressure sensor. A speckle tracking method was used by locating the maximum cross-correlation between multipixel kernels. Local tissue displacements were tracked during a stepwise quasistatic mechanical loading with a intracameral pressure increment from 17 to 25 mmHg (Figure 1). B-M mode OCT scanning was used to obtain 2-D cross-section scan from central 6-mm of cornea. Corneal axial strain tensor (perpendicular to the corneal surface) was calculated as, $E_{zz}(x,z) \equiv dU_z(x,z) \div dX$ where $U_z(x,z)$ represents the local axial displacements. Using the assumptions of homogeneity and uniform thickness, compressive (known as out-of-plane) Young's modulus was calculated.

Results: The average central corneal thickness of all three eyes was 480 microns. The axial strain profile was plotted (Figure 2) and the compressive Young's modulus was measured as 23.4 kPa, 48.1 kPa and 49.1 kPa for all three corneas.

Conclusions: The measured compressive Young's modulus is within the literature range of approximately 35 to 80 kPa. The OCE will be crucial for post-CXL biomechanical efficacy on intact corneal tissue under normal physiological pressure of 10 to 18 mmHg.

CONTROL ID: 3712194

SUBMITTER (NAME ONLY): Anna Duarri

TITLE: Nanoceria eye drops improve RPE cell therapy in the retinal degenerative RCS rat model

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Duarri, A. Salas, A. Badia, J. Rosell, V. Puntes, J. García-Arumí, Vall d'Hebron Institut de Recerca, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: Chronic inflammation is now regarded as a major pathogenic pathway common in retinal degenerative diseases. Current studies suggest that antioxidant therapies for chronic inflammation treatment are a feasible objective to stop disease progression and represent a promising strategy to improve the therapeutic benefits of regenerative medicine. In this line, nanoceria has been added to the group of antioxidant/anti-inflammatory substances with therapeutic properties. Nanoceria has a unique electronic structure that when reduced to the nanoscale behaves as an oxygen radical scavenger. Here, we developed a new generation of functional nanomedicine which integrates single and combined therapeutic functions involving nanoceria, specially designed for an eye drop formulation, together with retinal pigment epithelial (RPE) cell therapy for retinal degeneration.

Methods: Subretinal implantation of hiPSC-derived RPE cells in RCS rat model of retinitis pigmentosa was performed in the presence or absence of nanoceria eye drops. Four study groups were created: group 1 received subretinal injection of RPE cell suspension (10^5 cells/eye) under continuous nanoceria treatment; group 2 only received subretinal injection of RPE cell suspension; group 3 was injected with vehicle and treated with nanoceria; group 4 was injected with vehicle. Animals were tested at 1, 2, and 4 weeks after cell injection/treatment by OCT, FAF, and ERG to evaluate: 1) conservation of retina; 2) retinal function; 3) survival and integration of the implanted cells. After 4 weeks, animals were euthanized and eyes analyzed by ICP-MS, immunohistochemistry, qPCR, and western-blot.

Results: Ocular administration of nanoceria eye drops in the RCS rats reaches all eye parts without translocation inside the body. Nanoceria preserved the retina structure and RPE viability after transplantation and decreased the infiltration of activated microglia and reduced reactive gliosis. Transplanted RPE cells in presence of nanoceria expressed higher levels of specific markers bestrophin 1, MITF, and RPE65, and reduced glial activation. Moreover, transplanted RPE with nanoceria better preserved ONL compared to vehicle treatment

Conclusions: The combined therapy with RPE cell transplantation and the antioxidant and anti-inflammatory effect of the nanoceria eye drops is a potentially better therapeutic approach to protect the retina from degeneration.

CONTROL ID: 3712195

SUBMITTER (NAME ONLY): Hannah Dunbar

TITLE: Comparison of visual function in structurally defined sub-phenotypes of intermediate AMD: A MACUSTAR study report

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate whether reclassifying eyes with intermediate (i)AMD by additional imaging-based biomarkers identifies sub-phenotypes of iAMD with reduced visual function (VF).

Methods: People with no AMD and Beckman defined iAMD in the MACUSTAR study performed Best Corrected Visual Acuity (BCVA), Low Luminance Visual Acuity (LLVA), Moorfields Acuity Test (MAT), Pelli Robson Contrast Sensitivity (CS), International Reading Speed Test (IReST), Mesopic (MesAT) and Scotopic (ScoAT) average thresholds (S-MAIA microperimetry) and AdaptDx Rod Intercept Time (RIT), followed by multimodal imaging (colour fundus and confocal infrared photography, fundus autofluorescence and spectral domain optical coherence tomography). Images were graded by a central reading centre for presence of the following features: pigmentary abnormalities (PA), reticular pseudodrusen (RPD), incomplete and complete retinal pigment epithelium and outer retinal atrophy (iRORA and cRORA). Pairwise complete VF data were compared across three structurally defined

groups; no AMD, iAMD feature absent(-) and iAMD feature present(+) using nonparametric Kruskal-Wallis, followed by pairwise Wilcoxon tests. Being a signal seeking exploratory analysis, multiple testing correction was not applied.
Results: 224 people (n=56 no AMD [33F; mean age 68 yrs]; n=168 iAMD [106F; 71 yrs]) were included in this analysis. Of those with iAMD, 96(57%) had PA, 37(22%) had RPD, 18(11%) had iRORA and 7(4%) had cRORA. With the exception of IReST, those with iAMD and absent structural features had worse median VF than those with no AMD on all measures ($p<0.01$). LLVA, CS, MesAT, ScoAT and RIT were worse in those with iAMD+RPD compared to iAMD–RPD ($p<0.04$). LLVA, CS, MAT, MesAT and ScoAT were worse in those with iAMD+cRORA compared to iAMD–cRORA ($p<0.05$). CS was worse in those with iAMD+PA compared to iAMD–PA ($p=0.01$). There were no median differences between presence or absence of iRORA in any VF measure.
Conclusions: Though ascribed the same AMD disease stage, eyes with iAMD+RPD and iAMD+cRORA had poorer low luminance and contrast vision than other iAMD eyes. As the number of eyes with observed structural features is small, we aim to confirm our findings in a large longitudinal cohort and examine whether additional structural or functional features should be accounted for in AMD disease classification or used as entry criteria in treatment trials.

CONTROL ID: 3712196

SUBMITTER (NAME ONLY): Sara Haug

TITLE: Interim analysis of the Portal extension trial evaluating the long-term safety and efficacy of the Port Delivery System with ranibizumab (PDS) in neovascular age-related macular degeneration (nAMD)

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Haug, Southwest Eye Consultants, Colorado, UNITED STATES|N. Callaway, S. DeGraaf, S. LePogam, M. Rabena, R. Smith, G. Barteselli, Genentech, Inc., California, UNITED STATES|N. Callaway, Stanford University Byers Eye Institute, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The PDS is an innovative drug delivery system for the continuous delivery of a customized formulation of ranibizumab (RBZ) into the vitreous, approved for nAMD in the US. The Portal extension trial (NCT03683251) is evaluating long-term safety and efficacy of the PDS with RBZ 100 mg/mL (PDS 100 mg/mL) in patients (pts) with nAMD who completed the Ladder (NCT02510794) or Archway (NCT03677934) trials, or will complete the Velodrome (NCT04657289) trial. Interim efficacy data from Portal and long-term pooled safety data from Ladder, Archway, and Portal are reported.

Methods: In Ladder, pts received PDS (10, 40, or 100 mg/mL) with pro re nata (PRN) refills, or monthly intravitreal RBZ 0.5 mg injections (monthly RBZ). In Archway, pts received PDS 100 mg/mL with fixed 24-week refill-exchanges (PDS Q24W) or monthly RBZ (every 4 weeks). Once moved to Portal, pts receive PDS Q24W from day 1. Efficacy outcomes were assessed for Ladder-to-Portal pts treated with prior PDS 100 mg/mL PRN or prior monthly RBZ. Long-term safety was analyzed using pooled data from all pts who received PDS via optimized surgery procedure in Ladder, Archway, or Portal.

Results: For Ladder-to-Portal pts, BCVA remained stable from baseline (BL) to month 48 in prior PDS 100 mg/mL PRN (n=59) and prior monthly RBZ (n=41) arms; mean change from BL (letters; 95% CI) was 0.1 (–6.6, 6.8; n=31) and 2.3 (–9.4, 14.1; n=15), respectively. Center point thickness was also stable through month 48. ~95% of pts did not need supplemental treatment before each refill-exchange procedure. The PDS Patient Preference Questionnaire showed that 92% of Ladder-to-Portal prior monthly RBZ pts preferred PDS at week 40 over injections. In the all PDS safety population (n=555; mean follow-up 111 weeks), 137 (24.7%) pts had ≥1 ocular adverse event of special interest (AESI); most common ocular AESIs were cataract (11.4%), vitreous hemorrhage (6.1%), and conjunctival bleb/conjunctival filtering bleb leak (6.3%). Endophthalmitis occurred in 11/555 (2.0%) pts. Most AESIs were mild/moderate in severity.

Conclusions: Interim results from Portal suggest 48-month maintenance of visual/anatomical outcomes with PDS 100 mg/mL, with PDS preferred to monthly injections. The long-term safety profile of PDS is well characterized, manageable, and reveals no new safety signals.

CONTROL ID: 3712197

SUBMITTER (NAME ONLY): Gil Ben-David

TITLE: Cannabinoid 2 (CB2) receptor upregulation in experimental autoimmune uveitis (EAU)

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ben-David, Y. Nisgav, Y. Weinberger, M. Kramer, Ophthalmology, Rabin Medical Center, Petah Tikva, ISRAEL|M. Kramer, Sackler School of Medicine, Tel Aviv University, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To study the expression of CB2 receptor in the posterior segment of the eye and its response to intraocular inflammation (IOI).

Methods: EAU was induced in 53 C57BL/6J mice as previously published using the uveitogenic 161-180 amino acid fraction of human intra-retinal-binding-protein (hIRBP). Clinical and histopathological grading were performed on days 4, 10, 17, 21 and 24 post induction using indirect ophthalmoscopy and H&E staining respectively. CD4+ T Cells and CB2 receptor were stained in ocular sections and retinal whole flat mounts using immunofluorescence. Perfusion of Fluorescein isothiocyanate dextran conjugate (MW 500k, Sigma) was used for retinal blood vessels staining in flat retinas. Analysis was performed at different time points for cell volume and number using Confocal 3D microscopy and Imaris software.

Results: IOI occurred in 44 out of 53 (83%) mice with induced EAU. Clinical signs of inflammation appeared at 10 days, peaked at 17 to 21 days, and declined at 24 days, post EAU induction. Mice with high clinical scores exhibited more CD4+ cells and higher CB2 receptor positive cells in the vitreous, retina and choroid compared to mice with low grades of inflammation. In retinal flat mounts analysis, CB2 receptor was present in the retina of control mice and significantly upregulated on day 10 ($p<0.05$). CD4+ cells were located outside the retinal blood vessels, peaked on days 10-21 and diminished on day 24 post induction ($p<0.05$).

Conclusions: EAU proved to be a robust and reproducible model in our laboratory. CB2 receptor peaked in the retina earlier than the appearance of CD4+ cells which paralleled the clinical appearance of IOI. These preliminary results suggest that cannabinoids may have a potential effect on EAU.

CONTROL ID: 3712198

SUBMITTER (NAME ONLY): Nikolai Skiba

TITLE: Absolute quantification of phototransduction and other rod outer segment proteins using a novel technique of MS-Western

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.P. Skiba, T. Lewis, W.J. SPENCER, C. Castillo, V.Y. Arshavsky, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|A. Shevchenko, Molecular Cell Biology and Genetics, Max Planck Institute, Dresden, GERMANY|

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ABSTRACT BODY:

Purpose: Retinal photoreceptors are neurons generating electrical signals in response to light excitation. This function is performed by a set of phototransduction proteins localized in photoreceptor outer segments. Despite their well-known functions, the information about their absolute amounts is often conflicting, which impedes our deeper understanding of the relevant molecular mechanisms. In this study, we used a recently developed mass spectrometry-based protein quantification method, called “MS-Western”, for measuring absolute amounts of key functional proteins residing in rod outer segments.

Methods: MS Western quantifies proteins after co-digestion of a sample containing proteins of interest combined with a heavy-isotope labeled protein chimera composed of tryptic peptides representing each of these proteins and a reference protein (typically BSA). It relates the molar abundance of all analyzed peptides to a single reference protein (BSA) added to the sample as a standard. Our chimeric construct contained 3-5 reliably identifiable tryptic peptides representing 20 rod outer segment proteins along with 6 peptides representing BSA.

Results: By comparing the ion intensities of “light” and “heavy” peptides measured in a single mass spectrometry experiment, we simultaneously measured the absolute amounts of all 20 proteins of interest. The method’s accuracy was validated by confirming the equimolar amounts of protein subunits within the known stoichiometric complexes: PDE6α/PDE6β and RGS9/Gβ5/R9AP. The ratios of PDE holoenzyme and the RGS complex to rhodopsin in mouse rods were 1:120 and 1:450, respectively. Another example of this quantification is the 6:1 molar ratio between guanylyl cyclase 1 and 2, and their respective molar ratios to rhodopsin of 1:510 and 1:2,970. Altogether, this analysis provided an accurate quantification of 20 phototransduction and other functionally important outer segment proteins and resolved several discrepancies on their quantifications previously reported in the literature.

Conclusions: MS-Western is an accurate method for quantification of multiple proteins in a single mass spectrometry experiment. This approach is by far superior to a traditional Western blotting technique, which requires high quality antibodies and purified protein standards. MS-Western can be used to accurately measure the amounts of multiple proteins in any ocular tissue

CONTROL ID: 3712199

SUBMITTER (NAME ONLY): Laura Valdez

TITLE: Molecular Event in HRP Apoptosis

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.L. Valdez, Molecular Science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|

Commercial Relationships Disclosure: Laura Valdez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Human retinal pericytes (HRP) are contractile cells adjacent to and provide support for endothelial cells (EC) of capillaries, which are essential in the regulation of retinal vasculature. Early stages of DR are characterized by the loss of HRP, which leads to the development of advanced-stage pathology including angiogenesis. Although much is known about the etiology of DR, the apoptotic pathway that incites HRP loss remains unclear. Our preliminary studies reveal that monocyte-derived macrophages secrete TGF-β1, which induces the expression and secretion of a TGF-β1-Induced, pro-apoptotic BIGH3 protein (TGF-β–Induced Gene Human Clone 3) leading to apoptosis of HRP Eye, 30(12), 1639-1647Based on a preliminary study in renal cells (unpublished data), CTP (c-terminal peptide) with an RGD domain is released from BIGH3 by proteolysis leading to renal cell apoptosis. In the present study, we employed Western Blots to determine if a similar molecular event also takes place in the BIGH3 protein to induce HRP apoptosis.

Methods: HRP cells were obtained from Cell Systems and were cultured in complete media with 10% FBS, 1% penicillin/streptomycin, in a humidified 5% CO_2 incubator with a temperature of 37°C. Cells were harvested from passages 5-8 until reaching confluency. HRP were starved for 24hrs with media composed of only DMEM and 1% penicillin/streptomycin prior to getting treated 24hrs with and without 15ug/mL of TGF-β, 50ug/mL of Leupeptin (a protease inhibitor), and with both TGF-β and Leupeptin. Conditioned media was collected after 24hrs and stored in -80C until protein concentration assay and probed with an anti-BIGH3 polyclonal antibody, an in-house generated rabbit antibody generated against full-length recombinant BIGH3. Western blot analyses of the cleaved BIGH3 protein band were quantified using ImageJ.

Results: Western blots show two BIGH3 protein bands: un-cleaved protein (60kD) and cleaved (or truncated). Image analyses of band intensity of the cleaved proteins was significantly reduced (by five-fold) in the presence of Leupeptin (a protease inhibitor). Similarly, a two-fold reduction of the cleaved protein was also observed when Leupeptin was added to the cell media in conjunction with TGF-β.

Conclusions: Consistent with our previous observation, cultured HPR secret BIGH3 protein. Thus, our results are consistent with prior observations in renal cells that CTP release (by proteolysis) from BIGH3 is a molecular event in the HRP apoptosis.

CONTROL ID: 3712200
SUBMITTER (NAME ONLY): Douglas Parsons
TITLE: In vivo quasi-elastic light scattering eye scanner detects molecular aging in humans and mice
SESSION TITLE: Lens proteins and cataracts
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D. Parsons, S. Sarangi, O. Minaeva, J.A. Moncaster, L.E. Goldstein, Department of Radiology, Boston University, Boston, Massachusetts, UNITED STATES|D. Ledoux, D.G. Hunter, Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|D. Ledoux, D.G. Hunter, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J.I. Clark, Department of Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|L.E. Goldstein, Boston University Alzheimer's Disease Center, Boston, Massachusetts, UNITED STATES|
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ABSTRACT BODY:
Purpose: The absence of clinical tools to evaluate individual variation in the pace of aging represents a major impediment to understanding aging and maximizing health throughout life. The lens is an ideal tissue for quantitative assessment of molecular aging in vivo. Long-lived proteins in lens fiber cells are expressed during fetal life, do not undergo turnover, accumulate molecular alterations throughout life, and are optically accessible in vivo. The study purpose was to measure age-dependent signals in vivo in lenses of both healthy human subjects and wild-type C57BL/6 mice. We hypothesize that cumulative alterations in the lens may constitute an in vivo biomarker of molecular aging.
Methods: Quasi-elastic light scattering (QLS) was used to measure age-dependent changes in vivo in lenses of 34 healthy human subjects without history of eye disease (18 males, 16 females; ages 5–61), and in unanesthetized wild-type C57BL/6 mice aged 3–22 months-old. We also examined time-dependent effects of in situ oxidation on QLS signals obtained from water-soluble human lens protein extract (hLPE) during long-term incubation in vitro.
Results: Our results indicated that aging related QLS metrics can be acquired noninvasively in human subjects and in unanesthetized mice. Age-dependent QLS signal changes detected in vivo in humans and mice recapitulated time-dependent changes in hydrodynamic radius, protein polydispersity, and supramolecular order of human lens proteins during long-term incubation (~1 year) and in response to sustained oxidation (~2.5 months) in vitro.
Conclusions: Our findings demonstrate that QLS analysis of lens proteins provides a practical technique for noninvasive assessment of molecular aging in vivo.

CONTROL ID: 3712201

SUBMITTER (NAME ONLY): Paul GOIN

TITLE: Pre-dissected DMEK stored in bioreactor: feasibility study.

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. GOIN, S. POINARD, O. DORADO, C. PERRACHE, Z. HE, S. NINOTTA, F. MASCARELLI, P. GAIN, G. Thuret, Laboratoire de Biologie, Ingénierie et Imagerie de la Greffe de Cornée, BiiGC, EA2521, Faculté de Médecine, Université Jean Monnet Saint-Etienne, Universite Jean Monnet Saint-Etienne, Saint-Etienne, Rhône-Alpes, FR, academic, Saint-Etienne, Rhône-Alpes, FRANCE|P. GOIN, A. GAUTHIER, Ophtalmologie, Centre hospitalier regional universitaire de Besancon, Besancon, FRANCE|S. POINARD, O. DORADO, P. GAIN, G. Thuret, Ophtalmologie, Centre Hospitalier Universitaire de Saint-Etienne, Saint-Etienne, Rhône-Alpes, FRANCE|F. MASCARELLI, UMR S1138, Université Paris Descartes, Centre de Recherche des Cordeliers, Centre de Recherche des Cordeliers, Paris, Île-de-France, FR, academic/medres, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The number of endothelial grafts precut by corneal banks increases. Their shelf life is limited to a few days. We previously demonstrated the superiority of an active storage with the corneal bioreactor (BR) over organ culture (passive) for whole corneas. Aims: Measure endothelial viability of precut DMEK after 3 and 10 days of storage in our BR in a preclinical study.

Methods: Human pairs of corneas were included. The endothelial cell density (ECD in cells/mm^2), thickness and transparency of corneas were measured before graft preparation. Descemet's membrane (DM) was peeled using the no-touch technique leaving the graft attached to the center of the cornea (on approx. 1/mm^2). After randomization, one cornea was kept in organ culture (OC) and the other in the BR (21 mmHg, 2.6 µL/min) in the same medium (CorneaMax, Eurobio). The final viable ECD was determined using the triple staining with Hoechst-Ethidium-Calcein-AM. In addition, the expression of CD166 and NCAM (lateral membranes), ZO-1 (apical junctions), Na^+/K^+ATPase (endothelial pump function) and COX-IV (mitochondrial content) was studied by immunostaining to characterize endothelial cells after the storage.

Results: Initial ECDs were comparable: 2185±232 cells/mm^2 in BR versus 2276±328 cells/mm^2 in OC for the 3-day period and 2680±416 cells/mm^2 in BR versus 2644±420 cells/mm^2 in OC for the 10-day period. The DMs did not fold back in either BR or OC. Viable ECD did not differ significantly between BR and OC for either storage period: 2378±501 cell/mm^2 in BR versus 2342±503 cell/mm^2 in OC for the 3-day period (n=8 pairs and p=0.6238) and 2482±288 cell/mm^2 in BR versus 2579±315 cell/mm^2 in OC for the 10-day period (n=5 pairs and p=0.1756). Corneas were more transparent and thinner in BR than in OC after 3 days (916±86 versus 1193±136µm with p=0.0001) and 10 days (957±128 versus 1220±105µm with p=0.0625). The functional and structural markers studied were expressed in both groups after 3 and 10 days, some better preserved in BR.

Conclusions: The storage of precut DMEKs seems to be possible in BR and OC for at least 10 days. Interestingly, a precut endothelium continues to partially exert its pump function in the BR. In practice, this could allow the anterior part to be used for DALK. In addition to improving the storage of whole grafts, the BR allows the storage of precut DMEKs for up to 10 days with excellent endothelial survival.

CONTROL ID: 3712202

SUBMITTER (NAME ONLY): GianMarco Douglas

TITLE: Systemic treatment with Cucurbitacin I protects in light-induced retinal degeneration (LIRD) mice

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.L. Douglas, K. Bales, J.H. Boatright, Ophthalmology, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|M. Chrenek, J.T. Sellers, C. Reid, J.M. Nickerson, K. Bales, J.H. Boatright, Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tauroursodeoxycholic acid (TUDCA) is neuroprotective in retinal degeneration models. Cucurbitacin I has a chemical structure similar to TUDCA and has been shown to be protective in models of CNS neurodegeneration. Therefore, we sought to test whether systemic treatment with Cucurbitacin I is protective in a light induced retinal degeneration (LIRD) model.

Methods: Adult male (n=15) and female (n=14) BALB/cAnNCrl mice received two injections of either vehicle (10% DMSO+PBS, n=13) or Cucurbitacin I treatment (1.3 mg/kg; 10 µl/gram of mouse weight, n=16). After the first injection, mice were dark-adapted overnight and injected again 30-60 min prior to LIRD. Mice were either exposed to 2500 lux, to induce LIRD, or dim light (50 lux) for 4 hours. One week after light exposure, retinal function was assessed by electroretinograms (ERG) and eyes were collected for histology. Outer Nuclei Layer (ONL) counts were assessed in retinal sections stained with hematoxylin and eosin. Retinal sections were stained for GFAP and IBA1 to assess retinal glial inflammatory response. Two-way ANOVA was conducted to analyze data (mean±SD).

Results: Exposure to toxic light diminished scotopic ERG at 1 cd s/m^2 a- and b-wave amplitudes, compared to dim light exposure (-118µV±43.2 vs -256µV±57.9 and 370µV±130 vs 558µV±158, respectively; $p<0.04$). ONL nuclei counts were diminished to 70% in comparison to dim light exposed mice ($p<0.003$). Systemic treatment with Cucurbitacin I prevented the losses in ERG a- and b-wave amplitudes (-228µV±33.2 vs -256µV±57.9 and 526µV±91 vs 558µV±158, respectively; $p>0.28$) and ONL nuclei count ($p>0.5$), with outcomes statistically indistinguishable from dim light exposed groups. Retinal sections from vehicle-treated mice undergoing LIRD showed increased labeling of both GFAP ($p<0.03$) and IBA1 ($p<0.03$) compared to dim groups or mice undergoing LIRD but treated with Cucurbitacin I.

Conclusions: Systemic treatment with Cucurbitacin I protects against retinal degeneration. Injections of Cucurbitacin I protected both retinal function and structure of adult BALB/cAnNCrl mice model of LIRD. The suppression of inflammatory responses likely occurred in microglia and Müller glial cells. As CNS neuroprotection by Cucurbitacin I treatment is mediated by inhibiting JAK2-STAT3 signaling and preventing microglial overactivation, we plan future studies to examine these potential mechanistic pathways in retina.

CONTROL ID: 3712203

SUBMITTER (NAME ONLY): Christina Ohnsman

TITLE: Longitudinal Results and Test-Retest Variability of a Novel Optokinetic Nystagmus-Based Visual Acuity Test in Children with CLN2 Disease

SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Ohnsman, Clinical Development, REGENXBIO Inc, Rockville, Maryland, UNITED STATES|Y. Atiskova, J. Wildner, S. Dulz, Ophthalmology, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|A. Schulz, Pediatrics, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|

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ABSTRACT BODY:

Purpose: Vision loss is a prominent feature of neuronal ceroid lipofuscinosis Type 2 (CLN2) Batten disease, yet cognitive, motor, and language impairments prevent reliable measurement of visual acuity (VA) using standard methods. We previously described a novel VA test using optokinetic nystagmus (OKN) detection technology (Threshold Visual Acuity Test, University of Auckland, NZ), demonstrating high correlation between central retinal thickness (CRT) and VA-OKN as well as symmetrical VA-OKN between eyes in children with CLN2 disease. Here, we report longitudinal data for the same children, as well as test-retest variability.

Methods: Six to 10 months after initial VA-OKN measurement, binocular and monocular VA-OKN testing was performed at two consecutive visits two weeks apart in 23 children ages 3 to 9 years with classic CLN2 disease.

Results: Longitudinal data were available for binocular VA-OKN (OU) in 14 children, and for monocular VA-OKN in the right eye (OD) in 11 children and the left eye (OS) in 10 children. Eight of nine children (89%) who initially cooperated with monocular testing in both eyes did so at the second and third visits. Binocular VA-OKN ranged from 0.3 to 1.4 logMAR. Monocular VA-OKN remained highly symmetric between right and left eyes. Mean longitudinal change in VA-OKN over the 6 to 10-month testing period was 0.06 logMAR OU, 0.03 OD, and -0.05 OS. The 95% CI for test-retest limits of agreement on Bland-Altman analysis were 0.24 to -0.26 (mean difference = -0.01) OU, 0.30 to -0.30 (-0.03) OD, and 0.13 to -0.31 (-0.09) OS, with Pearson correlation coefficients of 0.93 OU, 0.88 OD, and 0.91 OS.

Conclusions: In children with the profound neurocognitive impairments associated with CLN2 disease that prevent use of standard VA methods, the novel, OKN detection-based Threshold Visual Acuity Test appears to be a valid measure, demonstrating satisfactory test-retest variability. More longitudinal data are needed to characterize the pattern and progression of VA loss in CLN2 disease.

CONTROL ID: 3712206

SUBMITTER (NAME ONLY): Ann Elsner

TITLE: Retinal changes seen on OCT and OCTA for diabetic subjects compared with cone distribution and vascular changes from AOSLO

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Elsner, T.J. Gast, B. Walker, R.N. Gilbert, V. Parimi, S.A. Burns, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic patients have a wider range of cone densities than controls and have capillary remodeling on AOSLO, even with normal total retinal thickness on OCT. To probe the relation of retinal vs. subretinal changes to cone distribution, we used OCT to localize lesions and OCTA for vessel remodeling and decreased flow.

Methods: Cone density and retinal vessels were imaged as previously for 10 diabetic subjects (29-79 yr, 54.5 +/- 12.7 yr). All subjects were consented and tested as approved by the Indiana University Institutional Review Board, which adhered to the Declaration of Helsinki. We performed OCT and OCTA (Heidelberg Spectralis II), then imaged cones and retinal microcirculation with AOSLO, using confocal and multiply scattered light images. We used reflectance mode and motion mapping for vessels, montaging images for the 6 x 6 deg central retina and temporal retina to 7 deg. Graders assessed OCT B-scans for cysts, exudates, microaneurysms, layer disruptions, subretinal fluid, and subretinal deposits and OCTA for lower flow and vessel remodeling. A 2-parameter exponential model of cone density, ln(cone density) = a * microns eccentricity + b, estimated total cones within the central 14 deg.

Results: Both total cones, 173,000 – 283,000, and vascular findings differed among subjects. All subjects had retinal microaneurysms and capillary remodeling seen shadowing cone maps and seen in inner retinal images on AOSLO. Retinal OCTA localized lesions in all subjects, but less capillary remodeling than AOSLO. Significant subretinal OCT or OCTA findings were not seen in either younger subject, with total cones 176,000 and 189,000, < the 95% CIs for age-similar controls. Similarly, no significant subretinal OCT findings were seen in the 3 older subjects with the lowest total cones. In contrast, there were subretinal deposits, indistinguishable from drusenoid deposits, in a 62 yr old with 273,000 total cones, the second highest of diabetics and within 95% CIs of controls. No subject had subretinal fluid on OCT.

Conclusions: Diabetic subjects with retinal thicknesses within normal limits can nevertheless have numerous retinal lesions, visible on OCT B-scans. Retinal vessel remodeling is visible on OCTA but to a lesser extent than with AOSLO. Our findings are inconsistent with early subretinal changes being necessary for low cone densities.

CONTROL ID: 3712207

SUBMITTER (NAME ONLY): Linda Kang

TITLE: Microbial keratitis isolates at a Midwestern tertiary eye care center

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Kang, M. Lu, L. Niziol, A. Thibodeau, T. Francis, M. Pawar, M.A. Woodward, Department of Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the causative organisms, antimicrobial susceptibility patterns, and demographic differences of microbial keratitis (MK) infections at a Midwestern tertiary eye center.

Methods: MK patients were identified in the University of Michigan electronic health record from August 2012 to February 2021. Laboratory tests (culture, stain, smear, polymerase chain reaction, antibody, antigen) from 7 days before to 90 days after MK diagnosis were identified and classified as lab-positive (any positive result) or lab-negative. Lab-positive infections were categorized as bacterial (gram-positive, gram-negative, acid-fast bacilli [AFB]), fungal, viral, Acanthamoeba, or polymicrobial. Antimicrobial susceptibilities were obtained. Patient demographics were compared between lab-positive and negative cases and between MK organism types using t-, Kruskal-Wallis, Chi-square, or Fisher exact tests.

Results: Of 2990 MK patients, 966 (32.3%) had labs performed, of which 517 (53.5%) were positive (289 females; 442 White, 45 Black, 9 Asian, 11 other races). Infections were bacterial in 72.7% (n=376) of patients, fungal in 6.6% (n=34), viral in 2.1% (n=11), Acanthamoeba in 0.8% (n=4), and polymicrobial in 17.8% (n=92). Of the bacterial infections, 72.1% (n=271) were gram-positive with coagulase-negative Staphylococcus (CoNS; 28.7%) and Staphylococcus aureus (S. aureus; 25.5%) as the most common pathogens. Bacteria were gram-negative in 26.1% (n=98) of cases, with Pseudomonas aeruginosa as the predominant pathogen (46.3%), and AFB in 1.9% (n=7). Methicillin-resistance occurred in 37% of S. aureus and 71% of CoNS; 100% were susceptible to vancomycin. Lab-positive patients were significantly older than lab-negative patients (mean ± standard deviation, 57.5 ± 20.5 years vs. 54.3 ± 20.3, p=0.015). White patients represented a larger percentage of bacterial, fungal, or polymicrobial infections than viral infections (87.0%, 97.1%, 88.9% vs 45.5%, all $p<0.05$). Black patients represented a larger percentage of viral infections than bacterial, fungal, or polymicrobial infections (45.5% vs 9.0%, 2.9%, 6.7%, all $p<0.05$).

Conclusions: Bacterial keratitis accounted for most MK cases. Gram-positive bacteria were the most common isolates, followed by gram-negative. CoNS and S. aureus were universally susceptible to vancomycin. Patients with positive labs were significantly older. There were significant differences between MK types with respect to race.

CONTROL ID: 3712208

SUBMITTER (NAME ONLY): Victoria Whitmore

TITLE: Comparative Assessment of Baseline and Longitudinal Higher-Order OCT Features in the Phase III VISTA Clinical Trial Based on Race

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Whitmore, S. Yordi, L. Lunasco, H. Cetin, G. Kalra, C.J. Mugnaini, K. Wise, C. Calabrise, K. Talcott, S.K. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the baseline and longitudinal higher order OCT features in the Phase III VISTA diabetic macular edema (DME) clinical trial based on race.

Methods: This was a post-hoc analysis of the Phase III VISTA-DME clinical trial, which included patients randomized 1:1 to receive 2mg IAI every 4 weeks or 8 weeks after 5 initial monthly doses. Higher-order OCT analysis conducted with a machine learning-enhanced feature extraction and multi-compartment segmentation platform enabled evaluation of volumetric fluid features and compartmental retinal integrity (e.g. EZ integrity). Specific features included mean central subfield thickness (CST), intraretinal fluid (IRF) volume, EZ-RPE panmacular volume and total EZ attenuation. Retinal anatomic dynamics and BCVA changes were compared and stratified by reported race. Patients self-reported as White (n=198), Black/African American (n=25), Asian (n=5), American Indian/Native Alaskan (n=1) and Not Reported (n=3). Only White (W) and Black/African American (B/AA) patients were included in analysis due to subject quantity.

Results: At baseline, age and clinical characteristics such as systolic blood pressure, BMI, duration of diabetes and BCVA were similar between W and B/AA (all $p>0.05$) (Table 1). Diastolic blood pressure was higher in B/AA (74.4 vs 77.7 mmHg, $p=0.033$). At Baseline and at Week 100, CST, IRF volume, EZ-RPE volume, EZ total attenuation and BCVA were similar between W and B/AA (all $p>0.05$).

From Baseline to Week 100 (Table 2), W and B/AA showed significant improvement in CST (-191.6±156.2µm, -236.8±200.5µm respectively, $p<0.01$ from baseline) and IRF Volume (-1.2±1.4 mm^3, -1.2±2.5 mm^3, $p=0.021$ from baseline). However, while W showed significant improvement in EZ-RPE volume (+1.3±0.2mm^3, $p<0.01$) and EZ total attenuation (-0.7±4.0%, $p=0.016$), B/AA demonstrated a nonsignificant improvement in both ($p=0.20$, $p=0.65$ respectively). W and B/AA showed significant improvement in BCVA during that period ($p<0.01$).

Conclusions: Higher order OCT DME features and longitudinal response to IAI demonstrated similar features and findings when comparing based on race. Both groups demonstrated significant anatomic and functional improvements with IAI.

CONTROL ID: 3712209

SUBMITTER (NAME ONLY): Cassandra Warden

TITLE: Arginine and citrulline induce angiogenic mechanisms and increase intracellular nitric oxide production in human retinal endothelial cells

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Warden, M.A. Brantley, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Cassandra Warden: Commercial Relationship: Code N (No Commercial Relationship) | Milam Brantley: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Purpose: We previously observed elevated plasma levels of both arginine and citrulline in patients with diabetic retinopathy compared to diabetic controls. Intracellularly, citrulline is converted to arginine, which serves as a substrate for both arginase and endothelial nitric oxide synthase (eNOS). In the current study, we tested whether arginine and citrulline could induce an angiogenic response in human retinal microvascular endothelial cells (HRMEC) and if arginine and citrulline activate arginase and/or eNOS in HRMEC.

Methods: Methods: HRMEC were treated with 30 μM citrulline, 70 μM arginine, or citrulline + arginine, and the angiogenic response was measured with cell proliferation, cell migration, and tube formation assays. To determine if citrulline and arginine activate arginase or eNOS in HRMEC, arginase activity was quantified by measuring urea, a product of arginase, and DAF-FM DA was used to stain for intracellular nitric oxide, a product of eNOS. Western blots were used to measure protein expression of arginase-1, arginase-2, total eNOS, and phosphorylated eNOS.

Results: Results: Individually, neither citrulline nor arginine resulted in an angiogenic response in HRMEC, but citrulline + arginine induced proliferation by 39.6% ($p = 0.018$), cell migration by 57.7% ($p = 0.011$), and resulted in tubes that were 36.2% longer ($p = 0.0042$) compared to untreated controls. There was no change in arginase activity or arginase-2 protein expression in HRMEC treated with citrulline and/or arginine, but citrulline + arginine resulted in lower protein expression of arginase-1 compared to untreated cells ($p = 0.0046$). Citrulline ($p = 0.012$), arginine (0.0029), and citrulline + arginine ($p = 0.025$) all increased NO production compared to controls. Arginine ($p = 0.028$) and citrulline + arginine ($p = 6.3 \times 10^{-4}$) led to greater total eNOS expression than in controls, and citrulline + arginine resulted in higher protein expression of phosphorylated eNOS compared to controls ($p = 0.029$).

Conclusions: Conclusions: These data demonstrate that arginine and citrulline together can induce an angiogenic response, increased nitric oxide production, and increase eNOS expression and phosphorylation with no effect on arginase activity in HRMEC. This suggests that elevated plasma arginine and citrulline could potentially contribute to progression of diabetic retinopathy.

CONTROL ID: 3712212

SUBMITTER (NAME ONLY): SUNDARARAJAN MAHALINGAM

TITLE: Consequences of eliminating ^{52}LFRTVL^{57} residues from the N-terminal domain of αA-crystallin on structure and function of the protein

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. MAHALINGAM, G. Shankar, P. Santhoshkumar, K. Sharma, Department of Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|K. Sharma, Department of Biochemistry, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported that deletion of ^{54}FLRAPSWF^{61} sequence from αB-crystallin results in gain of function. Since αA- and αB- have significant (~54%) sequence homology, we hypothesized that deletion of ^{52}LFRTVL^{57} from αA- will result in a gain of function. Thus, the present study was undertaken to see the effect of deleting 52-57 region on the structure-function of αA-crystallin.

Methods: Chaperone activities of the purified recombinant αA-wt and the deletion mutant (αAΔ52-57) were evaluated using one μM luciferase and 100 μg alcohol dehydrogenase (ADH) substrates. The ability of the proteins to inhibit $A\beta_{1-42}$ oligomerization and fibril formation in-vitro was examined under TEM. Cell integrity and ROS detection assays were performed to access the cytoprotective activity of the crystallins in sodium iodate-challenged ARPE-19 cells. The molecular size, hydrophobicity, and stability of the WT and mutant proteins were compared by standard methods.

Results: The average molar mass of αA oligomers increased from 710 kDa to 1036 kDa in αAΔ52-57. The hydrodynamic radii (Rh) of the mutant also showed a similar increase in size. The αAΔ52-57 mutant exhibited a 7-fold and 5-fold increase in chaperone activity compared to αA-wt with the unfolding luciferase and ADH, respectively. αA-mutant also suppressed $A\beta_{1-42}$ fibril formation in-vitro and showed 11 ± 0.39 % higher protection against $A\beta_{1-42}$-induced cytotoxicity in ARPE-19 cells compared to WT. Sodium iodate-induced cytotoxicity and ROS detection studies showed that the mutant αA protein has 20 ± 1.06 % greater anti-apoptotic activity than WT with equal concentration of chaperone tested and also showed 15 ± 0.68 % higher anti-oxidative activity than the wild-type in oxidatively stressed cells.

Conclusions: Our findings suggest that the residues 52-57 in αA-crystallin modulate oligomer size and chaperone activity. The deletion of the conserved 52-57 residues activates αA-crystallin. Further studies are required to understand the molecular basis for the activation of αA-crystallin after deletion of 52-57 sequence.

CONTROL ID: 3712215

SUBMITTER (NAME ONLY): Cissy Xiao

TITLE: Netrin-4 modulates corneal wound healing by enhancing corneal epithelium and nerve regeneration in vitro and in vivo.

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Xiao, D. Lara, Q. Zhou, T.T. Nguyen, M. Rosenblatt, V.H. Guaiquil, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the functional effects of Netrin-4, a known modulator of axon guidance, tumorigenesis, and angiogenesis, on corneal epithelium and nerve regeneration.

Methods: The endogenous expression of Netrin-4 was evaluated by immunofluorescent staining (IFS) in mouse cornea and trigeminal ganglia (TG) and human corneas. The recovery of Netrin-4 expression after corneal epithelium injury was confirmed by IFS and RT-qPCR. In vitro, human corneal limbal epithelial (HCLE) cells and freshly isolated TG neurons were treated with recombinant Netrin-4 in a dose-response manner. HCLE cells were cultured until confluency, and scratch assays were measured with time-lapse microscopy. TG neurons isolated from Thy1-YFP mice (N=3/treatment) were treated with medium only, NGF, or Netrin-4. Neuronal growth and neurite extension were then quantified with Neurolucida software. The in vivo effects of Netrin-4 were tested on mice (N=6/condition) using a corneal epithelial debridement model. Post-injury, mice were treated with topical drops of PBS or Netrin-4. Epithelial healing was evaluated with a slit lamp microscope and analyzed in Fiji. The corneas were flat mounted and stained on day 10 to assess subbasal nerve regeneration. Student’s t-test and ANOVA were used for statistical analyses.

Results: Netrin-4 was highly expressed in the mouse and human corneal epithelium and the neuronal cell bodies of TG. After injury, Netrin-4 was initially downregulated in these tissues and slowly returned to baseline levels of expression. The scratch assays on HCLE cells show that Netrin-4 at 25ng/mL induced significantly faster wound closure than control. Similarly, the in vivo data showed that mice receiving topical Netrin-4 had accelerated wound healing compared to control mice. The average neurite length was greater in isolated TG neurons treated with 25ng/mL Netrin-4 ($p=0.02$) and 50ng/mL NGF ($p<0.0001$) compared to the control. In vivo, the average length of subbasal nerves was greater for mice treated with Netrin-4 than for those treated with vehicle.

Conclusions: Netrin-4 was normally expressed in the corneal epithelium, and after injury, its expression slowly recovered to basal levels. Netrin-4 increased corneal epithelium and nerve regeneration both in vitro and in vivo. Ongoing studies aim to establish the optimal route of administration for Netrin-4 in corneal wound healing.

CONTROL ID: 3712217

SUBMITTER (NAME ONLY): Nishant Sinha

TITLE: mTORC regulation of autophagy in the corneal stroma following chemical injury

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.R. Sinha, Biomedical Sciences, University of Missouri, Columbia, Missouri, UNITED STATES|N.R. Sinha, R. Tripathi, P.K. Balne, S.L. Green, R.R. Mohan, Harry S. Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|R. Tripathi, P.K. Balne, S.L. Green, R.M. Laub, R.R. Mohan, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cornea is susceptible to accidental/intentional chemical injury. Chlorine (Cl_2) exposure to the eye causes corneal damage, redness, tearing, itching, and blurred vision. Autophagy and lysosomal biogenesis play a vital role in corneal homeostasis, repair, and transparency maintenance. This study tested if mTORC1-mediated dysfunctional autophagy and lysosomal biogenesis is associated with Cl_2 induced corneal damage.

Methods: Primary human stromal fibroblast cultures (hCSF) and ex vivo organ culture model using donor human corneas were used. hCSF cultures were exposed to +/- Cl_2 (0.5ppm liberated from 0.001% NaOCl) for 72h (n=6). Thereafter, cultures were fixed in 4% paraformaldehyde and generating protein lysates and mRNA and cDNA. The changes in autophagosomal and lysosomal signature genes (ATGs, LC3, SQSTM1/p62, LAMP1, mTORC1, and TFEB) were measured with qRT-PCR and proteins levels and distribution with western blotting and/or immunofluorescence. Ex vivo human corneas were exposed to 0.5ppm Cl_2 for 30 minutes and incubated for 2 months (n=3). mRNA and protein levels of autophagy markers (LC3, Beclin1, and p62) were analyzed with qRT-PCR, western blotting, and immunofluorescence.

Results: hCSF exposed to Cl_2 had decreased phosphorylated mTORC compared to vehicle. Cl_2 exposure to hCSF significantly increased mRNA and protein levels of LC3 ($p=<0.01$, $p=<0.01$), Beclin1 ($p=<0.01$, $p=<0.01$), and p62 ($p=<0.01$, $p=<0.01$) compared to vehicle. ICC of hCSF exposed to Cl_2 had higher levels of LC3 and Beclin1 with increased levels and accumulation of p62. Further, ICC showed TFEB distribution is greater in cytosol when exposed to Cl_2 compared to vehicle. LAMP1 is decreased in Cl_2 exposed hCSFs. IHC of ex vivo cultures showed increased protein levels of LC3, Beclin1, and p62 after Cl_2 exposure compared to vehicle.

Conclusions: Autophagy mechanism is involved in Cl_2 mediated toxicity to the cornea. Further ongoing studies are expected to offer additional mechanistic information regarding the role of autophagy in corneal injury, repair and homeostasis.

CONTROL ID: 3712218

SUBMITTER (NAME ONLY): Tobin Thuma

TITLE: The Big Warp: Registration of Disparate Retinal Imaging Modalities and an Example Overlay of Ultrawide-Field Photos and en-face OCTA Images

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.B. Thuma, K.B. Gunton, Pediatric Ophthalmology and Strabismus, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J.A. Bogovic, Howard Hughes Medical Institute Janelia Farm Research Campus, Ashburn, Virginia, UNITED STATES|J.S. Pulido, Retina Service and Vickie and Jack Farber Vision Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an algorithm and scripts to combine disparate multimodal imaging modalities and show its use by overlaying en-face optical coherence tomography angiography (OCTA) images and Optos ultra-widefield (UWF) retinal images using the Fiji (ImageJ) plugin BigWarp.

Methods: Optos UWF images and Heidelberg en-face OCTA images were collected from various patients as part of their routine care. En-face OCTA images were generated and ten (10) images at varying retinal depths were exported. The Fiji plugin BigWarp was used to transform the Optos UWF image onto the en-face OCTA image using matching reference points in the retinal vasculature surrounding the macula. The images were then overlayed and stacked to create a series of ten combined Optos UWF and en-face OCTA images of increasing retinal depths. The first algorithm was modified to include two scripts that automatically aligned all the en-face OCTA images.

Results: The Optos UWF image could easily be transformed to the en-face OCTA images using BigWarp with common vessel branch point landmarks in the vasculature. The resulting warped Optos image was then successfully superimposed onto the ten Optos UWF images. The scripts more easily allowed for automatic overlay of the images.

Conclusions: Optos UWF images can be successfully superimposed onto en-face OCTA images using freely available software that has been applied to ocular use. This synthesis of multimodal imaging may increase their potential diagnostic value. Script A is publicly available at https://doi.org/10.6084/m9.figshare.16879591.v1 and Script B is available at https://doi.org/10.6084/m9.figshare.17330048.

CONTROL ID: 3712219

SUBMITTER (NAME ONLY): Gabor Somfai

TITLE: Acute chorioretinal response after intense physical activity in senior sportsmen

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.M. Somfai, Ophthalmology, Stadtspital Triemli, Zurich, Zürich, SWITZERLAND|G.M. Somfai, I. Szalai, A. Csorba, Z. Nagy, Ophthalmology, Semmelweis Egyetem, Budapest, Budapest, HUNGARY|M. Tóth, Institute of Health Sciences and Sports Medicine, Testnevelesi Egyetem, Budapest, HUNGARY|J. Tian, D. Cabrera DeBuc, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Regular physical activity is important in healthy aging and is known to positively influence the retina and visual function. In order to elucidate the effect of physical activity on the retina we assessed the acute chorioretinal changes in senior athletes following short intense physical strain as assessed by optical coherence tomography (OCT).

Methods: Seventeen eyes of 17 healthy senior sportsmen (mean age 67.9 ± 7.4 years, 11 males and 6 females) were recruited for the study conducted at Semmelweis University, Department of Ophthalmology. The subjects performed a stepwise incremental exercise trial until exhaustion (vita maxima) or reaching a peak of maximum physiological age-related systolic blood pressure (calculated as 220/min - age) on a cycle ergometer. Macular scanning with a spectral domain (SD) OCT device was performed before and 1, 5, 15, 30 and 60 minutes following the exercise. The SD-OCT images were exported and segmented by our custom-built OCTRIMA 3D software and the thickness of the choroid and 7 retinal layers was measured. One-way ANOVA analysis was performed followed by Dunnett post hoc test. The level of significance was set at 5%.

Results: A significant thinning of the total retina was observed 1 minute post exercise which was followed by a significant thickening at 5 minutes (-1.56±1.1µm, p=0.000 and +1.05±1.0µm, p=0.012, respectively), with thickness values returning to baseline afterwards. The same significant trend was observed at the composite layer of the outer retina consisting of the outer plexiform and outer nuclear layer and the outer segment (-0.7±0.3µm, p=0.000 and +0.7±0.5µm, p=0.000 for 1 and 5 minutes, respectively). The outer region of the GCL+IPL complex showed also a significant thinning at 1 minute (-0.5±0.4µm, p=0.000). There was neither any significant change in choroidal thickness nor any correlation with the thickness changes of the intraretinal layers.

Conclusions: We could observe acute changes in senior sportsmen after strong physical strain involving the entire macula. These changes seem to be mainly present in the outer retina, independent of the choroidal vasculature. The observed trend is somewhat less pronounced, although seemingly similar to our previous observations in young sportsmen and warrants further research regarding its role in the healthy ageing of the retina.

CONTROL ID: 3712220

SUBMITTER (NAME ONLY): Martin Garcia

TITLE: Insulin in Combination with N-Acetylcysteine Protects Hypoxia Induced Toxicity in 661W Cells

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Garcia, L.L. Valdez, A.T. Tsin, Molecular Science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|

Commercial Relationships Disclosure: Martin Garcia: Commercial Relationship: Code N (No Commercial Relationship) | Laura Valdez: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Tsin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Proliferative diabetic retinopathy (PDR) is the leading cause of blindness among working-age adults. Photoreceptors are the most common and metabolically demanding cells in the retina thus oxygen is vital for retinal function. Hypoxia induced metabolic stress leads to photoreceptor atrophy and retinopathy. Furthermore, photoreceptor cell death is known to occur mainly via apoptosis. However, the protection of hypoxia-induced-cytotoxicity in cone photoreceptor cells has not been investigated extensively. The aim of this study was to determine whether co-treatment of insulin and the N-Acetyl-L-Cysteine (NAC) efficiently protects against hypoxia-induced cytotoxicity in 661W cells.

Methods: 661W were cultured at 5% CO2 at 37 C in DMEM with 10% FBS, 1% a penicillin/streptomycin. Cobalt (II) Chloride hexahydrate ($CoCl_2$) was used to induce hypoxia. Insulin was suspended in sterile water, and NAC was diluted in the culture medium. For recovery experiment, cells were pretreated with $CoCl_2$ for 24hrs, followed by replacing of medium with 100nM insulin and 3mM NAC alone, or with a combination of the two reagents for another 24hrs. Cell viability was determined by MTT assay in a 96 well plate. Morphological changes of the cells were observed and photographed under phase-contrast microscope and protein expression was measured by Western blot analysis. Statistical analysis was undertaken using independent two-tailed Students t-test using SPSS Statistics software.

Results: Treatment with $CoCl_2$ significantly inhibited cell proliferation, reduced the number of viability cells, and induced apoptosis, initiated PARP cleavage, and increased caspase 3 activation. In addition, $CoCl_2$ treatment led to oxidative stress, autophagy, and ubiquitination in the 661W cells. These effects, including cell proliferations were significantly reversed by the combination treatment of Insulin and NAC. In contrast, treatment with Insulin alone did not result in a similar protective effect and NAC partially protects against hypoxia induced toxicity.

Conclusions: Hypoxia induces significant apoptosis, oxidative stress, and protein ubiquitination in 661W cone photoreceptors. A combination treatment of Insulin and NAC completely reversed such hypoxia-induced cytotoxicity. Additional research on a combination therapy employing insulin and NAC may provide a promising therapeutic strategy for hypoxia-mediated cone photoreceptor cell damage.

CONTROL ID: 3712221

SUBMITTER (NAME ONLY): Will Edwards

TITLE: Identifying Neuroprotective Genes in Glaucoma Using Systems Genetics

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Edwards, D. Ashbrook, A.B. Stiemke, R. Williams, M.M. Jablonski, Ophthalmology, The University of Tennessee Health Science Center Department of Ophthalmology Hamilton Eye Institute, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a multifactorial, neurodegenerative disease characterized by the progressive loss of retinal ganglion cells (RGCs), optic nerve (ON) damage, and subsequent vision loss. Current treatments focus on lowering intraocular pressure (IOP); however, it is known that some patients continue to experience RGC death despite adequate IOP reduction. Our study aims to identify genes associated with ON health using systems genetics to provide insight for the development of neuroprotective agents.

Methods: A large cohort of the BXD family were aged to >13 months-of-age. ONs from 75 strains and the DBA/2J (D2) parent were harvested, sectioned, and stained with p-phenylenediamine. Numbers of healthy axons per ON cross-section were counted from 1–10 replicates per stain. Phenotype values were averaged per sex, and data were uploaded to GeneNetwork2 for mapping and systems genetics analyses. The trait was mapped using a linear mixed model utilizing the leave-one-chromosome-out method. Genome-wide significance levels ($P<0.05$) were obtained from 5,000 permutations of the data. Gene-phenotype correlations were performed and considered significant with a Pearson correlation coefficient <0.05.

Results: The number of healthy axons per ON varies 2.1-fold between the extremes and ranges from 30,000 in BXD98 to 62,000 in BXD20. QTL analysis identified a peak on Chr 9 ranging from 94.66Mb to 105.70 Mb with a logarithm of odds score of 4.27. This region of accounted for 424 positional candidate genes, 213 from the eye database and 211 from the retina database. Five candidates—armadillo repeat containing 8 (Armc8); mitochondrial ribosomal protein L3 (Mrpl3); Eph receptor B1 (Ephb1); Propionyl coenzyme A carboxylase, beta peptide (Pccb); nephronophthisis 3 (Nphp3)—passed stringent criteria and are high priority candidates. These genes were significantly correlated with higher numbers of live axons per ON (R^2= 0.38 – 0.46, P= 2.0e-3 – 9.26e-5).

Conclusions: A genomic region linked to ON health was located on Chr 9 in the BXD family of mice. Using stringent selection criteria, we identified 5 novel gene candidates associated with ON health. Further analysis is necessary to understand each candidate’s role as a plausible therapeutic target and would provide insight for development of future neuroprotective glaucoma treatments.

CONTROL ID: 3712223

SUBMITTER (NAME ONLY): Chris Louche

TITLE: Characterizing cellular senescence to prevent retinal ganglion cell loss in glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Louche, P. Manogaran, N. Colé, P. Westenskow, J. Galvao, Ophthalmology I2O, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|C. Louche, Universitat Basel Department Biozentrum, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Cellular senescence has been reported in human glaucoma patients and in a glaucoma mouse model. Mechanisms of senescence in the retina, and cell types implicated in this detrimental phenotype and propagation, remain incompletely understood. We aim to investigate the implication of senescence and identify the cells involved using the experimental model of retinal ischemia-reperfusion (I/R) injury in mice with the goal to prevent retinal degeneration.

Methods: Intraocular pressure (IOP) was increased in mice for 60 minutes by doing intracameral injection of elevated saline solution. In vivo and ex vivo measurements have been performed at different time points, up to 14 days post I/R injury. Visual acuity was evaluated using optokinetic response (OKR) tracking. Structural changes were assessed using optical coherence tomography (OCT). Retinal ganglion cell (RGC) degeneration was quantified on retinal flatmounts by counting BRN3A immunostained positive cells. qPCR on retinal lysates and immunohistochemistry was utilized in order to assess spatiotemporal patterns of senescence. For all analyses, the contralateral eye has been used as control and statistics have been performed using paired t-test.

Results: We observed a visual acuity dysfunction using OKR of the injured eye compared to control (-0.111 cycle/degree, p=0.016, n=4) at day 6. Despite being insignificant, thinning of the inner retinal layer after 14 days was noticed using OCT. RGC degeneration was measured with a loss of 59.24% at day 7 (p=0.018, n=4) and 36.28% at day 14 (p=0.030, n=6). We observed upregulation of senescence related genes in injured retinas compared to control at day 2: Cxcl1, Cdkn2b, Cdkn1a and day 7: Cxcl1, Il-1a. Using immunostaining, senescence markers were detected in injured retinas at day 2: P16INK4A and PAI1 were expressed in microglia and/or macrophages and Y-H2AX in RGCs and photoreceptors.

Conclusions: Evidence of cellular senescence is detectable in the retina following I/R insult. Several retinal cell types appear to be involved. However, what are the specific cell types that express and/or propagate the phenotype remain unclear. Therefore, to elucidate this we are planning to do single cell RNA sequencing to address these questions. In future steps will attempt to rescue the I/R senescent phenotype to improve visual acuity, with an ultimate goal of targeting cellular senescence in glaucoma patients for neuroprotection.

CONTROL ID: 3712226

SUBMITTER (NAME ONLY): Manik Bansal

TITLE: A novel method to determine axon-level IOP-induced insult

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Bansal, F. Zhong, Y. Hua, B. Wang, I. Sigal, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J. Reynaud, B. Fortune, Discoveries in Sight Research Laboratories, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|I. Sigal, Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To introduce an axon-centric approach to determine IOP-induced neural tissue insult in the optic nerve head (ONH).

Methods: Optical coherence tomography (OCT) images of a normal monkey ONH were acquired at IOPs of 10 and 40mmHg (Figure 1). IOP-induced ONH deformations were tracked using digital volume correlation (DVC). The non-collagenous ONH volume incorporating lamina cribrosa (LC) beam and pore details was formed by combining manual reconstructions from OCT images and polarized light microscopy of cryosections. The large blood vessels were later removed from the non-collagenous ONH volume. Axon paths from the retinal nerve fiber layer to the optic nerve were approximated by a custom fluid tracing technique. Experimental deformations were combined with local axon paths to determine the IOP-induced stretch along the axons (longitudinal) and the compression perpendicular to the axons (transverse). The largest longitudinal stretch and transverse compression over the whole axon were assigned as the “worst-case” insults for the axon. For analysis, the axons were grouped into six regions.

Results: The largest longitudinal stretch insult in the temporal region (range 5% to 21%) was 2.5x that in the superior (ST, SN) and nasal (IN, N) regions. The peak value of transverse compression insult in the inferior nasal region (7%) was 16% higher compared to all other regions.

Conclusions: Longitudinal stretch and transverse compression represent distinct mechanisms of potential axon damage. The presented approach has the potential to help identify the link between IOP-induced deformation and neural tissue damage and glaucoma.

CONTROL ID: 3712228

SUBMITTER (NAME ONLY): Alejandra de-la-Torre

TITLE: High prevalence of polyautoimmunity in patients with uveitis: A cross-sectional study

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. de-la-Torre, Immunology Unit, Universidad Del Rosario Escuela de Medicina y Ciencias de la Salud, Bogota, Capital District, COLOMBIA|A. de-la-Torre, W. Rojas-Carabali, C. Cifuentes-González, N.D. Barraquer, D. Polania, L. Boada-Robayo, D. Chacón-Zambrano, M.A. Fonseca-Mora, T. Muñoz, D.L. Cruz-Reyes, Neuroscience Research Group (NEUROS), Universidad Del Rosario Escuela de Medicina y Ciencias de la Salud, Bogota, Capital District, COLOMBIA|

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ABSTRACT BODY:

Purpose: Noninfectious uveitis is highly associated with immune-mediated diseases; however, its association with polyautoimmunity (PolyA) or familial autoimmunity is unknown. Therefore, this study aimed to analyze those phenomena in patients with noninfectious uveitis.

Methods: Cross-sectional study. Means and standard deviations were reported for the quantitative variables and absolute and relative frequencies for qualitative variables. Data were analyzed using hierarchical agglomerative cluster analysis. We first compared the collected variables with the “Index disease” and showed the p-value to find which variables had a statistical relationship to perform the clustering using the Gower coefficient. Then, we performed multivariate analysis and built a multinomial linear regression model. This model had “Index disease” as a dependent variable. The association measure was the β weights obtained. Next, to identify disease co-occurrence patterns to define PolyA spectra in uveitis, the R function “pheatmap” was used; this function allows heat maps to be drawn with the variables most related to PolyA. From the 218 recorded blocks of patients, it produces hard clusters, which were then used to study the co-occurrence of diseases.

Results: We analyzed 218 patients with noninfectious uveitis. Most patients were females (69.3%). The most common clinical characteristics were recurrent course (51.8%), persistent duration (60.6%), and insidious onset (62.4%). Anterior and panuveitis were the most common anatomical locations. Additionally, 36 patients (16.5%) had latent PolyA, and 100 patients (45.9%) had overt PolyA and, of which 22 (10.1%) had Multiple Autoimmune Syndrome. We found 22 index diseases and 28 diseases that coexist grouped in six hard clusters (Fig 1). Patients with PolyA had a mean of 2.3 diseases. One patient had 5 autoimmune diseases together documented. The most common index diseases were Idiopathic uveitis, Autoimmune uveitis, Sjögren’s syndrome, Juvenile idiopathic arthritis, and Ankylosing spondylitis. PolyA was associated statistically with epiretinal membrane (p:0.015) and optic disk edema (p:0.049).

Conclusions: PolyA is a common phenomenon among patients with noninfectious uveitis that can contribute as a risk factor in developing complications.

CONTROL ID: 3712229

SUBMITTER (NAME ONLY): Karina Cantu

TITLE: Role of Caspase-8 on Human Retinal Microvascular Endothelial Cell (HRMEC) Migration in Hyperglycemia

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Cantu, L.L. Valdez, A.T. Tsin, Molecular science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|

Commercial Relationships Disclosure: Karina Cantu: Commercial Relationship: Code N (No Commercial Relationship) | Laura Valdez: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Tsin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pathological angiogenesis is the hallmark of proliferative diabetic retinopathy (DR) at the advanced stage of this ocular disease. In response to prolonged tissue injury, human retinal microvascular endothelial (HRMEC) cells form new blood vessels to ensure the supply of oxygen and nutrients to the eye; however, progressive fibrovascular proliferation can eventually lead to retinal detachment and blindness. Caspase-8, the responsible protease for apoptosis has also been shown to modulate pathological and developmental angiogenesis but whether it exerts this role in a hyperglycemic environment has not yet been explored.

Methods: HRMEC were propagated using Complete Classic Medium with 1% Antibiotic-Antimycotic and 10% FBS. Conditioned medium was harvested from cells seeded into 24 well plates at a density of 800K and stored at -20°. HRMECs were treated with 5.5mM or 30mM of glucose, and the Casp-8 Glo assay was performed 24hrs following treatment. Cells were transfected with siRNA at 80% confluent. With a final concentration of siRNA solution 600pmol, samples were probed with p38 MAPK Antibody and Phospho-p38 MAPK. After transfected cells were confluent, they were starved in 2% FBS DMEM medium overnight. A wound was induced by scratching the cell monolayer with a P200 pipette tip. Cell migration was observed under the light microscope 24hrs after treatment.

Results: After 24 hours of glucose treatment, there were 232.5K viable cells in 5.5mM compared to 119K in 30mM glucose. Additionally, high glucose also increased VEGF secretion after 24hrs of glucose treatment (5.5mM of glucose 16.30pg VEGF/mL, 5.5 mM vs 22.41pg/mL 30mM). Hyperglycemic conditions also resulted in increased Pro-Caspase 8 expression, as the concentration of Pro-Caspase 8 expression from 1.25 fold change at 5.5mM to 2.5 fold (compared to 18S RNA). Western blots showed near-complete blocking of p38 phosphorylation in HRMEC with Caspase 8 KD.

Conclusions: In conclusion, caspase 8 activity was confirmed by Caspase-Glo assay in HRMEC when treated at both 5.5mM and 30mM of glucose, specifically at a luminescence of 1.75 RLU and 1.90 RLU, respectively. In addition, Caspase-8 KD resulted in a significant reduction of protein expression from 2.1-fold change to 1.1 along with an inhibition of cell migration.Taken together, our data strongly suggest that Caspase-8 promotes HRMEC migration via MAPK pathway involving p38 phosphorylation.

CONTROL ID: 3712230

SUBMITTER (NAME ONLY): Chen-Ching Peng

TITLE: Single vesicle analysis of aqueous humor reveals eye specific CD63-dominant subpopulation in pediatric ocular diseases

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Peng, L. Xu, J.L. Berry, The Vision Center, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|D. Im, S. Sirivolu, B. Reiser, L. Xu, J.L. Berry, Roski Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, California, UNITED STATES|P. Neviani, The Extracellular Vesicle Core, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Extracellular vesicles (EV) are detectable in aqueous humor (AH) from adult patients in previous studies. However, the presence of EVs in AH from pediatric diseased eyes has not been explored. Also, the expression profile of tetraspanins (CD9, CD63 and CD81) on AH EVs remains unclear. Herein, we measure the concentration of the pediatric diseased eye-derived AH EVs and analyze their size distribution and determine the phenotypic expression levels of tetraspanins of AH EV at single vesicle resolution.

Methods: Twenty-seven AH samples were obtained from 4 congenital cataract (CAT), 6 congenital glaucoma (GLC), 4 pediatric retinal disease (PRD) and 13 retinoblastoma (Rb) eyes. Rb eyes were further divided into treatment-naïve (Rb_Tn) and treatment-active (Rb_Tx) subgroups. Unprocessed AH samples were subjected to Nanoparticle Tracking Analysis (NTA) (Nanosight NS300) for size distribution and concentration, and to Single Particle-Interferometric Reflectance Imaging Sensor (SP-IRIS) (Exoview R100) for interferometric sizing and fluorescent-based immunophenotyping of EV marker expression (CD63, CD81, and CD9).

Results: By NTA analysis, the concentration of AH EVs is within 3.11×10^{9}~1.38×10^{10} vesicles per mL with a major population in an average modal size of 76.8~103 nm across pediatric disease states. SP-IRIS analysis revealed that tetraspanins, $CD63^{+}$, $CD81^{+}$ and $CD9^{+}$ EVs were detectable across all AH samples using the Exoview R100 platform. In addition, we identified a significant enrichment of CD63 single positive EV subpopulation in AH across 4 disease states (CAT + GLC + PRD + Rb_Tx): 54.9% of mono-$CD63^{+}$ EV among all fluorescent positive EVs. However, a mono-$CD63^{+}$ EV population composed only 28.3% of the AH EV population from Rb_Tn eyes ($P = 0.007$ when compared to 4 other disease states) suggesting a higher population of tumor-derived EVs in these eyes.

Conclusions: Small EVs are readily detectable in unprocessed AH with a dominant mono-$CD63^{+}$ EVs in AH regardless of pediatric eye disease states. Tetraspanin colocalization analysis indicates the clearance of tumor-derived EV heterogeneity by chemotherapy in Rb. This suggests an AH specific role of mono-$CD63^{+}$ EVs. These novel findings uncover a new direction in AH EV biomarker research.

CONTROL ID: 3712231

SUBMITTER (NAME ONLY): Yonju Ha

TITLE: Alterations of retinal pathophysiology following repeated blast injury resulting from reproduced open-field blast environment

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ha, E. Palacios, B. Luo, S. Li, F. Xia, H. Liu, W. Zhang, Ophthalmology, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|W. Zhang, Departments of Neuroscience, Cell Biology & Anatomy, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The number of military soldiers experiencing single or repeated blast injuries has increased with the development of explosive devices. Many of them suffer from visual deficits resulting from blast-induced eye and brain injury. The importance of studying visual deficits has been noticed due to their significant lifelong effects. However, the blast-induced visual deficit mechanism, which helps to diagnose and treat, is not fully understood because of its difficulty mimicking an open-field blast environment. In this study, we evaluated retinal pathophysiology following repeated blast exposure to the eye and brain using a custom-built advanced blast stimulator (ABS) reproducing an open-field blast environment.

Methods: The left side of the eye and head of WT mice (C57BL/6J, 12 weeks old) were exposed to three consecutive air blast shocks with a peak overpressure of 138 KPa using a custom-built ABS, and unexposed age-matched mice served as control. At 3 days after blast injury, the left eyes of blast-exposed and control mice were harvested, and TUNEL assay was performed. At 6 weeks after blast exposure, visual function was examined by visual acuity, pattern-evoked electroretinography (PERG) and positive scotopic threshold response (pSTR), and retinal sections were prepared for immunohistochemistry.

Results: At 3 days after blast injury, increased TUNEL positive cells in the ganglion cell layer were observed in blast-exposured retina. At 6 weeks after blast injury, there were significant reductions of visual acuity, PERG, and pSTR in blast-exposed mice compared to those in control mice, accompanied by a significant reduction of retinal ganglion cells.

Conclusions: Our study demonstrates that repeated blast exposure on the eye and brain results in severe pathophysiological damage in the retina. The blast injury model with ABS mimicking open-field blast is reproducible and may facilitate the study of biomarkers for diagnosis and neuroprotective mechanisms to explore therapeutic targets in sodiers suffering from blast injuries.

CONTROL ID: 3712233
SUBMITTER (NAME ONLY): Shermaine WY Low
TITLE: Decorin may Restore Endothelial Cell Integrity in the Retina
SESSION TITLE: Vascular Biology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Low, M. Beck, B. Mahaling, I. Kassem, D. Costakos, S.S. Chaurasia, Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|S. Low, I. Kassem, D. Costakos, S.S. Chaurasia, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|
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ABSTRACT BODY:

Purpose: The inner blood-retinal barrier (iBRB) mainly comprises of retinal microvascular endothelial cells (RMECs) regulating the transport of molecules such as ions, proteins and water required for the maintenance of retinal homeostasis. Small leucine rich proteoglycans, such as decorin, constitute an integral component of the endothelial cell extracellular matrix (ECM). Since decorin can elicit diverse molecular signals to modulate cell permeability, migration, and survival of RMECs, the present study aims to study the role of decorin in restoring hypoxia-induced damage to the endothelial cell integrity in the retina.

Methods: Human retinal microvascular endothelial cells (HRMECs) were cultured to confluency and subjected to hypoxia +/- 200 nM human recombinant decorin for 24 h. Cells were analysed in real time using xCELLigence system for 7 days. iBRB was evaluated using FITC-dextran permeability and tight junction proteins, including ZO1 by immunohistochemistry and western blotting. Cellular proliferation and scratch wound migration assays were also performed. Cell media was collected to measure the decorin levels using ELISA.

Results: Biochemical and immunoassays characterized the localization and release of decorin by HRMECs. Furthermore, decorin treatment to HRMECs exposed to hypoxia effectively reduced cell permeability and restored tight junction function. Additionally, decorin prevented aberrant endothelial cell proliferation and migration.

Conclusions: Decorin may counteract the hypoxia-induced iBRB disruption in the retinal microvascular endothelial cells, thereby presenting new therapeutic strategies for the management of retinal vascular disorders.

CONTROL ID: 3712234

SUBMITTER (NAME ONLY): Ekaterina Loskutova

TITLE: Lutein, Zeaxanthin, and Meso-Zeaxanthin Supplementation Improves Multisensory Integration in Open-Angle Glaucoma.

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Loskutova, J.S. Butler, G. Lingham, J. Loughman, Centre for Eye Research Ireland (CERI), Technological University Dublin, Dublin, Dublin, IRELAND|A. Setti, School of Applied Psychology, University College Cork, Cork, Cork, IRELAND|C.J. O'Brien, Department of Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: To determine the effect of supplementation with Lutein (L), Zeaxanthin (Z) and Meso-Zeaxanthin (MZ) on multisensory integration (MSI) performance among individuals with open-angle glaucoma (OAG).

Methods: The European Nutrition in Glaucoma Management study (ENIGMA, ClinicalTrials.gov id: NCT04460365) is a placebo-controlled, double-masked randomized trial evaluating the effects of 18 months of carotenoid supplementation in OAG. 62 participants (24 female) with a diagnosis of OAG were enrolled, of whom 42 were randomized to active treatment (10 mg L, 10 mg MZ, 2 mg Z [MacuShield®]), and 20 to placebo. Macular pigment optical density (MPOD) was measured in the study eye using dual-wavelength autofluorescence (Heidelberg Spectralis OCT). MSI was assessed using the sound induced flash illusion (SIFI), where participants indicated the number of visual flashes observed on screen, while simultaneously presented with a congruent or incongruent number of auditory beeps. Participants susceptibility to the SIFI illusion, where individuals misperceive the number of flashes displayed in the incongruent condition, was assessed as an indicator of MSI efficiency.

Results: Mean MPOD increased by 60% in treated participants over the study duration, indicating effective carotenoid tissue deposition. A 2 (treatment: active and placebo) by 2 (time: baseline and 18 months) mixed repeated-measures ANOVA revealed a statistically significant interaction of treatment and time ($F(1,48) = 4.518$, $p = 0.039$) for the incongruent SIFI condition, indicating improved MSI performance following supplementation in those treated with carotenoids, but not placebo.

Conclusions: MSI performance improved significantly in response to supplementation with L, Z and MZ in people with OAG. MSI deficiencies have been reported in older individuals prone to falling, an issue known to affect people living with glaucoma. This finding indicates that MSI performance, a factor potentially linked to daily life issues affecting people with glaucoma such as risk of falls, driving safety concerns and general impact on quality of life, may be improved by supplementation with a mix of L, Z and MZ carotenoids.

CONTROL ID: 3712235

SUBMITTER (NAME ONLY): Thomas Clahsen

TITLE: Tyrosinase reduces expression of vascular endothelial growth factors and improves corneal graft survival

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Clahsen, N. Hatami, C. Cursiefen, Department of Ophthalmology, Uniklinik Koln, Koln, Nordrhein-Westfalen, GERMANY|T. Clahsen, C. Cursiefen, University of Cologne Center for Molecular Medicine Cologne, Cologne, Nordrhein-Westfalen, GERMANY|C. Büttner, A. Reis, Institute of Human Genetics, University Hospital Erlangen, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: Lymphangiogenesis is critically involved in immune responses and corneal graft rejection. Recently tyrosinase has been identified as a novel regulator of developmental and inflammation-induced lymphangiogenesis. However, the underlying mechanisms are still unknown. Here we analyze the influence of tyrosinase on proliferation and expression of vascular growth factors in vitro and in vivo and test whether tyrosinase influences graft survival.

Methods: Proliferation of human dermal lymphatic endothelial cells (HDLEC) with/without tyrosinase was measured by using IncuCyte Zoom. Expression of vascular endothelial growth factors was quantified in HDLECs in vitro and in central cornea in vivo by using qRT-PCR. Balb/c mice were subjected to corneal transplantations and received a 1.5 mm graft from C57B/6 mice or albino C57BL/6 (B6N-Tyr^{cBrd}) mice. Graft survival was determined over 8 weeks and immune cell frequencies in draining lymph nodes were analyzed 3 days and 8 weeks post-transplantation.

Results: Treatment of HDLECs with recombinant tyrosinase inhibited proliferation in a dose-dependent manner. The treatment of HDLECs with recombinant Tyrosinase resulted in a significantly reduced mRNA expression of VEGF-D, VEGF-R2, and -R3 in vitro.

In order to further analyze the influence of tyrosinase on lymphangiogenesis in vivo, the limbal lymph vessel architecture of naive C57BL/6 and B6N-Tyr^{cBrd} mice was compared. B6N-Tyr^{cBrd} mice showed a significant increase in lymph vessel area and a significantly higher number of endpoints and branch points. The quantitative RT-PCR of isolated central corneal RNA showed a significantly higher expression of VEGF-A, -C, VEGF-R2, and -R3 in B6N-Tyr^{cBrd} mice compared to C57BL/6 animals. BALB/c mice receiving grafts from B6N-Tyr^{cBrd} mice showed significantly reduced graft survival compared to animals grafted from C57BL/6 mice. No significant differences in the infiltration of immune cells into draining lymph nodes could be observed between the two groups.

Conclusions: In this study, we identify tyrosinase as a novel regulator for the expression of vascular endothelial growth factors in vitro and in vivo. Furthermore, tyrosinase seems to be a key player in regulating limbal lymphatic vessel architecture and corneal graft survival. A potential mechanism of how tyrosinase is involved in corneal graft rejection is this novel lymphangiogenesis modulating activity.

CONTROL ID: 3712236

SUBMITTER (NAME ONLY): Jose Martinez

TITLE: IRBP in Diabetic retinopathy – Cell Culture & Ophthalmic Pathology Studies

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Martinez, L.L. Valdez, A.T. Tsin, Molecular Science, The University of Texas Rio Grande Valley, Edinburg, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Interphotoreceptor-Retinoid-Binding-Protein (IRBP) is restricted to the subretinal space by the external limiting membrane and RPE zonulae occludens. Its expression is reduced in diabetic retinopathy (DR) and increased expression is protective. Hypoxia decreases viable cone-like photoreceptors (661W) but increased VEGF, suggesting a role of photoreceptors in proliferative DR (PDR) (Rodriguez et al, Arch Clin Exp. Ophthal 3:23,2021). Here, we investigated the effects of high glucose and VEGF on IRBP expression by 661W and rod-like Y79 cells and distribution of IRBP and albumin in human globes with PDR and NPDR.

Methods: 661W and Y79 cells were cultured in DMEM or RPMI respectively with 10% FBS to 80% confluency and passaged to 65,000 cells/well for 24hrs prior to treatment and treated with 5.5mM and 30mM glucose with 10ng/mL of VEGF for 24 hrs. ELISA measured IRBP in the media. The expression of IRBP and albumin in human globes were examined by immunohistochemisry.

Results: During the 24hr treatment period, neither high glucose nor exogenous VEGF changed viable cell number. High glucose decreased of IRBP concentration in the media of 661W after the 24hrs (127+5nM IRBP in 5.5mM versus 69+5nM in 30mM glucose). VEGF also decreased in IRBP in the cell media (28+ 5nM IRBP in 5.5mM versus 0nM in 30mM glucose). Glucose and VEGF did not induce a similar decrease IRBP expression in Y79 cells (133nM in 5.5mM glucose, 133nM in 5.5mM with VEGF, 133nM in 30mM and 133nM in 30mM with VEGF). ANOVA showed significant treatment effects in 661W cells but not in Y79 ($F=0.83$ for 661W and $F=0.41$ for Y79). In control eyes IRBP was prominently expressed within the interphotoreceptor matrix (IPM); IRBP expression was markedly reduced in NPDR and PDR retina. Albumin was not detected in the IPM of control globes but was present in those with PDR.

Conclusions: High glucose and exogenous VEGF decreased IRBP expression in 661W but not Y79 cells. The decreased expression of IRBP in DR globes and entry of albumin into the subretinal space in PDR suggests a breakdown of the blood retinal barrier. Taken together, our data suggests that the mechanisms controlling the expression of IRBP are complex involving decreased IRBP transcription, and changes in the integrity of the junctional complexes normally restricting IRBP to the subretinal space.

CONTROL ID: 3712237

SUBMITTER (NAME ONLY): Vitus André Knecht

TITLE: Modulation of clinical neovascular AMD activity by systemic proteome – an analysis from the BIOMAC study

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Knecht, D. Frentzel, S. Rau, A. Rübsam, S.E. Künzel, S. Wolf, A. Joussen, Z. Oliver, Ophthalmology, Charite Universitatsmedizin Berlin, Berlin, Berlin, GERMANY|F. Dreher, M. Schütte, B. Lange, Alacris Theranostics, Berlin, GERMANY|H. Lehrach, M. Yaspo, Max Planck Institute for Molecular Genetics, Berlin, GERMANY|

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ABSTRACT BODY:

Purpose: To identify candidate systemic proteomic factors which may modulate the choroidal neovascularization (CNV) activity and subsequently determine the need for intravitreal anti-VEGF injections (IAI) in patients with neovascular AMD.

Methods: Cohort study on 46 patients with neovascular AMD, treated with anti-VEGF injections. The cohort was stratified by treatment need. One group (N=25) received regular IAI at intervals of 6 weeks or less, while still having signs of CNV activity (high frequency group – HF). The second stratum (N=21) included subjects with a treatment interval of 10 weeks or longer and having no signs of CNV activity (low frequency group – LF). Full ophthalmological profiling has been done and EDTA blood samples were collected. Proteomic factors were analyzed using Hyper Reaction Monitoring (HRM) mass spectrometry. Welch's two sample t-test was performed on log2-transformed data for statistical analysis. Proteins which were differentially expressed between HF and LF at a ratio of >1.5 and $p<0.05$ were considered as candidate proteins for further analysis.

Results: Both strata were well balanced with regards to age (HF 78.4±8.14; LF 79.7±7.00 years), gender (HF: 40% LF: 61.9% female) and BCVA (HF 61.4±15.7; LF 65.0±12.4). Central retinal thickness differed HF 352.2±98.0 vs. LF 274.8±45.7µm. 1'182 proteins represented by 20'826 peptide ion variants were quantified across all samples. Nine of these met the criteria. Six were up- and three downregulated in HF vs. LF. Up-regulated proteins: complement c1q subcomponent subunit b (C1QB) (95% CI HF 18.69-19.52; LF 18.09-18.66; ratio HF/LF=1,84; p=0.0068), cytosol aminopeptidase (LAP3) (95% CI HF 14.41-15.21; LF 14.16-14.66; ratio HF/LF=1.54; p=0.0318), and insulin-like growth factor-binding protein 3 (IGFBP3) (95% CI HF 13.44-14.90; LF 12.64-13.39; ratio HF/LF=4.1496; p=0.0106). Down-regulated proteins: Acidic leucine-rich nuclear phosphoprotein 32 family member A (ANP32A) (95% CI HF 8.19-12.63; LF 11.33-14.09; ratio HF/LF=0.67; p=0.0482).

Conclusions: Nine protein candidates were identified, which were differentially expressed between HF and LF. Factors with angiogenic potential such as C1QB, LAP3 and IGFBP3 were elevated in the high frequency treatment group, while factors with anti-angiogenic potential were increased in the low-frequency group. The data suggest a potential for systemic modulation of CNV activity.

CONTROL ID: 3712238

SUBMITTER (NAME ONLY): Heavenly Zheng

TITLE: Postoperative Complication Rates by Haptic Fixation Distance From Limbus in Sutureless Intrascleral Intraocular Lens Fixation

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zheng, G. Tsougranis, G. Sanchez, D. Mantopoulos, D.M. Miller, Ophthalmology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, UNITED STATES|

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ABSTRACT BODY:

Purpose: Flanged haptic intrascleral intraocular lens (IOL) fixation, commonly known as the Yamane technique, is a relatively new method of sutureless IOL fixation in patients who lack proper capsular support for traditional posterior chamber IOLs. We examined whether the distance of haptic fixation from the corneal limbus affected clinical outcome with particular attention drawn to the post-operative development of cystoid macular edema (CME), iris chafing, and intraocular inflammation.

Methods: Retrospective cohort study encompassing all patients who underwent secondary IOL placement via Yamane technique at Dartmouth-Hitchcock Medical Center from June 2015 to September 2021 was performed and totalled 60 procedures completed by two ophthalmologists. Data collected included gender, procedure laterality, age, sclerotomy distance (i.e. 2, 2.5, or 3 mm from the limbus), and postoperative incidence of CME, pigment dispersion, and inflammation. Rates of these postoperative complications were assessed by distance from the limbus. Inclusion criteria included (1) minimum follow-up time of two months and (2) no prior history of CME, pigment dispersion, and intraocular inflammation at the time of secondary lens implantation.

Results: Twenty-eight out of the total 60 patients met the inclusion/exclusion criteria and were further examined. The cohort's mean age was 68.1 ± 16.6 years with a mean follow-up time of 9.9 months. Overall, the incidence of postoperative CME, intraocular inflammation, and iris chafing at ≥2 months follow-up time was 29%, 54%, and 18%, respectively. The incidence of CME significantly increased with haptic fixation distance farther from the limbus, with a rate of 0%, 24%, and 66% at 2, 2.5, and 3 mm, respectively ($P = 0.043$). On the other hand, the incidence of both iris chafing ($P = 0.578$) and intraocular inflammation ($P = 0.424$) increased with haptic fixation closer to the limbus; however, these differences were not significant.

Conclusions: Presently, the placement of the haptics during Yamane IOL fixation has largely been a matter of surgeon preference and has ranged from 2 to 3 mm from the limbus. However, the distance from the limbus may hold clinical significance and should be considered given that differing rates of CME, iris chafing, and intraocular inflammation are seen due to these distances.

CONTROL ID: 3712240
SUBMITTER (NAME ONLY): Lindsey Morey
TITLE: Time-Course of Retinal Function during Zebrafish Retinal Regeneration
SESSION TITLE: Retina Development and Regeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Morey, D. Mitchell, D.L. Stenkamp, University of Idaho, Moscow, Idaho, UNITED STATES|P. Meighan, M.D. Varnum, Washington State University, Pullman, Washington, UNITED STATES|
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ABSTRACT BODY:

Purpose: Zebrafish regenerate their retinas following damage, resulting in restoration of function (McGinn et al., 2018 J Neurosci). Behavioral measures of visual function are restored more rapidly following a lesion that destroys inner retinal neurons and spares photoreceptors (PR) and glia (selective lesion; SL), than following a lesion that destroys all retinal neurons and spares only glia (extensive lesion; EL) (Sherpa et al., 2014 Dev Neurobiol). Here we evaluate recovery of visual function through characterization of the electroretinogram (ERG) over time following each type of retinal damage.

Methods: Right eyes of zebrafish (6mo–1.5yrs, both sexes) were lesioned with intravitreal injection of 10μM (EL) or 2μM (SL) ouabain, with left eyes as unlesioned controls. Function of retinal circuitry was analyzed at selected recovery times using ERG recordings in live zebrafish (n=3-13/timepoint). Eyes were then harvested for histological analyses of PKCα+ ON bipolar cells (BP) and parvalbumin (PARV)+ amacrine cell (AC) processes within the deep sublaminae of the inner plexiform layer (IPL), which receive input from ON BPs.

Results: A qualitative study of ERG waveforms focused on the “post-photoreceptor response” (PPR) to assess BP function and PR-BP connectivity, which in a healthy retina is dominated by the b-wave or ON BP response. There was a rapid reduction in amplitude of the PPR after both EL and SL, though the reduction was greater for EL. During early stages of functional recovery after each lesion type, we observed a deviated waveform, consistent with emergence of a d-wave (OFF BP response) elicited at light termination. At later time points (EL: 45 days post-injury (DPI), SL: 21DPI), the PPR amplitude increased and peaked sooner after the light stimulus compared to earlier DPIs, suggesting emergence of the b-wave. Later sampling times (EL: 60-90DPI, SL: 80DPI) continued to show PPRs with reduced amplitude and deviated waveforms, suggesting physiological abnormalities may persist. PKCα+ ON BP terminals and PARV+ AC processes became more reliably positioned within the deep sublaminae of the INL over recovery time after each lesion type.

Conclusions: ERG waveform topography suggests that PR-OFF BP component/connectivity may functionally recover and mature earlier during regeneration compared to the PR-ON BP component. Analysis with cell-specific markers suggests the gradual restoration of ON BP circuitry during regeneration.

CONTROL ID: 3712241

SUBMITTER (NAME ONLY): Kevin Borisiak

TITLE: Automated Image Quality Assessment for Spectralis SD-OCT Scans Utilizing Intrinsic Image Features and ML Confidence Score

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Borisiak, J. Whitney, E. Kanyo, H. Cetin, M. Bonnay, J.M. Bell, S.K. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|K. Borisiak, J. Whitney, E. Kanyo, H. Cetin, M. Bonnay, J.M. Bell, S.K. Srivastava, J. Reese, J.P. Ehlers, Ophthalmology, Tony and Leona Campane Center for Excellence in Image-Guided Surgery & Advanced Imaging, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an automated Random Forest (RF) machine learning model for evaluating Spectralis (Heidelberg) SD-OCT image quality.

Methods: This analysis utilized 52 SD-OCT Spectralis SD-OCT scans for training. Each scan was reviewed by two expert graders on a slice-by-slice basis. Each slice was assigned to one of three quality categories (Good, Moderate, Poor), with Good being defined as an image with no quality defects, Moderate being a gradable image with noticeable quality defects, and poor being an ungradable image. Following initial assessment, 4 additional limited quality scans were introduced to provide greater representation of “Poor” quality slice examples. Image features including intensity mean, median, variance, skew, kurtosis, and homogeneity were extracted. In addition to these features, a set of machine learning layer segmentation confidence scores were included in the feature vector for each image.
The computed features were used to train a series of random forest classifiers. To assess the impact of class imbalance on feature training, excess good and moderate scans were filtered from the training folds until a desired class balance (2:2:1) was achieved. Mean AUC scores for each class were computed via One vs. Rest binarization and micro-averaging over 10 independent runs of 5-fold cross validation.

Results: Following initial training, micro-averaged AUC scores of 0.90 ± 0.03, 0.85 ± 0.05, and 0.82 ± 0.12 for Good, Moderate, and Poor, respectively were achieved. Using the expanded dataset with increased representation of poor quality scans, the performance of the classifier on was improved (Good: 0.91 ± 0.06, Moderate: 0.82 ± 0.07, Poor: 0.90 ± 0.06). Class balancing the training sets via a filtering algorithm and including machine learning confidence scores resulted in similar but slightly improved mean AUC metrics (Good: 0.93 ± 0.03, Moderate: 0.84 ± .07, Bad: 0.90 ± 0.05) with more balanced confusion matrices.

Conclusions: The random forest model enabled reliable automated classification of “Good” and “Poor” quality Spectralis OCT images with minimal cross-over between these two classes. This tool has the potential to act as an image quality-gating system by providing rapid feedback during clinical trial image acquisition and advanced image analysis programs.

CONTROL ID: 3712242

SUBMITTER (NAME ONLY): Monica Pagliara

TITLE: An ultrasound image-based radiomic model to assess regression of uveal melanomas after brachytherapy treatment .

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Tagliaferri, B. Fionda, L. Boldrini, V. Valentini, Radiotherapy Oncology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Lazio, ITALY|M.M. Pagliara, C. Caputo, M. Blasi, Ocular Oncology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Lazio, ITALY|F. Boselli, Ophthalmology Unit, Universita Cattolica del Sacro Cuore, Rome, Lazio, ITALY|

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ABSTRACT BODY:

Purpose: Tumor regression of uveal melanomas (UM) after radiotherapy has been confirmed as a strong prognostic factor for metastatis. The main and most commonly used diagnostic tool to control uveal melanoma response to brachytherapy treatment is A/B scan ultrasound. Changes in tumor height and internal reflectivity are the main outcomes for monitoring uveal melanoma regression after brachytherapy. Radiomics represents an innovative way of high throughput extraction of quantitative information from medical images to describe the heterogeneity of the lesions such as tumors.The purpose of this study was to determinate possible variations in the texture of the ultrasound imagines that could be correlated with the different pattern of regression of uveal melanoma after Ruthenium-106 or Iodine-125 plaque brachytherapy.

Methods: The dataset involved 50 eyes of 50 patients that underwent Ruthenium-106 or Iodine 125 plaque brachytherapy for uveal melanoma at the Ocular Oncology Unit of “Fondazione Policlinico Gemelli” in Rome. Each eye was classified in one of two regression pattern :“favourable” (progressive decrease in height and increase in internal reflectivity after brachytherapy) and “unfavourable” (stability or increase in size after brachytherapy and stable internal reflectivity). For the analysis, we selected and compared the same transversal and longitudinal ultrasound scans with greater tumor thickness at baseline, after 1 year and 3 years from treatment. The scans were performed by the same operator, with years of experience in the acquisition of ultrasound images for oncological purposes. These standardized images were put into a texture analysis program (Aliza) where a hand drawn region of interest (ROI) was created around whole tumor margins or in subregions of it. Furthermore, the ROI was analyzed both for semantic and agnostic features, such as intensity, shape, size or volume.

Results: Using features extracted from US images a deep learning-based model for the evaluation of pattern of regression of uveal melanoma after brachytherapy treatment was created An area under ROC curve (AUC) was generated to calculate sensitivity, specificity and accuracy of the model.

Conclusions: Deep learning-based radiomics analysis can be applied to quantify regression after brachytherapy treatment for uveal melanoma and can represent a decision support for retreatment and its timing.

CONTROL ID: 3712243

SUBMITTER (NAME ONLY): Kathleen Heng

TITLE: BDNF and cAMP promote retinal ganglion cell survival and function in a porcine model of traumatic optic neuropathy

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Neurotrophic factors play a key role in neuroprotection and regeneration of retinal ganglion cells (RGCs) as shown in rodent models of optic neuropathies. However, advancement towards clinical application has been limited by lack of data from large animal models. Here we tested the hypothesis that brain-derived neurotrophic factor (BDNF) and 8-(4-chlorophenylthio) (CPT)-cAMP together promote RGC survival in a porcine model of traumatic optic neuropathy.

Methods: Optic nerve crush (ONC) was surgically performed in Yucatan minipigs (5.5-6 months old) under general anesthesia. The contralateral optic nerves served as uncrushed controls. At the end of surgery, BDNF and CPT-cAMP (or 0.9% NaCl for vehicle control) were intravitreally injected into both eyes. Fundus exams, intraocular pressure measurements, and flash visual evoked potential (fVEP) recordings were performed prior to and 2 and 4 weeks after ONC. At week 3, eyes were injected with cholera toxin B subunit (CTB) to anterogradely label RGC axons in the optic nerve. At week 4, eyes and optic nerves were harvested and fixed. Retinas were dissected and immunostained for RBPMS (RGC marker), mounted, imaged by confocal microscopy, and quantified for RGC survival. Optic nerves were cryosectioned, imaged by fluorescent microscopy, and analyzed for RGC axon survival and regeneration.

Results: Fundus exam revealed edema of optic nerve head in the crushed eye and bilateral vascular attenuation after unilateral ONC. No change was observed in intraocular pressure. fVEP after ONC exhibited lower peak amplitude compared to uncrushed controls, and BDNF plus CPT-cAMP-treated eyes had decreased variation in peak latency compared to vehicle control. RBPMS immunofluorescence revealed increased RGC survival in retinal flatmounts treated with BDNF plus CPT-cAMP, and increased axon survival was observed in optic nerve sections from treated animals.

Conclusions: BDNF and CPT-cAMP treatment resulted in improved functional and histological outcomes for RGCs in a large animal injury model. This combination of neurotrophic factors has therapeutic potential for neuroprotection after optic nerve injury.

CONTROL ID: 3712245

SUBMITTER (NAME ONLY): Greta Chiaravalli

TITLE: The role of oxygen in the photoactivation of organic retinal protheses

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In 2020 the injection of Poly(3-hexylthiophene-2,5-diyl) (P3HT) nanoparticles (NPs) in retinitis pigmentosa model rats has proved to treat degenerative blindness (Maya-Vetencourt et al. 2020). Despite the effectiveness of this approach, the working principles are still matter of debate and any experimental investigation has not led to a conclusive interpretation. In this work we address the theoretical study of the interaction among the P3HT-NPs, the retinal electrolytic environment and a neuron membrane, aiming at highlighting the main working principles of such a complex system

Methods: The model takes into account 3 main blocks, shown in Fig.1: (1) model of photoactivation and transport phenomena in the bulk of NP (2) study of redox and capacitive phenomena at the NP-retinal oxygenated electrolyte interface, where superoxide O_2^- anion is produced;(3) model of neuron interaction with the NP-modified electrolytic environment. The description is performed through the Drift-Diffusion and Poisson-Nernst-Planck equations. Model calibration has been performed through electrochemical experiments of P3HT in oxygenated environment.

Results: Fig.2 shows neuron depolarization(left) and superoxide concentration c_{O2-}(right) as a function of oxygen partial pressure (Panel A) for two values of cleft thickness(10 and 100 nm) and as a function of the cleft thickness(Panel B). Predicted curve behaviors indicate that neuron depolarization and c_{O2-} production are strongly coupled mechanisms: as O_2^- is formed, it accumulates in the cleft region, inducing a significant neuron depolarization which may trigger action potential firing. As the cleft increases(Panel b), the superoxide is able to redistribute and the depolarization decreases

Conclusions: The proposed theoretical model has been used as a virtual laboratory to investigate biophysical mechanisms which are hardly accessible with experiments. Model predictions seem to suggest a correlation between the presence of superoxide ion and retinal neuron depolarization and highlight the crucial role played by the molecular oxygen and by the cleft size, thus helping shed light on the controversial working principles of the retinal prosthesis

CONTROL ID: 3712246

SUBMITTER (NAME ONLY): Sara Beqiri

TITLE: Qualitative comparison of AutoML explainability tools with bespoke saliency methods

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Google Cloud Platform (GCP) empowers clinicians to explore Artificial Intelligence (AI) via its code-free user interface. This, however, is associated with a low level of transparency and control over algorithm design. As a solution, the GCP Explainable AI features can produce saliency heatmaps with minimal coding, highlighting regions of model interest to guide clinician's understanding.

We present a qualitative evaluation of these explanations through a user survey, comparing them to the same saliency technique produced from a bespoke model.

Methods: We trained two algorithms for the binary classification of referrable vs non-referrable Diabetic Retinopathy (DR), using the same 60,133 fundus images from publicly available datasets. The AutoML and bespoke models reached accuracies of 93.7%, and 96.5% respectively, sufficient for our purposes of saliency map assessment.

12 test images were selected to represent varying degrees of AutoML prediction confidence. For each image, an XRAI saliency map was produced for both the AutoML and bespoke algorithms. The prior involved minimal coding, whereas the latter required a fully coded Jupyter notebook.

These maps were provided to a consultant ophthalmologist with 20 years of experience, who answered a survey of three specified questions per image, via a 5-point Likert scale. These focused on the map's localisation ability, clarity of information, and overall quality.

Results: Paired t-tests showed no statistically significant difference between the AutoML and bespoke map scores (3.25±0.75 vs 3.58±0.51) when comparing quality, however localisation ability and clarity of information were significantly higher for the bespoke model (2.75±1.14 vs 3.92±0.51, and 2.67±1.07 vs 3.83±0.58). A combined score for the three questions also showed a significant difference with a mean of 11.3±2.9 for bespoke and 8.67±1.44 for AutoML.

Conclusions: Our results showed that utilising the same saliency method and dataset in two different models can lead to significantly differing maps. Our qualitative evaluation depicted superiority of bespoke saliency maps in localisation and clarity when compared to the AutoML explainability tools.

CONTROL ID: 3712248

SUBMITTER (NAME ONLY): Chintan Patel

TITLE: A 6-Month GLP Toxicology Study of a Novel Hydrogel-based, Axitinib Intravitreal Implant (OTX-TKI) in Non-Human Primates

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Patel, E. Kahn, M. Priem, J. Iacona, A. Vanslette, E. Wong, C.D. Blizzard, P.K. Jarrett, M. Goldstein, R. Gurses-Ozden, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neovascular retinal diseases may be responsive to tyrosine kinase inhibitors (TKIs) which have a broader anti-angiogenic profile than anti-vascular endothelial growth factor agents alone. OTX-TKI is a novel, hydrogel-based, biodegradable, intravitreal implant designed to deliver the TKI axitinib for up to 6-9 months for the treatment of neovascular retinal diseases. The purpose was to evaluate the toxicology profile of OTX-TKI for 6 months in non-human primates (NHP).

Methods: Six cynomolgus monkeys were injected intravitreally with an OTX-TKI 700 µg implant in the right eye and saline in the left eye (control). Experimental dose represents a human equivalent dose of 1400 µg axitinib and 2.3x ocular dose safety margin when normalized to the vitreous volume between human and monkey. Ophthalmic exams with slit lamp biomicroscopy, intraocular pressure (IOP), optical coherence tomography (OCT) and confocal scanning laser ophthalmoscopy (cSLO) images were collected throughout the 6-month study period.

Results: Aqueous cell and flare, and vitreous cell and haze were graded a score of 0 at all timepoints through 6-months in all OTX-TKI and control eyes. No abnormalities were observed by ophthalmic exams. No clinically significant differences in IOP were observed between OTX-TKI and control eyes through 6-months. OCT imaging showed no clinically significant changes. Implants appeared idle and fully visible in the inferior vitreous up to 5-months. At Month 6, cSLO images showed implants in a majority of animals (4/6) had completely degraded and the implants in the remaining two animals were beginning to degrade.

Conclusions: OTX-TKI was generally well-tolerated with a favorable safety profile following administration in NHPs. No signs of intraocular inflammation or clinically significant changes in IOP and OCT images were observed. The safety and efficacy of OTX-TKI 600 µg intravitreal implant is currently being evaluated in humans for the treatment of wet age-related macular degeneration in a U.S.-based Phase 1b study.

CONTROL ID: 3712249

SUBMITTER (NAME ONLY): Khaldon Abbas

TITLE: Visual and safety outcomes of iris-claw Artisan intraocular lens implantation at a large Canadian setting

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Abbas, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|S. Qazi, B. Al-Qahtani, S. Sabeti, K. Baig, Precision Cornea Centre, Ottawa, Ontario, CANADA|B. Al-Qahtani, S. Sabeti, K. Baig, Department of Ophthalmology, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The iris-claw Artisan is an iris-fixated intraocular lens (IOL) used to correct aphakia in eyes without adequate capsular support. Limited long term follow-up data on efficacy and safety is available in Canada. In this study, we evaluate long term visual outcomes and complications following implantation of this secondary IOL.

Methods: This is a retrospective chart review including data of patients that underwent implantation of the Artisan IOL at a tertiary Canadian centre between January 2013 and December 2021. Clinical outcomes were assessed at standard of care post-operative follow-up visits at 1 day, 1 week, 1 month, and 3 months. Key outcomes assessed include uncorrected distance visual acuity (UCDVA), best corrected distance visual acuity (BCDVA), and complications.

Results: A total of 51 eyes from 47 patients were evaluated (49.0% male, 51.0% female). Mean patient age was 68 years (range 27-96). Retropupillary fixation was performed in 50 eyes and prepupillary fixation in 1 eye. Mean follow-up duration was 12 months (range 1-63 months). The most common indications for Artisan implantation were IOL dislocation (n=33; 64.7%), followed by aphakia (n=11; 21.6%), and IOL subluxation (n=7; 13.7%). The underlying causes to the above indications were surgical complications (n=13, 25.5%), pseudoexfoliation (n=8, 15.7%), trauma (n=3, 5.9%), and Marfan syndrome (n=2; 3.9%). Zonular weakness was regarded as the cause in 25 eyes (49.0%) with no other pertinent ocular history. The average LogMAR of the UCDVA prior to implantation and at 3-month follow-up was 1.053 (range; -0.1 to 2.8) and 0.413 (range; 0 to 2.3), respectively, and BCDVA was 0.658 (range: 0 to 2.3) and 0.602 (range: -0.02 to 2.8), respectively. Intraocular pressure increased from an average of 15.6 mmHg to 17.5 mmHg at 3-month follow-up. Visual acuity improved in 37 eyes (72.6%), remained the same in 4 eyes (7.8%), and decreased in 10 eyes (19.6%) after surgery. The most common complication at 3-month follow-up was pupil ovalization (n=8, 15.7%), followed by iris atrophy (n=3, 5.9%). Other complications included cystoid macular edema (n=1), cornea decompensation (n=1), and hyphema (n=1).

Conclusions: This is the largest study of patients that have undergone Artisan implantation in Canada. Iris-claw Artisan IOL is an effective and safe option for implantation in eyes without sufficient capsular support.

CONTROL ID: 3712250

SUBMITTER (NAME ONLY): Sangwan Park

TITLE: Single cell-RNA sequencing analysis of corneal endothelial cells in TAZ deficient mice

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Park, B.C. Leonard, M. Ferneding, S.M. Le, M. Ardon, C.J. Murphy, S.M. Thomasy, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California Davis, Davis, California, UNITED STATES|C.J. Murphy, S.M. Thomasy, Department of Ophthalmology & Vision Science, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|V. Raghunathan, The Ocular Surface Institute, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|V. Raghunathan, Department of Biomedical Engineering, Cullen College of Engineering, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mice deficient in Wwtr1, the gene that encodes transcriptional co-activator with PDZ-binding motif (TAZ), have a softer Descemet's membrane and decreased corneal endothelial cell (CEnC) density. To explore the underlying pathophysiology in TAZ deficient mice, single cell-RNA sequencing (scRNA-seq) was performed in wildtype (WT) and homozygous TAZ ($Wwtr1^{-/-}$) and heterozygous TAZ deficient ($Wwtr1^{+/-}$) mice at 2, 6, and 11 months of age.

Methods: Six corneas from 3 mice were pooled together and single cell suspensions were prepared for each genotype and age group. Cell suspensions were submitted for 10X Chromium Single Cell 3' library preparation and HiSeq 4000 sequencing. scRNA-seq analysis was carried out with Seurat using R. A cluster of CEnC was identified based upon the expression pattern of known marker genes for CEnC. Differential gene expression analysis was performed within the CEnC cluster to investigate the transcriptomic alterations between ages and genotypes. Differentially expressed (DE) genes were defined as genes with adjusted P-values < 0.05. Gene ontology (GO) term enrichment analysis was performed using ShinyGO v0.741; a false discovery rate (FDR) < 0.05 was applied.

Results: scRNA-seq revealed the presence of 13 cell clusters; cluster 11 showed higher expression of known marker genes (Col4a2, Col8a2, and Cdh2) for murine CEnCs. Within cluster 11, broader gene expression changes were observed between 2 and 11 months old $Wwtr1^{-/-}$ mice than between WT and $Wwtr1^{-/-}$ mice at the same age. GO analysis revealed (1) enrichment of ribosomal subunit assembly in 2-month-old $Wwtr1^{-/-}$ mice versus age-matched WT mice and (2) depletion of glycolysis and ribonucleotide metabolism in late endosome in 11-month-old $Wwtr1^{-/-}$ mice versus 2-month-old $Wwtr1^{-/-}$ mice. 11-month-old $Wwtr1^{-/-}$ mice had significantly higher expression of Plekhf1 gene versus age-matched WT and $Wwtr1^{+/-}$ mice, which is responsible for autophagosome transport and fusion with late endosomes.

Conclusions: Transcriptomics demonstrated that homozygous TAZ deficiency is associated with excessive autophagy in CEnCs. These results provide insights into the importance of TAZ signaling in the autophagy related degeneration of CEnCs.

CONTROL ID: 3712251

SUBMITTER (NAME ONLY): Amit Narawane

TITLE: Automated visualization of Henle's fiber layer and outer nuclear layer in retinal volumes using robotically-aligned optical coherence tomography

SESSION TITLE: New perspectives in technology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Narawane, P. Ortiz, M. Draelos, A.N. Kuo, J.A. Izatt, Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|R.P. McNabb, A.N. Kuo, J.A. Izatt, Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Standard optical coherence tomography (OCT) retinal imaging methods do not clearly distinguish outer nuclear layer (ONL) from Henle's fiber layer (HFL). HFL can be visually distinguished from ONL by de-centering the OCT beam pupil entry position, but this process requires operator skill and involves manual adjustment for every B-scan. Robotically-aligned OCT (RAOCT) automatically optimizes the pupil entry position per B-scan to acquire retinal volumes that offer complete radial visualization of HFL.

Methods: We mounted a custom swept-source OCT (1060nm) system on a collaborative robot with face and pupil tracking cameras (Fig. 1B) to enable real-time pupil tracking of imaging subjects. As seen in Figure 1A, a 2D fast steering mirror (FSM) conjugate to the retinal image plane modifies the pupil entry position of the OCT beam. Our custom software acquired retinal OCT volumes with radial B-scans and automatically adjusted the pupil entry position for each B-scan in an optimal path to visualize the HFL (Fig. 1C). With these B-scans, we reconstructed full retinal volumes that include HFL data throughout. We acquired such retinal volumes from consented subjects under an IRB-approved protocol.

Results: Figure 2 shows B-scans from retinal volumes acquired with and without the automated pupil entry adjustment. Fig. 2A shows a B-scan from a standard volume taken through the pupil center, and Fig. 2D shows a B-scan from the reconstructed volume, combining data from the B-scans in Fig. 2B and 2C. Arrows indicate areas of increased contrast due to reflectance from HFL.

Conclusions: We developed a technique for automated volumetric HFL visualization using a pupil entry adjusting RAOCT system. With this method, retinal volumes that distinguish HFL and ONL can be readily acquired, allowing for the investigation of ONL measurements as potential biomarkers in leading ophthalmic diseases.

CONTROL ID: 3712252

SUBMITTER (NAME ONLY): Ling Zhu

TITLE: Metallothionein is activated specifically in Müller cells in response to retinal stress

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zhu, T. Zhang, S. Zeng, Y. Chen, S. Lee, M. Yam, F. Zhou, X. Fan, M.C. Gillies, The University of Sydney, Sydney, New South Wales, AUSTRALIA|K. Jin, X. Fan, Zhejiang University, Hangzhou, Zhejiang, CHINA|Y. Chen, Sichuan University West China Hospital, Chengdu, Sichuan, CHINA|

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ABSTRACT BODY:

Purpose: Metallothionein 1 (MT1) is a metal transporter and antioxidative protein that is essential in maintaining cellular physiological and redox balance. While the oxidative stress-related neuroprotective effect of the MT1 in central nervous system disorders has been investigated, the role of MT1 in the retina is still not clear.

Methods: Macular explants and peripheral retinal explants from four human donors were exposed to intense light stress (32k lux, left eye) or dim light (5 lux, right eye of the same donor). We first used single-cell RNA sequencing technology to compare the different transcription profiles of different types of retinal cells in the human macula and peripheral retina in response to photic stress. We identified one of the top differentially expressed genes, MT1, expressed more in the peripheral-dominant Müller cells in response to stress than the Müller cells that dominate the macula. We explored further the expression pattern of MT1 in the macula and temporal mid-periphery. We stained the MT1 protein together with the Müller cell-specific marker, cellular retinaldehyde–binding protein (CRALBP). We also assessed the topographic protein expression of MT1 in retinal punches (2mm diameter) from the macula, including the fovea, to the periphery by Western blot. The changes of MT1 expression in Müller cells in response to retinal stress was explored further in a mouse model of subretinal neovascularization, the JR5558 mouse. To understand the protective roles of MT1 in Müller cells, we used siRNA to knock down the MT1 in human primary Müller cells in vitro and evaluate their response to photic stress. The viability of huPMCs with or without knockdown under photic stress was assessed by an AlamarBlue viability assay and LDH cell toxicity assay.

Results: The MT1 protein was specifically expressed in Müller cells and expressed more in the peripheral retina than the macula. The peripheral Müller cells upregulated their MT1 transcription levels in response to stress much more than the macular Müller cells. MT1 expression was also activated in the JR5558 mouse. MT1 knockdown in vitro significantly reduced the viability and increased cell cytotoxicity of human primary Müller cells under stress.

Conclusions: Increased levels of MT1 in Müller cells may protect the peripheral retina and help explain why the macula is more prone to develop certain degenerative conditions than the peripheral retina.

CONTROL ID: 3712255

SUBMITTER (NAME ONLY): Noha Sherif

TITLE: Evaluating a Deep Learning-based Algorithm for Automatic Segmentation of Geographic Atrophy on Fundus Autofluorescence Images

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.A. Sherif, T. de silva, T.D. Keenan, E.Y. Chew, C. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accurate and automated segmentation of geographic atrophy (GA) assists in disease detection, clinical decision-making, and clinical trial enrollment. In this study, we apply a deep learning approach to segment GA on fundus autofluorescence (FAF) images, assess algorithm accuracy, and identify GA features influencing algorithm performance.

Methods: A deep learning-based semantic segmentation model using DeepLabv3+ architecture was developed to automatically segment GA area on FAF images. The model was trained on 296 FAF images (163 eyes, multiple visits) from Age-Related Eye Disease Study 2 (AREDS2) with manually segmented GA areas. The performance was first validated on 47 FAF images after independently defining ground truth and subsquently on 620 FAF images (197 eyes, multiple visits) after manual verification of algorithm output. In both test sets, algorithm segmentation was compared to manual segmentation to quantify the accuracy of pixel area overlap, absolute percent error (PE), and area difference (AD). Algorithm performance was also evaluated on different GA features: configuration (e.g. horseshoe, ring, central solid); GA at center of macula, GA proximity to fovea, and variations in autofluorescence (AF).

Results: Evaluation of 47 test images exhibited GA pixel overlap accuracy = 0.94 and intersection over union = 0.86. Further validation in 620 test images indicated a mean PE of 9.56% (stdev=38.0%). A total of 414 images (66.8%) required no correction and 470 (69.1%) images demonstrated PE of ≤5%. Only 60 (8.8%) images had PE ≥25%. Bland-Altman comparison of the contours revealed bias of 0.26 mm^2 with 95% limits of agreement (-9.81, 10.32 mm^2). Segmentation error was highest in the presence of: decreased AF at the center of the macula (PE 48.41%, AD 2.79mm^2), decreased AF with halo of increased AF (PE 48.57%, AD -4.18mm^2), and area of decreased AF within the grid (PE 39.74%, AD 2.02mm^2). Segmentation error was lowest in solid GA with central involvement (PE 0.02%, AD -0.00mm^2). However, no statistical significance was observed in area differences amongst any GA features.

Conclusions: Deep learning models can reliably and accurately segment GA on FAF images. Although decreased AF near the fovea and decreased AF within the grid confounded the algorithm in some cases, it did not show any significantly diminished accuracy for different features analyzed.

CONTROL ID: 3712257

SUBMITTER (NAME ONLY): Donato Colantuono

TITLE: Secondary Sutureless Posterior Chamber Lens Implantation with Two Specifically Designed IOLs: Iris Claw Lens versus Sutureless Trans-Scleral Plugs Fixated Lens- Results of a 1 year follow-up

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Colantuono, D. Seknazi, A. Glacet, F. Amoroso, A. Miere, E. Souied, Universite Paris-Est Creteil Val de Marne, Creteil, Île-de-France, FRANCE|D. Colantuono, D. Seknazi, A. Glacet, F. Amoroso, A. Miere, E. Souied, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The management of patients with aphakia and/or lack of capsular support remains debated. The sutureless posterior chamber IOL (PCIOL) fixation is a very useful surgical option. The purpose of the study was to compare the one-year outcomes as well as post-operative best corrected visual acuity, refractive errors and complications of two different techniques of sutureless PCIOL secondary implantation.

Methods: Patients who underwent secondary implantation from December 2019 to January 2022 in the Department of Ophthalmology of Creteil Hospital were retrospectively included. Eyes implanted with the iris claw lens (Artisan Aphakia IOL model 205, Ophtec BV, Groningen, The Netherlands) were included in group 1, and eyes implanted with a newly developed sutureless trans-scleral plugs fixated lens (STSPFL, Carlevale lens, Soleko, Pontecorvo, Italy) were included in group 2.

Results: Twenty-five eyes of 25 patients were enrolled in group 1, and twenty eyes of 20 patients in group 2. No difference was found in visual acuity between two groups (0.38 +/- 0.24 logmar for group 1 and 0.26 +/- 0.54 logmar for group 2) ($p = 0.18$) at mean post-operative follow up (12.19 +/- 3.44 months for group 1 and 12.42 +/- 3.96 months for group 2) ($p = 0.13$). Both the mean refractive error (MRE) and induced astigmatism (IA) were greater in group 1 compared to group 2, respectively: the MRE was 0.99 +/- 0.57 vs. 0.46 +/- 0.36 ($p < 0.01$), and IA was 1.72 +/- 0.96 vs. 0.72 +/- 0.52 ($p < 0.01$). The most common complications in group 2 were conjunctival erosion (10%) and breakage of the plugs (10%).

Conclusions: No significant differences in terms of the recovery of visual acuity were found between the two groups. Group 2 (STPFL) gives better results in our sample due to less post-operative induced astigmatism and less refractive error.

CONTROL ID: 3712258

SUBMITTER (NAME ONLY): Afnan Mohammed K. Aladdad

TITLE: Retinal ganglion cells maintain survival and physiological properties when isolated using low-pressure FACS

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Aladdad, K. McLoughlin, A. Payne, A. Boda, K.E. Kador, Ophthalmology, University of Missouri Kansas City, Kansas City, Missouri, UNITED STATES|K. McLoughlin, Wellcome Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The culture of purified retinal ganglion cell (RGC) cultures has been a vital tool in the study of glaucoma and neural regeneration. Traditionally, RGCs are isolated from early postnatal animals using a two-step immunopanning (IP) technique, a procedure limited to RGCs of a specific maturity. This study aimed to develop a method using a low-pressure cell sorting protocol that will allow for the sorting of RGCs and their subtypes using optogenetic markers while maintaining the RGCs survival and electrophysiological properties, which can be affected using traditional fluorescence associated cell sorting (FACS).

Methods: Using a combined IP-FACS protocol that initially depletes macrophage and photoreceptors using IP before enriching for RGCs using low-pressure FACS against Thy-1 expression. RGC viability was compared against a two-step IP using a live/dead analysis. Cell phenotype was compared using immunohistochemistry for RBPMS and β-III-Tubulin, while properties such as axon outgrowth and neurite branching were also measured. Further, RT-qPCR was carried out to verify the purity of isolated cells. Functionality was compared using calcium imaging to determine isolated RGC response to both potassium chloride (KCl) and glutamate.

Results: RGCs purified by the IP-FACS method remained viable with no evident cytotoxicity and similarly extended their neurites to those purified by the IP method. RGCs isolated from both methods showed similar expression of RGC-specific proteins and similar gene expression levels. IP and IP-FACS methods resulted in no significant difference ($p > 0.05$) in a total number of neurites of 2.14 ± 0.3 and 2.47 ± 0.5, longest neurite length of 1098.14 ± 205.5 µm and 1184.15 ± 111.3 µm, total neurite length of 1765.5 ±367.7 µm and 2117.6 ± 23.3 µm and the average neurite length of 890.9 ± 148.9 µm and 882.2 ± 157.1 µm, respectively. Calcium imaging revealed that both populations respond to KCl and glutamate stimuli, confirming that cells are functional to standard calcium stimulus.

Conclusions: Our results showed that low-pressure FACS can isolate RGCs from rodents with comparable viability, phenotype, and function compared to the traditional method of immunopanning. This method opens the possibility of isolating embryonic RGCs or subtype populations by combining FACS isolation with optogenetically labeled transgenic rodents.

CONTROL ID: 3712259

SUBMITTER (NAME ONLY): Oswaldo Esteban Durán Carrasco

TITLE: Retinal sensitivity measured by photopic and scotopic microperimetry in type 1 diabetics without retinopathy, and its correlation with the thickness of the ganglion cell complex.

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Durán Carrasco, C. Fernández-Núñez, N. Pérez-Llombet Quintana, I. Fabelo Hidalgo, G. Quezada-Peralta, R. Abreu, Ophthalmology, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|I. Llorente-Gómez de Segura, Endocrinology, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|O. Durán Carrasco, I. Llorente-Gómez de Segura, R. Abreu, Universidad de La Laguna, La Laguna, Islas Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: DM1 is a growing pathology whose management is still under development. The age of diagnosis is usually between 10 and 14 years old, so early diagnosis is very important; We propose microperimetry (MP) as a part of this process and its correlation with the structure of the ganglion cell complex (GCC) evaluated by optical coherence tomography (OCT).

Methods: A descriptive, cross-sectional and comparative study was carried out in type 1 diabetic patients without signs of diabetic retinopathy (DR). Structural OCT was performed using a 9 mm macular cube with the Nidek RS 3000 Advanced 2 equipment (Nidek, Gamagori, Japan) and retinal sensitivity (RS) values were obtained by micropermitry in 13 specifically located points in scotopic and photopic mode using the Nidek MP3s (Nidek, Gamagori, Japan). Finally, the statistical analysis was carried out using SPSS version 25 (IBM, Armonk, NY, USA).

Results: 148 eyes of 75 subjects were analyzed, 36 diabetic patients without diabetic retinopathy and 39 healthy volunteers, the photopic mean retinal sensitivity (MRS) in the diabetic group was 30.5 +/- 1.98 dB, lower than the mean in the healthy group (31.12 +/- 1.27 dB, p = 0.05). In scotopic mode, MRS was lower (14.53 +/- 1.21 dB) than the mean of the control group (14.64 +/- 1.45 dB), however, they were not statistically significant (p = 0.063). Correlation between retinal sensitivity (RS), and GCC thickness has been found both in diabetics (0.279; p = 0.022) as well as in the control group (0.238; p = 0.007), however, it has not been seen that the group of diabetics present a significant decrease in the GCC thickness compared to the healthy group.

Conclusions: The average photopic MRS of diabetic patients is 30.68 +/- 1.92 dB, lower than the MRS in healthy volunteers with similar characteristics. Despite showing correlation between RS and GCC thickness in both groups; it has not been significantly lower in patients with DM1 without diabetic retinopathy signs, compared to healthy population.

CONTROL ID: 3712262

SUBMITTER (NAME ONLY): Caitlin Wuebbolt

TITLE: Reactive oxygen species (ROS) and adenosine triphosphate (ATP) levels in human corneal endothelial cells under ambient and physiologic oxygen conditions

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wuebbolt, S. Kilcullen, B. Calle Gonzalez, S.P. Patel, Ophthalmology, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|S.P. Patel, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The goal of our lab is to understand the pathophysiology of Fuchs endothelial corneal dystrophy (FECD) and why it is more common in women than men. Damage from ROS and decreased ATP production are prominent in FECD pathophysiology. The purpose of this study was to characterize the role of chronic hyperoxic stress (room air + 5% CO_2, $[O_2]_A$) vs. physiologic oxygen conditions (2.5% O_2 + 5% CO_2, balance N_2, $[O_2]_{2.5}$; environmental chamber, Billups-Rothenberg, Inc., Del Mar, CA) and estradiol (E2) on ROS and ATP levels in human corneal endothelial cells (HCEnCs). We hypothesized that $[O_2]_{2.5}$ would have lower ROS and higher ATP than $[O_2]_A$ and E2 would restore physiologic ROS and ATP levels under $[O_2]_A$.

Methods: Primary HCEnC cultures were prepared at $[O_2]_A$ and $[O_2]_{2.5}$. Cells were grown in growth medium until confluence and then matured for 7-10 days in minimal medium with 10 nM E2 in half of the cell samples. Cell lysates were analyzed for ROS levels (Cell Biolabs In Vitro ROS/RNS Assay, San Diego, CA) compared to an H_2O_2 standard curve and normalized to total protein concentration. ATP levels in cell lysates were measured with a luminescent ATP detection kit (Abcam, Cambridge, MA). Mean data were compared using ANOVA. Significant differences were explored with Tukey post hoc test with significance at $p<0.05$.

Results: There were no significant differences in ROS levels amongst O_2 and E2 conditions (p=0.53), and no differences were observed when data were analyzed separately for male (p=0.42) and female (p=0.40) donors (Table). E2 also had no effect on ATP levels. However, ATP levels were significantly different by O_2 condition (p= 0.01). ATP was significantly higher for cells at $[O_2]_{2.5}$−E2 than $[O_2]_A$−E2 (p=0.02). When data were stratified by sex, male HCEnCs had no significant differences in ATP levels in any condition (p=0.77), but female HCEnCs had significantly higher ATP levels at $[O_2]_{2.5}$−E2 than at $[O_2]_A$−E2 (p=0.01) (Table).

Conclusions: Our data show that O_2 and E2 do not regulate ROS in HCEnCs, but O_2 does affect ATP levels in a sex-specific manner. Alterations in HCEnC energetics may contribute to the pathophysiology of the sex difference in the prevalence of FECD.

CONTROL ID: 3712263

SUBMITTER (NAME ONLY): Harry Matundan

TITLE: The role of CD80 and HSV-1 ICP22 interaction on HSV-1 pathogenicity and latency-reactivation in infected mice

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Matundan, U. Jaggi, H. Ghiasi, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously we have shown that CD80 and not CD86 is suppressed in the corneas of mice ocularly infected with wild type (WT) HSV-1. This suppression of CD80 was mediated by binding of HSV-1 ICP22 to CD80 promoter. In addition, we found that ocular infection of mice with a recombinant HSV-1 expressing CD80 virus exacerbated eye disease in infected mice. In the current study, we investigated if any specific region of ICP22 is involved with the suppression of CD80 by using recombinant viruses lacking ICP22 gene or lacking ICP22 binding site to CD80 promoter.

Methods: BALB/c mice were scarified and ocularly infected with $2x10^5$ pfu/eye of a recombinant virus lacking ICP22 (D22) or lacking CD80 binding region (KOS-ICP22Δ40). Parental avirulent HSV-1 strain KOS (WT) was used as a control. Viral replication in the eye, corneal scarring, latency-reactivation, and exhaustion markers were determined in infected mice. Flow cytometry analysis was done to evaluate the expression of immune infiltrates into the cornea. CD80 promoter activity was monitored by luciferase assays after infection.

Results: Luciferase analysis of D22 and KOS-ICP22Δ40 infected cells compared with WT virus shown that ICP22 is involved in down-regulation of CD80 promoter in vivo and in vitro. At a functional level, both D22 and KOS-ICP22Δ40 viruses enhanced levels of effector CD8 T cell population and affected infiltrates in cornea of infected mice in a time-dependent fashion compared to WT virus. Suppression of CD80 in DCs was blocked in the absence of ICP22. The absence of ICP22 binding to CD80 promoter using both D22 and KOS-ICP22Δ40 viruses increased eye disease but latency and reactivation were not affected compared with WT virus.

Conclusions: Our results suggest that inhibiting the binding of HSV-1 ICP22 to CD80 promoter leads to increased HSV-1 pathogenicity. This is of particular interest, because it indicates that the absence of ICP22 leads to increased CD80 and CD8 expression in the eye of infected mice resulting in more eye disease. Thus, our data signifies that HSV-1 uses CD80 suppression by ICP22 as a mechanism of immune escape in order to protect the host from increased pathology.

CONTROL ID: 3712264

SUBMITTER (NAME ONLY): Ike Ahmed

TITLE: Preclinical evaluation of RTC-1119, a surface eroding intracameral implant composed entirely of a latanoprost acid prodrug, for long-term intraocular pressure control

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Battiston, S. Taghavi, H. Fischer, E. Baldwin, M. Statham, J. Day, A. Daley, I. Parrag, W. Naimark, Ripple Therapeutics, Ontario, CANADA|B. Muirhead, E. Hicks, J.J. Tian, H. Sheardown, Department of Chemical Engineering, McMaster University, Hamilton, Ontario, CANADA|I. Ahmed, Department of Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|I. Ahmed, Department of Ophthalmology, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|

Commercial Relationships Disclosure: Ike Ahmed: Commercial Relationship(s);Code C (Consultant/Contractor):Ripple Therapeutics;Code C (Consultant/Contractor):Aequus;Code C (Consultant/Contractor):Aerie;Code C (Consultant/Contractor):Akorn;Code R (Recipient):Alcon;Code R (Recipient):Allergan;Code C (Consultant/Contractor):Aquea Health, Inc;Code C (Consultant/Contractor):ArcScan | Kyle Battiston: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Shadi Taghavi: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Hans Fischer: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Emily Baldwin: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Matthew Statham: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Jonathan Day: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Adam Daley: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Ben Muirhead: Commercial Relationship: Code N (No Commercial Relationship) | Emily Anne Hicks: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Tian: Commercial Relationship: Code N (No Commercial Relationship) | Heather Sheardown: Commercial Relationship: Code N (No Commercial Relationship) | Ian Parrag: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics | Wendy Naimark: Commercial Relationship(s);Code E (Employment):Ripple Therapeutics

ABSTRACT BODY:

Purpose: Sustained release implants composed entirely from novel prodrugs have the potential to improve the safety and compliance of ophthalmic medications. The prodrug implants are non-swelling, exhibit surface erosion-based drug release, and avoid polymer-associated pro-inflammatory degradation products. The purpose of this work was to evaluate the preclinical ocular safety and pharmacokinetics of a prostaglandin prodrug intracameral implant (RTC-1119 IC implant) with >6 mo sustained release of latanoprost acid for primary open angle glaucoma and ocular hypertension.

Methods: RTC-1119 IC Implants were prepared by extrusion of RTC-1119, a prodrug of latanoprost acid, without the inclusion of a polymer carrier. Tolerability and surface erosion of RTC-1119 IC Implants was evaluated following IC administration in New Zealand white rabbits (4 rabbits, 7 eyes) for a duration of 7.5 months. Implants were visualized by gonioscopy. Safety was assessed through ocular exams, anterior segment optical coherence tomography, and histopathology. Quantification of latanoprost acid in aqueous humor and iris-ciliary body was assessed by liquid chromatography-mass spectrometry (Days 7, 28).

Results: The RTC-1119 IC Implant was well tolerated, with ocular exams indicating no adverse findings. No change in corneal thickness or implant associated inflammation was observed. Gonioscopy showed implants becoming smaller in diameter over time, supporting the surface erosion mechanism of drug release, and completely biodegrade without leaving behind any remnants due to the absence of a carrier system (Figure 1). Consistent levels of latanoprost acid were observed in the aqueous humor and iris-ciliary body at Day 7 and Day 28 (Figure 2).

Conclusions: The present study indicates that the RTC-1119 IC Implant is well tolerated in the rabbit eye, where it undergoes surface erosion to provide controlled release of latanoprost acid. Gonioscopic visualization of implants indicate that duration of drug release is >6 mo. Ongoing work is evaluating the IOP lowering effect of the RTC-1119 IC Implant in a canine model. This data supports the further development of the RTC-1119 IC Implant towards first-in-human clinical trials.

CONTROL ID: 3712265

SUBMITTER (NAME ONLY): Emmanuel Agu

TITLE: The Impact of COVID-19 on Periocular Non-Melanoma Skin Cancer in the Veteran Population

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mosenia, J.A. Lifton, L. Chan, K.G. Ligtenberg, R. Vagefi, S.R. Grob, R. Kersten, M. Ahmad, B. Winn, Department of Opthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|E.U. Agu, A. Mosenia, School of Medicine, University of California San Francisco, San Francisco, California, UNITED STATES|D. Saylor, Department of Dermatology, University of California San Francisco, San Francisco, California, UNITED STATES|E.U. Agu, J.A. Lifton, L. Chan, R. Vagefi, S.R. Grob, M. Ahmad, B. Winn, Department of Opthalmology, San Francisco VA Health Care System, San Francisco, California, UNITED STATES|D. Saylor, Department of Dermatolgy, San Francisco VA Health Care System, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite an increasing incidence of skin cancer over the last decade, studies have reported a decline in the diagnosis and treatment of skin cancer during the COVID-19 pandemic. We performed a retrospective cohort study using a large population-based cohort from the Veterans Health Administration (VHA) to determine how the pandemic has affected tumor size and morbidity in veterans with periocular non-melanoma skin cancer.

Methods: Electronic health records from all VHA sites were accessed through the VA Informatics and Computing Infrastructure (VINCI). Data were stored in the Observational Medical Outcomes Partnership (OMOP) model and queried via SQL Server. ICD-10 and current procedural terminology codes were used to identify patients who received Mohs surgery for periocular basal cell carcinoma (BCC) or squamous cell carcinoma (SCC) between 08/01/2018 and 09/10/2021. A combination of structured algorithms and manual review were used to extract patient demographics, lesion characteristics, and surgical outcome at three time points, ie. pre-COVID, early, and late COVID. Unpaired t-tests were used to assess statistical significance.

Results: Patient characteristics were similar between pre- and post-COVID cohorts in terms of gender, age, race, and tumor type. The average number of Mohs periocular surgeries performed per week were 23.1% (7.31 vs 5.62) and 13.1% (7.49 vs 6.51) lower in the early and later pandemic, respectively, compared to similar pre-COVID timeframes by month (Figure 1). Mean lesion size (maximum diameter) was 1.35 cm larger post-COVID compared to pre-COVID (95% CI 0.19 2.51, P=0.022); however, the defect size remained similar (Figure 2). Stratifying by tumor type, the same trends were noted in BCC, particularly early in the pandemic. However, mean SCC lesion and defect sizes did not vary over time.

Conclusions: Periocular Mohs surgery rates declined in the COVID pandemic across VHA. Lesions were larger particularly in the earlier phase of the pandemic for BCC. Future analyses using this cohort will attempt to determine if telehealth and travel time were associated with distinct outcomes.

CONTROL ID: 3712267

SUBMITTER (NAME ONLY): Elizabeth McCarthy

TITLE: The Impact of Hyperglycemia on Cognitive Function and Vision

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. McCarthy, Biology, American University, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Elizabeth McCarthy: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Type II diabetes (modeled in this research with hyperglycemia) has been shown to cause cognitive deficits and lead to retinopathy. Here, we looked at adult zebrafish to see if breakdowns in the blood-brain barrier and the blood-retinal barrier would be correlated with dysfunction on vision- and/or memory-guided behavioral assays. We hypothesized that our glucose-treated fish would have increased inflammatory markers (Rel-A) and decreased tight junction protein (Claudin-5) in the brain and retina, and that these markers would be consistent with glucose-treated fish having inferior performance on vision- and memory-guided assays.

Methods: To test our hypothesis, we maintained three groups of fish (roughly 10 per group), water-treated (stress control), mannitol-treated (osmotic control) and glucose-treated, in hyperglycemic conditions (or control) for 8 or 12 weeks while we collecting behavioral data. Every four weeks, fish were run through a three-chamber choice task (3CC) to assess cognition and, at the end of exposure, visually guided optomotor responses (OMR) were assessed and tissue samples were collected to determine changes in brain and retinal protein levels.

Results: At 8 weeks, no significant changes to memory were observed in glucose-treated fish. At 12 weeks, glucose-treated fish had significantly improved memory relative to water-treated fish ($p < 0.001$), though they were not significantly different from mannitol-treated fish. OMRs at 8 weeks revealed that glucose-treated fish performed better than both mannitol- ($p = 0.0166$) and water-treated fish ($p = 0.0394$). At 12 weeks, significantly more glucose-treated fish displayed positive OMRs compared to mannitol-treated controls ($p = 0.0166$). Preliminary molecular results show increased Rel-A and decreased Claudin-5 in both the brain and the retina of glucose-treated fish at both time points.

Conclusions: These results suggest that hyperglycemia-induced deficits in vision and cognition are controlled by different pathways; one involving osmotically-induced alterations and the other initiated by glucose specific mechanisms. Overall, hyperglycemia induced inflammation and decreased tight junction proteins seemed to be correlated with better performance on vision and memory guided behavioral assays.

CONTROL ID: 3712268

SUBMITTER (NAME ONLY): Andrew Bower

TITLE: Characterization of fluorescently labeled photoreceptors observed in carriers of choroideremia using multimodal adaptive optics imaging

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.J. Bower, N. Aguilera, S. Abouassali, T. Liu, J. Li, R. Lu, J. Giannini, R.N. Fariss, B.P. Brooks, W.M. Zein, L. Huryn, J. Tam, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|M. Smelkinson, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, UNITED STATES|A. Dubra, Department of Ophthalmology, Stanford University, Stanford, California, UNITED STATES|Z. Liu, D. Hammer, Center for Devices and Radiological Health, U.S. Food and Drug Administration, Silver Spring, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize patches of fluorescently labeled cone photoreceptors detected in female carriers of choroideremia (CHM) following intravenous injection of indocyanine green (ICG) dye using adaptive optics (AO) imaging (PMID:33796365).

Methods: Patches of fluorescently labeled photoreceptors (>50 cones) were identified using AO-ICG following multimodal AO imaging in 11 eyes from 6 carriers of CHM. Co-registered non-confocal split detection AO images were used to evaluate whether fluorescent patterns corresponded to cone photoreceptors, and outer retinal length (ORL) measurements were performed in AO-OCT volumes. For comparative purposes, histology of the outer retina from mice was obtained using custom-modified microscopes. Murine photoreceptors and retinal pigment epithelial (RPE) cells were assessed following both systemic injection of ICG as well as ex vivo incubation with ICG.

Results: In mice after systemic injection with ICG, RPE cells were labeled with ICG (PMID:27564519) but there was no observable ICG fluorescence in the photoreceptor layer. Photoreceptors were however readily labeled when detached from the RPE and incubated with ICG ex vivo, suggesting that the outer blood-retinal barrier function of the RPE prevents labeling of photoreceptors during normal physiologic conditions. In carriers, in addition to the ICG fluorescence pattern observed in the RPE mosaic, patches of ICG-labeled cone photoreceptors were also observed (23 distinct patches identified across 10 eyes). The excellent correspondence between fluorescently labeled photoreceptors visualized using AO-ICG and simultaneously acquired split detection images confirmed that these were indeed cones. There were no apparent differences in spacing, density, or ORL measurements of cones within these patches.

Conclusions: The discovery of ICG-labeled cone photoreceptors in patients, together with mouse histology data, suggests that there are focal disruptions to the outer blood-retinal barrier in carriers of CHM. These photoreceptors appear to be structurally normal and may be associated with interspersed enlarged RPE cells seen in CHM (IOVS 2021; 62:1900). These results demonstrate a possible novel application of AO-ICG as a functional assay for assessing the integrity of the outer blood-retinal barrier function of the RPE.

CONTROL ID: 3712269

SUBMITTER (NAME ONLY): Megan Vaughan

TITLE: Structural and functional assessment of photoreceptors in healthy individuals

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Vaughan, N. Tay, T. Kane, A. Kalitzeos, N. Singh, A. Zheng, M. Michaelides, E.J. Patterson, University College London, London, London, UNITED KINGDOM|M.H. Vaughan, T. Kane, A. Kalitzeos, N. Singh, A. Zheng, M. Michaelides, E.J. Patterson, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|M.R. Carmona, J.L. Barbur, City University of London, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Megan Vaughan: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Tay: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Kane: Commercial Relationship: Code N (No Commercial Relationship) | Angelos Kalitzeos: Commercial Relationship: Code N (No Commercial Relationship) | Navjit Singh: Commercial Relationship: Code N (No Commercial Relationship) | Adrian Zheng: Commercial Relationship: Code N (No Commercial Relationship) | Marisa Carmona: Commercial Relationship: Code N (No Commercial Relationship) | John Barbur: Commercial Relationship: Code N (No Commercial Relationship) | Michel Michaelides: Commercial Relationship: Code N (No Commercial Relationship) | Emily Patterson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Establishing the relationship between photoreceptors and visual function in the normal population is crucial for understanding the effects of progression and/or treatment of retinal disease. By using highly sensitive measures of photoreceptor structure and function, we aim to determine if there is a correlation between cone density, rod/cone function, and color vision in a group of healthy individuals.

Methods: Monocular data from ten healthy individuals were examined (6M, 4F, mean age: 29 years, range: 24-36 years). Functional assessment was carried out using Advanced Vision & Optometric Tests (AVOT), and included rapid flicker sensitivity, measured with cone- and rod-enhanced stimuli (at the fovea and in 4 quadrants located at 5 degrees eccentricity), as well as colour vision, measured using the Colour Assessment and Diagnosis (CAD) test. The CAD test yielded both red-green (RG) and yellow-blue (YB) chromatic discrimination thresholds. Photoreceptor structure was assessed using nonconfocal split-detection Adaptive Optics Scanning Light Ophthalmoscopy (AOSLO). Cone density was measured at 0.5, 1 and 5 degrees along the temporal meridian, using 55 x 55 μm regions of interests (ROIs). Three ROIs at each location were quantified twice by two independent graders.

Results: Measurements fell within the normal range for all AVOT and AOSLO assessments (Table 1). Agreement between cone density measurements of the two graders was excellent (intraclass correlation coefficient = 0.988, 95% confidence interval = 0.980-0.993). There were no statistically significant correlations between central cone density (0.5 or 1 degree) and either CAD or foveal cone-mediated thresholds (Pearson, $p > 0.05$). Nor were there any significant correlations between cone density at 5 degrees and peripheral rod- or cone-mediated thresholds (in the upper and lower temporal quadrants) (Pearson, $p > 0.05$).

Conclusions: Despite their current use as outcome measures in clinical trials for gene therapy, this is the first time the CAD, rod- and cone-mediated flicker tests and AOSLO have been validated against each other. Our data suggest that, in healthy individuals, natural variation in cone density does not have a significant effect on visual function.

CONTROL ID: 3712270

SUBMITTER (NAME ONLY): Marianna Weener

TITLE: Novel USH2A gene mutations and USH phenocopies described as a part of prospective Russian Usher syndrome clinical trial

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Weener, T.G. Markova, Research and Development, Oftalmic LLC, Moscow, RUSSIAN FEDERATION|T.A. Avanesova, Ophthalmology, Central Clinical Hospital under President Affairs, Moscow, RUSSIAN FEDERATION|V.A. Shibanova, Russian patient organization "LookToSee", Moscow, RUSSIAN FEDERATION|T.G. Markova, FGBU Rossijskij naucno-kliniceskij centr audiologii i sluhoprotezirovania Federal'nogo mediko-biologiceskogo agentstva Rossii, Moskva, Moskva, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: Usher syndrome (USH) is a rare genetic autosomal recessive (AR) disorder characterized by sensorineural hearing loss and retinitis pigmentosa. We performed prospective observational natural history clinical trial to clarify genotype-phenotype correlation of Usher syndrome patients in Russia for possible further treatment application

Methods: 118 syndromic RP patients with hearing loss of AR and sporadic inheritance were included under NCT03901391 and NCT03319524 protocols. Complete ophthalmic and audiology examinations were conducted in all the study subjects. DNA samples were extracted from patients' peripheral blood for whole exome sequencing (WES) analysis. Sanger sequencing was conducted for validating the identified mutations and cosegregation pattern in the families, MLPA was done for deletions borders clarification.

Results: USH patient group data is in Table 1. USH1 patients with biallelic mutations in MYO7A (14 cases), USH1C (1 case), CDH23 (2 cases), PCDH15 (2 cases) and CIB2 (1 case). USH2 patients with biallelic mutations in USH2A (71 cases), 15 of them are newly reported mutations in USH2A gene and are provided in Table 2. 7 patients had W3955X USH2A mutation – 3 homozygous and 4 – in compound heterozygous state with another confirmed pathogenic mutation, which are considered to be of founder effect from eastern Europe, one of the patients had deletion of 38 exon of USH2A c.7121-?_7303+? del, mutations in GPR98 (1 case), DFNB31 (2 cases). In 6 patients biallelic CLRN1 gene mutations were confirmed of USH3 group, 3 of those patients have known ancestors from Baltic region including Finland. Partially solved cases included USH2A: 1 heterozygous mutation, no second mutation found (3 cases), POC1B (1 case), EYS (1 case) – two compound heterozygous mutations, PRGR hemizygous mutation – but no genetic causes of hearing loss is found in these cases. GJB2 hearing loss genetically confirmed, but no genetic causes of vision loss found (3 cases). There were USH phenotype patients with confirmed another genetic disease: NIPBL (Cornelia de Lange syndrome 1), LOXHD1 (Deafness, autosomal recessive 77), PRGR (X-linked retinitis pigmentosa), PEX6 (Zellweger spectrum disorder). No any mutations found in 4 USH patients.

Conclusions: This study clarified main genetic causes of Usher syndrome and its phenocopies in Russian patients, 15 novel variants in USH2A gene were identified.

CONTROL ID: 3712271

SUBMITTER (NAME ONLY): George Thurston

TITLE: Analysis of kinetics of protonation pattern exchange for the eye lens protein, bovine gammaB crystallin

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Thurston, Physics, Rochester Institute of Technology College of Science, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: George Thurston: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To model the rapidity with which surface charge and consequent local near-surface voltage patterns change on a phase-separating globular protein, and to compare mean times for pattern change with characteristic times for translational diffusion to a neighboring protein, and for rotational diffusion to substantially different orientations in solution.

Methods: Our published, calibrated grand-canonical partition function model for the equilibrium charge regulation of bovine gammaB-crystallin indicates that to account for 95% of the coexisting charging patterns, approximately 400 distinct surface charge patterns are needed. Because of detailed balancing at equilibrium, such a model also gives ratios of rate constants describing protonation and deprotonation of each of the charged sites. We combine these ratios with existing literature data on typical rate constants for each type of titratable amino acid side chain and chain termini. By doing so we estimate individual rate constants for the rapidity of transitions between charging patterns connected by single protonation or deprotonation steps.

Results: The typical transition times between charging patterns range in general from microseconds to milliseconds, and in concentrated solutions can be orders of magnitude longer than typical times for translational diffusion to a neighboring protein (a few nanoseconds to microseconds), or for rotational diffusion through an angle of one radian, which is typically about 10 nanoseconds for this protein.

Conclusions: The implication of this kinetic model is that individual protein molecules that have a given charging pattern encounter many other protein molecules before their surface voltage patterns have a high likelihood of substantially changing. Because of this relative slowness of surface charge pattern changes, accurate modeling of the degree to which individual types of pairs are in close proximity, as well as how both direct energetic and hydrodynamic interactions affect their close-range mutual motion, can thus be accomplished, to a first approximation, by considering each such surface charge pattern pair independently.

CONTROL ID: 3712274

SUBMITTER (NAME ONLY): Birthe Dorgau

TITLE: Spatial transcriptomics of human pluripotent stem cell derived retinal organoids offers new insight in retinal development

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Dorgau, J. Collin, R. Queen, A. Rozanska, M. Lako, Bioscience Institute, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|

Commercial Relationships Disclosure: Birthe Dorgau: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Collin: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Queen: Commercial Relationship: Code N (No Commercial Relationship) | Agata Rozanska: Commercial Relationship: Code N (No Commercial Relationship) | Majlinda Lako: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although scRNA-Seq enables identification of distinct and changing cell populations during retinal development, the spatial resolution of those cell populations is missing. Spatial transcriptomics (ST) enables the visualisation and quantitative analysis of the transcriptome in spatial location, providing a novel tool for detailed studies of human retinal development. In this study ST is used for the first time on pluripotent stem cell derived retinal organoids to examine the spatial resolution of retinal cell-types during development.

Methods: Retinal organoids were cultured until day 210 of differentiation and collected at day 10, 20, 35, 45, 60, 90, 150 and 210 for ST and scRNA-Seq. experiments. ST experiments were performed using the 10xVisium Spatial Gene Expression Kit (10x Genomics). For this purpose, retinal organoids were fresh frozen and stored at -80°C. Cryosections of each sample were collected on individual 10xVisium Gene Expression slides and processed according to manufacturer's protocol. Whole transcriptome libraries were sequenced, analysed, and visualized using Space Ranger and Spaniel R package. For scRNA-Seq. retinal organoids were dissociated followed by cell capture and library generation using the Chromium Single Cell 3′ Library & Gel Bead Kit (10x Genomics). Uniform manifold approximation and projection plots were used to visualise the clusters.

Results: Early retinal organoids (day10) were dominated by a cell cluster expressing eye-field marker genes whereas later stages (day20/35) showed several progenitor cell clusters including retinal progenitor cells. Additionally, ocular surface epithelium and lens/cornea cells were found at these stages. Retinal ganglion cells appeared at day 35 and were detected throughout differentiation. Mid stages of retinal development revealed photoreceptor precursor expression at day 90, which matured to rods and cones in late developmental stages (day150/210), where also a bipolar cell cluster was evident. The comparison of ST and scRNA-Seq. data indicated comparable cluster distribution in development.

Conclusions: ST provides a powerful tool to investigate the spatial resolution changes within a tissue during development, demonstrating here for the first time on human retinal organoids. Thus, ST offers significant insights in normal retinal developmental and/or disease pathological mechanisms.

CONTROL ID: 3712281

SUBMITTER (NAME ONLY): Augustine Bannerman

TITLE: Creating a Mentorship, Research, and Virtual Shadowing Program for Underrepresented Minority Undergraduates During COVID-19

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bannerman, E.S. Lu, D. Bryant, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A. Bannerman, E.S. Lu, J.B. Miller, Retina Service, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|D. Bryant, Harvard University Faculty of Arts and Sciences, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Augustine Bannerman: Commercial Relationship: Code N (No Commercial Relationship) | Edward Lu: Commercial Relationship: Code N (No Commercial Relationship) | Douglass Bryant: Commercial Relationship: Code N (No Commercial Relationship) | John Miller: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon ;Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Genentech;Code C (Consultant/Contractor):Sunovion;Code C (Consultant/Contractor):Zeiss

ABSTRACT BODY:

Purpose: To offer early ophthalmology exposure to underrepresented minority (URM) premedical undergraduate students through clinical, research, and mentorship opportunities in an effort to increase URM trainees in the ophthalmology pipeline.

Methods: An ophthalmology mentorship program for URM undergraduate students was launched in the spring 2021 semester and continued through the fall 2021 semester. The program offered clinical experience through virtual shadowing sessions, research opportunities, and mentorship for applying to medical school and supporting career development. Twenty-two undergraduate students (including 13 returning students from the first session) were paired with 13 mentors composed of medical students, residents, and post-doctoral fellows. As part of the Virtual Shadowing Series, 8 ophthalmology faculty hosted 1-hour sessions during which they presented patient cases and surgical videos and shared their career paths.

Results: In a survey, respondents reported increased interest in ophthalmology (17/19, 90%), medicine (15/19, 83%), and research (13/19, 68%). Students attended an average of 3.5 (median 3) of the 8 virtual shadowing sessions offered. All respondents met with their mentor or attended a virtual shadowing session at least once, and all respondents indicated an interest in continuing to participate in the program. In addition to virtual shadowing, 3 students shadowed in the operating room for a half day, observing vitreoretinal surgery through a heads-up 3D surgery platform.

Conclusions: A program offering mentorship, research opportunities, and virtual shadowing experiences for URM undergraduate students increased interest in ophthalmology, medicine, and research for the majority of students, and may serve as a model for other institutions.

CONTROL ID: 3712285

SUBMITTER (NAME ONLY): Ameenat Lola Solebo

TITLE: Perceptions and experiences of health care service use during the pandemic for children with uveitis: UNICORNS-C19 study

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Solebo, S. Kellett, J. Rahi, R. Knowles, University College London Institute of Child Health Population Policy and Practice Research and Teaching Department, London, UNITED KINGDOM|A.D. Dick, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|V. Tadic, Greenwich University, UNITED KINGDOM|

Commercial Relationships Disclosure: Ameenat Lola Solebo: Commercial Relationship: Code N (No Commercial Relationship) | Salomey Kellett: Commercial Relationship: Code N (No Commercial Relationship) | Jugnoo Rahi: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Dick: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Knowles: Commercial Relationship: Code N (No Commercial Relationship) | Valerija Tadic: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: COVID-19 has disrupted provision of and access to healthcare. Children newly diagnosed with uveitis are particularly vulnerable to these disruptions. We aimed to describe the impact of the pandemic on the experiences and perceptions of care use for families of children newly diagnosed with uveitis.

Methods: UNICORNS-C19 is a cross-sectional study embedded within the Uveitis in Childhood National Prospective Cohort Study (UNICORNS), which is recruiting UK children with non-infectious uveitis in order to understand the sociodemographic, clinical and biological determinants of disease and treatment outcomes and quality of life.
We distributed (postally and electronically) a modified Health Foundation / Ipsos Mori survey, which comprises 13 questions (closed and open) around health and social care. Quantitative data were analysed using descriptive statistics, free text responses were analysed using qualitative thematic analysis. A framework was developed to index and chart data into themes through an iterative process.

Results: Response rate to date is 42 of the 95 UNICORNS families approached (44%). Of those who participated, 61% expressed concern over the impact of the pandemic on their health, with a third (31%) expressing difficulties in accessing essential medication, and 56% finding it harder to get basic food stuffs. Despite this, the majority expressed a positive experience with NHS services, with 72% being comfortable using their specialist hospital during the pandemic. Key themes identified in analysis included positive experiences of safety procedures and the adoption of digital health tools across different levels of care (primary to quaternary); negative experiences of poor co-ordination of care, or of delivery of synchronous telemedicine care of rare disease from primary / secondary health teams, and negative perceptions around the use of immunosuppression during the pandemic.

Conclusions: The UNICORNS study is well placed to provide useful data on patient experience for those starting a rare, chronic childhood disease care pathway during a global pandemic. Our findings suggest that primary and secondary care teams require additional support in delivering / co-ordinating care for those with rare disease. UNICORN C-19 findings will inform recommendations for future service planning.

CONTROL ID: 3712286

SUBMITTER (NAME ONLY): Dina Baddar

TITLE: Clinical and Genetic Characterization of a Cohort of Autosomal Recessive Bestrophinopathy Patients in an Egyptian Population

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Baddar, Ophthalmology, Research Institute of Ophthalmology, Giza, EGYPT|D. Baddar, C. Tawfik, Ophthalmology, Watany Eye Hospital, Cairo, EGYPT|C. Tawfik, Ain Shams University Faculty of Medicine, Cairo, EGYPT|N. Al Bagoury, H. Fathy, A. Abdel- Aleem, National Research Center, EGYPT|

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ABSTRACT BODY:

Purpose: To report the clinical and genetic characteristics of autosomal recessive bestrophinopathy (ARB) in Egyptian patients who are offspring to consanguineous parents. ARB is a rare inherited retinal disorder.

Methods: Prosepective study aiming to characterize the clinical picture, multimodal imaging and genetic findings in 13 patients with ARB from 11 consanguineous Egyptian families. All patients underwent complete ophthalmological examination and multimodal imaging including fundus photography, fundus autofluorescence (FAF) and optical coherence tomography (OCT). Full-field electroretinography (ERG) and electro-oculography (EOG) were performed as well as genetic testing of the BEST1 gene for biallelic mutations.

Results: The patients were comprised of 11 females and 2 males. The visual acuity ranged from counting fingers to 20/32. All patients exhibited retinal findings on multimodal imaging classically-described with ARB. These findings include hyperautoflourescent retinal flecks in the posterior pole and retinal midperiphery with corresponding hyperreflective RPE deposits on OCT, subretinal fluid in the fovea with overlying elongated photoreceptors in a stalactite-like arrangement and intraretinal cysts. One patient showed diffusely thinned neurosensory retina and RPE, but she had extinguished ERG and absent light rise on EOG. Her old retinal imaging demonstrated classic ARB findings. Another patient showed a large scar in the fovea markedly compromising vision. On electrophysiology, there was moderate reduction in ERG and absent light rise on EOG. Sequencing of BEST-1 gene revealed 2 previously-reported mutations c.122C>T, p.P41L, g.5952 C>T and c.424C>T- chr11:61724438C>T, p.R142W, and 2 novel mutations; c.245insCAG in a single patient and c.185G>C, p.R62P in 4 patients

Conclusions: Autosomal recessive bestrophinopathy is a recognizable phenotype caused by inherited mutations in the BEST1 gene. In this study, we present the clinical spectrum as well as a novel mutation found in 6 Egyptian patients from various regions. The novel mutation was not associated with a significant impact on retinal clinical picture.

CONTROL ID: 3712287

SUBMITTER (NAME ONLY): Noelia Kunzevitzky

TITLE:

Phase 1 Multicenter Study of Magnetic Cell Therapy for Corneal Edema

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Kunzevitzky, C. Fleming, J.K. Thoele, R. Goldberg, J.L. Goldberg, Emmecell, Menlo Park, California, UNITED STATES|R. Goldberg, Bay Area Retina Associates, Walnut Creek, California, UNITED STATES|J.L. Goldberg, Ophthalmology, Stanford University, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure: Noelia Kunzevitzky: Commercial Relationship(s);Code E (Employment):Emmecell;Code P (Patent):Emmecell | Christina Fleming: Commercial Relationship(s);Code E (Employment):Emmecell | Jennifer Thoele: Commercial Relationship(s);Code E (Employment):Emmecell | Roger Goldberg: Commercial Relationship(s);Code P (Patent):Emmecell;Code S (non-remunerative):Emmecell;Code O (Owner):Emmecell | Jeffrey Goldberg: Commercial Relationship(s);Code P (Patent):Emmecell;Code S (non-remunerative):Emmecell;Code O (Owner):Emmecell

ABSTRACT BODY:

Purpose:

To assess the safety and tolerability of magnetic cell therapy as treatment for subjects with corneal edema secondary to Fuchs' endothelial corneal dystrophy (FECD) or pseudophakic bullous keratopathy (PBK).

Methods: Human corneal endothelial cells were isolated from donor corneas, expanded in vitro and labeled with biocompatible magnetic nanoparticles to formulate EO2002, magnetic human corneal endothelial cells.

The safety and tolerability of a single intracameral injection of magnetic human corneal endothelial cells (EO2002) with and without endothelial brushing (EB) or Descemet stripping (DS) will be assessed in a phase 1, open-label, dose-escalating multicenter study. In total, 18 subjects with corneal edema will be enrolled in the study and will receive a single dose of EO2002 followed by the application of an external magnetic eye patch. Half of the subjects will only receive an injection of EO2002 and the other half will undergo EB or DS followed by EO2002 injection. Three doses will be studied over a 6-month follow-up period. The primary endpoints are the absence of inflammation and a stable intraocular pressure. The secondary endpoints will assess changes in corneal thickness and in best corrected visual acuity (BCVA).

Results:

Study enrollment for pseudophakic subjects that are surgical candidates for DSEK with BCVA <20/40 is ongoing. To date, 9 subjects were enrolled and treated with EO2002 with and without DS. No product-related SAEs have occurred.

Conclusions:

EO2020 injection in subjects with symptomatic corneal edema is well-tolerated, with no significant adverse events or changes in intraocular pressure. Forthcoming data from the remainder of the study should provide valuable information on the safety of all doses as well as essential data on secondary endpoints in this patient population.

CONTROL ID: 3712288

SUBMITTER (NAME ONLY): Michael Boachie-Mensah

TITLE: Microbiome Metagenomics in High-Fat Diet-Fed Mice Reveals Altered Microbial Metabolic Pathways Related to AMD

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Boachie-Mensah, J.Y. Zhang, J. Xiao, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|H. Lin, Duchossois Family Institute, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|H.A. Barba, N. Deng, D. Skondra, Ophthalmology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|U. Nadeem, Pathology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|A. Movahedan, Ophthalmology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|E. Chang, Medicine, Microbiome Medicine Program, Knapp Center for Biomedical Discovery, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The link between the gut microbiome and age-related macular degeneration (AMD) is not completely understood, but gut dysbiosis has been implicated in AMD pathogenesis. Our team previously showed that high-fat diet (HFD) intake induces changes in gut microbiota composition (gut dysbiosis), alters the retinal and choroidal transcriptome, and exacerbates choroidal neovascularization in mouse models. However, little is known about how HFD changes the functional profiles of microbes. The purpose of this study is to use shotgun metagenomics to determine the effect of HFD consumption on microbial metabolic pathways, thereby clarifying the link between HFD-induced gut dysbiosis and AMD.

Methods: C57BL/6 mice were placed on either a ND or 23% HFD for 8 weeks (4 mice/group). For shotgun metagenomic analysis, DNA was extracted from fecal pellets and Illumina compatible libraries were generated using the QIAseq FX Library Kit. Sequencing runs were performed on the Illumina NextSeq platform. Abundant microbial genes were identified and biological pathways associated with these genes were determined using the Kyoto Encyclopedia of Genes and Genomes.

Results: Between HFD and ND mice, we identified 29 significantly altered microbial metabolic pathways based on the Kruskal-Wallis Rank Sum Test (p-value < 0.05). The most significantly upregulated pathway in HFD mice was the biosynthesis of heparan sulfate (implicated in AMD pathogenesis due to its interaction with complement factor H). In contrast, significantly down-regulated pathways in HFD mice include N-glycan biosynthesis (important for intestinal barrier function), primary/secondary bile acid (BA) biosynthesis (BAs inhibit AMD features in vitro), polyphenol biosynthesis (protects against oxidative stress), glycerophospholipid metabolism (similarly altered in AMD patients), and sucrose/galactose metabolism (key for maintaining retinal homeostasis). Compared to HFD mice, ND mice exhibited significantly decreased degradation of terpenoids (eg, geraniol), a group of compounds with geroprotective properties.

Conclusions: HFD intake significantly dysregulates microbial metabolic pathways involving the metabolism of lipids, carbohydrates, amino acids, glycans, and terpenoids. Therefore, a HFD not only modulates gut microbiome composition, but is also associated with alterations in key microbial metabolic pathways that overlap with AMD pathogenesis.

CONTROL ID: 3712289

SUBMITTER (NAME ONLY): Anneka Joachimsthaler

TITLE: How the use of dim red-light pre-recording affects ERG responses of mice with long-wavelength shifted opsin

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Joachimsthaler, N. Stallwitz, J.J. Kremers, Ophthalmology, University Hospital Erlangen, Erlangen, Bavaria, GERMANY|A. Joachimsthaler, N. Stallwitz, Animal Physiology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|

Commercial Relationships Disclosure: Anneka Joachimsthaler: Commercial Relationship: Code N (No Commercial Relationship) | Nina Stallwitz: Commercial Relationship: Code N (No Commercial Relationship) | Jan Kremers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We investigated, how the ERGs of (LIAIS) mice, expressing a human L*-opsin instead of the native M-opsin, are affected by the use of visible red light, that may lead to photoisomerizations in the L*-opsin, during the preparations prior to ERG recordings.

Methods: Recordings were done on LIAIS mice, using wildtype (WT) littermates as control. Mice were dark adapted overnight and further handling was done either under dim red light or IR light with IR sensitive goggles performed in two separate sessions that were 2 weeks apart.

Anesthetized animals were placed on a heated platform in the Ganzfeld bowl and were dark adapted for 10 min before scotopic flash ERGs were recorded. Flash strengths increased from -3.7 to 0.8 log cd.s/m^2, with stimulus frequencies decreasing from 1 to 0.5 Hz and interstimulus intervals increasing from 10 to 120 sec.

For the following photopic flash ERG recordings the animals were adapted for 2 min to a 1.4 log cd/m^2 white background, before flashes with flash strengths increasing from -0.2 to 1.2 log cd.s/m^2 were presented upon the background.

All flash ERG responses were analyzed with regard to amplitudes and latencies of the prominent wave components.

Results: Preparation was substantially longer under IR light.

Responses to scotopic flash ERGs using red light were ≈14% smaller in LIAIS compared to WT mice. For both genotypes the use of IR light resulted in larger amplitudes of the scotopic a- and b-wave. This effect was stronger for LIAIS mice, where amplitudes increased by 22% (a-wave) and 28% (b-wave). In WT mice, a- and b-wave increased by 16% and 13%, respectively. OPs and implicit times did not depend on the light source used for preparation.

For the photopic flash ERGs, after the use of red light pre-recording the WT b-wave was 17% larger and 11% faster compared to LIAIS mice. The effect of IR light usage pre-recording was less pronounced. B-wave amplitudes were about 13% and 17% larger after IR preparation for WT and LIAIS mice, respectively.

Conclusions: The use of red light for mouse handling pre-recording has a slightly stronger effect on the red sensitive LIAIS mice compared to WT mice. However, the use of IR light resulted in larger ERG responses for both genotypes. Even though the use of IR light seems to ensure a more dark adapted state for the animals, handling is quite challenging and prolonged the total time of the experiment substantially.

CONTROL ID: 3712291

SUBMITTER (NAME ONLY): Varsha Srinivasan

TITLE: Identification and Validation of Biomarkers for Early Detection of Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Srinivasan, A. Upendran, Medical Pharmacology and Physiology, University of Missouri, Columbia, Missouri, UNITED STATES|A. Gangula, R. Kannan, Radiology, University of Missouri, Columbia, Missouri, UNITED STATES|D.P. Hainsworth, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|R. Kannan, Bioengineering, University of Missouri, Columbia, Missouri, UNITED STATES|A. Upendran, Institute of Clinical and Translational Sciences, University of Missouri, Columbia, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Varsha Srinivasan: Commercial Relationship: Code N (No Commercial Relationship) | Abilash Gangula: Commercial Relationship: Code N (No Commercial Relationship) | Dean Hainsworth: Commercial Relationship: Code N (No Commercial Relationship) | Raghuraman Kannan: Commercial Relationship: Code N (No Commercial Relationship) | Anandhi Upendran: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR), a retinal microvascular disease, is the major cause of preventable vision loss globally and is expected to affect ~191 million individuals by 2030. A major challenge in treating DR is its 'Clinical Silence'; wherein, the disease progression is not accompanied with easily observable symptoms. Currently, diabetic patients are annually examined using fundoscopy for onset or progression of vision threatening DR. However, fundoscopy, the gold standard for DR screening is time-consuming, expensive, uncomfortable, requires expertise and instrumentation. To overcome these limitations and to prevent DR-associated vision loss, we focused on identifying DR-associated biomarkers in urine, which would help in developing an alternative, rapid, and point-of-care (POC) screening procedure to predict the onset and progression of DR.

Methods: A total of 96 diabetic patients were recruited in a clinical study approved by the University of Missouri (MU) IRB committee. Four biomarkers that are related to onset of DR, 8-hydroxydeoxyguanosine (8-OHdG), Angiopoeitin-2, Membrane attack complex (C5b-9), Placental growth factor (PLGF), were chosen for evaluation. Urine samples were collected and the levels of four biomarkers were determined for various stages of DR as identified from the Fundus examination.

Results: The urinary biomarker levels were compared between mild and moderate stages of DR as this transition represents the clinically significant inflection point of disease. The average levels of three biomarkers (8-OHdG, Angiopoietin, and C5b-9) were found to be increased during mild to moderate transition, while for the PLGF the levels decreased. Classification into Low-risk and High-risk DR groups based on severity of the disease shows significantly higher levels of C5b-9 in high-risk groups compared to low-risk.

Conclusions: The change in the levels of the biomarker from mild to moderate stage of DR suggests their role as potential biomarkers for identifying progression of DR. Further analysis based on different demographic factors can provide crucial cues on onset of DR. However, it is important to validate the combination of biomarkers with larger sample set and subsequently integrate them into a single panel for a sensitive and reliable screening of DR. The design of POC lateral flow devices for the biomarkers is in progress.

CONTROL ID: 3712293

SUBMITTER (NAME ONLY): Salil Lachke

TITLE: The small Maf transcription factors Mafg and Mafk are required for embryonic lens development

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Lachke, S. Patel, D. Anand, Department of Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|S.A. Lachke, Center for Bioinformatics and Computational Biology, University of Delaware, Newark, Delaware, UNITED STATES|M. Yamamoto, Department of Medical Biochemistry, Tohoku University Graduate School of Medicine, Sendai, JAPAN|H. Motohashi, Department of Gene Expression Regulation, Tohoku University Smart-Aging Research Center, Sendai, JAPAN|F. Katsuoka, Department of Integrative Genomics, Tohoku University Tohoku Medical Megabank Organization, Sendai, JAPAN|

Commercial Relationships Disclosure: Salil Lachke: Commercial Relationship: Code N (No Commercial Relationship) | Shaili Patel: Commercial Relationship: Code N (No Commercial Relationship) | Deepti Anand: Commercial Relationship: Code N (No Commercial Relationship) | Hozumi Motohashi: Commercial Relationship: Code N (No Commercial Relationship) | Fumiki Katsuoka: Commercial Relationship: Code N (No Commercial Relationship) | Masayuki Yamamoto: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The small Maf transcription factors (TFs) Mafg and Mafk belong to the basic leucine-zipper (bZIP) protein family. Previous data showed that Mafg$^{-/-}$:Mafk$^{+/-}$ compound knockout (KO) mice develop cataract from age 4-month onward. Interestingly, Mafg$^{-/-}$:Mafk$^{-/-}$ double KO mice exhibit lens defects significantly early, prior to birth. However, the role of Mafg and Mafk in embryonic lens development has not been examined. Therefore, we sought to characterize lens defects in embryonic stages in Mafg$^{-/-}$:Mafk$^{-/-}$ double KO mice.

Methods: Appropriate crosses were set-up to generate Mafg$^{-/-}$:Mafk$^{-/-}$ mice and immunostaining and fluorescence microscopy was used for characterization of lens markers. High-throughput RNA-sequencing (RNA-seq) was performed on embryonic day (E) 16.5 Mafg$^{-/-}$:Mafk$^{-/-}$ and control lenses in biological triplicates. Differentially expressed genes (DEGs) in E16.5 Mafg$^{-/-}$:Mafk$^{-/-}$ lenses were validated using RT-qPCR or immunostaining.

Results: At E16.5, the anterior epithelium of the lens (AEL) in Mafg$^{-/-}$:Mafk$^{-/-}$ animals appears abnormally multilayered. Further, Mafg$^{-/-}$:Mafk$^{-/-}$ lenses exhibit abnormal abundance of F-actin near the “fulcrum” region. To gain insights into the molecular basis of these defects, RNA-seq of Mafg$^{-/-}$:Mafk$^{-/-}$ E16.5 lenses was performed. Over 200 DEGs were identified in Mafg$^{-/-}$:Mafk$^{-/-}$ lenses. These DEGs were further prioritized based on iSyTE analysis, gene ontology (GO) analysis and relevance to lens biology. Among the prioritized candidates, Epha5 (Eph receptor A 5) is found to be significantly reduced in Mafg$^{-/-}$:Mafk$^{-/-}$ lenses but not in control or Mafg$^{-/-}$:Mafk$^{+/-}$ lenses. Because deletion of ephrin-A5 (Efna5), an established ligand of the Epha5 receptor, is shown to cause lens epithelial cell adhesion defects, it is possible that Epha5 reduction contributes to the multilayered AEL defect in Mafg$^{-/-}$:Mafk$^{-/-}$ lenses. Further, other candidates with functional relevance to the cytoskeleton, cell cycle and extracellular matrix were also among the DEGs in Mafg$^{-/-}$:Mafk$^{-/-}$ lenses and may contribute to the lens defects.

Conclusions: These data demonstrate that Mafg and Mafk are necessary for proper development of the lens during embryogenesis. Further, these data uncover new downstream regulatory targets of Mafg and Mafk in the lens. Because these TFs are expressed beyond the lens, these new regulatory relationships may inform on small Maf-based control in non-lens tissues.

CONTROL ID: 3712295

SUBMITTER (NAME ONLY): Erin Burnight

TITLE: Development of a CRISPR dCas9-KRAB based strategy for treatment for dominant retinal degenerative blindness

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Inherited retinal disease is a major cause of blindness worldwide. The most common disease-causing mutation in patients with RHO-associated retinitis pigmentosa (RP) is a dominant gain-of-function missense variant at amino acid residue 23 (Pro23His). Treatment for this disease and other dominantly inherited retinal dystrophies will require knockdown or ablation of mutant allele expression. To that end the purpose of this study was to develop a CRISPR-Cas9-mediated transcriptional repression strategy capable of suppressing RHO expression.

Methods: We created CRISPR-Cas9 transcriptional knockdown reagents using catalytically inactive S. aureus Cas9 (dCas9) fused to the Krüppel associated box (KRAB) transcriptional repressor domain and evaluated four guides targeted to transcriptional regulatory elements in the promoter region of RHO. Using a reporter construct carrying GFP cloned downstream of the RHO promoter fragment (nucleotides -1403 to +73), we assayed GFP knockdown in cells treated with our RHO promoter-targeted CRISPR-dCas9 reagents. Following functional confirmation, reagents were packaged into AAV5 vectors and delivered to human retinal explants (N=3) and Pro23His mutant retinal degenerative swine (N=4). RHO knockdown was demonstrated via Western blot analysis and immunocytochemistry.

Results: Quantitative RT-PCR analysis of cells treated with CRISPR-dCas9 and reporter plasmids demonstrated ~74%-84% reduction in GFP expression when compared to control cells treated with reporter plasmid only. The guide with the greatest knockdown in this assay (sag94) was cloned into AAV5 cassette plasmids along with dCas9-KRAB and used in downstream ex vivo and in vivo experiments. Western blot analysis demonstrated significant RHO knockdown (50%) in human retinal explants treated with AAV5-RHOpCRISPRi vector compared to untreated controls. When we extended these studies into the Pro23His rhodopsin mutant swine model, we observed a 20% knockdown of rhodopsin in CRISPRi-treated retinae compared with untreated contralateral control retinae at two-weeks post injection.

Conclusions: We have generated a dCas9-KRAB gene repression system suitable for suppressing RHO expression in vivo. This work may provide a paradigm from which to develop CRISPR-dCas9 therapies to treat dominantly inherited retinal dystrophies.

CONTROL ID: 3712297

SUBMITTER (NAME ONLY): Sanja Petrovic Pajic

TITLE: Relative preservation of central retinal layers in LHON in comparison to other optic neuropathies

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate thickness of retinal layers in Leber hereditary optic neuropathy(LHON) compared to non-mitochondrial optic neuropathies in atrophic stage with the aim to see if in LHON any specific patterns can be found.

Methods: 14 patients(24 eyes),10 males/4 females,mean age 37.5 years, with confirmed LHON (LHON group) were compared to 13 patients(23 eyes)with optic neuropathy, mean age 46 years, 7 males/6 females, with LHON-negative genetic testing(mtDNA+WES) and without identified aetiology of the bilateral optic atrophy (nonLHON group). Seven eyes were excluded due to confounding factors. Peripapillary RNFL (pRNFL) measurement and segmentation analysis of macular region retinal layers was performed using the Heidelberg Engineering Spectralis SD-OCT. Published normal segmentation data were used for controls.

Results: In LHON group RNFL, GCL and IPL layers were thinner in all ETDRS fields compared to nonLHON group, except for the central circle where LHON group had significantly better preservation of these layers (p=0.012,p=0.006 and p=0.011). The LHON group RNFL was significantly thinner in the pericentral middle ring (p=0.005), whilst IPL was significantly thinner in both middle and outer ring (p=0.019 and p=0.04). LHON group had thicker INL even compared to controls in the central circle (p=0.008) and the outer ring (p= 0.024), whilst the INL layer in nonLHON group was not significantly thicker than in controls. The LHON group also had thicker INL in the central circle (p=0.004) compared to nonLHON group. The ratio between the middle ETDRS ring and the central circle for RNFL (0.83–2.62), GCL (0.76-2.88) and INL (0.84-3.16) thicknesses were lower in LHON group compared to non LHON group (1.45-3.46, 1.72-3.57 and 1.14–3.30). Interestingly, in 3 LHON patients with VA improvement, the ratios were similar to results of nonLHON group. This may represent a new LHON biomarker. The two groups also significantly differed in temporal (p=0.045) and temporal superior region (p=0.001) pRNFL thickness.

Conclusions: The retinal ganglion cell complex thickness (RNFL-GCL-IPL) is relatively preserved in central ETDRS circle in LHON compared to non-mitochondrial optic nerve atrophies. LHON patients also showed thickening of INL layer compared to healthy controls. Our findings might represent novel biomarkers and the structural basis for possible recovery in some LHON patients.

CONTROL ID: 3712298

SUBMITTER (NAME ONLY): Anastasios Stavrakakis

TITLE: Peripapillary changes of Retinal Nerve Fiber Layer after a successful surgery for rhegmatogenous retinal detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Stavrakakis, A. Vlachou, M.K. Tsilimbaris, Ophthalmology, Panepistemiako Geniko Nosokomeio Erakleiou B Cheirourgikos Tomeas, Heraklion, Heraklion, GREECE|P. Tsoka, M.K. Tsilimbaris, Laboratory of Vision and Optics, Panepistemio Kretes Iatrike Schole, Heraklion, Crete, GREECE|

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ABSTRACT BODY:

Purpose: To investigate possible changes in peripapillary retinal nerve fibre layer (RNFL) after successful surgery for rhegmatogenous retinal detachment (RRD).

Methods: Forty eyes, which underwent surgery for primary RRD, were included in the study. Successful surgery was performed either by pars plana vitrectomy, retinopexy and SF6 gas tamponade or pneumatic retinopexy. Exclusion criteria were known conditions that can cause changes to the RNFL (e.g. history of glaucoma) or surgery that demanded extensive manipulations. Spectral-domain optical coherence tomography (SD-OCT) was used for the measurement of the peripapillary RNFL. Values calculated by the device in 6 peripapillary sectors were used. Pre-operative measurements and at 1, 3 and 6 months time post-operative were compared. Control eye was the fellow eye at each time point. Demographic and clinical characteristics of patients were also recorded. Eighteen patients have completed the 6 month follow up .

Results: 18 patients have completed the six month follow up and were compared. Initially, the peripapillary RNFL values of the 18 affected (detached) eyes were measured in each follow up (at 1, 3 and 6 month post operatively). Only segments that are corresponding to the detached area were compared. Analysis was performed with one-way Anova and post-huc Tukey test. 17 eyes. Statistically significant changes were noticed in 15 eyes at least in one segment related to the detached area. Out of these, 5 eyes had statistically significant change in all RNFL segments corresponding to the detached area and 10 eyes at least in one segment. Finally, RNFL segments related to the detached retina were compared in each follow up between the two eyes. Two-tailed T-test was used for the analysis. 14 out of 18 eyes showed statistically significant difference in each follow up, 2 had no significant difference and 2 had statistical differences only in some time points.

Conclusions: The peripapillary RNFL values in the segments related to the detached retina seem to be affected over time despite successful retinal detachment repair.

CONTROL ID: 3712300

SUBMITTER (NAME ONLY): David Eveleth

TITLE: A Phase 1/ Phase 2 Study Evaluating the Safety and Efficacy of TTHX1114 on the Regeneration of Corneal Endothelial Cells in Patients with Corneal Endothelial Dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Eveleth, T. Tremblay, Trefoil Therapeutics, Inc, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the safety and tolerability of TTHX1114.

Methods: Protocol was reviewed/ approved by the IRB and informed consent obtained from all subjects. TTHX1114 was administered as a weekly 10mcL IC injection at doses of 1ng, 3ng, or 10ng or vehicle x 4 weeks. The study included patients with Fuchs endothelial corneal dystrophy (FECD), central endothelial cell (CEC) density < 2000 mm^2 in the study eye; adequate function in the fellow eye; and no other co-morbid conditions that would interfere with the assessment of safety or efficacy. 22 subjects were enrolled/randomized; 17 subjects received TTHX1114 (1ng [7], 3ng [3], or 10ng [7]) and 5 received placebo. Assessments included specular microscopy, slit-lamp examination, BCVA, central corneal thickness (CCT), and IOP.

Results: Of the subjects enrolled, 19/22 (86.4%) were female, 100% were White, with a mean age of 74.5. All subjects received all injections and completed the study. There did not appear to be any meaningful changes in slit-lamp, BCVA, CCT, or IOP. A total of 88 10mcL injections were administered and the mean and median change from pre-injection IOP was -1.9 and -2, respectively; the highest increase was 4mmHg. There were no deaths, SAEs, or DLTs. No AEs were considered related to TTHX1114 by the Investigator, but 4 AEs were considered related to the IC injections procedure; these events were all mild, reported only in 1 subject each, and included conjunctival hemorrhage, eye irritation, foreign body sensation in eye, and photophobia. Analysis of specular microscopy is ongoing.

Conclusions: Standard ocular assessments were sufficient to assess the safety and tolerability of TTHX1114 and an injection volume of 10mcL which appeared to be safe and well-tolerated. The MTD was not exceeded and the RP2D was determined to be 10ng/10mcL delivered by IC injection. The study was originally designed to also obtain a preliminary estimate of efficacy by assessment of CEC densities but this was confounded by the presence of guttae and the inability to reproducibly image the same geographic location at subsequent visits. Further dose/volume escalation should be conducted and exploration of relevant efficacy endpoints which may include eligibility criteria requiring significantly abnormal baseline measurements and/or more reliably imageable patients in additional studies.

CONTROL ID: 3712301

SUBMITTER (NAME ONLY): Robert Gunzenhauser

TITLE: Impact of COVID-19 Pandemic on Teleretinal Screening using Optical Coherence Tomography at the Veterans Health Administration

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In 2019, a novel teleretinal imaging program was implemented at the Veteran Affairs (VA) Greater Los Angeles Healthcare System providing remote OCT evaluation with prompt retinal specialist evaluation. The purpose of this study was to determine how the COVID-19 pandemic affected the tele-OCT screening program in its second year of implementation.

Methods: Retrospective chart review study of patients evaluated by a retina specialist through asynchronous tele-OCT evaluation in 2019 and 2020. Electronic medical records were used to obtain patients' demographic and clinical characteristics, tele-OCT consult results, and patient adherence to tele-OCT follow-up plans.

Results: There were 108 tele-OCT consults in 2020 compared to 158 tele-OCT consults in 2019, a 32% decrease. There was no significant difference in overall patient adherence to follow-up between the two years. In 2020, patients who had diagnosed anxiety were less likely to be adherent compared to 2019 (37.5% v. 71.4%, $p=0.023$). In 2020, the retinal diagnosis was less likely to be changed after teleretinal consultation compared to 2019 (12.96% v. 29.1%, $p<0.01$).

Conclusions: The decrease in tele-OCT use reflects the decrease in patients presenting to referring clinics that utilized the consult mechanism during the COVID-19 pandemic. Patient anxiety should be considered when addressing compliance. The teleretinal program is providing an education benefit to referring providers.

CONTROL ID: 3712302

SUBMITTER (NAME ONLY): Davide Ortolan

TITLE: Single cell resolution map of retinal pigment epithelium helps discover subpopulations with differential disease sensitivity

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Ortolan, R. Sharma, A. Volkov, A. Maminishkis, L. Huryn, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|N. Hotaling, National Center for Advancing Translational Sciences, Bethesda, Maryland, UNITED STATES|S. Di Marco, S. Bisti, Istituto Italiano di Tecnologia, Genova, Liguria, ITALY|

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) is susceptible to regional atrophy in several retinal degenerative diseases, such as age-related macular degeneration (AMD). Variations of RPE phenotype and function with retinal location influence the development of Geographic Atrophy, a late stage of AMD. Understanding the precise location and the nature of RPE phenotypic and molecular differences will be invaluable to study retinal diseases. In this work, we provide a detailed and comprehensive morphometric map of the entire human RPE and show how it changes in AMD.

Methods: RPE/choroid flatmounts were generated from more than 20 human non-AMD and AMD eyes. The entire flatmounts were stained for RPE cell borders and imaged. An open-source software for image analysis, based on machine learning, was developed to quantify RPE morphometry. Spreadsheets with raw data and heatmaps were generated to compare regional RPE differences.

Results: RPE cell area analysis of non-AMD eyes revealed the presence of 5 statistically different subpopulations, which we named as P1 to P5. P1 corresponded to fovea and parafovea (median: 147.2 ± 15.4 μm^2 sd), while P5 corresponded to far-peripheral RPE (median: 331.9 ± 27.2 μm^2 sd). Interestingly, a peripheral ring of smaller RPE cells (P4) was discovered (median: 176.8 ± 18.7 μm^2 sd) that is closer in size to perifoveal RPE cells (median: 177.6 ± 15.7 μm^2 sd). RPE aspect ratio increased gradually with retinal eccentricity, while hexagonality decreased correspondingly. The morphometric differences between RPE subpopulations, seen in non-AMD eyes, decreased in AMD eyes. Each subpopulation had greater variability compared to non-AMD (30-70% higher standard deviation). Analysis of RPE atrophies in AMD eyes and ultra-widefield retinal images of patients with Late-Onset Retinal Degeneration (L-ORD) and Choroideremia (CHM) showed that P1, P4 and P5 were most affected in AMD, while mid-peripheral subpopulation P3 was the most affected in L-ORD and CHM.

Conclusions: Overall, the study provides the first exhaustive morphometric map of the human RPE and a geographic reference of RPE subpopulations for future studies. The analysis of AMD eyes will help to predict disease progression using RPE morphometry progression. Future studies will focus on finding molecular markers for RPE subpopulations to understand the etiology of retinal diseases.

CONTROL ID: 3712303

SUBMITTER (NAME ONLY): Omer Iqbal

TITLE: The potential roles of IL-6 and NKG2C in the pathogenesis of Stevens Johnson Syndrome/Toxic Epidermal Necrolysis

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Iqbal, Opthalmology/Pathology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|H. El-Khateeb, Opthalmology/Pathology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|A. Dharan, Microbiology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|C.S. Bouchard, Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stevens Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) are mainly drug-induced severe cutaneous adverse reactions with increased morbidity and mortality. It also involves the eyes causing ocular surface disease leading to visual impairment and blindness. The pathogenesis is not completely understood. HLA-E-specific activating receptor CD94/NKG2C is reported to trigger T-cell receptor-independent cytotoxicity in cytotoxic T cells. Several cytokines are known to play a role in the pathogenesis of this condition. The role of IL-6 and NKG2C in causing ocular surface disease and keratinocyte apoptosis is not fully explored. Determination of the expression of IL-6 and NKG2C studied by immunofluorescence microscopy will enable better understanding of their potential roles in the pathogenesis of SJS/TEN. It is hypothesized that IL-6 and NKG2C play a crucial role in the pathogenesis of SJS/TEN and may correlate with the degree of severity of skin detachment and ocular surface disease.

Methods: In order to validate this hypothesis, the specific aim is to determine the expression of IL-6 and NKG2C in the skin of patients with biopsy confirmed SJS/TEN compared to the lichen planus controls by immunohistochemistry and correlation with severity of skin detachment. Under a current, Loyola IRB approved protocol, 12 collected and archived unstained slides of skin and blood plasma samples from patients with biopsy confirmed SJS/TEN will be used for this study. Deconvolution Immunoflourescence (IF) will be performed using IL-6 and NKG2C antibodies using a Delta Vision microscope equipped with a digital camera.

Results: Deconvolution immunofluorescence performed on skin biopsy confirmed SJS/TEN slides showed expression of IL-6 and NKG2C using a DeltaVision microscope.

Conclusions: IL-6 and NKG2C may be involved in the pathogenesis of SJS/TEN. Further studies are warranted to establish their roles in the severity of disease.

CONTROL ID: 3712304

SUBMITTER (NAME ONLY): Sanjeeb Bhandari

TITLE: Visual acuity results at ten years in participants with age-related macular degeneration enrolled in the Age-Related Eye Disease Study 2

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Bhandari, E. Konstantinou, E. Agron, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|T.E. Clemons, The EMMES Corporation, LLC, Rockville, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To present data on long-term (10 years) follow-up of visual acuity results in participants with age-related macular degeneration (AMD) enrolled in the Age-Related Eye Disease Study 2 (AREDS2), a clinical trial of oral supplementation for the treatment of AMD

Methods: Participants (n=4203) 50 to 85 years with bilateral large drusen or unilateral late AMD were enrolled in the AREDS2 study from 82 retinal specialty clinics in the US between 2006–2008 and followed until the conclusion of the clinical trial in 2012. After the end of the trial, an additional 5-year of follow-up was conducted in a subset (2923 participants) via telephone every 6 months until 2018. A subset of the AREDS2 participants (709 participants[1418 eyes]) was also evaluated in a final in-clinic study visit (at 10 years) to collect data on best-corrected visual acuity (VA), AMD status evaluated with color fundus photographs(CFP) and optical coherence tomography that were graded centrally by the reading center (AMD progression assessed with AREDS severity scale for AMD), and treatment. Late AMD was defined as the presence of neovascularization or geographic atrophy on CFP.

Results: The mean (SD) age of the 709 participants at baseline was 70 (7.5) years. The mean (SD) VA of 76.6 (16.8) letters (Snellen equivalent of 20/30) at baseline remained stable in the initial five years but dropped to a mean of 63.1 (24.8) letters (Snellen 20/60) at the 10-year visit (Table 1, Figure 1A). The proportion of eyes with VA≥20/40 dropped from 85% at baseline to 57% over 10 years while those with VA<20/200 increased from 4% to 15% (Table 1, Figure 1B). Late AMD increased from 18% at baseline to 74% at 10 years. Another analysis showed that at year 10, 650 of 1414 eyes (46%) had ≥10 letters loss compared with baseline. Of all the participants with vision loss, 293/650 (45%) had developed late AMD by year 5 that increased to 471(72.7%) over 10 years.

Conclusions: Half of the cohort followed had maintained good VA (20/30 on average) over 10 years. The mean VA dropped by year 10 with 72% progressing to late AMD. Only a small proportion of eyes experienced severe vision loss.

CONTROL ID: 3712306

SUBMITTER (NAME ONLY): Jon Whitney

TITLE: Comparative Assessment of Multiple Model Implementation Systems for Multi-Layer Retinal Segmentation: Single Line, Two-Line, and ROI training.

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Whitney, H. Cetin, E. Kanyo, M. Bonnay, S.K. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate potential performance improvements from using varying levels of global information in deep learning layer segmentation.

Methods: All models were trained with a dataset of 141,000 annotated OCT B-scans, and trained where full images were compressed into 128x128 patches. First, a lowmag model considered the internal limiting membrane (ILM) segmentation alone. A second model used both the ILM and Brooks Membrane (BM) as segmentation targets (two-line model). This focused the model on global OCT architecture. The third model was trained on ILM to BM region of interest (ROI), which then applied the segmentation to the top of the identified region. These models were evaluated on a high-pathology holdout test set of 451 annotated images, and performance was compared using the average deviation away from manual annotations in pixels.

Results: The single line lowmag model had an average offset of 25.38 pixels, heavily impacted by blank sections where the model was unable to detect any ILM line (Figure 1). The two-line model performed better on average than single line segmentations, with an average offset of 2.18 pixels, potentially due to more robust segmentations in high pathology samples. The two-line model also performed better than the ROI model, which had an average offset of 5.65 pixels. Interestingly, the ROI model was less precise than the two-line model, which suggests that there is something useful about both identifying the specific boundaries in the image relevant to the segmentation goal, as well as information regarding the broader context.

Conclusions: Both global and local information are important for making accurate annotations of biological structures which are impacted by pathology and unusual circumstances. This work examines the effect of different levels of global information on deep learning model segmentation performance.

CONTROL ID: 3712307

SUBMITTER (NAME ONLY): Tyler Najac

TITLE: Follow Up Metrics in Primary Care Clinics after Implementation of an Artificial Intelligence Assisted Telemedicine Screening Program for Diabetic Retinopathy

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We aim to determine the effects of implementing an artificial intelligence (AI) diabetic retinopathy (DR) screening system on the rate of patient follow-up and time to follow-up in patients of the North Philadelphia community with more-than-mild (MTM) DR.

Methods: A retrospective chart review of patients screened for DR with Eyenuk's (Los Angeles, CA) EyeArt software at three primary care offices between 10/1/2020–12/31/21. Inclusion criteria were diabetics 18 or older who had a DR screening. Photos were taken on a non-mydriatic fundus camera. EyeArt interpretation was based on the International Classification of Diabetic Retinopathy (ICDR) criteria. Results were reported as “referable” for uninterpretable images or MTM DR (ICDR 2-4 +/- evidence of macular edema) or “not referable” (ICDR 0-1 and no evidence of macular edema). Temple ophthalmology office staff reviewed the EyeArt database to schedule follow up appointments for referrable patients. Screening outcomes and time to follow up exams were recorded and compared to a control group that were interpreted by an optometrist without AI between 3/2018 and 3/2020.

Results: 41 patients were screened for DR at 3 clinic sites after implementing AI. 24/41 (58.5%) were referable by EyeArt. 17/41 (41.4%) patients were not referable. Of the referable patients, 3/24 (12.5%) were contacted by office staff, and all 3 completed a follow up exam. The average time to a follow-up exam was 126 +/- 25.7 days after the screening exam. Of 1902 screening exams prior to implementing EyeArt, 688 (35.1%) were referable. 157/688 (22.8%) had an appointment scheduled, and 133/157 (85.7%) showed up to their appointment. The average time from screening to interpretation was 30.5 +/- 43.2 days, and the average time from interpretation to appointment was 158.6 +/- 123.3 days. There was no significant difference between protocols for time to appointment (p=0.40).

Conclusions: We found no difference in time to follow up exam after AI implementation, due to delays at the appointment scheduling step. AI interprets the images immediately, but the follow-up exam is not scheduled until the ophthalmology office staff are notified. To effectively utilize AI, involving PCP office staff in scheduling follow up exams immediately after EyeArt interpretation is crucial.

CONTROL ID: 3712311

SUBMITTER (NAME ONLY): Amee Azad

TITLE: Race, Ethnicity, and Sex Differences in Retinal Detachment Repairs: A US Claims-Based Analysis

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.D. Azad, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Vail, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|A. Al Moujahed, D.M. Moshfeghi, N. Callaway, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal detachment is a sight-threatening ophthalmic emergency and timely repair is critical to optimize long-term visual outcomes. Sex and race/ethnicity health disparities have been previously identified in many fields but data for retinal detachments is limited. The purpose of this study is to investigate differences in rhegmatogenous retinal detachment (RRD) repair by race, ethnicity, and sex.

Methods: A retrospective study of a nationally representative claims database (Clinformatics^{TM} Data Mart Database [OptumInsight, Eden Prairie, MN]) for patients with an incident RRD between 2003-2019 was performed. Patients with pre-existing ocular conditions, discontinuous coverage, less than a year of coverage prior to the index diagnosis of RRD, and less than 30 days of follow-up after the index diagnosis were excluded. Two diagnoses of RRD were required for the primary outcome model. Models were adjusted for age, year of diagnosis, ocular comorbidities, systemic comorbidities. Primary outcomes were adjusted odds of receiving surgery, time to repair, and type of surgery.

Results: Among 10,339 eligible cases of incident RRD, 44% (n=4536) were women, 72% (n=7450) were White, 11% (n=1111) were Hispanic, and 11% (n=1137) were Black. The primary outcome model had 2755 confirmed RRD cases and 95% (n=2622) of these patients received surgery. Women had 20% reduced odds of receiving an RRD repair after adjustment (odds ratio [OR]: 0.80, 95% CI 0.74-0.87). Asian (OR 0.71, 0.57-0.90), Black (OR 0.83, 0.73-0.95), and Hispanic patients (OR 0.79, 0.69-0.90) also had lower odds of repair. Delays in RRD repair were not observed by sex, but Hispanic patients were more often delayed relative to their White counterparts (16 days, p=0.009).

Conclusions: In a retrospective national claims-analysis, women and racial/ethnic minorities were found to have significantly lower odds of rhegmatogenous retinal detachment repair relative to men and White patients, respectively. Hispanic patients experience delays in care relative to their White counterparts. While the reason for these differences is likely multi-faceted, health disparities and delays in care are known to have devastating implications on patient outcomes and warrant further investigation.

CONTROL ID: 3712312

SUBMITTER (NAME ONLY): Annastelle Cohen

TITLE: Developmental and adult estradiol signaling disruption alters expression of estrogenic pathway components in the zebrafish retina

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Cohen, V.P. Connaughton, Biology, American University, Washington, District of Columbia, UNITED STATES|L. Cassidy, Neuroscience, American University, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported that developmental manipulation to estradiol (E2) signaling causes long-term visual deficits in adult zebrafish. Here, we hypothesize that developmental exposure to environmentally relevant concentrations of bisphenol-A (BPA), an estrogen mimic, will cause long-term molecular changes in E2 signaling components within retina, including expression of estrogen receptors (ERs) and neural aromatase (cyp19a1b), similar to what has been well-established in the brain.

Methods: Zebrafish larvae and adults were transiently exposed to either low BPA (0.001μM), high BPA (0.1μM), vehicle control (DMSO, 0.003%), or water for 24 hours. Larval fish were returned to control conditions and reared until adulthood; adults were immediately sacrificed after exposure. Total RNA was extracted from adult retina and brain (N=2-3/treatment) and used in quantitative reverse transcription PCR (RT-qPCR) to quantify changes in mRNA expression of E2 transcriptional targets. Relative gene expression was determined with the comparative Ct method ($2^{-\Delta\Delta Ct}$).

Results: Preliminary results show upregulation of cyp19a1b and ERβ mRNA in retina and brain of adults exposed to BPA. Upregulation was concentration dependent in retina whereas low BPA caused the greatest expression in brain tissue, and at a greater overall relative expression than in retina (~300%). Adults developmentally exposed to low BPA, but not high BPA, exhibited upregulation of cyp19a1b (~600%) and ERα (250%) in retina; changes in ERβ expression were not detected in retina at either concentration. Larval exposures did not alter the expression of adult brain ERs or cyp19a1b.

Conclusions: Our results suggest that developmental disruption to E2 signaling through BPA exposure can have long-term molecular effects in retinal tissue. These differences were also observed in adults acutely exposed, suggesting that the effects of BPA both occur rapidly and sustain. The tissue-dependent differences observed suggest that retinal E2 signaling and regulation is unique to mechanisms well-studied in the brain, highlighting the significance of retinal-specific research on estrogenic pathways and the effects of disruption.

CONTROL ID: 3712314

SUBMITTER (NAME ONLY): Scott Greenwald

TITLE: Small and shallow optic cup morphology is associated with optic disc edema development during spaceflight

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.H. Greenwald, L.P. Pardon, S.S. Laurie, KBR, Houston, Texas, UNITED STATES|C.R. Ferguson, Aegis Aerospace, Houston, Texas, UNITED STATES|M. Young, B.R. Macias, NASA Johnson Space Center, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Approximately 70% of long-duration crewmembers develop signs of optic disc edema (ODE), a finding of spaceflight-associated neuro-ocular syndrome (SANS). The severity of ODE differs across individuals subjected to similar environmental factors on the International Space Station (ISS). Understanding the sources of this variability is of high priority because the incidence and severity of ODE may increase as mission durations are extended, potentially causing irreversible vision loss. We therefore tested the hypothesis that having crowded optic nerve head (ONH) morphology prior to flight confers a predisposition to spaceflight-induced ODE development.

Methods: Radial and circular OCT scans centered on the ONH were collected preflight and on flight day ~150 from both eyes of 31 crewmembers completing missions on the ISS. ODE was quantified as the change in total retinal thickness (TRT) from the annular region extending 250 μm from Bruch's membrane opening (BMO). ONH metrics included minimum rim width (MRW), cup volume, and cup-to-disc ratio. For each radial B-scan (≥24 per scan), the optic cup was defined as the region bounded by the internal limiting membrane and a cup reference line that was 200 μm anterior to a disc reference line connecting the BMO points. Circumpapillary retinal nerve fiber layer (RNFL) thickness and choroid thickness were also measured. Associations between the preflight variables and inflight changes in TRT were assessed using a linear mixed-effects model.

Results: Mild ODE was observed across the cohort during spaceflight, as evidenced by a mean (SE) increase in TRT of 38.3 (6.4) μm from baseline (392.0 (5.8) μm, $P < 0.001$). A greater increase in TRT during spaceflight was associated with shallower preflight optic cup depth (slope = -0.11 ± 0.03, $P < 0.001$) and smaller preflight optic cup volume (slope = -62.8 ± 18.9, $P = 0.002$). TRT changes were not associated with preflight cup-to-disc ratio ($P = 0.31$), MRW ($P = 0.14$), RNFL thickness ($P = 0.81$), or choroid thickness ($P = 0.38$).

Conclusions: Crowded ONH morphology represents a possible risk factor for the development of spaceflight-induced ODE. However, variables outside of the optic cup (MRW, RNFL, choroid thickness) do not have an association with ODE. Crewmembers with small and/or shallow optic cups may benefit from additional ophthalmic monitoring during spaceflight and use of countermeasures against SANS.

CONTROL ID: 3712320

SUBMITTER (NAME ONLY): Erica Kahn

TITLE: A Safety and Pharmacokinetic Study of a Novel Hydrogel-based Axitinib Intravitreal Implant (OTX-TKI) in Non-Human Primates

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kahn, C. Patel, M. Priem, J. Iacona, A. Vanslette, E. Wong, C.D. Blizzard, P.K. Jarrett, M. Goldstein, R. Gurses-Ozden, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current anti-VEGF therapy for wet age-related macular degeneration (wet AMD) is rapidly cleared from the vitreous and requires injections every 1-2 months. OTX-TKI is a novel, hydrogel-based intravitreal implant designed to deliver a tyrosine kinase inhibitor, axitinib, for up to 6-9 months for the treatment of neovascular retinal diseases. Here we characterize the ocular distribution of axitinib from OTX-TKI implant following a single intravitreal injection in non-human primates.

Methods: Cynomolgus monkeys received intravitreal injections of either three 200 µg- (group 1, n=8), one 300 µg- (group 2, n=8) or one 600 µg- (group 3, n=8) OTX-TKI implant(s) bilaterally on Day 0. Experimental doses were selected to study the effects of dose and number of implants on distribution of axitinib. Ocular exams with slit lamp, intraocular pressure (IOP), confocal scanning laser ophthalmoscopy (cSLO) images and plasma samples were collected throughout the 9-month study. Subsets of eyes were enucleated at 3, 6 and 9 months to collect retina, choroid/retinal pigment epithelium (RPE), vitreous and aqueous humor tissue samples and analyzed for axitinib levels.

Results: OTX-TKI was well tolerated in all groups. No significant inflammatory response to OTX-TKI or clinically significant changes in IOP were observed. High axitinib levels in retina tissue were measured at Month 3 (>900 IC_{50}) and Month 6 (>16,000 IC_{50}) for all groups (Figure 1). Drug distribution in retina and choroid/RPE was higher in group 1 at Month 3, but comparable across all groups at Month 6. By Month 6, groups 1 and 2 implants released ~50% and group 3 implants released 35% of the dose in the vitreous. Daily release rates in group 1 implants were higher than groups 2 and 3 likely due to the larger surface area with the three implants used in group 1 only. Implant degradation was observed around Month 6 and released axitinib particles were visible in the vitreous at Month 9 (Figure 2). Plasma samples at Month 3 from all groups were below the level of quantification of axitinib (0.1 ng/mL) indicating minimal systemic exposure.

Conclusions: OTX-TKI delivered high levels of axitinib to retinal tissue and was generally well tolerated in non-human primates with no signs of significant inflammation. OTX-TKI is currently being investigated in humans for the treatment of wet AMD in a U.S.-based Phase 1b clinical trial.

CONTROL ID: 3712323

SUBMITTER (NAME ONLY): Tara Tovar-Vidales

TITLE: Transcriptome Profiling of TGFβ2 Treated Human Optic Nerve Head Astrocytes and Lamina Cribrosa Cells

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Tovar-Vidales, N. Lopez, R. Rangan, North Texas Eye Research Institute, Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, TX, US, academic/health, Fort Worth, Texas, UNITED STATES|Z. Zhou, Department of Biostatistics and Epidemiology, University of North Texas Health Science Center, Fort Worth, TX, US, academic/health, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optic nerve head (ONH) is the initial site of optic nerve damage. ONH-derived astrocytes and lamina cribrosa (LC) cells synthesize proteins to support the ONH. However, ONH cells are adversely affected in glaucoma and cause detrimental changes to the ONH. Previous studies have shown increased expression of the profibrotic cytokine transforming growth factor-beta 2 (TGFβ2) in the glaucomatous ONH. In glaucoma conditions, TGFβ2 promotes dysregulated signaling through the canonical and non-canonical pathways. The purpose of this study was to determine the differential gene expression profile between control and TGFβ2 treated ONH astrocytes and LC cells using RNA sequencing (RNA-seq).

Methods: Primary human normal ONH astrocytes (n=3 strains) and LC cells (n=3 strains) were derived from human donor eyes. ONH cells were grown to confluency and treated with or without TGFβ2 (5ng/ml) for 24 hours. Total RNA was extracted from ONH cells and RNA sequence libraries were prepared and sequenced on an Illumina Miseq2000. RNA seq analysis was performed to identify significant differentially expressed genes and was tested for pathway enrichment analysis using WEB-based Gene SeT anaLysis Toolkit.

Results: RNA-seq and pathway analysis identified several significant enriched gene sets (FDR<0.05) for ONH astrocytes and LC cells. These differential expressed genes were involved in the extracellular matrix and ECM structural constituents such as disintegrin and metalloprotease family members, collagens, and periostin. Other gene sets included metabolism and steroid hormone biosynthesis such as alcohol dehydrogenase, aldehyde dehydrogenase, and cytochrome P450.

Conclusions: TGFβ2 modulates the expression of several genes in cultured human ONH astrocytes and LC cells that may be responsible for pathogenic remodeling of the optic nerve head in glaucoma. New therapeutic targets or small molecule inhibitors may be identified that stop or slow the pathogenesis of glaucoma.

CONTROL ID: 3712326

SUBMITTER (NAME ONLY): Jendayi Dixon

TITLE: Selectively disrupting connexin-36 in rod photoreceptor cells alters light adaptation in photopic ERG amplitude

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Dixon, S. Modgil, S. Zhang, P. Iuvone, Ophthalmology, Vision Science, Emory University, Atlanta, Georgia, UNITED STATES|C. Ribelayga, Vision Sciences, University of Houston System, Houston, Texas, UNITED STATES|S. Zhang, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: When presented with a rod saturating background light, photopic ERG flash response amplitudes gradually increase as a function of time. This light-adapted response is disrupted when connexin-36 (Cx36) is knocked out in cone photoreceptors with b-wave amplitudes at a maximal level as soon as the background light is applied (Zhang et al., IOVS 2020;61(6)24). It is unknown if this response is due to eliminating cone-cone gap junctions or rod-cone gap junctions. To answer this question, we investigated the response to rod-specific disruption of Gjd2, the gene that encodes Cx36.

Methods: Mice of either sex aged 90 to 120 days were entrained to a 12h light/12h dark cycle. Three genotypes of mice were studied: Rho-iCre75; $Gjd2^{fl/fl}$ (rod-Cx36KO); $Gjd2^{fl/fl}$ (Cre-negative control); Rho-iCre75 mice with no floxed allele. Scotopic and photopic ERGs were recorded as described in Zhang et al. (2020) at mid-subjective night following dark adaptation. Optomotor responses were recorded under photopic conditions to assess visual acuity (spatial frequency threshold) and contrast sensitivity.

Results: There were no significant differences in scotopic ERG a-wave or b-wave amplitudes between rod-Cx36KO mice and controls (Rho-iCre and $Gjd2^{fl/fl}$ mice). The photopic b-wave amplitude of rod-Cx36KO mice was significantly higher than that of both control groups at all light-adaptation times ($p<0.01$). In contrast to the gradual increase in photopic b-wave amplitude of the control groups as a function of light-adaptation time, in the rod-Cx36KO mice, there was an immediate and constant increase in amplitude with little or no change over time. There was no significant difference in contrast sensitivity nor visual acuity between the groups ($p=0.06$ and $p=0.83$, respectively).

Conclusions: Our results show that mice with rod specific disruption of Cx36 appeared to enter a fully light adapted state immediately after the introduction of background light, which phenocopies the results observed in cone-specific Cx36KO mice. Thus, rod-cone gap junctions, rather than cone-cone gap junctions, regulate the photopic ERG light-adaptive response.

CONTROL ID: 3712327

SUBMITTER (NAME ONLY): Manpreet Johal

TITLE: Can SLT safely delay surgery in presurgical primary open angle glaucoma?

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Johal, H. Hamze, S. Sharma, A. Mohite, Ophthalmology, New Cross Hospital, Wolverhampton, Wolverhampton, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Selective laser trabeculoplasty (SLT) has been widely used as both a primary and adjunct treatment in glaucoma. Glaucoma surgery was significantly affected during the Covid-19 pandemic due to reduced theatre and clinic capacity. We looked at SLT as a temporary alternative to safely delay surgical intervention in presurgical primary open angle glaucoma (POAG).

Methods: This is a retrospective study that included 104 patients who had a diagnosis of POAG and received SLT treatment, with at least 1 year follow-up. Primary outcomes included: reduction in intraocular pressure (IOP), and number of glaucoma medications (NGM). The endpoint was defined as time to be listed for glaucoma surgery. All eyes that had progressive or advanced visual fields and were on 2 or more medications were included. Eyes with previous glaucoma filtration surgery or argon laser trabeculoplasty, diagnosed with normal tension glaucoma or that had significant angle closure disease (peripheral anterior synechiae >180) were excluded.

Results: The mean patient age was 73.4 ± years. At baseline, the mean IOP and NGM were 20.5 ± 4.9 and 2.8 ± 0.9 mmHg, respectively. At 12 months, the mean IOP was 16.5 ± 3.3 mmHg and the NGM was 2.7 ± 1.0. The IOP reduction was 3.7 ± 5.8 mmHg (14.5%, $p<0.01$) at 12 months follow-up, 3.4 ± 4.7 mmHg (15.5%, $p<0.01$) at 24 months follow-up, 3.7 ± 5.2mmHg (15.2%, $p<0.01$) at 36 months follow-up and 2.5 ± 5.9 mmHg (10.1%, $p=0.04$) at 48 months follow-up. No surgical intervention was needed in 96% of eyes within the first year of SLT. There was no significant difference in the NGM pre- and post- SLT.

Conclusions: With the current pandemic limiting the surgical capacities of eye hospitals, SLT can safely delay the need for glaucoma surgery for at least 1 year by reducing the IOP. This is particularly apparent in elderly patients or those poorly compliant to medical therapy. In addition, this could increase ophthalmology clinic capacity by reducing the number of post-operative follow ups.

CONTROL ID: 3712328

SUBMITTER (NAME ONLY): Uttio Roy Chowdhury

TITLE: Effect of the ATP-sensitive potassium channel opener diazoxide on retinal vessel diameter of C57BL/6J mice

SESSION TITLE: Blood flow and ischemia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Roy Chowdhury, M.P. Fautsch, Ophthalmology, Mayo Foundation for Medical Education and Research, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: ATP-sensitive potassium (K_{ATP}) channel openers (e.g., diazoxide) are known to increase blood flow in various non-ocular organ systems through vasodilation. K_{ATP} channel openers can also lower IOP, presumably by increasing aqueous humor outflow through the episcleral venous system. To determine if diazoxide could influence the retina vasculature, we evaluated retinal vessel diameter (RVD) in vivo.

Methods: RVD was measured by fluorescein angiography. Fundus images of retina from C57BL/6J mice treated intravitreally (single treatment, n=5) or topically once daily for 7 consecutive days (n=5) with diazoxide (5 mM) or vehicle, were captured by Phoenix Micron IV OCT. Predetermined retinal vessels were each measured at three separate locations in all retinas and averaged to obtain mean vessel diameter per retina. Imaging was performed in anesthetized mice at 15 min post treatment for intravitreal group and at 1 h and 23 h after the last topical treatment (day 7). Post treatment RVD was measured at 7 days after termination of diazoxide treatment in the topically-applied group.

Results: RVD increased by 30.0 ± 7.1% (n=5, $p<0.001$) from baseline, within 15 minutes of intravitreal diazoxide injection, while injection with vehicle caused no significant change (-4.1 ± 4.0%, n=5, p=0.07). When diazoxide was applied topically once daily for 7 days, RVD at 1 h after day 7 treatment was 20.0 ± 10.7% (n=5, p=0.007) greater than baseline values, with no change observed in vehicle treated eyes (-0.4 ± 3.2%, n=5, p=0.84). At 23 h after the Day 7 dose, RVD was 19.0 ± 5.2% (n=5, $p<0.001$) greater than baseline values with no significant change in the vehicle treated eyes (1.7 ± 1.6 %, n=5, p=0.07). Seven days following the last topical treatment, RVD returned to baseline levels (1.7 ± 3.5%, n=2, p=0.66).

Conclusions: Treatment with diazoxide causes dilation of retinal vessels and may influence blood flow to this region. This may have beneficial effects for some retinal pathologies.

CONTROL ID: 3712329

SUBMITTER (NAME ONLY): Andrew Santos

TITLE: Evaluating a Custom Targeted-Sequencing Panel for FEVR to Identify NDP Gene Variants

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Santos, W.A. Dailey, K.P. Mitton, Eye Research Institute, Rochester, Michigan, UNITED STATES|A. Santos, K.P. Mitton, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|K.A. Drenser, Associated Retinal Consultants LLC, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To confirm the usefulness of a novel orphan pediatric retinal disease panel for detecting variants in the NDP (Norrie Disease Protein) gene. Familial Exudative Vitreo Retinopathy (FEVR) and Norrie Disease (ND) can be caused by variants of the NDP gene (Norrin). A cohort of 76 subjects diagnosed with FEVR/ND and close relatives were sequenced using a custom Ampliseq panel that includes NDP and seven other genes linked to FEVR/ND and Retinoschisis (CTNNB1, TSPAN12, KIF11, FZD4, LRP5, ZNF408, RS1).

Methods: A custom Ampliseq targeted panel (180 amplicons) for 8 genes was designed with Illumina's DesignStudio Sequencing Assay Designer. The targeted panel was distributed into three pools (PCR reactions) per patient sample for complete coverage of 83 exons with 25 bp adjacent intron sequence. Target Genes were: NDP (ChrX), RS1 (Chr10); CTNNB1 (Chr3); TSPAN12 (Chr7); KIF11 (Chr10), FZD4 (Chr11), LRP5 (Chr11), and ZNF408 (Chr11). Ampliseq libraries were quality controlled by capillary electrophoresis and sequenced on the Illumina iSeq-100 platform at a scale of up to 50 samples per run. Variant impacts and allele frequency data were determined from ClinVar and The Genome Aggregation Databases (gnomAD).

Results: A total of 33 protein-altering variants were found in six FEVR/ND-related genes. Of note, 1/33 (3%) of the variants was present in the NDP gene. This patient was heterozygous for the NDP: His42Arg variant, pathogenic for ND. This mutation was found in a patient with a clinical FEVR grade of 4, indicating the diagnosis being ND rather than FEVR. The sequencing data revealed 95.5% of the base reads were > Q30 quality, the percent on-target bases passing filer was 92.2%, and the average sequencing depth coverage was 978.

Conclusions:

The custom Ampliseq targeted-sequencing Orphan Pediatric Retinal Disease panel was developed with the intention to detect genes associated with FEVR/ND and Retinoschisis. The panel's sequencing coverage was of sufficient depth to detect protein-altering variants in the NDP gene, the primary gene for ND.

CONTROL ID: 3712330

SUBMITTER (NAME ONLY): Ashley Nies

TITLE: Successful AAV2 readministration to porcine retinal ganglion cells and serum neutralizing antibody response

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nies, K. Heng, B. Li, R. Wen, A.Y. Wu, J.L. Goldberg, Byers Eye Institute, Spencer Center for Vision Research, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adeno-associated virus serotype 2 (AAV2) is a promising gene therapy platform for glaucoma and other optic neuropathies. However, pre-existing serum neutralizing antibodies (Nab) may significantly inhibit effective transduction and gene transfer. To investigate the effects of serum Nab on viral transduction in a large animal model, we delivered AAV2 to retinal ganglion cells (RGCs) in the porcine visual system at two timepoints and assessed transduction while monitoring serum Nab over time.

Methods: Yucatan minipigs (5.5-6 months old) were pre-screened for serum Nab titers, and animals with a positive titer were excluded. On day 0, AAV2-CMV-eGFP was intravitreally injected into the nasal and temporal aspects of the right eye, while the left eye served as a negative control. On day 14, the right eye was re-injected with AAV2-CAG-TdTomato in a similar fashion. On day 28, eyes were harvested and fixed in 4% PFA. The retinas were dissected, stained by immunofluorescence for RBPMS, flatmounted, imaged by confocal microscopy, and analyzed. To determine Nab titers, pig serum was collected on days 0, 3, 7, 14, and 28. Serial dilutions of pig serum were incubated with AAV2-Luciferase and subsequently with human embryonic kidney (HEK293) cells. Luciferase activity was measured and used to establish anti-AAV2 Nab titers.

Results: RGCs were transduced by viral administrations at both timepoints (AAV2-CMV-eGFP, day 0; AAV2-CAG-TdTomato, day 14) as evidenced by colocalization of eGFP and TdTomato with RBPMS immunofluorescence. In the negative control eye, the absence of eGFP and TdTomato expression was confirmed. Transduction efficiency was highest at the temporal and nasal retina near injection sites. Serum anti-AAV2 Nab levels increased over time beginning at day 7.

Conclusions: AAV2 can be successfully readministered over a short interval to porcine RGCs despite systemic production of anti-AAV2 Nab. Nab were produced in response to AAV2 exposure and increased over the study time course.

CONTROL ID: 3712331

SUBMITTER (NAME ONLY): Norianne Ingram

TITLE: Non-classical center-surround antagonism in the retina controls spatial and temporal filtering in scotopic light

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Ingram, F. Rieke, Physiology and Biophysics, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Norianne Ingram: Commercial Relationship: Code N (No Commercial Relationship) | Fred Rieke: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Center-surround antagonism(CSA) alters retinal ganglion cell(RGC) sampling of spatial inputs in bright light conditions but has appeared to be absent in scotopic light. While we confirm classical CSA in primate retina, we also observed non-classical effects due to surround input in dim light. Here, we investigated the non-classical spatial and temporal filtering properties of RGCs in dim light and probed the potential mechanisms mediating surround-dependent effects.

Methods: Electrophysiological recordings were made from ON parasol RGCs in RPE-attached, flat-mounted macaque retinas. RGCs were stimulated with spatially- and temporally-defined patterns with scotopic to low-photopic light. CSA was probed using spot-annulus stimuli to independently control the stimulation of the center vs surround. Short contrast steps and noise sequences were used to explore the temporal dependence on surround inhibition.

Results: Classic CSA was confirmed in RGC spatial receptive fields in mesopic and photopic conditions and was absent in scotopic conditions. Despite this, the center dimensions continued to narrow as background intensity increased. Pharmacology confirmed that the decreases in center persist without horizontal cell feedback. Subunits were also substantially larger in dim light and narrowed with increasing intensity. The time required for the receptive field to stabilize after the light was increased from 0.1 to 10 R^*/rod/s was ~30s. We found that surround activation shaped the kinetics of RGC responses in dim light. The responses to contrast steps and the noise-derived linear filters reached a peak more quickly when surrounds were illuminated. We simulated the responses to the steps by convolving the appropriate linear filter with the step stimulus. The predicted responses showed most of the surround-dependent differences in the time to peak of the recorded waveforms, but they did not fully explain the transience of the response following step onset.

Conclusions: CSA mechanisms drive temporal and spatial filtering in dim light. Alterations in kinetics are particularly notable in dim light since rod photoreceptor signaling is notoriously slow, providing ample opportunity for significant temporal filtering in downstream circuits. Modulation of inputs in the spatial and temporal domains are likely to determine threshold sensitivity for complex tasks like motion detection in dim light.

CONTROL ID: 3712333

SUBMITTER (NAME ONLY): Norberto Lopez-Gil

TITLE: THE USE OF SMARTPHONES FOR THE COLLECTION OF DIGITAL HABITS BIG DATA AND ITS CORRELATION WITH CLINICAL REFRACTION IN A UNIVERSITY POPULATION

SESSION TITLE: Machine Learning and Big Data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Lopez-Gil, R. Salmerón-Campillo, M. Jaskulski, Universidad de Murcia, Murcia, Murcia, SPAIN|A. Gonzalez-Diaz, D. Zarzoso-Fernandez, D. Aparicio, CNRS. Aix-Marseille Université, Marseille, FRANCE|

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ABSTRACT BODY:

Purpose: Recent studies justify the rise of late onset myopia in young people due to unhealthy digital habits (too much near work time, too near face-device distance, too low ambient illumination). University students are an especially vulnerable group due to the high volume of near vision tasks they normally perform in indoor illumination conditions. We performed a study to collect objective digital habits data in a university population and investigate their potential correlation with clinical subjective refraction.

Methods: 70 subjects aged 21±3 years, in their first or second year of university completed a clinical optometric examination, and used their own personal smartphones to install an app that continuously (at 1 Hz) measured their digital habits: face-device distance, ambient light level, daily screen time (measured only while looking at the screen); daily number of times the device was looked at (minimum interval between events of 20”. A statistical inference analysis was performed to know the relation between digital habits and the spherical equivalent of their refraction (SER), axial length (AL), and smartphone reading distance (SRD).

Results: A total of 60M of data points corresponding to 15M seconds, with at least 3600 s of data per subject, were obtained. Average daily screen time was 1.4±1.2h, with a maximum of 6.2 h, while the daily number of times the device was looked at was 74±59. The average intersubject face-device distance was 363±56 mm, while the SRD was significantly, ($p<10^{10}$) smaller, 296±59 mm. Mean+SD illuminance was 311±225 lux. The mean standard deviation of the intrasubject distance was 83 mm and illuminance was 714 lux. Lower SER values (larger myopia) and larger AL values correspond to a nearer face-device distance of lower ambient illumination, but the correlation was very weak ($R^2<0.03$).

Conclusions: Face-device distance and ambient illumination varied among subjects but also within the individual subjects’ data, indicating that a continuous measurement is needed to sample and estimate the real accommodating effort and illuminance. Within the context of the cohort size and study duration it was not possible to predict a strong correlation between SER or AL, with high variability in the digital habits data between subjects. A longitudinal study of several years would be needed to learn the effects of digital habits on myopia.

CONTROL ID: 3712334

SUBMITTER (NAME ONLY): Cezary Rydz

TITLE: “Aging mouse: functional vision decline and related molecular changes”

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Rydz, Q. Xu, V. Mai, D. Skowronska-Krawczyk, Department of Physiology and Biophysics, Center for Translational Vision Research, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|D. Lyon, Department of Anatomy and Neurobiology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A. Foik, International Centre for Translational Eye Research, Institute of Physical Chemistry, Polska Akademia Nauk, Warszawa, Mazowieckie, POLAND|

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ABSTRACT BODY:

Purpose: Aging leads to visual deterioration. Little is known about the molecular changes correlated with vision decline. Heterogeneity of retinal layers creates a challenge for isolated assessment. We aimed to identify age-related functional decline in mouse vision and examine aging impact at the molecular level.

Methods: Visual function was tested in 3-month and 18-month old mice using a comprehensive approach: 1.Visual acuity was assessed with Optomotor response (OMR) assay. 2.Rod and cone photoreceptor function was measured with scotopic and photopic electroretinography (ERG). 3.Visual system physiology was tested by performing recordings of Visually Evoked Potentials (VEPs). 4.RGC activity was assessed with recording of pattern ERG (PERG). For molecular analysis, the bulk RNAseq was performed. Gene set enrichment analysis was applied for differential expression comparisons between two groups of RNA-Seq samples.

Results: Optomotor response and ERG responses were significantly decreased in 18 month old animals in both scotopic and photopic conditions in comparison to 3-month old animals (p-value<0.0001). We observed a significant reduction of VEPs amplitudes recorded in the superior colliculus and the primary visual cortex. Interestingly pattern ERG recordings showed no statistical significance between young and old animals. Analysis of molecular changes revealed 1451 genes up-regulated (log2 fold>=1, FDR<0.05) and 2394 genes down-regulated (log2 fold<=-1, FDR<0.05) upon natural aging. Upregulated pathways in aged animals included inflammation, TNFa signaling and apoptosis. Downregulated pathways included DNA repair and fatty acid metabolism pathways.

Conclusions: Aging leads to a reduction in vision in mice. Significant decrease in photoreceptor function measured by ERG is coherent with behavioral measurements (OMR). Visual information processing is affected by aging; however, RGC function is preserved in old mice. The analysis of age-related molecular changes reveals transcriptional pathways impacted in aged retinas. Connecting functional and molecular approaches will lead to a better understanding of age-related diseases and may lead to novel therapies in the future.

CONTROL ID: 3712336

SUBMITTER (NAME ONLY): Yukun Guo

TITLE: A Deep Learning-based Method for Retinal Layer and Drusen Segmentation on Optical Coherence Tomography

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Guo, T. Hormel, M. Gao, T.S. Hwang, S.T. Bailey, Y. Jia, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To train and validate a convolutional neural network (CNN) to segment retinal anatomic layers and drusen in age-related macular degeneration (AMD) on volumetric optical coherence tomography (OCT) and quantify drusen area.

Methods: Study participants with non-exudative AMD were enrolled and underwent 6x6-mm central OCT scans on one eye with a 70-kHz commercial system (RTVue-XR Avanti; Optove, Inc.) A deep CNN takes OCT B-scans as input and outputs retinal layer boundaries (ILM, NFL/GCL, IPL/INL, INL/OPL, OPL/ONL, EZ, and RPE/BM. ILM - Inner limiting membrane; NFL – Nerve fiber layer; GCL – Gangling cell layer; IPL – inner plexiform layer; INL – inner nuclear layer; OPL – outer plexiform layer; ONL – outer nuclear layer; EZ – Ellipsoid Zone; RPE – retinal pigment epithelium; BM – Bruch's Membrane) [Fig. 1B]. In addition, a hybrid CNN [Fig. 1 G, H], which combines 3D and 2D convolutional layers to segment drusen, takes the thickness map, the minimum en face projection, and the volume data of the RPE slab as inputs and outputs the drusen distribution map. Image graders (Y.G., M.G.) manually graded the ground truth for these networks based on the B-scans and en face images. Five-fold cross-validation was used to evaluate our method on the entire dataset.

Results: We included 120 participants: 82 with nonexudative AMD and 38 healthy eyes. On the test sets, the networked achieved average Dice coefficients of 0.92 ±0.05 (mean±standard deviation) and 0.78±0.15 on the retinal layer and drusen segmentation, respectively. Since the network achieves accuracy in both of these tasks it represents an end-to-end approach and eliminates the need for graders to make subjective processing decisions such as manual correction of retinal layer boundaries. The proposed method showed high accuracy, even on small drusen [Fig.2, blue arrow] and did not produce false drusen segmentation in healthy eyes.

Conclusions: A CNN can accurately segment seven retinal layers and quantify drusen in nonexudative AMD eyes on volumetric OCT scans.

CONTROL ID: 3712337

SUBMITTER (NAME ONLY): Sophia Lam

TITLE: Clinical outcomes of retinal arterial macroaneurysms with vitreous hemorrhage managed with observation versus anti-VEGF versus pars plana vitrectomy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Lam, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|A. Shahlaee, M. Salabati, M. Klufas, Mid Atlantic Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the clinical outcomes of retinal arterial macroaneurysm (RAM) with vitreous hemorrhage (VH).

Methods: Retrospective analysis of eyes with RAM and VH seen between July 2013 and October 2021. Clinical and demographic data were reviewed including best corrected Snellen visual acuity (BCVA), treatment, comorbidities, and anticoagulation use. Treatment options included observation, intravitreal anti-VEGF injections (IVI), and pars plana vitrectomy (PPV). Patients with other retinal vascular pathologies requiring treatment were excluded.

Results: Of 50 eligible eyes analyzed, 33 underwent observation, 5 received IVI, and 12 underwent PPV. The mean number of injections in IVI group was 3.6±2.8 (range, 1-8). In IVI group, 100% were treated with bevacizumab. The incidence of subretinal hemorrhage was 18.2% in observation group, 25.0% in surgery group of which 8.3% had treatment with subretinal TPA, and 60.0% in IVI group. The mean time to intervention was 13±15.3 days for PPV and 38±69.9 days for IVI. There was no significant difference in age, gender, lens status, final BCVA, and duration of follow-up between the three groups (Table 1). All eyes showed a significant improvement in BCVA, but IVI and PPV groups had worse presenting BCVA and greater visual improvements compared to the observation group. There was no correlation between the number of injections and final BCVA (r=0.13, p=0.83). IVI and PPV groups used significantly more anticoagulants than observation group. However, there was no significant difference in final BCVA between patients using anticoagulant agents (0.52±0.53, Snellen 20/68) compared to those who were not (0.55±0.65, Snellen 20/71, p= 0.87).

Conclusions: Patients with RAM and VH are elderly and demonstrated significantly improved BCVA from baseline in all treatment groups and similar final visual outcomes. Improved BCVA was not impacted by the number of injections or anticoagulant use, suggesting that these factors may play a less important role in the treatment of RAM with VH.

CONTROL ID: 3712338

SUBMITTER (NAME ONLY): Kirk Stephenson

TITLE: Clinical and Genetic Re-Evaluation of Inherited Retinal Degeneration Pedigrees Following Initial Negative Findings on Panel-Based Next Generation Sequencing

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.A. Stephenson, J. Zhu, T. Burke, J. Turner, J.J. O'Byrne, D.J. Keegan, Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|A. Dockery, Next Generation Sequencing Laboratory, Mater Misericordiae University Hospital, Dublin, IRELAND|L. Whelan, G. Farrar, The School of Genetics & Microbiology, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Inherited retinal degenerations (IRDs) are the primary cause of working age blind registration in Western countries. These rare disease are genetically heterogeneous (>300 known genetic loci) and genetic diagnosis is required for many novel therapies (e.g., gene therapy). First-tier genetic testing of IRDs with panel-based next generation sequencing (pNGS) has a diagnostic yield of ~70-80% leaving the remaining more challenging cases to be resolved by second-tier testing methods.

Methods: Patients on a large hospital-based IRD register in Ireland were clinically and genetically assessed. 84% of this cohort was genetically resolved from 1st tier pNGS (250 genes). Non-resolved cases (n=69) were clinically reassessed with 26% (n=18) being reclassified as non-IRD disease. 34 patients were available for further genetic testing, all providing informed consent. Autosomal recessive cases with 1 candidate variant underwent single gene testing (introns and exons). Cases with inadequate pNGS coverage had repeat pNGS (250 genes) while those with adequate initial panel coverage had an expanded panel (351 genes) or trio whole exome sequencing (WES).

Results: Removing non-IRD cases from consideration and utilizing case-appropriate 2nd-tier genetic testing techniques, we genetically resolved 56% of previously unresolved pedigrees bringing the overall resolve rate to 92% (388/423). Resolution rate by test was pNGS 100% (n=5), single gene test 44% (n=4/9), trio WES 25% (1/4). 4 novel variants were found, 1 each in ABCA4, EYS, FLVCR1, and RPGR . 15.6% of the cohort resolved by 2nd line testing approaches are eligible for current gene therapy clinical trials (RPGR).

Conclusions: Though novel techniques like WGS will supersede current techniques, at present pNGS remains the most cost effective first-tier approach for molecular assessment of diverse IRD populations (€600 for NGS vs mean €1,222 for all other test types per positive result). Second-tier genetic testing should be guided by clinical (i.e., reassessment, multimodal imaging, electrophysiology) and genetic (i.e. single alleles in autosomal recessive disease) indications to achieve a genetic diagnosis in the most cost-effective manner. See Figure 1.

CONTROL ID: 3712339

SUBMITTER (NAME ONLY): Sandrine Joly

TITLE: Characterization of visual deficits in B cell-dependent experimental autoimmune encephalomyelitis: an improved mouse model of multiple sclerosis?

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Joly, J.B. Mdzomba, L. Rodriguez, V. Pernet, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|S. Joly, Ophthalmology, Inselspital Universitatsspital Bern, Bern, Bern, SWITZERLAND|J.B. Mdzomba, V. Pernet, Inselspital Universitatsspital Bern Universitatsklinik fur Neurologie, Bern, Bern, SWITZERLAND|F. Morin, L. Vallières, Neuroscience Unit, University Hospital Center of Quebec, Universite Laval, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: To study the visual impairments associated with multiple sclerosis (MS), experimental autoimmune encephalomyelitis (EAE) is a standard animal model induced by immunizing mice with myelin oligodendrocyte glycoprotein peptide (MOG_{35-55}). However, this form of EAE idoes not involve B cells, in contrast to MS. The present study aimed to characterize the visual symptoms in a B cell-dependent EAE to better mimic human MS.

Methods: B cell-dependent EAE was induced with an antigen called bMOG. After the induction of EAE with bMOG in C57BL/6J male mice, changes in visual function were followed by electroretinography and optomotor acuity tests. Motor deficits were monitored in parallel with a standard clinical scoring method. Retinal neuron survival, gliosis, microglia activation, optic nerve demyelination and opsin expression were examined by histological and Western blot analyses. Gene expression changes were determined by RNA sequencing.

Results: bMOG EAE mice showed persistent loss of visual acuity. In contrast, the electroretinogram (ERG) and the motor function spontaneously recovered after deficits culminating in the inflammatory disease phase. Visual acuity loss was associated with retinal inflammation, gliosis and synaptic impairments, as suggested by histological observations and transcriptomic results. Interestingly, chromatic ERG recordings revealed significant alterations in the M-cone pathway.

Conclusions: The visual changes induced by bMOG in mice present similarities to those reported in multiple sclerosis and neuromyelitis optica. Therefore, bMOG EAE offers a new model to test experimental treatments for MS in the visual system.

CONTROL ID: 3712341

SUBMITTER (NAME ONLY): Alireza Karimi

TITLE: Biomechanics of Human Trabecular Meshwork in Healthy and Glaucoma Eyes via Dynamic Schlemm's Canal Pressurization

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To explore poorly understood mechanisms that maintain IOP within a normal range. The trabecular meshwork (TM) consists of ECM embedded with collagen and elastin fibers and studies have shown that TM stiffness is considerably higher in glaucoma eyes. Emerging data indicates that the TM moves dynamically with transient IOP fluctuations, resulting in dynamic aqueous outflow. Soft biological tissues exhibit time-dependent/viscoelastic behavior under dynamic loading, but little is known about time-dependent TM behavior. We calculated the viscoelastic mechanical properties of the TM in n=2 healthy and n=2 glaucoma eyes obtained within 72 hours postmortem.

Methods: A quadrant of the anterior segment was mounted and submerged in a saline bath inside a pressure chamber to maintain 4 mmHg simulated episcleral venous pressure. A cannula connected to an adjustable saline reservoir was inserted into one end of Schlemm's canal (SC), with the other end open. A series of cross-sectional scans of the TM/SC complex were captured at 30 frames/second at two locations in each eye during pressure oscillation from 0 to 30 mmHg. A segmentation program delineated the TM boundaries in the OCT images to construct a 20-μm-thick volume finite element (FE) mesh of the TM/SC complex. Collagen and elastin fibrils were embedded in the model using our mesh-free penalty-based cable-in-solid algorithm (Fig). A pre-tension in the collagen and elastin fibrils and a pre-stress in the ECM of the TM were induced to mimic ciliary muscle contraction at the relaxed stage. The model was subjected to a normal optimized pressure function from 0 to 30 mmHg from the SC and the other boundaries were subjected to floating boundary conditions. An FE optimization algorithm was used to adjust the ECM/fiber mechanical properties such that TM/SC model and OCT imaging data best matched over time.

Results: Significantly higher short- and long-time ECM shear moduli, and collagen and elastin fibril elastic moduli, were present in the glaucoma eye TM compared to normal controls ($p<0.05$). The external region of the TM in glaucoma eyes (Fig) showed lower stresses versus the internal region.

Conclusions: Mechanical alterations are challenging to monitor clinically. We characterized the alterations in ex vivo healthy and glaucoma eyes. Our findings may contribute to enhanced understanding of glaucoma pathophysiology, diagnosis, and treatment.

CONTROL ID: 3712342

SUBMITTER (NAME ONLY): FULYA YAYLACIOGLU TUNCAY

TITLE: Practice Patterns and Needs Assessment of Ophthalmologists for Inherited Eye Diseases: Do we need a subspecialty as Ophthalmic Genetics?

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. YAYLACIOGLU TUNCAY, Medical Biology, Saglik Bilimleri Universitesi Gulhane Tip Fakultesi, Ankara, TURKEY|F. YAYLACIOGLU TUNCAY, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|E. KARAISMAILOGLU, Medical Informatics, Saglik Bilimleri Universitesi Gulhane Tip Fakultesi, Ankara, TURKEY|S. OZDEK, Ophthalmology, Gazi Universitesi Tip Fakultesi, Ankara, Ankara, TURKEY|

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ABSTRACT BODY:

Purpose: To evaluate the current practices, knowledge and needs of ophthalmologist at various clinical settings in Turkey regarding inherited eye diseases. Also, we aimed to understand the need for a subspecialty of ophthalmic genetics in a country where the rate of consanguinity and inherited eye diseases is higher.

Methods: A 29-question self-administered survey with branching algorithm was developed through Google forms and the survey link was sent to 2983 ophthalmologists practicing at various clinical settings in Turkey during February to June 2021. The survey assessed participants' occupational characteristics, current practices and preferences, knowledge about available diagnostic and therapeutic options, proposals to improve continuing education and healthcare services related to the inherited eye diseases.

Results: 414 (20.8%) ophthalmologists completed the survey, 236 of which (57%) were specialist, 178 (43%) were academic faculty. Of the respondents, 107 (25.9%) were in private practice, 71 (17.1%) in state hospitals, 129 (31.2%) in training and research hospitals, and 107 (25.8%) in university hospitals. 192 (46.4%) respondents were general ophthalmologists and 222 (53.6%) were subspecialist. Only 43.2 % of ophthalmologists reported presence of medical geneticist in their facility. Majority of the respondents reported being uninformed about genetic diagnostic tests (82.4%), available genetic tests in or near their facility (78.5%), and which genetic diagnostic tests were covered by health insurance system (93%). There was statistically significant difference in responses about management strategies of inherited eye diseases between subgroups with respect to affiliation ($p<0.05$, Table 1). Nearly 90% of ophthalmologists thought that training after residency was inadequate and 94% expressed the need for a subspecialty of ophthalmic genetics.

Conclusions: In the current era of next-generation genetic diagnostic tests and gene therapies, practice patterns and needs of ophthalmologists were revealed for the first time in a setting of higher disease rates due to consanguinity and fewer specialists interested in inherited eye diseases.

CONTROL ID: 3712343

SUBMITTER (NAME ONLY): Sanjay Kubsad

TITLE: Determining Patient Preferences at an Academic Ophthalmology Clinic: a Discrete Choice Experiment

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kubsad, A. Chen, Department of Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Sanjay Kubsad: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Eliciting patient perspectives can help inform in the design and improvement of an ophthalmology service to provide care that is respectful of and responsive to individual patient preferences, needs, and values. A discrete choice experiment is a survey technique where scenarios are presented for respondents to make trade-offs between two attributes by weighing the relative importance of each.

Methods: This study evaluated patient preferences at two academic ophthalmology clinics in Seattle, Washington. A discrete choice experiment was used to evaluate the relative importance of the following variables: out-of-pocket costs, expertise, wait times, appointment numbers, face-to-face times, and continuity of care. Forty-three patients were recruited from two ophthalmology clinics. Demographic data was collected. Patients were asked to rank the importance of each variable for their care. Additionally, eight choice-tasks were presented in random order and forced-choice preferences were elicited. The survey was translated into Spanish by the Harborview Interpreter Services, and telephonic or in-person interpreters were used when necessary. Ranked data was visualized. Choice data were analyzed using a binomial sign test.

Results: The relative importance of one attribute to another was measured first via a self-rank of attributes and second a discrete-choice questionnaire. Patients showed a wide variety of preferences across the different attributes. A self-ranking of attributes revealed high preferences for improved continuity of care, increased physician experience and increased face to face time. Discrete choice testing revealed that patients strongly preferred continuity of care ($P<0.05$). Face to face time was also the least preferred option when in conflict with other attributes ($P<0.05$).

Conclusions: Self-ranking and discrete-choice questionnaire matched in their evaluation of patient preferences for most attributes in terms of relative importance. In the latter, continuity of care was the most important attribute. Patients over-estimated the importance of face-to-face time with the provider when compared with a discrete-choice questionnaire evaluation. One limitation of this study was the small sample size. Future work with a larger study population could provide additional insight into attributes important for patient-centered care and help guide improvements to how care is delivered.

CONTROL ID: 3712344

SUBMITTER (NAME ONLY): Gabriella Guevara

TITLE: The Oculoplastic Selfie – is age a barrier to success?

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Guevara, H. Kandola, S. Kang, Adnexal, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Gabriella Guevara: Commercial Relationship: Code N (No Commercial Relationship) | Hardeep Kandola: Commercial Relationship: Code N (No Commercial Relationship) | Swan Kang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess if patients of all ages were able to submit self-generated photographs of presumed benign eyelid pathology. Still photographs supplement synchronous video consultations in the virtual oculoplastic clinic by providing superior resolution images to allow enhanced assessment of small eyelid lesions.

Methods: New patients referred with benign eyelid lesions were asked to submit self-captured photographs to a designated email inbox prior to a video consultation. Photographs for 300 consecutive patients between 29th April and 6th May 2021 were reviewed by two independent observers (GG and HK).

Each patient's submitted photographs were independently graded as either inadequate, adequate or excellent based on a previously agreed standard. Furthermore, observers also noted whether the images were adequately focussed and well lit.

Results: 300 patients submitted 895 photographs to the shared inbox in the time period. 57.3% (172) of participants were female and patient mean age was 42.5 years old (SD=16.37) ranging from 16 to 90. Mean number of photos submitted per patient was 2.98 (SD = 1.84) ranging from 1 to 15 images. 84.5% of photographs were graded as excellent (40.5%) or adequate (44.0%). There was no statistical difference in overall quality in different age groups (Chi Square test p-value = 0.79). There was also no statistically significant difference in ability to submit adequately focussed (Chi Square test p-value = 1.02) or well lit patients (Chi Square test p-value =0.78) among patients in different age groups. There was a weak correlation between age and number of photos submitted with younger patients more likely to submit a higher number (Pearson correlation -0.12 p = 0.03)

Conclusions: Age alone is not a barrier to successful patient generated photography of benign eyelid lesions. Quality improvement work is in progress to further improve image quality through patient education.

CONTROL ID: 3712345

SUBMITTER (NAME ONLY): Yvonne Adu-Agyeiwaah

TITLE: Oral administration of alpha-cyclodextrin reverses diabetic retinopathy in db/db mice

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Adu-Agyeiwaah, B. Asare-Bediako, M.D. DuPont, Vision Science Department, University of Alabama at Birmingham, School of Optometry, Birmingham, Alabama, UNITED STATES|S.S. Hammer, J.V. Busik, Deparment of Physiology, Michigan State University, East Lansing, Michigan, UNITED STATES|J. Floyd, The University of Alabama at Birmingham Department of Cell Developmental and Integrative Biology, Birmingham, Alabama, UNITED STATES|R. Prasad, S. Li Calzi, M.B. Grant, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|C.P. Vieira, Absorption Systems, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We hypothesized that high cholesterol levels leading to the formation of cholesterol crystals in the diabetic retina contribute to DR pathology and vision loss. Alpha-cyclodextrin, a cyclic oligosaccharide lowers cholesterol levels and improves atherosclerotic lesions. In this study, we investigated the effect of alpha-cyclodextrin on cholesterol crystals-induced retinal damage in DR.

Methods: Four-month-old db/db mice were given either oral alpha-cyclodextrin incorporated in their diet (21g/kg body weight) or a control diet. Mice were euthanized after 4 months of treatment. Measurement of Electroretinograms (ERG) and Optomotor kinetic (OKN) responses were undertaken to determine the retinal neural function and visual response respectively before euthanization. Eyes were collected for Scanning Electron Microscopy (SEM) and Immunohistochemistry for macroglia reactivity using Glial fibrillary acidic protein (GFAP).

Results: We observed the removal of cholesterol crystals from the retinas of diabetic mice with oral alpha-cyclodextrin treatment. GFAP reactivity was significantly reduced in the retinal macroglia cells of diabetic mice with oral alpha-cyclodextrin treatment (677.70 ± 204.51 vs 888.65 ± 218.29, $p<0.05$) compared to that of standard chow-fed diabetic mice. The a-wave in the ERG photopic response in alpha-cyclodextrin treated db/db mice was significantly improved compared to db/db mice (133.81 ± 20.58 vs 73.51 ± 36.6, $p<0.05$), and OKN responses were also improved in alpha-cyclodextrin treated db/db mice (0.41 ± 0.02 vs 0.37 ± 0.03, $p<0.05$) compared to the control diet treated db/db mice.

Conclusions: We demonstrate that cholesterol crystal-induced retinal pathology occurs in diabetes and contributes to DR which is improved by the use of oral alpha-cyclodextrin. We show that in addition to the reduction in retinal inflammation, treatment can preserve retinal neural cells, and subsequently retinal visual function and response can be restored using this therapy.

CONTROL ID: 3712347

SUBMITTER (NAME ONLY): Casey Keuthan

TITLE: Investigating the cell autonomous effects of NF1 mutation on human RGC development and survival

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Keuthan, S. Li, P. Zhang, C. Berlinicke, D.J. Zack, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|C. Anastasaki, D. Gutmann, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|Y. Zhu, Children's National Hospital, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Children with the cancer predisposition syndrome Neurofibromatosis type 1 (NF1) are prone to the development of optic pathway gliomas, where nearly 50% of affected individuals will exhibit vision deficits. These visual impairments are caused by axonal injury to, and potentially the eventual death of, retinal ganglion cells (RGCs), yet little is known how the NF1 gene/protein product, neurofibromin, contributes to RGC biology. This study was designed to investigate the effects that different NF1 mutations have on human RGC differentiation and survival.

Methods: Human iPSCs carrying various heterozygous (het) and homozygous (hom) NF1 mutations, and autologous control cells, were modified to contain a previously described BRN3B/tdTomato/Thy1.2 knock-in reporter/purification tag. NF1 wild-type (control) and mutant cells were then differentiated into 2D hRGC cultures and 3D retinal organoids using established protocols. Gene expression analysis was performed by qPCR and bulk RNAseq at time points throughout differentiation. Additionally, the differentiated hRGCs generated from the various NF1 mutant and control lines were purified and the effects of exogenous stressors on cell survival and neurite outgrowth were quantified by high-content image analysis.

Results: NF1 het iPSCs differentiated into tdTomato+ hRGCs similar to control lines, while NF1 hom cells differentiated with the same protocol showed reduced BRN3B/tdTomato/Thy1.2 reporter-expressing cells. Despite a decrease in pluripotency gene expression (e.g. POU5F1, NANOG) during 2D hRGC differentiation, NF1 hom iPSCs failed to express many early retinal development markers (e.g. LHX2, RAX, SIX3, SIX6). In preliminary attempts to differentiate NF1 cells into retinal organoids, NF1 mutant iPSCs successfully formed embryoid bodies, but some NF1 lines did not resemble control retinal organoids following neural induction. hRGCs differentiated from NF1 het lines were more sensitive to cell stressors, such as rotenone, in a mutation-specific manner.

Conclusions: NF1 mutant cell lines exhibit differences in RGC and retinal development, which are being further characterized. A high content screening approach, to identify compounds that can protect hRGCs from NF1-associated phenotypes, is currently underway. Together, this work provides a better understanding of potential cell autonomous mechanisms of NF1-associated vision loss.

CONTROL ID: 3712348

SUBMITTER (NAME ONLY): Suveera Dang

TITLE: Estimating Lifetime Risk of Retinal Disorders Among Patients with IBD Above Age 55 Years

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dang, H. Pakhchanian, P. Sohal, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|M. Dalal, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inflammatory bowel disease (IBD) is known to cause extraintestinal manifestations in at least a third of patients and is especially more common among the geriatric population. The purpose of this study is to estimate the lifetime risk of retinal disorders among patients with inflammatory bowel disease above the age of 55 years.

Methods: A retrospective cohort study was conducted using TriNetX (Cambridge, MA, USA), a federated research network composed of electronic medical records from over 80 million patients across 57 healthcare organizations. Individuals over the age of 55 with and without the diagnosis of inflammatory bowel disease (IBD) were identified using validated ICD-10 codes. Then, 1:1 propensity score matching (PSM) was utilized to create two same-sized cohorts balanced for comorbidities and demographics. After PSM, the lifetime outcomes of retinal disorders were compared with matched controls. A subgroup analysis was also conducted comparing Crohn's disease and Ulcerative Colitis.

Results: A total of 188,516 patients over the age of 55 were identified on TriNetX with a diagnosis of IBD. Subjects showed a statistically significant higher risk of having vitreous opacities (RR 2.01, 95% 1.86-2.18), puckering of macula (RR 1.78, 95% 1.63-1.95), macular degeneration (RR 1.64, 95% 1.56-1.73), retinal detachment or break (RR 1.53, 95% 1.37-1.7), cystoid macular degeneration (RR 1.53, 95% 1.30-1.80), retinal vascular occlusions (RR 1.46, 95% 1.28-1.65), central retinal vein occlusion (RR 1.45, 95% 1.14-1.84), retinal edema (RR 1.44, 95% 1.23-1.68), and vitreous hemorrhage (RR 1.26 95% 1.08-1.48) compared to controls. A subgroup analysis showed a statistically significant higher risk of vitreous hemorrhage (RR 1.32, 95% 1.03-1.69), puckering of macula (RR 1.18, 95% 1.04-1.34), and vitreous opacities (RR 1.15, 95% 1.03-1.28) in patients with Ulcerative Colitis compared to Crohn's Disease. Patients with Ulcerative Colitis were less likely to have retinal edema compared to Crohn's disease (RR 0.76, 95% 0.60-0.95).

Conclusions: Patients with IBD over the age of 55 years are at a significantly higher risk of developing retinal disorders compared to patients without IBD. Increased awareness of retinal disorders in this patient population could lead to improved patient care.

CONTROL ID: 3712349

SUBMITTER (NAME ONLY): Asad Durrani

TITLE: Risk factors for retinal detachment following open globe injury and outcomes of retinal detachment repair following ocular trauma

SESSION TITLE: Endophthalmitis & Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.F. Durrani, K. Li, Y. Zhou, P.Y. Zhao, M. Huvard, D.C. Musch, D.N. Zacks, Department of Ophthalmology and Visual Sciences, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|A. Toiv, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|D.C. Musch, Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report risk factors for retinal detachment (RD) following open globe injury (OGI) and the outcomes of RD repair following OGI.

Methods: Retrospective chart review of all OGI occurring between January 2000 and July 2017 at the University of Michigan. 587 eyes with OGI were surgically managed at our center with at least 30 days of follow-up. All eyes diagnosed with RD following open globe injury were included in this study. Multivariable regression was performed to identify risk factors for RD following open globe injury and predictors of poor vision following RD repair.

Results: 170/587 eyes (29.0%) were diagnosed with RD after OGI. The majority of patients were young males, 129/170 (75.9%) with mean age was 41.7 ± 24.2 years. Mean presenting logMAR visual acuity was 2.5±0.7, Snellen equivalent between hand motion and light perception. 25/170 eyes (14.7%) were diagnosed with RD on presentation, 79/170 eyes (46.5%) within 1 week, and 132/170 eyes (77.6%) within 1 month. Predictors of RD in multivariable regression included zone 3 injury (OR = 2.96, $p < 0.0001$), lens disruption (OR 1.54, $p = 0.0398$), vitreous hemorrhage (OR = 2.96, $p < 0.0001$), and presenting acuity worse than count fingers (OR = 2.37, $p=0.0023$). 105/170 eyes (61.8%) eventually underwent RD repair with 34 eyes (32.4%) re-detaching following repair. Of those eyes that underwent RD repair, mean final logMAR visual acuity was 1.95±0.95, Snellen equivalent between count fingers and hand motion. 40/105 eyes (38.1%) achieved vision count fingers or better vision at last follow-up. Predictors of poor vision, defined as worse than count fingers, following RD repair in multivariable modeling included aphakia (OR = 3.67, $p = 0.0190$), PVR at time of surgery (OR 4.38, $p = 0.0154$), and re-detachment (OR 2.78, $p = 0.0278$).

Conclusions: Retinal detachment commonly occurs within the first month following OGI. Posterior injuries, those with vitreous hemorrhage, lens disruption, or poor presenting acuity are more likely to develop retinal detachment after ocular trauma. Anatomic success was achieved in most patients who underwent repair, with just under half of these patients achieving ambulatory vision, suggesting surgery is worth attempting in many cases of retinal detachment following OGI.

CONTROL ID: 3712351

SUBMITTER (NAME ONLY): Grazyna Palczewska

TITLE: Two-photon excited scanning laser ophthalmoscope enables fundus imaging in healthy volunteers

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Palczewska, K. Palczewski, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|G. Palczewska, J. Boguslawski, M. Dabrowski, M. Wojtkowski, Institute of Physical Chemistry, Polish Academy of Sciences, POLAND|J. Boguslawski, D. stachowiak, G. Sobon, Faculty of Electronics, Wroclaw University of Science and Technology, POLAND|K. Palczewski, Department of Physiology & Biophysics, University of California Irvine, Irvine, California, UNITED STATES|M. Wojtkowski, International Center for Translational Eye Research, Polish Academy of Sciences, POLAND|

Commercial Relationships Disclosure: Grazyna Palczewska: Commercial Relationship: Code N (No Commercial Relationship) | Jakub Boguslawski: Commercial Relationship: Code N (No Commercial Relationship) | Michal Dabrowski: Commercial Relationship: Code N (No Commercial Relationship) | Dorota stachowiak: Commercial Relationship: Code N (No Commercial Relationship) | Grzegorz Sobon: Commercial Relationship: Code N (No Commercial Relationship) | Krzysztof Palczewski: Commercial Relationship(s);Code P (Patent):University of Washington, Case Western Reserve University | Maciej Wojtkowski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Two-photon excited fluorescence (TPEF) of the eye's fundus is a new imaging modality that has been recently demonstrated on humans. Using near-infrared fs laser pulses and two-photon excitation it is possible to probe retinal fluorophores with excitation spectra in the UV spectral range, impossible with one-photon imaging. This study was designed to verify the applicability of the newly developed instrument and imaging method with healthy volunteers without prior experience with this technique.

Methods: The study was performed using a TPEF scanning laser ophthalmoscope schematically shown in Fig. 1a. Fluorescence was excited with laser light at 780 nm, 76 fs pulse duration, pulse repetition rate of 6 MHz, and average power of 0.3 mW. Imaging was performed in a dark room with no prior dark adaptation or pupil dilation. Typically, 90-120 frames were recorded per eye and averaged in post-processing. We investigated a group of 13 healthy subjects with no history of ocular diseases in two age groups, 20-30 (n = 9) and 50-53 (n = 3) years old.

Results: In all cases, the recorded TPEF signal was significantly higher than the instrument noise and sufficient to reconstruct fundus images. With the first group of subjects, the mean fluorescence photon count per pixel was 45.8 x 10^{-3}, SD = 7.4 x 10^{-3} (n = 9). With the second group, mean fluorescence photon count per pixel was 48.7 x 10^{-3}, SD = 9.4 x 10^{-4} (n = 3). There was no significant difference between the two groups (Fig. 1b). Selected examples of images on naïve volunteers are shown (Fig. 1c). These results are comparable to those obtained on a trained eye (1 subject with substantial experience with this imaging modality, 10 sessions). Here, the mean photon count was slightly higher (89.9 x 10^{-3}, SD = 5.8x10^{-3}).

Conclusions: The results show that our novel imaging method is applicable to imaging untrained subjects and could be used clinically. The TPEF signal was significantly higher than the instrument's noise, and of the same order of magnitude as for an experienced subject; sufficient to reconstruct the TPEF image.

CONTROL ID: 3712352

SUBMITTER (NAME ONLY): Tyler Davis

TITLE: RimNet: a deep neural network for automated identification of the optic disc edge and neural rim

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.A. Davis, Computer Science, University of California Los Angeles, Los Angeles, California, UNITED STATES|E. Morales, L. Grassi, A. De Gainza, J. Caprioli, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|Z. Fei, University of California Los Angeles Jonathan and Karin Fielding School of Public Health, Los Angeles, California, UNITED STATES|Z. Fei, Department of Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|H. Rasheed, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accurate measurement of the neural rim based on optic disc imaging is an important aspect of glaucoma severity grading, often performed best by a trained glaucoma specialist. We aim to improve upon existing partially automated tools by building a fully automated system (RimNet) for direct rim segmentation and rim-to-disc ratio (RDR) calculation in glaucomatous eyes with images obtained in a retrospective observational study.

Methods: An database of 857 glaucomatous funduscopic images of 695 eyes were used for training, validation, and testing divided by an 80%/10%/10% random split. All rims were manually delineated by glaucoma specialists. The dataset consists of 591 patients (242 male, 349 female). Mean age was 60.4 years (±14.2). Any images deemed of insufficient quality by a glaucoma specialist were excluded. RimNet consists of a deep learning rim segmentation model and a computer vision RDR measurement tool. A random search algorithm was used to identify the best performing deep learning architecture for rim segmentation, as determined by intersection-over-union with the clinician segmentations. The measurement tool uses the model-generated rim segmentation to identify the thinnest section of the rim and calculate the RDR. The Drishti-GS dataset was used for an external validation of RimNet performance (Sivaswamy 2015).

Results: RimNet achieved a mean average error (MAE) of 0.06 (±0.04) for RDR on the test set. Figure 1 demonstrates training, validation, and test RDR results. An MAE of 0.13 (±0.09) was achieved for rim-to-disc area ratio (RDAR) on the test set. Bland Altman plots are shown in Figure 2. On the Drishti-GS dataset an MAE of 0.06 (±0.04) for RDR and 0.12 (±0.08) for RDAR was observed.

Conclusions: RimNet efficacious rim segmentation and RDR calculations, as demonstrated by the low MAEs and good agreements on both our test and DRISHTI-GS datasets. Such an automated algorithm would be a valuable component in an automated RDR-based glaucoma grading system. Further improvements could be made by improving the deep learning algorithm and expanding the variety of glaucomatous training images.

CONTROL ID: 3712353

SUBMITTER (NAME ONLY): Murtaza Adam

TITLE: Aqueous humor vascular endothelial growth factor pharmacodynamics in the phase 3 Archway trial of the Port Delivery System with ranibizumab

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Adam, Colorado Retina, Lakewood, Colorado, UNITED STATES|L. Barras, M. Maia, S. Gune, K. Maass, M. Chang, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Port Delivery System with ranibizumab (PDS) is a drug delivery system approved in the United States for neovascular age-related macular degeneration (nAMD). Following surgical implantation via the pars plana, the PDS allows for continuous intravitreal delivery of a customized formulation of the anti–vascular endothelial growth factor (VEGF) ranibizumab. In the phase 3 Archway trial of the PDS for nAMD (NCT03677934), aqueous humor (AH) samples were collected to characterize pharmacokinetics and pharmacodynamics of ranibizumab delivered via the PDS and intravitreal injection.

Methods: Archway assessed PDS 100 mg/mL and fixed refill-exchanges every 24 weeks (wks) vs monthly intravitreal ranibizumab 0.5 mg injections. All patients had ≥ 3 anti-VEGF intravitreal injections before screening and an intravitreal ranibizumab 0.5 mg injection at end of screening, 21–28 days before baseline (BL). Optional AH samples, each collected predose, were obtained and analyzed at BL and wks 24, 28, 48, and 52. Ranibizumab and free VEGF AH concentrations were measured using validated enzyme-linked immunosorbent assays with lower limits of quantitation of 20 ng/mL and 1.46 pg/mL, respectively. Significance was tested via Wilcoxon rank test with Bonferroni multiplicity correction.

Results: Optional AH samples were available for 102/248 and 65/167 patients at BL in the PDS and monthly ranibizumab arms, respectively. At BL, median AH ranibizumab and free VEGF concentrations (Table 1) were similar in both arms. At post-BL visits, ranibizumab concentrations were higher and free VEGF concentrations were lower in the PDS arm at 4 and 24 wks since dose, versus 4 wks since ranibizumab injection (PDS vs monthly ranibizumab, $P<0.01$ at each timepoint). In the PDS arm, free VEGF concentrations were similar at 4 and 24 wks since dose, indicating sustained free VEGF suppression throughout the 24-wk refill interval with the PDS. No correlations were observed between free VEGF concentrations and maintenance of BL best-corrected visual acuity or central subfield thickness at wk 36/40 in either arm.

Conclusions: The PDS delivered a more sustained concentration of ranibizumab versus monthly injections, resulting in improved longitudinal suppression of VEGF in AH.

CONTROL ID: 3712355

SUBMITTER (NAME ONLY): Wendy Teal

TITLE: Temporal and Spatial Expression of G Protein-Coupled Estrogen Receptor 1 (Gper1) in Developing Mouse Retina

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Teal, J. Ogilvie, Biology, Saint Louis University, Saint Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Wendy Teal: Commercial Relationship: Code N (No Commercial Relationship) | Judith Ogilvie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Gper1 is a G-protein-coupled estrogen family receptor known for rapid, non-genomic signaling with differential subcellular localization compared to the classic alpha and beta estrogen receptors. It has been demonstrated to be important for sensory system development and highly expressed in the developing zebrafish retina and optic nerve. The goal of this study is to determine Gper1's expression profile and localization in the developing mouse retina, which has not previously been elucidated.

Methods: We analyzed single-cell RNA-seq (scRNA-seq) data (Clark, et al. 2019, Neuron 102:1111-1126) using the R package Seurat to determine Gper1's expression profile. We used immunohistochemistry and western blot to determine Gper1 protein expression from P0-P21, using liver tissue and hippocampi as negative and positive controls, respectively.

Results: scRNA-seq analysis showed that Gper1 is expressed transcriptionally from E14-P8 in the mouse retina, with a transcriptional peak around P2. The transcript expression was most abundant in retinal progenitor and neurogenic cells with a subset of ganglion and other cell types also identified. The overall expression level was relatively low. Immunohistochemical data shows Gper1 protein localized to a subpopulation of cell bodies in the ganglion cell layer as early as birth, with Gper1 protein abundance peaking around P8 and then declining.

Conclusions: scRNA-seq analysis showed that Gper1 is expressed early in mouse retinal development, consistent with immunohistochemistry and western blot observations. Together, the data suggest that Gper1 may be expressed widely at low levels in neurogenic and retinal progenitor cells, but that gene and protein expression may become concentrated in a subpopulation of retinal ganglion cells around P2. Determining Gper1's temporal and spatial expression throughout development may provide insight into its function.

CONTROL ID: 3712357

SUBMITTER (NAME ONLY): Kennedy Hall

TITLE: Combined non-invasive brain stimulation and perceptual learning to enhance peripheral attention in individuals with macular degeneration

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hall, A. Chakraborty, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|B. Thompson, A. Chakraborty, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|B. Thompson, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Kennedy Hall: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Arijit Chakraborty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Individuals with central vision loss, for example, those in macular degeneration (MD), primarily use their peripheral for navigation and other daily living activities. Previously, we reported that peripheral attentive motion tracking, which is critical for navigation, can be improved by perceptual learning (PL) in individuals with MD. In this study, we investigated whether transcranial random noise stimulation (tRNS), a form of non-invasive brain stimulation, can enhance this perceptual learning effect.

Methods: 10 participants (42-65y, 6 males), including 6 with unilateral macular degeneration (UMD) and 4 with bilateral macular degeneration (BMD), were assigned into treatment (tRNS) and control (sham stimulation) groups using a stratified random sampling (3 UMD and 2 BMD in each group). Participants in both groups completed 5 x 40-min PL sessions across consecutive days, while tRNS/sham stimulation was delivered to the motion-sensitive extrastriate area MT+ (3 cm above and 5 cm to the left/right of inion). MOT speed thresholds (8 elements, starting speed 4°/s, partial report procedure) were measured for both hemifields separately during the preliminary baseline visit, pre- and post-intervention on each stimulation day, and then every 24h for 3 days after the stimulation day. tRNS/sham stimulation was applied on the MT+ contralateral; while MOT training was conducted in the hemifield ipsilateral to the affected eye (UMD) or eye with poorer visual acuity (BMD).

Results: MOT task performance improved in both the trained and untrained hemifield in all participants following perceptual learning. However, the tRNS group exhibited a larger improvement in both the trained (tRNS: 37 ± 18%, sham stimulation: 28 ± 11%; $p = 0.008$) and untrained (tRNS: 21 ± 9%, sham stimulation: 15 ± 11%; $p = 0.02$) hemifield than the sham group. In addition, the improvement in MOT performance in both hemispheres was sustained in the tRNS group for at least 72h (trained hemifield: 22 ± 10%, untrained 13 ± 8%, $p = 0.03$) after the final perceptual learning session. For the sham stimulation group, the improvement was sustained only for 48h in the trained hemifield and for 24h in the untrained hemifield.

Conclusions: These initial results suggest that tRNS boosts the efficacy of perceptual learning in enhancing peripheral attentive motion tracking in individuals with macular degeneration.

CONTROL ID: 3712358
SUBMITTER (NAME ONLY): Ryan Mock
TITLE: A real-time method for infrared (IR) reflectance image focus assessment
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Mock, H. Bagherinia, K. Romero, H. Solachuddin, P. Sha, S. Su, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: Many optical coherence tomography (OCT) systems incorporate IR fundus imaging for retinal preview and tracking. The acquisition reliability of OCT data depends on the quality of the IR fundus images' focus. This technique demonstrates a real time image focus measurement using a fast method which can aid an operator during patient alignment. The real time focus measurement is also essential for an automated acquisition system.
Methods: Our method first computes a focus value for each IR image by calculating the sum of the gradient magnitude above the 95th percentile of the gradient image as the focus value. Prior to the image gradient calculation, stripe artifacts are removed from IR images using a real time algorithm.

To test the algorithm, prototype software was used to collect a series of IR images (768x624 pixels over 11.52×9.36 mm2 with a pixel size of 15 μm/pixel) from a CLARUS^{TM} 500 (ZEISS, Dublin, CA) at a frame rate of 50 Hz, using normal and small pupil acquisition modes.

Sequences of roughly 700-800 images each were collected from 10 subjects (some of which had multiple sequences). Images with artifacts, such as blinks, were removed from the database, leaving roughly 5000 total images. The images that remained in the database could be in-focus or out of focus. The algorithm then determines a "Focus Value" for each image. The focus values are converted to probabilities by transforming the focus values using a cumulative distribution function (CDF) (Fig 1) determined from 5,005 IR images. This plot shows the probability that an image is in focus for a given focus value as determined by the algorithm.
Results: To evaluate the algorithm's performance, approximately 100 images were randomly selected from each of the 10 sequences for evaluation. 1,016 independent images (486 out of focus and 530 in-focus) were evaluated subjectively by an expert grader using large vessel sharpness as a measure of focus using two grades (in-focus vs out of focus). We used the grader's evaluation and the focus measurement calculated by the algorithm to compute receiver operating curves (ROC) (Fig 2). The area under the curve (AUC = 0.97) showed great performance of the algorithm with the test data.
Conclusions: We demonstrated a functional real time IR image focus assessment algorithm that can help operators with patient alignment and automated acquisition.

CONTROL ID: 3712359

SUBMITTER (NAME ONLY): Manoj Mohan Kulkarni

TITLE: A Calcium-Permeable AMPA Receptor Antagonist Reduces Aberrant Activity in Late-Stage Retinal Degeneration

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Kulkarni, Y. Wang, J. Gayet, K. Cosio, W.R. Taylor, T. Puthussery, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|M. Kulkarni, Y. Wang, W.R. Taylor, T. Puthussery, Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A hallmark of inherited photoreceptor degenerations is the development of aberrant spontaneous activity in retinal ganglion cells (RGCs). This activity can degrade the signal-to-noise ratio of residual visual signals as well as signals introduced by therapeutic interventions. We previously found that blocking calcium-permeable AMPA receptors (CP-AMPARs) reduces aberrant activity in AII-ACs and On-alpha RGCs in rd10 retina, likely by blocking rod-bipolar to AII-AC signaling. Our goal was to further investigate the mechanisms underlying aberrant activity during late-stage degeneration and determine whether specific cell types were differentially affected.

Methods: We studied rd10 mice at postnatal day 45-55, an age when rods have degenerated but some cones remain. We used two-photon calcium imaging (Cal520 AM) to record spontaneous calcium fluctuations from somas in the ganglion cell layer (GCL) in regions lacking residual light responses. Signals were measured for 1-5 minutes before and after applying the CP-AMPAR antagonist, IEM-1460 (IEM, 50 μM). Some retinas were later immunolabeled with cell-type specific markers (RBPMS, SMI-32, calbindin) to distinguish amacrine cells from RGCs, and to classify different alpha-RGC types. Data are mean ± 1 s.d.

Results: A subset of amacrine cells and RGCs displayed spontaneous, sustained (>10 sec) calcium fluctuations that were reversibly abolished by IEM-1460. The loss of the spontaneous fluctuations in sustained On-alpha RGCs reduced the signal variance by 48.0±11% (n=9 cells). Other alpha RGCs showed significantly less suppression (18±15%, n=15 cells, $p<0.0001$, unpaired t-test, 4 retinas). Overall, in 1423 ACs and GCs in 6 retinas, IEM reduced calcium-signal variance by 21.3±5.1% ($p=0.0007$, one sample t-test). The amplitude of the sustained fluctuations was positively correlated amongst the On-alpha RGCs in the same retinas, but anticorrelated between On-alpha sustained RGCs and putative Off-alpha RGCs.

Conclusions: A CP-AMPAR antagonist can suppress sustained aberrant activity in amacrine and ganglion cells after complete rod degeneration. The presence of anti-correlated activity in On-alpha sustained and putative Off-alpha RGCs is consistent with the involvement of AII-ACs. Our results suggest that CP-AMPARs may be a therapeutic target for suppressing aberrant activity in late stage retinal degeneration.

CONTROL ID: 3712362
SUBMITTER (NAME ONLY): Ellen Antwi-Adjei
TITLE: The AL-SIGHT Program: Participant Satisfaction in Year 1
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E.K. Antwi-Adjei, T.A. Swain, G. McGwin, A. Harbour, S. Register, I. Asif, C.A. Girkin, C. Owsley, L.A. Rhodes, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|
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ABSTRACT BODY:

Purpose: The Alabama Screening and Intervention for Glaucoma and eye Health through Telemedicine (AL-SIGHT) program was developed to engage at-risk populations living in rural Alabama who have limited access to eye care. AL-SIGHT utilizes remote optic nerve assessment to identify glaucoma and other eye diseases in patients seen at federally qualified health centers (FQHCs). This study aims to evaluate the satisfaction of participants enrolled in the first year of the AL-SIGHT program.

Methods: Three FQHCs in rural, underserved communities in Alabama enrolled participants with one or more risk factors: Black or Hispanic ≥ 40 years, White ≥ 50 years, diabetes, a pre-existing glaucoma diagnosis, and/or a family history of glaucoma. After demographic surveys and a brief eye health education program were administered, participants received visual acuity and IOP measurement, autorefraction, visual field testing, fundus photos, and optic nerve and macular optical coherence tomography. A satisfaction survey was then administered to the participant at the conclusion of the encounter with the research coordinator. Survey responses were analyzed with frequencies and percentages.

Results: Among the 340 participants enrolled, 297 (87.4%) were very satisfied and 42 (12.4%) were satisfied with the telemedicine program. 287 (84.4%) were very satisfied and 53 (15.6%) were satisfied with the time spent for the program. 312 (92%) found the location of screening very convenient and 27 (7.9%) found it convenient. 323 (95%) were very likely and 17 (5%) were somewhat likely to recommend the program to others.

Conclusions: The AL-SIGHT program had near total participant satisfaction. Participants also found the program location in the FQHCs where the participants also receive their primary care to be convenient. High satisfaction levels can be used to promote telemedicine programs to patients and increase access to eye care services especially in rural areas.

CONTROL ID: 3712364

SUBMITTER (NAME ONLY): Brian Cheng

TITLE: Association of health literacy and utilization of ocular hypotensive medication among adults with glaucoma

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.T. Cheng, A.P. Tanna, Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Brian Cheng: Commercial Relationship: Code N (No Commercial Relationship) | Angelo Tanna: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch & Lomb, Ivantis, Sandoz, Zeiss

ABSTRACT BODY:

Purpose: Previous studies have shown patients with glaucoma and low health literacy have increased difficulty with eye drop administration and greater risk of disease progression. However, the association of low health literacy and utilization of ocular hypotensive medications is not well-delineated. We conducted a retrospective, cross-sectional analysis to test the hypothesis that patients with low health literacy utilize more glaucoma medications and have higher rates of polypharmacy.

Methods: Data were analyzed of adults (≥18 years) enrolled in the Medical Expenditure Panel Survey (MEPS) from 1996-2017. The MEPS is an annual, representative survey of individuals, families, their healthcare providers, and pharmacies in the United States. National Assessment of Adult Literacy (NAAL) score was used to stratify into low (NAAL <226) and high health literacy (NAAL ≥226). Multivariable regression models adjusted for insurance type were constructed to examine the impact of literacy on prescription medications, health expenditures, and polypharmacy (≥3 medications prescribed for glaucoma).

Results: There were 7846 adults enrolled in the MEPS who self-reported diagnosis of glaucoma. There were increased rates of low health literacy associated with self-reported glaucoma (23.9% vs 9.7%, adjusted OR [95% CI]: 2.43 [2.25-2.62], P<.0001). Among adults with glaucoma, low health literacy was associated with a greater number of glaucoma prescription medications (adjusted risk ratio: 1.06 [1.01-1.12], P=0.03) and increased healthcare spending on these medications (adjusted β: $57.05 [$30.22-83.87], P<.0001). Moreover, adults with low health literacy were more likely to report polypharmacy (adjusted OR: 1.28 [1.11-1.47], P=0.0005).

Conclusions: Self-reported diagnosis of glaucoma was associated with low health literacy. Moreover, low health literacy was associated with a greater number of glaucoma prescription medications, increased expenditures, and higher likelihood of polypharmacy. Glaucoma patients with low health literacy may benefit from careful patient education and close treatment monitoring.

CONTROL ID: 3712366

SUBMITTER (NAME ONLY): Fiammetta Catania

TITLE: Low rate of pterygium recurrence in patients under chronic treatment with low dose oral tetracycline

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Catania, P. Vinciguerra, A. Di Maria, Humanitas Mirasole SpA, Rozzano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: Low dose of systemic doxycycline (LD-OD) has been proven to produce antiangiogenic effects and to inhibit both the expression and activation of matrix metalloproteases (MMP)-2 and MMP-9, whose expression is particularly relevant to pterygium progression.The aim of the study is to assess the outcome of both primary and recurrent clinically significant pterygium after surgical excision and conjunctival graft apposition in a cohort of patients undergoing chronic treatment with LD-OD for chronic refractory blepharitis.

Methods: Retrospective analysis of patients that underwent surgical excision and conjunctival graft apposition was conducted.Included patients were under LD-OD treatment before surgery and were affected by pterygium involving > 5 keratoscopic rings.Patients were divided in two groups: primary pterygium and recurrent pterygium.Rate of recurrence in both groups 1 year postoperatively was registered.Surface regularity, visual quality and dry-eye symptoms at 1-month, 3-months and 6-months follow-up were also monitored.

Results: In primary pterygium group 1/36 patients (2.77%) showed recurrence at 1-year follow-up.Best corrected visual acuity(BCVA) improved at 6-weeks follow-up (p=0.037), with a significant decrease in astigmatic refractive error (p = 0.021). Surface asymmetry index(SAI) and corneal total root mean square (RMS) were significantly lower at 1-year follow-up (p=0.042 and p =0.039 respectively).Ocular surface disease index (OSDI) score significantly reduced at 6-weeks follow-up (p=0.025).In recurrent pterygium group clinical relapse was detected in 1/24 patients (4.16%) at 1-year visit. BCVA significantly increased (p<0.001) and astigmatic refractive error significantly decreased (p=0.002) at 6-weeks examination. They also experienced a decrease in SAI(p=0.004), longitudinal spherical aberration (LSA)(p=0.021), Symmetry Index of Curvature (IC)(p=0.043), RMS(p=0.036), high-order aberrations (HOAs)(p=0.041) and OSDI score (p=0.005).

Conclusions: LD-OD treated patients with primary or recurrent pterygium show a lower rate of recurrence at 1-year follow-up compared to data in literature. Surface regularity and symptoms also improve in these patients after surgery.Prospective studies on a larger population are encouraged.

CONTROL ID: 3712367

SUBMITTER (NAME ONLY): Maria Grazia Saita

TITLE: Safety and Stability of PEA+DHA Ophthalmic Topical Formulation for Potential Treatment of Dry Eye

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Saita, S. Mangiafico, B. Melilli, D. Aleo, F. Spitaleri, M. Cro, R&D, Medivis srl, Tremestieri Etneo, Catania, Italy, ITALY|

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ABSTRACT BODY:

Purpose: Aim of our research was to develop an ophthalmic eye drops (MDV1601) able to intervene in any event of “dry eye cascade” as defined by DEWS II, by employing two endogenous molecules, Palmitoylethanolamide (PEA) and Docosahexaenoic acid (DHA), showing well documented neuro-regenerative and anti-inflammatory activities and which are very difficult to stabilize in a safe eye drops.

Methods: MDV1601 shelf-life stability studies were performed in two different final packaging: LDPE bottle (10mL) with ODS system and single-dose pouches (0.5 mL) according to International Conference on Harmonization (ICH) stability guidelines: 25°C (±2°C/ NMT 60% R.H) and 40°C (± 2°C/ NMT 75% R.H). Safety of the new patented formulation was evaluated by cellular viability using an in vitro human corneal cells model (HCE-SkinEthic), through MMT assay.

Results: MDV1601 is an isotonic and safe eye drop solution preservative free. PEA and DHA are highly stable for 6 months at 40° and for at least 24 months at 25°C, meeting ICH stability requirements for the storage at room temperature. The MMT results after 30 min (irritation test) and 24h (cytotoxicity test) of MDV1601 contact time suggested absence of direct toxicity and no epithelial surface damage (viability >98% versus negative control-PBS).

Conclusions: MDV1601 is the first formulation based on two very active endogenous molecules (PEA and DHA) potentially able to stabilize tear film and to protect ocular surface in dry eye syndrome, in line with the DEWS II definition of dry eye. The presence of PEA+DHA combo links anti-inflammatory and neuro-regenerative activity potentially able to improve signs and symptoms of the disease. Moreover, the absence of preservatives may result in improved ocular safety. MDV1601 could represent the “ideal artificial tear” for physiological restoration of ocular surface in dry eye syndrome.

CONTROL ID: 3712368

SUBMITTER (NAME ONLY): Andreas Pollreisz

TITLE: Three-dimensional reconstruction of human retinal pigment epithelium (RPE) permits a novel view of the RPE – photoreceptor outer segment (OS) interface

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Pollreisz, A. Sedova, M. Lindell, U. Schmidt-Erfurth, Medical University of Vienna, AUSTRIA|D. Kar, K.R. Sloan, C.A. Curcio, University of Alabama at Birmingham, Alabama, UNITED STATES|O. Packer, Y.J. Kim, D.M. Dacey, University of Washington, Seattle, Washington, UNITED STATES|Z. Arsenault, M. Marsh, Object Research Systems ORS Inc, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: RPE cells and their interaction to photoreceptor OS are the first microconnectome of the visual system yet our understanding of the morphology relies on limited data from electron microscopy (EM). Our goal was to use volume EM to provide a detailed and unprecedented description of human RPE cells and their contact with OS.

Methods: A parafoveal retinal volume from a 28-year-old male Caucasian with an unremarkable macula was prepared by serial block-face scanning EM. The RPE cell membrane was reconstructed manually using TrakEM2 software (ImageJ). The cell body organelle content was reconstructed using advanced automated image segmentation methods (Dragonfly, Object Research Systems).

Results: Surface area and volume of a single complete RPE cell was 16898 μm^2 and 6042 μm^3, respectively. AP (n=808) originate from the apical part of the CB and comprised 85% and 21% of the total RPE surface area and volume. AP are elongated (mean length±SD: 6926±4353 nm) and form specialized interactions with overlying OS of cones and rods. Diameter of an AP ranged from 135 to 615 nm. The cell contained 546 pigment granules (lipofuscin/ melanolipofuscin/ melanosome), with a total surface area and volume of 5028 μm^2 and 734 μm^3. Details of volume coverage percentage of organelles are listed in the Table. We identified 438 mitochondria in the cytoplasm with a surface area and volume of 3607 μm^2 and 271 μm^3. The nucleus showed a total surface area and volume of 274 μm^2 and 375 μm^3. Membranous tubules and sacs in the cytoplasm resembling endoplasmic reticulum, yet to be confirmed by histochemical analysis, showed a total surface area and volume of 5321 μm^2 and 988 μm^3.

Conclusions: The apical surface of RPE and its relationship to photoreceptor OS is more extensive and complex than previously appreciated from light microscopy and single section EM studies. The surface area for molecular exchange vital for vision is vast. Cytoplasmic organelles are important clinical imaging signal sources. Our data will assist the interpretation of clinical high-resolution optical coherence tomography in early detection of neurodegenerative retinal diseases including age-related macular degeneration, for explicating the viral vector route in subretinal gene therapy, and benchmarking cells used for cell-based therapy and disease modeling.

CONTROL ID: 3712369

SUBMITTER (NAME ONLY): Kavitha Anbarasu

TITLE: TBK1 as a therapeutic target for Retinal Ganglion Cell neuroprotection in optic neuropathies

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Anbarasu, Indiana University Department of Medical and Molecular Genetics, Indianapolis, Indiana, UNITED STATES|M. Surma, J.S. Meyer, A. Das, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|K. Anbarasu, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|K. Huang, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|J.S. Meyer, A. Das, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mitochondrial dysfunction is implicated in optic neuropathies such as normal-tension glaucoma (NTG) and a missense mutation in the mitophagy gene Optineurin ($OPTN^{E50K}$), has a strong association (17% prevalence) with NTG. To date, mechanism to improve mitochondrial homeostasis in human RGC neurons for developing RGC neuroprotection is unclear. Here, using human stem cell differentiated RGC neurons and cutting-edge cell biology approaches, we set out to identify RGC protection mechanism by improving mitochondrial homeostasis

Methods: Small molecule-based stem cell differentiation and immunopurification (MACS) was done to obtain pure, well characterized RGCs (originally developed in Don Zack lab). CRISPR mutated human embryonic stem cells with $OPTN^{E50K}$ mutation was used for glaucoma modeling. Mitochondrial damage was inflicted by potent stressor, CCCP. Literature evidence suggests Tank-binding kinase1 (TBK1) inhibits mitochondrial biogenesis and we tested if TBK1 inhibition by a potent inhibitor BX795 could promote mitochondrial biogenesis. Mitochondrial mass was measured by immunofluorescence (Tom20), western blot (Tom70) and flow cytometry. Activation of mitobiogenesis was measured by qPCR and western blot of biogenesis genes (AMPK, PGC1a). Statistical comparison between two independent data sets was done using student's t-test.

Results: Mitochondrial homeostasis or Mitochondrial quality control (MQC) process is maintained by biogenesis of healthy mitochondria, fission/fusion, and degradation of damaged mitochondria (mitophagy). Our data shows hRGCs promote mitochondrial biogenesis under mitochondrial stress. Aggregates of $OPTN^{E50K}$ are dissolved by TBK1 inhibitor, BX795, ($p<0.05$, 24hrs; <0.005, 48hrs) treatment. Furthermore, TBK1 inhibition also enhanced mitochondrial mass (<0.05, WT and <0.01, E50K hRGCs) by activating biogenesis pathway and improved cell viability ($p<0.01$, WT and <0.05, E50K hRGCs) with reduction in caspase activity ($p<0.01$, WT).

Conclusions: Protein aggregates are often found in neurodegenerative conditions and increased mitochondrial biogenesis is often seen as a stress response. TBK1 inhibition leads to dissolution of $OPTN^{E50K}$ aggregates, with increased mitochondrial biogenesis resulting in neuroprotection of both WT and E50K hRGCs. Our study, for the first time, shows RGC neuroprotection mechanism by improving MQC, which is applicable for multiple optic neuropathies.

CONTROL ID: 3712371

SUBMITTER (NAME ONLY): Michelle Giarmarco

TITLE: Efficiency of gene therapy via intravitreal injection in primate cones

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Giarmarco, R. Barborek, J. Rowlan, D. Rezeanu, B. Bembry, J. Neitz, M. Neitz, J.A. Kuchenbecker, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal delivery of gene therapy vectors to the retina carries lower risk of adverse events compared to subretinal injections, but has thus far exhibited less therapeutic potential in animal studies. We developed a new adeno-associated virus (AAV) vector for intravitreal delivery of genes to cone photoreceptors. The virus carries an expression cassette with a cDNA encoding an engineered opsin fused to the gene for green fluorescent protein (GFP) under the control of regulatory elements directing expression to long- and middle-wavelength (L/M) cone photoreceptors. The purpose of this study was to evaluate the expression pattern of the opsin-GFP fusion protein after intravitreal injection of the vector in a primate eye.

Methods: The expression cassette was packaged in the 7m8 AAV capsid and 8.5×10^{10} viral genomes in a volume of 50 microliters was injected into the vitreous of an adult macaque eye. The eye was harvested 5 weeks after the injection and retinal cryosections were labeled with antibodies against short-wavelength (S) and L/M opsin. Following confocal imaging, volumes of fovea (400 µm wide, 20 µm deep) were analyzed in TrakEM2 to count individual GFP-expressing, S, and L/M cones.

Results: GFP fluorescence was confined to the fovea. Across the fovea around 25% of cones expressed GFP, with expression highest at the center. GFP was localized primarily in the outer segments, and diffusely along the plasma membrane. While the majority of transduced cones were L/M, surprisingly a small fraction (~5%) were S cones.

Conclusions: A gene therapy vector designed for intravitreal delivery directed robust expression of an engineered opsin to foveal cones in a primate. This finding is promising for the next phase of ocular gene therapy in humans.

CONTROL ID: 3712372

SUBMITTER (NAME ONLY): Mark Ellison

TITLE: Size and shape matters: Evaluation of endothelial cell viability for preloaded Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) grafts in two different carriers

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.S. Ellison, M.M. Straiko, K.D. Tran, Research, Lions VisionGift, Portland, Oregon, UNITED STATES|P.K. Dye, D.T. Tsering, R. Hubbs, M.T. Hikes, K. Odell, Processing, Lions VisionGift, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine endothelial cell loss (ECL) associated with DSAEK grafts preloaded in the Tan EndoGlide Ultrathin or a circular glass Jones tube.

Methods: Twenty-seven donor corneas (age 42-73) were pre-cut for DSAEK with a microkeratome, trephinated, and loaded into either a Tan EndoGlide or glass Jones tube. Grafts were stored in a Life4C filled Krolman viewing chamber for 24 hours and then removed from their carriers using retina forceps (Tan EndoGlide) or via ejection (Jones tube) onto a bed of calcein AM-supplemented viscoelastic. Grafts were then imaged and analyzed for ECL by FIJI segmentation. ECL was determined for DSAEK grafts in the different cohorts and statistical significance was determined using one-way ANOVA and Tukey's post-hoc analysis.

Results: There were no significant differences in donor characteristics (including age, pre-processing endothelial cell density, death-to-preservation, lens status or diabetes status) for grafts loaded into a Tan EndoGlide or Jones tube. The EndoGlide is oval-shaped with a 3.5mm x 2.2mm opening, while the Jones tube has a 3mm diameter round lumen. ECL for grafts loaded into a Tan EndoGlide was 10.3% ± 2.3% (graft thickness: 60 – 189μm, n = 9). ECL for thin grafts (34 – 69μm, n = 9) loaded into the Jones tube was 24.0% ± 5.0%, while ECL for thick grafts (92 – 119μm, n = 9) was 34.2% ± 6.1%. ECL for grafts loaded into the Tan EndoGlide is significantly less than those loaded into the Jones tube ($P<0.001$). Thin grafts loaded in the Jones tube also had significantly less ECL than thick grafts loaded into the Jones tube ($P<0.001$).

Conclusions: The size and shape of the carrier can influence the cell viability of preloaded DSAEK grafts. The Tan EndoGlide and Jones tube differ in both internal shape and diameter. The higher ECL in the grafts loaded into the circular Jones tube was likely produced by endothelial-to-endothelial surface contact as well as excessive stromal folds inside of the carrier. Thinner grafts had less ECL when loaded in the Jones tube, but still showed characteristic patterns of cell loss along tissue folds.

CONTROL ID: 3712373

SUBMITTER (NAME ONLY): Guan Xu

TITLE: Assessing biomechanics of aqueous veins and perilimbal sclera in crosslinked porcine globes using multiwavelength photoacoustic imaging

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The inability to predict the outcome of micro-invasive glaucoma surgeries (MIGS) on lowering intraocular pressure (IOP) is a critical barrier to providing safe and effective interventions for patients. To address this critical barrier, our goal is to advance knowledge on the dynamic mechanisms of the distal aqueous humor drainage in the aqueous veins in the perilimbal sclera. We have developed an optical resolution photoacoustic (PA) microscopy system for resolving the deformation of aqueous veins and perilimbal sclera in porcine and human eyes in three dimensions (3D) as a function of IOP. In this study, we will induce variations of the biomechanical properties in whole eye globes by crosslinking and examine the performance of our methods.

Methods: Whole porcine eyes were treated with 5% genipin for crosslinking. During the imaging experiment, the globes were first pre-conditioned to a physiological state, then perfused at a constant flow rate with 0.25% indocyanine green (ICG) to steadily increase the IOP under continuous monitoring. PA images were taken at 5 mmHg IOP intervals at 790 and 1200 nm wavelengths, targeting the ICG-perfused aqueous veins and collagen-rich perilimbal sclera, respectively. The displacement of the spatial features within the tissue components were tracked throughout the image series. Strain fields in each tissue components were calculated using a finite element analysis (FEA) method.

Results: The biomechanical tensile tests on perilimbal tissue samples determined that the genipin crosslinking procedure results in moderately altered tissue stiffness (tangent modulus) and viscoelastic relaxation times. Results from preliminary whole globe experiments show strain gradients at the vein-sclera interface in untreated whole globes. Studies are ongoing to examine the performance of the PA and strain analysis methods to discern biomechanical differences in the observed tissue components of the untreated and crosslinked globes.

Conclusions: PA imaging combined with data driven FEA will advance understanding of the tissue biomechanics of the complex aqueous veins-perilimbal scleral system and role in IOP regulation. Advancing this knowledge on biomechanics and aqueous humor dynamics will enable clinicians to improve MIGS outcomes by choosing the appropriate surgery for a given patient based on characteristics of the distal outflow system.

CONTROL ID: 3712378

SUBMITTER (NAME ONLY): Robert Shanks

TITLE: Transcriptomic and Proteomic Analysis Identifies a Role for a Bacterial Stress Response Regulator in Cytotoxicity to Corneal Epithelial Cells and Biofilm Formation

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Shanks, N.A. Stella, K.M. Brothers, E.G. Romanowski, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bacterial keratitis is a vision threatening infection of the cornea. Serratia marcescens causes contact lens associated bacterial keratitis and experiences a hostile environment on the ocular surface. Mutation of the stress regulator gene gumB in S. marcescens strongly reduces the bacteria's ability to induce corneal inflammation. The goal of this study was to gain insight into the mechanisms responsible for this conserved stress response system protein in regulating ocular microbial pathogenesis.

Methods: Transcriptomic analysis of S. marcescens contact lens isolate K904 and an isogenic gumB mutant. RNA-sequencing, NanoString, and qRT-PCR were used to measure RNA from bacteria grown in lysogeny broth and in New Zealand White rabbit corneas. Proteomics on surface fraction from cultures grown in lysogeny broth was performed. Cytotoxicity was measured with PrestoBlue and Calcein AM staining. Genes for individual candidate cytotoxic factors were cloned and expressed from plasmids. Protease activity was measured from normalized culture filtrates using azocasein. Surface proteins and type I pili were assessed using PAGE and yeast agglutination analysis. Biofilm formation was assessed by the microplate-crystal violet assay.

Results: Approximately 15% of the S. marcescens genome had significantly altered expression in the gumB mutant ($p<0.05$). Of interest, major changes include reduction of toxic and host-pathogen regulator genes including flagella, pili, hemolysins, and serralysin metalloproteases. The gumB mutant secretomes were defective in protease activity (down 65±5% verus WT, $p<0.001$) and cytotoxicity to ocular surface cells (down 50±10% versus WT, $p<0.01$). Expression of serralysin, but not the ShlA cytolysin, PhlA phospholipase, or FlhDC virulence regulator restored cytotoxicity to the gumB mutant indicating that serralysin protease expression could complement the gumB mutant defect. Biofilm formation by the gumB mutant was defective (down 87±7% versus WT, $p<0.05$) and data suggest that this was due to loss of pilus biosynthesis rather than extracellular polysaccharide levels.

Conclusions: This study indicates that GumB is a major regulator of virulence genes and bacterial interactions with ocular cells through transcriptional control of secreted metalloproteases and biofilm promoting adhesins.

CONTROL ID: 3712379

SUBMITTER (NAME ONLY): Linjiang Lou

TITLE: Blue Light Rearing Does Not Affect In Vivo Retinal Function in Infant Rhesus Monkeys

SESSION TITLE: Myopia: Mechanism of Emmetropization and Eye Growth

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Lou, L.J. Frishman, K.M. Beach, L. Hung, Z. She, E.L. Smith, L.A. Ostrin, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|K.M. Beach, L. Hung, E.L. Smith, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Blue light hazard refers to potential retinal phototoxicity from short-wavelength “blue” light exposure. Blue light is ubiquitous in both natural and artificial light sources, including, most notably, sunlight. Light emitting diodes (LEDs) are a common source of artificial blue light. Speculation exists whether blue light from LED-backlit electronic devices may lead to retinal toxicity. The purpose of this study was to determine the effects of long-term exposure to narrowband short-wavelength ambient lighting on retinal function in rhesus monkeys that were part of experiments examining the effects of blue light on refractive development (Hung et al., 2021).

Methods: Infant rhesus monkeys were reared under short-wavelength “blue” light (n=7; 465 nm, 20 nm half-max bandwidth;183±28 lux) on a 12-hour light/dark cycle starting at 26±2 days of age. Age-matched control monkeys were reared under broadband “white” light (n=8; 504±168 lux). Light- and dark-adapted full-field flash electroretinograms (ERGs) were recorded in anesthetized monkeys at 330±9 days of age. Photopic stimuli were brief duration (<5 ms) red flashes (0.04-5.68 cd.s/m^2) on a rod-saturating blue background and the ISCEV standard white flash (3.0 cd.s/m^2 on a white 30 cd/m^2 background). Monkeys were dark-adapted for 20 minutes and scotopic stimuli were ISCEV standard white flashes of 0.01, 3, and 10 cd.s/m^2. A-wave, b-wave, and photopic negative response (PhNR) amplitudes were measured.

Results: For ISCEV standard light-adapted ERGs, there were no significant differences in a-wave (43.1±9.6 vs. 39.9±4.4 μV; P=0.35), b-wave (176.1±40.1 vs. 160.1±30.6 μV; P=0.49), and PhNR (16.4±8.7 vs. 8.7±10.0 μV; P=0.15) amplitudes between control and blue light reared monkeys. For red flashes on a blue background, there were no significant differences in a-wave, b-wave, and PhNR amplitudes between groups for all flash energies (P>0.05 for all). Similarly, dark-adapted a- and b-wave amplitudes were not significantly different between groups (P>0.05 for all). There were no significant differences in a- and b-wave implicit times between groups for all ISCEV standard stimuli (P>0.05 for all).

Conclusions: Long-term exposure to narrowband blue light did not affect photopic or scotopic ERG responses in infant monkeys. Findings suggest that exposure to 12 hours of daily blue light for approximately 10 months does not result in altered retinal function.

CONTROL ID: 3712380

SUBMITTER (NAME ONLY): Manuel Garza Leon

TITLE: Non-invasive tear rupture time geographical patterns in healthy patients versus with evaporative dry eye.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Garza Leon, P. Quintanilla, D.C. Correa-Sandoval, F. Amparo, Clinical Science, Universidad de Monterrey Division de Ciencias de la Salud, San Pedro Garza Garcia, Nuevo León, MEXICO|F. Amparo, Cornea Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate if there is a difference in the geographical pattern of non-invasive tear film rupture in healthy patient's vs with evaporative dry eye (DED).

Methods: Retrospective, cross-sectional and observational study. Patients with evaporative dry eye and healthy individuals who had dry eye assessments included Ocular Surface Disease Index questionnaire, meibum expressibility, lid margin abnormality, ocular staining, non-invasive tear film break-up time, and meibography were included.

Healthy patients were defined as OSDI<13, NIKBUT>10 seconds, and no ocular staining. Patients with DED were included according to the criteria of the International Workshop on MG Dysfunction (OSDI score>12 points, NIKBUT<10 seconds, degrees of expressibility 1 to 3, and liquid secretion score MGYLS>3).

The NIKBUT was calculated using the Antares topographer according to the manufacturer's protocols. The topographic definition of the tear film rupture was carried out by dividing the 12 rings projected into 6 central and 6 peripherals. In addition, for the definition of the lower and upper quadrants, and line was drawn from 1 to 180 grades of the tear rupture map, as well as from 90 to 270 grades for the identification of the nasal, and temporal quadrant. The evaluation was made by two independent observers.

Results: Seventy-two eyes of 72 patients were studied, with an average age of 34.94 ± 25.07 (range 18 to 77), 51.4% of the male sex, 36 with DED, and 36 healthy patients. 100% of the patients with DED had some rupture vs 50% of the healthy patients. We found that the initial rupture of the tear film in the lower temporal quadrant is more frequent in patients with DED compared to healthy patients. (22 vs 9, p=0.003), with an OR of 4.17 (95% CI 1.75,13.15). In addition, there was a difference in the initial NIKBUT (13.83±3.84 and 5.43 ± 2.13, p = 0.003), age, (40.44 ± 16.89 vs 29.42± 13.13 years, p= 0.003), thickness of the tear film (67.08 ± 18.80 vs 82.92 ± 31.97 microns, p=0.005), loss of meibomian glands in the upper eyelid (21.89±9.17 vs 16.43±6.33%, p=0.005) and lid margin abnormality (1.77±0.86 vs 1.00±0.75, p=0.0003) between the patients with DED and the healthy ones respectively

Conclusions: In our population, the tear film ruptured more frequently in the lower temporal quadrant in patients with evaporative dry eye than in healthy patients.

CONTROL ID: 3712381

SUBMITTER (NAME ONLY): Debresha Shelton

TITLE: Subretinal expression of Galectin-3 after light-induced retinal damage

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Shelton, J.T. Sellers, M. Chrenek, T. Getz, V. Summers, P.E. Girardot, S. Modgil, J.H. Boatright, J.M. Nickerson, Department of Ophthamology, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Galectin-3 (Gal-3), is a β-galactoside-binding protein is purported to be a prognostic biomarker in patients with severe disease (e.g., heart failure or depression). We hypothesized that manipulation of the Vitamin A cycle during light-induced retinal damage (LIRD) could reveal whether increased Gal-3 expression is a predictor of microglia/macrophage deposition within the RPE during damage resolution.

Methods: High activity Rpe65 (L450 ($^{L/L}$)) and the low activity variant (M450 ($^{M/M}$)) were bred to Cx3CR1-GFP-mice on C57Bl/6J background. Light damage was conducted at 50,000 lux for 5 h during the dark phase of the circadian cycle. Mice were imaged and sacrificed at days 1, 3, & 7 after damage (age= P60-P365, n=3-4/group). Retinal thickness and morphology were measured via SD-OCT, cSLO, and histopathology. Tissue was collected for RPE flat mounts. GFP+ (microglia/macrophages) and Gal-3+ cells were counted and classified. ZO-1 spatial patterns were measured with CellProfiler and Imaris.

Results: Differences in damage patterns and kinetics between RPE 65 $^{M/M}$ and RPE65$^{L/L}$ mice were evident in both functional and morphological outcomes. On days 1 & 3 post LIRD, GFP^{+} cells were not significantly different in number between genotypes. Later, on day 7, more GFP^{+} cells were observed in the RPE 65 $^{L/L}$ mice compared to RPE65 $^{M/M}$ and no damage controls [BJ1] ($p<0.0001$). Notably, the RPE65$^{L/L}$ mice lost most of their ERG a-, b-, and c-wave amplitudes within the first 24-72 hours post LIRD induction compared to RPE65$^{M/M}$ mice ($p<0.005$). This phenotype worsened by day 7 post LIRD induction ($p<0.001$). Retinal detachments occurred earlier in RPE65$^{L/L}$ animals than in the RPE65$^{M/M}$ mice. Expression of Gal-3 in RPE65$^{M/M}$ mice was comparable to RPE65 $^{L/L}$ during early stages of damage (up to day 3 post LIRD induction); however, at day 7, RPE65$^{M/M}$ mice exhibited low levels of Gal-3 while RPE65$^{L/L}$ animals continued to express high levels of the protein heterogeneously in both RPE cells and CX3CR1-GFP^{+} cells. The distribution of GFP^{+} cells was correlated with Gal-3 expression patterns in RPE cells in a time-dependent manner after LIRD induction

Conclusions: Changes in subretinal expression of Gal-3 correlate to CX3CR1-GFP^{+} cell deposition and correspond to functional and morphological damage. Significance: Galectin inhibitory drugs may therapeutically modulate sub-retinal damage via microglia/macrophage-RPE interactions

CONTROL ID: 3712382

SUBMITTER (NAME ONLY): Piotr Strzalkowski

TITLE: Impact of government-imposed lockdown due to the COVID-19 Pandemic on admissions and severity of retinal detachments in a referral eye hospital in Germany.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Strzalkowski, C. Reiter, S. Dithmar, Ophthalmology, HELIOS Dr Horst Schmidt Kliniken Wiesbaden, GERMANY|

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ABSTRACT BODY:

Purpose: To analyze the patient characteristics and severity of retinal detachments (RDs) in a referral eye hospital during the COVID-19 pandemic with a corresponding timeline a year before.

Methods: Retrospective cohort study based on electronic patient records of all patients with confirmed diagnosis of RD from February 22, 2020 (lockdown imposed by German Government) to May 4, 2020 (end of lockdown) and following 2 weeks after lockdown period (LP) in the Department of Ophthalmology, Helios Dr. Horst Schmidt Klinikum (HSK), Wiesbaden, Germany, were analyzed and compared to the equivalent pre-COVID-period (p-Cp) from February 22, 2019, to May 4, 2019).

Results: During LP 26 patients were diagnosed with RD compared to 60 patients in the p-Cp (-56.7%, $p<0.01$). Within 2 weeks after LP a total of 13 with RD were admitted. A year before, two weeks after p-Cp 26 patients with RD were admitted, respectively (-50%, $p<0.01$). There was no statistical difference in age between LP group and p-Cp group (65.3±11.5 vs. 69.1±12.3 years ($p>0.05$)). Time between initial symptoms and ophthalmological examination was significantly longer in LP group ($p<0.01$). While usage of gas tamponade and silicone oil tamponade was similar in both LP and p-Cp group, there was a significant increase of proliferative vitreoretinopathy (PVR) RD needing silicone oil tamponade within two weeks after LP ended in Germany (LP 53.8% vs. p-Cp 23.1%) ($p<0.01$).

Conclusions: During government-imposed lockdown caused by COVID-19 pandemic, the rate of patients admitted with RD dropped significantly compared to the same p-Cp. Time between initial symptoms and ophthalmological examination was significantly longer in LP group, with consecutively more PVR-RD needing silicone oil tamponade within the following two weeks after lockdown period ended. While policymakers have focused primarily on containing chains of infection with SARS-CoV-2, it has had a massive impact on the medical care of ophthalmic emergencies with worsening prognosis after retinal detachment.

CONTROL ID: 3712387

SUBMITTER (NAME ONLY): Frederick Collison

TITLE: Chart-based contrast sensitivity in luminance noise: effects of age and simulated optical abnormality

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.T. Collison, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|F.T. Collison, The Chicago Lighthouse, Chicago, Illinois, UNITED STATES|J. McAnany, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|E. Kopidlansky, Precision Vision, LLC, Woodstock, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effects of age and simulated optical abnormality on contrast sensitivity (CS) in luminance noise using a novel booklet-based letter CS test.

Methods: Sixty-eight subjects with no known visual deficits who recently underwent a comprehensive eye exam participated in this study (age range 18-85, with at least 10 subjects per decade between ages 20 and 70 years). Subjects were tested using the right eye only and asked to identify letters that spanned a broad range of Weber contrast (0.001 to 0.56) printed in a novel booklet-based test. The letters were presented against a uniform gray background (no-noise condition) and in the presence of static spatial luminance noise (noise condition), which consisted of light and dark checks. A subset of 5 subjects (age range 26-35 years) performed the same test under three additional conditions: (1) simulated cataract (Simuspecs Blur/Glare Cataract filter #20776), (2) +2 diopters (D) of blur, and (3) low room luminance (illuminance reduction of approximately 20x). CS for these three conditions was compared to the standard condition using paired t-tests with Bonferroni correction ($p = 0.05/3$).

Results: In the no-noise condition, contrast sensitivity was independent of age (mean log CS of 1.7) until approximately 54 years, and declined linearly for older subjects (CS loss of 0.1 log unit/decade). CS measured in noise was independent of age across the range of ages tested (mean log CS of 0.9); the slope of a linear regression function fit to these data was not significantly different from 0. Manipulations of simulated cataract and +2D blur significantly reduced CS in the no-noise condition (both $p < 0.05/3$), whereas these optical manipulations did not significantly affect CS in noise. Reduced room illumination did not significantly affect CS in the presence or absence of noise.

Conclusions: The results suggest that measurements of CS in luminance noise may be valuable, as these measures appear to be independent of age and certain forms of optical degradation. Furthermore, the results support CS measurements in noise in patients with retina or optic nerve disease, as noise may minimize possible artifacts arising from optical effects such as media opacities or defocus.

CONTROL ID: 3712388

SUBMITTER (NAME ONLY): Eileen Hwang

TITLE: Comparison of segmentation methods for measuring collagen fiber density in confocal reflectance images of the vitreous

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Hwang, D. Morgan, M. Hartnett, Ophthalmology, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|B. Coats, Mechanical Engineering, University of Utah, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Spatial variation in vitreous collagen fiber density may play a role in vitreous aging. Methods for quantifying fiber density across the eye are not well developed. Our objective was to evaluate the performance of different image segmentation methods for detecting variation in vitreous collagen fiber density in confocal reflectance images.

Methods: Four right fresh young adult porcine eyes were sectioned in the sagittal plane at the nasal limbus. Two-dimensional 70um x 70um confocal reflectance images were obtained every 1mm along an anterior-posterior axis originating at the nasal limbus. Three methods were used to quantify fiber density: 1) manual fiber counting by a single grader; 2) automated fiber counting using the Fiji ridge detection plugin; 3) automated pixel thresholding using the Fiji moments algorithm. Pearson correlation was used to compare methods. Simple linear regression was used to evaluate anterior-posterior density trends.

Results: Confocal reflectance images of porcine vitreous demonstrated a network of linear fibers with a diameter of 1.18 ± 0.51um (mean ± SD). Manual fiber counting yielded an average density of 0.019 ± 0.006 fibers/um^2, whereas automated fiber counting yielded an average density of 0.032 ± 0.014 fibers/um^2. Automated pixel thresholding resulted in an average of 23 ± 9% of pixels occupied by signal. There were strong correlations between manual fiber counting and automated fiber counting (R-squared=0.80, $p<0.0001$) and between automated fiber counting and automated pixel thresholding (R-squared=0.85, $p<0.0001$). All three methods demonstrated a significant trend of decreasing density from anterior to posterior. The density was found to vary by 7.1% per mm (95%CI 4.0-10.2%; $p<0.0001$) by manual fiber counting and 8.2% per mm (95%CI 3.9-12.6%; $p=0.0005$) by automated fiber counting, and 7.1% per mm (95%CI 3.3-10.9%; $p=0.0006$) by automated pixel thresholding.

Conclusions: High correlation was observed between three methods for quantifying fiber density in vitreous confocal reflectance images. By all three methods, collagen fiber density was greater anteriorly, near the vitreous base, which is consistent with prior research. These results support the use of these methods for assessing relative differences in vitreous collagen fiber density.

CONTROL ID: 3712389

SUBMITTER (NAME ONLY): Jenay Yuen

TITLE: Outcomes and risk factors for noncompliance in glaucoma suspects identified by teleretinal screening in a safety net patient population

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yuen, B. Xu, B. Song, L. Daskivich, B. Wong, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|L. Daskivich, B. Wong, Los Angeles County University of Southern California Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate risk factors for in-person follow-up compliance and diagnosis of glaucoma in patients with glaucomatous findings via teleretinal diabetic retinopathy screening (TDRS).

Methods: Retrospective chart review was conducted on diabetic patients with large or asymmetric cup-to-disc ratios identified by teleretinal screening in Los Angeles County's primary care-based TDRS program between 1/1/2016 to 12/31/2018. Demographic and clinical information were extracted from medical records. Risk factors for in-person visit compliance and diagnosis of glaucoma were analyzed with multivariable logistic regression in compliant patients.

Results: 837 patients with optic discs suspicious for glaucoma on teleretinal screening were included. 542 patients (64.8%) successfully completed an in-person visit with 87.6% of those diagnosed with glaucoma-related pathology (60.8% as glaucoma suspect and 26.8% as glaucoma). Patients 50-65 years old were 1.52 times as likely of being compliant with in-person visits compared to those <50 years old (p=0.048). Caucasian patients were 3.04 times as likely to be non-compliant compared to Latino patients (p=0.041). For every $10,000 increase in zip-code median income, patients were 10% less likely of being complaint (p=0.019). Those screened at sites with associated ambulatory optometry clinics were seen in-person faster than those at tertiary care medical centers, with 8% fewer days between screenings and initial in-person visits (p=0.046). Patients >65 years old were more likely to have confirmed glaucoma than those <50 years old (p <0.001). Compared to Latino patients, African American and Caucasian patients were 3.18 (p<0.001) and 7.32 times (p=0.024) as likely to have confirmed glaucoma, respectively.

Conclusions: In this safety net patient population with suspected glaucoma on teleretinal screening, patients who were younger, Caucasian, or from higher-income neighborhoods were less likely to follow up for an in-person evaluation. Compared to Latino patients, African American patients and Caucasian patients were at higher risk for confirmed glaucoma diagnosis.

CONTROL ID: 3712390

SUBMITTER (NAME ONLY): Rodrigo Vilares-Morgado

TITLE: EFFECT OF REPEATED INTRAVITREAL INJECTIONS IN GLAUCOMA SPECTRUM DISEASES

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Vilares-Morgado, A. Moleiro, F. Alves, A. Melo, S. Estrela-Silva, J. Araújo, J. Tavares-Ferreira, M. Silva, A. Rocha-Sousa, Â. Carneiro, J. Barbosa-Breda, Department of Ophthalmology, Centro Hospitalar Universitario de Sao Joao, Porto, Porto, PORTUGAL|V. Correia, Faculty of Medicine of the University of Porto, Porto, Porto, PORTUGAL|R. Vilares-Morgado, A. Moleiro, J. Barbosa-Breda, UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine of the University of Porto, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: To evaluate whether repeated intravitreal injections are associated with glaucomatous progression in eyes with glaucoma spectrum diseases.

Methods: Retrospective longitudinal study of patients with ocular hypertension (OHT), glaucoma suspects (GS) or definite glaucoma that received ≥8 total intravitreal injections per eye and had ≥2 SD-OCT RNFL thickness measurements at least 12 months apart, having received ≥1 intravitreal injection during the study period. We excluded eyes with poor OCT quality and if the baseline global RNFL thickness was < 50 µm. Our primary outcome was the variation in RNFL thickness. Linear mixed effects models were constructed, including a multivariable model.

Results: 118 eyes from 104 patients were included. Average baseline age was 70.75±10.90 years with a follow-up of 39.91±23.14 months. 41% of eyes had primary open angle glaucoma (POAG), 36% OHT or GS, 16% secondary OAG and 6% angle-closure glaucoma (ACG). 40% had exudative AMD, 26% venous occlusion, 25% diabetic macular edema and 9% other retinal disorders. Average number of intravitreal injections during the study period was 22.10±14.19. RNFL thickness decreased significantly (85.97±20.14 to 79.70±20.69 µm; p<0.001; -2.10±7.36 µm/year), with no significant changes found in visual fields MD (p=0.382). There was a significant difference in RNFL variation among glaucoma spectrum diseases, with more thinning in eyes with secondary OAG (-11.24±16.95 µm; -3.79±6.19 µm/year), followed by POAG (-8.64±14.39 µm; -3.35±6.23 µm/year), ACG (-8.13±11.08 µm; -3.78±5.64 µm/year) and OHT/GS (-0.94±15.69 µm; -0.04±8.74 µm/year) (p<0.001). A higher number of study time injections was significantly associated with higher RNFL thinning (p=0.008). The proportion of eyes under glaucoma medical treatment increased from 73.7% to 82.2% (p=0.049), as well as the average number of glaucoma medications per eye (p=0.018); more eyes underwent selective laser trabeculoplasty (p<0.001) and surgical implantation of tube shunts (p=0.002). IOP decreased significantly from 18.64±7.10 to 15.05±4.04 mmHg (p<0.001). In a multivariable linear mixed model, higher baseline RNFL thickness (p<0.001), higher baseline IOP (p<0.001), lower central corneal thickness (p<0.001) and type of glaucoma spectrum disease (p=0.017) significantly predicted higher RNFL thinning.

Conclusions: Routine optic nerve evaluations should be performed in patients undergoing regular intravitreal injections.

CONTROL ID: 3712391

SUBMITTER (NAME ONLY): L. Jay Katz

TITLE: Successful reduction in topical medication burden in glaucoma patients at 3 years with iDose intracameral therapy versus timolol

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Katz, Glaucoma Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|L. Katz, L. Doan, D. Applegate, C. Davis, K. Stephens, T. Navratil, Glaukos Corp, Laguna Hills, California, UNITED STATES|

Commercial Relationships Disclosure: L. Jay Katz: Commercial Relationship(s);Code E (Employment):Glaukos;Code I (Personal Financial Interest):Glaukos | Long Doan: Commercial Relationship(s);Code E (Employment):Glaukos;Code I (Personal Financial Interest):Glaukos | David Applegate: Commercial Relationship(s);Code E (Employment):Glaukos;Code I (Personal Financial Interest):Glaukos | Christian Davis: Commercial Relationship(s);Code E (Employment):Glaukos;Code I (Personal Financial Interest):Glaukos | Kerry Stephens: Commercial Relationship(s);Code E (Employment):Glaukos;Code I (Personal Financial Interest):Glaukos | Tomas Navratil: Commercial Relationship(s);Code E (Employment):Glaukos;Code I (Personal Financial Interest):Glaukos

ABSTRACT BODY:

Purpose: Topical prostaglandin analogues are first line therapy for the treatment of open-angle glaucoma (OAG). Although effective if dosed properly, patient adherence with eyedrops is poor and worsens in proportion to increased medication (med) burden in terms of both number of bottles and frequency of dosing. Additional drawbacks include ocular surface disease and cosmetic side effects. To address these drawbacks, two travoprost-eluting intraocular implants (iDose) were developed. We conducted a Phase 2, randomized, double-masked, multicenter trial to compare the safety and efficacy of these implants to timolol 0.5% BID in reducing IOP in OAG or ocular hypertension. This submission provides analysis of the subset of patients on the same or lesser topical IOP-lowering therapy at 36 months vs screening.

Methods: Randomized patients on 0 to 3 medications at screening received iDose-FE (fast eluting; n=51), iDose-SE (slow eluting; n=54) or underwent sham procedures and received timolol BID (n=49). iDose patients received placebo eyedrops. Additional topical IOP-lowering meds were added per protocol for patients with IOP >18mmHg at any visit. In this analysis, the proportion of patients on the same or lesser number of topical IOP-lowering meds at month 36 vs screening were evaluated. Mean change from 8AM baseline IOP was evaluated at month 36 in this population. Adverse events and safety parameters were evaluated.

Results: iDose-FE and iDose-SE demonstrated a clinically relevant IOP-lowering effect of 8.3 and 8.5mmHg, respectively, vs 8.2mmHg for timolol control. 70% of iDose-FE and 68% of iDose-SE subjects were well controlled on iDose with the same or lesser topical med burden at 36 months vs screening, vs 46% of subjects on timolol. iDose was generally well tolerated with no adverse events of conjunctival hyperemia, periorbital fat atrophy, clinically significant endothelial cell loss, and only a single adverse event of iris color change.

Conclusions: Robust, sustained IOP-lowering was achieved with both iDose models. The therapy was generally well tolerated over a period of 36 months. A responder analysis demonstrates substantial reduction in topical med burden for iDose-treated eyes, thus making iDose an attractive alternative to topical IOP-lowering therapy. iDose is currently being evaluated in two Phase 3 pivotal trials with results expected in late 2022.

CONTROL ID: 3712392

SUBMITTER (NAME ONLY): Michael Chen

TITLE:

Long-term comparison of Kahook Dual Blade excisional goniotomy and Gonioscopy-assisted Transluminal Trabeculotomy

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chen, Z. Zhang, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|O. Adeleye, Tulane University, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure: Michael Chen: Commercial Relationship: Code N (No Commercial Relationship) | Olufunke Adeleye: Commercial Relationship: Code N (No Commercial Relationship) | Ze Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Kahook Dual Blade (KDB) Goniotomy and gonioscopy-assisted transluminal trabeculotomy (GATT) both target the trabecular meshwork to increase aqueous outflow. We aimed to compare the efficacy and safety of KDB and GATT in patients with open angle glaucoma (OAG) with at least one year of follow-up.

Methods: A retrospective chart review was performed of adult patients at two centers who underwent KDB or GATT (with or without phacoemulsification) for treatment of OAG with at least one year of follow-up. Data collected included visual acuity, intraocular pressure (IOP), glaucoma medications, visual field results, diagnosis, adverse events, and additional glaucoma procedures. The primary outcome included surgical success (defined as 20% or more IOP reduction). T-test and chi-squares were used for analysis.

Results: Forty-four eyes were enrolled in the study, with 22 eyes in each group. Age, gender, and other demographics were similar in both groups. The mean preoperative IOP was 17.9 + 7.1 mm Hg and 22 +7.8 mmHg ($p= 0.041$) on 2.6 + 0.9 and 3.8 +0.8 medications ($p<0.001$) in the KDB and GATT groups, respectively. At 1 year, the mean IOP reduction 0.5 ± 7.1 mm Hg and 8.4 ± 7.7 mm Hg ($p=0.05$) in the KDB and GATT group, respectively. KDB eyes had 38.5% success while GATT eyes had 84.6% success. At 6 months, the mean medication reduction was 0.47 + 1.07 and 1.32 + 1.14 ($p=0.02$) in the KDB and GATT groups respectively. At 1 year, mean medication reduction was 0.568± 1.56 in the KDB group and 0.15± 0.55 ($p=0.088$) in the GATT group. There was no statistically significant difference in adverse events between the two groups.

Conclusions: Our study showed both KDB and GATT are safe and can effectively lower IOP and reduce medication burden. At one-year follow up, GATT appears to be show greater IOP reduction and more likely to achieve at least 20% reduction in IOP at 1 year despite a higher preoperative IOP and medication burden than KDB. There was no significant difference in medical reduction between the two groups, though it is notable the GATT group had a higher preoperative drop burden. This is the first study to show a significant difference in IOP reduction and surgical success between GATT and KDB with one year of follow up. A more extensive study is warranted to study this difference further.

CONTROL ID: 3712394

SUBMITTER (NAME ONLY): Jeremy Bohl

TITLE: Blockade of alpha7-nicotinic acetylcholine receptors decreases calcium signaling in starburst amacrine cells in the mouse retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bohl, Z. Sharpe, M. Ayub, T. Ichinose, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Jeremy Bohl: Commercial Relationship: Code N (No Commercial Relationship) | Zachary Sharpe: Commercial Relationship: Code N (No Commercial Relationship) | Mahnoor Ayub: Commercial Relationship: Code N (No Commercial Relationship) | Tomomi Ichinose: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal motion detection is dependent on the excitatory and inhibitory outputs of the starburst amacrine cell (SAC), Acetylcholine (Ach) and GABA respectively. We recently found that blockade of alpha-7 nicotinic acetylcholine receptors (α7-nAChRs) decreased the direction selectivity of on-off direction-selective ganglion cells, which was attributable to cholinergic feedback to bipolar cells. To examine whether the direction selectivity of SACs is controlled by cholinergic feedback to bipolar cells, we carried out two-photon calcium imaging on light-evoked responses from SACs in the presence and absence of Methyllycaconitine (MLA).

Methods: Oregon Green BAPTA (OGB-1) or GCaMP6m was used for calcium imaging. Electrophoretic injection of OGB-1 was conducted with a sharp electrode placed onto tdTomato labeled SACs. Recording of calcium responses in labeled SACs took place 1-2 hours after injection of OGB1. For GCaMP6 introduction, AAV9-GCaMP6M was injected into the intravitreal space of ChAT-Cre mouse eyes. Distal dendrites of SACs were imaged, and a 180° bidirectional moving bar stimulus was projected onto the photoreceptors on the ventral half of the retina by a UV LED. After calcium imaging was captured in a control solution, MLA (100 nM) was bath applied. Two-photon imaging occurred at 15 frames per second in a recording window of 256x124 pixels. Calcium fluorescence was analyzed using Fluoanalyzer in MATLAB.

Results: In response to two-directional stimulation, we observed brighter responses to preferred motion, centripetal direction, and dimmer responses during null, centrifugal direction. The application of MLA decreased the calcium responses in both directions for the SAC. After washout of MLA, preferred directional response increased to near control conditions, but null directional responses remained dimmer. These results indicate decreased synaptic output from the SACs, which is consistent with our previous observation of reduced direction selectivity in on-off direction-selective ganglion cells.

Conclusions: Our results show that α7-nAChR blockade by MLA decreases the overall calcium response in distal SAC dendrites. These new results confirm our previous work that cholinergic feedback to bipolar cells from SACs plays a role in SACs' direction selectivity, resulting in a reduced direction selectivity in on-off direction-selective ganglion cells.

CONTROL ID: 3712396

SUBMITTER (NAME ONLY): Hanieh Mirhajianmoghadam

TITLE: Axial length changes in response to myopic defocus under different ambient light intensities

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Mirhajianmoghadam, L.A. Ostrin, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies have shown that axial length (AL) changes in response to myopic optical defocus in young adults. However, the range of myopic defocus used has been limited (≤ +3 D). Moreover, the interaction between myopic defocus and ambient light intensity on AL is not well-studied. The goal of this study was to assess AL change in response to increasing increments of myopic defocus under three different ambient light conditions.

Methods: Healthy participants (ages 28.5±6.1 years, n=15) underwent three experimental sessions in a randomized order. At each session, participants first viewed a movie at 2 meters for 10 minutes. The room light was then adjusted to one of the three ambient light intensities (dim: <50 lux, moderate: ~500 lux, bright: ~2000 lux) and after 15 minutes, a Lenstar biometer was used to measure baseline AL. +2D was then added to the left eye. Participants continued to watch the movie, and AL was measured in both eyes after 15 minutes. Each 15 minutes, the defocus was increased to +4D and +6D, and Lenstar repeated. Upon removal of the final lens, recovery was assessed at 15 minutes. For each eye, the AL difference between the baseline measurement and each time point was calculated. The difference in AL between experimental and control eyes was analyzed with repeated measures ANOVA for sequential time points (four 15-minutes intervals) and light intensity (dim, moderate, bright).

Results: Spherical equivalent refractive error and axial length were comparable between right and left eyes (control: -0.6±1.3 D and 23.56±1.00 mm; experimental: -0.6±1.3 D and 23.57±0.96 mm; P=0.49 and P=0.76, respectively). There was no significant AL change across the four time points (P=0.96) or between the three light intensities (P=0.83). Additionally, there were no significant interactions between time point and light intensity (P=0.81).

Conclusions: Axial length did not significantly change in experimental eyes compared to control eyes following 15 minute intervals of monocular myopic defocus from +2D to +6D, regardless of ambient light intensity. Our results suggest that if axial length changes occur in response to myopic defocus, they may not be detectable with a Lenstar biometer.

CONTROL ID: 3712398

SUBMITTER (NAME ONLY): Thangal Yumnamcha

TITLE: Endoplasmic Reticulum-Mitochondria crosstalk in Retinal Pigment Epithelium dysfunction: Implications for age-related retinal diseases

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yumnamcha, E. Abdul Shukkur, E.A. Berger, L. Pukhrambam, A. Ibrahim, Ophthalmology, Visual, and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|A. Ibrahim, Pharmacology, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: Endoplasmic reticulum (ER) stress is linked with several retinal degenerative diseases including age-related macular degeneration (AMD). Chronic ER stress during ageing leads to retinal pigment epithelium (RPE) dysfunction, which is a hallmark of AMD. However, the role of mitochondria in ER stress-induced RPE dysfunction remains poorly investigated. Therefore, the objective of the present study is to explore the crosstalk between the ER and mitochondria (MT) in ER stress-induced RPE dysfunction and cell death.

Methods: Methods: A human RPE cell line (ARPE-19) was treated with an ER stress inducer (tunicamycin (TM), 1µg/mL,) for 48 h. Protective effect of various pharmacological inhibitors and mitochondrial targeted antioxidant, MitoQ, were assessed. Mitochondrial ROS (mt-ROS), membrane potential (Δψm), and intracellular ATP level were measured by Mitosox, JC-1, and ATP assays, respectively. Cell death was determined by lactate dehydrogenase (LDH) leakage. Barrier integrity was assessed by electric cell-substrate impedance sensing (ECIS) system. qPCR and western blot were performed to determine ER stress and apoptotic markers expression. Statistical analysis was performed using ANOVA or Student's t test.

Results: Results: Treatment of ARPE-19 cells with TM significantly upregulated several ER stress markers gene, including XBP1s, ATF4, CHOP and PDI. Furthermore, TM-treatment resulted in an increase in mt-ROS, decreased Δψm, less ATP, and cell death. Interestingly, JNK kinase inhibitor pretreatment attenuated TM-induced cell death. Bid, a mitochondrial proapoptotic protein, was also increased in TM-treated ARPE-19 cells and pretreatment with BI-6C9, an inhibitor of Bid, reduced TM-induced cell death. Finally, MitoQ pretreatment attenuated disruption of membrane integrity and cell death induced by TM.

Conclusions: Conclusions: Our results demonstrate that ER stress induces apoptosis in ARPE-19 cells by causing mitochondrial damage. We further show that blocking mitochondrial apoptotic pathway or addition of mitochondria-targeted antioxidant have a protective effect against ER stress-induced cell death.

CONTROL ID: 3712399

SUBMITTER (NAME ONLY): Susan Ostmo

TITLE: Ultra-widefield optical coherence tomography in retinopathy of prematurity

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.R. Ostmo, T. Nguyen, S. Ni, S. Khan, X. Wei, Y. Jia, D. Huang, Y. Jian, J. Campbell, Ophthalmology, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S. Ni, S. Khan, X. Wei, Y. Jia, D. Huang, Y. Jian, Biomedical Engineering, Center for Ophthalmic Optics and Lasers, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) has the potential to provide objective diagnosis of ROP, however, integration of OCT into ROP diagnosis has been limited. We investigate whether an investigational 140 degree field of view OCT has the potential to assist with ROP diagnosis in awake neonates.

Methods: We review our experience imaging 35 unique patients, more than 100 imaging sessions, in the neonatal intensive care unit (NICU) who met criteria for ROP screening (birthweight ≤ 1500g or gestational age ≤ 30 weeks). Patients underwent ophthalmoscopic exam and OCT imaging using a 400-kHz, portable, contact swept-source system with a real-time feedback display, following placement of an eyelid speculum and pharmacological dilation. RetCam imaging was performed in some cases for comparison. Experience with OCT-based diagnosis versus ophthalmoscopic diagnosis was qualitatively compared by a single, unmasked examiner.

Results: The full ICROP classification could be made in all imaging sessions unless research imaging was deferred for medical reasons. The field of view of the contact-based design appeared wider than Retcam 130 degree lens (Figure 1). In addition to documentation of the extent of peripheral stage, in some cases, it was possible to visualize the ora serrate and document full vascularization of the retina (Figure 2). Anecdotally, it was easier to visualize the peripheral stage through small pupils compared to ophthalmoscopy, and while not formally measured, the exam seemed to be faster and better tolerated by the babies.

Conclusions: Early experience with an investigational contact-based UWF-OCT suggests that OCT-based screening may provide objective documentation and diagnosis of the full spectrum of Zone, Stage, and Plus disease in ROP. Although not formally studied here, our experience suggests that OCT-based screening also has the potential to be faster, less stressful to the neonate (and preferred by NICU nurses) compared to the ophthalmoscopic examination or standard fundus imaging.

CONTROL ID: 3712400

SUBMITTER (NAME ONLY): Ehtesham Shamsher

TITLE: Is Dark Chocolate (Resveratrol) neuroprotective in a model of Alzheimer's disease?

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shamsher, L. Guo, B. Davis, V. Luong, N. Ravindran, M. Cordeiro, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|E. Shamsher, Jules-Gonin Eye Hospital, Universite de Lausanne, Lausanne, Vaud, SWITZERLAND|S. Somavarapu, School of Pharmacy, University College London, London, London, UNITED KINGDOM|M. Cordeiro, Ophthalmology Research Group, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Alzheimer's disease (AD) is the major cause of dementia in the world with increasing evidences of the retina being affected. Since no cure exists, there is an urgent unmet need to find new treatments. Resveratrol, a natural polyphenol found in dark chocolate and red wine, has been advocated as a potential neuroprotectant in this disease. However, resveratrol has a low solubility and bioavailability limiting its clinical translation. In this study, we assessed a novel formulation of resveratrol in vitro and in vivo in a triple transgenic Alzheimer's disease (3xTg-AD) mouse model.

Methods: Resveratrol nanoparticles (RNs) were formulated using a thin rehydration technique. They were assessed in vitro on R28 cells against glutamate excitotoxicity and cobalt chloride induced hypoxia. Next, 3xTg-AD mice received intranasally either RNs (n=7) or an equivalent vehicle (n=6) 5 days a week for 3 months. After 3 months of treatment, animals were imaged using Detection of Apoptosing Retinal Cells (DARC). DARC count was defined as the number of fluorescent spots counted by a masked investigator. After sacrifice, their brains were harvested and immunostained for amyloid-beta (Aβ) and phosphorylated tau (pTau). Retinas were immunostained with Brn3a, a retinal ganglion cell (RGC) marker.

Results: RN formulation incorporating over 10 mg/ml resveratrol was stable over 90 days. RNs were able to protect R28 cells exposed to glutamate compared to the vehicle (IC_{50} 25.1±0.4 vs 14.4±1.0 mM, $p<0.0001$) but did not show any neuroprotection against cobalt chloride induced hypoxia compared to the vehicle (260.3±16.5 vs 200.7±22.3 μM, $p>0.05$). In vivo, DARC count was reduced with RN treatment compared to the vehicle (7.7±2.1 vs 49.1±13.3, $p<0.01$). However, these results did not correlate with a higher RGC density compared to the vehicle (1205±203 vs 1015±100 cells/mm^2, $p>0.05$). Interestingly, Aβ and pTau depositions in the brain were reduced with RN treatment compared to the vehicle (3.6±0.2 vs 4.5±0.2 Aβ score, $p<0.01$ and 2.1±0.5 vs 6.6±1.9 pTau score, $p<0.05$). No adverse effects were seen in vivo either systemically or in the eye.

Conclusions: These promising results show that RN is non-toxic and neuroprotective in vitro and in vivo when administered intranasally. However, DARC imaging failed to show a correlation with RGC density. Further studies are needed to confirm these results.

CONTROL ID: 3712402

SUBMITTER (NAME ONLY): Sukhvinder Singh

TITLE: Adenosine treatment ameliorates bacterial endophthalmitis by promoting antimicrobial activity and inhibiting inflammatory milieu

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Singh, Z. AHMAD, S. Das, A. Kumar, Ophthalmology, Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recently, we performed global metabolomics and transcriptomic analyses to determine key signaling pathways perturbed during experimental S. aureus endophthalmitis. We observed dysregulation in purine metabolism with a significant decline in “adenosine” levels. Here, we sought to determine the role of adenosine signaling in the pathobiology of bacterial endophthalmitis.

Methods: Bacterial endophthalmitis was induced in C57BL/6 mice by intravitreal (IVT) injection of S. aureus (SA) strain, RN6390. Retinal tissue was used for metabolomics and transcriptomic studies. The physiological role of adenosine was determined by IVT injection 6 h post-SA infection. Disease progression was evaluated by a daily eye exam and ERG analysis and assessment of bacterial burden and inflammatory cytokines. Mechanistic studies were performed using cultured human retinal Müller glia, mouse bone marrow-derived macrophages (BMDMs), and challenging them with S. aureus in the presence/absence of adenosine or specific inhibitors/activators.

Results: Our temporal metabolomics and transcriptomic analyses revealed a time-dependent decrease in adenosine levels and its signaling pathway genes in S. aureus-infected mouse retina. Interestingly, intravitreal administration of adenosine significantly reduced bacterial burden and intraocular inflammation resulting in preserved retinal functions. The supplementation of adenosine enhanced the expression of its signaling pathway genes CD73 and ADORA1. Moreover, adenosine treatment enhanced the expression of antimicrobial peptides viz. S100A7/A8 in Muller glia and BMDMs, resulting in increased bacterial phagocytosis and killing. Adenosine treatment exhibited anti-inflammatory properties in SA-infected cells.

Conclusions: Our study demonstrates reduced adenosine and impairment of its downstream signaling during bacterial endophthalmitis. Adenosine derivatives could be used as an anti-inflammatory/anti-bacterial therapy to improve visual outcomes in endophthalmitis.

CONTROL ID: 3712403

SUBMITTER (NAME ONLY): Houbin Zhang

TITLE: Intelligent Quantification of Retinal Ganglion Cells in the Entire Mouse Retina Based on Improved YOLOv5

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zhang, F. Yang, Sichuan Academy of Medical Sciences and Sichuan People's Hospital, Chengdu, Sichuan, CHINA|J. Zhang, Y. Huo, J. Yang, X. Wang, B. Yan, X. Du, J. Liu, L. Liu, Y. Liu, University of Electronic Science and Technology of China, Chengdu, CHINA|

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ABSTRACT BODY:

Purpose: To develop an automatic method to count specifically-labeled mouse retinal ganglion cells (RGCs) with improved accuracy and efficiency. This method can be used to assess the status of RGC degeneration in glaucoma mouse models.

Methods: An automated algorithm was developed based on improved YOLOv5. Five channels instead of a single channel with the Squeeze-and-Excitation block added was used to improve the accuracy of counting. The complete number of RGCs in an intact mouse retina is obtained by dividing the retina into small overlapping areas and counting followed by merging all divided areas together using the Non-Maximum Suppress algorithm. The degeneration of RGCs was induced by intravitreal injection of NMDA. RGCs were labeled with an anti-BRN3A antibody.

Results: The automated quantification result shows a very strong correlation (mean Pearson correlation coefficient approximately equal to 0.993) with that of manual counting for both normal mice and a glaucoma mouse model. Our model achieves a mean average precision of 0.981. Furthermore, the GPU calculation time for each mouse retina is less than one minute.

Conclusions: We have developed a new automatic RGC counting technique with great accuracy and speed. It will provide a convenient tool for researchers who are engaged in glaucoma research using mouse models to understand the pathogenesis of glaucoma and develop potential therapeutic drugs.

CONTROL ID: 3712404

SUBMITTER (NAME ONLY): Rajalakshmy Ayilam Ramachandran

TITLE: The biomolecular composition of extracellular vesicles released by corneal epithelial cells during Pseudomonas aeruginosa infection

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ayilam Ramachandran, D.M. Robertson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Rajalakshmy Ayilam Ramachandran: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Robertson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pseudomonas aeruginosa (PA) is a major cause of infectious keratitis. Extracellular vesicles (EVs) are membrane bound nanovesicles secreted by cells that play a key role in cell communication. The purpose of this study is to characterize the biomolecular cargo in corneal epithelial-derived EVs released during PA infection in the corneal epithelium.

Methods: Telomerase-immortalized human corneal epithelial cells were infected with a standard invasive test strain of PA (strain PA01) for six hours. EVs were isolated from cell culture supernatants by size exclusion chromatography. Pooled fractions F1/F2 contained EVs and pooled fractions F4/F5 contained secretory proteins. Uninfected cells and planktonic PA were used as controls. Immunoblotting was performed for EV markers CD63, CD9, CD81, TSG101 and flotillin; size and concentration were determined by nanoparticle tracking analysis (NTA). Mass spectrometry was performed by the Proteomics Core at UTSW. Protein abundance values were log2 transformed and analyzed using a two-tailed t-test. Proteins with $p<0.05$ were subject to analysis using functional enrichment analysis tool (FunRich) software.

Results: All of the tested EV markers were detected in EVs. Protein concentration was lower in EVs than the secretory fraction. Using NTA, the average EV particle size was 30 ± 150 nm. PA infection did not alter EV particle number. Comapring protein abundance, 132 proteins in EVs released from PA-infected cells were significantly different than EV released from non-infected cells. Of these, 72 proteins were upregulated in response to PA-infection. Gene enrichment analysis indicated that among the 132 differentially expressed proteins, most genes belong to energy and metabolic pathways. Of the 72 upregulated proteins, gene enrichment analysis showed that the highest percentage of genes were related to G alpha and IL-8 signaling, energy pathways, signal transduction, metabolism, and hydrolase activity.

Conclusions: While PA infection does not alter the number of EVs released by corneal epithelial cells, it does alter the proteomic profile. Bioinformatics analysis indicates that proteins related to critical biological process including immune signaling, energy metabolism and cell communication pathways are enriched in corneal epithelial EVs released during PA infection.

CONTROL ID: 3712405

SUBMITTER (NAME ONLY): Dion Kevin III

TITLE: Two-color full-field stimulus thresholds under scotopic and photopic conditions in inherited retinal degenerations

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kevin III, University of Mississippi, University Park, Mississippi, UNITED STATES|D. Kevin III, J.C. Park, N. Sabbia, J. McAnany, R.A. Hyde, Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The full-field stimulus test (FST), a measure of visual sensitivity typically obtained under dark-adapted conditions, is correlated with the most sensitive location of the visual field measured by dark-adapted static perimetry. The purpose of this study was to perform a comprehensive analysis of the FST under dark-adapted (DA) and light-adapted (LA) conditions with red and blue light, and to determine their relationship with visual field area assessed by kinetic perimetry.

Methods: Eleven subjects with a known diagnosis of an inherited retinal degeneration (IRD) participated. Visual field area was determined using an Octopus 900 kinetic perimeter with three target sizes (V4e, III4e, and I4e). Area of scotomata, if present, were subtracted from the recorded field area. FST thresholds were obtained with photopically matched (cd/m^2) red (632 nm) and blue (468 nm) stimuli under LA and DA conditions. DA-FST (red and blue) thresholds were compared with LA-FST (red and blue) thresholds. DA-FST (red and blue) and LA-FST (red and blue) thresholds were also compared with the visual field areas.

Results: FST thresholds for red and blue stimuli were highly correlated under DA ($r = 0.94$, $p < 0.001$) and LA ($r = 0.95$, $p < 0.001$) conditions. For 9 of the 11 subjects, DA-FST threshold was approximately 2.2 log units higher for the red stimulus than for the blue stimulus. The remaining 2 subjects had equal red and blue DA-FST thresholds, consistent with their clinically apparent lack of rod function. LA-FST threshold was approximately 0.2 log units higher for the red stimulus than for the blue stimulus. For subjects with nearly normal visual fields (where $\log_{10}$ (visual field area [$degrees^2$]) > 3.5), FST values varied widely, with no measurable dependence on visual field area. In contrast, for subjects with reduced visual field areas, FST thresholds increased as visual field area decreased.

Conclusions: FST threshold differences between red and blue stimuli were consistent with predictions based on the scotopic and photopic spectral sensitivity functions, allowing the quantification of full-field rod- and cone-pathway sensitivity in this cohort of IRD patients. For subjects with marked field loss, FST thresholds were associated with kinetic field area.

CONTROL ID: 3712406

SUBMITTER (NAME ONLY): Steven Shen

TITLE: Long-term effects of anti-VEGF therapy versus panretinal photocoagulation (PRP) on retinal vessel caliber in eyes with proliferative diabetic retinopathy (PDR)

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.L. Josic, Jaeb Center for Health Research, Tampa, Florida, UNITED STATES|S. Shen , J.W. Pak, S. Meuer, A. Domalpally, B.A. Blodi, Wisconsin Reading Center, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The DRCR Retina Network Protocol S trial was a non-inferiority study that compared ranibizumab (RBZ) to PRP in eyes with high-risk PDR. To better understand the long-term effects of anti-VEGF therapy, we performed a post-hoc evaluation of retinal vasculature in PDR eyes treated with RBZ versus PRP.

Methods: Fundus photographs of study eyes were evaluated for retinal vessel caliber at Baseline (BL), 2-Year (Y2), and 5-Year (Y5) time points. The Integrative Vessel Analysis (IVAN) software was used to measure Central Retinal Artery/Vein Equivalents (CRAE/CRVE) and the arteriovenous ratio (AVR) of vessels at 1 disc diameter from the optic nerve. Changes in CRAE, CRVE, and AVR over the 3 time points were analyzed between the RBZ and PRP groups using mixed linear regression models. Sensitivity analyses included censored eyes in each randomization group that received the alternate treatment.

Results: 107 eyes (83 participants) with gradable images for all 3 timepoints were analyzed: 48 eyes (35 participants) in the RBZ group and 59 eyes (48 participants) in PRP group. CRAE decreased significantly more in the PRP versus (vs) RBZ arm at Y2 (mean (SD) = -12 (17) μm vs. -2 (12) μm p=0.003), and there was a trend towards greater decrease in the RBZ arm between Y2 and Y5 (-1 (17) μm vs. -8 (18) μm, p = 0.13) with no difference between the groups at Y5 (-13 (18) vs. -9 (17), p = 0.22). CRVE decreased consistently in the PRP vs. RBZ arm at Y2 (-19 (25) vs. -14 (22), p = 0.26), with a larger decrease in the PRP arm at Y5 (-28 (27) μm vs. -18 (21) μm, p = 0.01). However, this decrease was not sustained following sensitivity analysis. In the RBZ group, the mean (SD) number of injections was 22.0 (11.4) at Y5 with no difference between BL/Y2 and Y2/Y5. In the final models, inclusive of ocular factors, BL demographics and randomization stratification factors, the only additional factor associated with changes in CRAE and CRVE was BL diabetic retinopathy.

Conclusions: Decreases in arteriolar and venular caliber were seen over 5 years in both the RBZ and PRP groups. While most of the arteriolar narrowing occurred within the first 2 years for the PRP group, it occurred after 2 years in the RBZ group, suggesting that these treatments may affect the retinal vasculature at differential rates.

CONTROL ID: 3712407

SUBMITTER (NAME ONLY): Jens Kiilgaard

TITLE: The clinical applicabillity of IHC staining for BAP1 for prognostication of uveal melanoma

SESSION TITLE: Not all who wanders is lost - Prognostication, diagnosis, and treatments of ocular tumors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.F. Kiilgaard, C. Faber, M.M. Bagger, Dept. of Ophthalmology, Rigshospitalet, Copenhagen, DENMARK|J.F. Kiilgaard, C. Faber, S. Heegaard, Kobenhavns Universitet, Kobenhavn, DENMARK|S. Heegaard, D. Scheie, Dept. of Pathology, Rigshospitalet, Kobenhavn, DENMARK|

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ABSTRACT BODY:

Purpose: To evaluate the value of IHC staining for BAP1 and PRAME in a routine clinical setup

Methods: Patients treated for uveal melanoma from 2017 to 2021 were included in the study. IHC stainings were performed on both cytospin, enucleated eyes and cell blocks using self-clotting technique

Results: A total of 222 patients were diagnosed with uveal melanoma at the Copenhagen University clinic. 143 patients were treated for Choroidal melanoma, 13 for ciliary body melanoma and 66 for iris melanoma. One patient with iris melanoma chose not to be operated.One Patient was treated for bilateral uveal. melanoma.Of the 65 Patients with iris melanoma 64 were treated with local resection and one patient was enucleated. Of the 156 patients with posterior melanoma, 45 had TransVitreal-RetinoChoroidal biopsy (TVRC) followed by enucleation of the eye and.4 patients had only enucleation. A total of 103 patients with posterior melanoma had TVRC and Brachytherapy and 1 patients was only treated with brachytherapy..

55 of 65 Iris patients had BAP1 IHC performed.. One patient had too little material for analyses and one sample was inconclusive, leaving 53 (96%) sample diagnostic. 47 of 49 enucleates eyes were analysed for BAP! IHC and only 1 was inconclusive leaving a total of 46 samples diagnostic (98%). For the TVRC this number was only 55% (73 of 133 patients)

Conclusions: BAP1 IHC yields a high outcome when "true" histology is availble, but is not very stable in cytological preparations.

CONTROL ID: 3712408

SUBMITTER (NAME ONLY): Deepak Poria

TITLE: Investigating the effect of a llama-derived transducin nanobody on mouse rod function

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Poria, J. Luu, K. Palczewski, V. Kefalov, Ophthalmology, Gavin Herbert Eye Institute, University of California Irvine, Irvine, California, UNITED STATES|G. Iyer, Brown School of Social Work, Washington University in St Louis, St Louis, Missouri, UNITED STATES|H. Leinonen, School of Pharmacy, University of Eastern Finland, Kuopio, FINLAND|V. Kefalov, Physiology and Biophysics, University of California, Irvine, California, UNITED STATES|K. Palczewski, Physiology and Biophysics, and Biochemistry, University of California, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rhodopsin mediates light detection by activating the G protein transducin, a heterotrimeric complex of G_{α}, G_{β} and G_{γ} subunits. Upon activation, G_{α} dissociates from $G_{\beta\gamma}$ and initiates downstream signaling to produce the photoresponse. Proper G_{α} function is required for light detection, while dysregulated $G_{\beta\gamma}$ signaling could lead to neurological and carcinogenic conditions. Recently, a llama-derived nanobody (Nb5) was shown to bind the $G_{\beta\gamma}$ heterodimer, covering the G_{α}-binding site and potentially modulating G-protein signaling. Here, we investigated the function of rods in transgenic mice expressing the Nb5 nanobody.

Methods: We generated transgenic mice expressing Nb5 under the rhodopsin promoter. To facilitate detection, Nb5 was flanked by a FLAG domain. The animals were bred on a C57Bl/6 background, maintained on a 12hr light/dark cycle, and dark-adapted overnight for experiments. The Nb5 effects on rod function were studied by scotopic in-vivo electroretinography (ERG), ex-vivo transretinal recordings, and optokinetic behavior experiments. Retina histology was studied by FLAG and peanut agglutinin immunohistochemistry. Nb5 expression in the retina was quantified by western blotting.

Results: In-vivo ERG revealed a 50% reduction in maximal a-wave response amplitude in mutant mice versus controls. Dark-adapted fractional sensitivity, estimated from dim flash transretinal responses, was reduced by 30% in the mutants versus controls. Scotopic visual acuity and contrast sensitivity both were reduced by 30% in the mutants versus controls. Western blots showed robust Nb5 expression in the mutants, and immunohistochemistry confirmed Nb5 expression in rods. The presence of Nb5 down-regulated G_{α} subunit expression by 75% in the mutant retinas. Histological studies did not reveal any retinal degeneration in the mutants up to 5 months relative to controls. However, the immunohistochemistry revealed a non-uniform Nb5 expression in the outer nuclear layer of mutant retinas.

Conclusions: We conclude that the transducin nanobody likely remains bound to the $G_{\beta\gamma}$ complex, leading to reduced rod sensitivity and visual acuity, but without inducing degeneration. Together, our results demonstrate that expression of Nb5 in rods partially suppresses their function without adverse effects on their long-term survival, advancing development of new types of G protein-coupled receptor targeting drugs.

CONTROL ID: 3712409
SUBMITTER (NAME ONLY): Valeria Lopez
TITLE: Contrast Sensitivity Application for Augmented Reality Wearable Device
SESSION TITLE: Machine Learning and Augmented Virtual reality
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Johnson, N. Rady, G. Mijares, M. Abou Shousha, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|V. Lopez, M.K. Durbin, A. Nicklin, OD, M. Abou Shousha, Heru, Inc., Miami, Florida, UNITED STATES|
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ABSTRACT BODY:

Purpose: The Pelli-Robson (PR) chart measures contrast sensitivity by presenting letters of decreasing contrast to determine a patient's threshold contrast. The purpose of this study is to demonstrate the comparability of a contrast sensitivity application developed for a wearable augmented reality platform to the PR contrast sensitivity test.
Methods: Fourteen participants with and without contrast sensitivity deficits were recruited to complete the Heru contrast sensitivity (HCS) application and PR chart test. Randomization determined which eye, OD or OS, was tested for each participant. The PR chart test was administered to participants with full refractive correction. The Heru contrast sensitivity application (HCS) was installed on a Magic Leap 1, size 2 headset, and uses a tumbling E presentation on a light background with a shrinking staircase thresholding strategy. Trial lenses were inserted into the headset to correct using the distance spherical equivalent. To improve our sampling of the lower end of the contrast sensitivity range, participants repeated HCS and PR tests using neutral density filters with 2x and 3x attenuation (ND2 and ND3). Contrast sensitivity values were compared between the two tests using Bland Altman analysis.
Results: Our study included 14 eyes, 79% female, with an age range of 24-80 years old (mean age of 49 years). Fourteen eyes from 14 subjects were independently tested with both methods using no filter and using a neutral density filter with an attenuation factor of 2 (ND2). Eleven of those eyes were also tested with a neutral density filter with an attenuation factor of 3, but two of the results were invalid because the subject could not see the PR chart. The overall mean difference was -0.08 dB with limits of agreement from -0.7 to 0.75 dB, showing significant variability. The mean difference and total number of outliers increased with the use of a neutral density filter (-0.03 with no filter, -0.14 with ND2, and -0.08 with ND3 (Figure 1), with outliers of 7%, 21% and 22% respectively.
Conclusions: It is possible to implement a contrast sensitivity test on a wearable device, and for the tested population the mean log contrast sensitivity matches well on average to the Pelli-Robson.

CONTROL ID: 3712410

SUBMITTER (NAME ONLY): Rupesh Agrawal

TITLE: Anti-Tubercular Therapy in the Treatment of Tubercular Uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.V. Agrawal, Ophthalmology, Tan Tock Seng Hospital, Singapore, SINGAPORE|R.V. Agrawal, Singapore Eye Research Institute, Singapore, SINGAPORE|V. Gupta, Ophthalmology, Post Graduate Institute of Medical Education and Research, Chandigarh, Chandigarh, INDIA|B. Betzler, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, SINGAPORE|J.H. Kempen, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|I. Testi, C. Pavesio, Uveitis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|I. Putera, R. La Distia Nora, Universitas Indonesia, Depok, Jawa Barat, INDONESIA|O. Kon, Respiratory Medicine, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To quantitatively evaluate the efficacy of anti-tubercular therapy (ATT) in tubercular uveitis (TBU) patients.

Methods: In this systematic review and meta-analysis, a search of PubMed, EMBASE and Cochrane Library was conducted for articles on ATT outcomes in TBU published between 1st January 2000 and 1st August 2021. Study details, demographics, clinical features, investigations that led to a diagnosis of TBU, treatment regimen (ATT, corticosteroids and immunosuppressants), and information on target treatment outcomes was extracted independently by three reviewers. A meta-analysis of proportions was performed. Main outcome measures include inflammation recurrence; inflammation reduction; complete resolution of inflammation; improved visual acuity (VA); ability to taper corticosteroids to < 10 mg/day without inflammatory progression; use of adjunctive immunosuppressants while on ATT. This review is prospectively registered in PROSPERO (CRD42020206845)

Results: Forty-nine studies reporting data for 4,017 TBU patients were included. In comparative studies, the odds ratio (OR) of inflammatory recurrence was 0.33 (95%CI: 0.19-0.60) for TBU patients treated with ATT versus no ATT. For TBU patients treated with ATT, the pooled absolute incidences of inflammatory recurrence, inflammatory reduction, complete resolution of inflammation and of visual acuity improvement were 13% (n=310/2,216; 95%CI: 9-18), 81% (n=217/276; 95%CI: 62-95), 83% (n=1,167/1,812; 95%CI: 77-89), and 65% (n=347/542; 95%CI: 51-78) respectively. Corticosteroids were tapered to <10 mg/day without inflammatory progression in 91% (n=326/395; 95%CI: 78-99) of patients, 9% (n=121/1,376; 95%CI: 6-13) of whom were administered concomitant immunosuppressive agents alongside ATT.

Conclusions: Treatment of TBU with ATT is associated with a high level of control or improvement of inflammation, followed by a two-thirds improvement in the risk of inflammatory recurrence in TBU patients; only one-seventh of TBU patients have recurrences during follow up. Visual acuity improved in most patients. However, more prospective studies with detailed reporting of ATT regimens, patient subgroups and outcomes are required to elucidate the effectiveness of ATT about other outcome measures.

CONTROL ID: 3712411

SUBMITTER (NAME ONLY): Preet Sohal

TITLE: Analyzing the effect of the COVID-19 pandemic on patient outcomes following keratorefractive surgery

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Sohal, B. Murdock, D. Belyea, Ophthalmology, The George Washington University, Washington, District of Columbia, UNITED STATES|H. Pakhchanian, I. Ali, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of the COVID-19 pandemic on keratorefractive surgery outcomes by comparing rates of post-operative complications prior to and during the pandemic.

Methods: A retrospective cohort study was conducted using TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple large health organizations in the United States. Patients were identified based on using validated CPT procedure codes for keratorefractive Surgery and were separated into two cohorts based on if they received their procedure before the pandemic protocols (Jan 1, 2019-Mar 17, 2020) or during the pandemic (Mar 18, 2020 to Dec 1, 2020). Then, 1:1 propensity score matching was utilized to create two same-sized cohorts which matched for various demographic and medical conditions. Subsequently, the relative risk for 11 specific post-operative complications between was compared between the two cohorts. Relative risks between cohorts were calculated and outcomes with $p<0.05$ were considered statistically significant.

Results: A total of 2,626 patients were included in analysis with 1,313 in each of the pre-pandemic and pandemic cohorts after propensity matching. Dry eye had a greater risk (RR 1.29; 95 CI, 0.94, 1.77) among the pandemic cohort, however the results were not statically significant ($P>0.113$). Similarly, retinal detachment was observed to have a lower risk (RR 0.83; 95% CI, 0.36, 1.92) among the pandemic cohort but the results were not statistically significant either ($P >0.663$). No statistically significant differences in the remaining post-operative complications were observed including recurrent corneal erosion, secondary corneal erosion, corneal scar/opacity, diffuse lamellar keratitis, corneal neovascularization, vitreous degeneration and hemorrhage, retinal edema, and cystoid macular degeneration.

Conclusions: The COVID-19 pandemic undoubtedly affected surgical practice of many ophthalmologists, and many operating rooms adopted new protocols after safety concerns for surgeons and ancillary staff. The results show that there was no statistically significant difference in the rate of post-operative complications for patients undergoing keratorefractive surgery before and during the pandemic. This suggests that despite the new safety protocols implemented in operating rooms, the quality-of-care patients received during the pandemic was not impacted.

CONTROL ID: 3712412

SUBMITTER (NAME ONLY): Annette Hoskin

TITLE: The International Globe and Adnexal Trauma Epidemiological Eye Study (IGATES) registry.

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Hoskin, S.L. Watson, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|A.K. Hoskin, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|R.V. Agrawal, Tan Tock Seng Hospital, Singapore, SINGAPORE|Y. Irawati, JEC Eye Hospitals and Clinic, Jakarta, INDONESIA|M. Shah, Drashti Netralaya, Dahod, INDIA|P.S. Subramanian, University of Colorado, Denver, Colorado, UNITED STATES|M. Soleimani, Farabi Eye Hospital, Tehran, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|A. Sen, Sadguru Netra Chikitsalaya, Chitrakoot, Kolkata, INDIA|S. Natarajan, Aditya Jyot Eye Hospital Pvt Ltd, Mumbai, Maharashtra, INDIA|J. Dalma, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|E. Pradhan, Tilganga Institute of Ophthalmology, Kathmandu, NEPAL|A. Ayachit, MM Joshi Eye Institute, Hubli, Karnataka, INDIA|D. Giridhar, Giridhar Eye Institute, Kochi, Kerala, INDIA|M. Agarwal, Dr Shroff's Charity Eye Hospital Delhi, New Delhi, Delhi, INDIA|A. Awan, Shifa International Hospitals Ltd, Islamabad, Islamabad, PAKISTAN|K. Bhattacharjee, Sri Sankaradeva Nethralaya, Guwahati, Assam, INDIA|

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ABSTRACT BODY:

Purpose: Purpose: With few exceptions, analysis of eye injuries, has been limited to relatively small-scale studies and currently there is no internationally adopted registry to collect data on eye injuries. This study reports analysed data collected from a new international eye injury registry.

Methods: Data was collected from 18 participating centers across 8 countries; Indonesia, India, USA, Iran, Nepal, Mexico, Guatemala and Pakistan utilizing a freely accessible online platform, the International Globe and Adnexal Trauma Epidemiological Eye Study (IGATES) registry. The mechanism and location of injury, clinical management and visual outcomes were analyzed. All data were anonymized and participating sites obtained ethics from their local ethics review board.

Results: 1988 eyes (representing 1922 patients) with a male to female ratio of 3.7 and mean age of 30.6 years were included in the analysis. The male to female ratio was highest in Guatemala (7.1) and lowest in Mexico (2.0). More than 9/10 injuries (93%) were accidental/unintentional with 52.9% occurring in the home and 23.9% in the workplace. Iran had the highest rate of workplace injuries (53.7%) and the USA and Mexico the highest rate of domestic eye injuries, 63.0% and 67.0%, respectively. Eye protection was reported as worn in 7/1859 (0.4%) of all patients.

Conclusions: The majority of eye injuries were accidental and occurred at home, there were significant differences found amongst the surveyed countries. This may have implications for public health interventions such as education of the public in regards to the risks in the home. IGATES will provide an opportunity to use big data to analyze eye injuries, to help improve outcomes and ultimately reduce their incidence with real-time, informed prevention strategies.

CONTROL ID: 3712414

SUBMITTER (NAME ONLY): José Arteaga Rivera

TITLE: Combined Intense Pulsed Light and Low Level Light Therapy Vs. Oral Azithromycin for the treatment of moderate to severe hypersecretory meibomian gland disfunction.

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.Y. Arteaga Rivera, D. Jimenez-Collado, N. Macriz-Romero, A. Ramírez-Miranda, C.A. Müller-Morales, A. Navas, E.O. Graue-Hernandez, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To compare subjective and objective clinical outcomes in patients treated with oral azithromycin or intense pulsed light (IPL) + low level light (LLLT).

Methods: This is a retrospective observational study in 20 patients with moderate to severe hypersecretory meibomian gland disfunction (MGD). Twelve patients were treated with oral azithromycin 1g once a week for 3 weeks, and 11 patients with IPL+LLLT using the Eye-Light® and My Mask® (Espansione Marketing S.p.A, Bologna, Italy) respectively, following the eye-light treatment protocol once a week for 3 weeks. Both groups were reevaluated 1 month after finishing treatment.

Patients with any medication or condition that could modify the ocular surface, macrolide hypersensitivity, pregnant and breastfeeding women were excluded. Variables analyzed were: non–invasive tear break-up time, meibography, tear meniscus height (TMH) and conjunctival redness (OCULUS Keratograph® 5M, Wetzlar, Germany). Uncorrected and corrected visual acuity, tear break-up time (TBUT), Schirmer I test, Oxford scale for fluorescein staining and OSDI scores were also recorded.

Results: Mean patient age was 57.65±10.43 years. All pretreatment variables were similar in both groups ($p>0.05$). When compared to their baseline measurements the group treated with IPL+LLLT showed statistically significant differences ($p<0.05$) in TMH (0.34±0.26 to 0.40 ±0.28)), Oxford score (1.32±1.04 to 0.55±0.59), dry eye sensation (3.18±1.60 to 1.55±1.63), eyelid redness (1.82±2.27 to 0.73±1.34), eyelid telangiectasia (1.27±1.00 to 0.27±0.46), eyelid edema (1.09±0.83 to 0.27±0.46), ocular mucus secretion (0.64±0.80 to 0.00) and OSDI scores (44.09±20.29 to 19.09±17.86). The azithromycin group showed significant differences ($p<0.05$) in TBUT (5.79±4.41to 9.88±10.52), dry eye sensation (3.25±1.48 to 1.75±1.76), eyelid hyperemia (1.41±0.66 to 1.08±0.66) and OSDI scores (36.5±18.68 to 22.25±13.63). When comparing IPL+LLLT group with the azithromycin group, no significant differences were observed.

Conclusions: Both treatments confer improvement in the subjective and objective parameters studied. Despite the fact that no significant differences were observed when comparing both groups, patients treated with IPL+LLLT showed improvement in more variables suggesting that it might be superior for the treatment of hypersecretory MGD.

CONTROL ID: 3712416

SUBMITTER (NAME ONLY): Gabriella Rogers

TITLE: Inorganic polyphosphate-collagen complexes improve corneal epithelial cell function under glucose starvation and enhance corneal wound healing

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.M. Rogers, D. Myung, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|D. Myung, Ophthalmology, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure: Gabriella Rogers: Commercial Relationship: Code N (No Commercial Relationship) | David Myung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal injuries collectively represent a major global human health challenge, affecting hundreds of millions of people each year. Thus, there is a critical need for treatments that drive proper corneal wound healing. Polyphosphate (PolyP) is a biocompatible inorganic linear polymer composed of phosphate units. In the past few years, studies have shown that PolyP functions as a storage reservoir for ATP, regulates cell responses to stress, and increases cell proliferation. In this study we hypothesized that collagen crosslinked via electrostatic interactions using PolyP will form complexes that can support corneal wound healing by providing additional energy to facilitate cellular growth and normal cell function.

Methods: PolyP-collagen complex was formed by adding PolyP45 to bovine collagen type 1. The presence of PolyP in the complexes was confirmed by adding DAPI and reading the fluorescence intensity using excitation/emission settings of 350/550 nm. Corneal epithelial cells (CECs) were seeded on PolyP-collagen complexes. Cell phenotype and morphology were evaluated via staining with CK3, ZO-1 and phalloidin. The intracellular content of PolyP and mitochondrial morphology was evaluated using DAPI and TOM 22 respectively, after 16 hours of cell starvation. Corneal wound healing was evaluated using an ex vivo model of organ culture. A lamellar keratectomy was performed in rabbit corneas followed application of PolyP-collagen. Corneal wound size was monitored daily using fluorescein.

Results: CECs seeded on PolyP-collagen expressed CK3, ZO-1 and were able to proliferate forming a monolayer. Serum and glucose-starved CECs that were not treated with PolyP-collagen exhibited reduced intracellular PolyP and fragmented mitochondria morphology. Starved CECs treated with PolyP-collagen showed increased intracellular PolyP and normal tubulated mitochondrial morphology. PolyP-collagen treated rabbit corneas had 75% of the wounds healed by day 5 compared to 0% from the untreated group.

Conclusions: CECs showed normal phenotype and biocompatibility in the presence of PolyP-collagen complexes. In addition, CECs were able to uptake PolyP-collagen that may have helped supply ATP to maintain normal mitochondrial function under starvation conditions. We suggest that intracellular PolyP levels may contribute to enhanced corneal wound healing and tissue regeneration

CONTROL ID: 3712418

SUBMITTER (NAME ONLY): Ricky Paramo

TITLE: Unraveling how Corneal Schwann cells Affect Axonal Regeneration

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Paramo, R. Mohan, P. Bargagna-Mohan, Neuroscience, UConn Health, Farmington, Connecticut, UNITED STATES|R. Paramo, R. Mohan, University of Connecticut School of Medicine, Farmington, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Ricky Paramo: Commercial Relationship: Code N (No Commercial Relationship) | Royce Mohan: Commercial Relationship: Code N (No Commercial Relationship) | Paola Bargagna-Mohan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal Schwann cells (cSCs) are glial cells that ensheath axons and provide trophic support for axons. Surgical procedures that lesion stromal axons often result in aberrant axonal regeneration with impaired sensation. This study aims to illuminate temporal and regio-specific changes in myelinating (m) and non-myelinating (nm) cSCs during injury by exploiting the proteolipid protein 1-enhanced green fluorescent protein (Plp1-egfp) mouse.

Methods: Anesthetized adult male and female Plp1-egfp mice were subjected to stromal micropocket injury. Corneas were harvested 7, 14, and 30 days post-injury and processed for whole mount immunohistochemistry using antibodies against L1CAM (nm-cSCs), beta III-Tubulin (bIIITub), and NF-200 (m-SCs). Samples were analyzed by epifluorescence microscopy. NeuronJ (FIJI software) was used to quantify axonal and cSC network from high-resolution tiled images. The limbus-to-limbus corneal diameter was set at 3.8 mm and an internal 1.6 mm diameter for the central cornea. Statistical analysis was performed using ANOVA with Tukey's multiple comparison test and results were considered significant with $P < 0.05$.

Results: Comparisons of the L1CAM, NF200, and eGFP staining in control corneas for both total and central networks revealed significantly higher density for L1CAM and eGFP over NF200 in the central cornea. Upon injury, all markers were reduced significantly at 7 d, but returned at 14 d post-injury and exceeded controls levels. The network of eGFP cells in the central cornea at 14 d exceeded that of NF200. At 30 d post-injury, the total network of eGFP cells remained the highest. In the central cornea, the eGFP network was equivalent to L1CAM but significantly greater than NF200 cells. At 30 d the eGFP network was greater than that of NF200 and bIIITub at the peripheral cornea, identifying regional differences in the regeneration of SCs and axons.

Conclusions: Our data suggest that differential expression of L1CAM and NF200 during SC restoration could contribute to aberrant axonal regeneration in the repairing central cornea. Regenerating cSCs apparently also initiate a pro-myelination repair program. This immunolocalization study examining the temporal and regio-specific changes in different cSC biomarkers could help advance our understanding of how these critical glial cells influence axonal growth and restore sensory function in injury and disease paradigms.

CONTROL ID: 3712419

SUBMITTER (NAME ONLY): Francisco Figueiredo

TITLE: Differences in acute chemical injury severity grading between Cornea specialists and non-Corneal specialists

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.C. Figueiredo, Biosciences Institute, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|F.C. Figueiredo, B.L. Teh, M. Shaw, J. sandhu, Ophthalmology, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Ocular chemical injuries (OCI) require prompt medical attention, including immediate assessment with appropriate treatment, as they are potentially blinding. Severity grading assessment of OCI on presentation is important both for management and prognosis.

This study aimed to look at inter-rater reliability between Cornea specialists and non-Corneal specialists in grading acute chemical injury severity.

Methods: This is a prospective study in a United Kingdom (UK) tertiary hospital in two different time periods: September 2017–June 2018 and September 2021–December 2021.

Consecutive patients presenting to the Eye Emergency Department (EED) with a history of acute OCI within those two time periods were included. Patients were initially assessed by non-Corneal specialists of different grades (specialty trainee to consultant) using Roper-Hall classification, with treatment initiated as per local protocol. They were then assessed by Cornea specialists within 24 hours of presentation to compare the chemical injury severity grading.

Results: Forty eyes of 31 patients had acute OCI. Most of the patients were male (77%; n=24) with mean age of 42 (range:19-84; SD:18). The majority (55%; n=17) had alkali injuries and 65% (n=20) of them were accidents at workplace or home.

Thirty-five eyes (87%) had a mild chemical injury (Grade 1 and 2) and carried a good prognosis. Seven eyes with mild chemical injury and four eyes with moderate-severe chemical injury of Grade 3 and 4 were due to assault.

There was a 70% (n=28 eyes) agreement between Cornea specialists and non-Corneal specialists. The remaining 10% (n=4 eyes) were under-graded and 20% (n=8 eyes) were over-graded. Of those under-graded eyes, there was no change in management in 3 eyes, including two which required perilimbal conjunctiva resection and human amniotic membrane transplant. One had additional topical therapy and had a full recovery.

For the over-graded eyes, six eyes had their topical therapy regime simplified. Two eyes were admitted to hospital for treatment and discharged earlier following re-grading of the injury.

Conclusions: There is good inter-rater reliability between Cornea specialists and non-Corneal specialists in grading OCI severity. Over-grading may increase treatment cost with avoidable admission whilst under-grading may compromise patient care. Further data collection is needed to allow for two comparable time period.

CONTROL ID: 3712422

SUBMITTER (NAME ONLY): Wai Lydia Tai

TITLE: Histone deacetylase 11 deficiency promotes PC12 cell proliferation and differentiation

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Tai, X. Wang, A. Ashok, K. Cho, S. Jiang, D. Chen, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|X. Wang, Weifang Medical University, Weifang, Shandong, CHINA|

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ABSTRACT BODY:

Purpose: Epigenetic factors play dynamic roles in neuronal development, progenitor cell proliferation, differentiation, and neural regeneration. Histone modification by histone deacetylases (HDACs) represents a key mechanism by which neurons regulate transcriptional profile during proliferation and differentiation. Accumulative studies have highlighted the therapeutic potential of HDACs inhibitors in neurological disorder. Therefore, we aimed to find HDAC that correlates with retinal ganglion cells (RGCs) development, which may provide a target of HDAC inhibitor in retinal degenerative diseases.

Methods: HDACs (members 1-6, 8-11) mRNA levels in retinal ganglion cells (RGCs) isolated from mouse at embryonic (E16) and postnatal (P0, P10) stages were analyzed by quantitative polymerase chain reaction (qPCR). PC12 cells were transduced with lentivirus carrying shRNA against HDAC11. Over 25 different transductants were generated with HDAC11 mRNA level knockdown ranged 20% to 70%. The transductants were subjected to proliferation assay, evaluated by 5-ethynyl-2'-deoxyuridine (EdU) incorporation before and after treatment of nerve growth factor (NGF; 30 ng/ml). Neurite outgrowth was quantitatively assessed 3 days after NGF-induction of neural differentiation.

Results: Initial screening of HDACs mRNA revealed a unique temporal increase of HDAC11 from E16 to P10, indicating an inhibitory contribution of HDAC11 to RGC growth capacity. To test this hypothesis, we established HDAC11 knockdown cell lines using neuron-like PC12 cells and examined their performance in proliferation and differentiation. In the absence of NGF, transduced cell line with about 50% knockdown in HDAC11 showed significantly increased number of dividing cells compared to naïve control PC12 cells while it also showed significantly more neurite outgrowth following NGF treatment, suggesting HDAC11 deficiency can enhance both proliferation and differentiation.

Conclusions: Our data show that HDAC11 may play a role in mediating neural progenitor cell proliferation and neuronal differentiation. These findings may suggest a novel target for promoting neuronal regeneration.

CONTROL ID: 3712423

SUBMITTER (NAME ONLY): Ye Sun

TITLE: c-Fos regulates retinal angiogenesis through modulating photoreceptor-released inflammatory proteins

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Sun, S. Kaneko, T. Wang, D.I. Tsirukis, E. Lam, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pathological proliferative angiogenesis causes irreversible blindness in vascular eye diseases such as retinopathy of prematurity (ROP). Inflammatory mediators are known key regulators in retinopathy and inflammation is often thought to come from infiltrating inflammatory cells, but we recently found that photoreceptors also can signal for blood vessel growth through inflammatory signals via c-Fos in a mouse model of retinal angiogenesis. However, the underlying molecular and cellular mechanisms of photoreceptor control in ROP via c-Fos remain to be determined.

Methods: Photoreceptor specific c-Fos knockout mice (c-Fos cKO) wss generated by crossing c-Fos flox/flox mice with rod photoreceptor specific Rhodopsin improved Cre mice (Rho-iCre). The oxygen induced retinopathy (OIR) mouse model was generated as a ROP preclinical mouse model. RNA Isolation, real-time PCR, western blot and immunohistochemistry were used to analyze gene expression and protein localization. Confocal imaging, fundus fluorescein angiography and HE staining were used to identify phenotypes. Adeno associated virus (AAV) was used to modulate gene expression. CUT&Tag sequencing was used to examine the targets of c-Fos. GraphPad Prism (v8.0) was used for statistical analysis.

Results: c-Fos expression was significantly induced and robustly activated in OIR retinas including photoreceptor layer at postnatal (P) 13. c-Fos deficiency in rod photoreceptors significantly reduced NV by 30% (p=0.007, n=16-26) without influencing VO (p=0.33) compared to littermate floxed controls. Pharmacologic treatment with c-Fos (AP-1) inhibitor (SR11302) and photoreceptor specific AAV shRNA subretinal delivery targeting c-Fos significantly suppressed retinal neovascularization in OIR model. CUT&Tag sequencing data showed that over 200 genes potentially bind to c-Fos at P14 only in retina with OIR not in normal control. In contrast, there were over 150 genes potentially bind to c-Fos at P14 only under normal condition but not in OIR condition.

Conclusions: These data suggest that c-Fos in photoreceptors mediates neovascularization through modulating photoreceptor-released inflammatory proteins in OIR retinas. Targeting c-Fos protected against neovascularization and may be a potential therapeutic for treating retinal angiogenesis.

CONTROL ID: 3712425

SUBMITTER (NAME ONLY): Ratnakar Tripathi

TITLE: Evaluation of delayed/chronic corneal toxicity and clinical manifestations for 4-month after mustard gas exposure to rabbit eyes in vivo

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Tripathi, N.R. Sinha, P.K. Balne, A. Hofmann, S.L. Green, L.A. Suleaiman, P. Sinha, N. Hesemann, R.R. Mohan, Ophthalmology, University of Missouri System, Columbia, Missouri, UNITED STATES|R. Tripathi, N.R. Sinha, P.K. Balne, A. Hofmann, P. Sinha, N. Hesemann, R.R. Mohan, Ophthalmology, Harry S Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|S.S. Chaurasia, Ophthalmology, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sulfur mustard (SM) gas exposure to the eye causes severe toxicity to the cornea called mustard gas keratopathy (MGK). This study investigated delayed/chronic corneal toxicity and clinical manifestations at 1-, 2-, and 4-months in rabbit eyes in vivo exposed to SM.

Methods: The study was approved by the institutional animal care and use committee and followed ARVO guidelines. New Zealand White rabbits (n = 36) were exposed to SM vapor at a target concentration of 200 mg-min/m^3 for 8 minutes. Clinical eye manifestations in live rabbits were performed with the slit-lamp microscope, confocal HRT3 microscope, Fante's grading system, fluorescein staining, Schirmer’s tests, pachymetry, applanation tonometry, and optical coherence tomography. At the endpoints, rabbits were humanely euthanized, and corneas were collected for histological, molecular, and cellular analyses.

Results: SM exposed rabbit corneas showed a significant corneal haze (Fante’s scores 2-4; $p<0.0001$), central corneal thickness (749-560 ± 40.7; $p<0.0001$), tear flow (18-21± 2.3 $p<0.0001$), and corneal edema, decreased in keratocyte density, loss of endothelium cell number and corneal neovascularization (NV) compared to naïve untreated control corneas up to 2-month post-SM exposure. At 4-month post-SM exposure, rabbit corneas developed additional pathologies including severe ulcer of varying sizes, epithelial defects, and NV at the peri-limbal plexus regions. Also, few of the SM-exposed rabbit eyes showed ruptured cornea with iris plugged the hole and prolapsed. In these rabbits, significantly decreased central corneal thickness ($p<0.001$) and severe epithelium-erosion were observed. The clinical quantitative analyses matched typical delayed/chronic corneal pathology. Histological and molecular studies are underway.

Conclusions: Mustard gas exposure to eyes cause severe delayed/chronic corneal toxicity in rabbits in vivo. Additional analysis is warranted.

CONTROL ID: 3712426

SUBMITTER (NAME ONLY): Kamran Rahmatnejad

TITLE: Comparison of Combined Phacoemulsification with Ahmed Glaucoma Valve implantation and Combined Phacoemulsification with Xen Gel Stent Implantation in Patients with Primary Open Angle Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Rahmatnejad, F.J. Gross, Ophthalmology, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|N. Chaganty, Mathematics and Statistics, Old Dominion University, Norfolk, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Kamran Rahmatnejad: Commercial Relationship: Code N (No Commercial Relationship) | Fredric Gross: Commercial Relationship: Code N (No Commercial Relationship) | N Rao Chaganty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the effect of combined phacoemulsification with Ahmed glaucoma valve implantation and combined phacoemulsification with Xen gel stent implantation on intraocular pressure (IOP) of patients with primary open angle glaucoma (POAG)

Methods: In this retrospective study, we enrolled 12 patients who underwent combined phacoemulsification with Ahmed glaucoma valve implantation (group 1) and 15 patients who underwent combined phacoemulsification with Xen Gel stent implantation (group 2). All 27 patients had preoperative IOP of 18 mm Hg or higher. We compared the IOP and number of IOP-lowering medications at baseline and postoperative month 3 (POM3) between the two groups.

Results: The age mean +/- standard deviation (SD) was 64.08+/-13.50 years for group 1 and 65.53+/-9.73 for group 2. Male composed 58% in group 1 and 60% in group 2. White gender composed 41.7% and 46.7% in group 1 and 2, respectively. After confirming the normality assumption, two sample t-test was performed for the difference between the two groups. At POM3, mean IOP decreased to 14.33+/-3.45 mm Hg (44% decrease) in group 1 and 18.53+/-8.38 (26.8% decrease) in group 2 (P=0.11). The number of IOP-lowering medications decreased from 3.08+/-0.90 to 1.33+/-1.16 in group 1, and from 3.13+/-1.30 to 1.27+/-1.39 in group 2 at POM3 visit (P=0.91).

Conclusions: In this study, phacoemulsification combined with Ahmed glaucoma valve implantation was more effective at lowering IOP in comparison to phacoemulsification combined with Xen gel stent implantation, although this difference did not reach a statistically significance level. Further studies with a larger sample size might be able to show a statistically significant difference between the two procedures.

CONTROL ID: 3712429

SUBMITTER (NAME ONLY): Bryan Le

TITLE: Anti-Inflammatory and Anti-Fibrotic Activities of Human Corneal Stromal Stem Cells and Their Extracellular Vesicles Measured by in vitro Assays

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Le, R. Knight, S. Robertson, S.X. Deng, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|B. Le, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Bryan Le: Commercial Relationship: Code N (No Commercial Relationship) | Rob Knight: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Robertson: Commercial Relationship: Code N (No Commercial Relationship) | Sophie Deng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Human Corneal Stromal Stem Cells (CSSC) have been shown to promote regeneration of transparent stromal tissue and suppress inflammation in wounded mouse corneas. Small extracellular vesicles (sEV) secreted by these CSSC have been implicated to play a crucial role in this process. It is important to identify those CSSC that display high regenerative capacity. This study investigated the capacity of CSSC and their sEVs to suppress inflammation and fibrosis using in vitro assays.

Methods: Conditioned media of primary human CSSC were collected for sEV isolation and assay analysis. Anti-inflammatory response was evaluated using a RAW 264.7 cell assay, in which osteoclast differentiation was induced by receptor activator of nuclear factor kappa-B ligand (RANKL) and Concanavalin A. Cell morphology and mRNA level of matrix metalloproteinase 9 (MMP-9), Tartrate resistant acid phosphatase (ACP5), and Cathepsin K (CTSK) was quantified by qRT-PCR. Anti-fibrotic activity was assessed by a differentiation protocol in which primary human corneal fibroblasts differentiated into myofibroblasts after TGF-β1 treatment and were assayed for pro-collagen I alpha-1 (pro-COLIa1) level via ELISA and the protein expression of myofibroblast markers, α-smooth muscle actin (αSMA) and fibronectin extra domain-A (EDA-FN) by immunohistochemistry.

Results: Conditioned media and sEVs from primary CSSCs were capable of significantly reducing gene expression of MMP-9 (5.37 folds and 2.07 folds, respectively, $p<0.05$), CTSK (2.1 and 3 folds, $p<0.05$), and ACP5 (2.2 and 2.1 folds, $p<0.05$) compared to the positive control in the RAW 264.7 cell assay. CSSC conditioned media potency correlates with their sEVs' potency to prevent monocyte-to-osteoclast differentiation. In anti-fibrotic assays, sEVs from CSSC reduced pro-COLIa1 level by 40.9% relative to the positive control and lowered αSMA-positive cells by 32% ($p<0.001$). Among these different CSSC derived from multiple donors, one distinct donor CSSC produced sEVs that repeatedly demonstrate a higher anti-inflammatory and anti-fibrotic capacity than other CSSC ($p<0.001$).

Conclusions: The anti-fibrotic activity of sEV could be quantified using in vitro assays. There is donor variation among CSSCs and their sEVs in respect to their anti-inflammatory and anti-fibrotic capacity. The factors didact the activities of sEV remain to be elucidated.

CONTROL ID: 3712430

SUBMITTER (NAME ONLY): Ying Zhu

TITLE: Intraocular Pressure (IOP) Performance with 25-Gauge Dual-Cutting 20,000cpm Beveled Vitrectomy Probes During Vitreous Removal

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhu, C. Garufis, V. Wuyyuru, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Ying Zhu: Commercial Relationship(s);Code E (Employment):Alcon | Carrie Garufis: Commercial Relationship(s);Code E (Employment):Alcon | Vara Wuyyuru: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: This study aims to 1) understand the IOP performance of 25+® Gauge (Ga) dual-cutting, 20K cuts per minute (cpm) beveled vitrectomy probes used for vitreous removal during a vitrectomy; 2) understand the operation time of vitreous removal during a vitrectomy.

Methods: 25+® HYPERVIT® beveled 20K cpm vitrectomy probes were driven by a CONSTELLATION® Vision System (Alcon Vision, LLC.) to aspirate vitreous in a hollow acrylic eye model. A digital transducer (OMEGA, PX409-001GUSBH) was connected to the bottom of eye model to detect IOP change during aspiration. 4cc of fresh porcine vitreous was filled into the eye model per testing. Six samples were tested under core duty cycle, vacuums of 250mmHg, 450mmHg and 650mmHg and cut rate of 20,000cpm. Both system IOP control enabled and disabled were used with 30mmHg as the initial IOP setting. Average IOP fluctuation during aspiration, final stable IOP, average operation time of vitreous removal were calculated for each test setting. Statistical analyses were performed on average IOP fluctuation rate using Welch's t- test with $p<0.05$.

Results: Without IOP compensation, the average fluctuation rate was -0.035 ± 0. 006mmHg/s for 250mmHg, -0.105 ± 0.008mmHg/s for 450mmHg and -0.175 ± 0.021mmHg/s for 650mmHg, which showed significant differences between each vacuum setting($p<0.05$). After enabling IOP compensation, average IOP fluctuation rate significantly reduced to 0.001±0. 005mmHg/s, 0.004 ±0.007 mmHg/s and 0.005±0.010 mmHg/s at vacuums of 250, 450 and 650mmHg($p<0.05$). There was no significant difference of IOP fluctuation rate between vacuum settings ($p>0.05$). Without IOP compensation, the final stable IOPs after removing vitreous at vacuum settings of 250mmHg, 450mmHg and 650mmHg were 22.11±1.80mmHg, 15.12± 0.41mmHg and 7.11± 1.20mmHg. With IOP compensation, the IOP level maintained at 30.75 ± 0.24 mmHg, 30.72 ± 0.84mmHg, and 30.52 ± 0.92 mmHg for the same vacuums. Corresponding operation times of complete removal of vitreous were 206s, 145s and 129s respectively.

Conclusions: During vitreous removal at the maximum cut rate, 25+® Ga 20K cpm vitrectomy probes with IOP compensation maintain IOP at improved levels with less fluctuations compared with no compensation. Using IOP compensation and 20K cpm vitrectomy probe in a 25G vitrectomy procedure can help surgeons to achieve a stable and efficient vitreous removal process.

CONTROL ID: 3712431

SUBMITTER (NAME ONLY): Lucas Kim

TITLE: Long-Term Outcomes and Histopathology from Ebola Virus Persistence in Ocular Tissues and Fluids (EVICT) Study

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Kim, T. Fashina, S. Yeh, University of Nebraska Stanley M Truhlsen Eye Institute, Omaha, Nebraska, UNITED STATES|L. Kim, Mercer University School of Medicine, Macon, Georgia, UNITED STATES|J. Shantha, University of California San Francisco Department of Medicine, San Francisco, California, UNITED STATES|X. Zeng, United States Army Medical Research Acquisition Activity, Fort Detrick, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ebola virus disease (EVD) survivors are at increased risk of uveitis and sequelae including cataract, which can lead to vision disability. Prior work in the EVICT study explored the short-term outcomes of cataract surgery in survivors but the long-term outcomes and the potential for Ebola virus to reside in cataract materials requires further study.

Methods: We performed a long-term analysis on EVD survivors who were enrolled in the EVICT study underwent manual small incision cataract surgery (MSICS). Patients underwent anterior chamber taps for Ebola virus (EBOV) RNA RT-PCR; those who tested negative were eligible for MSICS. Follow-up data on visual acuity (VA) and ocular complications at 3–4-months, 6 months, and 12 months post-surgery were analyzed. Histology and In situ hybridization (ISH) for EBOV RNA were performed on lens and capsular material from MSICS surgery.

Results: Clinical outcomes of 34 EVD survivors who underwent MSICS surgery were analyzed. Median preoperative logMAR (VA) was 2.65 (VA Counting fingers - Hand motions). Post-operatively, median logMAR VA improved to 0.18 at 3-4 months ($p < 0.01$) but showed slight worsening to 0.48 ($p < 0.01$) at 6 months and 0.60 ($p < 0.01$) at 12 months. Nine patients underwent an additional YAG capsulotomy procedure. Ocular adverse events within 1-3 months included recurrent uveitis (n=1, 3%). Adverse events observed at 3-4 months included vitreous opacity (n=3, 8.8%), epiretinal membrane (n=1, 3%) and panuveitis (n=1, 3%). Recurrent uveitis was observed between 6-12 months in 11 patients (32%). Other findings observed included vitreous opacity (n=5, 14.7%), epiretinal membrane (n=1, 3%), tractional retinal detachment (n=1, 3%) band keratopathy (n=1, 3%), Histopathology of cataracts and cataract nuclei (n=7) showed lens fiber vacuolation and morgagnian globules, Anterior capsules (n=2) showed mineralization and thickened capsule. Further ISH analysis of 7 lens samples showed no evidence of EBOV RNA within lens or capsular material.

Conclusions: Twelve month outcomes from the EVICT study showed that cataract surgery is safe and restored vision with no evidence of EBOV RNA within lens or capsular tissues. Secondary cataract, recurrent uveitis and retinal findings were observed although our analysis was limited by patient dropout and sample size. MSCIS surgery in EVD survivors was well-tolerated but patients required ongoing monitoring.

CONTROL ID: 3712432
SUBMITTER (NAME ONLY): Yota Inoue
TITLE: The Effect of Injector Tip Shapes on Insertion During Intraocular Lens Implantation.
SESSION TITLE: Cataract surgery II
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y. Inoue, T. Hishida, T. Sobajima, S. Nagasaka, Kabushiki Kaisha Nidek, Gamagori, Aichi, JAPAN|
Commercial Relationships Disclosure: Yota Inoue: Commercial Relationship: Code N (No Commercial Relationship) | Takahiro Hishida: Commercial Relationship: Code N (No Commercial Relationship) | Tatsuya Sobajima: Commercial Relationship: Code N (No Commercial Relationship) | Shinji Nagasaka: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: At ARVO 2021, our team reported on the effect of differing tip shapes on IOL injectors. The study indicated resistance during insertion could be affected by shape, size, material, and surface roughness of the injector. The current study investigates the effect on insertion due purely to tip shapes using three parameters, bevel angle, slit length, and diameter of the nozzle .

Methods: We prepared a sample that was scaled up from the actual injector.
The study evaluated a control sample consisting of a round polypropylene bar (6 mm in diameter). The treatment samples included:
(1) Slit length (3, 4, 5 mm *slit width 1.2 mm) (6 mm in diameter)
(2) Bevel angle (35, 45, 55°) (6 mm in diameter)
(3) Diameter of the nozzle (4 mm from the tip – 7.0, 7.5, 8.0 mm)

The following testing procedure was used:
A silicone sheet (thickness=0.4 mm) was used to simulate a cornea. After making an incision of 6.5±0.1 mm, the injector tip was inserted in the silicone at a speed of 2 mm/sec with a universal material testing machine (AGS-50NX). (1) and (3) were inserted for 4.6 mm depth to pass common use . (2) was inserted for 9 mm depth to pass the bevel root.
The maximum value of the resistance during insertion was measured 17 times for each master model injector. The resistance values were compared between control and treatment samples. $P<0.05$ was considered statistically significant.

Results: The maximum value of insertion resistance (N) was significantly lower at all bevel angles compared to the control group as reported below:

Control group: 6.88 ±0.564 N
Bevel angle: 35 degree = 5.11 ±0.587 N ($P < 0.05$), 45° = 3.81 ±0.337 N ($P < 0.05$), 55° = 2.77 ±0.316 N ($P < 0.05$)
Slit length: 3 mm = 6.73 ±0.728 N ($P = 0.25$, t-test), 4 mm = 7.34 ±0.660 N ($P < 0.05$),
5 mm = 7.91 ±0.769 N ($P < 0.05$)
Diameter of the nozzle : 7 mm = 7.00 ±0.513 N ($P = 0.26$), 7.5 mm = 7.82 ±0.839 N ($P < 0.05$),
8 mm = 8.13 ±0.517 N ($P < 0.05$)

Conclusions: The outcomes of this study suggest that the bevel angle had the greatest effect on the ease of injector insertion. With a sharp bevel tip, the bevel root angle is more obtuse, and sudden resistance on the injector is less likely, reducing the chances of the bevel root being stuck in the incision. Therefore, injectors with a sharp bevel tip experienced significantly lower resistance when the bevel root passed through the silicone sheet.

CONTROL ID: 3712434

SUBMITTER (NAME ONLY): Cathy Sun

TITLE: Predicting progression to proliferative diabetic retinopathy

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Sun, Y. Guo, S. Yonamine, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|C. Sun, FI Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a prediction model for progression of non-proliferative diabetic retinopathy (NPDR) to proliferative diabetic retinopathy (PDR) and to determine if incorporating additional clinical time points improves model performance.

Methods: Using de-identified electronic health records from an academic medical center, we identified a cohort of patients with NPDR at the index date. This cohort included patients with age ≥18 years, presence of type 1 or 2 diabetes mellitus, and no prior diagnosis of PDR. Patients who progressed to PDR or were lost to follow-up (censored) ≤6 months from the index date were excluded. Figure 1 illustrates our study design. Four types of models were compared: Cox proportional hazards, Cox with backward selection, Cox with lasso regression, and Random Survival Forest (RSF). Covariates were included in the models if they were significant (p-value <0.05) in the univariable Cox models or clinically relevant. For each model, three sets of covariates were compared: covariates at the index date (static model 1), covariates updated at 6-month follow-up (static model 2), and covariates at the index date plus change of time-varying covariates during the 6-month observation period (dynamic model). The data were split into 80% training and 20% testing. The model performance was evaluated by the concordance index (0-1; perfect prediction= 1).

Results: The cohort of 1107 patients had a median age of 66 years (IQR 56-74) and 547 (49%) were female. The cohort consisted of 32% white, 30% Asian, 14% Latinx, 11% black and 11% other races. The insurance types included 48% Medicare, 23% PPO/HMO, 15% Medi-Cal/Self-Pay and 14% other. 89 (8.0%) patients progressed to PDR with a median event time of 22.8 months (IQR 11.7-40). The concordance index of the trained models assessed on the test dataset are shown in Table 1. The dynamic model using RSF had the best predictive performance at a concordance index of 0.848. In this model, the variables ranked as most important were insurance, age, number of outpatient visits before the index date, mean Systolic Blood Pressure (SBP) and change in mean SBP during the observation period.

Conclusions: We developed a set of prediction models for progression of NPDR to PDR that achieved high performance (concordance index >0.7). The dynamic model that incorporated the change in clinical variables during the 6-month observation period had the best performance.

CONTROL ID: 3712435

SUBMITTER (NAME ONLY): Robert Zawadzki

TITLE: Progress on measurements and interpretation of the optoretinograms (ORG) in mice: implementation of Full Field Swept Source Optical Coherence Tomography (FF-SS-OCT)

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.J. Zawadzki, R.K. Meleppat, P. Zhang, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|R.J. Zawadzki, D. Valente, K.V. Vienola, R.S. Jonnal, Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|S. Lee, N. Doble, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|P. Zhang, School of Optoelectronic Engineering and Instrumentation Science, Dalian University of Technology, Dalian, Liaoning, CHINA|

Commercial Relationships Disclosure: Robert Zawadzki: Commercial Relationship: Code N (No Commercial Relationship) | Ratheesh Meleppat: Commercial Relationship: Code N (No Commercial Relationship) | Denise Valente: Commercial Relationship: Code N (No Commercial Relationship) | Soohyun Lee: Commercial Relationship: Code N (No Commercial Relationship) | Kari Vienola: Commercial Relationship: Code N (No Commercial Relationship) | Pengfei Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Ravi Jonnal: Commercial Relationship: Code N (No Commercial Relationship) | Nathan Doble: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To give an update on our recent progress in measurements and interpretation of the optoretinograms (ORGs) i.e., detection of light-evoked functional retinal responses using Optical Coherence Tomography. To present the design and implementation of mouse retinal Full Field Swept Source Optical Coherence Tomography (FF-SS-OCT) system for high-speed measurements of mouse retinal ORGs.

Methods: Albino mice were imaged in vivo with a custom mouse retinal FF-SS-OCT employed with a light stimulation channel to allow measurements of high-speed mouse retinal ORGs. For comparison, the same mice were evaluated using our standard ORG probing setup using Scanning Light Ophthalmoscopy / Optical Coherence Tomography (SLO/OCT) retinal imaging system. Before the ORG experiments, mice were dark-adapted. Both intensity-based ORG analysis (time-dependent changes of the depth scattering profiles of retinal layers), and phase-based ORG analysis (time-dependent changes of the phase difference (path length) between retinal layers) have been extracted from the ORG data sets.

Results: The depth scattering ORG profiles extracted using the SLO/OCT system and FF-SS-OCT reveal similar correlations between depth positions and intensity of different retina bands. The phase-based ORG signals extracted from the same data sets, although more sensitive to retina motion and more computationally demanding, provided an order of magnitude higher sensitivity of detecting changes in retina layer positions. The application of FF-SS-OCT system allowed observation of the fast ORG responses in mouse retina with much higher precision if compared to the ORGs extracted using raster scanning SLO/OCT retinal imaging system.

Conclusions: Successful implementation of phase-based ORG signal analysis in mice for data acquired with the SLO/OCT system and FF-SS-OCT allowed direct comparison of the results. Implementation of FF-SS-OCT for extraction of ORG signals opens the possibility of future studies of the fast ORG response in mice, potentially allowing separation of Cone and Rod-based ORGs and direct correlation of the ORGs with the ERGs (electroretinograms). However, slow ORG signals connected with light-evoked water movements between different compartments of the retina can still be more efficiently studied with our standard raster scanning SLO/OCT retinal imaging system.

CONTROL ID: 3712436

SUBMITTER (NAME ONLY): Emeline Nandrot

TITLE: Retinal atrophy phenotypes associated with light sensitivity and inflammation in the new MerTK-cleavage resistant mouse model

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.F. Nandrot, S. Réty, J. Enderlin, Q. Rieu, S. Augustin, E. Vanoni, S. Roux, F. Sennlaub, Institut de la vision, Paris, Île-de-France, FRANCE|I. Tabas, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The MerTK tyrosine kinase receptor is a key element of the retinal pigment epithelial (RPE) phagocytic machinery required for photoreceptors (PRs) survival. Recently, we showed this receptor is subjected to the cleavage of its extracellular domain as a way of finely controlling its function. We thus investigated the ocular phenotype of MerTK cleavage-resistant ($MerTK^{CR}$) mice devoid of the cleavage site.

Methods: $MerTK^{CR}$ and control mice were monitored between the ages of 3 and 18 months using fundus photography (FP), autofluorescence (AF) detection, optical coherence tomography (OCT), electroretinography (ERG), optokinetic behavioral tests as well as paraffin-embedded and electron microscopy (EM) tissue sections. Survival of bone-marrow macrophages (BMMs) was assessed in pig primary RPE co-cultures. Mitochondrial activity and energy sources use were evaluated with the Seahorse technology on freshly-dissected RPE/choroid and retina tissues.

Results: Our first cohorts showed large degenerative areas in the central retina associated with AF, in males and then in females, only when followed monthly by OCT plus FP/AF but not by OCT alone. We thus hypothesize that $MerTK^{CR}$ mice might be light-sensitized by the FP and AF lamp bulbs. Besides thinning of the photoreceptor layer, macrophages infiltration was observed by OCT. Though, $MerTK^{CR}$ BMMs do not survive more than controls in primary RPE co-cultures, suggesting that observed macrophages could be linked to decreased RPE immunosuppressivity rather than to increased BMMs survival potential. At the EM level, RPE anomalies were detected including phagosomes retained in the apical area and abnormal mitochondria. Accordingly, mitochondrial function and energy production are reduced in RPE/choroid tissues.

Conclusions: Current experiments are testing which cell type carries the light sensitivity, assessing macrophages infiltration after laser impacts and exploring in vivo BMMs survival after adoptive cross-transfers between $MerTK^{CR}$ and control mice. As well, the RPE phagocytic profile is being explored both in vitro and in vivo. All together, this new mouse model displays a novel phenotype that could prove useful to understand the interplay between RPE and PRs in inflammatory retinal degenerations and highlight a new role for MerTK in the maintenance of the immune privilege in the retina.

CONTROL ID: 3712439

SUBMITTER (NAME ONLY): Fatima Abukunna

TITLE: Engineering the inner neural retina using electrospun scaffolds and extrusion-based bioprinting

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.E. Abukunna, A.M. Aladdad, R. Nolan, M. Vierra, K.E. Kador, Ophthalmology, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: 3D bioprinting technique has been used to recapitulate the cellular organization of several tissues throughout the body, including the cornea, limbus, and parts of the retina. However, the capacity to recreate these tissues is derived not just from the placement of the printed cells but also in the "bio-ink" material used to print cells and the scaffold substrate on which the cells are printed, both of which can affect the cell survival, gene expression, and cell migration. Here, we will study the effect of different bioink materials on the 3D printing of retinal ganglion cells (RGCs) and astrocytes, studying the survival of the printed cells and the interactions of the two cell types in our model system.

Methods: RGCs and astrocytes were isolated from early postnatal rodents and suspended in bioinks prepared from alginate, RGD peptide conjugated alginate, collagen, matrigel, or mixtures of these gels and printed using an extrusion based bioprinter. Astrocytes and RGCs were printed separately on electrospun radial scaffolds and survival evaluated by live dead analysis and cell morphology / neurite outgrowth. Samples were then printed on the same scaffolds with astrocytes in the scaffold center and RGCs surrounding to test the ability of the astrocytes to secrete factors that polarize RGC growth and to evaluate the ability of the astrocytes to migrate across the scaffold.

Results: RGCs and astrocytes were able to survive the extrusion printing process in all bioinks at a high percentage, however, RGCs were unable to extend neurites and astrocytes were unable to stretch on bioinks that did not include matrigel. On samples where astrocytes and RGCs were printed on the same scaffold, astrocytes secreted factors were only able to polarize RGC growth within 100 μm of the printed astrocytes. On these samples, RGCs were observed entering the matrigel printed at the scaffold center, while astrocytes were able to migrate from the matrigel onto the radial scaffold.

Conclusions: Electrospun scaffolds combined with 3D bioprinting represent a potential device providing an in vitro model for understanding retinal development and the interaction between RGCs and astrocytes.

CONTROL ID: 3712442

SUBMITTER (NAME ONLY): Tia Kowal

TITLE: Differences in primary cilia amongst retinal ganglion cell subtypes

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kowal, O. Dhande, K. Ning, B. Wang, Q. Wang, W. Liu, Y. Hu, Y. Sun, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|N. Berbari, Biology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary cilia are sensory organelles that project from the surface of most differentiated cells. These microtubule-based structures coordinate several signaling pathways that are involved in cell proliferation, migration, and differentiation. It is known that primary cilia play critical roles in eye development and photoreceptor function; however, less is known about what role the primary cilia might play in mature retinal ganglion cells (RGCs). To begin to understand these organelles, we assessed the presence or absence of a cilia membrane marker Arl13b and a widely distributed neuronal cilia marker AC3 in different subtypes of mouse RGCs.

Methods: Immunofluorescent staining for primary cilia axoneme markers, Arl13b and AC3, and basal body marker centrin 3 was performed on retinas isolated from adult (P25-P35) transgenic mice in which fluorophores were specifically expressed in only one known subtype of RGC. Additional subtype protein markers were analyzed using immunostaining. Subtype marker specificity was confirmed by colocalized with the pan-RGC marker RBPMS, and ARL13b or AC3 signal was only considered a primary cilium if adjacent to centrin 3 signal. Statistical analyses were performed using Student's t-test, and $p<0.05$ was considered statistically significant.

Results: The presence of prototypical cilia markers Arl13b and AC3 in defined subtypes of retinal ganglion cells was analyzed. These markers were not expressed equally amongst the RGCs. Primarily AC3 positive cilia were found on alpha-RGCs identified by protein markers osteopontin (53% AC3 – 17% Arl13b), calretinin (53% AC3 – 44% Arl13b) and SMI32 (47% AC3 - 27% Arl13b). Whereas directionally selective RGCs either CART positive or Trhr positive differentially localize Arl13b or AC3, respectively in their primary cilia. Intrinsically photosensitive RGCs differentially localize Arl13b and AC3 based on melanopsin expression. Cilia in antibody labeled melanopsin cells primarily had Arl13b (30%), whereas transgenic mouse melanopsin (opn4) labeled RGCs primarily have AC3 (54%) positive cilia.

Conclusions: Primary cilia may be differentially organized between the subtypes of retinal ganglion cells. Further analyses are required to better understand what implications this may have on RGC subtype specific function.

CONTROL ID: 3712443

SUBMITTER (NAME ONLY): Mindy Xu

TITLE: Outcomes of Pediatric Myasthenia Gravis with Ocular Involvement

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Xu, M.S. Borchert, M. Chang, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M.S. Borchert, M. Chang, Ophthalmology, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pediatric myasthenia gravis (MG) is uncommon, and earlier studies on ocular outcomes were published prior to the widespread adoption of newer treatments such as rituximab. We report outcomes of pediatric MG in patients treated at our institution over the last 10 years.

Methods: We conducted a retrospective chart review of all children (<18 years) seen at our pediatric ophthalmology department from 2011 to 2021 with a diagnosis of MG and at least 1 year of follow-up. We collected data on demographics, treatments, and outcomes in three groups of patients: 1) generalized MG with ocular involvement at presentation 2) ocular myasthenia gravis (OMG) with later generalization and 3) OMG only. Cox proportional hazards regression analysis was conducted to identify factors associated with outcomes.

Results: Of 41 patients, 18 presented with generalized MG with ocular involvement, 6 presented with OMG that later generalized, and 17 had OMG without generalization. The median age at diagnosis was 3 years, and the median duration of follow-up was 6 years. Medical treatments included pyridostigmine (100%), steroids (42%), intravenous immunoglobulin (22%), and steroid sparing agents including rituximab, eculizumab, azathioprine, and mycophenolate mofetil (24.4%). Thymectomies were performed in 67% of patients with generalized MG (groups 1 and 2) and 12% of patients with OMG (group 3, p=0.002). Among patients with ocular presentation who later generalized, the median time to generalization was 0.8 years (range 1 month to 4 years). At last follow-up, 5% of patients had active myasthenia with fluctuating symptoms, 73% were stable on medications, and 22% were resolved off medications. Residual amblyopia was diagnosed in 7%. There were no significant differences in these outcomes among groups. Failure to stabilize symptoms was associated with younger age at presentation (p=0.03). Lack of symptom resolution was associated with use of steroids (p=0.02) and steroid-sparing immunosuppressive agents (p=0.01). There were no factors associated with residual amblyopia or generalization (in patients with ocular presentation).

Conclusions: In our cohort of pediatric MG patients with ocular involvement, rates of stabilization and resolution were similar to earlier studies. The use of steroids and steroid-sparing agents were associated with worse outcomes, likely indicating more difficult to control disease.

CONTROL ID: 3712444

SUBMITTER (NAME ONLY): Swarup Swaminathan

TITLE: Improved Prediction of Perimetric Loss in Glaucomatous Eyes Using Latent Class Mixed Modeling

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.S. Swaminathan, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A.A. Jammal, F. Medeiros, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate whether the identification of distinct subpopulations among glaucoma patients improves the estimates of future perimetric loss.

Methods: Eyes with ≥5 reliable visual fields were identified in the Duke Glaucoma Registry. Standard automated perimetry (SAP) mean deviation (MD) and visual field index (VFI) values were collected with associated timepoints. The dataset was split at the patient level, with 80% used for model training and 20% for testing. Rates of change were modeled using latent class mixed models (LCMM) and ordinary least square (OLS) regression. LCMM can identify subpopulations clustered around different average rates. Bayesian Information Criteria was used to identify the LCMM with the optimal number of classes. The LCMM was presented with the first 3, 4, 5, & 6 visual fields of eyes from the test set to predict subsequent SAP MD or VFI values. Model performance was compared to OLS with mean square prediction error (MSPE) using Wilcoxon signed-rank test. Analysis was completed in R.

Results: The full dataset contained 52,900 visual fields from 6,558 eyes of 3,981 subjects, with an average of 8.1±3.7 visual fields per eye. The optimal LCMM for SAP MD contained 3 classes with rates of -0.08, -0.17, & -1.33 dB/year (84.0%, 11.4%, & 4.6% of the population respectively). The optimal LCMM for SAP VFI contained 4 classes with rates of -0.21, -0.66, -2.96, & -6.77%/year (82.6%, 10.1%, 5.7%, & 1.5% of the population respectively). For both SAP MD and VFI, MSPE was significantly lower with LCMM compared to OLS regardless of the number of tests used ($p<0.001$ for all comparisons; Figure 1). Notably, MSPE from LCMM was significantly lower than that of OLS when using only the first 3 visual fields of test eyes (4.90 vs. 60.19 for MD respectively, $p<0.001$; Figure 2). MSPE of fast progressors was significantly lower with LCMM versus OLS (27.30 & 79.59 respectively, $p= 0.01$).

Conclusions: LCMM successfully identified different groups of progressors in a large glaucoma population and significantly improved the prediction of future test estimates. LCMM had superior accuracy for future prediction even when using a small number of visual fields, suggesting that it could more easily identify eyes at risk for significant visual field loss.

CONTROL ID: 3712445

SUBMITTER (NAME ONLY): RUTH ESHETE

TITLE: Differences in Select Medication Use in Patients with Age-Related Macular Degeneration and in Controls

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. ESHETE, A.M. Lynch, N. Mandava, A. Palestine, M. Mathias, B.D. Wagner, N. Manoharan, C. Fonteh, R. Navo, J. Patnaik, Ophthalmology, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Globally, age-related macular degeneration (AMD) is a leading cause of vision loss for individuals of ages 50 years and older. The different subtypes of AMD are early, intermediate, and advanced including geographic atrophy (GA) and neovascular (NV) AMD. Medications such as nonsteroidal anti-inflammatory drug (NSAIDs), metformin, hormone therapy (HT) and Age-Related Eye Disease Studies (AREDS) supplements have been shown to play a role in AMD. However, there is a paucity of literature on the effect of these medications in the different subtypes of AMD. The purpose of this study was to determine whether there is an association between the use of NSAIDs, metformin, HT, and AREDS in the different subtypes of AMD compared to controls.

Methods: A case-control study was conducted using the University of Colorado AMD registry (July 2014 - December 2021). For this analysis, AMD status was categorized into 3 groups: controls, early/intermediate and advanced (NV and GA AMD) using multimodal imaging. The current use of NSAIDs, metformin and AREDS at enrollment and past and/or current use of HT were reported. The associations between the use of NSAIDs, metformin, HT and AREDS and AMD categories and controls were determined using adjusted odds ratios (ORs) from multinominal logistic regression.

Results: Of all study patients (n=1167) included in the analysis, there were 931 cases and 236 controls. Among the cases, 42.5% had early/intermediate AMD and 57.5% had advanced AMD. Cases were significantly more likely to use AREDS (37.0% advanced AMD and 52.5% early/intermediate AMD when compared to controls (0.9%). The use of AREDS remained significantly higher in cases compared to controls after adjusting for confounders. HT was used significantly more in controls (27.1%) compared to cases (12.7% of advanced AMD patients and 16.3% of early/intermediate AMD patients). After adjusting for age and history of chronic hypertension, the odds of HT was 0.54 (95%CI:0.33-0.90) for patients with early/intermediate AMD and 0.46 (95% CI:0.27-0.77) for advanced AMD as compared to controls. Metformin and NSAIDs use did not significantly differ between the three AMD groups.

Conclusions: We found that AMD cases were much more likely to use AREDS and less likely to use HT compared to controls. The protective effect of HT may provide important insights into systemic mechanisms related to the risk of macular degeneration.

CONTROL ID: 3712446

SUBMITTER (NAME ONLY): Pablo Pérez-Merino

TITLE: Novel methodology for intraocular lens power calculation based on simulated optical performance: application in post-LASIK eyes

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Pérez-Merino, IMEC, Interuniversitair Micro-Elektronica Centrum, Leuven, Vlaams-Brabant, BE, other/research, BELGIUM|J. Aramberri, Miranza Begitek, SPAIN|J.J. Rozema, Universiteit Antwerpen Faculteit geneeskunde en gezondheidswetenschappen, Wilrijk, BELGIUM|A. Vásquez Quintero, Ghent University Faculty of Engineering and Architecture, Universiteit Gent Faculteit Ingenieurswetenschappen en Architectuur, Gent, Oost-Vlaanderen, BE, academic/eng, BELGIUM|

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ABSTRACT BODY:

Purpose: To predict the post-operative refractive error in cataract surgery eyes with previous corneal refractive surgery.

Methods: A total of 75 patients with previous myopic and hyperopic LASIK (40 female / 35 male; age: 66 ± 6 y.o.; axial length range: 20.85 - 29.84 mm; RMS HOAs range: 0.11 - 0.81 microns for a 4-mm pupil) were included in the study. Anterior and posterior corneal Zernike coefficients (from Pentacam, Sirius and MS39 corneal topographers), axial distances (corneal thickness, post-operative effective lens position and vitreous chamber depth) and IOL geometry (SN60WF, ALCON Laboratories; Precizon Toric, OPHTEC BV) were exported to ZEMAX (Radiant ZEMAX; Focus software) where the patient-specific eye models were built. Optical quality was described in terms of the metric Visual Strehl (VSOTF). The defocus and astigmatism producing the maximum VSOTF was taken as the optimal target and compared with the post-operative subjective refraction.

Results: The Bland-Altman analyses of the data show the agreement between the predicted refraction of the proposed optimized methodology for IOL power calculation and the post-operative subjective refraction. The bias and limits of agreement (LoA) were -0.02±0.52 [LoA: -1.05, 1.00], -0.03±0.20 [LoA: -0.43, 0.35] and -0.03±0.19 [LoA: -0.39, 0.38] D for M, J_0 and J_{45}, respectively. Average spherical equivalent was -0.36±0.80 D (subjective) and -0.35±0.73 D (predicted), average power vector J_0 was 0.10±0.33 D (subjective) and 0.10±0.37 D (predicted), and average power vector J_{45} was -0.03±0.12 D (subjective) and -0.02±0.15 D (predicted), with ICC of 0.79 for M, 0.71 for J_0 and 0.55 for J_{45}, respectively; showing high reliability between the predicted refraction and the post-operative subjective refraction in all patients. The percentage of eyes within ±0.5D was of 82.6% (M), 84.1% (J_0) and 82.6% (J_{45}), while the agreement within ±1.0D was of 93.3% (M), 98.6% (J_0) and 97.3% (J_{45}).

Conclusions: We develop a patient-specific method for IOL selection based on virtual ray tracing. Strong agreement between the predicted refraction and the post-operative subjective refraction in a large case series of cataract surgery eyes with previous corneal refractive surgery suggest that the proposed optimized methodology provide an accurate tool for IOL selection. The predicted refraction was influenced by the presence of corneal aberrations.

CONTROL ID: 3712447

SUBMITTER (NAME ONLY): Andrew Powers

TITLE: GeneTAC™ small molecules reduce toxic nuclear foci and restore normal splicing in corneal endothelial cells derived from patients with Fuchs endothelial corneal dystrophy (FECD) harboring repeat expansions in transcription factor 4 (TCF4)

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Powers, K. Cheung, H. Schehr, N. Osgood, C. Livelo, N. Levin, M. Safadi, J. Kerr, C. Zhang, N. Chilcoat, A. Bhat, Design Therapeutics, Carlsbad, California, UNITED STATES|T.A. Rinkoski, K.H. Baratz, M.P. Fautsch, Department of Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|E.D. Wieben, Department of Biochemistry and Molecular Biology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Most cases of FECD are caused by a CTG trinucleotide repeat expansion in intron 3 of the TCF4 gene leading to production of toxic RNA foci, global splicing dysregulation, and cellular dysfunction. The mainstay of FECD management is keratoplasty; no disease-modifying therapies are currently approved. GeneTAC™ molecules are small molecule gene targeted chimera compounds designed to target specific genomic sequences through a DNA-binding moiety and modulate transcription. In this study, we evaluated GeneTAC™ molecules designed to selectively target the expanded CTG repeats in TCF4 intron 3 for their effects on RNA foci formation and mis-splicing.

Methods: GeneTAC™ molecules were synthesized and selected for RNA foci-reducing activity in immortalized F35T corneal endothelial cells (CECs). Primary FECD patient-derived CEC lines (n=4) were treated continuously for 2 to 9 days with 7 unique GeneTAC™ molecules at concentrations up to 300 nM. Toxic nuclear RNA foci containing expanded CUG repeats were evaluated using fluorescence in situ hybridization, and disease-related splicing defects in MBNL1, MBNL2 and NUMA1 were evaluated using PCR.

Results: In FECD patient-derived primary CEC lines harboring mono- and biallelic TCF4 repeat expansions, treatment with GeneTAC™ molecules reduced the average number of foci by 40 to 99% in a time- and concentration-dependent manner. Changes in splicing of MBNL1, MBNL2 and NUMA1 mRNA demonstrated that the most active GeneTAC™ molecules corrected splicing to levels observed in unaffected CECs at concentrations > 33 nM.

Conclusions: Treatment with GeneTAC™ molecules corrected key molecular hallmarks in FECD patient-derived CECs. These findings support continuing development of GeneTAC™ molecules as a potential disease-modifying therapy for FECD.

CONTROL ID: 3712448

SUBMITTER (NAME ONLY): Heather Heitkotter

TITLE: Evaluation of EZ reflectivity normalization across different OCT devices

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Heitkotter, J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|K. Vang, J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|M. Gaffney, Biomedical Engineering, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|M. Gaffney, Biomedical Engineering, Marquette University, Milwaukee, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Heather Heitkotter: Commercial Relationship: Code N (No Commercial Relationship) | Koua Vang: Commercial Relationship: Code N (No Commercial Relationship) | Mina Gaffney: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Carroll: Commercial Relationship(s);Code F (Financial Support):AGTC, MeiraGTx, Optovue;Code C (Consultant/Contractor):AGTC;Code I (Personal Financial Interest):Translational Imaging Innovations

ABSTRACT BODY:

Purpose: Ellipsoid zone (EZ) reflectivity has potential to serve as a biomarker of photoreceptor integrity, but there is variability in the methods used to extract reflectivity values. Here we evaluate normalization methods of EZ reflectivity across four different OCT devices.

Methods: Horizontal 6mm line scans (20 averaged B-scans) were acquired in five control eyes using the Cirrus, Bioptigen, Optovue Avanti, and Spectralis OCT devices. Eight longitudinal reflectivity profiles (LRPs; each 7 pixels wide by 250 pixels in depth) were extracted using ImageJ from each OCT between 0.5–2.0mm (0.5mm intervals) from the fovea. Boundaries of the ganglion cell and inner plexiform layers (GCIPL) and the peak and full width half max (FWHM) of the EZ were identified. Intensity values between the GCIPL boundaries were averaged. Intensity values between the EZ FWHM were averaged, and peak EZ intensity was extracted. Values were averaged across LRPs for each scan. The average intensity of a 300x50 pixel vitreous region was also extracted from each scan. Four intensity normalization methods were evaluated with ICC and Friedman's test: 1) peak EZ, 2) EZ FWHM, 3) GCIPL normalization (EZ FWHM/GCIPL), and 4) vitreous normalization (subtract vitreous from 3 before taking ratio).

Results: The ICC for mean peak EZ (-0.11) and mean EZ FWHM (-0.09) intensity across devices were poor. Friedman test revealed significant differences in peak EZ intensity across devices ($Q(3)=86.2$, $p<0.0001$). Dunn's multiple comparisons test indicated peak EZ differed across all devices except between Optovue vs Spectralis. Mean EZ FWHM across devices also significantly differed ($Q(3)=66.0$, $p<0.0001$), and Dunn's test revealed values from the Bioptigen were significantly different from the other devices ($p<0.0001$). The ICC for GCIPL normalization across devices was poor (-0.21), and Friedman test revealed significant differences across devices ($Q(3)=13.6$, $p=0.0001$), including Spectralis vs Bioptigen ($p=0.009$) and Spectralis vs Optovue ($p=0.018$). The ICC for vitreous normalization across devices was poor (0.042), with significant differences revealed by Friedman test ($Q(3)=11.2$, $p=0.002$), specifically between Bioptigen vs Optovue ($p=0.009$).

Conclusions: Our data demonstrate that the normalization method alters the relationship of EZ reflectivity across devices. Such variability poses challenges to utilization of EZ reflectivity as a biomarker in clinical studies.

CONTROL ID: 3712449

SUBMITTER (NAME ONLY): Raba Thapa

TITLE: Skin Carotenoid Assessment to Detect Vitamin A Deficiency in Children and Pregnant Women in Nepal

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Thapa, Vitreo-Retina, Tilganga Institute of Ophthalmology, Kathmandu, 3, NEPAL|R. Thapa, E. Addo, P.S. Bernstein, Ophthalmology and visual science, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|S. Ruit, Cataract and Cornea, Tilganga Institute of Ophthalmology, Kathmandu, 3, NEPAL|

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ABSTRACT BODY:

Purpose: Vitamin A deficiency (VAD) is a continuing public health problem among children and pregnant women of Nepal. We conducted a comparative cross-sectional study to assess skin carotenoid measurement as a rapid noninvasive screening tool for VAD in children and pregnant women.

Methods: We enrolled 162 pregnant women and 164 children (8 to 12 years old) from three public hospitals in three ecological regions (Mountain, Hill and Terai) of Nepal in this study. Skin carotenoid levels were assessed noninvasively with reflection spectroscopy using the Veggie Meter® (Longevity Link Corporation, Salt Lake City, Utah, USA). The primary outcome was whether skin carotenoid measurement can successfully identify subjects with VAD. Detailed eye evaluations were conducted in subjects with low skin carotenoid scores (<150 RU) and those with symptomatic night blindness. Serum retinol and serum carotenoid levels were measured using high performance liquid chromatography (HPLC). Intra-class correlation coefficients were calculated. P values were considered significant if less than 0.05.

Results: A total of 8.6% of pregnant women and 12.8% of children were VAD (serum retinol <200 ng/ml) even though only four had present or past ocular clinical signs of VAD. There was significant correlation of total skin carotenoids with serum retinol among the pregnant women ($r= 0.255$, $p= 0.001$) and children ($r=0.253$, $p=0.001$). There was significant correlation of skin carotenoids with serum carotenoids among the pregnant women ($r=0.314$, $p <0.001$) and children ($r=0.510$, $p < 0.001$). There was significant correlation of total serum carotenoids with serum retinol among the pregnant women ($r= 0.447$, $p= 0.001$) and children ($r=0.530$, $p<0.001$). When we performed initial statistical analysis using a cutoff of 200 RU, the Veggie Meter® detected VAD with 71.4% sensitivity and 66.0% specificity in pregnant women and with 71.4% sensitivity and 54.6% specificity in children.

Conclusions: Although sensitivity and specificity were moderate for detecting VAD with the Veggie Meter®, skin carotenoid assessment using this rapid noninvasive portable device could still have immense value as a biomarker for high-risk VAD screening in Nepal and similar developing countries with limited access to laboratory measurement of serum vitamin A levels.

CONTROL ID: 3712450

SUBMITTER (NAME ONLY): Gavin Li

TITLE: Assessment of Sex Differences in Clinically Significant Dry Eye and Associated Autoimmune Disease Prevalence

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Li, D. Cui, J. Zeng, P. Mathews, S. VanCourt, E.K. Akpek, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Gavin Li: Commercial Relationship: Code N (No Commercial Relationship) | David Cui: Commercial Relationship: Code N (No Commercial Relationship) | Julia Zeng: Commercial Relationship: Code N (No Commercial Relationship) | Priya Mathews: Commercial Relationship: Code N (No Commercial Relationship) | Shanna VanCourt: Commercial Relationship: Code N (No Commercial Relationship) | Esen Akpek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate sex differences in dry eye diseases with regards to objective dry eye parameters and autoimmune disease.

Methods: Dry eye patients presenting at a tertiary academic medicine center, evaluated by an ophthalmologist between 3/2015 and 7/2021 were identified using international classification of disease codes (M35.0, H16.222, H04.123, 710.2, 375.15). Patient sex at presentation was obtained using billing records and confirmed with medical record review. A total of 343 (21.0%) male and 1288 (79.0%) female patients were identified. Review of electronic medical records was conducted to evaluate demographics, objective dry eye parameters at baseline visit, autoimmune or inflammatory disease, and ocular comorbidities.

Results: A total of 100 patients, 50 male and 50 female, were included. Mean age was 62.5 years and 81.0% self-identified as White, with no demographic differences based on sex (P>.05). There was no statistically significant difference (all P>.05) for objective dry eye parameters at baseline presentation for mean lissamine green conjunctival staining (2.8 women vs 2.5 men), corneal fluorescein staining (2.0 women vs 1.9 men), Schirmer's test without anesthesia (9.8 women vs 11.2 men), and tear osmolarity (304.7 women vs 304.0 men). Approximately two-thirds (68% men, 66% women; P=.812) had primary dry eye without an autoimmune disease or dry eye-related ocular comorbidity. More women had an established autoimmune disease at baseline visit (14% vs 2%; P=.027), an equal number were diagnosed with an autoimmune disease during follow-up (12% women vs 8% men; P=.505).

Conclusions: No statistically significant difference was observed with regards to demographics and objective dry eye parameters. Prevalence of existing autoimmune disease was greater in women at presentation, however diagnosis incidence during follow-up was similar, indicating autoimmune disease may be underdiagnosed in men on presentation. Additional and larger studies evaluating clinical differences of sex in dry eye patients are warranted.

CONTROL ID: 3712452

SUBMITTER (NAME ONLY): Emily Tom

TITLE: Impaired polyunsaturated fatty acid (PUFA) synthesis disrupts RPE phagocytosis

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Tom, Q. Xu, D. Skowronska-Krawczyk, Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|F. Gao, D. Skowronska-Krawczyk, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Emily Tom: Commercial Relationship: Code N (No Commercial Relationship) | Fangyuan Gao: Commercial Relationship: Code N (No Commercial Relationship) | Qianlan Xu: Commercial Relationship: Code N (No Commercial Relationship) | Dorota Skowronska-Krawczyk: Commercial Relationship(s);Code C (Consultant/Contractor):Visgenx

ABSTRACT BODY:

Purpose: ELOVL2 (Elongation of Very Long Chain Fatty Acids-Like 2) encodes a transmembrane protein that plays critical roles in the biosynthesis of omega-3 docosahexaenoic acid (DHA) (22:6n-3) and very long-chain polyunsaturated fatty acids (VLC-PUFAs), which are highly enriched in photoreceptors and essential for maintaining healthy visual function. Adjacent retinal pigment epithelial (RPE) cells are responsible for daily phagocytosis and subsequent degradation of lipid-rich photoreceptor outer segment tips. The aim of this study was to investigate the functional role of ELOVL2 in RPE cells and to what extent alterations of DHA and VLC-PUFA synthesis contribute to RPE dysfunction.

Methods: We used small interfering RNAs (siRNAs) directed against ELOVL2 in ARPE19 cells and performed immunohistochemistry and fluorescent microscopy studies. To investigate phagocytic function, cells were challenged with FITC-labelled rod outer segments (FITC-ROS) and stained with lysosomal marker LAMP1. The proportion of surface-bound and internalized ROS in control (n=9) and ELOVL2 knockdown (n=9) cells was quantified using ImageJ and normalized to the number of nuclei. Two-tailed Student’s t-test was used for statistical analysis.

Results: ELOVL2 knockdown ARPE19 cells showed ~30% decrease in phagocytosed ROS ($p<0.001$) compared to control. In addition, lysosomal size and distribution differed between the two groups. In normal ARPE19 cells, lysosomes exhibited a perinuclear distribution, while in ELOVL2 knockdown ARPE19 cells, LAMP1 signal was localized to the cell periphery.

Conclusions: Overall, the findings of this study support our hypothesis and suggest that ELOVL2 knockdown and subsequent decline in DHA and VLC-PUFA synthesis result in impaired phagocytic function of RPE cells. This study not only provides insight into the molecular mechanisms of RPE phagocytosis but also opportunities to explore therapeutic treatments for pathologic states such as age-related macular degeneration (AMD) using lipid supplementation.

CONTROL ID: 3712453

SUBMITTER (NAME ONLY): Tomas Aleman

TITLE: Preparation for a Gene Augmentation Trial for RDH12-Associated Retinal Degenerations

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.V. Pendyala, Scheie Eye Institute, Department of Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|T.S. Aleman, B.A. Bell, S. Chomistek, J. Sun, M. Weber, A.M. Maguire, J. Pham, I. Shpylchak, S. Zhou, A. Luo, P. Margaritis, Z. Wei, J. Bennett, Center for Advanced Retinal and Ocular Therapeutics (CAROT), Scheie Eye Institute, Department of Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in RDH12, which encodes a retinol dehydrogenase localizing to photoreceptor inner segments, cause early onset retinal degeneration. We defined changes in retinal structure and function in pediatric patients with Leber congenital amaurosis (LCA) due to RDH12 mutations. We also initiated safety evaluations of AAV8 delivering a photoreceptor-driven human codon optimized (hco) RDH12 cDNA in non-human primates (NHPs).

Methods: Twenty-six patients (ages 2-21 years) with RDH12-LCA underwent a complete ophthalmic exam and imaging with SD-OCT and 20 of these individuals were evaluated longitudinally over 3 years. In animal studies, 4 macaques already enrolled in an AAV vaccine study received bilateral subretinal i(SR) injections of AAV8.RK1.hcoRDH12 in a dose-ranging study (3E10 – 3E11vg). One additional animal was injected with a similar vector that incorporated eGFP. Follow-up was performed with protocols that matched those used in patients. Animals were evaluated for transgene expression and histopathology 4 weeks post-injection.

Results: In the patients, visual acuity ranged from 20/40 to 20/800 and remained stable in most patients. SD-OCT showed early foveal thinning in all patients but detectable outer nuclear layer (ONL) at greater eccentricities from the fovea. ONL extent and thickness declined over the course of the study. FST sensitivities were rod-mediated and reduced on average by ~2.5 log units and declined by about 5 dB over 3 years. In NHPs, retinas developed pigmentary changes outlining the area of subretinal injection similar to that seen in other SR injection studies. SD-OCT imaging revealed injection-related alterations in retinal structure. Histologic analyses revealed minimal inflammation at 3E10 or 1E11 vg and rare monocytic peri-vascular infiltrate at 3E11vg. RDH12 immuno-staining was specific to photoreceptors, as was GFP in retinas treated with AAV.RK1.eGFP

Conclusions: Detectable but dysfunctional photoreceptors in the pericentral and peripapillary retina of patients with RDH12-LCA suggest these regions may be targets for gene augmentation. Subretinal delivery of AAV8.RK1.hcoRDH12 in NHP was safe at 1E11vg with only mild inflammation at 3E11vg. The RK1 promoter limited expression to photoreceptors. The data support plans for a formal GLP preclinical toxicity study prerequisite to a human clinical trial.

CONTROL ID: 3712454

SUBMITTER (NAME ONLY): Vrathasha Vrathasha

TITLE: Mitochondrial transplantation to rescue retinal ganglion cell function in optic neuropathies

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Vrathasha, M. Pyfer, J.M. O'Brien, V.R. Chavali, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is the leading cause of irreversible blindness worldwide. The role of mitochondrial dysfunction leading to retinal ganglion cell (RGC) death has been implicated in the pathogenesis of primary open-angle glaucoma. In addition to supporting the high bioenergetic needs of RGCs, mitochondria also play a central role in oxidative stress, calcium dysregulation, and apoptosis pathways. Restoring mitochondrial function by transplantation is a recent development and has been a target of therapeutic intervention.

Methods: Mitochondria were isolated from hSkMCs by magnetically binding to the TOM22 surface protein. Western blot and PCR analysis with gene-specific primers for mitochondrial DNA confirmed the purity of the isolated mitochondria. The integrity of the purified mitochondria was confirmed by transmission electron microscopy. We incubated human induced pluripotent stem cell-derived RGCs (hiPSC-RGCs) with exogenous mitochondria from metabolically active human skeletal muscle cells (hSkMCs). SkMCs were transduced with lentiviral mito-GFP to label donor mitochondria for identification. To test the functional impact of mitochondrial transfer, we treated hiPSC-RGCs with rotenone to induce oxidative stress. The effects of exogenous mitochondria in hiPSC-RGCs were evaluated for oxygen consumption by Oroboros, mitochondrial membrane potential, reactive oxygen species (ROS), and ATP production.

Results: Treatment of hiPSC-RGCs with 730 nM of rotenone induced significant mitochondrial depletion by 12 hours of exposure and thereby decreased ATP production while increasing ROS and superoxide production. hiPSC-RGCs incubated with isolated mitochondria accept them by 1 hour, and the uptake increases with mitochondrial dosage, incubation time, and presence of PEP-1 peptide. ATP production and oxygen consumption by hiPSC-RGCs under oxidative stress improved following mitochondrial transfer. Furthermore, intravitreally injected exogenous mitochondria into C57BL/6 mouse eye were detected in the ganglion cell layer of the murine retina, and its expression co-localized with BRN3, TUJ1, and TOM22 markers.

Conclusions: Through our studies, we hope to demonstrate that mitochondrial transplantation is a viable, novel therapy to rescue RGC function and can be used as a mitigating treatment for glaucoma and other optic neuropathies before the occurrence of permanent vision loss.

CONTROL ID: 3712455

SUBMITTER (NAME ONLY): Tarek Safi

TITLE: An artificial-intelligence-based decision support tool for the detection of Cornea guttata and the assessment of the donor corneas in the eye bank.

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Safi, L. Daas, B. Seitz, Ophthalmology, Universitatsklinikum des Saarlandes und Medizinische Fakultat der Universitat des Saarlandes, Homburg, Saarland, GERMANY|G. Kiefer, M. Nadig, M. Sharma, M. Sakha, A. Ndiaye, M. Deru, J. Alexandersson, Cognitive Assistants, Deutsches Forschungszentrum fur Kunstliche Intelligenz GmbH Standort Saarbrucken, Saarbrucken, Saarland, GERMANY|

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ABSTRACT BODY:

Purpose: Cornea guttata (CG) prevalence post keratoplasty varies from 15 to 18%, with 1 to 2% of the cases presenting with significant negative outcomes. The purpose of this research project is to create a program based on artificial intelligence (AI) that helps with the detection of CG in the donor corneas (DC) in the eye bank.

Methods: Preoperative corneal endothelial images (PCEI) of patients who underwent keratoplasty were collected and classified into 2 groups according to the postoperative CG grade. Group 1 included healthy corneas and those having mild postoperative CG, while group 2 included corneas with severe postoperative CG. Using previously tested semi-quantitative morphological criteria along with other characteristics such as donor age and lens status, the PCEI were analyzed and used to create and train an AI-based tool for the detection of CG. The underlying concept of the tool compares previous cases with comparable properties to the DC in test. The postoperative CG grades of previous cases similar to the DC in test determine the prediction for its CG grade. Finally, the features and CG grade of the analyzed DC are stored in the database for future use.

Results: In total, 6221 PCEI belonging to 1078 patients were used to create a transparent and explainable decision support tool for the detection of CG through a hybrid approach combining 2 components. (1) Graphical analytic tools, whereby the PCEI pass multiple OpenCV-based image processing steps including the Watershed transform algorithm. In this step, cell membranes are delineated, and abnormally large cells or cell depleted areas are marked in red. Several other cell representations such as “honeycomb” representation are created for an enhanced visualization of the endothelial layer (EL). (2) Machine learning (ML) classifiers including Case-Based Reasoning were created to detect CG. Initial experiments showed a performance comparable to humans (4-fold evaluation yielded precision: weighted F1 score:0.93).

Conclusions: We presented an AI-based program able to facilitate the detection of CG in the DC in the eye bank by comparing the PCEIs with relevant previous cases, using ML classifiers and offering an enhanced visualization of the EL. The evaluation and optimization of this program will follow as the next stage of our project.

CONTROL ID: 3712456

SUBMITTER (NAME ONLY): Wei-Chun Lin

TITLE: Machine Learning for Predicting Early High Postoperative IOP After Trabeculectomy

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Lin, M. Hribar, Medical Informatics & Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|A. Chen, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Trabeculectomy is the most commonly used surgical method for advanced glaucoma. Many factors may impact the success of a trabeculectomy, such as patient selection, surgical technique, and postoperative management. Studies have shown that IOP control at the early postoperative period is crucial for successful trabeculectomy. Physicians may adjust the frequency of visits, steroid frequency, or other procedures to manage postoperative IOP. Yet, accurately predicting postoperative IOP is difficult due to various factors associated with wound healing. This study aims to develop predictive models to determine which glaucoma patients have higher risk of early high postoperative IOP.

Methods: We identified 1,005 adult glaucoma patients who underwent trabeculectomy from 2010 to 2021 and had at least 5 follow-up visits before surgery at OHSU. Early high postoperative IOP was defined as IOP ≥ 21 mmHg within 1-month postoperatively. Two types of data were extracted and used: static and time-series features. Static features included demographic data, eye exams and medications before surgery, and the highest preoperative IOP and VA. Time-series features included IOP, VA, and medications in the last 5 visits before surgery. We developed several machine learning models with static features to predict whether the patient has a higher risk of early high postoperative IOP, including XGBoost, random forest, and support vector machine. Also, to explore the importance of time-series features, we developed multimodal and long short-term memory (LSTM) models (figure 1). Area under the receiver operating characteristic curve (ROC), precision, recall, and F1 score were used to evaluate the performance.

Results: Figure 2 shows the ROC curves and AUC scores of 5 models. The XGBoost model had the highest AUC score (0.71) and F1 score (0.51). The LSTM and multimodal models showed lower performance, indicating that the fluctuation of eye measures from the visits before surgery is less associated with early postoperative high IOP. The top three important predictors identified in the XGBoost model were age, surgeon, and the highest preoperative IOP.

Conclusions: Machine learning models with secondary use of EHR data can be used to predict early postoperative high IOP patients. The work has implications in improving trabeculectomy postoperative management. In the future, we may incorporate text data into models to improve prediction accuracy.

CONTROL ID: 3712457

SUBMITTER (NAME ONLY): Luis García Onrubia

TITLE: Correlation between cytokine and chemokine levels in tear and plasma in the follow-up of uveitis patients

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. García Onrubia, M. Mateos, A. Enriquez-De-Salamanca, C. García-Vazquez, L. Cocho Archiles, J. Herreras Cantalapiedra, Instituto de Oftalmobiologia Aplicada, Valladolid, Castilla y León, SPAIN| L. García Onrubia, M. Mateos, L. Cocho Archiles, J. Herreras Cantalapiedra, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|

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ABSTRACT BODY:

Purpose: To determine whether tear levels of cytokines and chemokines could be used as a potential reliable biomarker in patients with uveitis and its correlation with plasma levels.

Methods: Twelve cytokines/chemokines were measured in tear and plasma samples of 22 patients diagnosed with active anterior, intermediate, posterior or panuveitis. Patients underwent standard treatment for uveitis were followed longitudinally over 6 months. At that time tear and plasma samples for measurements of the same of cytokines. Levels of these molecules in tears and plasma were compared and associated with degree of activity of the uveitis.

Results: Tear interleukin (IL)-6 percentage of detection was significantly reduced in the inactive phase ($p<0.05$). Tear concentration of epidermal growth factor (EGF), Fractalkine, IL-8, IL-1RA, interferon-inducible protein (IP)-10/CXCL10, vascular endothelial growth factor (VEGF) and IL-6, comparing the active and inactive period were not statistically different. Plasma concentration of EGF, Fractalkine, IL1-β, IL-17A, IL1RA, IL-2, IL-23, IL-8, IP-10, tumour necrosis factor-alpha, VEGF and IL-6, comparing the active and inactive period was not statistically significant. The levels of EGF, fractalkine, IL1-β, IL-17A, IL-1RA, IL-2, IL-23, IL-8, IP-10, TNF- α and IL-6 in patients with uveitis in their active/inactive phase were statistically different ($P<0.05$) to their counterpart levels in plasma. However, the difference between the tear and plasma levels of VEGF was not statistically significant ($P>0.05$).

Conclusions: No isolated cytokine/chemokine in the tear has been found, which concentration could be used as a potential biomarker of treatment response. Furthermore, apart from the VEGF, the cytokine/chemokine concentration in tears was independent of the plasma counterparts.

CONTROL ID: 3712459

SUBMITTER (NAME ONLY): Najnin Sharmin

TITLE: Real-time mimicking of accommodative microfluctuations by a tunable lens and monocular sensing of the sign of defocus

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Sharmin, B. Vohnsen, School of Physics, University College Dublin, Dublin, Leinster, IRELAND|

Commercial Relationships Disclosure: Najnin Sharmin: Commercial Relationship: Code N (No Commercial Relationship) | Brian Vohnsen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Accommodative microfluctuations may potentially play a role in the detection of the sign of defocus. The aim of this study was to examine the temporal dynamics of accommodation with and without microfluctuations in the young adult eye. This can provide insight into whether defocus is sensed by the eye and its possible relation to emmetropization.

Methods: Real-time accommodation, with and without microfluctuations (MFs), was analyzed in a monocular vision system with a Hartmann-Shack wavefront sensor (HS-WFS) capturing up to the 4^{th} radial Zernike order at 25 Hz, used along a tunable lens (TL), and a near-IR beacon at 850 nm. Subjects viewed with the right eye a green Maltese cross target (0.86°) on a dark computer screen placed at 1-m distance with a 3 mm pupil. The power of the TL was coded both to trigger an accommodative response and, when desired, to replicate and cancel MFs during the accommodative process using the defocus signal from the HS-WFS. Three subjects (2 emmetropes, 1 myope) were analyzed. In the first set of measurements, it generated constant defocus step changes (from 0 D to the comfortable accommodative range of the subject) at random time intervals (within 5 to 9 s). In the second set of measurements, the TL made the same random-time defocus step changes while mimicking, with opposite sign, detected MFs.

Results: The accommodation followed defocus steps accurately both with and without MFs for all of the subjects. Some accommodation overshooting was noticed when the MFs were mimicked by the TL. The reaction time was found to be in the range of 300 – 750 ms and the response time was found in the range of 250 – 1500 ms. It was noticed that almost in 50% of the cases, the reaction and response time was longer when MFs were compensated by the TL, while for the remaining cases both times were either similar or even faster with MFs compensation.

Conclusions: The findings show that in the absence of MFs accommodation is still in the correct direction. The accommodative response time increased with an increased magnitude of step changes and with the increased measurement time but was only weakly affected by the removal of the MFs cue. Thus, MFs may predominantly aid to maintain an average accommodation level rather than to provide the required direction of accommodation.

CONTROL ID: 3712465

SUBMITTER (NAME ONLY): Alexander Suh

TITLE: The Effectiveness of Telemedicine Screening for Retinopathy of Prematurity in the Remote Midwest United States

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.W. Suh, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|J. Martin, K. Wang, Avera Health, Sioux Falls, South Dakota, UNITED STATES|D. Suh, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Alexander Suh: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Martin: Commercial Relationship: Code N (No Commercial Relationship) | Katherine Wang: Commercial Relationship: Code N (No Commercial Relationship) | Donny Suh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinopathy of Prematurity (ROP) is the worldwide leading cause of preventable childhood blindness. In remote areas of the United States as well as developing countries, in-person screening for ROP by a trained ophthalmologist can be a significant hurdle. In this study, we aim to assess the effectiveness of telemedicine screening for retinopathy of prematurity (ROP) in premature infants in South Dakota.

Methods: A retrospective review of medical records for premature infants were screened for ROP at neonatal intensive care units (NICUs) in Sioux Falls, South Dakota from September 1, 2017 to December 31, 2021. RetCam Shuttle (Natus Medical Inc., Pleasanton, CA) retinal images were posted on a secure server for evaluation by a pediatric ophthalmologist. Patients who were suspected to progress to Stage I ROP or greater were referred to Children's Hospital and Medical Center in Omaha, Nebraska where they received comprehensive examination and, if necessary, anti-vascular endothelial growth factor (VEGF) treatment. The remaining patients received an outpatient comprehensive examination by a pediatric ophthalmologist within two weeks of discharge.

Results: 250 telemedicine examinations were performed on 70 infants during the study period, averaging 3.6 examinations per infant. Of the 70 infants, 6 (8.6%) were transferred for referral-warranted ROP. Remote telemedicine screening for referral-warranted ROP had a sensitivity of 100% and specificity of 97%. We had a positive predictive value of 67% and negative predictive value of 100%. Four of the six infants transferred for referral-warranted ROP required treatment with anti-VEGF, all of whom had good outcomes. No patients progressed beyond stage 3 ROP.

Conclusions: Remote telemedicine screening in at-risk premature infants detected referral-warranted ROP at a high accuracy with no poor outcomes throughout the four-year period. This study demonstrates the efficacy and functionality of telemedicine in screening for ROP and lays out implications for further utility in developing countries.

CONTROL ID: 3712467

SUBMITTER (NAME ONLY): Nadine Rady

TITLE: Impact of Corrective Lenses on the Supra-threshold Visual Field Test with Augmented Reality Headsets

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Rady, C. Johnson, G. Mijares, M. Abou Shousha, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|V. Lopez, M.K. Durbin, A. Nicklin, OD, M. Abou Shousha, Heru, Inc., Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Nadine Rady: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Johnson: Commercial Relationship: Code N (No Commercial Relationship) | Valeria Lopez: Commercial Relationship(s);Code E (Employment):Heru Inc. | Georgeana Mijares: Commercial Relationship: Code N (No Commercial Relationship) | Mary Durbin: Commercial Relationship(s);Code E (Employment):Heru Inc. | Alexandra Nicklin, OD: Commercial Relationship(s);Code E (Employment):Heru Inc. | Mohamed Abou Shousha: Commercial Relationship(s);Code E (Employment):Heru Inc.

ABSTRACT BODY:

Purpose: The suprathreshold visual field (SVTF) test using augmented reality (AR) headsets offers a method of portable screening for visual field defects. For patients with refractive error, the current standard of practice utilizes corrective lenses while testing. In this study, we explore whether the omission of corrective lenses impacts the efficacy of the SVTF as a screening tool for visual field loss.

Methods: Twenty-one adult patients with refractive errors were recruited over a two-week period at a tertiary academic eye institute to take the STVF test using the Heru re:Imagine full threshold strategy (Heru, Inc, Miami, FL) implemented on MagicLeap 1 AR headset (MagicLeap, Plantation, FL) with and without lens correction. Of these patients, fifteen underwent full threshold visual field testing. Patients were alternated between taking the STVF with or without correction first. Correction was achieved using classic trial lenses attached to a lens-holder and inserted in the headset. One or both eyes were tested depending on the presence of refractive error. STVF were deemed abnormal if two or more stimuli, other than those in the blind spot, were missed. Measures of sensitivity, specificity, and kappa statistic were calculated.

Results: Our study included 28 eyes, 76% females (n = 16), 57% Hispanic or Latinos (n = 12), with a mean age of 53.6 years. All the patients wore corrective eyeglasses. The mean myopic spherical equivalence was -3.60, and the mean hyperopic spherical equivalence was +2.13. The majority (57%) of the participants had cylinder power in their prescription (n = 12). Relative to the full threshold VF, the sensitivity of the STVF with correction was 57%, while without correction was 29%. The specificity of the STVF test with correction was 92%, while without correction was 58%. The kappa statistic for inter-rater reliability is 0.3, suggesting a fair agreement with a 75 percent observed agreement.

Conclusions: Our data suggest that the use of corrective lenses is of value for the efficacy of the supra-threshold test as a screening tool. Future directions include a larger sample size with a particular focus on patients with high cylinder power, and high-myopes and hypermetropes.

CONTROL ID: 3712468

SUBMITTER (NAME ONLY): Aftab Taiyab

TITLE: Understanding the requirement of AP-2β in development of the Trabecular Meshwork

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Taiyab, J. Dham, F. Shirazee, M. Akula, J.A. West-Mays, McMaster University, Hamilton, Ontario, CANADA|T. Williams, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of ocular structures of the anterior segment is critical for proper aqueous humor production and outflow. Previously, we have demonstrated that deletion of AP-2β from the neural crest and the developing periocular mesenchyme (POM) results in abnormal development of anterior angle structures including the TM, Schlemm's canal and the cornea. In order to determine the specific and the cell-autonomous role of AP-2β in TM development, we have recently developed a new mouse model by deleting AP-2β later during TM development using a tamoxifen-inducible ubiquitin cre recombinase (Ubc-Cre-ERT2) system; a cre recombinase system that allows us to manipulate the time of deletion of AP-2β.

Methods: UbCre$^{ERT2+/-}$; Tfap2b$^{+/-}$ mice were bred with Tfap2b$^{lox/lox}$; tdTomato$^{lox/lox}$ mice to generate pups containing UbCre$^{ERT2+/-}$; Tfap2b$^{-/lox}$; tdTomato$^{lox/+}$ (mutant) and UbCre$^{ERT2+/-}$; Tfap2b$^{+/lox}$; tdTomato$^{lox/+}$ (control). The eyes of all the pups were topically treated with 5μL tamoxifen solution (5mg/mL) three times per day starting post-natal day (P) 4 until P7. The pups were euthanized at P14 and the eyes were enucleated, fixed and processed for paraffin sectioning. H&E and immunohistochemistry (IHC) using antibodies for AP-2β and the TM markers, αSMA and myocilin, were performed on paraffin sections from mutant and control eyes.

Results: The H&E staining of P14 mutant eyes showed adhesion of iris to the cornea near the anterior angle, and fewer TM cells when compared to their control littermates. The morphology of the other anterior structures including the cornea remained unaffected in the mutants (n=6 eyes per genotype). The AP-2β deletion was confirmed by IHC in the anterior ocular structures including the anterior angle and the cornea of the mutant mice. The decrease in the TM cell population in mutants was further confirmed by the reduction in αSMA and myocilin staining (n=6 eyes per genotype).

Conclusions: The absence of TM cells from the anterior angle upon deletion of AP-2β from P4 to P7, after the specification of POM is complete, suggests a cell-autonomous role of AP-2β in TM development. The reduced number of TM cells in the mutants may be primarily responsible for the adhesion of iris to the cornea at the anterior angle. The reduced expression of TM cell markers and TM cell population suggests that AP-2β is critical for proper development and differentiation of TM.

CONTROL ID: 3712472

SUBMITTER (NAME ONLY): Willy Carpio Rosso

TITLE: Characterization of subretinal hyperreflective material and short-term visual acuity in patients with neovascular age-related macular degeneration treated with antiangiogenic agents

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Carpio Rosso, S. Meneses, S. Rosenstiehl, F. Rodriguez, Fundacion Oftalmologica Nacional, COLOMBIA|

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ABSTRACT BODY:

Purpose: To associate morphological characteristics of subretinal hyperreflective material (SHRM) with short-term visual outcomes in patients with neovascular age-related macular degeneration (nAMD) treated with intravitreal antiangiogenic therapy (anti-VEGF).

Methods: An analytical observational study was carried out in eyes with nAMD treated with 3 loading doses of antiVEGF. SHRM optical coherence tomography (Cirrus) characteristics and measures were analyzed including reflectivity, borders, homogeneity, localization, width and the presence of ELM/EZ. Correlations were performed to evaluate the association between OCT characteristics and short-term visual outcomes.

Results: A total of 65 eyes (65 subjects), with a median age of 75,5 years (IQR 16,0) were included. All the subjects had SHRM. Median best-corrected visual acuity (BCVA) pre-treatment was 0,8 (IQR 0,7) LogMAR and post-treatment was 0,7 (IQR 0,6) LogMAR. We found a positive correlation before and after treatment in BCVA (r=0,8) (p=0,001), SHRM extension (r=0.7) (p=0,001), low reflectivity (p=0,017) and non-defined borders (p=0,037) that were statistically significant. The parameters that were associated with an improvement in BCVA after treatment were SHRM characteristics: low reflectivity (p=0.048), non-homogeneity (p=0.048) and width (p=0.043), presence of external limiting membrane (ELM) (p=0.002) and ellipsoid zone (EZ) (p=0.017).

Conclusions: Findings associated with improved short-term visual outcomes were SHRM low reflectivity, non-homogeneity, shorter width and the presence of ELM/EZ. Studies with a larger sample are required to assess the relevance of OCT features with the final visual prognosis.

CONTROL ID: 3712473

SUBMITTER (NAME ONLY): A. Brooke Still

TITLE: Systemic treatment with methylsulfonylmethane protects against light-induced retinal degeneration

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Still, J.T. Sellers, M. Chrenek, J.M. Nickerson, J.H. Boatright, Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|J.H. Boatright, Center for Visual and Neurocognitive Rehabilitation, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|

Commercial Relationships Disclosure: A. Brooke Still: Commercial Relationship: Code N (No Commercial Relationship) | Jana Sellers: Commercial Relationship: Code N (No Commercial Relationship) | Micah Chrenek: Commercial Relationship: Code N (No Commercial Relationship) | John Nickerson: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Boatright: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously reported that dimethyl sulfoxide (DMSO) acts as a neuroprotectant in light-induced retinal damage (LIRD) and the retinitis pigmentosa Pdeb6$^{rd10/rd10}$ (rd10) mouse models. Because DMSO has side effects, such as halitosis and body odor, we decided to test a metabolite of DMSO, methylsulfonylmethane (MSM), for protection. MSM, the oxidized form of DMSO, has no known side effects and is designated as Generally Recognized as Safe (GRAS) by the FDA. We tested the hypothesis that systemic treatment with MSM would be protective in a LIRD mouse model.

Methods: 90-day-old male BALB/c mice were intraperitoneally (IP) injected the afternoon before and morning of bright light exposure with either 4025 mg/kg MSM, 3.5 ml/kg (3.85mg/kg) DMSO, or saline vehicle. Mice were dark-adapted overnight prior to bright light (2500 lux x 4h) or dim light (50 lux x 4h) exposure. Retinal function was assessed by electroretinogram (ERG) with increasing flash intensities from 0.001 to 10 cd s/m^2 one week later, and outer nuclear layer (ONL) quantification was completed using hematoxylin and eosin (H&E) staining in sagittal retina sections of eyes collected afterward.

Results: When compared to vehicle dim, a-wave and b-wave amplitudes at the highest flash intensity decreased 83% and 76%, respectively, for the vehicle bright group ($p<0.0001$), but only 56% and 42% for the MSM bright group ($p<0.0001$) and 31% and 15% for the DMSO bright group ($p<0001$). The differences between mean amplitudes of the vehicle bright group versus either of the drug bright groups were also statistically significantly different ($p<0.0001$). Compared to vehicle dim mice, vehicle bright mice lost 63% of their ONL nuclei ($p<0.0001$), but MSM bright mice only lost 17.8% ($p<0.02$) and DMSO bright mice only lost 3.21% (n.s.). The differences between the vehicle bright group versus either of the drug bright groups were also statistically significantly different ($p<0.0008$).

Conclusions: MSM is protective against LIRD-induced losses in retinal function and in the number of remaining ONL nuclei. MSM was not as protective as DMSO. We believe this may be due to a difference in molar ratio between the drug concentrations (49.29 mmol/kg for 3.5 ml/kg DMSO compared to 42.76 mmol/kg for 4025 mg/kg MSM). Overall, given the lack of side effects compared to DMSO, the current data suggest that MSM should be further pursued as a retinoprotectant.

CONTROL ID: 3712474

SUBMITTER (NAME ONLY): Mallory Suarez

TITLE: Sutureless Sclerotomy: The Efficacy of Platelet Rich Plasma (PRP), Clotted Whole Blood, and Polymerized ReSure Sealant

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Suarez, R.M. Sappington, B. Hayes, Ophthalmology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|R.M. Sappington, Neurobiology and Anatomy, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Mallory Suarez: Commercial Relationship: Code N (No Commercial Relationship) | Rebecca Sappington: Commercial Relationship: Code N (No Commercial Relationship) | Bartlett Hayes: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pars plana vitrectomy incisions can be self-sealing, sutured, or sealed with ocular adhesives. Complications such as leaks, hypotony, endophthalmitis, inflammation, astigmatism, and suture breakage raise questions regarding what technique and material modifications can improve scleral wound closure. The purpose of this study is to evaluate the effectiveness of combining the patient's own tissues with products that are already FDA approved in a novel technique for scleral wound closure in pars plana vitrectomy.

Methods: Cadaveric Yorkshire porcine eyes (n=3) were manually vitrectomized and a 23-gauge trocar was used to create a scleral wound which leaked saline infusion fluid at baseline. 200µL of platelet rich plasma (PRP) was mixed with 100µl of thrombin for PRP clot formation. In one trial, A 2mm dermatological hole punch was used to mold the clotted plasma. A pair of 23-gauge Grieshaber MAXGrip Forceps delivered the clot through the 23-gauge trocar into the scleral wound. In another trial, the 23-gauge trocar was removed and a 2-20µl pipette delivered the clotted plasma into the wound. The MAXGrip Forceps were used as a plunger to push the clot through the micropipette tip and into the wound. A mixture of whole blood and thrombin were aspirated into 16-,18-, and 20-gauge angiocath tips creating clotted whole blood. The IV angiocath tips were then cut into 6-8mm pieces, creating cylindrical clots. The clots were delivered through the 23-gauge trocar into the scleral wound. This methodology of clot delivery was also used for polymerized ReSure Sealant.

Results: A PRP clot was delivered through a 2-20µl pipette tip using the MAXGrip Forceps, preventing ocular wound leakage up to a pressure of 60 mmHg. A clot of whole blood molded from the 20G IV angiocath tip was successfully delivered through the 23G trocar with no ocular wound leakage at baseline. However, it was dislodged during the Seidel test.

Conclusions: This study provided preliminary evidence that clotted PRP and clotted whole blood could be feasible options for scleral wound closure. Further well controlled, randomized, and live animal studies will be required to determine the efficacy and long-term stability of the outlined materials and methodology of clot formation and delivery, but further studies have the potential to shape the approach to sclerotomy closure.

CONTROL ID: 3712475

SUBMITTER (NAME ONLY): Hartej Singh

TITLE: Quantitative assessment of venting techniques to facilitate intraocular perfluorocarbon removal

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Singh, K. Astafurov, Rutgers Robert Wood Johnson Medical School New Brunswick, New Brunswick, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Hartej Singh: Commercial Relationship: Code N (No Commercial Relationship) | Konstantin Astafurov: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

Perfluoro-n-octane (PFO) is a useful adjuvant for the repair of retinal detachments due to its transparency and high density. However, intraocular PFO retention has been implicated in inflammation, visual field defects, and retinal toxicity. Thus, the total removal of PFO at the end of surgery is critical but, at times, difficult due to corneal edema and intraocular lens fogging. PFO's high vapor pressure in operating room conditions with continuous air venting aids its intraocular elimination. This study seeks to quantitatively characterize optimal conditions for the removal of residual PFO via evaporation during vitreoretinal surgery.

Methods: A standard, 25-gauge (25g) vitrectomy system (Alcon Constellation) and an anatomically-sized model plastic eye (Phillips Studio, UK) were used for the experimental setup. Valved trocars were placed 3.5mm from the corneal limbus, and low, clinically-relevant PFO volumes were instilled into the model eye. The evaporation rates were measured under varying venting conditions with humidified air infused at 40 mmHg by the Alcon Constellation. Four 25g venting methods were examined, a chimney-vent, a needle, and an extrusion cannula with and without a silicone tip. The needle and extrusion cannula trials were conducted at the mid-vitreous position and near the PFO interface.

Results: At the volumes tested, PFO evaporated linearly with all venting methods. The 25g chimney vent offered the fastest evaporation rate (0.019±0.002 cc/min). The 25g extrusion cannula with a silicone tip showed slower evaporation rates both at the mid-vitreous position and close to the PFO interface (0.006±0.0002 cc/min, 0.008±0.001 cc/min, respectively). Removing the extrusion cannula's silicone tip marginally increased the evaporation rate (0.012±0.001 cc/min, near the PFO interface). The 25g needle yielded the slowest evaporation rate (0.005±0.0003 cc/min, near the PFO interface).

Conclusions: Residual PFO can be removed from the eye using air venting due to PFO's high vapor pressure. We show that, with 25g instrumentation, a chimney-vent is the optimal PFO venting method, and, with air infused at 40 mmHg, five minutes are sufficient for eliminating PFO volumes up to 0.1 cc. Our quantitative data would be useful to vitreoretinal surgeons who may encounter challenges with visualization of complete PFO removal not infrequently seen at the end of long surgical procedures.

CONTROL ID: 3712477

SUBMITTER (NAME ONLY): Dania Abuleil

TITLE: Visual cortex anodal transcranial direct current stimulation (a-tDCS) does not alter GABA concentration

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Abuleil, D.L. McCulloch, B. Thompson, University of Waterloo, Waterloo, Ontario, CANADA|D. Gorbet, J. Steeves, York University, Toronto, Ontario, CANADA|B. Thompson, Center for Eye and Vision Research, HONG KONG|

Commercial Relationships Disclosure: Dania Abuleil: Commercial Relationship: Code N (No Commercial Relationship) | Diana Gorbet: Commercial Relationship: Code N (No Commercial Relationship) | Daphne McCulloch: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Steeves: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Thompson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Anodal transcranial direct current stimulation (a-tDCS) of the primary visual cortex can alter visual perception in individuals with normal vision and in those with amblyopia. The mechanisms that underpin this effect are unknown. When applied to the primary motor cortex, a-tDCS reduces the concentration of the neurotransmitter GABA within the stimulated region. We investigated whether this effect occurs when a-tDCS is delivered to the primary visual cortex.

Methods: Thirteen adults with normal vision participated in a within-subjects study design consisting of two MRI sessions, one involving active a-tDCS and the other a placebo (sham) a-tDCS to the visual cortex. Each session began with the measurement of binocular rivalry dynamics (oblique gratings, 6.1° size, 0.5 cpd, 60-second viewing time). GABA and glutamate concentrations (magnetic resonance spectroscopy; MRS) and resting state functional connectivity (functional MRI) were then measured before (baseline) and immediately after application of a-tDCS. For MRS, a 2.5 cm^3 voxel-of-interest (VOI) was centered on the calcarine sulcus and positioned so that it covered only brain tissue. For functional MRI, brain volumes were acquired using whole-brain echo-planar imaging with a T2-weighted sequence.

Results: Active a-tDCS stimulation had no effect on visual cortex GABA concentration nor on resting state connectivity. However, there was a trend towards increased glutamate concentration following active stimulation ($p=0.045$). In addition, higher visual cortex glutamate concentrations at baseline were associated with longer piecemeal percepts during binocular rivalry ($r=0.561$, $p=0.046$).

Conclusions: Unlike motor cortex, visual cortex a-tDCS does not appear to be mediated by a reduction in GABA concentration. Unexpectedly, temporal dynamics of binocular rivalry are associated with higher visual cortex glutamate concentration.

CONTROL ID: 3712478
SUBMITTER (NAME ONLY): Emaan Chaudry
TITLE: Post COVID-19 Vaccine Uveitis: A Case Series
SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Chaudry, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|N. Hanna, H. Bedi, Y. Khan, Ophthalmology, McMaster University, Hamilton, Ontario, CANADA|G.S. Nijjar, The University of British Columbia, Vancouver, British Columbia, CANADA|
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ABSTRACT BODY:

Purpose: With the recent emergence and worldwide distribution of COVID-19 vaccines, many side effects may be underreported and possibly unknown. Cases of vaccine-associated uveitis have been linked to almost all vaccines administered in the past, however, there is scarcity of literature providing insight into post COVID-19 vaccine associated uveitis / episcleritis. By documenting patients presenting with uveitis / episcleritis after the administration of mRNA Pfizer and Moderna vaccines, this case series significantly advances our current understanding of potential COVID-19 vaccine ocular complications.

Methods: Patients with ocular symptoms consistent with uveitis / episcleritis within 15 days of the administration of the Pfizer or Moderna COVID-19 vaccine were included in this study. Ocular assessment included a Snellen best-corrected visual acuity (BCVA) converted to logMAR, intraocular pressure (IOP) with Goldmann Applanation Tonometry, pupil check, anterior and dilated posterior segment assessment with slit-lamp, and optical coherence tomography (OCT) imaging. Patients were anonymized and demographics including sex, race, age, and other necessary clinical data were recorded.

Results: A total of 9 patients (6 female and 3 males) with a mean age of 42.9 (range, 19-83) were included. 7 patients received a Pfizer vaccine and 2 received a Moderna vaccine. 5 patients presented with symptoms after their first dose, 2 after their second dose, and 1 after both doses. The mean time of ocular symptoms post vaccine was 6.15 days (range, 1-14) and the mean BCVA was 0.657.

Patients were diagnosed with bilateral anterior granulomatous uveitis (case 1), unilateral nongranulomatous anterior uveitis (case 2, 6-9), bilateral nongranulomatous anterior uveitis (case 3-4), and episcleritis (case 5). Case 1 and 9 have been highlighted and summarized in figure 1 and 2, respectively.

Conclusions: The pathogenesis of vaccine induced uveitis is not properly understood, however, the outcomes of this case series aids in establishing a temporal association between the Pfizer and Moderna COVID-19 vaccines and the onset of uveitis / episcleritis. As the rate of COVID-19 vaccinations increase globally, it is imperative for physicians to be aware of the possible association and presentation of these ocular findings and diagnoses to effectively treat patients.

CONTROL ID: 3712480

SUBMITTER (NAME ONLY): Shigeo Tamiya

TITLE: Rho effector Arp2/3 is involved in myofibroblast transdifferentiation of retinal pigment epithelial cells

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tamiya, G. Jagatheesan, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Shigeo Tamiya: Commercial Relationship: Code N (No Commercial Relationship) | Ganapathy Jagatheesan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Myofibroblast transdifferentiation of retinal pigment epithelial (RPE) cells has been implicated as key event in fibrotic complications such as proliferative vitreoretinopathy or fibrosis associated with exudative age-related macular degeneration. We previously demonstrated that Rho GTPase plays a key role in this process. Interestingly, ROCK, one of the main downstream Rho effector, was not involved in this process. The purpose of this study is to examine the role of Arp2/3, another key downstream Rho effector involved in actin polymerization, in myofibroblast transdifferentiation of RPE cells.

Methods: Primary cultured porcine RPE cells were used for experiments. Second passage RPE cells cultured on collagen hydrogels were stimulated with TGF-beta2 to induce myofibroblast transdifferentiation. Expression of myofibroblast markers, alpha-smooth muscle actin and tropomyosin-1, was examined by western blot analyses. Myofibroblast function was assessed by collagen hydrogel contraction. The cell permeable C3 transferase and CK-666 were used to inhibit Rho and Arp2/3, respectively.

Results: As previously reported, TGF-beta2 stimulation of second passage RPE cells induced myofibroblast transdifferentiation, which was demonstrated by significant increase in expression of myofibroblast marker proteins as well as enhanced contraction of collagen hydrogel. Rho inhibitor and Arp2/3 inhibitor significantly reduced myofibroblast marker expression as well as collagen hydrogel contraction.

Conclusions: Rho and its downstream effector Arp2/3 is involved in myofibroblast transdifferentiation of RPE cells. Actin polymerization is a key process in mechanosignaling that affects multiple downstream signaling molecules. Alteration of Rho-Arp2/3 pathway or its downstream targets may lead to therapeutic treatment of fibrotic complications such as proliferative vitreoretinopathy or fibrotic complications of exudative age-related macular degeneration in which RPE cell transdifferentiation to myofibroblasts play a significant role.

CONTROL ID: 3712481

SUBMITTER (NAME ONLY): Niharika Bhatia

TITLE: Estimation of structural integrity of Rayner RA0600C intraocular lens in a model of transscleral fixation with the Gore-Tex suture

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Bhatia, A. Gorrai, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES|K. Astafurov, Department of Ophthalmology, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Niharika Bhatia: Commercial Relationship: Code N (No Commercial Relationship) | Ananya Gorrai: Commercial Relationship: Code N (No Commercial Relationship) | Konstantin Astafurov: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Sutured intraocular lens (IOL) fixation is used for fixating IOLs in the absence of capsular support. Various IOLs have been employed in the past for this including CZ70BD (Alcon Laboratories, Inc), Akreos AO60 and, most recently, enVista MX60 and MX60E (Bausch & Lomb, Inc). Some of these IOLs have substantial disadvantages, including fracture of IOL eyelets. The purpose of this study was to determine the maximal tensile strength of the eyelet in a newly FDA approved IOL RayOne RAO600C (Rayner, Inc) and compare it to the other commonly used IOLs.

Methods: We tested Rayner RAO600C and CZ70BD lenses. The IOLs were suspended in a testing platform with the optic held by a clamp and a simple pass GoreTex 8-0 suture passed through an eyelet. Gradually increasing downward force was applied to the GoreTex suture/eyelet by adding weight until the fracture of the eyelet was recorded. The resultant force applied to IOL eyelets was calculated. Statistical analysis to compare the mean tensile strength was completed by the two-tailed Mann Whitney U-test.

Results: The mean eyelet fracture force was 0.2609 N ± 0.0305 N for the CZ70BD (n=4) and 1.002 N ± 0.0878 N for the RAO600C IOL (n=4), which was statistically significantly greater (p=0.02857; Mann Whitney U-test). The absolute mean difference was 0.741 N (95% [0.6252, 0.8947]).

Conclusions: The eyelet-haptic complex of Rayner RAO600C lens endured significantly greater (3.8 times) tensile force than that of the CZ70BD. In a prior similar investigation, CZ70BD fractured at a greater force than we observed, which may be related to differences in experimental set-up. Further, in this prior study, CZ70BD had the same tensile strength when compared to Envista MX60E, and 2.3 times lower tensile strength when compared to Akreos AO60 IOL. Extrapolating those results to our data, RAO600C eyelet-haptic complex is potentially significantly stronger than Envista MX60E and may be as strong as Akreos AO60. It also has advantages of being a foldable IOL and could be passed through a small 2.2mm corneal incision. Overall, our findings suggest that the RAO600C may be a sustainable option for transscleral sutured IOL fixation.

CONTROL ID: 3712482

SUBMITTER (NAME ONLY): Alireza Kamalipour

TITLE: Combining OCT and OCT-Angiography Longitudinal Measurements for the Prediction of Visual Field Progression in Glaucoma with Artificial Intelligence

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kamalipour, S. Moghimi, V. Mohammadzadeh, T. Nishida, E. Micheletti, J. Wu, G. Mahmoudinezhad, M. Christopher, L. Zangwill, R.N. Weinreb, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|P. Khosravi, University of California Irvine, Irvine, California, UNITED STATES|T. Javidi, Electrical and Computer Engineering, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To use longitudinal OCT and OCT-Angiography (OCTA) measurements to predict visual field (VF) progression in glaucoma suspect and glaucoma patients with a supervised machine learning approach.

Methods: 110 eyes of glaucoma suspect (33.6%) and glaucoma (66.4%) patients with a minimum of five 24-2 VF tests over an average follow-up duration of 4.1 years were included. Participants were required to have at least three pairs of optic nerve head and macula OCTA images during follow-up. VF progression was defined based on a composite measure including either a “likely progression event” on Guided Progression Analysis, a statistically significant negative slope of VF mean deviation, or a positive pointwise linear regression event. Gradient Boosting Classifier was used to predict the probability of VF progression based on different subsets of baseline and longitudinal OCT and OCTA input features at the global and regional levels. Areas-under-ROC curves (AUROC) were used to compare the classification accuracy of different models.

Results: VF progression was detected in 28 eyes (25.5%). The model that used combined baseline and longitudinal OCT and OCTA features at the global and regional level had the best classification accuracy for the prediction of VF progression (AUROC = 0.89 [95% CI: 0.82, 0.95]). Models including combined OCT and OCTA features had higher classification accuracy compared to those with individual subsets of OCT or OCTA features alone. Moreover, including regional measurements significantly improved the classification accuracy of the models compared to using global measurements alone. The addition of longitudinal rates of change of OCT and OCTA measurements as input features (AUROCs = 0.80-0.89) considerably increased the classification accuracy of the models with baseline measurements alone (AUROCs = 0.60 0.63). (Figure 1, all P-values for pairwise comparisons < 0.05)

Conclusions: Artificial intelligence techniques combining longitudinal OCT and OCTA measurements can predict clinically-relevant glaucomatous VF progression. Longitudinal OCTA measurements complement OCT-derived structural metrics for the prediction of functional VF loss in glaucoma patients.

CONTROL ID: 3712483

SUBMITTER (NAME ONLY): GUOQIN WEI

TITLE: Erucamide targets microglia to regulate the retinal angiogenic microenvironment and function as a neurotrophic factor

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Erucamide, a highly hydrophobic fatty acid amide synthesized by photoreceptors, maintains the structure and function of retinas, but its mechanism of action remains unknown. Here we used multiple biochemical techniques to identify erucamide's target cells, binding proteins, and potential mechanism of neurotrophic action.

Methods: Surface functionalized porous silicon nanoparticles (pSiNPs) were used to efficiently deliver erucamide into the retina. BODIPY-erucamide probes were synthesized to facilitate visualization of erucamide in vivo. Photo affinity labeling proteomics were performed to identify the binding proteins of erucamide. Gene profiling experiments were conducted to elucidate molecular pathways in the target cells.

Results: We used silane-modified pSiNPs to overcome the chanllage of delivering hydrophobic erucamide in vivo. Both intravitreal and subretinal injection of erucamide-pSiNPs resulted in wide-spread activation of GS-Lectin positive cells that were subsequently found to be CD11b+ microglia. BODIPY-labelled erucamide was taken up by CD11b+ cells three days after injection, suggesting that microglia may be directly targeted by erucamide. Angiogenic cytokines like VEGF, PDGFa, FGF, IL-6, TNFa were upregulated after erucamide treatment in both microglia sorted from injected mouse retinas or human iPSC derived microglia. Photo sensitive probes of erucamide were designed, synthesized and used for photo affinity labeling proteomics of the human microglial cell line HMC3. Results from these experiments were used to identify potential binding targets of erucamide. Several novel binding protein candidates were subsequently found to be essential for activation of microglia regulated by erucamide.

Conclusions: We hypothesize that, as a known angiogenic factor itself, erucamide may also work in a paracrine fashion to regulate and maintain a neurotrophic microenvironment in the retina. Microglia can be a direct target of erucamide both in vitro and in vivo. This neurotrophic paracrine activity may be mediated by a number of novel microglial-associated erucamide-binding proteins that are responsible for the activation of, and angiogenic cytokine secretion from, microglia. Modulation of these pathways may represent novel targets for drug discovery in the treatment of neurovasculoglial degenerative retinal diseases.

CONTROL ID: 3712484

SUBMITTER (NAME ONLY): Sangeetha Kandoi

TITLE: Modeling autosomal dominant retinitis pigmentosa associated with copy number variants in rhodopsin and rescue using Photoregulin3 in patient-specific retinal organoids

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Copy number variants in wild-type rhodopsin (RHO) have been reported as a novel cause of autosomal dominant retinitis pigmentosa (adRP) in a 68-year-old male (first reported in ARVO 2019). The current study focuses on (i) modeling the disease phenotype using 3D retinal organoids (RO), and (ii) attenuating the overexpression of wild-type RHO using Photoregulin3 (PR3), a small molecule inhibitor of upstream regulator NR2E3.

Methods: Induced pluripotent stem cells (iPSCs) reprogrammed (n=3 clones/subject) from the patient with adRP associated with four copies of RHO and an unaffected first-degree relative with two copies of RHO (control) were differentiated into RO. RO collected at various time-points of differentiation days (D) - D120 (rod photoreceptor birth), D200 (early maturation), and D300 (late maturation) were assessed for morphology (Bright-field, Transmission electron microscopy; TEM), RHO expression (quantitative real-time PCR; qRT-PCR, bulk RNA-seq), protein localization and quantification (Immunofluorescence; IF and western blotting; WB). Patient RO of D300-350 was treated with varying doses of PR3 (0.5, 0.25, and 0.1 μM) for one week and assessed for RHO levels and localization (qRT-PCR and IF).

Results: Morphological evaluation of patient-specific iPSC-RO displayed delayed maturation or absence of outer segments (Bright-field/TEM), ~6-10-fold increased RHO expression (qRT-PCR, bulk RNA-seq), impaired localization of Rhodopsin (Rho) protein within the cell body as opposed to being present in the outer segments (IF), and ~4-fold elevated Rho (WB) at all the time points compared to control. PR3-treated patient RO showed a substantial decrease in the RHO mRNA levels (10- to 30-fold) in a dose-dependent manner compared to the vehicle-treated RO, along with a partial rescue in the transport of Rho from cell bodies to the inner and outer segments. All data are represented as Mean±SEM (n=3 independent experiments).

Conclusions: Tight regulation of RHO is essential for rod photoreceptor function and maintenance. This study provides a proof-of-principle for personalized medicine by utilizing (a) patient-specific iPSC to model disease and (b) investigated a small molecule approach as a clinically viable strategy to target and modify the disease progression in patients with adRP associated with RHO-overexpression.

CONTROL ID: 3712488

SUBMITTER (NAME ONLY): Khadija Agsalud

TITLE: Hydroquinone as a model of smoking-induced oxidative stress in cultured porcine endothelial cells

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Agsalud, J.J. Bu, A. Abbas, E.N. Finburgh, P. Shaw, N.A. Afshari, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effect of hydroquinone (HQ), an oxidative component of cigarette smoke, on inflammatory markers in porcine corneal endothelial cells, and to find an optimum treatment time and concentration for hydroquinone as a model of smoking-induced oxidative stress in corneal cells.

Methods: Four porcine eyes were harvested. The corneoscleral rim was separated from the rest of the eye and treated with 0.5% trypsin for 15 minutes. Corneal endothelial cells were then scraped from Descemet membrane and plated into one well of a 12 well plate. Cells were proliferated to confluency in a low growth factor medium, then passaged three times onto one well of a 6 well plate, two wells of a 6 well plates, then twelve wells of a 12 well plate for treatment. The treatment groups were as follows: HQ for 1, 2, and 4 hours at 200, 250, and 300 μM (9 wells total), and an untreated control group (3 wells). Total RNA was extracted using the RNEasy Mini Kit and then converted to cDNA using the iScript Reverse Transcription Supermix. Expression of inflammatory markers IL-6, TNF-alpha, and p38, and the reference gene GAPDH, were quantified using real-time quantitative PCR (RT-qPCR). The experiment was repeated to obtain 3 biological replicates per treatment group. The delta-delta Ct method was used to calculate relative gene expression, and statistical tests were calculated using delta Ct values.

Results: Single-factor analysis of variance (ANOVA) revealed a statistically significant effect of HQ on TNF-alpha expression ($p<0.005$) and a marginally significant effect on IL-6 expression ($p<0.10$). No significant effect was observed on p38 expression ($p=0.51$). Pairwise t-tests were then conducted on TNF-alpha and IL-6 expression for each treatment group versus the untreated controls, revealing that for both TNF-alpha and IL-6, increase in expression became significant at treatment time of 2 hours at 250 and 300 μM ($p<0.05$), and at treatment time of 4 hours for 200, 250, and 300 μM ($p<0.05$).

Conclusions: HQ treatment beginning at 2 hours and 250 μM significantly increases expression of the inflammatory markers IL-6 and TNF-alpha, but not p38. Higher treatment times and concentrations should be chosen with caution due to increasing HQ cytotoxicity and low RNA yield. HQ may be useful as a novel smoking-induced oxidative stress model in corneal endothelial cells.

CONTROL ID: 3712492

SUBMITTER (NAME ONLY): Wesley Jackson

TITLE: Antibody-hyaluronic acid conjugates for sustained treatment of neovascular ocular disease

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Jackson, L. Brier, A. Barnebey, J. McFarland, A. Twite, Valitor, Inc, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-VEGF therapy continues to be the gold standard to minimize the risk of vision loss due to neovascular ocular disease, including wet age-related macular degeneration (AMD) and diabetic macular edema (DME). However, current anti-VEGF biologics require frequent intravitreal (ITV) injections, and poor compliance to redosing protocols has been linked to losses in efficacy over the long-term. To solve this problem, Valitor's multivalent protein (MVP) conjugation technology was designed to enable sustained anti-VEGF therapy after ITV injection, thereby substantially reducing the required treatment frequency. The stability of the MVPs after administration is highly dependent on the anti-VEGF biologic, and thus our goal was to engineer an antibody that can maintain the stability of an MVP in the vitreous humor.

Methods: Using phage-display screening and literature searches, we developed a library of single domain anti-VEGF antibodies (anti-VEGF VHH) with variable peptide linkers to facilitate conjugation. We synthesized MVPs comprising multiple copies (i.e. valency) the VHH antibodies conjugated to soluble, long-chain hyaluronic acid. We initially ranked the unconjugated antibodies and MVPs based on their thermal stability. We further tested top MVP performers in stability studies at ~10X the anticipated clinical ITV concentration in a vitreous mimetic buffer at 37C for up to 9 months. Periodically, we assessed stability based on changes in either VEGF binding affinity or hydrodynamic radius.

Results: Using our library, we identified several anti-VEGF VHH constructs that had high thermal stability, were compatible with our MVP conjugation platform, and were able to confer high stability following conjugation. Further, we identified specific VHH sequence characteristics and peptide linkers that enabled anti-VEGF MVPs to maintain their size and remain highly potent and soluble after more than 6 months at in situ conditions.

Conclusions: Based on our findings, we have developed a consensus sequence for in situ stability comprising key VHH and peptide linker characteristics. We then engineered a novel optimized anti-VEGF VHH that has been incorporated into our anti-VEGF product candidate (VLTR-557) that will enable long-acting treatment of wet AMD. We are currenting scaling the manufacturing of VLTR-557, and we plan to initiate IND-enabling preclinical studies in mid-2022.

CONTROL ID: 3712493

SUBMITTER (NAME ONLY): Jacob Light

TITLE: Value of Diagnostic Vitrectomy in Impacting Clinical Management

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diagnostic vitrectomy can provide useful information in cases of intraocular inflammation or opacity in which initial work-up has failed to elucidate an underlying etiologic process. Studies have reported a wide range of diagnostic yields, but few have focused on the impact of results on clinical course/management. We hypothesized that patients in whom diagnostic vitrectomy directly impacts subsequent clinical management will have different visual outcomes than patients in whom it does not. Furthermore, we aimed to provide up-to-date information about the rates of positive infectious, inflammatory, and neoplastic diagnostic vitrectomy results.

Methods: A retrospective chart review of the patients who underwent diagnostic pars plana vitrectomy and vitreous biopsy from January 2015 through April 2021 was performed. Baseline characteristics including presumptive diagnosis was collected from the charts and compared with final pathology reports to assess the role of diagnostic vitrectomy. Visual acuities were recorded immediately pre-operatively, at post-operative months 1, 6, and 12, and at the final visit. Changes in visual acuity relative to pre-op were calculated. The microbiologic and pathologic results of each vitrectomy sample were reviewed, the final post-op diagnosis was recorded and categorized by etiologic subtype, and the patients in whom the results led to significant change in diagnosis and/or clinical management were identified.

Results: A total of 117 eyes of 117 patients (57.3% female, mean (±SD) age 63.2 (±18.7); range 4-93 years) were included in this study. Patient characteristics, follow-up, and procedure gauge are summarized in Table 1. The mean (±SD) pre-vitrectomy logMAR visual acuity was 1.20 (±0.95) and mean (±SD) 1 month post-vitrectomy logMAR visual acuity was 0.97 (±0.93; p=0.046), The mean (±SD) 6 month post-vitrectomy logMAR visual acuity was 0.93 (±0.91; p=0.023). Analysis of vitrectomy results and impact on clinical management is presented in Table 2. In 24.8% of cases, vitrectomy result led to change in clinical management.

Conclusions: Diagnostic vitrectomy results lead to a change in clinical management in a minority of cases. Prognosis for visual outcome in these cases may be poorer, possibly due to more severe conditions being more likely to yield positive results. Neoplastic etiologies tend to be underestimated clinically prior to diagnostic vitrectomy.

CONTROL ID: 3712496

SUBMITTER (NAME ONLY): Anastasiya Vinokurtseva

TITLE: Comparison of acetylsalicylic acid and mitomycin C in Tenon's capsule fibroblasts: distinct effects on cytokine-induced myofibroblast activity and implications for glaucoma surgery.

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Vinokurtseva, J.J. Armstrong, C. Hutnik, Ophthalmology, Western University Schulich School of Medicine & Dentistry, London, Ontario, CANADA|E. Li, Western University, London, Ontario, CANADA|H. Liu, Saint Joseph's Health Care London, London, Ontario, CANADA|C. Hutnik, Ivey Eye Institute, London, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Inflammation-driven scarring is associated with high rates of surgical failure in trabeculectomies and in minimally invasive glaucoma procedures alike. The current gold standard anti-scarring adjuvant mitomycin C (MMC) has variable effectiveness in controlling fibroproliferation and is associated with significant cytotoxic effects. Acetylsalicylic acid (ASA) is unique among non-steroidal anti-inflammatory drugs, exerting its effects through covalent enzyme modifications. When delivered locally, ASA repurposes the typically pro-inflammatory cyclooxygenase (COX-2) enzyme to resolve inflammation, rather than simply suppressing it. By resolving inflammation, it reduces likelihood of inflammation-mediated fibroproliferation and fibrosis.

The aim of this study is to determine whether ASA decreases inflammatory cytokine-induced scarring activity in human Tenon's capsule fibroblasts (HTCFs) and to compare the effects of ASA to MMC in in vitro model of subconjunctival scarring.

Methods: Glaucoma patient-derived HTCFs in 2D and 3D models were co-treated with inflammatory cytokine TGFβ1 with and without ASA (concentrations ranging 100-1600µg/ml), or MMC (0.05-0.2mg/mL), to assess their effects on HTCF activity via Western Blot, immunofluorescence, MTT, LDH and 3D collagen contraction assays. ASA-triggered lipid mediators were measured using liquid chromatography tandem mass spectrometry (LC-MS/MS).

Results: ASA treatment decreased HTCF-mediated collagen contraction, TGFβ1-induced HTCF metabolic activity, and myofibroblast-associated protein expression, in the absence of cell necrosis. In comparison to MMC, ASA was as effective in reducing markers of inflammation and scarring, while being less cytotoxic.

Within cytokine-activated HTCFs, ASA significantly impaired prostaglandin production and significantly increased secretion of the pro-resolving lipid mediators 5-hydroxyeicosatetraenoic acid (HETE), 15-HETE and 18-hydroxyeicosapentaenoic acid (HEPE).

Conclusions: ASA reduces cytokine-induced myofibroblast transdifferentiation in human Tenon's capsule fibroblasts, being non-inferior to MMC in vitro. ASA's unique effects are associated with unique lipid mediator expression profile. ASA-driven resolution of inflammation may be a promising strategy to mitigate cellular events associated with cytokine-mediated scarring.

CONTROL ID: 3712498
SUBMITTER (NAME ONLY): Tara Pahlevan
TITLE: Comparison of 10-2 and 24-2 visual field event analyses
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: T. Pahlevan, G.C. Lee, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|A. Iwase, Tajimi Iwase Eye Clinic, Tajimi, Gifu, JAPAN|
Commercial Relationships Disclosure: Tara Pahlevan: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Aiko Iwase: Commercial Relationship(s);Code F (Financial Support):Carl Zeiss Meditec, Inc.;Code R (Recipient):Carl Zeiss Meditec, Inc. | Gary Lee: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc.

ABSTRACT BODY:

Purpose: The 10-2 visual field (VF) provides more information in the center of the VF compared to 24-2. An extension of the HFA guided progression analysis (GPA) adding event (i.e. change from baseline) analysis for 10-2 was recently proposed[1]. In this preliminary, retrospective study, we compare the results of the GPA event analyses in 24-2 and 10-2 VFs.

Methods: A retrospective series of VFs were analyzed from 22 eyes of 11 clinically managed glaucoma subjects with at least 5 visits each with 10-2 and 24-2 (or 30-2) SITA Standard VFs using HFA™ II-i or HFA3 (ZEISS, Dublin, CA). 10-2 and 24-2 VFs were typically alternated between visits. 24-2 VFs were extracted if the 30-2 VF was available. VFs were selected to cover the same follow-up period for the shorter of the 10-2 or 24-2 series. A GPA Alert result of “Possible” or “Likely” Progression was considered a progression event. Cohen’s kappa was used to assess agreement between the proposed 10-2 and reference 24-2 GPA event analyses.

Results: Age at first exam ranged from 32.2 to 74.1 years (see Table 1). Mean 24-2 and 10-2 MD at first exam were -1.16 (standard deviation, SD: 3.00, range: -12.47 to 1.43) dB and -0.88 (SD: 2.87, range: -12.33 to 1.08) dB, respectively. Mean follow-up time for the 24-2 series was 5.3 (SD: 2.8, range: 1.2 to 10.0) years, with a mean inter-visit interval of 0.4 (0.1, range: 0.3 to 0.6) years.Mean follow-up time for the 10-2 series was 5.2 (SD: 2.8, range: 1.4 to 9.9) years, with a mean inter-visit interval of 0.6 (0.3, range: 0.3 to 1.2) years. 21/22 cases (95.5%) were observed to agree, resulting in a kappa of 0.83 (95% CI: 0.51 to 1.00).

Conclusions: In this preliminary study, strong agreement was observed overall between the event analysis results for a proposed 10-2 GPA and a reference 24-2 GPA. This may suggest the potential clinical utility of using change from baseline analyses for 10-2 VFs to highlight progression in the central VF that may or may not be detected in the 24-2 VF. Further work may include more extensive comparisons between 10-2 and 24-2 GPA event analyses in cohorts with clinically confirmed diagnoses of progression or non-progression.

References

[1] Durbin et al. IOVS 2021; 62(8): Abstract 3482.

CONTROL ID: 3712499

SUBMITTER (NAME ONLY): Sarah Giles

TITLE: Patient iPSC-RPE implicate mitochondrial defects in Macular Telangiectasia

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Macular Telangiectasia Type 2 (MacTel) is a rare, late-onset, degenerative retinal disease with an extremely heterogenous genetic architecture. MacTel has been linked to metabolic defects including reduced circulating levels of serine and glycine, and increased levels of deoxysphingolipids (dSLs). However, there is likely to be serine/glycine/dSL-independent factors contributing to the onset of MacTel as many patients have normal metabolite levels, and multiple MacTel GWAS loci have been identified that are not clearly linked to serine/glycine/dSL metabolism. Here, we differentiated retinal pigment epithelium from induced pluripotent stem cells (iPSC-RPE) derived from a cohort of MacTel case and control patients with diverse genetic backgrounds to screen for functional defects and identify common cell-intrinsic pathological mechanisms that may drive disease.

Methods: We differentiated iPSC-RPE from 9 MacTel patients and 5 unaffected family members. iPSC-RPE differentiation and functional maturity were validated by cell type specific gene expression and measuring polar secretion of VEGF (apical) and PEDF (basal) over 18 weeks. We measured secreted serine and glycine abundance using mass spectrometry. iPSC-RPE phagocytosis ability was measured by the uptake of fluorescently conjugated porcine outer segments (POS). RNAseq and subsequent GSEA pathway analysis were performed as an untargeted screen to identify common defects. Lastly, we measured oxygen consumption rate (OCR) and mitochondrial function using the mitochondrial stress test with a Seahorse Analyzer.

Results: We observed that MacTel iPSC-RPE had elevated expression of enzymes in the serine synthesis pathway, and reduced levels of serine (21%) and glycine (15%) secretion indicating a defect in serine and glycine metabolism. Phagocytosis of POS and secretion of VEGF and PEDF were comparable between MacTel and control iPSC-RPE. GSEA pathway analysis of RNAseq differential expression identified an enrichment of cellular stress pathways (for example hypoxia, NFKB, Complement) and dysregulation of central carbon metabolism in MacTel iPSC-RPE. Lastly, MacTel iPSC-RPE showed a significant reduction in basal OCR (17%) and maximal OCR output (24%).

Conclusions: We provide a comprehensive analysis of MacTel patient-derived RPE to both validate iPSC-RPE as a model for cellular pathologies linked to MacTel, and discover new disease-associated metabolic phenotypes.

CONTROL ID: 3712500
SUBMITTER (NAME ONLY): Erik Gunnarsson
TITLE: Assessing Macular Vasculature in Schizophrenia
SESSION TITLE: OCT Angiography Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. Gunnarsson, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|V. Chen, O. Saeedi, Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|H. O'Neill, E. Hong, Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|
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ABSTRACT BODY:

Purpose: Schizophrenia is a neurodegenerative disorder that poses a significant burden on society. Optical coherence tomography (OCT) has shown pathology in the retina of patients, mainly retinal nerve fiber layer and ganglion cell layer thinning, but the neurobiological bases of these changes are unknown. One possible source may be vascular abnormalities that have contributed to these changes. The purpose of this study was to use OCT-angiography (OCTA) to analyze macular vessel density (VD), vessel skeleton density (VSD), foveal avascular zone (FAZ) size and acircularity in subjects with Schizophrenia Spectrum Disorder (SSD) and controls to establish whether SSD is associated with macular vascular changes.

Methods: We recruited 50 SSD patients (mean ± SD age: 35.3 ± 11.2 years) and 39 age-matched controls (mean ± SD age: 35.8 ± 13.5 years). We obtained 3x3-mm OCTA images centered on the fovea at three depths: whole retina, superficial capillary plexus (SCP), and deep capillary plexus (DCP). Image analysis was conducted using ImageJ software. To analyze VD and VSD, images were binarized with the local Phansalkar method, then the Early Treatment of Diabetic Retinopathy Study (ETDRS) grid was overlaid to allow regional analysis in superior, nasal, inferior, and temporal quadrants (figure 1). We measured FAZ size and acircularity using whole retina images. IBM SPSS software with a General Estimating Equation was used for statistical analysis.

Results: The mean VD for the whole retina for the SSD group was 50.8 ± 3.0 and for the control group was 51.0 ± 2.5 ($p=0.717$). There was also a non-significant difference in VD between SSD and control groups in SCP ($p=0.523$) and DCP ($p=0.980$) as well as in all quadrants individually. The mean VSD for the whole retina for the SSD group was 9.0 ± 0.6 and for the control group was 9.0 ± 0.5 ($p=0.790$). There was also a non-significant difference in VSD between SSD and control groups in SCP ($p=0.647$) and DCP ($p=0.711$) as well as in all quadrants individually. No significant difference was found between groups in FAZ size ($p=0.381$) or acircularity ($p=0.178$).

Conclusions: Our results suggest that macular vascular structures as measured by VD, VSD, FAZ size and acircularity appeared similar in SSD patients compared with age-matched controls. Other potential causes for the retinal neural tissue changes previously found in SSD should be investigated.

CONTROL ID: 3712501

SUBMITTER (NAME ONLY): Michelle Sun

TITLE: Impact of Type 2 Diabetes Mellitus and Insulin Use on Progression to Glaucoma Surgery in Primary Open Angle Glaucoma

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.T. Sun, S. Pershing, J.L. Goldberg, S. Wang, Spencer Center for Vision Research, Byers Eye Institute, Stanford University, California, UNITED STATES|

Commercial Relationships Disclosure: Michelle Sun: Commercial Relationship: Code N (No Commercial Relationship) | Suzann Pershing: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Goldberg: Commercial Relationship: Code N (No Commercial Relationship) | Sophia Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The complex interaction between diabetes, hyperglycemia, insulin treatment and glaucoma remains incompletely understood, and is particularly relevant given insulin has recently emerged as a potential therapeutic target in glaucomatous degeneration. We aimed to investigate outcomes of primary open-angle glaucoma (POAG) patients with and without type 2 diabetes mellitus (T2DM) on either oral hypoglycemic agents or insulin.

Methods: Retrospective observational study using U.S nationwide healthcare insurance claims database. Patients aged ≥40 years old with a diagnosis of POAG were included. A diagnosis of T2DM and use of either oral hypoglycemic agents or insulin therapy were the primary predictors. The main outcome measure was time to first glaucoma surgery. Multivariable Cox proportional hazards regression models evaluated factors associated with POAG progression requiring surgery. Insulin use was analyzed as a time-varying co-variate with the date of first fill considered the start date.

Results: A total of 829,562 POAG patients were included for analysis, of which 212,164 (25.6%) had T2DM. Mean age was 68.7 years (SD 10.7) and 57% were female. There were 211,055 patients taking oral hypoglycemic agents, while 82,413 were on insulin. While T2DM was a significant predictor of progression to glaucoma surgery in univariate analyses (HR 3.50, 95%CI 3.43-3.57, $p<0.001$), this was no longer significant once adjusted for HbA1c, demographic (age, gender, socioeconomic status, race) and glaucoma factors (severity, baseline medications, previous laser trabeculoplasty). When evaluating only POAG patients with T2DM, compared to patients only taking oral hypoglycemic agents, we found that insulin use was associated with a 1.11 higher hazard of requiring glaucoma surgery (95%CI 1.07-1.15, $p<0.001$), and remained an independent predictor in multivariate analyses after adjusting for confounders (HR 1.08, 95%CI 1.04-1.13, $p<0.001$).

Conclusions: Insulin use amongst POAG patients with T2DM may be associated with a higher rate of progression requiring glaucoma surgery. Additional studies are required to better characterize this relationship.

CONTROL ID: 3712502

SUBMITTER (NAME ONLY): Cigdem Yasar

TITLE: Novel retinopathy in pediatric retinal vasculitis: long term follow up

SESSION TITLE: Posterior Segment Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Yasar, H. Ghoraba, J. Regenold, C. Or, M. Halim, G. Uludag, J. Hwang, I. Karaca, A. Mobasserian, A. Akhavanrezayat, H. Khojasteh, Y.J. Sepah, D.V. Do, Q.D. Nguyen, Ophthalmology, Byers Eye Institute at Stanford Univesity, Palo Alto, California, UNITED STATES|M. Yasar, Ophthalmology, Bingol Devlet Hastanesi, Bingol, TURKEY|

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ABSTRACT BODY:

Purpose: In this case series, we aim to report long term follow up data of novel retinopathy associated with pediatric retinal vasculitis.

Methods: Pediatric patients diagnosed with retinal vasculitis at a tertiary uveitis clinic were reviewed between January 2020 and December 2021.Eyes with novel retinopathy were included if follow-up period was more than 12 months.The retinopathy was characterized by three findings: dark retinal areas on Optos wide angle fundus photography (WAFP) with corresponding hypoautofluorescence and ellipsoid zone disruption on optical coherence tomography (Figure).

Retinal vasculitis was graded using fluorescein angiography (FA) per the Angiography Scoring for Uveitis Working Group score.Lesion area was calculated using Image-J.Full field electroretinogram (ffERG) was also performed.Demographic and clinical data including lesion area and FA severity score were collected at 3 time points: baseline, within 2 months from ffERG and at last follow-up visits.

Results: 17 pediatric patients (27 eyes) with retinal vasculitis and novel retinopathy were included. Mean age was 12.7±3.4 years and 35 % were female.Mean follow up duration was 29.4±12.1 months.FA scores decreased from 8±5.04 at baseline to 2.1 ± 2.1 at the last follow up visit (P<0.001). 30% of eyes did not show any disease activity at the last follow-up visit.

The retinopathy persisted in all eyes at the last follow-up visit.However, mean lesion area significantly decreased from 407.6±239.5 mm2 at baseline to 378.4±222.6 mm2 at last follow-up visit (P=0.04).FA scores at baseline were significantly correlated with lesion areas at both baseline (P=0.01) and last follow-up visit (P=0.01).However, FA scores at the last follow-up visit did not correlate with the lesion areas (P=0.9).

ffERG was performed in 19 eyes.Lesion areas, at the time of ffERG, were negatively correlated with amplitudes of scotopic rod b wave (P=0.03), mixed a wave (P=0.05), mixed b wave (P=0.001), cone b wave (P=0.05), and 32 Hz flicker (P=0.006).Delayed 32 Hz flicker timing was also correlated with lesion areas (P=0.009).

Conclusions: Pediatric retinal vasculitis is associated with a novel retinopathy whose area is correlated with decreased retinal function and higher initial disease activity.The retinopathy can persist even after resolution of inflammation.

CONTROL ID: 3712503

SUBMITTER (NAME ONLY): Jason Strawbridge

TITLE: Maternal sociodemographic risk factors for retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Strawbridge, A. Chu, Pediatrics, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|C. Janzen, Obstetrics and Gynecology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|I. Tsui, Retina and Vitreous Diseases, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Maternal medical comorbidities and pregnancy complications have been previously studied as risk factors for retinopathy of prematurity (ROP). The relationship between maternal sociodemographic characteristics and ROP risk remains unclear. Therefore, the purpose of this retrospective cohort study was to include maternal sociodemographic data with variables that have been previously found to be significant in assessing an infant's risk for ROP.

Methods: We analyzed data from preterm infants born at a single institution who were referred for ROP screening between 2011 and 2021. Demographic and clinical data for each infant and mother were collected via review of the electronic medical record. Collected maternal data included age at delivery, insurance type, medical comorbidities, pregnancy complications, and smoking status in pregnancy. Self-reported race/ethnicity was recorded and included: Hispanic, black, white, Asian, and other. Collected infant data included gestational age (GA) and comorbidities. The primary outcome measure was the presence of any-stage ROP in either eye. The presence of ROP requiring treatment (type 1 ROP) was examined as a secondary outcome measure. Univariate and multivariate logistic regression models were used to evaluate each predictor for potential association with ROP.

Results: Of 324 preterm infants, 99 (30.6%) developed any-stage ROP and 33 developed treatment-requiring ROP (10.2%). The mean gestational age (GA) for the cohort was 28.8 weeks (range 22-38 weeks). Variables independently associated with increased risk of any-stage ROP included public insurance coverage (OR 7.3; 95% CI 2.6-20.8; $p<0.001$) and maternal smoking during pregnancy (OR 12.3; 95% CI 2.4-62.0; $p=0.002$). Maternal Hispanic ethnicity demonstrated an independent association with treatment-requiring ROP (OR 4.6; 95% CI 1.07-20.0; $p = 0.040$).

Conclusions: We observed a higher risk of treatment-requiring ROP for infants born to Hispanic mothers. In addition, public insurance coverage and maternal smoking during pregnancy were found to be independent modifiable risk factors for developing any-stage ROP. These findings suggest that both maternal comorbidities and sociodemographic factors may independently contribute to ROP risk. Future studies which examine additional socioeconomic determinants should be considered to identify other sources of health inequities and guide intervention efforts.

CONTROL ID: 3712504
SUBMITTER (NAME ONLY): OLIVIA KILLEEN
TITLE: Barriers to Wearing Eyeglasses Among U.S. Youth
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: O. KILLEEN, J. Cho, S. Raven, G. Wang, M.A. Woodward, P. Newman-Casey, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|A. Mubeen, A. Claus, L. Kim, University of Michigan College of Literature Science and the Arts, Ann Arbor, Michigan, UNITED STATES|T. Chang, Family Medicine, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|
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ABSTRACT BODY:

Purpose: Uncorrected refractive error (URE) is the most common cause of visual impairment in youth. We aimed to identify barriers to wearing eyeglasses among a contemporary sample of U.S. youth.
Methods: A five question, open-ended poll about experiences with eye problems, refractive correction, and reasons youth do not wear eyeglasses if they need them was distributed to the MyVoice Text Message Cohort of U.S. youth aged 14–24 years (www.hearmyvoicenow.org). Respondent demographics were analyzed. Low socioeconomic status (SES) was defined as receiving free or reduced-price lunch. Text message responses were coded using a modified grounded theory approach.
Results: Out of 1204 recipients, 88.3% (n=1063) responded. Mean age was 20.3 ±2.4 years (range 15-24 years); 58.8% (n=625) were male; 74.0% (n=787) were white; and 41.4% (n=440) had low SES. Many (65.8%; n=699) had experienced trouble with their eyesight, including need for eyeglasses or contacts (63.6%; n=676) or medical eye problems (14.9%; n=158). Some youth (2.4%; n=21) reported vision problems consistent with URE that impacted daily life, e.g. "I've been having blurry vision and not seeing clearly for a while now and I'm worried since I'm driving." Some (14.2%; n=96) had discontinued eyeglasses or contacts, often because youth felt they no longer needed refractive correction (51.0%; n=49; e.g. "I stopped because my eyesight got better"), they were a hassle (14.6%; n=14; e.g. "I no longer use them because they need a lot of care and that annoys me"), or they were lost, broken, or expired (14.6%; n=14; e.g. "I don't wear them anymore because I had broken them about 5-6 years ago"). Concerns over appearance (52.0%; n=553; e.g. "they look dorky") and cost (16.1%; n=171; e.g. "the cost of glasses can be expensive especially without insurance") were the most common reasons youth might not wear eyeglasses if they needed them.
Conclusions: Major barriers to correcting refractive error among U.S. youth include cosmesis and cost. Future work should focus on making eyeglasses and contact lenses that are not only appealing, but also affordable for U.S. youth.

CONTROL ID: 3712505

SUBMITTER (NAME ONLY): Nathaniel Parsons

TITLE: Regulatable complement inhibition of the alternative pathway mitigates age-related macular degeneration pathology

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Parsons, B. Rohrer, Ophthalmology, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|B. Rohrer, Research Services, VA Medical Center Ralph H Johnson, Charleston, South Carolina, UNITED STATES|

Commercial Relationships Disclosure: Nathaniel Parsons: Commercial Relationship: Code N (No Commercial Relationship) | Baerbel Rohrer: Commercial Relationship(s);Code P (Patent):US 14/043,317

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) occurs after age 65. AMD has two forms, dry (atrophic) and wet (angiogenic). AMD is a multifactorial disease; risk factors include aging, smoking, and complement dysregulation. The amplification loop of the complement alternative pathway (AP) is responsible for the majority of complement activation on cell surfaces and extracellular membranes in animal models of this disease. The AP is inhibited naturally by circulating complement protein factor H (fH). Complement component C3 (C3) protein increases and decreases respective to complement activation. In wet AMD, complement effector molecules increase angiogenesis, activate microglia and recruit immune cells, amplifying the complement-microglia inflammatory feedback loop, leading to tissue damage.

Methods: The C3 promoter (−1005 to +251), pC3, was cloned into a pTR backbone and plasmids (pC3-mCherry/CR2-fH) were synthesized and utilized to generate adeno-associated virus serotype 5 (AAV5) vectors. pC3 activation was determined in transiently transfected ARPE19 cells stimulated with H_2O_2 and normal human serum (+/- TT30 or NAC). Laser-induced choroidal neovascularization (CNV) was analyzed in mice treated with AAV5-pC3-mCherry/CR2-fH, using imaging (optical coherence tomography), functional (electroretinography, ERG), molecular (western blotting, complement activation) and histologic (microglia activation and migration) readouts.

Results: Proof of concept was provided that pC3 is modulated in a complement and oxidative stress-dependent manner in human ARPE19 cells, examining mCherry fluorescence. Safe concentrations of AAV5-pC3-CR2-fH, when injected subretinally, were identified using ERG and OCT (10^{10} - 10^{11} vg/mL). The expression of CR2-fH significantly reduced CNV in a dose dependent manner, with a maximum reduction of lesion size of ~35% when compared to mCherry-treated animals. CR2-fH expression reduced CNV-associated ocular C3 activation as assessed by western-blotting for the C3a breakdown products C3d/C3dg. We expect to document a reduction in microglia migration into the subretinal space.

Conclusions: Here we demonstrated that regulating AP inhibition in a complement-dependent manner can ameliorate pathology, and hypothesize this effect to be due, in part, by reducing microglial activation and the proinflammatory microenvironment.

CONTROL ID: 3712506

SUBMITTER (NAME ONLY): Carl Regillo

TITLE: Efficacy, durability and safety of KSI-301 antibody biopolymer conjugate in wet AMD – Year 1 primary endpoint results from the pivotal DAZZLE study

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Regillo, Mid Atlantic Retina, Philadelphia, Pennsylvania, UNITED STATES|D.V. Do, Stanford University School of Medicine, Stanford, California, UNITED STATES|J.S. Ehrlich, D. Janer, P. Velazquez-Martin, R. Zawadzki, V. Perlroth, Kodiak Sciences Inc., Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reducing the treatment burden currently required for optimal management of high-prevalence retinal exudative and vascular diseases is a key focus of next-generation therapeutics development. KSI-301 is an antibody biopolymer conjugate designed to provide potent and long-lasting intraocular vascular endothelial growth factor (VEGF) suppression. Early clinical studies in treatment-naïve patients showed strong efficacy with clinical durability of up to 6-months in patients with wet age-related macular degeneration (wAMD) with an encouraging safety profile. The objective of the pivotal DAZZLE study is to demonstrate that KSI-301 is non-inferior to aflibercept while providing a clinically meaningful reduction in intravitreal injection burden.

Methods: In this prospective, double-masked, multicenter, pivotal clinical trial, treatment-naïve patients with wAMD were randomized 1:1 into two treatment arms: KSI-301 (5 mg) or aflibercept (2 mg). Each subject was scheduled to receive three monthly loading doses of their assigned treatment. Thereafter, subjects in the aflibercept arm continued on every-other-month dosing. The dosing regimen for the KSI-301 treatment arm was every 3 to 5 months based on protocol-specified disease activity assessments. The primary efficacy endpoint was the mean change from baseline in best corrected visual acuity (BCVA) at Year 1 (Figure 1).

Results: 557 subjects across 69 sites in the United States and Europe were randomized and received study treatment. The mean age at randomization was 76.4 years and 62.1% were female. At baseline, mean BCVA was 63.6 ETDRS letters with 44% of patients having a Snellen equivalent of 20/40 or better; mean baseline central subfield thickness (CST) was 354.9 um. The primary efficacy, durability and safety results of this pivotal clinical study will be presented for the first time at the meeting.

Conclusions: Treatment outcomes with currently available anti-VEGF therapies are dependent on a treatment frequency that is challenging to sustain or inaccessible in real-world clinical settings. The DAZZLE study's efficacy, durability and safety results will provide important confirmatory evidence on the potential role for KSI-301 as a more durable anti-VEGF treatment option for patients with wet AMD.

CONTROL ID: 3712509

SUBMITTER (NAME ONLY): Min Zhao

TITLE: Contribution of the vascular mineralocorticoid receptor in diabetic retinal neuropathy in a mouse model of type 1 diabetes

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhao, E. Gelizé, V. Dinet, F.F. Behar-Cohen, Team 17, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|M. Zhao, E. Gelizé, V. Dinet, F.F. Behar-Cohen, Team 17, INSERM UMRS1138, Paris, Ile de France, FRANCE|J. Guegan, Plateforme de Bioinformatique/ Biostatistiques – iCONICS, IHU-A-ICM, Paris, Ile de France, FRANCE|F. Jaisser, Team 1, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy remains a major cause of vision loss worldwide. MR pathway overactivation has been recognized in the pathogenesis of diabetic nephropathy and retinopathy. We previously showed that MR antagonism reduced retinal inflammation and edema in a rat model of type 2 diabetes. We aimed to decipher the role of vascular MR in diabetic retinopathy.

Methods: Diabetes was induced by streptozotocin (STZ) in mice with MR invalidation specifically in vascular endothelial cells (Tie2-MR-KO) or in smooth muscle cells/pericytes (SMA-MR-KO). Electroretinography was performed 2 months after STZ injection. The neuroretina was used for transcriptomic analysis. Human vascular smooth muscle cells (VSMCs) were cultured in high glucose media and treated with aldosterone alone or associated with MR antagonist to validate the MR-regulated genes in diabetic condition.

Results: We observed impairment of scotopic and photopic ERG in diabetic wild-type mice that was improved in SMA-MR-KO mice but not in Tie2-MR-KO mice. Transcriptomic analysis identified a gene encoding stanniocalcin-1 (STC1), a neuroprotective glycoprotein expressed in the smooth muscle cells. Indeed, the expression of Stc1 was significantly downregulated in the retina of diabetic wild-type mice but upregulated in the retina of diabetic SMA-MR-KO mice. In human VSMCs cultured with high glucose, aldosterone downregulated the STC1 and MR antagonist inhibited the aldosterone-induced STC1 decrease.

Conclusions: Vascular smooth muscle/pericyte MR may contribute to the neuropathy in the diabetic retina through regulation of STC1. This hypothesis will be further investigated by the injection of recombinant STC1 in wild-type mice and/or siRNA in SMA-MR-KO mice.

CONTROL ID: 3712510

SUBMITTER (NAME ONLY): Emmanuel Kofi Addo

TITLE: The Lutein and Zeaxanthin in Pregnancy (L-ZIP) Trial – Initial Results

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Addo, A. Gorusupudi, S. Allman, P.S. Bernstein, Department of Ophthalmology and Visual Science, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|E. Addo, P.S. Bernstein, Department of Nutrition and Integrative Physiology, The University of Utah Department of Nutrition and Integrative Physiology, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Emmanuel Kofi Addo: Commercial Relationship: Code N (No Commercial Relationship) | Aruna Gorusupudi: Commercial Relationship: Code N (No Commercial Relationship) | Susan Allman: Commercial Relationship: Code N (No Commercial Relationship) | Paul Bernstein: Commercial Relationship(s);Code F (Financial Support):Kemin Health;Code C (Consultant/Contractor):Tesseract ;Code P (Patent):For resonance Raman spectroscopic measurement of carotenoids in retina, skin, and other tissues

ABSTRACT BODY:

Purpose: Recently, prenatal multivitamins with added lutein (L) and zeaxanthin (Z) have been introduced into the American market with claims of improving maternal and infants' health. Although these claims are physiologically plausible, no evidence exists to support them. Hence, we conducted a prospective controlled trial (NCT03750968; still ongoing) to determine whether prenatal carotenoid supplementation counteracts maternal carotenoid depletion, particularly in the third trimester, and if it can enhance maternal and infants' systemic and ocular carotenoid status.

Methods: In this trial, 47 participants were randomized 1:1 to receive standard-of-care daily prenatal vitamins with or without 10 mg of L and 2 mg of Z for 6 to 8 months. The primary outcome was maternal carotenoid status in the serum, skin, and eye measured at the end of each trimester and postpartum with HPLC, resonance Raman spectroscopy, and dual-wavelength autofluorescence, respectively. The secondary outcome assessed infants' carotenoid levels in the umbilical cord blood, skin, and eyes using similar techniques as above but optimized for infants. Linear regression analysis was used to explore the association between maternal and infants' carotenoid status. A p-value of 0.05 was considered statistically significant.

Results: Participants' mean (±SD) age was 29.7 (±3.7) years. Masked study analysis of all subjects shows a significant increase in maternal serum L+Z, skin carotenoids, and macular pigment optical density and volume at 9^{o} eccentricity (MPOV9^{o}) from the first trimester, a peak at the third trimester, and a decline postpartum. Postpartum maternal serum L+Z levels are significantly associated with umbilical cord blood L+Z levels ($r=0.83$, $p<0.001$) and infants' skin carotenoids ($r=0.66$, $p<0.001$). There was a statistically significant positive correlation between postpartum maternal MPOV9^{o} and cord blood L+Z levels ($r=0.52$, $p=0.003$) and infants' skin carotenoids ($r=0.48$, $p=0.007$).

Conclusions: Unmasked study results will be available in early February 2022, and we will then know whether prenatal carotenoid supplementation prevents maternal carotenoid depletion and enhances infants' foveal development. Our findings may serve as a basis for future large-scale research in normal and high-risk pregnancies and could guide policy decisions about prenatal carotenoid recommendations.

CONTROL ID: 3712511

SUBMITTER (NAME ONLY): Irina Saltykova

TITLE: GADD34 does not affect the translational rate in P23H RHO mouse retina

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Saltykova, A. Zhylkibayev, M.S. Gorbatyuk, University of Alabama at Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Irina Saltykova: Commercial Relationship: Code N (No Commercial Relationship) | Assylbek Zhylkibayev: Commercial Relationship: Code N (No Commercial Relationship) | Marina Gorbatyuk: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: P23H Rho mice, mimicking retinitis pigmentosa in humans, manifest chronic unfolded protein response activation during retinal degeneration (RD). GADD34, the UPR mediator and protein phosphatase 1 catalytic subunit, permits protein synthesis through dephosphorylation of eukaryotic initiation factor 2a (eIF2α) in cells. We hypothesized that further upregulation of phosphorylated (p) eIF2α modulates the rate of protein synthesis and affects vision loss in mice with RD.

Methods: C57BL/6, P23H Rho, and P23H Rho GADD34$^{-/-}$ mice were used in this study. Mouse retinas were collected on postnatal (p) day 30 to study protein and RNA expression by western blot and RT-PCR analyses. Retinal function was assessed using electroretinography. The SUnSET method was applied for the in vivo assay of protein synthesis. Apoptotic cells were assessed via TUNEL staining of P22 retinas. Lipopolysaccharide (LPS; 10 mg/kg of body weight) was injected intraperitoneally into mice to induce a pro-inflammatory response at P30.

Results: The P23H Rho mice demonstrated a decrease in protein synthesis associated with sustained phosphorylation of eukaryotic initiation factor 2a (p-eIF2a) compared to the C57BL/6 mice. Knocking out GADD34 resulted in further elevation of p-eIF2α in the degenerating retinas. Surprisingly, this elevation was not associated with a more pronounced decline in the rate of translation or restoration of the p-mTOR axis in P23H Rho GADD34$^{-/-}$ mice. Moreover, sustained upregulation of p-eIF2α was associated with a 30% decline in the a-wave amplitude of the scotopic ERG, while the b-wave was not affected. The ERG recordings were supported by a 50% increase in apoptotic cells in the P23H Rho GADD34$^{-/-}$ retinas compared to the P23H Rho retinas. Because GADD34 controls the expression of inflammatory cytokines in immune cells, we further analyzed IL6 and Tnfa gene expression in the retinas of LPS-treated mice. We found that a 4-fold reduction in Il-6 and a 2.7-fold upregulation in Tnfa expression in P23H Rho GADD34$^{-/-}$retinas.

Conclusions: Our results indicate that GADD34 deficiency does not affect the rate of protein synthesis during chronic ER stress, suggesting that p-eIF2α is not the major point of translational control in progressive RD. GADD34 may control the inflammatory response of P23H Rho retinas, and its deficiency may alter pro- and anti-inflammatory cytokine ratios, thus resulting in compromised photoreceptor homeostasis.

CONTROL ID: 3712512

SUBMITTER (NAME ONLY): Urikhan Sanzhaeva

TITLE: Investigating the functional role of β4B-tubulin in vision

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Sanzhaeva, V. Ramamurthy, Department of Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|S.E. Boye, Department of Ophthalmology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|V. Ramamurthy, Department of Ophthalmology and Visual Sciences, West Virginia University, Morgantown, West Virginia, UNITED STATES|

Commercial Relationships Disclosure: Urikhan Sanzhaeva: Commercial Relationship: Code N (No Commercial Relationship) | Shannon Boye: Commercial Relationship: Code N (No Commercial Relationship) | Visvanathan Ramamurthy: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Microtubules, polymers of αβ-tubulin heterodimers, are essential for cell division, intracellular protein trafficking, ciliogenesis, and ciliary function. Recent studies showed a link between autosomal dominant missense mutations in β4B-tubulin isotype (TUBB4B) and Leber congenital amaurosis (LCA) and severe hearing loss. However, the mechanism underlying the diseases caused by TUBB4B mutations and the role of β4B-tubulin in photoreceptor cells remains to be elucidated and is the focus of this study.

Methods: CRISPR-Cas9 generated Tubb4b knockout (KO) and Tubb4b R391H or R391C knockin (KI) murine models were utilized to understand the importance of β4B-tubulin in photoreceptors and the mechanisms behind LCA. Protein and mRNA levels were measured by quantitative immunoblotting and reverse transcription PCR. Electroretinography was performed to measure the response of photoreceptors to light stimuli. Immunofluorescence analysis was used to assess the morphology of the retina. All experiments were performed with wild-type littermates as controls. A two-tailed Student's t-test was used for statistical analysis.

Results: Photoreceptor function and the morphology of the retina were not affected in mice lacking β4B-tubulin, suggesting that other β-tubulin isotypes may compensate for the loss of this particular tubulin isotype in the retina. Indeed, β6-tubulin transcripts and protein levels were upregulated in the Tubb4b$^{-/-}$ retina. Intriguingly, Tubb4b KI mice did not recapitulate patient phenotype as photoreceptor function was normal in these animals. Analysis of published single-cell RNA sequencing of the human and murine retina revealed a species-specific difference in β4B-tubulin expression in photoreceptor cells. Indeed, β4B-tubulin was localized to photoreceptors only in non-human primate retina, while in the mouse retina, it was expressed throughout the retina and localized to photoreceptors and downstream neurons.

Conclusions: This study shows that the β4B-tubulin is not essential for photoreceptor development and maintenance in mice. We found that β6-tubulin transcript and protein levels were upregulated in the absence of β4B-isotype, suggesting functional compensation by β6-tubulin. We demonstrated that the β4B-tubulin is differentially expressed in the mouse and non-human retina. Altogether, our findings indicate that the Tubb4b mice model may not be suitable for investigating mechanisms behind LCA linked to TUBB4B mutations.

CONTROL ID: 3712513

SUBMITTER (NAME ONLY): Shelly Mishra

TITLE: Intraocular Pressure Response of Selective Laser Trabeculoplasty in Phakic and Pseudophakic patients in an Urban City Academic Glaucoma Practice

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mishra, J. Dossantos, S. Lesche, A. Ahmed, D. Belyea, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Shelly Mishra: Commercial Relationship: Code N (No Commercial Relationship) | Jason Dossantos: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Lesche: Commercial Relationship: Code N (No Commercial Relationship) | Aseef Ahmed: Commercial Relationship: Code N (No Commercial Relationship) | David Belyea: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Selective laser trabeculoplasty (SLT) is a procedure used as a therapy option in glaucoma to lower intraocular pressure (IOP). Currently, there is limited data on statistically significant IOP effects of SLT in pseudophakic eyes vs phakic eyes.1,2,3 This study investigates the postoperative change in IOP in phakic vs pseudophakic eyes with glaucoma.

Methods: This is a retrospective observational study on patients who visited George Washington University Department of Ophthalmology from January 1, 2015 to January 1, 2019 with primary open-angle, pseudoexfoliation, pigmentary, or normal-tension glaucoma and received 360 degrees SLT. Patients were excluded if they had laser or glaucoma surgery either 6 months prior to or 12 months following SLT, other glaucoma types, or used steroids. Demographics were collected and the pre- vs post-SLT IOP were analyzed using Wilcoxon signed rank test.

Results: 160 patients (N=103 African American, 64%, N=37 Caucasian, 23%, N=7 Asian, 4%, N=6 Hispanic or Latino, 4%, N=6 Other, 4%) were included in this study. Mean IOPs for phakic and pseudophakic eyes were collected at baseline, 6-week, 6-month, and 12-month visits (Table 1). P-values comparing interval mean IOP points to the baseline IOP and were found to be significant ($P<0.05$) for phakic and pseudophakic groups. P-values comparing mean IOP between phakic and pseudophakic eyes at baseline, 6-week, 6-month, and 12-month are listed in Table 1.

Conclusions: Our study not only includes a larger study group of 160 patients, but also a novel analysis of a diverse demographic population (64% African American) compared to other studies with an average of 50 participants and exclusively focused on Caucasian populations. Previous history of cataract surgery does not negatively impact decrease in mean IOP 6 weeks, 6 months, and 12 months post-SLT. However, our results are consistent with previous studies in showing no significant IOP reduction between phakic and pseudophakic eyes post-SLT. Further investigation with a diverse population is required to comprehensively understand the correlation between pseudophakia and IOP reduction post-SLT.

CONTROL ID: 3712514

SUBMITTER (NAME ONLY): Song Li

TITLE: Astrocytic Secreted Phosphoprotein 1 (SPP1) Protects Retinal Ganglion Cells in glaucoma

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Li, T.C. Jakobs, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Li, T.C. Jakobs, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Song Li: Commercial Relationship: Code N (No Commercial Relationship) | Tatjana Jakobs: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Reactive optic nerve astrocytes protect retinal ganglion cell (RGC) survival and visual function in glaucoma and traumatic optic neuropathy. To better understand the molecular mechanism of astrocyte-mediated neuroprotection, we conducted gene expression profiling of the optic nerve head and identified Secreted Phosphoprotein 1 (SPP1, also called osteopontin) as one of the leading candidate genes. Here, we directly test the hypothesis that SPP1 acts as a neuroprotective factor that promotes RGC survival, and improves visual function in glaucoma and traumatic optic nerve injury.

Methods: We generated a new transgenic mouse line that combines GFP expression from the endogenous Spp1 locus with the incorporation of loxP sites for conditional deletion of the Spp1 gene and activation of red fluorescent protein after cre recombination. This strain was crossed to B6.GFAP-cre mice to generate an astrocyte-specific Spp1 knock out. Using the microbead model of glaucoma and optic nerve crush, we tested how RGC numbers and visual function (pattern ERG, visual acuity) were affected by astrocyte-specific knock-out of Spp1. Immunohistochemistry, qPCR, and RNA-sequencing were used to identify signaling pathways and molecular mechanisms of neuroprotection. Mitochondrial respiration was measured in cultured astrocytes using a Seahorse metabolic analyzer.

Results: SPP1 expression was increased in optic nerve astrocytes in glaucoma and optic nerve traumatic injury and was driven by the TGF-β1/Runx1/E2f1 signaling pathway. Conditional knock-out of Spp1 in astrocytes led to more pronounced RGC loss and visual impairment in glaucoma and optic nerve traumatic injury. RNA-sequencing showed that in $Spp^{-/-}$ astrocytes genes associated with neuroinflammation were up-regulated, whereas neurotrophic factors, genes associated with phagocytic activity, synaptogenesis, and especially oxidative phosphorylation were down-regulated. Conversely, exogenous SPP1 strongly induced VDAC1 expression and promoted oxidative phosphorylation in astrocytes.

Conclusions: SPP1induces a neuroprotective state in astrocytes, promotes mitochondrial function and VDAC1 expression, and protects RGCs and vision function in glaucoma.

CONTROL ID: 3712515

SUBMITTER (NAME ONLY): Rajan Adhikari

TITLE: Bicarbonate accelerates flash response kinetics and amplitude and extends dynamic range in murine retinal rods.

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.D. Adhikari, P. Geva, C. Cornwall, C.L. Makino, Physiology and Biophysics, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Rajan Adhikari: Commercial Relationship: Code N (No Commercial Relationship) | Polina Geva: Commercial Relationship: Code N (No Commercial Relationship) | Carter Cornwall: Commercial Relationship: Code N (No Commercial Relationship) | Clint Makino: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In darkness, there is a current that circulates through the rod; Na^{+}along with some Ca^{2+}enters the outer segment through cyclic-nucleotide-gated (CNG) ion channels and K^{+}exits the inner segment through voltage gated ion channels. Photon stimulation hydrolyzes cGMP, closes CNG channels and suppresses the circulating current. By stimulating rod outer segment guanylate cyclase (ROS-GC) to synthesize cGMP at a faster rate in a Ca^{2+}-dependent fashion. bicarbonate has been shown to affect the circulating current in darkness as well as the photon response amplitude and kinetics in amphibian rods. Here, we wanted to see how bicarbonate impacts the physiology of murine rods, which are considerably smaller in size, operate at higher temperature and generate faster photon responses.

Methods: The ex vivo electroretinogram (ERG) was recorded from retinas of mice deficient in cone transducin, in order to isolate the rod response to photic stimulation. Retina were perfused with Ames solution containing either 20μM bicarbonate or equimolar Cl^{-}in place of bicarbonate. 50μM DL-AP4 and 100μM BaCl2 were added to block post-photoreceptoral and glial responses, respectively. Solutions were maintained at 35°C and bubbled with 95% O2/5% CO2. Retinas were stimulated with 20ms flashes at 500nm and with 10s steps at 540nm through various neutral density filters.

Results: Murine rods responded reversibly to bicarbonate with an increased in circulating current by 1.4-fold(n=7). The integration time of dim flash response decreased by 1.3-fold(n=6) indicating faster flash response recovery. Sensitivity to flashes were reduced by 1.7-folds(n=3).

The time in saturation, measured from midflash to 20% recovery of circulating current, were lower for bicarbonate experiments. Flash almost 2-fold brighter was required to hold rods in saturation.

Bicarbonate decreased the step sensitivity of rods by 1.4-fold (for 540nm light), this is attributed to 1.3-fold lower integration time of dim flash response.

Conclusions: In contrast to 20μM bicarbonate used here, previously observed in amphibian rods, bicarbonate at 50mM increased circulating current by 17± 3% with similar dim flash response as in murine rods. Amphibian's sensitivity to flashes was reduced by 52± 10%, while that of murine rods reduced by 7± 0.5% (n=3).

CONTROL ID: 3712516

SUBMITTER (NAME ONLY): Ke Zeng

TITLE: Effects of Socioeconomic Deprivation on Visual Acuity in Diabetic Vitreous Hemorrhage

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Zeng, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|N.H. Siegel, M.L. Subramanian, S. Ness, X. Chen, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Ke Zeng: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Siegel: Commercial Relationship: Code N (No Commercial Relationship) | Manju Subramanian: Commercial Relationship: Code N (No Commercial Relationship) | Steven Ness: Commercial Relationship: Code N (No Commercial Relationship) | Xuejing Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Socioeconomic deprivation is associated with earlier and increased prevalence of diabetic retinopathy. We conducted a retrospective clinical case study to investigate how socioeconomic deprivation affects visual acuity (VA) outcomes in vitreous hemorrhage (VH) secondary to proliferative diabetic retinopathy (PDR).

Methods: This is a retrospective analysis of eyes with PDR presenting with acute VH at a safety-net academic medical center between May 1, 2015 and December 31, 2019. Subject addresses were used to calculate the Massachusetts Area Deprivation Index (ADI), from 1 to 10 with 10 being the most disadvantaged. Two-tailed Welch two-sample t-tests determined differences between low (1-5) and high (6-10) ADI groups. One-way ANOVA was used for measurements involving visual acuity (VA) due to non-normal distributions. The primary outcomes were mean VA, change in VA, and appointment frequency. Subgroup analysis was conducted for different endpoints, including resolution without surgery, progression to surgery, and unresolved cases such as those lost to follow-up. A secondary outcome included time to surgery.

Results: A total of 183 patients were included. The groups of low (n = 86) and high ADI (n = 97) had the same age of presentation (59.2) and similar VA (LogMAR 1.36 v. 1.32). Overall change in VA from presentation to endpoint (resolution without surgery, surgery, or unresolved) was LogMAR -0.53 in the low ADI group versus -0.58 in the high ADI group (△0.05, 95CI -0.20 to 0.30, P=0.68). Low ADI group averaged 5.56 appointments compared to 5.01 in the high ADI group (△0.55, 95CI -0.34 to 1.44, P=0.23). Examining study endpoints, 31.4% achieved resolution without surgery in the low ADI group (vs 21.7% high ADI, P=0.14) and 26.7% in the low ADI group were lost to follow-up or remained unresolved (vs 35.6% high ADI, P=0.23). Among those who progressed to surgery, the low ADI group averaged 7.78 weeks compared to 9.75 weeks in the high ADI group (△-1.98, 95CI -7.36 to 3.40, P=0.47).

Conclusions: There was no statistically significant difference in VA changes and appointment frequency between patients in the low and high ADI groups. The study suggests that there may be a trend for low ADI to be associated with a shorter time to surgery and to achieve resolution without surgery.

CONTROL ID: 3712517

SUBMITTER (NAME ONLY): Elisa Cornish

TITLE: Outcomes of eyes with central geographic atrophy or subretinal fibrosis in neovascular age-related macular degeneration when treatment is switched to from a proactive to a reactive regimen

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.E. Cornish, V. Nguyen, D. Barthelmes, M.C. Gillies, Save Sight Institute, The University of Sydney Faculty of Medicine and Health, Sydney, New South Wales, AUSTRALIA|G. Ming, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|D. Barthelmes, UniversitatsSpital Zurich, Zurich, SWITZERLAND|A.L. Vincent, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|

Commercial Relationships Disclosure: Elisa Cornish: Commercial Relationship: Code N (No Commercial Relationship) | Vuong Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Gemmy Cheung Chui Ming: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Vincent: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Barthelmes: Commercial Relationship(s);Code C (Consultant/Contractor):Walter and Gertrud Siegenthaler Foundation Zurich, Switzerland and the Swiss National Foundation | Mark Gillies: Commercial Relationship(s);Code C (Consultant/Contractor):NHMRC practitioner fellowship;Code F (Financial Support):Novartis;Code F (Financial Support):Bayer

ABSTRACT BODY:

Purpose: We assessed the outcomes of eyes with neovascular age-related macular degeneration (nAMD) in routine clinical practice that switched to a reactive (ie. pro re nata) treatment regimen from proactive (treat and extend) after developing macular atrophy (MA) or submacular fibrosis (SMFi).

Methods: We analysed data from the Fight Retinal Blindness! (FRB!) Project database, a prospectively designed registry of “real-world” outcomes from 2006 to 2021. Treatment-naive eyes starting vascular endothelial growth factor (VEGF) inhibitors for nAMD that went on to develop MA or SMFi were included. Patients from Australia, France, Ireland, Netherlands, New Zealand, Singapore, and Switzerland were included.

Results: There were 2125 treatment-naïve eyes with nAMD commencing treatment with anti-VEGF injections who did not have MA/SMFi at baseline from the Registry’s database that were eligible for the present analysis because they subsequently developed one or both complications at the fovea on treatment. Of these, 821 (35%) eyes were diagnosed with MA and 1166 (55%) eyes were diagnosed with SMFi. 7% (MA) and 9% (SMFi) of eyes were switched to reactive treatment regimen likely due to their visual prognosis. Vision was 56 (19.7) & 51 (22.54) letters is those eyes that developed MA and SMFi and continued proactive treatment (SD). Vision of eyes that switched to reactive treatment was 45 letters (28.5) in fluid tolerant MA, 47 letters (22.8) in fluid intolerant MA, 31 letters (23.8) in fluid tolerant SMFi and 38 letters (26.9) in fluid intolerant SMFi lesions (SD). Vision was maintained at a similar rate to proactive regimen to 12 months for eyes with MA and inactive SMFi lesions but not for eyes with active SMFi. Reactively treated eyes had an 8% chance of a large retinal haemorrhage leading to significant vision loss 12 months from switching regimen. The eyes with fluid tolerant SMFi lesions had the highest risk at 15%.

Conclusions: Reactive treatment of nAMD in eyes that develop MA or SMFi carries an 8% risk of a large retinal haemorrhage with significant vision loss. Vision deteriorates at a similar rate as with proactive regimen except for eyes that have active SMFi lesions. Clinicians should be cautious when switching treatment regimens to reactive, particularly in eyes with active SMFi lesions.

CONTROL ID: 3712518

SUBMITTER (NAME ONLY): Jae Kang

TITLE: Long-Term Alcohol Consumption and Risk of Exfoliation Glaucoma among US Health Professionals

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Kang, B. Rosner, Medicine, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|A. Hanyuda, Medicine, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|J.L. Wiggs, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.R. Pasquale, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Jae Kang: Commercial Relationship: Code N (No Commercial Relationship) | Akiko Hanyuda: Commercial Relationship: Code N (No Commercial Relationship) | Bernard Rosner: Commercial Relationship: Code N (No Commercial Relationship) | Janey Wiggs: Commercial Relationship(s);Code C (Consultant/Contractor):Aerpio pharmaceuticals;Code F (Financial Support):Allergan, Editas, Maze, Regenxbio, Avellino | Louis Pasquale: Commercial Relationship(s);Code C (Consultant/Contractor):Twenty Twenty, Skye Bioscience, Eyenovia

ABSTRACT BODY:

Purpose: High alcohol consumption decreases the bioavailability of dietary folate, a possible factor important for exfoliation glaucoma (XFG). We assessed the association between alcohol intake and incidence of XFG in a prospective study.

Methods: We followed 195,408 participants of the Nurses' Health Study (1980–2018), the Health Professionals Follow-up Study (1986–2018), and the Nurses' Health Study II (1991–2019) biennially. Eligible subjects at each 2-year risk period were 40+ years old and free of XFG with available data on diet and ophthalmic examinations. We evaluated cumulatively-averaged total alcohol (primary exposure); information for individual alcoholic beverages including beer, wine, and liquor were obtained from validated dietary food frequency questionnaires repeated every 2-4 years. The main outcome of XFG incidence was confirmed by medical records. We used per-eye Cox proportional hazards models, accounting for inter-eye correlations, to estimate multivariable-adjusted relative risks (MVRRs) and 95% confidence intervals (CIs)

Results: During 6,878,075 eye-years of follow-up, 702 eyes with XFG were documented. Greater total alcohol consumption was significantly associated with XFG risk: the MVRR for cumulatively averaged alcohol consumption ≥15+ g/day vs. non-drinking was 1.54 (95% CI, 1.16–2.05; P_{trend}=.02). Long- and short-term alcohol intake was significantly associated with XFG risk, with the strongest associations with cumulatively-averaged alcohol intake as of 4 years before diagnosis (MVRR ≥15+ g/day vs. non-drinking=1.62 [95% CI, 1.23–2.14; P_{trend}=.003]). Stratifying alcohol consumption by type of beverage revealed a significant trend for liquor. Compared to non-drinkers, consuming 3.6+ drinks per week of beer, total wine or liquor was associated with the following MVRRs for XFG: 1.25 (95% CI, 0.88–1.77; P_{trend}=.43), 1.34 (95% CI, 1.03–1.73; P_{trend}=.10) and 1.41 (95% CI, 1.11–1.79; P_{trend}=.02), respectively. We did not observe interactions by age, latitude, residential tier, intakes of folate or vitamin A ($P_{interaction}$>.40); however, the association between alcohol and XFG was suggestively stronger for those without family history of glaucoma ($P_{interaction}$=.10).

Conclusions: Alcohol consumption was associated with higher risk of XFG, an association that provides more clues regarding the etiology of XFG

CONTROL ID: 3712520

SUBMITTER (NAME ONLY): Jessica Girgis

TITLE: Evaluating Donut-Shaped Hypertransmission Defects on En Face Optical Coherence Tomography in Patients with Age-Related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Girgis, A. Gutierrez, N.K. Waheed, New England Eye Center, Boston, Massachusetts, UNITED STATES|E. Moult, S. Chen, J.G. Fujimoto, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|J. Girgis, A. Gutierrez, N.K. Waheed, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|L.S. Mendonca, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

Commercial Relationships Disclosure: Jessica Girgis: Commercial Relationship: Code N (No Commercial Relationship) | Eric Moult: Commercial Relationship(s);Code P (Patent):VISTA-OCTA | Siyu Chen: Commercial Relationship: Code N (No Commercial Relationship) | Alfredo Gutierrez: Commercial Relationship: Code N (No Commercial Relationship) | Luísa Mendonca: Commercial Relationship(s);Code C (Consultant/Contractor):Gyroscope Therapeutics | James Fujimoto: Commercial Relationship(s);Code F (Financial Support):Topcon;Code I (Personal Financial Interest):Optovue;Code P (Patent):Optovue, VISTA-OCTA | Nadia Waheed: Commercial Relationship(s);Code C (Consultant/Contractor):Nidek Medical Products, Boehringer Ingelheim, Topcon;Code F (Financial Support):Carl Zeiss Meditec, Heidelberg, Nidek Medical Products, Topcon;Code I (Personal Financial Interest):Ocudyne, Gyroscope Therapeutics ;Code E (Employment):Gyroscope Therapeutics

ABSTRACT BODY:

Purpose: To describe and evaluate donut-shaped hypertransmission defects on en face sub-RPE optical coherence tomography (OCT) imaging and the associated findings seen on OCT B-scans in eyes with intermediate and advanced age-related macular degeneration (AMD) using a retrospective, observational study.

Methods: This study included 21 eyes with intermediate or advanced AMD imaged at the New England Eye Center. A donut-shaped hypertransmission defect was defined as a hypertransmission defect surrounding a central area of hypotransmission on en face OCT. Donut-shaped hypertransmission defects on custom en face sub-RPE slabs and their associated B-scans were acquired using a 3 μm, 128 kHz A-scan rate ultrahigh resolution spectral-domain OCT (UHR SD-OCT) and/or commercial SD-OCT devices.

Results: A total of 40 donut-shaped hypertransmission defects from 21 patients were identified on en face OCT. The donut-shaped hypertransmission defects were found to be associated with RPE migration, drusen with heterogenous or non-reflective homogenous contents, incomplete retinal pigment epithelium and outer retinal atrophy (iRORA), and/or complete retinal pigment epithelium and outer retinal atrophy (cRORA) on associated commercial and UHR SD-OCT B-scans. In each case, the hypertransmission on en face OCT corresponded to choroidal hypertransmission secondary to RPE disruption on associated B-scans. In 9 lesions, a clump of preserved RPE in the center of iRORA or cRORA lesions was observed with associated relative hypotransmission into the choroid, as seen in Figure 1; this area of preserved RPE corresponded to the central area of hypotransmission on en face OCT.

Conclusions: Donut-shaped hypertransmission defects on en face OCT sub-RPE slabs were evaluated and found to be associated with various findings on SD-OCT B-scans, including RPE migration, drusen with homogenous or heterogenous contents, iRORA, and/or cRORA. Future longitudinal studies may be performed to determine if the presence of donut-shaped lesions is associated with faster progression to advanced AMD.

CONTROL ID: 3712521

SUBMITTER (NAME ONLY): Youngho Jung

TITLE: Noninvasive high-contrast in vivo imaging of conjunctival goblet cell using moxifloxacin-based fluorescence microscopy in a rabbit model with ocular surface damage induced by 0.2% benzalkonium chloride.

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the non-invasive examination of conjunctival goblet cells (GCs) by moxifloxacin-based fluorescence microscopy (MBFM) in a rabbit model with ocular surface damage (OSD) induced by 0.2% Benzalkonium Chloride (BAC)

Methods: Moxifloxacin-based axially swept wide-field fluorescence microscopy, which can image the conjunctiva with 2.0-μm resolution, 1.2 × 1.2 mm field of view, 2.2-mm depth of field, and 1-fps imaging speed, was used in the study. Four control and eight OSD rabbits were used. For the OSD rabbit model, 0.2% BAC was topically instilled once daily to one eye of each rabbit for 7 days. The same procedure was performed in the control group using Balanced Salt Solution (Alcon, Fort Worth, TX) instead of BAC. MBFM imaging of the superior bulbar conjunctiva was conducted after topical instillation of moxifloxacin 0.5% ophthalmic solution (Vigamox®; Alcon). The imaging was conducted longitudinally every 7 days for 21 days and the changes of GC density were analyzed. Clinical examinations, including fluorescein staining and tear film break-up time (TBUT), were conducted together to measure dry eye severity.

Results: In-vivo GC imaging of rabbits was possible without significant motion artifacts. Longitudinal MBFM imaging of the BAC-induced OSD rabbit model showed significant GC density loss at days 7 (447±246 GCs/mm^2) and 14 (470±260 GCs/mm^2) post administration compared to that at the baseline (877±181 GCs/mm^2) and their recovery at day 21 (833±437 GCs/mm^2). The GC density of control rabbits was unchanged during the longitudinal MBFM imaging for 3 weeks. The corneal staining score and TBUT significantly worsened at days 7 (8.1±2.2, 3.4±1.5 s, respectively) and 14 (6.4±1.6, 4.3±1.3 s, respectively) compared to those at the baseline (1.8±0.5, 6.8±1.6 s, respectively), and had recovered on day 21 (0.8±0.9, 8.4±1.2 s, respectively). They showed strong correlations with GC density.

Conclusions: MBFM visualized conjunctival GCs of rabbit models non-invasively with high-contrast. In the OSD model, the changes of GC density, observed with MBFM, were correlated with clinical severity, demonstrating the potential of MBFM for clinical GC evaluation in ocular surface diseases.

CONTROL ID: 3712522

SUBMITTER (NAME ONLY): Ryo Kawasaki

TITLE: Cardiovascular Disease Risk Prediction using Retinal Images via Explainable-AI based models with Traditional CVD risk factor estimation

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Traditional cardiovascular (CVD) risk estimation requires information from blood test. Recently, a deep learning (DL) model based on retinal images to estimate CVD risk has been proposed. However, it is still in black-box how the retinal image-based risk prediction performs. We developed explainable AI-based CVD risk prediction model with explicitly estimating individual traditional CVD risk factors with coupled with image-based risk estimation with a proposal to be speculated in the future potential in CVD screening process not requiring blood test.

Methods: We used a subset data from UK Biobank which contains 52,297 entries. We developed a DL model to predict 5-year cumulative incidence of major cardiovascular events (MACE) using multiple combinations of traditional CVD risk factors and retinal images. A two-stage deep learning neural network is proposed. The first stage is a multi-task learning network which takes the retinal images as input and estimates 10 individual CVD risk factors as outcomes (fig). These estimated risk factors are being used as inputs of the second-stage network to estimate the MACE. We compared variation in the risk prediction models combining CVD risk factors and retinal images.

Results: In terms of MACE prediction, our two-step model xMACE (ROC-AUC 0.738 [95%CI 0.710-0.766]) outperformed the traditional score-based model of SCORE (0.682 [0.640-0.719], and at similar range to the neural network model based on traditional CVD risk factors (0.758 [0.729-0.784]).

Conclusions: MACE risk predicted by the deep learning algorithm from retinal images can perform as good as blood test based risk prediction model, and still providing individualized recommendation for which risk factors to be intervened to reduce the risk of CVD.

CONTROL ID: 3712523

SUBMITTER (NAME ONLY): Luisa Colorado

TITLE: CORNEAL DENDRITIC CELL DYNAMICS ARE ASSOCIATED WITH CLINICAL FACTORS IN TYPE 1 DIABETES

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.H. Colorado, L. Beecher, N. Pritchard, N. Efron, K. Edwards, Centre for Vision and Eye Research, Queensland University of Technology Faculty of Health, Brisbane, Queensland, AUSTRALIA|K. Al Rashah, Security Forces Hospital Program, Riyadh, Riyadh, SAUDI ARABIA|C. Dehghani, University of Canberra, Canberra, Australian Capital Territory, AUSTRALIA|A. Russell, Princess Alexandra Hospital, Woolloongabba, Queensland, AUSTRALIA|R. Malik, Weill Cornell Medicine - Qatar, QATAR|

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ABSTRACT BODY:

Purpose: Immature dendritic cells (imDCs) have recently been reported to migrate at a speed of approximately 1 μm/min in the healthy human cornea, as seen with time-lapsed imaging using in vivo confocal microscopy (IVCM). Mature, immature, and putative sub-epithelial dendritic cell density (DCD) and imDC dynamics were explored in people with and without type 1 diabetes.

Methods: Twenty participants with type 1 diabetes (age 55 ± 11 years, duration of diabetes: 29 ± 14 years) from the LANDMark study (a 7-year, two-site, natural history study of type 1 diabetic participants) and 10 age- and gender-matched participants without diabetes (age 55 ± 17 years) underwent IVCM at the whorl region of the nerve plexus to quantify the density of immature, mature and putative dendritic cell phenotypes. Trajectory (length travelled/time) and displacement (distance from to and end points/time) speeds as well as persistence ratio (displacement/trajectory) were calculated from at least three imDCs per cornea. Blood biochemistry and metabolic measures from plasma (including hemoglobin A1C) and urine samples were retrospectively analysed.

Results: Mature DCD was higher in diabetic participants compared to controls (12 ± 13 vs 4 ± 4 cell/mm2, p=0.02). Other cell dynamics and DCD did not differ between groups. Significant associations were found between imDC density and high-density lipoprotein (HDL) cholesterol (mmol/L) (ρ=0.6; p=0.01) and triglycerides (mmol/L) (ρ=-0.6; p=0.01). Putative DCD correlated with HDL cholesterol (mmol/L) (ρ=-0.5; p=0.02). Average imDC trajectory path (μm/min) correlated with duration of diabetes (ρ=-0.5; p=0.03) and estimated glomerular filtration rate (eGFR) (mL/min) (ρ=0.5; p=0.03). Average imDC displacement associated with duration of diabetes (ρ=-0.5; p=0.03), eGFR (mL/min) (ρ=0.7; p<0.01). Average imDC persistence (ratio) correlated with eGFR (mL/min) (ρ=0.6; p=0.01).

Conclusions: This study suggests that metabolic parameters may be reflected in the cornea as observed by imDC dynamics using IVCM and provides evidence of the link between imDCs dynamics and lipid levels, renal function, and duration of type 1 diabetes.

CONTROL ID: 3712525
SUBMITTER (NAME ONLY): Arthur Sit
TITLE: Method for Objective Grading of Tonography Tracings
SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Tonography is the standard method for non-invasive measurement of outflow facility, a critical component of aqueous humor dynamics. With this technique, a pressure decay curve is obtained when a weighted tonometer probe is placed on the eye for several minutes. However, obtaining high quality tracings can be challenging and use of poor-quality tracings can adversely affect the validity of measurements. Also, assessment of tracing quality has typically been subjective, leading to potential bias. The purpose of this study was to develop an objective method for assessing quality of tonography tracings.

Methods: Pneumatonography tracings were obtained from an ongoing multicenter study of aqueous humor dynamics (ClinicalTrials.gov NCT04412096) in participants with glaucoma or ocular hypertension within the Eye Dynamics and Engineering Network (EDEN). IOP was captured digitally at 40 Hz over 2 minutes with a 10 gram weighted probe. A linear best-fit line was obtained for each tracing and root mean square error (RMSE) was calculated as a measure of fit quality. Each tracing was also graded by 7 experienced tonographers using a 1 (worst) to 10 (best, Fig 1) scale for quality (Expert score). A Reference set of 35 tracings was used to determine the relationship between RMSE and Expert score using a logarithmic curve. This relationship was used to calculate a predicted score in a second Test set of 20 tracings. The differences between the predicted scores and the Expert scores were evaluated using Bland-Altman analysis.

Results: The relationship between Expert scores and RMSE was described by the equation: EDEN score= -4.236 ln(RMSE)+7.6569, where the EDEN score is the predicted quality score using a 1-10 scale. For the Test set, there was a very strong correlation between EDEN predicted scores and Expert scores (R=0.94, Fig 2A) using this equation. The mean difference between Expert and EDEN scores was -0.30 ± 0.86 (SD), and the limits of agreement were between -1.99 and +1.39 (Fig 2B).

Conclusions: Objective assessment of pneumatonography tracings can be performed using RMSE of a fitted line and calculation of predicted EDEN quality score on a 1-10 scale. Mean EDEN scores are slightly higher than mean Expert scores, which may result in acceptance of tracing that may be deemed poor quality by expert grading. Further research is needed to determine appropriate cutoff values.

CONTROL ID: 3712527

SUBMITTER (NAME ONLY): Nicole Macriz-Romero

TITLE: Thin-layer Rheology of Meibum using Quartz-Crystal Microbalance with Dissipation in Meibomian Gland Dysfunction Patients and Controls

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Macriz-Romero, J.Y. Arteaga Rivera, J. Guerrero, C.A. Muller Morales, A. Ramírez-Miranda, A. Navas, E.O. Graue-Hernandez, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|C.J. Radke, University of California Berkeley, Berkeley, California, UNITED STATES|S. Jonguitud-Flores, B. Yáñez-Soto, Instituto de Física UASLP, San Luis Potosí, San Luis Potosí, MEXICO|G. Espinosa-Pérez, Universidad Michoacana de San Nicolas de Hidalgo Instituto de Fisica y Matematicas, Michoacan, MEXICO|

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ABSTRACT BODY:

Purpose: The main purpose of the lipid layer in the tear film is to prevent evaporation. The integrity of the lipid layer depends on its rheology, but information regarding individual patients is lacking. We tested the hypothesis that Meibomian gland dysfunction (MGD) patients present lipid with different rheological properties when compared to controls using an experimental model.

Methods: Ten participants over the age of 18 with MGD and 10 healthy controls were included. Exclusion criteria included the use of topical or systemic drugs, ocular disease with the exclusion of MGD, autoimmune disease, contact lens use, history of eye surgery and pregnant or breastfeeding women. Meibum was mechanically expressed from both eyes using cotton swabs and collected in a clean glass slide. It was then immediately dissolved in 1 ml of chloroform and stored at -80 C until analysis. The samples were measured with a quartz crystal microbalance with dissipation. Lipids from single patients at variable concentrations were placed in a clean gold-coated quartz sensor and chloroform was allowed to evaporate. The frequency of oscillations and the dissipation were monitored at 25 C. Samples were then heated to 38 C and the shift in frequency and dissipation recorded. Lastly, samples were allowed to cool down to 25 C. The results of the frequency and dissipation shifts were adjusted to a Kelvin-Voigt viscoelastic model.

Results: The results obtained at 25 C are consistent with the presence of two layers, a thin viscoelastic layer at the interphase (elasticity ≈ 2 MPa and viscosity ≈ 4 cP) and a viscous fluid layer (viscosity ≈ 10 cP). Upon warming the samples to 38 C, the layers lose organization and become a single viscous layer with a viscosity of 8 cP. The two layers reformed and returned to basal values when the samples' temperature decreased to 25 C. The thickness of the viscous layer is greater in controls (≈ 30 nm) when compared to MGD patients (≈ 10 nm) (p value <0.05).

Conclusions: Meibum in MGD patients is less elastic and organized when compared to controls, which may explain its enhanced evaporation. The published information measures viscoelastic characteristics of meibum composed of a pool of samples, not single patients. This method is useful to assess individual patients as it is capable of determining rheological properties in minuscule amounts of sample.

CONTROL ID: 3712528

SUBMITTER (NAME ONLY): Alexi Melki

TITLE: Efficacy of a drug-soaked contact lens to achieve target pupillary dilation for UV light treatment of light adjustable IOLs.

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Melki, K. Makhoul, F. Kahale, J. Brenner, Boston Vision, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cataract extraction with light adjustable lens implantation allows post-operative power titration with UV light to attain the desired refractive outcome. The treatment requires exposure of the IOL optic through a pupillary dilation of at least 7 mm at several intervals in the postoperative period. We intend to show that pupillary dilation is reached faster by applying a contact lens soaked in dilating drops compared to a single application or multiple application of eye drops. If shown to be effective, the soaked CL method would significantly improve clinic workflow, reduce patient inconvenience as well as the burden of the postoperative UV light adjustments.

Methods: We recruited 10 patients who had undergone bilateral cataract surgery and received RxSight's Light Adjustable Lens (LAL). We compared three methods of dilation: a one-time set of drops, a 5-minute interval administration, and a CL soaked in dilating drops. One set consisted of one drop each of 1% Tropicamide, 10% Phenylephrine, and 1% Cyclopentolate. The CL was soaked in a solution of the drops for ten minutes. In each patient we placed the soaked contact lens in one eye and simultaneously began either the interval drop regimen or the one-time administration in the other eye. We measured the time needed to achieve a 7mm dilation through each method.

Results: The eyes that received the contact lens soaked method achieved 7 mm pupil dilation faster than one time application of eyedrops and similar at intermittent eye drops application. We noted empirically that dilation with soaked CL lagged behind interval and singular set drops in the early stages before catching up or surpassing over time. Patients reported that the soaked CLs was the most convenient method of dilation. Technicians and physicians had fewer interruptions to their clinical schedule with one-time administration of drops and soaked CLs, which improved workflow efficiency.

Conclusions: Our results show that administration of a soaked CL produced adequate dilation for LAL treatments. It was comparable to administering drops at 5-minute intervals, and outperformed one-time drop administration. This confers a significant benefit to patient comfort in the clinic and minimizes interruptions to the clinic schedule during the dilation period. A study with a larger sample is required to validate these results and to quantify ideal CL soaking time.

CONTROL ID: 3712530

SUBMITTER (NAME ONLY): Eduardo Lage

TITLE: Inter- and intrasession reproducibility of an open-field portable wavefront autorefractor with and without fogging lenses

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Lage, C.S. Hernandez, A. Gil Ruiz, I. Casares, A. de Lara, Electronics and Communications Technology, Universidad Autonoma de Madrid, Madrid, Madrid, SPAIN|E. Lage, I. Casares, A. de Lara, Instituto de Investigacion Sanitaria de la Fundacion Jimenez Diaz, Madrid, Madrid, SPAIN|C.S. Hernandez, A. Gil Ruiz, J. Poderoso, A. Wehse, D. Lim, S. Dave, PlenOptika Inc, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: High repeatability portable autorefractors may enable effective deploy of global-health initiatives to mitigate uncorrected refractive error worldwide. For example, in studies to evaluate the effectiveness of different measures, repeatability has a direct impact on the statistical power and sample size required, while in screening applications, contributes to increased sensitivity and specificity. This work presents a preliminary assessment of the inter- and intrasession repeatability of an affordable autorefractor (QuickSee, PlenOptika Inc) under two separate measurement conditions, with and without fogging lenses.

Methods: 6 volunteers (29,8 ± 8,1 years old) were measured at 2 different sessions spaced 1-week. Each subject was tested 6 times per session with the QuickSee, 3 times in standard mode and 3 using a modified version of the device eyecup to allow over-refraction through fogging lenses (+2.0 D). Intersession measurements were spaced 5 minutes apart and the complete alignment procedure was repeated for each measurement. After converting autorefractor readings into power vectors (M, J0, J45), repeatability was evaluated using the Bland-Altman method to compare differences between all possible combinations from each subject (inter- and intrasession). Repeatability coefficients (RPC), estimated as the 95% limits of agreement, and the mean absolute errors were also evaluated. In all cases, only results for the right eyes were analyzed.

Results: Participants had an average Spherical Equivalent (SE) refraction of -0.75 ± 2.06 D, (Min -5.11 D, Max 0.175 D). A total of 36 samples per dataset were obtained for the intrasession analysis while 54 samples per dataset were used in the intersession comparison. In all cases the mean difference was practically 0 indicating no bias for any of the vector components. SE RPCs for intrasession test were 0.15 D in standard mode and 0.29 D with the fogging lenses. Intersession RPCs were 0.29 D and 0.4 D without and with the fogging lenses, respectively. Detailed results for all vector components are shown in Table 1.

Conclusions: This preliminary analysis shows that the device can provide excellent RPCs in standard mode, which decrease moderately with the use of the fogging lenses. Further work exploring improvements in the eyecup design and measurement averaging techniques may further enhance the RPC values in over-refraction mode.

CONTROL ID: 3712531

SUBMITTER (NAME ONLY): John Fitzpatrick

TITLE: Cytokine Profiles of Normal Eyes in the INflammatory MediatorS in the PathophysIology of Diabetic REtinopathy (INSPIRE) Study

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Fitzpatrick, A. Nair, S. Al-Awamlh, K. Scavelli, P. Mallory, J. Sheng, S. Gangaputra, S.J. Kim, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: INSPIRE is a prospective, randomized, 3-year study, with aims of characterizing the role of aqueous cytokines with diabetic retinopathy progression. This analysis establishes the cytokine levels in eyes without diabetic retinopathy or other ocular inflammatory conditions. These levels will serve as a normal for comparison with diabetic retinopathy and other inflammatory ocular conditions.

Methods: 104 eyes of 104 non-diabetic patients were enrolled. All eyes underwent unilateral vitrectomy for non diabetic causes such as epiretinal membrane, macular hole, vitreous opacities, vitreous hemorrhage, and retinal detachment. Approximately 0.2 mL of undiluted aqueous sample was obtained with a 30 gauge needle at the time of vitrectomy. These samples were collected and stored at -80 degrees C and later analyzed for 24 pro and anti inflammatory cytokine levels using the Millipore Multiplex Human Cytokine Kit (Millipore Corporation, Burlington, MA) according to the manufacturer's instructions.

Results: Baseline characteristics of the cohort are shown in Table 1. The mean age was 68.4 years +/- SD 7.91. 48 patients were phakic, 55 patients were pseudopakic, and 1 was aphakic. Four patients were on systemic immunosuppressive mediations including methotrexate, fingolimod, azathioprine, and imatinib for systemic autoimmune conditions. Six patients were on topical prostaglandin analogs and one patient was on fluorometholone drops. Six patients had systemic inflammatory diseases including gout, psoriasis, multiple sclerosis, Crohn's disease, and undifferentiated connective tissue disease.

24 cytokines were measured in all 104 eyes. The most clinically relevant cytokines measured included VEGF, TNF-a, IL-8, IP-10, IL-6, IL-1b, IL-17A, IL-10. These cytokine levels are summarized in Table 2. Additional cytokines also detected included FGF-2, Eotaxin, G-CSF, Fit-3L, GRO, MCP-3, MDC, PDGF-AA, PDGF-AB/BB, sCD40L, IL-1RA, IL-2, IL-4, MCP-1, MIP-1b, and RANTES.

Conclusions: To our knowledge, this is the first large scale characterization of normal cytokine levels in eyes without diabetic retinopathy or other ocular inflammatory conditions. This data will be integral to better understand the inflammatory drivers of diabetic retinopathy progression and subsequent therapeutic targets.

CONTROL ID: 3712532

SUBMITTER (NAME ONLY): Tyler Pfister

TITLE: Mediating factors in the link between visual impairment and psychiatric disorders

SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Pfister, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|J. Wilson, L. McKernan, Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|S. Gangaputra, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual Impairment (VI) is strongly associated with psychiatric disorders. However, recent research indicates that depression may be less related to quantitated vision loss than it is to the secondary impact of decreased functional status. It remains unclear what functional aspects of vision influence the development of anxiety and depression associated with vision loss. We analyzed the relation between instrumental and non-instrumental activities of daily living (IADL and ADL) and self-reported VI and how the inability to perform tasks may mediate depression and anxiety.

Methods: Cross-sectional responses from the 2016 National Health Interview Survey (n=15,690) were analyzed using a structural equation modeling (SEM) approach to calculate the direct effect of subjective VI on the frequency of anxiety and depression symptoms and the indirect effect mediated by impairment in ADLs and IADLs. Unstandardized regression coefficients were estimated after controlling for baseline demographics, socioeconomic status, and comorbid disease using the Charlson Comorbidity Index. A separate SEM assessed the impact of near and distance vision dysfunction on the severity of anxiety and depression.

Results: IADLS: Both cleaning and communicating difficulty showed a significant mediating effect for anxiety and depression, while shopping difficulty only had a significant relation to depression but not anxiety. Interestingly, transportation difficulty did not mediate either relationship. ADLS: Bathing, dressing, mobility and toileting limitations all demonstrated a significant mediating effect between VI and anxiety frequency (collective $p < 0.0005$), while feeding did not. Only dressing limitations were a significant mediator for depression frequency. Lastly, distance VI was found to be a significant predictor of anxiety and depression frequency ($p = 0.001$, 0.002), but near VI was not ($p = 0.755$, 0.171).

Conclusions: ADL and IADL dysfunction may contribute to depression and anxiety symptoms induced by VI. The indirect effects were minor compared to the direct effects indicating that other factors that could not be studied may play a larger role in the severity of psychiatric illness. These results may help inform which activities should be targeted by low vision and visual rehabilitation providers.

CONTROL ID: 3712534

SUBMITTER (NAME ONLY): Larry Park

TITLE: Evaluation of novel YP-P10 Peptide in animal models of inflammatory dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.C. Park, K. Park, Naason Science, Inc, Cheongju-si, Chungbuk, KOREA (THE REPUBLIC OF)|L. Gharat, Y. Hu, Yuyu Pharma Inc, Jung-gu, Seoul, KOREA (THE REPUBLIC OF)|J. Alam, Z. Yu, C.S. De Paiva, S.C. Pflugfelder, Baylor College of Medicine, Houston, Texas, UNITED STATES|G.D. Novack, PharmaLogic Development, Inc, San Rafael, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study is aimed to investigate the efficacy of YP-P10 Peptide in several animal models of dry eye disease

Methods: Sprague-Dawley rats were subjected to extraorbital lacrimal gland excision (ELGE) or sham surgery. Seven days after surgery, animals were dosed with Topical ocular YP-P10 Peptide (0.1, 0.3, 1 & 3%) or vehicle BID 14 days. Corneal staining using NEI scale was observed biomicroscopically after instillation of 1% fluorescein. C57BL/6J mice were subjected to desiccating stress (<30% relative humidity) and cholinergic blockage for 1 day (DS). Mice received topical ocular YP-P10 Peptide (0.3, 1 or 3%) or vehicle BID 3 days before starting DS and continued during DS. Additional controls were naïve mice not subjected to DS, and DS mice dosed with ocular dexamethasone sodium phosphate. Tears were collected using capillary tubes and inflammatory mediators were measured using Luminex immunoassay. Cornea and conjunctiva were excised and lysed in RNA lysis buffer and subjected to qPCR for a panel of inflammatory markers that have been implicated in dry eye.

Results: Rats: A statistically significant ($p<0.001$) increase of the fluorescein-stained cornea score based on the NEI scoring scale was observed on the eyes of the ELGE group compared to the SHAM group. Treatment with YP-P10 Peptide reduced corneal damage. Mice: DS increased mRNA levels of G-csf in cornea and Il6, Ccl20, Mmp3, Tnf in conjunctiva. A dose-dependent decrease in several inflammatory mediators associated with dry eye (Il1b, Ccl5 and Cxcl10) was observed in the cornea and conjunctiva, reaching statistical significance compared to vehicle and showing activity similar to dexamethasone in the conjunctiva. This was accompanied by significant decrease in CCL5 and an increase in IL-10 in tear fluid of YP-P10 Peptide treated animals.

Conclusions: Topical ocular YP-P10 Peptide reduced corneal epithelial disease in a rat ELGE dry model and several inflammatory mediators in DS-induced dry eye disease in mice. This anti-inflammatory effect suggests that YP-P10 Peptide might have efficacy in the treatment of dry eye induced ocular surface inflammation.

CONTROL ID: 3712535

SUBMITTER (NAME ONLY): Emma Wood

TITLE: Comparison of Adeno-Associated Virus Serotype Tropism in Human Retinal Explants and Non-Human Primates Retinal Explants

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Wood, S. sun, W. Su, J. Xie, R. He, P.W. Tai, E. Bilsbury, S. Doherty, H. Lin, G. Gao, B. Tian, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: As improvements are made in engineered and recombinant AAV serotypes that are potentially more potent than naturally occurring serotypes, there is an urgent need to explore an effective and direct method for testing the transduction efficiency and tropism of these AAV serotypes in human retinal tissue. Human retinal explants serve as a robust, informative model to evaluate transduction efficiency and tropism in human cells, while the efficacy of non-human primate (NHP) retinal explants needs to be directly compared to human tissue to determine its use as a predictive model. Herein, this study examines the transduction efficiency and tropism of ten different AAV serotypes in the human retinal and non-human primate (NHP) retinal explants ex vivo.

Methods: AAV-3b, AAV-6.2, AAV-6TM, AAV-9rh, AAV-32.33, AAV-PHP.B, AAV-PHP.eB, AAV-rh10, AAV-rh39, AAV-rh43 were tested. AAV2/2 and AAV2/8 served as positive controls. All vectors driving expression of GFP under control of the CB6 promoter packaged by the University of Massachusetts Chan Medical School Vector Core. Three independent experiments were performed, each using a different human donor and NHP eye. Retinal explant cultures were maintained for 7 days post transduction. Immunohistochemistry was performed for GFP and the total number of GFP+ cells was calculated using ImageJ manually. Retinal cell tropism for each AAV serotype was evaluated qualitatively by recording whether cells of the inner nuclear layer (INL) or outer nuclear layer (ONL) that were GFP+ overlapped with markers of different retinal cell types, 7G6, PNA, GS, rhodopsin, and arvalbumin.

Results: AAV-32.33 and AAV-rh10 have the high transducing efficiency for photoreceptor cells and Muller cells, compared with AAV2/2 and AAV2/8 in NHP and human retinal explants. Furthermore, the retinal cell tropism in NHP retinal explants for all serotypes was consistent with retinal cell tropism in human retinal explants.

Conclusions: Our study shows that AAV-32.33 and AAV-rh10 could be useful candidates for intraocular gene delivery to photoreceptor and Muller cells. These results show that human retina explants serve as an effective and direct method for predicting transduction efficiency and tropism of new AAV serotypes in human retina.

CONTROL ID: 3712537

SUBMITTER (NAME ONLY): Katie Williams

TITLE: Genetic associations of OCT-derived measures of macula and fovea curvature in UK Biobank participants

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Williams, A. Olvera-Barrios, P.L. Mueller, A. Warwick, C.A. Egan, A. Tufail, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|P.G. Hysi, A. Olvera-Barrios, A. Warwick, C.A. Egan, A. Tufail, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|K. Williams, P.G. Hysi, C.J. Hammond, King's College London Faculty of Life Sciences and Medicine, London, London, UNITED KINGDOM|P.L. Mueller, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|Y. Kihara, A.Y. Lee, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The aim of this study was to identify genetic variants associated with novel measures of the curvature of the posterior globe derived from macular optical coherence tomography (OCT) scans in a large UK-based cohort.

Methods: A total of 73,032 participants from the UK Biobank study who underwent macular spectral-domain OCT as part of their ophthalmic examination were analysed. A deep learning model was used to segment the scans and polynomial fit was used to calculate the curvature of the macula and fovea. Genome-wide association analyses were performed on individuals of European ancestry using BOLT-LMM with adjustment for age, sex and population structure. Given that foveal curvature is highly dependent on retinal pathology individuals were excluded with diabetes or with ocular diagnoses affecting retinal thickness. Given that macula curvature, synonymous with dome-shaped macula configuration, is associated with myopia further analyses with adjustment for refractive error were performed.

Results: Analyses were performed on 77,324 and 58,348 participants for macula and fovea curvature respectively. Genetic variants associated with macula curvature clustered at 37 unique autosomal genomic regions at genome-wide significance (P<5x10-8) and the most significant locus was LAMA2 ($p=3.40x10^{-49}$). This and several other loci were previously associated with refractive error and myopia. After adjustment for refractive error the most significant locus was DGKD ($p=6.60x10^{-65}$). A larger number genome-wide significant variants were associated with fovea curvature (n=315) which clustered at 128 unique autosomal genomic regions including LINC00461 ($p=5.50x10^{-76}$), ADCY5 ($p=5.90x10^{-73}$) and FLT1 ($p= 9.90x10^{-27}$).

Conclusions: This study has identified a large number of genetic loci influencing the curvature of the macula and fovea. The identified genetic determinants could provide additional insights into axial elongation, macula staphyloma (a risk factor for myopic maculopathy), dome-shape macula configuration and foveal development.

CONTROL ID: 3712539

SUBMITTER (NAME ONLY): Stanley Saju

TITLE: Comparison of Quantitative Retinal and Choroidal Measurements in Eyes with Neovascular Age Related Macular Degeneration Using Fully Automatic Software Versus Native Spectralis Software

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Saju, S.J. Chiu, G. Jaffe, D.S. Grewal, Retinal Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine agreement on quantitative retinal and choroidal measurements obtained with Duke Reading Center's automatic segmentation software, DRCVisualizer and native Spectralis Heidelberg Eye Explorer (HEYEX) OCT software in eyes with neovascular age related macular degeneration (nvAMD) under treatment in a clinical trial.

Methods: Eighty eyes of eighty participants from a phase 2 nvAMD clinical trial dataset with good quality images were randomly selected. Images were acquired with a 20x20 degree 97-line High Resolution scan protocol. For each scan, the standard nine-field ETDRS grid was centered at the fovea, and the HEYEX software (Version 1.10.4.0) automatically segmented the internal limiting membrane and Bruch's membrane on each B-scan image. Any segmentation errors were manually corrected in HEYEX and all scans were then imported into DRCVisualizer (Version 2.1.1). We compared the following automatically computed parameters generated by both DRCVisualizer and HEYEX: Central Subfield Thickness (CST), Central 1mm Volume, and Total ETDRS Grid Volume. The following parameters were manually annotated on both software by a trained grader: Center point thickness, foveal neurosensory retinal thickness, foveal subretinal hyperreflective material thickness, foveal subretinal fluid thickness, subfoveal choroidal thickness, and Horizontal and Vertical extent of pigment epithelium detachment. Intraclass correlation coefficients (ICC) were used to determine agreement between measurements obtained.

Results: There was excellent agreement between HEYEX and DRCVisualizer for all automatically computed thickness and volume parameters as well as for all manually annotated measurements. ICC were excellent (Table 1) for all parameters (range 0.99-1.00). Measured values were very similar using the two software and percent differences between the measured values for all 10 parameters ranged from 0.048 to 1.513% (Table 2).

Conclusions: Semiautomatic retinal thickness and volume measurements and manually annotated anatomic features generated by the Duke Reading Center's DRCVisualizer software have excellent agreement with and are very similar to the values generated by the Spectralis HEYEX software in eyes with nvAMD in a clinical trial setting.

CONTROL ID: 3712540

SUBMITTER (NAME ONLY): Raiza Perez Lucena

TITLE: Validation of lens thicknes (LT) measurement. Artificial intelligence versus clinician.

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Perez Lucena, D. Roca, J. De La Cruz, A. Arteaga, A. Gonzalez, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to validate the lens thickness (LT) measurement process by anterior segment OCT images, manually and with artificial intelligence.

Methods: A retrospective chart review of patients that underwent uncomplicated FLACS at the Illinois Eye and ear Infirmary was done. 329 anterior segment OCT images of the LenSx Femtosecond platform were reviewed. Lens thickness measurements were done by 4 physicians and interobserver agreement was determined. Using artificial intelligence (AI), the same measurements were made and subsequently compared.

Results: Of the 329 anterior segment images, 36 were excluded because bad quality. Mean LT was 520.3 ± 549.6 µm. Interobserver agreement was high across all 4 physicians. Afterward, LT measurements were compared with AI results. The LT measured by anterior segment OCT showed excellent agreement.

Conclusions: Sensitivity and specificity were high for AI LT measurements. This can improve refractive outcomes when used in biometric formulas.

CONTROL ID: 3712541

SUBMITTER (NAME ONLY): Jason Comander

TITLE: The Genetic Basis of Rod-Cone versus Cone-Rod Dystrophies

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Comander, S. Chorfi, E. Place, C. Weigel Difranco, R.M. Huckfeldt, Ocular Genomics Institute, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|J. Comander, S. Chorfi, E. Place, C. Weigel Difranco, R.M. Huckfeldt, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRDs) are classically diagnosed and classified by the electroretinogram (ERG) rod and cone response amplitudes, and the pattern of ERG responses is associated with various clinical diagnoses. Certain gene defects cause primarily cone dysfunction, such as CNGA3, which causes achromatopsia. Other gene defects can cause a cone-rod dystrophy (cone>rod dysfunction), such as ABCA4. Some genes defects cause rod-cone dystrophies (rod>cone dysfunction), known as retinitis pigmentosa (RP), including rhodopsin.

Methods: This study compares residual cone and mixed rod-cone response amplitudes across 5095 ERGs of 1239 subjects with IRDs caused by 84 different genes. The mixed rod and cone response was elicited by 0.5 Hz white flashes at 0.22 cd*s/m2 after dark adaptation. The cone specific response was elicited by 30 Hz flashes after light adaptation. The residual of a curve fit of the cone versus mixed response amplitudes was calculated, which can be considered as a type of cone/rod amplitude ratio.

Results: The lowest cone/rod ratio, indicating primary cone dysfunction, was seen in KCNV2 defects, which causes “cone dystrophy with a supernormal rod electroretinogram”. AIPL1 defects, which also cause an unusual ERG, also had large residual rod signals with low cone signals. These two genes, along with achromatopsia genes such as CNGA3 & CNGB3, have the lowest cone/rod ratios. The highest cone/rod ratios, indicating primarily rod dysfunction, were frequently seen in genes that cause dominant RP, such as rhodopsin, KLHL7, and IMPHD1. (Different relative rankings are obtained with amplitude-independent calculations.) ABCA4, and to a lesser extent RPGR, showed a wide spectrum of ratios, consistent with their ability to cause RP versus cone-rod dystrophy in different subjects. Findings for additional genes are discussed.

Conclusions: This study shows, in an unbiased way, which IRD genes cause more rod versus cone-specific defects, in many human subjects. This pattern likely reflects the underlying biology of the different gene functions and might have implications for therapeutic approaches to gene replacement for IRDs.

CONTROL ID: 3712542

SUBMITTER (NAME ONLY): Meher Saleem

TITLE: Phosphatidylserine transport is impaired in the trabecular meshwork of primary open angle glaucoma

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Saleem, K. Jasti, K. Ramlakhan, S.K. Bhattacharya, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|M. Saleem, Georgetown University School of Medicine, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: In primary open angle glaucoma (POAG), the trabecular meshwork (TM) has been found to have decreased levels of cytosolic/plasma membrane phosphatidylserine (PS) and the ATPase phospholipid transporting 8B2 (ATP8B2) compared to controls. We hypothesize that PS transport is impaired in the POAG TM, and that the flippase ATP8B2 is specifically responsible for the transport of PS in the TM.

Methods: Primary TM cells were derived from normal cadaveric eyes (n=20) with equal gender distribution. All collections followed the tenets of the Declaration of Helsinki. To evaluate PS transport, TM cells were incubated with nitrobenzoxadiazole (NBD)-PS (excitation=433 nm, emission=540 nm) and imaged with a confocal microscope. This transport method with suitable modifications was also adapted for POAG TM tissues (n=20) and control TM tissues (n=20) with equal gender distribution. POAG and control TM tissue ages were 75±5.5 and 68±4.5 years respectively. Knockout (KO) of the ATP8B2 gene was performed with a CRISPR/Cas9 lentivector in primary TM cells. To complement this experiment, artificial unilamellar vesicles embedded with ATP8B2 and control unilamellar vesicles were incubated with PS. Bligh and Dyer lipid extraction was performed on ATP8B2 KO TM cells, control TM cells, ATP8B2 embedded unilamellar vesicles, and control unilamellar vesicles. The extracted lipids were analyzed with TSQ Quantum Access MAX Triple Quadruple Mass Spectrometer with Equisplash™ internal standard to assay the specificity of ATP8B2. Statistical analysis was performed with a two-way ANOVA test.

Results: The kinetics of NBD-PS transport from the extracellular matrix into primary TM cells occurred over the course of 15 minutes. These kinetics were consistent in control TM tissue, but occurred at a 3-5-fold slower rate in POAG TM tissue. A repertoire of PS lipids (acyl chain length 16-22) exhibited reduced transport in ATP8B2 KO TM cells compared to controls. Unilamellar vesicles embedded with ATP8B2 exhibited increased PS transport compared to controls.

Conclusions: Our results are consistent with the occurrence of impaired PS transport in the POAG TM, and also with the transport of PS by ATP8B2 in the TM. These findings are consistent with the finding of decreased levels of ATP8B2 in the POAG TM, and could indicate that the decreased levels of ATP8B2 could be contributing to impaired PS transport in the POAG TM.

CONTROL ID: 3712543

SUBMITTER (NAME ONLY): Brittany Bowman

TITLE: Remote and In-Lab Eccentric Viewing Training in Patients with Central Vision Loss

SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Bowman, N. Ross, P.J. Bex, New England College of Optometry, Boston, Massachusetts, UNITED STATES|J. Skerswetat, P.J. Bex, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Currently, there are no standardized methods to select, quantify or train eye movements in patients with central vision loss (CVL). We developed 2 eccentric viewing (EV) training systems, in-person and remote, to implement and compare alternative feedback methods for CVL rehabilitation.

Methods: CVL patients (n=8 in-lab (median age=71years ± 20 standard deviation); n=8 remote (61 ± 11); n=9 normally-sighted controls (28 ± 5)) were recruited. The remote system, consisting of a laptop and eye tracker (Tobii EyeX or GazePoint GP3), was mailed to participants. Matlab speech and an experimenter on Zoom guided participants through the remote experiment. The in-lab system was led by a researcher and utilized an Eyelink eye tracker. In both systems, a PRL in the inferior visual field was trained with audio, contracting ring, gaze-contingent ring, image of a hand, and tactile feedback in random order and were compared to free viewing. The contrast sensitivity function (CSF) at the PRL was assessed via bandpass-filtered HOTV letters, updated using an adaptive algorithm; fitted after 25 correct responses; maximum 50 trials per condition.
Bivariate-Contour-Ellipse-Areas (BCEAs), Area-Under-the-CSF (AUCs), and CSF Acuities were calculated to measure oculo-motor and perceptual performance, respectively. Analysis-of-variance models and planned multiple comparisons were used to determine statistical effects.

Results: We were able to measure the CSF and BCEAs of all subjects both in-lab and remotely, however, eye tracking data loss was higher in remote-CVL patients, likely due to EV. BCEA was significantly reduced in all feedback conditions in the remote-control group ($p=0.003$), but not for the in-lab control group. In all groups, there were no significant differences in Acuity or AUC across feedback mechanisms.

Conclusions: We developed a novel remote EV training system, which successfully measured contrast-sensitivity in CVL patients and successfully tracked eyes in a subset of participants. Although the present feedback methods did not affect the visual function endpoints tested in this study, this system may be used to evaluate other rehabilitation approaches and functional outcomes.

CONTROL ID: 3712544

SUBMITTER (NAME ONLY): Nahomy Ledesma Vicioso

TITLE: Assessment of diversity and inclusion information in ophthalmology residency program websites

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ledesma Vicioso, G. Sun, Weill Cornell Medicine, New York, New York, UNITED STATES|F. Woreta, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prospective ophthalmology applicants, particularly racial and ethnic minorities, heavily consider program factors related to program culture and commitment to diversity when researching residency programs. We performed a cross-sectional study to evaluate for the presence of predetermined diversity and inclusion criteria in US ophthalmology program websites. We tested the hypothesis that larger programs and high program rank were more likely to be associated with presence of the diversity and inclusion criteria.

Methods: A complete list of 125 US ophthalmology residency programs was obtained from the Fellowship and Residency Electronic Interactive Database (FREIDA) in May 2021. A total of 121 program website links were found through FREIDA or Google Search and were included in the analysis.

Program characteristics like program size (number of PGY2- PGY4 residents) and whether the program ranked within the top 20 “Best Hospitals for Ophthalmology” per the 2020 U.S. News & World Report were collected. A descriptive analysis was performed. Fisher’s exact tests were used to compare proportions.

Results: Out of 121 program websites reviewed, 29 (24%) met at least 1 of the 6 predetermined diversity and inclusion criteria. Of these 29, 9 (7%) had mention of diversity in mission statement, program director’s statement or department chair’s message, 17 (14%) had a standalone diversity statement, 9 (7%) had information about a rotation or elective for minority students, 11 (9%) had mention of diversity initiatives, 7 (6%) had a diversity page or section, 6 (5%) mentioned appointed diversity leadership. Programs with more than 12 residents (OR 3.58; CI 1.39-9.55; p=0.0039) and programs ranked within the top 20 “Best Hospitals for Ophthalmology” (OR 3.28; CI 1.05-10.1; p=0.023) were more likely to have at least 1 of the diversity and inclusion criteria on their website.

Conclusions: The majority of ophthalmology residency programs do not have mention of, or information regarding, diversity and inclusion on their websites. Larger and higher-ranked programs are more likely to mention or portray their commitment to diversity on their residency website.

CONTROL ID: 3712545

SUBMITTER (NAME ONLY): Arthur Nassaralla

TITLE: Diabetic microangiopathy: prevalence of assumed diabetic glomerulopathy in diabetic retinopathy patients in follow-up care in a medical retina clinic

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nassaralla, B.A. Maciel, C. Junqueira de Carvalho, J.L. Orefice, Centro Oftalmológico de Minas Gerais, Belo Horizonte, BRAZIL|A. Sasse, Faculdade de Medicina São Leopoldo Mandic, BRAZIL|

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ABSTRACT BODY:

Purpose: To assess the prevalence of diabetic glomerulopathy findings in patients diagnosed with diabetic retinopathy (DR) for over 5 years having follow-up care in Medical Retina (MR) clinic.

Methods: Thirty-three patients were invited randomly and consecutively evaluated in one day in our MR clinic. Along with indirect ophthalmoscopy to evaluate the patients' retinas, various tests and questions to assess the risk factors and presence of kidney damage were performed. Semi-quantitative urine test strips were the main test to detect kidney damage, while questions about patient's lifestyle, past history and knowledge about the disease, medications in use were the main determinant of patients' risk factors. The results were, then, correlated.

Results: Among mild, moderate and severe retinopathy patients, 78,8% (26) had, beyond diabetes, hypertension, other possible etiology for kidney damage. 30,3% (10) had swollen lower limb history and 39,3% (13) reported foamy urine. Using a system to grade the severity (1-4 from mildest to severe), the semi-quantitative urine test strips, were used to analyze proteinuria, hematuria, and glycosuria. 66,6% (22) of the patients presented at least some kind of renal damage. Proteinuria was found in 30,2% (10) of the patients (grade 1- 12,1%; grade 2 - 15,1%; grade 3 - 3%; grade 4 - 0%). Meanwhile 42,2% (14) of the patients manifested glycosuria (grade 1- 6%; grade 2 - 6%; grade 3 – 27,2%; grade 4 - 3%). Lastly, hematuria appeared in 24,2% (8) of the patients (grade 1- 12,1%; grade 2 - 9,1%; grade 3 - 3%; grade 4 - 0%). While 21,2% (7) of the patients had previous knowledge about their proteinuria, only 12,1% (4) of them reported awareness of the renal damage.

Conclusions: Diabetic nephropathy is one of the three most common manifestations of diabetes. In patients diagnosed with diabetic retinopathy for over 5 years undergoing clinical follow-up in a MR clinic the prevalence of renal damage was 66,6%, when compared to only 30% in most studies about diabetes manifestations epidemiology. Therefore, we may infer that, diabetic retinopathy may be a biomarker for diabetic nephropathy in diabetic patients.

CONTROL ID: 3712546

SUBMITTER (NAME ONLY): Irina Balikova

TITLE: High myopia and vitreal veils in a patient with Poretti-Boltshauser syndrome due to a novel homozygous LAMA1 mutation

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Balikova, N. Faizi, I. Casteels, Ophthalmology, University Hospital Leuven, Leuven, Please select, BELGIUM|P. Coucke, M. De Bruyne, E. De Baere, Department of Biomolecular Medicine, Center for Medical Genetics, Ghent University Hospital, Ghent, BELGIUM|

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ABSTRACT BODY:

Purpose: We describe a patient from non-consanguineous Caucasian parents who presented at the age of 1 year with nystagmus, reduced visual contact and high myopia. Fundoscopic examination revealed optically empty vitreous and vitreal veils. The electroretinogram (ERG) under general anesthesia showed reduced scotopic and photopic responses, which remained stable during the follow up of 16 years. She had mild axial hypotonia that resolved with age. Her general development was normal. A cerebral MRI was performed at 1 year and 17 years of age and revealed dysplasia of the cerebellum with presence of cysts and atrophy of the superior peduncles with a molar tooth like sign. In the differential diagnosis Stickler and Wagner syndrome were considered. The purpose of this study was to identify the genetic cause of the vitreoretinopathy in this patient.

Methods: Firstly targeted genetic testing using next generation sequencing of COL2A1, COL11A1 and COL11A2 was performed. Secondly, a Next generation sequencing based gene panel analysis was carried outusing a NovaSeq 6000 platform (Illumina). The analysis was performed on a gene panel including RetNet related genes

Results: No pathogenic variants were identified in the COL2A1, COL11A1 and COL11A2 genes. The analysis of the Retnet genpanel showed an interesting homozygous potentially pathogenic variant c.8446C>T, p.(Arg2816Ter) in exon 59 in the LAMA1 gene. This variant creates a premature stop codon in 59/63. Segregation testing of the parents showed that they are both heterozygous carriers of the mutation.

Conclusions: We present a patient with severe early onset myopia and vitreal veils carrying a novel homozygous LAMA1 mutation. Mutations in this gene are shown to underly the Poretti-Bolthauser syndrome (OMIM 615960). The patients have intellectual disability, ataxia and cerebellar abnormalities. Ocular abnormalities described are myopia, oculo - motor apraxia, and retinal dystrophy. Here we show a patient with severe myopia and vitreal veils and no psychomotor retardation except for transient axial hypotonia. These are ocular features typically described in Wagner and Stickler syndromes. We show that Poretti-Bolthauser syndrome should be considered in the differential diagnosis of the vitreoretinopathies together with Stickler, Wagner and Knobloch syndromes.

CONTROL ID: 3712549

SUBMITTER (NAME ONLY): Anse Vellappally

TITLE: A novel method of enhancing in vivo OCT lamina cribrosa visualization for automated segmentation

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vellappally, P. Alexopoulos, Z. Ghassabi, T. Lee, R. Zambrano, J.S. Schuman, H. Ishikawa, G. Wollstein, Department of Ophthalmology, NYU Langone Health, NYU Grossman School of Medicine, New York, New York, UNITED STATES|D. Szezurek, L. Shijie, J. Fishbaugh, G. Gerig, Department of Computer Science & Engineering, NYU Tandon School of Engineering, Brooklyn, New York, UNITED STATES|T. Lee, J. Hu, Departments of Population Health and Environmental Medicine, NYU Langone Health, New York, New York, UNITED STATES|J.S. Schuman, Departments of Biomedical Engineering and Electrical & Computer Engineering, NYU Tandon School of Engineering, Brooklyn, New York, UNITED STATES|H. Ishikawa, Departments of Ophthalmology, Casey Eye Institute, and Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|G. Wollstein, Department of Biomedical Engineering, NYU Tandon School of Engineering, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Automated segmentation of in-vivo lamina cribrosa (LC) has been challenging, owing to the complex 3D structure and decreased visibility in the lamina depth. Frangi's vesselness filter, which was originally developed for angiogram segmentation, have been successfully demonstrated in segmenting the ex-vivo LC from micro-CT and second harmonic generation microscopy images. In this project we are proposing a new approach of segmenting the in vivo LC from OCT scans, incorporating the Frangi's vesselness principle to facilitate in vivo LC image analysis in much greater detail compared to our previously described 3D analysis method.

Methods: In-vivo spectral-domain OCT scans (Leica, Chicago, IL) were acquired from healthy non-human primates. Scans of varying degree of image quality were selected for the analysis and underwent automated brightness and local contrast enhancement. 3D Frangi's vesselness filter was applied using a fixed setting for scans of all qualities. Our previously described segmentation algorithm was then used to quantify the LC microstructure. The measurements generated from the Frangi analysis and from our own conventional method were compared with a standard reference (manually segmented LC by an expert). Paired t tests were performed to compare if the differences between standard reference and conventional method are greater than the differences between standard reference and Frangi analysis. The visibility of analyzable lamina and dice coefficient were also compared to the conventional method using the same test.

Results: In vivo scans acquired from 5 rhesus macaques (3 males, 1 female, aged 4.3-10.7 yrs) were used for the analysis. No significant difference was detected for LC microstructure parameters between Frangi's approach and conventional method with respect to the standard reference, except for significantly higher pore count in Frangi's method ($p=0.003$; Table). Furthermore, visibility (Figure) was significantly higher for the Frangi method compared to the conventional approach ($p<0.001$) with no difference detected for the semantic segmentation, as reflected by the dice coefficient.

Conclusions: The use of Frangi analysis substantially increase the analyzable lamina while providing similar quantification of the LC microstructure compared to our previous 3D analysis method. This improves the potential for automated and thorough volumetric analysis of in vivo OCT LC image.

CONTROL ID: 3712550

SUBMITTER (NAME ONLY): Liang Li

TITLE: In Vivo Evaluation of Naïve and Diseased RGC Activities at Single-Cell Level

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Li, F. Fang, X. Feng, P. Zhuang, H. Huang, P. Liu, J. Liu, N. Sredar, L. Liu, Y. Sun, J.L. Goldberg, Y. Hu, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|F. Fang, Department of Ophthalmology, The Second Xiangya Hospital, Central South University Xiangya School of Medicine, Changsha, Hunan, CHINA|S. Zhang, X. Duan, Department of Ophthalmology, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|D.A. Miller, H. Zhang, Department of Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The characteristic feature of optic nerve injury and glaucoma is the progressive degeneration of RGCs and their axons. However, the neuronal activities of RGCs and their changes in disease models have not been studied longitudinally in vivo. Here we demonstrate the feasibility of directly visualizing light-evoked RGCs activities by cSLO-mediated high throughput RGC Ca^{2+} imaging. The powerful population and single-cell analytic strategies we developed revealed, for the first time, distinct dynamic RGC activity changes in optic nerve crush(ONC) and glaucoma models.

Methods: Due to the superb optical accessibility of the retina, fluorescence-labeled RGCs can be imaged noninvasively in vivo by cSLO. We specifically delivered Ca^{2+} indicators, jGCaMP7s, to the mouse RGCs by AAV2 and mSncg promoter. Thus, we employed cSLO customized with UV stimulation and jGCaMP7s, to optically record light-evoked activities of about 1200 RGCs/retina simultaneously in naïve living mice, as well as longitudinal recording RGC activities at multiple time points in ONC and glaucoma mice.

Results: In naïve retinas, 47 RGC clusters were recognized by unsupervised algorithms, and then hierarchically re-grouped into 9 groups with distinct ON, OFF, and ON-OFF responses to UV stimulation. Consistent with distinct transcriptomic changes in trauma and glaucoma, population analysis of longitudinal RGC Ca^{2+} imaging reveals initial increase, but later rapid loss of ON-RGC activities in ONC, versus mild decreased but well-preserved ON- and OFF-RGC activities in glaucoma. More strikingly, single-cell Ca^{2+} imaging tracing uncovers unprecedented conversions of RGC activities, majority of ON-to-OFF conversion in trauma and OFF-to-ON conversion in glaucoma. Thus, not static as assumed, individual RGC's light-evoked activity is rather vibrant with unique transformation patterns in different diseases.

Conclusions: Our results demonstrate the potential of in vivo RGC Ca^{2+} imaging as a reliable, sensitive, direct and noninvasive RGC functional measurement at single-cell level, but with high throughput capability. This proof-of-concept study lays out the foundation for in vivo RGC function classification and evaluation with more visual stimuli under normal, disease, and therapeutic conditions, at both population and single-cell levels, which is invaluable in understanding RGC pathophysiology and identifying functional biomarkers for diverse optic neuropathies

CONTROL ID: 3712551

SUBMITTER (NAME ONLY): Sachin Rajpal

TITLE: Evaluation of Patient Acceptance for Visual Field Testing with a Wearable Device

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rajpal, Ophthalmology, Howard University Hospital, Washington, District of Columbia, UNITED STATES|M. Durbin, PhD, A. Nicklin, OD, B. Spencer, V. Lopez, S. Sanchez, M. Abou Shousha, MD, PhD, Heru, Inc, Florida, UNITED STATES|R. Sanchez, D. Williams, OD, C. Tagayun, MD, See Clearly Vision, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current methods of ophthalmic exams can be cumbersome, time consuming, and a burden to administer. This study was performed to evaluate acceptability of a software application on a virtual reality/augmented reality headset. If users and patients accept such tools, they may ultimately lead to increased patient satisfaction and workflow.

Methods: A cross-sectional study was performed at a single center, 5-physician ophthalmology practice in the greater Washington D.C. area. The testing was administered by three technicians to 73 patients all of whom were surveyed. The survey included 18 questions, 13 of which used a Likert scale for answers (strongly disagree to strongly agree). Patient data was deidentified and no patients were excluded.

Results: Of patients who have had experience with other perimeters, 88.5% of patients preferred this device to the gold standard Humphrey Visual Field for visual field testing. 89% of patients would recommend this device to other people compared to 1% [1 individual] who would not [7 patients remained neutral]. 84.9% of patients voted the Heru personality was very helpful in guiding them on how to perform the test compared to 11% [8 patients] who voted somewhat helpful and 4.1% [3 patients] who voted neutral. 93% of appointments had a shorter duration as gauged by technicians due to the implementation of the device.

Conclusions: This device was well received by the patients, technicians, and physicians at this practice. By maximizing effectiveness with time management, ease of use, and consistent patient engagement this device meets many goals of healthcare delivery. Although there are limitations to this study, it is likely that this device will be useful in a variety of clinical settings including larger volume clinics, possibly even at home testing in the future.

CONTROL ID: 3712555

SUBMITTER (NAME ONLY): Jihye Kim

TITLE: Does age modify the relation between genetic predisposition to glaucoma and various glaucoma traits in the UK Biobank?

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Aschard, Institut Pasteur, Paris, Île-de-France, FRANCE|J. Kang, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|J.L. Wiggs, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Khawaja, NIHR Barts Biomedical Research Centre, London, London, UNITED KINGDOM|L.R. Pasquale, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|J. Kim, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine whether associations between a glaucoma polygenic risk score (GPRS) and various glaucoma traits is modified by age.

Methods: We included UK Biobank participants with demographic information, genetic data, and various glaucoma trait data: intraocular pressure (IOP; n=118,153), macular retinal nerve fiber layer (mRNFL; n=42,132), macular ganglion cell inner plexiform layer (mGCIPL; n=42,042), and prevalent glaucoma status (n=192,283). We generated a GPRS for each individual using 2,673 genetic variants and their estimated effect sizes reported by a recent multi-trait genomic analysis. To assess modification by age of the relation between GPRS and glaucoma traits, we used multivariable linear regression for IOP, mRFNL, and mGCIPL; multivariable logistic regression for prevalent glaucoma risk; and analyzed the associations by age quartiles (Q1: <51, Q2: 51-57, Q3: 58-62, and Q4: ≥63 years), with tests for interactions. All analyses were adjusted for age, age2, sex, ethnicity, social deprivation, body mass index, blood pressure, diabetes, cardiovascular disease, spherical equivalent, and various lifestyle factors. We also sub-stratified interaction effects of GPRS and age for each glaucoma trait by sex.

Results: For IOP and glaucoma, interactions between GPRS and age were significant (P-interactions<2.3e-4). The association between the GPRS and IOP increased with age (mean differences in IOP (mmHg) per standard deviation (SD) of GPRS = 0.95, 1.03, 1.18, and 1.24 for 1st, 2nd, 3rd, and 4th quartile of age; P<2.5e-25). Similar trends were observed with glaucoma risk (odds ratio per SD of GPRS = 2.39, 2.58, 2.80, and 2.75 for 1st, 2nd, 3rd, and 4th quartile; P≤0.001). However, for mRNFL or mGCIPL, we did not observe any interactions between GPRS and age (P-interactions>0.05). We observed that the interactions of GPRS and age were significant (P-interaction<0.02) within each sex stratum, with no differences by sex (P-interaction of PRS, age, and sex = 0.70 for IOP and 0.68 for glaucoma).

Conclusions: A glaucoma genetic predisposition score was more strongly associated with higher IOP and greater glaucoma prevalence in older versus younger adults in the UK Biobank. These data may inform how to prioritize glaucoma screening in genetically predisposed individuals.

CONTROL ID: 3712556

SUBMITTER (NAME ONLY): Lincoln Shaw

TITLE: Interaction of Metformin and Other Medications in Reducing the Risk of Age-Related Macular Degeneration in a Diabetic Cohort

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Shaw, A. Blitzer, S. Khanna, S. Amin, S. Hariprasad, D. Skondra, Department of Ophthalmology & Visual Science, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|M. Hyman, S. Ham, J. Soo, A. Flores, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our group recently found that metformin protects against the development of age-related macular degeneration (AMD) in a large case-control study. The purpose of this subgroup analysis is to assess the interaction of metformin and other medications in protecting against the development of AMD in diabetic patients.

Methods: This is a case-control study analyzing data from a large health insurance claims database. In our prior study, subjects aged 55 years and over and with a new diagnosis of AMD were included as cases and were matched 1:1 with controls. This study is a subgroup analysis of diabetic cases compared to diabetic controls from the initial matching process. An adjusted regression model was used to identify interactions among diabetics taking metformin and other commonly prescribed medications divided into 5 categories: insulin, sulfonylureas, glitazones, other diabetic medications (exenatide, sitagliptin, or pramlintide), and statins.

Results: 81,262 cases were identified compared to 79,497 control subjects. Analysis revealed an independent protective effect against AMD development with the use of metformin (OR 0.95 [CI 0.93-0.97], $p < 0.001$), insulin (OR 0.92 [0.90-0.95], $p < 0.001$), and sulfonylureas (OR 0.94 [0.92-0.96], $p < 0.001$). When used in combination with metformin versus neither medication, insulin (OR 0.89 [CI 0.83-0.97], $p = 0.004$) and sulfonylureas (OR 0.91 [CI 0.84-0.98], $p = 0.01$) demonstrated a protective effect as well. Subjects taking insulin or sulfonylureas alone had a similar risk of developing AMD as those taking metformin alone (OR 0.96 [CI 0.89-1.01] and OR 0.98 [CI 0.90-1.05), respectively). Those taking other diabetic medications (exenatide, sitagliptin, or pramlintide) were at higher risk of developing AMD (OR 1.08 [CI 1.05-1.11], $p < 0.001$), although when taken with metformin the increased risk was no longer demonstrated (OR 1.04 [CI 0.97-1.13]). Lastly, subjects taking sulfonylureas with metformin demonstrated a further decreased risk of AMD development compared to those taking metformin alone (OR 0.94 [CI 0.91-0.97], $p < 0.001$).

Conclusions: Our results suggest that metformin, insulin, and sulfonylureas are protective against the development of AMD in diabetic patients. Other diabetic medications may place diabetics at a higher risk of developing AMD, but this risk is alleviated when taken in combination with metformin.

CONTROL ID: 3712557

SUBMITTER (NAME ONLY): ERIN ONG

TITLE: Nasal Paracentral Corneal Melt Associated with Bacterial Dacryocystitis

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. ONG, A. Serrano, D.T. Tse, E.C. Alfonso, C.L. Karp, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|S.C. Pflugfelder, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe six patients presenting with central or nasal paracentral sterile corneal melts in which dacryocystitis was felt to be a risk factor for keratolysis in all cases.

Methods: The medical records of six patients presenting to the Bascom Palmer Eye Institute with non-infiltrated central or nasal paracentral corneal melts and concurrent dacryocystitis.

Results: All patients presented with central or nasal epithelial defects, stromal ulceration, or corneal perforations. All corneal melts were focal and lacked a culture-positive stromal infiltrate. Dacryocystitis was a concurrent diagnosis in all cases. The cultures of the lacrimal sac drainage were positive for Staphylococcus aureus, Streptococcus sp., Pseudomonas aeruginosa, and Propionibacterium acnes. Three patients with corneal perforation required surgical management. The corneal pathology stabilized after treatment of the dacryocystitis.

Conclusions: Nasal or paracentral corneal melts may be associated with an underlying chronic dacryocystitis, suggesting that inflammatory mediators and impaired tear outflow in the setting of bacterial dacryocystitis may create a favorable environment for keratolysis. Prompt management of the lacrimal drainage system infection can lead to stabilization or resolution of the keratolytic process.

CONTROL ID: 3712558

SUBMITTER (NAME ONLY): Tonatiuh Garcia Ruiz

TITLE: Retinal ex vivo live imaging indicates microglia interaction with synaptic sites in experimental glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Garcia Ruiz, A.K. Yu, J. Hyer, L. Della Santina, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the CNS, microglia have been shown to be important for synaptic pruning during development but its role during neurodegenerative processes is not well understood. Our previous work demonstrates that after intraocular pressure (IOP) elevation, microglia proliferate, activate, and increase their colocalization with synapses. Here we use live imaging to record microglia movement and their interaction with retinal ganglion cell (RGC) post-synaptic puncta in the inner plexiform layer (IPL).

Methods: Adult Cx3cr1-GFP mice had one eye undergo laser-induced ocular hypertension, a model in which IOP is transiently elevated and returns to baseline by 7 days. Prior to IOP elevation, some animals underwent intravitreal injection with AAV-PSD95-RFP, resulting in RGCs that express fluorescently labelled post-synaptic puncta. Contralateral eye served as control. Animals were euthanized 7 days post-laser. Time-lapse z-stack images of ex vivo retina was acquired with a spinning disk confocal every 30 seconds for a total of ten minutes. Statistics were performed using Student’s t-test.

Results: After IOP elevation, IPL microglia increase in number and exhibit morphological change consistent with activation. Increased movement is seen in the microglia from the lasered eye, where there is active filament displacement, extension, and retraction. In response to IOP elevation, microglia show greater process displacement length (2.14 um in laser (SE=0.45) vs. 0.79 um in control (SE=0.19); P=0.03) and faster process speed in the lasered (0.01 um/s; SE=0.005) in comparison to control (0.002 um/s; SE= 0.0005; P=0.02). Microglia contact with PSD95 is seen in both control and lasered eye. However, microglia in the control eye exhibit less process displacement and motility, and furthermore, microglia contact with PSD95 is more superficial in the control condition. In contrast, after IOP elevation activated microglia appear to have engulfed PSD95.

Conclusions: Activated microglia increase their motility, survey their environment, and possibly engulf synaptic proteins. Whether this activity is neuroprotective or neurodegenerative remains a subject of ongoing study.

CONTROL ID: 3712559

SUBMITTER (NAME ONLY): Weijie Lin

TITLE: Progression of Keratoconus in a Pediatric Population

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.V. Lin, G. Rand, D. Trief, L.H. Suh, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine risk factors for progression of keratoconus in a pediatric cohort

Methods: Retrospective consecutive series of keratoconus pediatric patients seen by cornea specialists at the department of ophthalmology at Columbia University Medical Center from February 2015 to September 2020 were included. Mann Whitney U tests and Fisher exact tests were carried out to identify risk factors for progression of keratoconus. Subgroup analysis of older (>14 years of age) pediatric patients was carried out. Advanced keratoconus was defined as a pachymeter measurement of <400um in at least one eye.

Results: Of the 33 included pediatric patients, 7 met the definition of advanced keratoconus. Of the advanced keratoconus patients, age, sex, and reported seasonal allergies were not statistically significant. 4 out of 10 patients of the age <14 cohort presented with advanced keratoconus, compared with 3 out of 20 patients in the age >14 group ($p = 0.161$). The median income of the zip codes of these patients showed a trend (although did not reach statistical significance) of lower incomes in the advanced keratoconus group ($52,200 vs $76,200) ($p = 0.074$). 21 patients showed progression by their second visit. No statistically significant differences were found between the group (in terms of age, sex, and presence of reported allergies) that showed progression and the group that did not. The Kmax value for those that progressed by the second visit was statistically significantly higher (61.8) than the patients who did not progress by the second visit (55.0, $p = 0.042$).

Conclusions: Cross linking treatment for keratoconus is currently approved for age >14 years but not for the very young pediatric population. In our study,here was a non-statistically significant trend for patients of age <14 and for patients from lower income zip codes to present more frequently with advanced keratoconus. The majority of patients progressed by their second visit. Kmax values were shown to be statistically significantly different in the group that showed progression by the second visit Although our retrospective data collection had a limited number of patients, our data suggests that risk factors for presenting with advanced keratoconus may include coming from an area of lower median income, which may be an important factor to note as a social determinant of health.

CONTROL ID: 3712564

SUBMITTER (NAME ONLY): Maryam Ghiassi

TITLE: TNFa and other Select Cytokines in Patients with Intermediate Age-Related Macular Degeneration (iAMD)

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ghiassi, B.D. Wagner, A. Palestine, N. Mandava, A.M. Lynch, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age related macular degeneration (AMD) is a leading cause of blindness worldwide. The disease affects the local microenvironment of photoreceptors and retinal pigment epithelium causing an irreversible cell loss and subsequent decline in vision. It has been shown by our group that patients with iAMD have significantly altered levels of several inflammatory biomarkers, including complement factors and CCLx chemokines, in cases with iAMD compared to control patients without AMD. Building on this research that supports a role for systemic inflammation in patients with iAMD, we embarked on this study to compare levels of plasma cytokines namely, TNFa, IL-6. IL-8, IL-1ra, IL-4, and VEGF in patients with iAMD compared to controls with no AMD.

Methods: Patients with iAMD who were part of the University of Colorado IRB approved AMD registry were included in this study. Imaging studies and blood plasma samples were obtained from both iAMD and control patients. Cases and controls were defined using the Beckmann classification and multimodal imaging. The cytokine analysis was conducted using current established laboratory protocols. Wilcoxon rank-based tests were used to compare cytokine levels between the two groups.

Results: There were 211 patients with iAMD and 100 controls. The iAMD and control groups were comparable in smoking status, BMI, hypertension, cardiac and vascular disease. We found TNFa levels to be significantly higher in cases with iAMD compared to control patients ($P<0.01$). Levels of IL-6, IL-8, IL-1ra, IL-4 and VEGF levels did not differ between cases and controls (Table-1).

Conclusions: Patients with iAMD had higher levels of TNFa, a key regulator of the inflammatory response, compared with controls. TNFa is produced by macrophages, monocytes and other cells and has been shown to have direct effects on retinal pigment epithelial cells including induction of complement expression and up-regulation of VEGF production. These findings support our hypothesis that systemic inflammatory markers can distinguish patients with and without iAMD. Serum TNFa levels can potentially be used as a biomarker to identify high risk patients with iAMD.

CONTROL ID: 3712565

SUBMITTER (NAME ONLY): Amy Schefler

TITLE: Morphological Biomarkers Related to Visual Acuity in Patients with Radiation Retinopathy Treated with Intravitreal Ranibizumab

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Schefler, Ophthalm, Houston Methodist, Houston, Texas, UNITED STATES|A.C. Schefler, S. Trejo, H. Yu, C. Moore, Ophthalmology, Retina Consultants of Texas, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Radiation therapy is an effective treatment for a variety of ocular cancers, yet these radiotherapies can damage the retina, resulting in radiation retinopathy (RR) 6 months to 3 years post-radiation. In this post-hoc analysis[ST1] , we monitor and investigate retinal morphological outcomes via spectral-domain optical coherence tomography (SD-OCT), slit lamp, and/or direct ophthalmoscope to identify the most relevant biomarkers related to visual acuity.

Methods: Forty eyes with active RR were randomly assigned to cohorts A, B, and C for intravitreal ranibizumab (RBZ, 0.5 mg) treatment: (A) monthly RBZ injections for 48 weeks (n = 8), (B) monthly RBZ injections for 48 weeks plus targeted retinal photocoagulation to areas of peripheral retinal ischemia one week after the initial RBZ injection (n = 16), or (C) three consecutive monthly ranibizumab injections followed by as needed monthly RBZ injections (n = 16). At week 52, all cohorts entered a standardized treat-and-extend regimen until week 104. Best-corrected visual acuity and qualitative and quantitative SD-OCT parameters were assessed by frequency, univariate, multiple linear regression, and mixed model analyses.

Results: There was a significant difference in the presence of retinal hemorrhages at week 24, 48, 72, and 104 ($P < 0.0001$) and hard exudates at week 48 ($P = 0.016$) from baseline. A significant difference in the percentage of patients with neovascularization was found between cohorts ($P = 0.003$); cohort C had a significantly higher mean percentage of incidences of neovascularization (14.4%) compared to both cohorts A (0%) and B (4.01%). No significant differences were found between cohorts for the other graded parameters. Intraretinal cyst vertical size ($P < 0.001$) and EZ disruption ($P = 0.029$), were found to be most relevant to visual acuity due to their correlation with visual acuity by univariate analysis, with their significance confirmed in the mixed model ($P = 0.001$) and multiple linear regression model ($P = 0.01$), respectively.

Conclusions: This study helps characterize the course of vision in patients with RR by confirming the relevance of intraretinal vertical cyst size and EZ disruption as morphological biomarkers of poor visual acuity from prior studies. Larger, multicenter studies are needed to fully understand and monitor morphological changes affecting visual acuity changes in RR.

CONTROL ID: 3712569

SUBMITTER (NAME ONLY): Andrew Shin

TITLE: The Accuracy and Repeatability of Biomechanical Measurements using the Brillouin Optical Scanner System (BOSS^{TM})

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Shin, C.S. Barnes, D. Chernyak, Intelon Optics, Lexington, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Andrew Shin: Commercial Relationship(s);Code E (Employment):Intelon Optics | Claire Barnes: Commercial Relationship(s);Code E (Employment):Intelon Optics | Dimitri Chernyak: Commercial Relationship(s);Code E (Employment):Intelon Optics

ABSTRACT BODY:

Purpose: Using Brillouin-scattering theory, the BOSS measures miniscule changes in the wavelength ('frequency shift') of laser light reflected back from an object, such as the cornea or crystalline lens. The measured frequency shift correlates with the material's stiffness, that is, its "longitudinal elastic modulus". In this study, BOSS measurements from water, plastic and porcine eyes were performed to investigate the data accuracy and repeatability.

Methods: A polystyrene cube filled with water was placed on the chinrest. Ten Brillouin frequency-shift measurements were made at each of 5 different positions of the cube, producing 50 Brillouin images for both water and plastic. Five individual old (5 months) and young (8 weeks) porcine eyes were obtained and mounted on a custom setup. In the lens experiment, 3 replicate scans were performed per lens, from the anterior to posterior lens though a single point. Three cornea exams were also performed on each porcine eye, with depth scans at 7 locations around the entire cornea.

Results: In the water and polystyrene experiment, the measured Brillouin frequency shifts were within 0.45% and 0.26%, respectively, of the formulated theoretical values and the coefficient of variation (CV) values were 0.4% and 0.3%, respectively, thus demonstrating exceptional accuracy and repeatability. In the porcine-eye lens experiment, the CV was 1.2% for the old eyes and 1.4% for the young eyes. The Brillouin stiffness of the old lenses (4.007±0.047 GPa) was significantly greater than that of the young lenses (3.699±0.051 GPa, P=0.0002). In the porcine cornea experiments, CV values of 1.0% and 1.4% were obtained for the old and young cornea samples, respectively.

Conclusions: The BOSS measured the biomechanics of various materials, including corneas and lenses, with high precision and repeatability. Consistent with the fact that the crystalline lens becomes harder with aging, this study showed greater Brillouin stiffness in old porcine eyes than in young. Based on the proven measurement accuracy and repeatability, there are many possible applications for biomechanical properties: diagnosis of ophthalmic disorders, such as keratoconus; providing reference parameters for cataract or refractive surgeries; and functioning as a tool to prove the efficacy of newly developed medicines such as lens-softening drugs for presbyopia.

CONTROL ID: 3712570

SUBMITTER (NAME ONLY): Minal patil

TITLE: Optical coherence tomography angiography in various types of amblyopia in an Indian pediatric cohort.

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. patil, Pediatric Ophthalmology, Drishti Eye Institute, Dehradun, Uttarakhand, INDIA|S. Luthra, Retina Department, Drishti Eye Institute, Dehradun, Uttarakhand, INDIA|G. Luthra, Cataract and refractive surgery department, Drishti Eye Institute, Dehradun, Uttarakhand, INDIA|

Commercial Relationships Disclosure: Minal patil: Commercial Relationship: Code N (No Commercial Relationship) | Saurabh Luthra: Commercial Relationship: Code N (No Commercial Relationship) | Gaurav Luthra: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the superficial and deep macular vessels density in various types of amblyopia in a pediatric cohort and to compare it with fellow and age-matched control eyes.

Methods: In this prospective cross sectional study,20 subjects each anisometropic (AA) and strabismic amblyopia (SA),31subjects of bilateral isometropic amblyopia (BA),in the age group of 3-15years and 21 age-matched controls of were included.Subjects with history of nystagmus, ocular surgery and retinal pathology were excluded.Macular vessel density (VD) in superficial and deep capillary plexus(SCPandDCP) in foveal,parafoveal region and the four quadrants(temporal, superior,nasal,inferior) were measured by optical coherence tomography angiography (OCTA AngioVue version 2018.0.0.18).VD in amblyopia eyes were evaluated and compared with fellow and control eyes.In BA group, right eyes were included for comparison. Foveal avascular zone(FAZ) was evaluated in amblyopia eyes and compared with fellow and control eyes.

Results: The mean SCP VD and DCP VD in foveal region (in the order AA , SA, BA, control) were 22.85±1.3, 22.53±8.3,23.9±7.8,21.97±7.6 and 36.33±7.7,39.25±10.8,37.77±8.4,35.77±8.9 respectively which did not differ between amblyopic eyes and control eyes ($p > 0.05$).

The mean SCP VD and DCP VD in parafoveal region (in the order in AA, SA, BA,control) were 51.03±4.2, 52.26±.9, 52.54±4.2, 53.96±2.5 and 53.55±3.7, 54.48±4.3, 54.34±5.5, 55.91±4.8 respectively.

In AA eye, the SCP and DCP VD in parafoveal region were reduced as compared to control eyes ($p<0.05$) however only the superior and nasal quadrant of SCP in parafoveal region showed reduced VD ($p <0.05$).

In SA eye the SCP VD in parafoveal region was reduced when compared with control eyes ($p<0.05$) in addition only the superior and inferior quadrant showed reduced VD ($p<0.05$). DCP VD in SA eye did not differ from control eyes.($p> 0.05$) Macular VD were similar in BA and control eyes($p>0.05$).

Area of FAZ showed no difference in any type of amblyopia and control eyes. When compared with fellow eye, AA eye showed reduced VD in SCP in parafoveal region and nasal quadrant ($p<0.5$) and SA showed no difference in macular VD in SCP and DCP($p>0.5$).

Conclusions: Of all the amblyopia, the anisometropic amblyopia children showed significant reduction in macular vessel density which can signify structural retinal involvement however needs a prospective study with larger sample size.

CONTROL ID: 3712571

SUBMITTER (NAME ONLY): Glenn Yiu

TITLE: Rhesus macaques with soft drusen share susceptibility genes with age-related macular degeneration in humans.

SESSION TITLE: AMD Translational Research

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Yiu, L. Huynh, K.P. Roszak, A. Moshiri, S.M. Thomasy, University of California Davis, Davis, California, UNITED STATES|J. Wang, Y. Li, R. Chen, Baylor College of Medicine, Houston, Texas, UNITED STATES|K. Choy, S. Farsiu, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nonhuman primates are the only mammals that possess a macula and exhibit soft drusen similar to those in human age-related macular degeneration (AMD). Here, we explored if aged rhesus macaques with soft drusen share similar susceptibility genes as human AMD.

Methods: We performed whole exome sequencing from 15 unrelated rhesus macaques from the California National Primate Research Center (CNPRC) with soft drusen identified on color fundus photography (CFP) and spectral domain-optical coherence tomography (SD-OCT), and compared with sequence data from a reference cohort of more than 1,800 rhesus macaques from various primate research centers. Variants falling within the exons of the orthologues of 34 candidate genes identified from genome wide association studies (GWAS) for human AMD were identified.

Results: Bilateral soft drusen were identified in 15 rhesus macaques with clinical exam, CFP, and SD-OCT. The mean number of macular soft drusen per eye was 25 +/- 31, with no evidence of advanced AMD features such as choroidal neovascularization or geographic atrophy in any study animal. Among genes associated with human AMD, we identified 6 new variants within 4 genes including COL4A3, TGFBR1, ADAMTS9, and CFH that are associated with soft drusen in macaques. All 4 of these genes are expressed in the retinal pigment epithelium (RPE). Although none of these novel variants correspond to human orthologues associated with progression to advanced AMD in humans, such as the well-characterized CFH Y402H variant, one identified variant in CFH appears to correspond to a critical binding position for C3b. Some variants such as those in TGFBR1 and ADAMTS9 also appear to be associated with drusen size and number in this cohort of animals.

Conclusions: Rhesus macaques with soft drusen share some susceptibility genes as those in human AMD including CFH, but not variants associated with progression to advanced AMD, consistent with the absence of advanced AMD features in this nonhuman primate model.

CONTROL ID: 3712572

SUBMITTER (NAME ONLY): Shilpa Kodati

TITLE: The Gut Microbiome in Ocular Inflammatory Diseases

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kodati, J. Lee, M. Maclean, P. Sherry, P.R. Nath, H. Lin, H. Sen, National Eye Institute, Bethesda, Maryland, UNITED STATES|C. Simpson, J. Jacobs, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Shilpa Kodati: Commercial Relationship: Code N (No Commercial Relationship) | Carra Simpson: Commercial Relationship: Code N (No Commercial Relationship) | Jung Lee: Commercial Relationship: Code N (No Commercial Relationship) | Mary Maclean: Commercial Relationship: Code N (No Commercial Relationship) | Patti Sherry: Commercial Relationship: Code N (No Commercial Relationship) | Pulak Nath: Commercial Relationship: Code N (No Commercial Relationship) | Henry Lin: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Jacobs: Commercial Relationship: Code N (No Commercial Relationship) | H Nida Sen: Commercial Relationship(s);Code E (Employment):Janssen Retina

ABSTRACT BODY:

Purpose: The contributory role of the microbiota to the development of autoimmune diseases has emerged in recent years including in mouse models of uveitis. However, less is known regarding the microbiota in uveitis patients. The purpose of this study is to investigate alterations in bacterial diversity and microbiota composition between healthy volunteers and patients with non—infectious uveitis as well as evaluate longitudinal changes in uveitis patients.

Methods: An observational, prospective single center study was conducted at the National Eye Institute, National Institutes of Health, enrolling patients with non-infectious uveitis and healthy volunteers. Stool samples were collected using a standardized stool sampling kit and samples analyzed using 16S ribosomal RNA sequencing. Participants also completed the Diet History Questionnaire (DHQ). Cross-sectional analyses included age, sex, BMI and diet as covariates.

Results: A total of 47 healthy volunteers and 55 patients with non-infectious uveitis were enrolled. Of those 55 uveitis patients, 34 patients were treatment naïve and longitudinal sampling was obtained from 12 patients. There were no significant differences in Alpha diversity, phylogenetic diversity, sample richness or bacterial abundances between uveitis patients and healthy volunteers. Similarly, on subgroup analysis, no significant differences in diversity measures were observed between active and quiet uveitis patients at baseline. However, patients with BCR had higher richness, alpha diversity, and phylogenetic diversity compared to other uveitis etiologies although this was not statistically significant. Differential abundance analyses revealed a significantly lower ($q < 0.001$) abundance of 15 bacterial amplicon sequence variants (ASV) in patients with quiet uveitis compared to active disease. Longitudinal cohort analysis showed that microbiota richness decreased with change in disease activity from active to quiet (coefficient = -56.81, $p = 0.038$).

Conclusions: Our preliminary results suggest that there are differences in the microbiota between active and inactive uveitis as well as longitudinal differences as disease activity changes. Further work is required including with metagenomics to validate these observations.

CONTROL ID: 3712573

SUBMITTER (NAME ONLY): Asik Pradhan

TITLE: Assessment of crystalline lens shape during accommodation using IOLMaster 700 B-scan images

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pradhan, R. Hughes, E. Pieterse, D.A. Atchison, S. Vincent, S. Read, A. Carkeet, Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|A. Pradhan, R. Hughes, E. Pieterse, D.A. Atchison, S. Vincent, S. Read, A. Carkeet, Centre for Vision and Eye Research, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The Zeiss IOLMaster 700® biometer offers image-based axial measurement of eye structures together with visualisation of the anatomical details in a longitudinal section. We aimed to analyse these B-scan images to determine crystalline lens shape changes induced by accommodation.

Methods: IOLMaster 700 B-scan images were acquired from 10 children (age: mean 11.1, SD 0.4 years) during 0D and 6D accommodation tasks. Scans were analysed using custom MATLAB software to determine the curvature measurements for anterior and posterior cornea and lens surfaces. The process involved segmenting the image to locate the corneal and lens surfaces (Figure 1), correcting for existing distortions in the image to reconstruct ray path distance maps, and using the maps with ray tracing to determine surface positions. Second order polynomials were fit to the surfaces to compute radii of curvature.

Results: The radius of curvature decreased significantly with accommodation for the anterior lens ($t_8 = 5.93$, $p = 0.0003$) (0D accommodation: mean 13.26mm, SD 2.19mm; 6D accommodation: mean 8.87mm, SD 0.94mm) but not for posterior lens ($p > 0.05$) (0D accommodation: mean -5.62mm, SD 0.64mm; 6D accommodation: mean -5.11mm, SD 0.52mm), nor for anterior and posterior cornea. Results for all surfaces are shown in Figure 2 with data for one image (6D accommodation) discarded due to eye movement artefacts.

Conclusions: This is a novel analysis of the data contained in IOLMaster 700 images. The measured changes in both anterior and posterior lens surface curvature were comparable to previous studies that demonstrate its potential of measuring lens shape during accommodation. Because of the wide availability of IOLMaster 700, this may be a useful research tool for studying crystalline lens shape. Further research is required to establish repeatability and accuracy of the technique.

CONTROL ID: 3712575

SUBMITTER (NAME ONLY): Daniel Chavez Velazquez

TITLE: Response to antiangiogenic treatment with mitomycin-C in corneal neovascularization

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Chavez Velazquez, K.M. Arteaga-Rivera, A.L. García-Terrazas, J. Guerrero, C.A. Muller Morales, A. Ramírez-Miranda, A. Navas, E.O. Graue-Hernandez, Cornea, External Diseases and Refractive Surgery, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: Maintaining transparency and avascularity is essential to preserve optimal vision. The administration of mitomycin-C (MMC) has been used intravenously for a hypoxic and embolic effect. This study aims to describe clinical outcomes of intravascular MMC for the treatment of corneal neovascularization.

Methods: A pilot study of 8 eyes with corneal neovascularization injection 0.1ml of MMC. Quantification of neovascularization was measured by an independent observer. ImageJ software (NIH, Bethesda Maryland) was used to trace and quantify vasculature in standardized clinical slitlamp photographs. Briefly all identifiable vessels were drawn upon and the number of pixels quantified. Each image was measured 3 times. Follow-up was done at 1 week, 1 month and 2 months post-injection. Preop and postop values were compared using t-test and statically significant value was set at $p < 0.5$.

Results: A total of 8 subjects were enrolled, of which 37.5% were female with an age range of 17-64 years (average of 37 years). In 62.5% of the cases the left eye was affected. The most frequent etiology responsible for the corneal vascularization was history of herpetic keratitis in 75% of the subject, phlyctenular keratoconjunctivis in 12.5%, and neovascularization secondary to intrastromal rings in 12.5%. One subject 12.5% presented herpes keratitis reactivation 7 days after injection, despite being on oral antiviral suppression therapy. Mean preoperative UDVA was 1.01 (+ 0.42), CDVA was 0.76 (+0.53) LogMAR. Postoperative UDVA was 0.91 (+0.42) and CDVA was 0.63 (+0.42) LogMAR with no statistically significant differences when preop and postop values were compared $p>0.05$. Two patients improved both UDVA and CDVA. Comparing photographs, there was an overall reduction of 60.27% of pixels in corneal vascularization at the las follow-up.

Conclusions: Corneal intrastromal MMC may be a potential therapeutic strategy to treat corneal neovascularization. Here we present short term results demonstrating that neovascularization may be reduced with clinically significant results, thus rendering this patients more suitable for optical surgical procedures. Despite regression of neovascularization visual acuity may not improve particularly if stroma is scarred. Further studies are needed to address its safety and long-term effects.

CONTROL ID: 3712576

SUBMITTER (NAME ONLY): Zhong-Lin Lu

TITLE: Predicting contrast sensitivity functions with digital twins generated by Hierarchical Bayesian modelling

SESSION TITLE: Machine Learning and Big Data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Lu, Division of Arts and Sciences, New York University Shanghai, Shanghai, Shanghai, CHINA|Z. Lu, Y. Zhao, Center for Neuroscience, New York University, New York, New York, UNITED STATES|L.A. Lesmes, M. Dorr, Adaptive Sensory Technology, Inc., San Diego, California, UNITED STATES|

Commercial Relationships Disclosure: Zhong-Lin Lu: Commercial Relationship(s);Code I (Personal Financial Interest):Adaptive Sensory Technology, Inc., Juehua Medical Technology, Ltd;Code P (Patent):Adaptive Sensory Technology, Inc., Juehua Medical Technology, Ltd | Yukai Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Luis Lesmes: Commercial Relationship(s);Code E (Employment):Adaptive Sensory Technology, Inc.;Code I (Personal Financial Interest):Adaptive Sensory Technology, Inc.;Code P (Patent):Adaptive Sensory Technology, Inc. | Michael Dorr: Commercial Relationship(s);Code E (Employment):Adaptive Sensory Technology, Inc.;Code I (Personal Financial Interest):Adaptive Sensory Technology, Inc.;Code P (Patent):Adaptive Sensory Technology, Inc.

ABSTRACT BODY:

Purpose: We developed a hierarchical Bayesian model (HBM) based on repeated measures of contrast sensitivity functions (CSF) obtained across three luminance conditions (Zhao et al., 2021). Here we use the HBM, which extracts covariant features within and between individuals and luminances, to generate digital twins for contrast sensitivity (CS) and predict yet-observed results.

Methods:

The HBM describes CS across a hierarchy of population, individual, and luminance, with hyperparameters at population/individual levels that quantify the covariant relationship between CS parameters (peak gain, peak spatial frequency, and bandwidth) across individuals and luminances. We evenly split 112 subjects in Hou et al. (2016) into Group I (N=56), in which CSF data included three luminances, and Group II (N=56), in which partial data from 0, 1, or 2 luminances were used to train and predict data observed in non-included conditions. Parameter uncertainty was quantified by half-width confidence intervals (HWCI), with smaller HWCI indicating higher model precision.

Results:

Group I data exhibited an average HWCI of 0.061 log10, which was expected to be lower than Group II, for which HWCIs decreased (from 0.101 to 0.089 and 0.084) as the number of training conditions increased (from 0 to 1 and 2). The mean absolute error of Group II predictions likewise decreased from 0.048 to 0.036 and 0.034. HBM predictions accounted for 77% and 83% of the variance of observed AULCSF values, using 1 or 2 luminances. Fig. 1 presents the example of one subject, with observed estimates for peak gain and peak frequency (left; top row), and CSF with confidence intervals (right, top row), in addition to digital twin predications for different training conditions (2^{nd}-4^{th} row). When predictions were used to seed analysis of the observed data, only 30-60% of the data collection was needed to reach the accuracy and precision of original analyses.

Conclusions: The HBM for contrast sensitivity extracted valuable information about covariant features within and between individuals and luminances. The HBM enabled the generation of digital twins for CS that predict yet-observed data, significantly reduces testing burden, and exhibits potential for improving real-world testing of functional vision.

CONTROL ID: 3712577

SUBMITTER (NAME ONLY): Kenny Nguyen

TITLE: The ophthalmology clinic as a gateway: Patients new to an academic ophthalmology clinic and the subsequent utilization of care with other healthcare providers within the health system

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Nguyen, A. Sun, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|M. Chen, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|M. Chen, University of Colorado Department of Ophthalmology, Denver Health Medical Center, Denver, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Kenny Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Ashley Sun: Commercial Relationship: Code N (No Commercial Relationship) | Michael Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Referrals generated from primary care networks have been shown to provide a multiplier effect in contributing value to the larger health system, but there have been few studies on the downstream effects of referrals generated from specialty clinics. We aimed to investigate the impact of an academic ophthalmology clinic on the larger health system by performing a cross-sectional retrospective study to analyze the subsequent utilization of care with other outpatient providers within the system following the initial visit.

Methods: Appointment records of patients aged 18 years and older who had a scheduled new appointment with an attending ophthalmologist at Penn State Health (PSH) Medical Center between January 1, 2019 and December 31, 2019 were analyzed. The patients who showed for this appointment were included for analysis. Patients were considered “Already established with PSH” if they had seen an outpatient healthcare provider within PSH within 3 years prior to the date of the eye appointment, and “Not already established with PSH” if they had not seen an outpatient healthcare provider within PSH within 3 years prior to the date of the eye appointment. Of this latter group, appointment records were analyzed to determine if and which other outpatient healthcare providers within the PSH system the patient received care from within one year after the eye clinic visit. The Institutional Review Board at the Penn State Hershey Medical Center deemed this study to be exempt.

Results: Of the 4628 new patient appointments in 2019, 3869 patients (83.6%) showed for their appointment and were included for analysis. Within this group, 1178 (30.4%) were “Not already established with PSH.” Within this group, 344 (29.2%) went on to see another outpatient healthcare provider within PSH within 1 year after their eye clinic visit. The type of outpatient healthcare provider seen included: another optometrist or ophthalmologist (n=169, 49.1%), another medical specialty (n=154, 44.8%), pre-operative anesthesia (n=65, 18.9%), and primary care (n=14, 4.1%). Some of these patients saw providers in multiple categories.

Conclusions: An academic ophthalmology clinic can serve as a significant gateway for patients to other departments within the larger academic health system.

CONTROL ID: 3712578

SUBMITTER (NAME ONLY): Ruikang Wang

TITLE: Does outer retinal thickness represent another clinical biomarker for predicting geographic atrophy growth?

SESSION TITLE: AMD Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.K. Wang, Q. Zhang, Z. Chu, Y. Cheng, H. Zhou, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R.K. Wang, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|Y. Shi, M. Shen, W.J. Feuer, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether the outer retinal layer (ORL) thickness measurement could serve as a clinical biomarker to predict the annual square root enlargement rate (ER) of geographic atrophy (GA).

Methods: Eyes with GA secondary to age-related macular degeneration (AMD) were imaged over a 12-month span with swept-source OCT (PLEX® Elite 9000 (ZEISS, Dublin, CA)) using a 6 x 6 mm scan pattern. GA lesions were manually identified and measured using the en face sub-retinal pigment epithelium (RPE) OCT images, and GA annual square root ERs were calculated. ORL thickness was measured using segmentation boundaries that extended from the upper boundary of outer plexiform layer to the upper boundary of RPE layer using a validated semi-automatic segmentation software. At baseline visit, the ORL thickness were measured in different sub-regions around the GA (Fig.1).

Results: A total of 38 eyes from 27 subjects were included in this study. The same eyes were previously used to compute the correlation between GA growth and the measurements of choriocapillaris (CC) flow deficits (FDs) and RPE-Bruch's membrane (BM) distances[1,2]. A negative correlation was observed between the ORL thickness and the annual GA growth in all the sub-regions (Table 1). The ORL thickness immediately around GA showed the strongest correlation with the GA annual square root ERs ($r=-0.457$, $p=0.004$ for a 0-300 μm rim around the GA). No correlations were found between ORL thickness and the previously published CC FDs in any sub-regions, whereas a significant correlation was found between the ORL thickness and the RPE-BM distances in the region immediately around GA ($r=-0.398$, $p=0.013$).

Conclusions: ORL thickness measurements around the GA showed significant correlations with the annual GA growth, but a significant correlation was also found between the ORL thickness and the RPE-BM distances, suggesting that the ORL thickness and RPE-BM distances do not independently influence the growth of GA. Due to the challenges of segmenting the ORL, RPE-BM distance measurements and CC FDs are sufficient to serve as the clinical biomarkers to predict the annual ERs of GA.

1. Shi Y, et al. Am J Ophthalmol. 2021;224:321-331.

2. Chu Z, et al. Am J Ophthalmol. https://doi.org/10.1016/j.ajo.2021.10.032

CONTROL ID: 3712579

SUBMITTER (NAME ONLY): Johanna Seddon

TITLE: Association between Dysfunctional Complement Factor I (CFI) Rare Variant Status and Progression to Advanced AMD

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Seddon, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|B. Rosner, Channing Division of Network Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Java, J. Atkinson, Nephrology and Rheumatology, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Johanna Seddon: Commercial Relationship(s);Code C (Consultant/Contractor):Laboratoires Thea ;Code I (Personal Financial Interest):Gemini Therapeutics;Code I (Personal Financial Interest):Apellis Pharmaceuticals | Bernard Rosner: Commercial Relationship: Code N (No Commercial Relationship) | Anuja Java: Commercial Relationship(s);Code C (Consultant/Contractor):Alexion, Novartis | John Atkinson: Commercial Relationship(s);Code C (Consultant/Contractor):Celldex Therapeutics, Achillion Pharmaceuticals, Annexon;Code I (Personal Financial Interest):Compliment Corporation, Gemini, Q32BIO INC

ABSTRACT BODY:

Purpose: To evaluate the associations between dysfunctional CFI rare variant carrier status and progression to advanced age-related macular degeneration (AMD), geographic atrophy (GA) and neovascular disease (NV) in a prospective analysis.

Methods: Analyses were performed using the Seddon Longitudinal Cohort Study (SLCS) of AMD (N=2116 subjects, 3901 eyes, mean follow-up 8.3 years, 22% progression rate to advanced AMD, PMID 30389371) and the Age-Related Eye Disease Study (N=2837 subjects, 5200 eyes, mean follow-up 9.2 years, 18% progression rate to advanced AMD). CFI rare variants with low serum factor I levels and decreased function in a serum based assay (PMID's 24036952 and 32908800), and other common and rare genetic variants related to AMD, demographic and behavioral factors, and baseline and follow-up macular status were evaluated. To estimate the effect of rare dysfunctional CFI variant status on AMD progression, independent of other variants related to progression, odds ratios (OR) were calculated based on Generalized Estimating Equations. Interactions between CFI carrier status and other variants were determined.

Results: Among the 4953 subjects (9101 eyes) in the combined cohort, 1% were rare CFI variant carriers and 44% of the carriers progressed to overall AMD compared with 20% of non-carriers ($P < .0001$). For advanced AMD subtypes, 30% of carriers versus 10% of non-carriers progressed to GA ($P < .0001$), and 18% of carriers and 11% of non-carriers progressed to NV ($P=.049$) over a 12-year follow-up period. CFI carriers were more likely to have a family history of AMD (CFI variant: 36% with 1 family member affected and 14% with 2+ family members affected; no CFI variant: 19% with 1 family member affected and 8% with 2+ family members affected; P for trend =.035). CFI variant carrier status was associated with progression to GA (OR 1.91, 1.03-3.52) but not with NV (OR 0.96, 0.54-1.71), after adjustment for demographic and ocular factors and other genetic variants (Figure). CFI rare variant carrier status was associated with the common CFI (PMID 18685559) and hepatic lipase C (LIPC, PMID 20385826) genetic variants, but no significant interactions between CFI carrier status and other genetic variants were noted for progression to advanced AMD, GA or NV.

Conclusions: These new findings suggest that carriers of dysfunctional CFI rare variants are at higher risk for progression to GA.

CONTROL ID: 3712580

SUBMITTER (NAME ONLY): Yorishige Matsuda

TITLE: Investigation of the therapeutic effect of adrenomedullin on experimental autoimmune uveitis

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Matsuda, S. Kakihara, K. Hirabayashi, A. Imai, Y. Iesato, T. Murata, Shinshu Daigaku, Matsumoto, Nagano, JAPAN|Y. Matsuda, S. Kakihara, K. Hirabayashi, A. Imai, Y. Iesato, T. Sakurai, A. Kamiyoshi, Y. Ichikawa-Shindo, M. Tanaka, H. Kawate, Y. Zhao, T. Shindo, Shinshu Daigaku Daigakuin Igakukei Kenkyuka Igakubu, Matsumoto, Nagano, JAPAN|

Commercial Relationships Disclosure: Yorishige Matsuda: Commercial Relationship: Code N (No Commercial Relationship) | Shinji Kakihara: Commercial Relationship: Code N (No Commercial Relationship) | Kazutaka Hirabayashi: Commercial Relationship: Code N (No Commercial Relationship) | Akira Imai: Commercial Relationship: Code N (No Commercial Relationship) | Yasuhiro Iesato: Commercial Relationship: Code N (No Commercial Relationship) | Takayuki Sakurai: Commercial Relationship: Code N (No Commercial Relationship) | Akiko Kamiyoshi: Commercial Relationship: Code N (No Commercial Relationship) | Yuka Ichikawa-Shindo: Commercial Relationship: Code N (No Commercial Relationship) | Megumu Tanaka: Commercial Relationship: Code N (No Commercial Relationship) | Hisaka Kawate: Commercial Relationship: Code N (No Commercial Relationship) | Yunlu Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Toshinori Murata: Commercial Relationship: Code N (No Commercial Relationship) | Takayuki Shindo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Adrenomedullin (AM) is a bioactive peptide isolated from human pheochromocytoma. AM is mainly secreted by vascular endothelial cells and has various physiological functions such as anti-inflammatory, anti-apoptotic, and anti-oxidative stress effects. We have reported that AM is also produced in the eye and that exogenous administration of AM ameliorates the pathogenesis of diabetic retinopathy and age-related macular degeneration (Am J Pathol. 2017, 2021). Experimental autoimmune uveitis (EAU) is an experimental model of human autoimmune uveitis and serves to investigate the mechanism of uveitis and evaluate therapeutics for ocular inflammatory diseases. In the present study, we investigated the therapeutic effect of AM-administration on EAU model in mice.

Methods: Female C57BL/6J mice aged 8 weeks were used. To induce EAU, N-terminal peptide fragment of human interphotoreceptor retinoid-binding protein (hIRBP(1-20)) emulsified with complete Freund's adjuvant containing Mycobacterium tuberculosis H37Ra was subcutaneously injected at the base of tails. Subsequently, pertussis toxin was intraperitoneally injected. In the AM group, human recombinant AM was administered subcutaneously using osmotic pump at infusion rate of 29 μg/kg/day for 14 days. PBS was administered to the control group in the same manner. On day 14 after immunization, clinical scores were evaluated. According to the severity of inflammatory findings, clinical scores were classified into 4 categories (0-3) as previously reported, with some modifications. The clinical scores were evaluated by two ophthalmologists in a blinded manner, and the average of both eyes was used as the score for each mouse.

Results: No significant difference was found in the clinical score between AM-treated (2.00±0.42, n=8) and control groups (1.31±0.49, n=8).

Conclusions: In the present study, we could not confirm the therapeutic effect of AM- administration on the clinical score of EAU. Since anterior ocular lesions of EAU have a large variability among individuals, pathological examination including posterior ocular lesions would be necessary for more detailed evaluation. Furthermore, the therapeutic effects of higher concentrations of AM and intraocular AM-injection should be considered in the next study.

CONTROL ID: 3712581

SUBMITTER (NAME ONLY): Meghan Knizak

TITLE: Effect of tactile meta-guidance on visual perception in people with and without central vision loss

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Knizak, N. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P.J. Bex, J. Skerswetat, Northeastern University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Meghan Knizak: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Ross: Commercial Relationship(s);Code R (Recipient):Eschenbach Optik | Peter Bex: Commercial Relationship(s);Code F (Financial Support):PerZeption Inc.;Code P (Patent):Northeastern University | Jan Skerswetat: Commercial Relationship(s);Code F (Financial Support):PerZeption Inc.; Adaptive Sensory Technology;Code P (Patent):Northeastern University

ABSTRACT BODY:

Purpose: Previous studies have reported visual perception improvements in the space around an observer's hands in normally-sighted participants. We examined whether similar benefits, using tactile meta-guidance, occur in peripheral vision of patients with central vision loss (CVL) across a range of visual functions.

Methods: We tested the effect in three groups of 8 individuals: CVL (median age: 63 years, ±16σ), age-matched controls (63±6σ), and young controls (24±1σ). Inclusion criteria- CVL: acuity of 20/300 or better in the better seeing eye and bilateral central scotomas verified by microperimetry; age-matched and young controls; acuity of 20/20 in the better seeing eye and no comorbidities. FInD (Foraging Interactive D-prime) psychophysics were deployed to measure detection thresholds for contrast, color, motion coherence, pattern coherence, and threshold-versus-contrast. Each of three charts contained a 4*4 grid of 6° cells, a random subset of which contained stimuli of varying signal intensity, ranging from easy to difficult levels, and updated by an adaptive algorithm using the observer's responses on previous charts. Participants completed 2 sessions in random order, either with or without touching with the left hand's index finger each cell before moving on to the next cell. Planned pairwise comparison t-tests were used to test within group differences with and without meta-guidance for each visual function. Analysis-of-variance models were used to compare groups and condition results for each visual function.

Results: A significant effect of visual impairment for all visual functions was found, however tactile meta-guidance did not significantly improve any of the investigated visual functions.

Conclusions: FInD psychophysics successfully detected deficits across a range of visual functions in people with CVL. The investigated visual functions showed deficits in CVL patients compared to control groups that are not improved by tactile meta-guidance. Future directions could explore the relationship of meta-guidance on fixation stability. However, these preliminary results suggest that tactile meta-guidance may not be an effective low vision rehabilitation strategy.

CONTROL ID: 3712582

SUBMITTER (NAME ONLY): Leila Chew

TITLE: Separating Glaucomatous vs. Aging-Related Effects in the Macular Region within a Bayesian Hierarchical Framework

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chew, E. Su, M. Mohammadi, V. Mohammadzadeh, R.E. Weiss, University of California Los Angeles, Los Angeles, California, UNITED STATES|S. Heydar Zadeh, K. Nouri-Mahdavi, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Leila Chew: Commercial Relationship: Code N (No Commercial Relationship) | Erica Su: Commercial Relationship: Code N (No Commercial Relationship) | Massood Mohammadi: Commercial Relationship: Code N (No Commercial Relationship) | Vahid Mohammadzadeh: Commercial Relationship: Code N (No Commercial Relationship) | Sepideh Heydar Zadeh: Commercial Relationship: Code N (No Commercial Relationship) | Robert Weiss: Commercial Relationship: Code N (No Commercial Relationship) | Kouros Nouri-Mahdavi: Commercial Relationship(s);Code F (Financial Support):National Institute of Health, Research to Prevent Blindness, Heidelberg Engineering

ABSTRACT BODY:

Purpose: To test the hypothesis that longitudinal glaucoma-related ganglion cell complex (GCC) thinning may be separated from aging-related changes within a Bayesian hierarchical linear model.

Methods: 63 eyes (45 patients) with suspected glaucoma (GS) and ≥2 years of follow-up and ≥3 macular OCT scans were recruited. The eyes in this cohort had suspicious optic discs but normal RNFL thickness and visual fields at baseline and final follow-up. The rate of RNFL thinning was required to be below 1 μm/year. GCC thickness at 36 3°×3° superpixels from the central 18° of macular volume scans were exported. Rates of GCC change at the superpixel level were estimated with a Bayesian hierarchical model with subject and superpixel-level random effects and residuals. One-sided Bayesian p-values were defined as the posterior probability that a given parameter was greater or less than zero (cutoff $p < 0.025$). The fixed effect of age was included in the model to assess the magnitude of aging-related GCC thinning. The main outcome measure was the difference in the magnitude of the GCC slopes between the longitudinal slopes and cross-sectional aging-related effects.

Results: Mean (SD) age, follow-up time, and number of OCT images were 61.3 (13.9) years, 3.5 (0.7) years, and 4.2 (1.0). The cross-sectional aging effect was significantly negative in 25 out of 36 superpixels with slopes of -0.56 to –0.22 μm per year in significantly changing superpixels. Longitudinal slopes were significantly negative in 34 out of 36 superpixels with slopes ranging from –1.38 to –0.36 μm per year in significantly changing superpixels. 33 of 36 superpixels had a steeper longitudinal slope compared to cross-sectional slope (Figure) and the differences were statistically significant in 9 of these 36 superpixels.

Conclusions: In this cohort, our proposed model was able to separate longitudinal glaucoma-related GCC thinning from aging-related effects; the longitudinal rates of thinning were significantly faster than the rates of change related to aging. To correctly estimate inner macular changes over time, longitudinal data with proper definition of the mean and variance structures are required.

CONTROL ID: 3712584
SUBMITTER (NAME ONLY): Yukai Zhao
TITLE: Visual acuity screen failures based on Snellen, ETDRS, and qVA Testing
SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y. Zhao, Z. Lu, Center for Neural Science, New York University, New York, New York, UNITED STATES|L.A. Lesmes, M. Dorr, Adaptive Sensory Technology, Inc., San Diego, California, UNITED STATES|Z. Lu, Division of Arts and Sciences, New York University Shanghai, Shanghai, Shanghai, CHINA|
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ABSTRACT BODY:
Purpose: During recruitment for retina trials, screen failure commonly results from discrepancies between inclusion criteria, real-world Snellen VA, and ETDRS VA verified at the study visit. This simulation study evaluated how failure rate is affected by different inclusion criteria and VA tests used for screening: Snellen, ETDRS and quantitative VA (Zhao et al. 2021).
Methods: To screen a population typical for retina (Fig.1 Kaiser 2009), we approximated a general patient (GP) distribution with piecewise uniform distribution of VA thresholds that varied from -0.2 to 1.8 logMAR, and VA range that scaled proportionally: VA range = 0.253 + 0.185 VA threshold (Zhao et al. 2021). We considered four inclusion criteria, bounded by 20/X and 20/320 (X= 25, 32, 40, or 50). To simulate recruitment, patients were randomly sampled from the GP, screened with a VA test (61-letter Snellen, 70-letter ETDRS, and 15-letter qVA), and verified with ETDRS. For each test and criterion, 1000 simulations that each comprised 1000 patient screenings, were used to calculate failure rate as the % of ETDRS scores verified outside of 20/X - 20/320.
Results: Fig. 2 shows that, across criteria, screen failure rates were highest for Snellen (12-15%), and lower for ETDRS (7-9%), and qVA (4-6%). Across tests, most failures were observed when screening for VA (20/50 – 20/320) known to exhibit the highest variability and worst Snellen-ETDRS discrepancy.
Conclusions: In simulations, the well-known deficiencies of Snellen VA lead to the highest screen failure rates (13%), which can be reduced but not eliminated using ETDRS (9%) and qVA (6%). The qVA's intelligent algorithm with 15-letter testing (5 rows of 3 letters) exhibits potential for feasible real-world screening that can improve patient recruitment for retina.

CONTROL ID: 3712585

SUBMITTER (NAME ONLY): Piotr Kopinski

TITLE: Mitochondrial and epigenomic gene transcription analysis in uveal melanoma

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.K. Kopinski, L.A. Dalvin, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Piotr Kopinski: Commercial Relationship(s);Code I (Personal Financial Interest):Regenxbio;Code I (Personal Financial Interest):Cabaletta Bio;Code I (Personal Financial Interest):Passage Bio;Code I (Personal Financial Interest):Oyster Pharmaceuticals | Lauren Dalvin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveal melanoma is a deadly cancer with high metastatic potential. Mitochondrial genetics and epigenetics are known to play a role in tumorigenesis, progression, and metastasis, while mitochondrial metabolites have recently been shown to cause changes in the nuclear epigenome. In this study, we describe the transcriptional state of genes involved in mitochondrial metabolism, chromatin remodelling, and histone modification in uveal melanoma in order to define targetable signaling pathways.

Methods: TCGA database of 80 primary uveal melanoma cases was queried for mRNA transcript levels of key mitochondrial metabolism enzymes and mitochondrial metabolism-dependent chromatin remodeling and histone modifying enzymes. These were selected a priori based on recently described metabolically-induced chromatin changes with known transcriptional outcomes (Kopinski et al. 2019, Picard et al. 2014). Transcription levels were compared against the group mean and samples were grouped based on key enzyme transcriptional profiles.

Results: Of the 80 analyzed samples, a third showed alterations in transcription co-activator PGC1α and citrate synthase (CS), a quarter in ATP-dependent citrate lyase (ACLY), and a fifth in mitochondrial polymerase γ (POLG). A third showed alterations in NAD-dependent deacetylases: Sirtuins 1 and 6 (SIRT1, SIRT6), of which 60% were discordant. Histone 3 lysine 9 (H3K9) demethylases (KDM3A, KDM3B, JMJD1C) were altered in a third of samples with high concordance. A quarter showed highly concordant alterations in DNA methyltransferases DNMT3A and B. Interestingly, Sirt1 expression was highly discordant with that of citrate synthase, while H3K9 methyltransferase showed discordance with H3K9 demethylases.

Conclusions: Primary uveal melanoma samples exhibit distinct transcriptional profiles with differential expression of mitochondrial metabolism and chromatin modifying enzymes, allowing identification of potentially targetable signalling pathways. Patterns of chromatin modifying enzyme expression suggest internally consistent conditions to promote a given chromatin state, with concordant expression of enzymes with similar function and opposing expression of those with opposite function. This suggests a personalized, transcriptonal profile-based metabolic intervention to disrupt these conditions may disable functional chromatin, thus providing a therapeutic target.

CONTROL ID: 3712587

SUBMITTER (NAME ONLY): Tais Estrela

TITLE: The Effect of Intraocular Pressure on Rates of Visual Field Loss in Eyes with Optic Nerve Drusen

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Estrela, A. A. Jammal, M. El-Dairi, F.A. Medeiros, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|F.A. Medeiros, Electrical and Computer Engineering, Pratt School of Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate rates of visual field loss in eyes with optic nerve head drusen (ONHD) and to investigate their relationship with intraocular pressure (IOP).

Methods: This was a retrospective cohort study involving patients with ONHD from the Duke Ophthalmic Registry. All records from eyes with at least 12 months of follow-up and at least 2 reliable standard automated perimetry (SAP) tests were included. Linear mixed models were used to estimate rates of SAP mean deviation (MD) loss over time. Rates of progression were classified in slow (slower than -0.5dB/y), moderate (between -0.5dB/y and -1db/y) and fast (faster than -1dB/y). Univariable and multivariable models were used to assess the effect of mean IOP and other clinical variables such as age, race and baseline MD, on rates of change.

Results: The study included 109 eyes of 66 subjects with ONHD followed for an average of 5.6 ± 4.3 years. 27 eyes (24.8%) were treated with IOP lowering drugs during follow-up. Eyes had a mean IOP during follow-up of 14.9 ± 2.5 mmHg. The mean rate of SAP MD change was -0.20 ± 0.18 dB/year, ranging from -1.10 to 0.22 dB/year. 102 (93.6%), 6(5.5%) and 1(0.9%) of eyes had slow, moderate, and fast progression, respectively. There was no statistically significant difference in rates of change between eyes receiving IOP lowering drugs and eyes that did not receive IOP lowering medication (P=0.441). Higher mean IOP during follow-up was not associated with faster rates of MD change in both univariable (P=0.131) and multivariable (P=0.435) models. In a multivariable model including mean IOP, age, gender, race, and baseline SAP MD, only age at baseline was significantly associated with faster rates of SAP MD loss with 0.07 dB/year faster rate of loss for each decade older (P=0.003).

Conclusions: Most eyes with ONHD have a slow progression of MD loss over time. We were not able to find a statistically significant relationship between mean IOP and rates of visual field loss, which suggests that there may not be a clear benefit of IOP lowering treatment in eyes with ONHD. Older age was significantly associated with faster rates of visual field loss.

CONTROL ID: 3712589

SUBMITTER (NAME ONLY): Eric Ruff

TITLE: Outcomes after Failed Pneumatic Retinopexy in Macula Off Retinal Detachments

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Ruff, J. Wallsh, N. Falk, J. Huz, P. Bhatnagar, Ophthalmology, Albany Medical Center, Albany, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macula off retinal detachments (RDs) represent a potentially visually devastating condition. Pneumatic retinopexy (PR) offers a prompt treatment option, but lower primary anatomic success rates than other surgical options. We aim to evaluate the visual outcomes of eyes with macula off RDs that failed initial PR compared to other primary surgical approaches.

Methods: Retrospective chart review of all patients diagnosed with a macula off RD was undertaken. Those eyes treated with PR were evaluated for anatomic success and final visual acuity (VA), amongst other data points. A comparative cohort was identified consisting of eyes treated with primary scleral buckle (SB) or scleral buckle and pars plana vitrectomy (SB/PPV) with pathology in which PR is an indicated treatment option. These cohorts were compared to the subset of eyes unsuccessfully treated with primary PR, most notably for final VA. Primary SB was also compared to secondary SB following failed PR and primary SB/PPV compared to secondary SB/PPV following failed PR.

Results: In total, 242 eyes were diagnosed with a macula off RD with 90 eyes (37.2%) treated primarily with PR. For all eyes undergoing PR, mean final VA was 0.36±0.05 logMAR (20/45). Pneumatic retinopexy was successful in 44 eyes (48.9%) with a mean final VA of 0.15±0.02 logMAR (20/29) and 90.1% achieving 20/40 or better final VA. Those eyes that failed PR required additional intervention with 33 (71.7%) secondarily treated with SB/PPV, 9 (19.6%) with SB and 4 (8.7%) with PPV. Failed PR undergoing secondary SB/PPV achieved a mean final VA of 0.53±0.11 logMAR (20/67) compared to 28 eyes primarily treated with SB/PPV with mean final VA of 0.59±0.11 logMAR (20/78; p=0.70). Both cohorts had comparable mean VA at initial presentation, 1.89±0.17 logMAR for failed PR versus 2.06±0.14 logMAR for primary SB/PPV (p=0.46). Similarly, failed PR undergoing SB reached mean final VA of 0.45±0.14 logMAR (20/56) compared to 9 eyes treated with primary SB with 0.42±0.18 logMAR (20/53; p=0.83).

Conclusions: When indicated, PR offers eyes with a macula off RD the potential for significant VA improvement and, even if primary PR fails, the VA results are comparable to primary PPV/SB and primary SB.

CONTROL ID: 3712590
SUBMITTER (NAME ONLY): Melinda Duncan
TITLE: The adult human lens transcriptome changes with age
SESSION TITLE: Lens Physiology
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: M.K. Duncan, A. Faranda, S.G. Novo, Y. Wang, M.H. Shihan, Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|J. d'Antin, Centre d'Oftalmologia Barraquer, Barcelona, Catalunya, SPAIN|
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ABSTRACT BODY:

Purpose: Aging is a major risk factor for cataract due to a combination of factors including age-related protein and lipid oxidation/damage, reduction in the ability of the lens to detoxify reactive oxygen species, and genetic alterations that could disrupt cellular structure. However, most tissues also alter gene expression with age even in the absence of pathology, and we found that the transcriptome of the aging mouse lens does as well, predicting pathways that could be either protective against cataract development or may exacerbate age-related declines in lens transparency. However, lab mice have a much shorter life span than humans thus the relationship between lens aging in mouse and human is unclear. This work seeks to fill this knowledge gap by investigating the transcriptomic changes of the aging human lens.

Methods: Young (20-30 years of age) and aged (70-89 years of age) human lenses were isolated from human cadavers during preservation of corneas for transplant by eye banks and immediately immersed in RNAlater prior to shipment to our laboratory. The lenses were dissected into central epithelium, equatorial epithelium, and cortical fibers, and total RNA prepared. RNA was converted to cDNA then sequencing libraries prepared using SMARTer Stranded Total RNA-Seq Kit-Pico kit and double strand sequenced by DNA Link. Read pairs were mapped to the human genome, data normalized and differential expression assessed using EdgeR. Differential expressed genes were mapped to pathways via iPathway Guide.

Results: Principal component analysis revealed that cell type (central epithelium, equatorial epithelium versus fibers) was the strongest factor driving lens gene expression, while age only accounted for 12% of the variance between samples. Aged lens fibers downregulate the expression of several hundred genes including the BMP regulator Crim1, numerous lens fiber cell markers and several enzymes responsible for glutathione metabolism, while less than 100 genes were upregulated with aging. Central and equatorial epithelial samples exhibit fewer gene expression changes with aging, while GSTM1 is the most downregulated gene in both cell types. Aged equatorial epithelium downregulates the expression of many lens marker genes consistent with the results in the cortical lens fibers.

Conclusions: Human lenses, like those of mice, differentially express numerous genes during aging, including many enzymes involved in glutathione metabolism.

CONTROL ID: 3712591

SUBMITTER (NAME ONLY): Theodore Jacques

TITLE: Vergence eye movements in patients with Parkinson's Disease

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Jacques, A. Lyu, A.M. Cheong, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|L.A. Abel, Deakin University, Burwood, Victoria, AUSTRALIA|P. Lee, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|R. Li, Pamela Youde Nethersole Eastern Hospital, HONG KONG|Y. Cheung, Queen Elizabeth Hospital, HONG KONG|A. Chan, Prince of Wales Hospital, The Chinese University of Hong Kong, HONG KONG|A.M. Cheong, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Theodore Jacques: Commercial Relationship: Code N (No Commercial Relationship) | Anqi Lyu: Commercial Relationship: Code N (No Commercial Relationship) | Larry Abel: Commercial Relationship: Code N (No Commercial Relationship) | Anne Chan: Commercial Relationship: Code N (No Commercial Relationship) | Yuk-fai Cheung: Commercial Relationship: Code N (No Commercial Relationship) | Paul H Lee: Commercial Relationship: Code N (No Commercial Relationship) | Richard Li: Commercial Relationship: Code N (No Commercial Relationship) | Allen Cheong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Parkinson’s Disease (PD) is associated with a variety of abnormalities in eye movements, and there is ample evidence for specific deficits in convergent eye movements. Often self-report or subjective judgements by clinicians, or objective eye-tracking measures are reported in the literature; but seldom both. Here we used both methods to describe the vergence deficits in PD patients.

Methods: 13 PD and 6 age-matched older adults (OA) were recruited to complete a smooth vergence task. A target mounted on a rod moved steadily closer and farther away (between 48 cm and 0 cm) at 3 different speeds (1, 2 and 4 cm/sec). Subjects fixated at the moving target and pressed a button when they perceived the approaching target as two (i.e. subjective break point). They also pressed the button when the retreating target became one (i.e. subjective recovery point). In addition to subjective reporting, subjects’ eye movements were captured using a binocular eye-tracking headset (Pupil Core 200Hz). The target positions at the time where convergence broke (i.e. objective break point) and at the time when the eyes recovered the binocular tracking (i.e. objective recovery point) were recorded. Each speed was measured twice and each trial comprised 3 cycles.

Results: Based on the objective measure, OA subjects maintained vergence until the target moved significantly closer (OA: 3.31 cm; PD:10.31 cm; $F(1,50) = 18.8$, $p<0.001$) and recovered vergence earlier (OA: 5.24 cm; PD:11.01 cm; $F(1,48) = 9.4$, $p<0.004$). We calculated the differences in target position between these objective points and the corresponding self-reported subjective points. PD subjects delayed in reporting the break point relative to OA (OA: 0.32 cm; PD: 2.22 cm; $F(1,51) = 4.65$, $p = 0.036$), but the groups did not differ in their reporting on the recovery point (OA: 1.70 cm; PD: 3.48 cm; $F(1,48) = 1.14$, $p = 0.29$).

Conclusions: Our PD patients showed expected deficits in objective measures of convergence and recovery. However, we found that PD subjects delayed in reporting a break in vergence but not for recovery. PD patients appear delayed in perceiving a loss of fusion but detect normally its restoration.

CONTROL ID: 3712596

SUBMITTER (NAME ONLY): Mitra Farnoodian-Tedrick

TITLE: Cell Autonomous Lipid Handling Defects in Stargardt iPS Cell-Derived Retinal Pigment Epithelium Cells

SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Farnoodian-Tedrick, D. Bose, M.M. Campos, R. Villasmil, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|I. Mariappan, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Purpose: Stargardt retinopathy is an inherited macular degeneration driven by mutations in gene ABCA4 and characterized by the accumulation of the lipid deposits in the retinal pigment epithelium (RPE), leading to its atrophy and photoreceptor death. The presence of ABCA4 in the apical membrane of human RPE cells suggests the involvement of this protein in RPE physiology and Stargardt disease pathogenesis. We developed Stargardt-iPS cells derived in vitro disease model to understand how ABCA4 loss of function promotes disease phenotype in the RPE - a primary injury site in Stargardt and other age-related maculopathies.

Methods: Fully characterized Stargardt- iPSCs (ABCA4 knock out and patient iRPE) were differentiated into RPE using a developmentally guided protocol. Stargardt-iRPE were cultured on semi-permeable membranes for six weeks to obtain a functionally mature and polarized monolayer tissue. Cells were evaluated for RPE-specific functions, including digesting photoreceptors outer segments. In addition, lipid accumulation phenotype was evaluated using a photoreceptor outer segment regimen to determine the human pathogenetic sequence.

Results: ABCA4 loss of function in Stargardt -iRPE triggers a cell-autonomous disease phenotype in RPE cells, including sub and intra-cellular lipid deposits while exposed to photoreceptor outer segment regimen. Stargardt -iRPE exhibited a reduced ability to digest photoreceptor outer segments that this defect was restored by lysosome acidifying drugs.

Conclusions: Our work shows Stargardt-iRPE offers a physiologically relevant in-vitro disease model for Stargardt disease and that ABCA4 loss of function initiates a cell-autonomous disease phenotype in RPE cells contributing to Stargardt disease pathology.

CONTROL ID: 3712597

SUBMITTER (NAME ONLY): Mallory Bowers

TITLE: Effect of Bimatoprost sustained-release intracameral implant on intraocular pressure and medication burden in patients with prior glaucoma surgery

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Bowers, M.K. Wong, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|R. Niknam, M.R. Moster, M.J. Pro, E. Dale, N.N. Kolomeyer, D. Lee, C.X. Zheng, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Ventimiglia, University of Maryland at College Park, College Park, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bimatoprost sustained-release (Bimatoprost SR, Durysta, Allergan) is a biodegradable implant that is administered intracamerally to reduce intraocular pressure (IOP) in patients with ocular hypertension or open angle glaucoma (OAG). To date, the efficacy and safety of Bimatoprost SR in patients with prior glaucoma surgery have not been examined. The aim of the present study is to evaluate outcomes of Bimatoprost SR implantation in patients with prior minimally invasive glaucoma surgery (MIGS) or incisional glaucoma surgery.

Methods: A retrospective chart review of 122 eyes that received Bimatoprost SR by six glaucoma specialists at Wills Eye Hospital between March 2020 and September 2021 was performed. Patients were included if they had prior iStent, goniotomy, trabeculectomy, or tube shunt surgery. Statistical analyses, including paired t-tests, were performed.

Results: A total of 41 eyes (39 OAG and 2 chronic angle closure) from 32 patients were included. Median age was 76 years and 24 (75%) patients were women. Of the 41 eyes, 25 (61%) had iStent implantation, 4 (10%) had goniotomy, 5 (12%) had trabeculectomy, 2 (5%) had tube shunt, and 5 (12%) had both trabeculectomy and tube shunt surgery prior to Bimatoprost SR implantation. Mean follow-up time was 26.9 ± 18.9 weeks after implantation. Mean IOP after Bimatoprost SR implantation (16.7 ± 5.0 mmHg) was similar to pre-treatment IOP (17.5 ± 4.5 mmHg, $p=0.37$). Patients required significantly fewer medications to control IOP after Bimatoprost SR implantation (1.2 ± 1.2) compared to baseline (1.9 ± 1.2, $p<0.001$). Two (5%) eyes required additional tube shunt surgery after Bimatoprost SR. No patient had long-term complications following Bimatoprost SR implantation.

Conclusions: Patients who received intracameral Bimatoprost SR with a history of prior glaucoma surgery subsequently required fewer IOP-lowering medications. The present data suggest that Bimatoprost SR may be a valuable alternative treatment option in patients with prior glaucoma surgery.

CONTROL ID: 3712598

SUBMITTER (NAME ONLY): Annie Ryan

TITLE: Diagnostic Electrophysiology in a Small Animal Model of Traumatic Optic Neuropathy (TON)

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ryan, M.A. Reilly, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Racine, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Traumatic optic neuropathy (TON) is a frequent, vision-threatening complication of head injury. No treatments are currently available and translational animal models are limited. The purpose of this study was to develop functional electrophysiologic diagnostic criteria for using a small animal model.

Methods: Male Sprague Dawley rats (~200g) were utilized, and all animal work was performed with IACUC approval. A series of light-adapted ERGs were conducted including flash ERGs (fERGs), flash Visual Evoked Potentials (fVEPs), and Photopic Negative Responses (PhNRs). ERG tests were conducted at least 7 days before injury (baseline), and 24 hours after injury (D1) to assess deterioration of visual function associated with the torsional TON. Rats were anesthetized with an intraperitoneal injection of ketamine/xylazine for each ERG session, and for the injury event (D0). All animals received baseline and D1 ERGs before sacrifice and tissue collection. The right eyes of all animals were injured utilizing a custom torsional injury-inducing device on D0. The left eyes of all animals remained uninjured. ERG signals were compared from baseline to D1 to determine differences in amplitudes and latencies at different time points.

Results: There was a reduction in the right eye amplitudes in fERG b-waves, fVEPs, and PhNRs at D1 as compared to baseline values. The left eye amplitudes at D1 were not significantly different to the left eye baseline amplitudes for fERG b-waves, and PhNRs. However, fVEP amplitudes were significantly different from baseline. Higher b-wave amplitudes in the ERG signal were observed in the left eye at D1 as compared to the right eye amplitude at D1.

Conclusions: A promising diagnostic technique for evaluation of the retina and visual system 24 hours after TON injury in a rat model. Comparing ERG and PhNR amplitudes between the ipsilateral and contralateral eyes may be a diagnostic for TON. Our small animal model detects the presence of visual system damage shortly after injury, which could allow for a promising diagnostic for humans in the future. Utilization of the differential amplitude between eyes may allow for diagnosis in humans where baselines are unavailable. Future work will evaluate changes at shorter time points and utilize these approaches to evaluate the safety and efficacy of candidate therapeutics for TON.

CONTROL ID: 3712601

SUBMITTER (NAME ONLY): Anita Ghosh

TITLE: Manganese porphyrin antioxidant alleviates particulate matter-induced allergic conjunctivitis

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Ghosh, Graduate Program in Biochemistry and Molecular Biology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|A.K. Ghosh, S. Iqbal, M. Bacellar-Galdino, N.E. Pappenhagen, S. Kaja, R&D Division, Experimentica Ltd, Forest Park, Illinois, UNITED STATES|S. Iqbal, Integrated PhD Program in Biomedical Sciences, Loyola University Chicago, Maywood, Illinois, UNITED STATES|S. Kaja, Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Particulate matter (PM) is a well-known trigger for the development of both acute and chronic forms of ocular surface disease. The purpose of this study was to evaluate the prototypic manganese porphyrin, manganese(III) tetrakis(1-methyl-4-pyridyl) porphyrin (Mn-TM-2-PyP), for its ability to protect against PM-induced damage.

Methods: Standardized Reference Material (SRM® 2786) consisting of fine atmospheric particulate of < 4 µm diameter was obtained from NIST. Rabbit corneal epithelial (SIRC) cells were exposed to a dose range of PM (1 - 300 µg/ml) for 24 h. Cell viability and motility assays were performed to evaluate the effect of PM and the protective effect of Mn-TM-2-PyP. The pharmacologic efficacy of Mn-TM-2-PyP (0.05% in saline, BID for 10 d) was tested in PM-induced allergic conjunctivitis in New Zealand White rabbits and assessed by ophthalmic exams and corneal fluorescein staining.

Results: MTT assay revealed dose-dependent loss of cell viability in response to PM exposure with IC_{50} of 13.6 µg/ml PM (n = 3 - 6), while lactate dehydrogenase (LDH) release increase dose-dependently with EC_{50} of 149.1 µg/ml PM (n = 3 - 6). Mn-TM-2-PyP (0.005% and 0.05%; 30 min pre-treatment) protected against PM (100 µg/ml)-induced LDH release (n = 3, $P < 0.05$). Exposure to PM (200 µg/ml) for 24 h significantly reduced motility of SIRC cells in scratch assays. Scratches were 54.4 ± 2.4% of the original width in untreated cells, while the scratch remained at 79.8 ± 2.6% in PM-treated cells ($P < 0.001$). In contrast, Mn-TM-2-PyP improved PM-treated SIRC motility beyond the level in untreated cells with scratch widths at 42.0 ± 1.9% ($P < 0.001$). In vivo, 10 d treatment with Mn-TM-2-PyP completely resolved PM-induced hyperemia (n = 4, $P < 0.001$) and corneal pathology (n = 4, $P < 0.001$) when compared to saline-treated eyes. Mn-TM-2-PyP had no effect on tear volumes.

Conclusions: Mn-TM-2-PyP protected against PM-induced cytotoxicity and impairment in motility in vitro and PM-induced allergic conjunctivitis in vivo. These data corroborate previous studies that have suggested generation of cellular oxidative stress as underlying mechanism of the deleterious effects of PM on epithelial cells. Our data suggest that oxidative stress is an etiological contributor to PM-induced allergic conjunctivitis in rabbits and support future therapeutic development of antioxidants for PM-induced ocular surface disease.

CONTROL ID: 3712602

SUBMITTER (NAME ONLY): Daniel Wang

TITLE: Quantitative Characteristics of Sickle Cell Maculopathy in Post Hematopoietic Stem Cell Transplantation Patients Using Optical Coherence Tomography

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Wang, J.I. Lim, Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|H. Liu, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hematopoietic stem cell transplantation (HSCT) for sickle cell disease (SCD) has enabled the conversion of hemoglobin SS genotype to either normal hemoglobin AA or to sickle cell trait (Hgb AS) with cessation of systemic crises. While peripheral vasculature abnormalities are the hallmark of sickle cell retinopathy (SCR), prior work by our group and others has shown maculopathy (SCM) characterized as macular thinning and vascular abnormalities on spectral-domain optical coherence tomography (SDOCT) and optical coherence tomography angiography (OCTA). The purpose of this study was to determine whether HSCT resulted in any change in the level of SCR or rate of SCM thinning.

Methods: A retrospective, cross-sectional chart review was performed. Post HSCT SCD patients were identified through a comprehensive chart review of the prospective SCR Study patient database. The SCR Study patients all underwent an annual complete ophthalmic examination, macular SDOCT, and OCTA imaging. A multivariate logistic regression analysis was performed to analyze the relationship between SDOCT thickness and patient transplantation status.

Results: A total of thirteen patients were followed longitudinally over a study interval of ten years and compared to those without HSCT. Best-corrected visual acuity was preserved over the study interval (Pre-HSCT: LogMAR: 0.0821, Post-HSCT: LogMAR: 0.0878, p=0.0023). Average macular thickness prior to HSCT was (312.94 +/- 16.88 μm) and post HSCT was (308.49 +/- 21.911 μm). Despite HSCT, study patients continued to demonstrate a generalized trend for continued macular thinning at rates similar to pre-transplantation (pre-HSCT: -0.276 μm/year; post-HSCT: -0.321 μm/year, p=0.572). No strong associations between SDOCT thickness/rates of thinning and parameters such as Hgb type, smoking status, hydroxyurea use, number of pain crises were identified for the HSCT subgroup.

Conclusions: Progression of SCM appears to occur despite HSCT. Further study using other imaging modalities such as OCTA may provide additional insight into the biological and pathophysiological mechanisms of SCM in HSCT patients.

CONTROL ID: 3712603

SUBMITTER (NAME ONLY): Jacquelyn Hamati

TITLE: Characterizing Prolonged Undifferentiated Postoperative Pseudophakic Iridocyclitis (PUPPI) at a Tertiary Care Provider Practice

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hamati, M. Salabati, R. Mahmoudzadeh, J. Dunn, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify and characterize patients with prolonged undifferentiated postoperative pseudophakic iridocyclitis (PUPPI) after uncomplicated phacoemulsification with posterior intraocular lens implantation (IOL).

Methods: Single-center, consecutive retrospective chart review conducted at Wills Eye Hospital (Philadelphia, PA, USA) to identify all new patients with PUPPI referred to our uveitis specialist between January 2015 and December 2020. Documented demographic features included visual acuity, intraocular pressure, comorbidities such as macular edema, and examination findings for each clinic examination.

Results: A total of 48 eyes of 30 patients were identified with PUPPI out of 1995 new patients (1.50%) during the study timeframe. Mean (SD) age was 68.8 (4) years. African-Americans and women were most commonly affected, making up 86% and 83% of the study population, respectively. Patients were followed for a mean of 10 months (range 0-54 months). The majority of patients remained on topical steroids for the entirety of their follow-up, including 84% of eyes at the 3-month visit, 75% at the 12-month visit, and 88% at the 24-month visit. The uveitis was suppressed in all patients by the 24-month visit when available. Mean visual acuity (MVA) was 20/50 at referral visit among patients with follow-up. There were no statistically distinct changes in MVA at subsequent visits. MVA was 20/36 at the 3-month visit (p=0.12), 20/36 at the 12-month visit (p=0.05), and 20/45 at the 24-month visit (p=0.70). Among patients with follow-up, cystoid macular edema was present in 20-30% of eyes throughout the study period (3-54 months). The MVA in eyes with CME was worse than in eyes without CME (20/66 versus 20/41, respectively) but the difference was not statistically significant (p=0.097).

Conclusions: PUPPI is more common in African-Americans and more chronic in women. Patients may require prolonged courses of topical steroids after surgery with fair visual outcomes. Poorer visual outcomes may be related to presence of CME.

CONTROL ID: 3712607

SUBMITTER (NAME ONLY): Krzysztof Palczewski

TITLE: In vivo two-photon excitation-based assessment of intracellular protein transfer to mouse retina

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Palczewski, S.W. Du, J. Zhang, R. Smidak, H.B. Yan, R. Holubowicz, G. Palczewska, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|K. Palczewski, S.W. Du, Department of Physiology & Biophysics, University of California Irvine, Irvine, California, UNITED STATES|G. Palczewska, Polgenix, POLAND|

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ABSTRACT BODY:

Purpose: Inherited eye diseases leading to degeneration of the retina predominantly result from genomic alterations to retinal proteins. Genome editing is especially attractive to correct mutations in genes associated with phototransduction, the visual cycle and other cellular processes essential for the viability of retinal cells. It is crucial to study and quantify the delivery of genome editors to the eye, to optimize editing efficiency and minimize toxicity in animals before clinical application.

Methods: All animal procedures were approved by Animal Care Committees at the University of California, Irvine and conformed to recommendations of the American Veterinary Medical Association Panel on Euthanasia and ARVO. We used mT/mG Cre reporter mice (Jackson #007676), which constitutively express membrane tdTomato in all cell types, and switch to membrane GFP after Cre-mediated loxP excision.

We assessed the efficiency of Cre delivery via intraocular injection to anesthetized mice, and compared numerous delivery strategies of recombinant Cre protein, including peptidic tags, small molecule labeling, and custom nanoparticle formulations.

Two-photon (2P) microscopy was performed in mouse eyes 6-8 days after intraocular injection of Cre. A 950 nm light was used to simultaneously visualize mT- and mG-labelled cells. Signals were directed into mT and mG channels based on the 2P emission spectra. Fraction of transfected RPE and photoreceptor cells was assessed for different delivery modalities.

Results: After injection of Cre with various delivery tags, we observed distinct color switching from tdTomato to GFP in photoreceptors and retinal pigment epithelium (RPE). The characteristic features of these cells were preserved, including the hexagonal shape and undisturbed mosaic of RPE cells, and outer segments, inner segments, nuclear layer and connecting outer fibers; all of which were clearly visible in photoreceptors. Many delivery tags were effective in the RPE, while some compounds were targeted to photoreceptors.

Conclusions: Clear 2P images were obtained from the entire retina ranging from the RPE to the ganglion cell layer, enabling 3D reconstructions and assessment of color switching. Thus, 2P excitation-based imaging in intact mouse eyes is an effective way to compare the relative efficacy of diverse delivery routes of genome editors by measuring transfection efficiency and impact on retinal structure.

CONTROL ID: 3712608

SUBMITTER (NAME ONLY): Hasan Cetin

TITLE: Machine Learning-Based OCT Detection of Geographic Atrophy Lesions in Non-neovascular Age-related Macular Degeneration

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Cetin, J. Whitney, E. Kanyo, M. Bonnay, S.K. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Advanced non-neovascular age-related macular degeneration (dry AMD) is a leading cause of vision loss. Recent clinical trials demonstrate the potential of emerging therapeutics for potential first-in-class treatment for geographic atrophy (GA). Identification and characterization of GA will be critical for optimal management with new treatment options. The purpose of this analysis was to assess the feasibility of an OCT-based automated machine-learning platform for detection of GA lesions.

Methods: This was an IRB-approved retrospective image analysis study evaluating eyes with dry AMD. A machine learning enabled multi-layer segmentation system was utilized to segment Bruch's membrane (BM), the ellipsoid zone (EZ), and RPE with manual correction. GA was defined by those areas with the EZ, RPE, and BM all intersection (i.e., total loss of RPE and EZ with only BM remaining. Automated training masks were created based on those areas of intersection of the segmentation lines. A U-Net architecture convolutional model was executed and evaluated on training datasets with varying ratios of annotated OCT images containing (positive) and not containing (negative) GA lesions in dry AMD. Overall, 10,271 B-scans from eyes with dry AMD were utilized including 1,456 B-scans that included GA lesions were utilized for training and tested on a self-generated validation set which including 1027 B-scans.

Results: Following model development, the feasibility of automated GA detection on OCT was demonstrated using a machine learning model (Figure 1). The F-score associated with this model which is tested on validation set was 0.68. Interestingly, the qualitative impression of model performance appeared to be quite good. Scan features that appeared to impact model performance, included low image quality, unusual posterior curvature, and slanted scans.

Conclusions: Automated detection of GA lesions on OCT using a machine learning model is feasible. Future research is needed to optimize performance across a highly diverse scan quality spectrum and evaluate the model for quantification of GA for longitudinal measurements.

CONTROL ID: 3712609

SUBMITTER (NAME ONLY): Tony Zhang

TITLE: Effect of Early Postoperative Aqueous Suppression Therapy on Surgical Outcomes of Valved Tube Shunts in Refractory Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.Z. Zhang, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|J. Wong, W.S. Shalaby, E. Dale, M.J. Pro, A. Shukla, D. Lee, J.S. Myers, R. Razeghinejad, M.R. Moster, Glaucoma, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|S.S. Lam, E. Dale, M.J. Pro, A. Shukla, D. Lee, J.S. Myers, R. Razeghinejad, M.R. Moster, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|W.S. Shalaby, Tanta University, Tanta, EGYPT|

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ABSTRACT BODY:

Purpose: To compare the effect of early vs late treatment with aqueous suppressants on the surgical outcomes of Ahmed glaucoma valve (AGV) FP-7 implants

Methods: Retrospective comparative cohort study on refractory glaucoma patients who underwent AGV implantation at Wills Eye Hospital from 2016-2021 who received topical aqueous suppressants either in the first 2 weeks (group 1; early) or after 2 weeks (group 2; late) postoperatively. The main outcome measures were incidence of hypertensive phase (HP), defined as an intraocular pressure (IOP) of >21 mmHg within 3 postoperative months, surgical failure at months 6 and 12 (defined as IOP<5 or >21 mmHg), progression to no light perception (NLP) vision, or further glaucoma surgeries.

Results: 199 eyes of 194 patients (group 1=140, group 2=59) were included. Mean age was 68.2±15.8 years old. At baseline, visual acuity (VA) was 1.0±0.9 and 1.2±0.9 (P=0.083), IOP was 36.8±10.7 mmHg and 35.6±11.8 mmHg (P=0.485), and number of glaucoma medications was 2.9±1.4 and 3.0±1.6 (P=0.629), in groups 1 and 2 respectively. 43% of patients had primary open angle glaucoma and 52.7% had severe disease. HP developed in 35.7% of group 1 eyes and 50.8% of group 2 eyes (P=0.011). At month 6 (n=177) the surgical failure rate was similar in both groups (22.8% vs 20.0%, P=0.748). At month 12, (n=137) failure was also similar between groups (25.3% vs 39.5%, P=0.238). Reasons for failure were similar (P=0.055) and included IOP>21 mmHg (45.5%), further glaucoma surgeries (38.6%), and NLP vision (9.1%). Kaplan-Meier survival analysis comparing cumulative probability of failure at 12 months showed no significant difference between groups (P=0.461). Multivariate logistic regression analysis suggests that development of HP was a significant predictor of month 12 failure (P=0.044). Age, sex, race, late use of aqueous suppressants, glaucoma type and severity, baseline VA, IOP, narrow angle, and medication number were not significant predictors of failure.

Conclusions: Our findings suggest that early aqueous suppressant use after FP-7 AGV implantation was associated with decreased occurrence of a HP. Although surgical failure rate was similar between groups, HP was a significant predictor of month 12 failure. Longer-term follow-up with larger sample size studies are warranted on this subject.

CONTROL ID: 3712612

SUBMITTER (NAME ONLY): Sara Aurora Garcia y Otero Sánchez

TITLE: Use of Gonio-Photographs with the GS-1 Automated Gonioscope to Assess the Basic Knowledge for SLT Application.

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Garcia y Otero Sánchez, J.A. Paczka, O. andrea, A.M. Ponce Horta, A. Tornero-Jimenez, R. Monserrat, Research department, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|O. andrea, A.M. Ponce Horta, A. Tornero-Jimenez, Research department, Asistencia e Investigacion en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Selective Laser Trabeculoplasty (SLT) is a useful method to decrease intraocular pressure (IOP) for glaucoma and ocular hypertension(OHT) patients.Upskilling for SLT increase the proficiency of the clinical skills of ophthalmologyst,such as gonioscopy.The purpose of this study is to investigate agreement and correlation of decision-making elements regarding SLT treatment using gonio-photographs (GP)among ophthalmologists inexperienced in SLT.

Methods: A set of 10 GP GS-1 automated gonioscope; Nidek,Japan)with different clinical findings were presented to three ophthalmologists with scarce experience with SLT.They were instructed to follow a 4-step process, which consisted on:(1)selecting aiming beam spot size,(2) a 5-minute review of 10 GP,(3)judgement of the level of difficulty to identify relevant gonioscopic findings helpful to decide about how to perform SLT, and(4)placement of a graphic representation of a SLT spot with a specific energy value(0.1 mJ-1.0 mJ)in the pretended region(s)to treat the same 10 GP.The results of an experienced glaucoma specialist(reference rater or RR)were used to analyze each examiner's results.Inter-rater agreement analysis, rank,concordance and intra-class correlations were used.A p-value of ≤ 0.05 was considered statistically significant.

Results: All participants finished the four-step process.Two raters selected the same spot-size as compared to the reference.Level of discerning clinical findings was poorly correlated.Number of spots had a good inter-rater agreement between the reference observer and one of the inexperienced ones(weighted Kappa=0.55, SE=0.17; 95% IC, 0.23-0.87).Total energy per GP was good and significantly correlated between RR and the same inexperienced observer(rho=0.63; p=0.049).Intraclass correlation was fair regarding totally energy(0.48; 95% IC, 0.16-0.79)and number of spots (0.56; 95% IC, 0.24-0.83).Precision and accuracy had poor correlation among raters (≤0.9). Mean energy used per GP was statistically different in the RR(5.69±1.0mJ)as compared to the others(4.75±1.1mJ, 4.51±0.8mJ, 2.11±0.9mJ).

Conclusions: Unexperienced ophthalmologists' responses in this model based on GP derived from the GS-1 device had poor agreement in most of the studied variables when compared with an experienced ophthalmologist.Further studies using GP are warranted in order to assess the impact of teaching interventions.

CONTROL ID: 3712613

SUBMITTER (NAME ONLY): Neha Raparla

TITLE: The Effect of COVID-19 on Corneal Graft Rejection

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the impact of COVID-19 on corneal transplant failure.

Methods: A retrospective cohort study was conducted using TriNetx (Cambridge, MA, USA), a national electronic health records research network encompassing multiple large health organizations. Patients who underwent corneal transplantation were identified via Current Procedural Terminology (CPT) codes. They were then divided into those who contracted COVID-19 after corneal transplantation (n=678) and those that did not (n=37,930). Cohorts were matched for age, BMI, gender, primary hypertension, diabetes mellitus, respiratory disease, heart failure, nicotine dependence and alcohol-related disorders. The primary outcome was corneal graft failure over a 120-day post-operative period. Outcomes were compared between both groups.

Results: Prior to propensity matching, there was a significant increase in corneal graft failure in those infected with COVID-19 (RR 1.7, CI 1.11-2.62, p-value 0.014). Underlying medical disease was more prevalent in this group with the greatest difference observed for BMI (57.67% versus 35.49%), hypertension (55.52% versus 28.25%), and diabetes mellitus (33.48% versus 13.73%). After propensity matching, a total of 1354 patients were included in the analysis, with 677 in the negative COVID-19 group and 677 infected with COVID-19. There was no statistically significant difference in corneal graft failure between the two groups (RR 1.31, 95% CI 0.69-2.49, p-value 0.405).

Conclusions: COVID-19 did not have a statistically significant impact on corneal transplant outcomes.

CONTROL ID: 3712616

SUBMITTER (NAME ONLY): Lisa Keay

TITLE: PrevenTing Falls in a high-risk, low vision population through specialist ORientation and Mobility services: the PlaTFORM randomised trial

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the Lifestyle-integrated Functional Exercise fall prevention programme for older people with low vision or blindness (v-LiFE).

Methods: A single-blinded randomised controlled trial evaluated the v-LiFE program compared to usual care. Primary outcomes were the activity normalised fall rate over 12 months, measured using prospective falls calendars and function and participation (Late Life Function and Disability Instrument, Function sub-scale LLFI, Rasch scored). Activity was estimated using a wrist worn accelerometer over 1-week periods at baseline, 3 months and 12 months. Multiple imputation was used when accelerometer data were missing, based on self-reported physical activity. The rate ratio (RR) for falls were modelled using a negative binomial regression, mean differences were calculated with 95% Confidence Intervals (CI) for continuous measures, all analyses were on an intention to treat basis with pre-planned sub-groups (high physical activity, peripheral field loss and multiple fallers). The Short Physical Performance Battery (SPPB) was used to investigate if the v-LiFE program led to improvements in strength and balance

Results: 588 participants were randomised and 532 (90%) completed the trial. Mean age was 74 years, 346 (59%) were female, median visual acuity was 1.0 logMAR, (inter-quartile range 0.4-1.9) and 497 (85%) used a mobility aid. The annual falls rate was 2.1±3.5 and similar in the intervention and control groups (RR 0.89, 95% confidence interval, CI 0.69-1.13). The LLFI score was also similar (-0.02 95% CI -0.06-0.03). There was no difference in the rate of falls requiring medical care (RR 1.04 (0.79,1.36). There were no differences in the sub-groups for the primary outcomes. The SPPB total score was similar between groups (0.13 95% CI -0.24-0.51). Cadence in the 4m walk was better in the intervention group (0.20, 95% CI 0.06-0.34 steps/metre), but the timed sit-to-stand, 4m walk time and standing balance scores were not different.

Conclusions: Though strength and balance training has been shown to prevent falls in older people, this trial involving older people with low vision did not demonstrate any benefit. It is possible that a higher dose program and/or a

different approach to implementation will be required to reduce falls and improve function in older people with low vision.

CONTROL ID: 3712617

SUBMITTER (NAME ONLY): Ayesha Girach

TITLE: Variability of outer retinal hyper-reflective bands detected using optical coherence tomography

SESSION TITLE: Pediatric Ophthalmology - Pathophysiology and Imaging Modalities and Oculoplastics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Melanin is a major contributor to the intensity and width of the retinal pigment epithelium (RPE) on optical coherence tomography (OCT). It is hypothesized, high melanin concentrations cause scattering making the RPE appear as a thick band and obscures adjacent layers. A split band appearance of the outermost hyperreflective band has been demonstrated in Albinism, meaning the RPE and Bruch's Membrane appear as two separate bands. We performed a cross-sectional observational study to test the hypothesis that a reduction in melanin causes an increased ability to differentiate the hyperreflective bands seen on OCT images of the outer retina.

Methods: Using the UK Biobank dataset, we generated a randomised sample of 300 participants with specific inclusion and exclusion criteria. Inclusion criteria was an age between 40 to 65, visual acuity better than 0.60 logMAR, no ocular pathology, and measurable OCT images of both eyes. We analysed three ethnic groups: White (n=100), Asian (n=100) and Black (n=100). The OCT images of the participants' left eyes were qualitatively analysed for the number of outer retinal hyperreflective bands at the fovea and parafovea. We also analysed the proportion of cases with foveal hypoplasia (FH). FH was graded using the Leicester OCT structural grading system described by Thomas MG et al. 2011.

Results: A significantly less number of outer retinal hyperreflective bands are seen at the fovea (X^2=7.23, p=0.027) and parafovea (X^2=16.24, p=0.0003) in the black ethnicity group compared to the other ethnicity groups. Although there was a higher proportion of cases of grade 1 FH in the white and asian groups compared to the black group this was not statistically significant (p=0.09). No significant (p=0.69) difference in visual acuity is observed between the groups.

Conclusions: We highlight the potential role of melanin in our ability to resolve outer retinal structures using OCT. Higher concentrations of melanin in black populations could be associated with fewer outer retinal hyperreflective bands. As previously described in albinism, the additional outer retinal bands visible are likely due to hypopigmentation. Outer retinal thickness measurements should be interpreted with caution when derived from automated segmentation algorithms.

CONTROL ID: 3712618

SUBMITTER (NAME ONLY): Sunil Srivastava

TITLE: A phase 2 randomized controlled trial of the Janus Kinase (JAK) inhibitor filgotinib in patients with noninfectious uveitis

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Noninfectious uveitis (NIU) is a major cause of visual impairment with limited treatment options. We performed a randomized, placebo-controlled, double-masked trial of filgotinib, a JAK1 preferential inhibitor, to assess its efficacy and safety in NIU.

Methods: Adults with intermediate-, posterior- or pan-uveitis that was active despite at least 2 weeks of treatment with 10-60 mg prednisone were eligible for this trial. Patients were randomized 1:1 to receive either filgotinib, 200 mg daily, or placebo for up to 52 weeks. On study day 1, all patients began a protocolized prednisone taper beginning at 60 mg to 0 mg by the beginning of Week 15. The primary endpoint was the proportion of patients failing treatment by week 24. Treatment failure was defined as a new chorioretinal and/or retinal vascular lesion, worsening of best corrected visual acuity by ≥15 letters, or an inability to achieve an anterior chamber cell or vitreous haze grade 0.5+ at week 6 or a 2-step increase after week 6. Patients who took study drug and completed at least week 6 of the study were considered evaluable. While in progress, the trial was terminated before full enrollment (planned N = 248) for business reasons. As a result, all hypothesis testing was done without multiplicity adjustment.

Results: Seventy-four (74) patients were randomized. The majority (57%) had idiopathic uveitis. Patients with missing data were imputed as treatment failures. Of the 66 evaluable patients, the proportion failing treatment was 12 of 32 (38%) in the filgotinib arm and 23 of 34 (68%) in the placebo arm ($p = 0.006$). The median time to treatment failure was 22 weeks in the placebo arm and was not estimable in the filgotinib arm as more than half the patients in the filgotinib arm did not have treatment failure (hazard ratio 0.309; 95% CI [0.144 to 0.663]) [Figure]. Adverse events were reported more frequently in patients who received filgotinib than placebo (81% v. 69% adverse events and 14% v. 6% serious adverse events). There were no arterial or venous thromboembolic events, no major adverse

cardiovascular events, no opportunistic infections and no cases of tuberculosis or herpes zoster reported.
Conclusions: In patients with vision threatening NIU, filgotinib 200 mg reduced the risk of uveitis flare compared to placebo and was generally well tolerated.

CONTROL ID: 3712623

SUBMITTER (NAME ONLY): Catherine Johnson

TITLE: Correlation Between SITA Fast Visual Field Strategy Measurements and Augmented Reality-Based Heru re:Vive Visual Field Strategy Measurements

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The SITA Fast (SF) visual field (VF) strategy was developed as a faster alternative to the SITA Standard (SS) VF strategy and is routinely used in clinical centers due to its shorter duration. In this study, we correlate visual field measurements of SF on the Humphrey Field Analyzer (HFA) (Carl Zeiss Meditec, Inc, Dublin, CA) with those of the Heru re:Vive VF strategy (Heru Inc, Miami, FL) downloaded onto an augmented reality (AR) headset.

Methods: Thirty-seven eyes from thirty-five subjects underwent visual field testing with SITA Fast and Heru re:Vive strategies. Subjects with a range of neurologic and ophthalmologic pathology were recruited from a tertiary eye institute during their regular clinic visit. Subjects either had a same-day SF VF scheduled or had been tested with SF within three months of study visit, with either the 24-2 (n = 28) or 30-2 (n = 9) field patterns. Eyes with visual acuities of 20/400 or worse or having had intraocular surgery within 6 months of study date were excluded. Heru re:Vive testing was done in a darkened room using the Magic Leap 1, size 2 headset (Magic Leap, Plantation, FL) and lenses were inserted into the headset for refractive correction. For the two tests, HFA and Heru, the correlation coefficient was determined for metrics of mean deviation and mean sensitivity and test duration was compared.

Results: Strong correlations between Heru and HFA tests were found for metrics of both mean sensitivity ($R=0.82$, $p<0.001$) (fig. 1) and mean deviation ($R=0.83$, $p<0.001$) (fig. 2). Sensitivity analysis included all 37 eyes tested and mean deviation analysis included 28 eyes, excluding the 9 eyes tested with the 30-2 VF pattern. Mean test time of both tests were similar (4.27 minutes for Heru versus 4.38 minutes for HFA).

Conclusions: VF measurements of mean sensitivity and mean deviation obtained using the Heru re:Vive strategy installed on a portable headset correlate well to those from the SITA Fast HFA test among neurologic and ophthalmologic patients.

CONTROL ID: 3712624

SUBMITTER (NAME ONLY): Bradley Gundlach

TITLE: Use of Serial Anti-VEGF Injections in Patients with Severe Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Anti-Vascular Endothelial Growth Factor (Anti-VEGF) agents have revolutionized the treatment of many diseases in ophthalmology, and have begun to find increased use in the treatment of Retinopathy of Prematurity (ROP). Although the use of Anti-VEGF agents has demonstrated benefits in severe (i.e., Type 1) ROP, many questions remain about its optimal use and long-term outcomes. Here, we investigate the need for multiple Anti-VEGF injections and factors which may predict a reduced response to treatment requiring repeat therapy for ROP.

Methods: Retrospective chart review study of patients screened for ROP as inpatients in the Neonatal Intensive Care Unit (NICU) between 2011-2021 who also received anti-VEGF treatment. Electronic medical records were used to obtain patient demographics as well as ophthalmic and non-ophthalmic treatments and outcomes. Patients were stratified by whether they received single or multiple anti-VEGF injections.

Results: 32 patients (59 eyes) were identified as receiving at least one injection, and 5 patients (8 eyes) receiving two injections. The mean post-menstrual age of those receiving a single injection was 24.6 weeks [range:22.1-31.7] and for two injections was 23.8 weeks [range:23.3-25.7]. Receiving multiple injections was not correlated with birthweight ($p=0.121$) or gestational age ($p=0.14$), but was associated with decreased age at first injection (OR = 0.31-0.82; $p=0.006$). The mean corrected gestational age at first injection for those receiving a single injection was 36.3 weeks [range:31.5-47.4] and for two injections was 33.1 weeks [range:31-36.6]. Age at first injection was not significantly correlated with gestational age ($R^2 = 0.281$) or birth weight ($R^2=0.062$).

Conclusions: Infants with severe ROP requiring anti-VEGF treatment at earlier ages may be more likely to require repeat therapy at later ages. This data may be helpful when counselling parents during initial treatment discussions, and highlights the importance of close follow-up of these patients to assess the need for additional treatment.

CONTROL ID: 3712625

SUBMITTER (NAME ONLY): Julia Kim

TITLE: Functional imaging of mitochondria using flavoprotein fluorescence and its correlation with intraocular pressure in treated glaucoma patients

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Increased intraocular pressure (IOP) is believed to induce oxidative stress and lower antioxidant defenses in the optic nerve, leading to retinal ganglion cell death. A noninvasive retinal metabolic imaging device measures flavoprotein fluorescence (FPF), a potential biomarker for mitochondrial dysfunction and early apoptosis due to oxidants and other stimuli. We evaluated the relationship between FPF and IOP to investigate the functionality of the device and the pathophysiology underpinning glaucoma.

Methods: 52 eyes from 52 patients with glaucoma or suspect glaucoma were imaged. FPF scores were obtained at the optic nerve head (ONH) and macula using OcuMet Beacon (OcuSciences Inc., Ann Arbor, MI). Optical coherence tomography obtained the retinal nerve fiber layer (RNFL) and macular ganglion cell complex (GCC) thicknesses. The association between IOP and FPF, adjusting for age, sex, and RNFL, was evaluated by linear regression.

Results: Glaucoma eyes (n=34) on average had lower IOP (13.4 vs. 16.4mmHg), thinner RNFL (72 vs. 90μm), and thinner macular GCC (66 vs. 79μm) compared to suspects. All glaucoma eyes were treated and most were on IOP-lowering drugs. Among these, higher IOP correlated with a higher FPF score at the ONH but was not statistically significant (p=0.23). For suspect eyes, the opposite relationship was observed between IOP and FPF (p=0.03), but this was not significant when RNFL thickness was taken into account by using the ratio of FPF to RNFL (FPF/RNFL). Two glaucoma eyes were outliers with low IOP (7 and 10mmHg) and high FPF/RNFL. In multivariable analysis, older age, male sex, and greater RNFL thickness were associated with higher FPF scores.

Conclusions: IOP may not be the sole contributor for mitochondrial dysfunction in treated glaucoma patients. Since the majority of glaucoma patients are stable on IOP-lowering drugs, this result may reflect that little RGC stress and apoptosis occur in controlled disease. These drugs are also thought to exert additional antioxidant activity. The two outliers had more advanced glaucoma (RNFL: 49 and 55μm) and may represent greater mitochondrial stress and progressing disease despite adequate IOP control. Longitudinal studies with a wider disease severity spectrum are needed to better establish the relationship between IOP and FPF.

CONTROL ID: 3712626

SUBMITTER (NAME ONLY): Vladimir Kefalov

TITLE: Understanding how the G90D and G90V rhodopsin mutations cause night blindness

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A wide range of blinding disorders have been associated with mutations in the rod visual pigment rhodopsin. Point mutations of Glycine 90 to Aspartate (G90D) or to Valine (G90V) have been reported to cause congenital stationary night blindness (CSNB) and retinitis pigmentosa (RP), respectively. In vitro studies have shown that the G90D/G90V mutations cause decreased stability of both chromophore-bound rhodopsin and chromophore-free opsin. This lower stability could produce persistent activation of rod photoreceptors even in darkness and interfere with normal light detection, causing CSNB or RP. However, the molecular mechanism by which these mutations cause abnormal photoreceptor function and degeneration remains controversial.

Methods: Using CRISPR/Cas9 technology, we created homozygous mutant mice with either G90D or G90V rhodopsin and performed their initial characterization. Retinal morphology was analyzed by hematoxylin and eosin staining of retinal cross-sections. Scotopic function was assessed by in vivo electroretinography (ERG). Pigment content and stability of its 11-cis-retinal Schiff base in the dark were measured by spectrophotometry of dodecyl maltoside extracts from whole mouse eyes, in the absence or presence of hydroxylamine (HA), respectively.

Results: The morphology of the retina in both G90D and G90V mutant mice was normal up to 4 months of age, with good preservation of both outer nuclear and photoreceptor layers. However, the rod maximal response (ERG a-wave) in G90V and G90D mice at 2 months was suppressed to ~70% and ~50%, respectively, compared to controls. The rod photosensitivity was also reduced to a greater degree in the G90D than in G90V mice. The amount of rhodopsin in eyes of 2-month-old G90V mice was reduced to 25% of wild type levels. However, its 11-cis-retinal chromophore was not readily accessible to HA in the dark. In contrast, the level of rhodopsin in the eyes of G90D eyes was 35% of that in controls and its chromophore was accessible to HA.

Conclusions: Our preliminary data suggest that both G90D and G90V opsins in mouse rods have reduced chromophore binding. However, unlike in wild type and G90V rhodopsin, the covalent link between chromophore and opsin in G90D rhodopsin appears unstable and susceptible to hydrolysis. We conclude that G90V and G90D mutations in rhodopsin can cause night blindness by two different mechanisms that are being investigated further.

CONTROL ID: 3712628

SUBMITTER (NAME ONLY): Johnson Huang

TITLE: Increased Post-Cataract Surgery Refractive Surprise in Glaucoma Patients

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: An important part of cataract surgery is having excellent postoperative refractive outcomes. Therefore, postoperative refractive surprise is a challenge of significant interest in achieving desired vision. As populations age around the world, the incidence of glaucoma and cataract continue to rise. Further understanding of refractive outcomes in glaucoma patients undergoing cataract surgery is essential. In this study, we investigate post-cataract refractive outcomes of glaucoma versus non-glaucoma patients without any concomitant visually significant co-morbidities.

Methods: Patients who underwent uncomplicated phacoemulsification cataract surgery from 2007 to 2018 were enrolled in this retrospective cohort study. The first eye of each patient that qualified was included. We excluded patients with visually significant ocular or systemic comorbidities, prior non-refractive eye surgeries, combined cataract surgeries, and patients requiring additional procedures post op. Refractive outcome at postoperative 1 month was evaluated between control and glaucoma groups, as well as among glaucoma types.

Results: A total of 503 patients (354 in non-glaucoma and 149 in glaucoma) were included. Among the control group, 67.8% and 95.2% of patients fall within 0.5D and 1.0D of target respectively compared with 65.7% (P=0.659) and 89.9% (P= 0.027) in the glaucoma group. Refractive outcomes were compared between glaucoma types and no significant difference were found in percentage of patients within 0.5D and 1.0D of target (P=0.172 and P=0.9 respectively).

Conclusions: Patients with glaucoma are more likely to have postoperative refractive surprise compared with the general population. This is seen in patients without visually significant comorbidities, which suggest glaucoma plays a role in refractive outcomes not accounted for by current IOL calculations. Of note, the increase in refractive surprise seen in glaucoma patients appears to be irrespective of glaucoma type.

CONTROL ID: 3712630

SUBMITTER (NAME ONLY): Roberta McKean-Cowdin

TITLE: Differences in Vision-Specific Quality of Life with Visual Acuity by Race, Ethnicity in the Multiethnic Ophthalmology Cohorts of California Study (MOCCaS)

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. McKean-Cowdin, B. Burkemper, K. Ding, X. Jiang, Population and Public Health Sciences, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|R. McKean-Cowdin, B. Burkemper, X. Jiang, B. Xu, Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M. Torres, R. Varma, Southern California Eye Institute, CHA Hollywood Presbyterian Medical Center, Los Angeles, California, UNITED STATES|D.J. Grisafe, Medicine, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Roberta McKean-Cowdin: Commercial Relationship: Code N (No Commercial Relationship) | Dominic Grisafe: Commercial Relationship: Code N (No Commercial Relationship) | Mina Torres: Commercial Relationship: Code N (No Commercial Relationship) | Bruce Burkemper: Commercial Relationship: Code N (No Commercial Relationship) | Kaili Ding: Commercial Relationship: Code N (No Commercial Relationship) | Xuejuan Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Xu: Commercial Relationship: Code N (No Commercial Relationship) | Rohit Varma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare racial, ethnic differences in visual acuity (VA) on vision-specific quality of life (VSQOL)

Methods: In the MOCCaS, the impact of VA on VSQOL measured by the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) was evaluated in a population-based sample of African American (AA), Chinese American (CA), and Latino (LAT) adults. A total of 17,071 adults 40 years of age and older participated in a comprehensive ophthalmologic examination and in-person interviews from 2000 to 2018. Distance VA was measured during a detailed ophthalmologic examination using standard ETDRS protocol at baseline. VSQOL was assessed at the end of the clinical examination using the NEI-VFQ-25. Vision-related daily tasks (VRDT) and well-being composite scores were calculated using item response theory (IRT); classical test theory (CTT) was used to score 11 subscales with values ranging from 0 to 100, with higher scores representing better visual functioning.

Results: 14,570 participants (5,171 AA, 4,151 CA, and 5,248 LAT) with complete data were included in the analysis. Predicted VRDT and well-being composite scores were significantly lower for Latinos across level of presenting VA compared to AA or CA participants. An inverse relationship was found with significantly lower levels of patient reported ability to complete vision-related daily tasks after adjustment for covariates using IRT. A 2-line change in VA was associated with a 4.6 point change in vision-related daily tasks score for LAT participants, 3.9 for CA participants, and 2.9 for AA participants. The difference was greater for those 65 years of age and older. No significant differences in change for well-being were identified by race,ethnicity (3.2 Latino, 3.0 Chinese, 3.0 African American). Classical test theory revealed significant interactions for driving difficulty with VA, age, and race.

Conclusions: Each 2-line loss in VA has a significant impact on patient reported ability to complete vision-related daily tasks. The 2 line difference in VA corresponds to a lower difference in VRDT for African American as compared to Latino adults. Disparities in health are at times attributed to differences in income, education, and barriers to care however differences in VA and VSQOL persisted by race, ethnicity after controlling for measured socioeconomic and clinical variables.

CONTROL ID: 3712633

SUBMITTER (NAME ONLY): Theresa Landry

TITLE: Long-term Outcomes of Standalone Excisional Goniotomy using the Kahook Dual Blade in Eyes with Primary Open-Angle Glaucoma

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Landry, Clinical and Medical Affairs, New World Medical Inc, Rancho Cucamonga, California, UNITED STATES|M. ElMallah, Ocala Eye, Ocala, Florida, UNITED STATES|B. Williamson, C. Nelson, Williamson Eye Center, Baton Rogue, Louisiana, UNITED STATES|

Commercial Relationships Disclosure: Theresa Landry: Commercial Relationship(s);Code E (Employment):New World Medical | Mohammed ElMallah: Commercial Relationship(s);Code F (Financial Support):New World Medical;Code F (Financial Support):Ivantis;Code F (Financial Support):Glaukos | Blake Williamson: Commercial Relationship(s);Code F (Financial Support):New World Medical;Code C (Consultant/Contractor):New World Medical ;Code C (Consultant/Contractor):Sight Sciences;Code C (Consultant/Contractor):Glaukos;Code C (Consultant/Contractor):Zeiss;Code C (Consultant/Contractor):Johnson and Johnson;Code C (Consultant/Contractor):B&L | Cade Nelson: Commercial Relationship(s);Code F (Financial Support):New World Medical

ABSTRACT BODY:

Purpose: Purpose: To describe the long-term safety, intraocular pressure (IOP) lowering effect, and reduced surgical burden of the Kahook Dual Blade® (New World Medical, Rancho Cucamonga, California) as a standalone procedure when used to excise trabecular meshwork in eyes with primary open angle glaucoma (POAG).

Methods: Methods: This is a retrospective chart review of 39 eyes from 2 sites in the United States that included data collection of IOP, IOP-lowering medications, and additional glaucoma procedures at months 12, 24, 36, and 48. Eyes were not washed out of their previous IOP-lowering medications for this analysis. Intra- and postoperative adverse events were tabulated

Results: Results: Analysis from 39 eyes showed a mean IOP reduction from a baseline of 20.4 to 15.0 mmHg at month 48 (26.4% reduction, $p < 0.001$) Medication use at 48 months was similar to baseline ($p=0.123$). 33/39 (85%) eyes required no further surgery to manage IOP. One case of mild iritis related to the procedure was reported.

Conclusions: Conclusion: Excisional goniotomy with KDB effectively decreases IOP over long-term follow up when utilized as a standalone procedure in eyes with POAG. The device also shows a favorable safety profile in line with other minimally invasive glaucoma surgical interventions. Notably, the vast majority of patients (85%) did not require additional surgical intervention to further lower IOP for the duration of the study.

CONTROL ID: 3712636

SUBMITTER (NAME ONLY): XIAOGANG WANG

TITLE: Comparison study of the two biometers based on swept-source optical coherence tomography technology

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. WANG, Shanxi Eye Hospital, Taiyuan, Shanxi, CHINA|J. Dong, First Hospital of Shanxi Medical University, Taiyuan, Shanxi, CHINA|

Commercial Relationships Disclosure: XIAOGANG WANG: Commercial Relationship: Code N (No Commercial Relationship) | Jing Dong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the potential differences in parameters, including axial length (AL), central corneal thickness (CCT), anterior chamber depth (ACD), lens thickness (LT), flat keratometry (Kf), steep keratometry (Ks), mean keratometry (Km), astigmatism, white-to-white (WTW) distance, acquired rate, and intraocular lens (IOL) power, between the two swept-source optical coherence tomography (SS-OCT) biometers, the ANTERION (biometer A) and IOLMaster 700 (biometer B).

Methods: As a prospective observational comparative case series study. We enrolled 198 eyes undergoing cataract surgery. The AL, CCT, ACD, LT, Kf, Ks, Km, astigmatism, WTW, acquired rate, and IOL power were assessed. McNemar tests compared the acquired rate and paired sample t-test compared the quantitative measurement results, between groups.

Results: Nineteen eyes were excluded owing to missing AL data for either biometer. Finally, data from 179 eyes were analyzed. Between the two devices, no significant difference was found in AL, astigmatism magnitude, J0, and J45, while significant differences existed in CCT, ACD, LT, Kf, Ks, Km, WTW, astigmatism axis and IOL power; no statistical significance was found in AL acquired rate (biometer A, 90.9% and biometer B, 93.9%). Approximately 65.4% of eyes demonstrated ≥ 0.5 D difference in IOL power between the two biometers.

Conclusions: The two biometers showed significant differences in all measurements (CCT, ACD, LT, K, WTW, astigmatism axis and IOL power), except for AL.

CONTROL ID: 3712639

SUBMITTER (NAME ONLY): James Gibson

TITLE: Resident cataract surgery outcomes and complications in a large urban safety-net hospital

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gibson, P. Lang, D. Im, S. Kang, A. Kolluru, B. Wong, USC Roski Eye Institute, Keck Hospital of USC, Los Angeles, California, UNITED STATES|B. Wong, Los Angeles County University of Southern California Medical Center, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: James Gibson: Commercial Relationship: Code N (No Commercial Relationship) | Paul Lang: Commercial Relationship: Code N (No Commercial Relationship) | Deborah Im: Commercial Relationship: Code N (No Commercial Relationship) | Sara Kang: Commercial Relationship: Code N (No Commercial Relationship) | Ajay Kolluru: Commercial Relationship: Code N (No Commercial Relationship) | Brandon Wong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Public safety-net hospital patients have high rates of ocular comorbidities, which can occur in the setting of chronic disease and may affect cataract surgery outcomes. In a retrospective case series, we aimed to characterize the outcomes and complications, as well as identify risk factors for poor outcomes and complications, of resident-performed cataract surgeries at an urban public safety-net hospital.

Methods: The study population included all patients undergoing cataract surgery at LAC+USC with a resident as the primary surgeon from July 2015 to June 2016. Exclusion criteria included cases performed by a fellow; cataract cases combined with retina, glaucoma or corneal surgeries; and cases with inadequate documentation. Pre-operative, surgical, and post-operative characteristics were recorded. Primary outcomes were major intraoperative complication rate, risk factors for major intraoperative complications, rates of visual improvement, and risk factors for poor visual outcome. A multivariable Firth's logistic regression tested risk factors for statistical significance.

Results: 811 eyes were analyzed. 599 (73.9%) cases resulted with post-op best corrected visual acuity (BCVA) 20/40 or better, with 641 (80.9%) cases showing at least two lines of visual improvement. 119 (14.7%) cases had at least one intraoperative complication, most commonly posterior capsule tear (8.6%) and vitreous loss (7.2%). Ocular risk factors significantly associated with lower odds of post-op BCVA of 20/40 or better included history of proliferative diabetic retinopathy (PDR) (OR=0.25; 95% CI=0.14-0.44; p<0.001), intravitreal therapy (IVT) (OR=0.40; 95% CI=0.16-0.99; p=0.047), and vitreous hemorrhage (VH) (OR=0.33; 95% CI=0.15-0.70; p=0.004). Patients with history of VH (OR=0.33; 95% CI=0.15-0.72; p=0.005) were also significantly less likely to improve vision by two lines. History of panretinal photocoagulation (PRP) was associated with significantly increased odds of intraoperative complication (OR=5.22; 95% CI=1.42-19.27; p=0.013).

Conclusions: Several ocular comorbidities and ocular therapies—including PDR, VH, IVT—were significantly associated with poor visual outcomes, while PRP was associated with intraoperative complication, in resident-performed cataract surgery at a public safety-net hospital. These results can better inform both resident education and pre-surgical counseling for this underserved patient population.

CONTROL ID: 3712641

SUBMITTER (NAME ONLY): Ryan Duong

TITLE: Pre-operative prognostic risk factors in patients undergoing 27-g Pars Plana Vitrectomy for diabetic tractional retinal detachment

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Duong, X. Cai, N. Ambati, Y. Shildkrot MD, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Ryan Duong: Commercial Relationship: Code N (No Commercial Relationship) | Xiaoyu Cai: Commercial Relationship: Code N (No Commercial Relationship) | Naveen Ambati: Commercial Relationship: Code N (No Commercial Relationship) | Yevgeniy Shildkrot MD: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: As 27-gauge (27g) pars plana vitrectomy (PPV) for treatment of diabetic tractional retinal detachment (DM-TRD) becomes more widely practiced, there is a growing necessity to determine in which patients the procedure would be the most beneficial. We seek to evaluate pre-operative prognostic indicators for 27g PPV repair of diabetic tractional retinal detachment using a retrospective interventional case series analysis.

Methods: Visual and anatomic outcomes of 110 eyes that underwent 27g PPV for repair of DM-TRD from 2013-2020 were evaluated with respect to various past medical history parameters via linear regression analysis.

Results: The retina was successfully flattened at the end of all cases except one, and overall re-detachment rate was 10.9% (n=12). Pre-operatively, 80.2% (n=88) of patients were legally blind (logMAR > 1) compared to 56.3% (n=40) at postoperative month 6 ($p<.001$). Higher pre-operative logMAR visual acuity was associated with both greater odds of re-detachment (OR 4.95, $p=.002$) and worse visual acuity at month 6 ($p<.001$). Among the patient history parameters assessed, pre-operative use of dialysis ($p=.038$) and neovascularization of the iris (NVI) ($p=.045$) were associated with significantly worse visual acuity at month 6. Longer duration of diabetes in years was also associated less improvement in visual acuity from baseline at 6 months ($p=.037$). No medical history risk factors were identified for re-detachment.

Conclusions: Our results suggest that 27g PPV remains a viable option for repair of DM-TRD with the additional finding that duration of diabetes, dialysis use, and presence of NVI prior to surgery represent negative risk factors of visual outcomes. Comprehensive pre-operative evaluation is required to better estimate prognosis and identify diabetic patients who may most benefit from smaller gauge vitrectomy repair of DM-TRD

CONTROL ID: 3712642
SUBMITTER (NAME ONLY): Eric Gaier
TITLE: Pathologic interocular suppression after monocular deprivation
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E.D. Gaier, D. Bowen, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|E.D. Gaier, D. Bowen, D. Montgomery, M.F. Bear, Brain and Cognitive Sciences, Massachusetts Institute of Technology Picower Institute for Learning and Memory, Cambridge, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: Eric Gaier: Commercial Relationship(s);Code C (Consultant/Contractor):Luminopia, Inc., Stoke Therapeutics, Inc. ;Code P (Patent):Luminopia, Inc. | Daniel Bowen: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Montgomery: Commercial Relationship: Code N (No Commercial Relationship) | Mark Bear: Commercial Relationship(s);Code C (Consultant/Contractor):Luminopia, Inc.

ABSTRACT BODY:

Purpose: Amblyopia results from abnormal visual experience during development and is a leading cause of visual impairment in children and young adults. Pathologic interocular suppression of the amblyopic eye by the fellow eye serves as a quantifiable property and pathogenic driver of amblyopia. Recently development and implemented “dichoptic”/antisuppression amblyopia therapies have produced mixed results. We aimed to deepen the understanding of pathologic interocular suppression in the context of amblyopia at the level of the visual cortex using a mouse model.
Methods: Juvenile mice underwent chronic electrode implantation prior to visual stimulus presentation at P35. A 3D monitor and polarized lenses were used to selectively present phase-reversing sinusoidal grating stimuli to each eye. Awake visual evoked potentials (VEPs) elicited by a 45-degree grating presented to the contralateral eye were monitored as the concordant or discordant (135-degree) orientation was gradually presented to the ipsilateral eye.
Results: In naïve animals, binocular discordant stimuli significantly reduced VEP magnitudes compared with concordant stimuli primarily through disruption of the late, positive component of the VEP waveform. Reversing the contrast ramp direction showed the same monocular-binocular differences, suggesting these observations were not an artifact of presentation order. VEP responses recorded through the opposite hemisphere showed similar effects of rivalrous binocular stimulation on the VEP waveform. Introducing the discordant orientation in the same, contralateral eye produced a similar suppressive effect but carried a higher contrast threshold, suggesting interocular modulation of cross-orientation suppression. Incrementally adjusting the ipsilateral eye stimulus from concordant to discordant reveals a 15-degree threshold for interocular cross-orientation suppression. Seven days of monocular deprivation disrupted suppression of the early, negative VEP component by binocular discordant stimulus presentation but did not alter effects on the late component.
Conclusions: We have established a useful model of binocular rivalry to study interocular suppression. Disruption of interocular suppression that accompanies monocular deprivation serves to validate this model as tool to study the interplay between interocular suppression and amblyopia development and recovery.

CONTROL ID: 3712643

SUBMITTER (NAME ONLY): Mark Fields

TITLE: Use of iPSC-derived RPE to test the efficacy of elamipretide and SBT-272 in preclinical models of dry AMD

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Fields, J. Gong, H. Cai, L. Del Priore, Ophthalmology, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Mark Fields: Commercial Relationship(s);Code C (Consultant/Contractor):Stealth BioTherapeutics;Code F (Financial Support):Stealth BioTherapeutics | Jie Gong: Commercial Relationship: Code N (No Commercial Relationship) | Huey Cai: Commercial Relationship: Code N (No Commercial Relationship) | Lucian Del Priore: Commercial Relationship(s);Code C (Consultant/Contractor):Stealth BioTherapeutics

ABSTRACT BODY:

Purpose: Identification of compounds that may be of therapeutic benefit in inhibiting progression of AMD is limited by the absence of good animal models as well as a clear understanding of the biology of disease progression. Dysfunction of retinal pigment epithelial (RPE) cells is a key feature of AMD pathogenesis and likely occurs early in the disease. Somatic cells harvested from AMD patients can be reprogrammed to form RPE and model patient-specific disease. We have reported previously that iPSC-derived RPE from AMD patients exhibit a retinal degenerative phenotype and a distinct transcriptome compared to controls. Here, we use an in vitro aged Bruch's membrane model to evaluate the therapeutic efficacy of elamipretide and SBT-272 on RPE derived from AMD patients.

Methods: iPSC-derived RPE were generated from AMD patients (2 atrophic; 1 exudative) and patients with no history of AMD (n = 3). To test the therapeutic efficacy of elamipretide and SBT-272, cell viability was analyzed on nitrite-modified extracellular matrix (ECM), a typical modification of aged Bruch's membrane, for 48 hrs. DNA microarrays were used to elucidate gene expression in AMD-derived RPE cultured on nitrite-modified ECM.

Results: AMD-derived RPE exhibited reduced ability to survive on nitrite-modified ECM. Treatment with both elamipretide and SBT-272 significantly improved cell viability on nitrite-modified ECM. Hierarchical clustering analysis reveals that the AMD-derived RPE segregate into two distinct clusters on nitrite-modified ECM vs. unmodified ECM. Nitration of ECM increases expression of complement component genes, complement C1R (C1R), complement component 3 (C3) and complement C4A (C4A), among others. Both compounds reverse this trend. Both drugs increase expression of complement regulatory genes including complement factor H-related protein 2 (CFHR2). Both drugs also alter the pattern of many mitochondrial-related genes such as glutaminase.

Conclusions: Treatment with elamipretide and SBT-272 significantly improve the ability of AMD-derived RPE to survive on nitrite-modified ECM. Treatment with elamipretide and SBT-272 alter expression of mitochondrial and complement-related genes after nitration of ECM. Disease models using patient-derived iPSC-derived RPE may help pave the way for the development novel therapeutic strategies for AMD.

CONTROL ID: 3712644

SUBMITTER (NAME ONLY): Colin Tan

TITLE: Sensitivity of multicolor imaging in diagnosing age-related macular degeneration and Polypoidal Choroidal Vasculopathy

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.S. Tan, Ophthalmology, National Healthcare Group Eye Institute, Singapore, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Colin Tan: Commercial Relationship(s);Code R (Recipient):Roche

ABSTRACT BODY:

Purpose: To evaluate the accuracy of multicolour imaging compared to standard colour fundus photography (CFP) in differentiating AMD from normal eyes, and in detecting features of PCV.

Methods: In a prospective study of 50 consecutive patients presenting with PCV or AMD, standardized multimodal imaging (CFP, multicolour imaging, fluorescein and indoyanine green angiography) was performed. PCV was diagnosed using specific diagnostic criteria, with ICGA as the gold standard. CFP and multicolor images were graded using standardized grading protocols to determine sensitivity, specificity, positive and negative predictive values (PPV and NPV) in differentiating AMD from normal eyes, and in detecting features of PCV.

Results: The mean age of the patients was 70.0 years. Of 100 eyes, 44 had PCV, 11 had neovascular AMD, 21 non-neovascular AMD and 23 were normal. Of 44 eyes, polyps appeared as dark green oval lesions in 39 (88.6%) using the multicolour channel, while the branching vascular network (BVN) appeared as mottled grey lesions in 16 (36.4%) using the infrared channel. Multicolor had superior specificity (73.9% vs. 52.2%) and NPV (94% vs. 85.7%) compared to CFP for detecting all types of AMD. The sensitivity was similar for both multicolor and CFP (97.7% vs. 97.4%). For the detection of PCV, multicolour had higher sensitivity (86.4% vs. 59.1%) and NPV (89.3% vs. 74.3%) compared to CFP. In contrast, the specificity (89.3% vs. 92.9%) and PPV (86.4% vs. 86.7%) were similar between the two. PCV lesions were best visualized on the infrared multicolour images. Using BVN as a parameter, infrared imaging had very high specificity (96.6%) and PPV (88.9%) for detecting PCV.

Conclusions: Multicolour imaging is superior to CFP in differentiating AMD from normal eyes and detecting features of PCV. The presence of BVN on infrared imaging and dark green oval lesions should alert ophthalmologists to the presence of PCV.

CONTROL ID: 3712645

SUBMITTER (NAME ONLY): Amy Lu

TITLE: Optical coherence tomography angiography in inherited retinal disease

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lu, J. Sundstrom, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Amy Lu: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Sundstrom: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diagnosis of inherited retinal diseases (IRD) remains difficult as some diseases do not demonstrate obvious findings on clinical exam. Optical coherence tomography angiography (OCTA) is an emerging, non-invasive imaging modality that may provide new information regarding these diseases. However, studies involving OCTA and IRD generally involve small case series that focus on specific IRDs. Here, we perform a database search to examine global as well as disease-specific changes in OCTA in different IRDs.

Methods: A systematic review and meta-analysis was performed by searching Pubmed. Studies utilizing OCTA in IRD were included. Search results that did not utilize OCTA, did not include eyes diagnosed with IRD, not available in English, not primary research articles or case series, or did not involve human eyes were excluded.

Results: Database search identified 25458 records. After removal of duplicates, 6603 records were subjected to inclusion/exclusion based on manual review of titles and abstract. 153 articles were included for full-text review. The most common reasons for exclusion were no diagnosis of IRD and no use of OCTA. Specifically, 1142 (17%) of non-duplicated search results included eyes that were diagnosed with IRD, of which 153 (13%) these utilized OCTA imaging. 128 (84%) of studies that were included were published between 2018 and 2021. 22 different IRDs were represented after inclusion/exclusion. Most highly represented IRD diagnoses were retinitis pigmentosa, Best disease, Stargardt's disease, choroideremia, adult onset foveomacular vitelliform dystrophy, and X-linked retinoschisis. Preliminary analysis suggests that multiple IRDs demonstrate patterns of enlarged superficial foveal avascular zone (FAZ) and decreased vessel density compared to healthy controls, and compared to earlier forms of the disease. Further, differences in FAZ and vessel density are more prominent to specific deep or superficial layers and capillary beds, and these differ between diseases.

Conclusions: OCTA has been increasingly utilized in characterizing different IRDs as well as different stages of IRD progression. OCTA has also been incorporated in initial reports describing novel IRD entities and novel mutations in known IRDs. OCTA adds new understanding to the pathology of IRD and should be considered in the workup and continued management of IRD patients.

CONTROL ID: 3712646

SUBMITTER (NAME ONLY): Ashley Brown

TITLE: Multimodal tracking of subretinal ARPE-19 cells labeled with indocyanine green contrast in rabbits for potential AMD treatment

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Brown, V. Nguyen, Y.M. Paulus, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|X. Wang, Y.M. Paulus, Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Ashley Brown: Commercial Relationship(s);Code F (Financial Support):University of Michigan | Van Phuc Nguyen: Commercial Relationship(s);Code E (Employment):University of Michigan | Xueding Wang: Commercial Relationship(s);Code E (Employment):University of Michigan | Yannis Paulus: Commercial Relationship(s);Code E (Employment):University of Michigan

ABSTRACT BODY:

Purpose: Vision loss from age-related macular degeneration (AMD) is currently irreversible as the retinal photoreceptors lack regenerative capacity. Regenerative cell therapies offer a promising treatment in restoring retinal function through transplanted stem cells, but face challenges in tracking the cells in vivo. This study used indocyanine green contrast (ICG) and multimodal imaging to longitudinally monitor the movement and growth of transplanted stem cells in vivo.

Methods: A model of 12 New Zealand White rabbits with localized retinal pigment epithelial (RPE) lesions from photocoagulation represented the RPE cell atrophy causing vision loss in patients experiencing AMD. Optical coherence tomography (OCT) was used to visualize the structural layers of the retina and guide an injection of progenitor human retinal pigment epithelium cells (ARPE-19) labeled with ICG into the lesions. The ICG increased the cell signal sensitivity to allow a noninvasive, multimodal system of photoacoustic microscopy (PAM), OCT, and fluorescence imaging to longitudinally track the distribution of ARPE-19 cells in vivo for 28 days.

Results: PAM and fluorescence imaging optimally visualized ICG labeled ARPE-19 cells at 700 nm. After an injected dose of 30 µL labeled ARPE-19 cells at a concentration of 10^6 cells/mL, PAM and fluorescence imaging tracked cell movement and growth. PAM signals (0.2±0.01 a.u. pre-injection) increased 20-fold (3.93±0.05 a.u.; $P<0.001$) and were detectable for 28 days. Fluorescence signals (0.07 ±0.01 a.u. pre-injection) initially increased by 37-fold (2.41 ±0.01 a.u.; $P<0.001$) and were also detectable for 28 days. Both signals detected stronger concentrations of ARPE-19 cells localized to photocoagulation lesions in the RPE. As a control, injected ICG without ARPE-19 cells did not localize to the lesions and was cleared from the body within 7 days. Histological staining with hematoxylin and eosin (H&E), as well as immunohistochemistry staining with RPE65 antibody confirmed localization and growth of ARPE-19 cells in the photocoagulation lesions as seen in OCT images.

Conclusions: The movement and growth of subretinal transplanted ARPE-19 cells labeled with ICG can be longitudinally tracked in vivo for up to 28 days using a noninvasive multimodal system of PAM, OCT, and fluorescence imaging.

CONTROL ID: 3712647

SUBMITTER (NAME ONLY): Andrea Vincent

TITLE: Characterising the natural history of retinal degeneration progression associated with a founder mutation in the PDE6B gene.

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Vincent, E. Edgar - Nemec, S. Hull, Ophthalmology, New Zealand National Eye Centre, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND| A.L. Vincent, S. Hull, Eye Department, Greenlane Clinical Centre, Auckland, NEW ZEALAND|

Commercial Relationships Disclosure: Andrea Vincent: Commercial Relationship: Code N (No Commercial Relationship) | Elena Edgar - Nemec: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Hull: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the rate of progression of vision and retinal parameters in PDE6B-associated rod cone retinal dystrophy, in a cohort of Māori patients, over a 9 year period, in New Zealand/Aotearoa. All carried at least one copy of the same pathogenic variant, (c.2197G > C, p.(Ala 733Pro)).

Methods: Retrospective review of patients identified from the the New Zealand Database of Inherited Retinal Disease with the PDE6B founder variant. Clinical notes were reviewed to determine best corrected visual acuity at each visit. Sequential Spectralis OCT scans through the fovea and shortwave autofluorescence (SW-AF) were reviewed, with the ellipsoid line identified and measured. The hyperautofluorescent ring was marked and measured in the horizontal and vertical meridian. Progression rates for width of the EZ, AF ring diameters and area, and BCVA were estimated using linear mixed models.

Results: 19 patients were identified (53% female) with an average age at first visit of 47 years (range 21-68 years) and average follow-up of 3.2 years (range 1-9 years), and 16 were homozygous for the p.(Ala 733Pro) allele. Almost all patients in this study had an initial baseline measurement of <3000µm for EZ line width and SW-AF ring diameters, EZ-line widths decreased by 350µm per year, area of SW-AF ring diameters decreased by 2.2mm2 per year and average horizontal and vertical hyper SW-AF ring diameters decreased by 320µm and 430µm per year, respectively. Estimated mean rate of LogMAR visual acuity decline, based on the slope of each patient was 0.0529 increments per year.

Conclusions: This study characterises the rate of progression of a cohort of patients with the same unique PDE6B founder mutation. Consistent with previous studies, disease progression rate was observed to be a function of initial baseline measurement. This study also provides information on the rate of progression for patients with more advanced stages of the disease (<3000µm for EZ line). Documenting the natural history is a prerequisite for preparedness for any gene-directed treatment.

CONTROL ID: 3712649

SUBMITTER (NAME ONLY): Alexandra Castillejos

TITLE: Structural and Functional Assessment of Glaucoma Progression in Patients with Boston Keratoprosthesis Type 1

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Castillejos, C. Saini, J. Chodosh, L.Q. Shen, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the assessment of glaucoma progression in patients with Boston Keratoprosthesis type 1 (KPro) by optical coherence tomography retinal nerve fiber layer (OCT RNFL) and Humphrey Visual Fields 24-2 (HVF), to clinical determination.

Methods: Retrospective analysis of all KPro patients at Massachusetts Eye and Ear between 1990 and 2021. Of 1358 KPro patients, 67 patients had undergone Cirrus OCT RNFL imaging, of which 9 patients had three or more OCT images without significant artifacts and with signal strength ≥6. 101 patients had undergone HVF testing, of which 22 had three or more reliable HVFs (FL<33%, FP<20%, FN<20%). Progression by OCT was defined as >5µm loss of average RNFL thickness or >7µm for superior and inferior quadrants. HVFs were assessed for trend-based and event-based progression using previously published criteria. Clinical determination of progression was based on an increase in cup-to-disc ratio of 0.2 on clinical exam or an escalation of glaucoma therapy.

Results: Sufficient OCT and/or HVF data for progression analysis was available for 24 KPro patients (66.7% male, 83.3% white, mean age 60.9±11.9 years) with follow-up of 5.5±3.3 years. At the time of baseline testing, the average visual acuity was logMAR 0.51±0.47, the RNFL thickness was 88.1±15.1µm, and the mean deviation was -12.5±6.5dB. Glaucoma progression based on OCT and/or HVF was noted in 20.8% (5/24) of patients. 2 out of 9 patients progressed based on OCT, while 3 out of 22 progressed based on HVF. In 6 of the 22 patients (27.3%) with reliable HFVs, progression could not be assessed due to severe loss at baseline. Clinical assessment showed progression in 16.7% (4/24) of patients. Overall, OCT and HVF testing identified an additional 4 progressors (16.7%), who were not identified by clinical assessment (Table 1).

Conclusions: Although the use of structural and functional measurements to detect glaucoma progression is limited in patients with KPro, our data suggest that HVF and OCT can be complementary to conventional clinical assessment of glaucoma in this patient population.

CONTROL ID: 3712652

SUBMITTER (NAME ONLY): Erin O'Neil

TITLE: Central Structural and Functional Abnormalities in Choroideremia: Longitudinal and Cross-sectional Observations from a Large Cohort of Patients

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. O'Neil, Ophthalmology, The Children's Hospital of Philadelphia Division of Ophthalmology, Philadelphia, Pennsylvania, UNITED STATES|K.E. Uyhazi, K. O'Connor, Y. Jiang, A.M. Maguire, J.I. Morgan, J. Bennett, T.S. Aleman, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|K.E. Uyhazi, E. Shagena, A.M. Maguire, J.I. Morgan, J. Bennett, T.S. Aleman, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|K. Scavelli, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe in detail the natural history of the central retinal structural and functional changes of a large group of patients with choroideremia (CHM).

Methods: Patients with CHM, ages 6 to 70 years (n= 133), had a comprehensive ophthalmologic evaluation and retinal imaging with spectral domain optical coherence tomography (SD-OCT). OCT cross sections were quantified along the horizontal meridian and related to co-localized visual thresholds measured with automated two-color static perimetry. A subset of patients (n=45) had longitudinal evaluations, which were used to validate predictions from much larger cross-sectional observations.

Results: Most patients (88%) retained visual acuity (VA) better than 0.3 logMAR until the fifth decade of life. VA decline below this level was associated with shortening of the inner segment ellipsoid (EZ) to RPE/BrM band thickness to ~half the normal value, coinciding with approximation of the transitions zones (TZs) of degeneration to the foveal center. No such relationship was identified between VA and outer nuclear layer (ONL) thickness or foveal sensitivity. Earliest abnormalities in regions with normally appearing retinal pigment epithelium (RPE) were the loss of the photoreceptor outer segment (POS) and RPE interdigitation zone associated with rod dysfunction. We confirmed that cone function may remain normal over an extended range when rod sensitivity has fallen well-below normal limits and prior to demonstrable changes in ONL thickness. TZs from relatively preserved retina to severe ONL thinning and inner retinal thickening moved centripetally with age, in either cross-sectional or longitudinal observations. In general, RPE abnormalities paralleled photoreceptor degeneration although there were regions with detectable but abnormally thin ONL co-localizing with severe RPE depigmentation and choroidal thinning.

Conclusions: We found that visual acuity decline in choroideremia relates well to shortening of the POS but not as well with ONL thickness or foveal sensitivity as measured by static perimetry. We confirmed that rod sensitivity loss is the earliest and most sensitive measure of visual function. These results have implications for further gene therapy clinical trials. The relationships established may help outline the eligibility criteria and outcome measures for clinical trials for CHM.

CONTROL ID: 3712653

SUBMITTER (NAME ONLY): Stephen Phillips

TITLE: Prevalence of Diabetic Retinopathy in Patients with Limited English Proficiency

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Phillips, Z. Gill, A. Strong Caldwell, J.L. Patnaik, N.C. Grove, L. Mudie, M. Wagner, A. Marin, N. Mehta, S.C. Oliver, L. Seibold, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: This retrospective observational study compares the prevalence and severity of diabetic retinopathy (DR), and the likelihood of receiving anti-vascular endothelial growth factor (anti-VEGF) treatments in limited English proficiency (LEP) patients compared to English proficient (EP) patients.

Methods: We used the Cataract Surgery Outcomes Database to analyze the records of patients who underwent cataract surgery at the University of Colorado between 2014 and 2019. LEP was defined as a need or preference for an interpreter during medical encounters. Demographic and pre-operative characteristics analyzed included gender, race/ethnicity, age, prevalence of diabetes, history of macular edema, and history of DR. Comparisons between groups were made using logistic regression analysis with general estimating equations to account for patients with two eyes included in the study.

Results: A total of 868 LEP and 12,722 EP patients were analyzed. LEP patients had a significantly higher rate of type 2 diabetes (44.9% vs 21.5%, $p<0.0001$), macular edema (9.8% vs 2.9%, $p<0.0001$), and DR (18.1% vs 5.8%, $p<0.0001$). In patients with DR, LEP patients were more likely to receive anti-VEGF injections (34.4% vs 23.5%, $p=0.028$) and have more severe DR (severe non-proliferative DR 8.3% vs 6.5%, proliferative DR 58.6% vs 42.9%, $p=0.023$). LEP patients receiving anti-VEGF injections were less likely to receive >25 injections (2.3% vs 11.3%) and more likely to receive <10 injections as compared to EP patients (73.3% vs 65.5%, $p = 0.111$).

Conclusions: Our data suggests that LEP patients are at increased risk for DR and associated complications. Interestingly, we found that while a greater proportion of LEP patients receive anti-VEGF injections, they are less likely to receive as many injections overall compared to EP patients. This may suggest that LEP patients receive less consistent follow-up care. While this study represents a first step towards examining the relationship between EP status and DR, further studies are needed to better understand how language influences patient outcomes.

CONTROL ID: 3712654

SUBMITTER (NAME ONLY): Jayoung Moon

TITLE: Therapeutic Efficacy of pH-Responsive Cyclosporine A-eluting Contact Lenses in a Rabbit Model of Experimental Dry Eye.

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Moon, R. Jin, H. Yoon, J. Kim, H. YOON, K. Yoon, Ophthalmology, Chonnam National University Hospital, Gwangju, Gwangju, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Topical application of cyclosporin A (CsA) is a widely adopted method for treating ocular inflammatory diseases. However, achieving therapeutic levels of CsA in ocular tissues is challenging due to its significant molecular weight and hydrophobicity and the natural defense system of the eye. The purpose of this study was to investigate the effects of two different types of pH-responsive CsA-eluting contact lenses on the ocular surface of experimental dry eye (EDE) in rabbits.

Methods: CsA-eluting contact lenses were developed using two pH-responsive materials (pH-responsive immine cross-linking hyaluronic acid and pH-responsive cellulose polymer drug-eluting systems). Dry eye was induced using 0.1% benzalkonium chloride in rabbits, subdivided into the normal, EDE, 0.05% CsA, naïve soft contact lens (CL), immine cross-linking hyaluronic acid contact lens (CL type 1), or cellulose polymer contact lens (CL type 2) groups (n=18). CsA release profiles of the CsA-eluting contact lenses were evaluated with high-performance liquid chromatography analysis at pH 7.4 and 37°C, the same environment as the human ocular surface. Tear volume, tear film break-up time (TBUT), and corneal staining scores (CSS) were measured after 7 and 14 days. Periodic acid-Schiff staining for conjunctival goblet cells and TUNEL assay for corneal apoptotic positive cells were performed after 14 days.

Results: CsA was continuously released without an initial rapid release for 24 hours in both types of CsA-eluting contact lenses. All treatment groups showed a significant improvement in tear volume, TBUT, and CSS compared to the EDE group at 7 and 14 days. The CL type 1 and CL type 2 groups exhibited a significant improvement in the clinical parameters than the 0.05% CsA and CL groups after 7 and 14 days. In addition, compared to the EDE group, the CL type 1 and CL type 2 groups had higher goblet cell density and fewer TUNEL positive cells after 14 days ($p < 0.05$).

Conclusions: Two types of CsA-eluting contact lenses manufactured using two pH-responsive substances showed sustained drug release under conditions similar to the ocular surface. Both CsA-eluting contact lens types 1 and 2 could improve clinical signs, increase conjunctival goblet cells, and decrease TUNEL positive cells in a rabbit model of experimental dry eye.

CONTROL ID: 3712655

SUBMITTER (NAME ONLY): Anser Abbas

TITLE: Anti-inflammatory effect of prescription eye drops on porcine corneal endothelial cells with induced oxidative stress

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abbas, J.J. Bu, K. Agsalud, D.F. Hakim, T. Noguchi, P. Shaw, N.A. Afshari, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess inflammatory markers in a porcine model of smoking-induced oxidative stress in corneal endothelial cells after treatment with three commonly used eye drops: cyclosporine (0.05%), lifitegrast (5%), and tacrolimus (0.1%).

Methods: The corneoscleral rim was separated from eight harvested porcine eyes and treated with 0.5% trypsin for 15 minutes. Corneal endothelial cells were scraped from Descemet membrane, plated into one well of a 12-well plate, proliferated to confluency in a low growth factor medium, and passaged three times until reaching 12 wells of a 12-well plate for treatment. Hydroquinone (HQ) was used to induce oxidative stress. Cells were exposed to medium containing 250 μM HQ and one of the following nine eye drop treatments: 10%, 5%, or 2.5% cyclosporine (Restasis 0.05% eye drops diluted ten-, twenty-, and forty-fold respectively); 10%, 5%, or 2.5% lifitegrast (Xiidra 5% drops diluted respectively); and 5%, 2.5%, and 1.25% tacrolimus (0.1% drops diluted respectively). All treatments were two hours and tested in biological triplicate. Control groups were: each eye drop condition without the addition of HQ (N=3 each), HQ alone (N=5), and untreated (N=7). Total RNA was extracted using the RNEasy Mini Kit and converted to cDNA using the iScript Reverse Transcription Supermix. Expression of inflammatory markers IL-6, TNF-alpha, and the housekeeping gene GAPDH, were quantified using real-time quantitative PCR. The delta-delta Ct method was used to calculate relative gene expression, and statistical tests were calculated using delta Ct values.

Results: Cells with hydroquinone-induced oxidative stress had significantly reduced IL-6 expression when treated with cyclosporine ($p<.05$), lifitegrast ($p<.01$), and tacrolimus ($p<.05$), compared to cells with hydroquinone alone. Single-factor analysis of variance (ANOVA) did not reveal significant differences based on each level of eye drop concentration. In the absence of hydroquinone-induced oxidative stress, eye drop treatment did not significantly impact inflammatory marker expression.

Conclusions: Cyclosporine, lifitegrast and tacrolimus can protect against inflammatory marker expression in corneal endothelial cells in an induced oxidative stress model. More research is needed on these effects at various eye drop concentrations.

CONTROL ID: 3712656

SUBMITTER (NAME ONLY): Ana Chucair-Elliott

TITLE: Cell-specific Studies Through Novel Mouse Model Reveal the Transcriptomic Response of Retinal Müller Glia to Aging

SESSION TITLE: Animal Models of Age Related Macular Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.J. Chucair-Elliott, S. Ocañas, K. Pham, M. Van Der Veldt, D. Stanford, W. Freeman, Genes & Human Disease, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, UNITED STATES|M.H. Elliott, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|S. Ocañas, A. Cheyney, M.H. Elliott, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|W. Freeman, Oklahoma City VA Medical Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is the major risk factor for age-related macular degeneration (AMD) but how aging contributes to AMD pathogenesis is unclear. Epigenetic modifications, mainly methylcytosine (mC) and hydroxymethylcytosine (hmC), regulate the genome and gene expression, and are altered with advanced age. DNA methylation analyses of AMD patient blood and retinas suggest differential methylation resulting in gene expression changes during development of AMD. In addition, Müller glial cells (MGC) are activated in AMD patient retinas. The aim of this study is the validation and demonstration of a cre/ERT2-NuTRAP mouse model for the paired interrogation of differential mC/hmC genome-wide and the translatome specifically in MGC with retinal aging.

Methods: Female NuTRAP $^{flox/flox}$ and male Aldh1l1-cre/ERT2$^{+/wt}$ mice were bred to generate Aldh1l1-cre/ERT2$^{+/wt}$; NuTRAP$^{flox/wt}$ (Aldh1l1-cre/ERT2^{+}; NuTRAP^{+}) mice. After systemic tamoxifen treatment mice were euthanized at 6 or 24 months of age and their retinae harvested and processed for: immunohistochemistry of mCherry, EGFP, GS, CD11b, and GFAP expression in retina sagittal sections via confocal microscopy; MGC ribosome bound RNA isolation via TRAP and stranded RNAseq profile; MGC nuclei isolation via INTACT method for bisulfite amplicon sequencing (BSAS) and nuclear RNAseq.

Results: Specific co-localization of EGFP, mCherry, and the MGC marker GS was observed in the Aldh1l1-cre/ERT2^{+}; NuTRAP^{+} retinae. RNA-seq bioinformatic analysis revealed MGC-specific transcriptomic changes associated to inflammation in response to aging, such as purinergic receptor and cytokine-mediated signaling pathways. Nuclear RNAseq data supported the MGC identity of the INTACT-DNA isolates. BSAS showed site-specific decrease of mC in the promoter region of the MGC-specific gene Kcnj10 and hypermethylation in the promoter region of the photoreceptor gene Rho in INTACT-DNA positive fraction relative to input.

Conclusions: Our data show the Aldh1l1-NuTRAP model as a suitable tool for the paired interrogation of DNA methylation and gene expression, specifically in MGC. Differential transcript expression with overrepresentation of pathways and processes related to inflammation was found specifically in MGC in response to aging.

CONTROL ID: 3712657

SUBMITTER (NAME ONLY): Bruno Maciel

TITLE: Peripheral neuropathy evaluation of diabetes mellitus patients in follow-up care in a medical retina clinic

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.A. Maciel, A. Nassaralla, J.L. Orefice, Centro Oftalmológico de Minas Gerais, Belo Horizonte, Minas Gerais, BRAZIL|

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ABSTRACT BODY:

Purpose: To assess the prevalence of peripheral neuropathy findings in patients diagnosed with diabetic retinopathy (DR) for over 5 years having follow up care in Medical Retina (MR) clinic.

Methods: Thirty-three patients were invited randomly and consecutively evaluated in one day in our MR clinic. Along with indirect ophthalmoscopy to evaluate the patients' retinas, various tests to assess the presence and severity of peripheral neuropathy were performed. Semmes-Weinstein monofilament test, abnormalities in posterior tibial and dorsalis pedis pulse, presence of active or inactive diabetic foot ulcers (DFUs), and questions such as history of DFUs or inadequate outdoor footwear were made throughout the examination. The results were, then, correlated.

Results: Among mild, moderate and severe retinopathy patients: 39,4% presented abnormal Semmes-Weinstein monofilament test; 42,5% and 30,3% showed weak or absent pulse (posterior tibial and dorsalis pedis respectively); While 24,2% reported history of diabetic foot ulcer, only 9,1% demonstrated active DFUs and 3% had amputation history. The inadequate outdoor footwear use was reported by 39,4% of the patients.

Conclusions: Peripheral neuropathy is a common manifestation of diabetes in patients diagnosed with diabetic retinopathy for over 5 years undergoing clinical follow-up in a MR clinic. Therefore, we may infer that, being two of the three most common diabetes manifestations, diabetic retinopathy may be a biomarker for peripheral neuropathy in diabetic patients. Furthermore, patients presenting peripheral neuropathy from diabetic foot that were never submitted to a fundoscopic evaluation have a good chance of presenting undiagnosed diabetic retinopathy.

CONTROL ID: 3712658

SUBMITTER (NAME ONLY): Jianqing Li

TITLE: Multimodal Imaging and En Face OCT Detection of Calcified Drusen in Eyes with Age-Related Macular Degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Li, J. Liu, R. Laiginhas, M. Shen, Y. Shi, O. Trivizki, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|N.K. Waheed, New England Eye Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: En face optical coherence tomography (OCT) imaging was investigated as a method for the detection and monitoring of calcified drusen in eyes with non-exudative age-related macular degeneration (AMD).

Methods: A retrospective review of a prospective study was performed of same-day color fundus (CF), near infrared (NIR), fundus autofluorescence (FAF), and en face swept-source OCT (SS-OCT) images to identify eyes with non-exudative AMD and calcified drusen. The appearance and subsequent progression of these lesions were compared using the different imaging modalities.

Results: Two hundred twenty eyes from 139 patients with non-exudative AMD were studied with 42.7% of the eyes containing calcified drusen either at baseline or during their follow-up visits. On the en face sub-RPE SS-OCT slabs, calcified drusen appeared as dark focal lesions referred to as choroidal hypo-transmission defects (hypoTDs). The corresponding B-scans showed drusen with heterogenous internal reflectivity and a hyper-reflective cap. In the majority of the calcified drusen, choroidal hyper-transmission defects (hyperTDs) were observed to develop over time around the periphery of the hypoTDs giving them the appearance of a donut lesion on the en face SS-OCT images. These donut lesions were associated with significant attenuation of the overlying retina, and the corresponding FAF images showed hypo-autofluorescence at the location of these lesions. The donut lesions fulfilled the requirement for a persistent hyperTD and is synonymous with complete retinal pigment epithelium and outer retinal atrophy (cRORA). Six eyes displayed regression of their calcified drusen without developing cRORA. B-scans at the location of the regressed calcified drusen showed deposits along the RPE with outer retinal thinning in the regions where the calcified lesions previously existed.

Conclusions: En face rendering of OCT images is a useful method for the detection and monitoring of calcified drusen and future studies will document the evolution of these drusen as they form donut lesions and foci of cRORA.

CONTROL ID: 3712659

SUBMITTER (NAME ONLY): Jenny Zhang

TITLE: A Novel ex-vivo Model for Studying Early Pressure-Induced Retinal and Optic Nerve Head Responses in The Human Eye

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.W. Zhang, J.M. Sivak, Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, CANADA|J.W. Zhang, D. Chan, J.M. Sivak, Donald K. Johnson Eye Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, CANADA|D. Chan, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

Commercial Relationships Disclosure: Jenny Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Darren Chan: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Sivak: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Early pathological changes in the human retina and optic nerve head due to elevated intraocular pressure (IOP) remain elusive due to the unique biomechanical properties of human eye in the context of glaucoma. We generated a new model of acute IOP elevation based on a recently characterized organotypic whole-globe human eye perfusion approach. This system enables us to study the initial response of ex vivo human retina and lamina cribrosa (LC) to pathologically relevant pressure insult.

Methods: Human eyes received from the Eyebank of Canada within 24 hours of enucleation were immersed in Neurobasal-A Medium with supplements. Physiological fluid convection was restored in the eyes by infusion of synthetic aqueous humor into the anterior chamber over 6 hours. For each pair of eye, one was perfused to maintain a physiological IOP of 18-21mmHg, and the contralateral eye was maintained at an elevated IOP of 30-50 mmHg. Following perfusion eyes were fixed in 4% paraformaldehyde and sectioned for confocal microscopy. RBPMS staining and TUNEL assay were quantified to assess retinal ganglion cell (RGC) survival. GFAP and Iba1 staining were quantified to assess astrocyte reactivity and microglial activation in the retina and LC. Two-tailed paired student's t-test was used for statistical analysis.

Results: Whole-globe human eyes maintained a sustained physiological or elevated IOP for 6 hours, for at least three pairs. The retina and LC ctyoarchitecture were well preserved in all samples. There was minimal loss in the number of RBPMS-positive RGC ($p=0.50$) after IOP elevation. TUNEL assay also showed no apoptosis in the ganglion cell layer in both normal or elevated IOP eyes. IOP elevation led to significant activation of retinal microglia ($p=0.015$), indicated by changes in their distribution. IOP elevation showed a trend of increased GFAP intensity in the retina and LC, indicating potential early astrocyte reactivity.

Conclusions: Our model produces sustained, elevated IOP in ex-vivo whole globe human eyes. The pressure insult induces rapid microglial activation that precedes visible neuronal injury. These changes replicate findings in other early-stage glaucoma models, and provide insight into pathological events relevant to early human glaucoma. With further optimization, this model will be used to study IOP-dependent molecular changes in human eyes relevant to glaucoma pathogenesis.

CONTROL ID: 3712660

SUBMITTER (NAME ONLY): Chloe Khoo

TITLE: History of Systemic Corticosteroid Use Prior to Pars Plana Vitrectomy – Long-term Outcomes at 1 Year

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Khoo, H. Pakhchanian, C. Culp, B. Bernstein, M. Nasseri, M. Dalal, Ophthalmology, The George Washington University, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study the outcomes at 1 year after pars plana vitrectomy (PPV) in patients with a history of systemic corticosteroid use prior to PPV.

Methods: A retrospective cohort study was performed using TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple health organizations in the United States. Patients who underwent PPV were identified using a series of ICD-10 codes and stratified into 2 cohorts - with or without a history of systemic corticosteroid use prior to PPV. Each subject was matched to a control based on age, sex, BMI and the presence or absence of hypertension, diabetes mellitus, chronic lower respiratory diseases, heart failure, nicotine dependence and alcohol related disorders. The primary endpoint of the study was the incidence of vitreous hemorrhage (VH), choroidal hemorrhage, retinal detachment or break, iridocyclitis, retinal edema, cystoid macular degeneration, macula pucker, glaucoma, cataract, corneal edema, central retinal vein occlusion (CRVO) and central retinal artery occlusion (CRAO).

Results: A total of 25,752 patients were included in the analysis with 12,876 patients in each of the cohorts after propensity matching. At 1-year post-PPV, the cohort with a history of systemic corticosteroid use prior to PPV were at greater risk for choroidal hemorrhage (RR 2.16; CI 1.42, 3.28), retinal detachment or break (RR 1.09; CI 1.04, 1.15), iridocyclitis (RR 1.59; CI 1.38, 1.82), retinal edema (RR 1.27; CI 1.15, 1.41), cystoid macular degeneration (RR 1.61; CI 1.45, 1.8), macula pucker (RR 1.42; CI 1.35, 1.5), glaucoma (RR 1.42; CI 1.34, 1.51), cataract (RR 1.28; CI 1.2, 1.36) and corneal edema (RR 2.37; CI 1.55, 3.62).

Conclusions: Patients with a history of systemic corticosteroid use prior to PPV are at greater risks of long-term complications at 1-year post-PPV, possibly from a heightened inflammatory response from an underlying disease process treated by the corticosteroid. These findings can facilitate pre-operative counseling with patients regarding potential surgical risks and post-operative complications.

CONTROL ID: 3712661

SUBMITTER (NAME ONLY): Shivam Amin

TITLE: Outcomes of drive-by paintball shootings at a tertiary academic center

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Amin, A. Farooq, H. Shah, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|V. Otti, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the sequela of ocular paintball injuries from drive-by shootings with a focus on the range and severity of injuries sustained, clinical management, and visual outcomes.

Methods: Retrospective analysis of 20 patients who suffered ocular paintball injuries from drive-by shootings and were evaluated at a tertiary medical center from July 18, 2020, until November 8, 2021.

Results: Mean follow-up interval was 1.7 months from the time of initial evaluation (range: 0 days - 11.4 months). The average age of patient at the time of presentation was 36.6 years (range: 13 - 64 years-old). Fourteen patients (70%) had an initial visual acuity (VA) of hand-motion (HM) or worse. Six patients (30%) suffered ruptured globe injuries requiring urgent surgical repair, of whom three (15%) underwent subsequent evisceration. Nine patients (45%) presented with vitreous hemorrhage, eight (40%) with traumatic hyphema, four (20%) with iridodialysis, three (15%) with traumatic cataract, two (10%) with choroidal rupture, and one (5%) with a retinal tear/detachment. Fourteen patients (70%) suffered two or more ocular injuries. Seventeen ocular surgeries were performed on eleven patients (55%) at our institution with three patients referred to in-network providers for definitive surgical management. A total to fourteen patients (70%) suffered ocular injuries requiring surgical intervention. Final VA was NLP in five patients (25%).

Conclusions: The severity of injury following paintball-induced ocular trauma is higher in this case series than what has previously been reported in the literature. To our knowledge this is the first study to date that specifically characterizes ocular paintball injuries suffered from drive-by shootings where paintball projectiles were used as a means to cause intentional harm. The use of paintballs and paintball guns in unregulated settings bears further scrutiny given their potential to cause devastating ocular injury.

CONTROL ID: 3712662

SUBMITTER (NAME ONLY): Deeba Husain

TITLE: Urinary Mass Spectrometry Metabolomic Profiles in Age-related Macular Degeneration (AMD)

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Husain, I. Lains, K.M. Mendez, J.B. Miller, D.G. Vavvas, I.K. Kim, J.W. Miller, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|R. kelly, J. Lasky-Su, Brigham and Women's Hospital Channing Division of Network Medicine, Boston, Massachusetts, UNITED STATES|J.Q. Gil, J. Murta, R. Silva, Coimbra Univ, PORTUGAL|L. Liang, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with age-related macular degeneration (AMD) and across different severity stages have been shown to have distinct plasma metabolomic profiles compared to controls. Urine is a biofluid obtained non-invasively and, in other fields, urine metabolomics has been proposed as a feasible and more accessible alternative to plasma biomarkers. However, to our knowledge, no studies have evaluated urinary mass spectrometry (MS) metabolomics in AMD. This study aimed to assess urinary metabolomic profiles of patients with different stages of AMD and a control group.

Methods: We conducted a prospectively designed, multicenter, cross-sectional study including patients with AMD and a control group (>50 years old). At our two study sites – Boston, US and Coimbra, Portugal – participants had a complete ophthalmological exam and were imaged with color fundus photographs for AMD classification and staging (AREDS classification scheme). At the same visit, fasting urine samples were collected, which were used for metabolomic profiling (Ultrahigh Performance Liquid chromatography – Mass Spectrometry, Metabolon, Inc). Multivariable logistic and ordinal logistic regression models were used for analysis, accounting for age, gender, body mass index and use of AREDS supplementation.

Results: We included 484 participants, 389 with AMD (89 early, 201 intermediate and 99 late AMD) and 95 controls. Six urinary metabolites differed significantly ($p < 0.01$) across the severity stages of AMD (early, intermediate and late stage) with pathway analysis revealing an enrichment of sphingolipid metabolism. Of note, two of the metabolites (sphingosine and phosphoethanolamine) have been previously shown by our group to also differ in the plasma of patients with AMD compared to controls and all across AMD severity stages.

Conclusions: This is the first investigation of urine metabolomics using Mass Spectrometry in AMD. We identified some differences across stages of disease that support our previous findings using plasma, supporting the potential of these metabolites as biomarkers for this common, blinding disease.

CONTROL ID: 3712664

SUBMITTER (NAME ONLY): Christiana Han

TITLE: Wnt Signalosome Assembly by Small Molecule Wnt-Mimic

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Han, C. Bonnet, C. Zhang, J.J. Zheng, S.X. Deng, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: One key precursor to Limbal Stem Cell Deficiency is insufficient Wnt-β-catenin signaling pathway; however, therapeutic tools are underdeveloped as manipulation of hydrophobic WNT proteins proves challenging. This study explored the effect of our small molecule WNT-mimic(MFH-ND) on Wnt-β-catenin signaling pathway using an experimental model of 293STF cells treated with MFH-ND and Wnt3a.

Methods: HEK 293 (293STF) cells were treated with vehicle (DMSO), 0-4000 ng/mL recombinant human Wnt3a protein with carrier, 0-800 μM of MFH-ND for 18 hours. Cell viability and firefly luciferase activity was measured using TOP-Flash assays following manufacturer's protocol. Microplate Reader was used to measure cell viability and firefly luciferase activity. The Wnt pathway activity was expressed as the ratio of fluorescence intensity to firefly luciferase. Figure 1 is displayed as Mean ± Standard Error of Mean (SEM). Figure 2 graphs were interpolated from sigmoidal standard curves(Model: Sigmoidal, 4PL, X is concentration) using GraphPad. Hill Coefficient(Model: Specific binding with Hill slope) using Graphpad.

Results: Per. Figure 1

At MFH-ND concentrations starting from 200 uM to 800 uM, across all the Wnt concentrations, there is a drastic increase in WNT Signaling Activation.

Hill Coefficient was calculated to be 1.113.

Conclusions: MFH-ND alteration of the Wnt-β-catenin pathway seemed to be an enhancement of the Wnt3a ability to activate the Wnt pathway. Evidence of cooperative binding(n=1.113 and Figure2) as well as boosted Wnt pathway activation(Figure1) point to evidence of signalosome assembly. Wnt3a alone was sufficient to activate the signalosome complex but had a much lower activation when compared to the high concentrations MFH-ND at the same Wnt3a concentration, suggesting MHF-ND was able to recruit a higher activation through a second mechanism, possibly cooperative binding. Figure 1 shows how Wnt pathway activation can be finely altered, which is important when trying to reach a certain therapeutically ideal target. Prospective animal trials will provide more in-vivo understanding of MFH--ND with in-vivo Wnt-β-catenin signaling to see if MFH-ND could be used as potential therapeutic target to Limbal Stem Cell Deficiency, caused by reduced Wnt-β-catenin pathway activation.

CONTROL ID: 3712665

SUBMITTER (NAME ONLY): Rachel Tam

TITLE: Spatial analysis of ellipsoid zone loss in eyes with hydroxychloroquine toxicity

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Tam, T. de silva, G.K. Jayakar, C.A. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hydroxychloroquine (HCQ), which is used to treat autoimmune diseases, can cause retinal toxicity which manifests photoreceptor loss and damage to the retinal pigment epithelium (RPE), ultimately leading to irrecoverable central vision loss. Structural evidence of retinal toxicity is provided by disruption of the ellipsoid zone (EZ) reflectivity band and change in outer retina thickness (ORT), both of which are detectable on spectral-domain optical coherence tomography (SD-OCT) imaging and display different patterns based on various demographic characteristics. This work investigates spatial differences in retinal susceptibility to these changes to better understand and detect retinal toxicity after HCQ treatment.

Methods: 87 patients (average age, 58.8±12.1 years) on long-term HCQ (14.1±7.3 years) enrolled in a case-control study (NCT01145196) underwent imaging with SD-OCT (Heidelberg Spectralis). Of the 32 patients who demonstrated evidence of toxicity, 20 were White, 6 were Black, 3 were Asian, and 3 were of unknown race. 2D enface maps of EZ loss and ORT were generated with automated algorithms and analyzed within each eye relative to the fovea location and demographic data, including race and ethnicity.

Results: In eyes without foveal involvement, the pattern of EZ loss demonstrated that the location of EZ loss closest to the fovea occurred most commonly in the inferotemporal sector (17/30). Eyes had a range of EZ loss areas and patterns (EZ loss area, Asian=29.88±21.48 mm^2, Black=21.60±16.35 mm^2, Caucasian=9.23±9.43 mm^2, p=0.000254). For eyes without foveal involvement (EZ loss>250 μm from the fovea), areas of EZ loss were greater in Black and Asian eyes. For eyes with large amounts of EZ loss (>20 mm^2), more Asian and Black eyes (6/8) maintained EZ loss further from the fovea (>250 μm). Analyses of ORT in the foveal B scans revealed the differences between affected and unaffected eyes to occur further from the fovea in Black and Asian affected eyes than in Caucasian eyes.

Conclusions: Quantitative analyses of structural changes in HCQ toxicity can reveal differences in retina spatial involvement within an eye and between patients. Causes for differential involvement may be due to gradients within the retina and differences in cellular distributions between patients which may be affected by race. This has implications for screening participants as well as for the development of interventions.

CONTROL ID: 3712668

SUBMITTER (NAME ONLY): Naveen Karthik

TITLE: Effects of Iris Pigmentation on Degree of Anterior Chamber Inflammation after Cataract Surgery using Automated Analysis by Spectral Domain Optical Coherence Tomography

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Karthik, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|N. Karthik, S. Sharma, R. Gans, K. Baynes, E. Fisher, C. Chen, P.K. Kaiser, A. Venkat, C.Y. Lowder, S.K. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anterior Segment Optical Coherence Tomography (AS-OCT) has shown utility for imaging and quantifying anterior chamber (AC) inflammation after cataract surgery. The objective of this study was to elucidate the effects of iris pigmentation on the degree of AC inflammation after cataract surgery using AS-OCT.

Methods: This was an IRB-approved, observational, prospective case series of patients who underwent cataract surgery by one surgeon (RG) at the Cleveland Clinic Cole Eye Institute. Anterior chamber volume scans were obtained using AS-OCT (Avanti, Optovue Inc, Fremont, CA) at designated time points after cataract surgery including postoperative day 0 or 1 (POD0/1), postoperative week 1 (POW1), and postoperative month 1 (POM1). AS-OCT images were analyzed by an automated, proprietary algorithm, which identified inflammatory cells within the AC as previously described. Iris color was designated by the operating surgeon. Cell fluid density (number of inflammatory cells per mm3 of AC volume) was correlated to iris pigmentation.

Results: 155 eyes of 117 patients were analyzed. 40% of patients were female (n=47), and the average patient age was 69 years (range: 44-91 years). Distribution of iris color was 28% blue (n=43), 51% brown (n=79), 7% green (n=11), and 14% hazel (n=22). On automated analysis, no significant difference (p=0.16) was noted in average cell fluid density between blue (65.2 ± 102.9 cells/mm3) and brown (41.8 ± 48.8 cells/mm3) eyes at POD0/1. Average cell density of brown eyes (4.47 ± 8.87 cells/mm3) was significantly (p=0.04) greater than average cell density of blue eyes (2.11 ± 1.80 cells/mm3) at POW1. Likewise, at POM1, average cell density of brown eyes (2.01 ± 3.50 cells/mm3) was significantly greater (p=0.01) than average cell density of blue eyes (0.75 ± 0.72 cells/mm3).

Conclusions: Eyes with brown irises demonstrated significantly greater inflammatory cell density within the AC compared to eyes with blue irises at the POW1 and POM1 time points after cataract surgery. Brown irises, with greater levels of pigment, may be associated with prolonged inflammation after cataract surgery compared to iris colors with less pigment. Further work into the role of iris pigmentation on the inflammatory response after cataract surgery in larger cohort studies is needed to guide postoperative therapy considerations.

CONTROL ID: 3712669

SUBMITTER (NAME ONLY): Supriya Arora

TITLE: Three-dimensional choroidal contour mapping in pathology:comparison with healthy controls

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Arora, Ophthalmology, Princess Margaret Hospital, New Providence, Nassau, BAHAMAS|S. Arora, Bahamas Vision Centre, New Providence, Nassau, BAHAMAS|B. Rosario, J. Chhablani, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|A. Selvam, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|V. Sant, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|J.A. Sahel, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|M.N. Ibrahim, K.K. Vupparaboina, J. Chhablani, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study the choroidal contour map in central serous chorioretinopathy (CSCR) and age related macular degeneration (AMD) and compare with healthy controls.

Methods: Retrospective analysis on 13 healthy eyes, 12 eyes with CSCR and 8 eyes with AMD was performed. Volumetric scans were captured using a widefield swept source optical coherence tomography and CIS and COS in 3D were obtained using previously validated residual U-net (ResUnet) deep learning model for choroidal segmentation. Qualitative analysis of CIS and COS was performed using custom built MATLAB based 3D visualization tool and the choroidal contour shapes were determined in the order of decreasing steepness. Quantitative analysis was based on maximum principal curvature (Pmax) of the surface which was calculated at the center, superior, inferior, nasal and temporal macula.

Results: Qualitative evaluation of CIS demonstrated the shape of a bell, hump, crescent, arc and cupid's bow in 4,3,2,2 and 2 in normal eyes; 2,6,4,0,0 in CSCR eyes and 0,5,2,1,0 in AMD eyes respectively. Qualitative analysis of COS demonstrated the shape of a bell, hump, crescent, arc and cupid's bow in 2,6,2,1,2 in normal eyes; 2,8,1,0,1 in CSCR eyes and 0,6,1,1,0 in AMD eyes. On quantitative analysis of CIS, Pmax at central macula was -0.23, 0.45 and -0.02 in normal eyes, CSCR and AMD respectively (p=0.015). Similarly, Pmax in superior, inferior and temporal macula was significantly different between the 3 groups (p=0.001,0.029,0.019).The difference between CIS and COS was the highest for AMD group (-6.73±2.2) as compared to normal eyes (-2.5±0.4) and CSCR (-2.8±1.7)(p=0.038). On making a comparison within the group, the central Pmax, superior Pmax, inferior Pmax and temporal Pmax between the CIS and COS of normal eyes (p=0.0002,0.00003,0.004,0.003), CSCR (p=0.006,0.001,0.0003,0.033) and AMD (p=0.009,0.005,0.006,0.005) were significantly different from each other.

Conclusions: Choroidal contour was steeper in CSCR and flatter in AMD as compared to normal eyes. More data is continuously being added and will be presented at the meeting.

CONTROL ID: 3712670

SUBMITTER (NAME ONLY): Taariq Mohammed

TITLE: Validation and quantification of optical coherence tomography angiography decorrelation at high and low intraocular pressures in a non-human primate model

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Mohammed, V. Chen, O. Saeedi, Ophthalmology, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) is a noninvasive angiographic method that compares the decorrelation signal over time to identify areas of changing signal. Erythrocyte Mediated Angiography (EMA) uses autologous ICG-labelled cells to permit the visualization and absolute quantification of retinal capillary flowrates. We aimed to compare and validate EMA with OCTA and then to compare the OCTA decorrelation and flow values at low and high pressures in a non-human primate model.

Methods: Sequential OCTA and EMA was acquired in two sessions of two non-human primate (NHP) eyes at high and low intraocular pressures (Figure 1). OCTA was acquired using Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany), and EMA was acquired using previously described methods (Tracy 2019). OCTA decorrelation within capillaries of the superficial vascular plexus (SVP) was measured using manual segmentation. We then compared the values of OCTA decorrelation with EMA in the same vessels. We further compared OCTA decorrelation values at high and low IOPs.

Results: In 15 SVP capillaries at low IOP and 11 at high IOP, EMA velocity was 0.61 +- 0.07 mm/s and 0.54 +- 0.21 mm/s respectively and OCTA decorrelation was 0.61 +- 0.06 and 0.56 +- 0.11 respectively (Figure 2). OCTA decorrelation values correlated with absolute EMA velocity ($r = 0.50$, $p < 0.05$). In ten perifoveal SVP capillaries at high and low IOP, the mean OCTA decorrelation at a low IOP (Mean IOP = 14.5 mm Hg, OCTA decorrelation = 0.69 +- 0.11) was significantly higher than at high IOP (Mean IOP = 27.75 mmHg, OCTA decorrelation =0.49 +- 0.08, $p < 0.05$).

Conclusions: In our analysis, a large and statistically significant difference was observed between OCTA decorrelation at low and high IOP, and was correlated with changes in absolute erythrocyte velocity as measured with EMA. This potentially validates the decorrelation values of OCTA.

CONTROL ID: 3712672

SUBMITTER (NAME ONLY): Manuel Salinas-Lugo

TITLE: Genetic alterations associated with keratoconus, a bioinformatic research and a functional analysis.

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Salinas-Lugo, M.E. Quiroga-Garza, D. Bastán-Fabián, J.E. Arreola, R.E. Ruiz, M. Sepulveda-Villegas, V. Treviño, J.C. Hernandez-Camarena, J. Valdez-Garcia, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: The aim of this project is the search of related genetic mutations of keratoconus. Previous results were published by our research group, where 37 genes directly related to this ectasia were proposed (Gomez, Lopez, el tal. 2019). This research was continued and the updates are presented here.

Methods: Via a bioinformatic approach using the Pubterm tool, we searched and curated genes and abstracts associated with keratoconus; afterwards, these publications were analyzed in order to classify the genetic alterations into those with evidence of functional variant, and those with other evidence of genetic alterations. Finally, a functional analysis was made according to the signaling pathway implied for each gene.

Results: 405 abstracts were retrieved mentioning 304 relevant genes. After exclusion of non-human genes and those without genetic variants, 74 genes remained. Of these, 25 had evidence of functional variant, including 13 new genes in comparison to the previous publication; such as: VANGL1, miR-184 and FLG. The remaining 49 genes stand for other evidence of genetic alterations including 23 new genes, such as: SOD1 and ADAMTS8. A total of 36 new genes were retrieved. Genes were grouped according to the relevant molecular pathways in which they are involved: Immune regulation, apoptosis, transcription factors, signaling pathways, collagen and cytoskeleton properties. The following genes have the most citations: VSX1, COL4A,TGFB1, miR-184, DOCK9, FLG and ZEB1.

Conclusions: After retrieving these genes and performing a functional analysis, the findings exhibited that different genes from multiple molecular pathways may be involved in keratoconus pathophysiology. These genes could be contemplated for screening purposes as risk factors analysis for Keratoconus; nevertheless, differences across ethnic groups need to be taken into account on a case by case basis.

CONTROL ID: 3712673

SUBMITTER (NAME ONLY): SeIn Kim

TITLE: Neural information of artificial vision varies depending on mean firing rate and spiking duration

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kim, H. Roh, M. Im, Brain Science Institute, Korea Institute of Science and Technology, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|H. Roh, Division of Electrical Engineering, Korea University, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|M. Im, Division of Bio-Medical Science & Technology, University of Science and Technology, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Recent clinical trials demonstrated the feasibility of retinal prostheses for somewhat useful artificial vision. Although the healthy retina is known for transmitting remarkable amount of neural information, the amount of artificial visual information created by prosthetic devices is still unknown. The quality of prosthetic vision is likely to be at least partially dependent on how much information would be transmitted. Here, we investigated neural information as a function of mean firing rate and spiking duration of retinal ganglion cells (RGCs).

Methods: We used neural computational methods to generate correlated spike trains and calculate the amount of information of those simulated RGC spiking activities. First, we created five groups of 1-sec-long spike trains with different mean firing rates using a modified version of ‘Brian 2’, an open-source simulator for spiking neural networks. Second, we created five groups of spike trains that have 60 Hz average firing rate but different spiking duration. Then, we calculated the amount of neural information for each group to examine the effects of varying mean firing rate and spiking duration.

Results: The mean firing rates of the first five groups were 20, 40, 60, 80, and 100 Hz. The amounts of neural information transmitted by 15 cells of each group were 2.95±0.11,4.32±0.15,5.19±0.13, 5.96±0.16, and 6.38±0.13 bits (mean±std), respectively. The spiking duration of the second five groups were 0.2, 0.4, 0.6, 0.8, and 1.0 sec. In each group, 15 cells transmitted neural information 1.54±0.07, 2.82±0.09, 3.76±0.09, 4.37±0.10, and 5.19±0.13 bits, respectively. In both cases, the higher firing rate or the longer spiking duration, the more neural information was transmitted as expected. However, the effects of increments in both parameters were gradually diminished. For example, when the spiking duration was 0.2 sec, the neural information increased by 0.77 bits for the mean firing rate change from 20 Hz to 60 Hz. When the duration was 1.0 sec, the neural information increased by just 2.24 bits for the same change in mean firing rate. Although the duration was 5 times bigger, the information was only ~2.9 times more.

Conclusions: Our results indicate that we can transfer more information as the mean firing rate and spiking duration increase but energy-information efficiency should be considered.

CONTROL ID: 3712675

SUBMITTER (NAME ONLY): Jeffrey Sims

TITLE: The feasibility and reliability of a remote teleophthalmology reading center for improving access to care

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sims, D. Chen, V. Patel, L.A. Al-Aswad, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|G. Maestre, J. Melgarejo, Faculty of Medicine, Universidad del Zulia, Maracaibo, Zulia, VENEZUELA, BOLIVARIAN REPUBLIC OF|G. Maestre, Department of Neurosciences and Department of Human Genetics, The University of Texas Rio Grande Valley School of Medicine, Brownsville, Texas, UNITED STATES|M. Petitto, Glaucoma and Retina Units, Eye Clinic of Maracaibo, Maracaibo, Zulia, VENEZUELA, BOLIVARIAN REPUBLIC OF|J. Melgarejo, KU Leuven Department of Cardiovascular Sciences, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|

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ABSTRACT BODY:

Purpose: Early detection is key in the management and long-term outcomes of numerous ophthalmic disorders, such as glaucoma and diabetic retinopathy, many of which can present insidiously with symptoms unnoticed prior to advanced disease. Teleophthalmologic screening presents a major opportunity to reach populations that traditionally lack access to routine care. The goal of this study is to evaluate the feasibility and reliability of a remote international reading center using ocular imaging.

Methods: 50 patients (mean age 58.5 years, 48/50 female) presented for comprehensive eye exams from an ophthalmologist (Reference Standard, or “Ref”) in Venezuela, and fundus photography and optical coherence tomography (OCT) images were sent to two outside ophthalmologists (Reader 1 and Reader 2, or “R1” and “R2”) blinded to the in-person exam. Features assessed included cup/disc ratio (CDR) on fundus photos and retinal nerve fiber layer thinning on OCT. Fundus findings were compared for reliability and accuracy, with the in-person exam treated as the best available assessment; while OCT findings were compared between R1 and R2 for reliability.

Results: While agreement on exact CDR between the readers and Ref was relatively low (17.6-29.4%), CDR findings were fairly well correlated (r 0.614-0.649, $p<0.01$), with moderate reliability among all evaluators (intraclass correlation 0.665 for right eye, 0.698 for left eye; Table 1). Agreement was higher for CDR estimate on fundus photo (r 0.865-0.848, $p<0.01$). When assessing for CDR > 0.5, accuracy improved (76.5-83.3% agreement) and moderate interrater reliability was observed. On remote OCT assessment, percent agreement between readers were 72% (right eye) and 64% (left eye), with fair reliability (Cohen’s kappa coefficient 0.323 for right eye, 0.236 for left eye; Table 2).

Conclusions: Although CDR agreement rates between in-person fundoscopic exam and remote fundus photography reading were low, findings were well correlated and improved when assessing for the clinically relevant distinction of CDR > 0.5, suggesting that remote screening may be reliable and accurate in assessing for abnormal CDR. Lower reliability of remote OCT assessment was driven by a high disagreement rate between these readers, reflecting the need for consensus, standardization, and further evaluation with a larger pool of readers in a sample better representing the general population.

CONTROL ID: 3712677

SUBMITTER (NAME ONLY): Nilesh Raval

TITLE: Assessment of Optical Coherence Tomography Findings Based on COVID-19 Status and Demographics

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Raval, Department of Ophthalmology and Visual Sciences, Montefiore Medical Center, Bronx, New York, UNITED STATES|Y. Steinberg, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|I. Rusu Jutagir, M. Messilaty, J.N. MBEKEANI, Surgery (Ophthalmology), Jacobi Medical Center, Bronx, New York, UNITED STATES|A. Parsikia, Department of Research Services, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|I. Rusu Jutagir, J.N. MBEKEANI, Department of Ophthalmology and Visual Sciences, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The full scope of ophthalmic manifestations of coronavirus disease 2019 (COVID-19) has yet to be appreciated. We used optical coherence tomography (OCT) to compare subjects with a history of COVID-19 disease and those without evidence of past disease across qualitative and quantitative metrics.

Methods: Subjects diagnosed by reverse-transcriptase polymerase chain reaction with COVID-19 or presence of SARS-CoV-2 antibodies (N=25) and those with no history or antibody evidence of disease (N=25) were prospectively assessed using a Zeiss Cirrus HD OCT Model 5000. Retinal nerve fiber layer (RNFL), macular ganglion cell complex (GCC), and foveal thickness were tabulated. Retinal structural findings were evaluated by a retina specialist. Results were stratified by age, race, ethnicity, gender, and presence of comorbidities (diabetes and hypertension). Student's t-test, linear and logistic regression, univariate analysis with COVID+ subjects, and multivariate analysis with all subjects were performed. Significance was set at $p<0.05$.

Results: COVID+ subjects did not show significant differences compared to COVID– subjects across any parameters. There were significant differences across demographic groups. Univariate analysis showed that COVID+ Asians had thinner RNFL (p=0.014, right; p=0.018, left) and GCC (p=0.041, right; p=0.051, left) than COVID+ Blacks and Whites. COVID+ Hispanics had decreased foveal thickness compared to COVID+ non-Hispanics (p=0.019, right; p=0.004, left). Multivariate analysis confirmed that Blacks (p=0.015, left) and Whites (p=0.010, left) had thicker GCC than Asians and that Hispanics had decreased foveal thickness (p=0.041, left) compared to non-Hispanics. The middle age group had thinner GCC (p=0.022, right; p=0.024, left) than the youngest age group. While COVID+ Blacks were more likely to have retinal structural changes than COVID+ subjects of other races with a trend toward significance (OR=5.00, p=0.084), multivariate analysis did not confirm this disparity.

Conclusions: Analysis of this cohort did not reveal significant differences between COVID+ and COVID– individuals. However, comparison of demographic parameters did show significant differences across age, race, and ethnicity. The reasons for these disparities are obscure. Further studies with a greater number of subjects may reveal differences based on COVID-19 status.

CONTROL ID: 3712679

SUBMITTER (NAME ONLY): Qian Li

TITLE: Establishing a Hybrid Control for Conjunctival Allergen Challenge Studies for Allergic Conjunctivitis

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q.H. Li, H. Li, Statistics and Data Corporation, Arizona, UNITED STATES|P.J. Gomes, G. De Moraes, M.B. Abelson, Ora, Inc, Massachusetts, UNITED STATES|G. De Moraes, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Randomized, vehicle-controlled, and double-masked conjunctival allergen challenge (CAC) studies have been successfully used to support marketing applications for treatments of allergic conjunctivitis. These studies have been conducted using standardized challenge methodologies and the endpoints have been evaluated with consistent approach, therefore it may be feasible to use hybrid control arms in future CAC trials. The purpose of hybrid control is to pool the trial control subjects and certain historical control subjects based on adequate statistical matching, such as propensity score (PS). The advantage of using a hybrid control is to expose fewer subjects to allergens for whom there will be no benefit from the vehicle treatment.

Methods: Among three completed Phase II and III CAC studies for the allergic conjunctivitis indication, two are used as historical control and one is selected as a reference. We compare the outcomes between the historical control and the reference trial control, after controlling PS, to evaluate the similarity in vehicle treatment responses. The PS matching incorporates prognostic factors such as age, sex, and baseline post-challenge itchiness and redness. We construct a hybrid control arm for the reference trial using PS matching between the trial treatment group and the historical control. The results of the treatment effect using the hybrid control are compared with the results using the trial control.

Results: The reference study was randomized in a 2:1 ratio to treatment (91 subjects) or control (47 subjects). The combined historical control includes 75 subjects from the two studies. Figure 1 shows the post-challenge mean scores of itchiness and redness for the baseline, 16 hours post treatment time points, and 15-minutes post treatment, displayed by individual study and matched groups using PS matching. The mean differences between the two matched groups are reduced to less than or equal to 0.24. Table 1 shows that the conclusions on treatment effect are unchanged using the hybrid control in the reference trial. The least squares mean differences are less than or equal to 0.17 between the trial and hybrid controls.

Conclusions: Introducing hybrid control arms in CAC studies maintains study integrity and validity. The use of a hybrid control could potentially reduce costs and improve subject safety.

CONTROL ID: 3712680

SUBMITTER (NAME ONLY): Yuxuan Cheng

TITLE: Automatic segmentation of geographic atrophy in OCT scans using deep learning

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Cheng, Z. Chu, H. Zhou, Q. Zhang, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|M. Shen, R. Laiginhas, J. Liu, Y. Shi, J. Li, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|R.K. Wang, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To automatically identify, segment, and quantify geographic atrophy (GA) based on optical attenuation coefficients (OACs) and optical coherence tomography (OCT) datasets using deep learning algorithms.

Methods: Normal eyes and eyes with GA secondary to age-related macular degeneration (AMD) were imaged with swept-source OCT using a 6x6 mm scan pattern. Depth-resolved OACs were calculated from OCT scans. For each OCT scan, three images were generated and combined to produce pseudo-color images (Figure 1): (1) the OAC-identified RPE elevation from Bruch's membrane (BM), (2) the sum OAC projection between the inner limiting membrane and BM, and (3) the sub-retinal pigment epithelium slab projection (subRPE) extending from 64 to 400μm below BM. An attention improved U-net model was trained to segment the composite images with a focal loss for a better classification of evolving GA lesions. All GA lesions were manually labeled from the subRPE slabs by senior graders for evaluating the model. User-friendly software with the model was developed to test the algorithm in clinical settings. The performance of the model was evaluated using DICE similarity coefficients (DSCs). The areas of the GA lesions were calculated and compared with manual segmentations using Pearson's correlation and Bland-Altman analyses. Both the model output and the manual outlines excluded GA lesions with greatest linear dimension less than 250μm.

Results: A set of 153 GA eyes, 30 drusen only eyes, and 60 normal eyes were used to develop and test the model. The dataset was split 80:20 for training:validation. Another 30 AMD eyes with GA lesions were prepared for testing. The model reached the dice coefficients of 0.958, 0.941, 0.930 on the training, validation, and testing after 300 epochs of training, respectively. The mean area difference on the testing set was 0.106 mm^2 between manual segmentation and the model, and the Pearson's correlation was 0.957. Figure 2 shows a working example of the software on a case with GA lesions.

Conclusions: The proposed model using composite color images derived from OCT scans effectively and accurately identified, segmented, and quantified GA lesions.

CONTROL ID: 3712681
SUBMITTER (NAME ONLY): Sangly Srinivas
TITLE: Transcorneal fluorescence lifetime spectroscopy
SESSION TITLE: Drug delivery
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S.P. Srinivas, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|Y. Sun, Y. Povrozin, N. Redes, B. Barbieri, ISS Inc, Champaign, Illinois, UNITED STATES|
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ABSTRACT BODY:
Purpose: As an intrinsic property, the fluorescence lifetime of a fluorophore is independent of its concentration but is influenced by electrolyte levels, pH, temperature, membrane potential, and refractive index. Thus, lifetime measurements can probe the dynamics of biophysical/biochemical parameters in transparent tissues. Here our goal is to establish a dedicated ophthalmic time-resolved confocal scanning microfluorometer (OTR-CSMF) for intensity and lifetime measurements across the cornea.
Methods: We established a prototype of OTR-CSMF comprising a fiber-optic-based confocal fluorometer, corneal perfusion system, multiple solid-state pulsed lasers (445, 488, and 532 nm), nanostage, and electronics for rapid lifetime acquisition by digital frequency-domain approach. Next, we developed software for data acquisition, depth scanning, laser control, and data analysis, based on Vinci™, a standard tool for desktop fluorometers. Finally, we have tested and validated OTR-CSMF with references dyes and porcine corneas ex vivo.
Results: By focusing 488 nm laser at the coverglass:water interface using the 40x (0.8 NA; water) objective, depth vs. scatter produced a peak with FWHM of ~1.3 μm. The instrument point spread function (PSF) was assessed by fluorescence correlation spectroscopy (FCS) measurements of fluorescein in water, which led to the axial FWHM and radial beam waist estimates of 1.2 and 0.33 μm, respectively. These confirm the axial resolution and demonstrate the system's single-molecule detection sensitivity. Using rhodamine 110 in water (lifetime = 4 ns) as the standard, we found the lifetime of rhodamine B, fluorescein, and Ruthenium phenanthroline (RuPhen) to be close to values reported previously. Finally, transcorneal measurements with freshly isolated porcine corneas and multiple dyes demonstrated the principal functionality of OTR-CSMF (Figs. 1-2). Since fluorescein and RuPhen are hydrophilic, we secured their accumulation across the cornea by injection into the anterior chamber.
Conclusions: OTR-CSMF transcends the microfluorometer described earlier by Srinivas and Maurice (IEEE Trans Biomed Eng, 39(12): 1283-1291, 1992). It enables transcorneal lifetime measurements (resolution of 50 ps; dynamic range of 100 ps – 1 ms) at a high axial resolution (~1.3 μm) and fluorescence sensitivity (~100 pM of fluorescein).

CONTROL ID: 3712682

SUBMITTER (NAME ONLY): Andrew Thomson

TITLE: Telemedicine Assisted Postoperative Care Following Microincision Vitrectomy Surgery

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Thomson, N. Garcia-O'Farrill, A.A. Hunter, Oregon Eye Consultants, LLC, Eugene, Oregon, UNITED STATES|A.C. Thomson, Ophthalmology, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Andrew Thomson: Commercial Relationship: Code N (No Commercial Relationship) | Noraliz Garcia-O'Farrill: Commercial Relationship: Code N (No Commercial Relationship) | Allan Hunter: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Microincision vitrectomy surgery (MIVS) studies have shown low complication rates. In the setting of the COVID-19 pandemic and rural satellite clinics, we investigated the role of telemedicine as an alternative to postoperative visit (POV) regimens after uncomplicated MIVS.

Methods: This IRB approved, prospective single-site, and single-surgeon study included patients without any history of glaucoma, ocular trauma, or severe systemic or ocular disease who underwent uncomplicated MIVS for any indication between January-August 2021. Prophylactic topical pressure-lowering drops were prescribed if POV intraocular pressure (IOP) was ≥22 mmHg. POVs included the same day after surgery, week(s) 1, 2, 8, and 12. Patients were randomly assigned (1:1) into two arms: telemedicine (TM) or In-person (IP). Weeks 1 and 8 POV utilized protocol-based and questionnaire guided undilated exams performed by an ophthalmology fellow that were conducted either TM or IP, according to arm assignment. Any patients with concerning symptoms identified at these visits were scheduled for dilated exams with the surgeon. All patients underwent dilated exams performed by the surgeon on the same day after surgery, weeks 2 and 12. Primary endpoint was mean best corrected visual acuity (BCVA). Secondary endpoints included changes in intraocular pressure (IOP), retinal nerve fiber layer thickness, and number of additional visits. Statistical analysis included Mann Whitney U and chi-square tests.

Results: Fifty-two eyes from 50 patients (33 female, 17 male; p-value=0.02) with mean ages of 68.4±6.8 years underwent 55 total surgeries with 25 or 27G MIVS platforms. Forty-seven patients have completed all POVs. Mean preop BCVA logMAR was 0.53±0.55 and 0.40±0.45, and at 12 weeks, they were 0.39±0.45 and 0.26±0.33 for the TM and IP groups, respectively. No significant between-group differences were found for primary or secondary outcomes. All cases of abnormal IOP resolved by the following POV with pressure lowering drops. Concerning symptoms were identified in five patients requiring additional visits, revealing two cases of worsening macular edema (1 TM and 1 IP) and one case each of cataract progression (TM), vitreous hemorrhage (IP), and macular hole recurrence (TM). No complications presented at the TM or IP visits.

Conclusions: Telemedicine-assisted POV regimens may be a safe and convenient alternative for patients undergoing uncomplicated MIVS.

CONTROL ID: 3712683

SUBMITTER (NAME ONLY): Shahna Shahul Hameed

TITLE: Human neuritin 1: Therapeutic Strategy for Juvenile Open-Angle Glaucoma

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shahul Hameed, R.C. Miller, T.P. Sharma, Department of Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|S. Shahul Hameed, R.C. Miller, T.P. Sharma, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Juvenile open-angle glaucoma (JOAG) has early childhood disease manifestation and is associated with significant vision loss. Intraocular pressure (IOP) in these patients sometimes ranges over 40 mm Hg. JOAG has a strong genetic component and clinical management of JOAG can be quite challenging with current treatment options only limited to lowering IOP. We have previously shown that the secreted human protein neuritin 1 (NRN1) exhibits neuroprotection, regeneration and preservation of retinal ganglion cell (RGC) function after axonal injury. We propose to model JOAG by culturing human posterior eyecups within our novel ex-vivo Translaminar Autonomous System (TAS). In this system, we will overcome elevated IOP mediated RGC degeneration by over-expressing NRN1 as a therapeutic strategy.

Methods: Human donor eyes were obtained from eye banks. To recapitulate JOAG glaucomatous conditions in an ex-vivo environment, dissected human posterior cups (n=4) were cultured in the TAS model at elevated IOP conditions over 6 days with and without recombinant hNRN1. To induce translaminar pressure changes, the flow rate of the perfusion medium was adjusted and calculated using automated pumps and software. We assessed the survival of retinal ganglion cells with and without NRN1 treatment by TaqMan array analysis of apoptosis/inflammatory markers (retina). Expression of FN and COLIV was examined from the conditioned medium of both groups by Western blot analysis.

Results: We successfully maintained IOP: ICP differentials over 6 days (n=4). The RGCs degenerated faster in non-treated conditions compared to NRN1 treated eyes. In contrast to the controls, the treated group significantly decreased expression of FN and COLIV ($p<0.05$, n=4). We observed downregulated expression of GFAP ($p<0.001$, n=4), BAX and TLR4 expression ($p<0.05$, n=4) after NRN1 treatment.

Conclusions: Our data identified that NRN1 treatment promotes RGC survival under pathological conditions of glaucoma. This study suggests that hNRN1 could be utilized as a potential therapeutic to save RGC and a plausible treatment option for JOAG.

CONTROL ID: 3712684

SUBMITTER (NAME ONLY): Xinxin Zhao

TITLE: Hyperbranched EPC polymer enhanced anti-angiogenic activity and the cellular uptake of aflibercept

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhao, X. Su, Institute of Molecular and Cell Biology, Singapore, SINGAPORE|J.Y. Lim, X. Loh, Institute of Materials Research and Engineering, SINGAPORE|

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ABSTRACT BODY:

Purpose: Intravitreal injection anti-vascular endothelial growth factor (anti-VEGF) for the treatment of retinal diseases is invasive and potentially associated with sight-threatening complications. We previously reported the using of nanomicelle form EPC (nEPC) to topically deliver Aflibercept to the retina in a mouse in-vivo model. EPC is a copolymer, made up by covalently linked polyethylene glycol (PEG), polypropyl glycol (PPG) and polycaprolactone (PCL). We hypothesized that hyper-branched poly(PEG/PPG/PCL/Glycerol urethane) (EPCGs), with additional PEG branches on polymer backbone, will improve cellular penetration. The biological effect from the branched structure was then evaluated based on in-vitro biocompatibility, cellular uptake and ex-vivo angiogenic mice choroidal explant.

Methods: - To introduce PEG branches:
Glycerol (0.25 and 0.75%) was added during the synthesis of EPC
- To form nanomicelles with Aflibercept
Polymers were dissolved in the buffer containing required amount of aflibercept.
-To quantify cellular uptaken
aflibercept was covalent linked with rhodamine
- Biological assays:
Biocompatibility of EPCG was evaluated using human umbilical vein endothelial cells (HUVECs) with LDH cytotoxicity assay
Intracellular uptake was assessed by both direct confocal microscopy and flow cytometry.
The anti-angiogenic activity of nanomicelles was evaluated by ex-vivo mice choroidal explant.

Results: The hyperbranched EPCGs are biocompatible with HUVECs. EPCGs were able to inhibit blood vessel sprouting after 48hr exposure to EPCG nanomicelles in a concentration and branching dependent manner. Aflibercept complexed with nanomicelles had increased intracellular uptake into HUVECs and human corneal epithelial cells (hCECs), also in a concentration and branching dependent manner.

Conclusions: Hyperbranched EPCG is biocompatible with HUVEC cells in-vitro. Increased branching induced by glycerol was found to enhance the performance of EPC nanomicelles in two ways: (1) Inhibition of vessel sprouting in mice choroidal explant, (2) Increase intra-cellular uptake of aflibercept, which may potentially translate to increase cornea penetration. This suggests that hyperbranched EPCG might be suitable as a platform for topical drug delivery. Further tests are underway to confirm this.

CONTROL ID: 3712685

SUBMITTER (NAME ONLY): Preeti Gupta

TITLE: The ageing visual function system and functional health in multi-ethnic older adults: The PIONEER study

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Gupta, A.T. Gan, R.E. Man, E.K. Fenwick, E.L. Lamoureux, Population Health Research, Singapore Eye Research Institute, Singapore, SINGAPORE|P. Gupta, R.E. Man, E.K. Fenwick, E.L. Lamoureux, Population Health Research, 2.Duke-NUS Medical School, Singapore, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Preeti Gupta: Commercial Relationship: Code N (No Commercial Relationship) | Alfred Gan: Commercial Relationship: Code N (No Commercial Relationship) | Ryan Man: Commercial Relationship: Code N (No Commercial Relationship) | Eva Fenwick: Commercial Relationship: Code N (No Commercial Relationship) | Ecosse Lamoureux: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the cross-sectional associations between components of the visual function system (VFS) and functional health outcomes, in multi-ethnic Asians aged ≥60 years.

Methods: We included individuals from The PopulatION HEalth and Age-Related SEnsory Decline PRofilE (PIONEER), a cross-sectional population-based study of Singaporean Chinese, Malays, and Indians aged ≥60 years. VFS assessments comprised visual acuity (VA, logarithm of the minimum angle of resolution (LogMAR)), contrast sensitivity (CS, Pelli-Robson), and depth-perception (DP, Frisby). Functional health outcomes included instrumental activity of daily living (IADL, using Lawton Scale), mobility (via 4m-walking speed), and self-reported falls in the last 12 months. VFS impairments in the better eye were defined as follows: presenting visual impairment (PVI) as presenting VA worse than 6/12 (logMAR > 0.3); CS impairment (CSI) as CS <1.55 log CS; and DP impairment (DPI) as binocular DP≥150 arc sec. Logistic regression models were used to determine the independent relationship between the VFS and functional health outcomes.

Results: Of the 1,782 participants (mean age [SD]: 72.7 [8.2] years; 54.7% females), 303 (17.0%), 363 (20.4%), and 502 (28.2%) had PVI, CSI and DPI, respectively. Slow gait speed (<0.8m/s), low IADL (IADL score <24 for women and <15 for men) and at least one fall, was present in 662 (37.9%), 264 (17.6%) and 289 (19.2%) individuals, respectively. In multivariable-adjusted analyses including all VFS impairments simultaneously, PVI was associated with higher odds of poor IADL (odds ratio [OR]=1.53, 95% confidence interval [CI]: 1.06-2.21), while CSI was associated with an increased likelihood of poor IADL (OR=1.92, 95% CI: 1.37-2.69) and slow gait speed (OR=2.15, 95% CI: 1.63- 2.85). In turn, DPI significantly increased the odds of having experienced any falls by over 40% (OR=1.43, 95% CI: 1.06- 1.92).

Conclusions: CSI and DPI, independent of VA, are associated with a higher risk of poor functional health outcomes. Strategies such as highlighting steps or uneven surfaces may be warranted to potentially reduce the risk of poor functional health in older adults with low vision.

CONTROL ID: 3712687

SUBMITTER (NAME ONLY): Hyo Seon Yu

TITLE: Effect of curcumin through NLRP3-inflammasome pathway inhibition on oxidative stress-injured retinal pigment epithelial cells.

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yu, E. Hong, Y. Shin, M. Seong, H. Cho, Hanyang University, Seongdong-gu, Seoul , KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Oxidative stress is the major cause of retinal pigment epithelial (RPE) cell death. Among the inflammatory mechanisms triggered by oxidative stress, the activation of the NLRP3 inflammasome pathway has been known to be associated with the pathogenesis of age-related macular degeneration (AMD). We used oxidative stress-injured RPE cells to investigate the effects of the curcumin, a strong antioxidant, on the NLRP3 inflammasome pathway.

Methods: ARPE-19 cells were treated with several concentrations of curcumin and 300μM hydrogen peroxide (H_2O_2). Cell viability was measured with cell counting kit-8, MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) and lactate dehydrogenase assay. To evaluate the effect of curcumin on ARPE-19 proliferation, we performed wound healing assay. The activity of reactive oxygen species (ROS) was also evaluated. Intracellular NLRP3 inflammasome protein levels in various concentration of curcumin treatment were compared using western blotting and Immunocytochemistry.

Results: 300μM H_2O_2 reduced the viability of ARPE-19 cells. However, when treated with 7.5μM curcumin, ARPE-19 cells showed increased viability and decreased cell toxicity. Curcumin also reduced free radical in the H_2O_2-induced damaged cells, promoted the expression of survival-related proteins and attenuated H_2O_2 dependent expression of the NLRP3 inflammasome and its related signaling proteins.

Conclusions: Taken together, these results suggest that curcumin has protective effects on oxidative-stress in RPE cells by attenuating the activation of the NLRP3 inflammasome. Although further researches may be needed, curcumin may have potential therapeutic or protective effect on the pathogenesis of AMD.

CONTROL ID: 3712688

SUBMITTER (NAME ONLY): Sanjoy Bhattacharya

TITLE: Age-related functional vision loss in Sphingosine-1-phosphate receptor 3 knockout mouse

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.K. Bhattacharya, V. Krishnan, S.D. Meehan, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Sanjoy Bhattacharya: Commercial Relationship: Code N (No Commercial Relationship) | Varun Krishnan: Commercial Relationship: Code N (No Commercial Relationship) | Sean Meehan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To characterize the retinal morphology and visual function of sphingosine-1-phosphate receptor 3 knockout (S1PR3KO) mice.

Methods: Spingosine-1-phosphate receptor 3 (S1PR3KO) and C57BL/6J mice of both genders, ages 1-10 months, Rpbms, Iba-1, CRALBP, GFP, RPE65, Neuroligin2, Synaptophysin, PSD95 and other antibodies. Pattern and flash electroretinogram (PERG and FERG), embedding, fixation and confocal microscopy. All results were subjected to statistical analysis. The retina and optic nerve samples were also subjected to biochemical and mass spectrometric analyses following published protocols.

Results: We found significant functional PERG differences in S1PR3KO mice between 7 and 8 months of age. There was significant reduction in PERG amplitude at 8 months (5±2 μV) of age in S1PR3KO compared to that at 7 months (20±5 μV) of age, whereas FERG remained unaltered [results are mean± standard deviation for n=6 (equal male and female mice)]. Control C57BL/6J mice showed no difference during 7-10 months of age for these assessments. At 7 months of age the average individual PERG amplitude for S1PR3KO is a little (2-6 μV) less than that for C57BL/6J of the same age but average for n=6 mice in each group the difference was not statistically significant. We found largely single retinal ganglion cell (RGC) layer in S1PR3KO mice at all ages; C57BL/6J mice showed a 2-3 RGC layer. For S1PR3KO mice, although hematoxylin-eosin staining showed no difference in gross morphology of the retina, the PSD95 and Neuroligin2 showed a disordered pattern at 8 months of age compared to that at 7 months. C57BL/6J mice showed consistent patterns throughout the assessment period of 7-10 months. All data were subjected to Student’s t-test or two-way ANOVA as appropriate. The PERG amplitude differences were found to be statistically significant.

Conclusions: S1PR3KO mice shows both morphological and functional electrophysiological changes at 8 months of age compared to that at 7 months of age suggesting dramatic age-related retinal alteration in these mice.

CONTROL ID: 3712689

SUBMITTER (NAME ONLY): Erica Su

TITLE: A Bayesian Hierarchical Spatial Longitudinal Model Improves Estimation of Local Macular Rates of Change in Glaucoma Eyes

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Longitudinal analyses of local structural or functional measures frequently use repeated simple linear regression (SLR) to estimate eye-specific rates of change (RoC). We developed a novel Bayesian hierarchical spatial longitudinal (HSL) model to improve estimation of local macular structural RoC in a prospective cohort of glaucoma patients and compared the results to those of SLR.

Methods: 111 eyes (111 patients) from the Advanced Glaucoma Progression Study with 4 OCT scans and 2 years of follow-up were included. Ganglion cell complex (GCC) thickness within 7x7 arrays of superpixels from Spectralis OCT macular volume scans were exported and analyzed. The current version of our Bayesian HSL model includes superpixel intercept and slope random effects, global patient intercept and slope effects, patient-superpixel interaction intercepts and slopes, and visit effects to improve accuracy of superpixel-patient RoC estimates. Superpixel-patient specific estimates and their posterior variances were calculated from the HSL model and compared with those obtained from Bayesian SLR performed on longitudinal data from each superpixel-patient separately. We considered superpixel-patient specific RoC as worsening or improving (significantly negative or positive) when the upper or lower limit of the 95% credible interval was less than or higher than 0, respectively.

Results: Mean (SD) baseline 10-2 visual field mean deviation was –8.9 (5.9) dB. Mean (SD) follow-up time was 3.6 (0.4) years with 7.3 (1.1) OCT scans per eye. Across 5,419 superpixel-patient curves, the posterior variances from HSL were smaller than SLR for 87% of intercepts and 83% of slopes. The mean (IQR) ratio of posterior variances of SLR over HSL for intercepts and slopes were 4.0 (1.5-4.9) and 3.9 (1.3-4.4), respectively. HSL identified a higher proportion of significant negative slopes (17.6% vs. 15.6%; $p<.001$) and lower proportion of significant positive slopes (1.2% vs. 4.6%; $p<.001$) as compared to SLR.

Conclusions: A novel Bayesian HSL model improves estimation accuracy of local GCC rates of change. The proposed model is 4 times as efficient as SLR for estimating superpixel-patient intercepts or slopes and identifies a higher proportion of deteriorating superpixels when compared to SLR while minimizing false positive detection rates.

CONTROL ID: 3712691

SUBMITTER (NAME ONLY): Jacob Kanter

TITLE: Salvaging the conventional outflow pathway in neovascular glaucoma (SCOPING) – Pilot results from a multidisciplinary treatment protocol

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Kanter, D. Dao, L. Shaw, A. Mackin, R. Komati, P. Amin, D. Skondra, M. Qiu, Ophthalmology and Visual Science, The University of Chicago Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: For NVI/NVG eyes with open angles, we propose a protocol to medically salvage the conventional outflow pathway and reduce the need for subsequent IOP-lowering surgeries. We also propose a novel strategy for utilizing GATT to surgically salvage the conventional outflow pathway in NVG eyes.

Methods: Patients with first-time NVI and/or NVA and at least partially open angles were treated with 6 intravitreal bevacizumab (IVB) injections interspersed with PRP at the discretion of the retina service. IVB injections were encouraged to be spaced by 28 days. Elevated IOP was treated at the discretion of the glaucoma service.

Results: Seven eyes from 6 patients were treated with SCOPING. The etiologies of NVG included PDR (5), CRVO (1), and OIS (1). The median presenting VA was 20/40 (range 20/25 to 20/1250). Median presenting IOP was 38 mmHg (range 15 to 47) on 0 meds at baseline. The median duration between IVBs was 35 days (range 23 to 77), and the median total duration from IVB#1 to IVB#6 was 203 days (range 152 to 224). The median number of PRP sessions during the protocol period was 3 (range 1 to 4). At 1 month after IVB #6, the median IOP was 15 mmHg (range 9 to 19) on median 0 meds (range 0 to 2). All 7 eyes had prompt regression of NVI/NVA and no recurrence throughout the protocol period. Five eyes had 100% open angles upon presentation; each maintained adequate IOP control without surgery. The 2 eyes with 50% PAS upon presentation developed progressive synechial closure; 1 patient elected GATT, and 1 elected Baerveldt 350 in the sulcus. After the protocol was completed, the eye with OIS developed NVA 80 days after IVB#6, and the eye with CRVO developed NVA 119 days after IVB#6. One eye with PDR developed vitreous hemorrhage 152 days after IVB #6 and received 4 subsequent IVB injections. The 5 eyes with PDR did not develop any recurrence of NVA after a median follow-up of 56 days (range 28 to 245) after IVB#6.

Conclusions: Our protocol demonstrates the value of aggressive anti-neovascular treatment for NVI/NVG with completely or partially open angles. In SCOPING, 6 monthly IVBs lead to immediate regression of NV while PRP exerts a long-term effect. If the angle develops partial synechial angle closure, GATT can be attempted to salvage the conventional outflow pathway if the patient and team are committed to close follow-up and ongoing treatment.

CONTROL ID: 3712692

SUBMITTER (NAME ONLY): Jonathan Gong

TITLE: Impact of Disrupting Lactate Dehydrogenase a (LDHa) on Retinal Metabolism and Photoreceptor Function

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The mature mammalian retina remains metabolically active to support visual function and life-long photoreceptor outer segment renewal. Recent studies suggest that rodent photoreceptors rely heavily on aerobic glycolysis for both energy supply and cellular anabolic activities. Lactate dehydrogenases are important enzymes that catalyze the bidirectional conversion between pyruvate and lactate. In this experimental study, we assess the impact of disrupting LDHa in both wild-type (WT) and degenerating retinas by performing molecular genetic and biochemical analyses.

Methods: Murine rod photoreceptor-specific LDHa gene deletion was conducted in both WT and Rds/Prph2(P216L) backgrounds using Rho-iCre. Perturbation of LDHa protein was detected using immunocytochemistry. LDH enzymatic activity assay was carried out in WT and Rds mutant retinas. Impact of LDHa rod deletion on the outer nuclear layer (ONL) was examined using rod and cone photoreceptor marker immunolabeling and confocal imaging. Visual function was assayed by electroretinography (ERG) at P51, P84, and P180.

Results: Using an in situ enzymatic assay, the highest LDH activity was detected in the inner segment (IS) of retinal photoreceptors. Rod-specific deletion of LDHa gene resulted in the near abolishment of the LDH protein in the ONL without affecting its inner retina expression. In the WT background, deletion of LDHa in rods did not produce an apparent decrease in ONL thickness or visual function changes as measured by ERG. LDHa rod deletion did not appear to accelerate degeneration in the Rds mutant background. However, ERG detected significant deterioration of photopic b-wave. Furthermore, immunostaining detected abnormal cone cell morphological changes including exuberated opsin mislocalization and lateral dendritic sprouting.

Conclusions: These results show that LDHa is the major LDH enzyme expressed by photoreceptors. The main site for LDH activity in the retina is the photoreceptor IS, suggesting the proximity of LDHa protein localization with mitochondria in the photoreceptor IS. Further, rod-specific LDHa deletion can affect cone cell morphology and function in the Rds background. The apparent lack of disruption of photoreceptor morphology and function in the WT retina likely reflects the metabolic resilience and adaptability of the retinal network.

CONTROL ID: 3712693

SUBMITTER (NAME ONLY): Laura Tiedemann

TITLE: Lower eyelid reconstruction practice patterns among U.S. oculoplastic surgeons

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is no accepted standard of care for the reconstruction of full-thickness lower eyelid defects unable to be repaired by semicircular flaps or primary closure. We present a cross-sectional study of the preferred practice patterns and reconstructive techniques for these defects among U.S. oculoplastic surgeons surveyed 01/2021–03/2021.

Methods: We designed a survey to determine surgeon use and preference for the modified-Hughes procedure, transposition/advancement flap with free tarsal graft, Mustarde flap, bipedicle flap plus free tarsal graft, and free tarsal graft with free skin graft when treating lower eyelid defects. 596 oculoplastic surgeons who completed an oculoplastics fellowship were contacted by email or Doximity messenger. Contact information was obtained via practice and hospital websites, and the corresponding author section of Ophthalmic Plastic and Reconstructive Surgery. Retired physicians and pure cosmetic surgeons were excluded. Pearson chi-square testing compared surgical techniques and respondent demographic data.

Results: 120 surgeons responded (20.1%) with no statistically significant differences in response rate across U.S. regions. Median age range was 41-50 years (29.1%), with most respondents aged 70 or less. The majority of surgeons were in practice for 1–10 years (35.8%), with only 7 surgeons practicing for >40 years. Group practice was the most common practice setting (44.5%). The modified-Hughes procedure was the most common technique (92.5%), followed by the transposition/advancement flap with free tarsal graft (52.5%) and then the Mustarde flap (40.8%). The free tarsal graft with free skin graft was the least commonly used technique (8.3%). Most surgeons performing the Hughes and transposition flap techniques were in their first 20 years in practice (63.1%, 55.6%). The bipedicle flap with free tarsal graft was more common in academics (16 patients) and group practices (8) than solo practices (6). Middle-aged surgeons were more likely to perform free tarsal grafts with free skin grafts (70.0%) than other age groups.

Conclusions: While U.S. oculoplastic surgeons use various techniques for repair of full-thickness lower eyelid defects, the Hughes procedure was the most common in this study. Further quantitative examination is necessary to determine physician justification for technique preference.

CONTROL ID: 3712694

SUBMITTER (NAME ONLY): Hosein Hoseini-Yazdi

TITLE: Sustained increase in human choroidal thickness associated with brief stimulation of the optic disc with short-wavelength blue light

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Hoseini-Yazdi, S. Read, M.J. Collins, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|T. Schilling, H. Bahmani, Dopavision GmbH, GERMANY|

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ABSTRACT BODY:

Purpose: Environmental light regulates ocular growth, through mechanisms that may be mediated by melanopsin retinal ganglion cells (mRGCs). This study aimed to examine the choroidal thickness (ChT) changes following brief stimulation of the melanopsin-expressing axons of the mRGCs at the optic disc with blue light in a group of healthy emmetropic and myopic subjects.

Methods: The sub-foveal ChT of 10 emmetropic and 10 myopic subjects (ages 28 ± 6 years) was measured with enhanced-depth imaging optical coherence tomography before and during a 60-min period after stimulation of the optic disc with a 15 Hz flickering short-wavelength blue light for 1-min. ChT was also assessed following 1-min of no light stimulation on all subjects and following 1-min of optic disc stimulation with a 15 Hz flickering long-wavelength red light on a subset of subjects (3 emmetropes and 3 myopes). These control conditions were assessed on separate days at a similar time of day. Linear mixed model analysis was performed to examine the main effects and interactions of light, time, and refractive group upon changes in ChT.

Results: Averaged across all time points post-stimulation, the ChT increased significantly following the optic disc stimulation with blue light (4 ± 1 μm), compared to the no light (0 ± 1 μm) and red light (0 ± 1 μm) conditions (both $p < 0.001$). Significant choroidal thickening was observed across all measured time points following the stimulation of the optic disc with blue light compared to no light stimulation in emmetropes (change at 60-min post-stimulation, 10 ± 2 μm vs 4 ± 2 μm, $p < 0.001$), but not in myopes (4 ± 2 μm vs 0 ± 2 μm; $p > 0.05$). No significant changes in ChT were observed following the stimulation of the optic disc with red light compared to the no light condition in either refractive group (all $p > 0.05$). The increases in ChT associated with blue light stimulation of the optic disc were significantly greater in emmetropes than myopes after 30 (8 ± 2 μm vs 0 ± 2 μm), and 60 mins (10 ± 2 μm vs 4 ± 2 μm) post-stimulation (both $p < 0.05$; Fig 1).

Conclusions: A refractive error-dependent sustained thickening of the human choroid was observed with brief stimulation of the optic disc with blue light. This choroidal response may relate to a short-wavelength sensitive mRGCs' signaling pathway, given the lack of response of the choroid with red light stimulation.

CONTROL ID: 3712695

SUBMITTER (NAME ONLY): Kin Ho Chan

TITLE: Corneal Power Profile Derived from Both Meridians is Better Correlated with the Peripheral Refractive Profile in Myopic Children

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In children receiving corneal reshaping therapy, the myopia progression rate is associated with the change in corneal power, possibly due to its ability in reflecting refractive power changes towards peripheral fields, i.e., peripheral refractive profile – a hypothetical optical cue related to myopia development. As the peripheral refractive profile is typically acquired from refractive powers derived from two meridians (spherical-equivalent error, SE), it is unclear how well conventional topographic powers (axial, tangential, & refractive), which are derived from only a single meridional plane, can represent the peripheral refractive profile. This study compared the abilities of corneal power profile generated by the mean power (derived from the average of the steepest and flattest meridians) vs. conventional topographic powers in representing the peripheral refractive profile for myopic children.

Methods: A hundred fifty low-to-moderate myopic children (Age: 8 to 13 years, SE: –1.00DS to –5.75DS, Cylindrical error ≤1.50DC) with unremarkable ocular health were recruited. Peripheral refractive profile was determined using an open-field autorefractor along the horizontal field up to ±20° eccentricity in a 10° step. Corneal topography was measured by a Placido-disc based corneal topographer. Second-order polynomials ($y=ax^2+bx+c$) were fitted to refractive and corneal power data (y) as a function of eccentricity (x) for each individual. The a-coefficients represent the refractive and corneal power shifts towards the periphery and were used for data analyses.

Results: Pearson's correlations indicated that the peripheral refractive profile obtained from the open-field autorefractor were significantly correlated with the corneal power profiles derived from the mean (r=0.40), tangential (r=0.37), axial (r=0.20), and refractive power (r=0.17, all $P<0.05$). The correlation coefficient for mean power was significantly stronger than for refractive and axial powers (Fisher-Z-transformation, both $P<0.005$), but similar to the tangential power (P=0.31).

Conclusions: Corneal power profile derived from two meridians showed the highest correlation with the peripheral refractive profile, indicating the potential weakness of inferring peripheral refractive profile from the corneal powers derived from just one meridian.

CONTROL ID: 3712696

SUBMITTER (NAME ONLY): Kin-Sang Cho

TITLE: RvD1 suppresses microglia activation and improved spatial vision of mice with microbead-induced glaucoma

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Cho, L. PAN, A. Rajagopalan, D. Chen, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L. PAN, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Suppressing microglia activation has been suggested to be an appealing approach to rescue neuronal degeneration in glaucoma. Recently, specialized pro-resolving mediators such as Lipoxin A4 (LXA4) and Resolvin D1 (RvD1) have been shown to play a key role in resolving inflammation. This study investigated the roles of LXA4 and RvD1 in mediating microglial inflammation and neuroprotection in a microbead (MB)-induced glaucoma mouse model.

Methods: First, we pre-treated mouse microglial cultures with 10-7 M LXA4 or RvD1 for 6 hours followed by incubating with 10-7 M ATP. Naïve microglia and ATP-treated microglia were included as negative and positive controls, respectively. After 24 hours, mRNAs were extracted and RT-PCR detection of proinflammatory markers Cox2 and IL-1b were performed. One-way ANOVA followed by Dunnett's multiple comparable test was used for statistical analysis. Next, we induced unilateral elevation of intraocular pressure (IOP) by anterior chamber injection of MB in adult male and female C57BL/6 mice. The IOP levels were measured at day 3, 7, and then every 7 days post-MB injection until day 28. 2.8x10-5 M LXA4, RvD1 or vehicle was injected into the vitreous at day 3, 10, 17 and 24 post-MB injection. At day 14 and 28, retinal ganglion cell function and spatial vision were measured by recording the positive scotopic threshold response (pSTR) and optomotor response (OMR), respectively. Two-way ANOVA followed by Tukey's multiple comparable test was used for statistical analysis.

Results: ATP induced upregulation of Cox2 and IL-1b ($P<0.01$) in microglia cultures. LXA4 and RvD1 significantly reduced expression of Cox2 ($P<0.01$) and IL-1b. pSTR and OMR showed a gradual decline in vehicle treated glaucoma mice. RvD1 treated mice showed a slight increase in pSTR. RvD1 but not LXA4 treated mice significantly increased of both contrast sensitivity ($P<0.05$) and visual acuity ($P<0.01$) at 4 weeks post-MB injection comparing to the vehicle treated mice.

Conclusions: LXA4 and RvD1 suppressed pro-inflammatory cytokine/marker expressions of ATP-treated microglia. RvD1 but not LXA4 significantly improved the spatial vision of contrast sensitivity and visual acuity in glaucoma mice. Further understanding the mechanism of RvD1 on neuroprotection would unfold its therapeutic potential in glaucoma.

CONTROL ID: 3712697

SUBMITTER (NAME ONLY): Olusola Olawoye

TITLE: A short online course successfully trains non-ophthalmic diabetic retinopathy graders to recognize glaucomatous optic nerves in low-resource settings

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Olawoye, V.F. Chan, T. Peto, A. Azuara-Blanco, N.G. Congdon, Centre for Public Health, Queens University Belfast, Belfast, Antrim, UNITED KINGDOM|O. Olawoye, Ophthalmology, University of Ibadan College of Medicine, Ibadan, Oyo, NIGERIA|N. Pham, H. Thu Huong, Orbis International, VIET NAM|N. Lam, Hanoi Medical University, Hanoi, VIET NAM|C. Hunter, N.G. Congdon, ORBIS International, New York, New York, UNITED STATES|K. Fowobaje, Epidemiology, University of Ibadan College of Medicine, Ibadan, Oyo, NIGERIA|C. Ross, M. Coote, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Recent evidence (Tang J et al Lancet Glob Health 2019) suggests that glaucoma screening may be cost-effective in developing countries although it is generally not in high income countries. Screening of two major blinding eye diseases (glaucoma and diabetic retinopathy (DR) using the same resources is likely to further improve cost-effectiveness. The aim of this study was to test the efficacy of a one-week online course in training non-ophthalmic DR graders to recognize glaucomatous optic nerves in Vietnam.

Main Research Question: Can non-ophthalmic DR graders be trained inexpensively to accurately screen for glaucoma?

Methods: In this uncontrolled, interventional before-and-after study, 43 non-ophthalmic DR graders participating in an NGO program (primarily nurses and internists) took part in a self-taught, one-week online course on recognizing glaucomatous optic nerves. Their performance (% of images graded correctly as to 'refer/no refer and 'reason for referral' compared to a panel of glaucoma specialists) on a test set of optic nerve photos from the GONE website, population studies and patients taking part in the DR screening program was assessed before and after training, and was compared with 29 local, non-glaucoma-specialist ophthalmologists not taking the course.

Intervention: Self-paced participation in an online course describing various aspects of a glaucomatous optic nerve over one week.

Results: The mean±SD age of the non-ophthalmic graders was 32.3±7.3 years, with a mean±SD working experience of 8.2±7.1 years, compared to 32.6±5.5 and 7.2±5.2 years years for ophthalmologists. Non-ophthalmic graders' test performance improved from a mean of 33.3±14.3% pre-training to 55.8±12.6% post-training ($P<0.0001$). Their post-test performance did not differ from that of ophthalmologists (58.7±15.4%, $p=0.384$). Results (significant improvement with training, no difference between post training graders and ophthalmologists) were consistent regardless of the origin of the optic nerve images (GONE website, population study, local images from the Vietnam program).

Conclusions: Non-ophthalmic graders could significantly improve their accuracy in detecting glaucoma after a brief online course, and had performance comparable to ophthalmologists. This model could contribute to low-cost glaucoma screening in underserved settings.

CONTROL ID: 3712698

SUBMITTER (NAME ONLY): Machelle Pardue

TITLE: Rod-only Retina Maintains Protective Effect of Scotopic, but not Photopic Lighting on Lens-induced Myopia in Mice

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.T. Pardue, P. Datta Roy, K. Hogan, D. Brown, Q. Paulus, R. Mazade, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|M.T. Pardue, P. Datta Roy, K. Hogan, D. Brown, R. Mazade, Biomedical Engineering, Georgia Institute of Technology College of Engineering, Atlanta, Georgia, UNITED STATES|Q. Paulus, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous work by our lab has shown that both scotopic and photopic ambient lighting is protective for lens-induced myopia (LIM) in wild-type mice (Landis et al., IOVS 2021). Evidence suggests that both mouse rod and cone photoreceptors can detect photopic lighting (Tikidji-Hamburyan et al., Nat Commun 2017). To investigate the origins of the protective effect of photopic lighting in myopigenesis, we measured the response to LIM in transgenic mice with rod-only retinas exposed to different ambient light levels.

Methods: Rod, cone, and melanopsin photoreceptors were targeted using Gnat1+/+, Gnat2-/-, Opn4-/- mice, respectively, creating mice with rod-only retinas. Mice were used as naïve controls (control, n=20) or received a monocular -10 D lens over the right eye (LIM, n=21). Animals were placed in one of three ambient lighting conditions: 1 lux (scotopic, n=14), 50 lux (mesopic, n=13), or 10,000 lux (photopic, n=14) on a 12:12 light:dark cycle. Refractive errors, corneal curvature and ocular axial parameters were tested at baseline, 1- and 2-weeks post-goggling using an automated photorefractor, keratometer, and SD-OCT. Myopic shifts were calculated as the difference in refractive error between the right and left eyes.

Results: Myopigenesis occurred in all LIM mice over the treatment period, while no myopia developed in control mice (0.02±0.39D). However, the degree of myopigenesis was influenced by light levels ($p<0.001$). LIM mice exposed to ambient 50 lux and 10,000 lux lighting developed comparably severe myopic shifts, (-5.90±0.42 D and -6.68±0.49 D, respectively, p=n.s.). In contrast, LIM mice exposed to ambient 1 lux lighting developed significantly less myopic shift compared to the mice in 50 and 10,000 lux lighting (-3.97±0.35 D, $p<0.01$). Other measured outcomes did not change with LIM or light exposure.

Conclusions: Here, we exploited a transgenic mouse model with intact rod, but disrupted cone and melanopsin, signaling to determine which photoreceptor pathways underlie the protective effect of photopic lighting in LIM. Our results indicate that a rod-only retina provided the needed signaling for the protective effects of scotopic lighting during LIM, while not contributing to the protective effect of photopic lighting for myopic eye growth. Future studies will examine the effects of a cone only retina on LIM under different ambient light levels.

CONTROL ID: 3712700
SUBMITTER (NAME ONLY): Homa Rashidisabet
TITLE: Real-World Data Generalization for Glaucoma Prediction
SESSION TITLE: Data science, machine learning, and AI
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: H. Rashidisabet, R. Chan, T.S. Vajaranant, D. Yi, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|
Commercial Relationships Disclosure: Homa Rashidisabet: Commercial Relationship: Code N (No Commercial Relationship) | R.V. Paul Chan: Commercial Relationship: Code N (No Commercial Relationship) | Thasarat Vajaranant: Commercial Relationship: Code N (No Commercial Relationship) | Darvin Yi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Despite the rapid growth of AI in ophthalmology research, translations to clinical settings remain challenging. This study aims at showing AI models trained on standardized publicly available datasets perform well while they are not generalizable to the complex real-world clinical data for predicting glaucoma.

Methods: To compare the relative impact of using public datasets compared to hospital datasets, we used data from three well-studied public fundus datasets (REFUGE, Drishti-GS, and RIM-ONE-DL) as well as data from the Illinois Eye and Ear Infirmary. Given the limited available number of glaucoma images (n=362) in public data, we randomly sampled the same number of non-glaucoma images to create a balanced dataset. Consistently, we sampled 362 images per class from IODA. Using state-of-the-art residual networks, we classified images as glaucoma or non-glaucoma. We created two classification models: (1) a model trained on public data, and (2) another model trained on real-world (RW) data. To investigate the generalizability of these two models, we tested each model on both RW and public test sets. We will refer to each result as a train-test pair (e.g. the model trained on RW data and tested on public data is the RW-public result). We further compared the explainability of each model for predicting glaucoma based on fundus images using Grad-CAM Visualization.

Results: The Public-Public model has significantly higher accuracy (0.88) and AUC (0.95) than the RW-RW model. However, the public dataset model fails to generalize on real-world data as the accuracy and AUC respectively drop by 9% and 18% once tested on RW data. On the other hand, the RW model results in similar accuracy (0.80) and AUC (0.86) regardless of being tested on RW or Public data. Further, based on Grad-CAM visualization, the RW dataset model shows more consistent localization on the Optic Disc (OD) region than the Public dataset model which matches clinical insight for diagnosing glaucoma.

Conclusions: Our results show that standardized publicly available fundus data are not a good representation of RW data resulting in bias models that do not generalize to the RW data. We found the heterogeneous RW data can be used to develop AI models that potentially enable clinical translations.

CONTROL ID: 3712701

SUBMITTER (NAME ONLY): Austin Pereira

TITLE: Proof of concept analysis of a deep learning model to conduct automated segmentation of optical coherence tomography images for macular hole volume

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pereira, N. Choudhry, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|J.D. Oakley, Voxeleron LLC, San Francisco, California, UNITED STATES|S. Sodhi, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Austin Pereira: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Oakley: Commercial Relationship: Code N (No Commercial Relationship) | Simrat Sodhi: Commercial Relationship: Code N (No Commercial Relationship) | Netan Choudhry: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Modern-day staging of a full-thickness macular hole (MH) requires manual caliper measurement of the minimum linear diameter (MLD) on optical coherence tomography (OCT) images. However, these 2-dimensional measurements are technician and OCT segmentation software dependent, with literature demonstrating high inter-user variability in same-eye MLD observations. The aim of this study was to determine if an automated artificial intelligence (AI) model could assess MH volume on swept-source OCT images to improve MH size characterization.

Methods: In this proof-of-concept case series between 2017-2019, patients with an idiopathic full-thickness MH undergoing pars plana vitrectomy surgery with 1-year follow-up were considered for inclusion. Swept-source OCT images were taken at the preoperative, postoperative 1-month and 1-year time-points. MHs were manually graded from preoperative OCT images to delineate MH volume. This information was used to train a 3-dimensional convolutional neural network (CNN) for automatic segmentation. Cross-validation was used to assess performance across all subject eyes. The primary outcome was correlation of manual MH volume to automated volume segmentation.

Results: Twenty-four eyes were included in analysis. The correlation between manual and automated MH volume was R^2=0.94. The average dice coefficient between manual and automated metrics was 0.73 [0.65 - 0.86]. The mean preoperative automated MH volume was 1.3nL ± 1.54 (range 0.04 - 7.18nL); all MHs were closed at the 1-year postoperative follow-up. Automated MH volume metrics demonstrated higher correlation to MLD compared to manual MH measurements (R^2=0.72 and 0.61, respectively). Automated macular hole volume demonstrated significantly higher correlation to change in visual acuity from preoperative to the postoperative 1-year time-point compared to MLD (volume: R^2=0.53, MLD: R^2=0.39).

Conclusions: This deep learning CNN represents the first AI model to analyze MH volume. Fully automated segmentation demonstrated high correlation to manual MH volume measurements. The resulting automated volume assessment creates less inter-user variability and offers improved prognostic considerations for postoperative visual outcomes following MH surgical intervention compared to MLD.

CONTROL ID: 3712702

SUBMITTER (NAME ONLY): Sun Young Lee

TITLE: Exosome based anti-VEGF drug delivery combined with active targeting of choroidal neovascularization (CNV)

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lee, D. Pollalis, G. Gopinadhan Nair, Ophthalmology, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|S. Lee, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|C. Kang, D. Kim, Department of Pharmaceutical sciences, College of Pharmagy, Oklahoma City, Oklahoma, UNITED STATES|A. Nanda, The University of Oklahoma College of Medicine, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: To employ an active targeting strategy for intraocular anti-VEGF drug delivery for the management of CNV, we have developed ASL-exosomes composed of Anchor, Spacer, and Arg-Gly-Asp acid (RGD) Ligand modification. Our recent work demonstrated that decorating exosomes with RGD, one of the major integrin binding ligands, allowed selective delivery of exosomes to the area of CNV because integrins are essential in VEGF signaling in CNV. In current study, we aimed to study whether aflibercept (Eylea®) loaded ASL-exosomes enhance the efficacy of anti-VEGF agent in CNV suppression by active targeting of CNV.

Methods: Fluorescent labeled ASL-exosomes were engineered using mouse retina-derived exosomes and loaded with Eylea. Either Eylea loaded ASL-exosomes (4g Eylea/$5x10^7$ exosomes/1l), naive exosomes ($5x10^7$ exosomes/1l), Eylea (40g/1μl) or PBS (1μl) was intravitreally injected in a laser-induced CNV mouse model 3 days after laser treatment (n=6-11 in each group). Retinal sections or choroid/RPE flat mounts at 7 days after exosome treatment were stained with GSA and anti-integrin α_V antibody to assess CNV induction, integrin expression. Total volumes of CNV lesion were quantified and compared between the groups. Retinal sections were also stained with GFAP to assess an immediate reactive retinal gliosis 1 day after intravitreal exosome treatment.

Results: Integrin α_V was highly expressed in CNV lesion. Intravitreally delivered Eylea loaded ASL-exosomes improved CNV suppression by 12 % ($p < 0.05$) compared with Eylea alone treatment despite ASL-exosomes contained 0.1 times of Eylea in Eylea alone treatment group that is relevant to the clinical dose. Intravitreal injection of Eylea-loaded ASL-exosome treatment did not induce immediate reactive retinal gliosis.

Conclusions: ASL-exosomes may be useful for active targeting strategy by targeting CNV, therefore upgrading the functionality of the intraocular drug delivery system. Further study is needed to translate active targeting strategy and exosome based intraocular drug delivery platform for the management of posterior eye diseases.

CONTROL ID: 3712705

SUBMITTER (NAME ONLY): Joshua Taylor

TITLE:

Prevalence of diabetic retinopathy in Indigenous and non-Indigenous Australians: a systematic review and meta-analysis

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Taylor, A. Turner, Lions Eye Institute, Perth, Western Australia, AUSTRALIA|M. Chia, P. Foster, P. Keane, University College London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of blindness worldwide and Indigenous Australians suffer disproportionately from diabetic-related blindness. Exploring ethnic variation in disease is useful for service planning and can lead to identification of ethnic-specific modifiable risk factors. Existing studies on DR prevalence in Indigenous diabetic patients have reported variable results. We performed a systematic review to summarise the evidence-base relating to DR prevalence amongst Indigenous and non-Indigenous Australians.

Methods: This study was conducted following Joanna Briggs Institute (JBI) guidance on systematic reviews of prevalence studies (PROSPERO ID:CRD42022259048). We performed database searches of Medline (Ovid), EMBASE, and Web of Science up to October 2021 using a search strategy designed by an information specialist. We included studies reporting DR prevalence amongst diabetic patients (type 2 or mixed) in Indigenous and non-Indigenous Australian populations, with last data collected after January 2000. Two independent reviewers performed risk of bias assessments using a 9-item appraisal tool developed by the JBI. Meta-analysis was performed using double arcsine transformation and a random-effects model comparing Indigenous and non-Indigenous subgroups.

Results: Of 801 records identified through database searches, 14 studies met inclusion criteria and were included in the quantitative synthesis. The Indigenous subgroup scored significantly lower on the appraisal tool compared to the non-Indigenous subgroup (mean score 51% vs 78%, p=0.04). Pooled DR prevalence in the Indigenous subgroup was 29% [95% CI:22-37%] compared to 25% [95% CI:17-33%] in the non-Indigenous subgroup, although there was significant heterogeneity in the pooled results ($p<0.01$, $I^2>94\%$). Of 3 studies reporting within-study comparisons, all 3 found higher DR prevalence amongst Indigenous patients.

Conclusions: Indigenous studies scored lower for methodological quality compared to non-Indigenous studies. Pooled subgroup differences in DR prevalence were inconclusive due to the presence of significant heterogeneity. Further analysis into sources of heterogeneity is needed. Within-study comparisons suggest that DR may be more common amongst Indigenous Australians. Analysis of modifiable risk factors contributing to ethnic variation requires further exploration.

CONTROL ID: 3712706

SUBMITTER (NAME ONLY): Sean Kim

TITLE: Evaluation of Ultra-Widefield Fundus Photography as a Screening Tool for New Onset Flashes and Floaters

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.D. Kim, D. Rosen, R. Wang, E.M. Bowie, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Sean Kim: Commercial Relationship: Code N (No Commercial Relationship) | David Rosen: Commercial Relationship: Code N (No Commercial Relationship) | Rui Wang: Commercial Relationship: Code N (No Commercial Relationship) | Esther Bowie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: New onset flashes and floaters are common symptoms presenting to ophthalmology clinics. Patients undergo an urgent, thorough dilated ophthalmic exam in order to rule out retinal breaks, holes, or detachments that may require intervention. Utilization of ultra-widefield (UWF) fundus imaging as a screening tool may expedite care received by patients with new symptoms and help guide ophthalmologist examination and intervention. Furthermore, UWF photography may identify breaks not seen on clinical exam to allow earlier detection of retinal breaks, leading to improved outcomes.

Methods: The study protocol was reviewed and approved by the Penn State College of Medicine Institutional Review Board. All adult patients presenting to Penn State Eye Center urgent care with new onset flashes or floaters from 12/1/21 to 1/6/22 were identified as potential subjects. Participating subjects underwent a full standard of care indirect ophthalmoscopy by a resident physician. The findings were confirmed with an attending ophthalmologist. Subjects then underwent a UWF photography with the Optos California icg. The results of resident exam, attending ophthalmologist exam, and UWF photography reviewed by a vitreoretinal surgery attending were compared. Descriptive statistical methods were used to compare the results.

Results: 29 patients met the inclusion criteria. Twenty-four eyes of 12 subjects were included in the study (41%). Posterior vitreous detachment was detected in 20 eyes by attending examination, compared to 20 eyes by residents (100%) and 14 eyes by photography (67%). Retinal breaks were detected in 3 eyes by attendings, compared to 2 eyes (67%) by residents and 2 eyes (67%) by photography. 1 retinal detachment was detected by all modalities. 18 out of 24 eyes (75%) were described to have significant obstruction of peripheral view of retina by the upper and lower lids and lashes on photography.

Conclusions: While limited by lack of depth perception and inability to visualize the entire retina, UWF photography may still serve as a useful tool for documenting various retinal pathologies, particulaly in settings without access to ophthalmologists or in resident education to aid in visualization of retinal pathologies. More data is required to assess the effectiveness of UWF photography as a screening tool for evaluating new onset flashes and floaters.

CONTROL ID: 3712707

SUBMITTER (NAME ONLY): James Samson

TITLE:

Birdshot Retinochoroidopathy: Characteristics of Patients Treated at a Tertiary Care Center

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Samson, G. Fridman, B. Glick, C.M. Samson, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|J.M. Samson, Biology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe characteristics of a cohort of patients diagnosed with Birdshot Retinochoroidopathy (BRC) at a tertiary care center.

Methods:

Retrospective chart review of patients diagnosed with BRC at the Manhattan Eye Ear, Throat Hospital from January 2017 to July 2021. Outcome measures included age of onset, HLA-A29 positivity, laterality, visual acuity and function, presence of cystoid macular edema, need for immunomodulatory therapy (IMT), and disease course.

Results:

Forty-three patients were analyzed. The average age of onset was 50.9 years and 81.4% of patients were female. Forty-two patients (97.7%) were HLA-A29 positive. All patients had bilateral involvement and were visually functional across the time frame of the study. Six patients (14.0%) were blind in one eye. Thirty-five patients (81.4%) experienced cystoid macular edema at some point in their disease. Thirty-five patients (81.4%) required IMT and 30 patients (69.8%) completed at least two years of therapy prior to discontinuing treatment. Of those, 73.3% were free of inflammation for five years, while 20% had recurrence of inflammation. Ten patients (27.9%) of the cohort remained on IMT during the course of the study.

Conclusions:

The characteristics of BRC in our cohort resembled those reported in other studies. Treatment of severe disease with IMT was associated with good visual outcome and disease remission.

CONTROL ID: 3712708

SUBMITTER (NAME ONLY): Eugenia Custo Greig

TITLE: Choriocapillaris Impairment Prior to Nascent Geographic Atrophy Development

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Custo Greig, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|E. Moult, J.G. Fujimoto, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|I.N. Despotovic, N.K. Waheed, New England Eye Center, Boston, Massachusetts, UNITED STATES|L.A. Hodgson, R.H. Guymer, Z. Wu, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Eugenia Custo Greig: Commercial Relationship: Code N (No Commercial Relationship) | Eric Moult: Commercial Relationship: Code N (No Commercial Relationship) | Ivana Despotovic: Commercial Relationship: Code N (No Commercial Relationship) | Lauren Hodgson: Commercial Relationship: Code N (No Commercial Relationship) | James Fujimoto: Commercial Relationship(s);Code I (Personal Financial Interest):Optovue;Code P (Patent):Optovue;Code F (Financial Support):Topcon;Code P (Patent):VISTA-OCTA | Nadia Waheed: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis;Code S (non-remunerative):Nidek;Code C (Consultant/Contractor):Topcon;Code C (Consultant/Contractor):Roche;Code C (Consultant/Contractor):Boehringer Ingelheim;Code C (Consultant/Contractor):Regeneron;Code C (Consultant/Contractor):Apellis;Code C (Consultant/Contractor):Astellas | Robyn Guymer: Commercial Relationship(s);Code C (Consultant/Contractor):Roche;Code C (Consultant/Contractor):Genentech;Code C (Consultant/Contractor):Apellis;Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Bayer | Zhichao Wu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess whether choriocapillaris (CC) loss occurs prior to the development of nascent geographic atrophy (nGA) in intermediate age-related macular degeneration (iAMD) using optical coherence tomography angiography (OCTA) imaging.

Methods: Participants were enrolled as part of a prospective, longitudinal, observational study and underwent swept-source OCTA imaging (Zeiss PlexElite) at 6-month intervals. Only participants with reliable OCTA imaging in ≥2 visits and iAMD without nGA at baseline were included. CC flow deficit percentage (FD%; compensated for shadowing artifacts) and RPE volume/height measurements were determined for the visit prior to nGA development or final visit (n-1). Linear mixed models were utilized to examine the association between CC FD% and future nGA development at a global level and at a local level, defined by 120x120 µm superpixels (Figure 1).

Results: Of 105 eyes from 62 participants, 13 eyes from 10 participants developed nGA during the follow-up period. There was no significant difference in global CC FD% at the n-1 visit between eyes that developed nGA and those that did not ($P = 0.399$). In contrast, CC FD% was significantly higher in superpixels that developed nGA than those that did not ($P < 0.001$). However, the performance of CC FD% for predicting the development of nGA (area under the receiver operating curve [AUC] = 0.83) was not significantly different to the performance using RPE height alone (AUC = 0.83) or when using both CC FD% and RPE height (AUC = 0.84; $P \geq 0.48$) at the superpixel level.

Conclusions: CC flow deficits were significantly greater within local regions (superpixels) that subsequently developed nGA compared to those that did not. This did not hold true at the global level. Although CC FD% did not aid in the prediction of nGA development, these findings provide further insights into the potential patho-etiology of atrophy development.

CONTROL ID: 3712714

SUBMITTER (NAME ONLY): Yandong Bian

TITLE: Treatment Patterns of Ocular Surface Tumors in the United States: an IRIS Registry Analysis

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Bian, N. Hall, T. Elze, A. Lorch, J.W. Miller, H. Chang, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular surface tumors (OSTs) are a rare and vision-threatening condition of the conjunctiva and/or cornea. Potential treatments include observation for small, benign-appearing lesions, topical instillation or subconjunctival injection of medications such as interferon alpha-2b, and surgical excision with or without cryotherapy. We utilized the American Academy of Ophthalmology IRIS® (Intelligent Research in Sight) Registry to characterize the treatment patterns of OSTs in the United States (U.S.).

Methods: A total of 15,086 OST patients were identified in the IRIS Registry between 2013-2019 using ICD codes. Relevant procedures and/or injections of medications were identified using CPT codes. Descriptive statistics and frequencies were calculated for the types of procedures and injections undertaken.

Results: Of the 15,086 OST patients, 2,290 (15.18%) patients underwent a total number of 3,545 procedures and injections of chemotherapy or other agents. The median number of procedures or injections received by patients in the cohort was 2 (range 1 to 34). The majority of these patients underwent at least one surgical procedure (99.30%). Of the surgical procedures, 1982 patients (87.62%) underwent excision only procedures, 64 patients (2.83%) underwent cryotherapy only, and 216 patients (9.55%) underwent both excision and cryotherapy. Only 1.22% of patients underwent at least one injection of chemotherapy or other agent, the majority of which were interferon alpha (76.19%). Of patients who underwent injection of interferon alpha, 5 (21.74%) underwent a single injection while 18 (78.26%) underwent multiple injections. All patients who underwent a single injection of interferon alpha also underwent excisional procedures. Only 3 (16.67%) patients who underwent multiple injections of interferon alpha also underwent excisional procedures.

Conclusions: Our findings highlight frequencies of various treatments of OST patients in the U.S. Only 15.18% of OST patients underwent procedures (surgical or injection); the rest were either observed or treated with topical eyedrops. The majority of OST patients who received procedures underwent excisional procedures, while the majority of OST patients who underwent injection procedures received interferon alpha. Few patients who received multiple injections of interferon alpha also underwent excisional procedures.

CONTROL ID: 3712715

SUBMITTER (NAME ONLY): Courtney Goodman

TITLE: Composition of the gut microbiome in immune-mediated dry eye

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Goodman, D. Mehra, J. Betz, E. Locatelli, M. Hernandez, J. Hwang, A. Galor, University of Miami Miller School of Medicine, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|T. Doan, Francis I Proctor Foundation for Research in Ophthalmology, San Francisco, California, UNITED STATES|T. Doan, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gut microbiome alterations have been associated with various autoimmune diseases. There is limited data, however, on relationships between gut dysbiosis and immune-related dry eye (DE). The aim of our prospective, cross-sectional study was to evaluate the gut microbial composition of individuals with early or late markers of Sjögren's Syndrome (SS) compared to controls without DE.

Methods: We compared 20 individuals with positive early markers (anti-SP1, anti-CA6, anti-PSP IgG, IgA, andIgM) or late markers (anti-Ro/SS-A and anti-La/SS-B) of SS with no comorbid autoimmune diagnoses and 20 age- and sex-matched controls. Stool samples were collected and underwent deep RNA sequencing. The main outcomes measured were gut microbial composition and diversity.

Results: A total of 20 individuals with DE (mean age 61±13 years, Dry Eye Questionnaire-5 (DEQ-5) score of 15.2±3.4, Ocular Surface Disease Index (OSDI) score of 55.1±22.8, Schirmer of 7.1±5.2) were compared to 20 controls (mean age 59±12 years, DEQ-5 score of 4.8±3.8, OSDI score of 14.2±12.3, Schirmer of 21.9±9.1). No significant differences were observed in bacterial diversity (Shannon's index, $p=0.97$) or overall community structure (Euclidean PERMANOVA, $p=0.62$). A total of 41 species were differentially abundant between groups ($p<0.01$). Among these, 34 were relatively more abundant in the case group, including 10 species of Lactobacilli and 4 species of Bifidobacteria. A relative depletion of 7 species was found in the case compared to the control group, notably Fusobacterium varium and Prevotella stercorea.

Conclusions: Differences in gut microbiome composition were found in individuals with early or late markers of primary SS compared to an age- and sex-matched control group. Further studies are needed to elucidate the role of gut dysbiosis on immune dysregulation and disease activity in the eye. Gut microbiome modulation as a potential therapy for DE, such as through probiotic use or fecal microbial transplant, is another area of further research.

CONTROL ID: 3712716

SUBMITTER (NAME ONLY): Steve Gendi

TITLE: Characterization of COVID-19 Pre-Surgical Screening Amongst Ophthalmic Patients

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.W. Gendi, C. Akotoye, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|A. Kalur, J. Muste, C. Carvalho Soares Valentim, A. Iyer, K. Seth, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: During the COVID-19 pandemic, ophthalmologists were presented with the challenge of providing safe care to patients while limiting the spread of COVID-19. As a result, many institutions implemented universal pre-surgical COVID-19 screening prior to surgery for all patients. The goals of this study are to characterize the rate of COVID-19 positivity during pre-surgical screening at our institution, the surgical outcomes experienced in COVID-19 positive ophthalmic patients, and to report overall cost of universal pre-surgical screening.

Methods: This retrospective study included patients ≥ 18 years who underwent ophthalmic surgical procedures at a tertiary institution between May 11, 2020 and December 31, 2020. Patients without a valid pre-surgical COVID-19 test within the three days prior to their scheduled procedure, incomplete or mislabeled visits, and incomplete or missing data in their file were excluded. COVID-19 screening was completed by the Thermo Fisher TaqPath Polymerase Chain Reaction (PCR) kit.

Results: Of the 3,585 patients who met inclusion criteria, 2,044 patients (57.02%) were female, and the average age was 68.2 ± 12.8 years (mean ± standard deviation). 13 asymptomatic patients (0.36%) tested positive for COVID-19 via PCR screening. Three patients had known positive COVID-19 infection within the 90 days prior to surgery, thus 10 patients (0.28%) were found to have asymptomatic naïve COVID-19 infection via PCR. Testing was associated with a total charge of $788,700. Five of the 13 COVID-19 positive patients (38.46%) experienced a delay in their surgery. The average surgical delay was 17.23 ± 22.97 days (mean ± standard deviation).

Conclusions: Asymptomatic ophthalmic surgical patients experienced a low positivity rate with a limited impact on surgery scheduling at a significant cost. Further studies would be valuable in evaluating a targeted pre-surgical screening population as opposed to universal testing.

CONTROL ID: 3712717

SUBMITTER (NAME ONLY): Mallory deCampos-Stairiker

TITLE: Longitudinal Evaluation of Retinopathy of Prematurity Rates and Severity in India

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Singh, J. Kalpathy-Cramer, Harvard University, Cambridge, Massachusetts, UNITED STATES|R.V. Chan, University of Illinois Hospital and Health Sciences System, Chicago, Illinois, UNITED STATES|P. Sparizam, P. Shah, Aravind Eye Care System, Madurai, Tamil Nadu, INDIA|M.F. Chiang, National Institutes of Health, Bethesda, Maryland, UNITED STATES|M.A. deCampos-Stairiker, A. Gupta, M. Oh, A.S. Coyner, S.R. Ostmo, J. Campbell, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: The epidemiology of retinopathy of prematurity (ROP) changes over time as neonatal care improves across neonatal care units (NCUs). Prior work using an artificial intelligence (AI)-derived vascular severity scale (VSS) demonstrated that NCU-level ROP could be used for epidemiological monitoring and was associated with oxygen management in 13 NCUs in South India. In this study, we evaluated the change in NCU-level ROP severity over time in seven of these NCUs.

Methods: As part of the Aravind ROP tele-screening program, a VSS was derived from retinal fundus images collected during the first eye exam from babies screened at two different time periods: 2015–2017 and 2019–2020. Differences in VSS were evaluated using a one- or two-way analysis of covariance (ANCOVA) to control for gestational age (GA) or GA and NCU, respectively. The proportion of babies diagnosed with ROP was evaluated using a test of equal proportions.

Results: Between the two time periods studied, the proportion of babies diagnosed with ROP decreased across all NCUs from 32% (range: 7.0% – 75.0%) in the earlier time period to 11% (range: 7.1% – 13.1%, $p < 0.001$) in the later period. This was associated with an increase in mean birthweight and gestational age (Table). However, when controlling for GA, there was no clinically meaningful change in the mean ROP severity as assessed by the VSS (2.9 to 3.0), although this varied significantly by NCU and GA. The figure demonstrates the changes in one NCU, with lower VSS in babies born after 31 weeks and higher VSS (and more babies surviving to point of screening) in babies born before 31 weeks.

Conclusions: On average NCUs in South India are screening more babies for ROP now than five years ago, which may in part be due to improved survival especially in the youngest cohort as well as increased awareness of ROP among pediatricians and improvements in NCU care. The NCU-level VSS did not change at the population level but varied at the NCU level due to changes in demographics in each population, with higher VSS in the youngest babies being offset by many low-risk older babies with no disease.

CONTROL ID: 3712718

SUBMITTER (NAME ONLY): Tracy Lu

TITLE: Long-term real world teprotumumab outcomes

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lu, H. Bair, L. Amarikwa, C. Dosiou, A. Kossler, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|S. Diniz, P. Singh, D. Rootman, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|K. Clauss, S. Wester, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teprotumumab, an IGF-IR inhibitor, was approved for the treatment of thyroid eye disease (TED) in January 2020. Two clinical trials demonstrated efficacy in patients with active moderate-to-severe TED and excluded patients with other types of TED or previous therapy with orbital irradiation, surgery, glucocorticoid use (cumulative dose > 1 gm), or biologic treatments. This study is the first to report the long-term real world outcomes in patients treated with teprotumumab for TED.

Methods: The pooled data of consecutive patients treated with teprotumumab for TED from 3 academic institutions were reviewed. Patient data were collected at baseline, post-treatment, and at long-term follow-up. All patients who completed treatment with ≥4 infusions were included. The percentage of proptosis responders (≥2 mm reduction) and mean changes from baseline in proptosis, Gorman diplopia score (GDS), clinical activity score (CAS), and Graves' ophthalmopathy quality-of-life (GOQoL) score at post-treatment and long-term were calculated. The percentage of patients who had proptosis regression (≥2 mm increase from post-treatment to long-term follow-up) was also calculated.

Results: 48 patients with a mean age of 57.9 (range 30-90) and mean CAS of 4.1 (range 1-7) were included (Fig 1). The mean post-treatment and long-term follow-ups were at 28.9±SD 11.0 and 57.44±11.1 weeks after the first infusion, respectively. Compared to baseline, post-treatment metrics demonstrated a significant decrease in mean proptosis (2.91±2.18, n=47), GDS (0.67±1.22, n=43), and CAS (3.32±1.37, n=44), all $p<0.002$. No significant difference occurred in these values between post-treatment and long-term (n = 40, 39, 34 respectively). The mean GOQoL gain between baseline and post-treatment (19.8±17.6, n=15, $p<0.001$) was maintained long-term (22.7±14.8, n=11). 70.2% were proptosis responders (n=47) post-treatment, but 28.2% (n=39) had proptosis regression. Of the regressors, 81.8% (n=11) continued to have inactive disease (CAS of 0 or 1) (Fig 2).

Conclusions: Our results confirm the efficacy and durability of teprotumumab in consecutive patients with TED using the metrics reported in clinical trials. Although regression of the initially robust proptosis response may occur, most patients do not develop reactivation of active TED. Further investigation on the long-term durability of proptosis response and reason for proptosis regression in a portion of patients is warranted.

CONTROL ID: 3712719

SUBMITTER (NAME ONLY): Jay Chhablani

TITLE: Three-dimensional (3-D) analysis of the Haller's vessels in diseased eyes: comparison with healthy eyes

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chhablani, S. Singh, M.N. Ibrahim, A. Samanta, A. Selvam, V. Sant, M. Rasheed, J.A. Sahel, K.K. Vupparaboina, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze and report the 3-dimensional (3-D) structure, qualitative and quantitative parameters in Haller’s layer of the choroid in diseased eyes and compare with age-matched healthy eyes.

Methods: This was a retrospective study and included 3 groups (healthy, age-related macular degeneration (AMD), and central serous chorioretinopathy (CSCR) eyes). Previously validated end-to-end algorithm based on ResUnet, 3D tensor voting and geometrical modeling was used to segment, reconstruct and quantify Haller’s sublayer vasculature in 3D. A heat map showing the relative radius of the blood vessel, vascularity showing the blood flow in the vascular lumen was generated. A histogram showing the distribution pattern of the thickness of Haller's vessel was prepared. Qualitative parameters including symmetricity, arrangement, and branching pattern of vessels, rarefaction of vessel density, hot areas, and focal constriction were analyzed.

Results: A total of 34 eyes (14 healthy, 9 AMD, 11 CSCR eyes) were analyzed. The mean (±SD) Haller vessel radius in healthy, AMD and CSCR eyes was 86.4 ± 4.4 µm (range, 14.96 to 174.1 µm), 88.8 ± 6.4 µm (range, 14.7 to 179.2 µm) and CSCR: 88.3 ± 6.6 µm (range, 14.6 to 171.5 µm) respectively (Figure 1). However, the percentage of eyes with radius > 100 µm was more in AMD (17.7%) and CSCR eyes (16.8%) compared to healthy eyes (14.2%). Two eyes in CSCR and 3 eyes in the AMD group had an asymmetrical pattern of vessel arrangement whereas all the healthy eyes had a symmetrical pattern. Severe vessel rarefaction was seen in 1 healthy eye compared to 3 and 4 in AMD, and CSCR eyes respectively. Either focal or diffuse hot areas i.e., sites of vascular dilatation were seen in all 3 groups (healthy, focal: 8; diffuse: 2; AMD, focal: 6, diffuse: 2; CSCR, focal: 5, diffuse: 3). Focal constriction in Haller's vessels was seen in 2/14 eyes in healthy subjects compared to 7/9 eyes in AMD and 3/11 eyes in the CSCR group.

Conclusions: The diameter of Haller's vessels shows a wide range of variation in healthy as well as diseased (AMD, CSCR) eyes. However, both AMD and CSCR eyes showed a higher percentage of vessels with a radius > 100 microns compared to healthy eyes. Moreover, the qualitative analysis showed a higher percentage with symmetrical distribution, relatively fewer eyes with severe vessel rarefaction, and/ or focal constriction in healthy subjects compared to diseased eyes.

CONTROL ID: 3712721

SUBMITTER (NAME ONLY): Sarah Robertson

TITLE: Non-canonical Wnt signaling via Wnt16b improves human limbal epithelial stem/progenitor cell maintenance

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Robertson, C. Bonnet, J. Islam, S.X. Deng, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Understanding effective limbal epithelial stem cell maintenance is necessary to improve limbal stem cell deficiency (LSCD) treatment using ex vivo cultured limbal stem/progenitor cells (LSCs). We have previously demonstrated that canonical Wnt signaling is crucial for limbal stem cell maintenance and that Wnt2, Wnt6, Wnt11, and Wnt16b are upregulated in the limbus relative to the cornea. The purpose of this study is to investigate the effect and mechanism of supplementing Wnt16b in the LSC cultures on the expansion of the stem/progenitor cell population in vitro.

Methods: Wnt16b was overexpressed in 3T3 cells, which do not express Wnt16b, using a Wnt16b-IRES-GFP lentivirus vector. An IRES-GFP vector served as a control. Transduced 3T3 cells were sorted into low, medium, and high GFP expression groups. LSCs were isolated from five donors and cultured on low, medium, and high Wnt16b-expressing 3T3s compared to their respective GFP controls and an uninfected 3T3 control. After 12-14 days in culture, the cultivated LSCs were evaluated by quantifying cells expressing K12, K14, and high levels of p63α. Canonical and non-canonical Wnt pathway markers expressed in the cultivated LSCs were evaluated by quantitative real-time PCR (qRT-PCR).

Results: LSCs cultured on low Wnt16b-3T3 cells, which most closely corresponded to levels of Wnt16b in the human limbus in vivo, contained significantly higher percentages of p63α-bright cells and the non-canonical Wnt marker phosphorylated cJun than LSCs cultured on low GFP-3T3 cells. LSCs cultured on Wnt16b-3T3s also differentially expressed Wnt6, Wnt7a, and Wnt7b. Proliferation, colony-forming efficiency, and cell size were not significantly affected.

Conclusions: Wnt16b contributes to maintaining a fine balance of canonical and non-canonical pathways to regulate limbal stem cell proliferation, differentiation, and self-renewal in vitro.

CONTROL ID: 3712724

SUBMITTER (NAME ONLY): Lynn Shi

TITLE: Comparison of Bruch's Membrane Opening-Based Minimum Rim Width and Retinal Nerve Fiber Layer Rates of Change in Glaucoma Patients

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Shi, M. Mohammadi, V. Mohammadzadeh, E. Su, R.E. Weiss, J. Caprioli, K. Nouri-Mahdavi, Ophthalmology, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare longitudinal rates of change (RoC) in Bruch's membrane opening-based minimum rim width (BMO-MRW) and peripapillary retinal nerve fiber layer (RNFL) thickness as measured with Spectralis OCT in glaucoma eyes with moderate to severe damage at baseline.

Methods: Spectralis OCT optic disc volume scans from 113 glaucoma eyes (113 patients) with >2 years of follow-up and ≥4 OCT images were exported. BMO-MRW and RNFL raw OCT images were reviewed for centration, artifacts, and segmentation accuracy and incorrect segmentations were rectified. We estimated global and sectoral RoC with linear regression of MRW and RNFL thickness against time. Outcomes of interest were standardized global and sectoral RoC for the 2 outcome measures and proportion of worsening and improving rates (negative vs. positive rates of change with $p<0.05$). Standardized RoC were calculated by dividing absolute RoC by the standard deviation of regression residuals. We also used permutation analyses to control specificity with the 2.5% and 97.5%ile cutoff points used to define true worsening or improvement.

Results: Median (IQR) follow-up and OCT scan sessions were 2.5 (1.0-4.2) years and 5 (4-8), respectively. Baseline average (SD) global RNFL and MRW thickness were 63 (±14) µm and 158 (±50) µm. Baseline mean deviation was -9.2 (±5.8) dB. Based on simple linear regression, a higher proportion of significant negative RNFL rates was observed compared to MRW in the inferotemporal (35% vs. 20%; $p=0.015$) and inferonasal (42% vs. 17%; $p<0.001$) sectors. The proportion of improving sectors was similar except in the inferotemporal sector (2.6% vs. 9.7% for MRW; $p=0.04$). Permutation analyses also demonstrated a higher proportion of worsening RNFL rates than MRW in the inferotemporal ($p=0.026$) and inferonasal ($p<0.001$) sectors with overall lower positive RoC (Figure 1). Standardized RNFL RoC were significantly more negative than MRW globally, inferotemporally, superonasally, and inferonasally (Figure 2; $p\leq0.007$).

Conclusions: RNFL measurements are more likely to demonstrate faster negative rates of change and to detect disease deterioration compared to BMO-MRW in eyes with moderate to severe glaucoma damage. RNFL measurements had a better signal to noise ratio than BMO-MRW globally and in more sectors, suggesting that RNFL is the superior metric for monitoring change in moderate to severe glaucoma.

CONTROL ID: 3712726

SUBMITTER (NAME ONLY): Luis Antonio Rhoads Avila

TITLE: RABIN CONE CONTRAST SENSITIVITY TEST REPEATABILITY IN HEALTHY PATIENTS OF DIFFERENT AGE GROUPS

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Rhoads Avila, R. Garcia-Santisteban, J. García-Sánchez, J. Serrano-Aguilar, G. Salcedo-Villanueva, Retina, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|R. Garcia-Santisteban, Universidad Panamericana, Ciudad de Mexico, Ciudad de México, MEXICO|J. García-Sánchez, Universidad Anahuac Mexico, Huixquilucan, Mexico, MEXICO|L. Rhoads Avila, Medicine, Universidad La Salle, Mexico City, Mexico City, MEXICO|G. del Castillo Marquez, Medicine, Universidad Popular Autonoma del Estado de Puebla, Puebla, Puebla, MEXICO|J. Gonzalez Salido, Medicine, Universidad La Salle, Mexico City, Mexico City, MEXICO|E. Rueda Torres, Medicine, Benemerita Universidad Autonoma de Puebla, Puebla, Puebla, MEXICO|

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ABSTRACT BODY:

Purpose: Visual performance can be measured by different tests, such as contrast sensitivity (CS). The Rabin Cone Contrast Sensitivity Test (RCCST [Innova Systems]) is an easy way to evaluate CS. To our knowledge, this has not been validated before in subjects with apparently normal visual acuity (VA). The purpose of our study was to validate the RCCST's CS test in ophthalmologically healthy individuals to determine changes in CS with age and assess test-retest variability.

Methods: This was a retrospective, observational and comparative study performed in the Retina Department of the Asociación Para Evitar la Ceguera en México (APEC). Volunteers agreed to participate in CS testing and signed informed consent. The project was approved by the Institutional Review Board, and adhered to the Declaration of Helsinki.

Patients were aged between 18 and 65, ophthalmologically healthy with a refractive error between -2.00 to +2.00 D, and best corrected VA ≥20/20. Each subject was evaluated for CS 3 times to determine intraobserver repeatability (test-retest reliability). Subjects were grouped by age: 18-29; 30-39; 40-49; 50-60. Comparison between age subgroups was performed. Cronbach’s alpha and Intraclass Correlation Coefficient (ICC) were used to measure correlation between results. Kruskal-Wallis test (KW) was performed to determine differences among subgroups. Spearman's Correlation Coefficient (SCC) was performed to detect correlation between age and CS.

Results: 114 subjects were studied, consisting of 58 women and 46 men, with a mean age of 33.72, standard deviation (SD) 12.32, range 18 - 60. Mean CS was 1.61 CS logarithmic scale (CSLS), 0.10 SD, 95% confidence interval (CI) 1.59 - 1.63 (range: 1.25 - 1.98). Cronbach’s alpha resulted in a correlation of 0.725; ICC for average measures resulted in a correlation of 0.726, 95% CI 0.626 - 0.803 (P< 0.001). Hence, both tests returned “good” reliability of the system.

CS means by subgroups are shown in Table 1. KW resulted in a statistically significant difference between groups: Chi-squared of ranks=14.48, P=0.002. SCC between CS and age resulted in a correlation of -0.355 (P< 0.001) (Graph 1).

Conclusions: Repeatability of CS measurement by RCCST resulted in a “good” correlation. Differences among age groups existed, with a lower CS for older individuals. Therefore, we consider that CS can be accurately measured using the RCCST in a subset of healthy subjects.

CONTROL ID: 3712728

SUBMITTER (NAME ONLY): Maya Harrington

TITLE: Primary ophthalmic hospitalizations in the United States, 2016-2018

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Harrington, M. Turkiewicz, N. Arya, Mayo Clinic School of Medicine - Scottsdale Campus, Scottsdale, Arizona, UNITED STATES|A. Bhandarkar, M. Bydon, Mayo Clinic Department of Neurosurgery, Rochester, Minnesota, UNITED STATES|J. Shen, Mayo Clinic Department of Ophthalmology, Phoenix, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is little data on ophthalmic illnesses of the general population in recent years. In this study, we quantified the rates of hospitalization for ophthalmic disease and injury among all individuals in the United States, using the National Inpatient Sample – Healthcare Cost and Utilization Project(NIS-HCUP) database from 2016 to 2018.

Methods: We conducted a retrospective cross-sectional analysis of recent data from the NIS-HCUP database (2016-2018). This database is the largest all-payer inpatient-care database and provides a stratified random sample covering 97% of all discharges from hospitals in the United States. Individuals with primary ophthalmic illnesses were identified by filtering for those with an ICD-10 code related to disease of the eye or adnexa. Data analysis was conducted using R software.

Results: From 2016 to 2018, there were an estimated 23,423 ophthalmic inpatient admissions in the US. Most of these admissions were from non-traumatic disorders (77%). The most common diagnoses among the general population for ophthalmic diseases during this time period are: orbital cellulitis (9.6%), diplopia/visual disturbances (9.2%), orbital floor fracture (9.0%), optic neuritis (7.1%), and zoster ocular disease (5.5%). We compared our results with a previous study that quantified general population ophthalmic hospitalizations from 2001 to 2014.[1] Our results show that the rates of orbital cellulitis have decreased from 14.5% to 9.6% while the rates of optic neuritis have increased from 4.0% to 7.1%.

Conclusions: This is the first published data on ophthalmologic disease and injury hospitalizations in the US during the time period of 2016 to 2018. Our study shows that rates of orbital cellulitis have decreased from previous years while rates of optic neuritis have increased. More research is needed to understand what drives these trends and changes in prevalences in diseases. This will be valuable when applying interventions to reduce the incidence and financial burden of the most common ophthalmic diseases.

1. Iftikhar M, Junaid N, Lemus M, Mallick ZN, Mina SA, Hannan U, Canner JK, Latif A, Shah SMA. Epidemiology of Primary Ophthalmic Inpatient Admissions in the United States. Am J Ophthalmol. 2018 Jan;185:101-109.

CONTROL ID: 3712729

SUBMITTER (NAME ONLY): Fan Xia

TITLE: Epac2 deletion prevents retinal neuronal injury through attenuation of ER stress in a mouse model of retinal ischemia-reperfusion

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Xia, S. Shi, E. Palacios, W. Zhang, H. Liu, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ischemia is one of the most significant pathologies in various ocular diseases, including glaucoma, diabetic retinopathy and retinal vascular occlusion, and results in the death of retinal neurons. Exchange protein activated by cAMP (Epac) is a newly identified mediator of second messenger cAMP. We previously found Epac1 plays a critical role in retinal neurodegeneration. This study aims to investigate whether Epac2, the other isoform of Epac, has a role in retinal neuronal injury in a mouse model of retinal ischemia-reperfusion (IR).

Methods: IR was induced by elevating intraocular pressure to 110 mm Hg for 50 minutes via raising the saline reservoir, to which an infusion needle was connected and inserted into the anterior chamber of the right eyes. Retinal ganglion cells (RGCs) number, apoptosis/necroptosis, and molecules in the endoplasmic reticulum (ER) stress branches were determined by immunohistochemistry and TUNEL assay.

Results: We found that at 12 hours after IR, retinal neuronal apoptosis (TUNEL-positive cells) and necroptosis (p-RIP3-positve cells) were dramatically increased in wild type (WT) IR retinas, which were significantly mitigated by Epac2 genetic deletion. At 7 days after IR, RGCs were significantly preserved in Epac2$^{-/-}$ mice compared with age-matched WT mice. Mechanistically, the expressions of ER stress-related molecules including GRP78, p-PERK and CHOP, and ER stress response mediator ER oxidoreductin 1 (ERO1α) were significantly increased after ischemic injury and Epac2 deletion lowered levels of p-PERK, CHOP and ERO1 whose activation can lead to cell death.

Conclusions: These data indicate that Epac2 deletion is neuroprotective against retinal IR injury through attenuation of ER stress, and Epac2 blockade may be a favorable strategy in the treatment of retinal neurodegenerative diseases.

CONTROL ID: 3712731

SUBMITTER (NAME ONLY): Christopher Pandiscio

TITLE: Visualizing changes over time in the visual field using Static Perimetry Data

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Pandiscio, A.Y. Alibhai, Boston Image Reading Center, Boston, Massachusetts, UNITED STATES|N.K. Waheed, New England Eye Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Christopher Pandiscio: Commercial Relationship: Code N (No Commercial Relationship) | Agha Alibhai: Commercial Relationship(s);Code E (Employment):Boston Image Reading Center | Nadia Waheed: Commercial Relationship(s);Code C (Consultant/Contractor):Nidek Medical Products, Boehringer Ingelheim, Topcon;Code F (Financial Support):Carl Zeiss Meditec, Heidelberg, Nidek Medical Products, Topcon;Code I (Personal Financial Interest):Ocudyne, Gyroscope Therapeutics;Code E (Employment):Gyroscope Therapeutics

ABSTRACT BODY:

Purpose: 3-dimensional representations of the visual field and associated calculations of volume “under the hill” have been applied to perimetry data in clinical trials. Changes in volume have been used to monitor subjects and response to treatment. However, existing methods do not enable spatial correlation to volumetric changes. This study aims to develop techniques for calculating and visualizing volumetric changes over time in the Hill of Vision (HOV).

Methods: HOV software was built using MATLAB. HOVs were generated using four different interpolation functions: thin plate spline, natural neighbor, nearest neighbor, and linear interpolation. HOV software was then applied to perimetry data and visualized using plotting libraries. Difference HOVs (dHOVs) were constructed by first comparing a subject’s most recent perimetry data with their baseline, then applying an interpolation function to generate the dHOV. dHOVs were plotted using a green-red color scheme to demonstrate areas of visual improvement or decline respectively.

Results: Our software successfully generated interpolated HOVs and dHOVs. Each interpolation strategy produced distinct HOVs and dHOVS that varied in terms of smoothness. The dHOV was shown to be an effective way of spatially correlating changes in the visual field over time.

Conclusions: dHOV rendering can be easily implemented using several different interpolation strategies. Use of dHOV may prove to be a valuable way to visualize disease progression or visual function improvement.

CONTROL ID: 3712732

SUBMITTER (NAME ONLY): Yutao Liu

TITLE: Exosomes and their miRNA/protein profile in keratoconus-affected corneal stromal cells

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Liu, M. Khaled, T. Akoto, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|Y. Liu, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|D. Karamichos, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|D. Karamichos, Pharmaceutical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Exosomes are small secreted extracellular vesicles (30-150 nm) to mediate intracellular communication via their content of proteins, lipids, and nucleic acids. We aimed to characterize the exosomes secreted by primary corneal stromal fibroblasts (HCFs) from patients with or without keratoconus (KC).

Methods: Using primary HCFs derived from normal (n=4) and KC (n=4) patients, we collected and isolated exosomes using serial ultracentrifugation. Using nanoparticle tracking analysis (NTA) with ZetaView, we compared the size and concentration of isolated exosomes. Different exosomal markers were identified using a transmission electron microscope (TEM) (CD81) and western blot (CD9 and CD63). Exosomal miRNA profiles were determined by qRT-PCR using Exiqon Human panel I miRNA assays of 368 pre-selected miRNAs. Proteomics profiling was determined using the label-free spectral counting method with mass spectrometry. Differential expression analyses for miRNAs and proteins were done using the student's t-test with a significance cutoff of p-value ≤ 0.05.

Results: We successfully characterized exosomes isolated from HCFs using several complementary techniques. We found no significant differences in the size, quantity, or morphology between exosomes secreted by HCFs with or without KC. Expression of CD81 was confirmed by immuno-EM and expression of CD63 and CD9 with western blot in all exosome samples. We detected the expression of 72-144 miRNAs (threshold cycle Ct < 36) in all exosome samples. In KC-derived exosome samples, miR-328-3p, miR-532-5p, miR-345-5p, and miR-424-5p showed unique expression while let-7c-5p and miR-665 have increased expression. Protein profiling identified 157 proteins present in at least half of the exosome samples with 38 known exosomal proteins. We identified 12 up- and 2 down-regulated proteins in KC-derived exosomes. The proteins are involved in membrane-bounded vesicles, cytoskeletal, calcium binding, nucleotide binding. These genes could be regulated by NRF2, miR-205, and TGFβ1, which are involved in KC pathogenesis.

Conclusions: For the first time, we successfully characterized the KC-derived exosomes and profiled their miRNA and protein content, suggesting their potential role in KC development. Further studies are necessary to determine if and how these exosomes with differential protein/miRNA profiles contribute to the pathogenesis of keratoconus.

CONTROL ID: 3712733

SUBMITTER (NAME ONLY): Anddre Valdivia

TITLE: Association of Alzheimer's disease and age-related macular degeneration identified via a PheWas-based integrated bioinformatic analysis

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Valdivia, H. Nazari, Ophthalmology and Visual Neuroscience, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|M. Motamedi, Department of Ophthalmology and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Anddre Valdivia: Commercial Relationship: Code N (No Commercial Relationship) | Massoud Motamedi: Commercial Relationship: Code N (No Commercial Relationship) | Hossein Nazari: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A growing number of studies have suggested common pathological pathways between Alzheimer's disease (AD) and age-related macular degeneration (AMD) as evidenced by the progressive accumulation of proinflammatory protein, amyloid β (Aβ), in plaques of the AD brain and the drusen of AMD retina. To explore the shared genomic profile between AD and AMD, a bioinformatic pipeline approach was adapted to analyze disease related PheWAS datasets via an interaction predictor database followed by a pathways database.

Methods: Data were collected from the UKBioBank PheWAS datasets (AD: 430 cases and 400600 controls, and AMD: 2180 cases and 395156 controls). Top loci variants were identified as the single genetic variant with a minor allele frequency (MAF) range of 5e-5≤MAF<0.50. Genes corresponding to top loci variants were identified based on the single genetic variant proximity to nearest gene. PheWAS candidate genes were analyzed through the STRING database as 3 different groups, 1) AD only, 2) AMD only, and 3) AD+AMD. Within each group sub-clusters corresponding to a string of protein interactions were identified and further analyzed through the REACTOME pathway database (pathways p-value ≤ 0.05).

Results: STRING analysis revealed minimal protein-protein interaction enrichment (PPI-E) in the AD only group (p-value: 1) and the AMD only group (p-value: 0.072), while the AD+AMD group demonstrated significant PPI-E (p-value: 0.044). REACTOME pathway analysis demonstrated 3 shared pathways unique to the AD+AMD group: 1) glucagon signaling pathway (p-value: 0.024), 2) activation of GABA receptors (p-value: 0.018) and 3) aquaporin mediated transport (p-value: 0.033).

Conclusions: The application of an integrated bioinformatic analysis enabled us to identify three dominant pathways demonstrating the association between AD and AMD. Specifically, glucagon secretion has been shown to be regulated by activation of GABA receptors via an Akt-dependent manner. Glucagon has also been documented to increase the expression of aquaporin. Our findings highlight the convergence of AD and AMD pathologic pathways in the dysregulation of aquaporin with its potential contribution to defective Aβ secretion that may lead to Aβ accumulation in both AD and AMD.

CONTROL ID: 3712735

SUBMITTER (NAME ONLY): Soraiya Thura

TITLE: Timing of vitrectomy in patients with ocular inflammation and history of lymphoma

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Thura, L. Valdes, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the clinical course of patients and decision for vitreous biopsy, with history of lymphoma, who present with intraocular inflammation.

Methods: Retrospective chart review of patients who were diagnosed with vitreoretinal lymphoma who also have a history of lymphoma from a non-ocular site. Patients without a prior or concurrent diagnosis of non-ocular lymphoma, but who had eventual diagnosis of vitreoretinal lymphoma, were also assessed for comparison in terms of timeline from symptoms to vitreous biopsy.

Results: A small subset of patients have been identified between 2017 and 2022 at the University of Massachusetts Medical School who presented to Ophthalmology Clinic with uveitis in one or both eyes. All patients underwent vitrectomy with vitreous biopsy samples that came back positive for a diagnosis of intraocular lymphoma. One patient with a history of lymphoplasmacytic lymphoma was found to have a rare presentation of intraocular Richter's transformation, which has only been described a handful of times in the literature since 1928. Another patient with a history of testicular lymphoma was diagnosed initially with retinitis but vitreous biopsy results showed diffuse large B cell lymphoma. In comparison to patients without a prior history of lymphoma, the time to obtain vitreous biopsy from initial clinic presentation was decreased.

Conclusions: The decision to perform vitrectomy for definitive diagnosis in patients presenting with persistent panuveitis, who have a known history of lymphoma from a non-ocular site, can be expedited. In these particular instances, it is prudent to rule out malignancy, as atypical presentations of lymphoma can become evident.

CONTROL ID: 3712737

SUBMITTER (NAME ONLY): Warren Pan

TITLE: Small molecule PKM2 activators in the treatment of rd10 photoreceptor degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Pan, E. Weh, R. Fernando, S. Chaudhury, C.G. Besirli, T.J. Wubben, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is a blinding disease caused by multiple mutations in dozens of genes; therefore, a gene agnostic treatment approach to prevent photoreceptor (PR) degeneration is ideal. We previously demonstrated that pharmacological activation of pyruvate kinase M2 (PKM2) alters central glucose metabolism and is neuroprotective for PRs in a model of acute outer retinal nutrient stress. Additionally, microglia can adopt an inflammatory phenotype, which has been shown to contribute to PR degeneration in RP, and PKM2 has been shown to suppress this inflammatory phenotype in other systems. This study assesses the pharmacologic activation of PKM2 as a novel therapeutic avenue in the rd10 mouse model of RP.

Methods: We employed oral (PO) and intraperitoneal (IP) injections of a known PKM2 activator, ML-265, and a novel PKM2 activator, MCTI-566, in rd10 and wild-type mice from postnatal day 14 (P14) to 49 (P49). At various time-points, the overall retinal PK activity was measured using an enzyme coupled continuous assay that measures the depletion of NADH at 340 nm. In vivo retinal structure and function analyses quantitatively examined the effect of PKM2 activation on retinal degeneration in rd10 mice. Histology and flow cytometry characterized retinal morphology and microglia recruitment and polarization.

Results: PK activity is depressed by over 40% ($p < 0.001$) in rd10 retinas at P14 compared to age-matched wild type animals, prior to any observed PR degeneration. PO administration of ML-265 significantly increased PK activity in rd10 retinas by over 1.5-fold ($p < 0.01$), which was similarly demonstrated with IP MCTI-566. Flow cytometry demonstrated a significant increase in rd10 retinal microglial numbers with a shift toward the pro-inflammatory M1 phenotype.

Conclusions: We previously showed that enhancing retinal PK activity using a small molecule activator of PKM2 is neuroprotective in a model of acute nutrient deprivation. Our new data suggest that decreased PKM2 activity and altered microglial polarization may contribute to PR degeneration in the rd10 mouse model of RP. Therefore, the use of small molecule PKM2 activators as a non-gene-specific therapy may prevent these metabolic and immunologic perturbations in RP.

CONTROL ID: 3712738

SUBMITTER (NAME ONLY): Mary Munsell

TITLE: A Normative Database of Widefield Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA) Quantitative Vascular Metrics

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Munsell, I. Garg, M. Duich, R. Katz, R. Zeng, J.Y. Moon, E.S. Lu, D.N. Sayah, H. Wescott, J.B. Miller, Harvard Retinal Imaging Lab, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M.K. Munsell, I. Garg, R. Katz, R. Zeng, J.Y. Moon, E.S. Lu, D.N. Sayah, H. Wescott, N.A. Patel, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Clinical and research interpretation of WF SS-OCTA requires reference to control data using similar imaging and analysis tools. Literature on WF SS-OCTA with large sample sizes is sparse and often limited to only vessel density (VD). We aimed to analyze a large number of healthy eyes to create the first normative database using the ARI network (Zeiss Portal).

Methods: In this cross-sectional observational study, 383 eyes of 302 subjects were imaged using 3x3mm, 6x6mm, and 12x12mm scans centered on the fovea using 100kHz WF SS-OCTA (PLEX® Elite 9000) between December 2018 and September 2021. Robust exclusion criteria included presence of hypertension, diabetes, glaucoma, >2+ cataract, refractive error >±6D, trauma, and ocular pathology. VD and vessel skeletonized density (VSD) were calculated in the superficial (SCP), deep capillary plexuses (DCP), and whole retina, as well as foveal avascular zone (FAZ) perimeter, area, and circularity (Macular Density Algorithm v0.7.3). Mixed effects linear regression was used.

Results: Subjects had a median age of 54 (11-83) years. 48.3% were male, 72.2% were white, and 8.3% reported Hispanic ethnicity. Median values of OCTA metrics for each scan size are reported (Table). Both VSD and VD decreased significantly with age in most layers and scan types ($p<0.05$). FAZ circularity also declined with age on 3x3mm ($\beta=-0.001$,$p=0.001$) and 6x6mm ($\beta=-0.001$,$p=0.014$) scans. No difference between males and females nor any effect modification with age was observed. No significant differences between white, Black, and Asian patients were observed. Hispanic patients had significantly higher whole retina VSD on 6x6mm ($\beta=0.853$, $p=0.046$) and higher VSD and VD on all 12x12mm layers ($p<0.05$) than non-Hispanic patients. Worse visual acuity was associated with significantly lower VSD and VD ($p<0.05$) and more irregular FAZ in all layers for all scans.

Conclusions: We present the first normative database of OCTA metrics obtained using standardized ARI network algorithms. This represents an uncommonly large sample of control eyes and includes broad vascular metrics as well as scans ranging from 3x3 to 12x12mm. Our results provide a valuable reference for past and future studies using this device.

CONTROL ID: 3712739

SUBMITTER (NAME ONLY): Kristen Nwanyanwu

TITLE: Development of a risk stratification nomogram for the prediction of high-risk diabetic retinopathy

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.H. Nwanyanwu, J. Andoh, Ophthalmology and Visual Science, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|E. Chen, University of California San Francisco, San Francisco, California, UNITED STATES|Y. Xu, Y. Deng, Yale School of Public Health, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop and validate a risk calculator to identify individuals at high-risk for diabetic retinopathy (DR).

Methods: This study includes patients with diabetes from an urban, academic ophthalmology center. Patient demographic characteristics were generated using descriptive statistics. Univariable and multivariable cox proportional hazard model identified risk factors of high-risk diabetic retinopathy. Stepwise akaike's information criteria (AIC) was used to select the best multivariable model. Bootstrap estimate of calibration accuracy for 3-year survival probability showed the existence of model overfitting. The model was then validated using 200 bootstrap resamples to obtain the slope shrinkage factor which could be used to update the model to have better survival prediction. Nomogram and R Shiny app were developed to predict 3-year and 5-year survival probabilities. Statistical analyses were performed using R (The R Foundation, Vienna, Austria) and SAS 9.4 (Cary, NC).

Results: A total of 1363 patients (female, 51.7%) were included in this study. The mean age [SD] was 61.2 [13.5]. The mean hemoglobin A1C [SD] was 8.7 [2.5]. The ethnic and racial breakdowns were 42.9% white, 33.1% Black/African American, 27.5% Hispanic/Latino, and 3.65% Asian. Most patients had a current primary care provider (96.4%), primarily spoke English (80.3%), and had public insurance (63.7%). Patients had a history of the following diabetic and chronic health conditions: nephropathy (10.0%), neuropathy (17.8%), nonhealing ulcer (11.2%), dyslipidemia (31.3%), uncomplicated hypertension (47.5%), and complicated hypertension (2.1%). The validated predictive model included having a primary care provider (HR 2.61; Table 1), insurance provider (private [HR 0.90]; uninsured [HR 2.05]), hemoglobin A1C (HR 1.08), dyslipidemia (HR 0.70), uncomplicated hypertension (HR 1.31), and complicated hypertension (HR 1.66; Table 1). A nomogram was developed to predict 3-year and 5-year probability of developing DR (Figure 1).

Conclusions: Using a predictive model, we show that adult patients with diabetes can be stratified according to their risk of DR. Risk stratification methods may help to improve clinical and surgical decision-making for patients with DR.

CONTROL ID: 3712740

SUBMITTER (NAME ONLY): Jason Charng

TITLE: A wavelength-agnostic, deep learning algorithm segmenting the hyperautofluorescent ring in retinitis pigmentosa

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Charng, D.A. Mackey, F.K. Chen, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|J. Charng, Optometry, The University of Western Australia, Western Australia, AUSTRALIA|I. Viedma, D. Alonso-Caneiro, Optometry and Vision Science, Queesnland University of Technology, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Quantification of the hyperautofluorescent ring (HAR) is a key clinical trial outcome measure in retinitis pigmentosa (RP). Segmentation is currently done via traditional programming or manually. We applied a wavelength-agnostic deep learning (DL) algorithm to segment the HAR on fundus AF (FAF) images in RP eyes.

Methods: FAF images in RP patients were acquired using Heidelberg HRA2 in either blue or infrared AF (BAF /IRAF) mode, with a total of 1152 and 1099 images respectively.

For each modality, a fully semantic algorithm (single model) based on a Unet++ architecture with an InceptionV2 encoder was developed and trained with an approximate 50/20/30% data split (training/validation/testing). The same network was then trained using both BAF and IRAF images (dual model) to produce a wavelength-agnostic platform. Model performance was assessed using the Dice similarity coefficient of the AF class, with 1 indicating perfect match to manual delineation. Paired t-test compared the difference in Dice score between the single and dual model.

To test the wavelength-agnostic algorithm, we examined baseline FAF images from one eye (OD, if unavailable then OS) in patients with Usher syndrome. Manual and DL segmentation were performed in all images with HAR, with HAR horizontal extent and area extracted. Bland-Altman evaluated limits of agreement between manual and DL.

Results: For the BAF dataset, comparable mean (standard deviation) Dice coefficient were found in the single 0.952 (0.042) and dual 0.953 (0.048) model (t-test, p=0.14). Single IRAF 0.957 (0.054) and dual 0.959 (0.053) model dice scores were also similar (p=0.24).

In the Usher cohort (n=33), HAR was noted in 21 BAF and 22 IRAF images. In BAF, the mean difference (95% CI) between DL and manual delineation was 0.01 (-0.53 to 0.56) mm and -0.08 (-0.96 to 0.81) mm^2 for horizontal ring extent and area, respectively. In 4 images, poor agreement between DL and manual segmentation was due to low image quality. In IRAF, the mean difference for ring extent was -0.29 (-2.73 to 2.15) mm and -0.89 (-8.59 to 6.81) mm^2 for ring area. Poor agreement was due to low image quality (n=2) or indistinct HAR boundary (n=6).

Conclusions: The wavelength-agnostic DL algorithm was able to segment HAR in AF images, comparable to manual delineation, with manual correction required in a minority of images.

CONTROL ID: 3712741

SUBMITTER (NAME ONLY): Aparna Raghuram

TITLE: Characteristics of symptom reporting on convergence insufficiency symptoms survey (CISS) in adolescent concussion

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Raghuram, E.K. Wiecek, B.G. Jastrzembski, A. Shah, Opthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Raghuram, S. Marusic, E.K. Wiecek, B.G. Jastrzembski, A. Shah, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We aim to understand which CISS items are most frequently reported and if symptom reporting is impacted by age, sex, time since concussion and survey method.

Methods: Retrospective chart review was conducted to identify concussion patients from July 2014 to December 2020 through a multidisciplinary concussion clinic (MDCC) or a direct referral (REF) for evaluation. Patients either self-reported symptoms on the CISS using an iPad (MDCC) or responded verbally to the clinician administered CISS (REF). All individuals met inclusion criteria of < 18 years of age, < 1 year since concussion (sub-acute: 15-120 days, chronic: 121-365 days), 20/30 best-corrected visual acuity, and no ocular disease, strabismus or amblyopia. Age, sex, time since concussion, and CISS scores (15 items: 3 vision-related (CISS-V), 6 somatic (CISS-S), 6 cognitive (CISS-C)) were analyzed. Cronback's analysis was used to assess CISS-subscale inter-item consistency and analysis of covariance (ANCOVA) was used to understand group differences in CISS scores.

Results: Chart review identified 205 eligible patients (mean age 15 years ± 2.1; 141 female, 112 chronic, 105 MDCC). The mean CISS score (n= 205) was 27.80 ± 12.73. The most commonly reported symptoms were headaches (61% of patients reporting often or always), tired eyes (54%), losing concentration (52%), trouble remembering (44%) and uncomfortable eyes (44%). This trend was maintained across sex, time since concussion, and clinic type. Cronback's alpha was 0.70, 0.83, 0.86 for CISS-V, C and S, respectively, indicating excellent inter-item consistency. The highest mean subscale score was for CISS-S (2.05±1.2) followed by CISS-C (1.96±0.98) and CISS-V (1.24±0.98). ANCOVA indicated age was a significant covariate ($p < 0.01$). Higher scores were reported from the MDCC clinic (difference = 7.91; 95% CI: 4.22 – 11.61, $p<0.001$) and from sub-acute than chronic phase of concussion recovery (difference = 4.37; 95% CI: 0.68 – 8.06, $p = 0.02$).

Conclusions: Concussion patients most commonly reported somatic symptoms, such as headaches, tired and uncomfortable eyes. Patients who self-reported symptoms had higher symptoms scores, though symptoms reported were similar to clinician-administered. Clinicians administering the CISS may introduce a positive bias that lowers reported symptom intensity in post-concussion adolescents.

CONTROL ID: 3712742

SUBMITTER (NAME ONLY): Cristy Ku

TITLE: Light-induced retinal degeneration in immunodeficient mice.

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Ku, U. Park, P.A. Sieving, S.S. Park, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure: Cristy Ku: Commercial Relationship: Code N (No Commercial Relationship) | Un Chul Park: Commercial Relationship: Code N (No Commercial Relationship) | Paul Sieving: Commercial Relationship: Code N (No Commercial Relationship) | Susanna Park: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A model of retinal degeneration in immunodeficient mice would allow in vivo evaluation of the long-term effects of allogenic or xenogenic stem cell transplantation without concerns about immune rejection of transplanted cells. The ideal immunodeficient mouse for this purpose is the NOD-SCID (non-obese diabetic, severe combined immunodeficiency) mouse which is homozygous for mutations for the severe combined immune deficiency spontaneous mutation $Prkdc^{scid}$ and has an absence of functional T and B cells, lymphopenia, and hypogammaglobulinemia. This study tested the hypothesis that a nonhereditary model of retinal degeneration can be developed in NOD-SCID mice using light damage.

Methods: NOD-SCID mice (6 to 8 week males) were exposed to uniform white fluorescent light (10,000 lux) in a light box over varying durations: 30 minutes (2 mice), 1 hour (3 mice), and 3 hours (10 mice). Following light damage, ERG testing (LKC Technologies) and OCT imaging (Bioptigen) of the retina was conducted to evaluate the effect of light exposure on retinal function and morphology at 1 and 2 weeks after light exposure. OCT scan area included 1.4 mm temporal, nasal, inferior, and superior from the optic nerve head. At the end of the study, the mice were euthanized and the eyes harvested for histology.

Results: Light induced changes in outer retina with corresponding decrease in retinal function on ERG was observed in all mice exposed to light damage. OCT imaging showed loss of outer nuclear layer and IS/OS junction blurring as early as 1 week after light exposure with significant outer retinal atrophy at 2 weeks. The OCT outer retinal structural changes noted 2 weeks after light exposure did not vary with duration of exposure ranging from 30 minute to 3 hrs. ERG testing showed severe attenuation of rod and cone responses in all light exposed mice when compared to mice not exposed to light. The ERG changes correlated with OCT findings. Histologic evaluation is in progress.

Conclusions: Our preliminary data support the hypothesis that a model of light-induced retinal degeneration can be developed in immunodeficient mice that may be used for future studies in allogenic or xenogenic cell-based therapeutics. Work is in progress to evaluate the long term effects of the light induced retinal changes and to determine whether severity of retinal degeneration can be modulated by titrating light exposure.

CONTROL ID: 3712744

SUBMITTER (NAME ONLY): Rolake Alabi

TITLE: A sublamina-based approach to retinal vessel analysis using OCT angiography in glaucoma and glaucoma suspect eyes

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Alabi, A.W. Kong, L. Della Santina, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|O. Alabi, Neurosurgery, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|M. Jethi, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare macular vessel density across inner plexiform layer (IPL) depths in glaucoma suspects and patients with glaucoma

Methods: This is a retrospective cross-sectional study from a glaucoma clinic at a single center. 6 by 6 mm^2 en face OCT angiography (OCTA) macular images centered on the fovea were collected. 6 to 7 mm thick sections spanning the internal limiting membrane to the IPL/inner nuclear layer (IPL/INL) border (the outer IPL border) were extracted for each eye. A custom-written MATLAB code was used to distinguish small and large vessels in image stacks. Small and large vessel density (VD) were computed for each stack. A linear mixed effects (LME) model was used for statistical analysis. When comparing macular VD within stacks of a specific thickness in suspect versus glaucoma eyes, the LME model included a random effect for each patient (to account for multiple eyes per patient) and a fixed effect for glaucoma. Multivariable models included the potential confounding factors of age, history of hypertension, and/or history of diabetes.

Results: In the study, there were a total of 87 eyes (56 patients) that met criteria for analysis. Analysis using a LME model revealed glaucoma was associated with decreased small vessel density (SVD) starting 25μm above the IPL/INL border (effect size from -1.31 to -0.39, $p=3.6x10^{-4}$ to 0.045 with a peak negative effect size of -1.20 to -1.31 from 31 to 48μm above the IPL/INL border). To account for the contribution of confounders in the study population, a multivariate analysis that also included age, history of hypertension, and history of diabetes was completed. In this analysis, glaucoma was associated with decreased SVD specifically from 31 to 66μm (-1.17 to -0.54, p= 0.002 to 0.03) and from 79 to 96μm (-0.54 to -0.47, $p=9.2x10^{-4}$ to 0.002) above the IPL/INL border. Of the included confounders, only age demonstrated an effect on VD. Compared to glaucoma, the effect size of age on SVD was smaller in magnitude (-0.08 to -0.04 from 0-12μm and 25-30μm).

Conclusions: We quantified small and large vessel density across IPL depths using OCTA. In this analysis, glaucoma patients exhibited decreased SVD in the inner IPL compared to glaucoma suspects. How variable VD across IPL depths may result from or reflect differences in retinal ganglion cell resiliency and/or susceptibility in glaucoma are important questions for future study.

CONTROL ID: 3712745

SUBMITTER (NAME ONLY): Carolina Carvalho Soares Valentim

TITLE: Validation of an OCT-based deep-learning algorithm for the identification of full-thickness idiopathic macular holes (FTIMH)

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Carvalho Soares Valentim, A.K. Wu, W. Song, J.L. Cao, R.P. Singh, K.E. Talcott, Ophthalmology, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|V. Wang, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S. Yu, N. Manivannan, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Automated identification of OCT features can improve retina clinic workflow efficiency as they are able to detect pathological findings. The purpose of this study was to validate an OCT-based deep-learning algorithm for the identification of FTIMH features and stages.

Methods: In this retrospective study, subjects solely diagnosed with either FTIMH or Posterior Vitreous Detachment (PVD) were identified excluding secondary causes of macular holes, any concurrent maculopathy, or incomplete records. OCT scans (512x128) from all subjects were acquired with CIRRUS^{TM} HD-OCT 5000 (ZEISS, Dublin, CA) and reviewed for quality. In order to establish a ground truth classification, each OCT B-scan was labeled by two trained graders (Table 1). A retina specialist acted as a tie-breaker whenever there was a labeling disagreement. The FTIMHs were measured using the caliper tool on CIRRUS Review software and classified in stages according to the International Vitreomacular Traction Study. The accuracy of the algorithm to identify disease features in normal and FTIMH OCT B-scans was determined by dividing the number of B-scans in agreement by the total gradable scans labeled by the algorithm. Pearson's correlation was run to determine if the algorithm's probability score was associated with the stages of FTIMH.

Results: Ninety-nine OCT cube scans from 99 subjects (49 with FTIMH and 50 with PVD) were used. Among the FTIMH scans, 63% (n=31) were stage 4, 10% (n=5) were stage 3 and 27% (n=13) were stage 2. A total of 12,354 individual OCT B-scans were labeled gradable by the algorithm and yielded an accuracy of 90.6% in identifying OCT features of FTIMHs. A Pearson's correlation coefficient of 0.31 was achieved between the algorithm's probability score and the stages of the 49 FTIMHs cubes studied.

Conclusions: The OCT-based deep-learning algorithm was able to accurately detect FTIMHs features on individual OCT B-scans. However, there was a low correlation between the algorithm's output and FTIMH stages. The algorithm may serve as a clinical decision support tool that assists with the identification of FTIMHs. Further training is necessary for the algorithm to identify stages of FTIMHs.

CONTROL ID: 3712748

SUBMITTER (NAME ONLY): Liz Hitch

TITLE: Laminin-111 Expression in Extraocular Muscles of mdx Mice and the Potential Role of PITX2

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.M. Hitch, D. Fraser, L.K. McLoon, Ophthalmology and Visual Neuroscience, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Liz Hitch: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Fraser: Commercial Relationship: Code N (No Commercial Relationship) | Linda McLoon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Extraocular muscles (EOM) are spared in patients with Duchenne muscular dystrophy (DMD), a muscle wasting disease caused by mutations in the dystrophin gene. DMD limb skeletal muscle is highly susceptible to contraction-induced injury, leading to cycles of myofiber degeneration and regeneration. This results in increased extracellular matrix (ECM) deposition and fibrosis, severely impacting myofiber and myogenic precursor cell functions necessary for regeneration. Other labs showed that laminin-111 therapy reduced fibrosis and promoted muscle repair in mouse dystrophic limb muscle. It is expressed during embryological development but absent in adult limb skeletal muscle.

EOM contain a large population of myogenic precursor cells that express either Pax7 or Pitx2. Pitx2 is associated with the maintenance of many EOM-specific characteristics, and in its absence, the EOM begin to resemble limb skeletal muscle. As normal adult EOM express a number of proteins normally down-regulated in adult limb skeletal muscle, we assessed expression levels of laminin-111 in wildtype (WT) EOM and limb muscle and compared its expression to the mdx mouse model of muscular dystrophy and an mdx mouse deficient in Pitx2.

Methods: Immunohistochemistry was used to stain for laminin-111 expression at 3 months and 12 months in EOM and tibialis anterior (TA) muscles taken from WT normal mice, mdx mice, and mdx mice lacking Pitx2 expression.

Results: TA muscles at 3 months showed faint and discontinuous immunostaining for laminin-111. By 12 months in the WT mouse TA, laminin-111 expression was markedly decreased. In the TA from mdx and in mdx/Pitx2 null mice, levels of laminin-111 were extremely low. In the WT EOM, at 3 months there was robust immunostaining, which was maintained at 12 months. In the EOM from the mdx mice at both 3 and 12 months, the expression levels appeared similar to the WT controls. In the mdx/Pitx2 null mice, laminin-111 levels were reduced.

Conclusions: Laminin-111 was differentially expressed in limb muscle compared to EOM, and expression was maintained in the EOM at one year. In the mdx mouse EOM, laminin-111 was retained, but reduced in the EOM from the mdx/Pitx2 null mice. These data suggest that laminin-111 may play a role in EOM sparing in DMD, and that its continued expression at high levels appears to be related to retention of Pitx2 positive cells in the EOM.

CONTROL ID: 3712749

SUBMITTER (NAME ONLY): Chase Paulson

TITLE: Association of Non-Melanoma Skin Cancer with Exfoliation Syndrome in Utah

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Exfoliation syndrome (XFS) is a systemic disorder with ocular manifestations that is associated with irregularity in extracellular matrix deposition and remodeling. Given prior data suggesting an association between non-melanoma skin cancer (NMSC), i.e. basal and squamous cell cancers most often located in areas of sun exposure and XFS, a questionnaire was administered to clinic study patients to evaluate this relationship.

Methods: Participants answered a questionnaire designed to assess lifelong UV exposure, including leisure and occupational sun exposure, whether more likely to tan or burn in early life, eye and hair color, smoking behavior, vitamin D deficiency, skin cancer history, alcohol consumption and caffeine intake. The questionnaire was sent to 151 consented XFS study patients and their family members, recruited from the Moran Eye Center clinics. Of these, 53 patients completed the questionnaire and identified as non-Hispanic and white. Twelve respondents were excluded for: age (under 60y); missing birth date and basic demographic information; and unavailable electronic health records (EPIC system) to confirm absence or presence of XFS and medical history.

Results: Among these 41 eligible survey respondents ages 60y and older 31 had XFS (including 23 patients with chart-confirmed exfoliation glaucoma; XFG) and 10 respondents had no XFS diagnosis. These affected XFS and unaffected individuals did not substantively differ by gender, age, eye/hair color, or lifestyle (smoking, alcohol, caffeine consumption). XFS patients with XFG had a slightly higher frequency of NMSC (30%) compared with those unaffected by XFG (22%), and were more likely to reside at higher elevation (>5500 ft). There was an elevated proportion of XFS in those with highest quartile of sun exposure hours during young adult and adulthood (ages 21-64y) and XFS were somewhat younger at age of first sunburn.

Conclusions: Consistent with prior studies, patients with XFS/XFG appeared more likely to reside at higher elevations. Our limited, descriptive findings suggest that greater UV exposure over the adult life course may be associated with a somewhat higher risk of NMSC in XFS patients who have developed XFG. Identifying differences in UV exposure-related and other non-UV demographic and lifestyle risk factors and the development of NMSC between XFS, XFS with XFG, and unaffected individuals should be pursued in larger population-based studies.

CONTROL ID: 3712750

SUBMITTER (NAME ONLY): Xiaoyi Gao

TITLE: Exome analysis identifies novel genes associated with intraocular pressure in the UK Biobank cohort

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X.R. Gao, M. Chiariglione, A.J. Arch, Ophthalmology and Visual Sciences, Ohio State University, Columbus, Ohio, UNITED STATES|X.R. Gao, Biomedical informatics and human genetics, Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Xiaoyi Gao: Commercial Relationship: Code N (No Commercial Relationship) | Marion Chiariglione: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Arch: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is a major risk factor for glaucoma, the leading cause of irreversible blindness worldwide. IOP is also the only modifiable risk factor for glaucoma. Identifying rare variants that contribute to IOP help uncover the biological mechanisms regulating this trait, provide new therapeutic targets for IOP, and potentially glaucoma.

Methods: We conducted this study using the recent release of 450K whole exomes from the UK Biobank. IOP measurements were obtained using the Optical Response Analyzer (Reichert Corp., Philadelphia, PA). For this study, we used corneal-compensated IOP. The average of the right and left eye IOP measurements was used for downstream analysis. A total of 110,283 study participants who have IOP measurements were included in this analysis. We performed rare-variant analyses to identify the corresponding genes associated with IOP using REGENIE with adjustment for age, sex, and the first 10 principal components of genetic ancestry.

Results: We identified a novel gene, BOD1L1, that was significantly associated with IOP ($P = 5.92 \times 10^{-9}$). BOD1L1 is associated with the use of antiglaucoma preparations and miotics ($P = 3.8 \times 10^{-6}$). Another novel gene associated with IOP was ACAD10 ($P = 1.33 \times 10^{-10}$). ACAD10 is associated with glaucoma ($P = 1.6 \times 10^{-4}$). Further analyses may identify additional rare-variant associations with IOP.

Conclusions: We identified novel genes and rare variants associated with IOP. Our findings provide insights into the genetics of rare variants affecting IOP.

CONTROL ID: 3712752

SUBMITTER (NAME ONLY): Amy Huang

TITLE: Post-operative inflammation outcomes with the use of a sustained-release intracanalicular dexamethasone implant (Dextenza) following routine phacoemulsification

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Huang, M.K. Ertel, C. Ifantides, J.L. Patnaik, L. Seibold, Sue Anschutz-Rodgers Eye Center, Department of Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|M.K. Ertel, C. Ifantides, Department of Ophthalmology, Denver Health Medical Center, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study sought to characterize the need for adjunctive drop therapy with topical steroids or nonsteroidal anti-inflammatory drops (NSAID) in patients who received the Dextenza implant after routine phacoemulsification cataract surgery.

Methods: A retrospective chart review was performed. Patients who received a Dextenza implant after cataract surgery between January 2020 to July 2020 with at least 3 months of follow-up were included. Initiation of steroid or non-steroidal anti-inflammatory drop therapy, reason for therapy, and time of therapy initiation were collected.

Results: A total of 203 eyes were included for analysis with a mean patient age of 71.7 years. 59.1% were female and 87.7% self-identified as Caucasian. Anti-inflammatory drops (steroid, NSAID, or both) were started in 31.2% of eyes (62 eyes, excluding 3 eyes with unknown drop status and 1 eye started on drops after the 3-month follow-up period). Of all included eyes (excluding 9 eyes with unknown drop status), only 21.6% (42 eyes) were started because of persistent corneal edema, inflammation, post-operative pain, or cystoid macular edema. Of the 42 eyes started on drops due to clinical signs or symptoms, the majority of these (64.3%, 27 eyes) were started on topical steroids only. The remaining 35.7% (15 eyes) were started on both topical steroids and NSAIDs. In 72.6% of eyes requiring adjunctive therapy, treatment was started within the first week after surgery. The mean duration of adjunctive drop therapy was 36.6 days.

Conclusions: The majority of eyes that received Dextenza implantation after routine cataract surgery did not require topical anti-inflammatory therapy to control post-operative inflammation. Of those that did, most required the addition of a single drop, usually within the first week after surgery. This demonstrates that the sustained-release intracanalicular dexamethasone implant Dextenza is a viable platform for simplifying post-operative treatment regimens by reducing or eliminating the need for topical therapy after cataract surgery.

CONTROL ID: 3712753

SUBMITTER (NAME ONLY): Linus Amarikwa

TITLE: Teprotumumab-related hearing loss treated with oral corticosteroids

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Amarikwa, T. Lu, A. Kossler, Ophthalmology, Stanford Medicine, Stanford, California, UNITED STATES|C. Dosiou, Endocrinology, Stanford Medicine, Stanford, California, UNITED STATES|B. Winn, Ophthalmology, UCSF Medical Center, San Francisco, California, UNITED STATES|M. Inserra, Ear Associates and Rehabilitation Services Inc, San Jose, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teprotumumab is a novel IGF-1R inhibitor used to treat thyroid eye disease (TED). Hearing loss is a known adverse event, with an incidence of 10% in the clinical trials. However, recent reports suggest that the incidence of otologic symptoms, including hearing loss, may be up to 81%. To date, an effective protocol for managing hearing loss in this setting has not been determined. Here we present the first report of the successful treatment of teprotumumab-related hearing loss with prompt oral prednisone.

Methods: Case report with pre- and post-steroid therapy audiometric data.

Results: A 70-year-old woman with a 1-year history of Graves' disease controlled with methimazole presented with a 6-month history of active, moderate-to-severe TED. Initial treatment with oral steroids was ineffective. Five months later, teprotumumab was initiated due to worsening diplopia and a clinical activity score of 4. Ten days after teprotumumab initiation, the patient reported sudden hearing loss and tinnitus in the right ear. Audiogram demonstrated a mild down-sloping to moderately severe mixed conductive and sensorineural hearing loss with a pure tone average (PTA) of 33 dB HL (the conductive component was minimal and ranged from 10-15 dB). Hearing was normal in the left ear (Figure 1). She had no history of prior hearing problems, ototoxic medication use, exposure to loud noise, or infectious symptoms. Two days after hearing loss onset, she was treated with prednisone 60mg for 6 days with a 1-week gradual taper. Three weeks following steroid therapy a repeat audiogram demonstrated PTA improvement of 20 dB HL in her right ear which brought her to a normal level that was symmetric with her left ear (Figure 2). Word recognition scores improved from 92% at 70dB before steroid therapy to 100% at 55dB post-treatment. After improvement in hearing symptoms, the patient completed the 8-infusion treatment with no further hearing symptoms at 52-week follow-up.

Conclusions: Hearing loss is a concerning adverse event of teprotumumab therapy. Effective management of teprotumumab-related hearing loss should include risk factor assessment, patient education, baseline audiometric testing, early identification of hearing symptoms with repeat audiogram testing. If hearing loss is detected, prompt oral prednisone burst therapy should be considered.

CONTROL ID: 3712754

SUBMITTER (NAME ONLY): Brian Rosario

TITLE: Three-dimensional choroidal surface topography analysis in healthy eyes based on wide-field SS-OCT volume scans

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Rosario, A. Selvam, V. Sant, M.N. Ibrahim, K.K. Vupparaboina, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.A. Sahel, J. Chhablani, Department of Ophthalmology, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|S. Arora, Bahamas Vision Center, New Providence, Nassau, BAHAMAS|S. Arora, Princess Margaret Hospital, New Providence, Nassau, BAHAMAS|

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ABSTRACT BODY:

Purpose: To study the choroidal contour map in healthy eyes and make a qualitative and quantitative assessment of the inner and outer choroidal surface in a 3-dimensional (3D) view.

Methods:

This was a retrospective study based on wide-field swept-source optical coherence tomography (wide-field SS-OCT) volumes taken from 13 healthy subjects. Images were captured using a wide-field SS-OCT device (Carl Zeiss Plex Elite 9000) with a resolution of 12mm×12mm×3mm. Choroidal inner and outer surface in 3D were obtained using our previously validated residual U-Net (ResUnet) deep learning model for choroid segmentation. Qualitative analysis of inner and outer surfaces was performed using a custom built MATLAB based 3D visualization tool. Quantitative analysis was based on maximum principal curvature (Pmax) of the surface. A 4-quadrant grid with a 1mm circle centered around fovea.

Results:

Mean age of 13 healthy subjects was 30.7 ± 5.2 years. Qualitative evaluation of 13 healthy eyes demonstrated the inner surface of choroid (choroid-retinal interface) to be bell shaped in 4 eyes, hump shaped in 3 eyes, crescent shaped in 2 eyes, arc shaped in 2 eyes and cupid's bow shaped in 2 eyes. Outer surface (chorio-scleral interface) was bell shaped in 2 eyes, hump shaped in 6 eyes, crescent shaped in 2 eyes, arc shaped in 1 eye and cupid's bow shaped in 2 eyes. On quantitative evaluation, the mean central P_max at the inner and outer choroidal boundary was -0.23 ±1.27 and 1.09 ±3.63 respectively and were significantly different from each other (p=0.0002). Mean P_max in the superior, inferior and temporal macula were also significantly different between inner and outer choroidal surface (p=0.00003, 0.0004 and 0.003 respectively), while nasal curvatures were almost similar on both surfaces (p=0.011).

Conclusions:

A 3-dimensional view of inner and outer choroidal surface for the choroidal contour mapping is a unique way of evaluating choroid. The inner and outer choroidal contour curvature values are significantly different at the central macula, superiorly, inferiorly and at the temporal macula. Normative database for different age groups is being established and more data will be presented at the conference.

CONTROL ID: 3712755

SUBMITTER (NAME ONLY): Hendrik Scholl

TITLE: ALK-001 (C20-D3-Vitamin A) slows the growth of atrophic lesions in ABCA4-related Stargardt Disease: Results of a Phase 2 placebo-controlled clinical trial (TEASE study)

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|H.P. Scholl, Dept. of Ophthalmology, Universitat Basel Medizinische Fakultat, Basel, Basel-Stadt, SWITZERLAND|G. DeBartolomeo, L. Saad, Alkeus Pharmaceuticals, Massachusetts, UNITED STATES|I. Washington, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Hendrik Scholl: Commercial Relationship(s);Code C (Consultant/Contractor):Apellis Switzerland GmbH; Astellas Pharma Global Development, Inc./Astellas Institute for Regenerative Medicine; Belite Bio; Biogen MA Inc.; Boehringer Ingelheim Pharma GmbH & Co; Gerson Lehrman Group; Guidepoint Global, LLC; Gyroscope Therapeutics Ltd.; Janssen Research & Development, LLC (Johnson & Johnson); Novo Nordisk; ReNeuron Group Plc/Ora Inc.; Pharma Research & Early Development (pRED) of F. Hoffmann-La Roche Ltd; ReVision Therapeutics, Inc.; Stargazer Pharmaceuticals, Inc.; Tenpoint Therapeutics Ltd; Third Rock Ventures, LLC. ;Code F (Financial Support):Kinarus AG; Okuvision GmbH; Novartis Pharma AG | Gabrielle DeBartolomeo: Commercial Relationship(s);Code E (Employment):Alkeus Pharmaceuticals | Ilyas Washington: Commercial Relationship(s);Code P (Patent):Columbia University;Code C (Consultant/Contractor):Alkeus Pharmaceuticals | Leonide Saad: Commercial Relationship(s);Code E (Employment):Alkeus Pharmaceuticals

ABSTRACT BODY:

Purpose: To study the effects of ALK-001 on the progression of Stargardt Disease (STGD1). STGD1 is the most prevalent inherited macular dystrophy and results from defects in the ABCA4 gene that cause accelerated formation of vitamin A dimers in the retina. No treatment exists.

Methods: The TEASE study is a multicenter two-year Phase 2 double-masked, randomized, placebo-controlled clinical trial that randomized 50 patients with STGD1 and a well-delineated area of RPE atrophy. The investigational drug ALK-001 is a selectively deuterated vitamin A used as vitamin A replacement and taken orally once-a-day. Deuterium slows vitamin A dimer formation 4-5 fold without inhibiting the visual cycle. Patients were randomized 2:1 ALK-001:placebo during the first year, with 50% of placebo randomly crossed over to ALK-001 for the second year of treatment. The prespecified primary efficacy outcome measure is the rate of growth of the square root of atrophic lesions, as measured on short wavelength fundus autofluorescence imaging, and evaluated using a linear mixed model. The study was performed at 7 centers in the USA. 50 patients (38 white; 28 female) were randomized. Median age was 46 years (range, 18-60) and disease duration 9 years (0-36). Atrophic lesions were bilateral in 74% of cases with a ~5 mm^2 median area.

Results: The growth rate of the square root of atrophic lesions in the ALK-001 treated group was 21% slower than in the untreated arm ($p<0.001$). When using untransformed areas, the growth rate was 28% slower in the ALK-001 arm than the untreated arm. There were no clinically-significant changes in BCVA in either treated and untreated arms after 2 years as expected in this patient population. On average, ~90% of vitamin A was replaced with deuterated vitamin A, which was maintained over time. ALK-001 was well-tolerated with no unexpected adverse reactions, no report of night blindness or impaired dark adaptation, and no clinically-significant increases in liver enzymes.

Conclusions: These data represent the first time that a therapeutic intervention slows the progression of STGD1 in a clinically and statistically meaningful way. In addition, the data provides clinical evidence that vitamin A dimers contribute to the pathophysiology of STGD1, and that slowing vitamin A dimerization is beneficial even in advanced stages of STGD1.

CONTROL ID: 3712756

SUBMITTER (NAME ONLY): Matthew Kigin

TITLE: DMEK injectors with narrower lumen diameters may not directly correlate with increased endothelial cell loss

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kigin, C. Sales, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|M. Kigin, C. Sales, G. Schmidt, Iowa Lions Eye Bank, Iowa City, Iowa, UNITED STATES|S. Vigmostad, Roy J. Carver Department of Biomedical Engineering, University of Iowa College of Enginnering, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The relationship between endothelial cell loss (ECL) and DMEK injector lumen diameter remains poorly defined. We hypothesized that the LEITR glass injector, which has a narrower distal lumen compared to the Straiko glass injector, would be associated with increased ECL due to the DMEK scroll touching the walls of the narrower lumen. We further hypothesized that loading DMEK tissue into the LEITR injector through its proximal lumen, which is wider in diameter than its distal lumen, would reduce ECL compared to loading DMEK tissue through the proximal lumen.

Methods: A clinically significant difference in ECL was defined as ≥ 10%; for an alpha of 0.05, power of 0.9, and two-tailed tests, we designed the study to have 6 replicates for each comparison (LEITR vs. Straiko; LEITR narrow-lumen-loading vs. LEITR wide-lumen-loading). Surgical-grade mated corneal donor pairs were randomized to each group, prepared for DMEK by a trained technician, loaded into the injectors, expelled and flat-mounted, stained with Calcein-AM, and assessed for ECL using an inverted microscope and Fiji-ImageJ.

Results: We found no significant difference in ECL between the narrower LEITR injector and the Straiko injector (ECL $\Delta = 6.842\% \pm 5.61$, $p>0.05$). We did not observe a significant difference in ECL between DMEK tissues that were loaded through the LEITR injector's narrower distal lumen and tissues that were loaded through its wider proximal lumen (ECL $\Delta = 7.876\% \pm 5.38$, $p>0.05$). No consistent pattern of cell damage was observed between any of the groups, either.

Conclusions: Data from this modest sample of paired corneas suggest that narrower injector lumens may not directly correlate with increased ECL. This observation contradicts prior observations of incision size and ECL in DSAEK, a procedure that mechanically delivers the allograft into the eye rather than injects it with fluid. We hypothesize that DMEK tissue may behave as a deformable solid in a pipe and may thus be relatively insulated from the lumen walls by the no-slip condition described in Poisseuille parabolic flow. Further study is needed to test this hypothesis, which if true, would suggest that flow patterns and velocity may be more related to ECL than lumen diameter.

CONTROL ID: 3712757

SUBMITTER (NAME ONLY): HASSAN ESFANDIARIJAHROMI

TITLE: Optical Characterisation of Myopia Control Ophthalmic Lenses

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. ESFANDIARIJAHROMI, A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|A. Ho, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|A. BACK, Vision CRC USA, California, UNITED STATES|

Commercial Relationships Disclosure: HASSAN ESFANDIARIJAHROMI: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Ho: Commercial Relationship: Code N (No Commercial Relationship) | ARTHUR BACK: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Myopic defocus is considered a primary driver controlling myopia progression. Commercially available myopia control (MC) lenses incorporate positive powered lenslets in the treatment area and, through geometrical-based assumptions, are believed to produce a Net Myopic Defocus (NMD) at the retina. Utilising computer-based models and bench measurements we aim to verify the net focusing effect produced by several MC lenses.

Methods: Three MC lenses (Essilor Stellest™ and Hoya MiYOSMART™ spectacles, and Coopervision MiSight™ contact lenses) with comparable proportions of geometrically determined treatment areas were analysed. Designs were optically simulated in Zemax (-1.0 D). Simulations were converted to a power map with an aperture of 30 mm for spectacle lenses and 5 mm for the contact lens. Power map data was analysed using Matlab software to characterise the power across the apertures of lenses but excluding the central optical zones for the spectacle lenses. The average power of a sample of individual treatment regions were measured using the NIMO wavefront power profiler (Lambda-X, Nivelles). Hyperopic powers were subtracted from myopic powers for the calculation of NMD. The MTF was measured on an anatomically correct physical model eye (on-axis for the contact lens and off axis through the treatment region for spectacles) over a range of object vergences (-2.0 D to +5.0 D in 0.1 D steps) using a 5 mm pupil. The results were compared with the corresponding simulation to verify validity.

Results: The MTF confirmed good agreement between simulation and metrology (Figure 1). The MiSight lens showed a high NMD percentage for each analysis method (Table 1). However, both spectacles showed about equal distribution between myopic and hyperopic defocus in the optical analysis which differed substantially from the geometrical analysis of NMD where each treatment element is assumed to introduce only myopic focal points.

Conclusions: The distribution of defocus found with computer modelling and bench measurements were different to conventional geometrical based assumptions in the spectacle lenses studied. The NMD is substantially less than previously understood and the presence of hyperopic defocus was similar to myopic defocus in these spectacle designs. Animal and clinical trials using myopia control lenses incorporating myopic defocus and basing hypotheses on a geometrical rather than optical NMD may need to be re-evaluated.

CONTROL ID: 3712759

SUBMITTER (NAME ONLY): Phuc Nguyen

TITLE: In Vivo Tracking of Transplanted Progenitor Cells after Photocoagulation Using Multimodal Photoacoustic Microscopy, OCT, and Fluorescence Imaging

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Nguyen, Y. Liu, W. Zhang, J. Henry, X. Wang, Y. Paulus, University of Michigan, Ann Arbor, Michigan, UNITED STATES|W. Qian, B. Liu, IMRA America Inc., Ann Arbor, MI 48105, USA, Michigan, UNITED STATES|W. Fan, T. Zhu, S. Yuan, The First Affiliated Hospital of Nanjing Medical University, CHINA|

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ABSTRACT BODY:

Purpose: Stem cell therapy offers a great promise for retinal degenerations which have no current effective treatments, including age-related macular degeneration and retinal pigmentosa. To achieve optimized treatment outcome, it is important to utilize non-invasive imaging technology to track the behaviors of stem cells after transplantation. This study describes a multimodal photoacoustic microscopy (PAM), optical coherence tomography (OCT), and fluorescence imaging for noninvasive and real-time monitoring of stem cells delivered into the subretinal space and follows their biodistribution, survival, migration, and differentiation longitudinally for up to 3 months.

Methods: A precursor human retinal pigment epithelial cell (ARPE-19) were labeled with ultrapure chain-like clusters gold nanoparticle (CGNP) conjugated with indocyanine green and RGD peptide at 100 μg/mL for 24 h. PAM images were acquired at 578 nm and 650 nm were overlaid on the same image plane and on the OCT image. Rabbits were treated with retinal laser photocoagulation to induce RPE injury and received subretinal injection of 30 μL (10^6 cells/ μL) labeled cells into the subretinal space and monitored before and at 1, 3, 7, 14, 21, 28 days, 2 and 3 months after transplantation. All animal studies were approved by the UM IACUC.

Results: PAM images obtained at 578 nm show hemoglobin in retinal vasculature with high contrast. PAM images acquired at 650 show the distribution of ARPE-19 cells in the subretinal space due to strong absorption of the internalized CGNPs inside the cells and minimal absorption of hemoglobin at 650nm. ICG fluorescence imaging correlated well with the 650nm PAM images initially but rapidly lost fluorescent signal after only 1 week. The transplanted cells localized to areas of photocoagulation injury by day 7 post-injection. Subretinal injection of labeled ARPE-19 cells enhanced fluorescent intensity by 39-fold post-injection, PA signal by 30-fold post-injection, and OCT intensity by 180% post-injection. Immunofluorescentanalysis indicated that ARPE-19 cells were effectively localized to areas of damage corresponding to multimodal in vivo imaging.

Conclusions: This study represents an advanced technique for long-term tracking of the transplanted cells using multimodal PAM, OCT, and fluorescence imaging with the assistance of CGNP.

CONTROL ID: 3712760

SUBMITTER (NAME ONLY): Tala Al-Khaled

TITLE: The influence of ultra-wide field fluorescein angiography on the diagnosis and management of diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To study the influence of ultra-wide field (UWF) fluorescein angiography (FA) on the diagnosis and management of diabetic retinopathy (DR) when presented in addition to UWF color fundus and red free (CF/RF) images.

Methods: This cohort study was an online survey completed by experts who were asked to diagnose and manage DR cases based on different imaging modalities provided. Ten DR experts participated in the online survey. Experts independently reviewed 20 DR cases on a secure website and provided a diagnosis and management plan for each case, first based on UWF CF/RF images alone and again with the UWF CF/RF images and a corresponding UWF FA. Experts were also polled on their diagnostic confidence, their use of FA in clinical practice, and their opinions on the value of UWF FA in the cases presented. Primary outcomes included diagnostic sensitivity and specificity with and without the UWF FA based on the reference standard diagnosis. Secondary outcomes included intergrader agreement, expert confidence, management outcomes, and an analysis of experts' opinions on the clinical utility of UWF FA.

Results: Diagnostic sensitivity (95%CI) increased from 36% (29-43%) to 69% (62-75%, $p<0.05$) with the UWF FA. Intergrader agreement (Fleiss kappa statistic 0.29 [CI 0.21-0.27] vs. 0.44 [CI 0.40-0.47], $p<0.05$) and expert confidence (38% vs. 65%) also improved. Management changed from observation to treatment in 39% of responses. While 40% of experts did not request an FA when presented with UWF CF/RF images alone, 80% found the UWF FA

clinically useful when it was provided.

Conclusions: Diagnosis, treatment, and experts' opinions on the utility of FA all changed when a corresponding UWF FA was available. Incorporating UWF FA into clinical practice may improve DR grading accuracy, intergrader agreement, and expert confidence compared to diagnosis with UWF CF/RF images alone.

CONTROL ID: 3712761

SUBMITTER (NAME ONLY): Jacque Duncan

TITLE: Static perimetry over 2 years in the RUSH2A study: annual rates of change from mixed effects modeling

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.L. Duncan, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Jacque Duncan: Commercial Relationship(s);Code C (Consultant/Contractor):AGTC, DTx Therapeutics, Editas, Eyevensys, Gyroscope, Helios, Nacuity, Spark Therapeutics, SparingVision, ProQR Therapeutics, PYC Therapeutics, Vedere Bio II;Code F (Financial Support):Acucela, Allergan/Abbvie, Second Sight Medical Products, Biogen/Nightstarx Therapeutics, Neurotech USA;Code I (Personal Financial Interest):RxSight, Inc.

ABSTRACT BODY:

Purpose: Static perimetry (SP) provides quantitative measures of peripheral visual field in patients with inherited retinal degenerations (IRDs). There are few available estimates for rates of change in IRDs. Here we provide estimates of change over 2 years in 4 summary measures of SP from the Rate of Progression in USH2A-related Retinal Degeneration (RUSH2A) study using mixed effects models.

Methods: Participants with visual acuity ≥ 20/80, stable fixation, and kinetic visual field of ≥ 10° at baseline in the study eye had full-field static perimetry at baseline, 1, and 2 years. Summary measures were total hill of vision (V_{TOT}), hill of vision in the central 30° (V_{30}), V_{TOT}-V_{30} (V_{periph}), and mean sensitivity. Mixed effects models were used to estimate the annual rates of change and percentage rates of change using log transformed data with 95% confidence intervals. Models were applied to all eyes (N=102) and to a restricted group of eyes with baseline V_{TOT} > 5 dB-sr (N=88) to mitigate floor effects. A model excluding unreliable test results (false positives ≥ 15%) and a model down-weighting outlier rates of change were also applied to the restricted group.

Results: The average decline in V_{TOT} was 2.05 dB-sr/year (Table 1) or 8.3%/year (Table 2) in the entire cohort, but greater at 2.25 dB-sr/year or 8.8%/year in the restricted cohort. The average decline of V_{30} was 0.48 dB-sr/year or 5.2%/year in the entire cohort versus 0.56 dB-sr/year or 5.9%/year in the restricted cohort. The decline of peripheral visual field (V_{periph}) was 1.53 dB-sr/year or 16.0%/year in the entire cohort, and 1.68 dB-sr/year or 13.6%/year in the restricted cohort. The decline rate for mean sensitivity was 0.55 dB/year or 5.1%/year in the entire cohort and 0.60 dB/year or 5.4%/year in the restricted cohort. Excluding unreliable observations or down-weighting outliers reduced the estimated percentage of decline compared to using all eyes in the restricted cohort.

Conclusions: Estimates of the annual rates of decline of static perimetry measures were greater when the study cohort was restricted to eyes with room for worsening. The annual percentage change was greatest in V_{periph} after 2 years in eyes with USH2A-related retinal degeneration.

CONTROL ID: 3712762

SUBMITTER (NAME ONLY): Robert Hyde

TITLE: Adapting background illuminance modulates visual thresholds in patients with retinitis pigmentosa throughout the macula

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Hyde, J.C. Park, J. McAnany, Illinois Eye & Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Robert Hyde: Commercial Relationship: Code N (No Commercial Relationship) | Jason Park: Commercial Relationship: Code N (No Commercial Relationship) | J Jason McAnany: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To quantify patterns of threshold elevation under different light adaptation conditions throughout the macula in patients with retinitis pigmentosa (RP).

Methods: Nine subjects with RP (24 to 59 years old) and 10 visually-normal individuals (18 to 49 years old) participated. Threshold was measured at 7 locations along the horizontal meridian of the visual field (10^{o} nasal to 10^{o} temporal) using Goldmann size III targets. The field locations were grouped into three regions based on eccentricity from fixation: perifoveal (5^{o}-10^{o}), parafoveal (2^{o}) and foveal. Threshold was measured under DA conditions using long-wavelength stimuli and across a broad range of adaptation levels (DA to 50 cd/m^{2}) using short-wavelength stimuli. The relationship between threshold and adaptation level across the field was described using a standard "threshold-vs-illuminance" (TvI) model to derive absolute threshold (T_o), slope (n), and eigengrau (A_o). Repeated measures analysis of variance (ANOVA) was used to compare the three fit parameters between the two subject groups.

Results: Under DA conditions, thresholds for the short- and long-wavelength stimuli were similar throughout the visual field for 8 of 9 subjects, consistent with the cone pathway mediating threshold at all locations. Threshold elevation was greater for the RP subjects under DA and low adaptation conditions, compared to LA conditions. ANOVA indicated significantly elevated T_o and A_o for the RP subjects for each field location. The value of n was approximately independent of field location for the RP subjects and increased with eccentricity for the controls. This pattern resulted in significantly increased n in the fovea and significantly decreased n in the perifovea (both $p < 0.05$), with no significant difference in the parafovea ($p = 0.17$).

Conclusions: The approximately similar elevations in T_o and A_o for the RP subjects suggests that reduced quantal absorption may underlie threshold elevation throughout the macula in this cohort of RP subjects. Alternatively, the results may be attributed to the lack of rod function in these RP subjects, which would elevate DA threshold more than LA threshold.

CONTROL ID: 3712763

SUBMITTER (NAME ONLY): Destiny Hsu

TITLE: Choroidal tumor imaging using polarization diversity-optical coherence tomography (PD-OCT) with adaptive kernel degree of polarization uniformity (DOPU) processing

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hsu, M.V. Sarunic, School of Engineering Science, Simon Fraser University, Burnaby, British Columbia, CANADA|Y. Miao, T. Weaver, K. Paton, Z. Mammo, M. Ju, The University of British Columbia Department of Ophthalmology & Visual Sciences, Vancouver, British Columbia, CANADA|J. Song, J. Johnson, M. Ju, The University of British Columbia School of Biomedical Engineering, Vancouver, British Columbia, CANADA|M.V. Sarunic, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Our research focuses on investigating the utility of PD-OCT for imaging choroidal tumors in human eyes acquired in a clinical setting. Adaptive kernel-based DOPU images of lesions are compared to standard multimodal imaging techniques, including fundus photography, structural OCT, and fundus autofluorescence (FAF).

Methods: We used a custom-built swept-source OCT system for simultaneous detection of two orthogonal polarization signals over a >35° field-of-view (FOV). The melanin structures were segmented by measuring the polarization signal randomness with a novel adaptive kernel. The variability of this melanin specific measurement was assessed both longitudinally and across different demographics for healthy control subjects (N=10) to validate its quantitative measurement ability. In a clinic, two different types of patients, flat choroidal nevi (N=1) and elevated choroidal nevus (N=3) were imaged, and the DOPU contrast results were compared against standard imaging modalities for use in diagnosis and monitoring of pathology. The study received institutional ethics approval for human imaging.

Results: Selective identification of melanin using PD-OCT allowed accurate characterization of tumor dimensions and location within the choroid as shown in Figure 1. Fig. 1(a) shows overall morphological contrast, with the tumor visualized in (b)-(c) with DOPU contrast. Higher melanin concentration (red) signifies lesion presence against choroidal vasculature (blue). Blurring is seen in (b), whereas the adaptive kernel improves uniformity, and boundary and concentration estimates in (c).

Fig. 2(a) shows a healthy volunteer with uniform DOPU and clearly defined choroidal vasculature. Fig. 2(b) shows a flat nevus, highlighted in DOPU contrast by its melanin content in both en face and B-scan images, with a consistent RPE melanin signal. Fig. 2(c) shows a suspicious elevated nevus with associated subretinal fluid. Of note, there is RPE melanin signal loss in the B-scan.

Conclusions: Our proposed adaptive kernel-based DOPU process increases specificity and sensitivity of melanin molecule detection, with potential for improving choroidal tumor characterization, evaluation and follow-up over time.

CONTROL ID: 3712764

SUBMITTER (NAME ONLY): Xi-Qin Ding

TITLE: Inhibition of Ryanodine Receptor 1 Reduces Endoplasmic Reticulum (ER) Stress and Promotes ER Protein Degradation in Cyclic Nucleotide-gated Channel Deficiency

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Ding, F. Yang, H. Ma, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|R. Garg, A.S. Lewin, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cone photoreceptor cyclic nucleotide-gated (CNG) channel plays a pivotal role in cone phototransduction. Mutations in genes encoding the channel subunits CNGA3 and CNGB3 account for about 80% of all cases of achromatopsia and are associated with progressive cone dystrophies. CNG channel deficiency leads to cellular/endoplasmic reticulum (ER) calcium dysregulation and ER stress-associated cone apoptosis. This work investigated the role of the ER calcium channel ryanodine receptor 1 (Ryr1) in ER stress and cone degeneration in CNG channel deficiency.

Methods: The $Nrl^{-/-}$ and $Cnga3^{-/-}/Nrl^{-/-}$ mouse lines were used. The AAV-mediated CRISPR/SaCas9 genome editing was used to knockdown Ryr1 specifically in cones. Mice at postnatal day 5 (P5) received AAV2/5-SaCas9/gRNA-Ryr1 via subretinal injection ($4.4x10^9$ vg, 1.0 µl), and were analyzed for expression levels of Ryr1, cone specific proteins, ER stress markers, and ER retrotranslocation/ER-associated protein degradation (ERAD) proteins at P45-50 days, using western blotting and immunofluorescence labeling.

Results: The expression level of Ryr1 was increased in $Cnga3^{-/-}/Nrl^{-/-}$ retinas, compared with that in $Nrl^{-/-}$ controls. Treatment with AAV2/5-SaCas9/gRNA-Ryr1 nearly completely abolished this elevation. The expression level of cone arrestin (CAR) was reduced in $Cnga3^{-/-}/Nrl^{-/-}$ retinas, and treatment with the viral vector increased expression level of CAR by about 50%, compared with the vehicle-treated controls. The expression levels of the ER stress marker phospho-IRE1α and phospho-eIF2α were significantly elevated in retinas of $Cnga3^{-/-}/Nrl^{-/-}$ mice, and treatment with AAV2/5-SaCas9/gRNA-Ryr1 reversed these elevations. Furthermore, treatment with AAV2/5-SaCas9/gRNA-Ryr1 significantly increased expression levels of the ER retrotranslocation/ERAD protein E3 ubiquitin-protein ligase synoviolin 1 and degradation in ER protein 1 in $Cnga3^{-/-}/Nrl^{-/-}$ retinas, compared with the vehicle-treated controls.

Conclusions: This work demonstrates that Ryr1/ER calcium dysregulation contributes to ER stress/cone degeneration in CNG channel deficiency. The findings support strategies targeting ER calcium regulation to reduce cone degeneration.

CONTROL ID: 3712765

SUBMITTER (NAME ONLY): Langis Michaud

TITLE: Influence of pupil and reading distance on aberrations induced by multifocal soft lenses in young myopic adults

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Michaud, R. Marcotte-Collard, M. Malinowska, Optometry, Universite de Montreal, Montreal, Quebec, CANADA|

Commercial Relationships Disclosure: Langis Michaud: Commercial Relationship(s);Code F (Financial Support):Cooper VIsion ;Code C (Consultant/Contractor):VTI TEchnologies | Rémy Marcotte-Collard: Commercial Relationship: Code N (No Commercial Relationship) | Maja Malinowska: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare HOAs (total, spherical and coma) induced by 3 different soft multifocal lenses (SMFL) at different distances and to determine for each distance the relationship between the pupil diameter and HOAs vs lenses used.

Methods: Myopic young adults were randomly fitted with 3 types of SMFL (L1- Etafilcon A ; L2- Omafilcon A ; L3- Comfilcon A) . A 30 minutes break is observed between each test. Total HOAs, spherical aberrations (SA) and coma (C) are evaluated (OPD Scan, Nidek) without lenses, and while wearing each lens. Measurements are taken in distance vision, at 50 ,33 and 20 cm . The measurement of the pupil in dynamics was carried out with an open field refractor (Grand Seiko, Wam 5500) in photopic condition.

Statistical anlaysis was done by performing a two-factor within-subjects (3x4) repeated measures Anova. A post-hoc test is performed when significant differences are found. A Pearson correlation is established between aberrations, pupillary diameter, at each distance.

Results: The clinical population consisted of 9 M/18 F, aged 25.1 ± 1.6 years; being -2.75 ± 0.5 D. There is a significant increase in total HOAs with SMFL vs. naked eye . Every lens shows a reduction in HOAs with shorter reading distance.($F(2,54)=15.6$; $p < 0.01$; $\omega^2 = 0.151$) L3 demonstrates lower levels vs L1 and L2, statistically similar . There is a significant difference in total HOAs between all distances, except between 50 and 33 cm ($F(1,5 ;42,3)=30,4$; $p < 0.01$; $\omega^2 = 0,072$.) HOAs correlate strongly with pupil diameter ($r2 = 0.44$, $p <0.001$), for all lenses. SA seems to vary vs lens type. L3 generates less SA than L1 and L2, but this is not statistically significant. ($F(1.5; 41.6)= 3.0$; $p = 0.07$). SA is significantly reduced for all distances except between 50 and 33 cm (AS: $F(1.9; 49.3)=24.6$; $p < 0.01$; $\omega2 = 0.04$.) For C, the lens influences the results ($F(1,6 ;43,8)=8,7$; $p < 0.01$; $\omega2 = 0,13$.) L2 has lower levels than L1 and L3, the latter two being statistically similar.

Conclusions: Lens design and reading distance influence the levels of aberrations induced in the eye. In terms of design, the relationship of the add area vs. the pupil seems to be more important than the add power itself. For distance, it seems that reading at 20 cm reduces aberrations considerably. These results may influence how soft multifocal lenses are designed and used in a young adult myopic population.

CONTROL ID: 3712766

SUBMITTER (NAME ONLY): Alexander Robin

TITLE:

Corneal Hysteresis and Obstructive Sleep Apnea Syndrome

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Robin, V. Barquet, E. Sarmiento, M. Giovingo, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|D. Patel, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose:

To investigate the association between corneal hysteresis (CH) and obstructive sleep apnea (OSA) with regards severity of OSA based on apnea hypoxia index (AHI) and decibels of snoring.

Methods:

This is a cross-sectional observational study. We recruited patients who underwent sleep studies at Cook County Health. Each subject that agreed to participate underwent CH measurements using the Ocular Response Analyzer (ORA), Optical Coherence Tomography of the retinal nerve fiber layer (OCT RNFL), central corneal thickness measurements (CCT) measurements. Results of sleep studies were analyzed for AHI and mean decibels of snoring. ORA measurements were performed on each eye three times and results with a wave-front score <5.5 were excluded. Demographic information including age, gender, and race was collected. Patients were grouped by severity of OSAS as either normal/mild or moderate/severe. Data was analyzed with an ANOVA analysis for all factors recorded.

Results:

A total of 14 eyes have been analyzed, 8 eyes from patients with no or mild OSAS and 6 eyes from patients with moderate or severe OSAS. Patients in the none/mild OSAS group had an average CH of 10.8, patients in the moderate/severe OSAS group had an average CH of 9.1 (p=0.06). Patients were also analyzed to assess for a relationship between CH and decibles of snoring and showed a trend toward a negative correlation between increasing CH and decreasing decibles of snoring (p=0.08). There was no significant difference between groups in regards to average IOP (none/mild OSAS, moderate/severe OSAS: 17.1,17.2, p=0.95) or CCT (547, 522, p=0.14)

Conclusions:

CH had a negative correlation with the severity of OSA, as well as a negative correlation with decibels of snoring. This is potentially attributable to the previously identified upregulation of matrix metalloprotease expression in tissue of patients with OSA and the increased risk of glaucoma in patients with OSA, both of which are associated with lower CH. Another mechanism hypoxia

CONTROL ID: 3712767

SUBMITTER (NAME ONLY): Lingling Huang

TITLE: Automated Detection of Posterior Vitreous Detachment on Optical Coherence Tomography Images Using Computer Vision and Deep Learning Algorithms

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Huang, A. Li, J. Arnett, S. Baxter, D. Bartsch, D. Kuo, B. Radha Saseendrakumar, E. Nudleman, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|M. Feng, Z. Wang, J. Guo, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recognizing a posterior vitreous detachment (PVD) is important for pre-surgical planning and risk-stratification for retinal tears and detachment. Deep learning (DL) methods of optical coherence tomography (OCT) images have been trialed on several retinal diseases to assist diagnosis; however, reliable models capable of detecting PVD have not been established. Our studies aim to develop reliable computer algorithms for automated detection of PVD on OCT images.

Methods: Consecutive OCT volumetric scans of 800 eyes obtained with Heidelberg Spectralis from November 2020 to October 2021 were retrospectively reviewed. Eyes with poor image quality or history of pars plana vitrectomy were excluded. Four trained graders individually labeled the PVD status of each eye by reviewing the entire volume B-scans, in addition to the horizontal and vertical raster scans. A second review was performed by an expert grader if consensus review was needed.

Two computer algorithms were developed. A customized computer vision algorithm based on image filtering and edge detection was designed to localize the posterior hyaloid and identify the presence or absence of a complete PVD in OCT volume scan. A second DL image classification model based on ResNet-50 architecture was trained to detect PVD status on OCT.

Results: Both the customized algorithm and DL model detection results were largely in agreement with the PVD status labeled by trained graders, with the customized algorithm surpassing the DL model in F1-scores for per-volume PVD detection. The accuracy of the customized algorithm and DL model was 85.57%, and 76.90%, respectively. The sensitivity of the customized algorithm and DL model was 78.21% and 86.09%, while the specificity was 93.62% and 70.45%, respectively (Table 1).

Conclusions: Using both traditional computer vision and deep learning approaches, we successfully developed reliable models to recognize PVD status on OCT images, demonstrating the potential for automated image classification to detect vitreoretinal pathologies and assist with pre-surgical planning. Further optimization of the two algorithms are currently in process with plans for validation using a prospective, independent data set.

CONTROL ID: 3712769

SUBMITTER (NAME ONLY): Niroj Sahoo

TITLE: Longitudinal structural and functional changes in Central Serous Chorioretinopathy: A ten-year multimodal imaging-based study

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.K. Sahoo, Retina and vitreous, LV Prasad Eye Institute Kode Venkatadri Chowdary Campus, Vijayawada, Andhra Pradesh, INDIA|J. Ong, A. Selvam, J. Chhablani, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|D. Maltsev, military medical academy, RUSSIAN FEDERATION|R. Venkatesh, Narayana Nethralaya, Bangalore, Karnataka, INDIA|N. Reddy, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S. Madan, Giridhar Eye Institute, Kochi, Kerala, INDIA|L. Lima, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|V. Pramil, N.K. Waheed, New England Eye Center, Boston, Massachusetts, UNITED STATES|D. Giridhar, Giridhar Eye Institute, Kochi, Kerala, INDIA|G. Ledesma-Gil, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|E. Borrelli, Universita Vita Salute San Raffaele, Milano, Lombardia, ITALY|R. Sacconi, G. QUERQUES, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: To analyze the longitudinal changes in functional and imaging parameters in eyes with acute or chronic central serous chorioretinopathy (CSCR) over a minimum of 10 years.

Methods: This was a retrospective, multicentric, longitudinal, observational study in patients with a diagnosis of unilateral or bilateral CSCR. Trend in best-corrected visual acuity (BCVA), choroidal thickness (CT), area of double-layer sign (DLS), area of retinal pigment epithelium (RPE) alterations, and area of hyper-autofluorescence were analyzed.

Results: A total of 23 eyes of 16 patients (10 males and 6 females) were included in the study. The mean duration of symptoms prior to presentation was 20.6±50.6 months.

A slow worsening was seen in the chronic CSCR group, while it was relatively stable in the acute CSCR group (baseline 0.11±0.19 logMAR to final 0.08±0.13 logMAR in acute and baseline 0.31±0.47 to final 0.38±0.48 logMAR in chronic CSCR eyes). The trend in CT was more or less stable with a mild decrease in both acute and chronic CSCR groups over time (overall baseline 325±62.5 microns to final 314.8±71.8 microns). There was a slow rise in the area of RPE alteration and in a hyper-autofluorescent area in both acute and chronic CSCR with no overlap. However, there was a late dip in the values of hyper-auto-fluorescent areas. Duration of symptoms was significantly associated with poor final visual acuity in multivariate analysis.

Conclusions: Acute and chronic CSCR had different pattern of change in functional and imaging parameters. This could indicate a non-temporal relationship between acute and chronic CSCR forms.

CONTROL ID: 3712770

SUBMITTER (NAME ONLY): Yuliang Wang

TITLE: Effects of Atropine 0.01% on Refractive Errors in Myopic Children

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, X. Zhou, X. Qu, Fudan University Eye Ear Nose and Throat Hospital, Shanghai, Shanghai, CHINA|

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ABSTRACT BODY:

Purpose: To explore the effects of long-term usage of atropine 0.01% eye drops on spherical and cylindrical refractive errors in myopic Chinese children.

Methods: This study was a single-center randomized clinical trial. Children with myopia less than -6.0 D and refractive astigmatism (RA) less than - 2.0 D were enrolled and randomized to receive atropine 0.01% once nightly with single vision lenses or simply wear single vision lenses, then followed up every three months. Cycloplegic refraction and ocular biometric measurement of axial length and corneal curvature were obtained. The magnitude and direction of RA, corneal astigmatism (CA), and internal astigmatism (IA) were also evaluated during treatment.

Results: A total of 119 eyes (69 eyes in the atropine group and 50 eyes in the control group) were included in the final analyses at the 9-month visit. The atropine-treated eyes showed significantly less progression of myopia than those in the control eye (spherical equivalent: -0.35 ± 0.33 D vs. -0.56 ± 0.49 D, $P = 0.001$ and axial length: 0.20 ± 0.19 vs. 0.33 ± 0.19 mm, $P < 0.001$). Compared with the control eyes, a statistically significant increase of RA was observed in the atropine-treated eyes (-0.14 ± 0.29 D), which was mainly attributed to the increase of CA (-0.17 ± 0.26 D), instead of a minor decrease of IA (0.02 ± 0.32 D).

Conclusions: Atropine 0.01% is effective for preventing the progression of myopia and has potential effects on increasing refractive astigmatism in myopic Chinese children over 9 months of treatment.

CONTROL ID: 3712771

SUBMITTER (NAME ONLY): Erica Poole

TITLE: Color Vision Loss in Plaquenil Toxicity

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Poole, J.C. Rabin, University of the Incarnate Word Rosenberg School of Optometry, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure: Erica Poole: Commercial Relationship: Code N (No Commercial Relationship) | Jeff Rabin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Plaquenil (hydroxychloroquine, HCQ) is a highly effective drug which can cause maculopathy even after discontinuance. 2016 AAO guidelines (https://www.aao.org/clinical-statement/revised-recommendations-on-screening-chloroquine-h;) dismiss color vision testing as insensitive and non-specific. We question this assertion with new information exemplifying sensitivity of cone color testing for detecting HCQ toxicity.

Methods: Three patients referred by retinal specialists were assessed in our Visual Neurophysiology Service (VNS) for HCQ toxicity. Testing included refraction to best VA, Humphrey (HVF) central fields (10-2 SITA-Standard), spectral domain ocular coherence tomography (SD-OCT), multifocal electroretinograms (mfERGs; ISCEV standard www.iscev.org) which provide cone and cone bipolar cell function from multiple retinal sites, fundus autofluorescence (FAF), and cone specific contrast sensitivity (CS, Innova Systems, Inc.).

Results: An asymptomatic 71-YO HF with Rheumatoid Arthritis was taking 200mg HCQ daily for 20 years (total dose 1,460g). VA: 20/15 OD, OS, FAF: enhanced macular pigment mottling OU, HVF: parafoveal sensitivity loss, SD-OCT: inner retinal thinning OS>OD, mfERGs: reduced foveal & parafoveal >OS, CCT: borderline L cone CS, decreased M cone CS, OS>OD. A 50-YO HF with Systemic Lupus Erythematosus (SLE) took 400mg HCQ per day for 17 years (total dose 2,482g; FAF featured in: https://doi.org/10.3899/jrheum.181375). VA: 20/25 OD, OS, HVF: parafoveal scotomas OS>OD with nasal extension OS, SD-OCT: significant full-thickness macular thinning, foveal sparing OD only, FAF: Bull’s eye pattern of degeneration extending temporally OS consistent with HVF and mfERG results, CCT: significant decrease all cones, >OS. A 73-YO WF with SLE taking 200mg HCQ daily for 20 years (total dose 1,424g) reported decreased color vision for 5 years. VA: 20/30 OD, 20/40 OS, HVF: parafoveal loss OD and central loss OS, SD-OCT: diffuse foveal thinning OU, IS/OS deformities, “flying saucer” OD, FAF: Bull's eye maculopathy OS>OD, mfERGs: decreased centrally OS>OD, increased fovea/ring 2 ratio OU, CCT: severe CS loss all cone types.

Conclusions: Cone CS can be reduced in various stages of HCQ maculopathy, and its decrease can even constitute the only presenting symptom. We advocate its use for adjunctive testing of HCQ patients and plan prospective and retrospective studies to confirm its efficacy.

CONTROL ID: 3712775

SUBMITTER (NAME ONLY): Yu Jeong Kim

TITLE: Investigation of the effects of topical microRNA 16-5p mimic and inhibitor in a mouse model of inflammation-related dry eye

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kim, H. Cho, Y. Yeon, W. Lee, M. Kang, H. Lim, ophthalmology, Hanyang University, Seongdong-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: We previously reported that microRNA (miR) 16-5p were increased in tears of patients with Sjogren's syndrome compared to controls. In this study, we intend to investigate the effect of topical miR-16-5p mimic and inhibitor in a mouse model of inflammation-related dry eye syndrome.

Methods: We used 11-week-old NOD.B10.H2b mice, a model for primary Sjögren's syndrome. We measured baseline ocular staining score and tear production. And we topically applied miR-16-5p mimic, miR-16-5p inhibitor or the same volume of phosphate-buffered saline (PBS) four times a day for 1 week to both eyes of the mice. Seven days later, tear production was measured, and the corneal surface was observed for epithelial defects. The number of goblet cells was evaluated in the forniceal conjunctiva. The levels of proinflammatory cytokines were analyzed in the cornea, conjunctiva, and lacrimal glands.

Results: Topical miR-16-5p mimic increased ocular staining score in NOD.B10.H2b mice than PBS. And topical miR-16-5p inhibitor administration improved tear production and reduced corneal epithelial defects. The conjunctival goblet cell density was higher in miR-16-5p inhibitor treated eyes than in miR-16-5p mimic or PBS treated eyes. Mir-16-5p mimic increased the expression of proinflammatory cytokines in the cornea, conjunctiva, and intraorbital gland and miR-16-5p inhibitor suppressed them.

Conclusions: Inhibition of miR-16-5p had the effect of protecting the ocular surface and suppressing inflammation.

CONTROL ID: 3712776
SUBMITTER (NAME ONLY): Anne Claus
TITLE: U.S. Youth Perceptions of the Importance of Vision
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Claus, A. Mubeen, L. Kim, University of Michigan College of Literature Science and the Arts, Ann Arbor, Michigan, UNITED STATES|J. Cho, S. Raven, G. Wang, M.A. Woodward, P. Newman-Casey, O. KILLEEN, University of Michigan Department of Ophthalmology and Visual Sciences, Ann Arbor, Michigan, UNITED STATES|T. Chang, University of Michigan Department of Family Medicine, Ann Arbor, Michigan, UNITED STATES|
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ABSTRACT BODY:

Purpose: Uncorrected refractive error (URE) is common among U.S. youth. We aimed to understand how youth perceive eyesight compared to other aspects of their health, as valuing vision highly could facilitate treating URE.
Methods: An open-ended 5 question poll was distributed to the MyVoice Text Message Cohort of U.S. youth aged 14–24 years (www.hearmyvoicenow.org). Question 1 asked, “How important is your eyesight compared to other aspects of your health? Why?” Respondents’ demographic information was analyzed. Low socioeconomic status (SES) was defined as receiving free or reduced-price lunch. Text message responses were coded with modified Grounded Theory.
Results: Of 1204 recipients, 1063 (88.3%) responded. Mean age was 20.3 ±2.4 years (range 15-24 years); 625 (58.8%) were male; 787 (74.0%) were white; and 440 (41.4%) had low SES. Over half (n=609, 57.3%) reported eyesight was very important, 296 (27.8%) reported it was somewhat important and 90 (8.5%) reported that it was not important. Nearly half (n=507, 47.7%) reported eyesight was needed for daily life (e.g. “sight is one of the most important aspects of my health because in our time everything is technology and images”), 152 (14.3%) discussed personal or family experiences with vision problems (e.g. “very important, I've had two blind family members and I am hard of hearing so if my vision goes I'm very screwed”), and 68 (6.4%) expressed fear of developing eye problems (e.g. “very [important], I would be severely depressed if I lost [my eyesight]”).
Conclusions: U.S. youth value vision highly compared to other aspects of their health, yet there are high rates of URE in this population. Future research should focus on identifying barriers to eyeglasses.

CONTROL ID: 3712777

SUBMITTER (NAME ONLY): Bingyao Tan

TITLE: Imaging photoreceptor response in rodent eyes using phase-sensitive optical coherence tomography

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tan, H. Li, T. Ling, Nanyang Technological University, Singapore, Singapore, SINGAPORE|V. BARATHI, L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To measure the photoreceptor response in rodent eyes using phase-sensitive optical coherence tomography (OCT)To measure the photoreceptor response in rodent eyes using phase-sensitive optical coherence tomography (OCT)

Methods: Six Brown-Norway rats (age = 6 weeks) were used for this study. The animals were dark-adapted for 12 hours before being anesthetized using a cocktail of ketamine and xylazine. They were placed on a translational stage with 5 degrees of freedom, and the head was stabilized stereotaxically. A customized spectral-domain OCT system (central wavelength = 840nm, bandwidth = 145 nm) was applied to image the posterior eye, with a field of view of 20 degrees. A single cross-sectional position was traced temporally for 5 seconds, and at t = 1 second, a single 1ms visual stimulus (wavelength = 500 nm) was delivered to create a large and Maxwellian illuminance on the retina. The temporally sequenced cross-sectional OCT scans were registered, and the hyperreflective bands from inner segment and out segment of the photoreceptors were segmented automatically. The phase difference between the two layers was computed and traced over time.

Results: Visual stimulus-evoked nanoscopic photoreceptor response can be detected by phase-sensitive OCT, which is reproducible over different spatial locations on the retina (intra-class coefficient = 0.84). Stimuli with a bleach rate of 0.3% were associated with a transient optical path length change of 48.2 ± 16.4 nm. Signals from underneath retinal blood vessels decorrelated over time, likely due to the influence of the blood flow.

Conclusions: Phase-sensitive OCT provides a novel non-invasive approach to study photoreceptor response in rodents, and the current framework could be applied to investigate different animal disease models with photoreceptor abnormalities.

CONTROL ID: 3712778

SUBMITTER (NAME ONLY): Paripoorna Sharma

TITLE: Prevalence of peripheral retinal changes on ultra-widefield color fundus imaging

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Sharma, I. Shareef, F.P. Kalaw, V. Alex, E. Walker, S. Borooah, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The prevalence of peripheral retinal findings is unclear. We assess the prevalence of peripheral retinal abnormalities in retinal patients in an academic setting to understand how they associate with retinal diagnoses.

Methods: We performed a retrospective, observational clinical study. Ultra-widefield images (Optos P200DTx) were collated from the right eyes of consecutive retina clinic patients with demographic data attending Shiley Eye Institute, UCSD between 1st January and 30th November 2021. Images were included with unobstructed views of >60% of each quadrant and visibility of fourth order arterioles. The images were examined by a masked retinal specialist who recorded abnormal peripheral findings by quadrant (Fig, 1). Statistical analysis was performed using R software with fitted logistic regression models testing each peripheral change. Pearson's Chi-squared test was used for samples lacking logarithmic power.

Results: A total of 556 images were collated. After initial quality control, 312 patient images (mean age 61.9±19.5 years, 55.1% female) were analyzed. 152 (48.7%) patients had peripheral pathology, most commonly in the temporal quadrant. The most common peripheral findings were drusen (n=73, 23.4%) and laser marks (n=28, 9.0%). Diabetic retinopathy (DR) was associated with peripheral blot hemorrhages (P<.001), dot hemorrhages (P<.001), laser marks (P=.002), pigmentation (P=.049) and sclerosis of vessels (P<.001). Age-related macular degeneration (AMD) was associated with peripheral drusen (P=.001). Age was associated with general degeneration including chorioretinal atrophy (P<.001)(Fig. 2).

Conclusions: Peripheral retinal findings were common in our retinal patients, drusen being most prevalent. The findings were validated by associations of DR with common DR peripheral findings. AMD was correlated with drusen, validated by recent literature. New correlations between DR and pigmentation and vessel sclerosis need to be further investigated. This data is useful to retinal specialists using ultra-widefield imaging and can provide a platform for training AI algorithms in detecting peripheral pathology in ultra-widefield imaging.

CONTROL ID: 3712779

SUBMITTER (NAME ONLY): Brendon Lee

TITLE: Sebaceous cell carcinoma presenting as an ocular Marjolin ulcer following exposure to a common alkaline cleaning agent

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.W. Lee, M. Coroneo, Ophthalmology, University of New South Wales, Sydney, New South Wales, AUSTRALIA|D. Murrell, Dermatology, University of New South Wales, Sydney, New South Wales, AUSTRALIA|S.F. Taylor, Ophthalmology, The University of Sydney School of Medicine, Sydney, New South Wales, AUSTRALIA|A. Gal, Pathology, Histopath Diagnostic Services, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Marjolin ulcer is a rare and aggressive malignancy that originates from chronically inflamed, ulcerated, or scarred tissue. The potential for malignant transformation of ocular surface chemical injuries to a Marjolin ulcer is not well recognised. In fact, this progression may be accelerated by the immunosuppressive treatments often utilised to control the post-burn cicatrising process.

Methods: A 67-year-old, healthy and non-smoking, Caucasian lady presented with a 2 year history of pain, redness, tearing, and blurred vision in her right eye. She had suffered an alkaline burn of the right eye 4 years ago from a household cleaning agent. Right visual acuity was 6/400. Examination showed marked ocular surface disease and cicatrising conjunctivitis. Initial conjunctival biopsies returned negative for malignancy. Topical and systemic immunosuppression was underwent symblephara excision and amniotic transplantation. She eventually developed microbial keratitis and underwent an evisceration due to corneal perforation. Histopathological analysis showed high grade, poorly differentiated invasive sebaceous cell carcinoma with pagetoid intraepithelial spread and staining for BerEP4 and CK7 (Figure 1). To achieve tumor extirpation, an anterior exenteration was performed. No evidence of recurrence or metastasis was seen for 36 months.

Results: This is the second case of a sebaceous cell carcinoma Marjolin ulcer in the literature. We believe the theory most pertaining to an ocular Marjolin ulcer revolves around a co-carcinogen concept where the initial burn or injury acts to increase tissue susceptibility to other carcinogens such as ultraviolet radiation.

Conclusions: The potential for malignant transformation of ocular and pericoular chemical injuries into Marjolin ulcers needs to be recognised. Sebaceous cell carcinomas should be included in the potential spectrum of histopathology subtypes. We recommend that patients with previous chemical ocular burns, especially those initiated on immunosuppressive therapy, should be carefully evaluated, monitored, and counselled for the potential risk of Marjolin ulcer development.

CONTROL ID: 3712780

SUBMITTER (NAME ONLY): Sangeethabalasri Pugazhendhi

TITLE: Optical Coherence Tomography Angiography Features of Optic Nerve Ischemia

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Pugazhendhi, M. Yu, M. Shariati, Y.J. Liao, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|X. Zhou, Y. Cheng, R.K. Wang, Bioengineering, University of Washington College of Engineering, Seattle, Washington, UNITED STATES|R.K. Wang, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The hallmark of non-arteritic anterior ischemic optic neuropathy (NAION) is vascular compromise to the anterior optic nerve and peripapillary retinal nerve fiber layer (pRNFL) thinning and secondary degeneration of the retinal ganglion cell (RGC) body or macular ganglion cell complex (mGCIPL) thinning. This study investigates OCT and OCTA changes in chronic NAION and identifies imaging biomarkers that best predict disease.

Methods: We performed a retrospective cross-sectional study of 15 chronic NAION patients (20 eyes) and 23 age-matched controls (31 eyes) with swept-source (PLEX® Elite 9000) and spectral-domain OCT imaging, and static perimetry using Humphrey Field Analyzer (all instruments from Carl Zeiss Meditec, Inc, Dublin, CA). OCT pRNFL and mGCIPL were quantified automatically with commercial software, and OCTA were analyzed using custom MATLAB script to measure 12 parameters per eye after large vessel removal: vessel area density (VAD), flux, vessel skeleton density (VSD), vessel complexity index (VCI), vessel perimeter index (VPI), and vessel diameter index (VDI).

Results: Static perimetry mean deviation (MD) was significantly worse in NAION (-13.53 ± 2.36) than controls (-0.47 ± 0.72; $P < .001$), with 64 µm thinner pRNFL and 39.7 µm thinner mGCIPL in NAION eyes than controls ($P<.001$). Spearman correlation analysis show that VAD and flux are highly correlated with visual field MD and OCT measurements. Hierarchical clustering of OCT and OCTA data showed two distinct groups (NAION and control), where standardized measurements for NAION were generally lower than controls. Two-way mixed ANOVAs showed significant interaction between patient status (control and NAION) and structure (optic disc and macula) for annulus VAD and flux values and mean pRNFL and mGCIPL thickness. Post hoc tests showed this effect stems from lower peripapillary values in NAION than controls. Separate logistic regression models with LASSO regularization identified peripapillary VAD, VCI and VDI and macular VAD and flux as the best OCTA parameters to predict NAION.

Conclusions: Ischemic insult to the peripapillary region is more severe likely from primary degeneration while macula is affected by secondary retrograde degeneration and loss of RGC. Other than structural OCT measurements, peripapillary and macular vascular parameters such as VAD, flux, VCI and VDI are good predictors of optic nerve and retinal changes as a result of NAION.

CONTROL ID: 3712781

SUBMITTER (NAME ONLY): Shervonne Poleon

TITLE: Perceived utility of intervention strategies for improving medication adherence in glaucoma

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Poleon, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|L. Racette, The University of Alabama at Birmingham Department of Ophthalmology and Visual Sciences, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Shervonne Poleon: Commercial Relationship: Code N (No Commercial Relationship) | Lyne Racette: Commercial Relationship(s);Code C (Consultant/Contractor):Olleyes

ABSTRACT BODY:

Purpose: Interventions for improving medication adherence in glaucoma have had equivocal results due in part to a lack of stakeholder input. Incorporating patient and provider perspectives into intervention design may improve their ability to target key determinants of adherence. We assessed the perceived utility of the most effective interventions identified in the literature by sampling perspectives of glaucoma patients and providers.

Methods: We performed a literature review to identify studies that delivered interventions for improving adherence, and included only studies that used electronic monitoring and had at least three months of follow-up. We categorized the interventions based on the strategies delivered: education, reminders, motivational interviewing (MI), health coaching, instillation skill training, and combination vs polytherapy. We invited patients and providers to assess the utility of each strategy in day-to-day glaucoma management using a 4-point Not Useful to Very Useful Likert scale. We also used the Glaucoma Treatment Compliance Assessment Tool to assess patients' perceived glaucoma severity, susceptibility, treatment benefits, treatment barriers, and glaucoma knowledge. Patients (n = 13) were above age 40, used ocular hypotensive eyedrops, and had glaucoma for at least 2 years. Providers (n = 5) were optometrists or ophthalmologists who had at least 2 years' experience treating glaucoma.

Results: Only four strategies—education, reminders, MI, and health coaching led to a significant increase in adherence. For patients, education (median, IQR = 4.0, 0.25), health coaching (3.0, 1.0), and reminders (3.0, 2.0) had the highest utility, compared to MI (4.0, 0), reminders (3.7, 0.33), and education (3.5, 0.25) among providers. Higher glaucoma knowledge was associated with a preference for education (rho = .603, p = .03), and higher perceived glaucoma severity was associated with a preference for reminders (rho = .626, p = .02), instillation skill training (rho = .754, p = .003), and MI (rho = .754, p = .003).

Conclusions: The most effective strategies based on empirical data—education, reminders, MI, and health coaching—had the highest perceived utility in day-to-day management of glaucoma. Incorporating patient and provider perspectives into intervention design may improve their uptake and effectiveness, ultimately resulting in improved medication adherence in glaucoma.

CONTROL ID: 3712783
SUBMITTER (NAME ONLY): Jochen Straub
TITLE: Dewarping retinal and choroidal thickness maps in widefield optical coherence tomography volumes
SESSION TITLE: New improvements in imaging and development of biomarkers
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Straub, A. Noshadi, C. Leahy, J. Bumstead, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|A. Ohlendorf, S. Wahl, Carl Zeiss Vision GmbH, Aalen, Baden-Württemberg, GERMANY|A. Noshadi, Ambu A/S, Munich, GERMANY|
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ABSTRACT BODY:

Purpose: Recent developments in optical coherence tomography (OCT) have demonstrated single acquisition widefield imaging with an optical field of view (FOV) of up to 90°. The purpose of this study is to evaluate the previously developed OCT volume dewarping and normal incidence method, for the measurement of retinal and choroidal thickness maps in human eyes.
Methods: Our previous work (IOVS, Vol. 61, PB00103, 2020) has demonstrated that dewarping and measuring normal to the retinal pigment epithelium layer is a crucial step when analyzing structure and shape of the retina. The mathematical model predicted the results to be dependent on the retinal curvature and to increase as a function of FOV.

In this study we compare retinal and choroidal thickness measurements of 12 healthy right eyes of 12 subjects before and after applying the dewarping and normal incidence method. For each eye we have acquired 12x12 mm OCT volumes with 3 mm scan depth using PLEX® Elite 9000 (ZEISS, Dublin, CA). Axial eye length is needed for the dewarping algorithm and is measured using IOL Master® 500 (ZEISS, Jena, Germany).
Results: The relative difference between thickness measured along an A-scan and thickness measured using the dewarping and normal incidence method ranges between 0% and 4% for 12x12 mm OCT volumes which is consistent with the mathematical prediction. Furthermore, the difference varies in magnitude for every individual eye and increases with FOV. Figure 1 shows the results for all 12 human eyes.
Conclusions: Measurement of human eyes has confirmed that the dewarping and normal incidence method results in thickness maps that are different from the thickness maps calculated along A-scans. The range of differences measured in human eyes matched the previously published mathematical prediction. The results further confirmed that the magnitude of the difference increases with FOV and is different for every individual eye.

CONTROL ID: 3712784

SUBMITTER (NAME ONLY): Jiannong Dai

TITLE: The role of actin binding protein in the formation of cross-linked actin networks (CLANs) in trabecular meshwork cells

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Dai, N. Rayana, C.K. Sugali, W. Mao, Ophthalmology, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|W. Mao, Department of Biochemistry & Molecular Biology, IU, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cross-linked actin networks (CLANs) are a type of F-actin structure frequently found in glaucomatous trabecular meshwork (TM) cells and tissues. Also, TM cells form more CLANs after being treated with glaucoma-associated agents including TGFβ2 and glucocorticoids. Our recent studies showed that CLANs increase TM cell stiffness, decrease actin dynamics, and inhibit phagocytosis, which are very likely to contribute to elevated intraocular pressure. We previously showed that overexpression of a subset of calcium binding proteins increased CLANs formation. In this study, we determined the effect of gene knockdown of these proteins in primary human TM (pHTM) cells.

Methods: Primary HTM cells were first transfected with different siRNAs against caldesmon, calponin, tropomyosin and/or myosin light chain overnight. Non-targeting (NT) siRNA was used as a control. After siRNA transfection, the cells were treated with 5ng/ml TGFβ2 to induce CLAN formation for 6-7 days. At the end of treatment, the cells were fixed for immunostained with phalloidin-Alexa-568 and DAPI. The CLAN-positive cells (CPCs) over total number of cells per well was calculated and one-way ANOVA was used for analysis.

Results: The percentage of CPCs in the NT-siRNA control group was 13.5% and 21.5% in two different cell strains, respectively (N=4 for each strain). Knocking down of caldesmon, calponin, myosin light chain, or all four proteins (combo) showed a trend of inhibition of CLAN formation but it was not significant (likely due to small Ns). In contrast, the CPCs almost doubled in the tropomyosin knockdown group (24.6% and 45.9%, respectively; $P<0.05$ for both strains).

Conclusions: Our previous gain-of-function study showed that overexpression of tropomyosin did not affect CLANs. In this loss-of-function study, we found that tropomyosin knockdown enhanced CLANs. Therefore, tropomyosin is likely to be necessary, but not sufficient, for CLANs formation.

CONTROL ID: 3712785

SUBMITTER (NAME ONLY): Jay Wang

TITLE: Deep learning for quality assessment of optical coherence tomography angiography images

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) is a relatively novel technology that continues to improve, but variation in image quality remains problematic for reliable image analysis. We developed a deep learning-based system using convolutional neural networks for automated quality assessment of optical coherence tomography (OCTA) images.

Methods: We performed a single center, retrospective study of diabetic patients from August 2017 to April 2019. OCTA imaging with the Cirrus HD-OCT 5000 AngioPlex was performed. Manual grading of image quality was performed on 8x8 mm and 6x6 mm superficial slab images by two independent graders. An image quality score was assigned based on presence of motion and segmentation artifacts, media opacity, and visibility of fine capillaries. Machine-reported signal strength was also recorded. Each image was assigned a final image quality score from 0 to 4 based on a composite assessment from both graders. A ResNet152 neural network classifier pretrained using ImageNet was trained to classify the images. Because requirements for image quality may vary depending on the clinical or research setting, two models were trained – one to identify highquality images and one to identify low-quality images.

Results: 347 scans from 134 patients were included. Our neural network models demonstrated outstanding area under the curve (AUC) metrics for both low quality image identification (AUC=0.98, 95%CI: 0.96-0.99, κ=0.88) and high quality image identification (AUC=0.99, 95%CI: 0.99-1.00, κ=0.92), significantly outperforming machine-reported signal strength (AUC=0.78, 95%CI: 0.73-0.83, κ=0.27 and AUC=0.82, 95%CI: 0.77-0.86, κ=0.52 respectively).

Conclusions: Deep convolutional neural networks featuring skip connections were successfully trained to automatically classify between gradable and ungradable OCTA images, and have been made publicly available as a resource to other physicians and scientists. As OCTA becomes more widely utilized, flexible and robust methods for image quality control will be important.

CONTROL ID: 3712786

SUBMITTER (NAME ONLY): Abhishek Sethi

TITLE: Methods for Manual Segmentation of Hyper-resonant Foci to Identify a Ground Truth for Deep Learning Models

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sethi, M. Munro, J. Hallak, Illinois Eye and Ear Infirmary, Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|M.N. Alam, S. Goel, Biomedical Data Science, Stanford Medicine, Stanford, California, UNITED STATES|M. Pfau, Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M. Pfau, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|J. Hallak, AbbVie Inc, North Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The presence of hyper-reflective foci (HRFs) in the outer retina has been associated with age-related macular degeneration (AMD) and diabetic retinopathy (DR). We have previously employed a deep-learning (DL) model to perform semantic segmentation of HRFs. Here, we conducted a retrospective, observational clinical study to identify a ground truth for the DL model using manual segmentation.

Methods: Optical Coherence Tomography (OCT) images were retrieved of patients who received care at the retina service at the University of Bonn. The dataset included 3644 OCT (3044 AMD & 600 DR) images. Two separate teams of graders reviewed the images; team A consisted of one ophthalmologist, and team B consisted of a medical student and ophthalmologist. ImageJ was used to manually annotate the boundaries of HRFs found in the outer nuclear and/or outer plexiform layers for each OCT image. We measured the variability of manual segmentation of HRFs between two sets of graders and evaluated the accuracy of the DL model compared to manual segmentation by both teams.

Results: Overall, fewer HRFs were marked by the team B compared to team A; in fact, there were images where no HRF was annotated by the team B. Out of 3644 images, 3557 images (97.6%) had annotations which matched across both teams. When excluding images with zero overlap, the average intersection over union (IoU) was 0.285, and the average precision (AP) was 0.343 measured over 2303 images. When the DL model was trained with annotations by team A as the ground-truth, the IoU was 0.33, and the AP was 0.75. When the DL model was trained with the annotations by team B as the ground-truth, the IoU was 0.53, and the AP was 0.78.

Conclusions: There was considerable variability in the manual annotation of HRFs by the two teams of graders. This may be due to a low signal-to-noise ratio in several OCT images and challenges in delineating the outer retina from adjacent structures. A higher IoU was noted in the second set of annotations due to conservative delineation of HRFs and a larger team size. Therefore, a DL approach is essential for accurate and precise segmentation of biomarkers such as HRFs in OCT images.

CONTROL ID: 3712789

SUBMITTER (NAME ONLY): Sohaib Fasih-Ahmad

TITLE: Accuracy of Deep-Learning-Derived OCT Retinal Layer Segmentation in the Alabama Study on Early Age-Related Macular Degeneration 2 (ALSTAR2)

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Fasih-Ahmad, Z. Wang, Z. Mishra, C. Vatanatham, A.M. Jain, A. Ganegoda, Z. Hu, S.R. Sadda, Doheny Eye Institute, Pasadena, California, UNITED STATES|M. Clark, C. Owsley, C.A. Curcio, The University of Alabama at Birmingham Department of Ophthalmology and Visual Sciences, Birmingham, Alabama, UNITED STATES|S.R. Sadda, Department of Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Manual segmentation of early AMD features and associated retinal layers in SD-OCT images is tedious and time-consuming. Using only 5 OCT volumes of the ALSTAR cohort, we trained our existing deep-learning derived, graph-based algorithm to segment the outer-retinal layers in eyes with early AMD. Our goal was to evaluate the accuracy of this algorithm in ALSTAR2 cohort compared with manual segmentation.

Methods: Subjects ≥ 60 years old with healthy eyes or early AMD in at least one eye were enrolled in the Alabama Study on Early Age-Related Macular Degeneration 2 (ALSTAR2). Eye-tracked SD-OCT volumes (8.6x7.2mm, ART > 9, fovea centered) were acquired with Spectralis HRA + OCT2. The outer-retinal layers [inner segment myoid (ISM) (defined to span from the external limiting membrane to ellipsoid zone (EZ) center line), photoreceptor outer segment (EZ center line to outer surface of interdigitation zone), subretinal drusenoid deposits (SDD), retinal pigment epithelium (RPE), drusen, full choroid] were segmented manually by expert graders and fully automatically by our algorithm. Based on these segmentations, mean thickness, total volume, and total area of the 6 layers were computed in 9 ETDRS subfields, and mean measurement difference and correlation coefficients were calculated.

Results: The study cohort included 400 eyes (140 early AMD, 260 normal). The mean difference and correlation coefficients between segmentation methods are shown in Table 1. In general, mean thickness differences for most layers were <1μm (choroid by ~5-7μm) with a significant correlation between the automated and manual measurements for ISM, photoreceptor outer segments, RPE, and choroid layers. Correlations were not as good for drusen and SDD layers.

Conclusions: A deep-learning derived algorithm has promise in segmenting hyporeflective bands of ISM, photoreceptor outer segments, RPE, and choroid in normal and early AMD eyes. Further algorithm training using more OCT volumes with drusen and SDD lesions may be required to improve algorithm performance, and further statistical analysis is planned.

CONTROL ID: 3712790

SUBMITTER (NAME ONLY): Ian Sigal

TITLE: The lamina cribrosa vascular network is heavily interconnected with that of adjacent regions, not just the periphery, likely improving perfusion resilience

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.A. Sigal, P. Lee, M. Quinn, S. Waxman, A.P. Voorhees, B. Yang, Y. Hua, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|I.A. Sigal, P. Lee, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|B. Yang, Engineering, Duquesne University, Pittsburgh, Pennsylvania, UNITED STATES|T.C. Jakobs, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|B. Fortune, Devers eye institute, Legacy Health System, Portland, Oregon, UNITED STATES|J. Rizzo, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: A reliable blood supply to the optic nerve neural tissues is essential to prevent damage and vision loss. At the lamina cribrosa (LC) this is achieved by a complex network of capillaries intertwined with collagen beams. Conventional understanding has been that LC blood perfusion originates from the posterior ciliary artery (PCA) at the periphery of the canal and drains into the central retinal vein. To better understand the LC perfusion and potential challenges to perfusion that could lead to ischemia we map the LC 3D vasculature

Methods: The vasculatures of six normal monkey eyes were labelled post-mortem by perfusing lipophilic carbocyanine dyes through the carotid arteries. After enucleation serial coronal cryosections 16μm thick through the LC were imaged using fluorescence and polarized light microscopy to visualize the labeled vessels and label-free collagen, respectively. The collagen structures were registered and used to identify the LC and form an image stack from which the fluorescence was segmented to reconstruct the 3D vascular network. We performed both quantitative and qualitative analyses of the LC vessels

Results: Three of the six eyes exhibited vessel branches directly from the central retinal artery (CRA) to the LC (Fig 1). A watershed analysis revealed distinct perfusion regions for the initial branching levels, after which the vessels interconnected with the rest of the LC vascular network. The LC vessels were heavily interconnected with the adjacent vasculature (Fig 2). For example, in one eye there were 1100 anastomoses between the LC vessels and the exterior. The largest number of anastomoses was with the retro-laminar region (479), followed by the periphery (409), the pre-laminar region (159) and the central vessels (53). A substantial fraction (>20%) of neural tissues were further than 40μm from vessels, and thus at higher risk of ischemia

Conclusions: The LC vascular network is heavily interconnected with the PCA, but also with the CRA and with the pre- and retro-laminar regions. We postulate that multiple potential perfusion sources provide redundancy that can help protect tissues from compromised perfusion and ischemia, at all levels of IOP, particularly for tissues further away from the vasculature. More work is necessary to map more eyes, and develop the technology to measure LC blood flow and perfusion

CONTROL ID: 3712791

SUBMITTER (NAME ONLY): Morten Magno

TITLE: The Relationship Between adherence to a Mediterranean Diet and Dry Eye Disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.S. Magno, Department of Epidemiology, Universitair Medisch Centrum Groningen, Groningen, Groningen, NETHERLANDS|M.S. Magno, Department of Plastic and Reconstructive Surgery, Oslo Universitetssykehus, Oslo, NORWAY|E. Moschowits, T. Utheim, Department of Medical Biochemistry, Oslo Universitetssykehus, Oslo, NORWAY|M.W. Beining, Universitetet i Oslo Det medisinske fakultet, Oslo, Oslo, NORWAY|C.J. Hammond, Department of Twin Research & Genetic Epidemiology, King's College London, London, London, UNITED KINGDOM|T. Utheim, Department of Ophthalmology, Oslo Universitetssykehus, Oslo, NORWAY|J. Vehof, Department of Ophthalmology, Universitair Medisch Centrum Groningen, Groningen, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Lifestyle and dietary factors affect health and disease. A traditional Mediterranean diet, rich in unsaturated fats and oils, is often purported as a healthy diet. This study tested the hypothesis that a greater adherence to a Mediterranean diet is associated with a lower risk of dry eye disease (DED).

Methods: 58,993 participants from the Dutch Lifelines population-based cohort were included (aged 20-94 years, 60% female). The Women's Health Study (WHS) dry eye questionnaire was used to assess the primary outcome, WHS-defined DED. Level of adherence to a Mediterranean diet was quantified using a modified Trichopoulou's Mediterranean Diet Score (mMDS). The mMDS ranks participants across nine categories, yielding a sum score from zero to nine, with higher values indicating greater adherence. Logistic regression models were used to assess the relationship between WHS-defined DED and mMDS. Models were corrected for age and sex only (Model 1), age, sex, BMI, smoking status, and income and education level (Model 2), and all variables in Model 2 plus 48 traits and medical comorbidities associated with DED (Model 3). To assess possible reverse causality, participants with a diagnosis of dry eye were excluded, and the relationship between mMDS and symptomatic dry eye was assessed separately.

Results: 9.1% of participants had WHS-defined DED. Greater adherence to a Mediterranean diet was not linked to a decreased risk of dry eye. Contrarily, increasing mMDS values were significantly tied to an increased risk of WHS-defined DED in all models (odds ratio per mMDS unit 1.040, 95% CI 1.020-1.059, P<0.0001, Model 3). Higher mMDS scores were associated with a greater risk of symptomatic dry eye in all models, after excluding those with a diagnosis of dry eye (odds ratio 1.034, 95% CI 1.021-1.048, P<0.0001, Model 3).

Conclusions: Greater adherence to a Mediterranean diet was not tied to a lower risk of dry eye in this large, population-based Dutch cohort. In fact, higher mMDS scores were associated with an increased likelihood of having WHS-defined DED, which was also seen for symptomatic dry eye after excluding those with a clinical dry eye diagnosis. Causes of this observed effect should be explored further.

CONTROL ID: 3712793

SUBMITTER (NAME ONLY): Hong-Uyen Hua

TITLE: Feasibility of anterior chamber optical coherence tomography quantification of anterior chamber inflammation and cytokine and protein biomarker tear profile in pediatric uveitic patients

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Hua, S. Sharma, K. Baynes, S.K. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|S.T. Angeles-Han, T. Hennard, S. Thornton, A. Sproles, Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Examination and assessment of disease activity in pediatric non-infectious uveitis can be difficult and subjective. In this pilot study, we assess the feasibility of using quantitative imaging (anterior segment optical coherence tomography [AS-OCT]) and measuring biomarkers in tears to assess ocular inflammation.

Methods: This is an IRB approved study. Children with uveitis were deemed “active” or “inactive” by standard clinical examination graded by SUN criteria. Anterior segment OCT was obtained with Optovue Avanti (Fremont, CA, USA) and cells/mm3 were quantitated using automated software. Tears were collected using Schirmer’s strips. S100A8, A9, and A12 were measured using enzyme-linked immunosorbent assay. IL-18, IL-8, IP-10, MCP- 1, RANTES, and sICAM-1 were measured by Luminex assays.

Results: 10 eyes of 5 patients were included in this pilot study. 2 patients had active uveitis (intermediate uveitis and vasculitis and panuveitis); 3 patients had inactive uveitis (anterior scleritis, posterior scleritis, and intermediate uveitis). AS-OCT mean cells/mm3 in the active cohort was 15 cells/mm3 compared to .22 cells/mm3 in those with inactive disease. IP-10, MCP-1, sICAM-1, s100A12, and s100A8/9 were detected in all patients with sufficient sample. Comparing patients with active vs. inactive uveitis, mean sICAM-1 was 3349.58 pg/ML vs. 1808.07, s100A12 was 436.1 vs. 2219.1, mean IP-10 was 556.42 vs. 396.13, and MCP-1 was 4.77 vs. 9.03 respectively.

Conclusions: In this proof-of-concept study, we demonstrate that imaging-based metrics of inflammation and tear biomarker levels may differentiate active and inactive uveitis in children. AS-OCT quantification of AC inflammation was higher in those with clinically active uveitis. Furthermore, sICAM-1 and IP-10 in tears trended towards higher levels in patients with active uveitis, whereas S100A12 and MCP-10 trended towards lower levels. Imaging and tear-based biomarkers are promising non-invasive methods to monitor uveitis in children.

CONTROL ID: 3712794

SUBMITTER (NAME ONLY): Chaimae Gouya

TITLE: Absence of Interphotoreceptor Retinoid-Binding Protein (IRBP, RBP3) in Transgenic Rats Causes Photoreceptor Degeneration and Myopia

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Gouya, D. Kelly, O. Liu, Research, Research Mississippi Inc, Jackson, Mississippi, UNITED STATES|M. Kim, Clinical Research, Southern Therapy and Advanced Research, Jackson, Mississippi, UNITED STATES|B. Tieu, F. Gonzalez-Fernandez, Ophthalmology, University of Mississippi Medical Center, Jackson, Mississippi, UNITED STATES|F. Gonzalez-Fernandez, Research Service, G. V. (Sonny) Montgomery VA Medical Center, Jackson, Mississippi, UNITED STATES|B. Tieu, Ophthalmology, G. V. (Sonny) Montgomery VA Medical Center, Jackson, Mississippi, UNITED STATES|E. Lam, School of Medicine, University of Mississippi Medical Center, Jackson, Mississippi, UNITED STATES|V. Wilburn, R&D, Pathrd Inc., Jackson, Mississippi, UNITED STATES|

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ABSTRACT BODY:

Purpose: IRBP is the major protein component of the interphotoreceptor matrix (IPM) separating the retina from the RPE. Recently, its presence in vitreous and aqueous has been appreciated. Early expression of IRBP in rats suggests a critical role of the IPM in ocular development (Gonzalez-Fernandez and Healy, J Cell Biol 111:2775-84,1990). Although IRBP promotes the trafficking and protection of visual cycle retinoids in the adult, its function in retinal and ocular development is yet to be understood. Here, we seek to determine the effect of the absence of IRBP on postnatal eye growth and retinal integrity.

Methods: We generated an IRBP CRISPER/Cas9 knockout in a Sprague Dawley background. IRBP(-/-) and wildtype (WT) animals were reared from birth through p103 under dim cyclic light. Body and eye weight were determined together with globe dimensions via laser micrometry. Outer and inner nuclear cell densities were characterized morphometrically by QuPath image analysis of digitized sagittal histological sections oriented through the optic nerve. This data was correlated with scotopic and photopic ERGs, immunohistochemistry, and electron microscopy.

Results: WT animals showed IRBP immunospecific staining in the IPM; IRBP(-/-) did not express IRBP. Beginning at ~1.5 months globe weight was noticeably greater for IRBP(-/-) rats compared to age-matched WT animals. The maximal size difference, which occurred at ~4.5 months, was 18% and 16% for males and females respectively. Beyond that age, the difference in eye size did not increase appreciably further. The differences between age-matched IRBP(-/-) and WT globe size were independent of sex and body mass. Laser micrometry showed a slight increase in the anterior-posterior dimension for IRBP (-/-) which remains to be further studied. The outer nuclear layer began to gradually thin after weaning. The inner nuclear layer was spared relative to the outer nuclear layer. The degeneration was associated with the reduction of ERG A and B waves. Ultrastructural studies showed that the rod outer segments were irregular in contour and often broken.

Conclusions: Knockout of IRBP resulted in a gradual photoreceptor degeneration with concomitant globe enlargement. Transgenic absence of IRBP may provide a useful system not only to study the role of IRBP in the photoreceptor function and survival but also in ocular development and myopia.

CONTROL ID: 3712795

SUBMITTER (NAME ONLY): Sara Fard

TITLE: Orbital masquerade syndromes: When to pursue further evaluation in cases of biopsy proven painful non-specific orbital inflammation, a case series

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Fard, J.R. Lewis, J. N. Thayer, J. Carter, D.A. Hollsten, C.L. Fry, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|F. Zelun Jing, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|P. Chevez-Barrios, Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Painful non-specific orbital inflammation (NSOI) unresponsive to steroids should be re-examined, even in cases of compatible histopathology.

Methods: A retrospective case series of 3 eyes of 3 adult patients initially diagnosed as NSOI, based on clinical and histopathologic findings at University of Texas Health Sciences Center at San Antonio, is presented. These cases were re-evaluated given pain unresponsive to steroids. Follow-up ranged from 1 to 7 years. This study was approved by the Institutional Review Board and is compliant with the Health Insurance Portability and Accountability Act (HIPAA).

Results: Three patients had painful orbital inflammation initially diagnosed as NSOI by biopsy. However, the pain persisted in all despite oral immunosuppression with steroids. Re-evaluation included: repeat biopsy in two patients, expert ophthalmic pathology consultation in two patients, whole-body imaging in three patients, and several laboratory studies. The ultimate diagnoses were: one case of tuberculosis with secondary extraocular muscle amyloidosis, one case of granulomatosis with polyangiitis (GPA), and one case of metastatic lobular breast carcinoma without known primary.

Conclusions: The ophthalmologist must search for a more appropriate diagnosis in cases of biopsy proven painful NSOI unresponsive to steroids.

CONTROL ID: 3712797

SUBMITTER (NAME ONLY): Elahhe Afkhamnejad

TITLE: The Effect of Anti-Opioid State Laws on Prescribing Patterns in an Oculoplastic Practice

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Afkhamnejad, C. Stevenson, P. Gupta, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite three Texas laws since 2019 aimed at reducing opioid prescriptions, overdoses reached a national record high this year, leaving uncertainty about the efficacy of these measures. This retrospective chart review investigates the effect of these three policies on opioid prescribing practices at the University of Texas Medical Branch Oculoplastic Department.

Methods: This study included charts of approximately 520 participants over the age of 18 who underwent one of ten specified Oculoplastic procedures performed at the University of Texas Medical Branch between January 1, 2018 and July 1, 2021. Demographic data, type of surgery, and prescribed morphine milli-equivalents (MME) were extracted from the charts. T-tests and chi-square tests were utilized to detect significant differences in average MME prescribed per month. This data was analyzed for an overall change in the trend of prescribing patterns as well as individual changes between the timeframes pertaining to each policy.

Results: Out of the 520 subjects screened, 250 received a qualifying post-op opioid medication of any amount. Data shows a 15% decrease in opioid prescribing rates since January 2018 to present. Before any policies were passed, an average of 109.09MME were prescribed per month. This decreased to 98.23MME after the first law and 98.23MME after the second law. After the passage of the third anti-opioid policy, an average of 92.62MME/month were prescribed. Evaluation continues as to the significance ($p<.05$) of this overall decrease, as well as individual changes in average MME/month in timeframes after each law was enacted in September 2019, March 2020, and January 2021 [see Graph 1].

Conclusions: Implementation of the anti-opioid state laws in Texas made a demonstrable impact on the number of opioids prescribed by the Oculoplastic department at UTMB. Such success encourages the support of similar policies in other states. Conclusions will also identify other factors associated with higher MME prescriptions, such as specific patient demographics or type of surgery.

CONTROL ID: 3712798

SUBMITTER (NAME ONLY): Lin DU

TITLE: Growth Hormone releasing hormone (GHRH) promotes autoimmune uveitis by enhancing Th17 cell differentiation

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. DU, B. Ho, Y. Yip, C.C. Pang, W. CHU, Ophthalmology&Visual Sciences, The Chinese University of Hong Kong Faculty of Medicine, Hong Kong, HONG KONG|S. Chan, The Chinese University of Hong Kong School of Biomedical Sciences, Hong Kong, HONG KONG|J. Li, Department of Ophthalmology, Zhejiang University School of Medicine, Affiliated Hangzhou First People's Hospital, CHINA|

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ABSTRACT BODY:

Purpose: Autoimmune uveitis is a sight-threatening disease characterized by intraocular inflammation, which is usually accompanied with Th17 cells-associated systemic autoimmune disorders such as Behcet's disease. Thus, the role of Th17 cells in autoimmune uveitis and the novel treatments targeting Th17 cells are needed. GHRH, synthesized in the hypothalamus, controls the secretion of growth hormone in the pituitary. GHRH receptor (GHRHR) is also expressed in ocular tissues and T cells. We hypothesize that GHRH promotes autoimmune uveitis by regulating Th17 cell differentiation.

Methods: Ghrhr $^{lit/lit}$ mice (n=28) with non-functional GHRHR, were immunized with IRBP to induce autoimmune experimental uveitis (EAU). 21 days after immunization, EAU was assessed based on clinical examinations of cSLO, OCT and ERG. Eyeballs were collected for histology staining. Th17 cells isolated from spleen (SP), eye-draining lymph nodes (LNs) and eyes were evaluated for their activation, apoptosis and gene expression. GHRH agonist and antagonist were applied to wild-type (WT) mice (n=15 per group) immunized with IRBP to verify the role of GHRHR. $CD4^+$ T cells from IRBP-immunized WT and Ghrhr $^{lit/lit}$ mice were differentiated into Th17 cells in vitro following adoptive transfer into naïve recipient mice (n=8 per group) to determine the effect of GHRHR in the differentiation of pathogenic Th17 cells to induce EAU.

Results: Compared with WT mice, Ghrhr $^{lit/lit}$ mice have lower disease score ($p<0.0001$), decreased fold change of retina-choroidal thickness (RCT) ($p<0.0001$), higher amplitudes of b-wave in photopic and scotopic ERG ($p<0.001$). Ghrhr $^{lit/lit}$ mice have fewer $CD4^+$ IL-17a$^+$ T cells in the SP ($p<0.05$), LNs ($p<0.05$) and eye ($p<0.001$). Gene expression of Il17a, Il17f, Il22 and Csf2 is downregulated, while Il10 is upregulated. Compared with WT EAU mice treated with DMSO, mice treated with GHRH agonist have higher disease score ($p<0.05$), increased fold change of RCT ($P<0.05$) and increased Th17 cells ($p<0.05$), while EAU mice treated with GHRH antagonist have lower disease score ($P<0.01$), decreased fold change of RCT ($P<0.001$) and decreased Th17 cells ($P<0.01$).

Conclusions: Our results indicate that GHRH signaling is required in Th17-mediated autoimmune uveitis. GHRH signaling promotes EAU by increasing pathogenic Th17 cells, and Th17-lineage proinflammatory cytokines, but does not alter T cell activation and apoptosis.

CONTROL ID: 3712799

SUBMITTER (NAME ONLY): Blake Oberfeld

TITLE: Comparative Outcomes of Phacoemulsification combined with Hydrus or Kahook Dual Blade

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Oberfeld, N. Hall, D. Solá-Del Valle, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|B. Oberfeld, N. Hall, D. Solá-Del Valle, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Blake Oberfeld: Commercial Relationship: Code N (No Commercial Relationship) | Nathan Hall: Commercial Relationship: Code N (No Commercial Relationship) | David Solá-Del Valle: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Understanding the relative efficacy of different microinvasive glaucoma procedures (MIGS) is integral to clinical decision making. For the first time, this study compares outcomes of phacoemulsification combined with Hydrus Microstent (Phaco/Hydrus; Ivantis Inc., CA) or Kahook Dual Blade (Phaco/KDB; New World Medical, CA).

Methods: This retrospective study included patients who underwent Phaco/Hydrus or Phaco/KDB from January 2016 to 2021 at Massachusetts Eye and Ear. Baseline characteristics comprised demographic variables, corrected distance visual acuity, intraocular pressure (IOP), medication burden, glaucoma type, severity, and history of prior laser or surgery. Primary outcomes were IOP and medication burden evaluated by Generalized Estimating Equations (GEE). Two Kaplan-Meier Estimates (KM) assessed survival without additional glaucoma procedure or medication while maintaining: (1) IOP ≤21 mmHg and ≥20% IOP reduction or (2) IOP ≤ preoperatively designated goal.

Results: Mean preoperative IOP was 17.70 mmHg ± 4.91 (SD) on 0.28 ± 0.86 medications in the Phaco/Hydrus group (N=69) and 15.92 ± 4.34 mmHg on 0.19 ± 0.70 medications in the Phaco/KDB group (N=62). The Phaco/Hydrus group was more likely at baseline to have elevated IOP (p=0.02). All other baseline characteristics were statistically similar between surgeries. At 12 months, mean IOP was reduced to 14.98 ± 2.77 mmHg on 0.12 ± 0.60 medications after Phaco/Hydrus and 13.52 ± 4.13 mmHg on 0.04 ± 0.19 medications after Phaco/KDB. GEE models of IOP ($p<0.001$) and medication burden (p=0.04) had significant patterns of reduction across all timepoints, after adjusting for baseline IOP. There was no difference in the pattern of change in IOP (p=0.83) or medication burden (p=0.84) when evaluated over time between procedures, after adjusting for baseline IOP. Phaco/Hydrus and Phaco/KDB were not different in survival by KM1 (p=0.72) or KM2 (p=0.11).

Conclusions: Both Phaco/Hydrus and Phaco/KDB resulted in significantly reduced IOP and medication burden for more than 12 months. Reductions were not significantly different between surgeries. This study compared Phaco/Hydrus and Phaco/KDB for the first time to assert that the surgeries confer similar outcomes in IOP, medication burden, and survival estimates in a population with predominantly mild and moderate glaucoma.

CONTROL ID: 3712800

SUBMITTER (NAME ONLY): Lauren Mehner

TITLE: Effects of high altitude on development of retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.C. Mehner, B.D. Wagner, A.M. Lynch, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Lauren Mehner: Commercial Relationship: Code N (No Commercial Relationship) | Brandie Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Anne Lynch: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Low birth weight and gestational age are two of the most important risk factors for developing retinopathy of prematurity (ROP). Slow postnatal weight gain is also strongly associated with ROP. High altitude remains an important determinant of increased low birth weight rates in places such as Colorado, USA. The purpose of this study was to investigate whether maternal residence at high altitude alters the risk for ROP in premature infants.

Methods: This was a retrospective cohort study comparing elevation associated with the mother's residential zip code and rates of ROP in premature infants in a well characterized ROP registry cohort at a tertiary care facility in Colorado between January 2006 and December 2020. All infants in the study had a gestational age less than 31 weeks, birth weight less than 1500 grams, or an unstable clinical course according to current guidelines, as well as available maternal residential zip code information. Geocoding was performed in SAS by adding a latitude and longitude for the geographic center of each zip code. Coordinates for each zip code were exported and entered into https://apps.nationalmap.gov/elevation to obtain elevation. The resulting file was merged with the ROP registry dataset based on zip code.

Results: 1817 infants were included in the cohort, with 318 unique zip codes with associated elevation data (Figure 1). Elevation ranged from 0 to 10,000 ft, with the majority of births associated with elevations 4,000 - 7,000 ft. Higher elevation was associated with lower birth weight percentiles, higher gestational age and maternal age at delivery. These associations were similar when evaluating data specifically between 4,000 and 8,000 ft. Figure 2 demonstrates the nonsignificant distribution of ROP type by elevation. Severe ROP (type 1 or type 2) developed in 10.2% of infants (186/1817); there was no significant association between ROP and elevation after adjusting for gestational age, birth weight percentile and maternal age (p=0.25).

Conclusions: Despite the known increased rates of low birth weight in babies born to mothers living at high altitude, we found no significant association between altitude and ROP in premature infants in our cohort.

CONTROL ID: 3712801

SUBMITTER (NAME ONLY): Christine Kay

TITLE: Generation of qualitative evidence to support the content validity of the ViSIO-PRO and ViSIO-ObsRO in Retinitis Pigmentosa and Leber Congenital Amaurosis

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.N. Kay, University of Florida, Gainesville, Florida, UNITED STATES|I.S. Audo, Sorbonne Université, INSERM, CNRS, Institut de la Vision, CHNO des Quinze-Vingts, REFERET national rare disease center, INSERM-DGOS CIC1423, Paris, FRANCE|H. Bradley, M. Barclay, J. Sims, K. Boparai, N. Williamson, Adelphi Mill, Bollington, Cheshire, UNITED KINGDOM|F. Patalano, C. Naujoks, C. Spera, D. Viriato, J. Banhazi, Novartis Pharma AG, Basel, Basel-Stadt, SWITZERLAND|M. Fischer, Centre for Ophthalmology, University of Tübingen, Tübingen, GERMANY|M. Fischer, Oxford Eye Hospital, Oxford University NHS Foundation Trust, Oxford, UNITED KINGDOM|J. Green, Discipline of Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland, CANADA|T. Durham, Foundation Fighting Blindness Inc, Columbia, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual impairments associated with Retinitis Pigmentosa (RP) and Leber Congenital Amaurosis (LCA) have significant impacts on patients' vision-dependent activities of daily living (ADL) and broader health-related quality of life (HRQoL). Patient and observer-reported outcome (PRO/ObsRO) instruments can capture the patient or caregiver perspective in clinical trials and provide insights beyond clinical biomarkers. However, it is critical that such instruments have sufficient evidence of content validity (are appropriate for the target population). This study aimed to assess the content validity of the Visual Symptom and Impact Outcomes PRO (ViSIO-PRO) and ObsRO (ViSIO-ObsRO) instruments in RP/LCA.

Methods: Qualitative, semi-structured concept elicitation and cognitive debriefing interviews were conducted with 66 participants (33 adults, 10 adolescents, 8 children and 15 caregivers of children) in the US, France, Germany, and Canada. Patients had a clinical and genetic diagnosis of RP/LCA. Participants completed the ViSIO-PRO or -ObsRO instruments using a 'think aloud' technique to assess understanding, comprehension, and relevance of the items, instructions, response scales and recall period. Interviews were conducted in two rounds, allowing for modifications and subsequent retesting. Framework analysis of interview transcripts was performed.

Results: Participants demonstrated good understanding of the ViSIO-PRO and -ObsRO items (questions) and instructions across both rounds. Concepts assessed in the ViSIO-PRO and -ObsRO items were considered relevant to the majority of participants. The 7-day recall period and response scales were well understood and appropriately endorsed. Participant and expert clinician feedback supported the following modifications between rounds: 5 items were added to the instruments to assess additional concepts and 1 item was removed from the ViSIO-PRO due to

lack of relevance.

Conclusions: Findings support content validity of the ViSIO-PRO and ViSIO-ObsRO instruments as outcome assessments for use across RP/LCA genotypes. Further research to evaluate the psychometric validity of the instruments is underway and will support future use of the instruments as efficacy endpoints in clinical trials to support treatment benefit and in clinical practice to track disease severity.

CONTROL ID: 3712803

SUBMITTER (NAME ONLY): Sofia Padilla-Alanís

TITLE: Comparative Outcomes in Refractive Lens Exchange: Bilateral EDOF IOL vs. Mix and Match Approach in Emmetropic Presbyopic Patients.

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Padilla-Alanís, J.A. Nava-Garcia, J.C. Hernandez-Camarena, S. González-Godinez, G. Ortiz Morales, M.E. Quiroga-Garza, M.A. Salinas-Lugo, D. Bastán-Fabián, J.E. Arreola, J.E. Valdez, Institute of Ophthalmology and Visual Sciences, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To describe the refractive and visual outcomes at different distances (far and near) in different modalities in the approach of presbyopia in emmetropic patients.

Methods: We evaluated presbyopic patients with axial length (AL) between 22 and 24 mm who had undergone bilateral clear lens exchange. There were two surgical approaches: extended depth of focus (EDOF) only (n=16 eyes) and mix and match (MaM) approach (EDOF IOL in the dominant eye and trifocal IOL in the fellow eye), (n=12 eyes). At the 3-month postoperative visit, visual outcomes with undercorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), undercorrected near visual acuity (UNVA), corrected near visual acuity (CNVA) and refractive outcomes (residual spherical equivalent (SE)) were assessed.

Results: Mean age in all patients was 58.14 years and average AL was 23.39 mm. We had 8 male patients (2 in the MaM group and 6 in the EDOF only group) and 6 women (4 in the MaM group and 2 in the EDOF only group).

For the MaM group mean age was 54.4±4.27 years and mean AL was 23.12±6.45mm. CDVA and UDVA was 20/20 postoperatively. UNVA was Jaeger (J) 1 at 33 cm. Residual mean SE was -0.12±0.50 D. For the EDOF IOL mean residual SE was -0.08 D and for the trifocal IOL -0.16 D.

For the EDOF only group mean age was 61±8.05 years and mean AL was 23.58±0.47 mm. UDVA and CDVA was 20/20 postoperatively and UNVA was 20/20 at 33 cm. Residual mean SE was -0.50±0.58 D.

Conclusions: Visual outcomes were similar in both groups, both of which had high levels of visual satisfaction reported by the patient. We observed similar results in visual acuity both at far and near in both groups.

One of our limitations is that we have a small number of patients.

We are currently working in a larger patient data base along with taking into account more variables.

It is important to study more variables in order to determine which ones are relevant when deciding which approach we are taking in our patients giving them a more personalized surgical plan.

CONTROL ID: 3712804

SUBMITTER (NAME ONLY): Jie Gong

TITLE: Oxidative stress-mediated high-throughput screening identifies novel neuroprotective agents that protect RPE and rescues visual function in models of AMD

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gong, H. Cai, L.V. Del Priore, M.A. Fields, Department of Ophthalmology and Visual Science, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Jie Gong: Commercial Relationship: Code N (No Commercial Relationship) | Huey Cai: Commercial Relationship: Code N (No Commercial Relationship) | Lucian Del Priore: Commercial Relationship: Code N (No Commercial Relationship) | Mark Fields: Commercial Relationship(s);Code P (Patent):Yale University

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of visual impairment in the elderly. Oxidative stress and an aged or diseased Bruch's membrane contribute to the downstream dysfunction seen in retinal pigment epithelial (RPE) cells. The development of robust drug discovery platforms that can identify therapeutics that improve RPE cell function due to these insults would be beneficial. Herein, we demonstrate the use of a phenotypic high-throughput screening (HTS) platform to identify novel small molecules that improve RPE survival in vitro and a blue light damage model of retinal degeneration in vivo.

Methods: A HTS was conducted to identify compounds that protect RPE cells from oxidative damage. Cell viability was tested in models of RPE stress, including tert-butyl hydroperoxide (TBHP) exposure, ultraviolet-B (UV-B)-mediated light damage and nitrosative stress to the basement membrane. PCR and analysis of mitochondrial function were used to elucidate possible mechanisms of drug treatment. Sprague–Dawley CD-1 rats were exposed to blue light to induce dry AMD. Optical coherence tomography (OCT), hematoxylin and eosin, and immunofluorescence were performed to assess retinal structure. Electroretinography (ERG) was used to assess retinal function.

Results: Initial HTS of a library with 65,000 synthetic compounds (ChemDiv library) using TBHP, a chemical oxidizing agentidentified two compounds (M414 and M434) that significantly protect RPE from TBHP-induced cell death. M414 and M434 protected human RPE cells from UV-B light damage and enhanced cell viability on nitrite-modified basement membrane. Both compounds improved mitochondrial function and attenuated expression of mitochondrial apoptotic genes after oxidative damage to RPE cells. The retinal mid-layer thickness was significantly decreased after blue-light exposure in rats. The decreased retinal thickness and photoreceptor survival was improved after treatment with M414 and M434. Like the retinal structure changes, functional loss of ERG amplitude (from blue-light exposure) was restored after administration of both compounds.

Conclusions: Our data demonstrates the capacity of a HTS platform to identify novel small molecules that protect the retina from pathological factors associated with AMD.

CONTROL ID: 3712805
SUBMITTER (NAME ONLY): Manuel Quiroga-Garza
TITLE: Prevalence of corneal endothelial pleomorphism, polymegethism, and guttata in a Hispanic population.
SESSION TITLE: Corneal Endothelium
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M.E. Quiroga-Garza, G. Ortiz Morales, D. Bastán-Fabián, M.A. Salinas-Lugo, S. Padilla-Alanís, J.A. Nava-Garcia, D. Loya-Garcia, J.C. Hernandez-Camarena, A. Rodriguez-Garcia, J.E. Valdez, Ophthalmology, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|
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ABSTRACT BODY:

Purpose: To analyze the morphometric characteristics of the central corneal endothelium in healthy Hispanic adults 40-years and older from an eye health-care system.
Methods: A cross-sectional, descriptive, and analytical study was designed to assess central corneal specular microscopies of healthy adult Hispanic patients. Photographs of the central corneal endothelium were obtained using a Tomey EM-3000 non-contact specular microscope. We considered endothelial pleomorphism if <50% of cells were hexagonal, and polymegethism if the coefficient of variation was >40%.
Results: 702 eyes from 356 patients were included for study. The mean age was 69.76±10.72 years (range 42-93), with 195 female and 163 male patients included. The mean endothelial cell density (MCD) was 2255.09±488.07 cells/mm2; mean cell area was 458.85±166.62 µm2; and mean central corneal thickness was 522.37±39.97 µm. 75.64% of the patients had pleomorphic endothelium, with a significant difference in cell hexagonality between male and female patients ($p = 0.002$). Moreover, 48.43% of patients had polymegethism and 17.81% cornea guttata (CG); 64% of the CG patients were female.
Conclusions: MCD and cell hexagonality in this Hispanic population was lower than in other reports. A high rate of pleomorphism, polymegethism, and CG was observed. Considering the racial differences in the prevalence of CG established by other authors, our data reveal a high prevalence of this condition in this adult Hispanic population, with a higher preponderance of female patients. More information is needed regarding endothelial morphometric characteristics in Hispanics, as it represents a valuable tool to predict the stress response capability of this essential monolayer to insults. To our knowledge, this is the first study focusing on determining the prevalence of pleomorphism, polymegethism, and guttata in a Hispanic population.

CONTROL ID: 3712807
SUBMITTER (NAME ONLY): Abdullah Aleem
TITLE: Stabilized Optimization to Reduce Variance in Deep Learning Models Trained on Small Medical Datasets
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Aleem, R. Chan, P. Setabutr, D. Yi, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|
Commercial Relationships Disclosure: Abdullah Aleem: Commercial Relationship: Code N (No Commercial Relationship) | R.V. Paul Chan: Commercial Relationship: Code N (No Commercial Relationship) | Pete Setabutr: Commercial Relationship: Code N (No Commercial Relationship) | Darvin Yi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Deep learning models in the domain of (medical) computer vision have become increasingly complex and have a high capacity to learn any complex relationship in the data, but this comes at the cost of a high tendency to overfit which negatively impacts the model's ability to generalize and leads to poor performance on future data. Traditional methods of dealing with overfitting often fail due to limited amounts of data in the medical domain. This work presents the stabilized optimization method to train a deep learning model on small medical datasets with reduced variance.

Methods: Traditional methods to reduce overfitting which depend on regularization, drop out, input dimensionality, and batch size often fail on small datasets due to a limited validation set which is more prone to statistical variance and does not generalize well to our data. One naive method to reduce variance is ensembling multiple models and aggregating their predictions but this significantly increases the inference and training times.

Stabilized optimization is a two-step method to find a minimal variance model based on running metric performance. First, we stabilize the training process by finding optimal values for hyperparameters that affect training stability e.g. batch size by minimizing the metric running standard deviation. In doing so, we are actively selecting a model that has a stable performance on the validation set, which will most likely lead to a more generalizable performance outside that validation set. Once the training process is stabilized, we find optimal values for hyperparameters that improve performance e.g. learning rate by maximizing the metric running average to find the best model during the training process.

Results: We conducted experiments on UIC's ptosis dataset. Traditional methods maxed out on validation set for all hyperparameters and resulted in 98% AUCROC and 91% F1 score. An ensemble of 27 models improved performance to 99.5% AUCROC and 95.4% F1 score. The stabilized optimization method achieved 99.9% AUCROC and 96.4% F1 score and had 27 times faster inference time compared to the ensemble model.

Conclusions: Limited data in the medical domain makes it hard to use the traditional methods of handling overfitting. Stabilized optimization provides an effective and efficient method to train a deep learning model that generalizes well to the underlying small dataset and has less variance.

CONTROL ID: 3712808
SUBMITTER (NAME ONLY): Leticia Checo
TITLE: 24 month follow-up of Ahmed Clearpath® Glaucoma Drainage Device
SESSION TITLE: Clinical studies and trials
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: I. Wagner, S. Dorairaj, R.D. Ten Hulzen, Ophthalmology, Mayo Clinic Florida, Jacksonville, Florida, UNITED STATES|A. Ahuja, Charles E. Schmidt College of Medicine, Florida, UNITED STATES|A. Patel, Stanton College Preparatory High School, Florida, UNITED STATES|L. Checo, Research Collabotator Ophthalmology, Mayo Clinic Florida, Jacksonville, Florida, UNITED STATES|
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ABSTRACT BODY:

Purpose: To evaluate the efficacy of the new Ahmed ClearPath® glaucoma drainage device in the treatment of refractory primary open angle glaucoma (POAG).

Methods: Intraocular pressure (IOP), number of glaucoma medications, and complications were retrospectively reviewed in POAG patients over 18 years old who underwent Ahmed ClearPath® implantation surgery at our institution with 24 months of follow-up. Patients with previous ocular procedures such as phacoemulsification (n=11), Micropulse transscleral photocoagulation (n=7), and Xen gel stent implantation (n=4) were included.

Results: 12 eyes of 11 patients (mean age 72.3 ± 13.8 years) fit inclusion criteria and were enrolled. Most patients were Caucasian (n=9), female (n=11), and had severe POAG (n=11). Mean baseline IOP was 29.0 ± 7.6 and was reduced to 11.2 ± 3.9, 7.9 ± 4.2, 10.9 ± 5.6, and 11.2 ± 4.6 at 6, 12, 18, and 24 months respectively. Compared to baseline, IOP reductions were 61.4%, 72.8%, 62.4%, and 61.4%. 80% of patients who made the 24-month follow-up reached an IOP of ≤ 14 mmHg. Mean baseline number of medications was 3.0 ± 0.9 and was reduced to 0.67 ± 0.8, 0.57 ± 0.8, 0.7 ± 1.0, and 0.6 ± 0.5 at 6, 12, 18, and 24 months respectively. Compared to baseline, medication reductions were 77.7%, 81%, 76.3%, and 80%. Mild hyphema was noted as a post-operative complication in half of the population (n=6), but resolved during each one month follow-up. No long-term complications were observed.

Conclusions: To our knowledge, this is the first long-term study evaluating the efficacy of the Ahmed ClearPath drainage device in adult patients. The ClearPath device is safe and effective at reducing both IOP and medication burdens in patients with severe POAG. Additionally, minimal short-term complications were noted and no patients within our study experienced long-term adverse effects, increasing comfort for both the surgeon and the patient.

CONTROL ID: 3712811

SUBMITTER (NAME ONLY): Jean Adomfeh

TITLE: Association between sociodemographic factors and vision in adolescents in the United States

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Adomfeh, B.G. Jastrzembski, I. Oke, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Adomfeh, B.G. Jastrzembski, I. Oke, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Jean Adomfeh: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Jastrzembski: Commercial Relationship: Code N (No Commercial Relationship) | Isdin Oke: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Black, Hispanic, and children from less affluent homes are less likely to access eye health services. The aim of this study was to assess vision health disparities among United States (US) adolescents.

Methods: This cross-sectional study utilized the National Health and Nutrition Examination Survey (NHANES) from 2005-2008. Subjects included in the analysis were aged 12 to 18 years with a completed visual function questionnaire and eye examination. Outcomes included self-reported visual function and objective LogMAR visual acuity. Sociodemographic factors investigated included race, ethnicity, family income, and US citizenship status. Multivariable logistic and linear regression analyses were conducted to examine the association between the sociodemographic risk factors and each outcome, adjusting for age, sex, and all other covariates.

Results: The 3,006 participants included represent a survey-weighted 60 million US adolescents of which 15% were Black, 17% were Hispanic, 6% were non-US citizens, and 19% had a family income below the poverty threshold. There was increased odds of self-reported poor vision in subjects who were Black (OR=2.91; 95% CI=2.08-4.08; p<0.001), Hispanic (OR=2.96; 95% CI=1.82-4.81; p<0.001), and low-income (OR=2.39; 95% CI=1.59-3.59; p<0.001). There was a trend towards worse visual acuity in the worse-seeing eye in subjects who were Black (β=0.06; 95% CI=0.03-0.09; p<0.001), Hispanic (β=0.05; 95% CI=0.01-0.09; p=0.023), and non-US citizens (β=0.10; 95% CI=0.01-0.18; p=0.034). Similar relationships were observed in the visual acuity in the better-seeing eye.

Conclusions: Black race, Hispanic ethnicity, and low-income status increased the odds of self-reported poor vision and were associated with worse objective visual acuity in this nationally representative sample of US adolescents. Sociodemographic vision health disparities exist at an early age and interventions targeted towards younger children may be helpful to address future visual impairment.

CONTROL ID: 3712812
SUBMITTER (NAME ONLY): Lydia Kim
TITLE: U.S. Youth Opinions on Purchasing Eyeglasses Online
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Kim, A. Claus, A. Mubeen, University of Michigan College of Literature Science and the Arts, Ann Arbor, Michigan, UNITED STATES|J. Cho, S. Raven, M.A. Woodward, P. Newman-Casey, G. Wang, O. KILLEEN, University of Michigan Department of Ophthalmology and Visual Sciences, Ann Arbor, Michigan, UNITED STATES|T. Chang, University of Michigan Department of Family Medicine, Ann Arbor, Michigan, UNITED STATES|
Commercial Relationships Disclosure: Lydia Kim: Commercial Relationship: Code N (No Commercial Relationship) | Anne Claus: Commercial Relationship: Code N (No Commercial Relationship) | Amani Mubeen: Commercial Relationship: Code N (No Commercial Relationship) | Juno Cho: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Raven: Commercial Relationship: Code N (No Commercial Relationship) | Maria Woodward: Commercial Relationship: Code N (No Commercial Relationship) | Paula Anne Newman-Casey: Commercial Relationship: Code N (No Commercial Relationship) | Tammy Chang: Commercial Relationship: Code N (No Commercial Relationship) | Grace Wang: Commercial Relationship: Code N (No Commercial Relationship) | OLIVIA KILLEEN: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Online optical shops could improve access to eyeglasses, especially for youth, a generally technologically savvy segment of the population. We aimed to understand U.S. youth perceptions about purchasing eyeglasses online. We hypothesized that youth would be open to purchasing eyeglasses online.

Methods: An interactive text-messaging platform, MyVoice (www.hearmyvoicenow.org), sent five questions regarding eye care experiences to U.S. youth aged 14-24 years. Question five asked, “If you needed eyeglasses, how would you feel about getting them online?” The text message responses were coded by two investigators using modified Grounded Theory; disagreements were adjudicated by a third investigator.

Results: Of 1204 recipients, 88.3% (n=1063) responded. The mean age was 20.3 ± 2.4 years (range 15-24 years); 58.8% (n=625) were male; 74.0% (n=787) were white; 99.4% (n=1057) reported having access to technology, including laptops, desktops, smartphones, or tablets. Half (50.7%, n=539) felt positive about purchasing eyeglasses online (e.g. “I think it would be a good idea–more styles and cheaper”), while 35.4% (n=376) felt negative (e.g. “I would feel a little bit out of my depth, I think the optometrist would know best what to provide for eyeglasses”). Even some respondents who felt positive about purchasing eyeglasses online expressed specific concerns. The most prevalent concern among all respondents was a desire to try eyeglasses on prior to purchasing (n=102, e.g. “I would want to try them on first because I have a big head”).

Conclusions: Many U.S. youth are open to purchasing eyeglasses online, which could improve access to eyeglasses for this population. To overcome major concerns, online optical shops could offer the option to try frames before purchasing.

CONTROL ID: 3712815

SUBMITTER (NAME ONLY): Isaac Bleicher

TITLE: Outcomes of Far Posterior Open Globe Injuries: The Case for Zone 4

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Bleicher, G.W. Armstrong, E.D. Gaier, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|E.D. Gaier, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Isaac Bleicher: Commercial Relationship: Code N (No Commercial Relationship) | Grayson Armstrong: Commercial Relationship(s);Code O (Owner):Ocular Technologies Inc.;Code C (Consultant/Contractor):McKinsey & Company;Code C (Consultant/Contractor):Xenon-VR;Code C (Consultant/Contractor):Ophthalytics;Code C (Consultant/Contractor):Kriya Technologies;Code S (non-remunerative):American Medical Association | Eric Gaier: Commercial Relationship(s);Code C (Consultant/Contractor):Luminopia, Inc.;Code P (Patent):Luminopia, Inc.;Code C (Consultant/Contractor):Stoke Therapeutics Inc.

ABSTRACT BODY:

Purpose: Open globe injuries (OGIs) are categorized by zone of injury, with Zone 3 (Z3) defined as ≥5mm posterior to the corneal limbus. Heterogeneity in outcomes of Z3 OGIs precludes precise prognostication and surgical management decisions. We hypothesized that Z3 OGIs with far posterior wounds would have worse visual and anatomic outcomes.

Methods: We performed a retrospective review of Z3 OGIs with at least 30 days of follow-up treated at a tertiary care center over a 10-year period. Far posterior OGIs (pZ3) were defined as those with wounds extending ≥10mm posterior from the corneal limbus. Secondary surgeries, visual outcomes, and anatomic outcomes were compared between pZ3 and anterior Z3 (aZ3) eyes at presentation, the 3 months and the latest available timepoints after injury. Fisher's exact and Mann-Whitney U tests were used to compare pZ3 and aZ3 outcomes.

Results: Of 264 Z3 OGI eyes, 215 met inclusion criteria. Of these, 132/215 (61%) were classified as pZ3. pZ3 and aZ3 eyes underwent means (±SD) of 1.6±1.6 and 1.4±1.5 secondary procedures, respectively ($p>0.4$). At 3 months after injury, pZ3 eyes were less likely to maintain light perception or better vision (pZ3: 53%, aZ3: 77%), count fingers or better vision (pZ3: 28%, aZ3: 49%), or have ≥20/400 Snellen acuity (pZ3: 18%, aZ3: 39%)(p values≤0.01). These relationships were also seen at final follow-up for light perception (pZ3: 53%, aZ3: 71%), count fingers (pZ3: 27%, aZ3: 46%), and ≥20/400 acuities (pZ3: 17%, aZ3: 36%) (p values≤0.01). The effect of zonal group on count fingers and ≥20/400 acuity persisted even when excluding patients presenting without light perception (p values≤0.02). After OGI repair, pZ3 eyes were less likely to have improved visual acuity (pZ3: 34%, aZ3: 49%) and more likely to have reduced visual acuity (pZ3: 20%, aZ3: 7.2%) from presentation ($p<0.01$). A significantly greater proportion of pZ3 eyes became phthisical or were eviscerated/enucleated compared with aZ3 eyes (56% vs 40%, $p=0.02$).

Conclusions: Eyes with OGIs extending ≥10 mm posterior to the corneal limbus have poorer visual and anatomic outcomes compared to those limited to the more anterior Z3. While the potential for recovery in posterior OGIs necessitates careful assessment and emergent repair in all cases, further zonal categorization within zone 3 injuries may help improve prognostic precision and refine surgical approaches.

CONTROL ID: 3712816

SUBMITTER (NAME ONLY): Dawei YANG

TITLE: A deep-learning based diabetic macular ischemia classification on OCT-angiography images for predicting diabetic retinopathy progression and diabetic macular oedema development

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.G. YANG, C.Y. Cheung, A. RAN, F. Tang, The The Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Dawei YANG: Commercial Relationship: Code N (No Commercial Relationship) | Carol Cheung: Commercial Relationship: Code N (No Commercial Relationship) | Anran RAN: Commercial Relationship: Code N (No Commercial Relationship) | Fangyao Tang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously developed a deep-learning system (DLS) to identify diabetic macular ischemia (DMI) on superficial capillary plexus(SCP) and deep capillary plexus(DCP) of optical coherence tomography angiography (OCT-A) images. We aim to further investigate whether the DLS-based DMI classification provides prognostic values on diabetic retinopathy (DR) progression and diabetic macular oedema (DME) development in a cohort of patients with diabetes mellitus (DM).

Methods: This is a retrospective longitudinal study with 293 eyes from 164 patients with DM being followed up for at least 4 years.Image quality assessment and DMI assessment of all OCT-A images were first performed by the previously developed DL system. The presence of DMI was defined as images exhibiting disruption of fovea avascular zone (FAZ) or/and additional areas of capillary non-perfusion in the macula accorded with ETDRS protocols. Cox proportional-hazards model was used to evaluate the relationship of the binary DMI classification (presence or absence of DMI) to DR progression and DME development.

Results: Over a median follow-up of 54.09 ±4.67 months, 89 eyes (33.97%) had DR progression, and 34 eyes (12.98%) developed DME. SCP-DMI classification outcome (hazard ratio [HR], 3.451; 95% confidence interval [CI], 2.062 to 5.776; p <0.001) and DCP-DMI classification outcome (HR, 4.992; 95% CI, 2.884 to 8.645; p <0.001) were significantly associated with DR progression; while only DCP-DMI classification outcome (HR, 1.758; 95% CI 0.753 to 4.122; p <0.001) was associated with DME development after adjusting for age, duration of diabetes, fasting glucose, glycated hemoglobin, mean arterial blood pressure, baseline DR severity, average GCIPL thickness, and smoking status at baseline. Compared with the model based on identified risk factors alone, the addition of DMI classification outcomes improved the predictive discrimination of DR progression (SCP-DMI, C-statistics 0.741 vs. 0.696, p < 0.001; DCP-DMI, C-statistics 0.772 vs. 0.696, p < 0.01) and DME development (DCP-DMI, C-statistics 0.702 vs. 0.663, p = 0.076) in diabetic eyes.

Conclusions: The DL-based DMI outcomes demonstrated prognostic values for DR progression and DME development.

CONTROL ID: 3712818

SUBMITTER (NAME ONLY): Jorge Valdez

TITLE: Cataract surgery in challenging post refractive surgery scenarios.

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Valdez, S. Padilla-Alanís, G. Ortiz Morales, M.E. Quiroga-Garza, D. Bastan-Fabian, M.A. Salinas-Lugo, J.E. Arreola, J.A. Nava-Garcia, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To describe the refractive management, visual outcomes and patient satisfaction with refractive cataract surgery in challenging cases.

Methods: Retrospective chart review of selected cases. Throughout decision-making of refractive options after an exhaustive ophthalmological evaluation including IOL selection, aberrometry and surgical options was performed in agreement with all patients.

Results: Five challenging scenarios are reported with their management of refractive error. Case 1 presents a 54 year-old male with a history of LASIK surgery and clear lens, looking for refractive management. Multifocal IOLs were implanted in both eyes achieving UCVA of 20/20 in both eyes and UNVA of J1. Case 2 is a 72 year-old female with a history of LASIK surgery with a central island in the left eye presenting with bilateral cataract. Cataract surgery was performed with multifocal IOL in the right eye and monofocal IOL in the left eye, achieving a 20/20 uncorrected visual acuity (UCVA) and uncorrected near vision acuity (UNVA) of Jaeger (J) 1. Case 3 is a 59 year-old female with a history of RK presenting with bilateral cataract. Cataract surgery was performed with bilateral multifocal IOL implantation, achieving 20/20 UCVA in both eyes and UNVA of J3. Case 4 presents a 65-year-old female with a history of radial keratotomy (RK) with clear lens looking for refractive treatment. Right cornea was highly aberrated so monofocal IOL was implanted and a multifocal toric IOL in the left eye, achieving UCVA 20/20 in the right eye and 20/25 in the left eye, with a UNVA of J1.

Case 5 presents a 53-year-old male with a history of post-LASIK ectasia in the right eye, treated with penetrating keratoplasty (PKP) in which residual astigmatism was treated with LASIK plus enhancement 10 years later. The patient was seeking refractive management so a toric IOL was implanted, achieving a UCVA of 20/50.

Conclusions: Past history of refractive surgery and/or corneal disease makes for complex decision-making during the assessment for cataract surgery. Although challenging, the armamentarium of refractive options allows for excellent visual outcomes with great patient satisfaction.

CONTROL ID: 3712819

SUBMITTER (NAME ONLY): Radouil Tzekov

TITLE: Correlation between oscillatory potentials and photopic negative response amplitudes in a clinical setting

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.T. Tzekov, S. Safari, K. Tsay, Ophthalmology, University of South Florida, Tampa, Florida, UNITED STATES|R.T. Tzekov, C.L. Passaglia, Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|J.J. Kremers, Universitatsklinikum Erlangen Augenklinik, Erlangen, Bayern, GERMANY|D. Drucker, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: According to data presented before (IOVS 2019 v.60:5969), a strong correlation between the timing of retinal ganglion cell bursts and oscillatory potential (OP) peaks was observed when bright white flashes were presented in rats. Based on that, a hypothesis can be put forward about the existence of a correlation between OPs and the photopic negative response (PhNR) of the full-field electroretinogram (ERG). The purpose of the current study was to compare OP amplitude and PhNR parameters in patients with various retinal pathologies.

Methods: A retrospective chart review and data analysis of patients aged 18 and over undergoing routine ERG testing at USF Eye Institute (Tampa, FL) was conducted. The Photopic 3.0 ERG responses (LA 3.0) were analyzed. Ph3 responses were recorded using DTL electrodes, white xenon flash (2.5 cd.s/m^2) on a white background (30 c/m^2) with a digitization rate of 3750 Hz and bandpass filtering range of 0.3 to 1500 Hz. The ERG signal was filtered using high-pass 4^{th} order Butterworth filter with 58 Hz cut-off frequency. The root means square (RMS) of the filtered signal was calculated for the OP portion of the signal. The OP RMS values were compared (linear regression) to the amplitude of the PhNR response, determined in 3 different ways: measured from the isoelectric baseline (fB), measured from the b-wave peak (fP) and as an area under the curve (AUC).

Results: The records of 11 patients/20 eyes (2M, 9F); mean age 46.7 +/-14.6 yrs. were evaluated. The correlation between OP RMS and PhNR(fB) was moderate at R^2=0.5515 ($p<0.001$), while the correlation with PhNR(fP) was considerably better at R^2=0.8222 ($p<0.001$). Furthermore, several models of a linear regression between OP RMS and AUC extended to different time points after b-wave peak (every 5 ms form 5 ms to 50 ms after b-wave peak), which indicated a good correlation across the range (R^2 0.82 to 0.89) with the best regression model at 15 ms after b-wave peak (R^2 = 0.8875, $p<0.0001$).

Conclusions: A reasonably strong correlation was observed between OP parameters and PhNR amplitude. That supports a relationship between OP amplitude and PhNR under LA 3.0 recoding conditions, which has applicability in clinical practice, especially when determining the amplitude of PhNR with traditional methods is unreliable.

CONTROL ID: 3712820

SUBMITTER (NAME ONLY): Neha Sharma

TITLE: Macular Holes in Patients with Tractional Retinal Detachments due to Proliferative Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Sharma, C. Akotoye, A.K. Wu, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|R.C. Sastry, A.K. Wu, A. Rachitskaya, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Neha Sharma: Commercial Relationship: Code N (No Commercial Relationship) | Christian Akotoye: Commercial Relationship: Code N (No Commercial Relationship) | Resya Sastry: Commercial Relationship: Code N (No Commercial Relationship) | Anna Wu: Commercial Relationship: Code N (No Commercial Relationship) | Aleksandra Rachitskaya: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon, Zeiss, Novartis, Genentech;Code S (non-remunerative):Regeneron;Code F (Financial Support):Genentech, AGCT, Novartis, Appelis | Rishi Singh: Commercial Relationship(s);Code I (Personal Financial Interest):Novartis, Genentech, Regeneron, Alcon, Bauch and Lomb, 41 Gyroscope;Code F (Financial Support):Apellis, Aerie, Graybug

ABSTRACT BODY:

Purpose: Macular holes (MH) can be seen in patients with tractional retinal detachment (TRD) and proliferative diabetic retinopathy (PDR). However, there is a paucity of literature examining the characteristics of these macular holes and the visual outcomes after surgical intervention. This study aimed to characterize the features of TRD MHs in PDR patients, the rate of MH closure following surgical intervention, and the preoperative and intraoperative factors affecting hole closure and visual outcomes.

Methods: A retrospective chart review was conducted for adults diagnosed with a MH secondary to TRD who underwent pars plana vitrectomy (PPV) surgery at Cole Eye Institute between January 2015 and August 2021. Collected variables include patient demographics, procedure performed, rate of MH closure, visual acuity (VA) and OCT biomarkers at time of diagnosis and post-operatively at 3, 6, and 12 months. Fisher's exact test, paired t-test, and p=0.05 were used for statistical analysis.

Results: The final cohort consisted of 11 patients and 11 eyes (8 females, average age of 57.6 years old) who developed a MH secondary to TRD. The mean HbA1c was 8.35%. Five MHs (45.5%) were associated with subretinal fluid, 5 (45.5%) were associated with vitreomacular traction, and 2 (18.2%) were associated with epiretinal membrane. Average MH size was 383.1 μm. During PPV, 12 (85.7%) patients underwent concurrent procedures, including internal limiting membrane (ILM) peeling (2, 18.2%) and/or phacoemulsification and intraocular lens placement (7, 63.6%). Tamponade choice included C3F8 gas for most patients (n=7; 63.6%), air for 1 (9.1%), SF6 gas for 1 (9.1%), and silicone oil for 2 (18.2%). Nine patients (81.8%) achieved MH closure 3 months after surgery. One (9.1%) achieved MH closure after a singular re-operation. There was borderline significance between presence of concurrent procedure and successful MH closure (p=0.0545), and no significance between use of long-acting (C3F8) tamponade and successful MH closure at 3 months (p=0.4909). The mean VA at baseline and 12 months was 1.197 logMAR (20/315) and 0.981 logMAR (20/191), respectively (p=0.185).

Conclusions: This study showed that the majority (81.8%) of repaired MHs secondary to TRD remained closed at the 3-month follow-up without further re-operation. Despite closure, the long-term visual outcomes in patients with TRD macular holes are limited.

CONTROL ID: 3712821

SUBMITTER (NAME ONLY): Ashton Perlroth

TITLE: Visual Outcomes post-PPV for Tractional Retinal Detachment or Vitreous Hemorrhage in the Intelligent Research in Sight (IRIS) Registry

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.T. Perlroth, A. Brant, K. Mishra, H. Bair, C. Xu, D.V. Do, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|S. Pershing, D.V. Do, Ophthalmology, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|S. Pershing, Spencer Center for Vision Research, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with active Proliferative Diabetic Retinopathy (PDR) who develop non-clearing vitreous hemorrhage (VH) and macula-involving tractional retinal detachment (TRD) often undergo surgery with pars-plana vitrectomy (PPV). Our understanding of their visual prognoses remains limited. The purpose of this study was to determine visual acuity outcomes after PPV for TRD and VH patients in the IRIS Registry.

Methods: Patients were identified in the IRIS registry who received a new diagnosis of PDR who then developed either VH or TRD and underwent PPV within 90 days. The distribution of visual acuity in logMAR was evaluated at time points three months pre-PPV to one-year post-PPV, and the difference in mean logMAR one-year post-PPV was compared to one-week pre-PPV with an independent t-test. We further stratified by pseudophakic and phakic patients.

Results: Between 2016 and 2018, 1851 PDR eyes who developed VH underwent PPV and 553 with TRD underwent PPV. 18.8 % of VH eyes were pseudophakic preoperatively compared with 19.2% of TRD eyes, compared with 36.4% and 39.4% after one year post PPV. For TRD, preoperative visual acuity was 1.62 (phakic) and 1.59 (pseudophakic) logMAR and one-year postoperative VA was 1.35 and 1.35, and the difference was not significant (p=0.189 and p=0.260). For VH, preoperative visual acuity was 1.65 (phakic) and 1.73 (pseudophakic) logMAR and one-year postoperative VA was 0.84 and 0.83, and the difference was not significant (p=0.001 and p=0.001). On average, phakic eyes gained 0.82 logMAR and pseudophakic eyes gained 0.89 logMAR. Of note, for VH, the vast majority of improvement came within the first postoperative month.

Conclusions: Patients with PDR who developed TRD and underwent PPV on average presented legally blind (1.62 and 1.59 for phakic and pseudophakic) and did not significantly improve one year after PPV (1.35 and 1.35). Patients with PDR who developed VH and underwent PPV on average presented legally blind (1.66 and 1.73 for phakic and pseudophakic eyes) and improved significantly to 0.84 and 0.83 logMAR after one year, with the vast majority of improvement coming in the first month (1.06 and 1.13). For both TRD and VH, 1 week preoperative and 12 month postoperative VA was not significantly different between phakic and pseudophakic patients, and TRD and VH underwent post-PPV cataract surgery at similar rates.

CONTROL ID: 3712822

SUBMITTER (NAME ONLY): Medi Eslani

TITLE: Comparison between New Perimetry Device (IMOvifa®) and Humphrey Field Analyzer

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Eslani, T. Nishida, S. Moghimi, J.M. Arias, C. Vasile, V. Mohammadzadeh, R.N. Weinreb, Hamilton Glaucoma Center, Shiley Eye Institute, Viterbi Family Department of Ophthalmology,, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the performance of IMOvifa®, a new perimeter which performs visual field (VF) testing outside an examination darkroom, and compare with Humphrey Field Analyzer (HFA).

Methods: In this cross-sectional study, 138 eyes (including 25 healthy, 48 glaucoma suspects, and 65 primary open angle glaucoma) of 69 patients were evaluated. Patients were required to be experienced with the visual field testing performed on the HFA. All patients first underwent HFA 24-2 SITA-Fast and then IMOvifa® 24-2 AIZE-Rapid, which is comparable with SITA-Fast, for both eyes on the same day. Mean deviation (MD), pattern standard deviation (PSD), foveal threshold (FT), and visual field index (VFI) were compared between the two perimeters using Wilcoxon signed-rank tests, and Pearson's and Bland-Altmann correlation. Measurement time for performing VF for both eyes was also collected for each device.

Results: Measurement time was significantly faster for IMOvifa® compared to HFA (256sec vs 419sec, P<0.001). Rim artifacts were observed in 18 eyes (13.0%) with IMOvifa® and in 5 eyes (5.1%) with HFA. No differences were seen in mean MD (95% CI) -3.1 (-3.9, -2.4) dB for HFA vs. -3.1 (-3.8, -2.4) for IMOvifa®, and VFI 93.1 (91.1, 95.1) % for HFA vs 92.6 (90.4, 94.9) % for IMOvifa® (both P>0.05). Significant differences were seen in mean PSD 3.2 (2.7, 3.6) dB for HFA vs 4.1 (3.5, 4.6) for IMOvifa® (P<0.001), and FT 33.9 (33.1, 34.6) dB for HFA vs 30.6 (29.3, 31.9) dB for IMOvifa® (P<0.001). Pearson's r was strong for MD (r=0.90, P=<0.001), PSD (r=0.78, P<0.001) and VFI (r=0.94, P<0.001), but not for FT (r=0.21, P=0.023). Bland−Altman scatterplots showed reasonable agreement between the two perimeters (Figure 1).

Conclusions: IMOvifa® reduced measurement time by 38.9%. MD, PSD, and VFI values for IMOvifa® were highly correlated with HFA. This new perimeter appeared to reduce fatigue for both patient and examiner. Additional studies are needed to determine if it be useful for routine visual field testing of glaucoma.

CONTROL ID: 3712824

SUBMITTER (NAME ONLY): Ana Ponce Horta

TITLE: Functional Predictive Value of a Novel Classification System by Anterior Segment OCT in Assessing Filtering Blebs

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Ponce Horta, J.A. Paczka, A. Tornero-Jimenez, INSTITUTO DE OFTALMOLOGIA Y CIENCIAS VISUALES, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|D. Valencia Paredes, RESEARCH DEPARMENT, Unidad de Diagnóstico Temprano del Glaucoma, MEXICO (MEX), Jalisco, MEXICO|A.M. Ponce Horta, J.A. Paczka, A. Tornero-Jimenez, Asistencia e Investigación en Glaucoma, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Trabeculectomy is the most practiced surgery in glaucoma, and filtering blebs are usually studied with multiple classifications. The weak correlation of an anterior segment OCT (AS-OCT) classification with IOP in a preliminary cross-sectional study (ARVO 2021) suggested that the classification could have some predictive value. The objective of this study is to analyze the correlation between the Novel Classification System by AS-OCT (NOCTS) and the combination of NOCTS and the Würzburg classification (NOCTS+WC) with the filtering bleb functionality in a longitudinal study.

Methods: Longitudinal study of non-consecutive cases of patients with trabeculectomy. Fifty eyes of thirty-three patients were included. Filtering blebs were examined using the WC (score range, 0-12). A series of AS-OCT images were also evaluated using NOCTS (score range, 0-6) to evaluate 3 tomographic traits of the filtering bleb (wall thickness, cystic spaces and wall inner reflectivity). A weighted score was assigned to each item for every examined case. The blebs were subclassified into 4 types according to their outcome (complete success, qualified success with compression, qualified success with hypotensive drugs, and failure). The correlation between NOCTS, WC and NOCTS+WC with the baseline outcome and after one year of follow-up were analyzed, considering a p-value of ≤ 0.05 as statistically significant.

Results: Patients had a mean age of 60.1±17.7, predominantly female (72.7%), with POAG (51.5%), and pseudophakic (62%). The mean time after trabeculectomy was 49.5±64.1 months. The correlation of NOCTS with the baseline outcome was weak to moderate (r=0.372, p=0.008), and moderate at one year of follow-up (r=0.477 p=0.0001). The correlation of WC with the baseline outcome (r=0.623, p=0.0001) and at one year of follow-up were moderate to strong (r=0.689, p=0.0001). NOCTS+WC score had a strong correlation with the baseline outcome (r=0.788, p=0.0001), as well as at one year of follow-up (r=0.756, p=0.0001).

Conclusions: The combination of clinical and tomographic systems outperformed isolated evaluation with each of these systems, both at baseline, as well as at the one-year post-trabeculectomy outcome. Prospective studies with longer follow-up and larger samples are required to determine this new approach to classify filtering blebs.

CONTROL ID: 3712826

SUBMITTER (NAME ONLY): Zhidong Li

TITLE: M2 phenotype microglia polarization is neuroprotective in ischemic/reperfusion model of acute hypertensive glaucoma

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Li, W. Su, Y. Zhuo, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Zhidong Li: Commercial Relationship: Code N (No Commercial Relationship) | Wenru Su: Commercial Relationship: Code N (No Commercial Relationship) | Yehong Zhuo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ischemic/reperfusion injury induced neuroinflammation play crucial role in glaucomatous optic neuropathy. While the role of microglia in acute glaucoma and underlying mechanisms remain unclear. Here we investigate the effect and associated mechanism of microglia polarization in an acute hypertensive glaucoma model.

Methods: An acute hypertensive glaucoma model with substantial elevation of intraocular pressure (IOP) was established in adult C57BL/6 mice. Changes of miRNAs at different time point was detected by Real-time PCR. MiRNA-124 was administered intravitreally after model establishment. Retinal ganglion cells survival was evaluated by fluorescence stain and light microscopy. Inflammatory cytokines was detected by qRT-PCR. The number of CD86+ or CD206+ microglia in retina was measured by Flow Cytometry. Two-tailed Student's t-test was used for statistical analysis.

Results: Level of miRNA-155 were elevated in an early stage and remained for long period compared to control group, while miRNA-124 was elevated in a late stage. Treatment with miRNA-124 effectively increased retinal thickness and promoted ganglion cells survival(81.45±5.39%) compare to I/R injury alone(58.94±2.55%, $p<0.05$). Cytokines of IL-1β, iNOS and transcription factor C/EBP-α were suppressed, while TGF-β and Arg-1were promoted. Intravitreal miRNA-124 also decreased the number of CD11b+/CD86+ M1 microglia(36.4±2.35% vs 25.5±4.18%, $p<0.05$), and increased the number of CD11b+/CD206+ M2 microglia(21.3±3.64% vs 36.9±5.81%, $p<0.05$).

Conclusions: Our results indicated that miRNA-124 could alleviate retina injury and promote RGCs survival, by downregulating the expression of inflammatory cytokines. Intravitreal miRNA-124 altered the polarization of retinal microglia and regulate to neuroprotective M2 phenotype. Further experiments will be needed to understand underlying mechanisms.

CONTROL ID: 3712828

SUBMITTER (NAME ONLY): Siyan Zhu

TITLE: RPE utilizes proline through proline dehydrogenase to support retinal metabolism

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zhu, R. Xu, Y. Wang, J. Du, Ophthalmology, West Virginia University, Morgantown, West Virginia, UNITED STATES|S. Zhu, R. Xu, Y. Wang, J. Du, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|

Commercial Relationships Disclosure: Siyan Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Rong Xu: Commercial Relationship: Code N (No Commercial Relationship) | Yekai Wang: Commercial Relationship: Code N (No Commercial Relationship) | Jianhai Du: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously reported that the retinal pigment epithelium (RPE) preferentially metabolizes proline into TCA cycle metabolites and non-essential amino acids (NEAAs), which are exported to be utilized by the neural retina. Proline dehydrogenase (PRODH) is a key enzyme in proline catabolism. In this study, we aim to test the hypothesis that PRODH controls proline utilization and its metabolic support to the neural retina.

Methods: We obtained PRODH deficient (PRO/Re) mice and their parental control strain (C57BL/6J) from the Jackson Laboratory and validated the deficiency of PRODH expression in liver, RPE, and retina by Western blot. We measured the steady-state proline level in the plasma and RPE from PRO/Re mice by Gas Chromatography and Mass Spectrometry (GC MS). To study whether proline utilization was blocked in vivo in PRODH deficient mice, we delivered either ^{13}C or ^{15}N proline through retro-orbital injection to trace proline-derived TCA cycle metabolites and NEAAs using GC MS.

Results: In the wildtype (WT) C57BL/6J mice, PRODH protein was abundant in the liver and RPE, but much lower in the retina. In PRO/Re mice, however, PRODH protein was undetectable in the liver, RPE, and retina. We also found the steady-state proline was substantially accumulated in both the plasma and RPE from PRO/Re mice. These results validate that PRODH is deleted in the PRO/Re mice. Tracing isotope-labeled metabolites in vivo showed proline-derived TCA cycle metabolites and NEAAs were highly enriched in the RPE and retinas from the WT mice. However, in the PRODH deficient mice, both ^{13}C or ^{15}N proline were accumulated in the RPE, and proline-derived metabolites were almost abolished in the retina.

Conclusions: Proline catabolism through PRODH occurs mainly in the RPE but not the neural retina. RPE catabolizes proline into mitochondrial intermeidates and amino acids to provide substrates for retinal metabolism.

CONTROL ID: 3712829

SUBMITTER (NAME ONLY): Praruj Pant

TITLE: Retinal detachment after keratoprosthesis implantation: risk factors and visual outcomes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Pant, C. Robbins, C. Wisely, R. Gabriel, S. Fekrat, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Praruj Pant: Commercial Relationship: Code N (No Commercial Relationship) | Cason Robbins: Commercial Relationship: Code N (No Commercial Relationship) | Clayton Wisely: Commercial Relationship: Code N (No Commercial Relationship) | Rami Gabriel: Commercial Relationship: Code N (No Commercial Relationship) | Sharon Fekrat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare eyes that developed a retinal detachment (RD) after keratoprosthesis (K-Pro) implantation to those that did not.

Methods: Retrospective review of patients who underwent K-Pro implantation at Duke Eye Center between 2009 and 2018. Demographics, past ocular history, surgical outcomes, and visual outcomes were collected at 3 months, 12 months, 24 months, and 36 months after K-Pro and compared between two cohorts: 1) eyes that developed RD after K-Pro and 2) eyes that did not develop RD after K-Pro.

Results: 87 eyes that underwent K-Pro implantation were identified - 14 of which developed RD after K-Pro and 73 which did not. There was no significant difference in the age, sex, or race of patients who did or did not develop RD after K-Pro. There was no difference in past ocular surgical history or indication for K-Pro between the patients who did and did not develop RD after K-Pro. Among the 14 eyes that developed RD after K-Pro, RD developed between 72 and 229 days postop. Eyes with RD after K-Pro were more likely to have had a pars plana vitrectomy (PPV) prior to, at the same time as, or after K-Pro but before RD (11/14, 78.6%) when compared to eyes which did not develop RD (35/73, 47.9%), $p = 0.035$. Additionally, patients who developed RD after K-Pro were significantly more likely to have had PPV and endophthalmitis (4/14, 29%) compared to eyes which did not develop RD (3/73, 4%), $p = 0.002$. There was no difference in mean visual acuity between groups at 3 months, 12 months, and 24 months after K-Pro. Eyes that developed RD after K-Pro had significantly lower visual acuity at 36 months (20/8000) vs eyes that did not (20/800), $p = 0.036$.

Conclusions: Endophthalmitis and history of PPV either before or after K-Pro are risk factors for the development of RD after K-Pro. Eyes with and without RD after K-Pro had similar visual outcomes at 24 months but not 36 months after K-Pro.

CONTROL ID: 3712830

SUBMITTER (NAME ONLY): Caitlin Samson

TITLE: Pediatric Uveitis: Characteristics of Patients with both Arthritis and Uveitis Treated at a Tertiary Care Center

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.I. Samson, B. Glick, G. Fridman, C.M. Samson, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|C.I. Samson, Brandeis University, Waltham, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the characteristics of patients affected by both arthritis and uveitis.

Methods: Retrospective chart review of pediatric patients, age 18 or less, diagnosed with both uveitis and arthritis at the Manhattan Eye, Ear, and Throat Hospital between 2017 and 2021. Outcome measures included arthritis type, severity, course and relative severity of disease between uveitis and arthritis

Results: Thirty-three patient charts were reviewed. Thirty patients were female (90.9%). Anterior uveitis was the most common type, accounting for 97% of cases. Juvenile idiopathic arthritis (JIA) accounted for 90.9% of uveitis etiologies: oligoarticular (74.2%), polyarticular (22.6%), and psoriatic (3.2%). Thirty-two patients (97%) had bilateral involvement of uveitis. Thirty patients (90.9%) required immunomodulatory therapy. Arthritis severity was classified as follows: mild (60.6%), moderate (35.4%), and severe (3%). Uveitis was relatively more severe compared to arthritis in 72.7% of patients, less severe in 18.2% and equivocal in 9.1%. Of the 6 patients in whom arthritis was the more severe condition, 2 initially had uveitis as the more severe condition. No patients suffered functional disability from their arthritis.

Conclusions: In pediatric uveitis, arthritis often plays a significant role in the disease course and treatment choices. In some patients with severe uveitis, arthritis can later become the predominant clinical condition. Functional disability from arthritis was absent from this cohort.

CONTROL ID: 3712831

SUBMITTER (NAME ONLY): Akosua Asare

TITLE: Coarse stereopsis prior to strabismus surgery is associated with post-surgical ocular alignment in children

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Asare, E. Chang, C. Mulholland, C. Lyons, D. Giaschi, Ophthalmology and Visual Sciences, The University of British Columbia, Vancouver, British Columbia, CANADA|K. Meier, Psychology, University of Washington, Seattle, Washington, UNITED STATES|L. Wilcox, Psychology, York University, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Depth information can be extracted from small retinal disparities (fine stereopsis) and from large disparities that give rise to diplopia (coarse stereopsis). Previously, we showed retrospectively that some children with strabismus have intact coarse stereopsis when fine stereopsis is disrupted, and these children have better ocular alignment after strabismus surgery. Here we describe a prospective study to assess three pre-surgical measures that may predict ocular alignment after strabismus surgery: fine stereopsis, coarse stereopsis, and global motion thresholds, all of which have been shown to be sensitive to disruption of binocular vision.

Methods: Eleven children aged 4-14 years were assessed before and 4-15 months after alignment surgery. Depth-discrimination accuracy (nearer/farther) was measured for cartoon characters relative to a 0-disparity reference frame. 3D stimuli were presented using shutter glasses, with disparities categorized as fine (0.02, 0.17, 0.67 deg) or coarse (2.0, 2.5, 3.0 deg), based on previous work. The stimuli were aligned for each child and presented 20 times per disparity in random order. Global motion direction-discrimination (left/right) coherence thresholds were measured using a staircase procedure. The clinical outcome measure was ocular alignment (prism diopters) after surgery.

Results: Prior to surgery, depth-discrimination accuracy in the fine disparity range was near chance in all children regardless of post-surgical alignment. In the coarse disparity range, the association between pre-surgical depth-discrimination accuracy and post-surgical alignment was large ($r = -0.65$): children with higher accuracy showed smaller misalignment after surgery. For pre-surgical motion direction-discrimination, children with lower thresholds (better performance) showed smaller misalignment after surgery ($r = 0.82$). The association between coarse depth discrimination and motion direction discrimination prior to surgery was moderate ($r = -0.47$).

Conclusions: Our preliminary findings suggest that coarse, but not fine, stereoscopic performance may be useful for predicting ocular alignment outcomes after strabismus surgery. Coarse stereopsis matures before fine and may be important for coordinated binocular eye movements. Future research will determine if pre-surgical global motion perception provides independent information for predicting alignment outcomes.

CONTROL ID: 3712832

SUBMITTER (NAME ONLY): Darrian Kelly

TITLE: Detecting Molecular Features of the Interphotoreceptor Matrix and Outer Segments with Multiple Attenuated Internal Reflectance (MAIR) Infrared (IR) Spectroscopy

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kelly, C. Gouya, O. Liu, Research Mississippi Inc, Jackson, Mississippi, UNITED STATES|F. Gonzalez-Fernandez, Ophthalmology & Pathology, University of Mississippi School of Medicine, Jackson, Mississippi, UNITED STATES|A. Janorkar, Biomedical Materials Science, University of Mississippi Medical Center, Jackson, Mississippi, UNITED STATES|F. Gonzalez-Fernandez, Research and Development Service, Veterans Affairs Medical Center, Jackson, Mississippi, UNITED STATES|M. Kim, Clinical Research, Southern Therapy and Advanced Research, Jackson, Mississippi, UNITED STATES|

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ABSTRACT BODY:

Purpose: Challenges persist in determining the molecular features of intact retina tissue. IR spectroscopy measures the appearance of vibration and absorption for atomic bonds, and advances in MAIR allow IR to be applied to nontransparent samples. We sought to identify signature peaks in the complex retina spectra and assign them to anatomic and biochemical processes.

Methods: We obtained retina and RPE-choroid from adult albino Sprague Dawley rats for four experiments. Dissections were done in 10 min of bright light or under dim red light only. In two experiments, rod outer segments were isolated by titration and centrifugation at 15,000 xG for 5 min at 4 °C. The supernatant corresponded to the soluble interphotoreceptor matrix (IPM). Retinas, RPE-choroid, 50 ul of rod outer segment suspensions, purified outer segments and IPM supernatant were transferred to separate polyethene (PE) membranes. Sample tissue, extract and fluid were air dried on membranes to avoid a strongly absorbing H_2O IR peak. We used a PE membrane negative control to distinguish its peaks from sample peaks. The samples on membranes were analyzed by MAIR-IR spectroscopy.

Results: Washed and unwashed retina had complex spectra including peaks at 1737, 1652, 1584 and 1540 cm^{-1}. The RPE also showed these peaks, except the peak at 1737 cm^{-1} was distinctly absent. Peaks at 1737 and 1550 cm^{-1} were associated with the pellet (rod outer segments). Peak 1584 cm^{-1} was associated with the supernatant (soluble IPM extract). The fluid loosely associated with the retina did not match to purified hyaluronan and its spectra was interpreted to be protein-rich vitreal or aqueous material. Dissections in light and dark revealed changes in the 3000 – 2,800 cm^{-1} region, which may represent released visual cycle retinoids (all-trans retinol and retinal). The 1737 cm^{-1} peak was not affected by light. This peak matched purified docosahexaenoic acid.

Conclusions: Although the retina generates complex MAIR-IR spectra, assignments can be made. The 1737 and 1150 cm^{-1} peaks represent the rod outer segments. In contrast, the 1600 cm^{-1} peak represents the soluble IPM proteins. Changes in the 3000 – 2,800 cm^{-1} region may represent visual cycle retinoids. MAIR is a powerful approach to characterizing the retina in situ.

CONTROL ID: 3712834

SUBMITTER (NAME ONLY): Deepa Dhungel

TITLE: Effect of Virtual Transparency on Contrast Sensitivity of Disparity-driven Eye Alignments in an Augmented Reality Context

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Dhungel, W. Lew, D.R. Coates, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Augmented reality (AR) has been explored as a tool for lower-cost training in medical, industrial assembly, design, and education. Presentation of AR content requires a balance of its transparency without compromising the visibility of the surrounding physical objects. As a result, AR headsets can cause vergence-accommodation conflict and eye fatigue. It has been found that lower contrast drives weaker vergence and poorer depth perception. However, little is known about the effect of AR transparency on oculomotor eye alignment. Here, we determined the contrast thresholds for horizontal and vertical disparity-driven eye alignments for various levels of transparency.

Methods: Subjects(n=4) performed the task while wearing a pair of Epson Moverio BT300 AR smart glasses. The AR stimuli consist of a one-octave bandwidth filtered noise pattern of 2cpd with a disparity of 5 arcmin overlay on a background with zero disparity. We measured the contrast thresholds for producing a detectable nonius shift for 3 transparency levels (low, middle, and high) and 2 background conditions (grey and a black-and-white natural scene photograph) for horizontal and vertical disparity. Responses from the five staircase runs were combined into a single psychometric function, then fitted with a Weibull that converges to 82% correct performance.

Results: The contrast sensitivity was robust at middle and high transparency. Despite higher opacity at high transparency, there was no significant improvement of sensitivity when compared to the middle level. However, at low transparency, the contrast sensitivity reduced significantly. A cluttered background reduced the sensitivity at all transparency levels by two- to four-fold. There was no significant difference between horizontal vs. vertical results.

Conclusions: Even with a fusible background, the AR overlay with relatively low contrast is enough to drive the eye alignments. Mid transparency with the AR target and its surround in the middle visibility level is sufficient to drive contrast sensitivity of disparity-driven eye alignments. Lower transparency and cluttered background show a weaker drive to vergence, for both horizontal and vertical eye alignments, and may cause strain to the oculomotor systems. Careful manipulation of transparency and its contrasts should be taken into consideration when designing AR visual content.

CONTROL ID: 3712835

SUBMITTER (NAME ONLY): Josh Zhe

TITLE: Retinal degeneration in USH2A Mutant Rabbits Generated by CRISPR/Cas9 Technology

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zhe, V. Nguyen, Y.M. Paulus, Opthalmology, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|J. Song, Y. Li, Y. Sun, J. Xu, J. Zhang, Y. Chen, D. Yang, Center for Advanced Models for Translational Sciences and Therapeutics, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Usher Syndrome type IIA (USH2A) is a genetic disorder characterized by progressive photoreceptor degeneration due to retinitis pigmentosa (RP) and sensorineural deafness. Currently, there exists no therapy to stop or reverse the progressive photoreceptor death in USH2A. In order to understand and treat retinal degeneration in patients, it is essential to create a USH2A animal disease model. Since the Usherin protein is highly conserved in humans and rabbits, rabbits make a great model for USH2A. Furthermore, rabbit eyes have similar anatomical features to human eyes. In this study, we successfully created a USH2A knockout rabbit using CRISPR/Cas9 technology.

Methods: Rabbit embryos were injected with a mixture of 150ng/μL Cas9 mRNA and 50 ng/μL sgRNA at a dose of 2-5 pL. The guide RNA targets the rabbit USH2A gene on exon 12. Each recipient female rabbit received twenty to thirty injected embryos through embryo transfer surgery. Derived founder rabbits were bred to be homozygous for the USH2A knockout. The progression of retinal degeneration is then evaluated for up to 22 months using fundus photography, fundus autofluorescence (FAF), fluorescein angiography (FA), OCT, electroretinography (ERG), and slit lamp examination.

Results: In the three biallelic mutant rabbits, FAF spots were detected in the mid-periphery of the retina, and OCT images showed hyper-reflective disruptions of the photoreceptor layer. ERG signals of both rod and cone function were reduced in the USH2A mutant rabbits at 7 months and worsened at 15-22 months, indicating progressive retinal photoreceptor degeneration.

Conclusions: Due to similar anatomical features and disease progression as noted in humans, our USH2A rabbit model is a useful tool for studying retinal degeneration in Usher syndrome.

CONTROL ID: 3712836

SUBMITTER (NAME ONLY): Chaiyaporn Vatanatham

TITLE: Comparison of OCT retinal layer properties in normal and early AMD in the Alabama study on early age-related macular degeneration 2 (ALSTAR2)

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.C. Vatanatham, Z. Wang, Z. Mishra, S. Fasih-Ahmad, A. Jain, A. Ganegoda, Z. Hu, S.R. Sadda, Doheny Eye Institute, Los Angeles, California, UNITED STATES|M. Clark, C. Owsley, C.A. Curcio, The University of Alabama at Birmingham Department of Ophthalmology and Visual Sciences, Birmingham, Alabama, UNITED STATES|S.R. Sadda, Department of Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: While drusen and subretinal drusenoid deposits (SDD) are commonly associated with the initial diagnosis of age-related macular degeneration (AMD), early AMD patients are known to have scotopic deficits and presumed photoreceptor alterations. In this study, we sought to better characterize the structural alterations associated with the transition from normal aging to early AMD by quantifying the outer retinal layers on optical coherence tomography (OCT) volumes.

Methods: Subjects ≥ 60 years with either normal macular health (AREDS 1) or early AMD (AREDS 2-4) were enrolled as part of the Alabama Study on Early Age-related Macular Degeneration 2 (ALSTAR2). Eye-tracked SD-OCT macular volumes (1 per participant) were acquired with a Spectralis HRA + OCT2. A novel deep-learning-derived graph-based algorithm was used to segment 6 outer retinal layers (photoreceptor inner segment (inner segment myoid defined as external limiting membrane-ellipsoid zone (EZ) center line), photoreceptor outer segment (EZ center line-interdigitation zone outer surface), SDD, retinal pigment epithelium (RPE), drusen, choroid), and segmentation errors were manually corrected (fig. 1). Retinal layer mean thickness within 9 ETDRS subfields was computed and compared between the groups.

Results: The study cohort included 400 eyes: 140 early AMD and 260 normal. Table 1 shows comparison of mean thickness between normal and early AMD. In early AMD, increased mean thickness of drusen was observed in most subfields. SDD were numerically thicker in all subfields, but statistically significant in only a few. In contrast, the photoreceptor inner and outer segments were numerically thinner in all subfields but not statistically significant. No significant differences were observed in the RPE or choroid layer.

Conclusions: In the transition from normal to early AMD, drusen thickness increases consistently throughout the macula. SDD thickness increases in some subfields. The bacillary layer was thinner in early AMD, but the difference was not statistically significant. The choroid layer showed no difference in thickness in any subfield.

CONTROL ID: 3712837

SUBMITTER (NAME ONLY): Amirreza Naderi

TITLE: The Effect of Blocking Substance P in Treating the Allergic Red Eye

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Naderi, S. Wang, L. Liu, T. Blanco, Y. Xia, Y. Chen, R. Dana, Schepens Eye Research Institute of Massachusetts Eye and Ear, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, MA, US, academic/medres, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Allergic conjunctivitis and various conditions can cause conjunctival vessel dialation, leading to ocular redness (OR). Using an animal model of allergic OR, we evaluated the therapeutic efficacy of topical blockade of substance P (SP), which preferentially binds to neurokinin-1 receptor (NK1R) , in treating red eye.

Methods: Allergic OR was induced in guinea pigs with topical 1.5 mg/mL histamine. NK1R antagonist, L-703,606, was applied 10 minutes before or after OR induction as pre-induction or post-induction treatment, respectively. Animal eyes were imaged by a slit lamp (N= 12/group) every 30 seconds in the first 2 minutes, and at 6, 10, 20, 30, 40, 50, and 60 minutes. The redness was analyzed using the ocular redness index (ORI), a score between 0 to 100. After 60 minutes, tear fluid was collected to quantify SP levels by ELSIA (N= 6/group). Lastly, conjunctiva were harvested and stained with H&E to quantify the size of blood vessels and eosinophil and neutrophil infiltration (N= 6/group).

Results: With histamine induction, the ORI peaked at 10 minutes (maximum ORI: 17.04±0.99). Topical treatment of L-703,606 significantly ($P<0.05$) reduced ORI (pre-induction: 7.38±0.71; post-induction: 10.91±0.59). Compared to naive guinea pigs, histamine increased the conjunctival blood vessel diameter nearly three times (naive: 10.15±1.41; histamine: 30.66±4.12). Both pre- and post-induction treatment decreased blood vessels diameter (pre-induction: 16.84±2.21; post-induction: 23.69±2.36) but only pre-induction had significant ($P<0.05$) change. The tear concentration of SP was 71.64±19.16 pg/mL in the naive group, and 270.60±38.04 pg/mL in histamine-induced group. Pre-induction treatment significantly ($P<0.05$) decreased SP concentrations to 154.10±9.72 pg/mL and post-induction treatment lowered SP levels to 191.10±13.52 pg/mL. The numbers of eosinophils and neutrophils were 8.50±2.69 and 4.67±2.91 respectively in the conjunctiva of the naive group. Histamine increased the eosinophil count to 46.00±2.57 and neutrophils to 31.47±2.33. Post-induction treatment reduced eosinophils to 35.50±1.66 and neutrophils to 21.87±1.97, while pre-induction treatment significantly ($P<0.01$) decreased eosinophils to 26.00±2.92 and neutrophils to 14.53±2.31.

Conclusions: Topical administration of the NK1R antagonist effectively reduces allergy-induced ocular redness by decreasing SP release in the tear fluid and conjunctival leukocyte infiltration.

CONTROL ID: 3712840

SUBMITTER (NAME ONLY): Nazarul Hasan

TITLE: Role of LRFN2 in synaptic function of cone photoreceptors in mouse retina

SESSION TITLE: Photoreceptors and the OPL

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Hasan, R.G. Gregg, Biochemistry and Molecular Genetics, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|R.G. Gregg, Anatomical Sciences and Neurobiology, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure: Nazarul Hasan: Commercial Relationship: Code N (No Commercial Relationship) | Ronald Gregg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Daylight vision is mediated by cone photoreceptors in vertebrates. The synapse between cone photoreceptors and bipolar cells is functionally and anatomically complex and critical for normal visual function. ON cone bipolar cell dendrites make invaginating synapses and OFF cone bipolar cell dendrites make flat synapses with cone pedicles, however, the mechanism of whole synaptic assembly is not completely understood. Here we report a leucine-rich repeat (LRR) protein, LRFN2 that is expressed selectively at cone pedicles and involved in modulation of cone synaptic function.

Methods: Using an unbiased proteomic approach we identified LRFN2 as a candidate synaptic organizer protein in mouse retina, and generated a $Lrfn2^{-/-}$ mouse line using zinc finger nucleases. Immunohistochemistry was performed in retinal sections to localize protein expression. Biochemical interaction studies were performed in HEK293T cells expressing both LRFN2 and TRPM1. We characterized retinal function of $Lrfn2^{-/-}$ mice using electroretinogram (ERG) recordings.

Results: We show that LRFN2 expression is co-localized with PNA staining at the cone pedicles. We confirmed interaction between LRFN2 and TRPM1 in a heterologous system. In the absence of LRFN2, the synaptic markers: LRIT3, ELFN2, mGluR6, TRPM1 and GPR179 are properly localized. Similarly, LRFN2 expression and localization is not dependent on these synaptic proteins. Functional analysis showed a reduction in the amplitude of the photopic b-wave of the ERG in $Lrfn2^{-/-}$ mice.

Conclusions: Our data show that LRFN2 likely interacts with TRPM1 and is expressed exclusively at the cone pedicles. Further, its absence compromises normal synaptic transmission between cones and ON cone bipolar cells.

CONTROL ID: 3712841

SUBMITTER (NAME ONLY): Wei Wei Lee

TITLE: Imaging Predictors of Functional Outcomes Following Rhegmatogenous Retinal Detachment Repair

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Lee, R.H. Muni, Ophthalmology, University of Toronto, Toronto, Ontario, CANADA|

Commercial Relationships Disclosure: Wei Wei Lee: Commercial Relationship: Code N (No Commercial Relationship) | Rajeev Muni: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the microstructural optical coherence tomography (OCT) and fundus autofluorescence (FAF) imaging predictors of visual acuity, metamorphopsia and aniseikonia after retinal detachment repair.

Methods: Retrospective analysis of 614 eyes of 614 patients who underwent primary rhegmatogenous retinal detachment (RRD) repair. Best corrected visual acuity, metamorphopsia and aniseikonia were formally tested at 3 months post-operatively. Metamorphopsia and aniseikonia were quantitatively assessed with M-CHARTS and the New Aniseikonia Test. High-resolution spectral-domain OCT and FAF images were captured at 3 months post-operatively. Images were assessed for discontinuity of the outer retinal bands on OCT and retinal displacement detected by retinal vessel printings (RVPs) on FAF by 2 masked graders with disagreements adjudicated by a 3rd senior masked grader. Regression analysis was used to determine the imaging predictors of post-operative visual acuity, metamorphopsia and aniseikonia.

Results: Regression analysis indicated that significant early post-operative (at 3 months) imaging predictors of visual acuity were discontinuity of the external limiting membrane (ELM) (p=0.01) and presence of RVPs on FAF (p=0.033). Discontinuity of interdigitation zone (IZ) was a significant predictor of metamorphopsia [horizontal, MH (p =0.004); vertical, MV (p=0.056); average of MH+MV (p=0.008)] and presence of RVPs was a significant predictor of aniseikonia (p=0.04).

Conclusions: Post-operative discontinuity of the external limiting membrane and retinal displacement were significant predictors of post-operative visual acuity following RRD repair. Discontinuity of the IZ and retinal displacement were significant predictors of post-operative metamorphopsia and aniseikonia, respectively. Modifications of surgical techniques aimed to reduce post-operative discontinuity of the outer retinal bands and retinal displacement may improve functional outcomes after retinal detachment repair.

CONTROL ID: 3712842

SUBMITTER (NAME ONLY): Kyle Bolo

TITLE: Automated Expert-level Scleral Spur Detection and Quantitative Biometric Analysis on the ANTERION Anterior Segment OCT System

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bolo, G. Apolo, A. Pardeshi, B. Burkemper, B. Xu, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|A.S. Huang, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|M. Simonovsky, Heidelberg Engineering GmbH, Heidelberg, Baden-Württemberg, GERMANY|X. Xie, Eye Hospital of China Academy of Chinese Medical Sciences, CHINA|

Commercial Relationships Disclosure: Kyle Bolo: Commercial Relationship: Code N (No Commercial Relationship) | Galo Apolo: Commercial Relationship: Code N (No Commercial Relationship) | Anmol Pardeshi: Commercial Relationship: Code N (No Commercial Relationship) | Bruce Burkemper: Commercial Relationship: Code N (No Commercial Relationship) | Xiaobin Xie: Commercial Relationship: Code N (No Commercial Relationship) | Alex Huang: Commercial Relationship: Code N (No Commercial Relationship) | Martin Simonovsky: Commercial Relationship(s);Code E (Employment):Heidelberg Engineering | Benjamin Xu: Commercial Relationship(s);Code F (Financial Support):Heidelberg Engineering

ABSTRACT BODY:

Purpose: To perform a real-world validation of deep learning (DL) algorithms for automated scleral spur detection and measurement of scleral spur-based biometric parameters in anterior segment optical coherence tomography (AS-OCT) images.

Methods: Participants underwent AS-OCT imaging using the ANTERION OCT system (Heidelberg Engineering, Heidelberg, Germany). Three human graders (Reference, Expert, and Novice) provided labels of scleral spur locations. Scleral spur locations were also predicted using DL algorithms developed by Heidelberg Engineering that prioritize low false positive rate <4% (FPR4) or high true positive rate >95% (TPR95). Performance of human graders and DL algorithms were evaluated relative to the Reference Grader based on similarity of scleral spur locations, biometric measurements, and false negative and positive rates (FNRs and FPRs) of scleral spur detection.

Results: 1,308 AS-OCT images were obtained from 117 participants. Median scleral spur location differences of the FPR4 (52.6 ± 48.6μm) and TPR95 (55.5 ± 50.6μm) algorithms approximated that of the Expert Grader (61.1 ± 65.7μm). Inter-grader reproducibility of biometric measurements was excellent for all three (intraclass correlation coefficient [ICC] range 0.955-0.997). FNR and FPR of the TPR95 algorithm (1.0% and 15.8%) more closely approximated the Expert Grader (2.9% and 17.4%) than the FPR4 algorithm (12.6% and 4.0%). Performance of the Expert Grader and DL algorithms generally exceeded that of the Novice Grader.

Conclusions: DL algorithms on the ANTERION replicate expert-level measurement of scleral spur-based biometric parameters in a diverse real-world patient population. The algorithms could enhance clinical utility of AS-OCT imaging, especially for intraocular lens (IOL) calculations and evaluation of patients with angle closure.

CONTROL ID: 3712843

SUBMITTER (NAME ONLY): Tingyu Hu

TITLE: Terminable cell-encapsulating collagen-alginate composite device for sustained intraocular delivery as a therapy for retinal degenerative diseases

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Hu, B. Tam, Y. Chan, W. Lam, A.C. Lo, Department of Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Tingyu Hu: Commercial Relationship: Code N (No Commercial Relationship) | Brian K.C. Tam: Commercial Relationship: Code N (No Commercial Relationship) | Yau Kei Chan: Commercial Relationship: Code N (No Commercial Relationship) | Wai-Ching Lam: Commercial Relationship: Code N (No Commercial Relationship) | Amy Lo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal degenerative disease (RDD) is a sight-threatening disease with no effective treatment due to the lack of promising drug delivery for rescue of degenerated retinal neurons. Encapsulated cell therapy (ECT) with cellular release of fresh therapeutics enables local sustained drug delivery to the retina while avoiding repeated intravitreal injections. Glial cell-derived neurotrophic factor (GDNF) has shown its neuroprotective effect on photoreceptor cells. While photoreceptor cell death is common in most RDD, we hypothesized that continuous GDNF delivery by collagen-alginate composite (CAC) ECT device can rescue photoreceptor cells, finally slowing the RDD progression. Here, an injectable CAC ECT device equipped with a Tet-on Caspase 8 system was developed for sustained intraocular delivery of GDNF in rabbit eyes.

Methods: Intravitreal (IV) injection of CAC ECT device was performed on healthy New Zealand White rabbits. Three or six units of CAC ECT device were injected into the rabbit eye and kept for 2 weeks, after which rabbits were sacrificed, and devices were retrieved. CAC ECT device biostability was determined by evaluation of gel morphology, cell viability and internal structure. Its biosafety was examined by assessment of flash electroretinogram (fERG), intraocular pressure (IOP) and retinal histology. Rabbits receiving 3 ECT devices were also given 0.1mg/ml doxycycline in drinking water 7 days post-operation for 1 week to examine gel termination efficacy. Cell viability in retrieved devices was determined by MTS assay and Live-Dead assay.

Results: Our data showed that IV injection of CAC ECT device was safe and imposed no changes on retinal function and morphology. The retrieved CAC ECT device exhibited good mechanical stability, gel integrity with no material degradation, and no host tissue attachment with viable encapsulated cells. Scanning electron microscopy further revealed CAC interpenetrating network and colonies of living cells. A week of oral doxycycline treatment could effectively stop the CAC ECT device.

Conclusions: Our CAC ECT device was safe and terminable after IV injection. It demonstrated good mechanical stability while entrapped cells maintained their viability, suggesting that it is a promising drug delivery platform to treat RDD.

CONTROL ID: 3712846

SUBMITTER (NAME ONLY): Gabrielle Monterano Mesquita

TITLE: Relation between lens, pupil and ciliary muscle dynamics during accommodation from OCT images

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Monterano Mesquita, N. Truong, Y. Chang, F. Cabot, M. Ruggeri, S.H. Yoo, A. Ho, J. Parel, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|G. Monterano Mesquita, N. Truong, M. Ruggeri, F. Manns, Department of Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|F. Cabot, S.H. Yoo, Anne Bates Leach Eye Hospital, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|A. Ho, J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Knowledge of the lens dynamics during accommodation can provide insight into age-related changes that contribute to presbyopia. However, in addition to age-dependence, there are also significant inter-individual differences in accommodative responses. The goal of this study is to assess the sources of this variability by quantifying the dynamic changes of the lens, pupil, and ciliary muscle during accommodation from OCT images.

Methods: Following an IRB-approved protocol, OCT images of the left eye of 17 subjects (age: 16 to 70 years; mean: 34 ± 16 years) were captured during accommodation in response to a 2D step stimulus using two synchronized Spectral-Domain OCT systems coupled with an accommodative fixation target (Ruggeri et al, BOE, 2016): transscleral OCT for ciliary muscle imaging (1320nm, 13 fps, 7.5 μm axial resolution, 2.5 mm axial range, Thorlabs Telesto, Newton, NJ) and anterior segment OCT for lens and pupil imaging (840 nm, 13 fps, 8 μm axial resolution, 10.4 mm axial range). Images were recorded for 1.54 s before and 4.61 s after the stimulus for a total of 160 images. The time-dependence of lens thickness (LT), pupil diameter (PD), and ciliary muscle thickness (CMT) at mid-point were quantified. CMT-LT, PD-LT, and CMT-PD response diagrams were generated

Results: 8 out of 15 pre-presbyopic subjects responded to the stimulus. In these subjects, there was synchronous movement of the pupil, lens, and ciliary muscle. Figure 1 shows a typical result illustrating the sequence of pupil constriction followed by lens thinning and additional pupil constriction once the lens reached its asymptotic value. For the 7 eyes that did not respond and 2 presbyopes (>55 years), pupil response was inconsistent across subjects, with an increase in PD.

Conclusions: The combination of all 3 measurements (LT, PD, and CMT) is helpful in assessing the source of variability in accommodative responses and the role of the pupil in accommodation dynamics

CONTROL ID: 3712850

SUBMITTER (NAME ONLY): Prashanth Iyer

TITLE: Swept-Source Optical Coherence Tomography Detection of Bruch's Membrane and Choriocapillaris Abnormalities in Sorsby Macular Dystrophy

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.G. Iyer, M. Shen, Y. Shi, J. Liu, O. Trivizki, B.L. Lam, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|H. Zhou, Q. Zhang, Z. Chu, R.K. Wang, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Swept-source optical coherence tomography angiography (SS-OCTA) images were used to analyze Bruch's membrane (BM) and choriocapillaris (CC) abnormalities in undiagnosed relatives from a family with Sorsby macular dystrophy (SMD).

Methods: In a family with SMD (TIMP3 Tyr191Cys), SS-OCTA imaging was performed using the 6X6mm scan pattern and previously validated algorithms to detect abnormalities in BM and the CC, as well as the presence of reticular pseudodrusen (RPD) and macular neovascularization (MNV). Genetic analyses were performed for TIMP3 mutations.

Results: Of eight family members, two were previously diagnosed with SMD and six were asymptomatic (Figure 1). SS-OCTA imaging of the 33-year-old proband revealed type 1 MNV in the left eye and bilateral RPD, thickening of BM, CC thinning, and increases in CC flow deficits (FDs) (Figure 2). A TIMP3 mutation was confirmed. His niece, despite having no clinical evidence of SMD, showed BM thickening and CC thinning on SS-OCTA. A TIMP3 mutation was confirmed. The proband's younger nephew and niece also carried the TIMP3 mutation without clinical evidence of SMD. Two additional members had normal exams, unremarkable SS-OCTA findings, and no TIMP3 mutation.

Conclusions: SS-OCTA imaging can detect BM and CC abnormalities in vivo in subjects unaware of their TIMP3 status in a family with SMD.

CONTROL ID: 3712851

SUBMITTER (NAME ONLY): Ngoc Lan Vy Truong

TITLE: Quantification of ciliary muscle thickness changes during accommodation from dynamic transscleral OCT images

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Truong, G. Monterano Mesquita, Y. Chang, F. Cabot, M. Ruggeri, S.H. Yoo, J. Parel, A. Ho, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|N. Truong, G. Monterano Mesquita, M. Ruggeri, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|F. Cabot, S.H. Yoo, Anne Bates Leach Eye Hospital, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|J. Parel, A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: Ngoc Lan Vy Truong: Commercial Relationship: Code N (No Commercial Relationship) | Gabrielle Monterano Mesquita: Commercial Relationship: Code N (No Commercial Relationship) | Yu-Cherng Chang: Commercial Relationship: Code N (No Commercial Relationship) | Florence Cabot: Commercial Relationship: Code N (No Commercial Relationship) | Marco Ruggeri: Commercial Relationship: Code N (No Commercial Relationship) | Sonia Yoo: Commercial Relationship: Code N (No Commercial Relationship) | Jean-Marie Parel: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Ho: Commercial Relationship: Code N (No Commercial Relationship) | Fabrice Manns: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent studies have demonstrated the ability of OCT to quantify changes in ciliary muscle thickness with age and accommodation, giving insight into the potential role of the ciliary muscle in presbyopia. Prior studies have relied on measurements acquired statically at fixed accommodative demands. The purpose of this study is to quantify the dynamics of the ciliary muscle thickness changes during accommodation.

Methods: Following an approved protocol, transscleral images of the ciliary muscle of the left eye of 23 subjects (range: 16 to 71 y/o) with spherical equivalent refractive errors ranging from -7.5 to +1 D were acquired at 13 Hz during a response to a 2D accommodative step stimulus. A Spectral-Domain OCT system (1320nm, 28,000 A-lines/s, 7.5 μm axial resolution, and 2.5 mm axial range, Thorlabs Telesto, Newton, NJ) coupled with a custom accommodation module (Ruggeri et al, Biomed Opt Exp, 2016: 1351-1364) was used. For each subject, we acquired a series of 160 B-scans containing 897 A-lines. A MATLAB program was developed to measure the ciliary muscle thickness in each frame. Thickness was measured in the vicinity of the middle part of the muscle where the muscle boundaries could be clearly identified. The change in the muscle thickness was calculated as the difference between the average thickness obtained from the first 10 frames (unaccommodated state) and that obtained from the last 10 frames (accommodated state) of the dynamic recording. The relations between the change in thickness of the ciliary muscle and age as well as refractive error were quantified.

Results: Ciliary muscle thickness in the relaxed state was not found to be dependent on age ($p=0.951$) but was dependent on refractive error ($p<0.001$). The average of the ciliary muscle thickness change during accommodation of all other subjects was 0.062+/-0.074mm. There was not a statistically significant dependence on age (p-value > 0.005). The change in ciliary muscle thickness decreased with increasing myopia (p-value < 0.001).

Conclusions: Ciliary muscle thickness changes with accommodation were found to be independent of age but dependent on refractive error.

CONTROL ID: 3712852

SUBMITTER (NAME ONLY): Naoki Kiyota

TITLE: Constitutively active Ras promotes protection and axon regeneration in retinal ganglion cells after optic nerve injury

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Kiyota, K. Namekata, X. Guo, A. Kimura, T. Harada, Visual research project, Koeki Zaidan Hojin Tokyo-to Igaku Sogo Kenkyujo, Setagaya-ku, Tokyo, JAPAN|N. Kiyota, T. Nakazawa, Tohoku Daigaku Daigakuin Igakukei Kenkyuka Igakubu, Sendai, Miyagi, JAPAN|

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ABSTRACT BODY:

Purpose: Axons in the optic nerve do not usually regenerate when they are injured, causing permanent loss of vision. However, recent studies indicate that stimulation of PI3K/Akt and RAF/MEK/ERK signaling promotes axon regeneration and neuroprotection. In this study, we examined the effects of constitutively active Ras, K-Ras^{V12}, which powerfully activates these signaling, on retinal ganglion cell (RGC) protection and axon regeneration using an optic nerve crush (ONC) model.

Methods: K-Ras^{V12} was generated by site-directed mutagenesis and incorporated into an adeno-associated viral serotype 2 (AAV2) vector. AAV2-K-Ras^{V12} was injected intravitreally in C57BL/6J mice. One or two weeks after the injection, ONC was performed, and one or eight weeks later, cholera toxin B subunit (CTB647)-labeled regenerating axons were analysed. The number of RGCs was determined by immunolabeling using anti-RBPMS antibody in flatmounted retinas. EdU (50mg/kg) was intraperitoneally injected daily for examination of cell proliferation. Electron microscopy was performed for detailed histological analysis of axons.

Results: AAV2-K-Ras^{V12} treatment demonstrated increased number of RGCs compared with the control after ONC. As Ras is an oncogene, we examined the potential of cell proliferation, but found that RGCs were not proliferated by the AAV2-K-Ras^{V12} treatment. These data showed that the increased RGC number after ONC with AAV2-K-Ras treatment was due to neuroprotection. Furthermore, AAV2-K-Ras^{V12} treatment induced significant amounts of RGC axon regeneration even after 1 week, and some regenerating axons reached the optic chiasm after 8 weeks. These data indicated that AAV2-K-Ras^{V12} treatment induces powerful RGC axon regeneration. In addition, we found that AAV2-K-Ras^{V12} -induced regenerated axons were not myelinated, suggesting that combinatory treatment with promoting myelination may be required for functional recovery.

Conclusions: AAV2-K-Ras^{V12} may be useful for treatment of CNS axon injury in future, and it may be a good tool to study mechanisms for RGC axon regeneration and protection.

CONTROL ID: 3712853

SUBMITTER (NAME ONLY): Chandni Kapoor

TITLE: Moderate and Poor Visual Acuity in Pediatric Glaucoma Patients

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kapoor, University of California Davis, Sacramento, California, UNITED STATES|A. Jiang, Ophthalmology, Portland VA Medical Center, Portland, Oregon, UNITED STATES|J.D. Brandt, J. Chen, Ophthalmology, University of California Davis, Sacramento, California, UNITED STATES|J. Chen, Ophthalmology, Sacramento VA Medical Center, Mather, California, UNITED STATES|

Commercial Relationships Disclosure: Chandni Kapoor: Commercial Relationship: Code N (No Commercial Relationship) | Angela Jiang: Commercial Relationship: Code N (No Commercial Relationship) | James Brandt: Commercial Relationship(s);Code C (Consultant/Contractor):Théa;Code I (Personal Financial Interest):Glaukos;Code F (Financial Support):Santen USA | Jenny Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the characteristics of pediatric glaucoma patients with moderate and poor best corrected visual acuity compared to those with good visual acuity.

Methods: A retrospective review of electronic medical records from 2001 to 2019 was conducted for pediatric glaucoma patients or adults with history of pediatric glaucoma diagnosis or treatment. Visual acuity, failed amblyopia treatment, refractive status, axial length, strabismus, nystagmus, failed angle surgery, and media opacity were recorded. Patients without data for the best corrected visual acuity were excluded. Patients were categorized by their most recent WHO visual acuity (VA) status (poor VA <20/200, moderate VA <20/50 to 20/200, and good VA 20/20 to 20/50) and analyzed. One-way ANOVA testing was used to assess axial length differences among the VA groups, while Chi squared testing was used for the remaining variables.

Results: 233 glaucomatous eyes of 142 childhood glaucoma patients were identified. Average follow-up duration was 6.85 ± 4.46 years. 91 patients had bilateral glaucoma. There were 65 eyes with poor VA of which 22 (33.8%) had failed amblyopia therapy, compared to 16 (28.6%) of the 56 moderate VA eyes, and 1 (0.89%) of the 112 eyes with good VA who failed amblyopia therapy ($p<0.00001$). Failed angle surgery was observed in 29.2% of poor VA eyes, 35.7% of moderate VA eyes, and 25% of good VA eyes ($p=0.35$). The mean axial length for eyes with poor VA was 25.27mm, moderate VA 25.70mm, and good VA 23.91mm ($p=0.37$). Thirty of the 65 (46.2%) poor VA eyes had media opacity while 17 of the 56 (30.4%) moderate VA eyes and six of the 112 (5.36%) good VA eyes had media opacity respectively ($p<0.00001$). Strabismus was seen in 7.69% of poor VA eyes, 12.5% of moderate VA eyes, and 1.79% of good VA eyes ($p=0.02$). Similarly, nystagmus was found in 13.8% of poor VA eyes, 16.0% of moderate VA eyes, and 0.89% of good VA eyes ($p=0.0005$). Finally, anisometropia was found in 23.1% of poor VA eyes, 35.7% of moderate VA eyes, and 28.6% of good VA eyes ($p=0.31$).

Conclusions: Eyes with poor and moderate visual acuities tended to have increased rates of media opacity, failed amblyopia therapy, nystagmus, strabismus, and increased axial length though the latter was not statistically significant. Failed amblyopia therapy seems to be by far the most common association with poor vision. Failed angle surgery was not associated with poorer visual acuity.

CONTROL ID: 3712854

SUBMITTER (NAME ONLY): Shih-En Chen

TITLE: In vivo measurement of plexus-specific retinal erythrocyte velocity and acceleration in human subjects and NHPs

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Chen, V. Chen, J. Pottenburgh, O. Saeedi, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: We utilized multimodal imaging with Erythrocyte Mediated Angiography (EMA) and Optical Coherence Tomography Angiography (OCTA) to precisely quantify erythrocyte velocity and acceleration in perifoveal retinal arterioles, capillaries, and venules of humans and nonhuman primates (NHPs) at baseline and high intraocular pressure (IOP).

Methods: 15 eyes of 9 healthy human subjects and 4 eyes of NHPs underwent sequential EMA and OCTA. High intraocular pressure (IOP), defined as 18mmHg or higher, was induced in NHPs using a tight lid speculum. Systolic blood pressure, diastolic blood pressure, and IOP were measured to calculate mean ocular perfusion pressure (MOPP). Erythrocytes in capillaries were tracked using a semiautomated approach. To identify the corresponding vascular plexus, overlays were made using a time-lapse stack of EMA frames and OCTA images of the superficial vascular plexus (SVP), intermediate capillary plexus (ICP), and deep capillary plexus (DCP) (Figure 1). We compared erythrocyte velocity and acceleration in each plexus using generalized estimating equations for statistical analysis.

Results: In human subjects, overall mean capillary velocity was 1.7±1.6mm/s. Differences between capillary velocities were noted between SVP, ICP, and DCP ($p<0.01$ for all comparisons) (Table 1). Overall mean human capillary acceleration was 4.0±2.5x10-3mm/s2, which did not differ significantly between plexuses. In NHPs, overall mean capillary velocity (0.69±0.31mm/s) at baseline IOP was significantly higher than that of high IOP (0.39±0.18mm/s, $p<0.01$). Overall NHP mean capillary acceleration was significantly higher at baseline as compared to high IOP ($p<0.001$). While there were no significant differences between plexus velocities in NHPs at baseline, mean capillary velocities at high IOP varied significantly between DCP and ICP ($p<0.01$) and DCP and SVP ($p<0.01$). Mean capillary accelerations in NHPs at baseline IOP varied significantly between DCP and ICP ($p=0.015$). At high IOP, mean NHP capillary accelerations were significantly lower for SVP and ICP as compared to DCP.

Conclusions: In humans and NHPs, erythrocyte decelerate in arterioles then accelerate in venules as expected. We have shown that blood flow in the SVP, ICP, and DCP can be precisely quantified and can differ between plexuses. Furthermore, elevated IOP results in decreased erythrocyte velocity and acceleration.

CONTROL ID: 3712857

SUBMITTER (NAME ONLY): Adrian Hunt

TITLE: 36-month outcomes of VEGF inhibitors for treatment-naïve Central Retinal Vein Occlusion: Data from the Fight Retinal Blindness! registry.

SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: We performed a retrospective analysis of a large prospectively specified observational database of patients with central retinal vein occlusion (CRVO) treated with vascular endothelial growth factor (VEGF) inhibition from routine practice.

Methods: We identified 527 treatment-naïve patients with CRVO that commenced VEGF inhibitors between January 1, 2010-2018, with a mean (SD) age of 71 years (12), visual acuity (VA) of 41 letters (25). The primary outcome was mean change in VA from baseline to 36 months. Adjusted VA and central subfield thickness (CST) outcomes compared VEGF agents with generalised mixed effects models.

Results: In all eyes, mean VA change (95% CI) was +10 (7, 12) letters, 44% gained and 14% lost ≥15 letters, 37% had final VA ≥70 and 30% ≤35 letters. Mean CST change was -306µm. The adjusted mean VA change was similar with each VEGF inhibitor (+12 letters) despite significant difference in adjusted mean CST change with aflibercept (-310µm), ranibizumab (-258µm) or bevacizumab (-216µm; $P < 0.001$). VEGF switchers (19%) gained +11 letters like non-switchers (69%) but with more injections (20 vs. 10; $P < 0.001$). Eyes that were switched to steroid (12%) had lower mean baseline VA 38 letters, 46% had final VA ≤35 letters and no mean change in VA from baseline. Mean VA change in eyes with trial-eligible baseline VA (19-73 letters, 356/527, 68%) was +7 letters. Eyes outside this range with very-poor baseline VA (<19 letters, 129/527, 24%) gained +22 letters and eyes with very-good baseline VA (>73 letters, 42/527, 8%) lost vision by -7 letters. Completers (257/527, 49%) had a median of 18 injections over 26 visits. Suspension of therapy >180 days occurred in 141/527 (27%) eyes but only 62 (12%) eyes had no macular oedema during that time. Treatment status was known in 356/527 (68%) eyes – 55% were still receiving injections at 3 years while 45% had suspended therapy.

Conclusions: Patients with CRVO that commenced VEGF inhibitors in routine care had VA improvements of around 10 letters at three years - almost matching the outcomes of extension studies that followed RCTs. The choice of

VEGF inhibitor influenced CST but not VA outcomes. Half of all eyes were still being treated at 36-months.

CONTROL ID: 3712858

SUBMITTER (NAME ONLY): Christine Xu

TITLE: Trends for Proliferative Diabetic Retinopathy Vitrectomy Treatments in the IRIS® Registry (Intelligent Research in Sight)

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vitrectomies are necessary for treating non-clearing vitreous hemorrhage and tractional retinal detachments. We used the IRIS Registry to better understand vitrectomy rates and demographics that predict which Proliferative Diabetic Retinopathy (PDR) patients would be more likely to undergo a vitrectomy.

Methods: We identified patients with PDR between the years of 2016-2018 in the IRIS Registry and calculated the percentage of eyes with PDR undergoing vitrectomy each year. Multivariate regression was performed to identify how patient sex, age, and race/ethnicity as well as diagnosis influence odds of undergoing vitrectomy. We also compared the number of intravitreal anti-VEGF injections between 2016-2018 for eyes with PDR who underwent and did not undergo vitrectomy in 2018.

Results: Percentage of PDR eyes undergoing vitrectomies between 2016-2018 was 2.27% in 2016, 2.12% in 2017, and 2.40% in 2018 (Table 1). After adjusting for confounders, ages 41-60 (OR 3.0, 95% CI 2.59 - 3.48) and ages 61-40 (OR 2.72, 95% CI 2.42 - 3.05) had the highest odds of undergoing vitrectomy compared to patients aged 21-40. Similarly, compared with White race, Hispanics (OR 1.26, 95% CI 1.19 - 1.34) had the highest adjusted odds of undergoing vitrectomy and Asians (OR 0.72, 95% CI 0.62 - 0.83) and Blacks (OR 0.75, 95% CI 0.71 - 0.80) had the lowest. The mean number of injections for PDR patients who underwent and did not undergo vitrectomy in 2018 was respectively 2.96 and 0.93 ($p < 0.001$).

Conclusions: Within the IRIS Registry, there was no clear trend in the percentage of eyes with PDR undergoing vitrectomy between 2016, 2017, and 2018. Patients ages 41-60 were the most likely to undergo vitrectomy, possibly as a result of surgical candidacy. Interestingly, Hispanic patients had a 26% greater adjusted odds of undergoing vitrectomy than White patients, while Black and Asian patients respectively had a 25% and 28% lower adjusted odds. Eyes undergoing vitrectomy on average had 3 times more intravitreal anti-VEGF injections in the preceding two years than eyes that did not undergo vitrectomy.

CONTROL ID: 3712859
SUBMITTER (NAME ONLY): Amani Mubeen
TITLE: U.S. Youth Perceptions of Eyeglasses and Contact Lenses
SESSION TITLE: Eyecare delivery and economics
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Uncorrected Refractive Error (URE) among youth is associated with decreased school performance and productivity. We aimed to investigate youth experiences with glasses and contacts, as prior experiences with refractive correction are potential facilitators or barriers to correcting URE.

Methods: A five-question survey including open-ended questions about experiences with refractive correction was sent to the MyVoice Text Message Cohort of U.S. youth aged 14–24 years (www.hearmyvoicenow.org). Responses were coded by two team members independently using a modified grounded theory approach, and disagreements in coding were resolved by consensus.

Results: In total, 1063 participants out of 1204 responded (88.3%). The mean age of participants was 20.3 ± 2.4 years (range 15-24 years); 32.5% (n=346) were female; and 74.0% (n=787) were white. Nearly two thirds (65.8%; n=699) had experienced trouble with their eyesight, and 63.6% (n=676) had worn glasses and/or contacts. Some (31.7%, n=337) discussed a preference for glasses or contacts; of those, 83.7% (n=282) preferred glasses and 16.3% (n=55) preferred contacts. The most common reasons for preferring glasses were problems with contacts (12.8%, n=36, e.g. “I wear glasses because I cannot put contacts in for the life of me”) and convenience (4.3%, n=12, e.g. “I still wear my glasses because I think they're less work than contacts”). The most common reasons for preferring contacts were convenience (16.4%, n=9, e.g. “I wear corrective contacts so I can avoid the hassle of having glasses”), problems with glasses (12.7%, n=7, e.g. “I wear both, mostly contacts day to day because with masks they don't fog up like glasses do”), cosmesis (10.9%, n=6, e.g. “If I’m being active or planning on wearing makeup I’ll wear my contacts”) and preference for wearing contacts for sports (10.9%, n=6, e.g. “I do wear both, mostly contacts so that I can go swimming with ease”).

Conclusions: Glasses may be more popular than contact lenses among U.S. youth. Future work should address youth barriers to glasses to improve access to refractive correction.

CONTROL ID: 3712860

SUBMITTER (NAME ONLY): Karolina Roszak

TITLE: Multimodal corneal imaging of Boxer dogs with and without spontaneous chronic corneal epithelial defects (SCCEDs).

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.P. Roszak, R. Brady, C. Chang, M. Casanova, C.J. Murphy, S.M. Thomasy, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California Davis, Davis, California, UNITED STATES|C.J. Murphy, S.M. Thomasy, Department of Ophthalmology & Vision Science, School of Medicine, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Boxer dogs are known to be markedly overrepresented with SCCEDs. The clinical presentation of SCCEDs is well known, but the underlying pathophysiology of this condition in Boxers remains unclear. The purpose of this study was to perform multimodal corneal imaging of Boxers with and without SCCEDs to determine if corneal morphologic differences could be identified.

Methods: Eight control (9.5 ± +/- 2.0 yrs, 3 castrated males, 1 intact male, and 4 spayed females) and 15 SCCED-affected (8.5 +/- 1.3 yrs, 8 castrated males and 7 spayed females) Boxers were examined. An ophthalmic examination including Fourier-domain optical coherence tomography (FD-OCT) and in vivo confocal microscopy (IVCM) were performed in the central cornea of both eyes. One-way analysis of variance (ANOVA) was used to compare total corneal thickness (TCT), epithelial thickness, stromal thickness (ST), and density of keratocytes in the anterior stroma between SCCED-affected eyes, unaffected eyes of dogs with SCCEDs, and controls. Corneal endothelial cell density (ECD), cell size and cell side number were calculated using manual frame method (FM) and planimetry (PL) and compared between SCCED-affected and unaffected dogs using a Student's t-test.

Results: The TCT and ST were significantly higher in SCCED-affected eyes versus unaffected eyes of SCCED-affected Boxers with SCCEDs and controls ($P < 0.001$); no significant differences were found in epithelial thickness and anterior stromal keratocyte density between these three groups. Amongst SCCED-affected dogs, 6 had a low ECD with a mean ± SD of 768 ± 376 cells/mm^2 by FM and 892 ± 359 cells/mm^2 by PL. Furthermore, ECD was significantly less ($P < 0.05$) in dogs with SCCEDs (1488 ± 606 cells/mm^2 by FM, 1545 ± 559 cells/mm^2 by PL) versus unaffected dogs (1902 ± 293 cells/mm^2 by FM, 1898 ± 294 cells/mm^2 by PL). Finally, SCCED affected dogs showed significantly greater variability in cell size and side number versus control dogs ($P < 0.01$).

Conclusions: SCCED-affected Boxers had corneal morphologic features that differed from unaffected dogs including a low ECD in some. Additional Boxers are required to evaluate the prevalence of endothelial disease in this breed and its potential impact on the occurrence of SCCEDs.

CONTROL ID: 3712862

SUBMITTER (NAME ONLY): Eric Jung

TITLE: Initial experience with biosimilar bevacizumab-bvzr for intravitreal use in children: A Case Series

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.E. Jung, T. Lee, A. Nagiel, Roski Eye Institute, Department of Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|E.E. Jung, T. Lee, A. Nagiel, The Vision Center, Department of Surgery, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is ongoing research on the safety and efficacy of recently introduced anti-vascular endothelial growth factor (VEGF) biosimilars for the treatment of retinal disease, especially in the pediatric population. We report our initial experience with intravitreal bevacizumab-bvzr, a bevacizumab biosimilar FDA-approved in 2019 and recently introduced by our institution for off-label ophthalmologic use.

Methods: This was an IRB-approved single-institution retrospective case series of pediatric patients 21 years or younger who received at least one intravitreal injection of biosimilar bevacizumab-bvzr.

Results: 12 eyes of 9 patients were identified as having received intravitreal bevacizumab-bvzr, with a total of 13 injections performed. The mean number of injections performed per eye was 1.1 (range: 1 – 2 injections). The median follow-up time from first injection was 16 weeks (range: 4 – 33 weeks). The dose used was 0.125 or 0.625 mg in 0.025 ml for 7 retinopathy of prematurity (ROP) injections, and 1.25 mg in 0.05 ml for the remaining injections. Indications for injection included ROP (7/13), macular neovascularization (3/13), retinal vein occlusion (2/13), and Coats disease (1/13). All four patients with ROP experienced regression of Stage 3 disease, and all four patients with intraretinal or subretinal fluid on optical coherence tomography exhibited reduction or resolution of fluid following injection of bevacizumab-bvzr. No occurrences of post-injection inflammation, intraocular pressure anomalies, or endophthalmitis were observed.

Conclusions: This case series supports the continued use of intravitreal bevacizumab-bvzr as an anti-VEGF therapy option, including in the pediatric population. In light of its favorable cost profile compared to bevacizumab and other anti-VEGF agents, these results should encourage larger studies and its use in resource-poor settings.

CONTROL ID: 3712864

SUBMITTER (NAME ONLY): Siddharth Narendran

TITLE: Diet-induced inflammation and immune sexual dimorphism as driving factors for geographical and gender disparities in diabetic retinopathy prevalence

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Narendran, K. Ramasamy, Aravind Eye Care System, Madurai, Tamil Nadu, INDIA|

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ABSTRACT BODY:

Purpose: Previous epidemiological studies have reported significant geographical and gender disparities in the prevalence of Diabetic Retinopathy (DR) and vision-threatening diabetic retinopathy (VTDR). However, the drivers responsible for this heterogeneity are yet to conclusively determined. The two contiguous South Indian states, Tamil Nadu (TN) and Kerala (KL) possess similar geographical, genetic, and ethnolinguistic landscapes. Despite these similarities, the prevalence of several non-communicable diseases, including DR, has been reported to be significantly higher in KL compared to TN.

Methods: Data were evaluated by accessing the electronic health records of individuals presenting to five tertiary eye care facilities across South India from 2015-2019. The primary outcome was the diagnosis of DR or VTDR. Plasma Interleukin-6 (IL-6) concentration was measured using a commercial immunoassay. The secondary data from the National Sample Survey Organization was analyzed to study the per capita consumption patterns. Multivariate regression, Propensity score matching, Inverse probability treatment weighting, and doubly robust estimation, were employed to study the factors influencing the prevalence of DR and VTDR.

Results: A total of 922,158 patients were included in the analyses, among which there were 263,592 patients with Type II DM. After adjustment for individual confounders, Type II DM patients from KL were 2.05 times (adjusted hazard ratio, 2.056; 95% CI, 2.009 to 2.114; $P < 0.01$) and 2.27 times (adjusted hazard ratio, 2.272; 95% CI, 2.138 to 2.413; $P < 0.01$) more likely to be diagnosed with DR and VTDR respectively. Men were 1.6 (adjusted hazard ratio, 1.633; 95% CI, 1.508 to1.687; $P < 0.01$) and 1.84 (adjusted hazard ratio, 1.835; 95% CI, 1.752 to 1.922; $P < 0.01$) times more likely to be diagnosed with DR and VTDR respectively. Plasma IL-6 was significantly higher in patients with DR (2.44 vs 1.39 pg/ml), in men (2.27 vs 1.41 pg/ml), in patients from KL (2.23 vs 1.65 pg/ml), and in patients consuming a coconut oil-rich diet (4.05 vs 2.29 pg/ml).

Conclusions: The results of this study ascertain the existence of gender and geographical disparities in the prevalence of DR and suggest that elevated circulating levels of IL-6 could be a potential driving factor for both the gender and spatial heterogeneity in the prevalence of DR.

CONTROL ID: 3712865

SUBMITTER (NAME ONLY): William Tuten

TITLE: Spatial summation of increments and decrements in the human fovea.

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Measured with adaptive optics, the area of complete spatial summation (i.e., Ricco's area) for light increments delivered to the fovea has a diameter of ~2.5 arcmin. How the visual system integrates adjacent increments and decrements delivered within Ricco's area may yield insights into the mechanisms of spatial summation. To that end, we measured detection performance for various combinations of increments and decrements using an adaptive optics scanning light ophthalmoscope (AOSLO).

Methods: An AOSLO was used to image the retina and deliver stimuli to the central fovea in three subjects. Rectangular stimuli (1.0 x 1.3 arcmin; λ = 550 nm; duration = 187.5 ms; no compensation for fixational eye movements) were presented in pairs against a background of the same wavelength (~2900 cd/m^2). The component rectangles of the paired stimulus were positioned directly adjacent to one another. Stimuli were presented along various meridians in a two-dimensional stimulus space whose principal axes corresponded to the Weber contrasts (range: -100 to +233%) of the component rectangles. Stimulus directions included increment-only, decrement-only, increment-increment, decrement-decrement, and increment-decrement conditions. Detection was measured using a yes/no paradigm and psychometric function fits were used to derive isodetection contours. In one subject, detection for homotypic (incr-incr, decr-decr) and heterotypic (incr-decr) stimuli was assessed at five component rectangle separations ranging from 0 to 2.5 arcmin. Behavioral results were compared to computational observer (CO) simulations generated in ISETBio.

Results: In all subjects, homotypic stimuli exhibited linear summation, and heterotypic stimuli were less detectable than contrast-matched same-sign pairs, suggesting some cancellation of increments and decrements. In two subjects, the magnitude of this cancellation exceeded the amount plausibly accounted for by optical factors, as determined in the CO simulations. The change in detectability of homotypic stimuli as separation increased agreed with CO predictions, whereas heterotypic stimuli were less detectable than CO predictions for separations under 1 arcmin.

Conclusions: Our results suggest the partial cancellation of increments and decrements confined to Ricco's area reflects a combination of optical and neural factors, and may have implications for the underlying ON- and OFF- visual pathways.

CONTROL ID: 3712867

SUBMITTER (NAME ONLY): Jose Paczka

TITLE: Effect of Digital Compression on Intraocular Pressure after One Year of Trabeculectomy

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Paczka, A.M. Ponce Horta, A. Tornero-Jimenez, J. Escobedo Espinoza, Instituto de Oftalmologia y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|J.A. Paczka, A. Orozco Garcia, S. Garcia y Otero Sánchez, Research, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|A.M. Ponce Horta, A. Tornero-Jimenez, J. Escobedo Espinoza, M.A. Ibáñez-Sandoval, A. Orozco Garcia, Research, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|M.A. Ibáñez-Sandoval, Escuela de Medicina, Universidad LAMAR, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Trabeculectomy is still the method of choice for surgical treatment of glaucoma, especially for advanced cases. Follow-up and after-treatment manuevers are of outstanding importance for the postoperative clinical course and long-term outcomes. Ocular digital massage (ODM) is a commonly post-operative manuever that promotes aqueous flow through the surgical site, enlarging the bleb, reducing IOP and inhibiting scar formation. There is scarce information regarding the impact of ODM on trabeculectomy outcomes after at least one year of follow-up. The objective of this study is to evaluate the effect of ODM in a cohort of cases with at least one year of post-operative course.

Methods: A retrospective analysis of an electronic database of cases which underwent trabeculectomy in a glaucoma center (November 2017 - December 2020) was carried out. Cases with complete clinical information and a follow-up of at least one year after trabeculectomy were included in the study. The analyzed variables were best-corrected visual acuity, visual field stability, glaucoma stage of severity, number of antiglaucoma medications, time of trabeculectomy follow-up, site of ODM, effect of ODM on IOP and bleb formation. ANOVA analysis was performed for continuous variables. A p-value of ≤ 0.05 was considered as statistically significant.

Results: From 668 cases identified with trabeculectomy, 501 eyes of 416 patients (mean age, 64.2±13.9 years; 61% female; 68% POAG) were included in the study. One hundred and thirty one cases (25.9%) required ODM, and they were significantly younger (mean age, 59.5±.9.8 years, p=0.0012; 69% female; 52% POAG) and with higher pre-operative mean IOP, as compared with the eyes not requiring ODM (20.4±9.2 mm Hg vs 18.3±8.4 mm Hg, p=0.017). Eyes requiring ODM had an early (prior to 8 days) IOP of 16.6±.6.8 mm Hg, decreasing after the maneuver to 11.7±3.4 mm Hg (p<0.0001). After one year, mean IOP (15.3±6.0 mm Hg) of eyes not requiring ODM (n=478) was significantly greater (p=0.04) than IOP (14.0±5.1 mm Hg) of eyes requiring ODM (n=104). No persistent or serious complication was related to ODM.

Conclusions: Findings from the current report suggests that ODM after trabeculectomy is a post-operative maneuver that can induce a sustained benefit to reduce IOP and has to be investigated in well-designed trials in order to recognize its real applicability and limitations, in the long-term.

CONTROL ID: 3712868

SUBMITTER (NAME ONLY): Zahra Tajbakhsh

TITLE: Do vernal keratoconjunctivitis and allergic conjunctivitis have a different immune response at the ocular surface?

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dendritic cells (DC) density is increased in vernal keratoconjunctivitis (VKC) and allergic conjunctivitis (AC), and we have also shown altered morphology of DC in AC. This study compared the distribution of corneal and conjunctival epithelial DC in VKC, AC, and healthy controls to examine if allergy type causes differences in immune cell activation.

Methods: In vivo confocal microscopy (HRT III) was performed on the right eye of 60 participants (mean age 22.4±8.1 years, 70% male) based in Shiraz, Iran: 20 with limbal VKC, 20 with AC, and 20 healthy controls. Locations scanned included: corneal centre, corneal periphery (1mm inside limbus), corneal limbus, and bulbar conjunctiva (2-3 mm temporal to limbus). DC were counted manually, and corneal morphology was graded for cell body size, presence of dendrites, and dendrite appearance. Differences between groups and between locations were examined using linear mixed model analysis (density), Chi-Square test, Kruskal-Wallis test (morphology).

Results: DC density was higher in VKC, and AC compared to controls, at all locations ($p \leq 0.001$). DC density was significantly higher at the limbus of VKC participants compared to AC ($p < 0.001$), but there was no difference at other locations ($p \geq 0.08$). In all groups, DC density was highest at the limbus than at other locations ($p \leq 0.001$), with the fewest DC observed at the conjunctiva ($p < 0.01$). DC cell bodies were larger in VKC than AC at the corneal centre only ($p = 0.01$). DC cell bodies were larger in VKC, and AC compared to controls, at all corneal locations ($p \leq 0.001$). Dendrites were present on more DC in VKC, and AC compared to the controls, at the corneal centre and periphery ($p \leq 0.001$). VKC and AC groups had more long dendrites compared to the controls at the corneal periphery and limbus ($p \leq 0.001$). The VKC group had more long dendrites compared to controls at the corneal centre ($p = 0.04$) and more thick dendrites at the limbus ($p = 0.048$).

Conclusions: Increased DC density and altered morphology at the ocular surface were evident in both VKC and AC, a marker of the upregulated immune response. Greater DC density in both forms of ocular surface allergy, but higher density at the limbus may be a marker of the more severe VKC. Larger DC cell bodies and more with long dendrites could help to differentiate allergy from non-allergy and more severe forms of allergy from milder forms.

CONTROL ID: 3712870

SUBMITTER (NAME ONLY): Dominic Shayler

TITLE: Early photoreceptor trajectories towards a cancer-predisposed cone precursor state

SESSION TITLE: Retinal Development

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Maturing human cone precursors serve as the retinoblastoma cell of origin, yet the cone maturation-associated gene expression changes that contribute to retinoblastomagenesis are not defined. This study aimed to elucidate developmental trajectories and gene expression changes in early photoreceptor precursors and across cone maturation, define the role of cone-specific features in retinoblastoma genesis, and evaluate whether relevant cone maturation features are represented in human retinal organoids.

Methods: 794 single CD133+/CD44,CD49b- cells comprising cone and rod precursors and retinal progenitors were FACS- and microfluidics-isolated from 18 dissociated human fetal retinae (GW15-21). 867 single cells were FACS isolated from retinal organoids (55-225 DIC). After full-length scRNA sequencing, transcriptomes were clustered, and RNA velocity, differential expression, and SCENIC were used to define trajectories and identify cluster-specific gene expression and transcription factor regulons. Expression patterns were validated using RNA-FISH and immunofluorescence staining.

Results: Two post-mitotic photoreceptor precursor clusters were identified: common cone/rod precursors that co-expressed cone (THRB) and rod (NRL) regulons, formed bifurcating cone- and rod-directed trajectories, were marked by CHRNA1, and were detected by CHRNA1 FISH and NRL/RXRg staining; and rod-only precursors that solely expressed rod markers and regulons. Early cone precursor maturation was characterized by sequential expression of lncRNAs (CTC-378H22.2, HOTAIRM1, CTD-2034I21.2, and RP13-143G15.4), as validated by FISH, which marked distinct cone precursor domains. All maturing cone precursor states had high MYCN regulon activity and SYK expression, and inhibition of SYK impaired cell cycle entry in response to pRB knockdown. Retinal organoids did not show a common cone-rod precursor population or sequential cone lncRNA expression but had cone-specific SYK expression.

Conclusions: Full-length scRNA-seq of developing human retina revealed two potential routes to rods, features of common cone-rod precursors, lncRNAs that discriminate early cone maturation stages, and a role for intrinsically expressed SYK in the cone proliferative response. Retinal organoid cones failed to replicate several aspects of human cone development, which may influence the accuracy of retinal organoid development and disease models.

CONTROL ID: 3712871

SUBMITTER (NAME ONLY): Michelle Chen

TITLE: Quantification of the growth rate of prevalent and incident cRORA lesions in SD-OCT images

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Chen, T. de silva, A. Thavikulwat, H. Wiley, T.D. Keenan, E.Y. Chew, C.A. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: This work aims to quantify the growth and the characteristics of atrophy in age-related macular degeneration (AMD) using spectral domain optical coherence tomography (SD-OCT).

Methods: A 5-year prospective study of patients enrolled in a longitudinal study of dark adaptation (NCT01352975) with a range of AMD severities included annual imaging with SD-OCT (Spectralis, Heidelberg, Germany). Atrophy on SD-OCT was defined according to the Classification of Atrophy Meetings (CAM) guidelines as complete retinal pigment epithelium (RPE) and outer retinal atrophy (cRORA). SD-OCT volumes (30^{o}x25^{o}, 60 µm spacing) were first manually graded for presence/absence of cRORA and then a custom semi-automated algorithm contoured the cRORA regions in each OCT B-Scan. Enface 2D projection of the contoured cRORA regions was used to calculate the area atrophy (mm^2). The growth rate of atrophy was calculated for each eye by finding the slope of the best linear fit of the square root area measurements over available timepoints.

Results: Of the 31 patients with cRORA in either eye, 18 (58.1%) had unilateral cRORA whereas 13 (41.9%) had bilateral cRORA (i.e., total of 44 eyes with cRORA). Of these 44 eyes, 24 (54.0%) had cRORA already present at baseline (Group 1, median visual acuity 20/40), and 20 (45.5%) developed cRORA at follow-up visits (Group 2, median visual acuity 20/25). The mean (±SD) area of cRORA at the baseline visit for Group 1 was 2.88 ± 4.10 mm^2 and at the first visit with cRORA in Group 2 was 0.66 ± 0.70 mm^2. The median growth rate of atrophy in Group 1 (mean followup time 2.9 years) was 0.21 mm/year (range 0.024 - 0.64 mm/yr) and in Group 2 (mean followup time 1.3 years) was 0.17 mm/year (range -0.06 - 0.89 mm/yr). For eyes in Group 1, most visits (62.5%) had AMD severity scores 9 (non-central GA) or 10 (centrally involved GA) on color grading (range 5-10), while eyes in Group 2 had fewer visits (30%) with AMD severity scores of 9 or 10 (range 7-10).

Conclusions: Assessment of cRORA/atrophy in OCT can augment the current understanding of atrophy and its growth using color or autofluorescence imaging modalities. The detection and quantification of small, incident areas of atrophy could be used as a more sensitive outcome of advanced disease. The accurate quantification of the growth of these lesions is important in understanding disease progression and for the design of clinical trials.

CONTROL ID: 3712873

SUBMITTER (NAME ONLY): Alex McMullen

TITLE: Investigating the effects of surgical intraocular pressure on corneal endothelial cell viability using intact porcine eyes

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. McMullen, M. Buckley, Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|S. Chamness, J. Brunelle, J. Martiz, Carl Zeiss Meditec Cataract Technology, Inc., Nevada, UNITED STATES|Y.M. Khalifa, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|Y.M. Khalifa, Emory Eye Center, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although it is widely accepted that corneal endothelial cell (CEC) damage occurs during phacoemulsification surgery, it remains unclear if the elevated intraocular pressure (IOP) used during phacoemulsification contributes significantly to this damage. Using a novel experimental method enabling quantification of CEC damage in intact porcine eyes, we tested the hypothesis that elevated IOP under conditions relevant to phacoemulsification surgery leads to increased CEC damage.

Methods: Corneal endothelia of fresh, intact explanted porcine eyes were stained with two nucleic acid viability dyes and imaged through a fluorescence microscope without removing the cornea from the globe. The anterior chambers of the eyes were perfused with BSS to a pressure of 73.6mmHg (bottle height=100cm) for 10min (n=4) prior to restaining and reimaging. Baseline images were analyzed using custom algorithms to determine initial total cell counts (TC_1) and damaged/dead cell counts (DC_1). Images acquired after pressurization were analyzed to obtain final cell counts (TC_2, DC_2). CEC damage was quantified as the change in percent of cell damage/death, PCD ($PCD=100*DC_2/TC_2 - 100*DC_1/TC_1$). As a negative control, additional eyes were pressurized to a physiological IOP of 18.4mmHg for 10min (n=4). The experimental and negative control groups were compared using a two-tailed Student's t-test. As a positive control, one eye was perfused with deionized water at a pressure of 18.4mmHg for 10min.

Results: There was no significant difference in mean PCD values between the experimental (0.22%) and negative control (0.30%) groups (p=0.78). The positive control sample yielded a PCD of 84.5%, indicating that the method is able to detect CEC damage.

Conclusions: Our results suggest that the elevated IOP used over the duration of phacoemulsification surgery does not lead to a significant increase in CEC damage. However, further studies are needed to expand the sample size and ensure statistical power. Notably, the mean PCD measured in the experimental group was less than the yearly decrease in the central CEC density of healthy individuals (0.59%), strongly suggesting that surgical IOP alone does not result in clinically-significant CEC damage.

CONTROL ID: 3712874

SUBMITTER (NAME ONLY): Rachel Tandias

TITLE: Assessment of Microvascular Changes After Rhegmatogenous Retinal Detachment (RRD) Repair With Wide-Field Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA)

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Tandias, I. Garg, F. Vingopoulos, R. Katz, Y. Cui, M. Duich, R. Zeng, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|R. Tandias, I. Garg, F. Vingopoulos, R. Zeng, N.A. Patel, J.B. Miller, Retina Service, Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Cui, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To evaluate microvascular changes in the macula and extra-macular region on WF SS-OCTA and assess their association with visual acuity (VA) following RRD repair.

Methods: We conducted a retrospective, cross-sectional, observational study of 241 patients imaged with WF SS-OCTA (PLEX® Elite 9000) between Dec. 2018 and June 2021. The Advanced Retinal Imaging Network (Zeiss Portal) was used to obtain vessel density (VD) and vessel skeletonized density (VSD) of the superficial capillary plexus (SCP), deep capillary plexus (DCP), and whole retina as well as foveal avascular zone (FAZ) parameters from 3×3 mm, 6×6 mm, and 12×12 mm fovea-centered scans. Mixed-effects multiple regression models adjusting for age, presence of diabetes mellitus or hypertension, lens status, extent and duration of detachment, and interval from surgery to imaging were used for statistical analysis.

Results: We included 97 eyes of 92 patients who underwent successful repair of macula-off (n=54) or macula-on (n=43) RRD, 67 unaffected fellow eyes, and 185 control eyes of 149 healthy patients. Median interval from surgery to imaging was 13 (3-78) months. Compared to controls, RRD eyes showed reduced SCP VSD (β=-0.18, p=0.02), VD (β=-0.02, p=0.01), and FAZ circularity (β=-0.06, p=0.004) in 3x3 mm scans and lower VSD/VD in the SCP (β=-0.87, p=0.04; β=-0.03, p=0.03), DCP (β=-1.17, p=0.03; β=-0.03, p=0.03), and whole retina (β=-0.90, p=0.05; β=-0.03, p=0.04) in 12x12 mm scans. RRD eyes also had lower SCP VSD (β=-0.55, p=0.03), VD (β=-0.01, p=0.01), and FAZ circularity (β=-0.06, p<0.001) in 3x3 mm scans than fellow eyes. Postoperative VA at the time of imaging was associated with SCP VD (β=-1.07, p=0.04) in 3x3 mm scans. Macula-off eyes had lower FAZ circularity (β=-0.05, p=0.02) than macula-on RRD eyes, while eyes treated with cryopneumatic retinopexy showed increased FAZ perimeter (β=0.71, p=0.009) and reduced circularity (β=-0.13, p=0.01) compared to vitrectomized eyes.

Conclusions: Vessel densities in the SCP and DCP were reduced on 3×3 mm and 12×12 mm scans of postoperative RRD eyes compared to controls and fellow eyes. SCP VD was significantly associated with postoperative VA.

CONTROL ID: 3712875

SUBMITTER (NAME ONLY): eVhy Apryani

TITLE: Identification of cell populations and genetic mechanisms through single cell sequencing in proliferative vitreoretinopathy

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is the most common cause of failure of retinal reattachment surgery. The development of PVR occurs following a retinal tear and rhegmatogenous retinal detachment resulting in epiretinal and/or subretinal membrane formation that can redetach the retina and lead to blindness. Determining the specific cell types present in the membranes will allow us to have a better understanding of the disease process and may lead to the development of novel target therapies for the prevention of PVR. In this study, we sought to characterize the cell types and identify genes that are critical to the development of PVR.

Methods: Four idiopathic epiretinal membranes, 1 subretinal membrane and 1 ciliary body membrane were obtained from patients during surgery and were immediately processed for single cell isolation according to our previously published protocol. Single cell suspension of PVR membranes was prepared according to the protocol as specified by the 10x Genomics sample preparation guide (CG00053) and single cell RNA-seq (scRNA-seq) was performed using 10x Genomics Chromium Single Cell 3' Reagent Kits version 2. The single cell sequencing data were then analyzed using the open-source Seurat kit. The counts matrix was filtered to only include the top 5,000 variable features before clustering.

Results: The full dataset contains 33,694 features and 4,627 cells. Using the associated marker genes, five cell types were identified as retinal pigment epithelium (RPE), microglia, T cells, B cells and fibroblasts. Remarkably, about 56% of the total cells were categorized as immune cells. Heatmap analysis identified several genes that are involved in PVR development including genes involved in inflammation and epithelial-mesenchymal transition (EMT). Enrichment analysis based on gene ontology pathway analysis suggested that the common differential expressed genes were significantly enriched in oxidative phosphorylation and EMT.

Conclusions: This study illustrates how scRNA-seq may be used to understand the pathophysiology of PVR. Identification of specific cell types and genes that are critical to PVR development will provide the basis for discovery and development of novel treatments and PVR prevention. Our findings also highlight the role of immune cells in PVR pathobiology.

CONTROL ID: 3712876

SUBMITTER (NAME ONLY): Raju Rajala

TITLE: Phosphatidylinositol 5-Kinase (PIKfyve) Negatively Regulates Photoreceptor Neuroprotection

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.V. Rajala, Ophthalmology and Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|M.A. Bhat, K. Teel, A. Rajala, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|R.V. Rajala, Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Phosphatidylinositol-3-phosphate 5-kinase (PIKfyve) is a phosphoinositide 5-kinase that phosphorylates PI(3)P to generate $PI(3,5)P_2$. PI(3)P is generated from PI by the action of class III PI3K, Vps34. Vps34 loss in rods resulted in rod degeneration. The 5'-phosphatase (called FIG4) dephosphorylates $PI(3,5)P_2$ to PI(3)P. FIG4 loss also resulted in retinal degeneration. The role of PIKfyve in photoreceptor functions is unknown. This study examined the role of PIKfyve in the retina.

Methods: PIKfyve KO mice were generated under the control of retina-specific Chx10 (abbreviated as $^{ret}Pikfyve^{-/-}$) promoter. $PI(3,5)P_2$ levels were measured and immunoblot analysis with anti-PIKfyve, anti-rhodopsin, cone-arrestin, and sodium-potassium ATPase-alpha (NKAα) antibodies was performed in PIKfyve floxed and $^{ret}Pikfyve^{-/-}$ mouse retinas. Structure and function were assessed at 8 months of age. PIKfyve floxed and $^{ret}Pikfyve^{-/-}$ mice were subjected to light stress (LS) at 10,000 lux for 7 days. $PI(3,5)P_2$ is needed for late endosome and lysosome maturation. We examined the expression of NKAα, removed through the lysosomal degradation pathway. One week after LS, mice were subjected to ERG, followed by histological examination.

Results: $^{ret}Pikfyve^{-/-}$ retina had 70% less PIKfyve protein and more than 80% less $PI(3,5)P_2$ when compared to PIKfyve floxed retina. However, there was no significant difference in retinal function and structure between PIKfyve floxed and $^{ret}Pikfyve^{-/-}$ mice at 8 months of age. Light-stressed PIKfyve floxed mice exhibited photoreceptor degeneration; the structure was well preserved in light-stressed $^{ret}Pikfyve^{-/-}$ mice. Immunoblots showed no significant difference in the levels of rhodopsin, NKAα, and cone arrestin between PIKfyve floxed and $^{ret}Pikfyve^{-/-}$ mice without LS. Light-stressed PIKfyve floxed mice had significantly reduced levels of rhodopsin, cone arrestin, and NKAα compared with light-stressed $^{ret}Pikfyve^{-/-}$ mice. Light-stressed $^{ret}Pikfyve^{-/-}$ mice had a normal retinal function and well-preserved retinal structure, whereas light-stressed PIKfyve floxed mice had significantly reduced function and exhibited retinal degeneration.

Conclusions: The data suggest that PIKfyve-generated $PI(3,5)P_2$ regulates late endosome and lysosome maturation, and loss of PIKfyve promotes photoreceptor neuroprotection. Modulating the PIKfyve activity under retinal degenerative conditions may have therapeutic benefits.

CONTROL ID: 3712877

SUBMITTER (NAME ONLY): Gary Peh

TITLE: EVALUTAION OF VARIOUS RHO-ASSOCIATED KINASE (ROCK) INHIBITORS ON THE ATTACHMENT AND PROLIFERATION OF PRIMARY CORNEAL ENDOTHELIAL CELLS

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.S. Peh, F. Bandeira, H. Ong, K. Adnan, J.S. Mehta, Singapore Eye Research Institute, Singapore, SINGAPORE|G.S. Peh, Duke-NUS Medical School, Singapore, SINGAPORE|F. Bandeira, São Gonçalo Eye Hospital, BRAZIL|H. Ong, J.S. Mehta, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: The purpose of this study is to evaluate the use of various rho-kinase inhibitors (ROCKi) for the propagation of primary human corneal endothelial cells (HCEnCs).

Methods: Pairs of donor corneas unsuitable for transplantation were procured, isolated and expanded using a dual media approach. Several ophthalmic ROCKi (Netarsudil and its derivative (AR-13324, AR-13503), Verosudil (AR-12286), Ripasudil (K-115)), along with various classes of ROCKi compounds (Indazole, Aminofurazan, Amide, Benzodiazapiene) were comparatively evaluated for their effect on HCEnCs over a range of concentrations, and their capacity to improve cellular adherence. Control group was donor-matched HCEnCs treated with Y-27632. Initial experiments were performed using xCELLigence cell analyzer (n=3). Impedance readings from experiments were recorded and used as a quantitative measure to evaluate the effect of each ROCKi on HCEnCs. From the initial results, the two most efficacious ROCKi (AR-13324 and AR-13503) were further assessed for their capacity to improve HCEnCs proliferation using an EdU incorporation Click-iT assay.

Results: The classes of Indazole and Amide ROCKi compound, and K-115 were comparable to Y-27632 in terms of their working concentrations (100nM to 30mM). Both classes of Aminofurazan and Benzodiazapiene ROCKi had a negative impact on HCEnCs at 30mM, whereas the Y-39983 molecule were detrimental to the HCEnCs from 10mM. Of the AR-compounds, AR-12286 was comparable to Y-27632 at all 3 concentrations evaluated, whereas AR-13324 and AR-13503 negatively affected HCEnCs from 10mM. In fact, AR-13324 was cellular toxic from 10mM. Interestingly, at 100nM, both AR-13324 and AR-13503 significantly improved the attachment of HCEnCs over Y-27632. Proliferatively, both AR-13324 (100nM) and AR-13503 (1mM) were comparable to that of Y-27632 (10mM) even though lower concentrations were used.

Conclusions: We were able to demonstrate that various ROCKi evaluated including Ripasudil (K-115) and Netarsudil (AR-13324 and AR-13503) were comparable in their capacity to improve cellular attachment of HCEnCs at various concentrations. Subsequent evaluation revealed the Netarsudil molecules to aid proliferation of HCEnCs even when used at lower concentrations to Y-27632. Further functional assessment of Netarsudil within a cell injection rabbit model of bullous keratopathy is currently on going.

CONTROL ID: 3712879

SUBMITTER (NAME ONLY): Luis Garcia-Enriquez

TITLE: Happiness, Visual Function, and Quality of Life in Glaucoma Patients

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Garcia-Enriquez, D. Valencia Paredes, A. Orozco Garcia, Research, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|J.A. Paczka, L.A. Giorgi-Sandoval, A. Orozco Garcia, Research, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|L.A. Giorgi-Sandoval, L.A. Paczka-Giorgi, Research, Clínica para el Ojo Seco, Guadalajara, Jalisco, MEXICO|L.A. Paczka-Giorgi, Research, Telemedicine LATAM, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Patient-reported outcomes (PROs) provide patients' perspective of the disease. Positive psychological factors, such as happiness, have been credited with improving human functioning, and helping people live more successful lives. Happiness (a higher order concept, reflecting a more a stable state of being well) is not frequently used as a PRO in eye research. However, since an important goal of glaucoma management is the preservation of patients' visual function and quality of life (QoL), happiness could be a useful descriptor to interpret the wellbeing of patients with glaucoma. This pilot study attempts to measure the correlation between happiness and QoL, with the functional impact of the disease.

Methods: Telephone contact was carried out with patients identified in a database of a glaucoma center. Once their identity was confirmed and they provided verbal consent, they were invited to answer a set of questionnaires (OSDI, Subjective Happiness Scale or HSH, and NEI-VFQ-25). The local research board granted permission to perform this study. The analyzed variables were best-corrected visual acuity, glaucoma stage of severity (Hodapp et al classification), perimetry parameters (MD, PSD, VFI), average RNFL thickness (OCT), and number of antiglaucoma medications. The correlations between the variables were analyzed. A p-value of ≤ 0.05 was considered as statistically significant.

Results: Eighteen out of 23 contacted patients accepted to participate in the study. All patients had complete clinical information regarding glaucoma and underwent the entire set of questionnaires. The mean age of patients was 68.8±10.2 years (10 female, 8 male). All of them had POAG (7 mild, 6 moderate, 5 severe). General and specific information comparing three groups of glaucoma severity is presented in table 1. Scores of happiness had either a good or very good correlation (and statistical significance) with average RNFL thickness (OD, r=0.49, p=0.038; OS, r=0.65, p=0.003), OSDI (r=-0.51, p=0.03), severity of glaucoma (r=-0.50, p=0.033), and mean NEI-VFQ 25 score (r=0.79, p=0.0001).

Conclusions: Up to our knowledge, this preliminary study approaches happiness as a PRO for the first time in a glaucoma study. Our results suggest that this outcome can be a useful PRO to be added to other questionnaires, which can broaden the clinician perspective about the impact of glaucoma on patients' lives.

CONTROL ID: 3712880

SUBMITTER (NAME ONLY): Luis Vasquez

TITLE: Ocular Pain in Dry Eye Disease and its Association with Clinical Parameters

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.E. Vasquez, Z. Harbin, Z. Brooke, Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|J. Isteitiya, C. Villanueva, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular pain is an important symptom of dry eye disease (DED) which can substantially affect patients' quality of life. The purpose of this study is to evaluate severity and frequency of ocular pain in patients with DED and investigate their associations with other clinical parameters.

Methods: This cross-sectional study included 62 patients with DED. Using a questionnaire, they were asked to quantify the frequency and severity of their ocular pain using a 10-point scale with 10 indicating the most severe or most frequent pain, respectively. Patients also underwent a comprehensive ocular surface evaluation, including Ocular Surface Disease Index (OSDI) questionnaire, tear break up time (TBUT), corneal fluorescein staining, conjunctival lissamine green staining, and Schirmer test with anesthesia. The associations between severity and frequency of ocular pain with other clinical parameters were also investigated by regression analysis.

Results: There were 44 women and 18 men, with a mean age of 60.8 ±13.8 years (range, 27-87 years). The mean OSDI score was 53.4 ± 19.7. The mean values were 2.6 ± 2.7 for pain severity and 2.8 ± 3.3 for pain frequency. Regarding severity, mild pain (scores 1-4) was reported in 24 patients (38.7%), moderate pain (scores 5-7) in 8 (12.9%), and severe pain (scores 8-10) in 6 (9.7%). 24 (38.7%) did not report any ocular pain. Pain frequency was reported as infrequent (scores 1-4) in 21 (33.9%), moderately frequent (scores 5-7) in 8 (12.9%), and very frequent (scores 8-10) in 9 (14.5%). Severity and frequency of ocular pain demonstrated significant, but weak, correlations with the OSDI score ($P = 0.04$, $rs=0.26$, for both). Regression analysis showed a significant association between pain severity and Schirmer score ($P=0.001$, $\beta=0.28$). There were no significant associations between severity or frequency of ocular pain and age, sex, ethnicity, history of depression or anxiety, or clinical signs of DED.

Conclusions: Most patients with DED report experiencing ocular pain, which was mild and infrequent in majority. Ocular pain had only a weak correlation with OSDI and no significant association with other clinical parameters including signs of DED. In addition to routine questionnaires and clinical tests, a detailed evaluation of ocular pain symptoms is important in patients with DED.

CONTROL ID: 3712883

SUBMITTER (NAME ONLY): James Katz

TITLE: VEGA-1: Phentolamine Ophthalmic Solution as a Single Agent Improves Distance-Corrected Near Visual Acuity in Patients with Presbyopia

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Katz, The Midwest Center for Sight, Des Plaines, Illinois, UNITED STATES|A. Kolli, University of Michigan, Ann Arbor, Michigan, UNITED STATES|E. Lazar, eICON Medical Consulting, New York, UNITED STATES|R. Patel, K. Rahmani, M. Sooch, M.G. Brigell, Ocuphire Pharma, Inc., Michigan, UNITED STATES|J.S. Pepose, Pepose Vision Institute, Chesterfield, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the VEGA-1 Phase 2b presbyopia clinical trial, 0.75% phentolamine ophthalmic solution (POS) in combination with low dose pilocarpine (LDP) had a tolerable safety profile and met its primary efficacy endpoint by improving near vision by 3 lines. This abstract describes a pre-specified secondary analysis evaluating the efficacy of POS alone for improving distance-corrected near visual acuity (DCNVA) by 3 lines in presbyopia patients.

Methods: In the VEGA-1 trial, a Phase 2b, multi-center, randomized, placebo-controlled, double-masked clinical trial, a pre-specified secondary analysis evaluated the efficacy of POS alone for the treatment of presbyopia. Subjects with DCNVA of 20/50 or worse were randomized to receive POS vs placebo for 3-4 nights. The following morning at study visit 2, the percent of patients with ≥15 letters (3 lines) binocular photopic DCNVA improvement relative to baseline on an ETDRS chart in the POS and placebo arms were compared using logistic regression. We also assessed ≥ 10 letter (2 line) DCNVA improvement outcomes. Mean change in number of ETDRS letters read between treatment arms was compared using analysis of covariance. Percentage of subjects achieving DCNVA of 20/40 or better was also assessed.

Results: After randomization, 73 and 75 subjects received POS and placebo, respectively. Twelve or more hours after treatment, 30% of subjects in the POS arm and 14% in the placebo arm had a ≥ 15 letter binocular DCNVA improvement (p=0.027). POS compared to placebo resulted in more subjects achieving DCNVA improvements of ≥ 10 letters (53% vs 28%; p=0.005) and ≥ 5 letters (75% vs 55%; p=0.01). Compared to baseline, POS conferred a mean 10.2 letter improvement in DCNVA, significantly more than the 5.8 letter improvement with placebo (p=0.0008). Forty-one (56%) patients treated with POS and 27 (36%) treated with placebo had DCNVA of 20/40 or better (p=0.014). POS demonstrated similar improvements in monocular DCNVA. POS showed a favorable safety profile with only few mild adverse events and no headaches.

Conclusions: In this Phase 2b clinical trial, POS showed clinical efficacy to achieve a ≥15 letters improvement in DCNVA in presbyopia subjects. Given these results, advancement to Phase 3 trials is planned to evaluate the efficacy of POS alone and in combination with LDP for presbyopia.

CONTROL ID: 3712884

SUBMITTER (NAME ONLY): Liang Li

TITLE: Epitranscriptomic m^6A modification controls the development of late-born retinal progenitor cells

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Li, C. Lin, M. Wu, A.E. Davis, S. Wang, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|Y. Sun, Neurosurgery, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Liang Li: Commercial Relationship: Code N (No Commercial Relationship) | Yue Sun: Commercial Relationship: Code N (No Commercial Relationship) | Cheng-Hui Lin: Commercial Relationship: Code N (No Commercial Relationship) | Man-Ru Wu: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Davis: Commercial Relationship: Code N (No Commercial Relationship) | Sui Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: During retinal development, the cell cycle progression of retinal progenitor cells (RPCs) needs to be tightly controlled to ensure proper cell differentiation. CDKs (cyclin-dependent kinases), cyclins, CDK inhibitors, and several transcription factors are known to play key roles in regulating the cell cycle progression of RPCs. We looked for mechanisms that can bridge the regulation at the protein/kinase and transcriptional levels, and propose to elucidate the roles of post-transcriptional m6A (N^6-Methyladenosine) modification of mRNAs in regulating RPCs cell cycle.

Methods: We conditionally knocked out m^6A writer methyltransferase-like 14 (METTL14) from the beginning of retinal development. The histology of the METTL14 conditional knock-out (CKO) retinas was evaluated and compared to wild-type retinas at different development stages. The proliferation of RPCs was assessed by EdU cell proliferation assay. Cell cycle analysis was conducted by Fluorescence-activated cell sorting flow cytometry (FACs). RPCs lineage tracing was performed using retroviruses. The m^6A high-throughput sequencing (m^6A-seq) and single-cell sequencing technology were used to map out the differential gene expression profiles and the downstream signaling pathways.

Results: We found that the genes involved in directing m6A modification are expressed in the mouse retina. Mettl14 CKO retinas showed abnormal RPCs cell cycle arrest at neonatal stages. The majority of these arrested RPCs underwent apoptosis. A small fraction of them can bypass the apoptosis pathway and differentiate mainly into Müller cells. We further identified the m6A modified genes in the retina via m6A-seq and single-cell RNA-seq and uncovered their potential roles in regulating the RPCs cell cycle.

Conclusions: Our work demonstrates that epitranscriptomic m6A modification is essential for regulating the RPCs cell cycle during development. Manipulation of the m^6A modification pathways may provide promising control of abnormal cell proliferation observed in some retinal diseases.

CONTROL ID: 3712885

SUBMITTER (NAME ONLY): Susannah Waxman

TITLE: Astrocyte Morphology in the Collagenous Lamina Cribrosa Revealed by Multicolor DiOlistic Labeling

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Waxman, M. Quinn, I. Sigal, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|C. Donahue, L. Falo, Dermatology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|S. Salavatian, A. Mahajan, Anesthesiology and Perioperative Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|L. Falo, I. Sigal, Bioengineering, University of Pittsburgh Swanson School of Engineering, Pittsburgh, Pennsylvania, UNITED STATES|D. Sun, Massachusetts Eye and Ear Infirmary, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Susannah Waxman: Commercial Relationship: Code N (No Commercial Relationship) | Marissa Quinn: Commercial Relationship: Code N (No Commercial Relationship) | Cara Donahue: Commercial Relationship: Code N (No Commercial Relationship) | Siamak Salavatian: Commercial Relationship: Code N (No Commercial Relationship) | Aman Mahajan: Commercial Relationship: Code N (No Commercial Relationship) | Louis Falo: Commercial Relationship(s);Code P (Patent):Skinject | Daniel Sun: Commercial Relationship: Code N (No Commercial Relationship) | Ian Sigal: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Astrocytes in the lamina cribrosa (LC) play important roles in cell signaling and extracellular matrix remodeling, impacting the physiology of neural tissues necessary for vision. Although LC astrocyte morphology is known to undergo substantial changes throughout the pathogenesis of glaucoma, techniques to evaluate LC astrocyte morphology are limited. We hypothesized that multicolor DiOlistic labeling allows visualization of LC astrocytes and evaluation of key morphological features.

Methods: Gold microparticles were coated with all combinations of three fluorescent lipophilic dyes (DiI, DiD, and DiO) to create 7 different groups of microcarriers. Coronal vibratome sections were obtained through the LC of pig, sheep, and goat eyes (N = 2 sections each) at 200μm thickness. Dye-coated microcarriers were ballistically delivered into sections with a Helios gene gun. Cells were imaged via confocal microscopy and collagen was imaged via second harmonic generation (SHG). 25 total dyed astrocytes were segmented and morphological features quantified in Imaris.

Results: Microcarriers embedded within cells delivered dye that distributed across their respective cell membranes. Somas and fine ramified processes of astrocytes labeled with all 7 different combinations of dyes were visualized. Label density allowed visualization of individual astrocytes within LC pores. Distinct dye combinations allowed discerning individual astrocytes with processes in close proximity to one another, sharing spatial domains. SHG imaging allowed for visualization of astrocytes within the context of surrounding collagen beams. Average astrocyte branch number, length, depth, and straightness were 147.4 ± 106.7, 11.5 ± 10.2μm, 9.1 ± 5.3, and 0.9 ± 0.1.

Conclusions: Multicolor DiOlistic labeling in vibratome sections of collagenous LC is a suitable technique for visualization and morphological analysis of astrocytes. LC astrocytes demonstrated diverse morphologies and physical interactions with surrounding structures. Healthy LC astrocyte morphologies and interactions can later be compared with those in glaucomatous LCs to better understand the role of astrocytes in pathogenesis.

CONTROL ID: 3712886

SUBMITTER (NAME ONLY): Xiaoyu Cai

TITLE: NLRP3 inflammasome activation affects neuroretinal function in diabetic retinopathy

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Cai, B. Gelfand, J. Ambati, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|B. Gelfand, J. Ambati, Center for Advanced Vision Science University of Virginia, Charlottesville, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evidence suggests that inflammasome activity contributes to the pathogenesis of diabetic retinopathy (DR), but there remains uncertainty in the role of the NLRP3 inflammasome in DR. We sought to elucidate the timing of inflammasome activation and evaluate the involvement of NLRP3 inflammasome constituents including NLRP3, the adaptor ASC, and the protease Caspase-1 using a streptozotocin (STZ) induced DR mouse model.

Methods: The STZ model was used to induce diabetes (DM) in C57BL/6J wild type (WT) mice (male (m) N=60; female (f) N=20) as well as Caspase-1 knock out (KO) (m N=7; f N=5), ASC KO (m N=9; f N=9), and NLRP3 KO (m N=9; f N=8) mice. Vehicle control was used for control (CTL) mice of each genotype and sex. After one, three, and eight months of hyperglycemia, bilateral eyes were harvested with one eye being embedded for cryo-sectioning and the other being dissected for whole retina collection. Collected neuroretina were evaluated for inflammasome activity with immunoblotting. Gliosis and neuroinflammation were visualized through immunofluorescence staining of cryosectioned eyes for NLRP3 inflammasome constituents. Retinal neurodegeneration was also evaluated using scotopic electroretinography (ERG).

Results: At one and three months after STZ induction, immunoblotting of whole retinal lysates showed minimal increase of inflammasome activation in WT DM mice compared to WT CTL mice. On ERG evaluation at three months, there was a 23.1% decrease in a-wave and a 32.3% decrease in b-wave between DM and CTL WT mice. For Caspase-1 KO mice, there was a lesser decrease of 10.8% and 21.8% in a- and b-waves respectively, and in ASC KO mice there was also a lessened decrease of 5% in a-wave and 18.3% in b-wave between DM and CTL mice.

Conclusions: Our results suggest that while inflammasome activation may not be evident on protein analysis, on ERG evaluation there is a decrease in readings that may be indicative of a reduction in neuroretinal function by three months of DR. Additionally, the reduced loss of electrical function in both Caspase-1 KO and ASC KO mice may represent a partial rescue of neuroretinal function when components of the NLRP3 inflammasome are absent. This finding helps to establish a direct connection between inflammasome constituents to the pathological processes of DR. Further investigation is needed to elucidate the precise role of NLRP3 inflammasome activation in the pathogenesis of DR.

CONTROL ID: 3712888

SUBMITTER (NAME ONLY): Daniel Choi

TITLE: Evaluation of Long-Term Intravitreal Anti-Vascular Endothelial Growth Factor (VEGF) Injections on Renal Function

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Choi, B. McGeehan, B.L. VanderBeek, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Daniel Choi: Commercial Relationship: Code N (No Commercial Relationship) | Brendan McGeehan: Commercial Relationship: Code N (No Commercial Relationship) | Brian VanderBeek: Commercial Relationship(s);Code C (Consultant/Contractor):EyePoint Pharmaceuticals

ABSTRACT BODY:

Purpose: Studies have shown that intravitreal anti-VEGF can reduce plasma free-VEGF. However, the literature is sparse on the safety of long-term intravitreal anti-VEGF injections on the body, especially the kidney. We assessed the risk of developing chronic kidney disease or end-stage renal disease in patients receiving multiple anti-VEGF injections.

Methods: A commercial and Medicare Advantage medical claims database was used to identify all patients who were given an intravitreal anti-VEGF agent. The number of injections was then totaled for the proceeding 4 years following the initial injection. Exclusion occurred if patients at the time of the first injection were <18 years old, had <2 years of data in the plan or had any history of kidney disease (defined by either ICD code or estimated glomerular filtration rate). Patients were then divided into quartiles based on number of injections to compare the highest and lowest quartiles. Subanalysis was also done on those with individual disease states: neovascular AMD, macular edema due to RVO (MERVO), or diabetic retinopathy (DR). A weighted multivariable logistic regression analysis compared the odds of being diagnosed with chronic or end-stage kidney disease. A second time updating analysis, which did not require a specific time in the plan, used Cox proportional regression to assess an every 5-injection increase in the hazard of developing kidney disease.

Results: 13,895 patients in the lowest quartile (representing 1-3 injections) were compared to13881 in the highest quartile (≥21 injections). The nAMD had 6228 (1-4 injections) and 6172 (≥24); MERVO had 573 (1-2) and 580 (≥12); and DR had 523 (1-2) and 517(≥13) in the lowest and highest quartiles, respectively. Weighted analysis showed no association overall (OR=1.00, 95% CI:0.98-1.01, p=0.58) or in nAMD (OR=0.99, 95% CI:0.97-1.02, p=0.48), decreased odds in MERVO (OR=0.93, 95% CI:0.86-0.99, p=0.04) and increased odds in DR (OR=1.12, 95% CI:1.03-1.22, p=0.01) for the highest quartile. Time updating Cox analysis showed no association overall or for any subgroup (HR=0.97-1.01, p>0.27 for all comparisons).

Conclusions: While logistic regression showed some association of increased number of injections with kidney disease, time updating cox analysis was unable to confirm these findings, suggesting time was a confounder in the logistic regression analysis.

CONTROL ID: 3712889

SUBMITTER (NAME ONLY): Ming Chen

TITLE: Alternative oxidase expression slows photoreceptor degeneration due to RPE mitochondrial dysfunction

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chen, D. Vollrath, Department of Genetics, Stanford University School of Medicine, Stanford, California, UNITED STATES|Y. Wang, J. Du, Department of Ophthalmology and Visual Sciences, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Compromised RPE mitochondrial function has been implicated in the pathogenesis of AMD. We previously reported that ablation of Tfam in the mouse RPE (RPEΔTfam) results in OXPHOS deficiency, unexpected effects on RPE cell phenotype, and photoreceptor degeneration. We hypothesize that expression of alternative oxidases from C. intestinalis (AOX) and yeast (NDI1) in the RPE of RPEΔTfam mice will bypass loss of function of complexes III and IV (AOX) and complex I (NDI1), and restore respiration without ATP generation to the OXPHOS-deficient RPE in vivo. We sought to test this hypothesis and determine the effects of alternative oxidase expression on the RPEΔTfam retinal phenotype.

Methods: We used φC31 integrase-mediated site-specific transgenesis to generate C57BL/6J mice with Cre-conditional expression of epitope-tagged AOX and NDI1. BEST1-Cre;Tfam$^{fl/fl}$;tg:AOX-NDI1 mice were generated and assessed by immunoblot of RPE cell lysates and immunofluorescence imaging of RPE/choroid flatmounts. Cre expression, RPE morphology, and mean RPE cell area were assessed by flatmount staining. Oxygen consumption of eyecups in the presence of OXPHOS poisons was assessed with the Seahorse platform. Retinal structure and function were evaluated by OCT and ERG. Statistical analyses were done by two-tailed Student's t-tests.

Results: AOX and NDI1 proteins are specifically expressed in the RPE of BEST1-Cre;Tfam$^{fl/fl}$;tg:AOX-NDI1 mice and co-localize with Hsp60, a mitochondrial marker. Eyecups from AOX/NDI1 expressing mice maintain oxygen consumption in the presence of cyanide, consistent with AOX function. 18 week-old BEST1-Cre;Tfam$^{fl/fl}$;tg:AOX-NDI1 mice have a smaller mean RPE cell area (432 ± 28 μm^2) compared to RPEΔTfam mice (667 ± 101 μm^2; p=0.034, n=3 each). AOX/NDI1 expression slows retinal thinning at 22-24 weeks (242 ± 7 vs 208 ± 10 μm for RPEΔTfam; p=0.006, n=4 each), and AOX/NDI1 expression improves scotopic a-wave (p=0.044), scotopic b-wave (p=0.015), and photopic b-wave (p=0.013) amplitudes at 40-41 weeks (n=4 each).

Conclusions: AOX/NDI1 expression in the OXPHOS-deficient RPE of RPEΔTfam mice has significant beneficial effects on RPE cell phenotype, and photoreceptor viability and function in vivo. We are actively investigating which metabolic changes correlate with these profound phenotypic changes.

CONTROL ID: 3712890

SUBMITTER (NAME ONLY): Abdul Rasheed Mohammed

TITLE: Acute Idiopathic Posterior Vitreous Detachment And Fellow Eyes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mohammed, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|S. Sen, Aravind Eye Hospital, Madurai, Tamil Nadu, INDIA|B. Rosario, UPMC Eye Center, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J. Chhablani, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study the incidence and clinical presentation of acute idiopathic posterior vitreous detachment (PVD) at a tertiary care eye center.

Methods: Patients with less than 2 months of symptoms with any significant ocular history in the presenting eye were included in the study. Patients with symptoms of floaters/flashes longer than 2 months; significant ocular history including eventful cataract surgery, inflammation, trauma, YAG capsulotomy, ocular migraine were excluded. Between September 2019 and May 2021, a total of 101 consecutive patients with complaints of floaters and/or flashes in at least one eye underwent dilated fundus examination by a single retinal specialist to detect the presence of PVD. All patients were followed up by the same retina specialist at week 1, week 4, week 8, and then on an as-needed basis.

Results: This study included 101 patients presenting with 94.05% patients presenting with unilateral symptoms and 5.9% bilateral complaints. PVD was diagnosed in 129/202 eyes (63.9%) with 73 eyes (36.1%) having unilateral PVD and 56 eyes (27.7%) with bilateral PVD. A retinal break was identified in 15.5% of eyes with PVD. Prevalence of pre-existing PVD in fellow eyes was 20.7%, however, a further 13.7% unaffected eyes developed fresh PVD during follow-up. None of the study eyes developed additional new breaks during follow-up.

Conclusions: Patients presenting with symptoms suggestive of acute PVD unilaterally need to be screened for PVD in both eyes, as almost $1/5^{th}$ population may have fellow-eye involvement. Future screenings should be decided based on individual risk and PVD status at presentation.

CONTROL ID: 3712891

SUBMITTER (NAME ONLY): Changyow Kwan

TITLE: Corneal nerve changes on confocal microscopy after cenegermin treatment for neurotrophic keratitis

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kwan, C. Kim, Y. Shi, S. Garg, O.L. Lee, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cenegermin, a recombinant human nerve growth factor (rhNGF) eye drop formulation, was recently approved by the U.S. Food and Drug Administration for the treatment neurotrophic keratopathy (NK), a degenerative condition of the cornea characterized by decreased corneal sensation and poor corneal healing. This study aims to better understand the effects of cenegermin on patients with NK by analyzing corneal sensation, epithelial healing and corneal nerve structure through in vivo confocal microscopy (IVCM) before and after treatment.

Methods: This study included five eyes from five patients with NK stage 1 or 2 who completed a 6-week course of cenergemin treatment. Patients underwent clinical examination with assessment of corneal fluorescein staining, corneal sensation using a cotton wisp and examination of IVCM images of the corneal nerves in the basal epithelium neural plexus at baseline and after completing a 6-week course of treatment. The percentage area of corneal epithelial defect on fluorescein images was measured with ImageJ. IVCM images were analyzed for neuron density using NeuronJ (NIH, Bethesda, MD).

Results: Zero out of five eyes had visible corneal nerves on ICVM imaging prior to cenergemin treatment. After treatment, three out of five eyes had visible nerves on ICVM imaging (average density 2284.75 um/mm^2). The two patients who did not have visible nerves after treatment had comorbidities including corneal transplant and acanthamoeba infection. Epithelial fluorescein staining improved in all patients. The two eyes with stage 2 NK had epithelial defects at baseline examination, and both had complete resolution after treatment. Corneal sensation was stable in two out of five eyes and improved in three out of five eyes after treatment.

Conclusions: Treatment with cenegermin is effective in promoting corneal epithelial healing and nerve regrowth in patients with NK. Patients had improved epithelial appearance, corneal sensation and nerve density on IVCM after treatment with cenegermin. IVCM is a safe and minimally invasive imaging method that can be used to track structural response to cenegermin treatment.

CONTROL ID: 3712892

SUBMITTER (NAME ONLY): Praveen Bandela

TITLE: Role of accommodative microfluctuations in deciphering the sign of defocus for blur-driven accommodation

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.K. Bandela, A. Ho, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|P.K. Bandela, A. Ho, E. Papas, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|S.R. Bharadwaj, Brien Holden Vision Institute of Optometry and Vision Sciences, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S.R. Bharadwaj, Hyderabad Eye Research Foundation, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: While theoretical models envision the possibility that accommodative microfluctuations aid in deciphering the sign of defocus, empirical evidence for the same remains ambiguous. This study investigated this issue by determining the initial direction and dynamics of blur-driven accommodation through real-time manipulation of these microfluctuations.

Methods: A PlusOptix PowerRef3™ photorefractor recorded the ocular refraction of 10 young adults (23.8±3.8yrs) at 50Hz while they fixated on a Maltese cross stimulus that stepped between 1D and 3D demands with randomized onset time. The difference between two consecutive refraction data points was considered as an accommodative microfluctuation and its sign-reversed values were synchronously fed into an Optotune™ electrically tunable lens (ETL) to neutralise the microfluctuations in real-time. The initial direction, magnitude, latency and peak velocity of the step response was determined while manipulating the ETL accommodative microfluctuation feedback relative to baseline viewing.

Results: ETL manipulation of accommodative microfluctuations did not alter the proportion of step responses with correct initial direction (median(IQR) accommodation: 73.2 (56.1 – 81.8) %; disaccommodation: 75.0 (47.8 – 80.0)% or their response magnitudes (accommodation: 1.97±0.40D; disaccommodation: 1.95±0.40D), relative to baseline (correct response proportion 83.3 (73.0 – 92.3) %; response magnitude: 1.83±0.37D) ($p \geq 0.09$, for all). Response latency increased (accommodation: 275.8±38.1ms; disaccommodation: 322.3±82.6ms) and peak velocity decreased (accommodation: 5.37±1.6D/s; disaccommodation: 5.94±1.9D/s) with ETL manipulation, relative to baseline (latency: 276.8±59ms; peak velocity: 6.96±2.0D/s), but none were statistically significant ($p \geq 0.05$, for all).

Conclusions: The accommodative system responds in the desired direction despite neutralization of accommodative microfluctuations. While the response dynamics may have slowed-down in the absence of these microfluctuations, reflecting a conservative strategy, the change appears marginal and inconsequential for accommodation control. Overall, the results do not support the idea that accommodative microfluctuations aid in deciphering the direction of accommodation. Their role may be limited to maintaining the steady-state response.

CONTROL ID: 3712893

SUBMITTER (NAME ONLY): Paul Lang

TITLE: Impact of Delayed Corneal Cross-Linking in Keratoconus Patients

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Lang, A. Nguyen, M. Heur, G. Chiu, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Paul Lang: Commercial Relationship: Code N (No Commercial Relationship) | Annie Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Martin Heur: Commercial Relationship: Code N (No Commercial Relationship) | Gloria Chiu: Commercial Relationship(s);Code C (Consultant/Contractor):Glaukos;Code C (Consultant/Contractor):Acculens;Code C (Consultant/Contractor):BostonSight

ABSTRACT BODY:

Purpose: To highlight the impact of delayed corneal cross-linking (CXL) in patients diagnosed with progressive keratoconus.

Methods: Patients with progressive keratoconus were identified through retrospective chart review and eyes with a time interval of greater than 6 months between decision to perform cross-linking and treatment were included in analysis. Variables included in analysis were time to treatment, best corrected visual acuity (BCVA), manifest refraction, and tomographic data such as maximum keratometry (KMax) and pachymetry at the apex. A Wilcoxon rank test was used to compare measurements for statistical significance.

Results: 5 eyes of 3 patients were included in analysis. Mean time from decision to undergo crosslinking to treatment was 36±14.63 months. Reasons for delayed crosslinking included lack of insurance coverage, delayed insurance authorization, and lack of access to eye care during the pandemic. In this time interval, the mean change in manifest refraction was -6.051±5.64D (p=0.058), mean change in KMax was 3.94±6.08D (p=0.31), and mean change in pachymetry at the apex was -37.6±28.92µm (p=0.063). BCVA for 2 eyes worsened by 1 or more lines and all patients required the use of either scleral or rigid gas permeable contact lenses to achieve functional vision.

Conclusions: Keratoconus is characterized by progressive corneal thinning and steepening, and often associated with irregular astigmatism, corneal striae and central scars. Corneal cross-linking (CXL) aims to slow progressive keratoconus, and an FDA approved CXL protocol became available in the United States in 2016. Many barriers to prompt care still exist, however, that negatively impact visual function and quality of life for patients.

CONTROL ID: 3712894

SUBMITTER (NAME ONLY): ANANYA DATTA

TITLE: Transient Receptor Potential Nociceptors are Required for Contact Lens-Associated Corneal Parainflammation

SESSION TITLE: Contact lens

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. DATTA, J. Lee, H. Horneman, D.J. Evans, S.M. Fleiszig, Optometry and Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|H. Horneman, Department of Pediatrics Hematology/Oncology, University of California, San Francisco, San Francisco, California, UNITED STATES|D.J. Evans, COP, Biological & Pharmaceutical Sciences, Touro University California, Vallejo, California, UNITED STATES|

Commercial Relationships Disclosure: ANANYA DATTA: Commercial Relationship: Code N (No Commercial Relationship) | Justin Lee: Commercial Relationship: Code N (No Commercial Relationship) | Hart Horneman: Commercial Relationship: Code N (No Commercial Relationship) | David Evans: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Fleiszig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previously, we used a contact lens wearing murine model to show that lens wear was associated with corneal para-inflammation involving CD11c+ cells (24 h) and Ly6G+ cells (5-6 days). Recently, we showed transient receptor potential (TRP) ion-channels associated with corneal nerves were involved in corneal CD45+ and CD11c+ cell responses that correlated with protection against bacterial colonization. Here, we explored the role of TRP nociceptors in contact lens-mediated parainflammation.

Methods: Contact lenses were fitted onto one eye of C57BL/6 wild-type (WT) or double or single gene-knockout mice in TRPA1V1(-/-), TRPA1(-/-) or TRPV1(-/-). Contralateral eyes were used as controls. After 24 h or 6 days of lens wear, lenses were removed, and mice euthanized. Freshly enucleated eyes were fixed in ice-cold methanol or 2 % paraformaldehyde and corneal expression of MHC Class II+ cells or Ly6G+ cells detected using antibody labeling and imaging. Student's t-test and One-way ANOVA were used for statistical analysis and $P < 0.05$ considered significant.

Results: Lens-wearing corneas of WT mice showed a significant increase in MHC Class-II+ cells after 24 h, and in Ly6G+ cells after 6 days, vs. non-lens wearing controls ($P < 0.0001$, Student's t-test). Corneas remained free of visible pathology. Lens-wearing corneas of all TRP gene-knockout mice showed a significant increase in MHC Class-II+ cells at 24 h vs. respective baseline controls ($P < 0.0001$, Student's t-test). Non-lens wearing corneas of each TRP gene-knockout mouse showed significant reduction in MHC Class-II+ cells vs. WT at 24 h ($P < 0.0001$, One-way ANOVA). Corneas of lens-wearing TRP gene-knockout mice each showed a significant reduction in Ly6G+ cell infiltration vs. lens-wearing WT after 6 days ($P < 0.0001$, One-way ANOVA). Little or no corneal Ly6G+ cells were observed in 6 day non-lens wearing controls.

Conclusions: TRP nociceptors are required for contact lens-associated corneal para-inflammatory responses involving Ly6G+ cell (neutrophil) infiltrative after 6 days of lens wear, but not the MHC Class-II+ (CD11c+) responses after 24 h of lens wear. TRP nociceptors are involved in modulating baseline levels of corneal MHC-II+ cells. Specific role(s) for TRPA1 or TRPV1 in mediating these corneal phenotypes remains to be determined.

CONTROL ID: 3712896

SUBMITTER (NAME ONLY): Susmit Mhatre

TITLE: DEVELOPING A NOVEL LIPID-BASED SYSTEM OF DIALLYL TRISULFIDE (DATS) FOR SUSTAINED DELIVERY OF HYDROGEN SULFIDE FOR THE TREATMENT OF GLAUCOMA

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mhatre, C. Opere, S. Singh, Pharmacy and Health Professions, Creighton University School of Pharmacy and Health Professions, Omaha, Nebraska, UNITED STATES|

Commercial Relationships Disclosure: Susmit Mhatre: Commercial Relationship: Code N (No Commercial Relationship) | Catherine Opere: Commercial Relationship: Code N (No Commercial Relationship) | Somnath Singh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma, an ocular neuropathy, is characterized by progressive degeneration of retinal neurons. Current glaucoma therapies provide only symptomatic management by reducing IOP. Since glaucoma is reported even in normotensive patients, the ideal glaucoma medication should simultaneously lower IOP and confer neuroprotection to retinal neurons. Hydrogen sulfide (H_2S) has been reported to reduce IOP and elicit retinal neuroprotection in mammalian ocular tissues. Due to gaseous nature of H_2S and narrow therapeutic index, its delivery in ocular tissues involves unique challenges. Diallyl Trisulfide (DATS) is a lipophilic, potent, and fast H_2S donor reported to degrade rapidly under normal aqueous conditions. The objective of this study is to develop a novel lipid-based delivery system of DATS to provide sustain release of H_2S up to 8-9 hours upon topical application on cornea.

Methods: DATS content was determined by HPLC method in the concentration range of 3.12 – 100 µg/ml. The method was validated for specificity, linearity, accuracy and precision. The solid lipid nanoparticles (SLNs) loaded with DATS were prepared by using hot emulsification process and solvent evaporation method. DATS-SLNs characterized for particle size, zeta potential, drug loading and encapsulation efficiency. The in vitro release studies for both DATS and H_2S were performed by incorporating DATS-SLNs in PEG ointment base.

Results: A well resolved peak of DATS was detected at 2.8 mins run time. The method showed good linearity (R2 > 0.999) over the concentration range of 3.12-100 ug/ml. Particle size was higly dependant on the concetration of polymer, lipid and surfactant. In presence of surfactant (poloxamer 1%, soy lecithin 0.2%), the particle size was 238.6 ± 8 nm and 85 ± 4.5 nm for glyceryl behenate and glyceryl monostearate, respectively showing a corresponding decrease of 28 ± 0.56% and 66 ± 1.8%. PEG ointment base incorporated with DATS-SLNs showed a sustained release of DATS up to 9 hours releasing 67.89 ± 2.04% of the initial loaded amount with corresponding hydrogen sulfide concentration of 112 ± 2.16 µM.

Conclusions: A precise and accurate method for quantification of DATS was developed and validated in compliance of USP guidelines. A biocompatible system capable of sustaining H_2S release from DATS was obtained with a particle size less than 200 nm up to 9 hrs.

CONTROL ID: 3712898

SUBMITTER (NAME ONLY): JIE WANG

TITLE: Artificial Intelligence-assisted Projection-resolved Optical Coherence Tomographic Angiography (aiPR-OCTA)

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. WANG, T. Hormel, Y. Jia, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: JIE WANG: Commercial Relationship(s);Code P (Patent):Optovue Inc. | Tristan Hormel: Commercial Relationship: Code N (No Commercial Relationship) | Yali Jia: Commercial Relationship(s);Code F (Financial Support):OptoVue Inc;Code P (Patent):OptoVue Inc;Code P (Patent):Optos

ABSTRACT BODY:

Purpose: To improve the voxel-wise projection-resolved optical coherence tomographic angiography (PR-OCTA) using artificial intelligence.

Methods: In this study, a total of 4600 OCTA scans from 708 eyes, including 3224 AMD scans and 1376 DR scans, were acquired in the 3×3-mm central macular area. The projection-resolved ground truth was generated by allowing graders to adjust parameters within the rules-based PR-OCTA algorithm in order to independently optimize the appearance of flow signal in inner/outer retina, choroid and the area below the large vessels, separately. This enabled graders to ensure that residual artifacts were cleaned while real flow signal from posterior vessels, including pathological choroidal neovascularization, were preserved. The model in this study consists of a combined convolutional neural network and sequence-to-sequence network that produce the PR OCTA volume from volumetric structural OCT and uncorrected OCTA inputs. The performance of the proposed aiPR-OCTA algorithm was evaluated on 126 normal eyes by quantifying the vessel density (VD), flow signal-to-noise ratio (fSNR), vessel connectivity (VC), structural similarity between the vascular patterns in an en face angiogram and another formed by projection over all anterior layers, and the remaining artifacts in outer retina.

Results: Compared to the previous reflectance-based PR (rbPR-OCTA) algorithm, the aiPR-OCTA algorithm was able to remove more projection artifacts and preserve more flow signal. The aiPR-OCTA algorithm was able to remove large residual vessel patterns in the rbPR-OCTA (Fig.1 case1&2 B2) while preserving true anatomic detail at the capillary scale (Fig.1 case1&2 B3). The large vessel shadows caused by overprocessing in rbPR-OCTA (Fig.1 case1&2 C2) were also filled with capillary flow in aiPR-OCTA (Fig.1 case1&2 C3). Quantitative assessment also indicates that the aiPR-OCTA also increased both VD and VC (Table 1), which is consistent with aiPR-OCTA preserving more flow signal then rbPR-OCTA. Finally, aiPR-OCTA suppressed more background artifacts as the fSNR was improved and remaining artifacts in outer retina was reduced (Table 1).

Conclusions: The proposed aiPR-OCTA algorithm can remove more projection artifacts and preserve more flow signals than previous approaches. This voxel-wise aiPR-OCTA algorithm could enable reliable vascular quantification in deeper anatomic slabs.

CONTROL ID: 3712902

SUBMITTER (NAME ONLY): Nathan Dhablania

TITLE: The Prevalence and Risk Indicators of Uncorrected Refractive Error in African Americans: The African American Eye Disease Study (AFEDS)

SESSION TITLE: Refractive Error and Social Determinants of Vision Function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Dhablania, M. Torres, R. Varma, Southern California Eye Institute, Los Angeles, California, UNITED STATES|K. Ding, B. Burkemper, R. McKean-Cowdin, University of Southern California, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Nathan Dhablania: Commercial Relationship: Code N (No Commercial Relationship) | Mina Torres: Commercial Relationship: Code N (No Commercial Relationship) | Kaili Ding: Commercial Relationship: Code N (No Commercial Relationship) | Bruce Burkemper: Commercial Relationship: Code N (No Commercial Relationship) | Roberta McKean-Cowdin: Commercial Relationship: Code N (No Commercial Relationship) | Rohit Varma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the burden of uncorrected refractive error (UCRE) and the risk factors associated with UCRE in a population-based sample of African American adults.

Methods: A population-based sample of self-identified African Americans 40 years of age and older (n = 6347) from thirty contiguous census tracts in Inglewood, California, underwent a complete ophthalmic examination and an in-home-administered questionnaire to assess sociodemographic (e.g. marital status, employment status, education level, annual income level), lifestyle (e.g. smoking history), and biological and medical (e.g. weight and height, health and vision insurance, healthcare and eye care utilization) risk factors associated with UCRE. UCRE was defined as a ≥ 2-line improvement with refraction in the better seeing eye. Sex- and age-specific burden of UCRE were calculated and multiple regression analyses were used to identify independent risk factors.

Results: Of the 7957 eligible participants in AFEDS, 6347 (80%) completed both the in-home interview and the clinical examination. The overall prevalence of UCRE was 14.6% (n = 925). The prevalence of UCRE was higher for men than for women (15.9% and 13.8%, respectively, P = 0.02). There was no significant age-related trend in the burden of UCRE (P > 0.05). Annual household income of less than $20,000 and lack of vision care insurance were significant independent risk indicators for UCRE.

Conclusions: Our data confirm the high burden of UCRE in African Americans making it the leading cause of visual impairment in this population. Providing universal coverage for vision care and prescription lenses or glasses is an affordable and achievable health care intervention that would reduce the burden of visual impairment in African American adults and help improve vision health in this vulnerable minority population.

CONTROL ID: 3712903

SUBMITTER (NAME ONLY): William Gange

TITLE: Efficacy of intravitreal methotrexate and rituximab for intraocular diffuse large B-cell lymphoma

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.S. Gange, S.C. Oliver, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: William Gange: Commercial Relationship: Code N (No Commercial Relationship) | Scott Oliver: Commercial Relationship(s);Code F (Financial Support):Roche/Genentech, Regeneron, Aura Bioscience;Code C (Consultant/Contractor):Castle Bioscience

ABSTRACT BODY:

Purpose: To determine the relative efficacy of intravitreal methotrexate and rituximab for treatment of intraocular lymphoma.

Methods: Single-center retrospective chart review of patients with intraocular diffuse large B-cell lymphoma (either primary vitreoretinal lymphoma or secondary from a non-central nervous system primary) who received either intravitreal methotrexate or rituximab as part of their treatment course. Patients were excluded if they were diagnosed with central nervous system lymphoma prior to onset of eye involvement. Time to ocular remission (<1+ vitreous cells or vitreous tap with no evidence of disease), progression free survival (PFS), and overall survival (OS) were compared for patients receiving intravitreal methotrexate and rituximab. PFS was calculated as time from onset of treatment to recurrence of ocular disease (≥1+ vitreous cells or positive vitreous tap) and OS was calculated as time from onset of treatment to death.

Results: 18 eyes of 11 patients were included. 4/11 (36.3%) patients were female, and median age at diagnosis was 59 (range 42-83). 8/11 (72.7%) patients had primary vitreoretinal lymphoma and 3/11 (27.3%) patients had secondary intraocular lymphoma from a systemic non-central nervous system primary. 7 patients (10 eyes) received intravitreal methotrexate and 4 patients (8 eyes) received intravitreal rituximab as initial intravitreal therapy. All 18 eyes receiving intravitreal injections achieved ocular remission at some point during their course. Ocular remission occurred after a median of 3 injections (range 2-9) in the methotrexate group and 3 (range 2-7) injections in the rituximab group. Mean number of total injections in the entire sample was 10.4 (SD 4.2) per eye. Mean PFS was 54.6 ± 5.2 months (44.5 to 63.7 95% CI) for patients receiving methotrexate compared with 15.4 ± 3.4 months (8.7 to 22.1 95% CI) for patients receiving rituximab. Mean OS was 53.2 ± 5.8 months (41.8 to 64.6 95% CI) for patients receiving methotrexate and 48.5 ± 12.2 months (24.7 to 72.4 95% CI) for patients receiving rituximab.

Conclusions: Both rituximab and methotrexate are effective treatments for intraocular lymphoma, resulting in ocular remission after a median of 3 injections. Patients receiving methotrexate had a longer ocular progression free survival than those receiving rituximab, though mean overall survival was similar in both groups.

CONTROL ID: 3712904

SUBMITTER (NAME ONLY): Xi Lu

TITLE: RUNX3 expression in the retina and its effect on retinal neovascularization

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Lu, Y. Xu, X. Liang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Xi Lu: Commercial Relationship: Code N (No Commercial Relationship) | Yue Xu: Commercial Relationship: Code N (No Commercial Relationship) | Xiaoling Liang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the expression of Runx3 in murine retina, and the effects of RUNX3 overexpression on retinal neovascularization (RNV) in oxygen-induced retinopathy (OIR) mice, as well as to explore its effect on HIF1α-VEGF signaling pathway.

Methods: Neonatal C57BL/6J mice were randomly divided into four groups: control (CON) group, OIR group, RUNX3-overexpression-OIR (RUNX3-AAV-OIR) group and vector-OIR (GFP-OIR) group. RUNX3-AAV-OIR group and GFP-OIR group were intravitreal injected with RUNX3-overexpressing adeno-associated virus (AAV) vectors and scramble vectors on P3, respectively. Neonatal mice of OIR group, RUNX3-AAV-OIR group and GFP-OIR group were exposed to 75% O_2 for 5 days from P7 to P12, and then abruptly returned to room air. The size of neovascular area, avascular area, the number and morphology of tip cells were assessed and quantified by immunostaining in the flat-mounted retinas. The protein levels of HIF1α and VEGF in the retina were detected by Western blot.

Results: RUNX3 mainly expressed in retinal vascular endothelium, and also in ganglial cell layer and inner nuclear layer of neonatal C57BL/6J mice on P17. Compared to OIR group, the size of retinal neovascular aera and avascular area, and the number of tip cells of RUNX3-AAV-OIR group decreased significantly, and the number and length of filopodia increased significantly, the elevated level of HIF1α and VEGF in the retina of OIR were significantly reduced by overexpressing the RUNX3 gene; while there were few changes of GFP-OIR group compared to OIR group.

Conclusions: Overexpression of RUNX3 inhibited RNV as well as improved retinal vascular repair and remodeling of OIR, meanwhile decreased the expression levels of HIF1α and VEGF in OIR retina.

CONTROL ID: 3712906

SUBMITTER (NAME ONLY): Henry Bair

TITLE: Trends of PRP and Anti-VEGF for NPDR in the IRIS® Registry (Intelligent Research in Sight), 2016-2018

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Bair, C. Xu, Stanford University School of Medicine, Stanford, California, UNITED STATES|S. Pershing, Spencer Center for Vision Research, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|S. Pershing, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|A. Brant, K. Mishra, A.T. Perlroth, D.V. Do, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Though current treatment guidelines predominantly call for observation of non-proliferative diabetic retinopathy (NPDR), recent studies indicate that intravitreal anti-VEGF can reduce disease progression. In this study, we evaluated trends of intravitreal anti-VEGF and PRP administration to NPDR patients from 2016-2018.

Methods: We identified patients with an NPDR diagnosis from 2016-2018 in the IRIS registry and excluded patients once they developed proliferative diabetic retinopathy, vitreous hemorrhage, or macular edema. We calculated the percentage of NPDR patients receiving intravitreal anti-VEGF or PRP each year and performed a multivariate regression with patient characteristics of age, sex, and race/ethnicity to determine how these factors influence odds of treatment.

Results: In 2016, 2017, and 2018 there were 257,446, 400,301, and 504,001 eyes with NPDR, respectively. The yearly increase in number of eyes is in part due to an expanding number of clinicians participating in the IRIS Registry. In 2016, 2017, and 2018, 0.10%, 0.15%, and 0.15% of eyes received PRP, respectively; while 0.87%, 0.88%, and 0.94% of eyes received intravitreal anti-VEGF, respectively. Yearly increases in rates of PRP and anti-VEGF were significant ($\beta = 1.13$ and 1.04, respectively). Compared with white patients, Hispanic and Black patients were more likely to receive PRP (OR = 1.53 and 1.26, respectively) and less likely to receive anti-VEGF (OR = 0.85 and 0.73, respectively). Asian patients were less likely to receive anti-VEGF (OR = 0.68). Compared with patients aged 41-60, those aged 0-20, 61-80, and 81-100 were less likely to receive PRP (OR = 0.27, 0.66, 0.36, respectively); while those aged 0-20, 61-80, and 81-100 were more likely to receive anti-VEGF (OR = 2.69, 1.35, 1.83, respectively) and ages 21-40 were less likely (OR = 0.6).

Conclusions: Among NPDR patients, we found that 1) rates of PRP and anti-VEGF treatment increased slightly year-over-year; 2) Hispanic and Black patients were more likely to receive PRP and less likely to receive anti-VEGF than white patients, while Asian patients had comparable rates of PRP but were less likely to receive anti-VEGF; 3) patients aged 41-60 were more likely than other age groups to receive PRP except for those 21-40 (whose rates are comparable), and less likely than other age groups to receive anti-VEGF except for those 21-40 (whose rates are lower).

CONTROL ID: 3712907

SUBMITTER (NAME ONLY): Shuichi Makita

TITLE: High-density and >20-degree field-of-view en-face and three-dimensional posterior eye imaging by Lissajous scan optical coherence tomography and angiography

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Makita, Y. Yasuno, Computational Optics Group, Tsukuba Daigaku Igaku Iryokei, Tsukuba, Ibaraki, JAPAN|M. Miura, Department of Ophthalmology, Tokyo Ika Daigaku Ibaraki Iryo Center, Inashiki-gun, Ibaraki, JAPAN|S. Azuma, T. Mino, T. Yamaguchi, Kabushiki Kaisha Topcon, Itabashi-ku, Tokyo, JAPAN|

Commercial Relationships Disclosure: Shuichi Makita: Commercial Relationship(s);Code F (Financial Support):Topcon, Tomey, Kao, Yokogawa, Nikon, Sky Technology;Code P (Patent):Tomey | Masahiro Miura: Commercial Relationship(s);Code F (Financial Support):Novartis, Alcon, Santen;Code R (Recipient):Novartis | Shinnosuke Azuma: Commercial Relationship(s);Code E (Employment):Topcon | Toshihiro Mino: Commercial Relationship(s);Code E (Employment):Topcon | Tatsuo Yamaguchi: Commercial Relationship(s);Code E (Employment):Topcon | Yoshiaki Yasuno: Commercial Relationship(s);Code F (Financial Support):Topcon, Tomey, Kao, Yokogawa, Nikon, Sky Technology;Code P (Patent):Tomey

ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) and OCT angiography visualize in vivo human retina and its vasculature three-dimensionally with high-spatial resolutions. Involuntary eye movements make the trade-off between a field of view (FOV) and high-density sampling tight. We have developed a Lissajous scan OCT method that extends FOV with high-densely spatial sampling. The imaging capability of this method for diseased eyes is investigated.

Methods: A clinical prototype OCT device with a scan speed of 100,000 A-line/s is used. The OCT probe beam scans along with a modified Lissajous pattern. The continuous shifting of the Lissajous trajectory extends the FOV. Motion-free three-dimensional volumes and en-face OCT and OCTA images were generated by motion estimation and correction algorithms.

Twelve eyes of 12 subjects with branch retinal vein occlusion (BRVO) were scanned. The scanning range exceeded around 22-degree in diameter. After motion correction, data are remapped in 812 x 812 grid points. Eyes were also scanned with a raster scan of 320 x 320 pixels, and 20-degree (6-mm) scanning size by a commercial OCTA device (DRI-OCT, Topcon).

Results: Figure 1 shows en-face OCTA images of a representative case (79y, male). The en-face OCTA images of the superficial retinal slab with the Lissajous scan and the raster scan of the commercial device visualize the retinal vasculature. However, the enlarged images (the green box) show that the fine structure of retinal capillaries is visualized by the Lissajous scan method owing to high-spatial density. In 8 of 12 eyes, the capillaries around non-perfusion areas were better visualized.

The en-face slice and cross-sectional images of another patient’s eye (76y, male) are shown in Figure 2. The distribution of cysts and abnormal blood flow patterns can be visualized in en-face and arbitrary cross-sectional images.

Conclusions: We have shown that the Lissajous scan OCT enables high-dense en-face and three-dimensional posterior eye imaging more than >20-degree FOV. This technique will enable the assessment of biomarkers in more detail with a large FOV.

CONTROL ID: 3712908

SUBMITTER (NAME ONLY): Qiutang Li

TITLE: Gene therapy for Leber's hereditary optic neuropathy with mitochondrial ND4 mutation

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Li, C. He, Y. Tao, X. Zhang, A. Luk, B. Li, NEUROPHTH THERAPEUTICS INC, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Leber's hereditary optic neuropathy (LHON) is a rare genetic disease caused by mitochondrial gene mutations, such as MT-ND1, MT-ND4, and MT-ND6. MT-ND4 (G11778A) is the most common mutation causing LHON eye diseases worldwide. It causes sudden progressive vision loss in the affected patients, and there is no approved treatment currently available for LHON. This study aims to develop a gene replacement therapy product, NFS-01 (rAAV2-ND4), for the treatment of LHON associated with MT-ND4 mutation.

Methods: A recombinant AAV2-based therapeutic vector (NFS-01) was constructed to express a codon optimized human ND4 protein with a mitochondrial targeting sequence. After NFS-01 transduction, ND4 expression and cellular localization in 293T cells were examined by mitochondria/cytosol fractionation following by western blot. The NFS-01 function was investigated by comparing the productions of oxidative phosphorylated ATP and oxygen consumption rate in LHON patient-derived BLT2 hybrid cells with or without rAAV2-ND4 transduction. Furthermore, NFS-01 expression, tissue distribution, and biosafety were studied in rabbits and macaques after intravitreal (IVT) injection.

Results: ND4 protein expressed from rAAV2-ND4 vector was localized to mitochondria. ATP produced through oxidative phosphorylation in the mutant BLT2 cells was increased significantly after NFS-01 infection, indicating that NFS-01 at least partially restored ATP production in the mutant BLT2 cells. Consistently, rAAV2-ND4 significantly increased spare respiratory capacity of BLT2 cells as showed by Seahorse assay in the galactose medium condition. Furthermore, dose-response expression for ND4 gene was demonstrated in the rabbit retina after IVT injection. And the GLP toxicity studies showed no adverse effect or toxicity following IVT injection of NFS-01 in macaque. As part of the GLP studies, biodistribution of the vector was also performed and showed minimal spread of vector genome to spleen and lymph nodes. Neutralizing antibodies against AAV2 were either undetectable or no increase at 1- and 3-months post-injection.

Conclusions: Our gene therapy product NFS-01 allotropically expresses human ND4 protein in mitochondria and compensates for the loss function of ND4 in LHON derived cells. NFS-01 demonstrates effective retina delivery, expression, and safety post IVT injection in rabbits and macaques.

CONTROL ID: 3712909

SUBMITTER (NAME ONLY): Bin Sun

TITLE: A retrospective study of elderly patients with thyroid-associated ophthalmopathy

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Sun, Z. Zhang, L. Jing, C. Yan, Shanxi Eye Hospital, Taiyuan, Shanxi, CHINA|

Commercial Relationships Disclosure: Bin Sun: Commercial Relationship: Code N (No Commercial Relationship) | Zhaoxia Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Liping Jing: Commercial Relationship: Code N (No Commercial Relationship) | Chunfang Yan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Thyroid-associated ophthalmopathy (TAO) is most often seen in middle-aged patients with autoimmune thyroid disease, and immunosuppression is optimal therapy for active TAO. In elderly patients, TAO is less frequent but more severe. In this study, we aimed to determine the clinical characteristics and therapeutic schedule in elderly patients with TAO.

Methods: This retrospective study comprised 106 elderly patients with TAO (65.24±4.90 years). Data were obtained from a follow-up survey. The patients with active TAO received intravenous injection of methylprednisolone (MP) (39 cases) , or periocular injection of triamcinolone acetonide (TA) (16 cases) , or TA+oral cyclosporine A (TA+CsA) (35 cases). The NOSPECS classification, the clinical activity score (CAS) and $^{99m}T_c$-octreotide scintigraphy were used to evaluation of severity and activity of TAO before and after treatment.

Results: 106 elderly patients with TAO were identified (61 male, 45 female). At the time of initial diagnosis, 74.53% of the patients were hyperthyroid. 95.28% of the patients had bilateral TAO. Main symptoms were eyelid swelling (79.25%), exophthalmos (79.25%), eye movement limitation (81.13%) and double vision (75.47%). 12.26% of the patients had optic neurophathy. Orbital CT showed 86.79% of the patients had enlarged extraocular muscles. The exophthalmos, CAS score and NOSPECS grades of the patients with thyroid dysfunction were significantly higher than those with normal thyroid function ($P<0.05$). $^{99m}T_c$-octreotide scintigraphy was positive in active TAO patients (95%) with elevated uptake ratio (UR) ($P<0.05$). Smoking showed a significant correlation with CAS score ($P<0.05$), and age correlated with NOSPECS grade ($P<0.05$). Both UR and CAS scores of 90 patients with moderate to severe active TAO decreased significantly after treatment ($P<0.05$). The response rates of MP group and TA+CsA group were significantly higher than TA group ($P<0.05$), and with no significant difference ($P>0.05$).

Conclusions: The clinical manifestations of elderly patients with TAO were usually severe. Exophthalmos and eye movement limitation were the most common features and bilateral involvement. Thyroid dysfunction, smoking and age may increase the activity and severity of TAO. Intravenous corticosteroid pulse therapy and periocular injection of triamcinolone acetonide combined with cyclosporine A are effective for moderate to severe active TAO in elderly patients.

CONTROL ID: 3712910

SUBMITTER (NAME ONLY): Ebrar Al-Yasery

TITLE: Vitreo-Retinal Surgery in Diabetes: Demographic Associations in Victoria, Australia

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Al-Yasery, D.C. Sousa, B. Clark, P.J. Allen, P. van Wijngaarden, R. Dawkins, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|D.C. Sousa, P.J. Allen, P. van Wijngaarden, R. Dawkins, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy is one of the main causes of blindness among the working age Australian population. This study investigates the relationship between demographic factors and diabetic ocular complications requiring vitreoretinal surgery at the only tertiary eye hospital in Victoria, Australia.

Methods: Single-centre retrospective study using data extracted from the Australian and New Zealand Society of Retinal Specialists Registry (2015-2019). Demographic information for all patients who underwent surgery for complications of proliferative diabetic retinopathy (PDR) at the Royal Victorian Eye and Ear Hospital (RVEEH) were included. Population proportions were compared to 2016 Census of Population and Housing data for Victoria, and Primary Health Networks (PHN).

Results: A total of 594 vitreoretinal surgeries for vitreous haemorrhage and tractional retinal detachment (47%) in 424 patients (60% male) were identified. Working age patients (25-65 years) made up 75% of the study population. The great majority of patients (75%) included in the study were insulin dependent despite only 18% of patients having type 1 diabetes mellitus.

Of the study population, 18% were born outside of Australia (as compared to Census 26%), with 14% identifying English not as their first language. 1.4% of patients identified as Aboriginal and/or Torres Strait Islander (Census 0.8%).

Geographically, in Victoria the PHN with the highest number of included patients was the North Western metropolitan region making up 34% of patients (Census 29%). Of the total, 19% of patients were from regional and rural Victoria (Census 24%).

Conclusions: This study identifies working age men, who are insulin dependent as most at risk of PDR complications requiring surgery. There is also an association with geographical location, which may well be a proxy marker for socio-economic status. Aboriginal and / or Torres Strait Islander people appear to also be at higher risk. Interestingly, being born outside Australia, or from a regional / rural location do not seem to be risk factors in our population.

This work shows the importance of ocular screening in this population. Future work will involve characterization of ophthalmic screening access in the most at risk locations.

CONTROL ID: 3712911
SUBMITTER (NAME ONLY): Henry Marshall
TITLE: High polygenic risk is associated with earlier treatment initiation and escalation in glaucoma suspects
SESSION TITLE: Glaucoma Genetics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: H. Marshall, S. Mullany, G. Hollitt, E.C. Berry, L. Knight, R.A. Mills, J. Landers, J.E. Craig, Flinders University, Adelaide, South Australia, AUSTRALIA|X. Han, S. MacGregor, QIMR Berghofer Medical Research Institute, Herston, Queensland, AUSTRALIA|P. Healey, University of Sydney, South Australia, AUSTRALIA|A.W. Hewitt, University of Tasmania Menzies Institute for Medical Research, Hobart, Tasmania, AUSTRALIA|S.L. Graham, Macquarie University, Sydney, New South Wales, AUSTRALIA|R. Casson, The University of Adelaide, Adelaide, South Australia, AUSTRALIA|O. Siggs, Garvan Institute of Medical Research, Darlinghurst, New South Wales, AUSTRALIA|
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ABSTRACT BODY:
Purpose: To assess whether a polygenic risk score for primary open angle glaucoma predicts treatment commencement amongst treatment naive glaucoma suspects.
Methods: A prospective, longitudinal genetic association study combining a discovery cohort of glaucoma suspects who were treatment naive at enrollment into the Predicting Risk of Glaucoma: RElevant SNPs with Significant Association (PROGRESSA) study, and a replication cohort comprising of treated early manifest and suspect glaucoma cases.

In the discovery phase, a per-allele weighted polygenic risk score was calculated for 301 glaucoma suspects who were treatment naive at enrollment into the PROGRESSA study. Multivariable cox proportional regression analysis assessed the correlation between polygenic risk score and time to initiation of Intraocular pressure (IOP) lowering therapy. A replication analysis assessed the correlation between polygenic risk score and time to escalation of IOP lowering therapy amongst 539 suspect and manifest glaucoma cases who were on IOP lowering therapy at study enrolment.
Results: A higher glaucoma PRS was correlated with earlier initiation of IOP-lowering therapy after adjustments for age, gender, IOP, and family history of glaucoma (adjusted HR: 1.43/SD 95% CI: [1.04, 1.95] P=0.024). Participants in the highest normative population quintile demonstrated a 3.4-fold likelihood of requiring IOP-lowering therapy within 5 years than participants in the lowest quintile (HR: 3.38/SD 95% CI [1.12, 10.20] P=0.017).

A replication analysis then evaluated the correlation between polygenic risk score and escalation of therapy amongst participants on therapy at enrolment. A higher polygenic risk score for glaucoma was correlated with a greater risk of requiring treatment escalation (HR: 1.24 95% CI: [1.05, 1.24] P=0.009), and was correlated with maximum number of required IOP-lowering agents during monitoring (beta: 0.17/SD 95% CI: [0.07, 0.26] P<0.001).
Conclusions: This study demonstrates novel associations between polygenic risk of primary open angle glaucoma and time to initiation of IOP lowering therapy. It builds upon previous work highlighting the therapeutic utility of genetic

risk stratification in glaucoma.

CONTROL ID: 3712912

SUBMITTER (NAME ONLY): Matus Rehak

TITLE: Renal Parameters but not HbA1c Level Influence the Response to the Anti-VEGF Treatment in Patients with Diabetic Macular Edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Rehak, Ophthalmology, Justus Liebig Universitat Giessen, Giessen, Hessen, GERMANY|M. Rehak, C. Busch, C. Jochmann, D. Vollhardt, Ophthalmology, Universitat Leipzig Medizinische Fakultat, Leipzig, Sachsen, GERMANY|

Commercial Relationships Disclosure: Matus Rehak: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan, Bayer, Novartis;Code F (Financial Support):Novartis;Code R (Recipient):Alimera, Zeiss, Novartis | Catharina Busch: Commercial Relationship(s);Code C (Consultant/Contractor):Alergan;Code R (Recipient):Allergan, Bayer | Claudia Jochmann: Commercial Relationship(s);Code R (Recipient):Bayer | Daniela Vollhardt: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We evaluated the impact of the systemic metabolic and cardiovascular risk factors (e.g., HbA1c level, hypertension renal parameters or dyslipidemia) on the response to anti-VEGF treatment in patients with diabetic macular edema (DME).

Methods: In prospective, monocentric interventional study (LIPSIA Trial) in total 148 eyes of 90 patients with DME received clinical examinations as 24-hour blood pressure measurement and laboratory examination of metabolic, renal and cardiovascular parameters. These investigations were conducted prior to the montly aflibercept treatment and after 6 months. We investigated the correlation with demographic parameters, baseline best corrected visual acuity (BCVA) and the blood pressure levels as well as laboratory blood parameters.

Results: The mean age was 61.1±14.9 years. The mean body mass index (BMI) was 32.1±5.9 kg/m2. HbA1c values were >7.0% in 63% of all patients. The blood pressure (BP) of 77% patients was above the target values of systolic <140 mmHg and diastolic <80 mmHg. LDL cholesterol was above the target value of 1.4 mmol/l in 92% of patients. Worse baseline BCVA and lower age were associated with a more pronounced gain in BCVA 6 months after initiation of intravitreal therapy. Furthermore, patients with normal glomerular filtration rate (GFR≥ 90 ml/min/1.73m2) had a significant better functional outcome at 6 months compared to patient with reduced GFR (10.0 ± 11.7 letters vs. 2.9 ± 8.1 letters, EM mean [adjusted for baseline BCVA and age]: 7.7 ± 1.3 letters vs. 3.9 ± 1.1 letters, p=0.019). The better the baseline BCVA, the less likely a patient gained ≥ 5 letters at month 6 (OR: 0.913, 95% CI: 0.86 – 0.97, p=0.003). Patients with a GFR ≥ 60 ml /min /1.73m2 were more likely to gain ≥ 5 letters compared to patients with GFR <60 ml /min /1.73m2 (OR: 3.73, 95% CI: 1.28 – 10.92, p=0.016). HbA1c levels, fasting glucose or blood lipid levels did not show an association with visual outcome.

Conclusions: The DME patients in the LIPSIA study presented several systemic comorbidities that were mainly poorly controlled. The response to aflibercept intravitreal treatment correlated with the age, baseline BCVA, and the renal parameters, but not with the HbA1c level.

CONTROL ID: 3712914

SUBMITTER (NAME ONLY): Tierney Daw

TITLE: Simple and complex orientation selective ganglion cells in the retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.B. Daw, M. Thapa, G. Field, Neurobiology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Extracting oriented structure in natural scenes is a fundamental and highly conserved computation in the visual system. Orientation selective (OS) ganglion cells (osRGCs) have been identified in the retina, but many features of their responses remain unclear. Thus, we sought to understand the receptive field (RF) structure of osRGCs, how the retina produces OS, and whether OS is maintained across rod and cone vision.

Methods: We measured RGC responses to visual stimuli from ex vivo rat retinas using a large-scale multi-electrode array. We used drifting and contrast reversing gratings to identify osRGCs and determine their spatial frequency tuning. We used checkerboard noise to estimate RF structure. A linear-nonlinear model based on the estimated RF was used to determine the extent to which osRGCs perform linear spatial integration.

Results: Consistent with previous work, we found osRGCs with peak tuning along either the horizontal or vertical meridians. However, among osRGCs, we identified two distinct types of RFs. Some osRGCs exhibited RFs reminiscent of cortical simple cells: their responses had narrow spatial frequency tuning and were highly phase-dependent. Importantly, they had an OFF-center RF flanked by ON-responsive zones, producing an even-symmetric RF that accurately predicted visual responses, indicating a relatively linear RF. Other osRGCs exhibited RFs similar to cortical complex cells: their responses had broad spatial frequency tuning that weakly depended on phase. Furthermore, like cortical complex cells, their linear RF had a speckled organization with small ON and OFF subzones that poorly predicted their visual responses, indicating a nonlinear RF. Both kinds of osRGCs maintained tuning down to rod-mediated light levels, and tuning was largely eliminated by blocking GABAa receptors.

Conclusions: We demonstrate two distinct RF structures among osRGCs that parallel the division of simple and complex cells in primary visual cortex. These results suggest that the emergence of simple and complex OS tuning emerges first in the retina, at least in rodents. Both forms of tuning span rod to cone vision. Finally, both forms of tuning depend on GABAa receptors, suggesting that they are mediated by feedforward inhibition onto RGCs. Intracellular measurements will be needed to understand how these simple- and complex-like responses are achieved by retinal circuits.

CONTROL ID: 3712915

SUBMITTER (NAME ONLY): Blanka Golebiowski

TITLE: Estradiol and progesterone quantification in tears using ultrasensitive LC-MS

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Golebiowski, M. Phan, S. Kweon, F. Stapleton, School of Optometry and Vision Science, UNSW Sydney, New South Wales, AUSTRALIA|R. Desai, D. Handelsman, ANZAC Research Institute, Concord, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Analysis of sex hormones in tear fluid will aid understanding of their role in regulation of tear production and in dry eye disease. Levels of sex hormones in tears are unknown due to low tear volumes available and a lack of sufficiently sensitive quantification methods. This pilot study applied an ultrasensitive LC-MS method to estimate androgens and oestrogens in tears of pre- and post-menopausal women.

Methods: An ultrasensitive LC-MS method previously developed for serum sex hormones was applied. The accuracy of this method for tears was assessed by absolute recovery from pooled basal tears of pre-menopausal women spiked with three levels of known amounts of sex steroids. Flush tears (where 60 µL saline was applied to the ocular surface, collected using a microcapillary tube and samples pooled from both eyes/participant) from pre- and post-menopausal women (n=2/category) were subsequently analysed for testosterone (T), estradiol (E2) and progesterone (P4) concentration on an API-5000 triple-quadruple mass spectrometer equipped with an atmospheric pressure photoionization source. Recovery tests were run in six replicates and other analyses were run in duplicate.

Results: Excellent absolute recoveries were observed for all steroids analysed at the concentrations tested, with accuracy ranging from 93.7% (P4) to 99.3% (T) for basal tears. Concentrations of E2 were 2.90±1.01 pg/mL in flush tears of post-menopausal women and 8.40±1.70 pg/mL in pre-menopausal women. P4 was 0.30±0.07 ng/mL in flush tears of pre-menopausal women but was not quantifiable in all tear samples from post-menopausal women. T was not detectable in any of the flush tear samples.

Conclusions: The ultrasensitive LC-MS method showed high accuracy for analysis of sex hormones in basal tears. The method effectively quantified E2 and P4 in flush tears of pre- and post-menopausal women. Further work will explore this method for analysis of sex hormones in flush and saline-diluted basal tears to tackle the limitations of tear sample volume

CONTROL ID: 3712918

SUBMITTER (NAME ONLY): Manisha Malani

TITLE: Artificial intelligence and experimental studies to understand the transporters role in ocular toxicity of systemic drugs

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Malani, M.S. Hiremath, J. Nirmal, Pharmacy, Birla Institute of Technology & Science Pilani - Hyderabad Campus, Hyderabad, Telangana, INDIA|S. Sharma, M. Jhunjhunwala, C. Hota, Computer Science, Birla Institute of Technology & Science Pilani - Hyderabad Campus, Hyderabad, Telangana, INDIA|S.L. Gayen, Pharmaceutical Technology, Jadavpur University, Kolkata, West Bengal, INDIA|

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ABSTRACT BODY:

Purpose: Despite the ocular barriers, systemic drugs enter eye and causes toxicity. We hypothesize membrane transporters expressed in lacrimal gland (LG) to transport endogenous molecules from blood to tear, could falsely recognize the systemic drugs thereby gives access to eye. Hence, to understand the role of transporters (Organic Cation Transporter-1(OCT1)) in ocular toxicity, Artificial Intelligence (AI) methods and molecular docking studies were used to screen the drugs. Expression of OCT1 in LG and invivo tear kinetics study of predicted substrate (Cyclophosphamide(Cyc)) for OCT1 was performed to delineate the functional role of OCT1 in LG.

Methods: AI models were developed using a dataset of 193 drugs (substrate/non-substrates for OCT1) to predict drug-OCT1 interaction. Molecular Mechanics/Generalized Born Surface Area (MMGBSA) was used to calculate binding energy of protein (homology model of OCT1) and ligand (substrate/non-substrate/toxic drugs). Around 513 toxic drugs were screened through AI models and their binding energies were calculated using MMGBSA to classify them as substrate or non-substrate for OCT1. Expression of OCT1 in rabbit's LG was confirmed by real time polymerase chain reaction. Invivo tear kinetics was performed to validate AI predictions and the functional role of OCT1 in LG. Cyc was injected intravenously to rabbits (n=4) with or without topical OCT1 inhibitor (Atropine). Tear was collected using Schirmer strips at various time points and analyzed using HPLC. Data was presented as mean ± SD and analyzed using t-test. $P<0.05$ was considered to be significant.

Results: Developed AI models showed an accuracy of 81% to 83%. Binding energy of substrate molecules was found to be below -14613.30 kcal/mol. Many novel interactions were unrevealed between drugs and OCT1 (Table1). RNA expression confirms the OCT1 presence in LG. Tear secretion of Cyc was decreased with inhibitor, with a significant difference at 1h (870 ± 60 ng/ml without inhibitor, 570 ± 60 ng/ml with inhibitor), $p<0.01$.

Conclusions: Out of 513 systemic drugs causing ocular toxicity, 44% of them were predicted as OCT1 substrate. OCT1 expression in LG, molecular docking and tear kinetics studies confirms the functional role of OCT1 in the entry of systemic drugs (OCT1 substrates) into eye. Further studies will be carried in detail to delineate the role of OCT1 in LG.

CONTROL ID: 3712920

SUBMITTER (NAME ONLY): Hythem Abouodah

TITLE: Endoscopic pars plana vitrectomy outcome after open globe injury with corneal opacity

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Abouodah, K. Hamada, M. Pfannenstiel, R. Ajlan, Department of Ophthalmology, University of Kansas School of Medicine, Kansas City, Kansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The primary objective is to determine the surgical outcome of endoscopic pars plana vitrectomy (PPV) during or shortly after open globe repair. The secondary objective is to detect the number of patients who later required corneal transplantation.

Methods: This is a retrospective cohort study of patients who received endoscopic PPV during open globe repair or within one month later. Inclusion criteria involved adult patients with a history of open globe injury, corneal opacity, and endoscopic PPV. Data was collected for the period between 12/2018 and 8/2021. Patients with corneal pathology not obliterating the fundus view were excluded from the study. The University of Kansas institutional review board approved this study.

Results: Ten patients met the study inclusion criteria (3 females, 7 males) with an average age of 61± 22.6 years old. Indications for endoscopic PPV included: retinal detachment in five patients, vitreous hemorrhage in three patients (one with retinal tear, and one with choroidal hemorrhage), and intraocular foreign bodies in two patients. Final visual acuity ranged from 20/70 to no-light-perception (NLP). All patients had their retina successfully attached. Two patients developed phthisis bulbi after one year. Corneal opacity was treated with scleral contact lens in one patient, penetrating keratoplasty in two patients, and the remaining seven patients were deemed unsuitable to receive a corneal transplant due to poor visual potential.

Conclusions: Endoscopic PPV may be a useful tool to repair posterior segment pathology in patients with recent open globe injury and corneal opacity. It can help address posterior segment disease and postpone corneal transplant surgery until visual potential can be fully determined. A larger prospective study is needed to better elucidate the role of endoscopic PPV in similar patient cohorts.

CONTROL ID: 3712922

SUBMITTER (NAME ONLY): Kyung-Min Roh

TITLE: Evaluating multi-planar clear corneal incision architecture with microscope-integrated OCT (MIOCT)

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Roh, H. Goodell, J. Tian, E. Choi, T. Lai, J.A. Izatt, C.A. Toth, A.N. Kuo, Dept of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|D. Li, J.A. Izatt, C.A. Toth, A.N. Kuo, Dept of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|T. Lai, Dept of Ophthalmology, National Taiwan University Hospital, Taipei, TAIWAN|

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ABSTRACT BODY:

Purpose: Multi-planar clear corneal incisions (CCI) are the standard in cataract surgery for better wound closure and hence decreased risk of endophthalmitis. However, in previous limited experience examining cataract surgery incisions with OCT, we have not observed distinct incision multi-planarity. We sought to test the hypothesis that the manual multi-planar CCI may not actually be multi-planar.

Methods: Under controlled wetlab conditions, 4 ophthalmic surgeons with prior cataract experience (2 attendings, 2 residents) were re-familiarized with the multi-planar CCI and instructed to make 3 CCIs with a standard 2.4 mm keratome in porcine eyes. Each eye's anterior chamber was filled with viscodispersive prior to the 3 incisions. A research swept source MIOCT (1050 nm, 400 kHz) captured volumes at the CCIs (15 x 15 x 7.2 mm consisting of 750 B-scans x 750 A-scans x 950 depth pixels). For analysis, the anterior surface of each CCI was semi-automatically segmented. Each incision's center B-scan was refraction corrected and used to calculate the following metrics: incision length, length:width ratio, and internal angles. The internal angles were the angles between the incision's entry, center, and exit vectors calculated from the first 5%, mid 30%, and last 5% of incision length respectively (Fig. 1E). A Wilcoxon Signed-Rank test was performed to compare both sets of angles to the theoretical 90° of an ideal multi-planar incision and to 135° for a less acute multi-planar incision.

Results: Table 1 shows the metrics for each surgeon's CCIs. The null-hypotheses (entry and exit angles are part of distribution around 90°) were rejected in the t-tests ($p = 4.9 \times 10^{-4}$ and 4.9×10^{-4}). The result was the same with the t-test against 135° ($p = 4.9 \times 10^{-4}$ and 4.9×10^{-4}). All incisions had mean length:width ratios >=0.82.

Conclusions: CCIs created with a standard keratome do not appear to have multi-planarity in model porcine corneas. Despite this, length:width ratios show nearly square incisions, and the increased surface area from attempted multi-planar CCIs likely contributes to clinical incision closure.

CONTROL ID: 3712924

SUBMITTER (NAME ONLY): Helena Lam

TITLE: Phacoemulsification with Endocyclophotocoagulation or OMNI™ Ab-interno Canaloplasty/Trabeculotomy in Uveitic Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Lam, J. Olson, J. Yamanuha, Ophthalmology and Visual Neurosciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|N. Miller, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Helena Lam: Commercial Relationship: Code N (No Commercial Relationship) | Nathaniel Miller: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Olson: Commercial Relationship: Code N (No Commercial Relationship) | Justin Yamanuha: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is limited data regarding the role and efficacy of minimally invasive glaucoma surgery in the management of uveitic glaucoma (UG). We examined surgical outcomes in patients with UG after cataract extraction with lens implantation (CEIOL) plus endocyclophotocoagulation (ECP) or CEIOL plus OMNI™ ab-interno canaloplasty +/- trabeculotomy (Sight Sciences) (OMNI).

Methods: All patients aged >18 years with UG who underwent CEIOL + ECP or CEIOL + OMNI between August 2019 and September 2021 at a single academic center with a single surgeon were retrospectively reviewed. Surgical success was defined as intraocular pressure (IOP) ≤21 mmHg or reduction from baseline by 20% for two consecutive visits, without hypotony (IOP ≤5 mmHg), additional glaucoma surgery, or loss of light perception. Uveitic control was defined as less than a two-step increase in anterior chamber (AC) cell or lack of increase in steroid drop frequency. Outcomes were measured at three months post-operatively.

Results: Nine patients (14 eyes) were identified (eight ECP, six OMNI). Baseline pre-operative characteristics including IOP, AC cell grade, visual acuity (VA), age, sex, race, and affected eye(s) were not significantly different between groups. All cases were successful and had improved VA. In CEIOL + ECP and CEIOL + OMNI cases, IOP was reduced an average of 7.0 mmHg (p=0.06) and 8.9 (p=0.03) respectively. The number of glaucoma medications reduced by 0.3 (p=0.18) and 1.0 (p=0.04) respectively. Outcome differences between groups did not meet statistical significance. No cases had a two-step increase in AC cell, however there was an increase in steroid drop frequency for 50% of patients in each group. Post-surgical complications included cystoid macular edema (1/8 of ECP and 3/6 of OMNI cases), hyphema (2/6 of OMNI cases), and IOP spike (1/6 of OMNI cases).

Conclusions: Both ECP and OMNI with CEIOL improved VA, IOP, and glaucoma medication use, without a two-step increase in AC cell in UG at three months. An increase in steroid drop frequency may be the cost of a prolonged post-surgical inflammatory course related to the underlying uveitis. Further investigation with a larger population, longer follow-up, and prospective design are necessary.

CONTROL ID: 3712926

SUBMITTER (NAME ONLY): Jacqueline Lopez

TITLE: Risk Factors Predicting Loss to Follow-Up, Hospital Admission, and Medication Noncompliance Among Patients with Infectious Keratitis at a Public County Hospital

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.B. Lopez, L. Chan, M. Saifee, M. Yung, M.F. Chan, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|M.F. Chan, Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Infectious keratitis is a vision-threatening condition requiring close follow-up and disciplined eye drop administration to achieve resolution. Although patients presenting to county hospitals often have a more severe presentation, there is a paucity of risk and outcomes data in this setting. This study investigates social risk factors predicting loss to follow-up, medication noncompliance, hospital admission, and poor outcomes for infectious keratitis in the county setting.

Methods: We performed a retrospective case-control study at Zuckerberg San Francisco General Hospital and Trauma Center. Inclusion criteria were all patients who had corneal cultures for suspected infectious bacterial or fungal keratitis obtained between 2010-2021. Exclusion criteria were patients with viral keratitis only. Multivariable logistic regression was used to analyze the relationship of social and medical risk factors with loss to follow-up, medication noncompliance, hospital admission, worsened visual acuity, and delayed time to resolution.

Results: Of 174 patients with infectious keratitis, 69 (40%) were lost to follow-up. Unemployment was associated with increased risk of loss to follow-up (OR 2.58, p=0.049). There was a trend toward an association with homelessness and noncompliance (OR 3.48, p=0.095). 47 patients (27%) were hospitalized for treatment of corneal ulcers. Hospitalization correlated with unemployment (p=0.033), homelessness (p=0.033), and drug use (p=0.006). Unemployment was significantly associated with worse final visual acuity (p=0.001). Increasing age correlated with longer healing time of the ulcer, with each one-year increase in age associated with delayed resolution by 0.549 days (p=0.042).

Conclusions: Patients experiencing homelessness, unemployment, drug use, or increased age demonstrate higher risk for treatment barriers including loss to follow-up and medication noncompliance, resulting in worse visual acuity, risk for hospital admission, and delayed time to resolution. These risk factors should be considered when determining the need for hospitalization or more deliberate follow-up measures in patients with infectious keratitis.

CONTROL ID: 3712927
SUBMITTER (NAME ONLY): Angelina Covita
TITLE: Short term specificity of mixed 24-2C Guided Progression Analysis (GPA)
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Covita, G.C. Lee, T. Callan, S. Yu, N. Graves, C. Wu, Carl Zeiss Meditec, Inc., California, UNITED STATES|T. Severin, East Bay Eye Center San Ramon, California, UNITED STATES|I.A. Falkenstein, Glaucoma Specialists of San Francisco, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: In this study we use short term repeatability data to investigate the specificity of mixing 24-2C SITA visual field (VF) exams using the HFA GPA limits to detect change.

Methods: 24-2C SITA Standard (SS) and 24-2C SITA Faster (SFR), as well as 10-2 SS, and 10-2 SITA Fast VFs were acquired on an HFA3 Model 860 perimeter (ZEISS, Dublin, CA) at two repeat visits on one eye each for healthy and glaucomatous subjects. 24-2 VFs were extracted from 24-2C. 10-2 VFs were not used. All four visit series permutations having two baselines were comprised of the same SITA strategies (SS or SFR) were created (baseline order does not matter).

We also substituted 24-2C MD for the 24-2 MD in GPA to select change limits. Differences between Pattern Deviations (PD) of both follow-ups to the averaged baselines for each test point were compared to change limits used for analogous regions of the commercial 24-2 GPA.

Any change observed in this data was defined as a false positive because the repeated visits occurred over a short time period. False positive rates (FPR) with 95% confidence intervals (CI) were pooled from all 224 series and all 24-2C test points for both follow-ups. Specificity was defined as 1 – FPR. GPA excluded test locations where the MD or PD are too poor (marked as "out of range" or "X" on reports or analyses). FPR was calculated two ways: a) pooling all points and b) pooling only points not marked “X”.

Results: Mean age was 57.3 (standard deviation, SD: 7.6; range: 44.3 to 74.7) years for 28 healthy eyes and 71.3 (SD: 9.0; range 54.0 to 97.9) years for 28 glaucoma eyes (creating a total of 224 series permutations). Mean 24-2 SS MD was 0.38 (SD: 1.17; range: -1.89 to 2.62) dB and -7.92 (SD: 7.72; range: -23.42 to 1.63) dB in healthy and glaucoma eyes, respectively.

24-2C and 24-2 MDs showed strong agreement with an R^2 of 0.99 (slope: 1.04 and offset: 0.00). FPR was 0.060 (CI: 0.057 to 0.063) using all 27,776 pooled points and 0.066 (CI: 0.063 to 0.069) for the 25,300 pooled valid points, consistent with specificity of ~94%.

Conclusions: Short term specificity was ~94% for detecting change from baseline events in pooled test locations in 24-2C VF series consisting of mixed SITA exams using limits previously established for 24-2 GPA. This suggests that even without the temporal and spatial confirmation used in the standard commercial GPA, a mixed SITA 24-2C GPA may have reasonable specificity for determining progression.

CONTROL ID: 3712928

SUBMITTER (NAME ONLY): Johnny Li

TITLE: Comparison of Global and Hemifield Rates of Visual Field (VF) Progression in Glaucoma

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.X. Li, C.G. DeMoraes, N. Harizman, A. Leshno, Q. Wang, G.A. Cioffi, J.M. Liebmann, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare VF hemifield vs. global mean deviation (MD) rates of progression.

Methods: Eyes with ≥10 VF tests (Swedish Interactive Thresholding Algorithm 24-2) and ≥3 years of follow-up were included from patients at Columbia University Irving Medical Center. Rates of progression (dB/yr) in global, superior, and inferior hemifield mean deviation were calculated. The presence of rapid (worse than -0.5 dB/year), very rapid (worse than -1.0 dB/year), and catastrophic (worse than -2.0 dB/year) progression were determined.

Results: VFs from 4,217 eyes (average number of tests, 15.0; mean follow up, 9.3 years) of 2,435 patients were included. The rate of change in global, superior hemifield, and inferior hemifield MD were statistically different among all three groups (-0.30dB/year vs. -0.31 dB/year vs. -0.28 dB/year, respectively, $p < 0.01$) (Table 1). In the superior hemifield, a larger percentage of patients demonstrated rapid progression (26.9% vs. 25.4%), very rapid progression (11.0% vs. 8.7%), and catastrophic progression (2.0% vs. 1.2%) compared to global mean deviation. A similar result was seen in the inferior hemifield but only in those that demonstrated catastrophic progression (1.7% vs. 1.2%). Comparing symmetry of progression between the superior and inferior hemifield (Figure 1), although a plurality of eyes (82.1%) had minimal difference between hemifield change (superior minus inferior hemifield slopes between 0.0 and -0.5 dB/year), a substantial percentage of patients had asymmetry between the hemifields, with 17.9% of eyes having a difference greater than -0.5 dB/year and 5.5% greater than -1.0 dB/year.

Conclusions: Superior, inferior, and global VF MD rates of progression often differ, but a large difference may serve as an indicator for rapidly progressing glaucoma and necessitate a treatment change or earlier surgical intervention. Identification of these areas of regional, rapid progression can be used to individualize management and treatment decisions.

CONTROL ID: 3712929

SUBMITTER (NAME ONLY): Azadeh Mobasserian

TITLE: Optical coherence tomography angiography and microperimetric findings in non-paraneoplastic autoimmune retinopathy

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mobasserian, H. Ghoraba, J. Regenold, C. Or, S. Park, I. Karaca, N. Than, J. Hwang, G. Uludag, N. Yavari, W. Matsumiya, M. Zaidi, A. Akhavanrezayat, H. khojasteh, M. Hassan, Q.D. Nguyen, Byers eye institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this cross-sectional study, we aim to evaluate optical coherence tomography angiography (OCTA) and microperimetric findings in non-paraneoplastic autoimmune retinopathy (AIR).

Methods: Ten eyes (6 patients) with a diagnosis of AIR, using the criteria proposed by Sen et al., 2014 , were included along with ten healthy control eyes of five healthy age-matched subjects. Each eye underwent microperimetric evaluation using the CenterVue MAIA device (Padova, Italy) and OCTA examination using RTVue Avanti OCTA (Optovue Inc, Fremont, California, USA). Clinical and demographic data, including OCTA and microperimetry, were analyzed and compared between the 2 groups.

Results: Mean (SD) age for the AIR and control groups was 44.2 ± 25.2 and 37.2 ± 22.9 years, respectively (p=0.30). Mean LogMAR BCVA for the AIR and control groups was 0.29 ± 0.33 and 0, respectively (p=0.002).

Total and parafoveal superficial capillary plexus densities were significantly lower in the AIR group (45.6 ± 3.7% and 46.9 ± 4.8%, respectively) compared with the control group (52.2 ± 2.4% and 54.1 ± 1.8%, respectively), (p =0.001 and 0.003, respectively). Total and parafoveal deep capillary plexus densities were not significantly different between AIR and control groups (p=0.24 and 0.08, respectively). Foveal avascular zone (FAZ) area was not statistically different between AIR group (0.25 ± 0.06 mm) and control group (0.24 ± 0.04 mm), (p=1).

As for microperimetric findings, average threshold values were significantly lower in the AIR group (20.6 ± 5.4 dB) compared with the control group (26.6 ±1.7 dB), (p=0.006). Percentage reduced thresholds were higher in the AIR group (70.5 ± 36.8%) compared with the control group (20.3 ± 22.1%), (p=0.009). Fixation stability measurements (P1 and P2) were not statistically different between the 2 groups (p=0.8).

Conclusions: OCTA and microperimetry may show abnormal results in AIR patients. Both ancillary tests may be helpful in evaluation and management of this rare disease. Further studies are required to elucidate these findings.

CONTROL ID: 3712932

SUBMITTER (NAME ONLY): Shreya Shah

TITLE: Comparison of treatment cost and quality-of-life impact of thyroid eye disease therapies

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Shah, T. Lu, M. Yu, A. Kossler, Stanford University School of Medicine, Stanford, California, UNITED STATES|T. Lu, M. Yu, A. Kossler, Department of Ophthalmology, Stanford Medicine, Stanford, California, UNITED STATES|S. Hiniker, Department of Radiation Oncology, Stanford Medicine, Stanford, California, UNITED STATES|C. Dosiou, Department of Endocrinology, Stanford Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teprotumumab was approved as a treatment for thyroid eye disease (TED) in 2020, but some clinicians question whether its high cost is worth its benefits. Cost-effectiveness analyses (CEAs) can help answer this question, but the health utility scores required are rare in TED. In this study we compare costs of teprotumumab with other treatments and use the validated Graves' orbitopathy quality-of-life (GO-QoL) score to measure change (Δ) in QoL. Our aim is to help clinicians think critically about treatment costs for TED as health care shifts to focus on cost-effective solutions.

Methods: Analysis was limited to first and second-line therapies for moderate-to-severe active TED (as per the 2021 European Group on Graves Orbitopathy guidelines) with pre- and post-intervention GO-QoL scores available in the literature. The costs of these treatments were obtained from the Turquoise Health database using Medicare billing codes. Prices were then generated from 1,903 hospitals in 50 states. Full treatment costs, including costs of medication and infusion, were calculated using recommended dosing guidelines and standardized to a 70kg patient (Table 1).

Results: Costs of teprotumumab, rituximab, orbital radiotherapy (ORT), and IV methylprednisolone (IVMP) were analyzed. Among these, teprotumumab had the highest mean treatment-related cost at $386,424 (SD $65,217) followed by rituximab at $18,549 (SD $2,556), ORT at $4,316 (SD $1,183), and IVMP at $4,025 (SD $1,647). Teprotumumab yielded a ΔGO-QoL of 19.4 (SD 18.8), rituximab 17.9 (single study), IVMP 13.5 (SD 25.2), and ORT 6.6 (SD 27.8). Treatment cost/ΔGO-QoL for teprotumumab was greatest at $19,888, followed by rituximab at $1,036, ORT at $651, and IVMP at $298 (Table 2).

Conclusions: Treatment cost/ΔGO-QoL of teprotumumab is nearly 20 times that of rituximab and around 50 times that of IVMP. Long-term data regarding the effect of teprotumumab on reducing the rates of orbital and strabismus surgery and improving ocular sequelae, as well as studies evaluating the impact of treatment on QoL using quality-adjusted life years, are needed to be able to determine the cost-effectiveness of the various treatment options for TED.

CONTROL ID: 3712934

SUBMITTER (NAME ONLY): Karine Bigot

TITLE: Transferrin confers neuroprotection in ex vivo and in vivo glaucoma rat models

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bigot, J. Youale, E. Orhan, F.F. Behar-Cohen, T. Bordet, Eyevensys, Paris, FRANCE|J. Youale, T. Jaworski, F.F. Behar-Cohen, E. Picard, UMRS1138, INSERM, Paris, FRANCE|B. Kodati, Y. Fan, N. Nsiah, N. Pappenhagen, D.M. Inman, Pharmaceutical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Iron is essential for retinal metabolism, but excess iron can cause oxidative stress. In glaucoma eyes, progressive retinal ganglion cell (RGC) death has been associated with dysregulation of iron homeostasis. Transferrin (TF) is an endogenous iron transporter that controls iron ocular levels. Local administration of TF is neuroprotective in various models of retinal degeneration, controlling iron-induced oxidative stress without undesirable side-effects. Herein, we evaluated the protective effects of TF on RGCs in retinal explants exposed to various stresses and in a rat model of ocular hypertension (OHT).

Methods: Rat retinal explants (n = 6-10/stress condition) were subjected for 24 hours to 1mM $FeSO_4$, 100µM NMDA, or 100µM $CoCl_2$, and maintained in culture until 96 hours. TF (50 mg/mL) was added during the whole stress incubation period. Survival of Brn3a-immunolabeled RGCs was quantified at 96 hours. In vivo, OHT was induced by injection of magnetic microbeads into the anterior chamber of adult Brown Norway rats (n = 5/group). Animals then received four weekly intravitreal injections of TF or vehicle (BSS). Naïve rats served as normotensive internal controls. RBPMS-immunolabeling of flat-mounted retinas and PPD-stained optic nerve sections were used for, respectively, RGC and axon quantification at 4 weeks.

Results: All three stresses induced about 50% RGC cell loss in retinal explants. Incubation with TF significantly preserved RGCs against $FeSO_4$-induced toxicity (+49.5 %, p = 0.0354). Similarly, TF partly protected RGCs against NMDA-induced excitotoxicity (+42.2 %, p = 0.0027) or $CoCl_2$-induced RGC hypoxia (+54.4 %, p = 0.0053). In IOP rats, RGC density at 4 weeks was significantly decreased in BSS-treated animals in comparison to naïve animals (-49.7%) whereas RGC number was not statistically different from naïve animals in TF-treated rats (p = 0.2475). TF preserved RGCs by about 70% compared to BSS-treated animals with OHT (p = 0.0008). Similarly, the axon density at 4 weeks was not different from the naïve group in TF-treated rats (p = 0.2480), while preserving about 47% of the axons when compared to vehicle group (p = 0.0027).

Conclusions: These results indicate that TF can interfere with different cell death mechanisms involved in glaucoma pathogenesis and demonstrate the ability of TF to protect RGCs exposed to elevated IOP. Altogether these results suggest that TF could benefit glaucoma patients.

CONTROL ID: 3712935

SUBMITTER (NAME ONLY): Tzu-Ni Sin

TITLE: A spontaneous nonhuman primate model of myopic foveoschisis.

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Myopic foveoschisis involves splitting of retinal layers at the fovea in highly myopic eyes which can resemble changes in X-linked retinoschisis (XLRS). Here, we characterize a novel nonhuman primate model of myopic foveoschisis by clinical exam, imaging, genetic, immunohistochemical, and single-nuclei transcriptomic analyses, focusing on retinoschisin 1 (RS1) – the extracellular retinal protein involved in maintaining retinal architecture and defective in XLRS.

Methods: We identified a 27-year-old rhesus macaque with visual behavior of myopia and performed ophthalmic examination with streak retinoscopy and biometry. Multimodal imaging including fundus photography (FP), fluorescein angiography (FA), and optical coherence tomography (OCT) was performed to monitor progression over 16 months prior to necropsy. Sanger sequencing was performed using human primers for RS1. Antibodies against rhodopsin, M/L opsin, GFAP, and Iba-1 were used to evaluate photoreceptors, macroglia, and microglia in the right eye. Single-nuclei RNA-sequencing (snRNA-seq) was performed on macular tissue for clustering, differentially expressed genes (DEGs), and pathway analyses.

Results: Ocular examination showed a prominent choroidal pattern and peripapillary atrophy suggestive of myopia, with mean refractive error of -13.5D and axial length of 21.5mm in the two eyes. FA showed no active choroidal neovascularization, but OCT revealed foveal schisis in outer plexiform layer (OPL) of the macula that worsened over time. Sanger sequencing showed no coding defects in the RS1 gene. Immunohistochemistry showed increased GFAP expression within Müller glia in the OPL, and loss of ramified Iba-1+ microglia, but no definite disruption of photoreceptors. SnRNA-seq of the macula showed transcriptionally-distinct cell types including rod, cone, bipolar, horizontal, amacrine, Müller, and ganglion cells that were similar in proportion to controls. Most retinal cell types showed predominantly upregulated DEGs, especially in cones. SnRNA-seq showed RS1 expression primarily in cones and rods that did not differ significantly from control eyes.

Conclusions: This spontaneous nonhuman primate model of myopic foveoschisis demonstrates a structural phenotype resembling XLRS with activated glial cells, but does not exhibit photoreceptor degeneration, RS1 mutation or changes in RS1 expression pattern, suggesting different molecular mechanisms between the two conditions.

CONTROL ID: 3712938

SUBMITTER (NAME ONLY): Anderson Vu

TITLE: Characterizing recognition of optotypes used to evaluate visual acuity

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Vu, J.K. To, A. Browne, Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|D. Harris, Cornell University, Ithaca, New York, UNITED STATES|A. Browne, Institute for Clinical and Translational Science and Department of Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual acuity exams are the primary subjective exam to detect or track progression of ophthalmic disease. However, the ability to distinguish certain features to correctly identify objects is labeled “recognition” acuity and may interfere with accurate visual acuity measurements. Therefore, we sought to characterize the recognition of optotypes seen on common visual acuity exams.

Methods: Optotypes were displayed on a high-definition digital monitor and images were captured using cell phone placed behind a phoropter with various spherical, cylindrical and axis lenses. Using a custom in-house application, images with differing amounts of distortion were displayed to human subjects with normal best-corrected visual acuity in a “forced-choice” style multiple-choice exam. Subjects were forced to determine what optotype character was displayed. Test results were presented as heatmaps to optotype recognition accuracy for a range of optical distortions.

Results: 36 healthy human subjects completed the exam. Heatmaps of each optotype show accuracy of the 4 subjects evaluated for their recognition of each optotype. No optical distortion (0 sphere/cylinder with no axis of rotation) is displayed in top left corner. Allen and Wright (pediatric) optotypes had the highest recognition accuracy, whereas letter-based optotypes scored the lowest.

Conclusions: Optotypes have differing levels of recognition and could potentially result in a variation in performance on visual acuity exams. These results support findings that ETDRS and Snellen optotypes are not interchangeable, and this non-interchangeability applies to all optotypes. Additionally, visual acuity results may not be interchangeable unless the optotype used is fixed.

CONTROL ID: 3712941

SUBMITTER (NAME ONLY): Luis Acaba-Berrocal

TITLE: Novel Visible-Light Curable Hydrogel for Closure of Sclerotomy Wounds in Pars Plana Vitrectomy

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Acaba-Berrocal, G. Yazdanpanah, D. Schaumann, S. Melgreen, A. Xu, M. Verardi, C. Frisbie, A. Graham, P. Pfanner, L. Kalinoski, A.R. Djalilian, Y. Leiderman, R. Chan, Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|M.H. Berrocal, Universidad de Puerto Rico, San Juan, PUERTO RICO|

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ABSTRACT BODY:

Purpose: Current approaches to close sclerotomy wounds following pars plana vitrectomy (PPV), including (1) no-closure, (2) suturing, and (3) application of fibrin glue sealants (FG) are at risk for hypotony and endophthalmitis, potentially time-consuming to perform and uncomfortable for patients, and hard to prepare and apply, respectively. In this study, the efficacy and stability of a novel visible-light curable natural hydrogel (LC-COMatrix) was evaluated for closure of sclerotomy wounds following PPV in ex-vivo models.

Methods: The human corneoscleral tissues with exposed sclera (removed conjunctiva) were mounted on an artificial anterior chamber connected to a pressure pump and a pressure sensor. A sclerotomy wound was created 4-mm from the limbus using a 23g trocar. The created wounds were left unclosed (N=10), closed with FG (N=10), or closed with LC-COMatrix (N=10). Afterwards, the pressure was increased (0.2 ml/s) and the burst pressure was recorded. In addition, fresh adult porcine eyeballs underwent a 2-port 23g PPV with vitreous removal and replacement with saline. One of the created slcerotomy wounds on each eyeball was closed with LC-COMatrix (N=10) or left unclosed (N=10). The infusion pressure was increased (5 mmHg/s) and closure/failure pressure was recorded. Furthermore, 23g sclerotomy wounds on human scleras (N=12) were closed with LC-COMatrix and the tissues were subjected to rotational shake while incubated in corneal preservation solution. The scleral adhesivity of LC-COMatrix was followed up using anterior segment optical coherence tomography (AS-OCT) and slit lamp biomicroscopy for 30 days.

Results: The average burst pressure for human scleras closed with LC-COMatrix was 220.48 mmHg (range 75.1-400.0), which was significantly higher than those of FG (133.7 mmHg, range 5.0-430.0, $p=0.049$, and no-closure (20.5 mmHg, range 6.1-75.3, $p<0.001$). The average burst pressure of porcine eyeballs' sclerotomy wounds closed with LC-COMatrix was 234.9 mmHg (range 35.2-543.2), while the burst pressure in the control group was 25.4 mmHg (range 6.4-60.0) ($p<0.001$). Regular examination with slit-lamp and AS-OCT showed that LC-COMatrix was consistently attached to the human scleras during the 30 days of follow-up.

Conclusions: LC-Comatrix is a novel visible-light curable natural and easy-to apply hydrogel with potential application for closure of sclerotomy wounds following pediatric and adult PPVs.

CONTROL ID: 3712944

SUBMITTER (NAME ONLY): Cem Kesim

TITLE: Automated Henle's fiber layer segmentation from non-directional optical coherence tomography images with deep learning

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kesim, M. Hasanreisoglu, Ophthalmology, Koç University School of Medicine, Istanbul, TURKEY|S. Cansiz, Computer Engineering, Bilkent Universitesi, Ankara, Ankara, TURKEY|Z. Kulali, S. Bektas, Koç University School of Medicine, TURKEY|M. Hasanreisoglu, Koç University Research Center for Translational Medicine, TURKEY|C. Gunduz-Demir, Computer Engineering, Koc Universitesi, Istanbul, Istanbul, TURKEY|C. Gunduz-Demir, KUIS AI Center, Koc Universitesi, Istanbul, Istanbul, TURKEY|

ABSTRACT BODY:

Purpose: To develop a deep learning algorithm that performs Henle’s fiber layer (HFL) segmentation from non-directional optical coherence tomography (OCT) images of retina.

Methods: Directional OCT (D-OCT) images from the macular 20°×20° area of healthy subjects were acquired to manually segment HFL. A deep neural network was designed and trained to estimate these manual segmentations only from their corresponding standard non-directional OCT images. This deep learning algorithm was then validated by another set of standard non-directional OCT images of healthy subjects.

Results: Standard OCT images from 20 and 10 eyes were used for training and validation, respectively. The trained deep neural network segmented HFL on validation OCT images with 81.74 percent recall, 86.31 percent precision, and 83.70 percent f-score rates on the average. On the validation OCT images, the total HFL volume and the mean HFL thickness values calculated by deep neural network were 0.65 ± 0.07 mm^3 and 23.20 ± 2.51 μm respectively.

Conclusions: The current study shows that Henle’s fiber layer, which had been previously visualized and segmented with the help of D-OCT, could be segmented from standard, non-directional OCT scans by a deep learning algorithm, which proves to be a beneficial tool to improve HFL segmentation by reducing the need to perform D-OCT imaging.

CONTROL ID: 3712945

SUBMITTER (NAME ONLY): Josiah To

TITLE: Comparison of a Photogrammetry for Anatomical CarE (PHACE) system with other affordable technologies for 3D imaging of the orbit and adnexa

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.K. To, A.N. Vu, A. Browne, L.S. Ediriwickrema, Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|A. Browne, Department of Biomedical Engineering, Institute of Clinical and Translational Science, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Josiah To: Commercial Relationship: Code N (No Commercial Relationship) | Anderson Vu: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Browne: Commercial Relationship: Code N (No Commercial Relationship) | Lilangi Ediriwickrema: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A need exists for cost-effective standardized tools to objectively characterize morphology and volume of orbital and adnexal anatomy. We compared a custom Photogrammetry for Anatomical CarE (PHACE) system with other low and mid-cost 3D imaging technologies for quantitative facial modeling.

Methods: We compared two low-cost and two mid-cost 3D scanning technologies. The PHACE system and the iPhone Scandy Pro application (Scandy, USA) are low-cost systems (<$500), whereas the Einscan Pro 2X (Shining 3D Technologies, China) and ARC7 facial scanner (Bellus 3D, USA) are two mid-priced structured light sensing scanners (~$5000). Imaging was performed on human subject faces with Fitzpatrick skin types 2, 4 and 6, with and without 3D printed phantom lesions affixed above the brow line. The PHACE system used two Google Pixel 3 smartphones on two rotating turntables to acquire 90 photographs, which were then rendered into 3D models using Metashape (Agisoft, Russia) - a photogrammetry software. The rendered hemisphere volumes using PHACE, Einscan, Scandy, and ARC7 devices were calculated with CloudCompare (open-source point cloud software). The performance of each facial scanning technology was evaluated by quantitatively comparing digitally measured volumes to the calculated volumes of the 3D printed phantom lesions.

Results: The Einscan qualitatively (Fig. 1A) and quantitatively rendered 3D printed phantom lesions with greatest resolution and accuracy (mean difference of 2.2 ± 2.8% for 33.5 µL). The mean differences between the calculated volume of the small phantom lesion (124 µL) and the rendered volumes for the PHACE, Scandy, and ARC7 systems were 4.7 ± 3.7%, 9.1 ± 0.9%, and 22.0 ± 17.9%, respectively.

Conclusions: The PHACE system outperforms the Scandy and more expensive ARC7 system to accurately render volumes as little as 124 µL. The Einscan can accurately render volumes down to 33.5 µL but it is 10x the cost. We demonstrated an optimized system to generate 3D models of the human orbit and adnexa while balancing cost and performance.

CONTROL ID: 3712947

SUBMITTER (NAME ONLY): Bin Li

TITLE: rAAV2-ND1 gene therapy for Leber's hereditary optic neuropathy(LHON) with mitochondrial ND1 mutation

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Li, C. He, Y. Tao, C. Cheng, X. Zhang, A. Luk, Q. Li, Neurophth Therapeutics, CHINA|

Commercial Relationships Disclosure: Bin Li: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics | Congwu He: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics | Yu Tao: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics | Chao Cheng: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics | Xin Zhang: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics | Alvin Luk: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics | Qiutang Li: Commercial Relationship(s);Code E (Employment):Neurophth Therapeutics

ABSTRACT BODY:

Purpose: LHON is an inherited mitochondrial disorder characterized by bilateral vision loss due to the degeneration of retinal ganglion cells (RGC). Approximately 13%-25% of LHON cases are caused by G3460A point mutation in ND1 mitochondrial gene. There is currently no effective treatment for LHON. Drugs such as Coenzyme Q and various antioxidant exhibit limited beneficial effects. This study is to design and characterize the recombinant AAV2-based gene replacement therapy (rAAV2-ND1, NFS-02) for the treatment of LHON with ND1 mutation

Methods: The ND1 sequence was optimized by adjusting codon usage preference, sequence repeats, mRNA secondary structure stability, and GC composition. The codon optimized human ND1 protein was tagged with COX10 mitochondrial targeting sequence and inserted into rAAV2 viral vector. After transducing into 293T cells, ND1 expression and mitochondrial localization were examined by Western blotting and co-immunofluorescent microscopy, respectively. The NFS-02 rescue of ND1 deficiency on the LHON patient derived cells was evaluated by oxygen consumption rate measured with Seahorse assay in the galactose medium condition. The in vivo expression, tissue distribution, and biosafety were also studied in rabbit and macaque after intravitreal (IVT) injection

Results: NFS-02 was constructed with the codon optimized ND1 coding sequences showing higher translation efficiency in vitro. The exogenous ND1 protein from rAAV2-ND1 vector was co-localized with mitochondrial marker ATP5A1, suggesting its mitochondrial localization. Consistent with its role in mitochondrial complex I, rAAV2-ND1 transduction significantly increased spare respiratory capacity of LHON patient-derived ND1 mutant cells, suggesting its therapeutic efficacy in vitro. Dose-dependent ND1 expression in RGC was observed in rabbit retinas after IVT injection. No neutralizing antibodies against AAV2 were detected in rabbit eyes after 6-months of NFS-02 injection at 5E9 vg/eye dose, and the GLP toxicity studies on macaque showed no adverse effect or toxicity following NFS-02 injection

Conclusions: Our gene therapy product, NFS-02, can allotropically express human ND1 protein in mitochondria, which compensates for the loss function of ND1 in LHON mutant cells. IVT administration of NFS-02 can efficiently achieve RGC delivery and expression, without noticeable biosafety concern in rabbit and macaque eyes

CONTROL ID: 3712948

SUBMITTER (NAME ONLY): Kate Keller

TITLE: Effects of biomechanical cues on filopodia, tunneling nanotubes, and myosin-X in trabecular meshwork cells

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.E. Keller, Y. Sun, Y. Yang, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Kate Keller: Commercial Relationship: Code N (No Commercial Relationship) | Ying YIng Sun: Commercial Relationship: Code N (No Commercial Relationship) | Yong-Feng Yang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Tunneling nanotubes (TNTs) are modified filopodia, which emanate from the trabecular meshwork (TM) cell surface and are important for cellular communication. As a filopodia grows, their tips transiently engage the underlying extracellular matrix (ECM) via integrins before a second round of growth occurs. This suggests changes to the biomechanical environment could affect filopodia and TNT formation. Here, we describe the effects of substrate stiffness, or mechanical stretch, on filopodia and cellular communication via TNTs. In addition, we investigate Myo10-integrin interactions, which could aid stabilization of the growing filopodia.

Methods: Primary human TM cells were grown on: (1) surfaces mimicking the stiffness of normal TM (4 kPa) or glaucoma (50 kPa); or (2) collagen-coated FlexCell plates, which were subject to 24 hour static mechanical stretch. A fluorescent vesicle transfer assay was performed to measure cellular communication via TNTs. Western immunoblots measured Myo10 protein levels. TM cell lysates were immunoprecipitated using a Myo10 antibody and pull-downs were separated by SDS-PAGE. Western immunoblots were probed with antibodies against integrins α5, β1, αvβ5 and αvβ3.

Results: As substrate stiffness increased, there was a significant increase in fluorescent vesicles transferred between cells (34% (4kPa) vs 49% (50 kPa); n=39; p=0.001). However, filopodia length and the number of filopodia per cell were unaffected by substrate stiffness. Mechanical stretch produced a 7% increase in the number of fluorescent vesicles transferred between TM cells (n=74; p=0.015). Concomitantly, Western immunoblots and densitometry showed a small (5%), but significant increase in Myo10 protein levels (n=15; p=0.023). Co-immunoprecipitation assays showed interaction of Myo10 with integrins α5, αvβ5 and αvβ3, but not with β1-integrin.

Conclusions: Investigating the effects of substrate stiffness and mechanical stretch on filopodia and cellular communication via TNTs gives us further insight into how cellular communication could be affected in glaucomatous TM in situ, or in response to elevated intraocular pressure. Our results expand the repertoire of integrins to which Myo10 binds to. Further studies are required to investigate if Myo10-integrin interactions are necessary for filopodia growth, or the transition of filopodia to TNTs.

CONTROL ID: 3712951

SUBMITTER (NAME ONLY): Muhammad Qureshi

TITLE: Chronic Ocular GVHD Treatments at Two Distinct Geographic Locations of a Single Tertiary Referral Center

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.B. Qureshi, J.O. Garcia, Mayo Clinic Alix School of Medicine, Mayo Foundation for Medical Education and Research, Scottsdale, Arizona, UNITED STATES|C. Wentz, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|C.B. Nau, M. Schornack, Department of Ophthalmology, Mayo Foundation for Medical Education and Research, Rochester, Minnesota, UNITED STATES|J. Shen, Department of Ophthalmology, Mayo Foundation for Medical Education and Research, Scottsdale, Arizona, UNITED STATES|J. Quillen, C. Mead-Harvey, Department of Quantitative Health Sciences, Mayo Foundation for Medical Education and Research, Scottsdale, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Examine differences in baseline characteristics and treatment of chronic ocular graft versus host disease (oGVHD) patients in two geographically distinct locations.

Methods: Patients diagnosed with definite chronic oGVHD as defined by the International Chronic Ocular GVHD Consensus Group between 09/2014 and 09/2021 at two locations were identified. Clinic 1 (C1) is located in Arizona and Clinic 2 (C2) is located in Minnesota. IRB approved retrospective chart review was conducted and the following data was collected for initial and follow-up visits: demographic information, ocular surface disease index (OSDI), corneal fluorescein staining (CFS), and treatment (hot compresses, moisture chambers, punctal plugs, punctal cautery, autologous serum tears (AST), and scleral contact lenses). Differences by site were tested using Chi-Square tests or linear model ANOVA.

Results: C1 (n=79) and C2 (n=50) baseline mean age was 58.4 years and 57.5 years, respectively. Mean length of follow-up was 108.2 weeks for C1 and 115.9 weeks for C2. By last follow-up, mean OSDI change was -17.6 at C1 (95% CI -24.2, -11.1) and +5.3 (95% CI -1.4, 12.1) at C2. The difference in changes was statistically significant ($p<0.001$). At baseline, C1 mean CFS was significantly worse for both eyes than C2 mean CFS (OD $p=0.012$, OS $p<0.001$). By last follow-up, mean CFS OD change was -0.5 at C1 (95% CI -0.7, -0.2) and -0.1 (95% CI -0.4, 0.2) at C2. The mean CFS OS change was -0.5 (95% CI -0.7, -0.2) at C1 and +0.1 (95% CI -0.2, 0.4) at C2. The difference in changes was statistically significant for CFS OS ($p=0.006$) but not for CFS OD ($p=0.130$). Moisture chambers and scleral lenses were used in similar frequencies at C1 and C2 (14% vs 18%, 16% vs 18%, respectively). However, punctal plugs, punctal cautery, and AST were used more frequently at C1 than C2 (85% vs 60%, 67% vs 26%, 52% vs 8%, respectively).

Conclusions: oGVHD patients at C1 were associated with significant improvement in OSDI and corneal fluorescein staining in the left eye and were also associated with more frequent use of punctal plugs, cautery, and AST. The significance of these associations is limited by the retrospective nature of this review. Greater severity of baseline CFS at C1 supports previous studies showing that desert climate is associated with more severe signs of dry eye. Future prospective studies are needed to confirm the validity of these findings.

CONTROL ID: 3712954

SUBMITTER (NAME ONLY): Ecosse Lamoureux

TITLE: Relationship between Severity and Laterality of Age-Related Sensory Decline and Frailty In Multi-ethnic Elderly Asians

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.L. Lamoureux, R. Man, A.T. Gan, E.K. Fenwick, P. Gupta, Singapore Eye Research Institute, Singapore, SINGAPORE|E.L. Lamoureux, R. Man, E.K. Fenwick, P. Gupta, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate the relationship of the severity and laterality (i.e., unilateral or bilateral) of vision, hearing, and dual sensory impairments (VI, HI and DSI, respectively) with frailty in older Asians.

Methods: We included individuals from The PopulatION HEalth and Age-Related SEnsory Decline PRofilE (PIONEER), a population-based study of Singaporean Chinese, Malays, and Indians aged ≥60 years. Participants underwent visual acuity (VA) assessment using a LogMAR chart, and a hearing test using a portable audiometer at four frequencies (500, 1000, 2000, 4000 hertz). The Fried frailty phenotype was used to assess physical frailty, defined as meeting at least three out of five criteria comprising unintentional shrinking (BMI<18.5 kg/m^2); slowness (≤0.8m/s on 4m-gait speed); weakness (handgrip strength <30 kg (men) and <20 kg (women)); exhaustion (measured using the vitality domain of the 12-item Short-form survey); and low self-reported physical activity. Any, mild and ≥ moderate VI was defined as presenting distance VA >0.3 logMAR; 0.3< VA ≤0.48 logMAR; and VA >0.48 logMAR, respectively; and any, mild and ≥ moderate HI as an average threshold of ≥40 dB, 40≤ hearing loss <60 dB; and hearing loss ≥60 dB, respectively.

Results: Of the 1,510 PIONEER adults (mean±SD age 72.1 ±7.9yr), 44.0%, 43.7% and 23.1% had any VI, HI and DSI, respectively. Of these, 34.0% had bilateral VI only; 64.7% had bilateral HI only, and 18.3% had DSI+ comprising (a) bilateral VI/HI and unilateral HI/VI; or (b) bilateral VI and bilateral HI). Notably, 33.9% of participants were frail. In multivariable-adjusted analyses, the presence of bilateral VI or HI (any severity) was independently associated with almost twice the odds of having frailty (odds ratio [OR]: 1.82, 95% confidence interval [CI]: 1.25, 2.44; for VI; OR: 1.84, 95% CI: 1.32, 2.57; for HI) compared to those with no sensory impairment. Critically, those with DSI+ had even higher odds of being frail (ORs between 2.15-3.35). Unilateral VI, HI and DSI (i.e., unilateral VI and HI) of any severity were not associated with frailty.

Conclusions: Elderly Singaporeans with bilateral VI or HI of any severity; and DSI comprising any bilateral impairment are at high risk of frailty. Strategies to prevent and delay progression to bilateral sensory losses are warranted to reduce frailty in our ageing society.

CONTROL ID: 3712955

SUBMITTER (NAME ONLY): Wahbi Wahbi

TITLE: Macular OCT findings in patients with congenital nystagmus syndrome.

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wahbi, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|O. Nasser, Orasis World Class Eyecare Medical Center, ISRAEL|

Commercial Relationships Disclosure: Wahbi Wahbi: Commercial Relationship: Code N (No Commercial Relationship) | Orwa Nasser: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the macular optical coherence tomography findings in eyes of patients with congenital nystagmus syndrome compared to healthy subjects.

Methods: In this comparative cross-sectional observational study, a spectral-domain optical coherence tomography was conducted on eyes of congenital nystagmus syndrome patients and compared with those of healthy individuals (control group). ETDRS macular map was used in the analysis and average thickness of central 6mm (C6T), average thickness of central 1mm (C1T) and thinnest central thickness (CRT) were obtained and compared between the groups. Prevalence and grading of foveal hypoplasia and albinism were assessed in the patients group.

Results: 46 eyes of 23 congenital nystagmus syndrome patients and 46 eyes of 23 healthy individuals were included in the study. 80% of the eyes in nystagmus group had foveal hypoplasia. The mean grade of foveal hypoplasia is 3.45 ±0.9323 in the above group. 40% of patients with nystagmus had either ocular albinism or oculocutaneous albinism. CRT was 258.2 ± 48.31 µm in the nystagmus group compared to 189.3 ± 24.25 µm in the control group with a mean difference of 68.85 ± 7.97 µm ($P<0.001$). C1T was 267.2 ± 36.01 µm in the nystagmus group compared to 231.0 ± 26.0 µm in the control group with a mean difference of 36.20 ± 6.548 ($P<0.001$). C6T was 256.2 ± 26.15 µm in the nystagmus group compared to 279.1 ± 9.532 µm in the control group with a mean difference of -22.90 ± 4.104 µm ($P<0.001$).

Conclusions: The results of this study show that the majority of congenital nystagmus syndrome patients have foveal hypoplasia. Macular optical coherence tomography can be used to assess the foveal thickness and grading of foveal hypoplasia patients with nystagmus.

CONTROL ID: 3712956

SUBMITTER (NAME ONLY): Philip Chen

TITLE: Punctal stenosis associated with topical netarsudil use

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.P. Chen, T. Meirick, R.C. Mudumbai, M. Zhang, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Philip Chen: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Meirick: Commercial Relationship: Code N (No Commercial Relationship) | Raghu Mudumbai: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report a series of patients who developed punctal stenosis secondary to the use of topical netarsudil for treatment of glaucoma.

Methods: Patients using topical netarsudil for management of glaucoma and noted to have punctal stenosis ipsilateral to the eye(s) being treated with netarsudil were included. Each chart was reviewed to identify other potential causes of punctal stenosis and result of cessation of netarsudil.

Results: Sixteen patients had punctal stenosis; 13 developed unilateral punctal stenosis while using netarsudil unilaterally, and 3 patients developed bilateral punctal stenosis with bilateral use. Time from initiation of netarsudil to recognition of symptoms or documrntation of punctal stenosis ranged 2 to 35 months (mean 14.0 ± 8.7 months). Thirteen patients endorsed tearing, but two had no symptoms. Ectropion was seen in one eye. Corneal verticillata was noted in 14 (87.5%) patients. In 8 eyes, netarsudil was discontinued and the punctal stenosis was reversed, with resolution of associated symptoms.

Conclusions: Netarsudil use can lead to the development of reversible punctal stenosis, which may cause tearing and associated symptoms and which may be sufficiently severe as to require discontinuation of treatment. Patients reporting these symptoms while using netarsudil should not be assumed to have dry eye disease, ocular surface toxicity from topical medications, or other forms of acquired punctal stenosis.

CONTROL ID: 3712957

SUBMITTER (NAME ONLY): Idara Akpandak

TITLE: Risk of herpes zoster ophthalmicus following COVID-19 vaccination in a large US claims database

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Akpandak, D. Miller, Y. Sun, B.F. Arnold, N.R. Acharya, F.I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|B.F. Arnold, N.R. Acharya, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Idara Akpandak: Commercial Relationship: Code N (No Commercial Relationship) | D. Claire Miller: Commercial Relationship: Code N (No Commercial Relationship) | Yuwei Sun: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Arnold: Commercial Relationship: Code N (No Commercial Relationship) | Nisha Acharya: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine whether there is an increased risk of herpes zoster ophthalmicus (HZO) following COVID-19 vaccination.

Methods: Retrospective observational study utilizing OptumLabs® Data Warehouse, a longitudinal, real-world data asset with de- identified administrative claims and electronic health record data. A cohort study design and a self-controlled design were both utilized to investigate HZO following vaccination, defined by an ICD-10 diagnosis code within 30 days after vaccine administration (or up to the second dose if a second dose was administered), plus a new prescription or dose escalation of antivirals within 5 days of HZO diagnosis. Using a cohort design, COVID-19 vaccinated individuals from 12/11/2020- 6/30/2021 were compared to two influenza-vaccinated cohorts: a pre-pandemic group (1/1/2018-12/13/2019) and an early pandemic group (3/1/2020-11/1/2020). Cox proportional hazard models were used to identify unadjusted and adjusted hazard ratios for HZO. Using a self-controlled design, the incidence rate ratio comparing the risk of HZO in the risk intervals following COVID-19 vaccination to a control interval 60 to 90 days prior to the first dose was estimated using conditional Poisson regression.

Results: Among 3,567,715 patients in the COVID-19 vaccinated cohort, there were 60 post-vaccine HZO cases. Patients vaccinated against COVID-19 were not at increased risk of HZO compared to pre-pandemic influenza vaccinated patients (N= 5,101,709; HR= 0.84; 95% CI: 0.61 – 1.16; p= 0.29) and early pandemic influenza vaccinated patients (N= 4,060,412; HR= 0.93; 95% CI: 0.64 – 1.34; p= 0.69) after adjustment for demographics, comorbidities, zoster vaccine, and medication use. Additionally, HZO cases post-COVID-19 vaccination were less likely to be prescribed ophthalmic steroids compared to cases following pre-pandemic and early pandemic influenza vaccination (18.3% vs 29.6% vs 41.4%, respectively). In the self-controlled design, patients were not at increased risk of HZO after COVID-19 vaccination compared to their control interval (IRR= 0.74; 95% CI: 0.49 – 1.12; p= 0.15).

Conclusions: There is not an increased risk of HZO following COVID-19 vaccination. These results provide reassurance for the safety of the COVID-19 vaccine from an ophthalmic standpoint.

CONTROL ID: 3712958

SUBMITTER (NAME ONLY): Andy Morozov

TITLE: Personal Protection Equipment and Slit-lamp Breath Shield in the Ophthalmology Office Setting

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Morozov, S. Karageuzian, C. Morozova, D. Kamen, D.S. Boyer, H. Tabandeh, Retina Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: COVID-19 pandemic has become a major global public health challenge. The ophthalmology office setting involves close encounters between the patient and the health care workers increasing risk of viral transmission. Use of PPE decreases risk of person-to-person viral transmission. The purpose of the study was to evaluate breath-induced air currents in subjects without a facemask, with a procedure mask, with an improvised face, and in the setting of slit-lamp examination.

Methods: Breath-induced air currents were studied in healthy volunteers utilizing a vape pod system and videography during gentle and heavy breathing simulation. Video frames at 2 seconds after the initiation of expiration were captured and analyzed.

Results: A total of 210 recordings were made for 7 settings. Without a face mask, the aerosol moved forwards and spread vertically and horizontally reaching a mean distance of 23.1 inches for gentle, and 36.1 inches for heavy breathing at 2 seconds ($P < 0.001$). Using PPE the airflow patterns included: a) procedure mask- forward 0 cases, upward 19 (63%) cases, side 28 (93%) cases, downward 22 (73%) cases, and backward 22 (73%) cases. Adding a tape at the upper border of the mask eliminated upward flow in all cases. b) Improvised face mask- forward 0 cases, upward 0 cases, side 30 (100%) cases, downward 30 (100%) cases, and backward 17 (57%) cases. In 14 (47%) cases trace of aerosol was detected adjacent to the front surface of the mask. Adding a second layer eliminated the trace of aerosol in all cases. In the setting of simulated slit-lamp examination without the breath shield, the aerosol reached the chin rest in 9 (60%) cases during gentle breathing and in all cases during heavy breathing. The breath shield was effective in blocking forward airflow in all cases.

Conclusions: Use of a procedure mask by patients, while effective in blocking forward breath-induced airflow, redirects the flow upwards, potentially increasing the risk of contamination during an office procedure. An improvised facemask alters breath-induced air currents favorably and partially absorbs respiratory droplets.

CONTROL ID: 3712959

SUBMITTER (NAME ONLY): Xiaorong Xin

TITLE: Optic nerve crush elicits proteomic alterations in the rat retina

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Xin, Ophthalmology, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, Sichuan, CHINA|

Commercial Relationships Disclosure: Xiaorong Xin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic nerve (ON) injury and neurodegenerative disorders trigger a cascade of retinal ganglion cells loss, which leads to the failure of the ON to regenerate. Our current study was to explore the involvement of the alterations of proteome and key candidate proteins in the pathological event of ON degeneration in response to optic nerve crush (ONC).

Methods: In our current study, we established rat ON injury model through ONC. A quantitative comparison of the proteome in the rat retina was analyzed through TMT labeling, HPLC fractionation, LC-MS/MS and PRM proteomics analysis. Western blot was performed to validate the protein level of the candidate proteins following ON-crushed injury.

Results: ONC induced a total of 58 proteins downregulated and 13 proteins upregulated in the retina. Subcellular prediction was performed to characterize the subcellular localization of these differentially expressed proteins. ONC downregulated proteins that were mainly accumulated in the nucleus, extracellular domain, cytoplasm, and mitochondria. Most of the upregulated proteins were localized in the nucleus, cytoplasm, endosplasmic reticulum, mitochondria, extracellular region in response to ONC. For the biological process enrichment, the dysregulated proteins are important for maintenance of biological process including cellular metabolic process, phagocytosis, neurological system development, sensory perception, and visual perception. ONC elicited quantitative changes in proteins that associated with extracellular matrix, intermediate filament and cytoskeleton. The identified proteins predominantly participate in structural molecule activity, binding, transport, catalytic activity, and regulating molecular function. We found that longevity regulating pathway was significantly enriched through KEEG enrichment. Notably, of these differentially expressed proteins in the pathway, we noticed that AKT3, one of the isoform of AKT, was the most dysregulated after ONC. We further validated AKT3 protein level and our results showed a markedly decrease in its expression level responding to the ON injury.

Conclusions: Our proteomic analysis suggests that ON injury imposes a pathological impact on retina through altering proteomic profile. The identification of down-regulation of ATK3 provides a valuable clue that ATK3 is involved in the pathological cascade of ON degeneration and may be an important therapeutic target for ON regeneration.

CONTROL ID: 3712960

SUBMITTER (NAME ONLY): Mahesh Dev

TITLE: Effect of low light levels and target contrast on stepping accuracy in older adults with age-related macular degeneration

SESSION TITLE: Vision Impairment: Impact on Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.K. Dev, A.A. Black, D. Cuda, J.M. Wood, School of Optometry & Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

Commercial Relationships Disclosure: Mahesh Dev: Commercial Relationship: Code N (No Commercial Relationship) | Alex Black: Commercial Relationship: Code N (No Commercial Relationship) | Damian Cuda: Commercial Relationship: Code N (No Commercial Relationship) | Joanne Wood: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Older adults report difficulties performing daily activities, such as walking and stepping, under low light levels, particularly those with age-related macular degeneration (AMD). This study explored the effect of low light levels and target contrast on precision stepping accuracy in older adults with and without AMD.

Methods: Twenty-four older adults (12 AMD and 12 controls, aged over 65 years) walked along a 14-m level walkway containing stepping and distractor targets (10 each, 15x15cm). Participants stepped as closely as possible to the middle of stepping targets and avoided distractor targets. Stepping tasks were performed under three light levels (photopic, 440lx; 2 levels of mesopic, 10 and 3lx) and two stepping target contrasts (high 89% and low 54%). Foot placement during stepping was recorded using leg mounted cameras. Custom software determined anteroposterior (AP) and mediolateral (ML) stepping errors for each step (ball of foot to target centre), as well as absolute error (Euclidean distance).

Results: For absolute stepping errors, there were significant effects of group ($p=0.004$), light ($p<0.001$) and a significant group*light interaction ($p=0.015$), but no effect of contrast ($p=0.14$) (Figure). Controls showed similar errors under all light levels ($p=0.99$) but the AMD group had greater errors overall, and more errors under mesopic conditions compared to photopic ($p<0.001$). For both ML and AP stepping errors, there were significant effects of light ($p\leq0.008$) but no group effect ($p\geq0.13$); all participants stepped more laterally and posteriorly under low mesopic compared to photopic conditions. Target contrast had a significant effect on ML ($p=0.007$) but not AP stepping errors ($p=0.48$); all participants stepped more laterally for low compared to high contrast targets. There was a significant light*contrast interaction for AP ($p=0.019$) stepping errors; all participants stepped posteriorly for low compared to high contrast targets under photopic conditions.

Conclusions: Reduced light levels and lower contrast stepping targets negatively impacted stepping accuracy. Findings have implications for enhancing environmental design, including lighting and contrast, to promote safe mobility and minimise falls risk, particularly in older adults with AMD.

CONTROL ID: 3712961

SUBMITTER (NAME ONLY): Seong Joon Ahn

TITLE: Clock-hour Topography and Extent of the Photoreceptor and Retinal Pigment Epithelium Damages in Hydroxychloroquine Retinopathy: Functional Correlation and Implications for Classifications

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ahn, Hanyang University, Seongdong-gu, Seoul, KOREA (THE REPUBLIC OF)|K. Kim, Ophthalmology, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Seong Joon Ahn: Commercial Relationship: Code N (No Commercial Relationship) | Ko Eun Kim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the clock-hour topographic characteristics on the photoreceptor and retinal pigment epithelium (RPE) damages and correlate them with functional defects in eyes with hydroxychloroquine retinopathy

Methods: Among 152 eyes diagnosed with hydroxychloroquine retinopathy, those with coexistent retinal or macular diseases or those with poor image quality of optical coherence tomography (OCT) and fundus autofluorescence (FAF) images were excluded. In total, 149 eyes of 75 patients were included for the analyses and classified into parafoveal, pericentral, and mixed retinopathy according to disease pattern and also into early, moderate, and severe ones. Clock-hour topographic characteristics (from the fovea) and extents of the photoreceptor and RPE defects were evaluated by reviewing the OCT images obtained by 12 radial scans and wide-field FAF. The extent (numbers of involved clock-hour areas) of photoreceptor and RPE damages was correlated with perimetric parameters such as mean deviation (MD), pattern standard deviation (PSD), and visual field indices (VFI).

Results: Whereas the photoreceptor damages were most commonly noted at the 6 o'clock area in both parafoveal and pericentral retinopathy, the RPE damages were most commonly noted at the nasal area, peripapillary ones, in pericentral eyes. The extent of RPE damages was almost identical between OCT and FAF imaging, whereas that of photoreceptor defects was significantly greater in OCT, indicating superior sensitivity of OCT for the detection of the photoreceptor damages. The extent of photoreceptor damages significantly correlated with MD and VFI (both $P < 0.05$) and this seemed to better reflect the functional defects in eyes with the retinopathy, as the disparity in the visual function between moderate and severe eyes and the variability of the perimetric parameters in the same severity (moderate or severe) could be explained by the disparity or differences in the extent.

Conclusions: This study showed clock-hour topographic characteristics and extents of the photoreceptor and RPE damages in eyes with hydroxychloroquine retinopathy. From the significant correlation between the extent of photoreceptor damages and perimetric parameters, the information may be utilized for functional correlation and classification of hydroxychloroquine retinopathy.

CONTROL ID: 3712963

SUBMITTER (NAME ONLY): Jibran Mohamed-Noriega

TITLE: Prospective observational study of disc haemorrhages (POSH). Comparison of ocular and systemic variables between visits with and without disc haemorrhages.

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mohamed-Noriega, S. Aguilar Munoa, P. Praditsuktavorn, D.F. Garway-Heath, Glaucoma, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|G. Lazaridis, D.F. Garway-Heath, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|J. Mohamed-Noriega, Department of Ophthalmology, University Hospital and Faculty of Medicine, Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, MEXICO|G. Lazaridis, University College London Centre for Medical Image Computing, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Ocular and systemic variables previously reported to be associated with the presence of disc haemorrhages (DH) are compared in visits with and without DH.

Methods: Thirty patients with open-angle glaucoma and a new DH were recruited from Moorfields Eye Hospital for 5 visits (0, 1, 3, 6, and 12 months). The following examinations acquired in all visits were compared between DH+ and DH- visits: optic disc photography, nailbed capillaroscopy (4^{th} and 5^{th} fingers of the non-dominant hand), autorefraction, ocular response analyzer, heart rate and blood pressure, questionnaires to assess the number of days during the previous month with headache, aura, cold hands, hearing loss, insomnia, and reduced thirst, and the European Quality of Life-5 Dimensions (EQ-5D) questionnaire. A DH+ visit was defined as the presence of a DH in one or both eyes based on fundus photography. All visits started with the questionnaires and nailbed capillaroscopy; the patient and examiner were unaware of that visit DH status.

In all included participants and for all variables, the difference between the mean of DH+ visits was compared with a paired t-test with the mean value of DH- visits.

Results: Four patients were excluded from this analysis because all of their visits were classified as DH+. The 26 included participants attended 127 scheduled visits, 64 were DH+ and 63 DH-. Nailbed haemorrhages were identified in 24 (38%) of DH+ visits compared to 31 (49%) of the DH- visits (p= 0.183). In 44% of the visits, the same haemorrhage status was identified in the disc and the nailbed. Continuous variables are presented in Table 1. A higher corneal resistance factor (CRF) was identified in each eye during DH+ visits. Although it was not statistically significant, there was a trend toward more headaches during DH+ visits. IOP values were very similar between DH+ and DH-visits.

Conclusions: There was a tendency toward more headaches during DH+ visits. The CRF was higher in both eyes during DH+ visits, although it is unlikely to change between visits. The difference in CRF may be related to IOP or multiple testing. There was a high rebleeding rate in the disc and nailbed. The trends observed over only 5 visits in this small exploratory study warrant further investigations comparing systemic and ocular variables between DH+ and DH- visits.

CONTROL ID: 3712964

SUBMITTER (NAME ONLY): James Loughman

TITLE: Asian and Western refractive centile curves from meta-analysis of population refraction data

SESSION TITLE: Refractive Error and Social Determinants of Vision Function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Loughman, S. Harrington, D.I. Flitcroft, Technological University Dublin, Dublin, Dublin, IRELAND|K.J. Saunders, Ulster University, Coleraine, Londonderry, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To generate childhood refractive centile curves for Asian and Western populations in order to facilitate evidence-based myopia control.

Methods: 35,645 refraction measurements from 8 large population-based studies were included (12,965 European/North American eyes, and 22,680 Asian eyes). An individual meta-analysis of right eye SER was performed by region, age and gender. Quantiles were generated by age group and gender. Combined curves for each calculated centile were generated by weighted cubic spline interpolation according to the number of participants in each age group/study.

Results: Western and Asian population centiles differed at all ages (Figure 1). At age 6, median refraction was 1.33D and 1.34D in Western boys and girls, respectively and 0.25D and 0.24D in Asian boys and girls. Western children at the 97th centile were hyperopic at age 6 (0.11D boys; 0.18D girls). In Asia, 6-year-olds at the 97th centile were significantly more myopic (-1.71D boys; -1.77D girls). In the West, the median refraction did not reach the threshold for myopia (≤-0.50D) by age 18. In Asia, median refraction met the myopia threshold by age 10 in boys and age 9.5 in girls. Gender differences were most marked in hyperopes in the West, with boys 0.60D more hyperopic at age 7.5 at the 3rd centile. At age 10.5, girls were 0.22 D more myopic at the 97th centile, but by 18 the gender difference was <0.05D at all centiles. Median refraction varied less than 0.02D between sexes at all ages in the West. In Asia, gender differences were minimal (<0.20D) below age 11 but increased with age and were greatest in myopes. The gender difference in median refraction increased from age 6 to 15, with girls 0.55D more myopic by age 15, reducing to 0.40D by age 18.

Conclusions: Population-based centile analysis offers the prospect of monitoring the treatment efficacy of myopia control interventions outside a clinical trial, but must be gender- and region-specific. Historic data derived from the period before myopia treatments were introduced represent a valuable natural history resource on myopia progression. Pooling data from the large number of existing surveys provides a mechanism to standardize reference centile charts relevant to the management of myopia.

CONTROL ID: 3712965

SUBMITTER (NAME ONLY): Cori Jones

TITLE: Changes in eyelid position with scleral contact lens wear

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Scleral contact lenses (ScCL) are large diameter gas permeable contact lenses that enhance vision for a variety of ocular conditions. Several case reports have suggested ScCL can improve upper eyelid ptosis, but there have been no previous studies of the change in non-ptotic eyelid position with ScCL. In this observational clinical study, we hypothesize that ScCL wear increases interpalpebral fissure height (IPF) and margin to reflex distance (MRD).

Methods: IPF and MRD were measured on 115 eyes of 64 established ScCL patients from photographs incorporating a millimeter ruler at three time points: before insertion of the ScCL (control), 5 minutes after insertion of the ScCL, and after 2 or more hours of ScCL wear. ScCL diameter and sagittal depth (sag) on eye, longevity of ScCL wear, patient sex and age, and reason for ScCL wear were documented for each subject and controlled for during statistical analysis. Sag of the ScCL on eye at the 2 hour time point was measured with Oculus Pentacam. The caliper tool available with the Scheimpflug images was used to measure the distance from the apex of the ScCL to a line bisecting the pupil. A linear mixed effects model was utilized for analysis of mean difference in IPF and MRD between time points.

Results: Mean IPF of control conditions was 8.6±1.6mm. IPF measurement was greater after 5 min of ScCL wear than before ScCL placement (mean difference: 0.8mm, 95% CI 0.54, 1.06, $p<0.001$) and after 2 hours of ScCL wear than before ScCL placement (mean difference: 0.69mm, 95% CI 0.43, 0.95, $p<0.001$). There was no difference in IPF between 5 min and 2 hours of ScCL wear (mean difference: 0.11mm, 95% CI -0.15, 0.37, $p=0.595$). Mean MRD of control conditions was 3.4±1.4mm. MRD measurement was significantly greater after 5 min of ScCL wear than pre-ScCL insertion (mean difference: 0.35mm, 95% CI 0.14, 0.55; $p<0.001$) and after 2 hours of ScCL wear pre-ScCL insertion (mean difference: 0.28mm, 95% CI 0.08, 0.48, $p<0.001$). There was no significant difference in MRD between 5 min and 2 hours of ScCL wear (mean difference: 0.07mm, 95% CI -0.14, 0.27, $p=0.732$).

Conclusions: Study findings support the hypothesis that ScCL wear increases IPF and MRD in eyes without ptosis.

CONTROL ID: 3712968

SUBMITTER (NAME ONLY): Mervyn Thomas

TITLE: Truncating PAX6 mutations result in severe arrested retinal development with loss of cone photoreceptor specialisation: A multi-centre study

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.G. Thomas, H. Kuht, G. Maconachie, R. McLean, Z. Tu, V. Sheth, I. Gottlob, Ulverscroft Eye Unit, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|M. Tobin, Department of Health Sciences, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|J. Han, Institute of Vision Research, Yonsei University College of Medicine, Seodaemun-gu, Seoul, KOREA (THE REPUBLIC OF)|B.P. Brooks, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|E. Engle, Departments of Neurology and Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: PAX6 variants can be associated with pan-ocular phenotypes such as aniridia, keratopathy, anterior segment dysgenesis, cataracts, colobomas, foveal hypoplasia and optic nerve hypoplasia. Previous genotype-phenotype correlation studies have shown strong correlation between the severity of aniridia associated phenotypes and the type of PAX6 variants. In this multi-centre study, we aimed to specifically characterise the foveal phenotypes associated with PAX6 variants.

Methods: We established the foveal development investigators group (FDIG) aimed at exploring foveal phenotypes in developmental retinal disorders across different centres (n=10) in 8 countries. We included all patients with pathogenic PAX6 variants and high-resolution optical coherence tomography (OCT) scans of the fovea from FDIG and the literature. Variants were classified into truncating and non-truncating based on predicted effect. Foveal OCTs were graded by at least two expert graders and classified into grades of foveal hypoplasia according to the classification by Thomas MG et al. 2011. The groups were further classified into with cone photoreceptor specialisation (PRS+) and without (PRS-).

Results: We identified a total of 106 patients that met the inclusion criteria. There were more cases with truncating mutations (n=71) compared to non-truncating mutations (n=35). Grade 4 foveal hypoplasia was the most common (40.6% of cases). There was a significantly higher proportion of PRS- cases associated with truncating variants ($X2 = 12.6$, $p=0.0004$) compared to non-truncating variants. The visual acuity was significantly worse for truncating variants compared to non-truncating variants (median difference=0.35 logMAR, $p<0.0001$).

Conclusions: We show that truncating PAX6 variants are associated with severe arrested retinal development with loss of cone photoreceptor specialisation. These loss-of-function variants are predicted to generate no protein and hence result in relatively severe foveal phenotypes compared to missense variants. This also translates to poorer visual acuity in patients with truncating PAX6 variants.

CONTROL ID: 3712969

SUBMITTER (NAME ONLY): Jose M. Caminal

TITLE: MOUSE SUPRACHOROIDAL ORTHOTOPIC MODEL FOR SPONTANEOUS METASTASIS OF UVEAL MELANOMA

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is the most common intraocular malignancy in adults.
Currently, there is any effective therapeutic option for patients with metastatic disease since the UM is resistant to conventional chemotherapy and immune checkpoint blockade, showing poor response rates and limited overall survival.
Recent advances in the identification of early driver mutations and aberrant signaling pathways that contribute to the progression of UM, open new therapeutic strategies against specific targets.
To develop a mice xenograft model that mimics the metastatic process and that could to be used in pre-clinical studies to analyze the efficacy of new drugs or inhibitors that might interfere the growth of liver metastases.

Methods: We developed a xenograft model of human uveal melanoma in NSG (NOD-scidIL2Rgnull) strain mice that have severe immunodeficiency. UM cells have been orthotopically implanted in the suprachoroidal space by surgery of previously anesthetized mice. We had incorporated the luc2 gene into the cells and the bioluminescence signal in vivo was detected with the IVIS-LUMINA XR imaging system to follow the development of metastasis. Immunohistochemical studies were performed to verify the melanocytic origin.
Tissue samples were collected, paraffined, and immunohistochemical studies were performed to verify the melanocytic origin and cellular and molecular characteristics of the primary tumor and metastatic lesions developed in the mice.

Results: Our results show that 100% of mice injected with either $2x10^5$ OMM2.5 cells (n = 23) or MP # 41 cells (n = 24) have developed a primary tumor, which was detected at 10 ± 2 days after implantation. Enucleation of primary tumors was performed in all cases 16 ± 2 days after implantation. The bioluminiscence signal was detected at 23 ± 2 days and in liver at 31 ± 9 days after implantation of UM cells. Lung metastases were confirmed in 100% of the animals at necropsy (sacrifice per day 45 ± 11). Liver metastases were found in 87% of the animals that received OMM 2.5 cells and in 100% of those implanted with MP # 41. We also observed the presence of kidney metastases in 19% of mice on both lines. In contrast, only MP# 41 cells generated lymph node metastases.

Conclusions: We have successfully developed an in vivo mice metastatic model that allows to follow up the whole process of metastasis formation where new therapeutic strategies can be studied.

CONTROL ID: 3712970

SUBMITTER (NAME ONLY): shuo sun

TITLE: Retinal pigment epithelium-derived 2’3’ cGAMP contributes to AMD progression

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. sun, X. Li, Tianjin Key Laboratory of Retinal Functions and Diseases, Tianjin International Joint Research and Development Centre of Ophthalmology and Vision Science, Eye Institute and School of Optometry, Tianjin Medical University Eye Hospital, Tianjin, CHINA|S. sun, W. Su, E. Bilsbury, S. Doherty, E. Wood, A. Makhlouf, B. Tian, H. Lin, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|W. Su, Ophthalmology, Tianjin Medical University General Hospital, Tianjin, CHINA|A. Al Moujahed, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) dysfunction plays a central role in the progression of age-related macular degeneration (AMD). Our previous studies have shown that macular RPE cells of AMD patients have a notably increased accumulation of cytosolic damaged nuclear DNA (nDNA) fragments. This accumulation not only induced RPE cellular senescence and pro-inflammation via STING pathway, but also promoted the secretion of a variety of factors that are detrimental to the microenvironment of neighboring tissues. In the present study, we examined the role of paracrine effects exerted by dysfunctional RPE cells on neighboring cells in the pathogenesis of AMD, identified a novel culprit of this paracrine effect, and investigated the underlying mechanisms of these effects.

Methods: Since DNASE2A is essential for the degradation of cytosolic damaged nDNA fragments, CRISPR/Cas9 was used to generate DNASE2A$^{-/-}$ RPE cells that accumulate cytosolic nDNA, mimicking the AMD patients RPE cells. The levels of 2’3’ cGAMP and STING expression in macular RPE cells from AMD patients and DNASE2A$^{-/-}$ RPE cells were analyzed. Long-term treatment with 2’3’ cGAMP and/or a Volume-Regulated Anion Channel (VRAC) inhibitor was administered to wild-type and STING$^{-/-}$ ARPE-19 cells. Components of the STING pathway, pro-inflammatory factors and cellular senescence markers were tested. C57BL/6J mice were subretinally injected with 2’3’ cGAMP and examined by fundus photography and Optical Coherence Tomography (OCT). Activation of microglial cells, pro-inflammatory factors and complement system components were measured.

Results: We have identified 2’3’ cGAMP, the agonist in the STING-dependent cytosolic DNA sensing pathway, as a culprit for these paracrine effects. STING expression was increased in AMD donor RPE cells in a distribution pattern similar to that of RPE lesion formation. The level of secreted 2’3’ cGAMP was higher in macular RPE cells from AMD donors compared to age-matched controls. Chronic exposure to 2’3’ cGAMP can induce RPE degeneration in vitro, as well as outer retinal degeneration, microglial and complement activation in vivo. The deleterious effects caused by exposure to mediums containing 2’3’ cGAMP were ameliorated by STING knock-down and VRAC inhibition.

Conclusions: These findings suggest a potential role for 2’3’ cGAMP and STING in the progression of AMD, as well as new targets for the development of novel therapeutics.

CONTROL ID: 3712971

SUBMITTER (NAME ONLY): Sai Naga Sri Harsha Chittajallu

TITLE: Strength characterization of Human Cornea Against Sutures: Experiments

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chittajallu, H. Gururani, V. Chinthapenta, Department of Mechanical & Aerospace Engineering, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|S. Chittajallu, K. Tse, Department of Mechanical and Product Design Engineering, Swinburne University of Technology, Melbourne, Victoria, AUSTRALIA|A. Richhariya, Centre for Technology Innovation, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: To investigate the break starting strength (BSS) of human cornea inline with ISO: 7198 – 2016 to evaluate the suture tolerating strength of the cornea without losing its functionality.

Methods: 10 corneas with a suture bite distance of 2 mm from limbus were tested for a suture pullout test at a pulling rate of 3 mm/min. A lower pulling rate was used in the tests considering the physiology of the human eye. A steel wire of 0.4 mm is used for testing to negate the elastic effects of the sutures as per ISO 7198 – 2016. Tests were carried in a universal tensile testing machine with a 10 N load cell. Specimens were imaged while testing with the help of a microscopic imaging system with 16X magnification.

Results: BSS of the cornea is 4.072±0.859 N found at a 3 mm/min pull rate. The 10 N load cell is sensitive enough to capture the BSS, and the imaging system helps in situations where BSS is not visible in the load vs. time curve. The present system is efficient enough to evaluate BSS.

Conclusions: BSS of the cornea is evaluated with the help of a robust experimental setup.

CONTROL ID: 3712972

SUBMITTER (NAME ONLY): Shivakumara Reddy

TITLE: Extracellular vesicles as nanocarrier of avastin to inhibit neovascularization for longer duration in diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Reddy, A. Ballal, D. Upadhya, Centre for Molecular Neurosciences, Kasturba Medical College Manipal, Manipal, Karnataka, INDIA|S. S, Opthalmology, Kasturba Hospital Manipal, Manipal, Karnataka, INDIA|R. Chandrashekhar H, Pharmaceutical Biotech, Manipal College of Pharmaceutical Sciences, Manipal, Karnataka, INDIA|S. Adiga, Pharmacology, Kasturba Medical College Manipal, Manipal, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) is a common complication of diabetes mellitus demonstrating neovascularization and remains a leading cause of loss of vision. Treatment of DR focuses on targeting vascular endothelial growth factor (VEGF) to reduce neovascularization with repeated intravitreal injections. The complications with repeated intravitreal injections are retinal detachment, trauma, etc. To reduce the frequency of intravitreal injections, we loaded ant-VEGF drug into small extracellular vesicles (sEVs) as recent reports suggested the ability of EVs in sustained drug delivery. The ability of the anti-VEGF loaded sEVs were tested for their sustained antiangiogenic potential in STZ induced rat model of DR.

Methods: Small EVs were isolated from bone marrow-derived mesenchymal stromal cells (BM-MSC) and characterized. Avastin was loaded into sEVs by freeze-thaw, co-incubation 0.2% saponin, and sonication methods. Avastin loaded in EVs was checked for its antiangiogenic properties by chorioallantoic Membrane (CAM) assay in the egg chick embryo. To tract the avastin loaded EVs in the retina, FITC conjugated avastin was loaded into PKH26 labeled sEVs. Further, DR was induced in Wistar Albino rats through administration of streptozotocin. Blood sugar levels were monitored multiple times over months after the STZ injection, and the presence of exudates in the retina was confirmed by FITC-dextran perfusion. The effect of anti-VEGF-loaded EVs on neovascularization was evaluated at different time intervals using VEGF immunostaining.

Results: Characterization of EVs using NanoSight tracking demonstrated a mean size of 167nm, and TEM analysis revealed cup-shaped morphology, and western blot analysis revealed positive for TSG101 and CD 63 while negative for GM130. Significant amounts of avastin was loaded by all the tested methods. The avastin loaded EVs significantly inhibited the angiogenesis in the CAM assay. We have tracked avastin-loaded EVs in different retina layers in naive rats. In DR, avastin loaded EVs decreased the number of exudates in the retina, and the VEGF expression was low in the avastin loaded EV group compared to avastin alone group over a period of time.

Conclusions: Due to sustained drug delivery ability, avastin loaded EVs may be ideal for the controlled release of avastin for a longer duration to inhibit neovascularization in DR.

CONTROL ID: 3712973

SUBMITTER (NAME ONLY): Sora Im

TITLE: Suppression of choroidal neovascularization and epithelial-mesenchymal transition in retinal pigmented epithelium by adeno-associated virus-mediated overexpression of CCN5 in mice

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Chorodial neovascularization (CNV) is a defining characteristic feature of neovascular age-related macular degeneration (nAMD) that frequently results in irrversible vision loss. The current strategies for the treatment of nAMD are mainly based on neutralizing vascular endothelial growth factor (VEGF). However, anti-VEGF therapies are often associated with subretinal fibrosis that eventually leads to damages in macula. It was the aim of this study to investigate wheter an anti-fibrotic and anti-angiogenic protein CCN5 can a potential novel stratey for the treatment of nAMD with a capability to inhibit CNV and fiborsis stimultaneously.

Methods: To induce CNV in mouse eyes, laser photocoagulation was utilized. At 5 days after laser-induced CNV, recombinant adeno-associated virus serotype 2 encoding CCN5 (rAAV2-CCN5), rAAV2-virus-like-particle (VLP), and bevacizumab were administered via intravitreal injection. One week after injection, fundus fluorescent angiography (FFA), immunostaining, and cell counting were performed to determine rAAV2-CCN5 inhibits CNV leakage, retinal gliosis, change of retinal pigmented epithelium (RPE) cell morphology, and epithelial-mesenchymal transition (EMT) on RPE.

Results: Our data demonstrated that rAAV2-CCN5, but not a control viral vector, rAAV2-VLP, prominently attenuated both CNV lesions and angiogenesis. Bevacizumab, which was utilized as a positive control, exhibites similar effects on CNV lesion and angiogenesis. Upon laser photocoagualtion, RPE cells underwent significant morphological changes including cellular enlargement and loss of hexagonality. rAAV2-CCN5 significantly normalized these morphological defects, while bevacizuumab did marginally. Laser photocoagulation also led to fibrotic deformation in RPE cells through inducing EMT, which was completely blocked by rAAV2-CCN5. In a striking contrast, Bevacizumab as well ase rAAV2-VLP failed to exhibit any effects on EMT.

Conclusions: Our data demonstrate that rAAV2-CCN5 can inhibit CNV and EMT in RPE cells that are induced by laser photocoagulation in mice. Therefore, we suggest that rAAV2-CCN5 can be a safer yet efficient therapeutic modality for nAMD.

CONTROL ID: 3712974

SUBMITTER (NAME ONLY): Leopold Schmetterer

TITLE: A multi-regression model for improving the diagnostic performance of OCT to discriminate mild cognitive impairment and Alzheimer’s disease

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Schmetterer, J. Chua, C. Li, Singapore Eye Research Institute, Singapore, SINGAPORE|C. Chen, Memory Aging and Cognition Centre, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) has been proposed as a retinal biomarker for Alzheimer's disease (AD), however, current diagnostic performance is limited but may be improved by reducing the inter-individual variability of circumpapillary retinal nerve fiber layer (cpRNFL) measurements. We developed a multiple-regression framework including compensation for anatomical confounders, and combination of the cpRNFL and macular layers to increase discrimination between cognitively normal participants, mild cognitive impairment (MCI) and AD.

Methods: This cross-sectional study included 62 AD (n=92 eyes), 108 MCI (n=158 eyes), and 55 cognitively normal control (n=86 eyes) participants. Using an Early Treatment Diabetic Retinopathy Study circle at the macular level, thicknesses of the macular RNFL (mRNFL), macular ganglion cell layer (mGCL), macular inner plexiform layer (mIPL) were determined. Circumpapillary (cpRNFL) measurements were compensated for potential confounders including demographics (ethnicity and age), refractive error, optic disc (ratio, orientation, and area), fovea (distance and angle), retinal vessel density and signal strength. Thickness measurements of each layer and their corresponding areas under the receiver operating characteristic curves (AUCs) were compared between the groups.

Results: Age and gender did not differ among groups. In the multivariate analysis, MCI/AD participants showed significantly thinner measured and compensated cpRNFL, mRNFL, mGCL, mIPL, and altered retinal vessel density ($p<0.05$). Compensated RNFL outperformed measured RNFL for discrimination of MCI (AUC=0.74 vs 0.68; $p=0.02$) and AD (AUC=0.79 vs 0.71; $p=0.025$) from controls. Combining macular and compensated cpRNFL parameters further improved the detection of MCI (AUC = 0.79 vs 0.68; $p<0.001$) and AD (AUC=0.87 vs 0.71; $p<0.001$).

Conclusions: This study suggests that accounting for interindividual variations of ocular anatomical features in cpRNFL thickness measurements and incorporating information from macular layers may allow for a improve the identification of high-risk individuals with early cognitive impairment and dementia.

CONTROL ID: 3712975

SUBMITTER (NAME ONLY): Lujia Feng

TITLE: CCT5 Protects against MerTK-Associated Retinitis Pigmentosa in Retinal Pigment Epithelial Cells by Interacting with F-Actin and Activating the LIMK1/Cofilin Pathway

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Feng, Y. Zhuo, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|S. Zhang, Shenzhen Eye Hospital, Shenzhen, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP), characterized by the gradual loss of rod and cone photoreceptors that eventually leads to blindness, is the most common inherited retinal disorder, affecting more than 2.5 million people worldwide. However, the underlying pathogenesis of RP remains unclear and there is no effective cure for RP. Mutations in the Mer receptor tyrosine kinase (MerTK) gene induce the phagocytic dysfunction of retinal pigment epithelium (RPE) cells, leading to RP. Studies have indicated that filamentous actin (F-actin)—which is regulated by chaperonin-containing TCP1 subunit 5 (CCT5)—plays a vital role in phagocytosis in RPE cells. However, whether CCT5/F-actin signaling is involved in MerTK-associated RP remains largely unknown. Therefore, the present study explored the relationship between CCT5, F-actin, and RP, and the potential molecular mechanism underlying this disease.

Methods: In the present study, we specifically knocked down MerTK and CCT5 through siRNA transfection and upregulating CCT5 using CCT5-specific lentiviral vectors (CCT5-Le), then examined the expression of CCT5, F-actin, cofilin, LIMK1, and SSH1, the arrangement of F-actin, the cell proliferation, migration, and phagocytic function of human primary RPE (HsRPE) cells.

Results: We found that MerTK downregulation inhibited cell proliferation, migration, and phagocytic function; significantly decreased the expression of F-actin; and disrupted the regular arrangement of F-actin. Importantly, our findings firstly indicate that CCT5 interacts with F-actin and is inhibited by MerTK siRNA in HsRPE cells. Upregulating CCT5 using CCT5-Le rescued the cell proliferation, migration, and phagocytic function of HsRPE cells under MerTK-associated RP by increasing the expression of F-actin and restoring its regular arrangement via the LIMK1/cofilin, but not the SSH1/cofilin, pathway.

Conclusions: In conclusion, CCT5 protects against MerTK-associated RP in RPE cells by interacting with F-actin and activating the LIMK1/cofilin pathway. This finding provide a new perspective for research into the mechanisms underlying MerTK-associated RP and provide a new direction for future studies of the molecular mechanisms of RP pathogenesis.

CONTROL ID: 3712976

SUBMITTER (NAME ONLY): Tomohito Sato

TITLE: Expression patterns of systemic factors and vitreous fluid cytokines by cluster analysis in PDR

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sato, R. Okazawa, H. Someya, M. Takeuchi, Ophthalmology, National Defense Medical College, JAPAN|T. Enoki, Enoki Eye Clinic, JAPAN|M. Ito, Developmental Anatomy and Regenerative Biology, National Defense Medical College, JAPAN|

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ABSTRACT BODY:

Purpose: To identify the specific expression patterns of systemic factors and vitreous fluid (VF) cytokines in patients with proliferative diabetic retinopathy (PDR).

Methods: The study group (males / females: 18 / 7, mean age ± standard deviation [SD]: 58.6 ± 13.5 years old) was composed of 26 PDR eyes in 25 patients with type 2 diabetes mellitus, who underwent pars plana vitrectomy (PPV) for vitreous hemorrhage and/or tractional retinal detachment. The control group (males / females: 13 / 18, mean age ± SD: 71.2 ± 8.34 years old) consisted of 14 eyes patients with idiopathic macular hole and 17 eyes patients with idiopathic epiretinal membrane. As systemic factors, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure difference between SBP and DBP (PPD), heart rate (HR), international normalized ratio of prothrombin time (PT-INR), activated partial thromboplastin time (APTT), fasting blood glucose (FBG), hemoglobin A1c (HbA1c), and estimated glomerular filtration rate (eGFR) were measured. Undiluted VF was obtained at the beginning of PPV. IL-1ra, IL-6, IL-7, IL-8, IL-13, eotaxin, IFN-γ, IP-10, MCP-1, MIP-1β, TNFα and VEGF-A were measured by a multiplex bead array. Hierarchical cluster analysis was used to examine a comprehensive functional evaluation of systemic factors and VF cytokines as biomarkers in the pathology of PDR.

Results: In control group, the explanatory variables were broadly classified into one cytokine and two principal clusters: 1; IP-10, 2; a cluster composed of age, SBP, DBP, PPD, HR, FBG, eGFR and MCP-1, and 3; another cluster consisting of BMI, PT-INR, APTT, HbA1c and the remaining cytokines including VEGF-A. Age, SBP, DBP, PPD, HR, FBG, eGFR were grouped into a subcluster, and MCP-1 was proximately located to the subcluster. In PDR group, the explanatory variables were roughly divided into one cytokine and two principal clusters: 1; IP-10, 2; a cluster composed of MCP-1 and VEGF-A, and 3; another cluster consisting of all systemic factors and the remaining cytokines. VEGF-A was proximately located to MCP-1, not resembling to the arrangement in control group.

Conclusions: In PDR, the association between systemic factors and intraocular factors of inflammation and angiogenesis would be vulnerable, suggesting that the intraocular factors independently affect the pathology of PDR.

CONTROL ID: 3712978

SUBMITTER (NAME ONLY): Wen Zeng

TITLE: A new nonhuman primate model of desiccating stress-induced dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Zeng, L. Gong, B. Li, L. Pan, Sichuan Primed Shines, Ya'an, CHINA|S. Chauhan, W. Cho, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a desiccating stress-induced dry eye disease model using nonhuman primates (NHP).

Methods: Four to 5-year-old Rhesus macaque monkeys were housed in a controlled-environment room where relative humidity (RH), temperature (T) and airflow (AF) are regulated (RH = 6.4% ± 1.4%, T = 22.5°C - 25.3°C, AF = 12 L/min). Monkeys were placed in the controlled-environment room for 21 to 36 days to induce dry eye disease (DED). Post 21 days of DED induction, corneas were topically treated with 1 % Pred Forte or normal saline (placebo) thrice daily for 14 days. Corneal fluorescein staining (CFS), tear film break-up time (TFBUT), and proinflammatory cytokines in tears were measured to assess DED severity.

Results: A significant increase in corneal fluorescein staining (9.7 ± 1.8, $P < 0.001$) and proinflammatory cytokines levels (IL-17, $P < 0.01$; IL-2, $P < 0.05$) were observed on day 21 of controlled-environment room exposure. Moreover, TFBUT significantly decreased following DED induction (7.3 ± 2.4 vs. 4.4 ± 0.8, $P < 0.001$). Corticosteroid treatment significantly reduced CFS scoring (6.0 ± 1.2 vs. 9.3 ± 1.8, $P < 0.001$), restored TFBUT (6.1 ± 2.0 vs. 3.9 ± 0.6, $P = 0.001$), and prevented upregulation of tear proinflammatory cytokines, compared to the placebo treatment.

Conclusions: Desiccating stress induces dry eye disease in nonhuman primates, closely resembling the clinical symptoms and treatment response observed in human DED patients.

CONTROL ID: 3712979

SUBMITTER (NAME ONLY): Pablo Ortiz

TITLE: Robotically Aligned OCT Enables Synthetically Increased Field-of-View on Automatically Acquired Retinal Images.

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Ortiz, M. Draelos, A. Narawane, A.N. Kuo, J.A. Izatt, Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|R.P. McNabb, A.N. Kuo, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Robotically Aligned OCT (RAOCT) systems can image patients without a fixation target or stabilization (chin/forehead rest). Additionally, through robotic angular positioning control, RAOCT enables automatic acquisition of retinal images at different regions of interest (ROI), which can subsequently be montaged to synthetically increase the field-of-view (FOV) of the system.

Methods: Utilizing custom software, pupil tracking cameras estimated ocular pupil location and gaze of the eye, enabling autonomous alignment of a robotic arm mounted 20° FOV SSOCT retinal scanner (1050nm; Fig. 1A). The tracked gaze was utilized to control the orientation of the scanner relative to the optic axis of the eye, allowing control over the OCT beam's angle of incidence into the eye. Control of the angle of incidence allowed imaging multiple ROI by pivoting the scanner about the pupil (Fig. 1B). For each imaging session, the robot automatically aimed at and imaged 25 different ROIs over a 20° range. We subsequently montaged acquired volumes onto a single large FOV volume utilizing the gaze tracking information for localization and further optimized using b-spline based registration. We imaged consented freestanding subjects under an IRB approved protocol.

Results: Imaging performance on a healthy 26-year-old is demonstrated in Figure 2. Retinal montaging allowed us to synthetically double the FOV of the system from 20° to 40° with automatic alignment and aiming of the OCT scanner with minimal discontinuities along the retinal vasculature. The mean residual error corrected with registration was 0.21° across the entire field of view.

Conclusions: We demonstrated automatic retinal volumetric acquisition over multiple ROIs over a 20° range in freestanding subjects. With montaging, we demonstrated increased image FOV comparable to fundus photography.

CONTROL ID: 3712980

SUBMITTER (NAME ONLY): PO YIN WU

TITLE: The Utility of Strip Meniscometry in the Screening and Diagnosis of Dry Eye Disease in a Random Population-Based Cohort Study for Chinese Subjects Aged 50 and Over

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. WU, I. Wong, K.C. Shih, Department of Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|L. Tong, Cornea and External Eye Disease Service, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|L. Tong, Ocular Surface Research Group, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate the accuracy of strip meniscometry tube (SMTube) in dry eye screening and diagnosis in the context of a Chinese community.

Methods: This cross-sectional random population-based study initiated on 27 September 2021 and continuing until now. Chinese subjects aged 50 and above were recruited through randomized mail invitation in the Southern district in Hong Kong. Overall, the response rate was 96%, and cooperation rate was 49%. In total, 298 consecutive subjects underwent comprehensive dry eye assessment in order from least invasive to most invasive, including dry eye questionnaire (OSDI score), Non-invasive keratographic tear breakup time, tear meniscus height, tear breakup pattern, SMTube, NEI cornea staining score. The definition of dry eye was adopted from Asia Dry eye Society. Incremental (1 mm) strip meniscometry readings were tested for accuracy of dry eye diagnosis. The right eye of each subject was used for analysis.

Results: Among the 298 recruited individuals, mean age was 62.6 (± 7.20) years. Overall, 19.5% had dry eye disease (OSDI >/=13 and TBUT <10s). Among dry eye patients, random break was the most common tear breakup pattern, accounting for 62% of cases. Subjects with dry eye disease had significantly lower SMTube readings compared to those who did not have dry eye disease on Student’s t test. A low SMTube result had high specificity and high negative predictive value for dry eye disease, OSDI score >/=13 and presence of significant cornea staining. A cut off value of 3 mm was shown to be achieve optimum specificity and negative predictive value for dry eye disease (90.8% and 80.4%), cornea staining (94.1% and 64.8%) and OSDI score >/=13 (91.7% and 78.1%)

Conclusions: In a community setting, where dry eye prevalence is relatively low, an abnormal SMTube reading had high specificity and negative predictive value, suggesting excellent diagnostic value for an abnormal test result. A cut off value of 3 mm was proven to have the highest diagnostic accuracy for dry eye disease.

CONTROL ID: 3712981

SUBMITTER (NAME ONLY): Sean Mullany

TITLE: The APOE E4 allele is associated with faster rates of mGCIPL thinning in the PROGRESSA cohort

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mullany, H. Marshall, E. Souzeau, M. Hassall, J. Landers, O. Siggs, J.E. Craig, Ophthalmology, Flinders University, Adelaide, South Australia, AUSTRALIA|A. Agar, Department of Ophthalmology, University of New South Wales, Sydney, New South Wales, AUSTRALIA|A. Galanopoulos, R. Casson, Discipline of Ophthalmology and Visual Sciences, The University of Adelaide, Adelaide, South Australia, AUSTRALIA|P. Mitchell, P. Healey, Centre for Vision Research, University of Sydney - Camperdown and Darlington Campus Burkitt-Ford Library, Sydney, New South Wales, AUSTRALIA|S.L. Graham, Faculty of Health and Medical Sciences, Macquarie University, Sydney, New South Wales, AUSTRALIA|A.W. Hewitt, Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, AUSTRALIA|S. MacGregor, P. Gharahkhani, QIMR Berghofer Medical Research Institute, Herston, Queensland, AUSTRALIA|O. Siggs, Garvan Institute of Medical Research, Darlinghurst, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: This study sought to investigate the association between the apolipoprotein E (APOE) E4 allele and longitudinal retinal thinning in the 'Progression Risk Of Glaucoma: RElevant SNPs with Significant Association' (PROGRESSA) cohort, a prospective study of suspect and early manifest glaucoma.

Methods: Apolipoprotein E alleles and genotypes were determined in PROGRESSA, and an age- and ancestrally-matched normative cohort, the Blue Mountains Eye Study (BMES). Structural parameters of neuroretinal atrophy measured using spectral-domain optical coherence tomography (SD-OCT) including the macular ganglion cell complex (mGCIPL) and peripapillary retinal nerve fibre layer (pRNFL) were compared within the PROGRESSA cohort on the basis of genotype and presence of APOE E4 allele.

Results: Prospective rates of mGCIPL thinning were faster in participants harbouring at least one copy of the APOE E4 allele (beta coefficient=-0.13μm/year; $p=3.6x10^{-4}$). These participants also had a thinner average mGCIPL (70.9μm vs. 71.9μm; p=0.011) and pRNFL (77.6μm vs. 79.2μm; p=0.045) after a minimum of three years of longitudinal follow-up.

Conclusions: The APOE E4 allele was associated with faster rates of average mCGIPL thinning and a thinner average pRNFL, suggesting that the APOE E4 allele is a risk factor for retinal ganglion cell degeneration.

CONTROL ID: 3712982

SUBMITTER (NAME ONLY): Wai Chak Choy

TITLE: Retinoblastoma: Strata in Care Capacity and Mapping of Global Research Focus With Machine Learning

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Choy, W. Tang, E. Wong, Y. Zhang, J. Yam, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|E. Wong, Hong Kong Eye Hospital, Hong Kong SAR, China, HONG KONG|J. Yam, Hong Kong Hub of Paediatric Excellence, The Chinese University of Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Despite advancements in globe-preserving treatments, improvements in retinoblastoma (RB) outcomes are inconsistent across income levels and geographical locations. Both socio-economic factors and healthcare structure (SEH) were associated to the outcome. There are also regions with scarce literature coverage which hinder comprehension of the global landscape. We aim to use machine learning to categorize countries for care capacity with consideration to both socio-economic backgrounds and clinical services and identify differences in research focus.

Methods: We used hierarchical clustering to assess strata using 26 SEH variables from the World Bank and 10 clinical factors (e.g. treatment modalities) covering 129 countries. We collected literature published after Jan 1, 2001 from PubMed, Embase, ScienceDirect, Web of Science, and Global Index Medicus with search term ‘retinoblastoma’. A BERT model was trained to filter literature by relevance. Topic modelling was done with hierarchical Dirichlet Process (HDP). Abstracts and publication info were geotagged for relevant locations.

Results: 4 major country clusters with 10 subgroups were identified and interpreted with reference to SEHs and clinical delivery. BERT model attained 91.47% accuracy (sensitivity: 93.07%, specificity: 87.91%). 28,347 abstracts were identified as relevant. HDP identified 52 sub-topics over genetics of RB, genetics of associated diseases, clinical presentation and work-up, and treatment options. While coverage on clinical presentation and work-up were fairly sufficient across the world, genetics of both RB and associated diseases were rarely discussed in part of sub-Saharan Africa and the Middle-east and was predominantly dominated by localities of European descent. Stratification by our computed strata identified slim coverage of genetics presentation in Tier 1 and 2 countries and even distribution in Tier 4.

Conclusions: Capacity strata could serve as more comprehensive reference than income levels for targeted intervention, with implications on cross-border referral which should be considered when regional hubs are established. Our study proved machine learning can feasibly map existing knowledge on a disease. The scant evidence of RB genetics in ethnicity apart from the European descent should be tackled, which would implicate accuracy of genetics testing, identification of subtypes and general understanding of RB.

CONTROL ID: 3712983

SUBMITTER (NAME ONLY): Junghwan Lee

TITLE: Predicting 2-year and 5-year Late AMD Progression using Deep Learning with Longitudinal Fundus Images

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, Biomedical Informatics, Columbia University, New York, New York, UNITED STATES|J. Lee, F. Wang, Y. Peng, Population Health Sciences, Weill Cornell Medicine, New York, New York, UNITED STATES|Q. Chen, Z. Lu, National Center for Biotechnology Information, Bethesda, Maryland, UNITED STATES|T.D. Keenan, E.Y. Chew, National Eye Institute, Bethesda, Maryland, UNITED STATES|T. Wanyan, Intelligent System Engineering, Indiana University, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accurately predicting a patient's risk of progressing to late age-related macular degeneration (AMD) is difficult but crucial for personalized medicine. While current risk prediction models are useful, none utilizes a longitudinal series of images in patients' history to estimate the risk of late AMD in a given time interval. In this work, we seek to evaluate how deep neural networks capture the sequential patterns of longitudinal fundus images and improve the prediction of 2-year and 5-year risks of progression to late AMD.

Methods: We developed a hybrid architecture that consists of a Convolutional Neural Network and a Recurrent Neural Network, popularly known as CNN-RNN (Fig 1). Specifically, we used a ResNet to extract features from the images and applied an LSTM layer on top for the prediction. Two training strategies were used: (1) we used the ResNet trained on a late AMD detection task as a fixed feature extractor, and (2) we fine-tuned the weights of ResNet together with the LSTM in an end-to-end manner. We also compared our model with a ResNet which predicts AMD progression using a single image.

Results: We trained and evaluated the models using longitudinal fundus images from the Age-Related Eye Disease Study (AREDS). The AREDS dataset includes 4,315 participants, a large majority of whom had annual visits over 10 years. The dataset was split into train/validation sets with a 0.7:0.3 ratio. We evaluated models using the area under the receiver operating characteristic curve (AUC). Table 1 shows that the CNN-RNN model outperforms the baseline on 2-year (0.926 vs. 0.892) and 5-year (0.904 vs. 0.829) predictions. In the meantime, our model's performance increases with up to 5 visits, but drops with more visits in patient history. This might be due to the data imbalance and sparsity issues. We also observed that the end-to-end training did not show significant improvement.

Conclusions: We presented a CNN-RNN model for predicting late AMD progression for each patient in this study. Our experiments show that our model can capture dynamic sequential patterns and outperforms baselines. This study sheds light on the potential of deep learning to facilitate and support clinical decision-making on an individual basis.

CONTROL ID: 3712985
SUBMITTER (NAME ONLY): Haroon Rasheed
TITLE: DDLSNet: a novel deep learning-based system for grading glaucomatous funduscopic images for damage
SESSION TITLE: Data science, machine learning, and AI
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: Efforts at automatic identification of the optic disc and its neural rim have been reported, but have not been used to grade glaucoma severity with an accepted metric. In this retrospective observational study, we propose a DDLSNet pipeline consisting of a rim segmentation (RimNet) branch and a disc size classification (DiscNet) branch to automate glaucoma grading with the disc damage likelihood scale (DDLS).

Methods: To develop RimNet, funduscopic images from the UCLA Stein Glaucoma Division were randomly split into training, validation, and test datasets (80/10/10). Optic rims of the training set were drawn by glaucoma specialists. RimNet uses contrast enhancement, an InceptionV3/LinkNet rim segmentation model, and computer vision to identify the thinnest rim location and calculate the rim-to-disc ratio (RDR). To develop DiscNet, paired funduscopic images and OCT data from UCLA Stein Glaucoma Division were randomly split into training, validation, test datasets (80/10/10). DiscNet uses a VGG19 network to label disc size as small, medium, or large. The DDLS grade is calculated from RDR and disc size. Three glaucoma specialists graded the RimNet test set with DDLS (scale 1-10). The main outcome measure was a weighted kappa agreement with agreement defined as +/- 1 DDLS grade between graders and DDLSnet.

Results: RimNet was developed on 857 images (mean age=60.3 (±14.2) years, male:female ratio=0.42), and achieved an RDR mean absolute error of 0.06 (±0.04) on test set between RimNet and physician. DiscNet was developed on 8366 images (mean age=67.6 (±14.5) years, male:female ratio=0.57), and achieved 77% classification accuracy on test set. DDLSNet was evaluated on 87 images from the RimNet test set; Table 1 lists the agreements between DDLSNet and graders and between individual graders.

Conclusions: DDLSNet achieved acceptable performance as shown by fair weighted kappa agreement with grader 2 and 3. This illustrates the feasibility of developing an automated process such as DDLSNet for glaucomatous grading of optic disc images. Further improvements are required, and will be achieved by further training of graders, increasing sample size, and algorithm enhancement.

CONTROL ID: 3712986

SUBMITTER (NAME ONLY): Galo Apolo

TITLE: Age-related Changes in Dynamic Iris Behavior Assessed Using a Closed-Loop Iris Control System

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Apolo, N. Lazkani, A. Song, A. Pardeshi, B. Xu, Roski Eye Institute, Department of Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|S. Zhou, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|R.N. Weinreb, Hamilton Glaucoma Center, Shiley Eye Institute and Viterbi Family Department of Ophthalmology, University of California, San Diego, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop and test a closed-loop system for modulating iris activity and assessing the role of dynamic iris behavior in primary angle closure disease (PACD).

Methods: Participants aged 18 years or older were recruited from the University of Southern California Roski Eye Institute. Three consecutive videos of one eye per participant were recorded using the ANTERION OCT system (Heidelberg Engineering, Heidelberg, Germany). During recording, custom software was used to control a light-emitting diode (LED) and modulate ambient lighting to hold the iris in a dilated, constricted, or mid-dilated position. Dynamic iris behavior in the form of peak constriction velocity (PCV) and mid-dilated iris activity (MDIA) were measured in real-time. Linear regression analysis was performed to assess the relationship between participant age and PCV and MDIA.

Results: A total of 58 participants were recruited, with 40 (69.0%) being eligible for analysis based on patterns of iris behavior. Mean participant age was 50.0 (SD = 18.7) years. The system maintained a mid-dilated position for 69.0% of the participants with a mean difference of 0.071 (SD = 0.13) mm between the calculated and observed mean mid-dilated pupillary diameters. There was a negative linear correlation between PCV and age (slope= -0.02; $p < 0.01$) and MDIA and age (slope= -0.003 ; $p < 0.01$).

Conclusions: A novel closed-loop iris control system can modulate dynamic iris behavior and hold the pupil in a stable mid-dilated state. Dynamic iris behavior during pupillary constriction and in the mid-dilated state decrease with age. This system may be applied in the future to study dynamic disease processes involving the iris, including acute primary angle closure (APAC).

CONTROL ID: 3712987

SUBMITTER (NAME ONLY): Claus von der Burchard

TITLE: Improved Accuracy in Retinal Laser Therapy by Real-Time Temperature Control

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In retinal laser treatment, the tissue effect only partially correlates to laser energy due to differences in light absorption, light scattering and retinal pigmentation. Especially in subvisible laser treatment, the therapeutic accuracy is low. Thus, treatment reliability and reproducibility are limited.

We have previously reported on real-time temperature-guided retinal laser therapy to improve reproducibility. In this study, we report on the correlation of retinal temperature and laser-tissue effect.

Methods: A conventional 532nm continuous wave laser (Zeiss VisuLas 532) is used with a custom-build modulation module (Medical Laser Center Lübeck), which can measure the temperature rise in real-time with a rate of 3 kHz. Based on this, it controls the laser power in real-time such that a desired target temperature is quickly obtained and held for the rest of the irradiation.

Irradiations with target temperatures from 45 to 69 °C were performed in rabbits with a diameter of 200 µm and an exposure time of 100ms. With a laboratory PC-controlled module, we performed irradiations in 5 eyes of 3 rabbits. For an upcoming clinical study, it was converted to a microcontroller-based system, with which so far 1 eye of 1 rabbit was treated. Funduscopy, optical coherence tomography (OCT) and fluorescence angiography (FAG) were used for evaluation.

Results: With the PC system, the following ED-50 values were determined: Funduscopic visibility 60.2 °C, FAG visibility 60.2 °C, OCT visibility 59.4 °C. In OCT, the greatest linear diameter (GLD) of the lesions correlated better to temperature (R^2 = 0.62) than to laser power (R^2 = 0.47). The aim temperature was reached with an average error of 3.5%.

With the microcontroller system, comparable results could be reproduced. The average error in aim temperature was 2.3% (97% of lesions within a maximum error of 5%). ED-50 values were comparable in FAG (61.9 °C) and slightly higher in funduscopy (68.2 °C; pilot data with small sample size).

Conclusions: It could be shown that temperature-guided laser irradiations can improve accuracy in retinal laser therapy. Lesion strength is better correlated to temperature than to bare laser power. We are planning to begin a clinical study for temperature-guided non-damaging laser treatment in patients with central serous chorioretinopathy in early 2022.

CONTROL ID: 3712992

SUBMITTER (NAME ONLY): Alasdair Warwick

TITLE: Characterising individuals with retinopathy from retinal image grading data in UK Biobank

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The aims of this study were to identify individuals from the UK Biobank (UKBB) cohort with detectable retinopathy on retinal imaging and to describe their sociodemographic and clinical characteristics.

Methods: Colour fundus photographs and macular optical coherence tomography (OCT) scans were acquired using a Topcon 3D OCT-1000 Mark II system (Topcon, Japan). Grading was performed by trained and certified graders and clinicians of the Network of Ophthalmic Reading Centres UK (NetwORC UK-Belfast, Liverpool, and Moorfields Ophthalmic Image Reading Centres). Retinopathy was defined as the presence of one or more microaneurysms in either eye, with or without other retinal microvascular abnormalities on either imaging modality. Diagnosed diabetes (DM), diabetic retinopathy (DR) and hypertension (HTN) were ascertained from self-reported (verbal interview), linked hospital episode statistics and primary care records at the time of imaging. Self-reported medication history was obtained from touchscreen questionnaire responses. HbA1c >48mmol/mol was considered diagnostic of DM. Systolic or diastolic blood pressure (BP) measurements ≥140mmHg and ≥80mmHg respectively were considered diagnostic of HTN.

Results: Among 68,517 UKBB participants who underwent fundus imaging, 265 (0.4%) individuals were identified to have retinopathy from retinal imaging. The median age at assessment for this group was 59 years (interquartile range 52-64), 70.9% were men and 79.6% were of white ethnic background. When retinopathy grading data were compared against medical records, 69.8% and 49.8% had a diagnosis of DM and DR respectively. The majority (55.5%) had a HbA1c level in the diagnostic range for DM (mean 54.5 mmol/mol) and 47.2% self-reported using insulin. A diagnosis of HTN was recorded for 59.2%, while 55.1% self-reported taking anti-hypertensive medication and 73.6% had BP measurements in the hypertensive range. Overall, 95.1% had either DM or HTN (diagnosed or undiagnosed), while 63.0% had both. Of the 13 (4.9%) individuals without DM or HTN, 7 had only a single microaneurysm in one eye.
Conclusions: This is one of the largest prospective cohort studies containing validated grading data for retinopathy, showing a high prevalence of both DM and or HTN. These results demonstrate the quality of the retinal image grading and highlight the potential for detecting systemic pathology.

CONTROL ID: 3712993

SUBMITTER (NAME ONLY): Sayena Jabbehdari

TITLE: Visual Outcomes, Intraoperative and Postoperative Complications of Cataract Surgery: A Multi-Center Database Study

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Jabbehdari, A.B. Sallam, Ophthalmology, University of Arkansas for Medical Sciences College of Medicine, Little Rock, Arkansas, UNITED STATES|M.K. Soliman, Ophthalmology, Assiut University Faculty of Medicine, Assiut, EGYPT|

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ABSTRACT BODY:

Purpose: The visual acuity (VA) outcomes, intra- and postoperative complications of cataract surgeries complicated by posterior capsule rupture (PCR) or dropped nucleus fragments (DNF) have not been reported. Here, we report the results of a retrospective, multicenter study comparing uncomplicated cataract surgeries to those complicated by PCR or DNF.

Methods: After inclusion and exclusion criteria were met, we analyzed 178,859 eyes according to the VA at baseline and within three-month follow-up. Successful visual outcome was defined as VA≤0.3logMAR, and uncomplicated surgeries considered as reference group. Incidence of cystoid macular edema (CME), rhegmatogenous retinal detachment (RRD), and epiretinal membrane (ERM) were also analyzed. Statistical analysis between the pre- and postoperative VA and gains in Snellen lines was generated using ANOVA and chi-square tests with Bonferroni correction. Statistical significance was set at P<0.003. Multivariate logistic regression modeling to calculate the odds ratio between VA≤0.3logMAR and surgical complications at different time intervalswas also performed.

Results: DNF and PCR group eyes developed inferior visual outcomes compared to reference group (0.67±0.65 vs.0.43±0.55 vs.0.20±0.33, respectively, p<0.003) with mean change in VA of -0.32±0.86 vs. 0.34±0.72 vs.-0.42±0.5, respectively, (p<0.003). DNF and PCR group eyes gained ≥0.3logMAR (~3Snellen lines) in 46.8% and 50.9% of eyes, respectively, compared to the 62% in the reference group (p<0.003). Among those eyes in DNF group, 204 eyes (41.23%) were managed surgically with pars plana vitrectomy (PPV) (44.79±28.5 days between procedure and PPV) and 315 eyes (58.77%) were conservatively managed. Mean change in VA among those eyes with DNF managed by PPV was higher than eyes managed conservatively (-0.17±0.90 vs.-0.48±0.79, p<0.003). The odds ratio of having CME, ERM, and RRD among eyes with DNF or PCR was significantly higher than reference group (1.603, 2.133, 3.646 in DNF group, vs. 2.18, 1.28, 1.76 in PCR group, respectively, p<0.003).

Conclusions: We found that eyes are at risk of inferior VA when cataract surgery is complicated by DNF compared to eyes with PCR. In addition, eyes with PCR or DNF had worse VA and higher risk of CME, ERM, and RD compared to uncomplicated cases. Eye complicated with DNF that managed with PPV, had better VA compared to conservatively managed eyes.

CONTROL ID: 3712996

SUBMITTER (NAME ONLY): Mingguang He

TITLE: Axial shortening in myopic children after repeated low-level red-light therapy: evidence from a real-world study and a randomized controlled trial

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. He, W. Wang, Y. Jiang, Z. Zhu, J. Zeng, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|M. He, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|I.G. Morgan, Australian National University Research School of Biology, Canberra, Australian Capital Territory, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Myopia progression is characterized by axial elongation which is commonly considered as irreversible. In this study, we observed differences in the frequency and magnitude of axial shortening among myopic children following repeated low-level red-light (RLRL) therapy.

Methods: This prospective analysis was performed on a real-world study (RWS) and a subset sample of a randomized control trial (RCT). In the RWS, myopic children (cycloplegic spherical equivalent refraction [SER] of at least -0.50 diopter [D]) who completed RLRL treatment for at least 12 months were included in the analysis. In the 12-month RCT, children aged 8 to 13 years with myopia of cycloplegic SER of -1.00 to -5.00D, astigmatism ≤2.50D, and anisometropia ≤1.50D were recruited and randomly assigned to RLRL treatment (intervention group) or a single vision spectacle (control group). Children in the intervention group were included in the present analysis. Axial length (AL) was measured prior to cycloplegia. A subset of the RCT underwent swept-source optical coherence tomography where choroidal thickness (ChT) was obtained.

Results: Among the 434 myopic children in the RWS, 115 (26.50%), 76 (17.51%) and 20 (4.61%) of them had AL shortening according to cutoffs of 0.05 mm/year, 0.10 mm/year, and 0.20 mm/year, respectively. In the multivariable model, older baseline age, female gender and longer baseline AL were significantly associated with the presence of AL shortening. For AL shortened eyes, mean AL shortening (standard deviation, SD) was -0.142 (0.094) mm. Among the 111 children in the intervention group of the RCT, 26 (23.42%), 18 (16.22%) and 7 (6.31%) had AL shortening of 0.05 mm, 0.10mm, and 0.20 mm or more per year respectively, with mean of AL shortening (SD) of -0.156 (0.086) mm. In multivariate analysis, older baseline age was significantly associated with the presence of AL shortening, whereas among those with AL shortening, longer baseline AL was significantly associated with greater magnitude of AL shortening.

Conclusions: More than a quarter of the children had >0.05 mm AL shortening following RLRL therapy with a mean of -0.142 and -0.156 mm. This axial shortening cannot be explained by measurement error and/or choroidal thickening. Further studies are needed to explore mechanisms underlying axial shortening.

CONTROL ID: 3712999

SUBMITTER (NAME ONLY): Micalla Peng

TITLE: Electric Fields Direct Full-Length Optic Nerve Regeneration and Partial Restoration of Visual Function

SESSION TITLE: Neuroprotection and neuroregeneration

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Restoring vision in patients blinded by advanced optic neuropathies requires therapies that promote retinal ganglion cell (RGC) survival and direct RGC axon regeneration. Previously, we showed that electric fields (EFs) direct RGC axon growth towards the cathode (negative electrode), in vitro. Here, we hypothesized that exogenous application of EFs can be exploited to direct optic nerve regeneration in vivo using the optic nerve crush model.

Methods: Adult male Long-Evans rats underwent optic nerve crush injury with intra-orbital and intracranial electrode implantation. Five days later, rats were stimulated with various electrical waveforms for 5 hours daily for 10 or 30 days. Treatment efficacy was assessed via 1) histologic tests, such as RBPMS staining for surviving RGCs and CTB anterograde labeling of regenerated axons, 2) behavioral tests, such as optokinetic reflex and visual cliff tests, and 3) electrophysiologic studies, including visual evoked potential (VEP) and pattern electroretinogram (PERG) recordings. Analysis performed with ANOVA and Sidak's multiple comparisons test.

Results: 10 days of EF treatment directed 2-fold more RGC survival and 5-fold more axon regeneration at 250μm from crush site over untreated rats (n=5, $p<0.05$). Full length optic nerve regeneration was observed with 30 days of EF treatment. This was associated with 10-fold more RGC survival and 7-fold more axon regeneration at 250μm from crush site over the untreated rats (n=4, $p<0.05$). VEP recordings demonstrated partial recovery of visual function in 62% of superior colliculus sites in the 30-day treated rats (n=3, $p<0.05$) compared to 2% of the untreated (n=4). The PERG N95 amplitude (crushed nerve normalized to contralateral uncrushed nerve) was 0.66 in the 30-day treated rats (n=6, $p<0.05$) compared to 0.28 in the untreated (n=4). On visual cliff testing, 67% of 30-day treated rats (n=3) dismounted correctly (mean latency 184 sec) compared to no correct dismounts in the untreated (n=3).

Conclusions: Our results demonstrate that EF application can promote RGC survival and direct axon regeneration with partial recovery of visual function and suggests that EF application may be a viable therapeutic to help restore visual function in patients blinded by advanced optic nerve disease.

CONTROL ID: 3713000

SUBMITTER (NAME ONLY): Amandio Rocha-Sousa

TITLE: Optical Coherence Tomography Angiography Assessment of Retinal Microvasculature Before and After Carotid Endarterectomy

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rocha-Sousa, A. Moleiro, J. Rocha-Neves, R. Vilares-Morgado, J. Andrade, J. Barbosa-Breda, Faculdade de Medicina da Universidade do Porto, Porto, PORTUGAL|A. Rocha-Sousa, A. Moleiro, J. Rocha-Neves, R. Vilares-Morgado, V. Sousa, A. Silva, J. Barbosa-Breda, Centro Hospitalar e Universitário de São João, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: A growing body of research indicates that abnormal retinal microvascular features may serve as a novel biomarker reflecting the severity of underlying cardiovascular, neurodegenerative, and microvascular disease. Since blood flow to the retina is predominantly supplied by the internal carotid artery, we hypothesized that retinal microvasculature may change after carotid endarterectomy reflecting the disease status or therapeutic effects in patients with severe carotid stenosis.

Methods: Nine patients with carotid artery stenosis >70% underwent complete ophthalmic examinations and Optical Coherence Tomography Angiography (OCTA, Spectralis, Heidelberg) before carotid endarterectomy and 48 hours (h) and 3 months post-surgery. Image J software (National Institutes of Health, Bethesda, MD) was used to analyze OCTA images. Non-local means denoising filter, Phansalkar as adptative local thresholding methods and binarization algorisms were used to process the images. Eyes on the operated side constituted the ipsilateral eye group, and the other eye constituted the fellow eye group.

Results: : 8 male and 7 female were included, with a mean age of 73 years old.

In the ipsilateral eye group, FAZ area reduced significantly after endarterectomy (before vs 48h after surgery, p=0,012; before vs 3 months after surgery, p=0,012). FAZ area also decreases from 48h post-surgery to 3 months after surgery; however, this difference is not statistically significant (p=0,41). No differences in FAZ area were found in the fellow eye during follow-up (p=0,095).

Regarding vessel densities (VD), no statistical differences were found in the ipsilateral eye in macular or papillary scans both in superficial (SCP) and deep capillary plexus (DCP) ($p<0.05$), although a tendency for an increase in VD is evident in SCP of macula centered scans.

Similarly, no differences in vessel density were found during the follow-up in the fellow eye.

Conclusions: Endarterectomy for severe carotid stenosis reduce FAZ area in the immediate and midterm post-surgery.

CONTROL ID: 3713002

SUBMITTER (NAME ONLY): Srinidhi Singuri

TITLE: Clinical utility of Spectral-Domain Optical Coherence Tomography (SD-OCT) marker Disorganization of Retinal Inner Layers (DRIL) in Diabetic Retinopathy (DR)

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a vision-threatening microvascular complication that affects one-third of all diabetics. Fundus examination and imaging, commonly spectral domain optical coherence tomography (SD-OCT), are used to screen for, diagnose and monitor complications of DR. Disorganization of retinal inner layers (DRIL) is an understudied SD-OCT parameter. To investigate the clinical utility of DRIL in DR, we evaluate its relationship with several DR risk and progression factors.

Methods: A retrospective cohort study was conducted at a large academic center following Institutional Review Board approval. The cohort comprised 1,175 randomly selected, non-consecutive patients with ICD-9/10 codes for type 2 diabetes with and without retinopathy between September 2009 and January 2019 (n=2,083 eyes). Demographics, anti-hyperglycemic history, hemoglobin A1c (HbA1c), and VA were obtained by electronic medical record review. SD-OCT scans were evaluated for DRIL by two trained, double-blinded graders. Disagreement was arbitrated by a third blinded grader. Interrater reliability was tested with a kappa statistic. Generalized estimating equation logistic regression models were used to evaluate relationships between variables.

Results: Of 2,083 eyes, 28.08% (n=585) demonstrate presence of DRIL with high interrater reliability (K=0.88, 95% confidence interval (CI) [0.86-0.90]). Insulin users have more severe DR (p<.0001). DRIL is associated with worse VA (p<.001) and DR severity (p<.0001). Unadjusted, insulin usage appears to be associated with DRIL (OR 1.91, 95% CI [1.49-2.45]), however after accounting for DR severity, we find that DRIL is not associated with insulin usage (p=0.25).

The remaining DR-related factors (other anti-hyperglycemic usage, HbA1c, sex, race and age) are not associated with DRIL.

Conclusions: DRIL is a promising clinical parameter in patients with DR. SD-OCT marker DRIL is strongly associated with severity of DR and worse VA, supporting its utility as an unfavorable prognostic predictor. Initially, DRIL appeared strongly associated with insulin use, however after adjusting for DR severity, DRIL is not associated with insulin use. Thus, DR severity confounds the relationship between DRIL and insulin use.

CONTROL ID: 3713003

SUBMITTER (NAME ONLY): Marlies Gijs

TITLE: Pre-analytical sample handling effects on tear fluid protein levels

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the effect of pre-analytical sample handling on tear fluid protein levels.
We empirically tested variations of common tear collection and handling procedures.

Methods: We created sample sets that address the effect of tear collection, storage and extraction on protein recovery. Tear fluid was collected using Schirmer's strips from healthy subjects. Proteins were extracted by elution and centrifugation. The total protein content was measured with the BCA assay.

Results: Protein recovery was the highest after direct ('fresh') extraction. Minimal protein loss was found after intermediate storage at -80°C and -20°C (-3.1% and -4.5%, respectively). Protein concentration in the 'wet' storage condition of strips was 8.5 ± 6.0% higher compared to 'dry' storage. Protein recovery increased with increasing extraction volumes but also results in higher dilution of the sample. Sonication did not improve protein extraction efficiency. Protein concentration within the Schirmer's strip was the highest in the 0-5 (+head) mm region (1034.7 ± 72.7 µg/mL). Consecutive tear fluid collection did not greatly affect protein concentration. Protein recovery decreased with protein concentration but was independent of molecular weight.

Conclusions: There is a need to construct standardized operation procedures for pre-analytical handing of tear fluid in order to facilitate to build tear fluid biobanks and the use of tear fluid-based biomarkers in the clinical setting.

CONTROL ID: 3713004

SUBMITTER (NAME ONLY): Efrat Naaman

TITLE: PEDF-derived peptide inhibits Amyloid-β internalization and ameliorates retinal toxicity

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Amyloid-beta (Aβ) has been implicated in the pathophysiology of age-related macular degeneration. We have shown that Aβ species possess differential retinal neurotoxicity, where oligomeric and fibrillar assemblies of Aβ42 mediated the primary retinotoxic effects. The mechanism of internalization of extracellular Aβ42 species in the retina is not well defined. In the brain, Aβ binding to the 67kDa laminin receptor (67LR) mediated the internalization of oligomeric Aβ42 and related neuronal cell death. We have found that PEDF335, a pigment epithelium-derived factor derived peptide, can bind to 67LR. Here, we hypothesized that 67LR mediates Aβ42 uptake in the retina, and PEDF335 may limit extracellular Aβ internalization, thereby inhibit Aβ42 retinal toxicity.

Methods: ARPE-19 cells were cultured with PEDF335 for 6h before treatment with oligomeric or fibrillar Aβ42 for 24 h. Cell viability was determined by XTT assay. The uptake of Aβ42 was assessed using immunostaining. Wild type rats were treated with intravitreal injection (10µl) of PEDF335 (3mM) in each eye two days prior to administration of oligomeric or fibrillar Aβ42 to the right eye. Retinal function was assessed at baseline and thereafter through 6 weeks after the injection. At each time point, electroretinography (ERG) measures were compared between eyes. The presence of 67LR in ex-vivo retina was determined using immunostaining.

Results: PEDF335 treatment blocked amyloid internalization into ARPE-19 cells and maintained their viability in the presence of oligomeric and fibrillar Aβ42. ERG responses in rat eyes treated with oligomeric or fibrillar Aβ42 assemblies were near-normal in eyes previously treated with PEDF335, whereas those measured in eyes treated with Aβ42 alone showed pathologic attenuation through 14 days. No adverse effects were noted in response to PEDF335. Retinal immunostaining demonstrated the expression of 67LR in rats' retina.

Conclusions: Our results show that PEDF335 protects against oligomeric and fibrillar Aβ42 retinal toxicity, at least in part, via binding to 67LR and inhibition of Aβ42 internalization. These observations provide evidence on the importance of extracellular versus intracellular Aβ42 in the retina and suggest that the mechanism of toxicity of fibrils possibly involves secondary release of oligomers. Such insights may promote the mechanistic understanding of the retinal pathogenicity of Aβ.

CONTROL ID: 3713007

SUBMITTER (NAME ONLY): Ziqi TANG

TITLE: Using Deep Learning for Assessing Image-Quality of 3D Macular Scans from Spectral-Domain Optical Coherence Tomography

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. TANG, A. Ran, F. Tang, D.G. YANG, Y. Wong, C. Cheung, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|X. Wang, L. Luo, Q. Liu, P. Heng, Department of Computer Science and Engineering, The Chinese University of Hong Kong, Hong Kong, HONG KONG|X. Wang, Department of Radiation Oncology, Stanford University, Stanford, California, UNITED STATES|Y. Cai, Department of Electronic and Computer Engineering, The Hong Kong University of Science and Technology, Hong Kong, HONG KONG|H. Che, H. Chen, Department of Computer Science and Engineering, The Hong Kong University of Science and Technology, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Assessing image quality of optical coherence tomography (OCT) beforehand is very essential for subsequent retinal disease identification. We developed, validated, and tested deep-learning algorithms to assess the quality of macular scans obtained from two OCT devices.

Methods: This study was a retrospective analysis of OCT images obtained from the Chinese University of Hong Kong Eye Centre and Hong Kong Eye Hospital. The OCT images of different scanning protocols and devices (macular cube 512×128 B-scans from Cirrus OCT; and macular volume 512×31 B-scans, 1024×25 B-scans, and 1024×19 B-scans from Spectralis OCT) were included. The gradability of B-scan images and volume scans were labeled as gradable or ungradable. Gradable B-scan/volume scan was defined as absence of any artifact or; OCT artifacts affect less than 25% peripheral area or; fovea off centration presents in the central 50% area. Ungradable B-scan/volume scan was defined as OCT artifacts affect the central 50% area or fovea off centration is outside the central 50% area or fovea motion artifact. The ground truth was independently labeled by two masked well-trained graders. The discrepancy during the grading was resolved by adjudication by a senior grader. A total of 2,277 Cirrus scans and 33,633 Spectralis B-scans of 1,557 volume scans were divided into training (70%), validation (20%), test (10%), respectively. We developed, validated, and tested a 3D residual network (ResNet)-18 for Cirrus 3D cube scans, a dense convolutional network (DenseNet)-121 for Spectralis 2D B-scans, and a multiple-instance learning model for Spectralis 3D volume scans (Figure 1).

Results: In the primary validation of Cirrus cube scans, Spectralis B-scans, and Spectralis volume scans, the algorithms achieved the area under receiver operating characteristic curves (AUCs) of 0.930, 0.972, and 0.906 (Figure 2); sensitivities of 94.6%, 90.1%, and 86.5%; specificities of 83.3%, 94.2%, and 95.7%; and accuracies of 93.3%, 91.1%, and 87.2%, respectively.

Conclusions: The proposed deep learning algorithms achieved good performance, to distinguish gradable and ungradable OCT macular images. Incorporating with an artificial intelligence-based model, a volume-level quality indicator allows only gradable scans to be referred, which can smooth clinical operational flow for enhancing disease screening and diagnosis.

CONTROL ID: 3713008

SUBMITTER (NAME ONLY): Ursula Schmidt-Erfurth

TITLE: Ratio of photoreceptor to retinal pigment epithelium loss as an important predictor of GA growth and therapeutic efficacy

SESSION TITLE: AMD Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Schmidt-Erfurth, S. Riedl, W. Vogl, J. Mai, G.S. Reiter, D. Lachinov, C. Grechenig, H. Bogunovic, Ophthalmology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|A. McKeown, L. Scheibler, Apellis Pharmaceuticals Inc, Waltham, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the impact of the ratio between photoreceptor (PR) loss and retinal epithelium (RPE) loss in geographic atrophy (GA) on lesion growth as well as on the effect of pegcetacoplan treatment.

Methods: Spectral domain-optical coherence tomography (SD-OCT) volumes of patients included in the prospective, multicenter, randomized phase II FILLY trial, investigating the safety and efficacy of intravitreal C3 complement inhibition by pegcetacoplan in GA, were analyzed. All eyes were imaged with Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) were included. PR thickness as well as RPE loss were segmented automatically based on two separate deep learning algorithms. We investigated the difference in progression of RPE loss at year 1 between baseline quartiles of PR loss / RPE loss ratio as well as the effect of treatment within these quartiles. To this end, a multivariable regression model was calculated considering quartiles of PR loss / RPE loss at baseline and their interaction with treatment.

Results: GA growth in sham-treated eyes increased with higher baseline PR loss / RPE loss ratio quartiles (Figure 1). Lesions in the highest quartile showed statistically significantly increased growth of RPE loss of 284µm (95% CI: 84, 485; p=0.006) compared to lesions in the lowest quartile. Accordingly, the effect of monthly treatment also increased with higher PR loss / RPE loss ratio quartiles, reaching a statistically significant effect of -207µm, equaling a 57% growth reduction compared to SM treated eyes (95% CI: -408, -6,5; p=0.043) in the fourth quartile.

Conclusions: High baseline PR loss / RPE loss presents as a risk factor of increased GA growth. Furthermore, the treatment effect was observed to be dependent on baseline PR loss / RPE loss ratio, showing a significant RPE loss growth reduction for AM- compared to SM-treated eyes in the highest ratio quartile. These results highlight the importance of baseline characteristics for investigating treatment effects in GA. We expect such baseline characteristics identified by AI tools to be of relevance for defining robust criteria for patient selection as well as treatment guidelines for forthcoming clinical trials as well as clinical routine.

CONTROL ID: 3713009

SUBMITTER (NAME ONLY): Deborah Villafranca-Baughman

TITLE: A novel femtomolar hemodynamic modulation strategy reveals major microvascular defects in glaucoma at single-pericyte scale

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Villafranca-Baughman, J. Cueva Vargas, N.A. Belforte, F. Dotigny, A. Di Polo, Neuroscience, Universite de Montreal, Montreal, Quebec, CANADA|D. Villafranca-Baughman, L. Alarcon-Martinez, J. Cueva Vargas, N.A. Belforte, F. Dotigny, A. Di Polo, Neuroscience, Centre Hospitalier de l'Universite de Montreal Centre de Recherche, Montreal, Quebec, CANADA|L. Alarcon-Martinez, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Reduced blood flow and neurovascular deficits are recognized features of glaucoma, but the mechanisms underlying these alterations are poorly understood. Pericytes, the contractile cells that wrap around capillaries, regulate blood supply by modulating capillary diameter. Here, we developed a novel live imaging and femto-scale delivery system to study the role of single-pericyte hemodynamics in glaucoma.

Methods: Ocular hypertension (OHT) was induced by intracameral injection of magnetic microbeads in NG2-DsRed mice, which allow visualization of retinal pericytes. Two-photon laser scanning microscopy (TPLSM) was combined with a femtomolar delivery system (FemtoJet Microinjector) to visualize and modulate single-pericyte longitudinal responses in living mice. A micromanipulator was used to place the microneedle adjacent to a pericyte-capillary pair, and vasomodulators (e.g. ET-1:endothelin-1, NO donors) were delivered at a femtomolar scale. Capillary diameter was measured by placing a linear probe perpendicular to the plane of the vessel, and blood flow was quantified by counting the number of red blood cells crossing a pre-fixed vessel location.

Results: TPLSM adapted with a femto-microinjector provided high spatial-temporal resolution of single-pericyte-capillary responses without affecting neighboring vessels. Our data show decreased capillary diameter and blood flow at pericyte locations in glaucoma (sham: n=13 capillaries, OHT-2 wks: n=18 capillaries, N=5-7 mice/group, $p<0.01$). Femtomolar delivery of ET-1 in glaucomatous mice exacerbated the magnitude and duration of capillary constriction at pericyte locations and decreased blood flow relative to controls (vehicle: n=11 capillaries, ET-1: n=16 capillaries, N=3-5 mice/group, $p<0.001$). In contrast, NO donor administration rescued the ability of capillaries to dilate at pericyte locations enhancing blood flow despite OHT (vehicle: n=16 capillaries, NO donor: n=7 capillaries, N=3-5 mice/group, $p<0.01$), suggesting that microvascular defects in glaucoma are reversible.

Conclusions: We demonstrate the utility of combining TPLSM live longitudinal imaging and femtomolar delivery of vasoactive substances to study neurovascular defects caused by OHT. Our study identifies pericytes as critical regulators of capillary hemodynamics and unveils their potential as therapeutic targets to restore neurovascular function in glaucoma.

CONTROL ID: 3713011

SUBMITTER (NAME ONLY): Illes Kovacs

TITLE: The Sigma-1 Receptor Agonist Fluvoxamine prevents Dexamethasone-induced Ocular Hypertension in vivo.

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Lowering intraocular pressure (IOP) is currently the only treatment strategy to slow the progression of glaucoma. The increased IOP is attributed to abnormally elevated trabecular aqueous outflow resistance that can be caused by fibrosis of the trabecular meshwork (TM). We recently found that the specific sigma-1 receptor (S1R) agonist fluvoxamine (FLU) effectively reduces profibrotic factor-induced cytoskeletal rearrangement and cell proliferation of TM cells in vitro, therefore we propose that FLU may prevent TM fibrosis in vivo and thus can reduce IOP.

Methods: To induce IOP C57BL/6J wild type (WT) and S1R knock-out (KO) mice were weekly injected (n=8-12/group) with vehicle or Dexamethasone Acetate (Dex) through periocular conjunctival fornix to both eyes. FLU eye drops (30mM) were given bilaterally twice daily after 1 week of Dex. IOP was measured with Icare Tonolab weekly. After 4 weeks, the eyes were enucleated and bisected just posterior to the limbus. The retina, choroid, vitreous, and lens were removed carefully and the remaining anterior segments were frozen for further investigations. For S1R labeling fluorescent beads were injected intracamerally and TM regions with engulfed beads were imaged with confocal microscope.

Results: Dex increased the IOP in 7 month old WT mice after three weeks from baseline 17.26±1.46 to 18.61±1.05 mmHg (+7.82%; $p<0.05$) and two weeks of FLU eye drop treatment lowered IOP to 16.90±1.19 mmHg (-9.18%; $p<0.05$) compared to Dex group. In younger (2 to 5 month) WT mice IOP was elevated from baseline 17.66±1.01 mmHg to 19.65±2.00 mmHg (+11.27%; $p<0.05$) which is more pronounced than in aged mice. In KO mice the IOP increased from 16.81±1.41 to 18.72±1.04 mmHg (+11.36%; $p<0.05$). Of note the increase of IOP started earlier in KO mice (1 week) than in WT (2 weeks). As novelty, confocal images showed that S1R is present in the mouse TM region and preliminary PCR results revealed that the expression of key fibrosis elements (fibronectin and α-smooth muscle actin) were upregulated by Dex.

Conclusions: Fluvoxamine treatment effectively reduced the steroid-induced fibrosis and cytoskeletal rearrangement of trabecular meshwork tissue and prevented the increase in intraocular pressure in vivo. Thus Sigma-1 receptor agonists could be potential candidates for the development of a novel IOP-lowering drug.

CONTROL ID: 3713013

SUBMITTER (NAME ONLY): Alfrun Schönberg

TITLE: Effect of sCD83 on direct allosensitization after corneal transplantation

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.P. Schönberg, K. Hadrian, M. Hamdorf, C. Cursiefen, F. Bock, Department of Experimental Ophthalmology, Klinikum der Universitat zu Koln Zentrum fur Augenheilkunde, Cologne, Nordrhein-Westfalen, GERMANY|K. Peckert-Maier, E. Zinser, Department of Immune Modulation, University Hospital Erlangen, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: Immune-mediated graft rejections remain the most common cause for graft failure after organ and tissue transplantation. There is a great unmet medical need for pharmacologic strategies to promote graft survival without unduly compromising the health of the recipient. Recently, our group showed that pre-treatment of the corneal donor tissue with sCD83 improves graft survival. Here, we further elucidate the mode of action of pre-treatment of corneal donor tissue and determine the effect of sCD83 on direct allosensitization after corneal transplantation.

Methods: A murine model of high-risk corneal transplantation with C57BL/6N mice as donor and BALB/c mice as recipients was used. Corneal grafts were pre-incubated with sCD83 for 48 h. Excessive sCD83 was removed prior to transplantation by alternating incubation in hydrating and dehydrating medium (removal strategy). Corneal sCD83 content was assessed by immunoblotting and immunohistochemistry. Long-term allograft survival was determined by grading the graft opacity weekly for eight weeks. Moreover, the inflammatory phenotype of dendritic cells (DCs) and macrophages (Mφ) in the draining lymph nodes (dLNs) of the recipient was analyzed by flow cytometry eight weeks post transplantation.

Results: Applying the removal strategy to pre-incubated donor corneas resulted in a strong decrease of sCD83 in the stroma whereas sCD83 was still co-localized with immune cells of the donor cornea. Subsequent transplantation of those grafts into high-risk recipient beds improved long-term graft survival. Moreover, the frequencies of both regulatory DCs ($CD11c^+MHCII^+CD200R^+$) as well as Mφ ($F4/80^+CD200R^+$) were significantly increased in dLNs of mice that received sCD83-modulated grafts.

Conclusions: This study demonstrates that sCD83-induced corneal graft tolerance can be mediated directly by immune cells of the donor tissue and thereby modulates direct allosensitization in corneal transplantation. Thus, targeting the initial alloimmune response can already improve the long-term outcome. This new pharmacologic strategy of "direct allotolerance" could be a seeding point for novel therapeutic approaches in which pre-treatment of grafts with sCD83 could induce tolerance to the donor tissue and avoid lifelong immunosuppressive treatment of the patient.

CONTROL ID: 3713017

SUBMITTER (NAME ONLY): Jingqi Huang

TITLE: Circular RNA expression profile in human lens epithelial cells and cortical fiber cells through microarray

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, L. Xiong, Y. Sun, B. Chen, J. Chen, M. Huang, S. Huang, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Differentiation of lens epithelial cells (LECs) to lens fiber cells (LFCs) is a lifelong process involved in physiological lens development. Circular RNA, a class of covalently close-loop non-coding RNAs, plays important roles in lens development regulation. To unearth its potential specialized functions during human LECs differentiation, circRNA expression profiling in LECs and LFCs was analyzed.

Methods: Clear human lenses of five organ donors were obtained from Guangdong Eyebank and dissected into LECs and LFCs for RNA extraction. Matching RNA samples from two cell types were assessed by Agilent microarray to identify differentially expressed circRNAs (DEcircRNAs). Gene ontology (GO) enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses of the DEcircRNAs were performed to determine the related biological modules and pathways.

Results: There was a significant difference of circRNAs expression profiling between human LECs and LFCs, indicating that molecular regulation via circRNAs differs greatly in the process of LECs differentiation. A total of 218 DEcircRNAs were identified, among which 114 were up-regulated and 104 were down-regulated in LECs compared with LFCs. GO enrichment analyses revealed the DEcircRNAs were most signifcantly targeted to ephrin receptor signaling pathway (biological process), protein binding (molecular function) and cytosol (cellular compoment). Apoptosis, autophagy and Wnt signaling pathway were the most enriched pathway in KEGG analysis.

Conclusions: Our findings uncover the circRNA profiling in human LECs and LFCs, and analyzed the most related biological modules and signaling pathways of DEcircRNAs, which paves the way for futher characterization of potential regulatory mechanism of circRNA in LECs differentiation.

CONTROL ID: 3713019

SUBMITTER (NAME ONLY): Seung-Young Yu

TITLE: Seven-year clinical outcomes of Central Serous Chorioretinopathy according to age

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yu, J. Lee, K. Kim, E. Kim, Ophthalmology, Kyung Hee University Hospital, Dongdaemun-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To evaluate 7-year clinical outcomes in patient with central serous chorioretinopathy (CSC) according to age at presentation.

Methods: This retrospective study reviewed clinical and multimodal imaging data (color fundus photography, optical coherence tomography, fundus autofluorescence, fluorescein angiography, indocyanine green angiography) of 75 eyes of 71 patients with CSC. All subjects were followed up at least 7 years. The eyes were divided into 3 groups according to age at presentation, as <50 years old (Group 1, 28 eyes), 50 to 59 years old (Group 2, 28 eyes), and ≥60 years old (Group 3, 19 eyes). Best corrected visual acuity (BCVA), subfoveal choroidal thickness (SFCT), central subfield retinal thickness (CST), multimodal imaging were analyzed.

Results: At baseline, mean BCVA and mean CST among three groups were statistically different (BCVA; $p = 0.047$, CST; $p = 0.034$). Seven-year mean change of SFCT were -7.0 ± 56.7 μm in Group 1, -12.3 ± 51.0 μm in Group 2, and -66.4 ± 57.6 μm in Group 3. Mean SFCT in Group 3 significantly decreased compared to that of other groups ($p = 0.004$; compared to Group 1, $p=0.016$; compared to Group 2). Seven-year prevalence of shallow RPE elevation was 10.7% in Group 1, 25.0% in Group 2, 42.1% in Group 3. Seven-year prevalence of choroidal neovascularization (CNV) was 7.1% in Group 1, 14.3% in Group 2, 36.8% in Group 3. In older age group (over 50), advanced fundus autofluorescence patterns appeared and progressed during 7-year follow-up.

Conclusions: During 7-year follow up of CSC, mean subfoveal choroidal thickness decreased by 7.0 μm in age 30-49, by 12.3 μm in age 50-59, and by 66.4 μm in age over 60 which was significantly different. Age at presentation were associated with decreases of choroidal thickness. In CSC, long-term and planned researches are needed.

CONTROL ID: 3713020

SUBMITTER (NAME ONLY): Judit Hodrea

TITLE: The Protective Role of the Sigma-1 Receptor in Trabecular Meshwork Cells in vitro

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Trabecular meshwork (TM) is the main pathway for aqueous humor drainage from the eye. The fibrotic-like remodeling of the actin cytoskeleton in TM cells results in altered stiffness and impaired outflow which are the primary cause of increased intraocular pressure (IOP) leading to glaucoma. Thus, cytoskeletal-disrupting drugs could be a novel therapeutic approach to lower IOP. Recently, we proved that fluvoxamine (FLU), a specific Sigma-1 receptor agonist is antifibrotic in the kidney. Therefore, here we investigated whether FLU is effective in the prevention of cytoskeletal rearrangement and in vitro TM fibrosis in primary mouse- (MsTM) and non-glaucomatous human TM cells (HTM5).

Methods: Immunocytochemistry and Western blot were used to detect S1R on HTM5 and on MsTM cells. Primary MsTM cells from wild type (WT) and S1R knock-out (KO) mice and HTM5 cells were treated for 24h with 20 ng/mL platelet-derived growth factor (PDGF) combined with 10 μM of FLU. Cell proliferation was determined by thiazolyl blue tetrazolium bromide assay, cell toxicity by LDH assay, cell migration was measured by scratch assay, and F-actin was visualized by phalloidin staining and detected with fluorescent microscope. The fibrotic protein levels (fibronectin and αSMA) were measured by Western blot.

Results: S1R is present both in primary MsTM and HTM5 cells and is localized in the endoplasmic reticulum. Cell proliferation, migration, levels of fibrotic proteins (fibronectin, αSMA) and cytoskeletal rearrangement were induced by PDGF. FLU treatment was not toxic to the cells and ameliorated or even prevented the PDGF induced changes in all assays. Furthermore,upon PDGF treatment the integrated density of phalloidin staining increased with 19.73% in primary KO MsTM cells compared to WT and the formation of F-actin bundles and actin clumps was more pronounced in the absence of S1R suggesting its protective role in TM fibrosis.

Conclusions: FLU is non-toxic and effectively reduces profibrotic factor-induced cytoskeletal rearrangement and cell proliferation of TM cells. Therefore one can speculate that it might lead to lower outflow resistance also in animals and it could be an IOP-lowering drug candidate for glaucoma.

Grants: OTKA- K135398, LP2021-3/2021, 2020-4.1.1.-TKP2020-6183069269 (FIKP), 2020-4.1.1.-TKP2020-6183169273.

CONTROL ID: 3713022

SUBMITTER (NAME ONLY): Martin Michl

TITLE: Comparison of a human versus deep learning-based evaluation of fluid change in real-world OCT images of neovascular AMD

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Michl, B. Gerendas, P. Seeböck, E. de Llano, F. Goldbach, G. Mylonas, O. Leingang, W. Bühl, S. Sacu, H. Bogunovic, U. Schmidt-Erfurth, Ophthalmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|A. Gruber, Center for Medical Statistics, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To compare the clinical evaluation of intra- and subretinal fluid (IRF, SRF) presence and volume change between eye care professionals and a deep learning-based algorithm in real-world OCT images of patients with neovascular age-related macular degeneration (nAMD).

Methods: Patients were diagnosed with nAMD and treated at our retina department between 2007 and 2018 and are included in the Vienna Imaging Biomarker Eye Study (VIBES) registry. Five retinologists (RET), three ophthalmology residents (RES), three ophthalmologists working in private practice (PRIVO), three orthoptists (ORTH) and three certified readers from the Vienna Reading Center (VRC) subjectively graded the presence of IRF/SRF at two consecutive visits and the level of change (increase/no-change/decrease). There were 28 to 120 days between two visits and anti-VEGF injections were given at any timepoint between the two visits. For the presence of IRF/SRF, the majority vote of RET was used as ground truth and compared to the majority vote of each of the other four professional groups as well as to an algorithm for automated fluid quantification (fluid presence ≥5nl). For the comparison of fluid change (change ≥ ±5nl), the same algorithm served as the objective ground truth and was compared to all five professional groups.

Results: Spectralis OCT volumes of 248 visits (=124 visit pairs) were included in our analysis. Compared to RET, the agreement on IRF presence was 93% (RES), 93% (PRIVO), 92% (ORTH), 88% (VRC), 89% (algorithm); agreement on SRF presence was 92% (RES), 89% (PRIVO), 89% (ORTH), 94% (VRC), 90% (algorithm). Compared to the algorithm, agreement on IRF change was 84% (RET), 87% (RES), 85% (PRIVO), 80% (ORTH), 87% (VRC); agreement on SRF change was 87% (RET), 87% (RES), 85% (PRIVO), 83% (ORTH), 88% (VRC).

Conclusions: The consensus of human experts from different professional background appears to be consistent in respect to overall fluid evaluation. However, in quantitative terms, artificial intelligence allows a precise assessment of fluid change over time and thus a management of macular edema that is better or comparable to different human eye-care professionals.

CONTROL ID: 3713024

SUBMITTER (NAME ONLY): Gloria Gambini

TITLE: OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY ANALYSIS OF THE CORIO-RETINAL MICROVASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Gambini, T. Caporossi, U. De Vico, M.M. Carlà, M.C. Savastano, A. Baldascino, S. Fiore, E. De Lorenzis, S. Bosello, S. Rizzo, Universita Cattolica del Sacro Cuore, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: The study aims to evaluate the retinal and choriocapillary vascular density (VD) in a group of patients affected by Systemic Sclerosis (SSc) compared to healthy controls (HC) and to highlight a possible correlation between the (VD) at this level and the characteristics of the disease, the results of capillaroscopy and the organ involvement.

Methods: VD was assessed by Optical Coherence Tomography Angiography (Ultra-fast Spectral Domain OCTA, 6.4 mmmx 6.4 mm macular scan) at the level of the superficial (SCP), deep retinal capillary plexus (DCP), and the choriocapillary (CC) of 30 SSc patients compared to 30 subjects of the same sex and age without any retinal disease.

Results: 30 % of SSc patients (age 57.3 ± 10.0, female 86.7%) had a diffuse cutaneous variant ,a mean duration of disease of 10.4 ± 7.2 years, and patients with antibody positive-centromer and anti-Scl70 account respectively for 40.0% and 30.0%. Compared to HC, SSc patients showed altered VD at the level of the SCP (47.7 ± 3.6 vs 59.1 ± 3.5%, p = 0.009), of the DCP (50.0 ± 6.7 vs 54.3 ± 6.4%, p = 0.015), and CC (67.1 ± 2.2 vs 68.6 ± 1.7, p = 0.005). Furthermore, in the SSc group, the presence of digital ulcers (46.7%), telangiectasias (43.3%) and interstitial lung disease (46.7%) was related to reduced VD (46.8 ± 4 , 1 vs 50.3 ± 4.3%, p =. 033), of the CC (66.1 ± 1.4 vs 67.9 ± 2.4%, p = 0.004) and of the DCP (47.2 ± 8.8 vs 51.9 ± 4.3, p = 0.004). Finally, the mean capillary density at capillaroscopy showed a positive correlation with the VD at the level of the SCP (r = .474, p = .008), of the DCP (r = .414, p = .023) and of the foveal CC (r .482, p .007) and there was also a correlation between the density at CC and both DLco (r = .467, p = .009) and FVC / DLco (r = -. 436, p = .004) .

Conclusions: SSc patients in our cohort showed lower vascular density than healthy controls. Furthermore, the compromised VD at different levels of the eye is related to organ involvement and the degree of digital and pulmonary microvascular impairment. According to these data, OCTA could be proposed as a biomarker to study microvascular anomalies in SSc.

CONTROL ID: 3713025

SUBMITTER (NAME ONLY): Laura Valencia-Nieto

TITLE: Ophthalmic 0.1% Cyclosporine A Cationic Emulsion Improves Keratitis After the First Month of Therapy in Dry Eye Patients

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Valencia-Nieto, J. Pinto-Fraga, M. Blanco-Vázquez, I. Fernández, A. López-Miguel, C. García-Vazquez, M. González-García, A. Enriquez-De-Salamanca, M. Calonge, IOBA -Institute of Applied Ophthalmobiology, University of Valladolid, Valladolid, SPAIN|I. Fernández, M. González-García, A. Enriquez-De-Salamanca, M. Calonge, CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine), Carlos III Health Institute, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the short- (30 days) and mid- (90 days) term efficacy of 0.1% cyclosporine A cationic emulsion (CsA-CE) in dry eye (DE) patients exposed to normal (NCE: 23^{O}C, 50% relative humidity) and adverse controlled environment (ACE: 23^{O}C, 10% relative humidity, localized airflow).

Methods: This clinical trial (www.clinicaltrials.gov NCT04492878) included DE patients with moderate-severe keratitis. There were 3 visits: baseline, and 1 and 3 months after one daily instillation of CsA-CE in both eyes. Patients were evaluated 2 times in each visit, under NCE (pre-ACE) and 2 hr post-ACE. Symptoms were evaluated with the DE questionnaire (DEQ)-5, symptom assessment in DE (SANDE) II, and change in DE-symptoms questionnaire (CDES-Q). Clinical signs evaluated were: conjunctival hyperemia (Efron scale), meibomian gland secretion quality and expressibility, tear breakup time (TBUT), corneal fluorescein staining (Oxford scale), conjunctival staining (Oxford scale), and Schirmer test. To assess the effect of time and environment, linear mixed effects models or cumulative link mixed models were adjusted for quantitative (expressed as mean±standard deviation) or ordinal (expressed as median [interquartile range]) variables, respectively.

Results: Twenty patients were included. After 1 month of CsA-CE therapy there were significant improvements compared to baseline (in NCE) in: DEQ-5 (14.0±3.1 vs 9.7±4.3; $p<0.0001$), conjunctival hyperemia (2.5 [1] vs 2.0 [0]; $p<0.0001$), and corneal fluorescein staining (3.0 [1] vs 2.0 [1]; $p<0.0001$). These improvements were still significant ($p\leq0.001$) after 3 months. In contrast, TBUT, meibomian gland parameters, and Schirmer test did not change after treatment.

Comparing pre- and post-ACE evaluations, DE signs and symptoms worsened. However, corneal fluorescein staining post-ACE at 1 month (2.0 [2]) and 3 months (2.0 [2]) was significantly ($p<0.01$) better than baseline post-ACE values (3.0 [1.25]).

Conclusions: A short-term efficacy of 0.1% CsA-CE was observed, as keratitis and symptoms already improved after the first month, and were maintained after 3 months. In general, parameters worsened after ACE, although keratitis always remained lower than before treatment, meaning that patients treated with CsA-CE could be more protected when living under adverse environments.

CONTROL ID: 3713027

SUBMITTER (NAME ONLY): Jerome Roger

TITLE: Efficacy of CRX gene therapy for treating mouse models of dominant CRX-associated retinopathies and beyond.

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.E. Roger, E. Grellier, S. Lourdel, M. Perron, Neuro-PSI, Centre National de la Recherche Scientifique, Saclay, Île-de-France, FRANCE|J.E. Roger, E. Grellier, S. Lourdel, CERTO, Retina France, Colomiers, Haute-Garonne, FRANCE|

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ABSTRACT BODY:

Purpose: Efficacy and safety of gene therapies for retinal diseases (RDs) have been proven with preclinical success translated into clinical effectiveness. However, this approach is rarely chosen for dominant forms. Based on our previous published work, we focused on dominant-negative mutations in the transcription factor CRX. We developed a mutation-independent AAV vector that could circumvent the clinical and genetic heterogeneity of CRX mutations. We also tested the neuroprotective potential of our gene therapy product for CRX-independent retinopathies.

Methods: AAV-CRX is an AAV2/5 allowing the expression of human CRX specifically in photoreceptors, using Rhodopsin Kinase 1 promoter. The efficacy of AAV-CRX for different CRX-associated diseases was assess tested by injecting at P30 either $Crx^{Rip/+}$ mice, a model of Leber Congenital Amaurosis, or Tg(CRX^{R41W}) mice, carrying the human CRX^{R41W} mutation causing cone dystrophy. The effects on CRX-independent RD was also tested in rd10 mice by injecting at P14. The efficacy was assessed by immunohistochemistry, electroretinogram (ERG) and using a Dark/Light box test.

Results: AAV-CRX injection led to specific expression of CRX in photoreceptors with no toxicity. Three months after subretinal injection in $Crx^{Rip/+}$ mice, we observed: i) a rescue of rod and cone opsin expression, ii) a rescue of outer segment formation, iii) some degree of ERG response whereas it remained flat in controls iv) a fully restored behavioral response to light stress. Tg(CRX^{R41W}) characterization revealed a dose-dependent deleterious effect of CRX^{R41W} expression. Indeed, heterozygous Tg(CRX^{R41W}) carrying a single insertion displayed a functional retina while homozygous Tg(CRX^{R41W}) exhibited reduced retinal function after 3 months. These results support the relevance of increasing the amount of CRX^{WT} to counteract the dominant-negative effect of mutant CRX. The beneficial effects of AAV-CRX were observed in Tg(CRX^{R41W}) mutant mice with a cone only retina ($Nrl^{-/-}$ background). Finally, we showed that AAV-CRX has also a beneficial effect on CRX-independent RD by preserving rod photoreceptors in rd10 mice.

Conclusions: Overall, our gene therapy approach shows promising results for treating CRX-associated RDs, as well as CRX-independent retinopathies. It also highlights the potential interest of gene therapy to treat patients with RD carrying dominant-negative mutations.

CONTROL ID: 3713028

SUBMITTER (NAME ONLY): Aaron Brown

TITLE: Iterative Machine Learning: A Test Case for the Detection of Disc Hemorrhage

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Brown, K. Esquenazi, A. Harris, L.R. Pasquale, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|H. Cousins, Biomedical Data Science, Stanford University, Stanford, California, UNITED STATES|A.C. Brown, Y. Kim, C. Cousins, L.R. Pasquale, Department of Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|T. Elze, Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M.A. Coote, Glaucoma Research Unit, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Google AutoML, an online machine learning platform, has demonstrated comparable performance to hard-coded deep learning (DL) algorithms for the identification of pathology in fundus photos. Here we explore whether a small labeled training set can be leveraged to train AutoML to detect disc hemorrhages (DHs) in a large unlabeled test set using an iterative approach to prepare data with reduced time burden.

Methods: A retrospective analysis of fundus photographs of different resolutions and sources centered on the optic disc obtained from the Ocular Hypertension Treatment Study, New York Eye and Ear Infirmary of Mount Sinai, Massachusetts Eye and Ear, Thessaloniki Eye Study, and GONE datasets were included. Ground truth was established by the consensus of grades from two masked glaucoma specialists. We trained AutoML to distinguish DH positive and DH negative images. Predictions for a held-out validation set were obtained in batches. Positive predictions over a confidence threshold of 0.9 confirmed by a glaucoma specialist were added to the positive dataset to retrain the model. This process was repeated for the entire held out dataset. Area under the receiver operator curve (AuROC) for the AutoML model and a custom model based on the Inception v3 architecture were calculated.

Results: Baseline DH identification model was trained using 391 case and 990 control images. A held-out validation set of 80,000 images was partitioned into 8 batches. Classifications by the baseline model of the 1st batch yielded 2521 positives (out of 13530) with 51 true positives on review (Positive Predictive Value (PPV) = 0.020). AutoML Model v2 included these 51 positive images, testing with a 2^{nd} batch produced 1182 positive classifications (of 10912) with 27 positives on manual review (PPV = 0.023). Repeating this process for 8 iterations identified 275 DH positive images. The PPV of the final AutoML Model was 0.400 (Fig 1). The AutoML and Inception models achieved AuROCs of 0.79 and 0.64, respectively, in the final imageset. False positive examples depict challenges in learning the DH phenotype (Fig 2).

Conclusions: DHs are rare events in glaucoma patients and somewhat resistant to machine learning. Iterating on a baseline model using a large held out dataset led to a 20-fold increase in PPV.

CONTROL ID: 3713029
SUBMITTER (NAME ONLY): Ryan Man
TITLE: Identifying Content for an Item Bank to Measure the Quality-of-Life Impact of Myopia
SESSION TITLE: Refractive Error and Social Determinants of Vision Function
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: R. Man, K. Goh, E. Lee, A. Aranvindhan, A.T. Gan, M. Ang, Q.V. Hoang, C. Wong, S. Saw, E.K. Fenwick, E.L. Lamoureux, Singapore Eye Research Institute, Singapore, SINGAPORE|R. Man, M. Ang, C. Wong, S. Saw, E.K. Fenwick, E.L. Lamoureux, Duke-NUS Medical School, Singapore, SINGAPORE|Q.V. Hoang, Department of Ophthalmology, Columbia University, New York, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: Current myopia quality-of-life (QoL) questionnaires are burdensome to administer, have complicated scoring systems, and primarily assess vision functioning deficits. To address these issues, we are developing a myopia-specific QoL item bank (IB) that will be operationalized using a computerized adaptive testing (CAT) system to optimize administration and scoring. We report on the content generation and item refinement phases of this myopia specific IB; and compare its content with published literature.

Methods: Myopia-specific QoL domains and items were generated from: (1) existing visual and refractive-error specific questionnaires; (2) published articles; and (3) semi-structured interviews with patients with myopia (n=39); and healthcare practitioners (clinicians, optometrists, psychologists, and researchers; n=9) recruited from the Singapore National Eye Centre between 2020 and 2021. Following thematic analysis, items were systematically refined and subsequently tested using cognitive interviews with 24 additional patients across the myopia severity spectrum.

Results: Of the 39 participants with myopia (mean ± standard deviation age: 41.4±16.3 years; 76.9% female), 16 (41.0%) were spectacle wearers, 10 (25.6%) wore contact lenses regularly, 18 (46.1%) had undergone myopic refractive surgery, and 1 (2.5%) was on atropine drops. Ten (25.6%) patients had clinically-diagnosed pathologic myopia (PM). Whilst some myopia-specific QoL issues identified have been reported previously, e.g., activity limitation and mobility, others like work anxiety, refractive surgery and PM-related issues were novel. Initially, 912 items within seven independent QoL domains were identified: Activity limitation, Concerns, Emotional, Mobility, Management Comfort, Management Convenience, Management Concern, and Work. Following refinement, 249 items were retained, of which 69 (27.7%) were novel. During cognitive interviews, 14 items underwent amendment to improve clarity.

Conclusions: Our myopia specific IB comprises 7 QoL domains and 249 items, of which over a quarter are new. It will likely provide a comprehensive assessment of the broad impact of myopia and associated long-term complications, and the patient-centred effectiveness of myopia treatment. The IB will now undergo rigorous psychometric testing to generate item calibrations for the validation of a novel myopia CAT.

CONTROL ID: 3713035

SUBMITTER (NAME ONLY): Emilie van der Sande

TITLE: Atropine reduces axial elongation in a mouse model of syndromic myopia

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Atropine, a non-selective muscarinic receptor antagonist, is often used as a treatment for common childhood myopia, but it is unclear whether it is useful for the treatment of syndromic myopia. Here, we evaluate the effect of atropine on the regulation of eye growth in mice with a Foxg1-conditional knockout of low-density lipoprotein receptor-related protein 2 (Lrp2), which causes Donnai-Barrow syndrome characterized by extremely high myopia in humans.

Methods: Male (M) and female (F) C57BL/6 mice homozygous for both $FoxG1^{cre}$ and $Lrp2^{fl}$ (M n=9; F n=7) and littermates negative for $FoxG1^{cre}$ (M n=7; F n=4) were housed under full-spectrum 200 lux illumination (18h day/6h night). From postnatal day (P) 30 to 56, left eyes received one droplet 1% atropine sulfate daily, while right eyes received saline. Ocular biometry including axial length was measured using SD-OCT in anesthetized mice at P28, P30, P42 and P56.

Results: At P28, KO mice had significantly larger axial length (AL), compared to littermate controls (means±SEM KO M: 3269±38, Ctr M: 3166±19; KO F: 3262±50, Ctr F: 3102±30 µm; both M and F, $p<0.05$, unpaired t-tests). Atropine reduced AL growth significantly in both KO and Ctr mice (dAL, atropine minus saline treatment: KO M: -26±9; Ctr M: -42±7; KO F: -55±8; Ctr F: -62±4 µm, $p<0.01$ for treatment, MANOVA), which was mainly caused by a reduction of anterior chamber depth growth (KO M: -54±6; Ctr M: -42±6; KO F: -51±3; Ctr F: -47±3, $p<<0.0001$ for treatment, MANOVA). Lens thickness and vitreous chamber depth were not significantly affected by atropine.

Conclusions: Atropine reduced axial elongation in a mouse model lacking Lrp2, a protein which is directly implicated in controlling growth cues of the eye. This suggests that the mechanism of action of atropine is robust and that this treatment could be beneficial in humans with a syndromic cause of myopia.

CONTROL ID: 3713039

SUBMITTER (NAME ONLY): Lawrence Chan

TITLE: Characterization of Polymicrobial and Antibiotic-Resistant Infectious Keratitis in a County Hospital Setting

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chan, J.B. Lopez, M. Saifee, M. Yung, M.F. Chan, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|M.F. Chan, Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Infectious keratitis is an important cause of visual impairment worldwide, particularly in low-income communities. This study examines the social risk factors associated with polymicrobial infection and multidrug resistance, the spectrum of pathogens, and the impact on outcomes in a county hospital setting.

Methods: We performed a retrospective case-control study of patients at the Zuckerberg San Francisco General Hospital treated from 2010 to 2021 for infectious keratitis in inpatient and outpatient settings. Data on social, medical, and psychiatric risk factors were collected. Outcomes included final visual acuity, ulcer size, and time to resolution. Microbiological culture data and antibiotic sensitivities were documented. Multivariable logistic and linear regression analyses were performed.

Results: Of a total of 174 patients with infectious keratitis, 16.6% (n=29) of patients had polymicrobial infections confirmed by culture. The most common organisms in polymicrobial infections included coagulase-negative staphylococci (55%), coryneform bacteria (45%), Moraxella spp. (41%), Streptococcus viridans (21%), and Staphylococcus aureus (14%). 6.9% of all patients (12 of 174) were started on antibiotic eye drops prior to presentation to ophthalmology; of these patients, none had polymicrobial infections on culture, and there was no increased risk of multidrug-resistant organisms. Unhoused patients were 2.86 times more likely to present with a polymicrobial infection (P=0.047). HIV positivity, contact lens use, recreational drug use, smoking, and multiple corneal cultures were not associated with an increased risk of polymicrobial infection. The presence of a polymicrobial infection did not significantly impact ulcer size, final visual acuity, time to resolution, and need for tectonic keratoplasty/gluing.

Conclusions: Homelessness correlates with increased risk of polymicrobial infection, which supports initiating broad antibiotic coverage in this population. Initiation of antibiotic eye drops by a non-ophthalmology provider did not increase risk of polymicrobial infections. Polymicrobial infection did not significantly worsen clinical outcomes.

CONTROL ID: 3713040

SUBMITTER (NAME ONLY): Felix Yemanyi

TITLE: REV-ERBα regulates retinal function and protects against retinal degeneration in experimental retinitis pigmentosa

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Yemanyi, C. Liu, S. Huang, K. Bora, M. Maurya, A.K. Blomfield, Z. Fu, J. Akula, J. Chen, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: About 50% of retinitis pigmentosa (RP), an inherited retinal degenerative disease, results from mutations in >60 genes, yet gene therapy exists for only 1% of RP patients. Broad-spectrum therapies regardless of the RP-causing gene or other unknown factors are needed. REV-ERBα is a cytoprotective nuclear receptor that regulates development, metabolism, inflammation, and oxidative stress. We sought to determine whether REV-ERBα regulates retinal physiology in Rev-erbα-deficient (Rev-erbα$^{-/-}$) mice, and whether REV-ERBα activation could ameliorate photoreceptor loss in the rd10 mouse model of RP.

Methods: Localization and relative abundance of Rev-erbα were determined in C57BL/6J mice retinas via immunohistochemistry and laser capture microdissection. The role of Rev-erbα in retinal function and metabolism was analyzed in wild-type (WT) vs. Rev-erbα$^{-/-}$ mice retinas via electroretinography (ERG), Seahorse assay, microarray analysis, and RT-qPCR. The role of Rev-erbα in 661W cell (photoreceptor) metabolism following its knockdown was determined in vitro. Rd10 mice were injected intraperitoneally with REV-ERB agonist (SR9009) or vehicle from postnatal day (P) 7 to P30; retinal structure, apoptosis, and visual function were evaluated via histology, TUNEL staining, Western blotting, and scotopic ERG. Effect of SR9009 on photoreceptor cell survival and metabolism was determined in vitro.

Results: Rev-erbα localizes throughout the mouse retina and its transcripts are more enriched in the photoreceptor layer than the inner retina. Rev-erbα$^{-/-}$ mice showed markedly dampened visual function in ERG relative to WT, associated with reduced mitochondrial respiration, and without retinal thinning. Microarray expression from the Rev-erbα$^{-/-}$ vs. WT retinas also demonstrated altered expression of genes involved in metabolism, signal transduction and molecular transport. Rev-erbα knockdown in 661W cells supported its role in photoreceptor metabolism, signal transduction and molecular transport. Activation of REV-ERBα in rd10 mice significantly protected against photoreceptor thinning, apoptosis, and loss of visual function. Modulation of REV-ERBα in 661W cells corroborated its role in improving photoreceptor cell survival and metabolism.

Conclusions: These data suggest REV-ERBα regulates retinal function and metabolism, and may be activated to slow RP progression by promoting photoreceptor survival.

CONTROL ID: 3713041

SUBMITTER (NAME ONLY): Muhammad Hassan

TITLE: Assessment of Structural and Volumetric Choroidal and Retinal Indices in Eyes with Vogt Koyanagi Harada Disease

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare retinal and choroidal indices among patients with stable Vogt Koyanagi Harada (VKH) disease without macular edema and post-resolution of the macular edema.

Methods: Patients with a confirmed diagnosis of stable VKH between 2009-2017 were divided into two groups based on the absence of macular edema (Group 1) and history of resolved macular edema (Group 2). SD-OCT (Heidelberg Spectralis®) was utilized to capture 5-line High Definition (HD) raster scan with Enhanced Depth Imaging. Semi-automated segmentation tool of Heyex Software Version 6.2 was utilized to segment the retinal layers into 1) Full Retina (FR); 2) Retinal Nerve Fiber Layer (RNFL); 3) Ganglion Cell Layer (GCL); 4) Inner Plexiform Layer (IPL); 5) Inner Nuclear Layer (INL); 6) Outer Plexiform Layer (OPL); 7) Outer Nuclear Layer (ONL); 8) Photoreceptor Layer (PRL); 9) Retinal Pigment Epithelium (RPE). A manual segmentation of choroid was also performed. Similar segmentation was also performed on 22 normal eyes (11 Patients).

Results: Forty-two eyes (22 patients) with VKH disease were enrolled. 32 eyes were in Group1 and 10 eyes in Group 2. Mean of average thickness and volume for the segmented layers were compared between the two groups and between the groups and controls (Table 1 and 2). The RNFL and INL layers were significantly thicker and voluminous and ONL and PRL were thinner with lower volume in Group 2 compared to other groups. Both Study groups showed thickening and an increase in volume of OPL compared to normal eyes. The RPE layer was thickened with volumetric expansion in Group 1 but thinned out with a decrease in volume in Group 2. The mean central (1mm) choroidal thickness, average choroidal thickness, and choroidal volume were all significantly higher in group 1 compared to group 2 and controls. The choroidal indices were lower in group 2 compared to controls but failed to reach statistical significance.

Conclusions: VKH disease has a significant effect on different retinal layers despite having minimal impact on the FRT. Furthermore, it has a pronounced effect on both choroidal thickness and volume. Macular edema is a very rare complication of VKH and the significant changes in choroid of patients with macular edema underscores the role of choroidal vasculature abnormalities as underlying pathogenesis.

CONTROL ID: 3713042

SUBMITTER (NAME ONLY): Xiufeng Zhong

TITLE: Spatiotemporal development, transcriptome profile and enrichment of Müller glial cells in hiPSC-derived retinal organoids

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhong, R. Ning, D. Zheng, B. Xie, State Key Laboratory of Ophthalmology, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|J. Xu, B. Jiang, Key Laboratory of Brain Function and Disease, Faculty of Forensic Medicine, Sun Yat-sen University Zhongshan School of Medicine, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: The aim of this study is to clarify the developmental characteristics and transcriptome profile of Müller glial cells (MGCs) in an human induced pluripotent stem cells (hiPSCs)-derived retinal organoids (ROs), and establish protocols to enrich these cells, thus to facilitate the basic and translational study of MGC-related retinal diseases.

Methods: hiPSCs were maintained with mTeSR1, and differentiated into ROs according to our published protocol. ROs were sequentially collected to evaluate the temporal and spatial development of MGCs in ROs . Neural retina (NR) of ROs were collected and dissociated into single cells to amplify MGCs under adherent culture. Optical microscope was used to observe the morphology of the passaged MGCs, RNA-Seq and immunofluorescence staining to detect the expression of specific MGCs markers, and electronic microscopy to observe the ultrastructure of MGCs. The functional features of MGCs were also evaluated by the whole cell membrane clamp.

Results: In ROs, retinal progenitor cells (RPCs) progressively differentiated into SOX9+ Ki67- MGC precursors during differentiation day (D) 60 to D90, while mature MGCs markers CRALBP and GS did not appear until D120. Specific transcriptome profiles of MGCs were revealed by RNA-seq with ROs. Cells isolated from ROs aged older than D120 was an optimal source for the enrichment of iMGCs with high purity and expansion ability. They had typical features of human MGCs in morphological, molecular and functional aspects, and could be passaged serially at least 10 times, yielding large number of cells in a short period. The transcriptome pattern of the expanded MGCs was also revealed. MGC-related genes such as VIM, CRYAB, CD44, DBI and CCL2 were enriched in the passaged MGCs, while other retinal cell markers were down-regulated. SEM and TEM showed that MGCs had many microvillus projections, large nucleus with obvious nucleoli. The whole cell membrane clamp showed MGCs could depolarize in response to L-glutamate puff.

Conclusions: This study firstly clarified the timecourse of human MGC development in the RO model, where the MGCs could be enriched and expanded. The transcriptome pattern of MGCs was also revealed. These findings will pave the way for downstream investigation and application of MGC related retinal disorders.

CONTROL ID: 3713043

SUBMITTER (NAME ONLY): POONAM NAIK

TITLE: The Impact of Age and Sex on the host immune response in patients with Infectious endophthalmitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Endophthalmitis is a severe inflammatory disease following ocular surgery, or penetrating ocular trauma, associated with irreversible vision loss. Despite acknowledging the impact of biological variables along with the antibiotic susceptibility profile of the infecting agent on various diseases, its effect in human endophthalmitis is not fully elucidated. We therefore studied the impact of age and sex on cytokine production in patients with culture proven bacterial endophthalmitis

Methods: In this cross-sectional study, a total of 93 patients were stratified into three groups according to their age: A (0-30 years), B (31-54 years) and C (>55 years) and 20 patients with non-infectious retinal disorders as controls were included. Expression of IL-6, IL-10, IL-1β, IL-8, IL-17, TNF-α and LCN-2 were analysed in the vitreous fluids of these patients by magnetic bead based multiplex immunoassay (MILLIPLEX, Merck) and correlated with the demographics and its antibiotic susceptibility data.

Results: Patients in Group B, aged between 31-54 years exhibited higher IL-6, TNF-α, IL-17. On the contrary, group A showed higher level of IL-1β ($p < 0.05$), IL-10 ($p = 0.04$) and IL-8. LCN-2 was found be higher ($p = 0.01$) in the older age group (group C) only. Although IL-1β, IL-6 and IL-10 levels were comparatively higher in female patients, only IL-8 was found to be statistically significant ($p = 0.009$). Notably, patients infected with antibiotic resistant pathogens exhibited higher IL-1β, IL-8 and TNF-α ($p < 0.05$) compared to antibiotic-susceptible group indicating higher inflammatory response irrespective of age and sex.

Conclusions: Our study suggests that immunosenescence and drug resistant have a pivotal role in the incidence of bacterial endophthalmitis. Further work would focus on correlating these variables with systemic status and clinical outcome. The results of this study would help form strategies to differentially engage signalling pathways in the design of immunotherapeutic approaches for better prognosis in aging and drug-resistant endophthalmitis.

CONTROL ID: 3713044

SUBMITTER (NAME ONLY): Gareth Lingham

TITLE: Machine learning-estimated axial length is better than spherical equivalent for identifying higher-risk myopic eyes

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the performance of a machine learning-based algorithm in estimating axial length (AL) based on refraction and demographic data.

Methods: A machine learning-based algorithm (AL estimator) was trained using age, sex, spherical refractive error, astigmatism and corneal radius of curvature data derived from 4403 participants (aged 6-22 years) of Irish and Korean epidemiological studies. AL estimator performance was tested using right eye AL data from participants involved in myopia treatment trials (three Irish, one Australian). Bland-Altman statistics and linear regression were used to compare estimated and actual AL. Receiver operator characteristic analysis was used to assess the ability of the AL estimator to identify children with a high AL (≥26mm) and fast progressors (≥0.3mm axial elongation in 12 months), compared to spherical equivalent (SE).

Results: The AL estimator was tested on 507 participants (n=354, 69.8% Irish), of whom 437 (86%) had 12-month follow-up data [mean age: 11.3 years, range: 6-17; female: 304 (60%); mean AL: 24.8mm, range: 22.1-28.9]. Using baseline visit data, the mean difference in AL (actual – estimated) was -0.07mm (95% limits of agreement [LOA]: -0.97, 0.83; absolute mean error=0.36; R^2=0.80). When assessing 12-month AL progression, the mean difference between actual and estimated AL change was -0.001mm (LOA: -0.31, 0.31; absolute mean error=0.12; R^2=0.57). The AL estimator performed worse for Australian compared to Irish participants (respective mean errors: AL estimate=-0.16 vs -0.03mm, p=0.003; AL change=-0.04 vs 0.02, p=0.001). Compared to SE alone, the AL estimator was better at identifying eyes with an AL ≥26mm (area under the curve [AUC]: 0.97 vs 0.83) and eyes that progressed ≥0.3mm over 12 months (AUC: 0.90 vs 0.85; Figure 1).

Conclusions: In this cohort of myopic children, the machine learning model was able to provide a reasonably accurate estimation of actual AL. Importantly, the AL estimator demonstrated high diagnostic performance in identifying individuals with long AL and those who exhibited excessive axial elongation. Where biometry is unavailable, the AL estimator may represent a useful clinical tool for identifying children at risk of axial growth-related complications of myopia.

CONTROL ID: 3713045
SUBMITTER (NAME ONLY): Zeljka Smit-McBride
TITLE: Exosomes uptake by human retinal pigment epithelium cells
SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Z. Smit-McBride, R. Kolala, E. Lindgren, L. Morse, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|J. Anderson, Otolaryngology, University of California Davis, Davis, California, UNITED STATES|A. Grodzki, Molecular Biosciences, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|Z. Smit-McBride, R. Kolala, E. Lindgren, Vitreoretinal Research Lab, University of California Davis, Davis, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: The purpose of these experiments was to test and optimize uptake of mesenchymal stem cells (MSC) exosomes by human retinal pigment epithelium (ARPE-19) cell line utilizing the natural uptake mechanisms of exosomes by ARPE-19 cells.

Methods: We used human mesenchymal stem cells (MSC) exosomes labeled using ExoGlow (red-fluorescent dye) or human embryonic kidney 293 cells (HEK-293) exosomes X-Pack GFP-loaded (green-fluorescent protein). The concentrations of exosomes and the incubation period of transfected ARPE-19 were varied to determine which conditions allow for the highest transfection rate. ARPE-19 were labeled using an Oregon Green Phalloidin or CellTrace calcein red/orange AM and were imaged using an Olympus FV3000 confocal and ImageXpress Micro XL high-content microscopes. Assays were done in 96-well plates with four replicates, and plates were scanned on the ImageXpress Micro XL high-content screening system (Molecular Devices) at UC Davis IDDRC Biological Analysis Core. Additional images were obtained using a confocal microscope Olympus FV3000.

Results: Results indicate that ARPE-19 cells were able to uptake exosomes from two different heterologous sources, human mesenchymal stem cells (MSC) and human embryonic kidney 293 (HEK-293) cells. The highest transfection rate was achieved with 0.20 ug of exosomes added to 1x10^4 ARPE-19 cells/well, after a 5-hour incubation period. Imaging was best within the first 30 hours after exosomes were added to ARPE-19 cells. Signal diminished significantly after 30 hours. A higher quantity of exosomes did not equate to a higher transfection rate.

Conclusions: Exosomes are mediators of long-distance communication among different tissue and cells in the body. Exosomes carry cargo (proteins, mRNA, and microRNAs) to communicate messages to target tissues or cells. Our lab has previously identified a set of microRNAs (miRNAs) dysregulated in DR patients' ocular fluids, that may play a role in diabetic retinopathy (DR) pathogenesis. Our results strongly suggest that exosomes were quickly taken up by naïve recipient ARPE-19 cells by natural mechanisms. Our long-term goal is to develop miRNA-based therapies for DR using exosomes as natural carriers of miRNAs.

CONTROL ID: 3713046

SUBMITTER (NAME ONLY): Miguel Seabra

TITLE: TFEB-mediated reduction of autofluorescent granule load in retinal pigment epithelium

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Seabra, A.S. Falcao, M. Lopes-da-Silva, P. Antas, A.C. Fradinho, L. Lemos, S. Tenreiro, CEDOC, Nova Medical School, Lisbon, PORTUGAL|M. Seabra, C. Futter, Development, Aging and Disease, UCL Institute of Ophthalmology, London, UNITED KINGDOM|T. Ciossek, P. Nicklin, Research Beyond Borders, Boehringer Ingelheim, Biberach, GERMANY|

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ABSTRACT BODY:

Purpose: We are exploring pathways for autofluorescent granule (AFG) resolution by retinal pigment epithelium (RPE) cells to identify new therapeutic targets.

Methods: We are using an experimental model of RPE monolayers in culture where there is accumulation of AFGs similar to lipofuscin in vivo, after a single pulse of photoreceptor outer segments (POS). We previously observed that lysosomal dysfunction results in incomplete POS degradation and AFG accumulation. Here we are exploring gene therapy using adeno-associated viruses (AAV) and/or pharmacological approaches to target pathways that promote lysosomal function and biogenesis leading to AFGs reduced formation or its resolution, accessed by a variety of light and electron microscopical techniques, flow cytometry and western blot.

Results: We show that AAV-mediated over-expression of transcription factor EB (TFEB) reduces the load of AFG accumulation in RPE monolayers. Use of pharmacological inhibitors of mTOR leading to activation of TFEB, such as rapamycin, as well as other mTORC1 inhibitors, also led to a decrease in POS-dependent AFG accumulation in RPE.

Conclusions: These results suggest that viral or pharmacological approaches acting on the mTOR/TFEB axis may be beneficial in early/intermediate cases of AMD to delay progression of the disease.

CONTROL ID: 3713048

SUBMITTER (NAME ONLY): Megumi Fukushima

TITLE: Comparison of Subjective Ocular Refraction with Binocular Simultaneous Looking-in Type and Real Space

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We investigated the consistency of the subjective ocular refraction between Binocular Simultaneous Looking-in Type (Chronos, Topcon) and real space.

Methods: Twenty-eight healthy volunteers (21.2 ± 1.4 years old) participated in this study. The objective ocular refraction in all subjects was achieved by a conventional autorefractometer that measures eyes one by one (KR-800, Topcon Corp.) and Chronos. The subjects were undergone four times of visual acuity tests in four conditions randomly: performing the subjective refraction test with the Chronos value using the Chronos (Condition i); performing the test with the Chronos value using the real space (TCU-600, Fuji Kogaku Co., Ltd.) (Condition ii); performing the test with the KR-800 value using the Chronos (Condition iii); and performing the test with the KR-800 value using the real space (Condition iv). In both the real space and Chronos, the subjective refraction test distance was set at 5.0 m. The best-corrected subjective ocular refraction was defined as 0.18 logMAR. The subjective ocular refraction was converted to spherical equivalent (SE). Furthermore, astigmatism was transformed into a power vector. Then, the SE and astigmatism were compared between Chronos (merged Conditions i and ii) and real space (merged Conditions iii and iv).

Results: The SE was significantly and negatively greater in Chronos (−3.68 ± 2.83 D) than in the real space (−3.37 ± 2.85 D) ($P < 0.001$). No significant difference in J0 and J45 was observed between Chronos (J0, 0.28 ± 0.42 D; J45, −0.01 ± 0.18 D) and real space (J0, 0.29 ± 0.42 D; J45, −0.04 ± 0.16 D).

Conclusions: Chronos measured with an error of less than 0.50 D compared with the real space. We considered that Chronos is valuable for screening refractive errors and visual acuity in eye checkups.

CONTROL ID: 3713050

SUBMITTER (NAME ONLY): Ester Reina-Torres

TITLE: The relationship between pressure-dependent changes in outflow facility and dimensional changes in the anterior segment during perfusion of enucleated mouse eyes

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Reina-Torres, J. van Batenburg-Sherwood, D.R. Overby, Bioengineering, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Outflow facility (C) is typically determined by perfusing eyes over multiple pressure steps while measuring the flow rate (Q) into the eye and intraocular pressure (P), with C given by C=Q/P . In enucleated mouse eyes perfused via the anterior chamber (AC), C tends to increase with P. Yet in other species, C reportedly declines with P. In mice, the P-dependent rise in C may be related to the phenomenon of AC deepening that occurs when AC pressure exceeds that in the posterior chamber, causing retrodisplacement of the iris and lens that applies traction on the outflow pathway. The aim of this project was to assess whether dimensional changes associated with AC deepening are correlated with P-dependent changes in C in enucleated mouse eyes.

Methods: To visualise dimensional changes in the AC, enucleated eyes were imaged under a stereomicroscope with the anterior-posterior axis within the focal plane (15x, 1fpm). We examined two mouse strains: C57BL/6J (n=7) and FVB/N (n=5). We measured Q into the AC as P was increased stepwise from 4.5 to 21mmHg using iPerfusion. The last image from each step was used to estimate AC depth (ACD) and pupillary diameter (PD). We examined correlations between C, P, ACD and PD by linear regression (Bonferroni correction).

Results: P-dependent changes in C were more pronounced in C57BL/6J mice relative to FVB/N (400 vs 61% relative increase in C from first to last step). ACD was tightly correlated with P in both strains (R^2=0.8, R^2=0.7; p<0.001), while the relationship between PD and P was negligible (R^2=0.05, R^2=0.1). In C57BL/6J, changes in C were correlated with both ACD and PD (R^2=0.7, R^2=0.3; p<0.001). However, in FVB/N mice, changes in C were correlated with only ACD (R^2=0.5; p<0.001) and not PD (R^2=0.01; p=0.4).

Conclusions: These results reveal that in response to increasing AC pressure, there is significant deformation of the anterior segment in enucleated mouse eyes, including retrodisplacement of the lens and, to a lesser extent, expansion of the iris and widening of the pupil. These results suggest that the iris and lens both may apply traction to the outflow pathway to increase C, but the lens displacement appears to have a stronger effect on facility. Mouse strain differences, which exhibit different P-dependent changes on C despite similar dimensional changes, is worth further investigation.

CONTROL ID: 3713051

SUBMITTER (NAME ONLY): Pirro Hysi

TITLE: Performance of polygenic risk scores computed using sets of markers cosmopolitan for the prediction of glaucoma in ethnically diverse populations

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.G. Hysi, M. Simcoe, C.J. Hammond, King's College London, London, London, UNITED KINGDOM|M. Simcoe, A. Khawaja, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|A. Khawaja, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, England, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Aggregation of single-marker information into polygenic risk scores (PRS) is a popular glaucoma risk-prediction approach, but its implementation and utility is impeded by the variability of disease genetic architectures in ethnically diverse populations. The purpose of this study was to evaluate the factors that affect the performance of PRS built on genome-wide association study (GWAS) results from cohorts of predominantly European ancestry in populations of African and admixed genetic heritage.

Methods: Variable selection using Elastic Net models were conducted on markers previously reported as associated with glaucoma in a large GWAS among subjects participating in the UK Biobank cohort. The predictive models built on the selected markers in ethnically homogeneous groups were tested both in UK Biobank subjects (through a 80:20 holdout cross-validation) and in a fully independent cohort of European, African-Caribbean and “other” glaucoma cases and controls (576:287, 298:194 and 124:79, respectively) genotyped on a Human Omni Express Exome 8v1-2 BeadChip (Illumina) and imputed on 1000 Genomes haplotypes.

Results: Our optimized Elastic Net models effectively built sufficiently sparse pan-ancestral models that performed reasonably well, even in populations of non-European descent, including UK participants of African-Caribbean (Area Under the ROC Curve, AUC=0.65-0.71). These models performed better in the UK Biobank than in the smaller case-control cohorts (AUC difference of 0.05-0.10 in subjects of African and European ancestry), suggesting that the predictive performance of the PRS is in part affected by genotyping coverage and quality. Other factors likely affecting performance include similarity between training and testing datasets, levels of genetic admixture, and models shrinkage and scaling of parameters.

Conclusions: It may be possible to adapt the current European-driven information for effective PRS-based prediction in multiethnic populations. Future predictive PRS-based models will benefit from more ethnicity-specific GWAS information, but also from finer mapping of risk-associated genetic loci.

CONTROL ID: 3713052

SUBMITTER (NAME ONLY): Rahul Patil

TITLE: Unique structural differences between thin cornea and asymmetric keratoconus quantified using Polarization Sensitive – Optical Coherence Tomography (PS-OCT)

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.P. Patil, R. Narasimhan, Y. Patel, P. Khamar, R. Shetty, A. Sinha Roy, Narayana Nethralaya Foundation, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: To study changes in the birefringent properties of human cornea across healthy, thin corneas (< 500 µm), asymmetric and clinical KC.

Methods: In this study, the birefringent properties of 40 eyes from 20 subjects divided across 4 groups (healthy, thin, asymmetric KC and clinical KC corneas) were measured using our custom-built ultrahigh-resolution PS-OCT. Groups-1, 2 and 4 consisted of 10 eyes from 5 subjects each. Group-3 consisted of 5 eyes that showed normal topographical features, while their fellow eye showed classical KC features were put in Group-4 along with eyes having bilateral clinical KC. To achieve a near limbal-to-limbal scan field with uniform signal strength throughout the cornea a conical scan setup was incorporated in the PS-OCT design. Phase retardation (PR) enface maps from the posterior surface of the cornea were generated to obtain a succinct representation of the corneal fibril distribution.

Results: Figure-1 shows the PR enface maps of representative cases from each group and their corresponding axial curvatures (AC) maps. Columns 1 and 2 represent maps from a healthy cornea and a thin cornea. Columns 3 and 4 are from the same subject, with OD being the KC eye and OS being the contralateral eye having normal topography. While column 5 constitute the clinical KC eye. PR enface maps of healthy corneas showed the preferential arrangement of collagen fibrils with least retardation in apex and anchoring fibrils in the periphery. Thin corneas mimicked healthy eyes in collagen fibrillar arrangement. Asymmetric KC eyes followed common definitions of sub-clinical and forme fruste KC, but PR maps from PS-OCT confirmed a near-healthy collagen fibrillar distribution in these eyes. Clinical KC corneas showed large disruptions in collagen fibrillar arrangement at all annular zones ($p<0.05$) with complete loss of peripheral anchoring fibrils.

Conclusions: Distinctive changes in the structural arrangement of collagen fibrillar distribution were observed in KC, thin corneas, and healthy eyes. Spatial variations (zonal analyses) in polarization-sensitive information can assist in effectively minimizing the susceptive, erroneous classifications between healthy and diseased corneas in a clinical setting.

CONTROL ID: 3713053

SUBMITTER (NAME ONLY): Qian Ma

TITLE: Clinical and genetic analysis of Chinese patients with Möbius syndrome

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Ma, Y. Jiao, H. Jia, Q. Chang, D. Wang, Y. Liang, Beijing Tongren Hospital, Beijing, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: Möbius syndrome (MBS) is a rare disease with congenital limitation of ocular abduction and facial weakness, and frequently accompanied by multiple congenital malformations, including orofacial malformations, limb defects and musculoskeletal etc. The study aimed to investigate the clinical and genetic characteristics of Chinese MBS cohort.

Methods: Inclusion criteria were congenital, nonprogressive facial weakness and abduction deficit with full vertical motility and/or hypoplasia of CN6 and CN7 (MRI). All participants underwent standardized ophthalmologic examination, general physical examination, MRI of cranial nerves and WES.

Results: The study enrolled 17 unrelated patients (8 males, 9 females). Nobody had a family history, even if three patients were one of the twins. MRI revealed all patients had the hypoplasia of CN6 and CN7. 65% of patients (n=11, 11/17) showed bilateral facial weakness and the bilateral hypoplasia of CN7. 35% of patients (n=6，6/17) showed unilateral facial weakness (all were left), corresponding MRI revealed 3 of the patients were hypoplasia of left CN7，while the other three cases showed the hypoplasia of bilateral CN7. 82% of patients（n=14，14/17）showed bilateral abduction deficit and the bilateral hypoplasia of CN6. 12% of patients（n=2，2/17）showed unilateral abduction deficit (both were left), corresponding MRI revealed the hypoplasia of CN6, one was left and the other was bilateral. One patient (6%, 1/17) showed left facial weakness and full ocular motility, however, MRI revealed the hypoplasia of left CN7 and right CN6. In our cohort, 15 patients (88%, 15/17) also accompanied by other multiple congenital malformations, including tongue disfunction and abnormal development (n=13), dysarthria (n=7), high arched palate (n=6), limb defects (n=4) and poor listening (n=2). No causative mutations were found in REV3L, PLXND1 and other known pathogenic genes of CCDDs.

Conclusions: The genetic contributors to our Chinese MBS cohort were elusive. In our MBS cohort, facial weakness and abduction defects, as well as the hypoplasia of CN6 and CN7, were often bilateral involvement, and in cases with unilateral involvement, the left seemed to be more easily involved. Some atypical MBS patients showed facial weakness and full ocular motility, however, MRI revealed the hypoplasia of both CN6 and CN7, so we propose using MRI as an effective examination to obtain accurate clinical diagnosis.

CONTROL ID: 3713054

SUBMITTER (NAME ONLY): Emily Tan

TITLE: Do families prefer gaming to patching? A qualitative study on experiences and preferences with amblyopia treatment.

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Tan, A. Kadhum, H.J. Simonsz, S.E. Loudon, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|A. Treur, J. Bruijning, Hogeschool Utrecht, Utrecht, Utrecht, NETHERLANDS|M.V. Joosse, HMC Westeinde, Den Haag, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To explore parents' experiences and preferences with dichoptic action video gaming or patching as amblyopia treatment. In addition, information needs from parents to support patient participation in clinical decision making was investigated.To explore parents' experiences and preferences with dichoptic action video gaming or patching as amblyopia treatment. In addition, information needs from parents to support patient participation in clinical decision making was investigated.

Methods: In a prospective Randomized Clinical Trial (NCT 03767985) newly diagnosed children with amblyopia were recruited. Visual Acuity (VA) was measured using the crowded tumbling E-chart. After informed consent they were randomized to patching therapy: 2 hrs/day; compliance was monitored electronically using the Occlusion Dose Monitor; or dichoptic video game therapy using VR goggles: 1 hr/wk under direct supervision. Following completion, a qualitative study using semi-structured interviews was carried out. The parents of children who fulfilled their 6 weeks follow-up measurement were eligible for participation. The interviews were audio-recorded and transcribed verbatim. The data were analyzed thematically using Braun and Clarke's approach.

Results: So far, parents of 10 children have been interviewed. Three themes have emerged from the data in both the patching and gaming group: 1) misunderstanding the diagnosis of amblyopia and its treatment, 2) the need to establish a routine and 3) the influence of the child's age in explaining the need for treatment and child's participation with treatment. In the gaming group, parents reported the feeling of not being responsible for carrying out treatment themselves as a positive element. In the patching group parents experienced the treatment as flexible and easy to understand.

Conclusions: Despite the differences, parents described the efficiency and the effect of treatment as the most important aspects in choosing the sort of amblyopia treatment. However, they preferred to leave the choice of treatment to the professional.

CONTROL ID: 3713056

SUBMITTER (NAME ONLY): Nicholas Owen

TITLE: BMPR1B identified as a novel human ocular coloboma gene through cross-species meta-analysis

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Owen, M. Toms, R.M. Young, J. Eintracht, H. Sarkar, M. Moosajee, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|B. Brooks, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Moosajee, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|.. Genomics England Research Consortium, William Harvey Research Institute, Queen Mary University of London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Ocular coloboma arises from genetic or environmental perturbations which inhibit optic fissure fusion in early eye development. Despite high genetic heterogeneity, 70-85% of patients remain molecularly undiagnosed. We report BMPR1B as a novel causative gene using cross-species comparative meta-analysis.

Methods: Evolutionary conserved differentially expressed genes were identified through in silico analysis of mouse and zebrafish datasets over time points covering optic fissure closure. In situ hybridization, morpholino bmpr1b gene knockdown and human mRNA rescue experiments were performed in zebrafish to confirm spatiotemporal gene expression and phenotype. We interrogated the UK 100,000 Genomes Project for putative pathogenic variants within a cohort of genetically undiagnosed MAC (microphthalmia/anophthalmia/coloboma) probands.

Results: Nine conserved DEGs between zebrafish and mouse were identified. Expression was shown in the optic fissure, periocular mesenchyme cells or ciliary marginal zone. Knockdown of bmpr1b revealed a coloboma and microphthalmia phenotype. Novel pathogenic variants in BMPR1B were identified in 4 unrelated MAC families. We show BMPR1B rescued the knockdown phenotype, however mRNA carrying the patient-specific variants failed. confirming the loss of function impact of the variants on BMPR1B.

Conclusions: We demonstrate the utility of cross-species meta-analysis to identify novel coloboma disease-causing genes, including BMPR1B. There is potential to increase the diagnostic yield for new and unsolved patients, whilst adding to our understanding of the genetic basis of optic fissure morphogenesis.

CONTROL ID: 3713057

SUBMITTER (NAME ONLY): Laure Chauchat

TITLE: Comparison of four commercially available antiglaucoma drugs on the corneal healing process in the ex vivo eye irritation test (EVEIT) model

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chauchat, H. Rebika, C. Guerin, Horus Pharma, FRANCE|C. Panfil, N. Schrage, Aachen Centre Of Technology Transfer In Ophthalmology (ACTO), GERMANY|H. Rebika, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, FRANCE|

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ABSTRACT BODY:

Purpose: Corneal epithelial toxicity and effect on healing process have been already attributed to preservatives or some excipients. The goal of this study was to evaluate the corneal toxicity in high-frequency-application of 4 different latanoprost eyedrops formulated with or without preservatives, and containing more or less excipients with known effects as Macrogolglycerol hydroxystearate 40 (MGHS 40).

Methods: 4 different Latanoprost 0.005% formulations were tested: A. preservative free (PF); B. preserved with benzalkonium chloride (BAC) 0.02%; C. PF with MGHS 40 at 2.5% and D. PF with MGHS 40 at 5%. As references, negative control (-) PF Hyaluronic acid 0.18% eyedrops and positive control (+) BAC 0.02% were used. Eyedrops were applied over three days, six times daily on rabbit corneas cultured on an artificial anterior chamber the Ex Vivo Eye Irritation Test (EVEIT) system. Initially, four corneal abrasions (2.1–3.8 mm2) were induced. All defects were monitored by fluorescein stains and photographs. Corneal integrity (fluorescein permeability) and vitality (lactate and glucose quantification) were controlled during experiments.

Results: Total epithelial healing was observed for test products A, C and (-) at day 3. For test product D, a delayed healing of the initial lesions, not completed on day 3, was noted. As expected, B and (+) show increased and equally pronounced epithelial damage over the observation period. Additionally, the corneal barrier function was significantly affected for B and (+); Also, a higher permeability value of fluorescein was reported for D compared to A, C and (-). Daily quantification of the metabolic activity of each cornea showed an increase in lactate metabolism for B, D and (+). Glucose levels remained in physiological range for all tested items.

Conclusions: Delayed healing process and metabolic stress symptoms were highlighted for test products B and D containing notably BAC 0.02% and MGHS 40 at 5% respectively. BAC is already well known as toxic for ocular surface, and these results confirm EVEIT as an accurate and reproductible ex vivo model. Besides, MGHS 40, excipient with known effects, seems also to induce a concentration dependent corneal toxicity. Therefore, the use of this preservative and this excipient at high concentration in patients with epithelial defects should be a concern for corneal surface.

CONTROL ID: 3713058

SUBMITTER (NAME ONLY): Simon Lowater

TITLE: Non-invasive metabolic and structural retinal markers in patients with giant cell arteritis and polymyalgia rheumatica

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ellingsen, K. Byg, Department of Rheumatology, Research Unit of Rheumatology, Odense University Hospital, Odense, Syddanmark, DENMARK|S. Lowater, J. Wied, J. Grauslund, Department of Ophthalmology, Odense University Hospital, Odense C, Syddanmark, DENMARK|J.K. Pedersen, Department of Rheumatology, Svendborg Sygehus, Svendborg, Syddanmark, DENMARK|T. Ellingsen, Research Unit of Rheumatology, Department of clinical research, University of Southern Denmark, Odense C, Syddanmark, DENMARK|S. Lowater, J. Wied, J. Grauslund, Research Unit of Ophthalmology, Department of clinical research, Odense C, Syddanmark, DENMARK|

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ABSTRACT BODY:

Purpose: Giant cell arteritis (GCA) is a potentially sight threatening disease. Although it is associated with polymyalgia rheumatica (PMR), visual loss is not common in PMR. We performed an observational, cross-sectional study to investigate if retinal oxygen saturation and retinal vessel calibers in GCA- and PMR differed similarly from controls.

Methods: Retinal oximetry was performed with Oxymap T1 (Oxymap, Reykjavik, Iceland) on 20 GCA-patients (n=38 eyes), 18 PMR-patients (n=33 eyes) and 12 controls (n=20 eyes) at Odense University Hospital, Odense, Denmark. Age < 50 years, poor image quality (<6.0) and eyes with neurodegenerative-, severe retinal-, or optic nerve disease were excluded. Images were analyzed with Oxymap Analyzer software 2.5.0 (Oxymap, Reykjavik, Iceland). Cluster Robust Standard Error was used in a linear mixed model regression analysis adjusted for age and sex, to determine the principal outcomes consisting of retinal arteriolar- and venular oxygen saturation, retinal arterio-venular difference and retinal vessel diameters.

Results: Median age (interquartile range) for GCA, PMR and controls were 69.0 years (66.5-76.5), 69.0 years (67.0-72.0) and 75.5 years (71.5-81.0), respectively. According to the age- and sex-adjusted linear mixed model regression, the retinal arteriolar diameters were wider for GCA as compared to controls and PMR as compared to controls (13.4 pixels vs. 12.4 pixels, p=0.02 and 13.5 pixels vs. 12.4 pixels, p=0.04, respectively). There were no differences with respect to retinal venular diameters (17.4 pixels vs. 16.7 pixels, p=0.1 and 17.3 pixels vs. 16.7 pixels, p=0.2, respectively), retinal arteriolar oxygen saturation (92.9% vs. 91.4%, p=0.2, and 93.4% vs. 91.4%, p=0.1, respectively), retinal venular oxygen saturation (53.8% vs. 55.0%, p=0.7, and 52.8% vs. 55.0%, p=0.5, respectively) or retinal arterio-venular difference (39.1% vs. 36.3%, p=0.3, and 40.6% vs. 36.3%, p=0.1, respectively).

Conclusions: Compared to controls, patients with GCA and PMR both had wider retinal arterioles but unaffected retinal venular diameter and retinal metabolism. While this indicates a similar effect on the retinal vascular structure, prospective studies are needed to determine, if these parameters can be used to predict the clinical outcome.

CONTROL ID: 3713059

SUBMITTER (NAME ONLY): Eva Chamorro

TITLE: Daily changes in axial length in response to myopia control spectacles lenses: A pilot study

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Chamorro, M. Álvarez, C. Cano, J. Cleva, A. Díaz, I. Ortega, J. Alonso, Clinical Research, Indizen Optical Technologies, Madrid, SPAIN|J. Alonso, Applied Optics, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Studies have shown that diurnal rhythms of axial length (AL) are altered by imposed defocus, suggesting that small short-term changes in AL may be used to predict the efficacy of myopia control treatments. The goal of this study is to evaluate the influence of different types of myopia control spectacle lenses (MCL) on the diurnal AL changes of young adults.

Methods: AL measurements were obtained for 6 young adults (emmetropic or contact lens users) that were asked to wear spectacles with an MCL in the dominant eye having a plano central region and imposed peripheral defocus, and a plano control lens in the non-dominant eye. The peripheral defocus was induced with three different types of MCL: Type A (Miyosmart®, Hoya®, Malaysia), Type B (Stellest®, Essilor®, Malaysia) and Type C (a noncommercial prototype, IOT®, Spain). AL measurements were taken over 4 consecutive days. Baseline data without test glasses were collected in day 1. Each following day a new spectacle with an MCL was fitted and tested, in a randomize order. A Lenstar Myopia biometer (Haag Streit AG) was used to register 5 AL measurements within 2 hour intervals each day. Differences between control and treatment eyes for each MCL type and differences between the baseline and each treatment day for the dominant eye (eye with the treatment) were analyzed.

Results: Statistically significant differences were found between the control and treatment eye for MCLs B and C after 2 hours of use of the lenses, showing a significant increase of AL in the treatment eye. Non statistical differences between eyes were found for MCL A at any time while using the lens. When comparing AL change of the treatment eye between the baseline day and the treatment day, statistically significant differences were found for the 3 tested MCL types, showing that all the MCL treatments produce an increase of AL (figure 1). Minimal daily changes in AL were found during the baseline (control) day, showing variations lower than 0.01mm across all time intervals.

Conclusions: Myopia control spectacle lenses influence diurnal rhythms of AL in young adult human, producing a short-term small increase of AL that varies in intensity and time interval for each of the MCS. Additional studies with higher sample size and longer follow-up periods are necessary to confirm that short-term variations of diurnal rhythms can be used as predictor of myopia control efficacy.

CONTROL ID: 3713062

SUBMITTER (NAME ONLY): Víctor López-Soriano

TITLE: Integrated multi-omics analysis to dissect a cis-regulatory role of ultraconserved non-coding elements (UCNEs) in human developing and adult retina

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.R. Webster, Moorfields Eye Hospital, London, UK & Department of Visual Neuroscience, UCL Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|V. López-Soriano, A. Dueñas Rey, S. Van de Sompele, F. Coppieters, M. Bauwens, E. De Baere, Department of Biomolecular Medicine & Center for Medical Genetics, Ghent University & Ghent University Hospital, Ghent, BELGIUM|

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ABSTRACT BODY:

Purpose: Whole genome sequencing revealed an increasing number of pathogenic non-coding variants in inherited retinal diseases (IRD), with a majority of deep-intronic variants and only a few regulatory variants. Here we focus on the role of ultraconserved non-coding elements (UCNEs), defined as genomic regions >200 bp characterized by at least 95% human-chicken conservation. Regions under strong selective pressure are more likely to be involved in the cis-regulation of neighboring genes, mainly during development. However, most of these regions have not yet been functionally annotated, and their association with disease remains largely unknown. Therefore, we set out to assess a potential cis-regulatory role for active UCNEs in human retina using an integrated multi-omics analysis.

Methods: To predict active UCNEs, we integrated publicly available and published transcriptomic (bulk and scRNA-seq) and epigenomic (chromatin accessibility using ATAC-seq and DNase and histone modifications for active enhancers markers such as H3K27ac) datasets derived from developing and adult human retina. In order to characterize the genes within putative UCNE-associated genomic regulatory blocks we made a selection of genes with retinal expression. Whole genome sequencing (WGS) data from ~3,331 probands of the eye cohort of the UK 100,000 Genome Project Genomics England was mined.

Results: Interrogation of multi-omics human retina-derived data revealed a total of 1,349 retina-active UCNEs. Interestingly, 40 genes under putative UCNE control are linked to an eye disease phenotype. To assess their mutational load and their possible contribution to missing heritability in IRD, WGS data from the UK 100k Genome Project eye cohort was queried for sequence variants (SNVs) and structural variants (SVs) within UCNEs. A total of 79 SNVs and 10 SVs related to genes implicated in IRD or other eye phenotypes were identified. None of these are found in public genomic databases.

Conclusions: We identified 1,349 retina-active UCNEs potentially acting as CREs and representing an understudied target of non-coding variants that may explain missing heritability in IRD. Deciphering retinal UCNEs and their cis-regulatory landscapes contribute to functional genome annotations in the retina and to the non-coding morbid genome of IRD. Ultimately, they may represent novel targets for treatment.

CONTROL ID: 3713063
SUBMITTER (NAME ONLY): Noriaki Murata
TITLE: Automatic Visual Acuity Measurement by Using a Calibration-free Eye Tracking System
SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: N. Murata, H. Toda, H. Ubukata, T. Sonobe, A. Hasegawa, Department of Orthoptics and Visual Sciences, Niigata University of Health and Welfare, Niigata, Niigata, JAPAN|
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ABSTRACT BODY:
Purpose: The calibration-free eye tracker is equipped with a face recognition function that allows the examinee to start eye tracking when they sit on the device. We attempted to measure visual acuity automatically by combining this device with vertical stripe targets and investigated visual axis retention time at each spatial frequency of a visual stimulus.
Methods: A total of 44 eyes from 22 healthy participants (mean age: 20.2 years ± 0.7 years) were included in this study. The mean spherical equivalent of the right and left eyes were −4.6 D ± 2.2 D (range: −10.25 D to −1.5 D) and −4.5 D ± 2.2 D (range: −10.1 D to -1.5 D), respectively. Participants with visual field defects detected by a Humphrey field analyzer (24-2 Swedish Interactive Threshold Algorithm Fast Strategy) or with abnormal eye positions were excluded. Participants were seated in front of a calibration-free eye tracker (EMR ACTUS, Nac Image Technology, Tokyo, Japan) with an integrated monitor and freely observed a vertical stripe stimulus. Three types of stimuli (8.4, 12.9, and 25.8 cycles/degree [c/d]) were presented three times each. Areas of Interest (AOI) were set on the stripes, and the percentage of visual axis retention time in the AOI during the presentation of the stimuli was measured. A one-way repeated analysis of variance was used to compare the percentage of visual retention time for each stimulus. P values of less than 0.05 were considered significant.
Results: Among the 44 eyes, one (2.2%) was excluded from the analysis because of measurement error. The mean retention time per stimuli of the right eye were 79.9% ± 22.2%, 72.3% ± 27.9%, and 58.2% ± 30.7% at 8.4 c/d, 12.9 c/d, and 25.8 c/d, respectively, which were all statistically significantly different ($F = 12.9$, $p < 0.01$). In the left eye, the mean retention time per stimuli were 79.5 ± 22.7%, 77.4% ± 24.8%, and 61.0% ± 28.5% at 8.4 c/d, 12.9 c/d, and 25.8 c/d, respectively, which were all statistically significantly different ($F = 9.1$, $p < 0.01$). In both eyes, the percentage of visual axis retention time decreased with increasing spatial frequency.
Conclusions: The correct responses declined with the increasing spatial frequency even with the stripes displayed on the eye tracker. Further studies with a greater number of cases are needed to examine the correlation between LogMAR visual acuity and refractive error.

CONTROL ID: 3713065

SUBMITTER (NAME ONLY): Katerina Hufendiek

TITLE: Macular Vessel Density and Foveal Avascular Zone Metrics Using Optical Coherence Tomography Angiography in Fabry Disease. Long Term Follow Up

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hufendiek, M. Lindziute, I. Volkmann, D. Brockmann, C. Framme, J. Tode, K. Hufendiek, University Eye Hospital, Hannover Medical School, Hannover, GERMANY|J. Kaufeld, Division of Nephrology, Center for Internal Medicine, Hannover Medical School, Hannover, GERMANY|S. Hosari, B. Hohberger, C.Y. Mardin, Department of Ophthalmology, University of Erlangen-Nürnberg, Friedrich-Alexander-University of Erlangen-Nürnberg, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the long-term changes in macular microvasculature and explore a reliable retinal biomarker of Fabry Disease (FD).

Methods: Retrospective-prospective study of 26 eyes with FD (13 patients, 9 treated, 4 untreated) followed up to 48 months (mean 24, range 8-48). OCT Angiography (OCT-A) images (2.9x2.9 mm) were obtained using Heidelberg Spectralis II (Heidelberg, Germany). All OCT-A scans were analyzed using EA-Tool (Version 1.0), which was coded in MATLAB (The MathWorks, Inc., R2017b). Macular Vessel Density (MVD) was measured in three layers: Superficial Vascular Plexus (SVP), Intermediate Capillary Plexus (ICP), and Deep Capillary Plexus (DCP) in circular sectors (c1, c2, and c3). The Foveal Avascular Zone (FAZ) area (mm^2), horizontal and vertical diameters were manually measured in full-thickness scan, SVP, ICP and DCP.

Results: MVD decreased over time in SVP and ICP in c2 and c3 and in all sectors in DCP in FD patients ($p<0.04$). MVD reduction was predominantly seen in treated FD patients. FAZ full-thickness scan area and horizontal diameters increased at follow up in FD patients compared to baseline ($p<0.03$). FAZ at follow-up was larger in full-thickness scans and ICP in untreated vs. treated FD patients ($p<0.03$). Correlation analysis showed a moderate negative correlation between MVD in the inner most circle of SVP and DCP and FAZ in treated FD patients ($|r|>-0.6$). Extended results of MVD and FAZ follow up in all and treated vs. untreated patients are presented in Fig. 1 und Fig. 2.

Conclusions: This is the first long term follow-up OCT-A study in FD patients. MVD decreased in peripheral circle and deeper layers in follow-up in FD patients. Meanwhile FAZ increased at follow-up in the FD group. These changes over time are most likely linked to the vascular remodeling during the course of the disease. The reduction of MVD was predominantly seen in treated FD patients. This could be a result of enzymatic replacement therapy and could be potentially used as a reliable biomarker for monitoring the treatment of the disease. A baseline examination of MVD und FAZ before treatment initiation is meaningful. Larger studies are needed to establish the use of MVD und FAZ as biomarkers for treatment monitoring.

CONTROL ID: 3713066

SUBMITTER (NAME ONLY): James Bell

TITLE: The hierarchical response of human corneal collagen to controlled inflation

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bell, S.R. Morgan, E. Koudouna, S. Hayes, K.M. Meek, Cardiff University, Cardiff, Cardiff, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To elucidate the hierarchical deformation mechanisms of human corneal collagen under controlled inflation of physiological and pathological magnitudes.

Methods: 6 human donor corneas with scleral rim were mounted onto a bespoke sealed cell, which was connected via two pressure regulators and an expansion vessel to a source of compressed nitrogen. The cell included a window transparent to X-rays and was connected to translation and rotation stages inside beamline I22 at the Diamond Light Source synchrotron, UK. Images were acquired naso-temporally across the cornea from limbus to limbus at intraocular pressures of 5.5 mmHg, 17.5 mmHg and 40 mmHg. These increments were chosen for comparison with previous static results in the literature and to mimic the normal physiological state and ocular hypertension.

Results: The inflation apparatus was able to maintain pressure to an accuracy better than 0.1 mmHg. Features corresponding to collagen fibril diameter, spacing, D-period and orientation as well as tropocollagen spacing and orientation were measured simultaneously. Preliminary analysis revealed a radial distribution of strain (manifested as a change in D-period) across the cornea, which was accentuated in the outer periphery and limbus. In general, the interfibrillar spacing in the periphery and limbus (where collagen fibrils are arranged circumferentially) was found to increase with pressure.

Conclusions: The trends in D-period strain are indicative of bulging under increased pressure, which is pronounced at the limbus and the outer periphery. This agrees with the general consensus that the outer periphery and limbus act as a buffer zone, which takes up most of the strain under changes in intraocular pressure, and thus minimises changes in focussing power of the cornea. Further in-depth analysis of this data will allow us to calculate the supramolecular twist (which gives rise to a spring-like stretch in collagen fibrils) and examine in more detail the hierarchical response of corneal collagen to changes in intraocular pressures.

CONTROL ID: 3713067

SUBMITTER (NAME ONLY): Abhilash Goud Marupally

TITLE: Non-invasive Detection of Glycolytic Stress-induced Reactive Oxygen Species in Human Retinal Pigment Epithelium Cells using Autofluorescence Multispectral Imaging

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Marupally, A. Habibalahi, A. Anwer, E. Goldys, ARC Centre of Excellence for Nanoscale Biophotonics, Graduate School of Biomedical Engineering, University of New South Wales, Sydney, New South Wales, AUSTRALIA|A. White, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|N.A. Carnt, University of New South Wales School of Optometry and Vision Science, Sydney, New South Wales, AUSTRALIA|R. Casson, Ophthalmic Research Laboratories, South Australian Institute of Ophthalmology, Hanson Institute Centre for Neurological Diseases, Adelaide, South Australia, AUSTRALIA|R. Casson, Department of Ophthalmology and Visual Sciences, The University of Adelaide, Adelaide, South Australia, AUSTRALIA|N.A. Carnt, A. White, Westmead Institute for Medical Research, Westmead, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine auto fluorescent multispectral imaging (AFMI) signatures in a human retinal pigment epithelium (RPE) cell culture system under normal conditions and under glycolytic stress.

Methods: Human RPE cells (h1RPE7 cell line) were treated with a glycolytic inhibitor, iodoacetic acid (IAA) at 1 μM, 5 μM, and 10 μM concentrations for 24 hours. Cell viability was assessed using a fluorescent live/dead assay and dihydroethidium (DHE) was used to quantify cellular reactive oxygen species (ROS). Imaging was initially performed with routine confocal microscopy. ROS detection was then performed in the absence of exogenous fluorescent probes using a novel autofluorescence multispectral imaging (AFMI) microscopy method. A total of 33 spectral channels spanning specific excitation (345-505 nm) and emission (414-675 nm) wavelength ranges were used.

Results: A dose-dependent cell death occurred after 24 hours of exposure to IAA, peaking at 80% cell death at the 10 μM concentration. ROS production was significantly increased in cells under glycolytic stress ($p < 0.001$). There were highly significant changes in the patterns of spectral signals between treated and control groups using the AFMI microscopy ($p < 0.001$).

Conclusions: These results show that ROS can be detected using non-invasive multispectral imaging in retinal cells. This imaging technique may be adapted to in vivo use and has potential for the detection and monitoring of clinically relevant retinal disease states such as macular degeneration and glaucoma.

CONTROL ID: 3713069

SUBMITTER (NAME ONLY): Oksana Kutsyr

TITLE: Topical ocular GLP-1 (FNP120) administration preserves retinal function and morphology in a retinitis pigmentosa mouse model

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Kutsyr, P. Lax, N. Cuenca, Physiology, Genetics and Microbiology, University of Alicante, Alicante, Alicante, SPAIN|L. Fernández-Sánchez, V. Maneu, Optics, Pharmacology and Anatomy, University of Alicante, Alicante, Alicante, SPAIN|C. Lagunas, A. Fernández, R&D, Grupo Ferrer Internacional SA, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: Photoreceptor cell degeneration, inflammation, and oxidative stress are commonly associated with retinitis pigmentosa (RP), a retinal degenerative disease. Glucagon-like peptide-1 (GLP-1) is an endogenous neuropeptide synthesized by the retina that has exhibited neuroprotective effects in diabetic retinopathy. Therefore, this work aimed to evaluate a possible neuroprotective effect of a novel GLP-1 eye drop formulation (FNP120) in a mouse model of RP.

Methods: Rd10 mice were used as a model of RP. Topical ocular treatment with GLP-1 or vehicle was administered to rd10 mice from postnatal day 16 to P25 twice a day as eye drops in both eyes (5µL/eye). Three GLP-1 concentrations were tested (1, 2, and 4 mg/mL). Optomotor test and scotopic electroretinography (ERG) were used to evaluate mice retinal function after the treatment. Secondly, retinal cryostat cross-sections were performed to quantify the number of photoreceptor rows throughout the retina. Retinal morphology was analyzed using immunohistochemistry.

Results: Retinal function improved after 10-days of GLP-1 topical ocular administration. Rd10 mice treated with GLP-1 eye drops at a concentration of 2 mg/mL displayed significantly higher scotopic a- and b-wave amplitudes compared to vehicle-treated mice. Optomotor test also showed higher visual acuity found in 2 mg/mL treated rd10 mice. These functional findings correlated with a higher number of photoreceptor rows found in GLP-1 treated rd10 mice retinas. Also, these photoreceptors showed slightly better-preserved morphology and longer outer segments. GLP-1 administered at a concentration of 1 or 4 mg/mL did not achieve significant protective effects.

Conclusions: Topical administration of GLP-1 at 2 mg/mL was able to preserve retinal function loss and photoreceptor cells surviving in the retina of rd10 mice. These data support the view that GLP-1 may emerge as a new therapeutic strategy against retinal neurodegenerative diseases.

CONTROL ID: 3713071

SUBMITTER (NAME ONLY): Abhijit Sinha Roy

TITLE: Imaging of corneas after deep anterior lamellar keratoplasty using polarization sensitive optical coherence tomography

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sinha Roy, R.P. Patil, R. Narasimhan, Y. Patel, A. Pisharody, P. Khamar, R. Shetty, Narayana Nethralaya Foundation, Bangalore, INDIA|

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ABSTRACT BODY:

Purpose: To investigate the polarizing properties of corneas following deep anterior lamellar keratoplasty.

Methods: In this study, 20 patients were imaged using our custom-built ultrahigh resolution polarization sensitive optical coherence tomography (PS-OCT). A near limbal-to-limbal imaging field with uniform signal strength throughout the cornea was achieved using a conical scan setup. Cross sections (B-Scans) and enface maps of the cornea at various locations and depths were derived from the polarization sensitive information to observe localized changes in phase retardation (PR) and depolarization.

Results: PS-OCT provided an improved image contrast (Figure 1b) that can potentially assist in better diagnosis compared to the conventional intensity image (Figure 1a). Since tissue birefringence originated from alignment of collagen fibrils in the stroma, PR information showed strong birefringence at the graft-host interface (see Figure), indicating the microstructural alteration of collagen in those regions. Further, scar morphology and rupturing can also be precisely studied with using PR as a surrogate for wound healing.

Conclusions: PS-OCT can enable visualization of the alteration of tissue properties following corneal transplant and may reveal unique structural changes prior to graft failure.

CONTROL ID: 3713072

SUBMITTER (NAME ONLY): Fanny HENRIOUX

TITLE: Specific inflammatory answer of conjunctival and corneal cells in hyperosmolar context regarding NFAT5 activation

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. HENRIOUX, V. NAVEL, C. Belville, F. CHIAMBARETTA, L. Blanchon, V. SAPIN, iGreD UMR CNRS INSERM, Clermont-Ferrand, FRANCE|V. NAVEL, F. CHIAMBARETTA, Ophthalmology department, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, FRANCE|V. SAPIN, Biochemistry department, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, FRANCE|

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ABSTRACT BODY:

Purpose: In dry eye syndrome, hyperosmolarity is one of the main factors inducing ocular surface inflammation. The objective of this work is to decipher the cellular and molecular cascades in cornea and conjunctiva, which are involved in triggering inflammation, by focusing particularly on the nuclear factor of activated T-cells 5 (NFAT5) and its implication.

Methods: HCE (Human Corneal Epithelial) and WKD (Wong-Kilbourne derivative of Chang conjunctival cell) were cultured in normal medium or hyperosmolar medium (addition of 70 mM or 90 mM NaCl). Quantitative reverse transcription (RT-qPCR) and Western-Blotting assays were performed to analyze NFAT5 expression in corneal and conjunctival cells regarding medium (normal or hyperosmolar) and exposure times (6h, 12h and 24h). The activation of NFAT5 signaling pathway by hyperosmolarity cells was tested using Luciferase NFAT5 reporter assay system. Furthermore, cytokines expression analysis were performed by RT-qPCR and Multiplex assay, respectively at 24h and 48h, in both cells. Finally, the implication of NFAT5 in inflammation (cytokines production and release) was confirmed using the transfection of siRNA NFAT5.

Results: Our result demonstrate the NFAT5 induction and activation in both HCE and WKD in hyperosmolar context. Furthermore, among the inflammatory messages induced in hyperosmolar stress conditions, MCP1 levels were significantly reduced after inhibition of NFAT5 in WKD cells, and reduction of IL1 beta, TNF alpha and MCP1 levels in HCE cells.

Conclusions: These in vitro results highlight the major role of NFAT5 in the hyperosmolarity pro-inflammatory consequences but looks to be cell type specific between conjunctival and corneal epithelial cells.

CONTROL ID: 3713073

SUBMITTER (NAME ONLY): Qiu Ying Wong

TITLE: Changes in visual function in eyes with myopic traction maculopathy over 1 year

SESSION TITLE: Myopia: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q. Wong, Y. Dan, C.S. Chua, M. Ang, Q.V. Hoang, C. Wong, Singapore Eye Research Institute, SINGAPORE|Q.V. Hoang, Ophthalmology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the longitudinal change in macular thickness and visual function in highly myopic eyes with and without myopic traction maculopathy (MTM).

Methods: 109 eyes of 65 highly myopic patients were enrolled from the Myopic and Pathologic Eyes in Singapore (MyoPES) cohort and followed for at least 12 months. Axial length (AL) and logMAR best-corrected visual acuity (BCVA) were measured. Swept-source optical coherence tomography (SS-OCT) was performed, and images were evaluated for MTM and central subfield retinal thickness (CRT). Macular sensitivity (MS) was measured with MP-3 microperimetry.

Results: At baseline, mean age was 57.5±13.5 years and mean AL was 29.3±2.7mm and 20 eyes (18.4%) had MTM. On average, compared to eyes without MTM, eyes with MTM had significantly longer AL (30.8±1.7mm vs. 29.1±2.8mm, p=0.01), greater CRT (319±74um vs. 242±42um, p<0.001) and lower MS (19.8±4.1dB vs. 22.6±5.3dB, p=0.03). BCVA did not differ (0.33±0.39 vs. 0.24±0.29, p=0.22). At 1 year, MTM progressed in 5 eyes (25%) and resolved in 1 eye (5%). In eyes with progression, CRT increased from 302±57um to 359±83um (p=0.14). MS at 1 year in eyes with (20.2±4.1dB) and without MTM (21.8±5.5dB) did not significantly differ from baseline values (p=0.60 and 0.16, respectively).

Conclusions: Although visual acuity did not differ, visual function as measured by microperimetry was significantly worse in highly myopic eyes with MTM than those without at baseline. Over the span of 1 year, no significant change in macular sensitivity was observed in eyes despite MTM progression.

CONTROL ID: 3713074

SUBMITTER (NAME ONLY): Philipp Fuchs

TITLE: Analysis of AI-quantified fluid dynamics over time and their impact on visual acuity in real-world patients with neovascular age-related macular degeneration

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Fuchs, L. Coulibaly, H. Bogunovic, O. Leingang, A. Gruber, G.S. Reiter, U. Schmidt-Erfurth, Medizinische Universitat Wien, Vienna, Wien, AUSTRIA|D. Barthelmes, UniversitatsSpital Zurich, Zurich, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Fluid dynamics in neovascular age-related macular degeneration (nAMD) might negatively affect visual acuity (VA) during anti-VEGF treatment. The aim of this study was to investigate the differential effects of fluid fluctuations, fluid persistence and fluid volumes on VA using artificial intelligence algorithms (AI) (Vienna Fluid Monitor, RetInSight, Vienna, Austria) over a time period of three years in a real-world cohort.

Methods: Real-world data (OCT and electronic medical records) from patients with treatment-naive nAMD of the Fight for Retinal Blindness (FRB) Zürich database were extracted. Patients were included if ≥24 months follow up was available and if treated with Aflibercept, Bevacizumab or Ranibizumab. OCT scans were analyzed using AI to quantify intraretinal fluid (IRF), subretinal fluid (SRF) and pigment epithelial detachment (PED) in the central 1mm, adjacent 1-3mm and 3-6mm rings. Each persistent fluid parameter was defined as presence of either SRF, IRF or PED on ≥60% of the available OCT scans of each time window, respectively. The standard deviations of SRF, IRF and PED fluctuations were computed and sorted into quartiles. The effect of fluid parameters on change of VA after a loading dose was calculated using univariate mixed effect models.

Results: A total of 172 consecutive eyes from 135 treatment-naïve nAMD patients were included in the statistical analysis. Eyes with more frequent anti-VEGF treatments showed an increased change of VA from baseline to year 1 (p=0.040, estimate: -0.01 logMAR/injection). By year 2 and 3, eyes with the greatest IRF fluctuations (Q4) showed a worse VA in comparison to eyes with the least IRF fluctuations (Q1) (p=0.019, 0.11 logMAR, and p=0.012, 0.16 logMAR). Eyes with higher IRF volumes in the central area had a worse VA after 3 years of follow up. (p=0.031, estimate: 0.01 logMAR/nL). A correlation of the number of treatments and SRF dynamics in comparison to IRF dynamics could be identified (Figure 1).

Conclusions: Greater IRF fluctuations and greater IRF volumes are associated with worse VA after three years of follow up, while an increased number of injections improved VA gain in the first year. Fluid dynamics can be quantified using AI for real-time measurements and result in improved patient management in clinical practice.

CONTROL ID: 3713075

SUBMITTER (NAME ONLY): Lili Gong

TITLE: Inhibition of cGAS-STING by JQ1 alleviates oxidative stress-induced retina inflammation and degeneration

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Gong, M. Zou, Q. ke, R. Qi, X. zhu, W. liu, D.W. Li, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: cGAS-STING pathway is a key cytosolic DNA sensor signaling in innate immunity. Activation of cGAS-STING has been previously detected in retinal pigment epithelium (RPE) of Geographic atrophy (GA) patients, potentially contributes to pathogenesis of AMD [(1)]. We have recently shown that cGAS and STING are dose-dependently upregulated in RPE and retina of an experimental GA-like mouse model [(2)]. In the current study, we are aimed to identify drugs that can inhibits cGAS-STING signaling and prevents oxidative stress-induced RPE and retina injury.

Methods: X-ray irradiation (8 GY) was used to induce cytosolic DNA leakage in ARPE-19 cells. Immunofluorescence-based high-content analysis was used to screen an epigenetic library which contains 288 FDA-approved small molecules. Western blot and RT-PCR analysis confirmed the inhibitory effects of the identified molecules on cGAS and STING expression in ARPE and photoreceptor cell line 661W. Fundus photography, RPE flat mount and immunohistochemistry analysis determined the effects of the identified molecule on sodium iodate (SI) (35mg/kg)-induced RPE and retina degeneration.

Results: X-ray irradiation lead to obvious DNA damage and accumulation of cytosolic DNA. Drug screening identified BET inhibitor JQ1 exerts significant suppressive effect on cytosolic DNA release ($P < 0.05$). The RNA and proteins level of cGAS and STING were upregulated after irradiation or H_2O_2 treatment, whereas JQ1 treatment significantly represses such upregulation as well as the expression of downstream NFκB signaling ($P < 0.01$). Application of JQ1 (50mg/kg) after SI injection alleviates oxidative stress-induced RPE and retina inflammation and degeneration.

Conclusions: Together, we identified that JQ1 suppresses cGAS and STING expression in cells and in mouse retina and RPE upon oxidative stress. This study may provide new treatment strategy for GA.

CONTROL ID: 3713076

SUBMITTER (NAME ONLY): Marcin Marzejon

TITLE: Towards spectral sensitivity curve for two-photon vision mechanism

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The perceived brightness of different visible light sources can be compared with photometric units based on the standardized luminosity curves (300-780nm range). As reported previously (PNAS 111(50), pp. E5445-E5454 (2014)), near-infrared (NIR) radiation can cause isomerization of visual pigments by one- or two-photon absorption. The perceived color of the stimulus is red in the case of one-photon vision (1PV) or corresponds to half of the short-pulsed laser wavelength for the two-photon vision (2PV) mechanism. Since no luminosity curves for NIR range, comparison of such sources with photometric units is impossible. This study aims to provide an initial data for the 2PV spectral sensitivity curve (SSC).

Methods: We measured the scotopic visibility thresholds at fovea for 4 healthy dark-adapted subjects (2 males, 2 females; 27-43 y/o) between 750-1075nm. Up to 930nm, the total visibility threshold corresponds only to 1PV mechanism. For the 810-930nm, subjects distinguished 2 thresholds: the loss of half of the wavelength hue (2PV threshold) and total visibility (1PV) threshold. Starting from 950nm, only 2PV mechanism caused the visual sensation. The stimulus was a 0.5 deg diameter flickering circle projected in the retina by scanners. Two tunable pulsed light sources: OPO (750-990nm, F_{rep}=76MHz, τ_p=204fs) and fiber laser (872-1075nm, F_{rep}=51.5MHz, τ_p=205±9fs) were employed for psychophysical tests. The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of the Collegium Medicum, NCU.

Results: The 1PV thresholds agreed with the previous works (JOSA 37(7), pp. 546-554 (1947)). Within the 810-930nm range, a relatively high standard deviation of the 2PV thresholds was observed, as finding the disappearance of half of the wavelength hue is a relatively difficult task. 2PV thresholds slightly differ for OPO and fiber laser, which is explainable by differences in pulse durations and repetition rates. For ~1040nm, the 2PV threshold values agreed to the previous authors' results.

Conclusions: The 2PV sensitivity increased with wavelength of about 1 order of magnitude (810-1075nm range). Starting from 1010 nm, the shape of the obtained 2PV SSC differs from the wavelength-doubled scotopic luminosity curve for 1PV, corrected by the eye media transmittance. The maximum of 2PV SSC was not found. The results allowed us to obtain the first approximation of the 2PV SCC shape up to 1075nm.

CONTROL ID: 3713077

SUBMITTER (NAME ONLY): Sophie Glinton

TITLE: The Impact of Specific ABCA4 Variants on Retinal Function Using Regression Analysis of Electroretinography Data in a Large Patient Cohort

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Glinton, A. Calcagni, N. Pontikos, G. Arno, P.A. Keane, M. Michaelides, A.R. Webster, O.A. Mahroo, A.G. Robson, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|S. Glinton, N. Pontikos, S. Vermeirsch, G. Arno, P.A. Keane, M. Michaelides, A.R. Webster, O.A. Mahroo, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A. Calcagni, A.G. Robson, Department of Electrophysiology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|W. Lilaonitkul, Institute of Health Informatics, University College London, London, London, UNITED KINGDOM|W. Lilaonitkul, Health Data Research UK, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: ABCA4-retinopathy is the most common monogenic inherited retinal disease but current prognostic capability is limited by genetic heterogeneity with more than 1000 possible variants, for which combinations due to recessive inheritance result in a number of genotypes of at least n(n+1) / 2. Full-field electroretinography (ERG) is used clinically in the diagnosis and prognosis of ABCA4-retinopathy by measuring the activity of retinal cell populations in response to light stimuli. This study investigates whether regression analysis of genetic variants with ERG data can be used to derive coefficients relating to severity from a uniquely large single-centre patient cohort.

Methods: In this retrospective cohort study, multiple ISCEV-standard ERG parameters were labelled (DA 10, LA 3, and LA 30Hz ERGs) from 495 patients with confirmed ABCA4-retinopathy and compound heterozygous or homozygous pathogenic ABCA4 variants. ERG trace labelling was automated through custom peak-finding algorithms on additionally bandpass-filtered traces and labelled values normalised for ElasticNet regression analysis against the ABCA4 variant background of the cohort. ElasticNet is an extended regression method to deal with a large number of potentially correlated features.

Results: The analysis generated beta coefficients associated with individual variants. Within the 50 most frequent variants in the cohort, higher coefficient values were observed to be associated with previously identified milder variants including c.5882G>A p.(G1961E), c.5603A>T p.(N1868I) and c.4253+43G>A and lower coefficients with nonsense mutations and the severe intronic variant c.5461-10T>C. Many variants had intermediate coefficients consistent with partial function of the resultant protein. The resultant models had an average r^2 value of 0.726, and results were consistent for the derived coefficients across the measured ERG features DA 10 a-wave and b-wave, LA 3 a-wave and b-wave and LA 30Hz peak amplitude (avg. r=0825. (range 0.724-0.931)).

Conclusions: This analysis provides a novel quantification of the impact of specific ABCA4 variants on retinal function in a data-driven regression analysis based on clinical ERG recordings; the findings were consistent with previously described genotype-phenotype correlations.

CONTROL ID: 3713079
SUBMITTER (NAME ONLY): Agnieszka Zielinska
TITLE: Contrast Sensitivity Function of Two-Photon Vision
SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Zielinska, M. Szkulmowski, K. Komar, Institute of Physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Torun, Torun, POLAND|O. Kaczkos, J. Solarz-Niesluchowski, Faculty of Physics, University of Warsaw, Warsaw, POLAND|M. Marzejon, Department of Physical Chemistry of Biological Systems, Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, POLAND|M. Marzejon, Department of Metrology and Optoelectronics, Faculty of Electronics, Telecommunications and Informatics, Gdansk University of Technology, Gdansk, POLAND|K. Komar, International Centre for Translational Eye Research, Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, POLAND|
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ABSTRACT BODY:

Purpose: Humans can perceive pulsed near-infrared light as a visible about halved wavelength by two-photon absorption in photoreceptors (PNAS 111(50) (2014) pp. E5445-E5454). The contrast sensitivity function (CSF) of two-photon vision is not yet known. This study aimed to provide the first data to compare CSF for one- and two-photon vision.

Methods: A custom-built optical system employing 1040 nm and 520 nm pulsed laser beams (200 fs, 76 MHz) was used to measure two-photon and one-photon CSF, respectively, of 3 healthy volunteers (2 women, 1 man, age 24-43). The stimuli were tumbling E of 5 spatial frequencies (3, 6, 8, 15, 18 cyc/deg) formed by scanning laser beam. The background was obtained by Maxwellian view illumination of the retina with white LED. A contrast threshold was determined in a four-alternative forced-choice procedure: by finding the minimum stimulus brightness for which the subject was able to state the letter orientation in 4 of 5 trials correctly. The study was approved by the Ethics Committee of the Collegium Medicum, NCU.

Results: The CSFs were calculated as the reciprocal of Weber contrast. Since the background was one-photon in both cases and there is a lack of luminosity function for two-photon vision, the two-photon CSF was normalized to equalize sensitivities for the maximum value of one-photon CSF. Both curves show a decline from 3 cyc/deg to 18 cyc/deg. However, the two-photon CSF has a slightly broader range than the one-photon CSF – the differences between these ranges were 21, 7, 5 for the individual subjects.

Conclusions: CSF for two-photon vision was shown the first time. The obtained result may suggest that the two-photon CSF has a broader range than CSF of normal vision.

CONTROL ID: 3713080

SUBMITTER (NAME ONLY): Prayag bellur

TITLE: A Novel Methodology To Quantify and Visualize Progression Of Corneal Wound Healing Using OCT And Slit Lamp Data

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Singh, A. Tiwari, A. Gour, V. Singh Sangwan, Department of Cornea and Uveitis, Dr Shroff's Charity Eye Hospital Delhi, New Delhi, Delhi, INDIA|P. bellur, J. Rajput, B. Sangwan, M. Ben Thomas, T. Bhowmick, A. Chandru, Cornea, Pandorum Technologies pvt ltd, Bengaluru, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: Corneal defects measured by slit lamp/OCT incorporate several qualitative diagnostic readouts that include fluorescence which helps visualize the extent of epithelial debridement and raster scan which captures corneal inflammation. However, these multi-readout instrumentations have limited quantification capabilities. Herein, we have designed methodology to quantitatively assess the extent of corneal defect in a mouse model of alkali-induced stromal injury

Methods: Mice with deep alkali-induced stromal injury (penetrating lamellar keratoplasty, 2 mm wide and 50 µm depth, followed by 0.75 N sodium hydroxide for 30 s) were imaged using a slit lamp (AIA12 5 S /5 S L, Appasamy associates, India) and OCT (Avanti Widefield OCT, Optovue, Inc., USA) to obtain fluorescence images (blue filter) and corneal raster scans, respectively. A custom Matlab script (R2020b, The MathWorks Inc., USA) was generated for each readout and employed to extract quantitative measurements from the regions of interest by thresholding the raw images.

Results: The region of epithelial defect captured via the blue filter through slit lamp examination was quantified to have an area of 2.6mm^2 for mice at day 0 post alkali burn. The extent of inflammation from OCT data was quantified through hyper-reflectivity regions of the raster scan. The %reflectivity for healthy cornea was found to be <15% & mean pixel intensity <13. Thus, the progress of re-epithelization of the corneal wound along with the degree of inflammation was quantified over a study period of 4 weeks. Consequently, as the scar regenerated, the area of the wound and the hyper-reflectivity gradually reduced to 0 & <15% respectively, indicative of corneal wound healing.

Conclusions: Our results demonstrate a reliable quantitative methodology to visualize progression of corneal wound healing through standard slit lamp/OCT instrumentations for any animal model.

CONTROL ID: 3713082

SUBMITTER (NAME ONLY): Alexander Schmid

TITLE: Deep learning based segmentation of retinal fluids using optical coherence tomography (OCT) data

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Schmid, Digital Pathology, Carl Zeiss Meditec AG Oberkochen, Oberkochen, Baden-Württemberg, GERMANY|K. Patel, Center of Application and Research in India, Carl Zeiss India Pvt Ltd, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: OCT, a non-invasive imaging modality, plays a central role in ophthalmology. Efficient and precise segmentation of various abnormalities seen in OCT imaging can help detect and monitor disease progression, thus advising and supporting effective treatment decisions. For this purpose, we propose a new deep learning-based segmentation pipeline for retinal fluids in OCT.

Methods: The underlaying data is formed by an OCT B-scan dataset containing 1540 images and masks, split in 1291 training and 249 validation cases, annotated for three different retinal fluids: intraretinal fluid (IRF), subretinal fluid (SRF) and pigmented epithelial detachment (PED), captured by a CIRRUS™ HD-OCT 4000 (ZEISS, Dublin, CA). The performance of the model is also evaluated using the RETOUCH dataset, containing 70 SD-OCT volumes from three different OCT vendors. The segmentation model is based on a squeeze-and-excitation architecture including transfer learning strategies with partial freezing variants utilizing trained weights from ImageNet. The whole implementation is done using Tensorflow-Keras and the model is optimized using Tversky loss. The quantitative evaluation of the model prediction is performed using the Dice coefficient and the MeanIoU.

Results: According to the efficient interplay of transfer learning techniques across ImageNet and the OCT data, an overall validation Dice coefficient of 66.3 and MeanIoU of 69.6 percentage points could be achieved by training all fluid categories simultaneously. Figure 1 a) reveals the reached metric values for each individual label. In addition, the RETOUCH examinations resulted in the mentioned numbers in Figure 1 b).

Conclusions: This work constitutes that an individual adaptation of the network and the integration of domain-specific knowledge of other modalities through special transfer learning techniques enables semantic features to be learned even with minimal, complex data sets. Overall, adaptions and transfer learning scenarios of this network could increase the segmentation performance by 15.3 % measured by the Dice coefficient, compared to a standard segmentation implementation (nnUnet).

CONTROL ID: 3713083

SUBMITTER (NAME ONLY): Emilie Picard

TITLE: Endocrine disruptors induce cell death and phenotypic modifications in RPE cells

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Our environment is continuously enriched in pollutants that contribute to increase the prevalence of diseases or even the emergence of new pathologies. The effects of endocrine disruptors (EDs) on the eye remain unclear. Bisphenol A (BPA) is an ED widely used in the production of polycarbonate plastics leading to organ dysfunction and/or cancers. Fluoride, used to prevent tooth decay by its addition to municipal water supplies and dental products is now considered as ED. The aim of this study is to assess the effect of BPA and Fluoride on RPE cells.

Methods: ARPE-19 and hiPSC-derived RPE (iRPE) cells were exposed to different concentrations of BPA or Sodium Fluoride (NaF) during 1 or 7 days. Mitochondrial activity (MA) and transepithelial resistance (TER) were evaluated at 1 and 7 days on both cell lines. Cell viability and death were evaluated by flow cytometry on ARPE cells following 1 day of exposure. Immunofluorescence staining were used to evaluated iRPE cells phenotype following 1 day of exposure.

Results: Exposure during 24 hours of BPA at 0.5mM and NaF at 1.5mM significantly reduced MA by 90% and 55% respectively on ARPE cells. While BPA induced the loss of viability and the cell death, NaF had no effect on ARPE cells viability/death, as observed by cytometry. In iRPE cells exposed during 1 day, BPA at 0.5mM and 1mM decreased by 50% and 100% the MA and induced 100% of decrease of TER. At 0.1mM, BPA significantly slight increased MA without changes for TER. Following 7 days of exposure, 0.1mM of BPA slightly decreased MA and significantly decreased TER (50%). NaF exposure during 1 day had no effect on MA of iRPE cells even at 2 mM, but led to a dose-dependent increase of TER. After 7 days, 2mM NaF still not had effect on MA but decreased TER (20%). Immunostaining of iRPE cells shown a decrease of RPE65 intensity and an increase of vimentin intensity following 1 day of BPA exposure. NaF did not change the iRPE cells phenotype even at high dose.

Conclusions: Our results show that BPA induces a decrease of viability, cells death and loss of RPE phenotype, whom are increased with longer exposure. NaF induces a reduction of cell viability and cell death only at high dose. In conclusion, chronic exposure with ED may contribute to reduce function of RPE and promote the prevalence of neurodegenerative diseases.

CONTROL ID: 3713084

SUBMITTER (NAME ONLY): Joycelyn Arhin

TITLE: Prevalence of childhood cataract and associated factors among a pediatric population at a tetiary hospital in Ghana

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Arhin, K. Atia, D. Ben Kumah, I. Osei Duah Junior, E.K. Addo, A. Ahmed, K. Owusu Akuffo, Department of Optometry and Visual Science, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|D. Amankwa-Frempong, Department of Eye, Ear, Nose and Throat, Komfo Anokye Teaching Hospital, Kumasi, GHANA|E.K. Addo, Department of Ophthalmology and Visual Sciences, John A. Moran Eye Centre, University of Utah, Salt Lake, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Childhood cataract significantly impact the quality of life of children. Evidence from epidemiological studies are required in planning yet, there remains a dearth in data from sub-Saharan African countries including Ghana. The present study investigates the prevalence of childhood cataract and its associated factors among a pediatric population at a tertiary health facility in Ghana.

Methods: We conducted a retrospective chart review on 263 pediatric cataract cases examined (from January 2019 to December 2020) at the pediatric ophthalmology department of the Komfo Anokye Teaching Hospital, Kumasi, Ghana. Patient clinical data including sociodemographic, signs and symptoms, primary diagnosis and associated ocular complications were gathered and analyzed using Statistical Package and Service Solution (SPSS). Chi-square and regression statistics were used to summarize data at a significance of $p<0.05$.

Results: The prevalence of childhood cataract was 4.25% (263/6,188). The proportionate distribution of cataracts was congenital (39.5%), traumatic (33.1%) and developmental (26.6%). Over half (51.7%) of the subjects had unilateral cataract. The major complications of childhood cataracts were strabismus (5.70%), nystagmus (3.0%) and retinal detachment (1.90%). Older age (2-12 years, OR = 0.27, $p<0.001$;> 12 years, OR = 0.12, $p<0.001$) was significantly associated with reduced odds of congenital cataract. Similarly, increasing age (2-12 years, OR = 12.59, $p<0.001$; >12 years, OR = 7.57, $p = 0.004$) and female sex (OR = 0.58, $p = 0.038$) was significantly associated with decreased odds of traumatic cataracts. Conversely, older age (2-12 years, OR = 11.02, $p<0.001$; >12 years, OR = 26.57, $p<0.001$) and female sex (OR = 2.27, $p = 0.008$) were significantly associated with increased odds of developmental cataracts.

Conclusions: Over four in every hundred children had childhood cataract. This high prevalence is a major challenge, which warrants the institution and implementation of vision screening and eye health education programs to improve early detection and safety among the pediatric population.

CONTROL ID: 3713085

SUBMITTER (NAME ONLY): Andrew Moshfeghi

TITLE: Real-World Management of Neovascular Age-Related Macular Degeneration in the US

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the management of neovascular age-related macular degeneration (nAMD), factors that predict receiving treatment, and the relationship between treatment frequency and visual outcomes in routine clinical practice.

Methods: This retrospective analysis assessed electronic medical records from the Vestrum Health Retina Database for treatment-naïve eyes newly diagnosed with nAMD from January 1, 2014 that had ≥1 year of follow-up. Cumulative incidence of eyes receiving treatment was evaluated using the Kaplan–Meier (KM) method, and factors that predicted receiving treatment through one year were evaluated by logistic regression.

Results: Of 90,681 eyes included in the analysis, the percentage of eyes not receiving treatment was 23%, 16%, 15% and 13% at diagnosis and years 1, 2 and 3, respectively. The mean baseline visual acuity (VA) of eyes not treated and treated were 39 and 52 letters, respectively. Higher odds ratio (OR≥1.50, [95% CI]) of receiving treatment was found for eyes with baseline VA 20/40-20/100 vs ≥20/40 (1.52 [1.44, 1.61]); and for eyes with macular edema (3.26 [3.11, 3.42]), subretinal fluid (4.97 [4.75, 5.20]), or sub-retinal pigment epithelium fluid (1.64 [1.56, 1.72]). Lower OR (OR£0.50) for receiving treatment was found for patients with simultaneous bilateral diagnosis (vs. unilateral diagnosis, 0.32 [0.31, 0.34]);and for eyes with baseline VA<20/400 vs. ≥20/40 (0.29 [0.27, 0.30]). When treated within 1 month from diagnosis, eyes gained a mean (SD) of 5 (3) letters from baseline at 6 months, which was maintained at year 1. If treatment initiation was delayed 6 months from diagnosis, eyes gained a mean (SD) of 1 (0) letter at year 1. Mean BCVA change from baseline at year 1 was −1.21, 0.58, 4.31 and 5.6 letters in eyes treated with 1-3, 4-6, 7-9 and >9 injections, respectively. Within the subgroup of eyes that received 7-9 and >9 injections, those with baseline VA<20/400, gained 20.3 and 27.2 letters, respectively.

Conclusions: Almost one quarter of eyes with nAMD did not receive treatment at diagnosis. Simultaneous bilateral nAMD diagnosis and poor baseline VA (<20/400) were primary factors associated with not receiving anti-VEGF treatment. Greater VA gains were observed with prompt treatment and increasing number of injections, with eyes with poor baseline vision (<20/400) gaining a mean of ≥4 lines with ≥7 injections from baseline at year 1.

CONTROL ID: 3713086

SUBMITTER (NAME ONLY): Peter Heiduschka

TITLE: Nanoparticles made of pseudoproteins penetrate into mouse eyes

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kantaria, T. Kantaria, R. Katsarava, Chemistry and Molecular Engineering, Agricultural University of Georgia, Tbilisi, Tbilisi , GEORGIA|P. Heiduschka, W. Zhang, N. Eter, Ophthalmology, Westfalische Wilhelms-Universitat Munster, Munster, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Drug delivery to the eye still is a challenge. One way currently investigated is administration of drug-loaded nanoparticles (NP) that are able to penetrate ocular barriers. The purpose of this study is to check to what extent NPs made from pseudo-proteins loaded with the fluorescent dye Nile are able to penetrate ocular tissues and are taken up by cultured cells.

Methods: Biodegradable NPs of various types were prepared by nanoprecipitation of a pseudo-protein composed of L-leucine, 1,6-hexanediol and sebacic acid (8L6). Arginine-based cationic polyester amides 8R6 and comb-like polyester amides containing lateral PEG-2000 chains along with 8L6 anchoring fragments in the backbones were used to construct positively charged and PEGylated NPs. The NPs were loaded with fluorescein Nile red (NR) as a fluorescent probe. Suspensions of the NPs were given to cultivated pig microglial cells and retinal pigment epithelial (RPE) cells as well as topically or retrobulbary on eyes of C57BL/6 mice. Penetration of NPs into the eyes was checked by fluorescence analysis.

Results: Two different kinds of NP (TK-1 and TK-4) were prepared, loaded with Nile Red, and their physicochemical properties were characterised. Size of TK-1 was 128-131 nm, and of TK-4 164-190 nm. NP were stable over weeks and did not release the lipophilic dye. After topical administration, NP penetrated into the cornea, and we also found them in the sclera, as demonstrated by fluorescence and electron microscopy. Fluorescence was found in the cornea and the sclera 1 day and 3 days after both topical and retrobulbar administration. We also detected fluorescence in the isolated retina and lens, indicating that NP did reach the inner parts of the eyes. Fluorescence did vanish after 3-4 days, most probably due to wash-out. In cell culture, NP were taken up only by a small portion of RPE cells and apparently not at all by microglial cells. When BSA was omitted in the growth medium, microglial cells clearly took up NP.

Conclusions: The results show that the NPs made of pseudoproteins penetrate ocular tissues after topical or retrobulbar administration. This raises hope that the NPs may be useful carriers of therapeutic agents for ocular delivery. Future research should be directed at a longer presence of the NP inside the eye. For substances that should act inside the cells, NP should be modified in a way that they are taken up specifically by the target cells.

CONTROL ID: 3713088

SUBMITTER (NAME ONLY): Jack Greiner

TITLE: ATP's Potential Role as a Hydrotrope Thereby Preventing Intralenticular Protein Aggregation

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.V. Greiner, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T. Glonek, Clinical Eye Research of Boston, Winchester, Massachusetts, UNITED STATES|J.V. Greiner, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study provides evidence for the role of intralenticular adenosine triphosphate (ATP) as an endogenous hydrotrope for prevention of Protein Aggregation (PA) known to be an etiology of age-related cataractogenesis.

Methods: Calculation of ATP concentration and spectral line widths (indicators of atomic mobility) were determined in both H_2O and 98% D_2O buffers in intact (ex vivo) lens (N=12) among multiple species using a 200 MHz NMR spectrometer for phosphorus-31 detection. The line widths of each resonance multiplet of the three phosphorus atoms of ATP were determined during a time-course [baseline (0 hr) to 3 hr].

Results: Intralenticular concentration of ATP [2.4 ±0.15 millimolar (mM)] far exceeds the micromolar (μM) amounts required for intracellular metabolism. The field strength of the spectrometer permitted resolution of the spectral line width in the α-group phosphate (11.6 ±0.5 Hz) relative to the γ-group phosphate (18.8 ±0.5 Hz) of ATP ($P < 0.01$). When incubated in D_2O buffer, the line widths of the phosphates progressively narrow with time such that after 3 hr the line width of the α-group phosphate was 9.7 ±0.5 Hz and the γ-group phosphate was 8.9 ±0.5 Hz which indicates the direct interaction of the hydrogen atoms of water with the phosphate groups. With time, the γ-group phosphate line width narrows significantly more than the α-group phosphate line width ($P < 0.01$) indicating that the γ-group phosphate is interacting with the interstitial water, whereas the α-group is closer to the protein surface and less free to interact.

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Conclusions: 1. The large mM concentration of ATP in the metabolically quiescent lens is 3 orders of magnitude greater than what is believed to be required for all the known functions of ATP (metabolic or otherwise) combined. 2. Incubating in control H_2O buffer, the different signal widths of the α-and γ-phosphate signals indicate that the ATP is acting as a hydrotrope with the adenine moiety bound to and shielding the protein surfaces and the γ-phosphate extending into the interstitial water between neighboring α-crystallin protein molecules. 3. With incubation in D_2O buffer, the γ-group phosphate line width narrows significantly more than observed in the α-group phosphate. This data supports the hypothesis that ATP functions as a hydrotrope preventing cataractogensis secondary to PA. Prevention of PA is essential for maintaining lens transparency.

CONTROL ID: 3713089

SUBMITTER (NAME ONLY): Junya Hanaguri

TITLE: Beneficial effect of long-term administration of Febuxostat on retinal neurovascular coupling in type 2 diabetic mice

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hanaguri, H. Yokota, K. Takase, M. Watanabe, A. Ono, S. yamagami, T. Nagaoka, Nihon Daigaku Igakubu Fuzoku Itabashi Byoin, Itabashi-ku, Tokyo, JAPAN|A. Kushiyama, Meiji Yakka Daigaku, Kiyose, Tokyo, JAPAN|S. Kushiyama, Kokuritsu Kango Daigakko, Kiyose, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Febuxostat (FBX), which is a therapeutic agent for hyperuricemia, has an inhibitory effect on xanthine oxidase. Some previous studies reported that the inhibition of uric acid production by FBX may prevent diabetic nephropathy due to reduced oxidase stress and an anti-inflammatory effect. However, it remains unclear whether FBX has a beneficial effect on diabetic retinopathy. We investigated the effect of the long-term administration of FBX on impaired retinal blood flow regulation in response to flicker stimulation, which is an index of retinal neurovascular coupling, in type 2 diabetic mice.

Methods: Six-week-old db/db mice were randomly divided into an untreated group that received placebo (n=6) and a treated group, which received FBX (n=6). The longitudinal changes in retinal blood flow responses to systemic hyperoxia and flicker stimulation were evaluated every 2 weeks in diabetic db/db mice from 8 to 14 weeks of age. Retinal blood flow was assessed using laser speckle flowgraphy.

Results: Resting retinal blood flow was steady and comparable between the two groups throughout the study. In db/db mice treated with FBX, the blood flow responses to systemic hyperoxia and flicker stimulation were significantly restored from 10 weeks of age in comparison to diabetic mice in the untreated group ($P<0.05$, $P<0.001$), and these beneficial effects were observed until 14 weeks of age.

Conclusions: Our results suggest that the long-term administration of FBX can improve the impaired regulation of retinal blood flow in response to systemic hyperoxia and flicker stimulation in type 2 diabetic mice.

CONTROL ID: 3713090

SUBMITTER (NAME ONLY): Madeleine Carter

TITLE: Developing novel differentiation methods for the generation of 3D retinal organoids from cynomolgus macaque iPSCs

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Carter, V. Chichagova, B. Dorgau, M. Lako, Biosciences Institute, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|V. Chichagova, Newcells Biotech, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To develop a reliable in vitro protocol for generating 3D retinal organoids (ROs) from cynomolgus macaque iPSCs using a highly scalable multi-well plate (wp) format. This aims to inform knowledge of mammalian retinal differentiation and reduce the pre-clinical use of animal models.

Methods: Two iPSC lines from cynomolgus macaque (Macaca fascicularis) were exposed to several known and novel human retinal differentiation protocols, using early BMP4 addition, an IGF1 based media, or RPE conditioned media (-CM), in a 96-wp format. The differentiation protocols were applied using a timeline adjusted for the shorter macaque gestation, relative to human.

iPSC-derived ROs were characterised morphologically and molecularly throughout differentiation, for protein and gene expression of known neural-retinal and mature cell markers. Immunohistochemistry was performed using validated antibodies. RT-qPCR was performed on RNA from multiple organoids, using validated primers. Two-way ANOVA analysis of gene expression data was performed on two independent replicates.

Results: By adapting the timeline of human RO differentiation protocols to the shorter gestation of the macaque, macaque iPSC derived ROs were generated and maintained phase-bright retina and mature cell marker expression at day 120. Macaque ROs show the sequential expression of neural-epithelia (RAX, PAX6, SOX2), photoreceptor precursor (CRX), interneuron (AP2α, PRKCα), photoreceptor (ARR3, OPN1SW, OPN1LW/MW, RHO), and Müller glia (RLBP1) markers indicating some retinal development and maturation throughout differentiation. Method efficiency to generate ROs as determined by morphology was ~40% at day 120.

Macaque iPSC lines showed variable responses, with the IGF1-based protocol improving RO structure and photoreceptor gene expression (RCVRN, ARR3, CRX) significantly ($p<0.0001$) in both cell lines, and additionally significantly increasing Müller glia (RLBP1) and rod (RHO) expression ($p<0.0001$) in 1 cell line. RPE-CM addition from day 15 significantly increased Müller glia (RLBP1) and cone (ARR3) expression ($p<0.0001$) at late stages (day 90-120) in both cell lines.

Conclusions: The use of an adapted differentiation timeline and retinal stimulating factors, IGF1 and RPE-CM, resulted in high method efficiencies for differentiation of cynomolgus macaque iPSCs to ROs and confirms the amenability of production in a multi-well format.

CONTROL ID: 3713093

SUBMITTER (NAME ONLY): Vicente Zanon-Moreno

TITLE: Evaluation of the prevalence of non-intraocular pressure-related characteristics. A cross-sectional study of ocular hypertension and glaucoma patients.

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Zanon-Moreno, Universidad Internacional de Valencia, Valencia, Valenciana, SPAIN|M.D. Pinazo-Duran, N. Sala-Grau, C.C. borges, C. Garcia-Villanueva, Cellular and Molecular Ophthalmobiology Group, Universitat de Valencia, Valencia, Comunitat Valenciana, SPAIN|J. Garcia-Medina, Ophthalmology, Hospital General Universitario Jose M Morales Meseguer, Murcia, Murcia, SPAIN|E. Milla, Ophthalmology, Hospital Clinic de Barcelona, Barcelona, Catalunya, SPAIN|J.M. Salgado-Borges, Hospital da Boa Nova, PORTUGAL|

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ABSTRACT BODY:

Purpose: To evaluate the prevalence of non-intraocular pressure (IOP)-related characteristics in a cohort of individuals with ocular hypertension (OHT) and primary open-angle glaucoma patients (POAG) at risk of optic nerve degeneration (OND).

Methods: A multicenter, analytical, observational, cross-sectional study was performed using a representative sample of 412 volunteers of both sexes recruited from 8 hospitals (Spain and Portugal). Participants were classified as OHT subjects (n=198) and POAG patients at initial stage (n=214). Data from the clinical history, anamnesis, and ophthalmological examination (intraocular pressure -IOP-, central corneal thickness -CCT-, optical coherence tomography -OCT- and visual field -VF-) were recorded to define the study groups. Also, sociodemographics, anthropometric, endocrinologic, nutritional, toxic habits, psychotropic drugs, cardiovascular and respiratory variables were studied. Statistics were carried out by the SPSS 25.0 program.

Results: Mean age of the study population was 62 years. Gender distribution was 53% men and 47% women in the POAG group, and 39% men and 61% women in the OHT group. In the POAG group, IOP was 16 mmHg in the right eye and 18 mmHg, meanwhile in the OHT group was 20 mmHg in the RE and LE. Among the 14 potential risk factors for OND (age, gender, thyroid dysfunction, body mass index, coffee or tea consumption, smoking or drinking habits, psychotropic drugs, cold hands/feet síndrome, migraine, asthma, chronic obstructive pulmonary disease - COPD, and sleep apnea/hypopnea syndrome - SAHS) stood out in both groups for its prevalence the coffee habit (2/3 of the population, 64% POAG, 65% OHT), overweight (1/2 of the study volunteers, 34% POAG, 44% OHT) and psychotropic drug intake (1/3 of the participants, 36% POAG, 37% OHT), whereas the less frequent comorbidities were asthma (12% POAG, 9% OHT), COPD (5% POAG, 16% OHT) and SAHS (11% POAG, 13% OHT).

Conclusions: In this Spanish-Portuguese cohort, new non-IOP-related factors have been identified to help assess the risk of POAG and to prevent or delay OND and glaucoma blindness.

CONTROL ID: 3713094

SUBMITTER (NAME ONLY): Evan Berger

TITLE: Comparative Analysis of Face-Down Support Systems

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Berger, A. Wagner, K.G. Kapoor, Ophthalmology, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: E-commerce and expedited shipping have changed the landscape of patient options for access to face-down support systems (FDSS) for vitrectomy. The purpose is to compare the latest types of FDSS, their cost, and their expedited availability. A comparative analysis will help optimize patient preoperative counseling, help understand options to ensure positioning compliance post-operatively, and reduce cost surprises.

Methods: A Google search for “face down positioning equipment” and an Amazon search for “face down support” was conducted. On Amazon a search filter was used for products with a ≥ 4-star rating. A comprehensive list of FDSS was compiled. The device cost, shipping costs, option to rent vs. buy, and availability of next-day delivery were reviewed. The 1-week and 2-week costs for each FDSS was calculated.

Results: Three categories of FDSS were identified: face supports, seated supports, and sleep supports. Three online medical device companies were identified that offer FDSS (Table 1). Next-day shipping was available from two companies. On Amazon there were two popular FDSS available with free shipping through Amazon Prime. Table 2 provides a comparison of 1-week and 2-week costs. Regardless of shipping method, the most cost-effective FDSS type is a face support. Among ground shipped devices, the least expensive face/seated/sleep support package is The Standard Comfort Package 2. The most affordable option with next-day delivery is the face support from Vitrectomy.com. At 2 weeks it becomes less expensive to purchase this device. The Vitrectomy.com Ultimate Vitrectomy Package is the only face/seated/sleep support available with next-day shipping.

Conclusions: Patients that can wait for ground shipment have a number of FDSS options. Patients in need of next-day delivery have fewer options and will encounter significant delivery costs. These may be prohibitory for some patients as health insurance does not routinely cover FDSS. The optimal FDSS for a given patient will ultimately depend on their individual needs. This analysis helps vitreoretinal surgeons and their patients understand what FDSS options are available. The data can streamline preoperative counseling and increase the transparency of FDSS costs. In turn, this could lead to increased FDSS adoption, better positioning compliance, and possibly improved surgical outcomes.

CONTROL ID: 3713096

SUBMITTER (NAME ONLY): Kwadwo Akuffo

TITLE: Macular pigment optical density in the Bosomtwi District, Ghana

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.O. Akuffo, I. Osei Duah, D. Ben Kumah, S. Kyeremeh, Department of Optometry and Visual Science, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|L.N. Aduku, C. Apprey, Department of Biochemistry and Biotechnology, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|W. Eisenbarth, M. Lippok, Department of Applied Science and Mechatronics, Munich University of Applied Sciences, Munich, GERMANY|J.A. Hamidu, Department of Animal Science, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|B. Singh, Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|B. Singh, University Hospital, Kwame Nkrumah University of Science and Technology, Kumasi, GHANA|E. J. Johnson, Friedman School of Nutrition and Science and Policy, Tufts University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular pigments possess antioxidants, anti-inflammatory and light filtering properties implicated in visual function, and protection against retinal diseases, yet their average levels have not been previously determined in the general Ghanaian population. This study was designed to evaluate macular pigment optical density (MPOD) and its associated factors in a Ghanaian sample.

Methods: One hundred and fifty-four (aged 12 -72 years) subjects MPOD were determined in the best corrected visual acuity (BCVA) eye using customized heterochromatic flicker photometry. BCVA and Contrast sensitivity (CS) were assessed using LogMAR Early Diabetic Retinopathy Treatment Study (EDRTS) and Peli Robson charts respectively. Anthropometric assessment was performed following standard procedures and dietary carotenoid intake evaluated using a 3-day 24-hour dietary recall. Demographic and health status characteristics were gathered with a structured questionnaire. Data were summarized using frequencies, percentages, means, and standard error of means and associations between variables investigated with linear regression analyses at a significance level of $p<0.05$.

Results: The average MPOD at 0.5° and 1.0° retinal eccentricity were 0.22 ± 0.02 and 0.23 ± 0.01 density units whereas critical flicker frequency at the fovea and meso estimated at 17.31 ± 0.51 and 18.12 ± 0.36 Hertz respectively. MPOD was not influenced ($p > 0.05$) by age, sex, smoking, light exposure, body mass index, body fat, visceral fat and family history of eye diseases. Similarly, macular pigment was unrelated ($p > 0.05$) with BCVA, and CS.

Conclusions: Our results suggest lower average macular pigment levels than those obtained from previous investigations in Caucasians, Chinese, Europeans, and African descendants. Given the unsatisfactory mean MPOD levels, we recommend dietary interventional programs to help improve macular pigment levels in this sample.

CONTROL ID: 3713097

SUBMITTER (NAME ONLY): Tunde Peto

TITLE: Performance of a Diabetic Retinopathy Deep Learning Model for Ultra-widefield Imaging

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the performance of a deep learning model for diabetic retinopathy (DR) and diabetic macular edema screening when using ultra-widefield (UWF) imaging.

Methods: For model development, 67,200 UWF images were collected from DR programs and ophthalmology clinics worldwide. 30,836 images were double graded and adjudicated at 8 grading centres by 125 certified graders using ETDRS extension of the Modified Airlie House Classification of Diabetic Retinopathy following the JVN Clinical Trial Ultrawide Field Grading Manual v1.0. The grading system used traditional ETDRS 7-SF field definition as well as extended fields 3-7 to evaluate the retinal periphery. A further 36,364 UWF images were graded using a grading protocol based on the ICDR classification. The dataset was split into training, tuning and testing. The final DR model is an ensemble of 10 EfficientNet-b0 neural networks, independently trained with standard image augmentation techniques. For model validation, two independent sets of images were collected. Model performance was evaluated by comparing its predictions to the adjudicated ground truth for both sets of images.

Results: Prior to clinical validation, the model performance was internally evaluated on an independent set of 1967 images, of which 1050 were graded via adjudication as negative for more than mild diabetic retinopathy (mtmDR negative), and 917 as having referable diabetic retinopathy (mtmDR positive). The overall performance (Table 1) was weighted by target DR distribution. Clinical validation evaluated an independent data set of 420 images selected to achieve a target distribution that enabled appropriate confidence intervals for mtmDR sensitivity and specificity A panel of three graders adjudicated these 420 images and assessed 241 as mtmDR negative, 179 as mtmDR positive and 135 as vtDR positive. Model’s performance on the clinical validation set is shown in Table 2.

Conclusions: The deep learning model was developed with high quality graded UWF images and performed at a level that highly suggests usefulness in a clinical screening setting. A large, prospective multi-center clinical trial is currently evaluating the performance of a similar model in a real-world clinical setting.

CONTROL ID: 3713098

SUBMITTER (NAME ONLY): Benjamin Mc Clinton

TITLE: Characterization of Deletions using Oxford Nanopore Long-Read Sequencing

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Mc Clinton, L. Crinnion, M. McKibbin, R. Mukherjee, M. Ali, C. Inglehearn, C.M. Watson, C. Toomes, Leeds Institute of Medical Research at St James', University of Leeds, Leeds, Leeds, UNITED KINGDOM|L. Crinnion, C.M. Watson, Yorkshire and North East Genomic Laboratory Hub, Leeds, UNITED KINGDOM|M. McKibbin, R. Mukherjee, Eye Department, St James's University Hospital, Leeds, West Yorkshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Deletions in Inherited Retinal Disease (IRD) genes are a common cause of IRDs, but they can be time consuming to characterise. Short-read next generation sequencing (NGS) can struggle to characterise deletions accurately, particularly in exome or targeted sequence, where it may detect a deletion but fail to capture the breakpoints. Genome sequencing allows more effective characterisation of deletions, but many deletions occur due to the presence of repetitive elements, which inhibit accurate alignment of short-read sequences. The ability to characterise deletions efficiently is essential for confirming and defining breakpoints detected by NGS. The goal of this study was to develop a cost-effective long-range sequencing method to characterise deletions.

Methods: Four cases with large deletions in IRD genes, detected in exome sequence but not further characterised, were selected. These were amplified with Long Range PCR primers encompassing the deletion, using the Sequel Prep Long-Range PCR kit, to give 9.5kb, 4.4kb, 5.8kb and 4.2kb products. Samples were purified with an AxyPrep Mag PCR Clean Up Kit. Sequencing was performed on a MinIon using separate Flongle Oxford Nanopore adaptors. The resulting fast5 files were basecalled using Guppy, trimmed using Porechop and aligned using Minimap2. Filtering was performed using NanoFilt. Nanopore sequencing results were verified by Sanger Sequencing

Results: This method allowed fast, cost-effective characterization of deletion breakpoints in EYS, PRPF31, CNGA1 (see figure) and CNGB1. A high output was achieved for each case, with maximum 1.5Gb. A high proportion of reads were on target, up to 99.78% of generated bases were in the target loci. For three of the cases, Nanopore sequencing captured the breakpoint at a nucleotide level. The presence of repetitive Alu elements at the breakpoints of the PRPF31 deletion prevented nucleotide level characterization. For all cases, Sanger sequencing was then performed to confirm the sequence of the breakpoint.

Conclusions: This study has designed and tested a long-range, low-cost, labour efficient strategy to characterise breakpoints in deletions. This will allow for rapid characterisation of deletions detected by NGS.

CONTROL ID: 3713100

SUBMITTER (NAME ONLY): Cristina Martinez-Fernandez dela Camara

TITLE: RPGR^{ORF15} glutamylation impaired by mutations in its C-terminal basic domain

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Martinez-Fernandez dela Camara, J. Cehajic Kapetanovic, M.E. McClements, R.E. MacLaren, Nuffield Laboratory of Ophthalmology, Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|C. Martinez-Fernandez dela Camara, J. Cehajic Kapetanovic, R.E. MacLaren, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mutations in the RPGR gene represent a major contribution to retinitis pigmentosa. The photoreceptor-specific isoform, RPGR^{ORF15}, contributes to the intracellular cargo movement between inner and outer segments of rods and cones. Glutamylation of RPGR^{ORF15} by the enzyme TTLL5 is essential for its normal function and mutations in the glutamic acid-glycine rich region have been shown to impair this post-translational modification. The aim of this study was to evaluate the effect of disease-causing mutations in the C-terminal basic domain of RPGR^{ORF15} on its interaction with TTLL5 enzyme as a way of predicting the level of glutamylation in gene therapy vectors used in clinical trials.

Methods: RPGR^{ORF15} mutant constructs were generated by site-directed mutagenesis using a wild type (WT) construct as a template. RPGR WT and mutant constructs were transfected into HEK293 cells. The level of RPGR^{ORF15} glutamylation was assessed by western blot analysis using the GT335 antibody and a human RPGR antibody raised against the N-terminus. To analyse the interaction between the WT and mutant RPGR constructs with TTLL5, a proximity ligation assay was performed using the Duolink® detection technology from Sigma-Aldrich. The level of fluorescence was quantified in both assays to determine the level of glutamylation and the interaction between both proteins.

Results: GT335 western blot showed that the full-length RPGR^{ORF15} expressed with the wild type construct is strongly glutamylated. However, quantification of glutamylation levels by densitometry showed that all the mutations producing a truncated basic domain in RPGR^{ORF15} cause a decrease in the level of glutamylation, between 50 and 90%, compared to the full-length protein. However, the binding between truncated forms of RPGR and TTLL5 appeared not to be affected, suggesting that there are other mediators involved in the glutamylation of RPGR^{ORF15}.

Conclusions: Mutations in the C-terminal of RPGR^{ORF15} significantly reduce the level of glutamylation, despite apparently not impairing the binding to TTLL5. These results suggest that there are other proteins required for the glutamylation of RPGR^{ORF15}. Since glutamylation of RPGR^{ORF15} influences its stabilization and folding, and its interaction with other proteins in the connecting cilia, it is critical to ensure that gene therapy vectors provide the fully glutamylated protein to the retina in order to be biologically active.

CONTROL ID: 3713101

SUBMITTER (NAME ONLY): Tomasz Tomkiewicz

TITLE: Antisense oligonucleotide-based correction of the splicing defect caused by the c.769-784C>T variant in ABCA4.

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.Z. Tomkiewicz, S. Nieuwenhuis, F.P. Cremers, R.W. Collin, Department of Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|T.Z. Tomkiewicz, F.P. Cremers, R.W. Collin, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|A. Garanto, Radboud Universiteit Radboud Institute for Molecular Life Sciences, Nijmegen, Gelderland, NETHERLANDS|A. Garanto, Department of Pediatrics and Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Stargardt disease is an inherited retinal disease caused by mutations in the photoreceptor-specific gene ATP-binding cassette transporter type A (ABCA4). Interestingly ABCA4 has a high occurrence of splicing-affecting mutations. Here, we screened 9 antisense oligonucleotides (AONs) designed to correct pseudoexon (PE) inclusion due to a recurrent deep-intronic variant (c.769-784C>T) in ABCA4.

Methods: AON efficacy to induce PE exclusion in the ABCA4 transcript was assessed in three cell models carrying the c.769-784C>T variant. First, AONs were tested at a final concentration of 0.5 μM in HEK293T cells transfected with an ABCA4 midigene (splice reporter vector) carrying the deep-intronic change. Next, AONs were tested in patient-derived fibroblasts at the same final concentration. Based on the splicing-correction efficacy of each individual AON, the three most efficacious AONs were selected for a final assessment in photoreceptor-progenitor cells (PPC). Selected AONs were delivered at a final concentration of 0.5 μM and 1 μM. One-way ANOVA test with subsequent Bonferroni correction was used for statistical analysis.

Results: The AON screening using the HEK293T-midigene model indicated high efficacy of all AONs. Given these results, the same pool of AONs was evaluated in the patient-derived fibroblasts. Based on PE correction AON2, AON7 and AON5 were selected for further assessment in the patient-derived PPC model. AON2-mediated splicing correction was the most efficacious at the lower concentration (0.5 μM, $p<0.001$), followed by AON7 ($p<0.001$). AON5 was least efficacious reaching statistical significance at final concentration 1 μM only ($p=0.03$).

Conclusions: PE exclusion is a thoroughly researched therapeutic approach that has been shown to rescue protein function. It can be achieved using AONs, however it is crucial to select the most efficacious therapeutic molecule for further testing by employing different models. Taking this into account, AON2 and AON7 showed a high degree of PE skipping in PPCs, which provide a retina-like cellular context. Further research of AON2 and AON7 includes protein rescue studies and safety profile assessment in advanced retina models to mimic the cellular environment in patients.

CONTROL ID: 3713103

SUBMITTER (NAME ONLY): karim Elmowafi

TITLE: Combined Umbilical cord patching with amniotic membrane graft for corneal reconstruction

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Elmowafi, R. kamel, S. El Tarshoby, ophtalmology, Mansoura University Faculty of Medicine, Mansoura, EGYPT|

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ABSTRACT BODY:

Purpose: The aim of this study is Evaluation role of umbilical cord patch transplantation for corneal perforations and descemetoceles by assessment of healing of corneal perforation and increased corneal thickness in case with descemetoceles by using slit lamp bio microscopy and anterior segment optical coherence tomography.

Methods: After topical anesthesia for cases with corneal thinning patients and general anesthesia in corneal perforation cases. the base and surrounding of the ulcers were cleaned of necrotic tissue. The Umbilical cord patching with epithelium side facing up was trimmed to fit the shape and depth of the ulcer, and interrupted sutures were placed to anchor the UCP to the cornea. A large piece of the amniotic membrane with epithelium side up was applied over the entire cornea. Finally, bandage contact lens was applied. All patients were followed up daily throughout the first week, weekly for 1 month, then monthly for the first 6 months.

Results: There were 20 eyes with Corneal perforation or thinning. The diameter of corneal thinning ulcers of 3.5±2. 5mm.The anterior chamber in all 20 eyes formed at first postoperative day with improvement of preoperative photophobia foreign body sensation. The corneal thickness was increased in cases with corneal thinning from mean 86.00 ± 24µm to 194± 25µm postoperatively. Healing of corneal defect of cases with corneal perforation at average of 4 weeks. Best Correction Visual acuity in cases with thinning improvement from (-1.82 ± 3.455) by Log MAR to (-0.66 ± 1.942). While, cases with perforation there was an improvement from (-0.53 ± 0.548) to (0.79 ± 0.677)

Conclusions: The current study demonstrated the promising effects of combining UCP with amniotic membrane transplantation is a promising alternative for corneal insult, providing satisfactory reconstruction. Because of its stem cell therapy plus easy availability and efficacy .

CONTROL ID: 3713104

SUBMITTER (NAME ONLY): Jenny Youale

TITLE: Transferrin protects RPE cells from oxidative damages

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age-related Macular Degeneration (AMD) is a multifactorial disease involving oxidative stress, inflammation, complement activation and ferroptosis. Elevated retinal iron levels in AMD patients have been well documented and could contribute to all these pathophysiological hallmarks suggesting that iron chelation could benefit AMD. We previously demonstrated that local administration of Transferrin (TF), an endogenous iron chelator, is effective for reducing iron retinal content and oxidative stress and slowing down photoreceptor loss in various animal models of retinal degeneration. Here, we further explored the protective mechanism of action of TF in oxidative stress conditions at the retinal pigment epithelium (RPE) level.

Methods: Differentiated ARPE-19 (dARPE-19) and hiPSC-derived RPE (iRPE) cells were exposed for 24 hours to $FeCl_3$NTA or 4HNE in presence of TF. Viability of RPE cells was assessed by quantification of mitochondrial activity (CellTiter) and LDH release. Changes in the expression pattern of genes involved in iron homeostasis (TFR1, H-FT, L-FT, LCN2), oxidative stress (HMOX, SOD1), complement activation (C3), lipid metabolism (ABCA1), and ferroptosis (GPX4) was defined by RT-qPCR.

Results: Both $FeCl_3$NTA and 4HNE induced a dose-dependent decrease in dARPE-19 and iRPE cell viability. Incubation with TF significantly protected dARPE-19 and iRPE against $FeCl_3$NTA-induced toxicity (+101.1% and +91.2% viability, respectively), and against 4HNE-induced oxidative stress (+57.3% and +71.3% viability, respectively). 24h exposure of iRPE cells to $FeCl_3$NTA drastically decreased the expression of TFR1 (0.41-fold change) and increased the expression of H-FT and L-FT (2.47- and 3.39-fold change, respectively) and LCN2 (1.982-fold change). Moreover, a significant increase in C3, ABCA1, SOD1 and GPX4 genes was highlighted. Co-treatment with TF restored almost control levels of all genes impacted by $FeCl_3$NTA. Exposure to 4HNE drastically increased the expression of HMOX1 (11.77-fold change) which was significantly prevented by TF (2.39-fold change, $p < 0.0001$).

Conclusions: By controlling iron homeostasis, TF has the potential to counteract oxidative stress, complement activation and other pathways involved in AMD pathogenesis. The protective effect of TF in iron-independent stress condition suggests TF has activities beyond iron chelation.

CONTROL ID: 3713105

SUBMITTER (NAME ONLY): Consuelo Robles

TITLE: Inverted meniscus IOLs reduce retinal distortion in the peripheral visual field

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Robles, L. Hervella, Voptica SL, Parque Científico de Murcia, 30100 Murcia, SPAIN|P.M. Prieto, P. Artal, Laboratorio de Óptica, Universidad de Murcia, Campus de Espinardo, 30100 Murcia, SPAIN|J. Marin-Sanchez, E. Alcon, Oftalvist Murcia, Murcia, SPAIN|P. Taña, Oftalvist Alicante, Alicante, SPAIN|D. Christaras, H.S. Ginis, Department of Research, Athens Eye Hospital, Athens, GREECE|D. Christaras, H.S. Ginis, Diestia systems PC, Athens, GREECE|

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ABSTRACT BODY:

Purpose: Standard biconvex intraocular lenses (IOLs) are designed to optimize focus at the eye's central retina but degrade optical quality in the peripheral retina with respect to the natural crystalline lens. In order to prevent this drawback of current IOLs, a new lens with an inverted meniscus shape (ArtIOL, Voptica SL, Murcia, Spain) was developed to provide better image quality in the peripheral retina. Moreover, IOL implantation can be associated with image distortion. The aim of this study is to compare the inverted meniscus lenses with the standard biconvex with respect to the induced image distortion.

Methods: Pre- and post- cataract surgery fundus images were taken with an ultra-widefield retinal camera (CLARUS 500, Zeiss, Germany) in 55 eyes of patients implanted with a standard biconvex IOL (control group) and 43 eyes of patients implanted with the inverted meniscus ArtIOL lens. For each eye, retinal landmarks (such as vessel bifurcations) were identified and their relative radial position was identified using a purposely written MATLAB (MathWorks, Inc. Natick, MA, USA) script. Retinal distortion at these locations was obtained for both groups.

Results: Although there was a large variability among subjects, we have found distortion to be significantly lower in the ArtIOL group than in the control group. Furthermore, distortion was found to linearly increase with eccentricity roughly twice faster in the control group than in the ArtIOL group (see figure), therefore predicting even larger differences for higher eccentricities than the 40 deg range studied.

Conclusions: Its inverted meniscus design bestow ArtIOL lenses with a better performance on the peripheral field, significantly reducing distortion of the retinal image in pseudophakic eyes with respect to traditional biconvex IOLs. This may have an impact in the quality of vision affecting patients' tasks relaying in peripheral performance.

CONTROL ID: 3713106

SUBMITTER (NAME ONLY): Nicholas O'Connor

TITLE: Changes in Glaucoma Management Following Diurnal Home Tonometry

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. O'Connor, L.E. Hock, A. Shukla, N.N. Kolomeyer, R. Razeghinejad, L. Katz, J.S. Myers, D. Lee, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the effect of iCare HOME tonometry on clinical management of glaucoma patients who were progressing with low in-office intraocular pressures (IOP).

Methods: 72 eyes of 36 patients with primary open-angle glaucoma (n=36 eyes), low-tension glaucoma (n=20), pigmentary glaucoma (n=6), pseudoexfoliation glaucoma (n=2), chronic angle-closure glaucoma (n=2), open-angle glaucoma
suspects (n=2), and steroid response (n=2) were enrolled during office visits. Patients were asked to record IOP four times daily (around 8 am, 12 pm, 4 pm, and 8 pm) for 1 week using iCare HOME. Upon review of home tonometry readings, a decision was made whether to advance therapy. Home tonometry IOP mean, maximum, minimum, range, standard deviation, and coefficient of variation, as well as Goldman applanation tonometry (GAT) immediately prior to the home trial were compared retrospectively between patients who underwent changes in glaucoma therapy versus those whose management did not change.

Results: 42 eyes (58.3%) of 21 patients had changes in glaucoma management after review of iCare HOME readings. Of these, 30 (71.4%) changed medical therapy, 6 (14.3%) received selective laser trabeculoplasty, and 6 (14.3%) underwent surgery (Table 1). Patients for whom treatment was advanced demonstrated significantly greater maximum IOP (26.6 ± 10.5 mmHg vs 21.2 ± 7.3 mmHg, p = 0.01 and IOP range (17.6 ± 10.5 vs 12 ± 6.8, p = 0.01) than patients whose management was unchanged (Table 2). Mean IOP (15.3 ± 6.3 mmHg vs 14.1 ± 4.3 mmHg, p = 0.4) and GAT prior to the home trial (13.3 ± 4.2 mmHg vs 14 ± 3.3 mmHg, p = 0.4) were similar between the two groups.

Conclusions: The iCare HOME is a valuable tool for glaucoma specialists in determining whether to advance therapy among glaucoma patients who may be progressing despite meeting in-office IOP targets. Alternative iCare HOME testing may have value in assessing whether patients require additional treatment.

CONTROL ID: 3713110

SUBMITTER (NAME ONLY): Amy Babiuch

TITLE: Prediction of proliferative diabetic retinopathy (PDR) from nonproliferative diabetic retinopathy (NPDR) using real-world (RW) electronic health record (EHR) data

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.S. Babiuch, C.C. Valentim, A.K. Wu, A. Kalur, R. Sastry, A. Iyer, J. Muste, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|Q. Yang, S. Rizzo, J. Luu, G. Spicer, D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|D. Damopoulos, F. Benmansour, F. Hoffmann-La Roche Ltd., Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To develop and validate a survival analysis and machine learning algorithm to predict the individual future risk of NPDR worsening to PDR using RW EHR data.

Methods: In this retrospective study of 4408 patients with diabetes, NPDR, and ≥ 365 days of follow-up at Cleveland Clinic Cole Eye Institute from January 2012 to February 2020 (Babiuch A et al. Invest Ophthalmol Vis Sci. 2021;62(8):1120), EHR data from the NPDR index visit (diabetes type, age, race, gender, smoking status, BMI, Charlson Comorbidity Index [CCI] score, diabetic macular edema [DME] status, HbA1c, creatinine, systolic blood pressure, eGFR, BUN, insulin use, anti-VEGF treatment, logMAR letters) was used to build prognostic models of PDR progression. Data was randomly split into 80% development data and 20% test data. Both survival analysis and linear regression models were evaluated. To assess association of baseline characteristics with PDR progression, time-dependent Cox proportional hazards modeled PDR progression as time-to-event data. Median imputation addressed missing data in covariates. Linear regression models were trained for predicting probability of progression to PDR for 6 months (month [M] 6, M12, M18, M24) with respect to index visits. Performance of the Cox model was assessed using time-dependent dynamic area under the curve (AUC) and the linear regression model was evaluated using AUC and 95% CI.

Results: The Cox model performed well, with a dynamic AUC of 0.81 on average over the study period (Figure 1). The linear regression models predicted progression to PDR at M6 with an AUC (95% CI) of 89% (75%, 96%), at M12 with 89% (81%, 95%), at M18 with 86% (78%, 91%), and at M24 with 87% (79%, 92%; Figure 2). The Cox model revealed DME, Black race, and higher baseline CCI and HbA1c as significant positive associations with PDR progression, whereas anti-VEGF treatment and older age had significant negative associations. Linear models showed DME, higher CCI, and lower age as the most important predictors.

Conclusions: Results from 2 prototype models demonstrated feasibility in predicting PDR from individual NPDR patients using RW EHR data, which may inform clinical management of patients with DR; identified risk factors may also help clinical research of DR development in the RW.

CONTROL ID: 3713114

SUBMITTER (NAME ONLY): Juliet Moncaster

TITLE: α-klotho overexpression and age-related changes in mouse lenses across lifespan

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.A. Moncaster, D. Parsons, O. Minaeva, L.E. Goldstein, Radiology, Boston University, Boston, Massachusetts, UNITED STATES|J.A. Moncaster, O. Minaeva, C. Abraham, L.E. Goldstein, Alzheimer's Disease Research Center, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|C. Abraham, Biochemistry, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Klotho is a transmembrane proteins implicated in aging-related phenotypes (in brain, kidney, cardiovascular system, organism longevity) in humans and experimental animals. Klotho has been shown to be protective during aging and overexpression of it has been demonstrated to be neuroprotective in the brain. The klotho family of genes includes α-klotho, β-klotho and γ-klotho. α-klotho is expressed in the lens and the brain. However it is not known how α-klotho affects aging of the lens. Here we investigated the effect of α-klotho overexpression in the lens across the mouse lifespan.

Methods: α-klotho overexpressing transgenic and littermate non-trangenic mice were bred, maintained and genotyped at Boston University. Male and female mice were sacrificed at selected ages across the lifespan. Lenses were isolated and imaged under with a custom-adapted Zeiss stereophotomicroscope and digital Nikon camera.

Results: Aged mice displayed age-related cortical opacities. There was no overt different phenotype between the normal α-klotho expressing non-transgenic mice and the transgenic α-klotho overexpressing mice. In contrast to previously reported studies in the brain, overexpression of α-klotho did not appear to have any gross effect on aging lens phenotype.

Conclusions: Aged mice displayed age-related cortical opacities. There was no overt different phenotype between the normal α-klotho expressing non-transgenic mice and the transgenic α-klotho overexpressing mice. Further studies using α-klotho knock-out mice may provide further insight into the role of α-klotho in lens aging as has been reported for other tissues.

CONTROL ID: 3713116

SUBMITTER (NAME ONLY): Alba Paniagua-Diaz

TITLE: Optical Memory Effect of excised cataractous human crystalline lenses

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Paniagua-Diaz, C. Martínez, D. Simón, E. Moreno, P. Artal, Universidad de Murcia, Murcia, Murcia, SPAIN|I. Yago, J. Marin-Sanchez, Oftalmology, Hospital Clinico Universitario Virgen de la Arrixaca, El Palmar, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: Cataracts increase the amount of intraocular light scattering in the crystalline lens causing vision impairment by blurring and reducing the contrast in retinal images. Wavefront shaping techniques in combination with the Optical Memory Effect (OME) have been suggested for the optical (non-surgical) correction of scattering in cataractous lenses. In this context, we aim to characterize the scattering properties of excised human lenses by measuring their OME.

Methods: The Optical Memory Effect is an intrinsic correlation of scattering media that provides the isoplanatic patch of a cataract's correction imaging technique, determining how the transmitted speckle pattern changes with a tilt/shift of the incident beam. We measured it using a 594nm laser incident on cataractous lenses by recording the transmitted pattern. With the lens mounted on a shift/tilt holder, the similarity between the speckle patterns for different values of shift and tilt of the lens was examined via cross-correlation. We characterized the OME for different cataract stages. For each case, we also included other scattering metrics, as the straylight parameter, measured with the Optical Integration Method, the transport mean free path and contrast image quality, studying the variation of the OME with the measured scattering parameters. We measured a total of 22 lenses of donors aged between 29 and 67, leaving the cataract develop with time to increase the scattering range.

Results: We found that OME is non-negligible for cataracts, being strongly dependent on the scattering strength. For severe cataracts (straylight parameter Log10[s]=2.45 and image contrast below 16%), the OME was mainly limited by a tilt of 6 deg, whereas for weak cataracts (Log10[s]=1.32 and image contrast 90%) this range was extended up to 10 deg. We also found a linear relationship between the straylight parameter, image contrast and OME decorrelation, providing us with a new tool for the prediction of the OME range when only quantitative scattering measurements are taken.

Conclusions: The OME of cataractous excised human lenses has been measured for the first time. Together with quantitative scattering parameters measured simultaneously, it provides with a useful tool for the optical correction of cataracts using wavefront shaping techniques. This work paves the way to new potential approaches for the non-invasive and real-time correction of cataracts with wearable devices.

CONTROL ID: 3713118

SUBMITTER (NAME ONLY): Laxmi Raja

TITLE: Determinants of non-attendance in synchronous teleophthalmology clinics.

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Raja, S. Wagner, R. Struyven, P.A. Keane, J. Huemer, K. Balaskas, D. Sim, S. Kang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|J. Rahi, A. Solebo, Child Health, University College London Institute for Global Health, London, London, UNITED KINGDOM|S. Wagner, M. Cortina-Borja, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|P.A. Keane, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has accelerated the introduction and dissemination of telemedicine into ophthalmic secondary care. Yet this pivot to telemedicine-dominated care could exacerbate the differential in health outcomes for certain groups. This study seeks to quantify and characterise factors associated with non-attendance within a population of patients attending synchronous tele-ophthalmic hospital outpatient appointments.

Methods: A retrospective cohort study at a tertiary-level ophthalmic institution comprising a principal central site, four district hubs and five satellite clinics in London, UK between January 1st 2019 and October 31st 2021. Multivariable logistic regression modeled attendance status against sociodemographic, clinical and operational exposure variables for all new patient registrations.

Results: Between January 1st 2019 and October 31st 2021, a total of 6843 eligible patients (mean age of 45 +/- 32, 58.0% female) were newly registered to attend synchronous teleophthalmology clinics. Self-reported ethnicity identified 3.4% as South Asian, 1.4% Black, 25.3% Other Ethnic Group and 7.6% White. 62.3% did not report their ethnicity. Most appointments were in general ophthalmology (59.9%, n=4096), followed by cataract (20.2%, n=1379), adnexal (19.1%, n=1310), medica retina (0.1%,n=55) and glaucoma (0.0%,n=3).

Increased rates of non-attendance were associated with male sex (adjusted OR 0.74, CI 0.62-0.88), greater levels of deprivation (adjusted OR 0.88, CI 0.84-0.92), incompletion of self-reported ethnicity (adjusted odds ratio 0.3, CI 0.17 - 0.54) and a previously cancelled appointment (adjusted OR 0.65, CI 0.5-0.83) (all $p<0.001$). Individuals identifying as Asian or Black ethnicity had worse attendance in synchronous clinics with adjusted odds ratios of 0.42 (CI 0.20-0.90, $p = 0.02$) and 0.28 (CI 0.12-0.65, $p=0.0025$) respectively. Patients with diabetes were more likely to attend with an adjusted odds ratio of 1.03 (CI 0.3 - 3.55, $p = 0.9$).

Conclusions: With regards to synchronous teleophthalmology clinics, poorer attendance is associated with male sex, greater socioeconomic deprivation and self-reported Asian and Black ethnicities. Further study is warranted to evaluate whether enhanced surveillance of these cohorts could improve their non-attendance rates.

CONTROL ID: 3713119

SUBMITTER (NAME ONLY): Julian Esteve-Rudd

TITLE: Preclinical pharmacology and safety of GT005, an investigational gene therapy targeting the complement pathway for the treatment of Geographic Atrophy

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Esteve-Rudd, J. Francis, J. Hughes, S. Ellis, Gyroscope Therapeutics Ltd, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Report preclinical pharmacology and safety data of GT005, an investigational AAV2 expressing recombinant human Complement Factor I (hCFI), after subretinal delivery in non-human primates (NHP).

Methods: GT005 was assessed in a 6-month NHP GLP toxicology study after subretinal injection at low dose (LD) $7x10^{10}$ and high dose (HD) $3.5x10^{11}$ vg/eye (3 animals/sex/dose). Optical coherence tomography, intraocular pressure, electroretinography, vector shedding, ELISPOT, antibodies to capsid and hCFI, and hCFI levels in vitreous humor (VH) were measured throughout the study. Histopathology, vector biodistribution and hCFI expression in tissue were evaluated at termination.

Results: There were no systemic effects of GT005 and no treatment-related findings outside the eye. There were histopathology findings in the injection area for both doses, with variable severity. Mononuclear cell infiltrates were found in ocular tissues, optic nerve, optic disk, VH and iris/ciliary body. Loss of RPE and photoreceptors was detected from week (wk) 13. These changes correlated with a significant anti-hCFI antibody response in serum and VH of most treated NHPs at wk 13 and 26 ($P<0.01$). Serum levels of antibodies to AAV2 at wk 4 were weaker and remained constant at wk 13 and 26. No T cell responses to hCFI or AAV2 were found in NHPs, except for one animal in the HD group which developed a significant response against AAV2. Vector biodistribution was similar for both doses with levels highest at the dose site in ocular tissues and falling to below the limit of detection in most organs. Vector shedding was confined to tear samples up to wk 4. hCFI mRNA and protein expression was observed in the outer retina and hCFI protein was detected in VH from 2 wks up to 26 wks. Maximal levels of hCFI were found in the VH at wk 4 in the HD (1437±551 ng/mL) and at wk 13 in the LD (805±249 ng/mL). Reduced hCFI levels at later timepoints correlated with antibody titres to hCFI ($R=0.83$; $P<0.001$).

Conclusions: GT005 was well tolerated with no safety findings outside the eye. GT005 led to local hCFI expression. Ocular dose-dependent inflammation-induced changes were observed, and correlated strongly with anti-hCFI antibody generation. These were deemed to be species-specific and therefore unlikely to translate to the clinic. These data supported the clinical development of GT005.

CONTROL ID: 3713122

SUBMITTER (NAME ONLY): Noel Ziebarth

TITLE: Pilot Study to Increase Penetration of Rose Bengal in the Human Cornea

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ziebarth, Department of Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|J. Lai, H. Durkee, K. Leviste, P.A. Sepulveda Beltran, J. Martinez, E. Arrieta-Qintero, G. Amescua, J. Parel, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rose Bengal photodynamic antimicrobial therapy (RB-PDAT) has been shown to be an effective adjunct therapy for treating infectious keratitis. However, the average penetration depth of Rose Bengal (RB) as previously reported is insufficient to treat deeper infections such as those of acanthamoeba and fungus. The purpose of this study was to determine the effect of solvent and RB formulation (disodium versus lactone) on penetration depth within the cornea.

Methods: Eight pairs of human donor corneas were obtained from the Florida Lions Eye Bank. These corneas were initially received from donors to use as grafts in corneal transplant surgery but later were deemed unsuitable for transplant due to the donor's history or disqualifying medical indications. Prior to experiments, the corneal tissue was placed in Optisol medium and kept viable in sealed plastic containers at 4○C. The post mortem time was less than 15 days for all corneas. To test the effect of solvent, 5 pairs of corneas were soaked epithelial side down in a 0.01% solution of disodium RB in H_2O (OS) or in NaCl (OD) for 25 minutes. To test the effect of type of RB, an additional 3 pairs of corneas were soaked in a 0.01% solution of disodium RB in NaCl (OS) or a 0.01% solution of lactone RB in NaCl (OD). DAPI stain was applied to the endothelial layer of all corneas, and they were imaged via confocal microscopy. Penetration depth and corneal thickness was assessed from the Z-stack. Two tailed t-tests were used to evaluate statistical significance.

Results: Utilizing H_2O versus NaCl as the solvent for disodium RB had no effect on the mean corneal thickness after soaking (833±28μm in H_2O and 824±17μm in NaCl; p=0.55). The solvent also had no effect on the penetration depth of RB in the cornea (120±23μm in H_2O and 113±21μm in NaCl; p=0.62). The type of RB had no effect on the mean corneal thickness after soaking (938±16μm for disodium and 907±61μm for lactone; p=0.48). However, there was a significant difference between the penetration depth in the cornea of disodium compared to lactone RB (153±17μm for disodium and 202±13μm for lactone; p=0.016).

Conclusions: Our results suggest that the solvent used has no effect on penetration depth and that more hydrophobic RB groups will increase penetration depth. However, the swelling that occurred during soaking was higher than expected and requires more investigation before translation of this research into clinical treatment.

CONTROL ID: 3713123

SUBMITTER (NAME ONLY): Oliver Zeitz

TITLE: Phase I/IIa study examining the safety and tolerability of single and multiple rising intravitreal doses of BI 836880 in patients with wAMD

SESSION TITLE: AMD and Anti-VEGF

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Zeitz, Charite Universitatsmedizin Berlin, Berlin, Berlin, GERMANY|A. Edwards, Oregon Retina, a Division of Sterling Vision, Eugene, Oregon, UNITED STATES|A. Hu, Cumberland Valley Retina Consultants, Hagerstown, Maryland, UNITED STATES|B. Berger, Retina Research Center, Austin, Texas, UNITED STATES|G. Simons, D. Peter, Boehringer Ingelheim Pharma GmbH & Co KG, Biberach, GERMANY|M. ehrlich, Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, Connecticut, UNITED STATES|S. Sivaprasad, NIHR Moorfields Biomedical Research Centre, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To assess the safety and tolerability of BI 836880, a dual vascular endothelial growth factor (VEGF)/angiopoietin-2 inhibitor, in a two-part single rising dose (SRD) and multiple rising dose (MRD) study in patients with wet age-related macular degeneration (wAMD).

Methods: This Phase I/IIa open-label, non-randomized study (NCT03861234) includes patients with wAMD who, in the SRD part and the first cohort of the MRD part (1.00 mg), have progressed despite ≥3 prior anti-VEGF injections. The second cohort of the MRD part (2.00 mg) will enroll treatment-naïve patients with wAMD. In the SRD part, patients received one single intravitreous injection of BI 836880 (either 0.06, 0.18, 0.50, 1.00, or 2.00 mg) and were followed for up to 43 days. Based on the highest tolerated doses identified in the SRD part, patients in the MRD part will receive three consecutive 1.00 or 2.00 mg doses of BI 836880 over a 3-month period. The primary endpoint is the number of patients with dose-limiting ocular events in the SRD part and the number of patients with drug-related adverse events (AEs) in the MRD part. Secondary endpoints in the MRD part include change from baseline in best-corrected visual acuity (BCVA) and central subfield foveal thickness.

Results: In the completed SRD part, 15 patients received BI 836880 (n=3 per dose group); all were white with a mean age of 76 years. In total, 40% of patients had an AE; all were ocular. No AEs were dose-limiting or drug-related; one patient had a serious AE of wAMD in the fellow eye. Overall, 26.7% of patients had procedure-related AEs (vitreous floaters, conjunctival hemorrhage, dry eye). The mean change in BCVA from baseline to end of study in the SRD part was +5.3, +7.3, +0.3, +6.0, and +7.0 letters (doses of 0.06, 0.18, 0.50, 1.00, and 2.00 mg, respectively). In the ongoing MRD part, four patients have been enrolled and received 1.00 mg BI 836880 to date; all are white with a mean age of 76.5 years. Two patients have had a reported AE, one of which was ocular. Neither was serious, dose-limiting, or drug-related.

Conclusions: BI 836880 was well tolerated by patients in the SRD part and has been well tolerated by patients in the MRD part to date, with no dose-limiting or drug-related AEs reported. BCVA data from the SRD part demonstrate preliminary signs of efficacy, which are being further investigated in the ongoing MRD part.

CONTROL ID: 3713124

SUBMITTER (NAME ONLY): Kristina Frain

TITLE: Risk of Hepatitis B Virus reactivation in patients receiving systemic immunosuppressive therapies for uveitis: A Case Series

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Frain, E. Bober, C. de resende, E. Hindle, S. Sandhu, S. Hassan, I. Yeung, C. Pavesio, Uveitis Service, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|R. Lee, Barts Health NHS Trust, London, London, UNITED KINGDOM|J. Ma, Rheumatology, Royal Free London NHS Foundation Trust, London, London, UNITED KINGDOM|I. Ewing, Hepatology, Homerton University Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Oral Prednisolone (oPSL) at doses of ≥20 mg for ≥4 weeks is a well-documented moderate to high-risk factor for reactivation of chronic HBV (cHBV), especially in combination with immunosuppressants. Risk of iatrogenic cHBV reactivation in ophthalmology has not been reported. This retrospective case series describes cases of Uveitis with cHBV on oPSL and concurrent immunosuppressives to highlight the role for pre-treatment risk stratification for ophthalmologists.

Methods: Our large tertiary centre database was screened for uveitic patients receiving csDMARDs and had previous cHBV for inclusion. Patient records were retrospectively analysed and baseline patient characteristics, therapeutic, and serological data collected.

Results: 13 uveitic patients (8 female and 5 male) were included. Median age was 42 (±16.75). Sarcoidosis n=3 (23.1%) and VKH n=3 (23.1%) were the most represented uveitides. 11 patients (84.62%) received Prednisolone ≥20 mg for ≥4 weeks. Median duration in weeks oPSL >20mg was 10 (±37). Average maximum oPSL dose at each prescription was 60mg (±5). 6 patients (46.15%) were on Adalimumab. All patients were on csDMARD therapy. Of the 13 patients, 1 (7.69%) patient had reactivated HBV (rHBV) with a positive HbsAg during treatment. For the 1 patient with rHBV, the ALT level increased by 2857.69% from initial ALT measurement. 2 Patients (15.4%) required anti-HBV therapy.

Conclusions: This study demonstrated that Prednisolone can cause reactivation of cHBV in ophthalmology; our 7.69% reactivation rate is in keeping with the literature (<10%). Further higher-powered studies are warranted to identify causality and other independent predictors of reactivation in an ophthalmic patient population.

CONTROL ID: 3713125

SUBMITTER (NAME ONLY): Giulia De Rossi

TITLE: LRG1-driven phenotypic switch in pericytes is an early event in diabetic retinopathy

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. De Rossi, M.E. Da Vitoria Lobo, J. Greenwood, S.E. Moss, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Pericytes have a fundamental role in maintaining vascular homeostasis and their malfunction is thought to be an early event in diabetic retinopathy (DR). Cross-sectional studies have reported increased levels of leucine-rich α-2 glycoprotein 1 (LRG1) in the plasma and vitreous humor of diabetic patients but failed to establish whether LRG1 plays an active role in disease pathogenesis. Our study aimed to elucidate the role of LRG1 in the early microvascular events taking place in the diabetic retina using experimental models of DR.

Methods: We took advantage of two murine models of type I diabetes (STZ and Akita) to correlate Lrg1 expression to the retinal vascular changes happening over 6 months of hyperglycaemia. We also compared global Lrg1-deficient mice to wild-type littermates to identify the contribution of LRG1 to the vascular abnormalities in diabetic retinas (N=10/group, males, C57Bl/6). We then designed in vitro culture models incorporating human primary retinal pericytes (HRP) to assess the effects of LRG1 on the morphology, signalling and function of pericytes (N=3).

Results: We found increased LRG1 expression in diabetic retinas early after hyperglycaemia onset (4-8 wks). In both models, diabetic retinas were characterised by an increased number of semi-detached pericytes (or ‘pericyte bridges’), stretching their processes between adjacent capillaries of the deep plexus (50% increase at 16 wks). This increase did not occur in the diabetic retinas of Lrg1-deficient mice. Morphometric analyses revealed that these hyper-activated pericytes, and their processes, were almost-exclusively associated with bent capillaries (Fig.), suggesting that these structures can exert tractional forces on endothelial cells (ECs). Based on these observations, we subjected cultured HRPs to increasing doses of recombinant LRG1 and revealed a phenotypic switch towards a more star-shaped morphology coupled to an enhanced ability to contract collagen type I. This contractile phenotype was associated with increased expression of typical myofibroblast proteins (αSMA, vimentin, fibronectin).

Conclusions: We have shown that LRG1 is up-regulated early on after hyperglycaemia onset in the retina and triggers a myofibroblastic-like phenotype in pericytes. We believe that targeting LRG1 could prevent or revert EC-pericyte decoupling and normalise the vasculature, paving the way to more timely and effective treatments in DR.

CONTROL ID: 3713126

SUBMITTER (NAME ONLY): Ariel Zenouda

TITLE: The impact of luminance and disease stage on navigation performance in age related macular degeneration (AMD) - a MACUSTAR study report

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zenouda, Streetlab, Institut de la vision, Paris, Île-de-France, FRANCE|A. Abdirahman, A. Tufail, H.M. Dunbar, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|J. Sahel, S. Mohand-Said, M. Paques, INSERM-DHOS CIC 1423, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|A. Tufail, H.M. Dunbar, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|N. Zakaria, Novartis Institutes for BioMedical Research Inc, Cambridge, Massachusetts, UNITED STATES|N. Tyler, Pedestrian Accessibility Movement Environment Laboratory, University College London, London, London, UNITED KINGDOM|U.F. Luhmann, Research and Early Development, Translational Medicine Ophthalmology, Roche Innovation Center, Roche Pharma Schweiz AG, Basel, Basel-Stadt, SWITZERLAND|A. Schenk, C. Behning, Institute of Medical Biometry, Informatics and Epidemiology, Faculty of Medicine, University of Bonn, Bonn, GERMANY|

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ABSTRACT BODY:

Purpose: A navigation task was developed to study the impact of illumination and disease stage on navigation performance in people with AMD.

Methods: 64 subjects with AMD and 10 similarly aged healthy controls recruited to the MACUSTAR study at 2 sites; Quinze-Vingts CHNO (n=35, mean age: 72, AMD stage: 3 controls/27 early or intermediate[e/i]/5 late) and Moorfields Eye Hospital (n=39, mean age: 74, AMD state: 7/26/6) undertook a navigation task at Streetlab (S) and Pedestrian Accessibility Movement Environment Laboratory (P) respectively. 4 obstacle seeded mazes were developed at each site. Due to different platform sizes (S:9x5m, P:11x7m) and availability of obstacles maze configurations varied. Subjects navigated 1 of 4 randomly selected mazes under 1 transition (256 reducing to 1lux) and 3 static (256, 4, 1 lux) light conditions. Preferred walking speed (PWS) for an unobstructed path was measured under 256lux and %PWS calculated for each trial. A linear mixed model was constructed using %PWS as the outcome measure, adjusted for age and site. Disease stage, light condition and their interaction term were also included.

Results: A site effect was present with %PWS being 9 percentage points higher ($p < 0.001$) at S compared to P. Subsequent findings are adjusted for this effect. There were no direct effects of AMD stage or light level on %PWS, however their interaction term indicates %PWS is differentially affected by luminance depending on AMD stage. Specifically, e/i AMD had a significant interaction with the transition condition ($b = -5.87$, $p = 0.047$), whereas late AMD had significant interactions with 4 lux ($b = -7.68$, $p=0.04$) and transition condition ($b = -11.37$, $p = 0.003$).

Conclusions: Results indicate that whilst those with late AMD have poorer navigation performance under low and transient light conditions, people with e/i AMD do not experience a deleterious effect of static low light, but are negatively impacted by a sudden reduction in luminance. This may be a real-world manifestation of delayed dark adaptation and impaired vision in low luminance. These findings support the exploration of the utility of navigation-based endpoints for future novel treatment trials in both e/i and late AMD.

CONTROL ID: 3713128

SUBMITTER (NAME ONLY): Devika Verma

TITLE: Incidence of Ocular Herpetic pathologies in a hospital setting, United Kingdom

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Verma, R. Sharma, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UNITED KINGDOM|

Commercial Relationships Disclosure: Devika Verma: Commercial Relationship: Code N (No Commercial Relationship) | Rohit Sharma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The incidence of ocular herpetic pathologies, in particular Herpes Zoster Ophthalmicus (HZO), has seemingly been on a rise over the past years, especially among the elderly and immunocompromised. The nature of this rise is likely multifactorial ranging from access to Shingles vaccination programmes, potential increase in immunocompromised individuals, social factors and most recently, Covid-19 infection. The relationship between Covid-19 and ocular herpetic pathologies has anecdotal basis. Certain studies have hypothesized T-cell dysfunction as a mechanism of Varicella Zoster virus reactivation in patients affected by Covid-19. This retrospective, observational study analyses the pattern of incidence of ocular herpetic pathologies in a secondary care centre, United Kingdom (UK).

Methods: This study was set in an eye casualty clinic in Queens Hospital, Burton-on-Trent (University Hospitals Derby & Burton NHS, UK). Diagnoses of each patient was recorded in the Eye Casualty Patient Register. Data was extracted from three time periods – i. Pre-covid pandemic (July -December 2019), ii. Pandemic (July - December 2021) and iii. Post coronavirus vaccine introduction, UK (April and May 2021). Extracted data was pooled into the following groups – Herpes Simplex Keratits (HSK)/ HZO/ Shingles/Herpetic Kertatouveitis/ Herpes Zoster/Herpes Simplex/Herpes simplex endothelitis.

Results: The data between pre-pandemic and post-pandemic periods highlighted an increasing incidence of certain ocular herpetic conditions. Highest number of diagnoses were recorded as HSK and HZO. HSK accounted for the highest incidence across all time periods - 41% (pandemic), 34% (pre-pandemic) and 37.5% (after vaccine introduction). On the other hand, similar incidence is noted with HZO diagnoses - 32.9% (pandemic), 32.7% (pre-pandemic) and 37.5% (after vaccine introduction).

Conclusions: Overall, a gradual increase in incidence of ocular herpetic pathologies was observed from 2019 - 2021 at this centre. Multiple factors could be responsible for this rise, with Covid-19 infection as a potential factor. However, there is insufficient data to draw up a definitive association between the increasing incidence of such conditions and Covid-19, especially as the immune response to the infection and vaccinations are poorly understood. Larger, multi-centre studies would be required to assess the burden of incidence in the UK.

CONTROL ID: 3713129

SUBMITTER (NAME ONLY): Claus Cursiefen

TITLE: Corneal crosslinking ameliorates degree of corneal edema in subsequent acute keratoconus

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Cursiefen, W. Zhang, Y. hou, S. deng, A. Howaldt, F. Bock, Dept. of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Corneal edema in acute keratoconus is caused by a sudden break of Descemet membrane. This study aims to assess whether pre-treatment with corneal crosslinking (CXL) can ameliorate corneal edema in a subsequent hydrops.

Methods: Normal or keratoconic human tissue (obtained during penetrating keratoplasty; n=6 each) was incubated with Corneal Culture Medium (CCM) I for hydration for 1 day and then dehydrated with CCM II for 24 hours. Then either CXL with 30-minutes topical application of 0.1% riboflavin followed by a 30-minutes UVA irradiation (3mW/cm2) or riboflavin only (in controls) followed. Afterwards, tissues were incubated with CCM I and central corneal thickness was measured using OCT (before treatment: hydration, dehydration; after treatment: overnight, 1 day, 2 days, 4 days). In the vivo experiment, C57BL/6 mice received CXL or only riboflavin (controls). Fourteen days later, a linear perforating incision was performed as murine model of acute keratoconus. Corneal thickness was measured by OCT after incision at 15 and 30 minutes, 1 and 4 hours, 1, 7 and 14 days (thickness from 5 naïve mice as the baseline).

Results: In the ex vivo experiments, crosslinked normal and keratoconic tissue had a significantly reduced swelling after rehydration: For normal corneas (normalized to “Dehydration”), the percentage of increase in thickness between Dehydration and 24 hours was 15.87% in the CXL group and 89.3% in controls (P=0.0019). For keratoconus corneas, results were 6.53% in CXL-treated and 38.2% in controls (P=0.0323). In the in vivo experiment, the average corneal thickness was significantly reduced in the treatment group at 15 minutes, 4 hours and 1 day post treatment compared to the controls (P<0.05).

Conclusions: CXL seems to ameliorate acute swelling of normal and keratoconic human corneas. Also, it can ameliorate the degree of early corneal edema in subsequent acute keratoconus in the murine model.

CONTROL ID: 3713134
SUBMITTER (NAME ONLY): Bastien Leclercq
TITLE: Anatomical characterization of the choroidal nervous system
SESSION TITLE: Mechanisms of Refractive Error and Eye Development
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: B. Leclercq, M. Zhao, F. Behar-Cohen, UMRS1138, INSERM, Paris, Île-de-France, FRANCE|
Commercial Relationships Disclosure: Bastien Leclercq: Commercial Relationship: Code N (No Commercial Relationship) | Min Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Francine Behar-Cohen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The choroid vasculature, constituted by a network of arteries and capillaries, is essential to answer the metabolic needs of the outer retina. To avoid hypo or hyper-perfusion, which can lead either to ischemia or oedema, the choroidal blood flow is finely regulated by a very dense nervous system. This choroidal nervous system is known to be constituted by extrinsic components (autonomous and sensory) and by an intrinsic component (intrinsic choroidal neurons). While the choroidal vasculature has been thoroughly studied, the anatomy and the role of the choroidal nervous system and its implication in the etiology of pathologies is still poorly understood.

Methods: To better characterize the choroidal nervous system, choroids of mouse and rat, as well as human choroids, have been fixed and studied by histological approaches on transverse sections and/or flat-mounted tissue. Anatomical and neurochemical properties have been revealed by immunohistochemistry (IHC) using different markers of the autonomous and sensory nervous system such as TUBB3, myelin basic protein (MBP), neuropeptide Y (NPY) and calcitonin gene related peptide (CGRP). Furthermore, Electron microscopy (EM) has been used to analyze the ultrastructure of the nerve fibers and the myelination.

Results: The NPY-positive sympathetic fibers seem to be located close to the blood vessels, the labelling is almost exclusively concentrated around the vessels, probably at the synaptic level. There are very few CGRP-positive sensory fibers, the labelling is visible all along the fibers and these fibers are not preferably organized around the vessels, covering different zone of the choroid. EM analysis and IHC labelling on transverse sections showed both myelinated and unmyelinated nerves. Finally, IHC showed that a consequent quantity of fibers is located in the choriocapillaris, very close to the Bruch’s membrane.

Conclusions: The choroidal nervous system is a very dense and heterologous network. The sympathetic innervation seems to target preferably blood vessels, consistently with its role in the blood flow regulation. On the other hand, sensory nervous system displays a very different organization suggesting a different role in the choroid physiology. Moreover, the nervous fibers proximity with the Bruch’s membrane/retinal pigment epithelium complex could suggest a role of the choroidal nervous system in the regulation of the molecule efflux between the choroid and the retina.

CONTROL ID: 3713135

SUBMITTER (NAME ONLY): Dhanach Dhirachaikulpanich

TITLE: Investigating the effect of ageing on protein folding chaperones expression in RPE

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Dhirachaikulpanich, L.I. Paraoan, Eye and Vision Science, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Liverpool, UNITED KINGDOM|D. Dhirachaikulpanich, Mahidol University Faculty of Medicine Siriraj Hospital, Bangkok, THAILAND|J. de Magalhães, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Liverpool, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Protein folding chaperones have critical roles in proteostasis. In the human ageing brain and neurodegenerative disease, there is a significant decrease in the expression of these proteins. This study aimed to investigate their expression in relation to ageing in the retinal pigment epithelium (RPE).

Methods: The publicly available microarray transcriptome dataset GSE29801 of RPE/choroid was re-analysed to assess the ageing effect on gene expression in RPE/choroid. A linear model using limma was applied to find the differential expressed genes with age, and the respective significant genes were further subjected to gene set enrichment analysis. Fifteen RNA samples of human RPE/choroid (47-83 years old) were used to validate the significance of ageing for DNAJB1 (HSP40) gene. DNAJB1 expression was also assessed in ARPE-19 cells cultured on extracellular matrix exposed to glycolaldehyde to induce glycation end products (AGE) or exposed to lipid peroxidation (LPE) by qPCR and Western blot. Two-way ANOVA was performed for statistical analysis.

Results: The transcriptome data of 96 human RPE/choroid (9-93 years old) was analysed by limma. The analysis showed 620 genes differentially expressed with ageing (277 upregulated and 343 downregulated). Among the differentially expressed genes, gene-set enrichment analysis showed co-chaperone activity as a significant gene set (FDR<0.05), including down-regulation of DNAJB1, DNAJB4 and DNAJA1. The negative correlation of DNAJB1 transcription with ageing was validated in an independent set of 15 RPE/choroid samples by qPCR ($p<0.05$). There was an increase in mRNA expression but lower protein expression of DNAJB1 in ARPE-19 cells cultured in the presence of AGE and LPE ($p<0.05$).

Conclusions: Differential expression of the chaperone DNAJB1 in RPE/choroid of increased ageing was characterised using a publicly available human transcriptome RPE/choroid dataset, in-house human RNA samples extracted from human RPE/choroid and AGE-/LPE-exposed ARPE-19 cells. The results indicate the downregulation of DNAJB1 in ageing RPE. In the presence of AGE and LPE, DNAJB1 protein level is reduced in ARPE-19 cells, possibly due to increased turnover, but the cells might subsequently compensate by increasing mRNA expression of DNAJB1. Our results suggested that DNAJB1 could be a critical regulator of proteostasis in ageing RPE/AMD similar to the ageing brain and other neurodegenerative diseases.

CONTROL ID: 3713136

SUBMITTER (NAME ONLY): Rongjie Guo

TITLE: MSC-EVs treat dry eye disease by regulating dendritic cells and promoting tissue repair

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In this study, we explored the therapeutic efficacy of Mesenchymal stromal cells -derived extracellular vesicles (MSC-EVs) in a mouse model of dry eye disease (DED) and assessed its ability to modulate immune responses and promote tissue repair in dry eye disease.

Methods: DED was induced in female C57BL/6 mice by exposure to controlled environment chamber and subcutaneous injection of 0.5mg/0.2mL scopolamine hydrobromide four times per day for 14 days. Mice were grouped and treated with either MSC-EVs or PBS eye drops for comparison purposes. Samples of cornea, conjunctiva and draining lymph nodes were collected after treatment. Dendritic cells (DCs) were detected by immunofluorescence and flow cytometric analysis to assess its number and the expression of MHC-II and CD86. Th17 cells were detected by flow cytometric analysis to evaluate the antigen-presenting function of DCs. RT-PCR was performed to determine the mRNA expression of inflammatory cytokines in cornea and conjunctiva. In vitro, human corneal epithelial cells (HCEC) were cultured in hyperosmotic media and treated with MSC-EVs. Then cell viability was assessed by CCK8, and expression of inflammatory cytokines was detected by RT-PCR.

Results: MSC-EVs-treated mice presented more tear production ($P<0.05$) and lower corneal fluorescein staining scores ($P<0.05$). DED upregulated the number of DCs and their maturation level, and treatment with MSC-EVs effectively reduced the number of DCs ($P<0.05$) and suppressed the expression of MHC-II ($P<0.01$) and CD86 ($P<0.05$). Reduction of Th17 cells was also observed in cornea and draining lymph nodes. Compared with untreated control group, expression of inflammatory cytokines was downregulated in cornea and conjunctiva of MSC-EVs-treated mice. In vitro, MSC-EVs protected HCECs against loss of cell viability induced by hyperosmotic stress. MSC-EVs also reduced the expression of inflammatory cytokines, including TNF-α, IL-1β, IFN-γ and IL-6.

Conclusions: The results of our study revealed the role of MSC-EVs in regulating DC functions and promoting tissue regeneration in DED mice. MSC-EVs hold a great promise as a novel treatment method for DED and other ocular surface diseases.

CONTROL ID: 3713137

SUBMITTER (NAME ONLY): Noelia Blanco

TITLE: Effect of exosomes produced by corneal epithelium on the expression of virulence factors of bacteria.

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Blanco, V. Lozano-Iturbe, H. Ordiales Trabanco, L. Quirós, Department of Functional Biology, Universidad de Oviedo, Oviedo, Asturias, SPAIN|N. Blanco, V. Lozano-Iturbe, H. Ordiales Trabanco, I. Alcalde, L. Quirós, L. Fernández-Vega Cueto, C. Martín, J. Merayo-Lloves, Instituto Universitario Fernandez-Vega, Oviedo, SPAIN|L. Fernández-Vega Cueto, Instituto Oftalmologico Fernandez-Vega, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Infectious keratitis is one of the leading causes of blindness worldwide, frequently associated with the use of contact lenses. It is primarily due to the invasion of the corneal tissue caused by a great variety of microorganisms, mainly bacteria. Exosomes are nanovesicles of 30 to 150 nm in diameter involved in both physiological and pathological intercellular communication processes. Regarding eye diseases, the knowledge of their role is still very limited. Based on this, the hypothesis that arises is that microorganisms in contact with exosomes produced by human corneal epithelium cells (HCE), an experimental model, would produce changes in the expression of bacterial virulence factors.

Methods: Exosomes were isolated and purified from HCE and then added to Gram-positive (Staphylococcus epidermidis) and Gram-negative (Pseudomonas aeruginosa) bacterial cultures. Afterwards, the variation in the expression levels of genes encoding virulence factors were analysed by means of RT-qPCR over time compared to bacteria without any contact with exosomes.

Results: The expression levels of 7 virulence factors were studied at different times, from 30 minutes to 16 hours. When Staphylococcus epidermidis data was analysed, two clear tendencies were observed: while one group increased their expression up to 4-8 hours and then they remained stable, the other group, after a slight increase in the first 30 minutes, decreased over time. In the case of Pseudomonas aeruginosa, the genes analysed present a common trend, decreasing strongly in the first hours and recovering their expression levels over time.

Conclusions: Staphylococcus epidermidis, considered a commensal microorganism but also one of the main agents responsible for bacterial keratitis, increases the expression of genes encoding toxins and biofilm, while those related to quorum sensing are reduced over time. In the case of the pathogen Pseudomonas aeruginosa, the virulence factors related to biofilm establishment also modify their levels. Taking into consideration these results, it is deduced that bacteria have the ability to respond and change the expression of virulence factors in the presence of exosomes, with no need for direct tissue contact.

CONTROL ID: 3713138

SUBMITTER (NAME ONLY): Clare Futter

TITLE: Morphological heterogeneity of the lysosomes of the retinal pigment epithelium

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) has a high natural requirement for lysosomal degradation due to the daily phagocytosis and clearance of photoreceptor outer segments. Lysosomes are known to be heterogeneous in terms of morphology and content of classical lysosomal markers, but the functional significance of this is unclear. We aimed to characterise lysosomal heterogeneity in the RPE in order to determine the extent to which different lysosomal subpopulations represent stages in the lysosomal life cycle, which maintains the degradative capacity of the cell.

Methods: Morphology and content of lysosomal markers in primary porcine RPE and other cell models was determined by conventional and immuno-electron microscopy. To determine accessibility of lysosomes to the endocytic pathway cells were loaded with either fluorescent dextrans or colloidal gold particles and examined by live cell confocal microscopy and electron microscopy. Electron tomography was used to assess the 3-dimensional structure of RPE lysosomes.

Results: Vacuoles positive for lysosomal membrane proteins could be subdivided into those composed exclusively of lamellae, those with lamellar regions and those completely lacking lamellae. Endocytosed BSA gold particles were found exclusively in non-lamellar regions whilst the lamellar regions contained much of the lysosomal acid hydrolase, cathepsin D. Pulse chase experiments employing BSA gold showed that after degradation of the BSA that stabilises the gold particles, undigested aggregated gold particles were segregated into non-lamellar lysosomes. Parallel experiments employing sequential pulses of dextrans labelled with different fluorophores, separating the two pulses by up to 7 days, showed that a proportion of dextran-containing lysosomes lose accessibility to the endocytic pathway, suggesting that they have dropped out of the lysosome cycle. Electron tomography indicated multiple connections between lamellar lysosomes whilst at least some non-lamellar lysosomes have lost connection with this lysosomal network.

Conclusions: Morphologically heterogeneous lamellar and non-lamellar lysosomes within the RPE represent different stages in the lysosome cycle. Undigestible material is segregated into non-lamellar lysosomes that appear to lose the ability to interact with endosomes and lysosomes and drop out of the lysosome cycle.

CONTROL ID: 3713139

SUBMITTER (NAME ONLY): Helena Ordiales Trabanco

TITLE: Corneal surface glycosaminoglycans as receptors in Candida keratitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: One of the most frequent ocular pathologies worldwide is keratitis, which may be associated with infectious processes. Fungal keratitis is caused by a broad spectrum of microorganisms, which differs depending on the geographical area involved. The identification of the epithelial receptors which enable adherence and colonization is key with respect to fungal keratitis. Previous studies have shown that, in bacterial keratitis, pathogens specifically bind to certain regions of the glycosaminoglycans (GAGs) chains, which are usually highly sulphated. This study tested the hypothesis that GAGs can act as receptors of yeasts in corneal infection and possible changes in the gene expression of the modifying enzymes of the GAGs chains.

Methods: The adherence inhibition assays were performed on immortalized corneal epithelial cells (HCE-2) monolayers. Firstly, FITC-labeled yeast (Candida albicans, Candida glabrata or Candida parapsilosis) were co-incubated with heparan sulfate (HS), chondroitin sulfate A (CSA), chondroitin sulfate B (CSB), chondroitin sulfate C (CSC), or a mixture of the four, and then all incubated with HCE-2. Variations in the transcription levels of the GAGs chains modifying enzymes were analysed by RT-PCR. The data were analysed with statistical analysis. The mean values of two samples were compared using the Mann-Whitney U test with $p<0.05$ being considered as significant.

Results: The inhibition of adherence showed a decrease in the adherence of the 3 yeasts to the corneal cells although there are differences between fungal species and the interfering molecule used. HS and CSB showed the greatest inhibition in C. albicans, contrary to what occurs in C. parapsilosis, which were CSA and CSC. In C. glabrata, HS and CSC were those with the highest inhibitory capacity. The adherence of the fungus induced significant alterations in the expression levels of both HS and CS chains modifying enzymes. Among modifying enzymes of CS, 6 out of 9 enzymes showed sub-expressions induced by C. glabrata. In the case of modifying enzymes of HS, 10 out of 14 enzymes showed sub-expressions, although depending on the gene and yeast used.

Conclusions: Corneal surface GAGs are involved in the adherence of C. albicans, C. glabrata and C. parapsilosis. The interaction of the microorganism with cells induces alterations in the transcription levels of the GAGs chains modifying enzymes that are dependent at the yeast species.

CONTROL ID: 3713140

SUBMITTER (NAME ONLY): Siân Morgan

TITLE: An investigation into the impact of corneal rinsing during riboflavin/UVA corneal cross-linking

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Morgan, S. Hayes, A. Quantock, K.M. Meek, Cardiff University School of Optometry and Vision Sciences, Cardiff, Cardiff, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Corneal collagen cross-linking (CXL) using riboflavin and ultraviolet-A light (UVA) is a minimally invasive treatment used to prevent progression of keratoconus. Recently, some have advocated rinsing the cornea with balanced salt solution (BSS) prior to UVA exposure to remove the superficial riboflavin film and prevent UVA shielding. This study assesses the impact of rinsing on CXL effectiveness by examining the enzymatic resistance of the tissue following treatment.

Methods: 40 porcine eyes (with corneal epithelium removed) were assigned to 4 groups. Group 1 remained untreated. Groups 2, 3 and 4 received a 10-min application of 0.1% riboflavin/HPMC eyedrops. Group 3 was immediately exposed to 9 mW/cm^2 UVA for 10-mins and Group 4 received the same UVA exposure after a corneal surface rinse (0.25 ml BSS). Central corneal thickness (CCT) was recorded at each stage of treatment. Trephined 8.0 mm central corneal buttons (n = 5 per group) were subjected to 0.3% collagenase digestion at 37°C. The samples were monitored at 1-hr intervals for the first 30-hrs, and 2-10hr intervals thereafter, to determine the time required for complete digestion.

Results: A 10-min application of riboflavin/HPMC solution to the de-epithelialised cornea led to an increase in CCT (54 µm ± 26; $p<0.01$) (Fig. 1). During UVA exposure, the CCT of the unrinsed CXL corneas (Group 3) returned to pre-treatment levels but the CCT of the BSS-rinsed CXL corneas (Group 4) continued to rise above the pre-treatment value (75 µm ± 15; $p<0.01$). All CXL-treated corneas displayed a 3-to-4-fold greater resistance to collagenase digestion than non-irradiated corneas. Complete digestion occurred at 12 ± 0.9 and 12 ± 0.8 hours in the untreated (Group 1) and riboflavin only treated (Group 2) corneas respectively and at 36-49 hours in the CXL treated corneas (Groups 3 and 4). There were no notable differences in enzymatic resistance between the two CXL groups.

Conclusions: Both CXL protocols were equally effective at enhancing the resistance of the cornea to collagenase digestion, although BSS-rinse CXL may be advantageous for the treatment of thin corneas which require tissue swelling. Further studies are needed to assess the impact of different volumes of BSS rinse on CXL effectiveness.

CONTROL ID: 3713141

SUBMITTER (NAME ONLY): Ayesha Karamat

TITLE: Prediction of Activity in Eyes with Macular Neovascularization Due to Age-related Macular Degeneration Using Deep Learning

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Karamat, G. Corradetti, M.G. nittala, S.R. Sadda, Doheny Eye Institute, Los Angeles, California, UNITED STATES|N. Rakocz, J.N. Chiang, D.S. Boyer, D. Sarraf, E. Halperin, S.R. Sadda, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) can capture the microvascular structure of macular neovascularization (MNV) in eyes with age-related macular degeneration (AMD).In this study, we evaluated several deep learning algorithms designed to detect activity of MNV using en face OCTA images.

Methods: En face OCTA 6x6 mm images from 97 subjects with neovascular AMD imaged on RTvue-XR Avanti SD-OCTA (Optovue. Inc, Fremont, CA) device were included in this study and retrospectively analyzed. En face OCTA images of the MNV lesion were generated using a customized 10 microns thick slab,with the boundaries adjusted to display the maximum extent of the MNV lesion. Multiple machine learning models were trained to classify the presence of MNV activity on the OCTA images, using the presence of fluid on the structural OCT as the ground truth. Specifically, a five-fold cross-validation was applied to assess the different models' performance:four-fifths of the patients were used for training and a fifth for validation. This process was computed 20 times to generate a total of 100 different receiver operating characteristics (ROCs).The different performances were evaluated by using the ROC,its area under the curve (AUC). To further assess the ability of the algorithms to detect activity of MNV using en face OCTA images only, a leaky cross-validation approach was used.

Results: For 97 patients participated 637 en face OCTA scans were exported as .png images. Macular neovascularization (MNV) evident on en face OCTA images was a poor predictor of disease activity as defined by the presence of fluid on structural OCT. The algorithms used did not have a good performance and using the leaky cross-validation approach we conclude that even if a larger number of cases were used a substantial improvement in performance is not expected: Resnet (0.59 [0.47,0.71]), simple CNN (0.60[0.49,071]), LR+PCA (0.53[0.41,0.64]), Resnet-Scratch (0.62[0.54,0.70]). The leaky cross-validation applied to the top performing model, Resnet-Scratch, resulted in an AUROC of 0.67[0.60, 0.74].

Conclusions: In this study, we observed that en face OCTA images alone of MNV lesions are poor predictors of MNV lesion activity.This suggests that strong biomarkers of disease activity at a point time may not be encoded within the en face OCTA image.

CONTROL ID: 3713142

SUBMITTER (NAME ONLY): Brigitte Müller

TITLE: Age correlated reduction of photoreceptor connecting cilium length in XLRP mouse model and C57BL/6J mice

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Müller, A. Penner, K. Stieger, Ophthalmology, Faculty of Medicine, Justus-Liebig-University Giessen, Giessen, GERMANY|

Commercial Relationships Disclosure: Brigitte Müller: Commercial Relationship: Code N (No Commercial Relationship) | Annette Penner: Commercial Relationship: Code N (No Commercial Relationship) | Knut Stieger: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The C57BL/6-RPGR^{tm1Sti} mouse model for X-linked retinitis pigmentosa (XLRP model) carries a point mutation in the mutational hotspot exon ORF15 of the rpgr gene. To assess the reduction of photoreceptor connecting cilium (cc) length in the XLRP mouse model, immunohistochmically labeled cc were evaluated and compared to cc length in wildtype mice. Our central question was whether there is an age related reduction of cc length in photoreceptors (PRs) of the XLRP mouse model vs healthy wild type cc.

Methods: Hemizygous male or homozygous female mice (age: 3, 9 or 15 months) of the XLRP model and C57BL/6J wild type mice with respective age were sacrificed, enucleated and the eyes immediately frozen in embedding medium to cut frozen sections. Connecting cilium region was analyzed after immunohistochemical labeling with antibodies against Centrin, AcTub and RPGR using confocal laser scanning microscopy.

Results: Only Centrin and AcTub antibodies labeled the cc region of PRs in both mouse lines completely, in contrast to the RPGR antibody. Within each mouse line, the cc length got shorter with age. In XLRP mice, cc length is significantly shorter at 3 and 9 months compared to wild type retina. At 15 months, cc length in PRs of both mouse lines show no significant difference.

Conclusions: During the course of life cc length of PRs is decreasing significantly in both mouse lines investigated. In 3-months old XLRP mice, the cc length corresponds to 9-months old wild type mice. Therefore, age correlated reduction of photoreceptor cc length starts earlier in XLRP mouse model compared to wild type mice.

CONTROL ID: 3713143

SUBMITTER (NAME ONLY): hirotsugu kasamatsu

TITLE: Corneal higher-order aberration in corneal endothelial decompensation secondary to obstetrical forceps injury

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. kasamatsu, Y. Yagi-Yaguchi, T. Yamaguchi, J. Shimazaki, ophthalmology, Tokyo Shika Daigaku Ichikawa Sogo Byoin, Ichikawa, Chiba, JAPAN|

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ABSTRACT BODY:

Purpose: Corneal endothelial decompensation with Descemet's membrane (DM) breaks secondary to obstetrical forceps trauma is a rare condition, for which endothelial keratoplasty may be technically challenging due to abnormal contour of the corneal endothelial side. This study aimed to characterize the corneal high-order aberration (HOA) and corneal topographic changes in corneal endothelial decompensation with DM breaks.

Methods: This retrospective study included 18 healthy controls and 23 eyes of 21 patients diagnosed with corneal decompensation with DM breaks (nine men and 12 women; mean age of 54.0 ± 9.1 years) at Tokyo Dental College Ichikawa General Hospital. We classified the corneal topographic patterns obtained by anterior segment optical coherence tomography (AS-OCT, CASIA II, Tomey, Aichi, Japan) into five categories. We quantified HOA of the anterior and posterior surfaces and the total cornea using AS-OCT. We classified corneal topographic patterns (asymmetric, protruding, flat, posterior irregular pattern, and regular astigmatism) based on corneal topography maps. We evaluated the correlations between visual acuity and either corneal HOA, corneal opacity grading, or severity of corneal edema.

Results: The logarithm minimum angle of resolution of visual acuity was 1.45 ± 0.84 in eyes with corneal decompensation with DM breaks. The most common topography patterns were protruding and regular astigmatism (six eyes, each 26.1 %), followed by asymmetric pattern (five eyes, 21.7 %).HOA and coma within the diameters of 4 and 6 mm in corneal decompensation with DM breaks were significantly larger than those in healthy controls ($P<0.0001$). We found positive correlations between visual acuity and coma of the total cornea of 6-mm diameter, opacity grade, and corneal edema severity.
($r=0.482$, $P=0.023$, $r=0.695$, $P=0.0003$, $r=0.675$, $P=0.0006$, respectively)

Conclusions: Corneal HOA of total cornea and anterior and posterior surfaces were larger in patients with DM breaks secondary to obstetrical forceps injury than in normal individuals. Furthermore, coma significantly correlated with visual acuity, indicating that coma may be a useful parameter for assessing visual function in eyes with DM breaks.

CONTROL ID: 3713144

SUBMITTER (NAME ONLY): Sungjin Won

TITLE: The absorption of diethyl phthalate conventional hydrogel contact lens

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Won, J. Ahn, M. Choi, Optometry, Seoul National University of Science and Technology, Nowon-gu, Seoul , KOREA (THE REPUBLIC OF)|M. Choi, Convergence Institute of Biomedical Engineering and Biomaterials, Seoul National University of Science and Technology, Nowon-gu, Seoul , KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Diethyl phthalate (DEP) is commonly used in cosmetics, perfumes and is contained in contact lens cleaning solutions. Contact lenses float on the surface of the ocular and are used to correct vision. In addition to proteins and lipids, which are tear components, harmful substances in the atmosphere are adsorbed to the contact lens and their properties can be changed. The purpose of this study is to evaluate the binding strength between DEP and contact lens and the physical properties of contact lenses.

Methods: Daily disposable contact lenses, etafilcon A material 1-Day ACUVUE MOIST (Johnson& Johnson Inc.) and hilafilcon B material SofLens Daily (Bausch&Lomb Inc.), were used. All the contact lenses were washed to minimize the effect of multi-purpose solution by soaking the contact lenses in 3rd distilled water for 1 hour. Contact lenses were incubated with different concentrations of DEP solution; 2mL of 25μM, 50μM, 75μM, 100μM. The amount of absorbed DEP was measured using a UV-vis spectrometer at a wavelength of 228nm. Various parameters such as water content, and refractive power were measured.

Results: Both etafilcon A and hilafilcon B materials completed the binding reaction in 5 minutes. As the DEP concentration increased, the amount of absorbed DEP and the rate constants (k_{obs}) were increased. Among the two materials, etafilcon A showed the greater amount of absorbed DEP and the rate constants (k_{obs}). The water content of contact lenses tended to decrease as the amount of absorbed DEP increased. However, in terms of refractive power, there were only slight changes.

Conclusions: This study showed that DEP has a high binding effect on the contact lenses and reduces water content among several physical properties. Hilafilcon B has a nonionic-surface and etafilcon A has an ionic-surface. It is predicted that the difference in the amount of absorbed DEP and the rate constants (k_{obs}) were derived from this difference between the two materials. Contact lenses are in long-term contact with the ocular surface and the atmosphere, so adsorption of DEP can negatively affect ocular disease or wearability.

CONTROL ID: 3713146

SUBMITTER (NAME ONLY): Yoshiaki Yasuno

TITLE: Pseudo-degree-of-polarization-uniformity image generated from OCT intensity using deep neural network

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yasuno, K. Oikawa, S. Makita, Computational Optics Group, Tsukuba Daigaku, Tsukuba, Ibaraki, JAPAN|T. Yamaguchi, T. Mino, Kabushiki Kaisha Topcon, Itabashi-ku, Tokyo, JAPAN|M. Miura, T. Iwasaki, Department of Ophthalmology, Tokyo Ika Daigaku Ibaraki Iryo Center, Inashiki-gun, Ibaraki, JAPAN|

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ABSTRACT BODY:

Purpose: Polarization-sensitive OCT (PS-OCT) is expected to be the next generation OCT for clinical applications. The degree of polarization uniformity (DOPU) obtained by PS-OCT visualizes melanin distribution in retinal pigment epithelial cells (RPE) and depicts RPE abnormalities. However, the requirement of additional hardware for PS-OCT instrumentation has hindered the spread of PS-OCT. Here, we generated a pseudo-DOPU from ordinary OCT intensity using a convolutional neural network (CNN) and investigated its performance to detect abnormalities.

Methods: Fifteen eyes of 12 normal cases and 157 eyes of 123 abnormal cases were imaged by PS-OCT to obtain DOPU and OCT images. A CNN was trained to generate DOPU from OCT images using 10 eyes from 7 normal cases and 137 eyes from 103 cases of diseases.

Twenty eyes from 20 cases of disease and 5 eyes from 5 normal cases were used for evaluation. Ophthalmologist 1 extracted abnormal suprachoroidal regions from the OCT images, and ophthalmologist 2 identified RPE defects, thickening, prominences, and hyperintense retinal foci (HRF) in the DOPU and pseudo-DOPU faults at five locations within the regions. In normal eyes, the presence of abnormalities was assessed at five locations in each case.

Results: Representative pseudo-DOPU images of normal and abnormal cases which are not used in training are shown in Fig. 1. In these cases, pseudo-DOPU images well resemble DOPU images. In the disease case, RPE elevations (black arrows) and an RPE defect (white arrows) are in good agreement.

The recall and precision of pseudo-DOPU with respect to DOPU were as follows: for RPE deficiency (0.86, 0.37), for thickening (0.93, 0.65), for prominence (0.98, 0.98), and for HRF (0.74, 0.39). Of the 25 pseudo-DOPU cross-sectional images of normal eyes, 3 showed RPE defects, 1 showed RPE migration, and 1 showed abnormally low DOPU values, which were not confirmed by DOPU.

Conclusions: For the RPE abnormalities shown in DOPU, the pseudo DOPU did not show high precision but showed high sensitivity. For normal eyes, pseudo-DOPU seems to be similarly informative to PS-OCT, but we need to care about false abnormal findings.

CONTROL ID: 3713148

SUBMITTER (NAME ONLY): Antoine Rivail

TITLE: Deep Survival Prediction of Progression from Intermediate to Atrophic AMD from Longitudinal Retinal OCT

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Rivail, W. Vogl, S. Riedl, C. Grechenig, G.S. Reiter, U. Schmidt-Erfurth, H. Bogunovic, Department of Ophthalmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|R.H. Guymer, Z. Wu, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|R.H. Guymer, Z. Wu, Department of Surgery (Ophthalmology), The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure: Antoine Rivail: Commercial Relationship: Code N (No Commercial Relationship) | Wolf-Dieter Vogl: Commercial Relationship: Code N (No Commercial Relationship) | Sophie Riedl: Commercial Relationship: Code N (No Commercial Relationship) | Christoph Grechenig: Commercial Relationship: Code N (No Commercial Relationship) | Gregor Reiter: Commercial Relationship: Code N (No Commercial Relationship) | Robyn Guymer: Commercial Relationship(s);Code C (Consultant/Contractor):Bayer, Novartis, Roche Genentech, Apellis | Zhichao Wu: Commercial Relationship: Code N (No Commercial Relationship) | Ursula Schmidt-Erfurth: Commercial Relationship(s);Code F (Financial Support):Heidelberg Engineering, Apellis | Hrvoje Bogunovic: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In patients with intermediate age-related macular degeneration (iAMD), the risk of progression to advanced stages is highly heterogeneous and the prognostic imaging biomarkers remain unclear. Building optical coherence tomography (OCT)-based deep learning prognostic models is challenging due to large dimensionality of OCT scans and limited size of longitudinal datasets. We train a deep survival model, to estimate from OCT an individual risk of conversion to macular atrophy.

Methods: The deep learning model was trained on a development dataset consisting of 267 eyes (1459 OCTs) with iAMD imaged every 6 months with Spectralis OCT (512x49x496 voxels). The model learns a probability of a conversion to macular atrophy, with a prognosis for every 6 months up to 36 months in the future. The model is trained on raw OCTs with Logistic Hazard (LH) loss, combining the advantages of survival models and deep learning. We compared our model with a standard deep learning classification approach trained with a Binary Cross Entropy (BCE), as well as with a traditional survival model with Cox Proportional Hazards (CPH) trained on a set of clinically relevant quantitative OCT biomarkers. The models were evaluated with a five-fold cross-validation. In addition, an independent longitudinal OCT dataset with 240 eyes (240 OCTs) was used as an external test set. The model performance was measured with Concordance Index (CCI).

Results: The prognostic deep survival models achieved a CCI of 0.79+/- 0.03 on the cross-validation, and 0.74 on the external test set. The resulting population risk estimates in the form of Kaplan-Meier curves for the converter and censored eyes (conversion beyond 36 months) on the development set are shown in Fig. 1. The BCE model achieved CCI of 0.78 +/- 0.06 on the cross-validation, and 0.73 on the external test set. Finally, the CoxPh model obtained CCI of 0.75 +/- 0.1 on the cross-validation, and 0.73 on the external test set.

Conclusions: Deep survival models allow building risk estimators for progression from iAMD to macular atrophy. They successfully combine the advantages of deep learning that can learn from raw OCT images with survival modelling paradigm that accounts for censoring and predictions for multiple time intervals.

CONTROL ID: 3713149

SUBMITTER (NAME ONLY): Clemens Vass

TITLE: Along-the-bundle analysis of the retinal nerve fiber layer of glaucoma eyes compared to control as analyzed by plolarization-sensitive OCT

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Vass, F. Schwarzhans, S. Steiner, H. Resch, Department of Ophthalmology, Medical University of Vienna, Vienna, AUSTRIA|S. Desissaire, M. Pircher, C.K. Hitzenberger, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, AUSTRIA|G. Fischer, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Vienna, AUSTRIA|

Commercial Relationships Disclosure: Clemens Vass: Commercial Relationship: Code N (No Commercial Relationship) | Florian Schwarzhans: Commercial Relationship: Code N (No Commercial Relationship) | Stefan Steiner: Commercial Relationship: Code N (No Commercial Relationship) | Sylvia Desissaire: Commercial Relationship: Code N (No Commercial Relationship) | Hemma Resch: Commercial Relationship: Code N (No Commercial Relationship) | Georg Fischer: Commercial Relationship: Code N (No Commercial Relationship) | Michael Pircher: Commercial Relationship: Code N (No Commercial Relationship) | Christoph Hitzenberger: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To trace the retinal nerve fiber bundles (RNFBs) and to study the (mostly) decay of parameters describing the retinal nerve fiber layer (RNFL) along the RNFBs in healthy and early glaucoma eyes using polarization-sensitive optical coherence tomography (PS-OCT).

Methods: In this prospective cross-sectional study we used a prototype PS-OCT instrument to acquire wide-field scans composed of 7 times 3 volume scans in 21 early glaucoma (age 64.5 ±9.5 years) vs. 45 healthy eyes (age 50.7 ±13.7 years). The RNFL was segmented and the RNFBs were traced, starting at a 3 mm radius circle centered on the optic disc (OD) with 2 deg. spacing both towards the OD and the periphery. We focus on a sample of 5 RNFB traces at 40° (above the disc to fovea line), 20°, 0°, 340°. and 320°. The mean values and slopes along the bundles of RNFL-thickness (RNFL-T), RNFL-retardation (RNFL-R), RNFL-T times inter-trace distance (RNFL-TD), i.e. the bundle cross-sectional area, and RNFL-R times distance (RNFL-RD) were determined and compared between groups with t-tests for sections of 0.5 mm length.

Results: Glaucoma eyes showed statistically significantly reduced RNFL-T and RNFL-R over 2 to 6 mm depending on trace label. The largest difference between groups was observed temporal inferior (320°), where the significant differences extended over 5 to 6 mm for all parameters. For the 320° trace at 3 mm from the OD the difference between groups regarding the slopes of RNFL-T, and RNFL-TD was 6.0 µm/mm and 53.2 μm^2/mm ($p < 0.0005$ and $p < 0.005$) with the healthy eyes showing more negative slopes. The courses along the bundles are shown in fig. 1 and fig.2 for the mean parameter values and the mean slope values.

Conclusions: Early glaucoma shows significantly reduced RNFL-T and RNFL-R along large parts of the RNFBs. We find more negative slopes along the bundles for the healthy as compared to the glaucoma cases. The local slope of the parameters tested may contain information about the local number of remaining ganglion cells, which is to be confirmed in a future study.

CONTROL ID: 3713150

SUBMITTER (NAME ONLY): M Costello

TITLE: Extensive autophagy and unique nuclear excisosome formation from mitochondria characterize organelle degradation in lenses from Galago (bush baby) monkeys

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Schey, Biochemistry, Vanderbilt University, Nashville, Tennessee, UNITED STATES| M.J. Costello, K.O. Gilliland, Cell Biology and Physiology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: M Costello: Commercial Relationship: Code N (No Commercial Relationship) | Kurt Gilliland: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Schey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Our previous paper described the formation of the nuclear excisosome (NE) in Galago lenses from modified mitochondria that initiated the process in the presence of numerous autophagic vesicles within equatorial epithelium. Further examination revealed how elaborate autophagy processes near the fulcrum produced large degradative bodies in the young fiber cells as extended mitochondria and NE cores elongated into rod-like “beads on a string” structures that degraded nuclei at the organelle-free zone (OFZ).

Methods: Lenses from Galago (bush baby) monkeys (n=4, age 2-5) were fixed in formalin followed by paraformaldehyde, then Vibratome sectioned. Sections were fixed and processed for thin-section transmission electron microscopy or stained with fluorescent dyes for Airyscan confocal microscopy. Nuclei were stained with DAPI, actin with Alexa-phalloidin, lectins with WGA and membranes with DiI.

Results: Galago monkey lenses formed unique four-membrane organelles in the equatorial epithelium from modified mitochondria with collapsed cristae that condensed and surrounded core proteins with a single membrane. Enlarged beads appeared to assist in fusing smaller rods into longer ones as the complexes migrated into fiber nascent fiber cells and attacked nuclear envelopes near the OFZ. The high cellular activity in transition region was supported by extensive autophagy of the classical type and a new variation of expanded extracellular space (ECS) between epithelial cells where material to be degraded and degradative enzymes entered by exocytosis. These ECS autophagic vesicles became so prominent that they started a new complex interdigitation to isolate them as bounded degradative bodies in young fiber cells. Smaller autophagic vesicles were seen throughout the formation and degradation of organelles in the OFZ.

Conclusions: Autophagy plays a prominent role throughout the degradative process including formation of new large ECS based autophagic vesicles with single plasma membrane borders.

CONTROL ID: 3713151

SUBMITTER (NAME ONLY): Ayeswarya Ravikumar

TITLE: Contact Lens Induced Full- and Peripheral-Field Myopic Defocus on Choroidal Thickness with Time of Day

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ravikumar, L.A. Ostrin, Optometry, University of Houston System, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Ayeswarya Ravikumar: Commercial Relationship: Code N (No Commercial Relationship) | Lisa Ostrin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Short-term modulation of choroidal thickness may be an indicator of long-term myopia control. A previous study showed that the choroid thickens to full field spectacle lens myopic defocus, and more so in the evening than morning. Multifocal soft contact lens that provide peripheral myopic defocus have been shown to be effective in myopia control. The goals of this study were to assess short-term effects of full field or peripheral myopic defocus on choroidal thickness and to investigate time-of-day effects in young adults.

Methods: Healthy young adults (n=10) ages 28.2 ± 3.19 years participated in four sessions, separated by 1 to 4 days, two in the morning (9am) and two in the evening (5pm). For each session, participants first watched a movie for 10 min in a large screen at 2 m with single vision distance corrected contact lenses (+0.5 D for the working distance), and choroidal thickness was measured using optical coherence tomography(OCT) in both eyes. Then, the experimental lens, which provided an additional +2.5D full field or peripheral field defocus was placed on the left eye, and the participant continued to watch for 60 minutes. OCT was repeated. The distance-correction was replaced and recovery was measured after 20 minutes. Choroidal thickness change was determined for control and experimental eyes, and the difference between eyes was calculated. Repeated measures ANOVA with post-hoc Bonferroni correction was used to assess changes in choroidal thickness.

Results: Baseline choroidal thickness was similar in the morning (320.3±25.7 μm) and evening (335.6±26.6 μm, P=.4) and was similar between right and left eyes (P=.2). Following 60 min exposure to full field myopic defocus, the choroid of the experimental significantly thickened relative to the control eye in the morning (7.9±2.4 μm, P=.03), but not in the evening (6.0±2.7 μm, P=.15). Following 60 minutes exposure to peripheral field myopic defocus, the choroid did not significant change in the morning or evening (P=1 for both).

Conclusions: Findings show that short-term exposure to full field contact lens induced myopic defocus leads to significant thickening in the morning, but not in the evening. Peripheral field contact lens induced myopic defocus did not induce choroidal thickness changes. Future analysis including a larger sample size may be able to better distinguish small changes in choroidal thickness using OCT imaging.

CONTROL ID: 3713152

SUBMITTER (NAME ONLY): Matilda Biba

TITLE: Serum c-reactive protein (CRP) relationship with macular pigment and response to carotenoid supplementation in open-angle glaucoma

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Biba, E. Loskutova, G. Lingham, J.S. Butler, C.J. O'Brien, J. Loughman, Centre for Eye Research Ireland (CERI), Technological University Dublin, Dublin, Dublin, IRELAND|C.J. O'Brien, Mater Misericordiae University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: To evaluate CRP response to carotenoid supplementation and analyse its relationship to macular pigment optical density (MPOD) in glaucoma.

Methods: A randomised, double-blind, placebo-controlled clinical trial was conducted on 62 open-angle glaucoma subjects, with no known underlying systemic or ocular pathology. Subjects were randomly assigned (2:1 ratio) to treatment or placebo control groups and were required to ingest a daily dietary supplement for 18 months. The treatment group received the active capsule comprised of 10mg lutein, 2mg zeaxanthin and 10mg meso-zeaxanthin. Serum CRP levels, MPOD (Spectralis) and microperimetry (MAIA II) were measured at baseline and following 18 months supplementation.

Results: No significant differences in CRP and MPOD were found between treatment groups at baseline. MP volume was statistically significantly higher in the treatment group relative to placebo at 18 months ($p<0.01$; Table 1), but no significant difference in CRP was observed between groups. A statistically significant, inverse correlation was found between CRP and MP volume in the central 6^0 macular area (Fig. 1) and MPOD at 0.23, 0.51, 0.74 and 1.02 retinal eccentricities ($p<0.01$ for all). No significant correlation existed between CRP and glaucoma severity ($p=0.4$). To assess the direct effect of supplementation on CRP levels, a linear mixed model analysis was conducted with log(CRP) as the dependent variable and added fixed effects of time*treatment interaction. Baseline and 18 month data were used and participant ID was included as a random intercept to account for within-person correlation. No significant effect of supplementation on log(CRP) levels was found (estimate±SE: -2.5±1.64; t-test:-1.52; $p=0.13$).

Conclusions: The relationship between CRP and MPOD agrees with previous observations. The substantial increase in MP in response to supplementation, however, did not lead to a meaningful change in serum CRP (albeit that the treatment group mean CRP reduced and placebo group mean CRP more than doubled). Although further analysis is required with a larger study population, it appears that macular carotenoid supplementation has limited impact on this inflammatory marker among individuals with open angle glaucoma.

CONTROL ID: 3713155

SUBMITTER (NAME ONLY): Stephen LoBue

TITLE: The Association between Demodex and Ocular Symptoms in an Afro-Caribbean Population

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. LoBue, G. Kabarriti, C. Hampton, A. Song, G. Moustafa, S. Cheng, J. Park, Ophthalmology, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|

Commercial Relationships Disclosure: Stephen LoBue: Commercial Relationship: Code N (No Commercial Relationship) | Gabriel Kabarriti: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Hampton: Commercial Relationship: Code N (No Commercial Relationship) | Alex Song: Commercial Relationship: Code N (No Commercial Relationship) | Giannis Moustafa: Commercial Relationship: Code N (No Commercial Relationship) | Shuk Kei Cheng: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Park: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the association between the density of Demodex colonization, meibomian gland dysfunction (MGD) severity, and ocular symptoms in an Afro-Caribbean population.

Methods: The research study is a prospective, single-center, cross-sectional observational study. All enrolled participants will be analyzed in the following sequence: ocular surface disease index (OSDI) questionnaire, slit-lamp biomicroscopic examination, fluorescein tear film break-up time (F-BUT), and Demodex folliculorum count. Grading of the severity of MGD will be performed by a board-certified cornea specialist who will be blinded to the counting of Demodex specimens and OSDI score. Exclusion criteria include patients less than 18 years of age, active keratitis, intraocular surgery within three months, history of a pterygium, Sjogren syndrome, and uncontrolled autoimmune diseases. Demographics, ocular conditions, and comorbid medical conditions were collected and compared to patients without Demodex. Association with OSDI raw score and mite count will be calculated with Spearman correlation with the construction of 95% confidence interval.

Results: Twenty-eight patients ranging from 65 +/- 12 (mean +/- standard deviation) years of age met the criteria for inclusion. A total of 35.7% of patients were positive for Demodex colonization. The average count of Demodex was 1.37 +/- 1.00. No association with gender, age, OSDI score, or MGD severity was seen with Demodex colonization. Comorbid medical conditions such as DM and HTN were similar between patients with and without Demodex. Collarettes and scurf findings on clinical exam were associated with higher rates of Demodex, $p<.05$.

Conclusions: Demodex is relatively common in the Afro-Caribbean Population with higher rates among patients with collarettes and scurf. However, no association with worsening MGD or OSDI was linked to Demodex colonization.

CONTROL ID: 3713157

SUBMITTER (NAME ONLY): jihun shin

TITLE: The effect of pH on the surface charge of contact lens and lysozyme deposition

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. shin, S. Won, M. Choi, Optometry, Seoul National University of Science and Technology, Nowon-gu, Seoul, KOREA (THE REPUBLIC OF)|M. Choi, Convergence Institute of Biomedical Engineering and Biomaterials, Seoul National University of Science and Technology, Nowon-gu, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: jihun shin: Commercial Relationship: Code N (No Commercial Relationship) | Sungjin Won: Commercial Relationship: Code N (No Commercial Relationship) | Moonsung Choi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular pH has been measured for decades and reported to range from 6.5 to 7.7 and from 5.9 to 7.6 in normal; by a variety of factors, the ocular pH could be changed such as age, time, diseases, wearing contact lens, air pollution. The pH of the ocular surface could affect the ionization state of contact lens; protonation and deprotonation. In this study, we investigated the change of surface charge and protein deposition on contact lenses depending on the pH condition.

Methods: The etafilcon A material contact lens (1-Day ACUVUE MOIST, Johnson& Johnson Inc.) and 10mM phosphate buffer solutions were used throughout the study. The contact lenses were incubated in each buffer solution pH range from 6.0 to 8.0 for 48 hours to remove residual blister solution and reach equilibrium state. The surface charge of contact lens was evaluated via point of zero charge (POZC). The quantity of deposited lysozyme per unit area(mm^2) was calculated by dividing the total quantity of deposited lysozyme in each pH solution by its surface area(mm^2).

Results: The POZC of contact lenses were lower than each pH condition though they were increased under pH 7.2 and showed relatively constant values above pH 7.2. The surface area of contact lens was increased under pH 7.2 and showed relatively constant values above pH 7.2. The quantity of deposited lysozyme per unit area(mm^2) was increased under pH 7.2 and showed relatively constant values around and above pH 7.2.

Conclusions: The lower POZC than the given pH condition implies that the surface of contact lens has negative charge which attracts lysozyme that has positive charge. The POZC, surface area, and quantity of deposited lysozyme per unit area(mm^2) showed constant values above pH 7.2 which implies that the contact lens had fully ionized, and maximum amount of lysozyme had been deposited. It was found that the surface charge of contact lens is affected by the pH around them, and a maximum amount of lysozyme is deposited on contact lenses in physiological condition.

CONTROL ID: 3713159

SUBMITTER (NAME ONLY): Fergal Ennis

TITLE: Filters can negatively affect clinical stereopsis measures with the impact being greater in induced near exophorias.

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.A. Ennis, S. Cox, Optometry and Vision Sciences, Cardiff University College of Biomedical and Life Sciences, Cardiff, Cardiff, UNITED KINGDOM|

Commercial Relationships Disclosure: Fergal Ennis: Commercial Relationship: Code N (No Commercial Relationship) | Scott Cox: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Clinical stereopsis tests are known to give different thresholds but the underlying mechanism is not fully understood. Specifically why does the TNO threshold differ from other tests (e.g. Titmus)? The global versus local stereo theory has been disproved. The effect of illumination levels and filter impact has been partially explored but is inconclusive. Also, differences between compensated and decompensating individuals have not been fully explored. This preliminary study investigates to what extent clinically used anaglyphic (red/green) and vectographic cross-polarised filters impact on clinical stereo results in the presence and absence of an induced decompensating near exophoria.

Methods: Stereoacuities (SA) were measured using TNO and Titmus in 41 binocularly normal (i.e. fully compensated) participants (ages 19–32, mean age: 21.1 ± 2.5) both conventionally with their appropriate red/green or cross-polarised filters, and then with both filter options in place. This procedure was repeated in the presence of a base-out-prism-induced near exophoria (NXOP). The individual prism values required were calculated by manipulation of Sheard's criterion to give a base-out prism value that theoretically leaves the subject still fusing but with a consistently compromised state of compensation.

Results:

Combining filters only: There was no significant reduction in the TNO SA ($p = 0.246$) but there was a significant reduction in the Titmus ($p = 0.001$)

Inducing decompensation (NXOP) with single filters: There was a significant reduction in SA for both tests, more so for the Titmus (TNO $p = 0.044$, Titmus $p < 0.001$)

Combining filters and inducing decompensation (NXOP): There was a reduction in SA in both tests (TNO $p = 0.001$, Titmus $p < 0.001$). This reduction was greater than in either of the above single-manipulation scenarios.

Conclusions: The results of this pilot study suggest that the filters used to measure stereopsis may have a detrimental impact on stereopsis performance, especially in the presence of decompensating heterophoria: specifically the significant impact of red/green anaglyph filters on Titmus results suggest they may be more "invasive" than polarised filters and hence have a greater impact on the recorded threshold. Further research is needed to quantify this phenomenon and its relation to clinical data gathering and decision making.

CONTROL ID: 3713160

SUBMITTER (NAME ONLY): Zhe Pan

TITLE: Prevalence and Risk Factors of Macular Retinoschisis in highly myopic eyes: the Beijing Eye Study 2011

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Pan, Y. Wang, Beijing Tongren Eye Center, Beijing, CHINA|C. Zhang, Peking University Eye Center, Beijing, CHINA|

Commercial Relationships Disclosure: Zhe Pan: Commercial Relationship: Code N (No Commercial Relationship) | Ya Xing Wang: Commercial Relationship: Code N (No Commercial Relationship) | Chun Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the prevalence and risk factors of macular retinoschisis (MRS) in highly myopic eyes and their morphological features observed by optical coherence tomography (OCT) in Chinese population.

Methods: The population-based Beijing Eye Study 2011enrolled 3468 participants (1963 women, 56.6%) with a mean age of 64.6 ± 9.8 years (50 - 93). Spectral-domain OCT was applied in every participant, including the macula cube scan of 30× 25°centered in the fovea. High myopia was defined as a refractive error ≤ -6 diopters or an axial length ≥ 26.0 mm. MRS were detected by OCT images.

Results: A total of 213 highly myopic eyes of 129 participants were analyzed, with a mean refractive error of -8.5 ± 3.2 diopter, or a mean axial length 26.8 ± 1.4 mm. MRS was found in 36 subjects (48 eyes) with a prevalence of 27.9% (95% confidence interval (CI): 20.5%, 35.7%) per subject or 22.5% (95%CI: 16.9%, 28.6%) per eye. MRS was observed most frequently in the extrafoveal region (15 eyes, 65.2%), as compared with other locations, including 3 eyes in the foveal only region (13.0%), 2 eyes in the fovea plus part of parafoveal region (8.7%) and 3 eyes in the entire macular region (13.0%). The presence of MRS was more often seen in participants of a higher body weight (P=0.014), with more myopic refraction (P<0.001; OR, 0.75; 95%CI, 0.64, 0.88) (Figure 1), with a higher intraocular pressure (P=0.013), and with a wider parapapillary gamma zone (P=0.004), after multivariate analysis.

Conclusions: The prevalence of MRS was 27.9% in highly myopic participants in an older Chinese population. Body weight, intraocular pressure and gamma zone width may play a role in the development of MRS, besides the effect of myopic refraction.

CONTROL ID: 3713162

SUBMITTER (NAME ONLY): Madeline Evers Olufsen

TITLE: Estimation of retinal hole closure with and without amniotic membrane in a porcine model.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Olufsen, N.B. Sorensen, A.T. Christiansen, J.F. Kiilgaard, Dept. of Ophthalmology, Rigshospitalet, Copenhagen, DENMARK|M.E. Olufsen, S. Heegaard, J.F. Kiilgaard, Kobenhavns Universitet Sundhedsvidenskabelige Fakultet, Copenhagen, DENMARK|S. Heegaard, Dept. of Pathology, Rigshospitalet Diagnostisk Center, Copenhagen, DENMARK|J. Hannibal, Dept. of Clinical Biochemistry, Bispebjerg Hospital, Copenhagen, DENMARK|

Commercial Relationships Disclosure: Madeline Evers Olufsen: Commercial Relationship: Code N (No Commercial Relationship) | Steffen Heegaard: Commercial Relationship: Code N (No Commercial Relationship) | Nina Sorensen: Commercial Relationship: Code N (No Commercial Relationship) | Anders Christiansen: Commercial Relationship: Code N (No Commercial Relationship) | Jens Hannibal: Commercial Relationship: Code N (No Commercial Relationship) | Jens Kiilgaard: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Amniotic membrane (AM) transplantation has been used successfully in treatment refractory macular holes. We have previously shown that amniotic membrane has regenerative capacities in the retina. In this comparative study we investigate retinal hole closure with and without AM in a porcine model of retinal hole. Our hypothesis is that AM transplantation can close large retinal holes either by scar tissue formation or regeneration of retinal cells. The aim of this study is to evaluate the anatomical, functional, and histopathological outcomes after AM transplantation in a porcine model for retinal hole.

Methods: Danish landrace pigs were vitrectomized in full anesthesia and a subretinal bleb was created before cutting a retinal hole using a 23G vitrector. Pigs underwent either transplantation of humane freeze-dried amniotic membrane into the subretinal space or were left untreated. No tamponade was used, but sclerotomies were sutured with 7-0 Vicryl^{TM}. Prior to surgery and two and four weeks after surgery, the eyes were examined by Optical Coherence Tomography (OCT), multifocal electroretinogram (mfERG) and fundus photographs. At the end of follow-up, the eyes were enucleated for histology.

Results: Retinal hole closure seemed to be time dependent showing that some time passes before spontaneous closure. Furthermore, it was possible to calculate a hole closure rate. We found no spontaneous hole closure in retinal holes larger than 1350 um at 4 weeks. In the AM group all holes closed regardless of size.

Conclusions: We present a porcine model for retinal hole. Spontaneous hole closure is not a static event but happens over time. AM transplantation acts as a “band aid” or stimulator for retinal hole closure by glial scarring.

CONTROL ID: 3713163

SUBMITTER (NAME ONLY): Christiane Kafarnik

TITLE: Differentiation of Canine Adipose-derived Stromal Cells along the Keratocyte Lineage in vitro

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kafarnik, D.J. Guest, The Royal Veterinary College Department of Clinical Science and Services, Hatfield, Hertfordshire, UNITED KINGDOM|J.T. Daniels, Institute of Ophthalmology, University College London Faculty of Brain Sciences, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Christiane Kafarnik: Commercial Relationship: Code N (No Commercial Relationship) | Julie Daniels: Commercial Relationship: Code N (No Commercial Relationship) | Deborah Guest: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The objective of this study was to determine whether canine adipose derived mesenchymal stromal cells (adMSC) express keratocyte-specific phenotypic markers when cultured under conditions inducing differentiation of corneal stromal stem cells to keratocytes in 2D.

Methods: AdMSC were differentiated in keratocyte differentiation media (KDM) containing basic fibroblastic growth factor (bFGF) and ascorbic acid in the absence of serum for 3 weeks and compared to cells pre-cultured in corneal stromal stem cell media (CSSCM) containing ascorbic acid, platelet derived growth factor (PDGF), epidermal growth factor (EGF) and low serum for 7 days followed by 3 weeks KDM. This was performed in a biological triplicate and cells were characterized using quantitative RT–PCR and immunostaining. Statistical analysis included Shapiro-Wilk normality test, ANOVA, followed by the Tukey's post hoc test.

Results: AdMSC differentiated into KDC showed keratocyte-like morphology, expressed keratocyte associated proteins Keratocan, Lumican and ALDH1A3 and but not the stem cell marker Pax6 when cultured in KDM. Pre-culturing adMSC in CSSCM before differentiating in KDM increased the level of Keratocan and Lumican gene expression significantly but not ALDH1A3. AdMSC cultured in CSSC media showed a trend of upregulated Pax6 and N-cadherin, which was downregulated after keratocyte differentiation. Expression of differentiation markers was quantitatively lower than following the keratocyte differentiation of primary canine CSSC.
BFGF increased the cell expansion of adMSC-KDCs but retained a fibroblastic cell morphology. AdMSCs express α-smooth muscle actin (α-SMA) at the protein and mRNA level in the undifferentiated state and at all stages of differentiation.

Conclusions: Keratocyte-like cells derived from canine adMSCs may serve as a source of keratocytes but expressed myofibroblastic features when cultured in 2D.

CONTROL ID: 3713164

SUBMITTER (NAME ONLY): Masara Issa

TITLE: An Optimized, Patient-Customized Grid Maximizes Microperimetry Readouts in Geographic Atrophy: Evaluation of Average Threshold Test-Retest Reliability

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Issa, A. Lewis, F. Lopez, Allegan, an AbbVie Company, Irvine, California, UNITED STATES|K. Lashkari, Advanced Eye Centers Inc, North Dartmouth, Massachusetts, UNITED STATES|K. Lashkari, University of Massachusetts Dartmouth, Dartmouth, Massachusetts, UNITED STATES|K. Csaky, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Microperimetry is a useful assessment to evaluate visual function across the macula in detail. In geographic atrophy (GA), test points that fall within scotomas provide limited information. This study evaluates the feasibility and test-retest reliability of scotopic and mesopic microperimetry in patients with GA, using an optimized patient-customized grid.

Methods: This is a prospective pilot study conducted at 2 sites in the United States. At each of the 4 study visits (Baseline, Day 7, Months 3 and 6), scotopic then mesopic microperimetry were performed using an S-MAIA (CenterVue, Padova, Italy). Customized grids were generated by a reading center. Nine points were placed on the subject's preferred retinal locus and ~50 equidistantly spaced points were distributed in two concentric rings 200 and 450 µm from the lesion border. Test-retest reliability of average threshold sensitivities was assessed by evaluating data from the Baseline (test) and Day 7 (re-test) visits. Spearman correlations and Bland-Altman plots were used to evaluate association and equivalency between measurements, respectively. The coefficient of repeatability (CR) was also computed with 95% confidence intervals (CI) to quantify the smallest real difference between test and re-test. Values presented are means ± standard error of the mean unless otherwise stated. Statistical analysis was conducted using R Software (v4.1.2) under RStudio.

Results: Eleven subjects were enrolled (82% female). Median age was 80 years (range 63-91). GA lesion area was 19.8±1.5 mm^2, and mean best-corrected visual acuity was 56.5±5.3 letters. The average threshold sensitivity for each visit was: 7.3±2.2, 6.9±2.4, 5.4±2.5, and 5.2±1.9 dB for scotopic; 11.6±1.7, 12.1±1.7, 11.0±2.1, and 10.3±1.9 dB for mesopic conditions. In general, scotopic microperimetry was less reliable than mesopic (lower Spearman correlation and wider Bland-Altman limits of agreement). Similarly, average threshold sensitivity CRs were 13.6 dB for scotopic and 2.9 dB for mesopic, 95% CI [0, 17.2] and [0.1, 3.1].

Conclusions: This study demonstrates that patient-customized grids in GA offer a feasible and reliable way to conduct microperimetry in large scale clinical trials, particularly with mesopic microperimetry. Analysis of individual point sensitivity "by zone" and its reliability is currently ongoing.

CONTROL ID: 3713166

SUBMITTER (NAME ONLY): Peter Zhao

TITLE: Deep Learning for Automated Detection of Neovascular Leakage and Vascular Nonperfusion in Diabetic Retinopathy Using Ultra-widefield Fluorescein Angiography

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.Y. Zhao, N. Bommakanti, G. Yu, M.T. Aaberg, T. Patel, Y.M. Paulus, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neovascular leakage and vascular non-perfusion are angiographic features of diabetic retinopathy. The goal of this study was to determine whether these features could be accurately classified by a deep learning algorithm.

Methods: We used retrospective fluorescein angiogram images captured on the Optos ultra-widefield platform between January 2009 and May 2018. Images were randomly split into training (60%), validation (20%), and test (20%) sets. A ResNet-101 convolutional neural network that was pre-trained on ImageNet was trained on fluorescein angiogram images. The neural network was configured to output predictions on the presence of neovascular leakage and vascular non-perfusion. Predictions were compared to the ground truth labeled by masked, trained graders.

Results: 1452 images from 342 subjects were included. 60% of images were from female subjects, and 79% of images were from patients with type 2 diabetes mellitus. Mean hemoglobin A1c was 8.1% (SD=2.1%). Mean visual acuity was logMAR 0.35 (SD=0.30). Neovascular leakage was present in 21% of images, and non-perfusion greater than a pre-determined threshold (77.5 mm^2) predictive of development of proliferative diabetic retinopathy was present in 42% of images. The mean total non-perfusion area was 80.8 mm^2 (SD=63.3). The algorithm achieved an area under the curve (AUC) of 0.976 for neovascular leakage, and an AUC of 0.949 for detecting vascular non-perfusion. At operating points selected for high sensitivity, the algorithm achieved 97% sensitivity and 89% specificity for neovascular leakage, and 94% sensitivity and 79% specificity for non-perfusion. At operating points selected for high specificity, the algorithm achieved 75% sensitivity and 94% specificity for neovascular leakage, and 86% sensitivity and 86% specificity for non-perfusion.

Conclusions: A convolutional neural network was trained to recognize the presence of neovascular leakage and non-perfusion in ultra-widefield fluorescein angiography. Further research may help improve algorithm performance and better characterize the relationship between non-perfusion, neovascularization, and vision-threatening complications of diabetic retinopathy.

CONTROL ID: 3713168

SUBMITTER (NAME ONLY): Mallika Prem Senthil

TITLE: Associations between clinical measures and quality of life in refractive error

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Prem Senthil, Optometry, Flinders University, Adelaide, South Australia, AUSTRALIA|R. Chakraborty, Optometry, Flinders University, Adelaide, South Australia, AUSTRALIA|

Commercial Relationships Disclosure: Mallika Prem Senthil: Commercial Relationship: Code N (No Commercial Relationship) | Ranjay Chakraborty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Refractive errors are associated with structural and functional changes in the eye. While previous studies have assessed the impact of refractive error on quality of life, the association between the objective structural and functional measures of refractive error and quality of life has not been studied. This study aims to determine the association between clinical measures and quality of life in refractive error.

Methods: Fifty participants with corrected refractive error (spectacles, contact lens or refractive surgery) between the ages of 18 and 35 were recruited for this cross-sectional pilot study. Best corrected visual acuity, contrast sensitivity, and spherical equivalent refractive error (SER) were measured for all participants. Measurements of, axial length, corneal curvature and anterior chamber depth were obtained using the IOL Master, and macular thickness was measured using the optical coherence tomography. Vision related quality of life was assessed using the Quality of Life Impact of Refractive Correction questionnaire (QIRC).

Results: The mean age of the participants was 24.37±3.41 years (68% females). The mean spherical equivalent was -2.74± 1.87 D and the mean QIRC score was 44.07±6.61 logits. The QIRC based quality of life was significantly associated with axial length (r^2=0.16, p=0.004) and SER (r^2=0.12, p=0.013). A 1 mm increase in axial length reduced the QIRC scores by 2.41 logits and a one dioptre increase in SER caused a 1.03 logits reduction in QIRC scores. None of the other measured parameters were significantly correlated with the QIRC scores.

Conclusions: Quality of life positively correlated with spherical equivalent and negatively with axial length. Clinicians and researchers can use clinical measures to predict the quality of life in refractive error. Future studies should confirm these results in larger populations.

CONTROL ID: 3713169

SUBMITTER (NAME ONLY): Hoi-lam Li

TITLE: Mechanistic actions of baicalein in human trabecular meshwork cells

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Li, S. Shan, H.H. Chan, C. To, T. Lam, C. Do, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|D.W. Stamer, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|D.W. Stamer, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|H.H. Chan, C. To, T. Lam, C. Do, Centre for Eye and Vision Research (CEVR), 17W Hong Kong Science Park, HONG KONG|

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ABSTRACT BODY:

Purpose: Baicalein is a natural flavonoid derived from the dried roots of Scutellaria baicalensis Georgi. We have previously demonstrated that baicalein lowers intraocular pressure (IOP) by increasing trabecular meshwork (TM) outflow facility. In this study, we investigated the mechanistic effects underlying the baicalein-mediated increase in outflow facility.

Methods: Five independent strains of primary human TM (hTM) cells were used. The effects of baicalein on hTM cell volume regulation, cell contractility and cell migration were determined by electronic cell sorting, collagen gel assay and scratch assay, respectively. Measurements of phosphorylated myosin light chain (pMLC) were conducted by Western blot analysis. Differential protein expression profile after baicalein treatment for 3 hours was assessed using isobaric tag for relative and absolute quantitation (iTRAQ) based quantitative proteomics.

Results: Our results showed that baicalein (1-100 μM) had no effect on cell volume under iso-osmotic condition, but caused a concentration-dependent inhibition of regulatory volume decrease (RVD) by up to 70% under hypotonic condition. Similarly, baicalein exhibited a concentration-dependent hTM cell relaxation and retarded cell migration when compared to the vehicle control. At 100 μM, baicalein reduced MLC phosphorylation by 18±9% ($n=4$, $p<0.05$). After a 3-hour baicalein treatment, 47 proteins were significantly regulated in hTM cells ($n=3$, $p<0.05$). Consistent with in vitro findings, baicalein significantly altered the expression of pre-B-cell leukemia transcription factor-interacting protein 1 (PBXIP1, ↓60%), matrix metalloproteinase-14 (MMP-14, ↑14%) and cathepsin B (CTSB, ↑51%).

Conclusions: These findings suggest that baicalein triggers cell relaxation via MLC phosphorylation along with inhibiting RVD and migratory behavior in hTM cells. The baicalein-mediated changes in protein expression support the notion of altered extracellular matrix homeostasis, potentially contributing to a reduction of outflow resistance and thereby IOP.

CONTROL ID: 3713171

SUBMITTER (NAME ONLY): Catherine Hottin

TITLE: Osteopontin might mediate photoreceptor neuroprotection following GSK3 inhibition

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hottin, S. Lourdel, M. Perron, J.E. Roger, Institut des Neurosciences Paris-Saclay, Saclay, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Glycogen Synthase Kinase 3 alpha (GSK3α) and beta (GSK3β) kinases are key regulators of cell survival and death pathways. GSK3 inhibition has been a therapeutic approach for neurodegenerative disorders such as Alzheimer's and Parkinson's disease. In the retina, drug inhibition of GSK3 showed promising beneficial effects under pathological conditions. In our study, we aimed at deciphering the neuroprotective mechanism of GSK3 inhibition using mouse genetic models and identifying other therapeutic factors for new treatment.

Methods: Conditional mouse lines were generated using αPax6-Cre with retinal specific deletion of either isozyme of Gsk3 (Gsk3α/Gsk3β). Photoreceptor degeneration was induced in vivo using MNU, and ex vivo on retinal explant culture. RNA-Seq analysis was performed on control and MNU-injected mice carrying only one allele of Gsk3α (Gsk3α^{f+}β^{ff} α-Cre) expressed in the retina. Recombinant protein Osteopontin (OPN) was injected intra-vitreally or added to explant culture medium. Cell death was assessed with TUNEL assay.

Results: GSK3 is significantly inactivated during photoreceptor degeneration. Such inhibition was mimicked using mouse models with partial deletion of either Gsk3. In these models, induced-photoreceptor cell death ex vivo and in vivo following MNU injection was significantly decreased compared to controls. RNA-Seq analysis showed that most downregulated genes belonged to the phototransduction cascade. Upregulated genes identified were mostly related to inflammatory response and cell chemotaxis including secreted factors such as Spp1 and Fgf2. Increased transcriptomic and proteomic expression of both was confirmed between Gsk3α^{f+}β^{ff} α-Cre and Gsk3α^{f+}β^{ff} mice under degenerative and physiological condition. Immunostaining showed that OPN (Spp1) expression is limited to ganglion cells in WT and induced in Müller cells under different degenerative conditions. OPN treatment results in increased photoreceptor survival in ex vivo and in vivo degeneration model in WT mice. Interestingly, FGF2 expression was increased following OPN treatment.

Conclusions: Our work strongly suggests that the neuroprotective effects of GSK3 inhibition might be mediated by increased expression of OPN in Muller cells, triggering upregulation of FGF2 in photoreceptors. Such a feedback loop could be critical to modulate inflammatory response following retinal injury and sustain photoreceptor survival.

CONTROL ID: 3713172

SUBMITTER (NAME ONLY): Jesus Merayo-Lloves

TITLE: Corneal sensitivity with non-contact air jet esthesiometry compared with mechanical esthesiometry.

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Merayo-Lloves, I. Alcalde, Instituto Universitario Fernandez-Vega, Oviedo, SPAIN|J. Merayo-Lloves, L. Fernandez-Vega Cueto-Felgueroso, Universidad de Oviedo, Oviedo, Asturias, SPAIN|J. Lozano-Sanroma, A. Barros, J. Queiruga Piñeiro, A. Poo López, L. Fernandez-Vega Cueto-Felgueroso, Instituto Oftalmologico Fernandez-Vega, Oviedo, Asturias, SPAIN|

Commercial Relationships Disclosure: Jesus Merayo-Lloves: Commercial Relationship: Code N (No Commercial Relationship) | Javier Lozano-Sanroma: Commercial Relationship: Code N (No Commercial Relationship) | Alberto Barros: Commercial Relationship: Code N (No Commercial Relationship) | Juan Queiruga Piñeiro: Commercial Relationship: Code N (No Commercial Relationship) | Arancha Poo López: Commercial Relationship: Code N (No Commercial Relationship) | Ignacio Alcalde: Commercial Relationship: Code N (No Commercial Relationship) | Luis Fernandez-Vega Cueto-Felgueroso: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of the study was to assess the safety of the measurements taken with a new non-contact esthesiometer -Brill Engines esthesiometer (BEE) and to compare the sensitivity obtained with the Cochet-Bonnet esthesiometer (CBE).

Methods: Sixty eight eyes of thirty six healthy volunteers were included in the study. Corneal central sensitivity was measured with the new BEE and with the CBE, with a 0,08 mm of diameter nylon monofilament. Measurement was performed according with the manufacturer instructions. BEE was mounted in the slit lamp and CBE measurement was used manually. A sub-umbral esthesiometry strategy was performed. To assess whether the data followed a normal distribution, the Kolmogorov-Smirnov test was used. Likewise, the data obtained with the BEE were compared with those obtained with the CBE. A 95% confidence level was considered statistically significant. Measurements obtained with the CBE esthesiometer were converted to millibar for their comparison with the obtained with the BEE .

Results: Sixty eight eyes of thirty six consecutive healthy volunteers, 30,6% males and 69,4% females, underwent and complete the participation in the study. No adverse effected, ocular surface or corneal damage were detected and both test were well tolerated by volunteers. Correlation between both esthesiometers ICC was -0.123. (Table. 1). Bland Altman plots showed the great majority of data were inside the boundaries (2 SD). (Figure. 1).

Conclusions: A new non-contact air jet corneal esthesiometer was tested in healthy volunteers with good tolerance, no adverse effects. Values show that the lower force applied by CBE is more than 10 times higher than the BEE. This indicates, on the one hand, that it is not essential to exert so much force on the ocular surface to determine the sensitivity of a healthy cornea and, on the other, that BEE is more sensitive compared with CBE.

To confirm the pressure margins of BEE at each level and know the intervals in subjects with eye conditions, more studies will be conducted in the future with a more diverse population.

Brill Engines esthesiometer could be used as easy use, non-invasive and portable alternative of the Cochet Bonnet esthesiometer.

CONTROL ID: 3713175

SUBMITTER (NAME ONLY): Mary Carr

TITLE: Non-encapsulated Streptococcus pneumoniae is More Infective than Encapsulated S. pneumoniae in Early Keratitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Carr, K.M. Lovell, M. Robbins, H. Craddieth, M.E. Marquart, University of Mississippi Medical Center Department of Microbiology and Immunology, Jackson, Mississippi, UNITED STATES|A. Benton, Lake Erie College of Osteopathic Medicine Bradenton Campus, Bradenton, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The polysaccharide capsule of Streptococcus pneumoniae is an important factor in the pathogenesis of pneumococcal diseases such as pneumonia; however, the capsule is not required for bacterial conjunctivitis and its role in keratitis is poorly understood. The aim of this study was to investigate the importance of capsule using an in vitro corneal cell binding assay and a topical infection model of pneumococcal keratitis.

Methods: Adhesion to human corneal epithelial cells (HCECs) was determined for a keratitis strain of S. pneumoniae, K1544, and its isogenic capsule-deficient mutant, K1544Δcps. Each strain was inoculated onto the scratched corneas of 6-week-old A/J mice for acute experiments evaluating bacterial recovery (4 time points) and cytokine quantitation (2 time points) and long-term experiments evaluating clinical severity (1, 2, 3, 6, 8, and 10 days) and cytokine quantitation (10 days). Forty cytokines were quantified using antibody array densitometry.

Results: K1544Δcps binding to HCECs was significantly higher than that of K1544 ($p = 0.004$). Mouse corneas infected with K1544Δcps had significantly higher mean clinical scores than those infected with K1544 ($p = 0.033$; $n \geq 22$ per group) 24 hours post-infection. Beyond 24 hours and ending on day 10, there were no significant differences in clinical scores. All eyes were sterile by day 10 regardless of strain. Four and 8 hours post-infection, the mutant maintained significantly higher loads than the parent strain ($p = 0.014$ and 0.024, respectively). Bacterial loads were not significantly different at 12 or 24 hours. Protein levels of ocular IL-9, IL-10, IL-12-p70, MIG, and MIP-1-alpha were significantly higher for mice infected with K1544Δcps 24 hours post-infection compared to scratch controls or those infected with K1544 ($p \leq 0.043$; $n = 3$ per group). Cytokine levels were not significantly different 8 hours or 10 days post-infection.

Conclusions: Enhanced binding to corneal epithelial cells, retention of bacterial loads early in infection, and slightly higher clinical scores combined with an increase in cytokines one day after infection, suggest that non-encapsulated S. pneumoniae may have enhanced virulence in the cornea in the early stages of keratitis.

CONTROL ID: 3713177

SUBMITTER (NAME ONLY): Mezbah Uddin

TITLE: Topical latanoprost inhibits the developments of form-deprivation myopia and lens-induced myopia in the chick model

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Uddin, B. Zuo, K.P. Catral, C. To, D.Y. Tse, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|J. Wang, C. To, D.Y. Tse, Centre for Eye and Vision Research (CEVR), Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: To study the effects and the underlying mechanism of latanoprost on induced myopia in chicken

Methods: Myopia was induced in the right eyes of chicks using diffuser lenses (FDM) or -10D single vision lenses (LIM) for 12 days, while the left eyes were untreated control. One drop of topical latanoprost 0.005% or saline was administered daily in the treated and control groups, respectively. Refractive errors, tonometry and high-frequency A-scan ultrasonography were measured on days 0, 4, 8 and 12. Eyeballs were enucleated and processed for hematoxylin & eosin staining and western blot respectively. A total of 40 chicks were randomly divided into four groups (n=10). Data are presented as mean interocular differences ± standard deviation (SD).

Results: After 12 days of treatment, latanoprost inhibited both FDM and LIM. FDM control: -16.02±2.80D vs FDM latanoprost: -10.86±2.54D, $p<0.0001$. LIM control: -10.90±1.37D vs LIM latanoprost: -6.62±1.39D, $p<0.0001$) respectively. Intraocular pressure (IOP) was increased in FDM and LIM groups applied with saline, but decreased in those applied with latanoprost. Histology showed that latanoprost inhibited the thinning of sclera in the FDM and LIM groups. Latanoprost also upregulated retinal Early Growth Response 1 (Egr1) protein expression at the 12-day time point.

Conclusions: Topical latanoprost inhibit FDM and LIM in the chicken model and its effect was associated with a reduced IOP and upregulated Egr1 protein expression.

CONTROL ID: 3713178

SUBMITTER (NAME ONLY): Alberto Barros

TITLE: Corneal innervation changes after Sars-Cov-2 Infection. An In vivo Confocal Microscopy Study

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Barros, J. Lozano-Sanroma, J. Queiruga Piñeiro, A. Poo López, Optometry, Instituto Oftalmologico Fernandez-Vega, Oviedo, Asturias, SPAIN|I. Alcalde, J. Merayo-Lloves, Research, Fundacion de Investigacion Oftalmologica, Oviedo, Asturias, SPAIN|I. Alcalde, J. Merayo-Lloves, Instituto Universitario Fernandez-Vega, Oviedo, SPAIN|L. Fernandez-Vega Cueto-Felgueroso, Ophtalmology, Instituto Oftalmologico Fernandez-Vega, Oviedo, Asturias, SPAIN|L. Fernandez-Vega Cueto-Felgueroso, Universidad de Oviedo, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: To measure the innervation of the corneal subbasal nerve plexus of Covid-19 patients and compare the results with values of healthy patients.

Methods: A prospective, observational study was conducted analyzing 39 eyes of patients who had overcome Covid -19 and 46 eyes of healthy volunteers included as a control group (verified by antibody analysis and negative qPCR result) which underwent in vivo confocal microscopy with Rodstock Cornea Module© attached to Heildelberg HRT3©. Ocular surgery procedures, previous ocular infections or systemic diseases that could cause alteration in corneal innervation were exclusion criteria. At least 5 non overlapping images of each eye were selected and only one eye of each patient was included in the study. Following sub basal nervous plexus parameters were measured with ACC Metrics© software: Corneal Nerve Fiber Density (CNFD), Corneal Nerve Branch Density (CNBD), Corneal Nerve Fiber Length (CNFL), Corneal Total Branch Density (CTBD), Corneal Nerve Fiber Area (CNFA), Corneal Nerve Fractal Dimension (CNFrD). Data analysis was performed with SPSS® software for Windows 22.0 (SPSS® Inc, Chicago, IL.). The differences of age and sex between groups were checked with T-test and chi-square tests. The normality of the sample was checked with the Shapiro-Wilk test and the results were compared with the T test or the Man-Whitney U test based on the distribution of the data. The differences were considered statistically significant for $p<0.05$.

Results: There was no difference in the sex distribution between the groups ($p= 0.248$). The average age (± standard error) was 46.61±17.55 years for Covid-19 patients and 43.11±16.95 years for healthy control group ($p=0.353$) The mean of the analyzed variables (± standard error) from Covid-19 patients versus control group were CNFD: 16.09±6.92 and 23.03±8.31 fibers/mm^2 ($p=0,00008$), CNBD: 21.93±15.37 and 28.93±17.84 branches/mm^2 ($p=0.064$), CNFL: 11.61±3.61 and 14.05±3.71 mm/mm^2 ($p=0.002$), CTBD: 38.48±20.02 and 43.29 ± 23.94 ($p=0.41$), CNFA: 0.0057±0.0017 and 0.006±0.0023 mm^2/mm^2 ($p=0.853$), CNFrD: 1.46±0.041 and 1.47±0.037 ($p=0.007$).

Conclusions: According to the data obtained, corneal subbasal nerve plexus is decreased in Covid-19 patients compared to the healthy control group, statistically significant for density, length, and fractal dimension. The results show the presence of possible small fiber neuropathy induced by Covid–19 disease.

CONTROL ID: 3713179

SUBMITTER (NAME ONLY): Ashish Gupta

TITLE: Age-related changes in optical density and geometry of human crystalline lens measured with SS-OCT.

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gupta, E. Safarian Baloujeh, D. Ruminski, A. Jimenez-Villar, G. Gondek, I. Grulkowski, Faculty of Physics, Astronomy and Informatics, Uniwersytet Mikolaja Kopernika w Toruniu, Torun, Kujawsko-Pomorskie, POLAND|R.D. Toledo, P. Artal, Laboratorio de Óptica, Universidad de Murcia, Murcia, Murcia, SPAIN|

ABSTRACT BODY:

Purpose: To demonstrate in vivo three-dimensional imaging of crystalline lens in healthy eyes with SS-OCT. To objectively determine age-related effects on the crystalline lens by studying lens geometry and optical densities of back-scattered signals from sub-layers of the lens.

Methods: This study includes 50 eyes of 50 healthy volunteers (age range: 9-78 years old). Volumetric images of the crystalline lens were acquired for each eye using the SS-OCT system and the optical scatter index was measured using a double-pass system. The radius of curvature (ROC) and thickness of sub-layers of the lens was measured after refraction correction of the segmented layers. The enhanced intensity image is used to measure densitogram with the optical axis as the center of the image and to average the intensity values in the 54 μm region of interest (ROI). The Oxford nomenclature was used as a reference for the segmentation of distinct CL zones and the nucleus (figure 1). The enhanced intensity image is also used to determine the mean scattering index intensity of each layer of the crystalline lens.

Results: The thickness of the whole lens and measured thickness of the cortex increases with age. The mean ROC of the anterior cornea is 7.34 ± 0.24 mm, the posterior cornea is 6.39 ± 0.20 mm, the anterior lens is 10.1 ± 1.7 mm, the anterior nucleus is 4.06 ± 0.37 mm, the posterior nucleus is 3.67 ± 0.33 mm, the posterior lens is 5.90 ± 0.40 mm. ROC of anterior lens interface, anterior nucleus, and posterior nucleus decreases with age. However, there was no statistical correlation of age with ROC measured for the posterior lens ($R = 0.15$, $P = 0.298$). Thickness and mean intensity signal of each layer of the crystalline lens and their relationship with the aging of the eyes are presented in figure 2.

Conclusions: The SS-OCT imaging analysis of the lens indicated age-dependent development of sub-layers in the crystalline lens. SS-OCT for lens imaging is a useful tool for performing in vivo fundamental studies on the development and aging of the human lens.

CONTROL ID: 3713181

SUBMITTER (NAME ONLY): Ryan Imperio

TITLE: Enabling acquisition of optical coherence tomography angiography in cardiac surgery and intensive care

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We demonstrate the evolution of bedside, swept source, handheld optical coherence tomography (HH-OCT) and OCT angiography (OCTA) imaging with increasing scanning speeds for patients at risk for retinal ischemic events in infant and adult intensive care units (ICU).

Methods: We developed an investigational swept source OCT system at 100 kHz and increased scanning speed to 200 and 400 kHz to shorten the time of structural OCT capture and acquire OCTA. The handheld probe was lightweight and optimized for supine imaging. The increase in OCT speed required a heavier probe and was redesigned to fit comfortably and optimize balance in the operator's hand (Fig 1). We tested an ergonomic chair for stabilization body and forearm during imaging.

Results: At 100 kHz, we acquired OCT volumes without pharmacological pupil dilation in infants in the ICU. At 200 kHz, we readily obtained non-dilated OCT volumes in infants with congenital cardiac diseases and in adults before, during and after cardiac surgery. The 200 kHz OCTA capture was poor without pupil dilation, and was limited by pupil size and cardiac surgical motion. At 400 kHz, stabilization of the imager by an ergonomic chair decreased imager fatigue and imager-related motion artifacts. The decrease in OCTA scan acquisition time from 6 sec (at 200 kHz) to 3.6 sec (at 400 kHz) decreased motion artifacts and allowed for a stronger OCTA signal despite lack of pupil dilation.

Conclusions: The evolution of the handpiece, capture speed and ergonomic support, allowed capture of high quality structural OCT as well as OCTA with minimal artifacts. We are applying these advances to improve our understanding of the pathophysiology of retinal vascular events in cardiac patients.

CONTROL ID: 3713182

SUBMITTER (NAME ONLY): Duy Doan

TITLE: Automated machine learning (AutoML) models for diabetic retinopathy (DR) image classification from handheld retinal images

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To create and validate automated deep learning models for DR that are trained on handheld retinal images for community-based DR screening program (DRSP) in the Philippines.

Methods: AutoML Vision (Google Cloud) models were generated based on previously acquired 2-field retinal images (macula and disc centered, 1,600 images) from the Philippine DRSP. Image labeling was based on the International DR and DME classification obtained from primary grades and secondary adjudications by a reading center (RC). Images for the initial model were split 8-1-1 for training, validation and testing to detect referable DR [(refDR), defined as moderate nonproliferative DR or worse or any level of diabetic macular edema (DME). External testing of the autoML model was performed using a published image set (N=225 eyes) using the same devices in the same population, evaluated by the same RC. Sensitivity and specificity (SN/SP) for refDR were calculated.

Results: Training set distribution of DR severity by RC: no DR 66.0%, mild NPDR 10.7%, moderate NPDR 7.9%, severe NPDR 3.3%, PDR 5.6%, ungradable 6.5%. DME severity was: no DME 83.6%, DME 6.3%,center involved DME 7.4%, ungradable 2.7%. RefDR was present in 18.5% of images. Area under the precision-recall curve (AUPRC) was 0.947 (figure 1). The model’s overall accuracy for RefDR was 89.4%. External testing set DR/DME distribution: no DR 54.2%, mild NPDR 17.8%, moderate NPDR 9.8%, severe NPDR 3.3%, PDR 5.8%, ungradable 1.8%. DME severity was: no DME 62.7%, DME 6.2%, center involved DME 19.1%, ungradable 12.0%. RefDR was present in 39.1% of images. SN/SP for refDR on the external test set was 0.94/0.81. Table 1 shows a comparison with reported metrics from FDA approved algorithms.

Conclusions: This study demonstrates the accuracy and feasibility of autoML models for the identification of refDR developed for a DRSP using handheld retinal imaging in a low-resource setting community program. The performance approaches published diagnostic accuracy metrics of commercial models used for DRSP. Potentially, the use of autoML may increase access to machine learning models that may be adapted for specific programs that are guided by clinicians to rapidly address disparities in patient care.

CONTROL ID: 3713183

SUBMITTER (NAME ONLY): Erin Flynn

TITLE: Long Term Outcomes of Pre-operative Bevacizumab use in Diabetic Retinopathy patients needing Vitrectomy: A TriNetX Analysis

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Flynn, H. Song, M. Dalal, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|D. Akinbolue, H. Pakhchanian, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if there were differences in long term outcomes in patients requiring pars plana vitrectomy (PPV) for diabetic retinopathy (DR) with preoperative bevacizumab intravitreal injection versus without.

Methods: This retrospective cohort study utilized data from TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising 56 large health organizations in the United States. Patients who underwent PPV for DR were identified by CPT code and stratified by preoperative bevacizumab injection and no preoperative bevacizumab injection. Patients were matched for age, gender, and medical comorbidities (essential hypertension, diabetes mellitus, cerebrovascular disease, heart failure, nicotine dependence, alcohol related disorders, and body mass index). Primary outcomes measured over a year after the procedure included: vitreous hemorrhage (VH), choroidal hemorrhage, cystoid macular degeneration (CME), puckering of macula, glaucoma, cataract, dry eye syndrome (DES), central retinal vein occlusion, central retinal artery occlusion, vitreous opacities, ptosis, dislocation of lens, endophthalmitis, and retinal vascular occlusions. These long-term outcomes were compared between the cohorts after propensity score matching using logistic regression.

Results: A total of 6,810 patients were analyzed with 3,405 in each cohort after propensity matching. The preoperative bevacizumab cohort showed a significantly greater risk of developing VH (RR, 1.72; 95% CI, 1.36-2.17), Cataract (RR, 1.32; 95% CI, 1.14-1.53) and DES (1.66; 95% CI,1.29-2.14). The cohort without preoperative bevacizumab injection had a slightly greater risk of developing CME (RR, 1.36; p=0.034, 1.02-1.81) and increased risk of dislocation of lens (RR, 2.22; p=0.002 ,1.33-3.70). No other significant differences were found between the cohorts.

Conclusions: Preoperative treatment with bevacizumab before PPV for DR is a technique utilized in an attempt to lower intraocular VEGF levels and counter proliferation for the procedure. In this study, preoperative treatment of bevacizumab significantly increased risk of vitreous hemorrhage and cataract. However, lack of preoperative bevacizumab injection was associated with a more frequent occurrence of CME. This study illustrates that using bevacizumab preoperatively may have outcomes over a year after the operation.

CONTROL ID: 3713185

SUBMITTER (NAME ONLY): Daniel Chang

TITLE: Duration of Efficacy of AGN-190584 on Photopic Distance-Corrected Intermediate Visual Acuity in the GEMINI 1 and GEMINI 2 Pooled Phase 3 Studies

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Chang, Empire Eye and Laser Center, Bakersfield, California, UNITED STATES|W. Christie, Scott and Christie Associates, Cranberry Township, Pennsylvania, UNITED STATES|W. Pack, Y. Fang, Allergan, an AbbVie Company, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the duration of effect in photopic distance-corrected intermediate visual acuity (DCIVA) in presbyopia study participants treated with AGN-190584 on Days 1 and 30.

Methods: The durations of attainment of ≥3-line, ≥2-line, and ≥1-line improvement in photopic DCIVA were calculated in participants who received AGN-190584 bilaterally, once daily for 30 days (n=375). Intermediate visual acuity was assessed at a distance of 66 cm (26 in).

Results: On Day 30, the median final time point of sustained gains in photopic DCIVA was Hour 7 for a ≥3-line gain, Hour 8 for a ≥2-line gain, and beyond the 10-hour study visit duration for a ≥1-line gain in participants who achieved ≥3-line, ≥2-line, and ≥1-line gains, respectively (Figure). 96 study participants in the active treatment group achieved at least a 3-line gain, 205 at least a 2-line gain, and 312 at least a 1-line gain. On Day 1, the median final time point of sustained gains in photopic DCIVA was Hour 5 for a ≥3-line gain, Hour 7 for a ≥2-line gain, and beyond the 10-hour study visit duration for a ≥1-line gain in participants who achieved ≥3-line, ≥2-line, and ≥1-line gains respectively. 60 study participants in the active treatment group achieved at least a 3-line gain, 158 at least a 2-line gain, and 300 at least a 1-line gain.

Conclusions: In photopic illumination conditions, participants treated with AGN-190584 obtained ≥3-, ≥2-, and ≥1-line gains in DCIVA over the course of the 10-hour study visit on Days 1 and 30.

CONTROL ID: 3713186

SUBMITTER (NAME ONLY): Marion Munk

TITLE: LIGHTSITE III (Interim Analysis): Evaluation of Multiwavelength Photobiomodulation in Dry Age-Related Macular Degeneration Using the LumiThera Valeda Light Delivery System

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.R. Munk, Inselspital, University Hospital Bern, SWITZERLAND|V.H. Gonzalez, Valley Retina Institute, Texas, UNITED STATES|D.S. Boyer, Retina Vitreous Associates Medical Group, California, UNITED STATES|D.V. Do, Byers Eye Institute, California, UNITED STATES|S. Xavier, Florida Eye Clinic, Florida, UNITED STATES|A. Hu, Cumberland Valley Retina Consultants, Maryland, UNITED STATES|E. Lad, G. Jaffe, Duke Reading Center, Duke University School of Medicine, North Carolina, UNITED STATES|R.B. Rosen, New York Ear and Eye Infirmary of Mount Sinai, New York, UNITED STATES|T. Schneiderman, Retina Center NorthWest, Washington, UNITED STATES|A.C. Ho, Mid Atlantic Retina, New Jersey, UNITED STATES|S. Tedford, C. Croissant, C. tedford, LumiThera, Inc, Washington, UNITED STATES|R. Ruckert, Eyegnos Consulting, SWITZERLAND|D. Warrow, Cumberland Valley Retina Consultants, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry age-related macular degeneration (AMD) is a leading contributor to visual impairment across the globe. No current treatment exists to improve visual function or reduce disease progression outside of vitamin supplementation and lifestyle changes. LIGHTSITE III is evaluating multiwavelength photobiomodulation (PBM) therapy using the LumiThera Valeda® Light Delivery System in dry AMD

Methods: LIGHTSITE III (NCT04065490) is a prospective, double-masked, randomized, sham-controlled, parallel group, multi-center study to assess the safety and efficacy of PBM in dry AMD. Target enrollment was approximately 96 subjects (144 eyes). Subjects are treated with six series of PBM/Sham treatments (3x per week for 3 weeks) delivered over a 24-month period with a 13-month efficacy analysis of data. PBM therapy consists of low-level light exposure to selected tissues resulting in positive effects on mitochondrial output and improvement in cellular activity. Valeda is used to deliver multiwavelength PBM treatment using 590, 660 and 850 nm of light. Subjects are assessed for clinical and safety outcomes (i.e., best-corrected visual acuity (BCVA), low-luminance BCVA, contrast sensitivity, reading speed, color vision, VFQ-25 and perimetry). Independent OCT, FAF and color fundus imaging outcomes at selected timepoints are analyzed by a masked imaging reading center

Results: A total of 148 eyes from 100 subjects with dry AMD have been enrolled and randomized in a 2:1 design (PBM:Sham). The majority of subjects are female (68%) and Caucasian (99%). The average age at enrollment was 75 years and mean time since dry AMD diagnosis is 4.9 years. COVID-19 interference has been minimal and not significantly impacted subject enrollment or retention. Clinical and anatomical outcome data from the interim analysis conducted at Month 13 is presented. Results from the 21-month time point are expected at end of 2022

Conclusions: LIGHTSITE III provides the largest, randomized controlled trial evaluating the effects of PBM in dry AMD subjects. PBM therapy may offer a new treatment strategy with a unique mechanism and modality for patients with dry AMD

CONTROL ID: 3713188

SUBMITTER (NAME ONLY): Jade Harkin

TITLE: Enhanced reproducibility of retinal organoids enables the analysis of early human retinal fate specification

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Harkin, Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|K. Pena, S.S. Lavekar, K. Lentsch, Biology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|J.S. Meyer, Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|J. Harkin, S.S. Lavekar, J.S. Meyer, Stark Neurosciences Research Institute, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|E. Feder, Medicine, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Retinal organoids can be differentiated from human pluripotent stem cells (hPSCs) that effectively recapitulate the major stages of human retinogenesis. These organoids are becoming valuable tools for studying human retinogenesis and retinal diseases, yet shortcomings in the efficiency and reproducibility of current retinal organoid differentiation protocols have hindered their abilty to serve as effective models for the earliest stages of human retinal lineage specification.

Methods: In the current study, we refined an existing retinal organoid differentiation protocol using more standardized, quick reaggregation methods to generate highly reproducible 3D retinal organoids from human pluripotent stem cells (hPSCs). BMP signaling contributing to retinal specification was analyzed by treatment with either BMP4 or the BMP inhibitor LDN-193189, and differentiation efficiency was assessed at various time points based on morphological analyses and the expression of retinal markers. Additionally, to identify transcriptional changes that underly retinal fate dermination events, mRNA-seq analyses were conducted at the earliest stages of retinal specification.

Results:

Retinal organoids generated using quick reaggregation methods were highly reproducible in both their size and shape compared to more traditional methods. Following treatment of early aggregates with either BMP4 or LDN-193189, pure populations of either retinal or forebrain organoids were derived, respectively. Subsequently, RNA-seq methods analyzed the transcriptional profile of the earlies stages of retinal vs forebrain specification, long before these lineages have been reliably identified previously. These refined methods also yielded retinal organoids with greatly expedited differentiation timelines, with differentiated retinal neurons arising at earlier stages than traditional differentiation methods, also exhibiting higher levels of self-organization.

Conclusions: Taken together, this study provides a novel and highly reproducible method for generating retinal organoids suitable for analyzing the earliest stages of human retinal fate specification in an organoid model. These results elucidate some of the earliest transcriptional changes occurring at the most immediate stages of human retinal development, and provide a more optimized and rapid method for generating retinal organoids for translational applications.

CONTROL ID: 3713189

SUBMITTER (NAME ONLY): Kevin Harkin

TITLE: Deletion of Angiotensin II type 2 receptor (AT2) exacerbates retinal neovascularization and hemorrhage in oxygen-induced retinopathy (OIR)

SESSION TITLE: Retinal Vascular Diseases excluding Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Loss of endothelial cell integrity is a critical factor of ischaemic retinopathies. The pathogenesis is highly complex and multifaceted but the AT2 pathway has been implicated in vascular pathology in both the retina and brain. For example, in a murine model of cerebral malaria, deletion of AT2 augmented blood barrier breakdown and localized hemorrhage. This study tested the hypothesis that deletion of AT2 could lead to damaging effects in the retinal vasculature during ischaemic conditions.

Methods: AT2 knockout (KO) and C57BL/6J wildtype (WT) mice were subjected to the OIR protocol. At postnatal days 13 and 17 (P13; P17) eyes were enucleated, flat-mounted and the vasculature stained using lectin and TER119 (red blood cell marker). Using ImageJ, levels of retinal vasobliteration, neovascularization and hemorrhage were assessed. In a parallel in vitro experiment, vasopermeability was induced in Human Retinal Microvascular Endothelial Cells (HRMECs) monolayers with VEGF (50ng/ml) and/or treated with an endogenous agonist for AT2 (EA)(10^{-10} μM) with barrier function being assessed via xCELLigence.

Results: At P13 OIR, AT2KO mice (N=11) displayed an increase in retinal vasobliteration as compared to WT (N=12)($P<0.01$). $IBA1^{+}$ microglia, displayed regular and diffuse staining patterns within the WT retina coupled with highly ramified morphology, whereas the AT2KO mice, showed dense clustering of microglia along the avascular interface with the vasculature while displaying an amoeboid-like phenotype. At P17 OIR, AT2KO mice (N=13) had increased retinal neovascularization when compared to WT (N=12)($P<0.05$). Retinal hemorrhage was macroscopically visible in AT2KO mice, but not in WT. This was further supported via TER119 staining in murine retinas, where AT2KO (N=4) had a greater $TER119^{+}$ area than WT (N=5)($P<0.05$). HRMECs exposed to VEGF showed a reduction in endothelial integrity ($P<0.05$), which was attenuated upon pre-treatment with EA ($P<0.05$).

Conclusions: Genetic deletion of AT2 induced greater vasobliteration and neovascularization in OIR. AT2 is a key regulator of retinal vascularisation and barrier integrity with a lack of AT2 being detrimental and activation being protective. Taken together, our data suggest that activation of AT2, may provide a therapeutic option in strengthening tight junctions in diseases where endothelial integrity is compromised.

CONTROL ID: 3713191

SUBMITTER (NAME ONLY): Hagar Khalid

TITLE: Incident cardiovascular events following paracentral acute middle maculopathy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Khalid, Tanta University, Tanta, EGYPT|H. Khalid, S. Wagner, L. Raja, J. Huemer, D. Ferraz, K. Balaskas, D. Sim, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Paracentral acute middle maculopathy (PAMM), a retinal disease characterized by sudden-onset ischaemia of the deep vascular complex, could be the only presenting sign of incomplete central retinal artery or central retinal vein occlusion. Furthermore, isolated PAMM can be the presenting feature of carotid disease. PAMM has the potential to develop more severe ischemic disease which known as the ischemic cascade and may be the result of progressive vascular obstruction.

There has been equivocal evidence that PAMM may be associated with cardiovascular events. In this study, we explored the incidence of myocardial infarction and ischaemic stroke following a new diagnosis of PAMM at a large tertiary ophthalmic institution.

Methods: A total of 47 patients were newly diagnosed with PAMM by an ophthalmologist specializing in medical retina between January 1st 2008 and December 31st 2017 and had linked secondary care Hospital Episodes Statistics Admissions data. Myocardial infarction (MI) and ischaemic stroke were identified through previously validated International Classification of Diseases 10th Edition codes I21/I22 and I61-I64.

Results: Among the cohort, 28 were male and the average age was 59.0 (12.3) years at diagnosis. Three had myocardial infarctions, one prior and two of which followed an episode of PAMM; there were no cases of ischaemic stroke. Average age at time of MI was 75.3 (9.9) years. The two cases occurred 29 days and 1516 days following the diagnosis of PAMM

Conclusions: In this regional cohort of PAMM, there were no cases of ischaemic stroke and few cases of MI following an episode of PAMM. While underpowered to detect a difference with age-standardised rates of MI, our results did not identify a strong association between PAMM and elevated incidence of cardiovascular events.

CONTROL ID: 3713192

SUBMITTER (NAME ONLY): Colas Authié

TITLE: Development and validation of a mobility test for Inherited Retinal Disease in real and virtual conditions - preliminary results.

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although Inherited Retinal Disease (IRD) are well characterized in terms of anatomical and functional progression, their impact on patients' daily lives is often poorly understood and lacks standardized measures as performance-based outcomes (PerfO) evaluating the performance in daily-life tasks, such as orientation and mobility. We developed a new mobility test in real (IRL) and virtual (VR) conditions and performed a prospective, interventional non-invasive, longitudinal study (test-retest) to compare the performance of IRD patients and healthy participants in both conditions (IRL v.s. VR).

Methods: Fifteen retinitis pigmentosa patients and 15 age-matched healthy participants had to walk through a maze either physically presented (IRL) or displayed in a virtual reality headset (HTC Vive Pro Eye). In multiple light level conditions (between 1 Lux and 400 Lux in IRL), participants were instructed to step over two steps, pass under two flags, avoid a cone and two high obstacles, avoid a dead-end, and finally reach an end goal. Trial duration and errors were automatically recorded in VR condition. In IRL condition, errors were live coded by an experimenter and recorded by a different experimenter after the session. We computed a performance score taking in account duration and errors.

Results: Preliminary results indicate a good construct validity (discrimination between groups, ROC area>.9), a very good agreement of the performance score between sessions (ICC>.95) and between VR and IRL conditions (ICC>.9), and a good content validity (correlation with a visual score .41 and .65). Moreover, test duration was acceptable for 95% of participants (both conditions) and the VR experience was rated as enjoyable for 73% of participants. 78% of RP participants felt that the VR test was representative of their difficulties in daily life.

Conclusions: We have designed a locomotion test, both in real (IRL) and virtual (VR) conditions, that has excellent reproducibility and high agreement between both conditions. Additional data are awaited to confirm these results, and measure sensitivity to change which will determine its interest in monitoring the progression of a retinal disease and assessing the efficacy of new treatments.

CONTROL ID: 3713193

SUBMITTER (NAME ONLY): Huy Nguyen

TITLE: COVID-era influence on follow-up trends and the impact on retinovascular disease progression

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Nguyen, B.E. Ahearn, J. Sohn, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: COVID changed follow-up logistics starting 3/2020 in South Texas (STX). The incidence of proliferative retinovascular (RV) events in the emergent setting increased after shut down in STX. We investigate patterns of follow-up behavior in patients with and without proliferative complications of RV diseases.

Methods: We used CPT and ICD-10 codes in date range 1/2018 to 4/2021 to include patients diagnosed with diabetic retinopathy (DR) and retinal vein/artery occlusions (RVO/RAO) and analyzed them as two groups: anti-VEGF ± panretinal photocoagulation (PRP) (nonvitrectomy group) vs vitrectomies. We compared before and after COVID-era: appointment intervals and lapses, rate of progression in EDTRS staging for patients with DR.

Results: At initial encounter, 2/133/125 patients of 1503 had mild/moderate/severe DR. 40/5 patients had RVO/RAO. There were 429/1074 patients in the vitrectomy/nonvitrectomy group. Vitrectomy group had 123 non-clearing vitreous hemorrhages, 72 tractional retinal detachments, and 189 unclassified proliferative retinovascular complications. Prior to COVID, visit interval was 28.4 ± 43.2 vs 30.8 ± 47.8 days in the vitrectomy vs nonvitrectomy group ($p=0.61$). After COVID, the interval duration for the vitrectomy group increased to 39.8 ± 76.5 days with no increase in the nonvitrectomy group ($p<0.001$). Time to diagnosis of EDTRS-staged progression after COVID increased by an average of 21.5 days in the vitrectomy group and by 26.7 days in the nonvitrectomy group.

After COVID restrictions, missed appointments in the vitrectomy vs nonvitrectomy group changed from 24.5% to 30.8% vs 28.1% to 33.4%. Across all encounters, the vitrectomy versus nonvitrectomy group had 19.1% vs 21.9% cancellation rate (6.08 vs 5.85 appointments/patient) and 7.81% vs 8.39% no show rate (3.09 vs 2.97 appointments/patient). Overall, patients with DR who experienced EDTRS-staged progression missed 21.2% of appointments (6.8 per patient for those with missed appointments).

Conclusions: Patients who required vitrectomy versus those able to be managed in clinic missed appointments in the same proportion and quantity before COVID and increased appointment lapses similarly after COVID restrictions, but interval duration and variability was significantly higher in patients that eventually suffer a complication severe enough to necessitate vitrectomy.

CONTROL ID: 3713194

SUBMITTER (NAME ONLY): Jose Miguel Cleva

TITLE: Clinical validation of single-vision lenses optimized by considering user's accommodation

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The optimization of customized spectacle lenses often considers individual user parameters such as morphological data, frame parameters, and working distances to compensate oblique aberrations. Recently, it has been proposed a new optimization method that considers the accommodative ability of the user to optimize the lens in a more realistic object space and to modulate the oblique aberrations of the user in a more efficient way. The goal of this study is to compare the performance of single vision lenses (SV) optimized with this method against standard spherotorical lenses.

Methods: Double-blind study in which 66 non-presbyopic users were evaluated when wearing a spherotorical SV lens (control) and a customized SV lens optimized with a new method considering user accommodative ability (DRP2). Accommodative lag (LAG) was measured on-axis and 20 degrees off-axis using near retinoscopy at 40cm with a near fixation card attached to the retinoscope. Static visual acuity (VA) was measured on-axis and 20 degrees off-axis at 5.25m. Dynamic visual acuity (DVA) was measured using the software COI-Sport with a speed of 100cm/s at 5.25m. User experience (UX) was evaluated with a satisfaction survey after subjects used both pairs of lenses for 7 days each. Satisfaction rates in scale 1-5 and preferred lens choice were analyzed. Statgraphics Centurion XVI.II software was used to determine differences between lens designs.

Results: Significant higher dynamic VA and UX were found, showing better values for the lens DRP2. Non-significant differences were found in the LAG and static VA between both lenses at any of the viewing positions (Table 1). When the participants were asked to select their preferred lens, 51% preferred the DRP2 lens, 27% selected the control lens and 22% of the participants did not perceive differences between them.

Conclusions: Single-vision lenses optimized with a new optimization method that considers user accommodative ability provide better dynamic visual acuity and user experience than spherotorical lenses. Nevertheless, the accommodation lag of the user remains stable on and off-axis.

CONTROL ID: 3713196

SUBMITTER (NAME ONLY): Paul Gomes

TITLE: A multi-center phase 3 evaluation of bilastine 0.6% preservative-free eye drops for the treatment of allergic conjunctivitis

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.J. Gomes, Allergy, Ora, Inc., Andover, Massachusetts, UNITED STATES|P. Arranz, G. Hernandez, N. Fernandez, Faes Farma Vizcaya, Vizcaya, Bilbao, SPAIN|

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ABSTRACT BODY:

Purpose: Allergic conjunctivitis (AC) is a common ocular disease with a growing incidence rate. Novel topical therapies add to a physician's armamentarium. The efficacy of a new once-daily Bilastine 0.6% multi-dose preservative-free ophthalmic solution (BOS) for the treatment of the signs and symptoms of AC was evaluated. Non-inferiority testing was conducted between BOS and a marketed multi-dose formulation of ketotifen 0.025% (KOS).

Methods: This was a multi-center, double-masked, randomized, vehicle and active controlled, phase 3 study conducted to assess the efficacy for treatment of the signs and symptoms of AC, safety, and tolerability of BOS. The Ora-CAC® Allergen Challenge Model was used to assess acute ocular and nasal allergic responses. Subjects must have had a history of ocular allergies and a positive skin test reaction to a seasonal or perennial allergen. On Day 1, 228 adult subjects with AC were randomized to receive BOS N=91, KOS N=90, or vehicle N=47. A duration-of-action (16 hours post drop on Day 1) and an onset-of-action (15 minutes post drop on Day 15) visit was conducted. The primary efficacy endpoint was ocular itching. Statistical testing included superiority comparisons of BOS vs. vehicle at onset and duration of action and non-inferiority of BOS to KOS at onset.

Results: BOS showed efficacy reducing ocular itching at 15 minutes and 16 hours post treatment ($P<0.001$) while KOS showed efficacy at 15 minutes ($P<0.001$). BOS was non-inferior to KOS at onset. BOS demonstrated improvement over vehicle ($P<0.05$) for conjunctival/ciliary/episcleral redness, chemosis, eyelid swelling, tearing, rhinorrhea, ear/palate pruritus and nasal congestion at onset. BOS was safe and well tolerated. BOS was significantly more comfortable ($P<0.05$) than KOS immediately upon instillation and similar to vehicle.

Conclusions: Bilastine 0.6% preservative free eye drops developed by Faes Farma is effective at reducing ocular itching up to 16 hours post-treatment. Bilastine was safe and well tolerated. This multi-dose preservative-free formulation can be used as a once-daily treatment for the signs and symptoms of AC.

CONTROL ID: 3713198

SUBMITTER (NAME ONLY): Sergio Alonso-Alonso

TITLE: Comparison of mRNA expression in primary cultures of human anterior lens epithelium and human corneal endothelium.

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Alonso-Alonso, N. Vázquez, M. Chacon, M. Persinal-Medina, L. Fernández-Vega-Cueto-Felgueroso, J. Merayo-Lloves, A. Meana, Instituto universitario Fernández-vega-Fundación de investigación Oftalmologica-Universidad de oviedo, Oviedo, Asturias, SPAIN|N. Caballero-sánchez, Debreceni Egyetem, Debrecen, Hajdú-Bihar, HUNGARY|L. Nagy, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal endothelial dysfunctions are the main cause of corneal blindness in developed countries and to date, the shortage of endothelial tissue for its treatment represents an emerging problem. Therefore, finding substitutes to corneal endothelium in other tissues should be a priority in order to treat more patients. In this study we compare the gene expression from primary xeno-free cultures of human lens capsule epithelium and human corneal endothelium in order to evaluate the potential use of lens capsule epithelial cells as a surrogate of corneal endothelium.

Methods: Four corneal endothelia deemed inappropriate for surgery and four lenses were obtained from Asturias tissue bank. Corneal endothelium was dissected following the Schwalbe line and anterior lens capsule was dissected from the stroma. Both tissues were digested with TrypLE for 90 min at 37 °C and seeded on a culture plate and cultured until confluence. Subsequently, we performed bulk RNASeq in both cell types and analyzed their gene expression profiles. RNA was isolated using the Arcturus^{TM} PicoPure^{TM} kit followed by NEBNext Ultra II RNA library preparation. Samples were sequenced with Illumina NextSeq550. Additionally, cultured cells were fixed using ice-cold methanol for 10 min and immunocytochemistry of major corneal endothelial markers (Na^+/K^+ ATPase, ZO-1) were performed.

Results: We identified 19.677 similarly expressed genes out of 22.641 lens capsule epithelium and corneal endothelium genes. Essential genes for the correct function of the corneal endothelium such as, those responsible for the barrier function and ion pump (Na^+/K^+ ATPase, ZO-1) present a similar level of expression. Moreover, protein expression of major functional markers was confirmed by immunocytochemistry. The 2964 differentially expressed genes (DEGs) were mainly clustered in the gene ontology of epithelial cell proliferation, extracellular matrix organization and eye development.

Conclusions: Corneal endothelium and lens epithelium share substantial similarities in functional gene and protein expression, supporting the proposal to use lens capsule epithelial cells as a possible surrogate for corneal endothelium

CONTROL ID: 3713199

SUBMITTER (NAME ONLY): Pulak Nath

TITLE: High dimensional profiling and immune monitoring of Uveitis patients

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.R. Nath, M. Maclean, J. Lee, A. Kumar, H. Nadali, M. Yakin, S. Kodati, R.R. Caspi, H. Sen, Clinical and Translational Immunology Unit, Laboratory of Immunology of Immunology, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Maclean, Translational Immunology Section, National Institute of Arthritis Musculoskeletal and Skin Disease, Bethesda, Maryland, UNITED STATES|V. Nagarajan, R.R. Caspi, Immunoregulation Section, Laboratory of Immunology, National Eye Institute, Bethesda, Maryland, UNITED STATES|K. Kaya, Medical Genetics and Ophthalmic Genomics Unit, National Eye Institute, Bethesda, Maryland, UNITED STATES|J.J. Kuiper, Department of Ophthalmology, Universiteit Utrecht Faculteit Geneeskunde, Utrecht, Utrecht, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Uveitis is a significant cause of severe visual handicap. Evidence links induction of experimental autoimmune uveitis to T cell mediated pathogenesis which is believed to be regulated, at least in part, by natural killer (NK) cells. Here we present the unsupervised multimodal omics of the circulating NK cell compartment in a large cohort of 160 non-infectious uveitis patients (48% with systemic treatement and 52% with no systemic treatement at baseline) and 51 healthy controls.

Methods: Cases and controls were recruited and clinically phenotyped under a prospective clinical study (NCT02656381). We conducted 38-parameter flow cytometry [BD LSR-Fortessa] on freshly collected blood samples, bulk RNA sequencing and single cell RNAseq (scRNAseq) analysis of purified periperhal blood mononuclear cells (PBMCs) [Illumina NovaSeq 6000, 10x Genomics Chromium], and serum targeted proteomics using the Somascan array (SOMAlogic].

Results: Bulk RNA sequencing analysis revealed a clear distinction of PBMCs transcriptome between healthy donors and uveitis patients which was driven by a significant upregulation of NK biology gene (NCAM1, $P = 0.012$). At the single cell level, scRNAseq analysis could attribute these changes to the enrichment of a distinct subset of NK cells ($P < 0.05$) characterized by high FCGR3A gene expression in uveitis cases. Flow cytometric analysis confirmed a significant increase of CD16+ NK cells ($P = 0.003$), and a concomitant decrease of $CD56^{bright}$ NK subsets ($P = 0.002$) in the PBMCs of uveitis patients. SOMAlogic analysis revealed a significant decrease ($P = 0.028$) of NK-inhibitory soluble protein Thrombospondin-1 in the serum of uveitis patients.

Conclusions: The current data are in line with a role for NK cells as an active modulator of autoimmune responses in uveitis patients. A previous study involving blockade of IL2Ra (daclizumab) in uveitis patients showed expansion of $CD56^{bright}$ NK cells. Our current observation indicates expansion of activated NK cells and decrease in regulatory NK cells in uveitis patients. Further studies are needed to examine the role of NK cells in the development, progression and treatment of uveitis.

CONTROL ID: 3713201

SUBMITTER (NAME ONLY): Mary Ann Croft

TITLE: Accommodative movements of the lens, anterior hyaloid and choroid are correlated with accommodative amplitude but the relationships change with age

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Croft, G. Heatley, T. Nork, J. McDonald, A.W. Katz, P.L. Kaufman, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|P.L. Kaufman, Wisconsin National Primate Research Center, UW-Madison, University of Wisconsin-Madison, Madison, WI, US, academic, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify accommodative movements of the lens and choroidal movements in the human eye and the anterior hyaloid movements in the monkey eye, to determine if they are related to accommodative amplitude and presbyopia.

Methods: In eyes of 4 rhesus monkeys (aged 8-19 yrs), accommodative responses were induced by central electrical stimulation of the midbrain in a dose-dependent manner, from minimal to maximal accommodative responses. Accommodation was induced in the human eye by 4% topical pilocarpine. Accommodative amplitude was measured by Hartinger coincidence refractometry. OCT and ultrasound biomicroscopy (UBM; 50, 20 MHz) images were collected in the region of the lens, ciliary body and over the entire extent of the globe in monkey and human subjects in resting and accommodated states.

Results: Monkey: In this preliminary study, accommodative anterior hyaloid posterior movement was significantly related to accommodative amplitude in all 4 animals thus far measured (the more the anterior hyaloid moved posteriorly during accommodation, the higher the accommodative amplitude) but the relationship changed with age. In the young eye the average slope of the regression equation was 44.2 ± 5.5 diopters/mm (p= 0.001, n=2), but in the older eye it was 16.02 ± 3.23 diopters/mm (p= 0.007, n=2). Human: Lens accommodative thickening was significantly related to accommodative amplitude (26.02 ± 3.28 diopters/mm, n=22) but the relationship changed with age; young = 12.5 ± 6.6 diopters/mm (p=0.08, n=14); older = 3.72 ± 3.65 diopters/mm (p=0.35, n=8). In the older eye accommodative centrifugal choroidal movement around the optic nerve was negatively correlated with accommodative amplitude; the more centrifugal choroid movement the less accommodative amplitude (-0.63 ± 0.11 mm/diopter, p=0.028, r=0.97, n=4). Choroidal thinning was positively correlated with accommodative amplitude; the more the choroid thinned the higher the accommodative amplitude (43.5 ± 9.2 µm/diopter, p=0.042, r=0.96, n=4).

Conclusions: There are statistically significant accommodative movements of the choroid and various intravitreal structures. The posterior anterior hyaloid and choroidal movements may provide insights to the mechanism of accommodation, presbyopia, accommodating IOL function and perhaps glaucoma.

CONTROL ID: 3713202

SUBMITTER (NAME ONLY): Tim Murphy

TITLE: Retinal photographic feature localisation in diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Murphy, J. Armitage, A. Douglass, Deakin University School of Medicine, Geelong, Victoria, AUSTRALIA|P. van Wijngaarden, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|P. van Wijngaarden, The University of Melbourne Department of Surgery in Ophthalmology, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Diabetes affects 9.3% of the adult population globally and is a leading cause of preventable blindness. The burden of diabetic complications will increase rapidly in the coming decades. Effective detection of diabetic retinopathy offers the best strategy for timely intervention. As has been shown for glaucoma, systematic search strategies may enable more efficient grading, however there are no formalised strategies for grading diabetic retinopathy in clinical practice. Better understanding of the localisation of features of diabetic retinopathy may inform the development of a search strategy to aid the training of eye health care providers.

Methods: Three publicly available datasets of annotated retinal photographs were obtained, with a combined total of 757 images with diabetic retinopathy and 70 images of normal retinal vasculature. Annotations for venous beading, intraretinal microvascular abnormalities (IRMA) and neovascularisation were added to the existing annotations. Images were standardised to correct for centration, rotation and field of view. Vessel and lesion locations were extracted and collated into a frequency matrix. Heatmaps were generated showing frequency distributions of the location of arterioles, venules, microaneurysms, haemorrhages, exudates, cotton wool spots (CWS), IRMA, venous beading and neovascular changes.

Results: Retinal arterioles typically conform to two distinct temporal arcades, whereas the distribution of the temporal venular arcades is more heterogeneous (Figure 1). Microaneurysms and haemorrhages are diffusely distributed in the posterior pole. Exudates appear to cluster in the temporal macular region. CWS and IRMA occur most frequently in the peripapillary area. Neovascular changes are diffusely distributed in the posterior pole. Venous beading is clustered around the venular arcades in the peripapillary area (Figure 2).

Conclusions: Our study finds that diabetic retinopathy lesions are unevenly distributed in the posterior pole. The cause of exudate clustering at the temporal macular is not well understood and requires further study. These lesion distribution patterns will be used to derive a clinical algorithm to facilitate accurate diabetic retinopathy grading by trainee eye health care providers.

CONTROL ID: 3713204

SUBMITTER (NAME ONLY): Leina Lunasco

TITLE: Machine Learning-Enhanced Longitudinal Ellipsoid Zone Integrity Assessment on OCT in the VISTA DME Study

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lunasco, S. Yordi, H. Cetin, G. Kalra, C.J. Mugnaini, K. Wise, K.E. Talcott, C. Calabrise, S.K. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|L. Lunasco, S. Yordi, H. Cetin, G. Kalra, C.J. Mugnaini, K. Wise, K.E. Talcott, C. Calabrise, S.K. Srivastava, J. Reese, J.P. Ehlers, The Tony and Leona Campane Center for Excellence in Image-Guided Surgery and Advanced Imaging Research, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the longitudinal dynamics of quantitative ellipsoid zone (EZ) integrity on OCT in eyes with diabetic macular edema (DME) when treated with laser photocoagulation or intravitreal aflibercept injection (IAI) in the Phase 3 VISTA study.

Methods: VISTA was a randomized phase 3 study in DME patients. This post-hoc analysis included 361 eyes treated with laser photocoagulation, 2mg IAI every 4 weeks (2q4), or every 8 weeks following 5 initial monthly doses (2q8). OCT images were evaluated using machine learning-assisted retinal layer mapping software. EZ integrity parameters were EZ-RPE central subfield thickness (CST, μm), EZ-RPE panmacular volume (mm3), and percentage of partial and total EZ attenuation (proportion of macular area with 20μm or less and 0μm EZ-RPE thickness, respectively).

Results: There were no baseline differences in EZ metrics between the laser group and IAI groups. At week 4, laser eyes showed worsening integrity parameters with IAI eyes already improving. At week 100, the EZ-RPE CST and Volume were significantly higher in the IAI group ($p<0.0001$), while partial and total EZ attenuation were significantly lower ($p<0.0001$) compared to the laser group.

Specifically, the pooled IAI group demonstrated significantly improved EZ integrity parameters compared to baseline, while the laser group demonstrated significant worsening at week 100 (Table 1) despite ~41% of laser patients receiving IAI between weeks 24 and 100. At week 100, 2q4 demonstrated significant improvement in total EZ attenuation whereas the improvement in 2q8 did not reach statistical significance (-32.5%, $p<0.026$; -24.3%, $p=0.16$ respectively), although all other EZ metrics significantly improved in both groups. There were significant correlations between EZ metrics and BCVA at week 100 (Table 2).

Conclusions: IAI therapy for DME was associated with sustained improvement of outer retinal integrity parameters through week 100, whereas laser demonstrated significant worsening in EZ integrity despite a large proportion of patients receiving IAI treatment in addition to laser. This may explain some of the differences in functional outcomes between treatment approaches and provide a potential biomarker for outer retinal integrity in response to therapeutic interventions.

CONTROL ID: 3713206

SUBMITTER (NAME ONLY): Mattia Tomasoni

TITLE: Automatic Retinal Blood Velocity Estimation from XT Scans using Convolution Kernels

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tomasoni, A. Jacot-Guillarmod, J. Potic, T. Wolfensberger, C. Bergin, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|A.M. Dubis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A.M. Dubis, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Being able to precisely track bloodflow dynamic inv vivo is important in understanding a number of disease of the eye, CNS and systemically. Direct imaging of medium to large vessels is complicated due to relatively slow frame rates and aliasing artifacts, hence the development of XT (X direction by Time) imaging, whereby the slow scanner is paused for a period of the scan creating a normal rate structural image and a fast scan rate over the vessel of interest. The aim of this study is to design an algorithm to extract such measurements automatically from these images.

Methods: In the temporal portion of XT, blood cells move past the fast scanner resulting in a streak. Depending on the speed of the bood cell, the angle and length of the streak will vary. Streak orientation was selected by sliding a diagonal convolution kernel (consisting of a line of a certain slope) along the XT Scan, the fit of such kernel was evaluated at each pixel location. The speed of erythrocytes was automatically estimated by testing kernels with several slopes and selecting the best fit.

Results: The angles of lines belonging to the best fitting kernels were plotted against angles estimated by human graders. We evaluated our algorithm on 100 consecutive XT Scan frames from a BMC Apaeros AOSLO, revealing the known fluctuation of blood velocity and flow during the cardiac cycle. Plotting the graders' estimates against those produced by our algorithm resulted in a Pearson correlation coefficient = 0.70 (P=2E-35).

Conclusions: Here we present a pipeline to automatically detect time portions of XT images and extract streak angle, thus determining blood flow. Our method compared favorably with human graders, while taking a fraction of the time to compute. This pipeline can be used automatically within further analysis pipleines to determine new insights into diabetes and other vascular diseases.

CONTROL ID: 3713208

SUBMITTER (NAME ONLY): Anita Penkova

TITLE: Simulation of Thermally-Driven Buoyant Convection for Ocular Drug Delivery Enhancement

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The main purpose of this work is to computationally simulate the effect of thermal stimuli on fluid transport to enhance intravitreal drug delivery. The goal is to take into consideration the partial liquefaction of the vitreous due to syneresis.

Methods: In an earlier experimental investigation (Huang and M. Gharib), a thermal stimulus applied to an eye model showed an enhancement of fluid flow in the vitreous due to the density stratification resulting from thermal expansion. While this was done for a wholly liquid vitreous, in the current computational investigation the vitreous is considered to be partially liquefied due to syneresis. The vitreous is modeled as a Darcy fluid for the fibrous gel part and a Newtonian fluid for the liquefied part. A thermal stimulus consisting of a Peltier heater is applied over a 0.25-cm^2 circular area to provide a steady temperature of approximately 10C above the normal body temperature of 37C. The choroidal tissues and those surrounding the eye have been modeled with the Pennes bioheat equation for transport between the vitreous and the vasculature. The density changes in the ocular fluids due to heating create a gravitational body force and induces fluid motion over and above the normal physiological flow. The simulations were conducted for various eye orientations with respect to the direction of gravity. The liquefied region was kept as a simple spherical segment in the posterior region. The computational simulation was carried out using Star CCM+.

Results: The simulations show that after 5-10 minutes of heating at 10C above the body temperature at the cornea leads to fluid motion in the aqueous and the vitreous humors. As expected, the liquefied region within the vitreous experiences significant motion owing to the free mobility of the fluid therein. Fluid velocities up to 0.07 cm/s are predicted.

Conclusions: Thermal stimulation of the eye for approximately 10 minutes at the cornea by 10C elevation of the temperature provides substantial increase of the fluid velocity, particularly in the syneretic regions. This technique has the potential to significantly enhance intravitreal drug delivery to the retina. Detailed studies to further explore and quantify the degree of enhancement are needed along with clinical recommendations for ophthalmologists as well as patients.

CONTROL ID: 3713210

SUBMITTER (NAME ONLY): Margarete Karg

TITLE: Sex and Age-Related Changes in RPE Morphology and Function in Mice

SESSION TITLE: Animal Models of Age Related Macular Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Karg, E. Hoffmann, D. Krasniqi, D.Y. Shu, M. Moorefield, H. Philipose, B. Ksander, M. Saint-Geniez, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M. Karg, D.Y. Shu, B. Ksander, M. Saint-Geniez, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: While age is the major risk factor for developing AMD, age-matched comparisons found that women have a higher risk of developing wet AMD indicating an additional life-span-independent, sex-dependent risk factor. The primary cellular target of AMD is retinal pigment epithelial cells (RPE), which are post-mitotic and, as they age, undergo a slow degeneration leading to a loss of function. We hypothesize the increased susceptibility of women to AMD is caused, in part, by an age-related RPE degeneration that is more prominent and progresses faster in females than in males.

Methods: Functional and morphological analyses were performed on young (2-4 months) and aged (16-36 months) female (f) and male (m) C57BL/6 mice. Visual function was assessed by ERG a, b, and c- waves and optomotor reflex (OMR), which measured visual acuity and contrast sensitivity. Morphological analyses were performed by immunohistochemical staining of f-actin on RPE/choroid flat mounts. RPE cell density, cell area, and the number and size of RPE lesions (area with amorphic and enlarged cells) were quantified. P2ry12 immunostaining was used to monitor microglia recruitment to the subretinal space.

Results:

As expected, visual function was significantly reduced in aged mice as compared to young mice. However, aging female mice (18 months) displayed a significant decrease in contrast sensitivity vs age-matched males (mean % contrast 25.4 (f) vs 18.2 (m) at 0.267 cycl/deg, p=0.0001). This loss in vision coincided with a functional decline in RPE as shown by a significant reduction in the ERG c-wave (mean amplitudes [μV] 192 (f) vs 229.3 (m) at 24.1 cd.s/m^2, p=0.0001), while the a- and b-waves were not different. Highly geriatric mice (24-36 months) showed gross PRE morphological anomalies characterized by areas with amorphic and enlarged cells, which were significantly more frequent in females, 77% of RPE/choroid flat mounts (n=10 of 13) with at least 1 or more areas of aberrant RPE, as compared to males with < 10% (n=1 of 15). Interestingly, the loss of RPE morphology and function in female mice coincided with an increased recruitment of microglia to the subretinal space.

Conclusions: We conclude the age-dependent decline in visual function in mice is sex dysmorphic with females showing an accelerated loss of function that coincides with a decline of RPE. Implying RPE dysfunction may account for the AMD sex-dependent risk factor in women.

CONTROL ID: 3713212

SUBMITTER (NAME ONLY): Yuqin Yin

TITLE: Oncomodulin post-injury gene therapy enables full-length optic nerve regeneration

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yin, H. Gilbert, Y. Yang, L. Benowitz, Boston Children's Hospital, Harvard Medical School, Massachusetts, UNITED STATES|R.L. Neve, Gene Technology Core at Massachusetts General Hospital, Cambridge, Massachusetts, UNITED STATES|M.A. Stavarache, M.G. Kaplitt, Weill Cornell Medicine, New York, New York, UNITED STATES|L. Benowitz, Program in Neuroscience, Harvard Medical School, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optic nerve, like other pathways in the mature CNS, cannot regenerate after traumatic injury or degenerative diseases, leading to permanent vision loss. Altering the intrinsic growth ability of retinal ganglion cells (RGCs) by manipulating transcription factors or by activating growth factor-induced signaling pathways has resulted in appreciable levels of axon growth, but we are still far from achieving substantial visual recovery, underlining the need for therapies with higher efficacy. Oncomodulin (Ocm), an 11 kDa protein expressed by neutrophils and macrophages, is a critical mediator of optic nerve regeneration induced by intraocular inflammation. Intraocular inflammation combined with a cAMP analog and deletion of Phosphatase and tensin homolog (Pten) is one of the few treatments reported to promote optic nerve regeneration back to central brain target areas. This study's purpose is to obviate the need for intraocular inflammation and to apply treatments in a clinically relevant manner.

Methods: We incorporated the Ocm gene into the glial-specific shH10 virus, and injected this virus intraocularly together with AAV2 viruses expressing constitutively-activated adenylyl cyclase (AAV2-c/a-AC to elevate cAMP, a co-factor of Ocm) and shPten (AAV2-shPten) after optic nerve injury. Regenerating axons were labeled by an antereograde tracer cholera toxin subunit B (CTB) and quatified at different distances distal to the nerve injury site.

Results: After survival periods of up to 8 weeks, this combined treatment stimulated axon growth through the full length of the optic nerve, with 500-800 axons at the end of optic nerve and many axons crossing the optic chiasm and entering the brain.

Conclusions: Gene therapy directed at manipulating defined molecules and delivered after injury has occurred can promote substantial optic nerve regeneration and provides a model for future studies of brain target reinnervation.

CONTROL ID: 3713213

SUBMITTER (NAME ONLY): Mithun Santra

TITLE: Corneal stromal stem cell-derived extracellular vesicles transport TGF β3 to mediate anti-fibrosis effect on corneal scarring

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Santra, L. Weng, M. Louise Geary, T. yang, V. Jhanji, G. Yam, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Transparent cornea is paramount for vision. Corneal scarring is a top leading cause of global blindness. The conventional corneal transplantation has been challenging due to the scarcity of donor tissue. Alternative corneal stromal stem cell (CSSC) therapy was reported to successfully prevent the scarring development. The paracrine action of CSSC, mediated by extracellular vesicles (EVs), was shown to block corneal fibrosis and stimulate native tissue regeneration. This study investigated the role of anti-fibrotic transforming growth factor (TGF) β3 transported in CSSC-EVs in the scarless regeneration of mouse corneas after injury

Methods: Primary human CSSCs isolated from donor limbus were co-cultured with lipopolysaccharide-treated pro-inflammatory M1 mouse macrophages (RAW264.7) or conditioned media concentrates. The time course cellular and EV expression of hTGFβ1, 2 and 3 were examined by immunofluorescence and qPCR, respectively. Naïve CSSC or hTGFβ3 knockdown CSSCs were applied to mouse corneas after wounding by Algerbrush burring Corneal clarity (scar development), corneal thickness and the expression of inflammatory and fibrosis genes on mouse corneas were examined.

Results: hTGFβ3 was upregulated in CSSCs after stimulation with M1 RAW cells, in both co-culture and paracrine conditions. More importantly, EVs derived from the stimulated CSSCs contained increasing levels of hTGFβ3 mRNA transcripts. After CSSC application to injured mouse corneas, hTGFβ3 was significantly upregulated, in conjunction with the inhibition of mouse fibrotic genes. At day 14 post-injury, the treated corneas remained clear and the expression of fibronectin, hyaluronan synthase 2, SPARC, tenascin C, collagen 3a1, and α-smooth muscle actin were significantly reduced. CSSCs with TGFβ3 knockdown by specific siRNAs lost these therapeutic effects.

Conclusions: Our study revealed the paracrine action of human CSSCs on corneal scar prevention through EV-mediated delivery of TGFβ3 mRNA transcripts. The elevated TGFb3 expression in injured corneas could redirect the wound healing process to a reduced scarring or scar-free tissue regeneration, resulting in clear corneas.

CONTROL ID: 3713214

SUBMITTER (NAME ONLY): Ana Strat

TITLE: Engineering a 3D hydrogel system to study optic nerve head astrocyte morphology and behavior in response to glaucomatous insult

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Strat, A. Kirschner, H. Yoo, A. Singh, T. Bagué, H. Li, S. Herberg, P.S. Ganapathy, Ophthalmology and Visual Science, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|A.N. Strat, P.S. Ganapathy, Neuroscience, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In glaucoma, astrocytes within the optic nerve head (ONH) rearrange their actin cytoskeleton, while becoming reactive and upregulating intermediate filament glial fibrillary acidic protein (GFAP). Increased transforming growth factor beta 2 (TGFβ2) levels have been implicated in glaucomatous ONH dysfunction. A key limitation of using conventional 2D culture to study ONH astrocyte behavior is the inability to faithfully replicate the in vivo ONH microenvironment. Here, we engineer a 3D ONH astrocyte hydrogel to better mimic in vivo mouse ONH astrocyte (MONHA) morphology, and test induction of MONHA reactivity using TGFβ2.

Methods: Primary MONHAs (N = 6 independent preparations) were isolated from C57BL/6J mice and cell purity confirmed. To engineer 3D cell-laden hydrogels MONHAs (2.5 x 10^6 vs. 5.0 x 10^6 cells/ml) were mixed with photoactive extracellular matrix components (collagen type I, hyaluronic acid) and crosslinked for 5 minutes using a photoinitiator (0.025% riboflavin) and UV light (405-500 nm, 10.3 mW/cm2). Sholl analysis was used to assess MONHA process complexity over time (1-3 weeks) in hydrogels. MONHA-encapsulated hydrogels were cultured for 3 weeks, and then treated with TGFβ2 (2.5, 5.0 or 10 ng/ml) for 7 days. Treated hydrogels were evaluated for F-actin staining intensity, GFAP upregulation, and fibronectin/collagen IV deposition.

Results: MONHAs were ~95% positive for astrocyte marker GFAP, and <5% for oligodendrocyte marker OSP-1 and microglia/macrophage marker F4/80. Following encapsulation, MONHA retained high cell viability (~89%) in hydrogels and continued to proliferate over 4 weeks as determined by live/dead staining and MTS assays. Sholl analysis demonstrated that MONHAs within hydrogels developed increasing process complexity ($p<0.05$) with increasing process length over time ($p<0.0001$). Cell processes connected with neighboring cells, coinciding with Connexin43 expression within astrocytic processes. Treatment with TGFβ2 induced reactivity in MONHA-encapsulated hydrogels as determined by altered F-actin cytoskeletal morphology ($p<0.0001$), ~7.4-fold increase in GFAP expression ($p<0.0001$), and ~2.5-fold elevation in fibronectin ($p<0.05$) and collagen IV ($p<0.0001$) deposition.

Conclusions: Our data supports use of this 3D biomimetic ONHA-encapsulated hydrogel to further investigate ONHA behavior in response to glaucomatous insult.

CONTROL ID: 3713217

SUBMITTER (NAME ONLY): Thanvi Vatti

TITLE: Association of Macular Hole Intraretinal Fluid and Visual Acuity

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The degree of variability in intraretinal fluid (IRF) and configuration in patients with macular holes (MHs) has prompted studies to evaluate its prognostic value. This study investigates the association between preoperative intraretinal fluid (IRF) area and preoperative and postoperative in surgically repaired idiopathic MH. This study further evaluates other prognostic indices related to MH repair which may assist clinicians' understanding of MH operative management.

Methods: A retrospective cohort study of 251 patients who were diagnosed with idiopathic MH and IRF in the edges of the hole and underwent successful surgical repair were selected for the study. OCT scans were segmented by expert readers to obtain IRF area. Preoperative and postoperative best visual acuity (BVA) at 1,3, and 6 months were collected along with associated MH characteristics such as size, staging, postoperative closure status, type of closure (type I vs type II) and preoperative and postoperative central subfield thickness (CST). Associations between IRF area and these variables were evaluated using Spearman's correlation analysis.

Results: At preoperative baseline, the mean(SD) BVA was 46.4(19.03) and mean(SD) CST was 366.11(77.75). Preoperative IRF area was moderately correlated with preoperative BVA ($r = -0.32$, $p < 0.001$), negligibly correlated with postoperative BVA at 1, 3, 6 months ($r = -0.14$, $p = 0.026$; ($r = -0.21$, $p < 0.001$; $r = -0.19$, $p < 0.001$, respectively). Preoperative IRF area was strongly correlated with MH minimum linear diameter ($r = 0.56$, $p < 0.001$) and MH base diameter ($r = 0.65$, $p < 0.001$), moderately correlated with baseline CST ($r = 0.36$, $p < 0.001$) and negligibly with 6-month CST ($r = -0.2$, $p = 0.01$). Relationships between IRF and MH closure status ($r = 0.048$, $p = 0.45$) and closure type ($r = 0.047$, $p = 0.47$) were not statistically significant.

Conclusions: Preoperative IRF area in patients with idiopathic MH demonstrated a moderate correlation with preoperative BVA and a negligible/weak correlation with postoperative BVA up to 6 months, suggesting that vision may not have a clinically significant relationship with IRF in the setting of MH. Further, this study reinforced previous findings that preoperative IRF was strongly correlated with MH size.

CONTROL ID: 3713218

SUBMITTER (NAME ONLY): Ying Liu

TITLE: Pseudotime analysis of human stem cell-derived photoreceptor cell maturation following subretinal transplantation

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Photoreceptor transplantation is envisioned as a possible treatment for degenerative retinal diseases. In homeostasis, photoreceptor cell maturation and survival are partly regulated by extrinsic cues. However, in the transplantation context, the effect of extrinsic cues on the maturation and survival of donor cells following placement in the recipient niche is incompletely understood. Here, we aimed to investigate the maturation of transplanted human stem cell-derived photoreceptor cells in a mouse model of degenerative retinal disease.

Methods: Retinal organoids derived from Crx.tdTomato^{+} H9 human embryonic stem cells and cultured for 134 days were microdissected and subretinally transplanted into adult immunodeficient Rd1 mice. Age-matched organoids served as in vitro controls. After three months, we assayed photoreceptor maturation using single-cell RNA sequencing, immunohistochemistry, and patch-clamp electrophysiology.

Results: Genes expressed in mature cone and rod photoreceptor cells were upregulated in transplanted photoreceptor cells compared to the controls. By pseudotime analysis of gene expression changes, we found that the transcriptome of the transplanted photoreceptor cells was more closely aligned with that of normal adult human photoreceptor cells than the transcriptome of the control cells. Photoreceptors that expressed L/M opsin, S opsin, and rhodopsin were more abundant in the transplanted than the cultured organoids. In addition, we detected more abundant photoreceptor inner/outer segment-like structures, and presynaptic terminals, in the transplanted than in the cultured condition. Functionally, patch-clamp electrophysiological responses in the transplanted condition were consistent with cone outer segment maturation.

Conclusions: Human stem cell-derived photoreceptor cells that were transplanted in a mouse model of degenerative retinal disease showed maturation characteristics that exceeded those of in vitro controls. Pseudotime analysis of single-cell RNA sequencing data provides a facile method to assay the maturation of transplanted retinal cells by integrating the expression levels of thousands of genes in multiple cell populations.

CONTROL ID: 3713219
SUBMITTER (NAME ONLY): Vasileios Toulis
TITLE: Characterising the disease mechanisms of RP17 structural variants
SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: V. Toulis, J. Corral-Serrano, K. Hau, D. Ottaviani, M.E. Cheetham, A.J. Hardcastle, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|S. de Bruijn, S. Roosing, Radboudumc Department of Human Genetics, Nijmegen, NETHERLANDS|S. de Bruijn, S. Roosing, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, NETHERLANDS|U.S. Melo, Max Planck Institute for Molecular Genetics, RG Development & Disease, Berlin, GERMANY|U.S. Melo, Institute for Medical and Human Genetics, Charite – Universitatsmedizin, Berlin, GERMANY|S.J. Fliesler, Ophthalmology, Biochemistry, and Neuroscience Graduate Program, SUNY The State University of New York, Buffalo, New York, UNITED STATES|S.J. Fliesler, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|
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ABSTRACT BODY:

Purpose: We have identified complex structural variants (SVs) at the RP17 locus as a major cause of autosomal dominant RP (adRP). The genomic structure of each SV at the RP17 locus implicates altered topologically associated domain (TAD) structure and ectopic retinal enhancer-gene contact as a potential gain-of-function mechanism, with increased retinal expression of GDPD1. We explored this hypothesis by generating RP17 patient-derived 3D retinal organoids (ROs) and investigated the cellular and retina localisation of GDPD1.

Methods: Cells from RP17 patients were reprogrammed into induced pluripotent stem cells (iPSCs) using episomal vectors or lentiviral transduction, then differentiated into 3D ROs, alongside ROs differentiated from control iPSC. ROs were harvested at D200 and subjected to transcriptomic and lipidomic analyses (Lipotype GmbH), given the reported role of GDPD1 as a lysophospholipase. The GDPD1 gene was cloned into an expression vector for transient transfection in HEK-293 cells, and site-directed mutagenesis was used to create double and single mutants that are predicted to be catalytically inactive. GDPD1 was localized in HEK-293 cells and mouse retina using a commercial antibody to GDPD1 (Proteintech).

Results: iPSCs were developed from two individuals with the NL-SV1 and two individuals with the UK-SV2 SVs. All RP17 iPSC lines differentiated into ROs. The transcriptome of D200 RP17-SV ROs was compared to control ROs using RNAseq, and differentially expressed genes identified. Preliminary lipidomic analysis of RP17-SV vs. control retinal organoids revealed altered phospholipid ratios. The expression of wild-type and mutant GDPD1 was investigated in HEK-293 by immunocytochemistry and Western blotting. Immunohistochemistry demonstrated weak anti-GDPD1 immunoreactivity in photoreceptor inner segments in control ROs and mouse retina.

Conclusions: Our current data support the hypothesis that altered TAD structure leads to ectopic retina- specific enhancer-gene accessibility and interaction with GDPD1, resulting in increased retinal GDPD1 expression. Studies are underway to further test this hypothesis through transcriptomic, epigenetic, lipidomic and morphological analyses.

CONTROL ID: 3713220

SUBMITTER (NAME ONLY): Himanshu Gururani

TITLE: Investigation on rabbit corneal birefringence using digital photoelasticity technique

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Gururani, S.S. Chittajallu, M. Ramji, V. Chinthapenta, Mechanical and aerospace engineering, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|S.S. Chittajallu, A. Richhariya, Centre for technology innovation, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: To characterize the birefringence behavior of rabbit cornea using digital photoelasticity technique.

Methods: Eight rabbit corneas were subjected to intraocular pressure using an in-house designed anterior chamber. Then, the central 11 mm of the cornea was imaged using a polariscope in the transmission mode under white light. The images were captured at 20 mm of Hg pressure. The ten-step phase-shifting technique was employed, and the obtained phase maps were then unwrapped to obtain the full-field corneal birefringence data.

Results: The rabbit corneas exhibited a saddle-back distribution of isochromatic (contours of constant retardation). These isochromatics form their skeleton around the points of zero retardation, also known as isotropic points in photoelastic literature. The corneal isoclinics (contours of constant angle) were found to be distributed around the isotropic points as they pass through them. Further, the distance between isotropic points was found to vary amongst the tested corneas.

Conclusions: The birefringence of the cornea shows inter-individual variability yet maintains the saddle-back distribution. Since the isochromatics form their skeleton around isotropic points, it is proposed that the isotropic points are an implication of stable microstructure and curvature under pressure loading. Therefore, it is suggested that tracking the movements of these points during various interventions would be beneficial to clinical practice. However, detailed studies are required to test this hypothesis. Further, the analysis based on digital photoelasticity could be translated into clinical usage due to its simplicity and ability to capture full-field birefringence data.

CONTROL ID: 3713222

SUBMITTER (NAME ONLY): Cody Hayden

TITLE: Comparison of automated and manual segmentation of the foveal avascular zone in patients with and without diabetic macular edema using optical coherence tomography angiography

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hayden, M. Jacobs, N. Fowler, R. Higdon, R. Maldonado, Department of Ophthalmology and Visual Sciences, University of Kentucky, Lexington, Kentucky, UNITED STATES|

Commercial Relationships Disclosure: Cody Hayden: Commercial Relationship: Code N (No Commercial Relationship) | Mitchell Jacobs: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Fowler: Commercial Relationship: Code N (No Commercial Relationship) | Rebecca Higdon: Commercial Relationship: Code N (No Commercial Relationship) | Ramiro Maldonado: Commercial Relationship(s);Code C (Consultant/Contractor):ProQR Therapeutics

ABSTRACT BODY:

Purpose: Enlarged foveal avascular zone (FAZ) has been associated with lower visual acuity in diabetic patients. Accurate and automatic FAZ measurements could be a valuable tool in the management of diabetic macular edema. Here, we compare manual (MS) and automated segmentation (AS) FAZ tracings from 3 x 3mm optical coherence tomography angiography (OCTA) scans in healthy and diabetic macular edema (DME) patients.

Methods: This IRB approved study prospectively collected OCTA images in patients evaluated in a tertiary care center where 43 eyes from 43 healthy individuals and 36 eyes from 36 DME patients were included. The FAZ superficial vascular plexus was traced by three masked, trained graders using ImageJ. The raw images were analyzed with the Advanced Retinal Imaging (ARI) network algorithm. All images were analyzed for perimeter, circularity, and area. Paired t-tests were used to compare the manual and automated methods.

Results: For the healthy subjects, the FAZ area was 0.267 ± 0.149 mm^2, and 0.244 ± 0.189 mm^2 by MS and AS respectively (P=0.25). In DME patients, the FAZ area was 0.428 ± 0.222 mm^2 and 0.347 ± 0.217 mm^2 by MS and AS respectively (P=0.024). There was a statistically significant difference between the two methods for both perimeter and circularity in both cohorts of patients with AS underestimating perimeter (P=<0.001) and overestimating circularity (P=<0.001).

Conclusions: Our study shows that while automatic FAZ segmentation is reliable in healthy subjects, the reliability is reduced when estimating FAZ area in patients with DME.

CONTROL ID: 3713223

SUBMITTER (NAME ONLY): Qian Chen

TITLE: Reprogramming glutamine metabolism by supplement of dipeptide Alanine-glutamine improves retinal degeneration in STZ-induced rat model

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Chen, Y. Zhang, X. Wang, M. Wei, Y. Xu, W. Chen, Z. Liu, Eye Institute of Xiamen University, Xiamen, Hujian, CHINA|Q. Chen, Z. Liu, Xiamen University Faculty of Medicine and Life Sciences, Xiamen, Fujian, CHINA|

Commercial Relationships Disclosure: Qian Chen: Commercial Relationship: Code N (No Commercial Relationship) | Yuhan Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Xin Wang: Commercial Relationship: Code N (No Commercial Relationship) | Mingyan Wei: Commercial Relationship: Code N (No Commercial Relationship) | Yuan Xu: Commercial Relationship: Code N (No Commercial Relationship) | Wensheng Chen: Commercial Relationship: Code N (No Commercial Relationship) | Zuguo Liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a common and specific neurovascular complication of diabetes. Dysregulation of amino acid metabolism has been showed to be involved in the pathogenesis of DR. Glutamine is the most abundant and versatile amino acid in human and many other mammals and extensively involved in various metabolic pathways. The present study was designed to investigate whether reprogramming amino acids metabolism by supplement of Ala-Gln, serving as a substitute for glutamine, plays protective roles on the diabetic retinopathy in streptozotocin (STZ)-induced rat model.

Methods: Visual function of the rats was measured by electroretinogram (ERG). The expression of neurovascular markers and inflammation markers, such as glial fibrillary acidic protein (GFAP) and vascular endothelial growth factor (VEGF) were evaluated by western blot and immunofluorescence. The function of mitochondria was measured by immunostaining of TOM20. Regular body weight and blood glucose levels of rats were also monitored.

Results: Amino acid sequencing indicated the ratio of glutamate/glutamine was upregulated in the retinas of STZ-induced rat compared to normal control. The activity of ERG was declined in STZ-induced diabetic rats, while the supplement of Ala-Gln increased ERG activities in the diabetic rats. In addition, pro-inflammatory factors VEGF and VCAM-1 were decreased in diabetic rats treated with Ala-Gln compared to those treated with vehicle. Further, the protein expressions of glutamine synthase, GFAP were decreased in Ala-Gln treated diabetic rats. Immunostaining of GFAP indicated less of Muller cells were activated in the retina of Ala-Gln treated diabetic rats. The glycolysis indicated by levels of PKM2, LDHA and LDHB were significant increased after Ala-Gln treatment. The mitochondrial TOM20 was upregulated in the retina of Ala-Gln treated diabetic rats.

Conclusions: Our study has demonstrated that Ala-Gln has beneficial effects in diabetic retinopathy by improving the retinal neuronal function, reducing retinal glial activation and enhancing the glycolysis and the function of mitochondria in diabetic retinas. Therefore, reprograming metabolism by Ala-Gln may be a novel therapeutic avenue for retinal degeneration in DR.

CONTROL ID: 3713224

SUBMITTER (NAME ONLY): Svenja Sonntag

TITLE: Changes in fluorescence lifetime of the fundus after intravitreal ranibizumab injection in patients with exudative age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Sonntag, S. Schlunk, J. Kempska, S. Grisanti, Y. Miura, Department of Ophthalmology, University of Lübeck, GERMANY|Y. Miura, Institute of Biomedical Optics, University of Lübeck, GERMANY|

Commercial Relationships Disclosure: Svenja Sonntag: Commercial Relationship: Code N (No Commercial Relationship) | Stella Schlunk: Commercial Relationship: Code N (No Commercial Relationship) | Joanna Kempska: Commercial Relationship: Code N (No Commercial Relationship) | Salvatore Grisanti: Commercial Relationship: Code N (No Commercial Relationship) | Yoko Miura: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to compare the fluorescence lifetime (FLT) of the fundus before and after the intravitreal ranibizumab injection for exudative age-related macular degeneration (AMD).

Methods: Seventeen consecutive patients with exudative AMD were examined with fluorescence lifetime imaging ophthalmoscopy (FLIO: Heidelberg Engineering GmbH) before and 4 weeks after a scheduled intravitreal injection of ranibizumab. Number of past injection and the condition of the pre-treatment retina were not specified. The FLT was calculated for the separated macular areas defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. The relationship between the change in visual acuity and the change in FLT ($\triangle\tau_m$) or central retinal thickness ($\triangle$CRT) was assessed with an univariate regression analysis.

Results: The $\triangle$CRT after a single injection of ranibizumab ranged from -80 µm to 47 µm, with the median of 0 µm. The range of $\triangle\tau_m$ at the center was -166 ps to 293 ps, with the median of 8 ps for the short spectral channel (SSC: 498-560 nm), and -116 ps to 60 ps, with the median of 0 ps for the long spectral channel (LSC: 560-720 nm). In the inner ring $\triangle\tau_m$ ranged from -163 ps to 175 ps in SSC and from -68 to 28 ps in LSC, and in the outer ring from -126 ps to 9 ps in SSC and -49 ps to 26 ps in LSC. The results of the regression analysis showed that a decrease in FLT (negative $\triangle\tau_m$) is significantly associated with an increase in visual acuity ($p<0.01$) in all three analyzed areas in both channels. In contrast, there was no significant association between the change in visual acuity and the $\triangle$CRT.

Conclusions: The change in FLT induced by ranibizumab injection was shown to vary widely among individuals. However, it was shown that the shortening of FLT in the macula is associated with the improved visual acuity more strongly than the change in the morphology of the central retina. This presumably reflects activation of the metabolic state of the retinal cells. Therefore, using FLIO to evaluate the changes in FLT before and after anti-VEGF injection may be useful in evaluating the response of the metabolic state and function of the retina to anti-VEGF treatment.

CONTROL ID: 3713225

SUBMITTER (NAME ONLY): Megan Steinkerchner

TITLE: Long-Term Visual Outcomes in Patients with Idiopathic Macular Hole Surgery

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.P. Singh, K.E. Talcott, Center for Ophthalmic Bioinformatics, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|M.S. Steinkerchner, R.P. Singh, K.E. Talcott, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Megan Steinkerchner: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Singh: Commercial Relationship: Code N (No Commercial Relationship) | Katherine Talcott: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess long-term visual and anatomical outcomes following surgical repair of idiopathic full thickness macular holes (FTMH) with pars plana vitrectomy (PPV) and internal limiting membrane (ILM) peel in patients with 5 to 9 years of post-operative follow up

Methods: A retrospective study evaluated patients diagnosed with idiopathic full thickness macular hole who received surgical repair at a single academic tertiary center with at least 5 years of post-operative follow up. Data collection included demographic and pre-operative characteristics including best visual acuity (BVA), lens status, prior ocular history, and macular hole structural integrity as determined by spectral domain optical coherence tomography (OCT). Surgical techniques along with functional and structural improvement were assessed by collection of BVA and findings of ellipsoid zone (EZ) integrity and intraretinal fluid (IRF) on OCT at determined time points of 3 months, 6 months and each year until 9 years of follow up.

Results: The study comprised 90 eyes of 80 patients with a mean age of 67.2 +/- 6.8 years with an average post-operative follow up of 80.8 +/- 17.5 months (range 54-130 months). 61 eyes out of 70 phakic eyes (87%) received cataract surgery at the time of FTMH repair, with the remaining eyes receiving cataract surgery at an average of 9.5 +/- 4.6 months (range 5-18 months) post-surgery. Macular hole reoperation occurred in 4 eyes (4%) at a mean duration of 6.1 +/- 6.0 months (range 1-13 months). Over the study duration, EZ integrity was restored in 78% of eyes, with an absence of IRF in 96% on OCT. The pre-operative mean ETDRS BVA of 51 (Snellen equivalent 20/80-20/100) improved to a mean BVA of 76 (Snellen equivalent 20/25-20/30) at 5 years post operation, with an average gain of 25 letters at 1 year that remained stable over 5 years ($P<0.05$). >80% of eyes achieved a BVA > 65 (Snellen equivalent 20/50) 8 years after surgical repair.

Conclusions: Vitreoretinal surgery for idiopathic FTMH resulted in successful hole closure and sustained visual acuity improvement over long-term follow up.

CONTROL ID: 3713227

SUBMITTER (NAME ONLY): Stefano Gandolfi

TITLE: EFFICACY AND SAFETY OF A NOVEL AHMED VALVE INMPLANTAITON TECHINIQUE: A 5-YEAR RETROSPECTIVE STUDY

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Gandolfi, P. Mora, G. Calzetti, N. Ungaro, L. Varano, V. Tagliavini, S. Tedesco, M. Anna, Ophthalmology, Universita degli Studi di Parma, Parma, Emilia-Romagna, ITALY|

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ABSTRACT BODY:

Purpose: To measure longterm safety and efficacy of a novel less scarring Ahmed valve implantation technique.

Methods: Study design: retrospective comparative case series Methods: the clinical records of consecutive patients operated with an Ahmed valve implanted by adopting a novel technique (between 2012 - 2019) or with a more traditional approach (time frame between 2005 - 2011) were reviewed. Data analyzed: anti glaucoma medications,IOP, visual acuity,post-op complications. Surgical technique: "Group A" Ahmed valvei traditionally implanted and left open. "Group B": the tube was ligated and closed by a 7.0 polygalactin and the 9.0 nylon limbal mattress suture was placed by passing the needle "through" the tube, thereby allowing the aqueous to spill out through the tube's wall. In the expectations of the investigators, this approach was expected to lead to an anterior filtering bleb which scarred during a time-frame compatible with the dissoluiton of the peritubular 7.0 polygalacting suture. A flow of a less "inflamed" and "irritating" aqueous through the imiplant to the plate was then expected to occur, allowing the formation of the proper retroequatorial bleb with less chance of intense scarring. Statistical analysis: the data were analyzed by (a) parametric statistics (IOP) , (b) non paramteric statistics (medications, visual acuity, complications) . Kaplan-Meier survival curves were further created according to different cut-off levels of IOP (with or without medications).

Results: 235 patients, with at least 5-year follow up , (Group B) compared with n = 127 (Group A).
Group A: Pre-op IOP (mean, SD): 26.1 (9.1) , 5-yr IOP 15.7 (4.2), Pre-op medications: 2.8 (1.2), 5-yr medications: 1.5 (1.1). Group B: Pre-op IOP (mean, SD): 26.7 (9.3) , 5-yr IOP 13.6 (3.8), Pre-op medications: 3.5 (1.7), 5-yr medications: 1.2 (0.9). Both IOP values ($p < 0.001$ Student t test) and number of medications ($p < 0.01$, Chi Square test) were significantly different between the two groups 5 years after surgery. Post operative hypotony (11/235 and 15/168) and serous choroidal detachments (11/235 and 8/168) were comparable between the groups (Fisher exact tests, $p > 0.4$ for both variables). 4 hemorragic choroidal detachments occurred in group B and 2 in Group A. .

Conclusions: The described novel implantation technique for the Ahmed valve allows a better 5-yr IOP outcome compared with the traditional approach.

CONTROL ID: 3713228

SUBMITTER (NAME ONLY): Ian Pitha

TITLE: Cyclic strain-induced scleral myofibroblast escape from topographic confinement is ERK dependent

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.F. Pitha, A. Mozzer, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Ian Pitha: Commercial Relationship: Code N (No Commercial Relationship) | Annie Mozzer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Myofibroblasts are associated with pathologic scleral remodeling in myopia and glaucoma development.[1,2] We showed reduced myofibroblast alignment with collagen topography in human sclera can be modeled by cyclic strain exposure in vitro.[3] Here, we characterize the scleral myofibroblast response to cyclic mechanical strain.

Methods: Primary human peripapillary scleral (PPS) fibroblasts were cultured on topographically aligned grooves to promote cell alignment, exposed to TGFb (2 ng/ml) in the presence of vehicle or kinase inhibitors, and exposed to uniaxial strain (1 Hz, 5%, 12-24 hours). Alignment with grooves was determined at baseline, immediately following strain, and 24 hours after strain cessation with 0° being completely aligned and 90° being perpendicular to grooves. A wound healing assay was developed to investigate fibroblast migration across topographic cues in the absence of strain. Transcriptional profiling of myofibroblasts with or without strain was performed by RT-PCR and pERK, pSMAD2, and pSMAD3 levels were measured by immunoblot.

Results: Pre-strain alignment (6.2±1.5°) was significantly reduced after strain (21.7±5.3, $p<0.0001$) and restored 24 hours after cessation (9.5±2.6°). ERK and TGFbR1 inhibition preserved alignment after strain; however, loss of alignment occurred after ROCK, YAP, or SMAD3 inhibition. TGFb-induced myofibroblast markers were reduced by strain. While TGFb-induced phosphorylation of ERK and SMAD2 was unaffected by strain, SMAD3 phosphorylation was reduced significantly ($p=0.0004$). Wound healing across grooves was enhanced by ROCK and SMAD3 inhibition but not ERK or TGFbR1 inhibition.

Conclusions: Strain-induced myofibroblast migration across topographic confinement is ERK dependent and associated with pSMAD3 inhibition. These results inform potential mechanisms of pathologic scleral remodeling.

References

1. Oglesby EN, Tezel G, Cone-Kimball E, et al. Scleral fibroblast response to experimental glaucoma in mice. Mol Vis. 2016;22:82-99.

2. Wu H, Chen W, Zhao F, et al. Scleral hypoxia is a target for myopia control. Proc Natl Acad Sci U S A. Jul 24 2018;115(30):E7091-E7100. doi:10.1073/pnas.1721443115

3. Szeto J, Chow A, McCrea L, et al. Regional Differences and Physiologic Behaviors in Peripapillary Scleral Fibroblasts. Invest Ophthalmol Vis Sci. Jan 2021;62(1):27. doi:10.1167/iovs.62.1.27

CONTROL ID: 3713229

SUBMITTER (NAME ONLY): Camille Guerin

TITLE: In vitro permeation of Latanoprost eyedrops in a 3D human corneal tissue model

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Guerin, L. Chauchat, H. Rebika, M. Claret, Horus Pharma, FRANCE|Y. Kaluzhny, MatTek Corporation, Massachusetts, UNITED STATES|H. Rebika, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, FRANCE|

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ABSTRACT BODY:

Purpose: The permeability of the cornea to topically applied formulations is a major factor determining their clinical efficacy. Various agents could influence the corneal permeation including Benzalkonium chloride (BAC) or surfactants which help lipophilic agents solubilization. The purpose of the study was to evaluate the permeation of different Latanoprost formulations through an in vitro reconstructed human 3D corneal tissue model (EpiCorneal^{TM}).

Methods: EpiCorneal tissues are comprised of normal human corneal epithelial cells and attain morphology, barrier properties, and gene expression similar to the human cornea. 3 different formulations of 0.005% Latanoprost were tested: A. preservative-free (PF) and surfactant-free (SF) formulation; B. same SF formulation but containing BAC 0.02%; and C. different PF formulation but containing Macrogolglycerol hydroxystearate 40 (MGHS 40) at 5%. 100 µL of 1:5 diluted formulations were applied onto the EpiCorneal tissue surface and incubated at standard cell culture conditions (37°C, 5% CO2, 95% RH). Samples were collected after 0, 0.5, 1, 2, 3, 4, 5, 6, 8, 10, and 12 hr permeation and analyzed with a validated HPLC method for Latanoprost acid (LAT) detection (active form). Barrier integrity (TEER, Transepithelial Electrical Resistance) was determined before and after the permeation. For each formulation, plots of the cumulative amount of LAT that permeated through the tissue versus time were constructed. From the steady state flux region of the plot (<4 h), the permeation coefficient (Papp) was calculated.

Results: The transport profile of LAT formulations was linear from 2 to 12 hours for C and from 1 to 4 hours for A and B and then curved to reach a plateau. A and B had a similar permeation pattern, comparable at each timepoint. Papp was fastest and comparable for A and B (~8.5 cm.s^{-1}); C had the lowest Papp (3.14 cm.s^{-1}). Tissue integrity was maintained in all experiments.

Conclusions: The absence or presence of BAC within the formulations A and B did not influence the permeation profile as similar LAT cumulative amount and Papp were obtained. However, formulation C resulted in a lower and slower permeation pattern when compared to formulations A and B which may be due to the presence of MGHS 40. Thus, the EpiCorneal tissue model allowed us to anticipate the pharmacokinetics of LAT and the excipients' role. The results were confirmed in an in vivo rabbit model study.

CONTROL ID: 3713231

SUBMITTER (NAME ONLY): Mert Mestanoglu

TITLE: Pilot Data on Safety and Efficacy of Combined Corneal Crosslinking and Fine Needle Diathermy for Regression of Pathological Corneal Neovascularization and Corneal Stabilization Prior to High-Risk Keratoplasty

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mestanoglu, H. Heinen, F. Schaub, F. Bock, D. Hos, C. Cursiefen, Department of Ophthalmology, Universitat zu Koln, Cologne, Nordrhein-Westfalen, GERMANY|D. Hos, C. Cursiefen, University of Cologne Center for Molecular Medicine Cologne, Cologne, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Corneal neovascularization (CNV) causes decreased vision and is an important risk factor for graft rejection after (high-risk) keratoplasty (KP). Corneal crosslinking (CXL) and fine needle diathermy (FND) have previously been demonstrated to regress pathological CNV in both experimental and clinical studies. However, the impact of a combination of both treatment modalities on CNV has not been studied before. This pilot evaluation aimed to investigate whether combined CXL and FND are safe and efficient for regression of pathological CNV and corneal stabilization prior to high-risk KP.

Methods: This retrospective case series included ten patients (7 male, 3 female, mean age 58.1 years) with CNV and the need for high-risk penetrating KP. Patients were treated with CXL and FND followed directly by penetrating KP. Corneal vessel-covered areas were measured on pre- and postoperative slit-lamp images via a semi-automatic morphometric method. Patients were followed up for adverse events and graft rejection.

Results: Mean follow-up was 21.2 ± 7.8 weeks (range 4–31 weeks). No intraoperative complications were observed. In 4 eyes, wound leakage was observed during the early postoperative period. One of these patients required repeat-KP due to fungal keratitis, while two patients received amniotic membrane transplantation during the follow-up. One of these two patients developed endophthalmitis. Recovery of graft transparency was delayed in two eyes, and neurotrophic ulceration was observed in one graft. Combination treatment with CXL and FND resulted in a significant reduction of vascularized areas (mean reduction of 66.2%, ± 22.0%). Revascularization was not observed. All transplanted corneas remained clear and without immune reactions (except the one with fungal keratitis needing re-KP).

Conclusions: Combined CXL and FND prior to high-risk KP seems to be an efficient method to regress pathological CNV in this pilot evaluation. Leakage from corneal incision sites may be an early postoperative risk, possibly due to delayed corneal healing. Longer follow-up of the patients and future prospective studies are required to assess the impact of CXL and FND on long-term graft survival after high-risk KP and the potential of combined CXL and FND as a novel angioregressive method.

CONTROL ID: 3713232
SUBMITTER (NAME ONLY): Kevin Mendez
TITLE: Metabo-endotypes of Age-related Macular Degeneration
SESSION TITLE: AMD Translational Research
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: K.M. Mendez, I. Lains, J.B. Miller, D.G. Vavvas, I.K. Kim, J.W. Miller, D. Husain, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|K.M. Mendez, R. kelly, J.A. Lasky-Su, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|L. Liang, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|
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ABSTRACT BODY:
Purpose: Age-related Macular Degeneration (AMD) has a wide spectrum of both phenotypic and functional presentations. Yet, the contributing factors for this phenotypic variability remain not fully understood. Metabolomics reflects the downstream products of all the genetic transcription processes, making it appropriate to study multifactorial diseases like AMD. We hypothesize that there are distinct AMD endotypes (i.e. subtypes defined by functional or pathobiological mechanisms) that confer clinically meaningful differences. In this study, we aim to derive AMD endotypes based on metabolomics and correlate these endotypes with current AMD stage and retinal function.
Methods: Prospective, cross-sectional study including patients with any stage of AMD (n=196). All included participants had a complete ophthalmological exam and were imaged with color fundus photographs for AMD staging. Dark adaptation testing was performed with a 20 minutes protocol, and both rod intercept time (RIT) and area under the curve (AUDAC) were registered. Metabolomic profiling on fasting plasma samples was performed using ultra-performance liquid chromatography–mass spectrometry (LC-MS). Similarity Network Fusion (SNF) and spectral clustering were performed on the metabolomics and used to identify metabo-endotypes of AMD. Clinical differences across the metabo-endotypes were explored using one-way analysis of variance (ANOVA) for continuous variables and chi-squared test for categorical variables. Multivariable logistic regression models adjusted for covariates were then used to identify metabolomics drivers of each endotype.
Results: We identified 4 AMD endotypes using SNF and spectral clustering with metabolomics data. AMD stage (pval=0.002), RIT (pval=0.003), and AUDAC (pval=0.01) significantly differed across the endotypes. As shown in Figure 1, endotype membership tracked closely to RIT but appeared to be independent of the AMD stages. The most important drivers of the endotypes were amino acids (isoleucine, leucine, and valine metabolites), lipid metabolites (polyunsaturated and long-chain fatty acids), and nucleotides (purine metabolism).
Conclusions: Metabo-endotypes of AMD can be derived using metabolomics data and correlated with clinical and functional features. By interrogating the drivers of these metabo-endotypes, there is potential to better understand the pathophysiology behind AMD.

CONTROL ID: 3713233

SUBMITTER (NAME ONLY): Jana Sajovic

TITLE: Electroretinography as a biomarker to monitor Stargardt disease

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Sajovic, A. Meglič, M. Šuštar Habjan, M. Hawlina, A. Fakin, Department of Ophthalmology, Univerzitetni klinicny Center Ljubljana, Ljubljana, SLOVENIA|

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ABSTRACT BODY:

Purpose: To determine which electroretinographic (ERG) responses best correspond with disease progression in Stargardt disease (STGD1).

Methods: 42 patients with STGD1 (ABCA4 retinopathy) were included. Group 1 harboured two null mutations (8 patients, 3 male), while group 2 had other genotypes (34 patients, 10 male). Age at the time of exam, age at onset and decimal Snellen visual acuity were collected from the medical records. Full-field ERG and pattern ERG (24°X30° checkerboard) were recorded according to ISCEV standards. S-cone ERG was also recorded, according to the ISCEV approved extended protocol. The amplitudes of the following responses were analysed cross-sectionally with age: PERG P50, dark-adapted (DA) 0.01 ERG b wave, 3.0 ERG a wave and oscillatory potentials; light-adapted (LA) 30 Hz flicker ERG and 3.0 ERG b wave; and S-cone ERG. The right patients' eyes were taken for the analysis. Correlation between ERG responses and age at the exam was compared using simple linear regression. Mann-Whitney U Test was used for comparing age at the exam, age at onset, visual acuity and ERG amplitudes between the two groups.

Results: The median age of onset was significantly earlier in group 1 (8 vs 18 years; $p<0.01$); however, disease duration was similar between the two groups (12.5 and 12.0 yrs; $p>0.05$). Group 1 had also significantly worse visual acuity (0.02 vs 0.16; $p<0.01$) and significantly lower all ERG responses ($p<0.01$). Group 1 had no detectable macular function measured with PERG P50, whereas it was detectable in 79% of patients in group 2. Simple linear regression analysis revealed that in group 1, age had a significant effect on DA 0.01 ERG b wave ($\beta=-0.8$, $R^2=0.6$, $p<0.01$) and DA 3.0 ERG a wave ($\beta=-0.9$, $R^2=0.7$, $p<0.01$). In contrast, other ERG parameters did not show age dependency. In group 2, age was significantly associated with S-cone ERG amplitude ($\beta=-0.7$, $R^2=0.5$, $p<0.01$).

Conclusions: For double null patients, the best ERG biomarkers for follow-up were DA 0.01 and 3.0 ERG responses, representing retina rod system response. For other genotypes expected to confer residual ABCA4 function, the best ERG biomarker for follow-up was S-cone ERG. Different ERG responses may be best suited to monitor disease progression in different Stargardt genotypes. However, additional studies on larger datasets with precisely grouped genotypes would be needed.

CONTROL ID: 3713237

SUBMITTER (NAME ONLY): Jihong Kim

TITLE: Novel finding of morphologic characteristics of neovascular age-related macular degeneration (nAMD) with tolerable subretinal fluid (SRF)

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There has been a lot of debate about fluids in nAMD. Several studies have recently reported tolerating SRF in nAMD. However, none of the studies revealed the morphologic characteristics of nAMD with tolerable SRF. This study is aimed to present the morphologic characteristics of nAMD with tolerable SRF.

Methods: This is a longitudinal observational case series study. Tolerable SRF was defined as nAMD patient even with resistant SRF who maintained good visual acuity (VA) with no deterioration. Those patients with tolerable SRF at least 6 months were enrolled. They underwent additional anti-VEGF and observed for six-more months. Patients who showed deterioration of VA or appearance of hemorrhage and intraretinal fluid (IRF) during the study period were excluded. Structural OCT was performed to evaluate detailed PED and SRF morphology. OCT angiography was also performed to confirm CNV activity by evaluating morphology, size, and vascular density of CNV from en face images, and relative flow area from cross-sectional images. These parameters and visual acuity were assessed at 4 time points; SRF recurrence, study enrollment, last injection and last follow-up.

Results: A total of 25 eyes from 25 patients with nAMD with tolerable SRF were included in the study. The naïve diseases causing tolerable SRF were typical nAMD in 8 eyes (32%), PCV in 12 eyes (48%), and pachychoroid neovasculopathy (PNV) in 5 eyes (20%). During the study period, there were no statistically significant changes in VA, SRF height and CNV activity; size, vascular density and relative flow area, respectively (all $P>0.05$). Remarkably, during tolerable SRF span, all patients showed common morphological characteristics, which were vascularized shallow irregular PED with low activity, serous SRF, and absence of IRF.

Conclusions: Although initial CNV morphologic characteristics were different from each other, nAMD with tolerable SRF showed common morphological characteristics in OCT and OCT angiography. Hypothetically, remodeling of CNV following multiple treatments may eventually lead to this common morphology, Therefore, if a patient has eyes with nAMD with tolerable SRF could be managed with very relaxed Tx protocol

CONTROL ID: 3713239

SUBMITTER (NAME ONLY): Ralf Brinkmann

TITLE: Time-resolved 2D-temperature monitoring on RPE explants during laser irradiation by means of a fluorescent dye

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Brinkmann, L. Hoffmann, E. Seifert, D. Theisen-Kunde, Y. Miura, Medical Laser Center Luebeck, GERMANY|R. Brinkmann, X. Zhang, M. Mordmüller, Y. Miura, Institute of Biomedical Optics, University of Luebeck, Luebeck, GERMANY|M. Suzuki, Institute for Protein Research, Osaka University, JAPAN|

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ABSTRACT BODY:

Purpose: Subvisible retinal thermal laser treatments are becoming more popular, but lack an objective dosing control. This is very demanded since the laser-induced temperature rise differs largely due to inter- and intraocular variations of light scattering and pigmentation at the fundus. Therefore we developed an optoacoustic (OA) method to determine and control the average temperature rise during laser irradiation. In order to calibrate and analyse the OA-method, the time-resolved 2D-temperature distribution was investigated in this study by means of the thermosensitive fluorescent dye, ERthermAC, being taken up into the endoplasmic reticulum of the cells.

Methods: Porcine retinal pigment epithelium (RPE)/choroid-sclera explants were incubated with the dye for 30 min and then placed in a cuvette filled with phosphate buffer saline (PBS) for laser exposure. The samples were repetitively irradiated with a slitlamp-coupled Q-switched Nd:YLF-laser (527 nm wavelength, 250 ns pulse duration) on a spot diameter of 200 µm. ERthermAC absorbs between 480 and 590 nm and fluoresces from 560 to 700 nm. The fluorescence light was decoupled from the laser path with a dichroic mirror in front of the slitlamp. The laser spot was imaged enlarged on a sensitive camera. The OA transients were measured with an ultrasonic transducer embedded in a contact lens. Calibration curves were recorded by frequently exciting the probe with 9 µJ/pulse while heating the PBS with a rate of 2 °C/min from 20 to 60 °C. For laser-induced heating a repetition rate of 1 kHz with a pulse energy of 30 µJ was applied for 200 ms.

Results: The dye was well accumulated in RPE cells. An almost linear fluorescence intensity decay of 1.87 % per 1 °C was noticed for calibration. The fluorescence emission was stable and did not bleach over the irradiation time. Laser-induced heating revealed the expected temperature-correlated pressure rise by OA and the corresponding fluorescence decrease over time, strongest at the center of the spot. Both methods are in good accordance with an average difference in temperature rise of about 9.8 % after 200 ms.

Conclusions: The thermosensitive dye ERthermAC shows high affinity to ex-vivo RPE cells and enables time-resolved 2D-temperature monitoring during laser exposure. It shows a good accordance with the OA-method and is generally a useful tool to investigate temperature-related cellular effects.

CONTROL ID: 3713240

SUBMITTER (NAME ONLY): Lyes Toualbi

TITLE: Using non-viral S/MAR DNA vectors to restore protein expression in models of choroideremia

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Non-viral gene therapy could provide a safer alternative approach to conventional viral therapy for the delivery of large cDNAs in patients affected by inherited retinal diseases. We assessed the use of non-viral S/MAR vectors to produce functional protein in patient cellular and zebrafish models of choroideremia, an X-linked chorioretinal dystrophy caused by mutations in the CHM gene encoding Rab escort protein 1 (REP1), a protein involved in prenylation and intracellular trafficking.

Methods: S/MAR vectors were generated with human CHM coding sequence, the GFP reporter gene and ubiquitous promoters (CMV or CAG). The nanovector versions with minimal bacterial backbones were produced by Nature Technology.

Results: GFP expression was assessed in transfected patient fibroblasts and chm^{ru848} zebrafish micro-injected with the vector at the one-cell stage. CHM-S/MAR vectors restored REP-1 expression with a partial rescue of prenylation function in CHM patient fibroblasts. Human REP-1 expression was detected in micro-injected zebrafish at 6 days post-fertilisation. A mild but significant improvement in survival of 7.1 ±0.7 days (n=21) was observed in injected chm^{ru848} zebrafish compared to 5.9 ±1.2 days (n=43) in un-injected ($p<0.0001$). GFP expression was detected in the retinal photoreceptors.

Conclusions: S/MAR vectors have shown promise as a novel non-viral retinal gene therapy, warranting further development.

CONTROL ID: 3713241

SUBMITTER (NAME ONLY): Liang Wang

TITLE: Impact of Cataract Surgery on Low Luminance Visual Acuity Deficit Measurements

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Wang, Y. Shi, M. Shen, X. Jiang, P.G. Iyer, S.H. Yoo, T. Rose, R.G. Habash, G. Amescua, W.J. Feuer, G. Gregori, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Russell, Institute for Vision Research and Department of Ophthalmology and Visual Sciences, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The impact of cataract surgery on low luminance visual acuity deficit (LLVAD) measurements was investigated by comparing LLVAD measurements before and after cataract surgery.

Methods: Both normal luminance best-corrected visual acuity (NL-BCVA) and low luminance BCVA (LL-BCVA) were obtained using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts. LL-BCVA was measured by using a 2.0-log unit neutral density filter in front of the examined eye (Wratten filter; Kodak, Rochester, NY). LLVAD scores were calculated by subtracting the LL-BCVA letter score from the NL-BCVA letter score. To estimate the test-retest variability of these visual acuity measurements, we used data from a previously published study entitled Complement Inhibition with Eculizumab for the Treatment of Nonexudative Age-Related Macular Degeneration (COMPLETE) Study, where the NL-BCVA, LL-BCVA, and LLVAD measurements were obtained at an interval of three months. In the current study, the impact of cataract surgery on LLVAD measurements was analyzed by comparing the NL-BCVA, LL-BCVA, and LLVAD measurements before and after cataract surgery.

Results: In the COMPLETE study, a total of 37 eyes were included at baseline and at the month-3 follow-up visit. There were no clinically significant differences in the NL-BCVA, LL-BCVA, and LLVAD measurements between baseline and the month-3 follow-up visits with mean differences in ETDRS letter scores of -1.1 (P=0.02), -1.3 (P=0.11), and 0.1 (P=0.88). In the current study, a total of 25 eyes were assessed before and after cataract surgery. Not surprisingly, there were significant increases in the NL-BCVA (+7.3) and LL-BCVA (+10.2) letter score measurements after cataract surgery (both $P < 0.001$); however, a statistically significant decrease in the average LLVAD measurement (-3.0) was observed after cataract surgery ($P = 0.002$). This change was due to the greater impact of cataracts on LL-BCVA measurements compared to the NL-BCVA measurements.

Conclusions: A greater effect of cataracts on LL-BCVA than NL-BCVA measurements caused a significant change in LLVAD values after cataract surgery. Caution should be exercised when using LLVAD measurements as a predictor of disease progression in phakic eyes with age-related macular degeneration.

CONTROL ID: 3713242

SUBMITTER (NAME ONLY): Alessa Hutfilz

TITLE: Comparison between continuous wave and 10 kHz pulsed laser irradiation with regard to thermal damage on ex-vivo RPE explants

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hutfilz, C. Kren, C. Schmidt, D. Theisen-Kunde, R. Brinkmann, Medical Laser Center Lübeck, Lübeck, GERMANY|Y. Miura, Department of Ophthalmology, University Medical Center Schleswig-Holstein, Lübeck, GERMANY|M. Mordmüller, Y. Miura, R. Brinkmann, Institute of Biomedical Optics, University of Lübeck, Lübeck, GERMANY|

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ABSTRACT BODY:

Purpose: Photocoagulation of the retina is currently performed with different continuous wave (cw) and pulsed laser modalities. It is well known that the extent of laser induced tissue damage differs by inter and intraocular variations of scattering and fundus pigmentation. However, the influence of different laser modalities on the tissue denaturation has not been investigated in detail so far. Therefore, this work investigates the induced damage range on retinal pigment epithelium (RPE) explants between cw and pulsed irradiation in correlation to the temperature rise measured by optoacoustics (OA).

Methods: RPE/choroid/sclera explants from porcine eyes were irradiated via laser slitlamp on a 200 µm spot diameter with a cw laser at 532 nm wavelength, and with a Q-switched frequency doubled Nd:YLF laser at 523 nm with a pulse duration of 160 ns at a repetition rate of 10 kHz. The pulsed heating excites thermoelastic pressure waves, which contain the present RPE temperature. The pressure waves were detected with an ultrasonic transducer embedded in a contact lens and processed for real-time temperature evaluation. In an open-loop setup, the power of the cw laser and the pulsed laser were kept constant until the end of the irradiation period, where the final temperature was noticed. For a closed-loop feedback control, the pulse energy was actively modulated with respect to quickly achieve a desired aim temperature and by then keep this temperature constant for the rest of the irradiation time. The laser-induced RPE-cell damage was evaluated with Calcein-AM assay.

Results: Temperatures up to 70°C could be achieved in both modalities as well as with open- and closed-loop temperature-controlled irradiations. An average power of 60 mW in an open-loop setup for example revealed the same temperature of 44 °C in the cw mode as well as in the pulsed mode at the end of an 800 ms irradiation period at the same site of a low absorbing sample. The slopes of the temperature rise were almost identical.

Conclusions: It is shown that cw as well as pulsed irradiation with high repetition rate can be used to heat the tissue in a similar way. When using the same average laser power, the same temperature rise is achieved. The pulsed heating provides the unique feature that it additionally excites optoacoustic pressure waves, which can be used for real-time temperature monitoring and control.

CONTROL ID: 3713243

SUBMITTER (NAME ONLY): Christian Wolfram

TITLE: Real-world outcomes of anti-VEGF therapy: psychological, social and behavioral factors measured by the ALBATROS data collection instrument BPZ-9.

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wolfram, Ophthalmology, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|C. Wolfram, N. Pfeiffer, A.K. Schuster, Johannes Gutenberg Universitat Universitatsmedizin Medizinische Klinik und Poliklinik I, Mainz, Rheinland-Pfalz, GERMANY|T. Hudde, Eye Hospital Wolfsburg-Fallersleben, GERMANY|A. Klatt, Eye Center Klatt, GERMANY|B. Schnegelsberg, H. Midani-Oezkan, Novartis Pharma Nuernberg, GERMANY|F. Ziemssen, Universitatsklinikum Leipzig, Leipzig, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Ophthalmic questionnaires (e.g. NEI-VFQ-25) are validated to assess quality of life (QoL) in retinal diseases including neovascular age related macular degeneration (nAMD), diabetic macular edema (DME) or branch-/central retinal vein occlusion (B/CRVO). They do not thoroughly assess the patients' social and psychological status. We present the new BPZ-9, a novel, exploratory questionnaire which intends to capture a more comprehensive view on the patients' situation.

Methods: The BPZ-9 instrument consists of 9 questions which assess patient dependency and wellbeing in terms of requirement for domestic care, walking difficulties, accompanying person necessary, anxiety about visual impairment or their disease or treatment, satisfaction with treatment, information provided and eye examinations, evaluated at baseline.

Results: The BPZ-9 questionnaire was completed at 102 sites. No patient had previously received anti-VEGF injections. Data was collected from 1444 nAMD (mean 78 years), 445 DME (67 y), 233 BRVO (70 y) and 144 CRVO (71 y) patients. 27% of patients had walking difficulties, ranging from 18% (BRVO) to 29% in nAMD (DME 24%, CRVO 22%). 12-23% of patients needed an accompanying person (23% nAMD, 21% DME, 12% BRVO, 19% CRVO). Most patients reported anxiety concerning visual impairment: 77% of nAMD patients, 73% DME, 73% CRVO and 60% of BRVO patients. Concern about their disease or treatment was mixed: while 32% and 44% of nAMD patients were very/moderately distressed, distress about treatment and disease control was lower (11% very, 34% moderately distressed). Within the DME, BRVO and CRVO groups a lower proportion of patients was very distressed by the disease (26%,24%, 23%), the majority was “moderately distressed” (42%,47%, 42%). Concern about treatment and controls was at the same level compared to nAMD patients. Overall, most patients were very satisfied with their treatment (73%) and felt very well informed (81%).

Conclusions: When patients with retinal disease initially require anti-VEGF therapy, they might face impaired mobility, dependency on others, distress and anxiety about their retinal condition and therapy. These factors may lead to social and psychological concerns influencing their behavior and attitude towards their disease. More research on patient psychology, attitude and impairments in treatment outcome is needed.

CONTROL ID: 3713245

SUBMITTER (NAME ONLY): Jean Bennett

TITLE: A novel virtual reality orientation and mobility test to assess functional vision in patients with inherited retinal dystrophies

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bennett, E.M. Aleman, K. Maguire, A.J. Miller, M. Weber, A.K. Maja, A.M. Maguire, T.S. Aleman, Center for Advanced Retinal and Ocular Therapeutics (CAROT), Scheie Eye Institute, Department of Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a need in studies of patients with retinal disease for testing paradigms that can quickly, accurately, and reproducibly define the level of visual function as well as the patient's functional vision. We designed a virtual reality orientation and mobility (VR-O&M) protocol for such a purpose. The goal of this study was to initiate steps to validate this protocol in normal-sighted individuals as well as those with a diverse set of inherited retinal dystrophies (IRDs).

Methods: Using commercially available hardware and custom-generated software, we developed a task whereby individuals are tasked to follow a set of dimly lit red arrows to a 'course exit' while identifying obstacles that are adjacent to or directly in their path. Subjects with normal vision (n = 21, ages 10-66 y) as well as patients with IRDs (n= 16, ages 7-63 y) representing a spectrum of disease severity were invited to participate. All individuals first underwent a training and practice session and then were dark-adapted for 30 minutes. Subjects were asked to follow the VR-O&M courses presented at a range of increasing luminance levels using a set of 35 randomly selected configurations of similar difficulty. Performance was graded automatically by the software.

Results: Normal-sighted individuals were able to accurately navigate the course over a range of luminances and were able to identify over 90% of the objects at about 0.02 $cd.m^{-2}$. With the exception of one subject with light perception level of vision, all subjects with IRDs were able to complete the test. However, in the IRD group, light intensities allowing detection of the obstacles were significantly higher than in normal-sighted subjects. At the lowest level of luminance where normal subjects consistently detected nearly all objects, IRD patients could detect 10 to 80% of the presented objects which related to their disease severity.

Conclusions: This novel VR-O&M test promises to be a useful outcome measure for quantifying the impact of disease and treatments thereof on functional vision in inherited retinal degenerations.

CONTROL ID: 3713246

SUBMITTER (NAME ONLY): Sofie ten Brink

TITLE: Analysis of plasma HtrA1 concentrations in age-related macular degeneration

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.C. ten Brink, B. Bakker, C.C. Hoyng, Y.T. Lechanteur, C.C. Klaver, A.I. Den Hollander, Radboudumc Afdeling Oogheelkunde, Nijmegen, Gelderland, NETHERLANDS|C.C. Klaver, Ophthalmology/Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The responsible gene for the association at the Age-Related Maculopathy Susceptibility 2-High-temperature requirement protein A1 (ARMS2-HTRA1) locus with age-related macular degeneration (AMD) is still a matter of debate. A previous study demonstrated increased systemic HtrA1 protein concentrations in AMD, which were suggested to lead to subsequent degradation of Bruch's membrane and eventual choroidal neovascularization in AMD (Pan et al 2021, J Biol Chem 296:100456). We aimed to verify these results and therefore performed an enzyme-linked immunoassay (ELISA) targeting this protein in plasma samples of a case-control study.

Methods: A total of 200 advanced AMD patients and 200 controls without AMD were selected from the European Genetic Database (EUGENDA). An ELISA was performed for plasma HtrA1 concentrations. Multiple linear regression analysis with backward elimination based on adjusted-R^2 was used to assess the association between the HtrA1 plasma concentrations and AMD.

Results: We excluded 9 AMD and 3 control samples due to an absorption below the standard curve. Median plasma level of Htra1 was slightly higher in AMD patients (514 pg/ml) than in controls (500 pg/ml). However, the association between HtrA1 plasma level and AMD adjusted for age and age x AMD status was not significant (R^2 = 0.011; p = 0.10).

Conclusions: This study was unable to replicate the association between HtrA1 plasma concentrations and AMD. Further study is required to elucidate the causal gene dysfunction at the ARMS2-HTRA1 locus in AMD.

CONTROL ID: 3713247

SUBMITTER (NAME ONLY): Jennifer Adeghate

TITLE: Role of Metformin in the Development and Progression of Age-Related Macular Degeneration

SESSION TITLE: AMD Epidemiology & Systemic Therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a leading cause of irreversible blindness with limited treatment and management options. Metformin has been shown to have immunomodulatory roles which could influence the pathogenesis of AMD. This study investigates whether metformin confers a protective effect in delayed onset and slower progression of AMD.

Methods: This is a single-center retrospective cohort study, which included 18,431 patients aged 50-80 years, visiting ophthalmology clinics from September 2006 to August 2019. Among these, 132 patients with concurrent diagnoses of AMD and diabetes were further analyzed, stratified by metformin use. Data included demographics, presence and type of AMD, examination findings including visual acuity (VA), ocular coherence tomography (OCT) features and anti-VEGF injection frequency. These were compared between patients prescribed or not prescribed metformin.

Results: Among the 18,431 study patients, the average age was 63.7 ± 8.2 years in the metformin group and 63.0 ± 8.5 years in the non-metformin group (P = 0.0002). 74.6% of the metformin group had diabetes, compared to 9.3% of the non-metformin group (P < 0.0001). Incidence of AMD during the study period (4.2% compared to 5.1%, P = 0.049) and prevalence of AMD at the final visit (6.9% compared to 8.4%, P = 0.015) were found to be significantly lower in the metformin group compared to the non-metformin group. Several analyses were performed in a subset of 132 patients with concurrent diagnoses of AMD and diabetes. The metformin group exhibited less decline in VA (0.009 ± 0.041 logMAR/year), compared to the non-metformin group (0.013 ± 0.041 logMAR/year, P = 0.29) and less expansion of the area of geographic atrophy measured on OCT over time (1.10 ± 1.08 mm^2/yr), compared with the non-metformin group (1.66 ± 1.94 mm^2/yr, P = 0.33); however, these did not reach the level of statistical significance. A similar number of intravitreal anti-VEGF injections was required in the metformin group (2.2 ± 3.2 injections/year), compared with the non-metformin group (1.6 ± 2.1 injections/year) (P = 0.39).

Conclusions: Our data suggest that metformin may confer a protective effect against the onset and progression of dry AMD, though this protective effect may not apply to wet AMD.

CONTROL ID: 3713248

SUBMITTER (NAME ONLY): Joseph Abraham

TITLE: Exploration of Machine Learning-Enhanced Ellipsoid Zone Mapping and Radiomics-based Textural Features As Biomarkers for Risk of Geographic Atrophy Development in Dry AMD

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.R. Abraham, S. Sil Kar, H. Cetin, S.K. Srivastava, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|S. Sil Kar, A. Madabhushi, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate compartmental SD-OCT imaging biomarkers using machine learning-enhanced outer retinal segmentation and textural radiomics that are associated with the development of geographic atrophy (GA).

Methods: This was a retrospective image analysis study that included 114 subjects with dry age-related macular degeneration (AMD) without GA at baseline with 5 years of clinical and SD-OCT follow-up. All SD-OCT scans were analyzed using a machine learning-enhanced multi-layer retinal segmentation platform that enabled quantitative ellipsoid zone (EZ) integrity assessment and EZ-RPE compartmental extraction. Eyes were categorized as either GA developers or non-GA developers based on development of GA on SD-OCT by year 5 of follow-up. Baseline quantitative features between the GA developers and non-developers were compared using traditional statistics and a radiomic classification model combined with a Random Forest algorithm. Radiomic features were identified using a Minimum Redundancy Maximum Relevance feature selection method, and the 10 topmost features were used to train a Random Forest classifier.

Results: At baseline, eyes that developed macular GA (n = 33) significantly decreased EZ integrity as measured by mean EZ-RPE central subfield thickness (28.5 vs 36.2μm $p<0.001$) and EZ-RPE volume (1.23 vs 1.30 mm^3 $p=0.002$) compared to eyes that did not develop GA (n = 81). In addition, eyes that developed GA increased partial (5.4% vs 0.9%, $p<0.001$) and total EZ attenuation (2.6 vs 0.3%, $p<0.001$) compared to eyes that did not develop GA. Random Forest modeling utilizing identified radiomic features yielded a classifier performance of AUC=0.88±0.02 for GA development. Increased heterogeneity in the EZ-RPE compartment was associated with the development of GA.

Conclusions: The development of GA was significantly associated with reduced EZ integrity at baseline as well as radiomics-based EZ-RPE compartment textural features. These potential biomarkers could be key tools for risk-stratification of eyes for future development of GA and clinical trial enrichment.

CONTROL ID: 3713249

SUBMITTER (NAME ONLY): Hae Min Park

TITLE: Non-mydriatic cataract screening using ultra-widefield fundus imaging

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Currently, mydriatic slit-lamp examination is the gold standard for cataract evaluation. Discomfort following mydriasis, small pupil, and inability to dilate pupil may limit mydriatic examinations. Optomap is a widely used modality that captures ultra-wide fields without mydriasis. In clinical practice, peripheral cataract shadows are often visualized with a single, non-mydriatic ultra-widefield retinal imaging. In this study, we intended to evaluate whether non-mydriatic UWFRI can effectively screen cataracts.

Methods: Patients who underwent non-mydriatic ultra-widefield retinal imaging with Optomap were included in this study. Two ophthalmologists assessed cataract grading via 2 diagnostic modalities: (1) non-mydriatic ultra-widefield retinal imaging (UWFRI) and (2) mydriatic slit-lamp examination. Lens opacity classification system (LOCS II) was used as a reference grading scheme. Concordance of cataract gradings between the 2 modalities was evaluated. Red and green separation images, that can be generated via embedded software, were also evaluated and their utility in cataract grading was qualitatively assessed.

Results: A total of 170 eyes from 85 patients with cataract were included in this study. The mean age was 72.5 ± 10.4 years. Concordance between non-mydriatic UWFRI and mydriatic slit-lamp was 90.58%. With respect to cataract types, cortical opacity (CO) and posterior capsular cataract (PSC) had better concordance rate than nuclear sclerosis (NS). Qualitatively, grading of NS was most difficult when it was associated with vitreous disorders. 23 cases had cataract with vitreous opacity and red separation view was useful at differentiating cataract from vitreous opacity. On the other hand, green separation view was more useful at visualization of cataract itself.

Conclusions: Non-mydriatic ultra-widefield retinal image can be considered as a less inconvenient and effective tool for cataract screening. Various image modes provided by Optomap may aid clinicians to differentiate cataract from non-retinal posterior disorders.

CONTROL ID: 3713251

SUBMITTER (NAME ONLY): Jennifer Corwin-Buell

TITLE: Disinfection Efficacy Testing of a Triple Disinfectant System in an Investigational Multi-Purpose Solution Challenged against the Five Bacterial and Fungal Compendial Organisms

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Corwin-Buell, D. Callahan, D. McGrath, K. Millard, Vision Care, Microbiology, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Contact lens (CL) disinfection is critical for the prevention of microbial keratitis (MK) associated with contact lens wear. An investigational multi-purpose solution was designed as a low concentration, triple disinfectant system containing polyaminopropyl biguanide (PAPB), polyquaternium-1 (PQ-1), and alexidine. An evaluation of the investigational MPS was performed to determine the efficacy against the five ISO/FDA organisms, with and without the incorporation of organic soil. The organic soil was added with the organism preparation to further challenge the antimicrobial activity of the triple disinfectant system.

Methods: Testing was performed using Staphylococcus aureus (Sa), Pseudomonas aeruginosa (Pa), Serratia marcescens (Sm), Candida albicans (Ca), and Fusarium solani (Fs), prepared with and without organic soil, to achieve a final concentration from $1.0x10^5$ to $1.0x10^6$ colony forming units (cfu)/ml.

The test solution (10 ml) was dispensed into conical tubes and inoculated with each challenge organism (with or without organic soil). After 4 hours of disinfection, each test solution was neutralized with Dey-Engley Broth (DEB), plated in triplicate, and incubated. Additionally, an inoculum control (IC) was prepared in a suitable diluent to determine the initial concentration of each challenge organism.

Plates were enumerated for the recovery of organisms and log reduction values (LRV) were calculated, based on the mean log recovery of the IC. Three lots of the investigational MPS were tested and the mean LRV determined.

Results: The mean LRV for the bacterial organisms (Sa, Pa, and Sm) without organic soil were 4.7, 4.6, and 4.8, and with the incorporation of organic soil were 4.7, 4.6, and 4.7, respectively. The fungal organisms (Ca and Fs) without organic soil showed mean log reduction values of 3.4 and 4.5 and with the incorporation of organic soil were 4.6 and 4.4, respectively.

Conclusions: The investigational MPS containing the disinfectants PAPB, PQ-1, and alexidine, was efficacious and exceeded the ISO 14729 primary acceptance criteria for each challenge organism. Additionally, there was no decrease to the biocidal activity with the addition of organic soil.

The investigational MPS demonstrated a robust disinfectant system, formulated to reduce the potential risk for MK associated with contact lens wear.

CONTROL ID: 3713252

SUBMITTER (NAME ONLY): Sheldon Rowan

TITLE: Proteomic changes in the lens of a congenital cataract mouse model lead to reduced levels of glutathione and taurine

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rowan, E.A. Whitcomb, A. Taylor, Laboratory of Nutrition and Vision Research, Jean Mayer USDA Human Nutrition Research Center on Aging, Boston, Massachusetts, UNITED STATES|S. Rowan, A. Taylor, Department of Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|E. Bejarano, Envejecimiento celular y nutrición, CEU Universidad Cardenal Herrera, Moncada, Comunitat Valenciana, SPAIN|R.L. Pfeiffer, B.W. Jones, Moran Eye Center, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|K.L. Rose, K.L. Schey, Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Congenital cataracts develop through multiple mechanisms, but often lead to common endpoints, including protein aggregation, impaired fiber cell differentiation, and absence of fiber cell denucleation. It is now apparent that other metabolic abnormalities associate with cataractogenesis, including reductions in levels of amino acids, glutathione, and taurine. Here, we analyze the proteome and metabolome of mice expressing a mutant ubiquitin protein (K6W-Ub) to determine the molecular mechanisms underlying formation of its congenital cataract.

Methods: C57BL/6J wild-type or cataractous K6W-Ub transgenic mouse lenses were dissected at E15.5, P1, or P30 and proteins were analyzed via MS-based tandem-mass-tag (TMT) quantitative proteomics. Small molecules were spatially quantified using computational molecular phenotyping (CMP), a tool that enables acquisition of free amino acid fingerprints for every cell in the lens. Validation of proteomics findings was also performed using Western blot analysis and immunohistochemistry.

Results: Proteomic analyses revealed pathways that were altered during lens differentiation, by expression of K6W-Ub, or both. Prominent pathways included glutathione metabolism; glycolysis/gluconeogenesis; and glycine, serine, and threonine metabolism. Within the glutathione metabolism pathway, GSTP1 and GGCT were most strongly downregulated by K6W-Ub. Other consistently downregulated proteins were PGAM2, GAMT, and HMOX1. Proteins that were upregulated by K6W-Ub expression belonged to pathways related to lysosome, autophagy, Alzheimer's disease, and glycolysis/gluconeogenesis. Analysis of the metabolome via CMP revealed statistically significant decreases in taurine and glutathione and smaller decreases in glutamate, glutamine, aspartate, and valine in all ages of K6W-Ub lenses. Lens metabolites were spatially altered in the cataractous K6W-Ub lens.

Conclusions: K6W-Ub expressing lenses replicate many congenital cataract phenotypes and are useful disease models. The large reductions in levels of taurine and glutathione may be general signatures of cataract development, as human cataracts also have reduced glutathione and taurine. Key roles for amino acid metabolism and glycolysis/gluconeogenesis in cataractogenesis are emerging. Together our data point toward potential common metabolic/proteomic signatures of cataracts.

CONTROL ID: 3713254

SUBMITTER (NAME ONLY): Kristy Lee

TITLE: Optimizing Variant Curation Guidelines to Improve Clinical Genetic Testing for RPE65 Retinopathies Utilizing the ClinGen Framework

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Lee, J. Ross, W. Hankey, Genetics, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, UNITED STATES|A.R. Webster, UCL Institute of Ophthalmology, London, UNITED KINGDOM|L.S. Sullivan, Human Genetics Center, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|J.L. Duncan, University of California San Francisco, San Francisco, California, UNITED STATES|R. Ayyagari, Shiley Eye Institute, University of San Diego, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic testing for RPE65 retinopathies is critical to providing access to potentially sight preserving gene therapy to qualifying patients. Limiting the number of variants of uncertain significance (VUS) and increasing the number of accurately curated variants in public databases is vitally important to ensure that all patients who could potentially benefit from this clinical therapy are appropriately identified.

Methods: In 2015, the American College of Medical Genetics and Association for Molecular Pathology (ACMG/AMP) developed a framework to assess variant pathogenicity; however, the guidelines were written broadly. The Clinical Genome Resource (ClinGen), funded by the National Human Genome Research Institute, convened the Leber Congenital Amaurosis (LCA)/Early-onset Retinal Dystrophy Variant Curation Expert Panel (LCA VCEP) in July 2020 to develop rule specifications for curating variants in the REP65 gene through their Federatal Drug Administration approved process.

The LCA VCEP members meet monthly to specify ACMG-AMP rules, initially for the RPE65 gene, and to discuss resulting variant assertions. There are plans to expand this work to additional genes starting with GUCY2D, AIPL1 and CEP290 once rule specifications for the RPE65 gene are completed. Each rule was assessed for its appropriateness for the RPE65 gene and whether there would be any benefit to adding detailed criteria for its use and/or modifying its strength based on availability of evidence.

Results: Variant curation specifications were applied to 19 ACMG-AMP rule criteria and 9 rules were deemed not applicable to the RPE65 gene. Criteria modifications included setting allele frequencies in normal controls, defining phenotype criteria and conditions for adjusting rule strength. Fifty RPE65 variants were chosen for a pilot study to test the rule specifications, comprising of 20 pathogenic/likely pathogenic, 15 VUS and 15 benign/likely benign variants.

Conclusions: Results of this effort will aid clinical variant interpretation of the RPE65 gene and help standardize variant curations across laboratories. Expert level variant curation from this VCEP will be deposited in the ClinVar database for public access.

CONTROL ID: 3713257

SUBMITTER (NAME ONLY): David Monroy

TITLE: CONJUNCTIVAL KERATOACANTHOMA: A CLINICAL AND HISTOPATHOLOGICAL CASE SERIES

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Monroy, M. Zein, N. Venkateswaran, J. Matthews, P. Monsalve, A. Quann, A. Galor, G. Elgart, C.L. Karp, S.R. Dubovy, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conjunctival keratoacanthomas are rare, low-grade, hyperkeratotic crateriform tumors. The purpose of this study was to investigate the clinical, histopathological, immunohistochemical, and diagnostic imaging results that define conjunctival keratoacanthomas.

Methods: Retrospective chart reviews of 8 patients with pathologically confirmed conjunctival keratoacanthomas were performed. The demographics, clinical history, diagnostic testing (slit-lamp photography, high-resolution anterior segment optical coherence tomography, and high-resolution ultrasound biomicroscopy images), treatment modalities, histopathology, immunohistochemical testing, visual outcomes, and recurrences were extracted after identifying the patients in a database search of the Florida Lions Ocular Pathology Laboratory records.

Results: The mean age of the 8 identified patients was 54.5 years + 22.4 years. 75% (6/8) of patients were male and 62.5% (5/8) were of Hispanic ethnicity. All lesions were rapidly growing, white nodular lesions located on the bulbar conjunctiva located in the interpalpebral exposure zone. All lesions were surgically excised, and two underwent partial spontaneous resolution prior to surgery. No cases recurred at up to one year of follow-up. A prominent keratin-filled cup-shaped lesion with faulty maturational sequencing that extended full thickness with variably pale cytoplasm and foci of dyskeratosis and hyperkeratosis was present on histopathology in all cases. Hyper-reflective, thickened epithelium often overlying disorganized subepithelial tissue was seen on high-resolution anterior segment optical coherence tomography.

Conclusions: Conjunctival keratoacanthomas are rare lesions of the ocular surface with distinct clinical, histopathologic, and diagnostic features. Further research is required to better understand the clinical course and optimal treatment approach of this rare condition.

CONTROL ID: 3713258

SUBMITTER (NAME ONLY): Sandrine Zweifel

TITLE: Assessing choroidal nevi, melanomas and indeterminate melanocytic lesions using multimodal imaging – a retrospective chart review

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zweifel, S. Said, A. Bajka, M. Toro, M. Wiest, D. Barthelmes, M. Stahel, Ophthalmology, UniversitatsSpital Zurich, Zurich, SWITZERLAND|S. Zweifel, F. Geiger, D. Barthelmes, Universitat Zurich, Zurich, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Using multimodal imaging, literature proposed the following risk factors for choroidal nevus growth into melanoma: increased tumor thickness, subretinal fluid, decreased visual acuity, presence of orange pigment, ultrasound acoustic hollowness, and increased tumor diameter. This study investigated the presence of mentioned risk factors in choroidal nevi, choroidal melanomas, and indeterminate choroidal melanocytic lesions.

Methods: This retrospective, single-center chart review assessed choroidal melanocytic tumors with multimodal imaging. We defined our primary outcome as the cumulative presence of mentioned risk factors. Further, we evaluated various optical coherence tomography (OCT), ultrasound, and autofluorescence findings. Finally, we examined the electronic charts for any tumor-targeted therapeutic actions and tumor-related complications such as secondary choroidal neovascularization, accompanying retinal detachment, toxic tumor syndrome, or any form of metastases.

Results: We analyzed 51 tumors from 49 patients during the period from April 2008 to June 2021. Reviewing the diagnoses made in our archived consultation reports, we found 58.8% (30 of 51) choroidal nevi, 23.5% (12 of 51) choroidal melanomas, and 17.6% (9 of 51) indeterminate choroidal melanocytic lesions. During the entire observation period, no choroidal nevus and no indeterminate choroidal melanocytic lesion transformed into a choroidal melanoma. The median (IQR) age was 64.0 (56.0 to 70.5) years, with 23 of 49 (46.9%) patients being female. The follow-up time for all tumors was median (IQR) 25.0 (12.0 to 39.0) months. The choroidal nevi had a median (range) risk score of 0.0 (0.0 to 3.0), and the choroidal melanoma of 5.0 (3.0 to 6.0), with statistically significant different ratings ($p < 0.001$). Figure 1 shows an example tumor of an indeterminate choroidal melanocytic lesion with two risk factors present.

Conclusions: Multimodal imaging with fundus photography, OCT, autofluorescence, and ultrasonography, along with visual acuity assessment, creates a score that may help to distinguish choroidal nevi from melanomas objectively. Future studies should re-evaluate the above risk score using a larger study population.

CONTROL ID: 3713263

SUBMITTER (NAME ONLY): Vilas Wagh

TITLE: AMD in a dish: a novel platform based on sub-RPE deposit formation

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Wagh, Q. Hou, S. Farmer, C. Fox, V. Peterson, Genome and Biomarker Sciences, Merck Research Laboratories Boston, Boston, Massachusetts, UNITED STATES|K. Spencer, Discovery Chemistry, Merck Research Laboratories Boston, Boston, Massachusetts, UNITED STATES|A. Ogawa, Discovery Chemistry, South San Francisco Discovery Hub, South San Francisco, California, UNITED STATES|K. Bekkari, Genome and Biomarker Sciences, Merck Research Laboratories, Kenilworth, New Jersey, UNITED STATES|G. Addona, Quantitative Biology, Merck Research Laboratories Boston, Boston, Massachusetts, UNITED STATES|J. Nussbaum, Translational Medicine, South San Francisco Discovery Hub, South San Francisco, California, UNITED STATES|U. Lim, A.Z. Fernandis, Genome and Biomarker Sciences, MSD Singapore, Singapore, SINGAPORE|J. Lao, H. Qin, A. Chawla, A. Loktev, Cardiometabolic Disease Therapeutic Area, South San Francisco Discovery Hub, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly worldwide and it is estimated that nearly 300 million people will have advanced AMD with vision loss by 2040. No effective treatment exists for halting dry AMD progression, the form which affects 90% of all AMD patients. Early AMD is characterized by the presence of drusen, a protein-and lipid-rich deposits formed under Retinal Pigmented Epithelium (RPE) cell monolayer, or sub-RPE deposits. Efforts to understand how sub-RPE deposits, complement dysregulation and immune-cell recruitment contribute to AMD have been limited by the lack of relevant (age-dependent / cell-type-specific) models that faithfully recapitulate these pathogenic aspects of the disease.

Methods: Here, we describe a an in vitro AMD model based on isogenic RPE cell lines harboring a Fibulin-3 gene mutation that causes inherited macular degeneration with phenotypic similarities to AMD.

Results: Mutant RPEs secreted dense sub-RPE deposits after four-weeks of culture. Proteomic analysis of sub-RPE deposits showed striking similarity with protein composition of human drusen from AMD patients. Treating the cells with complement C3 inhibitor reversed of the phenotype.

Conclusions: These observations demonstrate that the model has pathophysiological relevance for AMD, allowing in vitro validation of drug targets and elucidation of molecular mechanisms underlying AMD pathogenesis.

CONTROL ID: 3713265

SUBMITTER (NAME ONLY): Brian Hafler

TITLE: Topological analysis of single-cell hierarchy reveals inflammatory glial landscape of macular degeneration

SESSION TITLE: Single cell analysis in retinal research in health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.P. Hafler, E. Song, M. Ige, A. Sheth, Y. Xing, G. Mourgkos, R. Dhodapkar, Ophthalmology, Yale University, New Haven, Connecticut, UNITED STATES|M. Kuchroo, Department of Neuroscience, Yale University, New Haven, Connecticut, UNITED STATES|M. DiStasio, Department of Pathology, Yale University, New Haven, Connecticut, UNITED STATES|L. Zhang, Department of Neurology, Yale University, New Haven, Connecticut, UNITED STATES|M. Menon, The University of Manchester, Manchester, UNITED KINGDOM|A. Tong, S. Gigante, J. Huang, S. Krishnaswamy, Computer Science, Yale University, New Haven, Connecticut, UNITED STATES|G. Wolf, Department of Mathematics and Statistics,, Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a neurodegenerative disease that is among the leading causes of blindness worldwide. The molecular pathways that lead to chronic inflammation and vision loss in AMD are not well understood. Our hypothesis is that functional changes in glia influence neurodegeneration in AMD, and these changes may be targeted to halt disease progression and preserve vision.

Methods: To identify cell populations that drive AMD progression, we isolated frozen retinal nuclei from the macula of lesion and non-lesion control samples and performed single-nucleus RNA-sequencing on 11 AMD tissue samples and 6 control tissue samples, creating the first single-cell dataset of AMD pathology. We used a suite of computational tools based on topological data analysis and data diffusion geometry to identify salient levels of the hierarchy, automatically characterize clusters, identify pathogenic populations, and rapidly compute differentially expressed genes between clusters of interest.

Results: We identified two populations of activated glia enriched in the nonexudative form of AMD, one microglial subset and one astrocyte subset. Applying our single cell dataset to other degenerative diseases revealed the same activated glial states in Alzheimer's disease and multiple sclerosis, indicating a common glial signature during neurodegeneration. In neovascular AMD, we identified a microglia-to-astrocyte signaling axis driving VEGFA expression and angiogenesis characteristic of disease pathogenesis. We validated this mechanism using in vitro and in vivo assays, identifying a possible new therapeutic target for AMD.

Conclusions: We apply our computational framework to a new dataset: the first single-cell transcriptomic atlas of AMD across disease stages. The algorithm identified and characterized specific subpopulations of microglia and astrocytes enriched in nonexudative AMD displaying activation signatures related to phagocytosis, lipid metabolism, and lysosomal function. This set of analyses has clear implications for potential therapeutics for AMD. Currently, anti-VEGF therapy is the primary intervention approved to treat AMD and is only effective in the most advanced stage of disease. Our unbiased topological analysis not only identified the cell-type specificity of VEGFA expression but also identified pathogenic signaling interactions that promote AMD disease progression.

CONTROL ID: 3713266

SUBMITTER (NAME ONLY): Farzad Pakdel

TITLE: CT-Scan Guided Intra-orbital Amphotericin Injection in COVID-19-associated Mucormycosis, a pilot study

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A high incidence of sinu-orbital Mucormycosis as a fulminant and opportunistic fungal infection happened following the COVID-19 pandemic. Traditionally, patients with apical or extensive orbital involvement are candidates for exenteration. We designed and applied CT scan guided orbital amphotericin C delivery. In this study we aimed to report this novel technique and results of this method in control of orbital mucormycosis with apical involvement.

Methods: A high incidence of sinu-orbital Mucormycosis as a fulminant and opportunistic fungal infection happened following the COVID-19 pandemic. Thus named as CAM. Traditionally, patients with orbital mucormycosis with apical or extensive involvement are considered hopeless for saving the eye. We designed and applied CT scan guided orbital amphotericin C delivery.

Results: A total of thirty patients with mean age of 52±11.86 were enrolled in this study. Twenty-three (76.7%) patients were male; group A: 11 (73.3%) and B: 12 (80%). The majority of the patients in both group were diabetics (A: 10 (66.7%), B: 10 (76.9%)). Most patients in both groups had received corticosteroids and antiviral therapy for their recent COVID-19, 23 (82.1%) and 25 (89.3%), respectively. No patient in group A underwent exenteration. Eleven (78.6%) patients in group B underwent orbital exenteration. Of the 6 expired patients, 5 (83.3%) were in group B ($P<0.0001$). Peri-orbital ecchymosis and intracranial air extension were observed in 2 (13.3%) and 1 (6.7%) in group A patients, respectively.

Conclusions: Intra-orbital amphotericin injection under CT-guidance can be considered as a highly effective method in patients with orbital mucormycosis. This method may decrease exenteration without increasing mortality of patients.

CONTROL ID: 3713268

SUBMITTER (NAME ONLY): Alicia Donahue

TITLE: Level of Agreement of Pelli-Robson and SpotChecks Contrast Sensitivity Tests in Seniors with Visual Impairment

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Donahue, A.G. Malkin, M. Knizak, B. Peterson, C. Idman-Rait, J.K. Ho, N. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|A.K. Bittner, M. Chun, M. Estabrook, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Testing for contrast sensitivity (CS) loss is valuable given its impact on visually-mediated tasks and to monitor ocular disease progression. The Pelli-Robson (PR)(a gold standard CS test) requires an in-person visit and that patients know the English alphabet. The SpotChecks (SC) CS test does not require this and may be feasible to complete remotely. SC has not been widely evaluated in people with visual impairment (VI). We evaluated the agreement between CS measurements on the PR and SC charts across a range of VI levels.

Methods: Better-eye distance visual acuity (VA) and binocular logCS measurements with the PR and SC tests were obtained using standard protocols in 25 subjects with VI due to various ocular diseases (mean age 70 years; range 55-89) enrolled in the Community Access Through Remote Eyesight (CARE) study. 95% limits of agreement (LoA; +/-1.96xSD) between the PR and SC tests were assessed according to subgroups for VA and age.

Results: As expected, the SC test overestimated logCS across all subjects when compared to the PR test since SC does not require optotype discrimination. Mean differences in logCS between tests were -0.16 (95% LoA:-0.64,+0.35; p=0.01) for VA <0.55 logMAR (n=13) and -0.12 (95% LoA:-0.43,+0.24; p=0.004) for VA 0.55-1.00 logMAR (n=7), these between-test differences were significant. For 5 subjects with VA >1.0 logMAR, the mean difference of -0.45 and LoA were larger (95% LoA:-1.31,+0.41; p=0.03). Mean differences between CS tests also increased significantly with age. The mean difference was -0.12 logCS (95% LoA:-0.40,+0.15; p=0.01) for ages 55-65 years (n=9), -0.20 (95% LoA:-0.80,+0.38; p=0.04) for ages 66-75 (n=8), and -0.25 (95% LoA:-1.10,+0.59; p=0.05) for ages 77+ (n=8). Age and VA were not significantly related (p=0.78).

Conclusions: The LoA between the PR and SC tests were largest in those with severe VI or the oldest subjects with VI. The 95% LoA between the PR and SC tests in all VI groups were larger than those of normally-sighted young adults in prior literature, reported as −0.24 to 0.09 right eye and −0.23 to 0.14 left eye. SC could be valuable in remote assessment and in patients with language barriers, illiteracy and aphasia, but SC results are not comparable to the PR. Future directions include evaluation in a larger sample (enrollment ongoing), assessment of test-retest repeatability and examining differences by ocular diagnosis.

CONTROL ID: 3713269

SUBMITTER (NAME ONLY): Hayette Rebika

TITLE: A comparative pharmacokinetics study of 3 Latanoprost eyedrops solutions containing various excipients in an animal model

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Rebika, L. Chauchat, C. Guerin, Horus Pharma, FRANCE|T. Amar, K. Viaud-Quentric, Iris Pharma, La Gaude, FRANCE|H. Rebika, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, FRANCE|

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ABSTRACT BODY:

Purpose: Benzalkonium chloride (BAC), the most common preservative used in anti-glaucoma eyedrops, has been described in the literature as increasing prostaglandin corneal penetration but to date, this fact seems to be controversial. In addition, surfactants may play a role in lipophilic agent solubilization and could, therefore, influence active substance (AS) penetration. The purpose of the study was to evaluate the role of formulation on the AS bioavailability by assessing the pharmacokinetics (PK) profile of different latanoprost eyedrops solutions on a rabbit model.

Methods: 3 different formulations of 0.005% Latanoprost were tested: A. preservative-free (PF) and surfactant-free (SF) formulation; B. same SF formulation but containing BAC 0.02%; and C. different PF formulation but containing Macrogolglycerol hydroxystearate 40 (MGHS 40) at 5%. The ocular concentration of Latanoprost free acid (LAT) was monitored according to GLP standards in 3 parallel groups of Dutch Belted rabbit following a single ocular administration of each tested items in the right eye (n=6). Aqueous humor (AH) and iris-ciliary body (ICB) samples were collected at the following timepoints: 0.5h, 1h, 2h, 3h, 4h, 8h, 24h post-dose. LAT concentrations were measured by RRLC-MS/MS validated method; statistical analysis (Fisher LSD) was performed. PK parameters (AUC, C_{max}, T_{max}, $t_{1/2}$) were calculated.

Results: In both AH and ICB, the concentration of LAT was statistically not different for A and B at each timepoint, except for t1h in ICB ($p=0.005$). However, LAT behavior in C was statistically inferior to A and B in AH and ICB from t30min to t3h ($p<0.05$). In terms of AUC, A (521 ng/mL.h; 300 ng/g.h) and B (470 ng/mL.h; 269 ng/g.h) were at least 2 times higher than C (210 ng/mL.h; 97 ng/g.h) in both AH and ICB respectively. C_{max} follow the same ratio for A and B vs C. T_{max} was 2h in AH and between 0.5 to 1h in ICB.

Conclusions: The absence or presence of BAC within the formulations A and B did not influence the PK profile as a similar behavior in LAT concentrations is described all over the study duration. Therefore, BAC for penetration purposes is no longer justified. However, these in vivo PK results highlighted the importance of formulation as a significantly lower absorption in AH and ICB is measured for the C formulation. This may be due to the presence of MGHS 40 which could be a matter of questioning.

CONTROL ID: 3713272

SUBMITTER (NAME ONLY): Sudan Puri

TITLE: Stimulation of Trigeminal Ganglion Neurons by Capsaicin Affects Corneal Leukocyte Migration Via Alterations in Neuropeptide Expression

SESSION TITLE: Corneal cell and molecular biology | Corneal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Puri, B. Kenyon, V.G. Sendra, D.L. Harris, P. Hamrah, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal nerves and resident leukocytes are closely associated, and we have previously demonstrated that trigeminal ganglion (TG) neurons express various chemotactic neuropeptides/chemokines. The purpose of this study was to characterize alterations in neuropeptide expression in the TG and their subsequent effect on migration of leukocytes following capsaicin stimulation.

Methods: We investigated if stimulation of TG neurons with capsaicin altered the expression of chemotactic molecules and affect the migration of leukocytes. To study the effect of capsaicin (30nM or 1mM) added to the culture media of TG neurons, mRNA and protein levels of neuropeptides were assessed in cultured TG neurons and media via RT-qPCR and ELISA. For the leukocyte migration assay, TG neurons with or without capsaicin treatment were co-cultured with splenic plasmacytoid dendritic cells (pDCs) isolated from pDC-GFP mice in a modified Boyden chamber, using transwell inserts with 5mm pore size.

Results: Capsaicin treatment of the TG neurons reduced the mRNA expression of neuropeptides Substance P (2.07-fold decrease), CGRP (3.09-fold decrease), and Somatostatin (1.60-fold decrease) compared to vehicle controls ($p<0.05$) and no change in Urocortin expression ($p>0.05$). The respective protein level was also significantly lower in the culture media of TG neurons treated with capsaicin compared to untreated TG neuron controls (Substance P ELISA, $p<0.05$). TG neurons treated with capsaicin and co-cultured in the modified Boyden chamber with pDCs in the transwell had less pDCs migrating through the transwell membrane after 24 hours incubation period, compared to untreated TG neurons co-culture (3.78-fold decrease; $p<0.05$).

Conclusions: Corneal nerves and resident corneal leukocytes share expression of neuropeptides and their respective receptors, suggesting a potential crosstalk. TG neurons exert chemotactic effects on leukocytes via neuropeptides and changes in expression levels of neuropeptides in the TG neurons following capsaicin stimulation affects the migration of leukocytes.

CONTROL ID: 3713274

SUBMITTER (NAME ONLY): Laura Whelan

TITLE: A nonsense variant in PEX5 is associated with an atypical peroxisome biogenesis disorder and retinitis pigmentosa.

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Whelan, A. Dockery, C. Shortall, P.F. Kenna, G. Farrar, The Smutfit Institute of Genetics, The School of Genetics and Microbiology, The University of Dublin Trinity College, Dublin, IRELAND|A. Dockery, Next Generation Sequencing Laboratory, Pathology Department, Mater Misericordiae University Hospital, Dublin, IRELAND|E. Duignan, P.F. Kenna, Department of Ophthalmology, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|S. Roosing, Department of Human Genetics and Donders Institute for Brain, Cognition and Behaviour, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: This study aimed to provide a genetic diagnosis for patients presenting with a mild peroxisome biogenesis disorder (PBD). Peroxisomes play a vital role in a variety of metabolic processes including β-oxidation of fatty acids and glyoxylate detoxification. Pathogenic variants in 13 PEX genes have been associated with PBDs. Clinical features vary but can include failure to thrive, developmental delay, retinal degeneration and liver disease. PEX5 encodes a peroxisomal import receptor protein and two isoforms exist in humans: PEX5S and PEX5L, the latter contains an additional exon.

Methods: Two affected siblings were recruited to the Target 5000 inherited retinal disease (IRD) study following a clinical diagnosis of PBD with retinitis pigmentosa. An unaffected sibling was also recruited. Targeted sequencing of the exons of 254 IRD genes was carried out on one affected sibling. Subsequently whole genome sequencing (WGS) was employed on the same individual as a more comprehensive sequencing measure.

Results: At last examination the patients were in their 8^{th} and 9^{th} decades of life. Following targeted sequencing no candidate variants were detected. WGS revealed a homozygous nonsense variant in PEX5, c.709C>T, p.(Arg237Ter), situated in the exon specific to PEX5L, leaving PEX5S unperturbed at the DNA level. This variant was present homozygously in both affected siblings while the unaffected sibling was homozygous for the wild-type base at this position. Pathogenic variants in PEX5 are typically associated with phenotypically severe PBDs. These patients did not display classical symptoms associated with a PEX5 defect including reduced life expectancy, epilepsy, growth delay or intellectual disability.

Conclusions: To the best of our knowledge, this is the first report of a significantly milder form of PBD than typically associated with PEX5 defects suggesting that the severity of the phenotype depends on the location of the given variant. Awareness of this unusual clinical presentation will allow for a more targeted diagnostic approach. This study highlights the value of WGS over targeted sequencing, where only the former was informative in terms of disease pathogenesis. The findings also underscore the importance of interrogating genes typically associated with more severe forms of disease even when the clinical presentation is relatively mild by comparison.

CONTROL ID: 3713276

SUBMITTER (NAME ONLY): Kumar Sambhav

TITLE: Implementation of Quality Improvement Measures For Inpatient Consults Improves Follow-up In Eye Clinic

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sambhav, D. Zhang, R. Michael, J. Hunt, M. Epps, S. Wetzstein, D. WuDunn, S. Grover, Ophthalmology, University of Florida Health Science Center Jacksonville, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients seen as inpatient consults are generally followed up in the eye clinics at some point in the future. This study was conducted to identify causes that reduce the follow-up rate of inpatient consults and analyze data before and after implementation of intervention to determine the quality improvement.

Methods: In this Department of Ophthalmology, starting July 1st 2021, certain interventions were implemented in order to improve the follow-up rate in the clinic. This included more robust communication with the in-patient and providing them with a clinic appointment at bedside along with a clinic contact number, more objective communication with the staff via e-mail regarding the date and time of appointment which would then be entered into the electronic medical records (EMR). This study analyzed the effect on quality improvement before and after the implementation of these measures. This IRB-approved study adhered to the tenets of the Declaration of Helsinki. Retrospectively, the pre-intervention data were collected and analyzed for a 3-month period between April – June 2020. The post-intervention data were analyzed for a one-year period between July 2020 – June 2021.

Results: In the pre-intervention period of 3 months, 46 inpatient consults were seen. Of these patients, 26 (56.5%) were seen for follow-up, 13 (28.3%) did not show for their initial follow-up and 7 (15.2%) patients did not have follow-up appointments in the EMR system.

After implementation of corrective measures, 348 inpatient consults were seen in a one-year period. Of these, 7 patients (2%) were referred to an outside facility. Of the remaining 341 patients tracked, only 30 patients (8.8%) did not have a follow-up in the EMR system. Thirty five patients had an appointment in the system after the cut-off date for analysis. Of the remaining 306 patients, 180 (58.8%) were seen as follow-up in the clinic and 96 patients (31.4%) did not show up.

Conclusions: There was a definite improvement in the number of patients seen as follow-up, the no-show rate remained similar to the University average no-show rate but there was a significant improvement in the number of patients who did not have a follow-up appointment. Implementation of these measures improved the quality of care and continuity of care provided to these patients.

CONTROL ID: 3713277

SUBMITTER (NAME ONLY): Emese Kanyo

TITLE: Comparative Assessment of Fully-Automated Machine Learning Enabled Fluid Feature Extraction to Expert-Reader Interpreted Fluid Segmentation in Diabetic Macular Edema and the Importance of Image Quality Stratification

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kanyo, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S. Yordi, H. Cetin, J. Whitney, L. Lunasco, K.E. Talcott, J. Reese, S.K. Srivastava, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optimization of deep learning models for fluid feature extraction to enable reader-independent assessment of fluid presence and characteristics in retinal disease is an important milestone for automated image processing. This analysis aims to compare a next generation fully automated deep learning model for fluid segmentation against human generated output in diabetic macular edema (DME).

Methods: This was a retrospective assessment of eyes with DME undergoing treatment with anti-VEGF therapy. All eyes had concurrent SD-OCT scans. All scans were initially analyzed with an earlier generation intraretinal fluid (IRF) segmentation system with subsequent expert reader manual correction, as needed. A next generation fluid segmentation model with enhanced sensitivity and specificity was evaluated with automated volumetric outputs and compared to reader-edited findings. An automated SD-OCT quality assessment system was used to stratify scan quality as “good”, “moderate”, and “poor” for image quality-based assessment of performance.

Results: A total of 1572 OCT scans were included in this analysis.The model correctly identified the presence or absence of IRF in 96% of the scans. Scans identified as “good” quality demonstrated significantly closer volumetric agreement to expert readers than “moderate” and “poor” quality scans ($p<0.001$).

Conclusions: This fully automated fluid model demonstrated overall strong agreement with human edited fluid segmentation. Image quality appears to have an important impact on agreement between automated and manually-edited results. Future assessments will include using the next generation system as foundational starting-point for expert reader corrections for future comparisons and assessing minimum quality standards for automated image analysis platforms.

CONTROL ID: 3713279

SUBMITTER (NAME ONLY): Stephanie Cox

TITLE: Ocular Surface Disease Patients with Microneuromas also have Reduced Nerves

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Cox, B. Bayraktutar, A. de Leeuw, G. Dieckmann, P. Hamrah, Department of Ophthalmology, Center for Translational Ocular Immunology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|S. Cox, B. Bayraktutar, A. de Leeuw, G. Dieckmann, P. Hamrah, Cornea Service, New England Eye Center, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The presence of microneuromas within the subbasal nerve plexus as identified via corneal in vivo confocal microscopy (IVCM) has been associated with corneal neuropathy, including with neuropathic corneal pain. However, the association of microneuromas with other nerve and immune cell parameters has not been established.

Methods: This is a secondary analysis of a retrospective study that involved the collection of IVCM images from ocular surface disease patients. All IVCM images were viewed by the grader, and presence or absence of microneuromas was determined for each patient based on all images. In addition, three representative images from the subbasal nerve plexus were selected for each patient. ImageJ with NeuronJ plug in was used to quantify each selected image for the total, main, and branch nerve densities and count. The results from these three images were averaged. In addition the number of immune cells were counted for each image and averaged. Patients with microneuromas were compared to those without using t-test or Mann-Whitney U test as appropriate.

Results: The patients showed an average of age of 58.3 ± 1.6 years and 76.2% were female. Compared to the non-microneuroma group (NMG), the microneuroma group (MG) had a lower average total density [11,995.28 μm/mm^2 (range: 3,580.00-14,173.55) vs 13,806.47 (range: 0.00-26,158.00); p=0.012], average total nerve number [6.7/frame (range: 1.7-10.3) vs 8.7 (range: 0.0-23.3); p=0.014], average branch nerve density [3,082.49 μm/mm^2 (range: 0.00-7,205.11) vs 4,553.88 (range: 0.00-14,601.73), p = 0.044] and average branch number [3.3/frame (range: 0.0-8.0) vs 5.0 (range: 0.0-19.3), p=0.024]. There was no significant difference in main nerve density (7,054.33 ± 541.44 μm/mm^2 for MG; 8,373.31 ± 271.68 for NG; p=0.070), main nerve number (2.9 ± 0.3/frame for MG; 3.5 ± 0.1 for NG; p=0.094), or immune cell density [14.6/mm^2 (range:0.0-175.0) for MG; 35.4 (range: 0.0-285.4) for NG; p=0.144].

Conclusions: Patients with microneuromas likely also have reduced nerve density, which is more apparent in branch nerves compared to main nerves, suggesting that patients with increased nerve loss have a higher likelihood of presenting with microneuromas.

CONTROL ID: 3713283

SUBMITTER (NAME ONLY): Vincent Yeung

TITLE: Corneal Myofibroblast Extracellular Vesicles Promotes Epithelial Corneal Wound Healing

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Yeung, L. Yuan, M. Parekh, A.E. Hutcheon, X. Guo, J.B. Ciolino, Department of Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Cortinas, E. Delavogia, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|T. Zhang, Independent Scholar, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Epithelial corneal wound healing is a multifaceted process that encompasses cell proliferation, migration, and communication from the corneal stroma. Upon corneal injury, bi-directional crosstalk between the epithelium and stroma via extracellular vesicles (EVs) has been reported. We previously demonstrated that human corneal epithelial cell (HCEC) EVs can promote corneal fibroblast (FB) to myofibroblast (MFB) differentiation; however, the mechanisms by which, corneal stromal EVs exert their effects on the corneal epithelium remains unclear. Here, we investigated the roles of corneal stromal (keratocyte (KER), FB, and MFB) EVs in epithelial corneal wound healing.

Methods: EVs were isolated from corneal KER, FB, and MFB conditioned media by using differential ultracentrifugation and characterized by western blotting (WB), transmission electron microscopy (TEM), Zetaview™ nanoparticle tracking analysis (NTA) and Zeta (ζ) potential. The HCEC's migratory ability and cell velocity following PKH26-labelled KER-/FB-/MFB-EV treatment was assessed in a scratch assay and determined by brightfield/immunofluorescent microscopy. HCEC's viability, proliferative and apoptotic activity following EV treatment was also assessed by a WST-8 and a Caspase-Glo® 3/7 assay. KER-/FB-/MFB-EV protein cargo was determined by mass spectrometry and ingenuity pathway analysis.

Results: WB revealed that FB-/MFB-EVs were enriched for CD63, CD81, INTGNAV and THBS1 compared to KER-EV, whilst all EVs were negative for GM130 as a negative control. All EVs showed minimal differences in biophysical properties (NTA, TEM and ζ-potential). MFB-EVs significantly increased HCEC migration and cell velocity in our scratch assay compared to KER-/FB-EVs and untreated controls. MFB-EV treatment elevated HCEC proliferation and lowered apoptosis levels compared to KER-/FB-EVs. At the proteomic level, we observed the MFB-EV protein cargo showed a >2-fold change in CXCL12, MMP1, COL6A1/-2/-3, TGFBI and EFEMP1 compared to KER-/FB-EVs; with other proteins unique to KER-/FB-EVs.

Conclusions: These findings highlight that MFB-EVs contains a unique protein cargo that promotes HCEC-migration, cell velocity, and proliferation compared to KER-/FB-EVs. Understanding these elements may offer novel modalities to accelerate epithelial corneal wound healing and future studies in promoting scarless-wound healing.

CONTROL ID: 3713287

SUBMITTER (NAME ONLY): Liangyu Zhou

TITLE: Near-infrared and eye tear triggered biocidal corneal bandage for bacterial keratitis therapy

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zhou, Y. Chen, Y. Chan, Department of Ophthalmology, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, Hong Kong, HONG KONG|Y. Deng, School of Chemical Engineering, Sichuan University, Chengdu, Sichuan, CHINA|

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ABSTRACT BODY:

Purpose: Antibiotics as the conventional treatment option for bacterial keratitis has raised the problems such as antimicrobial resistance and allergy, and these problems promoted innovation of alternatives for antibiotics. We designed an antibiotics-free biocidal corneal bandage with photo-sensitive nanocomposites embedded in enzyme-modified hydrogel. Nanocomposites and enzyme produce reactive oxygen species (ROS) to disinfect bacteria. The nanocomposites release ROS under near-infrared light (NIR) irradiation, and the enzyme in hydrogel produces ROS by catalyzing glucose in eye tear.

Methods: The generation of ROS was characterized using colorimetric analysis, and dyes that can react with ROS were used as the indicators. The antibacterial property of the bandage against Staphylococcus aureus (S. aureus) and Pseudomonas aeruginosa (P. Aeruginosa) suspended in medium was compared with the blank control group through spread plate method (N=3), Live/dead staining (N=3). The morphology of bacteria was examined by scanning electron microscopy (SEM). The ROS level in bacteria after treated by the bandage under NIR irradiation was also evaluated with DCFH-DA.

Results: Dyes were oxidized after treated with bandage under NIR irradiation, and the enzymes on the bandage could also oxidize dye in darkness in the presence of glucose. The living colonies decreased significantly to (52+/-2)% (S. aureus) and (27+/-2)% (P. aeruginosa) after treated by the bandage and NIR irradiation. The antibacterial rates from Live/dead staining were ((54+/-1)% to S. aureus and (83+/-2)% to P. aeruginosa). Severe damage on bacteria membrane and ROS signals were found only in bacteria that were treated by the bandage and NIR irradiation.

Conclusions: The catalysis of the dyes indicated that the biocidal corneal bandage produces adequate ROS in the presence of glucose with NIR irradiation. The decreasing of living colonies after treated by the bandage, indicated that our bandage has excellent antibacterial property. The in-vitro results suggested that our bandage has the potential to be a treatment alternative for bacterial keratitis, but further evaluations on ex-vivo and in-vivo models are required to justify its translational potential.

CONTROL ID: 3713288

SUBMITTER (NAME ONLY): Maria Parra

TITLE: Prevalence of retinopathy of prematurity in Colombia

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Parra, M. Hartnett, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|F. Arango, Universidad Autonoma de Bucaramanga, Bucaramanga, COLOMBIA|S. Granados, Universidad Javeriana de Cali, Cali, COLOMBIA|H. Rodriguez, Universidad Militar Nueva Granada, Bogota, COLOMBIA|

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ABSTRACT BODY:

Purpose: To describe the demographic and clinical and characteristics and risk factors of neonates with retinopathy of prematurity (ROP) detected in the ROP screening programs in Colombia

Methods: Cross-sectional analytical retrospective observational study. Records of neonates from Neonatal Intensive Care Units (NICU) were screened for ROP between 2015 and 2020. The screening criteria were: 32 or less gestational age (GA) in weeks or 1,500 grams or less of birth weight (BW). Indirect ophthalmoscopy was performed by retina specialists or pediatric ophthalmologists. The first examination was performed between the fourth and sixth weeks of life, with repeat examinations until retinal vascularization was complete. Eyes were graded for ROP severity based on the Classification International ROP (ICROP). A database was created in which demographic variables were recorded, maternal and neonatal risk factors, ROP classification and treatment.

Results: The records of 1,691 infants were reviewed and included 727 (43%) males and 94 (57%) females. Mean gestational age was 32.44 ± 2.6 weeks (range 24-39) and mean birth weight was 1,536 ± 404 grams (range 650-3,700). Mean postmenstrual age at the time of examination was 36.72 weeks (range 26-60). The mean gestational age of preterm infants with ROP was 28.66 ± 2.87 weeks (range 24-38); the mean birth weight was 1,230 ± 538 grams (range 650-2,100).

The proportion of ROP in less than 1,000 grams was 42.1%, and of them, 42.6% presented affection in zones I and II. The most frequent risk factors were sepsis and suplemmentary oxygen and 8.6% of neonates with ROP required surgical treatment.

Conclusions: The global prevalence of ROP was 17.5%, with a mean gestational age of 28.66 weeks and mean mean birth weigh of 1,230 grams.

CONTROL ID: 3713290

SUBMITTER (NAME ONLY): Hilde Rogeberg Pedersen

TITLE: Rod and cone dark adaptation in PAX6-associated aniridia

SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Pedersen, J. Stuart, T. Utheim, R.C. Baraas, National Center for Optics, Vision and Eye Care, Universitetet i Sorost-Norge, Kongsberg, Viken, NORWAY|E.S. Landsend, Ø.A. Utheim, T. Utheim, Department of Ophthalmology, Oslo Universitetssykehus, Oslo, NORWAY|

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ABSTRACT BODY:

Purpose: PAX6 mutations are associated with an underdeveloped macula, lower cone density and decreased cone-related visual function. How rod-related visual function and the retina are affected outside the macula is not known. We performed a cross-sectional study to measure dark adapted rod and cone sensitivity and association with retinal structure in congenital aniridia.

Methods: Dark-adaptation curves were measured after 5 minutes exposure to bright light in 25 participants with aniridia (8 males; 11–66 years) and 36 healthy controls of similar age with red (635 nm) and green (530 nm) 2° circular light stimuli presented at ~20 degrees temporal retinal eccentricity. A double-exponential model was fitted to each participant's responses to determine cone and rod thresholds over time. Thicknesses of the inner and outer retinal layers were measured from semi-automatically segmented spectral domain optical coherence tomography images of the macula in 20 of the aniridia patients and all the healthy controls. Examination of the anterior segment was performed to evaluate aniridia associated keratopathy (AAK, grade 0–3).

Results: Participants with aniridia had elevated thresholds for both the cone and the rod part of the dark-adaptation function compared with healthy age-matched controls [cone: −0.90±0.60 and −1.62±0.33 log cd/m^2, t(34.2)= -5.5, p<0.0001; rod: −3.62±0.65 and −4.26±0.29 log cd/m^2, t(30.7)= -4.6, p<0.0001, for aniridia and healthy controls, respectively]. The time to rod-cone break was similar between the aniridia and the control group (11.4±2.2 vs. 11.0±2.1 minutes, t(51)= -0.72, p=0.47). In aniridia, there was a significant correlation between foveal outer retinal layer thickness and final cone (r = -0.49, p=0.03) and rod (r = -0.45, p=0.03) threshold. The thresholds tended to be higher with more severe grades of AAK, but not significantly [H(2)=5.58, p=0.06 and H(2)=4.49, p=0.11 for cone and rod thresholds, respectively]. A multiple regression model indicated that foveal outer retinal layer thickness and age were the most important explanatory variables to predict both final cone threshold (r^2=0.38, p=0.016) and rod threshold (r^2=0.45, p=0.006) in aniridia when the AAK grade was 2 or less.

Conclusions: The results show that both rod and cone related function are affected and suggest that retinal changes in PAX6-associated aniridia are not confined to the central macula.

CONTROL ID: 3713291

SUBMITTER (NAME ONLY): Oliver Voecking

TITLE: Single cell transcriptome and gene knockout analysis reveals novel candidate genes with impact on anterior segment development

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Voecking, J.J. Smith, J.K. Famulski, Biology, University of Kentucky College of Arts and Sciences, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Periocular mesenchyme (POM) is a subgroup of neural crest cells, responsible for forming anterior structures, including the anterior segment (AS) of the eye. Despite the importance for the development of a healthy eye, molecular knowledge about this cell group is limited. The purpose of this study is to characterize genes involved in regulation of POM cells as they form the zebrafish AS. We employed scRNA analyses over the course of AS development to identify potential candidates and used CRISPR/Cas9 knockouts to analyze resulting phenotypes.

Methods: Larval eyes of transgenic zebrafish Tg(Foxc1b:GFP) and Tg(Lmx1b:GFP) were collected every 24 hours between 48hpf and 144hpf. GFP+ cells were isolated via FACS cell sorting and processed with the 10x genomics chromium single cell transcriptome kit. The subsequently resulting Illumina sequencing single cell transcriptomes were processed with the Cell Ranger pipeline. Analysis was done with the Cell Loupe Browser 5.0 and Monocle3. Gene expression was confirmed via in situ hybridization and gene function via Alt-R-CRISPR induced knockouts.

Results: Over 40,000 Foxc1b+ and Lmx1b+ cells from eyes only were collected. Transcriptome analyses showed that these cells were organized in re-occurring clusters during zebrafish anterior segment development. We identified and tracked clusters representing the iridocorneal angle (ICA) and the cornea. Our analysis revealed several genes associated within these clusters, including hgd, si:ch211-251b21.1, nusap1 and apoda1 with the cornea and ano9a, mdka, clu and zgc158463 with the ICA. Initial gene knockouts and drug treatments showed a crucial role in eye development for hgd and si:ch211-251b21.1. Specifically, the drug Nitisionone induced hgd inhibition, resulting in cloudy lenses and an overall maldeveloped eye morphology.

Conclusions: Our results provide the first single cell transcriptome atlas for AS development in zebrafish. Our efforts have identified several new genes previously not associated with AS development. Particularly, we have discovered that hgd and si:ch211-251b21.1 play roles in AS development. Ultimately, this type of approach is likely to advance potential for genetic screening of anterior segment related diseases and/or treatment of ocular diseases such as glaucoma.

CONTROL ID: 3713292

SUBMITTER (NAME ONLY): Amen Nigussie

TITLE: Incidence and risk factors for extremes in intraocular pressure after rhegmatogenous retinal detachment repair with pars plana vitrectomy.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nigussie, N. Ambati, O. Elghawy, J. Patrie MS, J. Bogaard MD, Y. Shildkrot MD, University of Virginia, Charlottesville, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acute drops and elevations in intraocular pressure are common post-surgical complications following rhegmatogenous retinal detachment (RRD) repairs. Predictors of acute intraocular hypertension (≥ 35mmHg) as well as hypotension (≤6mmHg) after RRD repair with pars plana vitrectomy (PPV) were evaluated. We tested the hypothesis that history of glaucoma, use of C3F8 and higher concentrations of expandable gases were responsible for extremes in IOP during postoperative day 1 (POD1) and postoperative week 1 (POW1). We designed a retrospective cohort study to assess these potential risk factors.

Methods: A chart review of 754 patients undergoing RRD repair at the University of Virginia between July 1, 2012 and July 1, 2020 was conducted. All cases of PPV with completed postoperative day POD1 and POW1 visits were included. 178 eyes of 178 patients met the inclusion criteria for this study. Demographics, past medical history, ocular history, surgical and postoperative notes were reviewed. Additionally, data was gathered to compare different tamponades (C3F8 vs SF6 vs silicon oil) utilized during surgery.

Results: 16 (9%) cases had IOP elevation on POD1 and 14 cases (7.9%) on POW1. Out of those 14 patients, 12 (85.7%) did not present with elevated IOP during their POD1 visit. We did not find a significant relationship between acute elevation in postoperative IOP and type of tamponade. There was an association with history of glaucoma and increased IOP only during POW1, but it was not statistically significant (P=0.076). 8 patients (4.5%) experienced hypotony during POD1 and 13 cases (7.3%) on POW1. Silicon oil and SF6 tamponade were positively associated with postoperative hypotony on both POD1 (P=0.037) and POW1 (P<0.001). However, we did not find correlations between fill concentrations and acute drops in IOP.

Conclusions: Our results revealed silicon oil and SF6 to have statistically significant correlations with acute drops in postoperative pressure (≤6mmHg). To our knowledge, there are no studies clearly stating these associations. Larger studies are needed to better understand the roles that silicon oil and SF6 tamponade play in postoperative hypotony. Finally, although we did not find significant risk factors for hypertony, we discovered that 12 cases (6.7%) had delayed spikes in IOP. This data highlights the utility of 1-week post-op appointments.

CONTROL ID: 3713294

SUBMITTER (NAME ONLY): Sharmila Masli

TITLE: Reduced tear Thrombospondin-1/Matrix Metalloproteinase 9 ratio can aid diagnosing Sjögren's syndrome related ocular surface inflammation.

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Masli, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|E.K. Akpek, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diagnosing Sjögren's syndrome (SS) underlying ocular surface inflammation is critical due to systemic co-morbidities and complications, however, currently not feasible using available tests. We tested the hypothesis that reduced tear levels of immunoregulatory Thrombospondin (TSP)-1, which also inhibits Matrix Metalloproteinase (MMP)-9, would reflect SS pathology. We performed a prospective observational case-control study to learn about changes in tear TSP-1 and MMP-9 levels in patients with ocular surface inflammation associated with SS vs. Non-SS causes.

Methods: Total 61 participants (healthy or with clinically significant ocular surface inflammation with or without a definitive diagnosis of SS) were included. In addition to tear sampling, clinical evaluations included non-invasive tear break-up time (BUT), tear osmolarity, Schirmer's test without anesthesia, and ocular surface staining (lissamine green for conjunctiva and fluorescein for cornea). Tear TSP-1 and MMP-9 levels were determined using custom magnetic bead-based multi-plex assay (MilliporeSigma, Burlington, MA, USA) in a masked fashion. Statistical analysis procedures included regression analysis and Fisher's Exact test.

Results: Average tear TSP-1 and MMP-9 levels in healthy participants (control group) were 322 and 12.2 ng/ml respectively. Significantly higher proportion of participants with SS-associated ocular surface inflammation than non-SS causes had tear TSP-1 levels below the control group average (55% vs. 29%, OR=3, 95%CI=1.64 to 5.35, $p<0.05$) and tear MMP-9 levels above the control group average (65% vs. 24%, OR=5.8, 95%CI=4.46 to 19.81, $p<0.05$). Tear TSP-1/MMP-9 ratio was significantly reduced when ocular surface inflammation was associated with SS as against non-SS causes (B= -2.36, 95% CI= -3.94 to -.0.79, $p<0.05$), regardless of tear MMP-9 levels. Patients with higher ratio were 72% less likely to have SS (OR=0.28, 95% CI= 0.1 to 0.75, $p<0.05$) and this ratio showed significant correlations with conjunctival and corneal staining scores (R= -0.3 and R= -0.29, respectively $p<0.05$).

Conclusions: Our results are consistent with our hypothesis and indicate that reduced tear TSP-1 level is associated with SS pathology underlying ocular surface inflammation. Thus tear TSP-1/MMP-9 ratio can be a useful test that aids in diagnosis of SS-associated ocular surface inflammation.

CONTROL ID: 3713296

SUBMITTER (NAME ONLY): Jim Bellingham

TITLE: Upstream variants causing reduced transcription and unusual presentation of recessive inherited retinal dystrophies

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bellingham, A.R. Webster, F. Motta, N. Jurkute, O.A. Mahroo, G. Arno, Institute of Ophthalmology - University College London, London, UNITED KINGDOM|A.R. Webster, N. Jurkute, O.A. Mahroo, G. Arno, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|G.C. Black, J. Ellingford, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, Manchester, UNITED KINGDOM|E. Lenassi, G.C. Black, J. Ellingford, Manchester Centre for Genomic Medicine, Manchester University NHS Foundation Trust, Manchester, Greater Manchester, UNITED KINGDOM|F. Motta, Department of Ophthalmology, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: To determine the effect of non-coding putative promoter/regulatory region variants in BBS10 and GUCY2D identified by whole genome sequencing (WGS) in trans with a protein altering variant in patients with atypical presentation of BBS10 and GUCY2D disease.

Methods: Patients underwent WGS as part of the UK's 100,000 genomes project followed by clinical variant interrogation identifying a single candidate coding region variant in BBS10 (patient #1) and GUCY2D (patients #2 & #3). Non-coding variant analysis of the suspected gene was performed including promoter region interrogation (Eukaryotic Promoter Database; https://epd.epfl.ch). Promoters were amplified, cloned into pGL3 vector, and suspected variants were introduced by site-directed mutagenesis. Luciferase reporter assays in HEK293 cells were used to determine the effect of promoter variants.

Results: Patient #1 harboured variants in BBS10: c.2119_2120delGT (p.Val707Ter), and c.-80dupC within a predicted promoter region. Patients #2 and #3 harboured GUCY2D c.-148T>C in the TAAT core (5'-TAAT-3' > 5'-TAGT-3') of a predicted CRX binding element in trans to c.2837C>A [p.(Ala946Glu)], and c.3043+5G>A (proven pathogenic impact via minigene assay), respectively. Luciferase assays showed that BBS10 c.-80dupC caused a ~70% decrease in activity compared to the wild-type promoter. For GUCY2D, the c.-148T>C variant only altered the luciferase activity when co-transfected with a CRX expression plasmid. In this instance, the mutant GUCY2D promoter exhibited ~75% ($p<0.02$) activity of the wild-type promoter.

Conclusions: Heterologous expression of luciferase under the control of BBS10 and GUCY2D promoters indicated that the candidate variants are likely to affect intrinsic expression of these genes in the retina. Patient #1 has no extra-ocular features of Bardet-Biedl syndrome at the age of 71 years, and patient 2 presented atypically for GUCY2D-Leber congenital amaurosis with a stationary retinal dystrophy affecting both rods and cones but retaining some visual function (BCVA 1/60 OD, 2/60 OS) at age 46 years. Patient #3 presented with LCA (no further details available at the time of writing). These findings suggest that in patients #1 and #2, the genotypes may be hypomorphic, evidenced by the clinical presentation at the mild end of the disease spectrum and retained promotor function (predicting about 30% for BBS10 and 75% for GUCY2D).

CONTROL ID: 3713298

SUBMITTER (NAME ONLY): Shervin Gholizadeh Moghaddam

TITLE: Long-term efficacy and safety of satralizumab in adults with AQP4-IgG-seropositive neuromyelitis optica spectrum disorder (NMOSD): results from the Phase 3 SAkura studies

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.L. Bennett, University of Colorado School of Medicine, Aurora, Colorado, UNITED STATES|S. Gholizadeh Moghaddam, Genentech, Inc.,, South San Francisco, California, UNITED STATES|E. Fox, Central Texas Neurology Consultants, Round Rock, Texas, UNITED STATES|B. Greenberg, University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|B.G. Weinshenker, Mayo Clinic, Rochester, Minnesota, UNITED STATES|A. Traboulsee, University of British Columbia, Vancouver, British Columbia, CANADA|M.R. Yeaman, David Geffen School of Medicine at UCLA, Los Angeles, and Division of Molecular Medicine, Harbor-UCLA Medical Center, Torrance, California, UNITED STATES|K. Blondeau, K. Weber, I. Vodopivec, F. Hoffmann-La Roche Ltd, Basel, SWITZERLAND|M. Levy, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. Levy, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Satralizumab reduced the risk of protocol-defined relapse (PDR) vs placebo in the double-blind periods (DBP) of two trials in NMOSD: SAkuraSky (NCT02028884; satralizumab + baseline immunosuppressants [IST]) and SAkuraStar (NCT02073279; satralizumab monotherapy). We present long-term efficacy and safety data from the DBP and open-label extension (OLE) of these studies.

Methods: Satralizumab or placebo was administered in the DBP; patients could then enter the OLE (satralizumab 120 mg Q4W). PDRs in the DBP were adjudicated by a Clinical Endpoint Committee; PDRs in the OLE were determined by the investigator (iPDRs). Current analyses included all aquaporin 4-immunoglobulin G seropositive (AQP4-IgG+) adults who received ≥1 dose of satralizumab in the DBP and/or OLE (overall satralizumab treatment [OST] period,

data cutoff: Feb 22, 2021). Efficacy analyses assessed the annualised iPDR rate (ARR), time to first iPDR, severe iPDR (≥2 point increase in the Expanded Disability Status Scale [EDSS] score), and sustained EDSS worsening (EDSS increase of ≥2, ≥1, or ≥0.5 points for patients with baseline scores of 0, 1–5, or ≥5.5, respectively, confirmed ≥24 weeks post-initial-worsening). Safety assessments compared rates of adverse events (AEs) per 100 patient-years (PY) in the OST period vs the DBPs.

Results: 106 AQP4-IgG+ adults were included (SAkuraSky: 44; SAkuraStar: 62). Median (range) duration of satralizumab exposure was 5.4 (0.1–7.0) years in SAkuraSky and 4.0 (0.1–6.0) years in SAkuraStar. The overall ARR (95% CI) in the OST was 0.11 (0.07–0.17) in SAkuraSky and 0.08 (0.05–0.13) in SAkuraStar; the ARR remained stable throughout the studies. At Week 192 (3.7 years) in SAkuraSky and SakuraStar, 74% and 73% of patients had no iPDR, 94% and 90% had no severe iPDR, and 89% and 86% had no sustained worsening of EDSS, respectively. Rates of serious AEs (95% CI) in the OST period were comparable with the DBP (serious AEs: SAkuraSky 13.7 [8.9–20.1]/100 PY; SAkuraStar 10.6 [6.9–15.6]/100 PY). Rates of infections and serious infections in the OST period were comparable with the DBP and did not increase over time. No deaths or anaphylactic reactions to satralizumab were reported in either study.

Conclusions: Satralizumab efficacy and its favorable safety profile are sustained with long-term treatment.

CONTROL ID: 3713301

SUBMITTER (NAME ONLY): Alice Le Meur

TITLE: Retrospective natural history of retinitis pigmentosa due to RHO, PDE6A, or PDE6B mutations: the PHENOROD1 study

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To better understand the natural history of cone and rod degeneration in patients with Retinitis Pigmentosa (RP) carrying mutations in the RHO, PDE6A, and PDE6B genes.

Methods: PHENOROD1 was a longitudinal retrospective study carried out at the national reference center for rare diseases (REFERET) at the Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts (Paris, France). A total of 110 patients with RP due to mutations in RHO, PDE6A, or PDE6B were enrolled, and the following parameters were collected from their medical records: best-corrected visual acuity (BCVA), binocular kinetic visual field (VF) (III4e), retinal sensitivity, color vision, full-field electroretinogram, optical coherence tomography, and fundus autofluorescence imaging. Differences between genotypic groups were analyzed using ANOVA, and the progression rates were estimated using a mixed error-component model.

Results: A total of 75 (68%) patients carried a mutation in RHO, 14 (13%) in PDE6A, and 21 (19%) in PDE6B. Mean age at onset was 23.4, 13.9, and 16.2 years in RHO, PDE6A and PDE6B patients, respectively ($p>0.1$).

There were no significant differences between genotypes with regard to the presentation of initial symptoms (night blindness and VF restriction), BCVA progression rates (on average +0.01 LogMAR per year in both eyes), and preservation of the ellipsoid zone.

In contrast, the evolution of VF and area of preserved autofluorescence between the ages of 20 and 60 was statistically different between genotypes, with a slower decline observed in the PDE6B group.

Interestingly, BVCA remained stable until ~40 years of age before starting to decline, while the inflection point for VF occurred earlier, in the patient's third decade.

Conclusions: The analysis of functional and structural visual parameters allowed to better define the natural history of rod-cone dystrophy according to underlying genotypes. This is of particular interest for the selection of patients in the development of photoreceptor rescue treatments such as SPVN06, a novel dual gene therapy based on the expression of neurotrophic factor RdCVF and thioredoxin RdCVFL, both encoded by the nucleoredoxin-like 1 gene.

CONTROL ID: 3713302

SUBMITTER (NAME ONLY): Spozmai Panezai

TITLE: Spatial amplitude modulation for vision improvement in cataractous eyes.

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Panezai, A. Jimenez-Villar, G. Gondek, I. Grulkowski, Uniwersytet Mikolaja Kopernika w Toruniu Wydzial Fizyki Astronomii i Informatyki Stosowanej, Torun, POLAND|A.M. Paniagua-Diaz, A. Aries, S. Manzanera, P. Artal, Laboratorio de Óptica, Universidad de Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To use spatial amplitude modulation method for vision improvement by deblurring the retina images in cataractous eyes.

Methods: The image formation on retina is the result of light propagation and focusing through crystalline lens, therefore the interaction of light with the opacities (cataractous lens) results in scattering and forming blur retinal images. We used spatial amplitude modulation method of masking the pupil plane, in such a way that light can only pass through the remained transparent parts of lens. The method depends on the imaging of pupil plane of cataract eye to estimate the spatial location of opacities to make an opacity map. This is used to design a complementary mask, which can be conjugated at the pupil plane by a spatial light modulator. The proposed method has been verified via simulation, where cataractous lens with opacities has been generated. The point spread function (PSF) was calculated by taking the FFT of the cataractous lens. Retinal image was calculated by convolving the PSF with ground truth image (I_g). The phase map of cataractous lens was used to generate a complementary binary mask to mask the pupil plane and retinal image was again generated by convolution of PSF of masked pupil with I_g. The quality of the retinal images was quantified by structural similarity (SSIM) index without and after applying the method.

Results: Cataractous lenses were simulated as phase elements with circular function acting as pupil with diameter 2.7 mm. Three levels of straylight described by $Log_{10}(s)$ = 1.75, 2 and 2.37 (at an angle of 6 degrees), corresponded to nuclear cataracts of rank 3 or higher in the Lens Opacity Classification System III (LOCS III) has been simulated. Images of sine-wave grating of 6, 12 and 20 CPD, were used as ground truth images. Measured SSIM has shown improvement for higher CPD for all grading's of cataract. For 20 CPD, the SSIM for $Log_{10}(s)$ = 1.75 has been improved from 0.33 to 0.38, for $Log_{10}(s)$ = 2, from 0.1 to 0.22 and for $Log_{10}(s)$ = 2.37, from 0.008 to 0.11.

Conclusions: Spatial amplitude modulation has been evaluated by numerical simulations of retinal images, corresponding to different grades of cataracts and by SSIM which has shown significant improvements after applying the method.

CONTROL ID: 3713304

SUBMITTER (NAME ONLY): Walter Yego

TITLE: An executive function task in mixed reality affects dynamic accommodation

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.K. Yego, R.C. Baraas, J. Stuart, E. Svarverud, National Centre for Optics, Vision and Eye Care, Faculty of Health and Social Sciences, University of South-Eastern Norway, Kongsberg, NORWAY|

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ABSTRACT BODY:

Purpose: The use of mixed reality (MR) displays in education and training have become increasingly commonplace. However, the inherent conflict between vergence and accommodation (VAC) causes concern that these technologies may have an effect on vision. We investigated dynamic accommodation in young adults before and after performing an executive function task in MR.

Methods: Dynamic accommodation (DA) in diopters (D) was measured (PowerRef 3) in 20 participants (11 males) age 20–24 yrs with habitual correction before and after performing an executive function task (Tower of London) in a head-mounted 3D display (HoloLens 2) for 30 min. The task involved arranging virtual objects at 50 cm distance to match a pattern presented on a physical 2D screen at 4 m. DA was measured over a 1 min period where participants binocularly viewed two accommodative targets, at 40 cm and 4 m, alternately at 3 sec intervals while instructed to keep the targets focused and fused. Data were analyzed using Wilcoxon and Kruskal-Wallis tests and Bonferroni corrections.

Results: The difference in accommodative change (ΔAC) between near and distance — before and after the MR task — was calculated. Accommodation behavior fell into two groups, those with no difference (<0.012 D, classified as stable) and those with a difference in ΔAC (unstable). Stable and unstable ΔAC median (interquartile range) were +0.10 (0.07) D and +0.26 (0.13) D, respectively, and significantly different from each other ($p<0.001$). Further analysis showed that those with unstable ΔAC either had contracted ΔAC (smaller ΔAC after the MR task, n=5) or expanded ΔAC (larger ΔAC, n=7). There was a statistically significant difference in ΔAC between the three groups (stable, contracted and expanded) ($p=0.002$, $H=0.70$) with pairwise comparisons showing significant differences between all groups ($p<0.001$). The mean (±SD) ΔAC of the groups were -0.44 (0.26) D, +0.27(0.12) D and 0.27 (0.12) D for the contracted, stable, and expanded groups respectively.

Conclusions: For some individuals, there was a large difference in accommodation behavior before and after performing the MR task. We hypothesize that the unstable ΔAC could be an effect of the VAC and that using MR over longer time periods could be disadvantageous for individuals with contracted ΔAC. An expanded ΔAC could imply a potential of increased flexibility in the vergence-accommodation system that may be beneficial for these individuals.

CONTROL ID: 3713306

SUBMITTER (NAME ONLY): Jing Jin

TITLE: A deep learning system for sickle cell retinopathy detection using retinal OCT images from children with sickle cell disease

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Jin, Ophthalmology/Surgery, Nemours Children's Hospital Delaware, Wilmington, Delaware, UNITED STATES|A. Bhattarai, C. Kambhamettu, Computer and Information Sciences, University of Delaware, Newark, Delaware, UNITED STATES|R. Miller, E. Kolb, Hematology/Oncology, Nemours Children's Hospital Delaware, Wilmington, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal damage in sickle cell disease (SCD) begins with vascular occlusion by sickled red blood cells. Inner retinal thinning due to tissue volume loss is the most common finding in OCT retinal images of SCD patients. Inner retinal thinning from neuronal migration is one of the characteristics of normal fovea. This project aims to develop and validate a deep learning system to detect retinal thickness changes due to sickle cell retinopathy (SCR) using retinal OCT from children with SCD.

Methods: We use a grid-based object detection algorithm, You Only Look Once (YOLO), to detect retinal thinning caused by SCR. Our dataset contains 3906 B-scans from 63 OCT studies of 33 SCD patients (14 male, 21 SS, 9 SC, 2 Sβ+ and 1 Sβ0, age 12.99±4.56, 5.35 to 20.26 years). Instances of SCR and fovea were annotated by an ophthalmologist using bounding boxes on each image. We divided the dataset into 5 sets, each containing approximately equal numbers of B-scans, to perform a 5-fold cross validation. The algorithm was trained 5 time, and each time on different 4 sets and tested on the remaining set using a Tesla V100 Graphical Processing Unit. We measured the training loss using Binary Cross-Entropy and Focal loss. Mean Average Precision (mAP) based on Intersection over Union between annotated and predicted bounding boxes was used as a performance metric.

Results: Our trained model achieved an average mAP of 96% and 72% on fovea and SCR detection, respectively. Figure 1 presents the corresponding confusion matrix. Low mAP on SCR detection can be attributed to the ambiguity and inconsistency in annotating SCR instances, as depicted by the Background column in Figure 1. Figure 2 compares SCR and fovea detection made by the trained model verses annotated images.

Conclusions: In this examination of retinal OCT images from children with SCD, a deep learning system has shown good precision in identifying SCR and differentiating disease injuries from similarly structured profiles of the normal fovea. Our future research combines the current approach with computer vision-based analysis of retinal layer thickness, extending our work towards predicting SCR progression by analyzing multiple OCT scans of re-visiting patients.

CONTROL ID: 3713307

SUBMITTER (NAME ONLY): Long Nguyen

TITLE: The relationship between sedentary behavior and dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Nguyen, M.S. Magno, T. Utheim, Department of Plastic and Reconstructive Surgery, Oslo Universitetssykehus, Oslo, NORWAY|T. Utheim, Department of Medical Biochemistry, Oslo Universitetssykehus, Oslo, NORWAY|J. Vehof, Department of Ophthalmology, Universitair Medisch Centrum Groningen, Groningen, Groningen, NETHERLANDS|J. Vehof, Department of Ophthalmology, Sykehuset i Vestfold HF, Tonsberg, Vestfold, NORWAY|M.S. Magno, Department of Epidemiology, Universitair Medisch Centrum Groningen, Groningen, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Sedentary behavior (SB) is a modifiable risk factor for several adverse health outcomes, such as cardiovascular disease and all-cause mortality, but its association with dry eye disease (DED) remains unclear. SB may increase low-grade systemic inflammation, which can contribute to DED, making it important to understand DED's relationship with this potentially modifiable risk factor. This large population-based, cross-sectional study aimed to test the hypothesis that SB is tied to an increased risk of DED.

Methods: We included participants from the population-based Lifelines cohort (n=48,418, 58% female, mean age = 51.4 years). DED was assessed using the Women's Health Study (WHS) dry eye questionnaire, and SB with the Marshall Sitting Questionnaire. We analyzed the relationship between DED and SB using logistic regressions, corrected for age, sex, BMI, smoking status, demographics, and 48 comorbidities. Additionally, we corrected for time of moderate to vigorous physical activity (MVPA) and stratified by WHO's recommendations of MVPA (<150 vs. ≥150 min/week) in analyses above. Finally, to investigate the impact of SB independent of computer screen exposure, the analyses were repeated for sitting time excluding time spent sitting behind a computer at home or at the office.

Results: In total, 9.1% of the population had WHS-defined DED. Greater SB was associated with an increased risk of dry eye (odds ratio (OR) 1.015 per hour/day, 95%CI 1.005-1.024, P=0.004). This result did not change after MVPA adjustment. Interestingly, the association between SB and WHS-defined DED was only significant for those with <150 min of MVPA/week (OR 1.022, 95%CI 1.002-1.042, P=0.027, n=11,783), and not in those with ≥150 min/week (OR 1.011, 95%CI 0.999-1.023, P=0.076, n=32,353). Lastly, when excluding time spent sitting during computer use, the relationship between SB and DED was substantially attenuated, and no longer significant (OR 1.009, 95%CI 0.996-1.023, P=0.19).

Conclusions: Supporting the hypothesis, we found that greater SB was tied to an increased risk of DED. However, sufficient physical activity appeared to mitigate the risk. Finally, as there was no association when only analyzing the subsample with <2 hours of daily computer use, future studies should investigate the impact of sitting time with and without computer use separately.

CONTROL ID: 3713308

SUBMITTER (NAME ONLY): Brendan Tamm

TITLE: Differences in keratorefractive surgery outcomes between patients with and without glucocorticoid use in the 12 months preceding surgery: A TriNetX analysis

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tamm, H. Pakhchanian, G. Martin, D. Belyea, Ophthalmology, The George Washington University Milken Institute of Public Health, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare differences in outcomes following keratorefractive surgery in patients who used glucocorticoids for the 12 months preceding surgery, and those who did not.

Methods: A retrospective cohort study was conducted using TriNetX (Cambridge, MA, USA), a federated electronic health record research network comprising multiple large health organizations in the US. Patients who underwent keratorefractive surgery were identified by CPT code and stratified cohorts based on glucocorticoid use. Cohorts were matched for age, gender, and comorbidities (essential hypertension, diabetes mellitus, cerebrovascular disease, heart failure, nicotine dependence, alcohol related disorders, and body mass index). Primary outcomes were Dry Eye Syndrome, Recurrent Corneal Erosion, Corneal Edema, Corneal Scar or Opacity, Corneal Ectasia, Acute Conjunctivitis, Diffuse Lamellar Keratitis, Corneal Neovascularization, Vitreous Degeneration (VD), Vitreous Hemorrhage (VH), Retinal Detachment or Break(RD/B), Retinal Edema, and Cystoid Macular Degeneration (CMD). Outcomes were compared between cohorts after propensity score matching using logistic regression and greedy nearest-neighbor matching algorithm.

Results: A total of 13,704 patients were included in analysis with 6,852 in each cohort after propensity matching. The glucocorticoid use cohort had a significantly greater risk of developing dry eye syndrome (RR, 1.61; 95% CI, 2.79-4.59), corneal neovascularization (RR,2.1; 95% CI, 0.99-4.46), vitreous degeneration (RR, 1.43; 95% CI, 1.17-1.75), vitreous hemorrhage (RR,1.82; 95% CI, 1.08-3.06), retinal detachment or break (RR,2.15; 95% CI, 1.61-2.87), retinal edema (RR, 2.17; 95% CI, 1.24-3.78), and cystoid macular degeneration (RR,1.98; 95% CI, 1.38-2.83). No significant difference was seen in development of recurrent corneal erosions, corneal edema, corneal scar, corneal ectasia, acute conjunctivitis, diffuse lamellar keratitis, or ischemic optic neuropathy.

Conclusions: Glucocorticoid use is an important consideration when evaluating for postoperative complications following keratorefractive surgery. Glucocorticoid users were more likely to develop dry eye, corneal neovascularization, VD, VH, RD/B, retinal edema, and CMD. These differences should be considered when evaluating patients and discussing outcomes with patients both pre and post-operatively.

CONTROL ID: 3713309

SUBMITTER (NAME ONLY): Karl Landheer

TITLE: An improved algorithm for the assessment of quantitative vitreous haze from fundus photographs

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Landheer, F. Sepehrband, J. Weyne, K. Chu, S. Hectors, P. Parasoglou, N. Gale, A. Murphy, J. Walls, M. Germino, Regeneron Pharmaceuticals, Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To improve the quantification of vitreous haze (VH), a key clinical feature of uveitis, we modified the Passaglia quantitative vitreous algorithm (PQVHA). The PQVHA was developed to improve upon the Miami Scale, which utilizes color fundus photographs (CFP) graded by an expert reader rating the VH as an integer from 0 (no haze) to 8 (extreme haze). The PQVHA addresses important limitations of the Miami Scale: dependence on an expert reader, subjective grading and a categorical scoring system. Our modifications to the PQVHA aim to reduce its sensitivity to variability of image acquisition and quality.

Methods: The data was from a phase 2 randomized, double-masked and placebo-controlled study to evaluate the efficacy and safety of Sarilumab in 58 patients with Non-infectious, Intermediate, Posterior or Pan-Uveitis. Each of the 5 PQVHA steps were modified. 1) The green channel of the CFP had the most contrast so was used for analysis, rather than a grayscale conversion. The images were then histogram normalized and gamma corrected. 2) A Gaussian kernel was used as a high-pass filter instead of a rect function, as the latter provides non-monotonic sinc-weighting to spatial frequencies. 3) Local entropy was not used because it can provide extreme weighting to small artifacts. 4) The magnitude spectrum was used instead of the power spectrum, as the latter's square function provides excessive weighting to a small number of high spatial frequencies. 5) The magnitude spectrum was integrated, and log transformed for a final value. Given the lack of ground truth to assess haze scores, the robustness of PQVHA and our algorithm were assessed by comparing the correlation of the scores with two expert readings in N=3245 images.

Results: The R^2 between our algorithm values and raters 1 and 2 was 0.33 and 0.50, respectively. For comparison, the R^2 between the values from the PQVHA and raters 1 and 2 were 0.10 and 0.08, respectively, and the R^2 between rater 1 and rater 2 was 0.34.

Conclusions: Our method builds upon the PQVHA to increase robustness against the particular experimental conditions between subjects and time points common to clinical trials.

CONTROL ID: 3713311

SUBMITTER (NAME ONLY): Maria Pinazo-Duran

TITLE: Starbust amacrine cells impairment in a rat model of chronic ocular hypertension.

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. Pinazo-Duran, S. Sanz-Gonzalez, Surgery-Ophthalmology Department at the Faculty of Medicine, Ophthalmic Research Unit Santiago Grisolia, VALENCIA, Valencia, SPAIN|A. Noailles, P. Lax, O. kutsir, N. Cuenca, Departmet of physiology, genetics and microbiology, Departmet of physiology, genetics and microbiology, Alicante, Alicante, SPAIN|A. Mayordomo-febrer, M. Lopez-Murcia, Veterinary, CEU Universidad Cardenal Herrera Servicio de Idiomas, Valencia, Valencia, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the retinal starbust amacrine cells (SBACs) by morphological and morphometrical approaches, in a rat model of chronic ocular hypertension (OHT).

Methods: Weekly intracameral injections of sodium hyaluronate (HYA) were used to induce chronic OHT in the left eye (LE), whilst salt solution was injected in the sham operated right eyes (RE) of seven male Wistar rats, during nine consecutive weeks. Intraocular pressure (IOP) measurements were done weekly, by means of a rebound tonometer. Retinal cryosections were obtained for immunohistochemical techniques (specifically ChAT antibody to SBACs), and morphometric approaches. Statistics were performed by the 28.0 SPSS program.

Results: The OHT was significantly higher and sustained during the follow-up in LE respect to RE at most timepoints. Considering that in the retinal ganglion cell (RGC) layer, the displaced amacrine cells (DACs) constituted up to 50% of all cells, and the SBACs account for 20% of the DACs population, mild-to-moderate OHT induced noticeable morphologic changes and a significant reduction in ON/OFF SBACs in the HYA-treated eyes (17.7 ± 2.9 cells/mm) with respect to the controls (24.8 ± 3.1 cells/mm), ($p<0.01$), contributing to the RGC layer global reduction.

Conclusions: The HYA intracameral injections in the rat eye induced a mild-to-moderate sustained IOP elevation and RGC loss, mimicking most human open-angle glaucoma milestones. The decreased density of SBACs and its deteriorated ON/OFF plexus in our chronic OHT model, probably started the fall off in the signal transduction and visual performance, that for the first time, may be related to specific anomalies in motion perception described in glaucoma patients.

CONTROL ID: 3713312

SUBMITTER (NAME ONLY): Philip Rosenfeld

TITLE: Impact of Central Choriocapillaris Flow Deficits on Low Luminance Visual Acuity Measurements

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.J. Rosenfeld, Y. Shi, J. Li, M. Shen, L. Wang, X. Jiang, W.J. Feuer, G. Gregori, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|X. Jiang, Sichuan University West China Hospital, Chengdu, Sichuan, CHINA|Z. Chu, Verana Health, Washington, UNITED STATES|Z. Chu, X. Zhou, Q. Zhang, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R.K. Wang, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The impact of central choriocapillaris (CC) flow deficits (FDs) on low luminance visual acuity (LLVA) measurements was investigated in pseudophakic normal eyes and in eyes with nonexudative age-related macular degeneration (neAMD) to determine if LLVA measurements correlated with the stage of AMD and its progression.

Methods: Both normal luminance best-corrected visual acuity (NL-BCVA) and low luminance BCVA (LL-BCVA) were obtained using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. LL-BCVA was measured by using a 2.0-log unit neutral density filter in front of the examined eye (Wratten filter; Kodak, Rochester, NY). LLVA deficit (LLVAD) scores were calculated by subtracting the LL-BCVA from the NL-BCVA letter scores. The percentage of central CC FDs (%FDs) was determined in a 1mm diameter circle centered on the fovea from 6x6 mm scans using swept-source OCT angiography (SS-OCTA) imaging (PLEX® Elite 9000, Carl Zeiss Meditec, Dublin, CA) along with a previously validated algorithm. Pseudophakic eyes were chosen since an ongoing study determined that cataracts have an unpredictable effect on LLVA measurements. Eyes with neAMD were categorized as drusen-only eyes and eyes with non-foveal geographic atrophy (nfGA). In eyes with nfGA, the posterior margin of atrophy could not be within 150 µm of the foveal center, and the area of nfGA could not comprise more than 10% of the central 1mm circle.

Results: In 30 normal eyes ranging in ages from 56 to 79, there were no statistically significant correlations between the central CC FD% and the NL-BCVA, LL-BCVA, and LLVAD measurements (all $|r|$ values ≤ 0.04, all p-values ≥ 0.85). However, in 27 drusen-only eyes ranging in ages from 67 to 90, significant correlations were found between the central CC FD% and the NL-BCVA ($r=-0.49$; $p=0.010$), LL-BCVA ($r=-0.65$; $p<0.001$), and LLVAD ($r=0.54$; $p=0.004$). Analysis of neAMD eyes with nfGA is currently underway.

Conclusions: In pseudophakic normal eyes, no correlations were identified between the central CC FD% and the NL-BCVA, LL-BCVAD, and LLVAD measurements; however, in drusen-only eyes, an increase in central CC FD% measurements were correlated with decreased NL-BCVA, decreased LL-BCVA, and increased LLVAD measurements. These correlations suggest that increased CC flow impairment impacts foveal photoreceptor function. The analysis of eyes with nfGA is ongoing.

CONTROL ID: 3713313

SUBMITTER (NAME ONLY): Harini Gudiseva

TITLE: Quantitative traits associated with primary open-angle glaucoma in African ancestry individuals

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.V. Gudiseva, V.R. Chavali, R. Salowe, J. He, R. Lee, S. Zenebe-Gete, E. Daniel, G. Ying, E.G. Miller-Ellis, V. Addis, P. Sankar, J. O'Brien, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|Y. Bradford, M. Ritchie, S.S. Verma, Genetics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: We conducted a genome-wide association study (GWAS) on African ancestry individuals, in order to identify genes associated with primary open-angle glaucoma endophenotypes.

Methods: The Primary Open-Angle African American Glaucoma Genetics (POAAGG) study population consists of self-identified Blacks, aged 35 years or older. Quantitative traits were collected on subjects during ophthalmic exams, including intraocular pressure (IOP), cup-to-disc ratio (CDR), central corneal thickness (CCT), visual acuity (VA), retinal nerve fiber layer (RNFL) thickness, mean deviation (MD), and pattern standard deviation (PSD). Genotyping on 5950 subjects including cases and controls was performed using the Multi-Ethnic Genotyping Array V2 (EX) consortium chip. After standard quality control, samples were imputed to the TOPMED phase 3 reference panel using the TOPMED imputation server, which resulted in ~15M variants at R^2>0.3 filter. Single variant, quantitative trait association tests were performed using generalized estimating equations (GEE) to account for inter-eye correlation, adjusting for sex and age at study enrollment, with the first five PCs included as fixed effects.

Results: Assuming independence of tests, the genome-wide quantitative trait association studies identified 351 significant SNP-trait associations (p-value<5x10-8) in 107 genomic loci. A total of 6 variants reached genome-wide significance for CDR, as well as 26 variants for baseline IOP, 27 variants IOP max, 99 variants for baseline PSD, 180 variants for MD, 7 variants for RNFL thickness, and 6 variants for VA. SNP association results for central corneal thickness (CCT) did not reach conservative genome-wide significance, assuming independence of all phenotypes evaluated in this study. The SNPs implicated in the associations analysis in our study mapped to genes that include SOX5, CSMD1, EVA1C, PHTF2, EXT1, ACE, CPXM2 and others. In silico and functional validation of the implicated SNPs is currently underway.

Conclusions: Our study recruited, genotyped, and deeply phenotyped the largest-ever cohort of African ancestry individuals with glaucoma from a single city, providing much needed genetic architecture for this most affected population. Glaucoma is an inherently complex and heterogenous disease, making this deep phenotyping necessary for understanding the pathophysiology of disease and to study the influence of genetic variations.

CONTROL ID: 3713314

SUBMITTER (NAME ONLY): Byung Ro Lee

TITLE: Novel aspect of epiretinal membrane (ERM) & it clinical significance: internal limiting membrane (ILM) Folds, underneath ERM vs. around ERM

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lee, J. Kim, Ophthalmology, Hanyang University Medical Center, Seoul, Seoul, KOREA (THE REPUBLIC OF)|B. Lee, J. Heo, Ophthalmology, Theoneseoul eye clinic, Seoul, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Byung Ro Lee: Commercial Relationship: Code N (No Commercial Relationship) | Jangwon Heo: Commercial Relationship: Code N (No Commercial Relationship) | Ji Hong Kim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously reported that ILM folds around ERM showed typical radiating hyporeflective lines pattern from margin of ERM, and they were shown excellently on both red-free image of confocal scanning laser ophthalmoscopy (cSLO) and 3D-rendering image of optical coherence tomography (OCT). In this study, we focused on ILM folds underneath ERM and assessed its prevalence, morphologic characteristics, and clinical Implications, which was not reported previously.

Methods: Retrospective, observational case study was performed in fifty five eyes of 48 patients with ERM. We developed a novel method of obtaining image of ILM folds underneath ERM. Using en face analysis mode of standard OCT macular volume scan, topographic surface images of ILM folds were acquired, then by adjusting frontal surface scan line, images of ILM folds situated underneath ERM and around ERM was acquired, respectively. We classified patterns of ILM folds underneath ERM group and compared them to those around ERM group. The prevalence of each patterns of ILM folds were obtained and compared between the two groups. In the patients with follow-up periods >5 years, anatomical & functional ERM progression was matched to that of the ILM fold patterns.

Results: Pattern of ILM folds were classified as radiating, irregular-random oriented and mixed. Among the 55 eyes, ILM folds around ERM group showed 52 (94.5%) eyes of radiating, 2 (3.6%) eyes of irregular and 1 (1.8%) of mixed pattern. Notably, ILM folds underneath ERM group showed 10(18.2%) eyes of radiating, 30 (54.5%) of irregular, 15 (27.2%) of mixed pattern. Irregular, random oriented pattern of underneath ERM group is composed of multiple gaps between ERM and retina. Immediately after ERM with ILM peeling, the ILM fold disappeared in both group of all eyes. ERM progression showed excellent agreement with ILM fold progression (kappa value [κ]= 1.0, 0.8, respectively in each group).

Conclusions: Our novel images using standard OCT showed that ILM folds underneath ERM has a random oriented, irregular pattern, which is remarkably different from typical radiating ILM folds around ERM. Particularly, this overview of ILM folds and gaps between ERM and retina provides us pre-surgical information and may aid to predict visual prognosis.

CONTROL ID: 3713315

SUBMITTER (NAME ONLY): Claire Mitchell

TITLE: Exosome release from RPE cells increased by lysosomal compromise

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.H. Mitchell, W. Lu, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Claire Mitchell: Commercial Relationship: Code N (No Commercial Relationship) | Wennan Lu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Understanding how injured RPE cells communicate trouble to neighboring cells is central. RPE cells are particularly susceptible to lysosomal compromise as they degrade photoreceptor outer segments released each day, and as they are post-mitotic cells, allowing chronic accumulation of toxins in the lysosomes. Given the pathways connecting lysosomes and multivesicular bodies (MVBs), and the role of MVBs in exosome release, we hypothesized that lysosomal compromise alteres exosome release from RPE cells.

Methods: Lysosomal compromise in iPS-RPE or ARPE-19 cells was induced by exposing cells to 20μM chloroquine for 7 days. Immunoblots were performed on vesicles collected from supernatant using ExoQuick. Vesicle size and quantity were analyzed with a Spectradyne system and exosome marker analysis performed with an ExoView chip system. C57BL6J mice received intraperitoneal chloroquine injections 50 mg/kg; 3x/wk for 6 weeks.

Results: Immunoblots showed a rise in exosome marker CD63 in vesicular material from the supernatents of iPS-RPE cells exposed to chloroquine. A similar rise in CD63 was observed in immunoblots from the supernatant of ARPE-19 cells exposed to chloroquine. Quantification of extracellular vesicle size confirmed these vesicles to be exosomes, with a mean diameter of 79.7 ±1.4 nm in control; particle size was not changed after exposure to chloroquine. However, Spectradyne analysis confirmed exosome number was increased by chloroquine. ExoView analysis showed chloroquine induced a differential increase in the number of CD63+ and CD81+ vesicles, with a smaller rise in CD9+ vesicles. Initial trials suggest supernatant from chloroquine-treated ARPE-19 cells reduced viable 661w cells, although chloroquine by itself did not. Increased staining for CD63 was found in RPE cells from mice, and in cultured RPE cells, treated with chloroquine.

Conclusions: These findings suggest lysosomal compromise increases exosome release from RPE cells. Links between exosome release and photoreceptor health require confirmation. Exosome markers CD63 and CD81 were previously identified in drusen from AMD patients; whether reducing lysosomal compromise can reduce these markers in drusen remains to be determined.

CONTROL ID: 3713316

SUBMITTER (NAME ONLY): Svenja Deuchler

TITLE: Virtual reality microsurgery training during medical school: data from implementation of Eyesi Surgical in ophthalmology clerkship in Germany

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Deuchler, J. Scholtz, F. Koch, Augenzentrum Frankfurt, Frankfurt am Main, Hessen, GERMANY|H. Ackermann, Institute for Biostatistics, Goethe-Universitat Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|F. Koch, Department of Ophthalmology, Klinikum der Johann Wolfgang Goethe-Universitat Frankfurt, Frankfurt am Main, Hessen, GERMANY|

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ABSTRACT BODY:

Purpose: Eyesi Surgical is an ophthalmologic microsurgery simulator that allows users to practice abstract microsurgical skills as well as more specialized clinical skills relating to cataract and vitreoretinal surgery. Currently, the simulator is usually introduced during residency or fellowship training for ophthalmologists. This study assessed the inclusion of microsurgical simulation training in the medical school ophthalmology clerkship.

Methods: 79 German medical students in their 10^{th} semester of undergraduate education were given the opportunity to complete up to two days of training on the simulator during their ophthalmology clerkship. They began with abstract modules which focused on instrument handling and microscope use and progressed to more ophthalmology-specific modules. They received an objective numeric score based on simulator performance and completed pre and post training subjective questionnaires.

Results: There was no relationship found between students' Eyesi Surgical performance scores and their specialty interests ($p=.790$). The majority of students (73.4%) subjectively rated their microsurgical skills to be higher after simulator training than before training ($p<0.001$). 92.4% of students found the Eyesi Surgical to be a useful component of the ophthalmology clerkship. Additionally, 15.2% of students indicated an interest in more simulator training during the clerkship than that which was offered. Objective scores from Navigation Training Level 1 showed that students achieved better results in the criteria categories of Completing Objects and Tissue Treatment than in the categories of Instrument and Microscope Handling. The mean Total Score was 25.71 out of a possible 100 points. A trend was found ($p=.078$) in the correlation between self-rated microsurgical ability and Navigation Level 1 total score on the Eyesi Surgical.

Conclusions: The inclusion of surgical simulation in the ophthalmology clerkship curriculum led to increased levels of confidence in the microsurgical skills of medical students. Offering surgical simulation training to medical students prior to residency can help to expose students to surgical fields, identify those that have particular talent and aptitude for surgery, and assist them in deciding which specialty to pursue in residency.

CONTROL ID: 3713317

SUBMITTER (NAME ONLY): Ram Nagaraj

TITLE: Peptains block retinal ganglion cell death in mice with ocular hypertension

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Nagaraj, A. Dhillon, R.B. Nahomi, M. Nam, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|D.L. Stankowska, G.A. Johnson, Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the neuroprotective effects of chaperone peptides (peptain-1 and peptain-3a) against retinal ganglion cell (RGC) death in vitro and two mouse models of ocular hypertension.

Methods: Rat primary RGCs were treated with peptain-1 or peptain-3a in the absence of trophic factors, and the apoptotic and dead cells were counted. Microbeads were injected into the anterior chamber of mice, and after 3 weeks, IOP was elevated. Peptains were injected intravitreally at 1 µg each in PBS and subsequently once a week for 3 weeks. Silicone oil was injected into the anterior chamber to elevate IOP and after 2 weeks the oil was removed and peptains were injected intravitreally at 1µg each in PBS.

Results: Peptains exhibited robust anti-apoptotic activity against neurotrophic factor deprivation in primary RGCs. The microbead-injected eyes had significantly higher IOP levels over a 6-week follow-up than the contralateral control eyes. The number of RGCs decreased by 31% following microbead injection, but peptain-1 and peptain-3a significantly decreased RGC death; to only 4% and 12%, respectively. IOP elevation reduced the anterograde transportation along the length of the optic nerve, but peptains ameliorated this effect. In eyes injected with silicone oil, RGC counts decreased by 39% after 2 weeks. Two weeks after silicone oil removal, the injection of peptain-1 and peptain-3a significantly reduced the RGC loss by 27% and 25%, respectively.

Conclusions: Peptain-1 and peptain-3a protect RGC somas and axons against ocular hypertension in mice. Our results suggest that they could be developed as neuroprotective agents for the treatment of glaucoma.

CONTROL ID: 3713318

SUBMITTER (NAME ONLY): Poria Dorali

TITLE: Cost-Effectiveness Analysis of Personalized Diabetic Retinopathy Screening Recommendations

SESSION TITLE: Health Economics and Health Care Delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Dorali, Z. Shahmoradi, T. Lee, Industrial Engineering, University of Houston, Houston, Texas, UNITED STATES|Z. Shahmoradi, Management, Policy & Community Health, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|C.Y. Weng, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|C.Y. Weng, Ophthalmology, Ben Taub Hospital, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Personalized screening policies for diabetic retinopathy (DR) can be effective in detecting DR while incorporating more accessible screening technologies such as teleretinal imaging (TRI) as a precursor to clinical screening (CS). This study conducts cost-effectiveness analysis comparing personalized and standardized screening policies for an urban, safety-net hospital system.

Methods: A partially observable Markov decision process model (POMDP) determined semi-annual personalized recommendations of either wait and watch (WW), TRI, or CS based on a patient's risk of having proliferative DR and screening compliance. A Monte Carlo discrete event simulation model was then utilized to compare the model-based personalized policy to standardized policies including annual CS (ACS), biennial CS (BCS) and annual TRI (ATRI) for a hypothetical cohort over their lifetimes. DR progression rates and patient-specific CS compliance were obtained from literature while patient-specific TRI compliance was derived from the TRI screening program at the Harris Health System, Houston, TX. Sensitivity analysis was conducted to examine cost-effectiveness of the screening policies across different A1C levels.

Results: For a base case population with an A1C level of 7% and TRI and CS compliance rates of 68.4% and 35%, respectively, the model-based personalized policy included 3.65% WW, 86.72% TRI and 9.62% CS (95% CI +/- 0.02%) on average during a patient's lifetime. The personalized policy was found dominant in 57.23%, 80.02%, and 67.75% (95% CI +/- 0.04%) for patients who followed them compared to ACS, BCS and ATRI, respectively (See Fig 1). At an A1C level of 13%, the personalized policy on average included 0.23% WW, 64.67% TRI, and 35.10% CS (95% CI +/- 0.03%). For this cohort, the personalized policy was found dominant for 71.99%, 94,53%, and 83.36% (95% CI +/- 0.04%) of patients compared to ACS, BCS and ATRI, respectively (See Fig 2).

Conclusions: For the majority of patients, following the model-based personalized screening policy provided more QALYs and was less costly when compared to other standardized policies, highlighting the potential benefit of personalized screening recommendations. This benefit increases for more at-risk patients, such as those with high A1C levels.

CONTROL ID: 3713319

SUBMITTER (NAME ONLY): Leonie Bourauel

TITLE: Spectral Analysis of Human Retinal Pigment Epithelium Cells in Healthy and AMD Affected Eyes

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Bourauel, L.A. von der Emde, M. Sassmannshausen, F.G. Holz, T. Ach, Department of Ophthalmology, University Hospital Bonn, Bonn, GERMANY|M. Vaisband, J. Hasenauer, Institute of Life & Medical Sciences, University of Bonn, Bonn, GERMANY|M. Vaisband, Department of Internal Medicine III with Haematology, Medical Oncology, Haemostaseology, Infectiology and Rheumatology, Oncologic Center; Salzburg Cancer Research Institute - Laboratory for Immunological and Molecular Cancer Research (SCRI-LIMCR); Paracelsus Medical University, Salzburg, AUSTRIA|K. Bermond, Department of Ophthalmology, Ludwigshafen Hospital, Ludwigshafen, GERMANY|I.S. Tarau, Department of Ophthalmology, Asklepios Klinik Nord-Heidberg, Hamburg, GERMANY|R. Heintzmann, Leibniz Institute of Photonic Technology, Jena, GERMANY|R. Heintzmann, Institute of Physical Chemistry and Abbe Center of Photonics, Friedrich-Schiller University Jena, Jena, GERMANY|C.A. Curcio, Department of Ophthalmology, University of Alabama at Birmingham, Alabama, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Individual retinal pigment epithelium (RPE) cells host hundreds of granules with AF properties (PMID: 32433758). Here, we characterized RPE cells in healthy and age-related macular degeneration (AMD) affected eyes by their AF spectra and correlate individual wavelengths with the amount of autofluorescent granules (lipofuscin, melanolipofuscin) per RPE cell body (RPECB).

Methods: Twenty-two RPE flat mounts of human donor eyes (7 AMD-affected (3 early AMD, 1 geographic atrophy, 3 neovascular) and 15 w/ unaffected macula (8<51 yrs; 7>80 yrs)) were imaged at three locations (fovea, perifovea, near periphery) using en face confocal AF (exc. 488 nm) and high-resolution structured illumination microscopy. Up to 110 cells/location/eye were marked manually and emission spectra were extracted (490-695 nm; 8.9 nm spectral channel width) from a projection image of each cell and stratified by disease status and location. Granules/cell were manually quantified and classified with computer-assistance. Mixed linear models were used to correlate spectra with the number of intracellular granules.

Results: Spectra of 5.549 RPE cells (<51yrs: 2.353, >80yrs: 2.053, AMD: 1.143) were included. Spectra of healthy cells showed similar emission spectral curves that peaked at 580 nm for the fovea and perifovea and between 575 and 580 nm for the near periphery. Compared to healthy, AMD spectral curves showed a 10 nm-shift towards shorter wavelengths (further statistical analysis in progress). The effect was strongest for the fovea and perifovea. Spectral curves at the perifovea appeared to be flattened at nAMD stage. Mixed linear models showed no statistically significant differences between the coefficients for wavelengths and granule load.

Conclusions: With the help of different microscopy techniques, identification of cellular (spectral AF) and subcellular (granules) properties of RPE cells allow to distinguish healthy from diseased RPE, especially at fovea and perifovea,

areas highly impacted by AMD related sub-RPE deposits A spectral shift in AMD in this large series of RPE cells confirms earlier microscopy findings (PMID: 12091448) from tissue cross sections. Future studies will examine the impact of individual granule spectra on the total RPE spectrum. Overall, our results will help to interpret the RPE's AF in studies using in vivo single cell imaging.

CONTROL ID: 3713320

SUBMITTER (NAME ONLY): Iwona Gorczynska

TITLE: Location of the retinal band containing photopigments in OCT images through human two-photon vision

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Gorczynska, M.M. Bartuzel, M. Sylwestrzak, P. Stremplewski, Institute of Physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Torun, POLAND|A. Consejo, Department of Applied Physics, Universidad de Zaragoza, Zaragoza, Aragón, SPAIN|

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ABSTRACT BODY:

Purpose: It is well established which band in OCT images corresponds to the photoreceptor layer, yet no in vivo experiments support it. Our goal is to demonstrate which retinal layer in OCT images contains visual photopigments through correlation with two-photon vision psychophysics experiments.

Methods: Two-photon (2P) vision is triggered when light from a pulsed light source is focused on the photopigments. SS-OCT device operating at 1.6MHz rate was used to trigger 2P vision and perform OCT imaging. 1.06μm wavelength light was seen by the subjects as green. OCT data were acquired in the fovea and 7° nasally from the fovea over 5°×5°FOV. The focal plane was moved across the retina over ±312μm from the photoreceptor layer in 31 steps. 6 data sets were taken at each. The same defocus steps were implemented in a random order in the 2P psychophysics experiment. A 5° horizontal line was scanned over the retina. For each defocus the subjects were matching the brightness of a green LCD screen placed in the eye fixation path to the apparent brightness of the OCT line providing a relative measure of the 2P perception intensity. 186 trials were completed. 4 normal subjects were tested. The accommodation was blocked with Tropicamide. The study was approved by the Bioethics Committee of NCU and was adhering to the Declaration of Helsinki.

Results: The effect of defocus on the OCT images was analyzed in C-scans by calculating speckle contrast. With increasing beam defocus from the selected retinal depth, the contrast was deteriorating. Maximum contrast was occurring at different retinal depths as the focal plane was moving across the retina. 2P vision deteriorated as the beam was defocused from the layer containing photopigments. The focal plane position at which the 2P vision was strongest correlates with the maximum contrast of the inner/outer photoreceptor segments junction (IS/OS).

Conclusions: 2P vision can be used to determine in which retinal layer in the OCT images the visual photopigments are located. We were able to determine that the strongest 2P perception correlates with the maximum contrast of the IS/OS layer, demonstrating in in vivo experiment that the light-sensitive band is indeed identified in OCT images as the photoreceptors layer.

CONTROL ID: 3713321

SUBMITTER (NAME ONLY): Sabine Kling

TITLE: Localized refractive changes induced by a new asymmetric intracorneal ring segment: a 3D Finite-element simulation

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kling, ITET, Eidgenossische Technische Hochschule Zurich, Zurich, Zürich, SWITZERLAND|S. Kling, ARTORG, Universitat Bern, Bern, Bern, SWITZERLAND|G. García de Oteyza, 1Clínica Oftalmológica García de Oteyza, SPAIN|J. Álvarez de Toledo, R.I. Barraquer, 3Centro de Oftalmología Barraquer, SPAIN|

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ABSTRACT BODY:

Purpose: To report the localized changes induced by an asymmetric intracorneal ring segment (ICRS) with varying base width and ring thickness in a finite-element simulation.

Methods: A 3D finite element model (FEM) was developed to simulate both a healthy and a keratoconic cornea. After creating a tunnel at 70% depth of corneal thickness, the displacements corresponding to the insertion of an ICRS of 160° arc length were enforced. Different ICRS designs were studied: (i) an asymmetric ICRS with increasing thickness (150 to 300 mm) and base width (600 to 800 mm) from one end to the other, and (ii) a symmetric ICRS with constant thickness (150, 225 or 300mm) and base width (600, 700, or 800mm) at all angular positions. The deformed geometry was assessed in terms of global curvature, sagittal curvature and optical aberrations; induced strains were assessed qualitatively.

Results: The asymmetric ICRS simulated implantation did correct vertical coma (-12.09 vs -8.34 mm), primary spherical aberration (12.98 vs 12.64 mm) and defocus (8.80 vs 8.29 mm) better than the simulated implantation of symmetric ICRS. Global curvature changes were dominated by ICRS thickness and less influenced by ICRS symmetry. Sagittal curvature showed a pattern of locally restricted flattening interior to the ring and local steepening on the opposite half of the cornea, which was more pronounced in the healthy than in the keratoconic cornea.

Conclusions: This study positions the asymmetric ICRS implantation as the most powerful vertical coma corrector. Correcting optical aberrations by ring design has the potential to prevent poor and disappointing results of ICRS surgery in asymmetric keratoconic phenotypes.

CONTROL ID: 3713322

SUBMITTER (NAME ONLY): Katherine Joltikov

TITLE: Experience with High Dose Infliximab and Biosimilar Infliximab-dyyb for Non-infectious Uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Joltikov, M. Munro, P. Bhat, A. Lobo, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Infliximab and biosimilar infliximab-dyyb are widely used for steroid sparing treatment of non-infectious uveitis. The purpose of this study is to report on the safety and efficacy of high-dose infliximab (INX) and biosimilar infliximab-dyyb (INXB), and immunogenicity of INXB, in the treatment of non-infectious uveitis.

Methods: A retrospective review of all patients with non-infectious uveitis treated with INX and/or INXB from 2016 to 2021 was conducted. Data collected included patient demographics, best corrected visual acuity (BCVA), INX/INXB dosage information and any adverse effects, additional immunosuppression medication, and clinical evidence of uveitis flare or quiescence. An active flare was defined as a two-step increase in the level of inflammation, and quiescence was defined as <1/2+ cell in the anterior chamber, no vitreous haze and no active posterior segment findings. Positive clinical immunogenicity was defined as an increased number of flares and/or decreased period of quiescence after starting INXB.

Results: A total of 35 patients met the inclusion criteria. The mean age was 42.6±13.6 years and 24 (69%) were female. Sixteen patients (46%) were African American, 13(37%) were Caucasian, and 5(14%) were Hispanic. Intermediate uveitis (8/35) was the most common diagnosis, followed by scleritis (7/35), anterior uveitis (7/35), and pan-uveitis (5/35). Seven patients had retinal vasculitis and 11 had a co-existing rheumatologic diagnosis (including 4 Bechet's, 3 sarcoidosis, and 2 rheumatoid arthritis). Eight patients received INXB; 4 patients were switched from INX to INXB due to insurance coverage, and 4 were started de-novo. The highest dosages of INX and INXB were 10mg/kg and 12.5mg/kg every 4 weeks, respectively. There were no significant adverse effects associated with high dose INX or INXB, and no significant uveitis flares in the 4 patients that were switched from INX to INXB.

Conclusions: The findings of this retrospective study provide insight into the safety and effectiveness of high-dose INX and INXB in the treatment of non-infectious uveitis. Biosimilar infliximab-dyyb was well-tolerated, safe, and appeared to be of similar clinical effectiveness to originator infliximab, and thus may be a potential cost-effective alternative.

CONTROL ID: 3713323

SUBMITTER (NAME ONLY): Christopher Lievens

TITLE: Extended Depth of Focus from AGN-190584 in GEMINI 1 and GEMINI 2 Pooled Phase 3 Studies

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lievens, Southern College of Optometry, Memphis, Tennessee, UNITED STATES|S. Kannarr, Kannarr Eye Care, Pittsburg, Kansas, UNITED STATES|W. Pack, Z. Zhang, Allergan, an AbbVie Company, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaluate the efficacy of AGN-190584 in extending depth of focus over the course of 30 days.

Methods: Analysis was pooled from identical phase 3 studies GEMINI 1 and GEMINI 2. Participants (N=750) were randomized to receive AGN-190584 or vehicle once daily, bilaterally for 30 days. Depth of focus was measured in diopters (D) using a phoropter in the dominant and non-dominant eyes at hours 0 and 1 post instillation on Days 1, 3, 7, 14, and 30.

Results: Mean depth of focus change from baseline in the AGN-190584 group for the dominant eye was 0.448, 0.484, 0.569, 0.663, and 0.726 D on Days 1, 3, 7, 14, and 30 at Hour 1 compared to a mean of 0.118, 0.114, 0.136, 0.178, and 0.191 D in the vehicle control group (Figure 1A). Mean depth of focus change from baseline in the AGN-190584 group for the non-dominant eye was 0.422, 0.462, 0.568, 0.664, and 0.699 D on Days 1, 3, 7, 14, and 30 at Hour 1 compared to a mean of 0.046, 0.119, 0.105, 0.156, and 0.157 D in the vehicle control group (Figure 1B). All data points for both the dominant and non-dominant eye were statistically significant at Hour 1 in favor of the active treatment group (achieving greater depth of focus). Mean letters of improvement in mesopic distance-corrected near visual acuity (DCNVA) at Hour 1 were 8, 8.9, 9.7, 10.6, and 10.8 in the AGN-190584 group on Days 1, 3, 7, 14, and 30 compared to 3, 4.1, 4.5, 5.1, and 5.3 in the Vehicle group (Figure 2). All data points were significantly higher in the AGN-190584 group compared to the Vehicle group with $p<.0001$.

Conclusions: Extended depth of focus was greater in the active treatment group compared to the vehicle control group as early as Day 1 Hour 1. Over the course of the 30 day study, a gradual increase in depth of focus was observed possibly suggesting a neuroadaptation response perhaps similar to what has been observed with Extended Depth of Focus (EDOF) Intraocular Lenses. With increased depth of focus and corresponding improvements in visual acuity from the pinhole effect there may be a learning period in which the visual cortex learns to process and utilize the EDOF. Letters of improvement in mesopic DCNVA at Hour 1 followed a similar upward trend over the 30 day studies.

CONTROL ID: 3713325

SUBMITTER (NAME ONLY): Elena Piotter

TITLE: Cas13 RNA base editing targeting stop mutation in ABCA4

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Piotter, M.E. McClements, R.E. MacLaren, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|R.E. MacLaren, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Elena Piotter: Commercial Relationship: Code N (No Commercial Relationship) | Michelle McClements: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Stargardt macular dystrophy (STGD1) is the most prevalent form of inherited macular dystrophy worldwide and is therefore highly clinically relevant. To date, a variety of gene supplementation approaches have been tested to create a therapy with some reaching clinical trials. Currently, however, no treatment exists. Newer technologies, such as RNA base editors, enable correction of pathogenic G>A and T>C mutation correction. ABCA4 has ~1200 known pathogenic mutations, of which ~63% are transition mutations amenable to this editing technology. Here, we investigated the use of a Cas13-ADAR RNA base editing system to correct an ABCA4 pathogenic stop mutation, c.206 G>A; p.W60*.

Methods: These experiments used a dual luciferase reporter assay comparing expression of Firefly luciferin to constitutively expressed Renilla luciferin. Fragments of the ABCA4 gene containing the desired mutation, c.206 G>A; p.W60* were inserted in-frame between the two luciferase elements with flanking F2A sites. As the insert contains a stop codon in frame, Firefly is not expressed but when mutation correction occurs, Firefly is expressed. The assay involved a triple transfection of HEK293T cells with the Cas13b-ADAR construct, the luciferase reporter plasmid, and the gRNA plasmid, for which 15 guide variants were tested. The output is the ratio of Firefly to Renilla expression.

Results: Initial findings indicate that all 15 guides show activity relative to the mutant plasmid and the non-targeting control (NTC), $p<0.0001$. Three guides showed statistically significant levels of editing, G6, G7, and G12, relative to the mutant plasmid. However, there was no significant difference between guides. When taken as a percentage of the wild-type (WT) plasmid ie no mutation, these guides showed between 28-34% of WT expression. Further, initial transcript analysis using EditR was performed, where 43-61% of transcripts showed the WT ‘G’ instead of an 'A' with guides 6, 7, and 12.

Conclusions: Overall, previous meta-analyses show 63% of pathogenic mutations in ABCA4 are amenable to Cas13b RNA base editing, particularly as there is no PAM-site constraint. This is a first look at RNA base editing targeting a mutation in ABCA4. The findings indicate that RNA base editing shows potential in targeting an ABCA4 sequence, thus indicating a clinical potential for Stargardt disease.

CONTROL ID: 3713326

SUBMITTER (NAME ONLY): Divya Pidishetty

TITLE: Defects in cone photoreceptor development and progressive retinal dystrophy in rd3 and abca4b knockout stable zebrafish models

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Pidishetty, P. Susaimanickam, S. Damera, I. Mariappan, Center for Ocular Regeneration (CORE), LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|D.A. Pidishetty, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|S. Boyenpally, Ophthalmic Pathology Laboratory, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|G. Kushawah, R. Mishra, Centre for Cellular and Molecular Biology CSIR, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: To knockout zebrafish rd3 and abca4b genes linked to retinal dystrophies and to study the effects of loss of function on retinal development and visual functions

Methods: Zebrafish rd3 and abca4b gene knockout models were generated by CRISPR-Cas9 based genome editing. The edits in the founder animals (F_0) was confirmed by T7 endonuclease assay followed by Sanger sequencing. Homozygous mutants were generated by interbreeding of heterozygotes. The wild type, $rd3^{-/-}$, $abca4b^{-/-}$ mutant fishes were euthanized at 3, 6 and 12 months of age and their retinal morphology was evaluated by immunohistochemistry. Visual assessment of these animals was performed using different functional test paradigms

Results: We report that the retina of $rd3^{-/-}$ mutants at 3 months have underdeveloped cones, with missing outer limiting membrane and lamination defects in the outer nuclear layer. Both rods and cones degenerate at later time points (6 and 12 months), with major loss in cone subtypes. In $abca4b^{-/-}$ mutants, a marked reduction in the cone nuclear layer and a corresponding increase in the number of rod nuclei suggest significant defects in cone precursor cell differentiation and maturation. The single blue cones are completely absent and the UV cones are underdeveloped with rudimentary inner and outer segments. The double cones develop normally, but undergo degeneration in older animals. In experimental paradigms to assess the feed capture response under normal photopic conditions (n=10), the mutant fishes failed to approach their feed/prey and displayed significantly higher latency than the wild type fishes. This visual behavioral deficit corroborates with the cone photoreceptor-specific developmental anomaly and retinal degeneration in mutant fishes

Conclusions: The zebrafish $rd3^{-/-}$ and $abca4b^{-/-}$ mutants show cone developmental defects and degenerative phenotypes that resemble the human disease. Defects in photoreceptor precursor cell differentiation, maturation and lamination indicates possible role(s) for these genes in the early retinal development

CONTROL ID: 3713332

SUBMITTER (NAME ONLY): Ashley Li

TITLE: High positive predictive value of fluorescein angiography contiguous perinerve retinal vascular leakage pattern for birdshot chorioretinopathy

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Li, L. Sobrin, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Ashley Li: Commercial Relationship: Code N (No Commercial Relationship) | Lucia Sobrin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Birdshot chorioretinopathy (BSCR) is a posterior uveitis with ovoid yellow-white choroidal lesions. If untreated, patients' vision declines, so early diagnosis is critical. While indocyanine green angiography (ICGA) is used to identify subtle lesions, ICGA is not always available. Fluorescein angiography (FA) is more common and a contiguous, perinerve retinal vascular leakage pattern has been described in BSCR patients. The purpose of this study is to determine the sensitivity and positive predictive value (PPV) of a contiguous, perinerve retinal vascular leakage FA pattern for BSCR diagnosis.

Methods: Mass General Brigham patients with a FA Common Procedural Terminology code and mention of BSCR in the free text of notes were identified. BSCR diagnosis required HLA-A29 positivity and typical lesions on fundus photos and/or ICGA hypofluorescent spots. Chart review was performed to confirm BSCR vs. other uveitis/retinal vasculitis diagnosis and symptom duration. The first FA was analyzed for a contiguous, perinerve pattern of leakage by two readers. A perinerve leakage pattern was defined as leakage primarily around the optic nerve and along the larger arcade vessels (Fig 1). We compared the rates of this FA pattern in BSCR vs. other posterior uveitis/retinal vasculitis patients using the chi-square test and determined the sensitivity and PPV of this FA pattern for BSCR diagnosis. All statistical analyses were performed in STATA.

Results: 54 BSCR patients and 42 patients with other posterior uveitis and/or retinal vasculitis were identified (Table 1). A perinerve FA pattern was more common in BSCR patients vs. patients without BSCR (53.7% vs. 4.76%, $p=3.63 \times 10^{-7}$). The sensitivity and specificity of the FA pattern were 53.7% and 95.2%, respectively. The PPV was 93.5%. BSCR patients with an FA perinerve pattern had a shorter time from symptom onset to FA vs. BSCR patients without the pattern (217 vs. 1510 days, p=.0015, t-test).

Conclusions: An FA contiguous, perinerve retinal vascular leakage pattern is a useful tool to identify potential BSCR for further imaging and serological testing. This pattern is more common when the interval between symptom onset and FA is shorter.

CONTROL ID: 3713333

SUBMITTER (NAME ONLY): Christine Orndahl

TITLE: Estimating power for a multi-site treatment study leveraging natural history ABCA4-related retinopathy data

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Orndahl, M. Abraham, S. Menezes, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|B. Brooks, B. Jeffrey, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Christine Orndahl: Commercial Relationship: Code N (No Commercial Relationship) | Maria Abraham: Commercial Relationship: Code N (No Commercial Relationship) | Supriya Menezes: Commercial Relationship: Code N (No Commercial Relationship) | Brian Brooks: Commercial Relationship: Code N (No Commercial Relationship) | Brett Jeffrey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A clinical trial of oral metformin for treatment of ABCA4 retinopathy was initiated at National Eye Institute (NEI) (ClinicalTrials.gov: NCT04545736). Power analysis was based on a single site (NEI) with high-resolution Optical Coherence Tomography (OCT) volume scans and equally spaced visits. To aid recruitment, an additional site with lower density volume scans is considered and unequally spaced visits introduced to account for missed visits due to the Coronavirus Disease 2019 pandemic. The aims were to determine the effects of adding a site that uses a mix of low- and high-resolution images and an increased number of natural history visits and spacing between visits on power.

Methods: A longitudinal spline regression is proposed for the primary outcome analysis, comparing growth rate in square-root transformed ellipsoid zone band loss area on OCT between the treatment phase (current study) and pre-treatment phase (natural history study), with a knot at the baseline visit when patients initiate treatment. Data were simulated using the observed mean, variance and inter-eye correlation for baseline values (from the last available pre-treatment visit) and pre-treatment growth rates from available natural history data at NEI; expected improvement in the primary outcome due to treatment; and other salient features of the study. Low-resolution values were derived from the natural history high-resolution images at NEI. The number of pre-treatment visits and spacing between visits were varied keeping other factors constant for a fixed sample size, while accounting for the appropriate resolution values at each site. The resultant power for detecting a treatment effect was estimated based on 2000 simulated datasets.

Results: The power estimated when accounting for a mix of low- and high-resolution values at the second site was the same as that with all high-resolution values at 80%. An increase from 4 to 6 pre-treatment visits increased power by 15% and increasing the spacing between visits from 6 to 12 months increased power by 6% for the study.

Conclusions: Increasing the number of pre-treatment visits and spacing between visits increased power. Derivation of low-resolution values from high-resolution images may be the reason for the high correlation between the two resolutions, which may explain why including a mix of low- and high-resolution values did not decrease power.

CONTROL ID: 3713336

SUBMITTER (NAME ONLY): Prince Akowuah

TITLE: Diet-reversal strategy for attenuating high fat diet-induced corneal dysregulation

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Akowuah, A. Burns, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|R. Rumbaut, A. Burns, Children's Nutrition Research Center, Baylor College of Medicine, Houston, Texas, UNITED STATES|R. Rumbaut, Center for Translational Research on Inflammatory Diseases, Michael E DeBakey VA Medical Center, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Prince Akowuah: Commercial Relationship: Code N (No Commercial Relationship) | Rolando Rumbaut: Commercial Relationship: Code N (No Commercial Relationship) | Alan Burns: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In addition to cardiometabolic changes, high fat diet (HFD) feeding causes loss of corneal sensitivity loss and impairs corneal wound healing. Diet reversal (DR) strategies effectively mitigate cardiometabolic effects of HFD and corneal sensitivity loss. Their utility for attenuating the impaired corneal wounding that accompanies HFD feeding, however, remains unclear. This study used a diet-induced obesity mouse model to test the hypothesis that in addition to attenuating corneal sensitivity loss, DR also attenuates impaired corneal wound healing induced by HFD.

Methods: 6-week-old C57BL/6 male mice were fed ad libitum, either normal diet (ND) or HFD for 10 weeks. Some of the HFD-fed mice were then switched to ND (DR group), with the rest continuing their respective feeding regimen for an additional 10 weeks. Mice were weighed weekly. Visceral adiposity was measured by epididymal adipose tissue (eAT) weight and adiposity index and fatty liver by liver weight. Corneal sensitivity was measured every 5 weeks using a Cochet-Bonnet aesthesiometer. At 10 and 20 weeks of feeding, a 2-mm diameter corneal epithelial abrasion wound was created, and wound closure monitored for 30h using sodium fluorescein staining. Data were analyzed with ANOVA. Significance was set at $p \leq 0.05$.

Results: Mice fed HFD-only gained ≥110 % more body weight ($p<0.0001$) and had ≥50% more visceral adiposity ($p<0.005$) than mice fed ND-only. Fatty liver was observed in mice fed HFD-only ($p<0.001$). DR markedly reduced body weight, visceral adiposity, and fatty liver. Corneal sensitivity was significantly reduced in mice fed HFD-only, corresponding to an ≥30% increase in pressure required to elicit a blink compared to mice fed ND-only ($p<0.05$). DR halted further progression of corneal sensitivity loss. After 5 and 10 weeks of DR, there was no difference in corneal sensitivity between DR group and age-matched ND group. At both 10 and 20 weeks of feeding, corneal wound closure was delayed (~6h) in mice fed HFD-only ($p<0.002$). DR for 10 weeks returned corneal wound closure to that of age matched fed ND-only.

Conclusions: The results are consistent with the hypothesis that DR attenuates HFD-induced corneal sensitivity loss and impaired corneal wound healing.

CONTROL ID: 3713338

SUBMITTER (NAME ONLY): Emmanuel Alabi

TITLE: Interrater reliability of the refractive measurements of plano-protective eyewear using the American National Standard Institute (ANSI) Z87.1 telescope approach

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.B. Alabi, Eye and Face Research, ICS Laboratories, Brunswick, Ohio, UNITED STATES|J. Hovis, Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|

Commercial Relationships Disclosure: Emmanuel Alabi: Commercial Relationship(s);Code E (Employment):ICS Laboratories | Jeffery Hovis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The optical testing requirements of plano-protective eyewear in national/international standards rely on subjective evaluation methods that are negatively impacted by factors such as differences in accommodation, depth of focus, field of view, criteria and resolving power of the telescope-human observer system. These challenges can lead to significant variation in the testing results provided by different test laboratories. This study examined how observer differences could affect the results by evaluating the interrater reliability of refractive measurements of plano-protective eyewear using the ANSI Z87.1 (2020) telescope approach.

Methods: Spherical and astigmatic power measurements were performed by two experienced observers on the left oculars of 52 pairs of military plano-protective eyewear in accordance with the method described in the ANSI Z87.1 standard. The observers were blind to each other's results. Briefly, the objective lens of a calibrated 8x telescope was mounted 35 feet from a combined sunburst-resolution test pattern in a controlled laboratory environment. The data was analyzed using a multiple rater, absolute-agreement, 2-way mixed-effects intraclass correlation (ICC) model for the spherical and astigmatic power measurements. SPSS-V26 was used for all statistical analysis and $p<0.05$ was used to determine statistical significance.

Results: The mean (±SD) refractive powers of the eyewear for raters 1 and 2 were spherical -0.005(±0.019), -0.006(±0.02) and astigmatism 0.031(±0.015), 0.026(±0.016), respectively. There was good reliability between the spherical power measurements, with an ICC of 0.813 and 95% confidence interval from 0.674 to 0.893 ($p<0.001$). The reliability between the astigmatic power measurements was lower. The ICC was 0.531 with a 95% confidence interval from 0.191 to 0.729 ($p<0.005$).

Conclusions: The ANSI Z87.1 telescope approach may provide reliable estimates of spherical power between raters for plano-protectors but less reliable interrater estimates of astigmatic power when using the same telescopic system. Objective refractive power measurement methods may improve this reliability further.

CONTROL ID: 3713339

SUBMITTER (NAME ONLY): Xuming Zhu

TITLE: Hedgehog signaling promotes expansion of Meibomian Gland stem cells in vivo

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Zhu, M. Xu, S.E. Millar, Black Family Stem Cell Institute, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|X. Zhu, M. Xu, S.E. Millar, Cell, Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|M. Grachtchouk, A.A. Dlugosz, Rogel Cancer Center, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|M. Grachtchouk, A.A. Dlugosz, Dermatology, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Xuming Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Mingang Xu: Commercial Relationship: Code N (No Commercial Relationship) | Marina Grachtchouk: Commercial Relationship: Code N (No Commercial Relationship) | Andrzej Dlugosz: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Millar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Meibomian glands (MGs) are specialized sebaceous glands (SGs) in which meibocytes are constantly replenished through proliferation and differentiation of acinar basal stem cells (SCs). However, specific markers for self-renewing SCs of MG (MGSCs) are poorly defined, and the signals that control their activity are incompletely understood. The Hedgehog (HH)/GLI pathway controls proliferation and differentiation of rat MG epithelial cells in vitro, and GLI2 is highly expressed in acinar basal cells and differentiating meibocytes but is absent from fully differentiated meibocytes in vivo. We hypothesize that MGSCs express similar marker genes as SCs of hair follicle SGs (SGSCs), and that GLI2 regulates MG homeostasis by coordinating proliferation and differentiation of MGSCs.

Methods: To determine whether the hair follicle SGSC markers Lrig1 and Lgr6, and the ubiquitous Wnt target gene Axin2, label self-renewing MGSCs we performed short- and long-term lineage tracing experiments using Lrig1-Cre^{ERT2}, Lgr6-Cre^{ERT2}, and Axin2-Cre^{ERT2} mice carrying the Rosa26^{mTmG} Cre reporter allele. To determine the effects of GLI2-mediated HH signaling on MGSCs we generated transgenic mice with forced expression of activated GLI2 (GLI2ΔN) in MG basal epithelial cells and carried out transcriptional profiling of laser captured MGs from control and GLI2ΔN-expressing mice. RNAscope and immunofluorescence were used to confirm RNA-seq results.

Results: Short-term lineage tracing data showed that Lrig1, Lgr6 and Axin2 label basal cells in MG ducts and acini. Long-term lineage tracing results showed that clones of labeled cells persist through multiple rounds of ductal and acinar renewal and give rise to differentiated progeny, identifying Lrig1+, Lgr6+ and Axin2+ ductal and acinar basal cells as self-renewing SCs. Forced expression of GLI2ΔN enhanced basal proliferation, caused expansion of Lrig1+ SCs, and lead to replacement of lipid-filled meibocytes by proliferative and poorly differentiated acinar cells. Transcriptional profiling of GLI2ΔN-expressing and control MGs revealed that forced GLI2ΔN expression caused greatly increased expression of Lrig1 and Lgr6 and suppressed expression of meibocyte differentiation genes.

Conclusions: (1) Lrig1^{+}, Lgr6^{+} and Axin2^{+} mark self-renewing basal SCs that replenish MG acinar and ductal epithelium in vivo. (2) GLI2-mediated HH signaling promotes proliferation and inhibits differentiation of MGSCs.

CONTROL ID: 3713340

SUBMITTER (NAME ONLY): Inês Pereira

TITLE: Magnetically actuated glaucoma drainage device for regulating intraocular pressure after implantation

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I.C. Pereira, H.M. Wyss, J.M. den Toonder, Mechanical Engineering, Microsystems Research Section, Technische Universiteit Eindhoven, Eindhoven, Noord-Brabant, NETHERLANDS|I.C. Pereira, H.M. Wyss, J.M. den Toonder, Institute for Complex Molecular Systems (ICMS), Technische Universiteit Eindhoven, Eindhoven, Noord-Brabant, NETHERLANDS|H.J. Beckers, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|

Commercial Relationships Disclosure: Inês Pereira: Commercial Relationship: Code N (No Commercial Relationship) | Hans Wyss: Commercial Relationship: Code N (No Commercial Relationship) | Henny Beckers: Commercial Relationship: Code N (No Commercial Relationship) | Jaap den Toonder: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The key risk factor for glaucoma is increased intraocular pressure (IOP). Glaucoma drainage devices have been developed to reduce IOP and thus stop disease progression, however, the lack of proper IOP control can lead to serious postsurgical complications. To have a better control of the IOP, we are developing an innovative magnetically actuated glaucoma implant with a hydrodynamic resistance that can be adjusted following surgery.

Methods: Our smart implant is comprised of a drainage tube and a housing element in which a magnetic “micro-pencil” valve is integrated (Figure 1A and B). The implant is made from poly(styrene-block-isobutylene-block-styrene), or ‘SIBS’.The magnetic microvalve was fabricated from SIBS containing homogeneously dispersed iron microparticles. “Micro-pencil” valves of this material were fabricated by replica molding using hot embossing, with femtosecond laser-machined fused silica glass molds (Figure 1C). The same technique was used to fabricate the housing element.

Results: Microfluidic experiments involving actuating the magnetic micro-pencil with a moving external magnet were carried out to confirm the valving function. The pressure upstream the implant, which would correspond to the IOP, was measured while the microvalve switched between open/closed states (Figure 2A). A pressure difference up to 10 mmHg was achieved which is sufficient to overcome hypotony, i.e. too low IOP (Figure 2B).

Conclusions: The femtosecond laser machining process has proved to be an effective technique to fabricate the molds for both the microvalve and the glaucoma device. The features in these molds were successfully transferred to a thermoplastic material like SIBS. Microfluidic experiments performed with the novel, magnetically actuated glaucoma implant have shown that, when in the closed state, the microvalve can provide a sufficient hydrodynamic resistance that can help to overcome hypotony.

CONTROL ID: 3713343

SUBMITTER (NAME ONLY): Dimitrios Stampoulis

TITLE: In vivo expression and efficacy following subretinal delivery of GT005, an investigational gene therapy for the treatment of geographic atrophy (GA)

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Stampoulis, J. Joel, A. Dreismann, E. Gardenal, J. Hughes, S. Ellis, J. Esteve-Rudd, Gyroscope Therapeutics Ltd, UNITED KINGDOM|

Commercial Relationships Disclosure: Dimitrios Stampoulis: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd | Josephine Joel: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd | Anna Dreismann: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd | Emanuela Gardenal: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd | Jane Hughes: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd | Scott Ellis: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd | Julian Esteve-Rudd: Commercial Relationship(s);Code E (Employment):Gyroscope Therapeutics Ltd

ABSTRACT BODY:

Purpose: Report non-clinical in vivo expression data and efficacy in the mouse laser-induced choroidal neovascularization (CNV) model after subretinal delivery of GT005, an investigational AAV2 gene therapy expressing recombinant human complement factor I (hCFI).

Methods: HEK-293 cells were transduced with GT005 to confirm expression of hCFI at both the mRNA and protein levels. Expressed CFI protein function was evaluated with a C3b cleavage assay. In rodent expression studies, GT005 was unilaterally, subretinally injected in mice at $2x10^7$-$2x10^8$ GC/eye. 28 days later ocular fluids and tissues were collected for expression analyses including qRT-PCR, ELISA, in situ hybridization and immunohistochemistry. In laser CNV model studies, GT005 or mGT005, which encodes for murine CFI, was subretinally injected in mice at $2x10^7$-$2x10^8$ GC/eye 28 days prior to lasering. Negative control animals received empty vector at $2x10^8$ GC/eye. Positive control mice received 80 ug aflibercept intravitreally after lasering. CNV leakage was assessed 4 and 7 days post-lasering by optical coherence tomography (OCT) and fluorescence angiography (FA). Lesion area was evaluated by staining RPE/choroid flatmounts with FITC-conjugated isolectin-B4 7 days after lasering.

Results: Expression and secretion of functional, processed hCFI was demonstrated in vitro after transduction of HEK-293 cells with GT005, and in vivo after subretinal injection of GT005 to mice. hCFI mRNA and protein were mainly localized in the outer retina and was enriched in the bleb area. In the CNV model, no significant difference was detected in CNV leakage at days 4 and 7 in mice treated with GT005 or a murine version (mGT005) compared to the negative control. However, both showed a dose-dependent effect in reducing CNV lesion size which was statistically significant at the $5x10^7$ and $2x10^8$ GC/eye doses (mGT005: P=0.040 and P=0.011 respectively).

Conclusions: GT005 leads to expression of functional CFI protein in vitro and in vivo in mice, localizing to the target tissues that are affected in dry age-related macular degeneration (AMD). GT005 shows therapeutic efficacy in the mouse CNV model, a model of wet AMD in which complement activation plays a key pathophysiological role. These data support the therapeutic potential of GT005 for the treatment of GA by complement system modulation.

CONTROL ID: 3713344

SUBMITTER (NAME ONLY): Christian Schmidt

TITLE: Towards thermal stimulation of the retina, RPE and choroid by temperature-controlled laser exposure

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Schmidt, Y. Miura, R. Brinkmann, Medizinisches Laserzentrum Lubeck GmbH, Lubeck, Schleswig-Holstein, GERMANY|M. Mordmüller, Institute of Biomedical Optics, University Lübeck, Lübeck, Schleswig-Holstein, GERMANY|

Commercial Relationships Disclosure: Christian Schmidt: Commercial Relationship(s);Code E (Employment):Medizinisches Laserzentrum Luebeck GmbH | Mario Mordmüller: Commercial Relationship: Code N (No Commercial Relationship) | Yoko Miura: Commercial Relationship: Code N (No Commercial Relationship) | Ralf Brinkmann: Commercial Relationship(s);Code C (Consultant/Contractor):Medizinisches Laserzentrum Luebeck GmbH;Code P (Patent):Medizinisches Laserzentrum Luebeck GmbH

ABSTRACT BODY:

Purpose: Subvisible, non-damaging retinal laser treatments are currently used for several retinal diseases. Due to strong inter- und intraocular variations of light scattering and pigmentation at the fundus the laser-induced temperatures differ widely. In order to overcome these uncertainties we developed an optoacoustic (OA) method allowing to determine and control the temperature rise during treatments. For treatment the currently used green and yellow wavelengths primarily address the retina and the retinal pigment epithelium (RPE) due to the strong melanin absorption in the RPE. The involvement of the choroid in the pathogenesis of chorioretinal diseases has been increasingly recognized, and the choroid is now being discussed as a target for treatment. Since IR wavelength are well suited for a choroidal thermal stimulation, this work attempts a combination of green and IR wavelength to achieve non-damaging stimulation of the retina, RPE and also the choroid with a proper temperature control.

Methods: Porcine RPE/choroid/sclera explants were placed in a cuvette filled with physiological saline solution. The specimen were irradiated via a laser slitlamp by a Q-switched Nd:YLF-laser (1053 nm and 527 nm wavelength) with a repetition rate of 10 kHz and pulse duration of 50 ns for 100 ms on a spot diameter of 200 µm. Acousto-optic modulators were used to modulate the laser pulse energies and clock ratio of the two wavelengths. OA transients induced by each laser pulse were recorded with an ultrasonic transducer embedded in a contact lens for temperature monitoring.

Results: OA transients were detected for every laser pulse of both wavelengths. Their ratios indicated a stronger absorption behind the RPE when combining both wavelengths compared to the 527 nm applied alone. For example, under the same average power of 35 mW, the maximum temperature of the RPE was measured to be 58,4 °C when irradiating with 527 nm and 3,5 µJ pulse energy, compared to 34,9 °C when 527 nm and 1053 nm were combined with 2,5 µJ and 4,5 µJ pulse energy, respectively, at 1:1 clock ratio.

Conclusions: This study is a first step towards a deeper thermal stimulation of the retina, RPE and choroid under proper temperature control. Future work will focus on temperature estimation at the choroid by the IR pulses. Further a feedback controlled irradiation with proper active temperature control will be implemented.

CONTROL ID: 3713348

SUBMITTER (NAME ONLY): Abdullah Aamir

TITLE: Phenotypic Characteristics as a Diagnostic Tool for Albinism: Sensitivity and Specificity Analysis

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Aamir, H. Kuht, G. Maconachie, R. McLean, Z. Tu, V. Sheth, F.A. Proudlock, I. Gottlob, M.G. Thomas, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|J. Han, Gangnam Severance Hospital Department of Ophthalmology, Gangnam-gu, Seoul, KOREA (THE REPUBLIC OF)|M.M. van Genderen, Bartimeus, Zeist, Utrecht, NETHERLANDS|R.W. Hertle, Akron Children's Hospital, Akron, Ohio, UNITED STATES|L. Kessel, Rigshospitalet, Kobenhavn, DENMARK|B. Brooks, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Albinism has significant genetic and phenotypic heterogeneity and can be difficult to distinguish from other causes of infantile nystagmus, particularly in a paediatric setting. Children with albinism are at risk of poor visual development and hence require timely diagnosis. We sought to identify clinical parameters specific to albinism, in order to contribute to the growing need for international consensus guidelines for the diagnosis of this complex condition.

Methods: Patients with nystagmus presenting to a paediatric ophthalmology department were screened in centres including Denmark, Korea, Netherlands, United Kingdom and the United States. Patients were stratified according to diagnosis through genetic confirmation. Ophthalmic examination, foveal hypoplasia (FH) and visual evoked potentials (VEP) were recorded. Receiver operating characteristic curves were plotted to assess the diagnostic ability of clinical parameters. Principal component analysis was used to identify unique-most variables. A binary logistic regression model was used to identify a single combined metric.

Results: 249 patients were included, of which 63% had molecular confirmation of albinism. Other diagnoses included FRMD7 (17%), PAX6 (8%), achromatopsia (8%) and congenital stationary night blindness (4%). Parameters with a positive correlation with albinism included fundus hypopigmentation (AUC=0.91), transillumination defect (TID) (AUC=0.91), FH (AUC=0.82) and VEP misrouting (AUC=0.73). Parameters with weak correlation included stereopsis (AUC=0.64), visual acuity (AUC=0.53) and altered head position (AUC=0.43). Regression modelling identified a single metric incorporating FH, TID and VEP with the highest predictive power (AUC=0.96). Removing VEP from the model revealed an AUC of 0.95.

Conclusions: Combining FH and TID may provide sufficient diagnostic power in suspected albinism and dismiss other causes of congenital nystagmus. VEP misrouting may only provide a marginal improvement in diagnostic ability.

CONTROL ID: 3713349
SUBMITTER (NAME ONLY): Matthew Driban
TITLE: Acute Posterior Vitreous Detachment
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: M. Driban, J. Chhablani, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|
Commercial Relationships Disclosure: Matthew Driban: Commercial Relationship: Code N (No Commercial Relationship) | Jay Chhablani: Commercial Relationship(s);Code C (Consultant/Contractor):Salutaris, Novartis, Allergan
ABSTRACT BODY:
Purpose: Posterior vitreous detachment (PVD) is a common ocular condition with myriad risk factors and complications that remain incompletely studied. In this retrospective clinical study, we analyzed the typical presentation of acute PVD, as well as the prevalence of various treatable findings and changes in the same and fellow eye.
Methods: This was a retrospective analysis of medical records from 2,346 patients with acute PVD. Patients with new cases of acute PVD were included in the study. Acute PVD was defined as patients presenting with new symptoms of PVD, including flashes or floaters in one or both eyes, or patients with diagnosis of PVD in their code. Patients with a history of any associated ocular disease, prior PVD, and intraocular injections were excluded. Descriptive statistics were generated on age, sex, contact date, visual acuity, and slit lamp and fundoscopy findings. Multivariate regressions were used to generate odds ratios with 95% confidence intervals (CI) to quantify associations between variables, such as demographics, seasonal presentation, and complications.
Results: A total of 4,692 eyes from 2,346 patients were analyzed. The majority of patients were female (60.5%) with an average age of 62.8-years-old. Mean visual acuity was 20/30 equivalent. Overall, 605 patients (25.8%) had any additional ocular finding on fundus exam, including pigmentation (N=184, 7.8%), lattice degeneration (N=158, 6.7%), tear (N=131, 5.6%), and hole (N=131, 5.2%). Unilateral retinal detachment was present in 26 patients (1.1%) and these patients demonstrated a similar rate (26.9%) of additional ocular findings compared to the entire sample size. Female sex (OR 1.21, 95% CI 1.03-1.43, p = 0.020) was independently associated with presentation during spring or summer.
Conclusions: In this study we describe the risk factors and prevalence of peripheral lesions and complications in acute PVD. We show associations between female sex and presentation during the spring or summer. Additionally, we highlight the incidence of previously unstudied ocular findings in acute PVD, which may be useful in predicting development of other ocular conditions or for identifying patients at risk for future PVD.

CONTROL ID: 3713352

SUBMITTER (NAME ONLY): Saoud Al-khuzaei

TITLE: Phenotypic appearances in a large ethnically diverse cohort of 178 patients with ABCA4 retinopathy

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Al-khuzaei, M. Shah, S. Broadgate, J. Yu, J.K. Jolly, R.E. MacLaren, P. Charbel Issa, S. Halford, S.M. Downes, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|S. Al-khuzaei, M. Shah, R.E. MacLaren, P. Charbel Issa, S.M. Downes, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|C.R. Foster, Pathlab Bay of Plenty, Tauranga, Bay of Plenty, NEW ZEALAND|J.K. Jolly, Anglia Ruskin University Vision and Eye Research Institute, Cambridge, UNITED KINGDOM|M. Shanks, P. Clouston, Oxford Medical Genetics Laboratories, Churchill Hospital, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Saoud Al-khuzaei: Commercial Relationship: Code N (No Commercial Relationship) | Mital Shah: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Broadgate: Commercial Relationship: Code N (No Commercial Relationship) | Jing Yu: Commercial Relationship: Code N (No Commercial Relationship) | Charlotte Foster: Commercial Relationship: Code N (No Commercial Relationship) | Jasleen Jolly: Commercial Relationship: Code N (No Commercial Relationship) | Morag Shanks: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship) | Peter Charbel Issa: Commercial Relationship: Code N (No Commercial Relationship) | Penny Clouston: Commercial Relationship: Code N (No Commercial Relationship) | Stephanie Halford: Commercial Relationship: Code N (No Commercial Relationship) | Susan Downes: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Stargardt disease STGD1/ABCA4 retinopathy (ABCA4R) is the commonest childhood onset inherited retinal dystrophy and can show marked phenotypic heterogeneity and is associated with a number of phenocopies. The characteristic phenotypic features of STGD1 are macular atrophy, flecks, and peripapillary sparing. In this study we aim to describe the broader phenotype in a cohort of 178 patients with ABCA4R to characterise further the spectrum of phenotypic features.

Methods: Patients with variants in ABCA4 were identified from the Oxford Medical Genetics laboratory database. Patients were only included if they had at least one retinal image, a minimum of 2 variants in ABCA4, or 1 variant with a phenotype consistent with an ABCA4R. Phenotyping included: colour fundus imaging (Optos or Topcon), fundus autofluorescence imaging (FAF), and optical coherence tomography (OCT). FAF imaging was primarily used to describe the phenotypic features in this study.

Results: The cohort included 151 patients with at least 2 ABCA4 variants and 27 monoallelic patients with phenotype consistent with ABCA4R. Typical phenotypes associated with ABCA4R were identified in 136 biallelic and 25 monoallelic patients and included: abnormal foveal AF with a ring of raised AF and minimal flecks; flecks but no macular atrophy; macular atrophy surrounded by a well confined ring of flecks; macular atrophy with minimal flecks; mottled macular AF; macular atrophy with flecks within the posterior pole; well defined lesion of macular atrophy surrounded by a heterogenous background AF; patchy areas of macular atrophy with a heterogenous background AF; and widespread chorioretinal atrophy. Atypical phenotypes were identified in 15 biallelic patients and 2 monoallelic patients and included macular atrophy surrounded by a ring of raised AF, heterogenous AF throughout the retina, cone rod dystrophy, retinitis pigmentosa, panretinal atrophy, punctate inner choroidopathy type appearance, and atypical foveal changes.

Conclusions: We present an ethnically diverse British cohort of 178 patients with a diagnosis of an ABCA4R demonstrating the wide spectrum of phenotypic features including atypical cases. Recognition of these different phenotypes in ABCA4R is key in diagnosis, with genetic confirmation, and will be important in selection of patients for inclusion for future therapeutic intervention.

CONTROL ID: 3713353
SUBMITTER (NAME ONLY): Robbie Holland
TITLE: Self-supervised pretraining enables deep learning-based classification of AMD with fewer annotations
SESSION TITLE: AI in the Retina
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Holland, M.J. Menten, D. Rueckert, BioMedIA, Imperial College London, London, London, UNITED KINGDOM|O. Leingang, H. Bogunovic, S. Riedl, U. Schmidt-Erfurth, Laboratory for Ophthalmic Image Analysis, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|A.M. Hagag, S. Sivaprasad, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|R. Kaye, A.J. Lotery, Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, Hampshire, UNITED KINGDOM|A.M. Hagag, S. Sivaprasad, Moorfields Eye Unit, National Institute for Health Research, London, London, UNITED KINGDOM|O. Leingang, Christian Doppler Laboratory for Artificial Intelligence in Retina, Christian Doppler Forschungsgesellschaft, Wien, AUSTRIA|M.J. Menten, Institute for AI and Informatics in Medicine, Technische Universitat Munchen, Munchen, Bayern, GERMANY|G. Traber, H.P. Scholl, Department of Ophthalmology, Universitat Basel, Basel, Basel-Stadt, SWITZERLAND|G. Traber, H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|L. Fritsche, Department of Biostatistics, University of Michigan, Ann Arbor, Michigan, UNITED STATES|T. Prevost, Nightingale-Saunders Clinical Trials & Epidemiology Unit, King's College London, London, London, UNITED KINGDOM|
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ABSTRACT BODY:
Purpose: Deep learning can detect and classify age-related macular degeneration (AMD), which are critical to patient monitoring and prognosis. Traditionally deep learning requires vast amounts of labelled data, which are time-consuming and costly to acquire. In this work we leverage self-supervised pretraining of deep-learning models to achieve high accuracy in classifying AMD while using fewer labelled training data.
Methods: Experiments were conducted on a dataset of 57,875 OCT images from the Southampton Eye Unit collected by the PINNACLE consortium. We trained multiple ResNet50 neural networks to classify between healthy eyes and early/intermediate AMD, and between early/intermediate and late AMD. For both tasks we measured the degradation in classification accuracy when limiting the amount of available training labels. We then repeated these experiments but used self-supervised pretraining, which learns from all images in the dataset even in the absence of labels. To this end, we used two different self-supervised pretraining methods: BYOL, which aims to maximize agreement between different views of the same image, and SimCLR which additionally aims to maximize disagreement between two views from different images.
Results: As expected, classification performance degraded as the number of training labels decreased. Without pretraining, classification between early/intermediate AMD and healthy eyes degraded from 0.92 to 0.64 area under curve (AUC) as the number of training labels decreased from 8299 to 20. Self-supervised pretraining restored performance, and furthermore elevated accuracy when all labels were available. Methods pretrained with BYOL/SimCLR decreased from 0.94/0.91 to 0.74/0.68 AUC for 8299 and 20 training labels respectively. Similar trends were observed when classifying between late and early/intermediate AMD.
Conclusions: Self-supervised pretraining significantly boosted the ability of deep learning to classify AMD in OCT images, especially when only small amounts of data were available as is typical in medical imaging. This motivates a

shift in focus towards procuring fewer, higher quality annotations and unlocks the benefits of deep learning for smaller datasets.

CONTROL ID: 3713355

SUBMITTER (NAME ONLY): Andras Komaromy

TITLE: Safety and efficacy of topically administered latanoprostene bunod (Vyzulta™) in glaucomatous dogs with ADAMTS10-open-angle glaucoma (ADAMTS10-OAG)

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Komaromy, M. Enfield, C. Harman, M. Matthews, A. Anderson, J.P. Steibel, Michigan State University, East Lansing, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Andras Komaromy: Commercial Relationship(s);Code F (Financial Support):Bausch & Lomb | Mary Enfield: Commercial Relationship: Code N (No Commercial Relationship) | Christine Harman: Commercial Relationship: Code N (No Commercial Relationship) | Marissa Matthews: Commercial Relationship: Code N (No Commercial Relationship) | Amanda Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Juan Steibel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate safety and efficacy of topically administered 0.024% latanoprostene bunod ophthalmic solution (Vyzulta™; Bausch & Lomb) in glaucomatous dogs with ADAMTS10-open-angle glaucoma (ADAMTS10-OAG).

Methods: Twenty glaucomatous Beagle dogs with ADAMTS10-OAG, 10 females and 10 males, between the ages of 2.4-4.9 years (median: 2.7 years) were used. In each dog, left or right eye was randomly selected for latanoprostene bunod treatment. Contralateral eyes were treated with generic 0.005% latanoprost ophthalmic solution with well established canine efficacy and safety. Part 1 (n = 15 dogs) consisted of a 4-week study with diurnal intraocular pressure (IOP) and pupil diameter being the main efficacy outcome measures: Following a baseline period (Week 1), dogs were treated once (q24h, Week 2) and twice daily (q12h, Week 3); Week 4 served as washout period. In Part 2 (n=11 dogs), IOPs were monitored for 8 hours following a 1-time drug administration. Safety was assessed by routine ophthalmic examination, gonioscopy and pachymetry. Differences in least square means of quantitative outcome measures were compared between latanoprostene bunod and latanoprost treated eyes by linear Gaussian model.

Results: Mean baseline IOP was 30.0 ± 3.1 mmHg (mean ± SEM). While there were significant decreases in IOPs and pupil diameters for both treatments ($p < 0.0001$), there were no differences in IOP treatment effects between latanoprostene bunod and latanoprost (q24h: 15.1 ± 1.3 mmHg vs. 15.9 ± 1.3 mmHg; q12hr: 13.1 ± 1.1 mmHg vs. 14.1 ± 1.1 mmHg). Furthermore, there was no difference in short-term IOP effect over 8 hours between the 2 drugs. Both latanoprostene bunod and latanoprost administration resulted in mild to moderate conjunctival hyperemia.

Conclusions: Once or twice daily administration of latanoprostene bunod and latanoprost were equally effective in lowering IOP in glaucomatous dogs with no detectable treatment effect resulting from latanoprostene bunod's nitric oxide (NO) donating moiety.

CONTROL ID: 3713356

SUBMITTER (NAME ONLY): Amit Gupta

TITLE: Determinants of Non-Attendance in Face-to-Face Ophthalmic Clinics Pre- and During the Coronavirus Pandemic

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gupta, S. Wagner, L. Raja, R. Struyven, P.A. Keane, J. Huemer, K. Balaskas, D. Sim, A. Solebo, S. Kang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|S. Wagner, R. Struyven, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|M. Cortina-Borja, J. Rahi, University College London Institute of Child Health, London, London, UNITED KINGDOM|P.A. Keane, NIHR Biomedical Research Centre at University College London, London, UNITED KINGDOM|J. Rahi, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Previous evidence suggests serial ‘non-attenders’ to clinic appointments are more likely to be socially disadvantaged, afflicted by poor health, and have higher use of emergency healthcare. This report seeks to quantify and characterise factors associated with non-attendance within a population of patients for face-to-face (F2F) outpatient appointments, pre—and during the COVID-19 pandemic.

Methods: This was a retrospective cohort study of all National Health Service (NHS) patients, aged 18 and over, who were newly referred to Moorfields Eye Hospital NHS Foundation Trust, a tertiary ophthalmic institution consisting of a principal central site, four district hubs and five satellite clinics in London between January 1st 2019 and November 1st 2021. We included patients referred to the adnexal, cataract, general ophthalmology, glaucoma and medical retina services. Only the patient’s first encounter (attendance or non-attendance) with MEH was included.

Results: A total of 70,328 of first appointments were F2F (mean age pre-pandemic: 54 and pandemic: 56 – IQR: 30 for both cohorts). The non-attendance rates for face-to-face pre-pandemic were 9.0% and face-to-face pandemic were 10.5%. Male sex (adjusted odds ratio pre-pandemic: 0.85, 0.80-0.91 and pandemic: 0.89, 0.82-0.97), greater levels of deprivation (adjusted odds ratio pre-pandemic: 0.89, 0.88-0.91 and pandemic: 0.91, 0.90-0.93), incompletion of self-reported ethnicity and a previously cancelled appointment (whether instigated by the hospital or patient) were strongly associated with non-attendance within this mode of care delivery ($p<0.01$).

Conclusions: Overall, male sex and greater socioeconomic deprivation are associated with poorer attendance. More specifically, non-attendance was higher amongst patients with self-reported Black ethnicity and early morning appointment times. Older patients, self-reported Caucasian ethnicity, those with diabetes and later appointment times were associated with higher levels of attendance. Further study is warranted to evaluate whether enhanced surveillance of certain cohorts could improve non-attendance rates in these groups.

CONTROL ID: 3713358

SUBMITTER (NAME ONLY): Faye Yu Ci Ng

TITLE: Bidirectional association of glaucoma and chronic kidney disease: a systematic review and meta-analysis of two million participants

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Ng, H. Song, B. Tan, C. Teo, National University Singapore Yong Loo Lin School of Medicine, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Faye Yu Ci Ng: Commercial Relationship: Code N (No Commercial Relationship) | Harris Jun Jie Muhammad Danial Song: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Kye Jyn Tan: Commercial Relationship: Code N (No Commercial Relationship) | Chong Boon Teo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma and chronic kidney disease (CKD) are both prevalent and debilitating conditions, with pathogenic pathways such as oxidative stress and fluid dysregulation common to both diseases. However, previous studies have yielded conflicting results regarding the association between them. We aim to determine if there is a bidirectional relationship between glaucoma and CKD, thus providing a comprehensive and evidence-based summary of their association.

Methods: We searched PubMed, Embase and Cochrane Library from inception until 15 June 2021. We included observational studies, published as full-length English articles in peer-reviewed journals, reporting on glaucoma and CKD as either exposure or outcome. We pooled odds ratios using random-effect meta-analysis and conducted subgroup meta-analyses and univariate meta regression. We assessed risk of bias using the Newcastle-Ottawa Scale (NOS) and quality of evidence using the GRADE framework. Our article is PROSPERO-registered and adherent to both PRISMA and MOOSE guidelines.

Results: We identified 3 retrospective cohort studies and 12 cross-sectional studies from 2,428 records and included 1,978,254 participants. Risk of bias was low to moderate. Participants with CKD at baseline had higher pooled odds of glaucoma (odds ratio[OR]=1.18, 95% confidence interval[CI]=1.04-1.33, I^2=66%, N=12) compared to participants without CKD. The association remained significant in the subgroups of longitudinal studies, diabetic participants, East Asian studies and primary open-angle glaucoma. In the reverse direction, participants with glaucoma at baseline had over two-fold higher odds of incident CKD compared to participants without glaucoma after 10-15 years of follow-up in longitudinal studies (OR=2.44, 95% CI=1.79-3.33, I^2=74%, N=2). All studies adjusted for age and sex, while most studies adjusted for comorbidities such as diabetes and hypertension. Meta-regression identified ethnicity (East Asians vs Non-East Asians) as a significant effect moderator. Associations were robust to trim-and-fill adjustment for publication bias, single-study influence and cumulative meta-analyses.

Conclusions: Our meta-analysis suggests a bidirectional association between glaucoma and CKD, particularly among East Asians. Further studies are required to elucidate the underlying mechanisms and account for the differential association by ethnicity.

CONTROL ID: 3713359

SUBMITTER (NAME ONLY): Harilaos Ginis

TITLE: Direct visualization of negative dysphotopsia in a physical model of the pseudophakic eye

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.S. Ginis, D. Christaras, S. Tsoukalas, A. Livir-Rallatos, Department of Research, Athens Eye Hospital, Glyfada, Attica, GREECE|H.S. Ginis, D. Christaras, diestia Systems, Athens, Attica, GREECE|P. Artal, Laboratorio de Óptica, Universidad de Murcia, Murcia, Murcia, SPAIN|

Commercial Relationships Disclosure: Harilaos Ginis: Commercial Relationship(s);Code C (Consultant/Contractor):Voptica S.L. ;Code P (Patent):Voptica S.L. | Dimitrios Christaras: Commercial Relationship: Code N (No Commercial Relationship) | Spyridon Tsoukalas: Commercial Relationship: Code N (No Commercial Relationship) | Angelos Livir-Rallatos: Commercial Relationship: Code N (No Commercial Relationship) | Pablo Artal: Commercial Relationship(s);Code I (Personal Financial Interest):Voptica S.L. ;Code P (Patent):Voptica S.L.

ABSTRACT BODY:

Purpose: Negative dysphotopsia (ND) is a photic phenomenon affecting pseudophakic eyes where a dark crescent or shadow is perceived in the peripheral temporal visual field. Although is it understood that the edge of the intraocular lens (IOL) and the space between the IOL's optic and the posterior iris are involved, the exact etiology remains unclear especially with respect to its clinical manifestation. The purpose of the study was to develop a physical model of the pseudophakic eye and to record ND at the retinal plane in a variety of conditions.

Methods: The eye model had realistic dimensions with a cornea made of PMMA (R=7.73mm, Q= -0.24) an iris at a depth of 3.55mm and an IOL holder with variable distance (0.5 to 1.5mm) from the pupil, simulating a pseudophakic anterior chamber depth (pACD) ranging from 4.05 to 5.05 mm. The eye was filled with distilled water. A board level camera (DFM 72BUC02-ML, Imaging Source, Germany) in a water-tight container with a 200μm glass window was used to record the retinal images. Negative dysphotopsia was investigated for two different types of IOLs (Acrysof SA60AT, Alcon, TX USA and ArtIOL, Art55, Voptica SL, Murcia, Spain), for two different pACD values (4.05 and 5.05 mm) and for two different pupil diameters (3 and 6 mm).

Results: A characteristic crescent appeared on the retina when a point source was positioned at an angle of 75 degrees with respect to the optical axis of the eye. The phenomenon was prominent for a pupil diameter of 6 mm and pACD of 5.05 mm. For 3 mm pupil diameter and for shallower pACD (4.05 mm) the phenomenon was not observed. When imaging an extended uniform field, a dark band having a width of approximately 4 degrees and brightness reduced at 74% of the field brightness appeared at the vicinity of 75 degrees. The crescent was less prominent for the meniscus lens (ArtIOL), presumably due to the smaller gap between the IOL edge and the posterior iris.

Conclusions: A peripheral crescent, corresponding to light that misses the IOL's optic results to the formation of a darker zone, between the light that is focused by the IOL and light that is missing the IOL. ND appeared only for large pupils and deep chambers and was reduced for inverted meniscus IOLs. However in clinical practice where IOL tilt and decentration can occur, ND could be manifested for smaller pupil diameters and pACD.

CONTROL ID: 3713360

SUBMITTER (NAME ONLY): Yiqin Du

TITLE: Therapeutics of stem cell secretome in dexamethasone-induced ocular hypertension mice

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Du, A. Kumar, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Yiqin Du: Commercial Relationship(s);Code P (Patent):University of Pittsburgh | Ajay Kumar: Commercial Relationship(s);Code P (Patent):University of Pittsburgh

ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of irreversible blindness worldwide. Stem cell-free therapy using stem cell secretome offers great hope for vision restoration. We investigated the protective roles of secretome from trabecular meshwork (TMSC) in dexamethasone (Dex) treated trabecular meshwork (TM) cells and Dex-induced ocular hypertension (OHT) mice.

Methods: Primary human TM cells were treated with 100nM Dex for 5 days and added TMSC secretome to be treated for another 5 days. For Dex-induced OHT, adult C57BL/6 mice were periocularly injected with 20 µl of Dex-acetate (Dex-Ac) at 10 mg/ml weekly for four weeks. Then the mice were periocularly injected with concentrated secretome from TMSC or corneal fibroblasts as well as Dex-Ac weekly for another 4 weeks and waited for 2 weeks before sacrifice. Immunofluorescent staining and qPCR were used to quantify expression levels of glaucoma-associated proteins/genes Myocilin (MYOC) and ANGPTL7. Intraocular pressure (IOP) was measured weekly by I-care tonometer. Statistical analysis was done using one-way ANOVA followed by Tukey posttest. $P<0.05$ was set as statistically significant.

Results: Both TMSC and fibroblasts showed high viability after 48-hr serum starvation and secretome harvesting, indicating good quality of secretome collection. TM cells had increased Myoc expression after Dex treatment, which was prevented and reversed by TMSC secretome. The increased expression of both Myoc and ANGPTL7 in response to Dex was significantly reduced by all three TMSC secretomes. CHI3L1 expression was diminished after Dex, which was preserved after TMSC secretome treatment. In OHT model, periocularly injected TMSC secretome successfully reduced the IOP elevation from week 4 (13.8±1.8 mmHg) after a single dose, as compared to Dex-treated mice (15.8±3.3 mmHg) and maintained to normal range till the end of the experiment at week 8, similar to that of vehicle controls. Fibroblast secretome was not able to reduce IOP (16.2±2 mmHg and 15.3±1.4 mmHg on week 4 and week 8 respectively), that was at similar levels to Dex-treated mice (week 4, 15.8±3.3 mmHg and week 8, 15.2±1 mmHg). Retinal ganglion cell function was preserved as evaluated by pattern electroretinography.

Conclusions: TMSC secretome protected both Dex treated TM cells and OHT mice by periocular injection. It opens an avenue for stem cell-free therapy for glaucoma with minimum invasive procedures.

CONTROL ID: 3713362

SUBMITTER (NAME ONLY): Miranda Scalabrino

TITLE: Cone function is dependent on rod rescue in a mouse model of Retinitis Pigmentosa gene therapy

SESSION TITLE: Neural retina: disease and repair

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Scalabrino, M. Thapa, E. Zhang, L. Peters, M. Pluenneke, J. Nolt, L. Chew, G. Field, Neurobiology, Duke University, Durham, North Carolina, UNITED STATES|A.P. Sampath, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|J. Chen, Cell & Neurobiology, University of Southern California, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Miranda Scalabrino: Commercial Relationship: Code N (No Commercial Relationship) | Mishek Thapa: Commercial Relationship: Code N (No Commercial Relationship) | Esther Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Lucy Peters: Commercial Relationship: Code N (No Commercial Relationship) | Molly Pluenneke: Commercial Relationship: Code N (No Commercial Relationship) | Jay Nolt: Commercial Relationship: Code N (No Commercial Relationship) | Lindsey Chew: Commercial Relationship: Code N (No Commercial Relationship) | Alapakkam Sampath: Commercial Relationship: Code N (No Commercial Relationship) | Jeannie Chen: Commercial Relationship: Code N (No Commercial Relationship) | Greg Field: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Gene therapy for inherited retinal diseases often fails to halt degeneration, likely due to intervening too late in the course of the disease or by not correcting enough cells. However, it is unclear whether any visual improvement following therapy will be retained by surviving cells for a long period of time. Our goal was to characterize how rod and cone visual transmission is impacted by early (30% rod loss), middle (50% rod loss), and late (70% rod loss) treatment timepoints in a mouse model of Retinitis Pigmentosa up to 6 months following therapy. Retinal function was measured by multielectrode retinal ganglion cell recordings, and useful vision assessed by a vision dependent task: a mouse's ability to track and capture a cricket.

Methods: We measured responses of retinal ganglion cells (RGCs) to artificial and natural visual stimuli under mesopic and photopic conditions using a mouse model of Cngb1-RP. In this model, rod death is a relatively slow process: rods progressively die until all are lost at 6-7 months. Importantly, this model can undergo genetic correction with tamoxifen, allowing us to measure responses from a model of a perfect gene therapy irrespective of inefficiencies in delivery, virus, or dosage. We measured RGC responses in animals at 1 month intervals following early, mid, or late treatment and compared responses to RGC recordings from WT and untreated mice out to 7 months. The cricket hunting behavior task was performed on treated, untreated, and WT mice by placing a mouse in a transparent recording box and introducing a cricket. Time to capture was compared across groups. Histology was also performed to correlate visual function to retinal structure.

Results: Untreated rods are non-functional in this model, however, gene replacement restored rod transmission at all treatment timepoints and persisted. In mid-treatment timepoints, rod responses increased quickly following therapy, reaching maximal information fidelity 2 months after treatment. Cone function also improved in response to gene replacement, but took >3 months. These responses were true for both cricket capture behavior and electrophysiology.

Conclusions: There is a known dependence of cone survival on rod survival: rod disorders such as Retinitis Pigmentosa also lead to eventual cone loss. However, this is the first instance of cone rescue also being dependent on first restoring rod structure and function.

CONTROL ID: 3713363

SUBMITTER (NAME ONLY): Sophia Marusic

TITLE: Myopia Screening Smartphone App: Validity in Assessing Refractive Error in a Pediatric Cohort

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Marusic, A. Raghuram, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|G. Luo, A. Raghuram, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G. Luo, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Sophia Marusic: Commercial Relationship: Code N (No Commercial Relationship) | Gang Luo: Commercial Relationship(s);Code P (Patent):Mass Eye and Ear;Code O (Owner):EyeNexo | Aparna Raghuram: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: With the rising prevalance of myopia, there is increasing need for validated screening tools to identify and monitor refractive error in pediatric populations. We conducted a prospective clinical study to compare the spherical equivalent (SE) refractive error measurements of a newly developed mobile app to manifest refraction (MR) and subjective cycloplegic refraction (SCR) performed in clinic.

Methods: Data was collected from 54 myopic subjects (61.1% female, mean age 11.7 ± 3.22 years). Eyes with astigmatism more than -1.75D were excluded. Refractive error was measured with the app before cycloplegia. Using a selfie camera to measure the viewing distance in real time, the app displayed three distance-compensated Tumbling E letters in 20/25 angular size. The subject's refractive error was estimated based on the far point distance at which they correctly identified the orientation of 2/3 letters. Pearson correlation (R) and Bland-Altman 95% limits of agreement were used to compare app measurements to clinical refraction.

Results: For the 95 eyes enrolled, the SE refractive error range was -0.75D to -6.38D as measured by SCR. 6 eyes with a difference in app measurement and MR more than 1.5x IQR (0.795) were outliers and excluded. The app measurement was highly correlated with MR ($R= 0.93$, $p<0.001$), as well as SCR ($R= 0.93$, $p<0.001$). A paired t-test showed that the app systematically underestimated SE refractive error by -0.306D ($p<0.001$) as compared to MR, and by -0.242D ($p<0.001$) as compared to SCR. The Bland-Altman 95% limits of agreement were [-1.46, 0.846] for the app and MR and [-1.37, 0.887] for the app and SCR. Clinically relevant limits of agreement are ±0.50D and 51.6% of eyes were within 0.50D of difference.

Conclusions: The moderate Bland-Altman agreement suggested that one-time measurement with the app may not be sufficiently accurate for some myopic patients. However, the high correlation and small systematic bias of the app with both MR and SCR may support its potential for screening for the presence of myopia and its relative progression in pediatric populations, if the agreement can be improved, for example, by repeated measurement. The similarities in comparing the app to MR and SCR demonstrated that the app could be used without cycloplegia and therefore operated by non-professionals.

CONTROL ID: 3713364

SUBMITTER (NAME ONLY): Sui Chien Wong

TITLE: Acute traction retinal detachment (stage 4) in retinopathy of prematurity: outcomes of endoscopic vitrectomy in 99 consecutive cases.

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Wong, R.H. Henderson, C.K. Patel, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|J. Wawrzynski, University College London, London, London, UNITED KINGDOM|D. Yeo, Alder Hey Children's Hospital, Liverpool, Merseyside, UNITED KINGDOM|C.K. Patel, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|S. Wong, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Sui Chien Wong: Commercial Relationship(s);Code C (Consultant/Contractor):DORC International;Code C (Consultant/Contractor):BVI | James Wawrzynski: Commercial Relationship: Code N (No Commercial Relationship) | Damien Yeo: Commercial Relationship: Code N (No Commercial Relationship) | Robert Henderson: Commercial Relationship: Code N (No Commercial Relationship) | Chetan Patel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the safety and efficacy of endoscopic vitrectomy (Endo-Vit) for stage 4 retinopathy of prematurity (ROP)

Methods: Consecutive non-comparative case series of surgery of all UK cases for traction RD in ROP (stage 4) between 2015-2021. Inclusion criteria was stage 4A or 4B ROP. Stage 5 cases were excluded. All cases had primary simultaneous high-resolution 19 gauge endoscopy and microscope-based visualisation, with standard 23 gauge vitrectomy

Results: Included were 99 eyes of 57 patients. Mean gestational age, birth weight and follow-up were 25.9 weeks, 789g and 27.4 months, respectively. RD stage was 4A in 54 eyes, 4B in 34 eyes and 4B/5 in 11 eyes. Prior laser was done in 84%, and intravitreal bevacizumab in 28%. Median number of surgeries was 1. Primary retinal re-attachment was 82% overall, 90% in stage 4A, 85% in stage 4B, and 36% in stage 4B/5. Primary lensectomy was required in 0%. Iatrogenic break occurred in 4 eyes. Postoperative cataract occurred in 4 eyes, all of whom developed 12 months after surgery. Visual acuity data was available in 92%, with overall fix and follow vision in 71%, logMAR 2.0 or better in 52%, and logMAR 1.0 or better in 29%.

Conclusions: Endoscopic visualisation significantly reduces the need for primary lensectomy in complex traction retinal detachment in retinopathy of prematurity, with favourable anatomic outcomes. It is a useful adjunct to microscope-based visualisation.

CONTROL ID: 3713365

SUBMITTER (NAME ONLY): Frederic Dargelas

TITLE: Extended 24-h release of topical eye drop Dexamethasone formulation with single dose using silica microparticle-silica hydrogel composite technology

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Dargelas, M. Vaahtio, M. Kaimainen, L. Leino, M. Reay, O. Leppänen, DelSiTech Ltd, Turku, FINLAND|H.R. Kamma, J. Vaczi, Optifye Therapeutics AG, SWITZERLAND|

Commercial Relationships Disclosure: Frederic Dargelas: Commercial Relationship(s);Code E (Employment):DelSiTech Ltd | Minna Vaahtio: Commercial Relationship(s);Code E (Employment):DelSiTech Ltd | Mika Kaimainen: Commercial Relationship(s);Code E (Employment):DelSiTech Ltd | Hanumantha Kamma: Commercial Relationship(s);Code O (Owner):Optifye Therapeutics AG | Janos Vaczi: Commercial Relationship(s);Code E (Employment):Optifye Therapeutics AG | Lasse Leino: Commercial Relationship(s);Code E (Employment):DelSiTech Ltd | Marcus Reay: Commercial Relationship(s);Code E (Employment):DelSiTech Ltd | Ossi Leppänen: Commercial Relationship(s);Code E (Employment):DelSiTech Ltd

ABSTRACT BODY:

Purpose: Topically administered therapies remain a standard of care for many ocular diseases. Frequent administration, as well as achieving stable therapeutic levels through the night poses a central challenge for effective maintenance of ocular health. As a result, the need to develop treatments with improved effective durations has gained significant attention. The purpose of this study was to investigate if a limited solubility therapeutic agent like dexamethasone (DEXA) could be efficiently encapsulated in Silica Matrix and demonstrate controlled release with a single 30 µL eye drop for 24 hours.

Methods: Two DEXA sustained release formulations, #09D and #12D) were tested. Dexamethasone was encapsulated in the Silica Matrix through sol-gel chemistry. New Zealand Rabbits were administered once with a single 30µL eyedrop in each eye. Tear samples were collected using a capillary up to 48 hours post dosing, and analyzed for DEXA by LC-MS/MS analysis from pooled left and right eye tear samples. In vitro DEXA and Si dissolutions were studied in sink condition and cumulative release as well as total dissolution and content was analyzed by spectrophotometry and HPLC. Intra ocular pressure (IOP) was monitored with Tonovet+ device.

Results: DEXA was successfully encapsulated in both silica microparticle-silica hydrogel formulations. In vivo pharmacokinetic data demonstrated extended controlled release of DEXA in rabbit tear fluid for 24 hours. Treatment was well tolerated and no changes in IOP were detected.

Conclusions: Efficient encapsulation of low solubility therapeutic agents like DEXA is possible by DelSiTech^{TM} Silica Matrix technology ensuring extended release in-vivo for 24 hours.

CONTROL ID: 3713366

SUBMITTER (NAME ONLY): Daniel Will

TITLE: Combined anti-VEGF injections and thermal laser photocoagulation for peripapillary and extrafoveal choroidal neovascular membranes in age related macular degeneration

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Will, Ophthalmology, Abington Memorial Hospital, Abington, Pennsylvania, UNITED STATES|A. Will, William Penn Charter School, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Daniel Will: Commercial Relationship: Code N (No Commercial Relationship) | Alexandra Will: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patients with neovascular AMD often require high treatment burden with first-line management using anti-VEGF injections. Lesions primarily located away from the central macula may be amenable to initial treatment with injections, reducing lesion size, followed by thermal laser destruction to maintain control of the disease with a reduced injection burden.

Methods: A retrospective electronic chart review was conducted on a series of 27 patients who had choroidal neovascularization (CNV) related to wet AMD and were treated initially with anti-VEGF injections and subsequently with thermal laser treatment. Demographics, lesion characteristics, clinical course, and outcomes were recorded. Patients were treated with laser if the lesions were relatively small in size and favorably positioned to minimize short-term and long-term risk of vision loss related to treatment.

Results: Chart review assembled 27 patients who were treated with anti-VEGF injections followed by thermal laser (24 peripapillary, 3 extrafoveal). 74% of patients had ceased injections following laser treatment at patient's last follow-up. Mean age was 80 years old (range 63-94). Average time without treatment following laser was 25.26 months (range 3-53 months): 4 patients had recurrent CNV and 3 developed new CNV during follow-up period. 89% of patients had stable or improved visual acuity. 3 patients had improved vision (gain of 2 lines or more), 20 had stable vision (VA within 1 line +/- of baseline acuity), 3 patients had worsened vision (vision loss of 2 lines or greater: 2 GA, 1 new CNV). No patients had reduced acuity due to laser. 33% (9 patients) had fovea involving disease of the fellow eye with reduced vision or need for anti-VEGF injections.

Conclusions: Carefully selected patients with appropriate lesion size and location may benefit from anti-VEGF treatment followed by thermal laser photocoagulation with a high percentage of patients maintaining vision without need for continued injections. A substantial number of patients can experience recurrent or new CNV and many have significant bilateral disease.

CONTROL ID: 3713367

SUBMITTER (NAME ONLY): Alex Gonzalez

TITLE: Development of a Mountable Filtering System for Enhancing Visual Perception of the Argus II Retinal Prosthesis

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gonzalez, M. Aguilar, C.J. Rowaan, J. Parel, Ophthalmic Biophysics Center, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B.L. Lam, N.Z. Gregori, Bascom Palmer Eye Institute,, University of Miami School of Medicine, Miami, Florida, UNITED STATES|N.Z. Gregori, K. Zann, Ophthalmology, Veterans Health Administration, Miami, Florida, UNITED STATES|J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The ability to interpret the artificial visual stimulus created by the Argus II retinal prosthesis can vary with the user's perceptual capabilities and the scene captured by the device's camera. Outcomes and proficient use may be improved through the introduction of filters as a rehabilitation tool. A mountable filtering system was developed allowing the user to transform the visual stimulus captured by the camera. This study investigates the feasibility of incorporating a filter as a tool to improve scene and pattern recognition.

Methods: Using CAD software and 3D printer, filter holders and an eyewear mount were developed (Fig. 1). During inpatient rehabilitation sessions, Eschenbach tints (17, 21, 31) were held over the user's camera to determine if visualization was improved. Gel film filters with comparable transmission characteristics (green 45%, plum 19%, grey 25%, clear control 99%) were mounted on holders with tactile marks for ease of identification. Each mount can hold up to 2 filters permitting the user to explore and combine filters. The filter system was deployed remotely to one Argus II user with the usage instructions and testing protocol. Filter comparisons were completed both indoors (lit/darkened room) and outdoors (sunny/overcast). The indoor scene consisted of observing a PC screen with a single white line in various orientations. The outdoor scene consisted of visualizing colored 2.5-inch balls with either grass or asphalt background. Filters were graded on a scale: -2 to +2 with zero indicating no change and the -/+ scores indicating decreases or increases in perception. The user was naïve that one filter was a control (Fig. 2).

Results: Indoor visualizations of the computer screen targets in a darkened room were improved with positive ratings, compared to no filter and the control. Conversely, indoor filter usage with incandescent illumination was rated negatively, compared to no filter. Outdoor usage of filters when identifying targets on various backgrounds did not improve visualization.

Conclusions: A mountable filtering system can be deployed to remote Argus II users, with preliminary data indicating indoor visualization improvements, as a function of room illumination. Additional user testing is required to understand the effects of the spectral characteristics of each filter.

CONTROL ID: 3713368

SUBMITTER (NAME ONLY): Brendan Kenyon

TITLE: pDC Secretome Promotes Corneal Nerve Survival and pDCs Modulate Cold Receptor Function

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kenyon, O. esteireiro, D.L. Harris, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|B. Kenyon, Program in Neuroscience, Tufts University Graduate School of Biomedical Sciences, Boston, Massachusetts, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Brendan Kenyon: Commercial Relationship(s);Code P (Patent):Tufts Medical Center | Olivia esteireiro: Commercial Relationship: Code N (No Commercial Relationship) | Deshea Harris: Commercial Relationship: Code N (No Commercial Relationship) | Pedram Hamrah: Commercial Relationship(s);Code P (Patent):Tufts Medical Center;Code S (non-remunerative):Novartis, Oyster Point, Dompe;Code C (Consultant/Contractor):Kala, Novartis, Dompe, Clementia, Novaliq, Santen, OKYO, Eyenovia

ABSTRACT BODY:

Purpose: We have previously reported that depletion of corneal plasmacytoid dendritic cells (pDCs) leads to a robust loss of corneal innervation. Herein, we demonstrate neurotrophic properties of the pDC secretome by concurrent pDC depletion and topical treatment with pDC-derived supernatant. Furthermore, we characterize functional alterations of corneal nerves by ex vivo electrophysiology.

Methods: For rescue studies, pDCs were sorted from adult C57BL/6J mice and cultured in serum-free media for 3 days, at which point supernatant was collected. Adult BDCA2-DTR mice were used for depletion of pDCs by subconjunctival injections of diphtheria toxin (DT; 30 ng/eye) at day 0 and repeated every 2 days and were compared to non-depleted controls In rescue studies, all BDCA2-DTR animals received DT injections every 2 days and were topically treated with pDC supernatant or serum-free media (control) 3 times/day for one week. Corneas were stained with β_{III}-tubulin, imaged by confocal microscopy, and nerve density quantified using NeuronJ. For electrophysiology studies, recordings were performed ex vivo on enucleated eyes using a glass recording micropipette at the ocular surface in a recording chamber perfused with 34°C physiologic solution. The activity of nerve terminal impulses (NTIs) was recorded at baseline and in response to cooling and warming ramps. Analyses were performed in Spike2 software.

Results: pDC supernatant treatment resulted in a significant increase in central cornea innervation compared to controls (131.49 + 10.49 vs 67.77 + 6.80 mm/mm^2; $p<0.01$). This effect was due to a rescue of the subbasal plexus (100.10 + 8.92 vs 30.34 + 7.40 mm/mm^2; $p<0.001$), as the stromal nerve density did not differ between groups. NTI activity of high-threshold cold receptors (HT-CRs) was altered by pDC depletion. Although background activity and cooling responses did not differ between groups. Interestingly, the cooling threshold, the temperature at which HT-CRs respond, was reduced in the pDC-depleted group (22.53 + 0.54°C vs 27.97 + 0.46°C).

Conclusions: These findings demonstrate that corneal pDCs are crucial for both the function and maintenance of corneal nerves. The structural and functional alterations following pDC depletion, as well as rescue of corneal innervation by pDC supernatant, may have relevant consequences for ocular diseases in which sensory abnormalities predominate.

CONTROL ID: 3713369

SUBMITTER (NAME ONLY): Khushboo Chauhan

TITLE: Evaluation of retinal layer metrics by SDOCT with reference to glycemic control and visual acuity in patients of type II diabetes.

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chauhan, B. Sharma, S. Karkhur, N. Yadav, L. Banerjee, R. Nyodu, Ophthalmology, All India Institute of Medical Science - Bhopal, Bhopal, Madhya Pradesh, INDIA|

Commercial Relationships Disclosure: Khushboo Chauhan: Commercial Relationship: Code N (No Commercial Relationship) | Bhavana Sharma: Commercial Relationship: Code N (No Commercial Relationship) | Samendra Karkhur: Commercial Relationship: Code N (No Commercial Relationship) | Nikita Yadav: Commercial Relationship: Code N (No Commercial Relationship) | Lagnajeeta Banerjee: Commercial Relationship: Code N (No Commercial Relationship) | Richa Nyodu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) is a non-invasive, in-vivo imaging technique that enables the cross-sectional examination of retinal layers. This study evaluates the correlation of retinal layer metrics with glycemic control (HbA1c) and visual acuity, in type 2 diabetics. Moreover, the variation in retinal layer metrics between diabetic and non-diabetic patients has also been studied.

Methods: It is a case control study of 146 patients. Macular cube scan of 512x218 protocol was done to assess central subfield thickness (CST) and average ganglionic cell layer (GCL) - inner plexiform layer(IPL) thickness in an elliptical annulus centered on fovea. Additionally, thickness was measured for inner retina (ILM-OPL) from the internal limiting membrane(ILM) to the proximal boundary of the outer nuclear layer(ONL); outer retina (ONL-RPE) from proximal ONL boundary to the retinal pigment epithelium (RPE); ellipsoid zone(EZ) to RPE(EZ-RPE) and total retina(ILM-RPE) from ILM to RPE at fovea, juxtafoveally at 1 mm nasal and temporal to the fovea. Average retinal nerve fibre layer (RNFL) thickness was evaluated using 200x200 protocol of optic disc cube centered on the optic disc.

Results: Inner retina including average RNFL thickness, average GCL-IPL thickness, foveal ILM-OPL thickness; EZ-RPE and total retina including juxtafoveal temporal and nasal thickness, showed significant reduction in diabetics. Visual acuity showed weak positive correlation with inner retinal layers. Additionally, total retina juxtafoveal nasal parameter had weak positive correlation with BCVA in diabetics. HbA1C showed weak negative correlation with inner retinal layers. Multivariate regression analysis showed increase in RNFL, GCL-IPL, inner retinal ILM-OPL juxtafoveal temporal and total retinal juxtafoveal nasal thickness were significantly associated with decreased visual acuity.

Conclusions: With the advent of OCT, quantitative assessment of different retinal layers, could help us detect signs of retinal neuro-degeneration and impending clinical diabetic retinopathy associated with chronic hyperglycaemia. Furthermore, it would serve as a biomarker to detect pre-clinical DR and initiate appropriate clinical interventions.

CONTROL ID: 3713372

SUBMITTER (NAME ONLY): Alexander Zeleny

TITLE: Utility of Fluorescein Angiography in Patients with Anterior Uveitis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zeleny, E. Oyeniran, S. Kodati, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. Zeleny, Georgetown University Medical Center, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Alexander Zeleny: Commercial Relationship: Code N (No Commercial Relationship) | Enny Oyeniran: Commercial Relationship: Code N (No Commercial Relationship) | Shilpa Kodati: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the utility of performing ultra-wide field fluorescein angiography (FA) in patients with anterior uveitis and to investigate the frequency of retinal vascular leakage in patients with anterior uveitis.

Methods: A retrospective chart review was conducted. Inclusion criteria included patients referred with a diagnosis of anterior uveitis who received a FA in the same visit at the time of presentation. Patients were excluded if they had evidence of posterior segment involvement on clinical exam. The FAs were reviewed to evaluate for the petaloid leakage consistent with cystoid macular edema (CME), optic disc leakage, and the presence of retinal vascular leakage (graded on a scale of none present, mild, and moderate/severe). The primary outcome was the presence of retinal vascular leakage on FA at presentation. Secondary outcomes included the presence of CME and optic disc leakage.

Results: A total of 30 patients (60 eyes) met the inclusion criteria (11 males, 19 females; mean age 52.6, range 26-83 years). FA grading revealed no retinal vascular leakage in 32 eyes (53.3%), mild leakage in 19 eyes (31.7%) and moderate to severe leakage in 9 eyes (15.0%). Further, 14 eyes (23.3%) showed petaloid leakage, and 3 eyes (5%) revealed disc leakage. Retinal vascular leakage was bilateral in 12 cases. FA was helpful in changing the presenting diagnosis in 5 patients (16.7%).

Conclusions: Our preliminary data suggests that anterior uveitis may be associated with retinal vascular changes. In some circumstances it may be helpful to obtain a baseline FA in anterior uveitis patients to ensure that the uveitis is appropriately characterized, especially given the treatment and prognostic implications.

CONTROL ID: 3713375

SUBMITTER (NAME ONLY): Zane Zemborain

TITLE: Deep Learning-based Segmentation of Nerves and Pathological Structures in Corneal Confocal Microscopy Images of the Subbasal Nerve Plexus

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Zemborain, S. Farsiu, Duke University Pratt School of Engineering, Durham, North Carolina, UNITED STATES|M. Soifer, N. Azar, H.M. Mousa, V.L. Perez, S. Farsiu, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To perform automated segmentation of corneal nerves and pathological structures in corneal confocal microscopy (CCM) images of the subbasal nerve plexus (SNP) in eyes with ocular surface disorders (OSD).

Methods: A novel, deep learning-based autoencoder was constructed to perform 4-class segmentation on SNP images using adversarial loss and clustering-based post-processing. The SNP autoencoder was trained/tested on 207 SNP images from 43 OSD patients, for which an expert manually segmented 4 tissue classes: background, nerve, foreign body, and neuroma. To remove the deleterious effects of applanation artifacts, an artifact-removal (AR) autoencoder was constructed to perform 3-class segmentation (Fig. 1 A-B). The AR autoencoder was trained on 450 SNP, 450 stroma, and 450 epithelium images from 27 patients, as well as examples generated from an auxiliary classifier generative adversarial network (Fig. 1 C-E).

Results: The training/testing split was performed patient-wise. Performance was quantitatively evaluated for the SNP autoencoder + AR autoencoder combination (Fig. 2) based upon tissue class precision, recall, and F1-score. The precision scores were 99%, 80%, 63%, and 73%; the recall scores were 99%, 73%, 84%, and 88%; the F1 scores were 99%, 77%, 70%, and 77% for the background, nerve, foreign body, and neuroma class, respectively.

Conclusions: It was possible to perform accurate segmentation of the SNP with a relatively high degree of precision and recall even under the constraints of a small dataset. This segmentation algorithm facilitates automatic quantification of the cornea’s nerve density, thickness, and tortuosity, which can be used to stratify OSD patients into subgroups that reflect specific pathophysiological mechanisms to the cornea’s immune response and pain experience.

CONTROL ID: 3713376

SUBMITTER (NAME ONLY): Dilsher Dhoot

TITLE: Suprachoroidal Delivery of RGX-314 for Diabetic Retinopathy: The Phase II ALTITUDE™ Study

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.S. Dhoot, California Retina Consultants, Santa Barbara, California, UNITED STATES|

Commercial Relationships Disclosure: Dilsher Dhoot: Commercial Relationship(s);Code C (Consultant/Contractor):Genentech, Novartis, Regeneron, Allergan, Alimera Sciences, Eyepoint Pharmaceuticals, Bayer, Apelis

ABSTRACT BODY:

Purpose: Sustained anti-VEGF delivery has been shown to decrease severity of diabetic retinopathy (DR) and reduce vision threatening complications, yet it is associated with a high treatment burden. RGX-314 is designed as a single gene therapy intervention utilizing the NAV AAV8 vector to deliver a soluble anti-VEGF fab transgene to potentially provide continuous anti-VEGF therapy. This study will evaluate RGX-314 for the treatment of DR without center-involved diabetic macular edema (CI-DME) utilizing an in-office, suprachoroidal delivery.

Methods: ALTITUDE is an open-label, controlled dose-escalation trial evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314 using the SCS Microinjector® in patients with a DR diagnosis of moderately severe or severe nonproliferative DR (NPDR) or mild proliferative DR (PDR). 20 patients in Cohort 1 were randomized to receive RGX-314 at a dose level of $2.5x10^{11}$ genomic copies per eye (GC/eye) versus observational control at a 3:1 ratio. Additional cohorts will include 40 patients randomized to receive RGX-314 at an increased dose level of $5x10^{11}$ GC/eye, in which enrollment is ongoing. Patients do not receive prophylactic immune suppressive corticosteroid therapy before or after receiving RGX-314. The primary outcome is the proportion of eyes with 2-step improvement in DR severity scale score (DRSS) at 48 weeks. Secondary outcomes include safety, and development and intervention of DR-related complications.

Results: As of September 29, 2021, RGX-314 was well tolerated in 15 patients in Cohort 1. One serious adverse event was reported in the fellow eye of a patient treated with RGX-314 and is considered not related to RGX-314. No intraocular inflammation was observed on slit-lamp exam. Common adverse events in the study eye were not considered drug-related and were predominantly mild. 5 of the 15 patients (33%) demonstrated a 2-step or greater improvement in DRSS from baseline at three months, compared to 0 of the 5 patients (0%) in the observational control group. In the 7 patients who had NPDR (DRSS 47-53) at baseline, 3 patients (43%) demonstrated a 2-step or greater improvement.

Conclusions: RGX-314 has the potential to provide sustained clinical outcomes in the treatment of diabetic retinopathy with a one-time treatment administered in-office.

CONTROL ID: 3713377

SUBMITTER (NAME ONLY): Cesar Hernandez Isidro

TITLE: Intracranial Pressure and its effects on Intraocular Pressure

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hernandez Isidro, Y.H. Mohamed, C.L. Passaglia, Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is increasing indication that intracranial pressure (ICP) may play a role in glaucoma since the lamina cribrosa of the optic nerve head is exposed to intraocular pressure (IOP) on one side and ICP on the other. The purpose of this study is to monitor ICP in awake and anesthetized animals to understand its dynamics, and how IOP responds to changes in ICP.

Methods: Experiments were done with adult Brown Norway rats housed in a 12-hr light-dark cycle with access to food and water ad libitum. Continuous recording of ICP in awake rats was done by implanting a fine cannula into the subarachnoid space through a hole in the skull. The cannula was connected to a custom wireless telemetry device attached to a jacket worn on the animal's back. ICP and IOP were concurrently recorded in anesthetized rats. Subarachnoid and ventricular ICP were recorded via a vented screw in the skull and a 25-gauge needle in a cerebral ventricle, respectively. Ventricular pressure was altered by varying the height of a fluid reservoir connected via a three-way stopcock to the needle. IOP was recorded via a 33-gauge needle in the anterior chamber of one eye. Data was analyzed in terms of means and variances. Variance was analyzed in randomly selected 1-hr samples of the ICP record.

Results: ICP was successfully recorded from 3 awake rats for 3 days to 4 weeks, and a diurnal ICP rhythm was observed in every animal. Mean ICP was 5.2 ± 1.8 mmHg during the light phase and 12.3 ± 4.2 mmHg during the dark phase ($p < 0.03$). ICP records of at least an hour in length were recorded from 6 awake rats and 6 anesthetized rats. Average variance of ICP fluctuations was 0.06 ± 0.04 mmHg for awake animals and 4.68 ± 4.49 mmHg for anesthetized animals ($p < 0.03$). IOP was observed to increase by 4.1 ± 4.0 mmHg after ICP elevation of 10 mmHg in 5 anesthetized rats ($p = 0.08$).

Conclusions: Our results show that ICP has a diurnal rhythm in conscious rats, with ICP being significantly higher during the animal's waking hours. We have previously shown that IOP is also higher at night, which implies that translaminar pressure is relatively stable throughout the day. ICP variance in conscious rats can be attributed in large part to animal activity as variance is greatly reduced by anesthesia. Effects of ICP elevation on IOP are reportedly due to changes in ocular blood volume and/or outflow facility and under further investigation.

CONTROL ID: 3713379

SUBMITTER (NAME ONLY): Moreno Menghini

TITLE: Intrafamilial phenotypic variability in a large family with autosomal dominant RP1 associated Retinitis pigmentosa, and novel RP1 variants in autosomal recessive RP

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Menghini, Ophthalmology, Ospedale Regionale di Lugano Italiano, Lugano, Ticino, SWITZERLAND|M. Menghini, D. Barthelmes, Ophthalmology, UniversitatsSpital Zurich, Zurich, SWITZERLAND|S. Koller, D. Grubich Atac, S. Feil, F. Kivrak Pfiffner, L. Bähr, I. Magyar, A. Bahr, W. Berger, Institute of medical molecular genetics, Universitat Zurich, Zurich, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Sequence variants in the RP1 gene account for a significant proportion of autosomal dominant (AD) cases, but are also found in autosomal recessive (AR) RP. No gene therapy has been developed so far for RP1 associated RP that shows a varying degree of severity. We investigated the phenotypic and genotypic differences of a large family with AD RP1 associated RP, and a family with compound recessive variants in RP1.

Methods: Clinical data from comprehensive ophthalmic exams, including multi-modal imaging and full-field ERG, were collected for all patients. Whole exome sequencing was performed for genomic analysis. The full length RP1 gene was cloned into an expression plasmid. Reference RP1 and mutant variants were expressed in cells and analyzed by Western blot and confocal microscopy for localization.

Results: The large Swiss family carrying an already described dominant RP1 variant showed varying degree of disease severity from almost complete loss of central vision at age 50 years to conservation of full central function at a similar age. The RP1 family with a recessive trait revealed two novel, compound heterozygous variants . The patient presented a typical RP phenotype with significant nyctalopia in early adulthood, and advanced visual field constriction. Autofluorescence showed a characteristic hyperautofluorescent perifoveal ring. The OCT confirmed retained photoreceptor layers at the fovea, and loss of the photoreceptor and outer nuclear layer outside of it. The father carrying the recessive frameshift variant did not show any signs of RP both clinically and electrophysiologically. The truncated RP1 from the AR family showed an increased nuclear localization, whereas the truncated protein from the AD family seems to be expressed more similar than the reference RP1 within the cell.

Conclusions: Frameshift variants in exon 4 of RP1 appear to not always be disease causing. The variant in the AD family appears to be quite frequent in patients of Swiss origin, and shows a great intrafamilial phenotypic variability. The variant in the AR family did not cause disease in the heterozygous state, but compound heterozygous state. Localization of expressed RP1 variants seems to differ according to their mode of inheritance. These observations are of utmost important when considering future therapeutic approaches.

CONTROL ID: 3713380

SUBMITTER (NAME ONLY): Thomas Schlegl

TITLE: Visualization of preretinal neovascularization (NV) using widefield swept source optical coherence tomography angiography (SS-OCTA)

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Schlegl, M. Niederleithner, A. Britten, P. Matten, W. Drexler, R.A. Leitgeb, T. Schmoll, Center for Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|H. Stino, U. Schmidt-Erfurth, A. Pollreisz, Department of Ophthalmology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|T. Schlegl, M. Niederleithner, L. De Sisternes, A. Britten, P. Matten, W. Drexler, R.A. Leitgeb, T. Schmoll, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: NV located above the vitreoretinal interface indicates proliferative diabetic retinopathy. However, in OCTA enface images it is often difficult to distinguish whether NVs have penetrated this interface. We developed a widefield SS-OCTA system that highlights NVs over a field of view of up to 90 degrees.

Methods: Our widefield SS-OCTA system scans the retina at an A-scan rate of 1.7 MHz, enabling fields of view of up to 90 degrees while maintaining Nyquist sampling density. The high scan speed keeps the acquisition time at a comfortable 15s. A deep neural network (DNN) is used for 3D denoising of the acquired data. For automated detection of NV we implemented a robust ILM segmentation algorithm. After a graph-cut search and flattening of the retina, 3D smoothing filters and morphological operations on the structural OCT data yield the segmentation of the ILM layer. The standard deviation of voxel gray values in the area above the ILM provides the neovascularization segmentation.

Results: Our prototype SS-OCTA device produced excellent image quality far out into the periphery. With this device, we have so far imaged nearly 100 subjects with diabetic retinopathy at various disease stages. Figure 1 shows a montage of two 18 mm x 18 mm scans of a healthy subject to an ultra-widefield 23 mm x 18 mm SS-OCTA image. The zoom-in in the bottom left corner highlights that even the smallest capillaries around the foveal avascular zone can still be resolved despite the large field of view. An SS-OCTA image of a diabetic patient with proliferative NV, where the automatic NV segmentation result was overlaid in red can be seen in Figure 2. It allows the ophthalmologist to distinguish between proliferative and non-proliferative vascular abnormalities at first glance.

Conclusions: Widefield SS-OCTA in combination with DNN-based image quality improvement techniques and segmentation algorithms enhances and simplifies the diagnosis and disease monitoring of preretinal NV. The occurrence, the corresponding spatial location, and the specific extent of vascular anomalies are accompanying signs of many retinal diseases. In future studies we will therefore aim at demonstrating the benefit of widefield SS-OCTA imaging beyond diabetic retinopathy.

CONTROL ID: 3713383

SUBMITTER (NAME ONLY): Fuensanta Vera-Diaz

TITLE: Effect of Peripheral Optical Quality in Accommodation Responses of Young Children

SESSION TITLE: Myopia and refractive error development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.A. Vera-Diaz, A. Jnawali, K.L. Kerber, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P.J. Bex, College of Science, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optical quality in the near periphery has been associated with refractive error development. We investigated whether peripheral optical quality in children at High (HR) or Low Risk (LR) for myopia affects their accommodation responses.

Methods: Young children (n=97, 7.58±0.96yrs) with functional emmetropia (SE OD +0.95±0.54D; AXL OD 22.79±0.75mm) were enrolled. Optical quality across the central horizontal ±30° was assessed using a scanning aberrometer. Strehl ratios, Defocus (Z4) and primary Spherical Aberration (SA, Z12) were computed for 4mm diameter pupils. Accommodation responses were assessed with an open-field WAM binocular autorefractor for a central target at 40cm (20° 'dead leaves' that mimic natural images). Linear regression models were used to test if the optical quality measures predicted accommodation responses, for all subjects and also when divided into HR and LR, based on parental myopia and baseline SE.

Results: Peripheral Strehl ratios significantly predicted central accommodation responses for the LR group (temporal retina: R^2=0.31, p=0.04; T25deg: β=-14.04, p=0.04; nasal retina: R^2=0.45, p<0.01; N10deg: β=-4.29, p<0.01), but not for children at HR for myopia. Central accommodation was also predicted by peripheral SA (temporal: R^2=0.335, p=0.05; nasal: R^2=0.48, p<0.01), and central SA (0deg: R^2=0.43, p<0.01). When split into LR and HR groups, only the nasal retina significantly affected accommodation responses for the LR group at N5deg (β=-7.97, p=0.03). Lastly, central accommodation was predicted by peripheral Defocus (nasal: R^2=0.48, p<0.01; temporal: R^2=0.39, p=0.02) and central Defocus (R^2=0.43, p<0.01). When split into HR and LR groups, nasal Defocus predicted accommodation responses only for the HR group (R^2=0.55, p<0.01). No significant differences were found between HR and LR groups in Strehl ratios, Defocus or SA, although a trend for more positive Defocus was found in the HR group and more positive SA (significant for T25deg and T15deg) in the LR group across the periphery.

Conclusions: Peripheral optical quality is associated with central accommodation responses in young children with functional emmetropia. Accommodation responses in children at LR for myopia are affected by their peripheral Strehl ratios and SA, and those at HR for myopia by peripheral Defocus. Peripheral optical quality, particularly in the nasal retina, may have implications in myopia development.

CONTROL ID: 3713384

SUBMITTER (NAME ONLY): Fritz Gerald Kalaw

TITLE: Comparison of Heidelberg Composite Images with Optos Ultra-Wide Field Images by Overlay using Artificial Intelligence vs Mathematical Warping

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.P. Kalaw, M. Cavichini, D.G. Bartsch, V. Alex, C.B. Galang, A. Heinke, A. Warter, W.R. Freeman, Ophthalmology, Joan and Irwin Jacobs Retina Center, La Jolla, California, UNITED STATES|J. Zhang, T. Nguyen, C. An, Electrical and Computer Engineering, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Wide angle imaging is an increasingly important area of retinal research as imaging the retinal periphery may aid in diagnosis of various retinopathies. This is currently being done easily with the Optos machine or, with little difficulty, using overlapping 55-degree scans across the fundus with the Heidelberg system. We aimed to determine if we could overlay images from these two imaging modalities to evaluate abnormalities seen on either machine. We evaluated and compared image alignment using mathematical warping of the images for comparison to Artificial Intelligence-assisted alignment as our group previously described with posterior pole imaging.

Methods: A total of 58 eyes were included in the study. Imaging was done on the same day. Single Optos image and 9 images of standard 55-degree fields were captured from multiple views using the Heidelberg machine.

Optos image was designated as a reference (i.e. fixed image) during alignment and each of the 9 Heidelberg images were aligned onto the reference. We assumed that both images were captured over a standard 3D spherical eyeball and the Optos camera has a fixed view with regards to the globe, as specified in DICOM standard. Therefore, we set up 3D keypoint coordinates for the Optos image and then estimated a 3D-to-2D (or vice versa) Direct Linear Transformation (DLT) matrix to warp the Heidelberg image.

Dice metric based on anatomical structures is adopted as the measurement to evaluate alignment quality. Retinal vessel maps were extracted from both images using third party segmentation algorithms. The Dice value was calculated over the vessel maps. Image masks indicating imaging circles are also applied to limit the computation in the overlapping areas between both images.

Results: Twenty-four eyes are currently being studied with a total of 240 images (10 image per eye). Four out of the 24 resulting composite images contain exaggerated patterns due to distortions which cannot be solved by the DLT method and manual labels, which are therefore excluded from the alignment evaluation. The average Dice values for the remaining 20 image pairs is 0.4652.

Conclusions: Ultra-wide angle from different instruments can be co-localized and this may permit better evaluation of abnormalities seen on the two instruments. AI-enhancement of mathematical warping is ongoing and will be presented in the final paper.

CONTROL ID: 3713386

SUBMITTER (NAME ONLY): Ying Li

TITLE: Oral supplementary nicotinamide riboside treats several components of the DBA/2J murine model of pigment dispersion glaucoma

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, N. Zhang, X. Zhang, M. Chrenek, P.E. Girardot, J. Wang, J.T. Sellers, J.M. Nickerson, E.E. Geisert, J.H. Boatright, Emory Eye Center, Emory University, Atlanta, Georgia, UNITED STATES|Y. Li , N. Zhang, X. Zhang, P.E. Girardot, J.H. Boatright, Center for Visual and Neurocognitive Research, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|B. Charles, Department of Diabetes & Cancer Metabolism, City of Hope Beckman Research Institute, Duarte, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test whether oral administration of nicotinamide riboside (NR), a nicotinamide adenine dinucleotide (NAD^+) precursor, protects retina ganglion cells (RGCs) against neurodegeneration in the DBA/2J (D2) mouse model of age-related inherited pigment dispersion glaucoma.

Methods: NR administration in drinking water and food (4000mg/kg of body weight per day) started when DBA/2J mice were 4 months old and continued until 12 months old. Control cohort identically received vehicle water and food with no added NR. Intraocular pressure (IOP) was measured every month until experiment completion. Pattern electroretinography (PERG) was recorded at 4, 6, 9 and 12 months old using a Celeris system (Diagnosys LLC, MA). Retinas were harvested for whole mount immunofluorescence staining with RGC marker Brn3a and imaged by fluorescent confocal microscopy. Retinal NAD^+ levels were enzymatically assayed (Abcam, CA). Iris depigmentation degree was assessed by transillumination pattern assay.

Results: The retina NAD^+ level of NR-treated aged D2 mice was significantly higher than untreated aged mice (220±21.5% vs 108±5.9% of young naïve D2 retina NAD^+ level, N=6-8, $p<0.05$). Brn3a-positive immunofluorescent cell counts were significantly higher in NR-treated aged D2 mice compared with untreated ones (1412±248 cells per field vs 475±378 cells per field, N=20, $p<0.05$). PERG P1 and N2 amplitudes were significantly higher from NR group than vehicle group (P1: 2.89±0.27uV vs 1.37±0.12uV, N=40, $p<0.05$; N2: (-5.85±0.5uV vs -3.11±0.24uV, N=40, $p<0.05$). The degree of iris atrophy in NR group was much less severe compared with vehicle group.(Fig.1)
The IOP in NR group was modestly but significantly lower than vehicle group when DBA/2J mice were 7, 8 and 9 months old; there was no significant difference at other time points.

Conclusions: NR oral supplementation significantly preserved RGC numbers and retina function in aging D2 mice. Interestingly, treatment also prevented iris atrophy, delayed IOP elevation associated with this glaucoma model, and elevated retinal NAD+ levels. NR oral supplementation thus treated several aspects of murine pigment dispersion glaucoma. Given parallels between this model and glaucoma in humans, our data indicate that NR is worth exploring as a therapeutic candidate in treatment of glaucoma.

CONTROL ID: 3713387

SUBMITTER (NAME ONLY): Frank Koch

TITLE: The use of hypersonic vitrectomy as a novel approach for retinal reattachment surgery

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.H. Koch, J. Scholtz, S. Deuchler, Augenzentrum Frankfurt, Frankfurt am Main, Hessen, GERMANY|F.H. Koch, Department of Ophthalmology, Klinikum der Johann Wolfgang Goethe-Universitat Frankfurt, Frankfurt am Main, Hessen, GERMANY|T. Knoch, Bausch and Lomb GmbH, Berlin, Berlin, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the safety and effectiveness of the Vitesse hypersonic vitrectomy device for retinal re-attachment surgery in proliferative (diabetic) vitreoretinopathy cases. Vitesse utilizes hypersonic technology to liquefy instead of cut the vitreous, providing an alternative to the traditional pneumatic guillotine cutter.

Methods: Patients with proliferative vitreoretinopathy or proliferative diabetic vitreoretinopathy where hypersonic vitrectomy was used for re-attachment of detached retina were analyzed. Effectiveness of hypersonic vitrectomy was evaluated, both subjectively using a questionnaire, and objectively by means of video documentation of procedures, device settings, and data collection of the patients' medical histories.

Results: In all 16 cases, Vitesse separated the vitreous from the detached retina completely with no iatrogenic tissue damage. Vitreous traction was only documented in one case. A conversion to a guillotine cutter was necessary in none of the cases. In 6 of 16 cases shaving of the vitreous base was performed after early fluid-air exchange with hypersonic vitrectomy as a safe procedure without any complications. No adverse events suspected to be related to hypersonic vitrectomy were documented in the follow-up visits.

Conclusions: The Vitesse device has potential advantages over traditional devices used for vitrectomy including reduced vacuum volumes which limited the amount of turbulence and avoid traction in the eye. Liquefaction directly in front of the probe entrance allows for continuous unrestricted fluid flow. A potential disadvantage of this procedure is a longer duration of procedure time for liquefying the vitreous. Investigation is ongoing to optimize the machine settings and device tip design.

CONTROL ID: 3713390

SUBMITTER (NAME ONLY): Sylvain POINARD

TITLE: Age-related changes in porcine lens deformability measured by a digital lens spinner

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. POINARD, J. PAPILLON, O. BEN MOUSSA, L. COULOMB, B. PEYRET, M. MENTEK, F. MASCARELLI, C. PERRACHE, Z. HE, P. GAIN, G. Thuret, Laboratory “Biology, Engineering, and Imaging of Corneal Graft”, BiiGC, Universite Jean Monnet Saint-Etienne, Saint-Etienne, Rhône-Alpes, FRANCE|S. POINARD, P. GAIN, G. Thuret, Ophthalmology, Centre Hospitalier Universitaire de Saint-Etienne, Saint-Etienne, Rhône-Alpes, FRANCE|F. MASCARELLI, Centre de Recherche des Cordeliers, Paris, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: The aging of the crystalline lens induces an increase in its rigidity responsible for the loss of accommodation. Research on presbyopia requires the use of a large number of animal lenses that are available without limit in the eyeballs of animals from slaughterhouses. The use of lenses from older animals, which are rarer, seems judicious to understand the physiopathology and to evaluate the effect of new treatments. The measurement of lens deformation at high speed (lens spinning) is one of the methods described to estimate lens rigidity. Objectives: To measure the deformability of the porcine lens as a function of the age of the animal using a new digital lens spinner.

Methods: 65 pairs of porcine globes aged from 6 months to 5 years were obtained from a local slaughterhouse and dissected within 2 h postmortem. We developed an original lens spinner integrating: 1/ a rotating support illuminated by a stroboscopic light synchronized with a CMOS camera; 2/ a software for acquisition and analysis of images in real time. Five parameters were measured on 8 positions of the lens in rotation and averaged. A measurement was performed at 75 rpm inducing no deformation (accommodated state) and then at 1500 rpm (non-accommodated state). The lenses were spun at t0 to estimate the initial comparability between the two lenses of the same animal. They were then stored in culture medium and one of the lenses was heated to 50°C to stiffen it while the other remained at 20°C. A second spin was performed after 6h. A linear mixed-effect model was used for statistical analysis.

Results: The anterior radius of curvature was the most sensitive parameter to deformation. The deformability of the 2 lenses of the same animal were very strongly correlated at t0, regardless of age (R^2=0.94, p<0.0001). Elasticity was inversely correlated with age (R^2=0.82, p<0.0001). Heating induced a stiffening by a factor of 5 compared to the fresh state, the more so the younger the animals were (p<0.0001). Storage at 20°C did not significantly alter elasticity.

Conclusions: Our lens spinner is suitable for the analysis of large series of lenses. The anterior radius of curvature is the least noisy parameter. This parameter is sensitive enough to measure age-related loss of elasticity in pigs. Heating artificially ages the lens and can be used as a model. The lens of aged pigs can serve as a model of presbyopic lens.

CONTROL ID: 3713394

SUBMITTER (NAME ONLY): Bryce Hwang

TITLE: Vitrectomy after Anti-VEGF or Pan-retinal Photocoagulation Therapy in Proliferative Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Hwang, N. Rayess, P. Mruthyunjaya, Stanford University School of Medicine, Stanford, California, UNITED STATES|E. Chen, University of California San Francisco, San Francisco, California, UNITED STATES|J.W. HINKLE, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R. Parikh, Manhattan Retina and Eye, New York, UNITED STATES|A.D. Azad, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Protocol S trial compared ranibizumab with PRP and found that treatment with ranibizumab leads to fewer vitrectomy procedures. The purpose of this study is to characterize the odds of pars plana vitrectomy (PPV) after pan-retinal photocoagulation (PRP) or anti-vascular endothelial growth factor (anti-VEGF) injections in the treatment of proliferative diabetic retinopathy (PDR).

Methods: A retrospective cross-sectional study from January 1, 2012 to December 31, 2017 was conducted using a nationally representative claims-based database, Clinformatics™ Data Mart Database (OptumInsight, Eden Prairie, MN). Newly diagnosed, treatment naïve adults (≥ 18 years old) with PDR as defined by ICD9/10 codes and continuous enrollment for at least two years after diagnosis were included. CPT codes were used to determine PDR therapy and PPV status. Eyes were analyzed separately and were stratified into two groups: eyes receiving only anti-VEGF therapy (anti-VEGF group) and eyes treated with PRP monotherapy (PRP group). Primary outcomes were rates of PPV and median time to PPV for each group.

Results: The cohort consisted of 2368 eyes with PDR. Overall, 52.8% of patients were male with a median age of 65 (54-71). Of these, 1787 eyes were treated with PRP only, and 581 were treated with anti-VEGF only. 3.4% (20/581) and 4.9% (87/1787) of eyes required PPV in the anti-VEGF and PRP groups respectively (p=0.150). Median time to PPV was 114 days and 188 days in the anti-VEGF and PRP groups respectively (p=0.079). Adjusted for gender and age, the odds of vitrectomy were not different between eyes treated with PRP only compared to those treated with anti-VEGF only (odds ratio [OR] 1.14, CI 0.69-1.96, p=0.629).

Conclusions: This study examines eyes with PDR treated with either anti-VEGF monotherapy or PRP monotherapy to determine the likelihood of vitrectomy in a large, nationally representative cohort. Although median time to vitrectomy was longer for anti-VEGF monotherapy compared to PRP monotherapy, both treatment modalities had the same odds of ultimately requiring a vitrectomy. These results suggest that PRP does not increase the odds of vitrectomy compared to anti-VEGF in PDR patients. The implications for clinical practice and patient counseling should be further explored.

CONTROL ID: 3713395

SUBMITTER (NAME ONLY): Matteo Posarelli

TITLE: Treatment of Patients with Neurotrophic Keratopathy and Concurrent Neuropathic Corneal Pain: Clinical Outcomes.

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Posarelli, L. Yavuz Saricay, B. Bayraktutar, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts School of Medicine, Boston, Massachusetts, UNITED STATES|M. Posarelli, L. Yavuz Saricay, B. Bayraktutar, P. Hamrah, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neurotrophic keratopathy (NK) is typically considered a disease with reduced corneal sensation and lack of symptoms of discomfort, although we have reported recently that some patients may have concurrent ocular pain, including neuropathic corneal pain (NCP). Our aim was to evaluate the clinical outcomes of patients treated for concurrent NK and NCP.

Methods: A retrospective case series of 19 patients with stage 1 NK and concurrent NCP who were seen at the New England Eye Center (Boston, MA, USA) between August 2016 and November 2021 was conducted. NCP was diagnosed based on clinical examination, proparacaine challenge test, and in vivo corneal confocal microscopy (IVCM) findings. Best-corrected visual acuity (BCVA), ocular surface disease index (OSDI), pain on visual analog scale (VAS), ocular pain assessment survey (OPAS), and corneal fluorescein staining (CFS) by National Eye Institute (NEI) grading system were reviewed retrospectively.

Results: Patients' mean age was 61.9±3.9. NK etiology included chronic dry eye disease (DED) (n=12, 63%), herpes simplex keratitis (n=4, 21%), and post-surgery complications (n=3, 16%). Among the 12 subjects with DED, 8 patients had a positive serology for autoimmune diseases (Sjögren's syndrome, rheumatoid arthritis, and small fiber neuropathy). At baseline, mean BCVA was 20/50, OSDI score was 64.5±5.2, VAS score was 5.7±0.6, pain severity on OPAS for the past two weeks was 5.4±0.4, and mean CFS was 7.8±0.8. All patients were treated with autologous serum tears (100%), 8 (42%) received recombinant human nerve growth factor (cenegermin), and 17 (89%) were prescribed oral medications (nortriptyline, low dose naltrexone, gabapentin). Following treatment (mean 25.3±7.3 months), BCVA increased to 20/30 ($p<0.01$), we observed an improvement in OSDI score (37.1±6.1, $p<0.001$), VAS score (1.7±0.3, $p<0.001$), and OPAS pain severity for the past 2 weeks (2.3±0.4, $p<0.001$), and CFS significantly decreased to 3.1±0.4 ($p<0.001$).

Conclusions: NK patients are typically thought to lack symptoms of discomfort, but they can present with concurrent NCP. Our data outline the importance of addressing both conditions to treat the ocular surface alterations and the ocular pain to improve the patients QoL. Topical growth factors and oral pain modulators can lead to a significant improvement in BCVA, CFS and ocular discomfort scores.

CONTROL ID: 3713396

SUBMITTER (NAME ONLY): William Samuel

TITLE: Inhibition of Sodium Iodate-Induced Apoptosis in Human RPE by the Stearoyl Coenzyme A Desaturase Inhibitor Sterculic acid

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Samuel, C. Vijayasarathy, S. Uppal, T. Duncan, T. Redmond, LRCMB, NEI / National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) cell loss or dysfunction caused by a variety of stressors is a factor in the onset of age-related macular degeneration (AMD). Sodium iodate ($NaIO_3$), an oxidizing agent causing selective RPE cell damage, is used in pre-clinical models of RPE damage. $NaIO_3$ damage to RPE mimics features of AMD and geographic atrophy, due to reactive oxygen species (ROS) generation by $NaIO_3$. We have found that fenretinide-induced apoptosis in ARPE-19 cells decreases stearoyl-CoA desaturase (SCD), important in regulating cellular functions by maintaining saturated/unsaturated fatty acid equilibrium. Here, we investigate the effect of the SCD inhibitor sterculic acid (SA) on $NaIO_3$-induced apoptosis in RPE cells.

Methods: Human RPE cells (ARPE-19) grown on tissue culture plates in MEM alpha medium with 1% FBS and antibiotic were differentiated for 4 weeks; media exchange was performed twice a week. Differentiated cells were treated with 5 mM $NaIO_3$ in the presence or absence of 10 mM SA in a serum-free medium for 20 h. The progression of apoptosis was followed by the extracellular release of LDH. Total RNA fractions were used to analyze mRNA and lncRNA expression using cell death pathway finder, inflammatory response, and autoimmunity PCR arrays by real-time RT-PCR.

Results: $NaIO_3$ induced apoptosis in ARPE-19 cells in a dose- and time-dependent manner as indicated by LDH release in the medium. Treatment with 10 mM SA blocked $NaIO_3$-induced apoptosis by ~90%. Of 98 lncRNAs assayed, 12 lncRNAs were upregulated, and 28 were downregulated, while out of 98 mRNAs assayed, 10 mRNAs were upregulated and 48 were downregulated, with a fold change of 2 or more, in cells treated with $NaIO_3$. $NaIO_3$ treatment increased GADD45a mRNA and SLC7A11-AS1 lncRNA expression by ~22- and ~34-fold, respectively. This increase was blocked by SA. Increase in expression, in response to $NaIO_3$ treatment, of HO-1, a stress response protein, and BCL2L11, a regulator of apoptosis via the intrinsic mitochondrial pathway, were also blocked by SA treatment.

Conclusions: Our results show that SA treatment effectively blocked $NaIO_3$-induced apoptosis in human RPE cells. The mode of action of this SCD inhibitor appears to be at the level of ROS generation. Thus, SA may be an effective agent in regulating the response of RPE to oxidative stress.

CONTROL ID: 3713397

SUBMITTER (NAME ONLY): Dionne Argyle

TITLE: Sexual dimorphism in antigen-independent angiogenesis inhibition of IgG1 antibodies

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Argyle, Experimental Pathology, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|J. Ambati, B. Gelfand, Ophthalmology, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|F. Pereira, Departamento de Oftalmologia e Ciências Visuais, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Full-length human IgG1 antibodies antagonize pathological angiogenesis independent of antigen binding, and thus may be a next-generation anti-angiogenic target for retinal disease like age-related macular degeneration and diabetic retinopathy. However, the extent to which sex influences this angioregulatory activity is unknown.

Methods: Laser photocoagulation was performed in male and female C57BL/6J mice, followed by intravitreous injection of a full-length humanized IgG1 antibody. Choroidal neovascular volume (CNV) was measured 7 days later. Male and female derived primary macrophages BL/6J and BALB/c mice and human single donors were analyzed for VEGF-A-induced chemotaxis in the presence or absence of humanized or human IgG1 antibodies, or human IgG2 (negative control).

Results: Human IgG1 induced a significantly greater reduction in CNV in male mice to female mice. In B6 and BALB/c macrophages, IgG1 inhibited Vegf-a induced chemotaxis to greater degree in male than female-derived cells. Similarly, primary human macrophages from male donors were significantly more sensitive to IgG1 inhibition than female donors. IgG2 treatment did not affect chemotaxis of male- or female-derived cells.

Conclusions: The effects of IgG1 antibodies are different between male and female systems with male models being significantly more sensitive to IgG1 than females. Future studies are needed to understand the hormonal and genetic causes of these sexually dimorphic responses. These findings may support sex-specific translational application of antigen-independent antibody activities, which may ultimately result in more personalized anti-angiogenic therapies.

CONTROL ID: 3713398

SUBMITTER (NAME ONLY): Breandan Kennedy

TITLE: Visual behaviour-based screening of a randomised chemical library identifies small molecules that restore vision.

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.N. Kennedy, J. Fehilly, J. O'Brien, UCD School of Biomolecular and Biomedical Science, University College Dublin, Dublin, IRELAND|B.N. Kennedy, J. Fehilly, J. O'Brien, UCD Conway Institute, University College Dublin, Dublin, IRELAND|M. Cerrada-Gimenez, S. Kaja, G. Kalesnykas, R&D Division, Experimentica Ltd, Kuopio, FINLAND|S. Kaja, Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Chicago, Illinois, UNITED STATES|R. Scoffin, Cresset BioMolecular Discovery Ltd, Litlington, Cambridgeshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinal and macular degenerations are conditions with progressive photoreceptor or retinal pigment epithelium (RPE) dysfunction resulting in blindness. Most patients lack effective treatments to preserve vision. Efficient and effective phenotypic screening of randomised compound libraries can uncover first-in-class drugs. Here, using a bespoke drug discovery workflow we identify drugs rescuing vision.

Methods: Phenotypic drug discovery was performed on the atp6v0e1^{UCD6} zebrafish model of impaired vision screening a Chembridge DIVERSet® randomised compound library. 80 compounds were combined into 18 orthogonal drug pools for plate testing. Visual behaviour was analysed at 5 dpf by optokinetic response.

Results: Proof-of-concept assays validated orthogonal drug pooling as appropriate for optokinetic response screening. The orthogonal pooling protocol successfully detected visual rescue of atp6v0e1^{UCD6} in Tubastatin A spiked pools (positive control) with 3-fold visual improvement. Of the 720 compounds screened, 86% of pools did not alter vision and 8% of pools showed overt toxicity. Two hit compounds were identified. UCD-OPGG-2C is a benzenedicarboxylic acid and dimethyl ester with a molecular weight (MW) of 277.28 UCD-OPGG-3E is a cyclohexanecarboxamide with a MW of 265.79. Re-purchased UCD-OPGG-3E elicited a significant ($p< 0.025$), two-fold improvement in vision in atp6v0e1^{UCD6} larvae.

Conclusions: We developed a novel workflow to efficiently detect compounds restoring vision in zebrafish. Future experiments will analyse retinal histology, and ocular safety and efficacy in rodent models. Computational approaches will identify novel structural analogues of UCD-OPGG-2C and UCD-OPGG-3E.

CONTROL ID: 3713399

SUBMITTER (NAME ONLY): Trupti Agrawal

TITLE: RB1 null iPSC-derived retinal precursors form atypical organoids with maturation and lamination defects

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Agrawal, S. maddileti, I. Mariappan, Center for Ocular Regeneration, Prof. Brien Holden Eye Research Centre, Hyderabad Eye Research Foundation, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|T. Agrawal, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|S. Kaliki, The Operation Eyesight Universal Institute for Eye Cancer, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: RB1 is a tumor suppressor protein that regulates cell cycle and its loss of function results in retinoblastoma. This study aims to generate RB1 null models of human induced pluripotent stem cells (hiPSCs) to understand the effects of loss-of function on retinal development and maturation in vitro.

Methods: Adipose-derived mesenchymal cells from familial retinoblastoma patient, harboring nonsense mutation in exon 18 of RB1 was reprogrammed into iPSCs, using episomal constructs expressing OCT4, SOX2, KLF4 and cMYC ($RB1^{+/-}$ hiPSCs). Isogenic mutant lines were also generated by CRISPR-Cas9 mediated, targeted editing within the exon 18 of human RB1 ($RB1^{-/-}$ hiPSCs). Stably expanding mutant iPSC lines were characterized by RT-PCR, immunofluorescence, western blotting and karyotyping. Healthy control and mutant iPSCs were differentiated into retinal lineage using established protocols.

Results: The patient specific heterozygous $RB1^{+/-}$ and CRISPR-edited homozygous $RB1^{-/-}$ iPSC mutant lines maintained their stemness, pluripotency, genomic integrity and formed embryoid bodies comprising of cell types of all three germ layers. Upon differentiation into retinal lineages, the $RB1^{+/-}$ hiPSCs formed normal eye-fields in 2D cultures at 4 weeks. About 30-40 eye-field primordial clusters (EFPs) were formed per million cells plated for differentiation (n=4) and this was comparable to that of the healthy control hiPSC line. However, the differentiation of $RB1^{-/-}$ hiPSCs resulted in about 25 folds reduction in eye-field numbers per million cells. The eye-field cells of all mutant lines expressed the early neuro-retinal precursor markers such as PAX6, RX, CHX10, MITF, SOX10 and also formed retinal pigmented epithelial patches, which suggested normal retinal lineage commitment. When the EFPs were excised and grown in suspension cultures, the retinal progenitors underwent self-organization and formed well laminated neuro-retinal cups in control and $RB1^{+/-}$ hiPSCs. However, the rare EFPs in $RB1^{-/-}$ hiPSCs formed only atypical retinal clusters with severe lamination and maturation defects.

Conclusions: The iPSC models confirm that either a partial or total loss of RB1 does not affect their stemness, pluripotency or retinal lineage commitment. However, the presence of at least one normal copy of the gene is necessary for proper differentiation, post-mitotic maturation and lamination of neuro-retinal precursors.

CONTROL ID: 3713400

SUBMITTER (NAME ONLY): Xi Chen

TITLE: Consistent Immunomodulatory Genes and the Competitive Endogenous RNA Networks in Keratoconus among Populations

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Chen, C. Liu, J. Zhuang, K. Yu, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Keratoconus (KC) is a progressive disorder of the cornea. Increasing evidence indicates that immune disorders play an essential role in KC progression. In addition, the manifestations of KC vary across populations. However, the immune-related etiology and concordant regulatory mechanisms in different populations remain elusive. Here, we comprehensively utilized bioinformatics approaches and experimental methods to explore the potential immunoregulatory mechanism of KC progression among populations.

Methods: Transcriptomics data contains two KC populations was derived from the public dataset GSE151631 (America: N=11; Saudi Arabia: N=15). Taking the intersection of genes across populations and known immunological genes to obtain immune-related differentially expressed genes (IRGs). Protein clustering algorithms were utilized to screen out the hub IRGs, which were further verified in the third populations (China: N=8). The underlying drug targets were predicted by drug-gene interaction analysis. Additionally, the KC-related immunoregulatory competitive endogenous RNAs networks (ceRNA) were constructed and experimentally validated.

Results: Overall, KC-associated common differentially expressed IRGs were obtained. After experimental validation, 15 hub IRGs were credible and not related to populations. Moreover, a total of 9 intersecting drugs targeting three genes, CCR2, CCR5, and F2RL1, were considered as potential druggable molecular targets for KC. Furthermore, upon ceRNA interaction network, we identified several lncRNAs and miRNAs as critical non-coding RNAs regulating the shared IRGs in different populations of KC patients.

Conclusions: The current study facilitated the understanding of KC-related immune processes and provided novel insights into developing new immunotherapies for KC. Moreover, finding commonalities in the onset and progression of KC in different populations would facilitate the generalizability of treatment.

CONTROL ID: 3713401

SUBMITTER (NAME ONLY): Karena Tien

TITLE: Pars Plana Vitrectomy Without Intravenous Anesthesia: Technique, Safety, and Outcomes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.X. Tien, E. Podesto, M. Adam, Rocky Vista University College of Osteopathic Medicine, Parker, Colorado, UNITED STATES|M. Adam, Colorado Retina Associates, Denver, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Karena Tien: Commercial Relationship: Code N (No Commercial Relationship) | Erica Podesto: Commercial Relationship: Code N (No Commercial Relationship) | Murtaza Adam: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan/AbbVie;Code C (Consultant/Contractor):EvePoint Pharmaceuticals;Code C (Consultant/Contractor):Genetech;Code S (non-remunerative):Dutch Ophthalmic;Code S (non-remunerative):Regeneron

ABSTRACT BODY:

Purpose: To describe the technique, safety profile, and outcomes of performing pars plana vitrectomy (PPV) without intravenous (IV) anesthesia. Benefits of performing PPV without IV anesthesia include increased patient satisfaction due to decreased out-of-pocket costs, no preoperative fasting requirements, and no IV-line placement prior to surgery.

Methods: Retrospective single-surgeon case series of patients who underwent PPV without IV sedation between September 2018 and December 2021. Patients elected to undergo PPV without sedation (N=23) or with oral sedation (N=261) via 0.125 to 0.25 mg sublingual triazolam administered 30 minutes preoperatively. A 5 cc sub-tenon's block with a 1:1 ratio of 0.75% bupivacaine and 2% lidocaine was slowly administered at the initiation of each case. A circulating nurse monitored patient vitals and electrocardiogram tracings without anesthesiologist support. Ocular and systemic adverse events, visual acuity, anatomic outcomes, supplemental block administration, and re-operation rates were examined.

Results: A total of 284 PPVs in 255 patients (68.53 ± 11.11 years old) were performed for a variety of surgical indications including floaters, intraocular lens/cataract surgery complications, retinal detachment, and epiretinal membrane. Patients elected to undergo surgery without IV sedation due to personal preference (N=251), insurance status (N=17), anesthesia risk (N=8), difficulty fasting prior to surgery (N=4), lack of IV access (N=2), anxiety (N=1), and pregnancy (N=1). For eyes with greater than 1 month of follow up (N=223), preoperative VA of 0.62 ± 0.70 LogMAR improved to 0.25 ± 0.38 LogMAR ($P<0.01$) postoperatively. No intraoperative complications, systemic adverse events, need to cease surgery prematurely, or conversion to intravenous sedation occurred. 1.77% of eyes (N=5) required intraoperative supplemental sub-tenon's block administration. Patient satisfaction was not measured; however, 96% of patients who underwent reoperation (N=4) or fellow eye surgery (N=19) requested the same method of anesthesia without IV sedation.

Conclusions: Vitreoretinal surgery with sub-tenon's block and oral sedation or no sedation can be safely performed without the support of an anesthesiologist. Additional trials should be performed to further quantify patient comfort and complication rates.

CONTROL ID: 3713402

SUBMITTER (NAME ONLY): Jae-Chiang Wong

TITLE: One-year outcomes of trabecular meshwork microstent placement in eyes with severe glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wong, S. Hallaj, N.N. Kolomeyer, A. Shukla, R. Razeghinejad, J.S. Myers, D. Lee, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Wong, Rowan University School of Osteopathic Medicine, Stratford, New Jersey, UNITED STATES|T.Z. Zhang, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|C. Haghshenas, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the one-year surgical outcomes of trabecular meshwork microstent placement for eyes with severe glaucoma

Methods: The retrospective cohort study included patients with a diagnosis code of severe stage glaucoma before trabecular meshwork (TM) microstent placement from 1/2014 to 6/ 2021. Patients with at least 6-months follow-up in the post-operative period were included. Demographic and clinical data were collected at the preoperative visit and post-operative visits for up to 1 year. Surgical failures were defined as eyes that required further glaucoma surgeries or progressed to no light perception.

Results: 40 eyes of 36 patients were included. Mean age was 74.9±7.5 years old. 37 (93%) eyes had iStent and 3 (7%) had Hydrus. 23 (58%) eyes had 1 microstent (first generation iStent or Hydrus) placed, 16 (40%) had 2 microstents (iStent inject), and 1 (2%) had 3 stents (iStent infinite). All (100%) microstents were placed in combination with cataract surgery. At the preoperative (pre-op) visit, Humphrey 24-2 visual field (VF) mean deviation was -9.2±8.1 dB (n=12), Octopus 30-2 GTOP VF mean defect was 13.5±8.8 dB (n=26), and mean cup-to-disc ratio was 0.8±0.2. Mean pre-op intraocular pressure (IOP) was 15.9±5.1 mmHg and mean number of pre-op medications was 2.6±1.2. Post-operative (post-op) mean IOP overall ranged from 13.8±3.9 to 16.7±7.2 mmHg and were only different at 3- and 6-month visits ($p<0.05$ for both). Mean number of glaucoma drops at the 6- and 12-month visits of 1.6±1.2 and 1.8±1.5 drops, respectively were also lower than baseline ($p<0.05$ for both). Within 3 months post-op, 1 (2.5%) eye developed IOP less than 5 mmHg without hypotony related complications and 16 (40%) eyes developed elevated IOP: 14 (35%) greater than 20 mmHg and 2 (5%) greater than 30 mmHg. There was no difference in drop regimen at 6- and 12-months comparing the use of 1 versus 2 microstents ($p>0.2$ for both). Within the first post-op month, 3 (7.5%), 18 (45%), and 4 (4.5%) eyes developed microhyphema, mild iritis (1+ cell and/or flare or worse), and corneal edema, respectively. 2 patients required further glaucoma surgery with 1 Xen gel stent and 1 Ahmed tube shunt.

Conclusions: Although not approved by insurance for severe glaucoma, any microstent placement demonstrated a possible benefit of decreasing medication burden for patient for up to 12 months with low surgical risk when combined with cataract surgery.

CONTROL ID: 3713403

SUBMITTER (NAME ONLY): Michael Simmons

TITLE: Classification of microcornea among patients with abnormalities of ocular development

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Simmons, Ophthalmology and Visual Neurosciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|E. Wen, V.V. Mootha, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|A. Mahindrakar, Srikiran Institute of Ophthalmology, Kakinada, Andhra Pradesh, INDIA|

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ABSTRACT BODY:

Purpose: To evaluate the performance of a 10mm corneal diameter threshold definition for microcornea among patients with disorders of ocular development and to explore the utility of inclusion of axial length in classification.

Methods:

This prospective cohort study recruited patients with microphthalmos, microcornea and coloboma who presented to the Srikiran Institute of Ophthalmology in Andhra Pradesh, India between 2014 and 2019. All patients underwent a full clinical examination. Only right eyes were included in the study. Patients were excluded if visual acuity was worse than hand motions or if no corneal diameter measurement was obtained.

Subjects were classified as having microcornea (uC) if their horizontal corneal diameter (measured with a ruler and external photo) was <10mm; otherwise, they were classified as having normal corneas (nlC). Subjects were classified as having coloboma if an optic fissure closure defect was identified in either the anterior or posterior segment. Subjects were defined as having microphthalmos if their axial length was <21mm; these subjects were further classified as having nanophthalmos if no other abnormalities were present.

Patients were divided into uC and nlC groups, then separately classified by the ratio of their corneal diameter and axial length with a cut off of 2.1 defining high axiocorneal symmetry (ACS). Chi squared analysis was performed to assess the proportions of patients with the various abnormalities of development between groups. Logistic regression analysis was run to evaluate associations between each classification system and visual acuity as well as corneal power.

Results: A total of 46 patients met inclusion criteria for the study. The mean corneal diameter was 8.5mm in the uC group (n=26) and 10.5 in the nlC group. The mean axial length was longer in the uC group than the nlC group (22.8mm vs 21.1mm (p=0.04)). The proportion of patients were significantly different in the high and low ACS groups (p<0.001), but there was no difference between the uC and nlC groups. There was a small but significant association between uC classification and visual acuity (p=0.047; adjusted R2=0.064).

Conclusions: Inclusion of axial length in classification of patients with microcornea distinguished patients with coloboma from others in the cohort. The presence of microcornea was associated with decreased visual acuity in this cohort.

CONTROL ID: 3713405

SUBMITTER (NAME ONLY): Peter Scanlon

TITLE: Assessing the impact of COVID-19 on visual acuity for diabetic macular edema patients treated with aflibercept in the UK

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure: Peter Scanlon: Commercial Relationship(s);Code F (Financial Support):Bayer PLC;Code C (Consultant/Contractor):Bayer PLC;Code R (Recipient):Bayer PLC;Code R (Recipient):Topcon | Charlotte Norridge: Commercial Relationship(s);Code F (Financial Support):Bayer PLC | Rajarshi Mukherjee: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Lotery: Commercial Relationship: Code N (No Commercial Relationship) | Tunde Peto: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis;Code R (Recipient):Roche;Code R (Recipient):Allergan;Code R (Recipient):Oxurion;Code R (Recipient):Heidelberg;Code C (Consultant/Contractor):Optos;Code C (Consultant/Contractor):Optomed | Romi Chhabra: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis | Clare Bailey: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis;Code R (Recipient):Janssen;Code R (Recipient):Roche;Code R (Recipient):Boehringer;Code R (Recipient):Alimera Sciences | Haralabos Eleftheriadis: Commercial Relationship(s);Code F (Financial Support):Bayer PLC;Code R (Recipient):Bayer PLC | Faruque Ghanchi: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis;Code R (Recipient):Allergan;Code R (Recipient):Alimera;Code R (Recipient):Alcon;Code R (Recipient):Roche | Colin Jones: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Assessing the impact of COVID-19 on visual acuity (VA) in eyes treated for Diabetic Macular Edema.

Methods: Anonymized data from 21 UK centers were extracted from Medisoft for eyes receiving treatment with aflibercept and with VA data in the pre-COVID baseline period (01/10/19 to 30/03/20, N=3,248). Comparisons for period 1 (01/04/20 to 30/09/20, N=2,077) – lockdown following RCOphth Medical Retinal Management Plan, period 2 (01/10/20 to 30/03/21, N=1,850) - intermittent lockdown and period 3 (01/04/21 to 30/09/21, N=1,111; 20 centers) - easing of COVID-19 restrictions.

VA change was compared for baseline VA, <7 vs. ≥7 injections before period 1 and for eyes losing ≥5 ETDRS letters in period 1.

Results: The mean change in VA for eyes with a baseline VA of ≤35 letters, was +4.9, +2.5 and +1.7 letters from baseline to period 1, period 1 to 2 and period 2 to 3, respectively. For baseline VA of 36-55 letters, +0.6, +1.7 and -0.2 letters, from baseline to period 1, period 1 to 2 and period 2 to 3, respectively. For baseline VA of 56-75 letters, +1.9, zero and -0.5 letters, from baseline to period 1, period 1 to 2 and period 2 to 3, respectively. For baseline VA of >75 letters, -4.3, -0.5 and zero letters, from baseline to period 1, period 1 to 2 and period 2 to 3, respectively.

For eyes receiving <7 injections before period 1, the mean change in VA was -1.9 letters (N=1,335) from baseline to period 1, +0.5 letters (N=992) from period 1 to 2 and +0.1 letters (N=592) from period 2 to 3. For ≥7 injections before period 1, the mean change in VA was -3.4 letters (N=742) from baseline to period 1, -0.4 letters (N=515) from period 1 to 2 and -1.1 letters (N=303) from period 2 to 3.

For eyes losing ≥5 letters before period 1, the mean change in VA when receiving ≥1 injection in period 2 was +3.9 letters (N=283) from period 1 to 2 and -0.1 letters (N=140) from period 2 to 3. For eyes not retreated in period 2, the

mean change in VA was -2.9 letters (N=162) from period 1 to 2 and zero letters (N=73) from period 2 to 3.
Conclusions: Visual gain between time periods was more likely for lower baseline vision. For eyes with <7 or ≥7 injections before period 1, the mean VA change was a loss in vision in the first period with little change in later periods. For eyes with ≥5 letter loss in period 1, subsequent visual gain was more likely if treatment continued.

CONTROL ID: 3713407

SUBMITTER (NAME ONLY): Patricia Gallego-Muñoz

TITLE: Improving corneal stroma repair with Silk Fibroin-derived membranes.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Gallego-Muñoz, E. Ontoria, M. Martínez García, Cell biology, Histology and Pharmacology, Universidad de Valladolid, Valladolid, Castilla y León, SPAIN|P. Gallego-Muñoz, E. Ontoria, M. Martínez García, Optical Diagnosis Techniques Research Group, Universidad de Valladolid, Valladolid, Castilla y León, SPAIN|M. Fernández Gutiérrez, R. Gutierrez-Contreras, P. Olaya, S. Marcos, Instituto de Óptica Daza de Valdés (IO-CSIC), Consejo Superior de Investigaciones Cientificas, Madrid, Madrid, SPAIN|S. Marcos, Centre for Visual Science; The Institute of Optics; Flaum Eye Institute., University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In recent years different biomaterials have been developed to improve corneal repair, among these, silk fibroin-derived biomaterials. In this study, we evaluated the corneal stroma cells response to silk fibroin-derived membranes (SFMs) following injury.

Methods: A stromal in vitro wound model, previously described by our group (Gallego Muñoz et al., 2017, 2018) was used to evaluate the effect of SFMs on the different processes occurring during stromal repair. Briefly, transparent SFMs were placed on the bottom of Petri dishes, on top of which human corneal stromal cells (HCSCs) were seeded and cultured. When HCSCs reached confluence a linear wound was made. Similar cultures without SFMs were used as control group. Wound closure time and cell organisation were evaluated by microscopy. Proliferation and myofibroblast differentiation were analysed by immunocytochemistry. Hepatocyte growth factor (HGF) secretion was measured by ELISA.

Results: SFMs induced a significantly faster wound closure than control showing complete closure at day 3 (Fig. 1A). HCSCs showed higher organisation on the substrate during the wound closure than in control (Fig. 1B). A peak of proliferation was observed at day 1 in both groups but it was significantly increased in HCSCs seeded on SFMs ($p<0.001$). On day 3, the percentage of proliferation decreased in both groups showing no differences. HGF secretion was significantly increased by SFMs at day 3 compared to control ($p<0.05$). No myofibroblast differentiation was observed in HCSCs seeded on SFMs at any study time compared to a low percentage of myofibroblasts observed in control at day 3.

Conclusions: We showed the positive effects of SFMs during the stromal wound closure. The SFMs could improve the corneal repair process and prevent the development of corneal opacities in view of the promotion of faster wound closure. The faster closure appears to be caused by an earlier proliferation peak in presence of SFMs, but may also indicate SFMs support of the migration process. The absence of myofibroblasts with SFMs may result from a higher HGF secretion, which has been shown to inhibit myofibroblast generation in the corneal stroma.

CONTROL ID: 3713408

SUBMITTER (NAME ONLY): Angels Fabra

TITLE: Role of exosomes in liver metastasis of uveal melanoma

SESSION TITLE: Where art thou tumor? - Ocular tumor physiology and metastases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Fabra, R. Ramos, E. Cabré, A. Vinyals, J. Vaquero, J. Piulats, E. Gonzalez Sanchez, I. Fabregat, ONCOBELL, Institut d'Investigacio Biomedica de Bellvitge, Barcelona, Catalunya, SPAIN|J. Caminal, D. Lorenzo, M. Gomá, C. Gutierrez, Ophthalmology Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: Exosomes are small membrane vesicles that carry functional biomolecules derived from donor cells and can be horizontally transferred to recipient cells.

We aim to analyze whether uveal melanoma -derived exosomes were able to condition liver cells to create a favorable niche for the metastatic colonization and outgrowth of uveal melanoma cells

Methods: We isolated exosomes by differential ultracentrifugation from primary and metastatic UM cell lines with a common genetic background. Secretome was obtained from cells growing in vitro either in 2D or 3D conditions. Exosomes were characterized by electron microscopy; proteomic analysis was performed by LC-MSMS (LTQ-Orbitrap), and exosomal biomarkers by immunoblot. The uptake of exosomes by human liver cells was assessed by immunofluorescence. Human liver stellate cells (LX2) and macrophages (THP1) in co-culture in vitro, were exposed to uveal melanoma-derived exosomes. Transcriptomic and proteomic analyses were studied after the exosomal treatments.

Results: We identified 3241 proteins in exosomes from the isogenic UM cell lines, 895 of which were differentially expressed between invasive and non-invasive UM cells and the identified targets were validated by immunoblot. Interestingly, bioinformatic analysis showed that invasive UM cells display an enrichment in proteins involved in cell migration, invasion and signaling pathways such as WNT, IGF-1R, TGFß and NFkB, as well as specific integrins and focal adhesion proteins.

Moreover, we assessed the uptake of UM-derived exosomes by macrophages (THP1 cells) which contribute to the activation and reprogramming of human hepatic stellate cells (HSCs). HSCs adopt then a proangiogenic phenotype by upregulation of VEGF, IL8 and IL1ß; a pro-inflammatory and pro-fibrotic environment via upregulation of extracellular matrix molecules such as FN1 and FN-EDA and CCN2 and a promigratory phenotype. These changes are at least in part, orchestrated by the induction of ZEB1 and PRRX1 transcription factors.

Conclusions: Our results indicate that uveal melanoma-derived exosomes have a key role in the education of the Human Liver Stellate Cells favoring the development of the pre-metastatic niche in the liver that tilt in favor of metastasis. Furthermore, uveal exosomes can be used as biomarkers of metastatic disease and their cargo reflect the plasticity of uveal melanoma cells and announces possible new therapeutic targets for uveal melanoma.

CONTROL ID: 3713410

SUBMITTER (NAME ONLY): mousa moradi

TITLE: Ensemble learning for AMD prediction using retina OCT scans

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. moradi, Y. Chen, Department of Biomedical Engineering, University of Massachusetts Amherst, Amherst, Massachusetts, UNITED STATES|T. Huan, J. Seddon, Department of Ophthalmology & Visual Sciences, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|X. Du, Department of Mechanical and Industrial Engineering, University of Massachusetts Amherst, Amherst, Massachusetts, UNITED STATES|Y. Chen, X. Du, University of Massachusetts Amherst Institute for Applied Life Sciences, Amherst, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a progressive retinal disease and a common cause of blindness in people over age 50. AMD pathology can be detected by optical coherence tomography (OCT) and categorized into advanced and non-advanced AMD based on presence of geographic atrophy and/or neovascularization. Here we propose a stack-based ensemble deep learning method and demonstrate that it can improve non-advanced and advanced AMD detection using retina OCT scans.

Methods: Images from 150 subjects and 278 eyes diagnosed as non-advanced or advanced AMD obtained by Zeiss Cirrus OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA) were used in this study. Low-quality images were excluded before processing. The cleaned dataset had 767 images labeled as non-advanced and 663 images labeled as advanced AMD. The quality of retina images improved by contrast limited adaptive histogram equalization. Each image was divided into 4 patches without overlap between each other. Two center patches near the fovea were used, resulting in 2860 patch images in total. The processed images were split into 80% for training, 15% for validation, and 5% for testing. Base learners include 3 custom sequential models with 15, 23, and 25 hidden layers trained by stochastic gradient descent (SGD), rmsprop, and Adam optimizers, respectively. The weights calculated from each base model were used as an input feature for a meta model. Figure 1 shows the block diagram of the proposed model.

Results: Classification results for the base and ensemble models are shown in Table 1. Model 3 trained by Adam achieved slightly higher accuracy (87%) than model 1 (85%) and model 2 (84%) using SGD and rmsprop optimizers. By stacking base learners, the ensemble model can improve the accuracy, specificity, sensitivity up to 91%, 92%, 90.9%, respectively, on the test set.

Conclusions: Stack-based ensemble deep learning can improve the detection of non-advanced and advanced AMD.

CONTROL ID: 3713411
SUBMITTER (NAME ONLY): Christian Viehland
TITLE: 400 kHz Handheld OCTA System for Bedside Imaging of Infant
SESSION TITLE: OCT Angiography Clinical Applications
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Viehland, C.A. Toth, J.A. Izatt, Duke University Pratt School of Engineering, Durham, North Carolina, UNITED STATES|X. Chen, D. Tran-viet, S. Mangalesh, R. Imperio, C.A. Toth, J.A. Izatt, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|
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ABSTRACT BODY:

Purpose: We report on the development of a 400 kHz handheld optical coherence tomography angiography (HH-OCTA) system for imaging of young children and infants in the operating room and the intensive care nursery (ICN). The high speed of the 400 kHz engine allows for rapid capture of 9x9mm OCTA images (750 A-scans/B-scan, 750 B-scans/Volume, 4 repeats per B-scan location, total acquisition time of 7.5 seconds). Images are montaged to produce a composite OCTA image with a nasal temporal field of view comparable to a contact fundus camera.

Methods: We developed a 400 kHz OCT engine based on a VCSEL swept source laser (Thorlabs inc.) and used our previously reported HH-OCTA scanner that has an ergonomic grip optimized for supine imaging. Imaging was performed in 8 normal adult subjects in a supine position, 47 children/infants in clinic or during exams under anesthesia (EUAs) in the operating room, and 9 infants in the ICN. Retcam (Natus Medical, Pleasanton, CA) fluorescein angiography (FA) images were obtained during some EUAs for clinical care. OCTA images were generated in post processing using speckle variance and graph cut based segmentation was used to create projections of the vasculature. OCTA images were montaged in post processing. Optical power was set in accordance with the ANSI Z80.36 standard Light Hazard Protection for Ophthalmic Instruments and all human subjects research was performed under protocols approved by the Duke University institutional review board.

Results: Representative HH-OCTA images from an infant undergoing exam under anesthesia are shown in fig. 1.

Conclusions: We demonstrated a 400 kHz HH-OCT system capable of capturing images at the infant bedside. These depth resolved OCTA images can show important pathological vascular features such as the extraretinal neovascular plaque and intraretinal vascular loops. When compared to a contact fundus camera fluorescein angiography the OCTA images provide superior, depth resolved visualization of the retinal microvasculature.

CONTROL ID: 3713412

SUBMITTER (NAME ONLY): Parinaz Rostamzad

TITLE: Indications for and effect of nasal and temporal partial tenotomy of the vertical rectus muscles in strabismus

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Rostamzad, H.M. van der Meulen-Schot, H.J. Simonsz, S.E. Loudon, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Nasal and temporal partial tenotomies of the vertical rectus muscles differentially correct vertical deviation (VD) in adduction, VD in abduction, V- or A-Pattern and ex- or incyclotropia. In an initial analysis of a large case series we defined clinical indications for this operation and differences in effect.

Methods: A retrospective analysis was carried out of patients who were treated between 1996 and 2021 in our clinic. All patients were included who had a nasal or temporal partial tenotomy of the vertical rectus muscles. Patients were excluded if postoperative measurements were missing. The changes in angle of strabismus in VD in adduction, in gaze ahead, VD in abduction, V- or A-pattern and ex- or incyclotropia were calculated by subtracting the measurement three months postoperatively from the pre-operative measurement. The Mann-Whitney U test was used in SPSS (version 27) to detect significant differences between effects.

Results: In total 126 patients were included, 100 of whom were treated by nasal and 26 by temporal partial tenotomy. Twenty-six patients were excluded due to missing postoperative measurements. The median age at operation was 48 years, range 8 - 70 years. Seventeen patients treated by nasal and seven patients by temporal partial tenotomy did not have sufficient binocular vision for a cyclotropia measurement. Sixteen patients had first strabismus surgery, 58 had re-operations, six had traumatic strabismus, 10 had an eye muscle palsy, 17 had vertical nystagmus, and 19 had unicoronal craniosynostosis. The change in angle of strabismus is depicted in the Figure. Effect of surgery was analyzed for inferior and superior rectus together and absolute values were used for change in angle. There was a statistically significant difference between nasal and temporal partial tenotomy for VD in adduction ($Z= 4.215$, $p<0.001$) and for VD in abduction ($Z=-2.365$, $p=0.018$) but not for pattern and cyclotropia.

Conclusions: The significant differences between the change of VD in adduction as compared to that in abduction, show that nasal and temporal partial tenotomies are suited for an isolated small VD in either ad- or abduction. It remains unclear why the change of cyclotropia by temporal partial tenotomies (N=19) was so small.

CONTROL ID: 3713413

SUBMITTER (NAME ONLY): Marie Kreikenbohm

TITLE: Effect of smoking on fluorescence lifetime of the ocular fundus

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kreikenbohm, G. Böhmerle, J. Schulz, S.R. Sonntag, S. Grisanti, Y. Miura, Department of Ophthalmology, University of Lübeck, GERMANY|Y. Miura, Institute of Biomedical Optics, University of Lübeck, GERMANY|

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ABSTRACT BODY:

Purpose: Nicotine can affect cellular metabolic states and is considered as a high-risk factor for various retinal diseases. The aim of this study is to determine, whether nicotine causes a change in the fluorescence lifetime (FLT) of the healthy ocular fundus using fluorescence lifetime imaging ophthalmoscopy (FLIO).

Methods: Twenty eight smokers (≥5 cigarettes/day, >2 years) aged between 20 and 37 years and 26 age-matched nonsmokers without systemic or retinal diseases were investigated. All participants were examined with routine ocular examinations including optical coherence tomography and FLIO (473 nm excitation, detection with the short spectral channel (SSC, 498-560 nm) and the long spectral channel (LSC, 560-720 nm)). FLT was analyzed for the macular areas using the Early Treatment Diabetic Retinopathy Study (ETDRS) grid.

Results: Compared to the non-smoking group, the smoking group showed significantly longer FLT (mean FLT: τ_m) in the SSC's inner ring of the ETDRS grid (Median: 211 ps non-smokers vs. 221 ps smokers), and a shorter τ_m in the LSC's outer nasal (244 ps non-smokers vs. 232 ps smokers) and outer superior (238 ps non-smokers vs. 227 ps smokers) ($p<0.05$). Variance analysis indicated a significant dose-dependent correlation between τ_m in the LSC and the cumulative nicotine dose, while an increased nicotine dose correlates with a shorter τ_m in the outer ring. There was no difference in retinal thickness between both groups and no correlation was found between retinal thickness and τ_m.

Conclusions: The results suggest a significant influence of smoking on the FLT of the ocular fundus, which might indicate metabolic or hemodynamic changes of retinal tissues by nicotine consumption.

CONTROL ID: 3713414

SUBMITTER (NAME ONLY): Shane Nau

TITLE: Cataract Surgery Outcomes in Patients with Non-ocular Autoimmune Disease

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Nau, R. Scott, J. Patnaik, A. Palestine, A.K. Reddy, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify whether patients with systemic autoimmune diseases without uveitis are at an increased risk for adverse outcomes following phacoemulsification surgery.

Methods: Medical records were reviewed of patients who underwent phacoemulsification cataract extraction with intraocular lens implantation between January 1, 2014, and December 31, 2019, at the University of Colorado Hospital. Exclusion criteria included history of uveitis and cataract surgery combined with another intraocular surgery. Data including sex, race/ethnicity, age, surgery length and cumulative dissipated energy (CDE), pre- and post-operative best-corrected visual acuity (BCVA) and intraocular pressure (IOP), and the presence or absence of post-operative persistent anterior uveitis (PAU) and post-operative cystoid macular edema (CME) were obtained. At our institution, patients with autoimmune diseases without uveitis receive the same post-operative corticosteroid regimen without additional pre-operative corticosteroids as compared to patients without autoimmune diseases.

Results: The charts of 762 eyes from patients with autoimmune diseases were reviewed. The control group of patients without autoimmune diseases comprised 10,201 eyes. Baseline demographics of the two groups were notable for a significantly higher percentage of females (76.4%, $p < 0.0001$) and younger age (68.3, $p=0.013$) within the autoimmune group. There was no statistically significant difference between the two groups with regards to race/ethnicity, surgery length, post-operative BCVA and IOP, and post-operative PAU and CME. For PAU specifically, 3013 eyes that had previously been reviewed for PAU made up the control group. In this control group, 2.4% of eyes developed PAU.

Conclusions: Patients with systemic autoimmune diseases without uveitis do not appear to be at higher risk for adverse outcomes, including persistent anterior uveitis, following phacoemulsification cataract extraction. These findings suggest that patients with autoimmune diseases without uveitis do not require a modified peri-operative corticosteroid regimen.

CONTROL ID: 3713416

SUBMITTER (NAME ONLY): Gustavo Ortiz Morales

TITLE:

Endothelial morphometric characteristics in primary cornea guttata.

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ortiz Morales, M.E. Quiroga-Garza, D. Bastán-Fabián, M.A. Salinas-Lugo, J.A. Nava-Garcia, D. Loya-Garcia, J.C. Hernandez-Camarena, A. Rodriguez-Garcia, S. Padilla-Alanís, J.E. Valdez, Institute of Ophthalmology and Visual Sciences., Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To describe the morphology of the corneal endothelium in healthy Hispanic patients with primary cornea guttata (PCG).

Methods: A retrospective, descriptive, and analytical study of specular microscopies was performed to study the central region of the corneal endothelium in healthy, surgery-naive Hispanic patients with PCG.

Results: 123 eyes from 76 patients with PCG were included for analysis. Mean age was 68.14 ± 10.55 years (range 45-88 years). Mean cell density (MCD) 1853.10±643 cells/mm2, the mean cell area was 596.1±263 µm2, and the mean central corneal thickness was 527.55±47.56 µm. 65% of patients had polymegethism and 80.5% had pleomorphism. 84% of patients had less than 25% total area affected. Females were the majority of PCG patients (64%), with higher rates of polymegethism (58.6%), and pleomorphism (63.6%).

Conclusions:

Hispanic patients with PCG show a lower than average MCD compared to the Hispanic population. A high rate of polymegethism and pleomorphism was observed, particularly in females, where PCG was more frequent.

CONTROL ID: 3713419

SUBMITTER (NAME ONLY): Dinah Chen

TITLE: Assessment of AI Algorithms for Diabetic Retinopathy Classification Using Model Cards

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In the last decade there have been vast advancements in artificial intelligence (AI) in ophthalmology. However, reporting in AI literature is highly unstandardized and algorithmic fairness remains challenging to assess. In this preliminary study, we evaluate 59 studies on the development, validation, and trialing of AI tools for referable diabetic retinopathy (RDR) diagnosis, on measures of transparency. To do so, we employ a scoring system using an AI model card, a framework for benchmarked assessment of algorithmic fairness.

Methods: We identified 59 studies on AI algorithms for RDR diagnosis using fundus photos. 17 studies reported on algorithm training and internal validation, 26 studies on external validation, and 16 studies on prospective, clinical validation of RDR algorithms. We apply our model card scoring system to these studies to broadly assess algorithm transparency. Model card scored elements include basic model details (i.e. model version), elements of intended use, input/output definitions and architecture, training and evaluation dataset details (i.e, source, size, demographics), performance measures (AUC, sensitivity (SE) and specificity (SP)), and ethical factors relating to algorithm bias.

Results: Out of a total possible score of 22, clinical validation studies scored an average of 16.7 (range 13- 20), representing a moderate level of transparency. Only 1 clinical validation study defined a clear scope of use and only 3/16 studies reported data on race. While nearly all reported sensitivity and specificity, only 9/16 studies reported AUC and only 4/16 reported imageability. Clinical validation studies were conducted on an average of 1094 patients, ranging from 143-4381 patients. Average AUC, SE and SP was 0.9305, 90.8%, and 85.8% respectively. Similarly, reporting on training and external validation varied widely. 6/43 studies reported race data. Training datasets ranged from 89 to 466,247 images, averaging 52,035 images. Average AUC, SE, and SP was 0.960, 90.9% and 89.46% for training algorithms respectively. Average AUC, SE and SP of externally validated algorithms was 0.942, 92.4%, and 86.17% respectively.

Conclusions: Our results demonstrate a high level of variability in reporting of AI algorithms for RDR, with many clinical validation studies demonstrating moderate or poor levels of transparency. Model cards may help in promoting fairness and standardization of AI reporting.

CONTROL ID: 3713420

SUBMITTER (NAME ONLY): Hannah Anderson

TITLE: Ocular Complications After Dexamethasone Implant Versus Intravitreal Triamcinolone in Patients with Post Vitrectomy Macular Edema

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Anderson, C.K. Liu, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|T. Wakabayashi, R. Mahmoudzadeh, M. Salabati, M. Spirn, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare complications of dexamethasone implants (DEX) and intravitreal triamcinolone (IVTA) in eyes with post-vitrectomy macular edema (ME).

Methods: A single-center, retrospective study was conducted at Wills Eye Hospital (Philadelphia, PA, USA). 0.7 mg DEX (Ozurdex; Allergan, Inc., Irvine, CA) and 2mg IVTA (Triesence; Alcon Laboratories, Fort Worth, TX) were injected in an office-based clinical setting. The medical records of patients who underwent DEX or IVTA for post-vitrectomy ME between July 2014 and May 2021 with a minimum follow-up of three months were reviewed. We reviewed the following parameters: age, gender, ophthalmic history, pre-treatment and post-treatment visual acuity, and post-treatment ocular complications.

Results: A total of 125 eyes from 124 patients were included in this study. There were 65 eyes from 65 patients in the DEX group (43% female, mean age 69.7 [±11.5] years) and 60 eyes from 59 patients in the IVTA group (% female, mean age 72.2 [±12.5] years). The total follow-up duration was 2.9 ± 1.7 years, with no significant difference between the two groups (p=0.059). The reasons for prior vitrectomy included rhegmatogenous retinal detachment (RRD), epiretinal membrane, macular hole repair, vitreous hemorrhage, proliferative diabetic retinopathy, retained lens fragments, vitreous opacities, and endophthalmitis. The reasons for DEX and IVTA treatments included post-vitrectomy ME, central retinal vein occlusion, branch retinal vein occlusion, and diabetic ME. The rate of ocular hypotony was significantly higher in the DEX group (9 eyes [14%]) compared with the IVTA group (1 eye [2%]) (p=0.029). The incidence of ocular hypertension was higher in the DEX group (24 eyes [37%]) compared with the IVTA group (12 eyes [20%]) but not statistically significant (p=0.059). There were no between-group differences in the incidence of vitreous hemorrhage (DEX 3 eyes [5%]; IVTA 1 eye [2%]; p=0.669) or RRD (DEX 2 eyes [3%]; IVTA 1 eye [2%]; p=0.944).

Conclusions: The risk of ocular hypotony was significantly higher and the incidence of ocular hypertension was higher after DEX treatment than after IVTA in eyes with a history of vitrectomy. There were no between-group differences in the other complications.

CONTROL ID: 3713421

SUBMITTER (NAME ONLY): Eduardo Martinez-Enriquez

TITLE: Estimation of the full shape of the crystalline lens from optical coherence tomography images using Eigenlenses.

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Martinez-Enriquez, A. Curatolo, J.S. Birkenfeld, A.M. Gonzalez, A. de Castro, S. Marcos, Instituto de Óptica, Consejo Superior de Investigaciones Cientificas, Madrid, Madrid, SPAIN|A. Mohamed, Ophthalmic Biophysics, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|A. Mohamed, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|M. Ruggeri, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Ruggeri, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|S. Marcos, Center for Visual Science. The Institute of Optics. Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Estimating the full 3-D biometry of the crystalline lens is important for understanding its changes with aging, accommodation or myopia development, and for improving intraocular lens calculations. In Martinez-Enriquez IOVS 2016, we proposed a 2-region parametric model (2RM) to estimate the full lens shape ex vivo and in vivo from optical coherence tomography (OCT) images. Martinez-Enriquez BOE 2020 described a novel method for the representation of the full shape of the lens ex vivo (Eigenlenses). Here we demonstrate the use of Eigenlenses to estimate the full shape of the lens in vivo, in comparison with the 2RM method.

Methods: OCT images were obtained on one eye of 17 human subjects (26±2 y/o; unaccommodated; 5 repetitions) using a custom-developed swept source OCT system (200K A-scans/s, axial depth=16 mm, pixel size=8.3 μm). Surface segmentation and distortion correction were performed to obtain 3-D models of the lens within the pupil. From these models, the full shape of the lens represented by 6 Eigenlenses coefficients was estimated using multiple linear regression. The following parameters were quantified: diameter (DIA), volume (VOL), equatorial plane position (EPP) and lens surface area (LSA). Results from the two methods (2RM and Eigenlenses) were compared in terms of repeatability (standard deviation of repeated measurements) and Pearson coefficient (ρ).

Results: The mean values of lens parameters across subjects were DIA=8.86±0.12/8.70±0.25 mm, VOL=140±7/136±9 mm^3, LSA=152±4/150±7 mm^2, and EPP=1.43±0.03/1.56±0.08 mm, for Eigenlenses/2RM, respectively. Repeatability was DIA_SD=0.06/0.11 mm, VOL_SD=2.3/3.3 mm^3, LSA_SD=1.8/3.1 mm^2 and EPP_SD=0.029/0.041 mm for Eigenlenses/2RM, respectively. The correlation between the parameters calculated with both methods were ρDIA=0.89, ρVOL=0.94, ρLSA=0.92 and ρEPP=0.88. R^2 from multiple linear regression between the first two Eigenlenses coefficients, which are related with the size and aspect ratio of the lens, and the DIA and VOL were R^2=0.98 and R^2=0.997 respectively. Using just these two coefficients only reduced the accuracy of DIA by 0.017 mm and VOL by 0.3 mm^3.

Conclusions: 2RM and Eigenlenses are both robust methods to estimate the full lens shape parameters in vivo. However, the Eigenlenses method is more repeatable and efficient, requiring only two coefficients for an accurate estimation of lens volume and diameter.

CONTROL ID: 3713422

SUBMITTER (NAME ONLY): Midhun Thomas

TITLE: Optimization of femto-laser assisted alkali wound model through 3D printed suction cup

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Thomas, P. bellur, A. Tiwari, J. Rajput, B. Sangwan, A. Chandru, T. Bhowmick, Pandorum Technologies Pvt. Ltd., INDIA|A. Singh, A. Tiwari, A. Gour, J. Rajput, B. Sangwan, V. Singh Sangwan, Dr. Shroff's Charity Eye Hospital, INDIA|

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ABSTRACT BODY:

Purpose: Femtosecond laser technology has been well established for cataract surgery and has also been attempted for animal corneal wound creation model. The femtosecond laser instrument uses a suction cup (a sterile component that is placed on the cornea) that generates a negative pressure which applanates the cornea to prepare it for the laser operation. This cup is designed to suit human eye and is not compatible for any animal model. In this study, we have prototyped a custom suction cup that is suitable for rabbit cornea for the optimization of wound model.

Methods: Femtolaser instrument (LDV Z8,Ziemer Ophthalmology GmbH ,Germany) was used to initially create the corneal wound (5mm diameter, x N NaOH, x seconds) using the standard suction cup. A 3 dimensional scan of the cup was used to extract the dimensions and used as a reference to redesign a modified suction cup based on the rabbit eye dimensions. The redesigned cup was first prototyped using Digital light processing until the validation stage. The final model was additively manufactured using direct metal laser sintering process using titanium.

Results: The standard suction cup suited for humans had an internal diameter of 12 mm,an external diameter of 20mm and a height of 3.5mm that created a pressure of 70mm-Hg to get the right amount of applanation for the surgery. The standard suction cup when used on the rabbit cornea generated a pressure lesser than 50 mm-Hg and hence the right applanation was not achieved for surgery. Four set of iterations was done to achieve the final desired results of the cup before it was printed in titanium. The final dimensions were reported to have an internal diameter of 9.5 mm, outer diameter of 16 mm and a height of 2.7mm and it achieved pressure of 70 mm-Hg.

Conclusions: A femto-laser assisted rabbit cornea wound model was optimized with the redesigned suction cup. The redesigned suction cup helped generate the right corneal applanation required to carry out the laser surgery and provides a reliable component that suits a rabbit cornea.

CONTROL ID: 3713423

SUBMITTER (NAME ONLY): Carl Danzig

TITLE: Patient characteristics from a post hoc analysis of nascent geographic atrophy progression following treatment with avacincaptad pegol from the GATHER1 study

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.J. Danzig, Rand Eye Institute, Deerfield Beach, Florida, UNITED STATES|

Commercial Relationships Disclosure: Carl Danzig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Avacincaptad pegol is a C5 inhibitor being investigated for the treatment of geographic atrophy (GA). Based on optical coherence tomography (OCT) changes that signify the evolution of the atrophic process, the atrophy can be subdivided as (1) complete retinal pigment epithelium (RPE) and outer retinal atrophy (cRORA), (2) incomplete RPE and outer retinal atrophy (iRORA), and (3) drusen. This post hoc analysis was conducted to better understand the impact of avacincaptad pegol treatment on earlier stages of GA and to investigate patient baseline characteristics that may be associated with progression of disease and response to avacincaptad pegol treatment.

Methods: GATHER1 was a Phase 2/3, randomized, double-masked, sham-controlled clinical trial. A post hoc imaging analysis of GATHER1 OCT data was performed by a masked analysis evaluating regions of OCT volume scans >500µm from the border of GA lesion(s) at baseline and months 6, 12, and 18 for progression of iRORA to cRORA and drusen to iRORA and/or cRORA.

Results: In the avacincaptad pegol 2-mg group, as compared to the sham group over 18 months, a smaller proportion of patients progressed from iRORA to cRORA (20% vs 42%, respectively) and from drusen to iRORA or cRORA (8% vs 27%, respectively). Baseline characteristic evaluation included prior ocular history, prior surgeries/procedures, visual acuity (Early Treatment Diabetic Retinopathy Study [ETDRS] and Snellen equivalent), low luminance ETDRS, fundus autofluorescence imaging assessments, and fluorescein angiogram imaging assessments. These baseline characteristics were assessed to determine which were potentially associated with progression from drusen to iRORA or cRORA, from iRORA to cRORA, and treatment response to avacincaptad pegol.

Conclusions: In this post hoc analysis of the GATHER1 trial, avacincaptad pegol 2 mg was associated with greater numerical reduction compared to sham in the progression of iRORA to cRORA, and in the progression of drusen to iRORA or cRORA over 18 months. Baseline characteristics potentially associated with GA progression and treatment response with avacincaptad pegol are identified.

CONTROL ID: 3713424

SUBMITTER (NAME ONLY): Bright Oduro

TITLE: Using scalar blur analyses to examine the effect of test criteria on performance of vision screening tests

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.A. Oduro, A.J. Logan, N. Strang, G. Loffler, G.E. Gordon, G. Kennedy, Vision Sciences, Glasgow Caledonian University, Glasgow, Glasgow, UNITED KINGDOM|J.M. Wood, S. Read, S. Hopkins, R. Cox, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: School vision screening programmes play a key role in the early detection of uncorrected refractive error and other ocular conditions in children. The efficacy of vision screening depends on the specific test protocol and criteria used. Here, we used scalar blur values (SBV; representing blur attributed to refractive error; Blendowske, 2015), derived from childhood refractive error data, to simulate the effect of modifying cut-off criteria on the accuracy of visual acuity (VA) in vision screening tests

Methods: Calculations were based on eye examination data from 255 primary and high school students aged 4-18 years in rural Queensland, Australia. Data included uncorrected monocular and binocular logMAR distance and near VA, distance VA with +1.50DS blur, and with cycloplegic autorefraction. The sphero-cylindrical autorefractor results (range of spherical equivalents -3.63D to +8.13D) were converted to SBV and used to classify the presence of refractive error. ROC curves were generated for a range of SBV and screening test performance simulated by calculating the effect of different VA cut-off values. The area under the curve (AUC) provided an overall diagnostic accuracy measure, a conservative 0.9 criterion was applied.

Results: Sensitivity and specificity depended on both VA cut-off values, and the magnitude of refractive error (SBV) considered significant. The 0.9 AUC criterion was achieved for myopes at SBV values of 1.25D and 1.50D for monocular and binocular measures respectively. Applying a cut-off value of 0.3 logMAR with these SBV yielded a sensitivity of 100% and specificity of 85% for myopes tested monocularly. For hyperopes, the same criterion was achieved at SBV values of 3.50D (monocular and binocular). Unlike near VA which did not improve SBV, adding a +1.50 blur test for hyperopes substantially reduced these values: 2.00D (monocular) and 2.25D (binocular).

Conclusions: The SBV approach allows the effect of different screening tests and criteria on sensitivity and specificity to be simulated and quantified. Distance VA measured in isolation was effective at detecting approximately 1D of myopia, compared to 3.5D of hyperopia. The inclusion of a +1.50DS blur test in children with good distance acuity substantially improved hyperopia detection. Using the SBV approach on larger datasets will help determine the most effective test protocol for school vision screening.

CONTROL ID: 3713425

SUBMITTER (NAME ONLY): Julia Xia

TITLE: Comparison of Cataract Surgery Outcomes in Patients with Type 1 versus Type 2 Diabetes

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.L. Xia, J.L. Patnaik, K.L. Christopher, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus in Aurora, Colorado, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Julia Xia: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Patnaik: Commercial Relationship: Code N (No Commercial Relationship) | Karen Christopher: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Existing studies on cataract surgery in diabetic patients have either looked at all types of diabetes combined or type 2 diabetes alone. This study aims to report the intraoperative and postoperative outcomes of cataract surgery in patients with type 1 diabetes (T1DM) compared to type 2 diabetes (T2DM). We hypothesize that T1DM eyes have greater prevalence of preexisting diabetic retinopathy, worse postoperative visual outcomes, and higher rates of postoperative cystoid macular edema (CME).

Methods: A retrospective chart review was performed for 8117 patients who underwent cataract surgery at the Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus from January 2014 to January 2020. Demographic data, ocular history, intraoperative and postoperative outcomes were compared using general logistic regression modeling with estimating equations to account for patients who had two eyes included. SAS version 9.4 software was used for the analyses.

Results: Our patient population was divided into T1DM (n=146), T2DM (n=1849), and patients without diabetes (n=6122). Patients with T1DM were diagnosed with diabetes at a mean age of 23.5 years and underwent cataract surgery after a mean of 29.9 years from diagnosis. Compared to T2DM eyes (n=3115), T1DM eyes (n=233) were more likely to have a history of proliferative retinopathy (63.1% vs 42.4%, $p<0.0001$), retinal detachment (9.0% vs 2.9%, $p<0.0001$), and were more likely to have undergone prior vitrectomy surgery (12.9% vs 4.0%, $p<0.0001$). T1DM eyes had worse postoperative best-corrected visual acuity (BCVA) (logMAR 0.27 vs 0.15, $p=0.0003$) despite having similar preoperative BCVA to T2DM eyes (logMAR 0.52 vs. 0.44, $p=0.092$). T1DM eyes had higher rates of posterior capsule opacification (PCO) requiring YAG capsulotomy compared to T2DM eyes (18.9% vs 9.0%, $p<0.0001$). The rate of postoperative CME was higher in T1DM compared to T2DM eyes but the difference did not reach statistical significance (5.2% vs 2.7%, $p=0.105$).

Conclusions: T1DM eyes have greater prevalence of preoperative diabetic retinopathy and have worse BCVA after cataract surgery compared to T2DM eyes. While there was more postoperative CME development in T1DM compared to T2DM eyes, this difference did not reach statistical significance. Additionally, there were higher rates of PCO requiring YAG capsulotomy in T1DM compared to T2DM eyes.

CONTROL ID: 3713426

SUBMITTER (NAME ONLY): Andres De la Hoz

TITLE: Scleral deformation under air pulse – a finite element study

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. De la Hoz, J.S. Birkenfeld, S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|S. Marcos, Center for Visual Science, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mechanical properties of the sclera are relevant for the understanding of tissue remodelling and potential new treatments of myopia. Air pulse deformation imaging has been used to characterize the mechanical properties of the cornea in vivo, and has shown some potential for use in characterizing the sclera's mechanical properties. In this work, we studied the influence of parameters such as material preoperties, intraocular pressure (IOP), and tissue thickness on scleral deformation, using a parametrized finite element model of the porcine sclera.

Methods: A three-dimensional finite element model of the porcine eye globe was created in ANSYS Mechanical. IOP was incorporated as an internal fluid volume. A one-term Ogden hyperelastic model was used to describe the non-linear elastic behavior of the tissue. A range of values were evaluated for each variable: thickness of .58 to 0.78 mm at site of air pulse loading, IOP of 15 to 30 mmHg, material model μ value of 0.01 to 0.1 MPa. Central displacement, central-peripheral deformation ratio, applanation time, and peak-to-peak distance were calculated from the deformed sclera. A multiple regression was done to quantify the influence of the independent variables.

Results: Unlike results in the cornea, applanation and peak-to-peak distance do not appear to be suitable descriptors of deformation, as higher scleral rigidity produced small values in these parameters. Central displacement was found to be highly correlated to material properties (correlation coefficient R^2=0.90), but thickness (R^2=0.06) and IOP (R^2 =0.02) were poorly correlated. The influence of thickness and IOP was more pronounced for the upper range of deformation values (>1mm central displacement). At the lower range (>0.4mm), deformation is driven primarily by material coefficient.

Conclusions: Porcine scleral deformation is influenced by elastic material properties, IOP, and thickness, with the former being the primary influence in the lower deformation range. Results suggest that air pulse deformation imaging could be used to estimate the elastic mechanical properties of the sclera in vivo.

CONTROL ID: 3713427

SUBMITTER (NAME ONLY): abdul hannan

TITLE: Csk regulates lacrimal gland development by controlling YAP activity

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. hannan, ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: abdul hannan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Lacrimal gland (LG) is the tear secreting gland which keeps eyes moistened. Dysfunction of the lacrimal gland can lead to the aqueous-deficient dry eye disease and even corneal damage. In this study, we find that C-terminal Src kinase (Csk) plays a key role in the development of lacrimal gland in a YAP dependent manner.

Methods: Csk was deleted in the lacrimal gland using a LG epithelial specific Cre during embryogenesis. Csk-deleted mouse was sacrificed, and the phenotype of the lacrimal gland was examined at various postnatal stages by fixing the glands with 4% paraformaldehyde followed by immunofluorescence and H&E staining. Primary LG epithelial cells were collected from P1-4 mouse pup and cultured for one week and treated with Csk inhibitor.

Results: We observed that the Csk-ablated lacrimal gland could not differentiate into a functional LG, instead we found dilated acini and ducts with complete loss of suppressive Src phosphorylation (pSRC-527Y) and the presence of active nuclear YAP. By RNA-seq analysis of the FACS-sorted LG epithelial cells, we also observed a significant increase in Yap target genes. Remarkably we could also rescue the dilated phenotype of the LG by homozygous deletion of YAP in the Csk deletion background, which supports our hypothesis that Csk regulates LG development via regulating YAP activity. Hippo pathway is known to regulate YAP by S-127 phosphorylation on its N terminal domain, which results in the inhibition of YAP function and cytoplasmic retainment. On the other hand, phosphorylation of YAP at Y-357 by Src family of kinase leads to the nuclear localization of YAP and enhanced transcriptional activity. WB analysis shows that treatment of LG epithelial cell with Csk inhibitor did not change the phosphorylation pattern of YAP at the S-127 site, but it led to a significant increase of Y-357 phosphorylation, suggesting that Csk regulates Yap activity independent of Hippo signaling.

Conclusions: Our results demonstrate that Csk regulates lacrimal gland morphogenesis by controlling the Yap activity. Deletion of Csk results in the activation of Src kinase which activates YAP by phosphorylating Y-357 and results in the dilation of the lacrimal gland.

CONTROL ID: 3713430

SUBMITTER (NAME ONLY): Valentina Tonelotto

TITLE: Exploring The Therapeutic Potential of Ergolide as An Anti-Cancer Agent for Uveal Melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Tonelotto, H. Sundaramurthi, B.N. Kennedy, University College Dublin, Dublin, IRELAND|V. Tonelotto, Xenopat S.L., Barcelona, SPAIN|S. Marcone, The University of Dublin Trinity College, Dublin, IRELAND|L. Jensen, BioReperia AB, Linköping, SWEDEN|G. Zoltán, Pharmahungary Group, Szeged, HUNGARY|

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ABSTRACT BODY:

Purpose: Metastatic uveal melanoma (MUM) is a poor prognosis cancer wherein approximately 85% of patients diagnosed do not survive beyond one year. There is no standard of care for MUM. Therefore, it is vital to understand and identify novel pharmacological based drugs for MUM. Ergolide, a sesquiterpene lactone isolated from the flowers of Inula species (a medicinal herb), exerts anti-cancer properties. The objective of this study is to: 1) evaluate whether Ergolide reduced MUM cell survival/viability in vitro and in vivo; and 2) understand the Ergolide mechanism of action.

Methods: Clonogenic cell survival assays assessed the ability of uveal melanoma (UM) cells derived from primary (Mel285 and Mel270) and metastatic (OMM2.5) tumours to proliferate following treatment with Ergolide. Cells were treated with 1, 5 or 10 μM Ergolide (N = 3) for 96 hours and additionally cultured for 10 days with fresh media. DiI labelled OMM2.5 cells were transplanted into the perivitelline space of 2 days old zebrafish larvae, treated with 0.5% DMSO or 2.5 μM Ergolide for 3 days and analysed for changes in primary xenograft cell fluorescence. Methods to isolate extracellular vesicles from OMM2.5 cells and UM patient samples are being optimised.

Results: Ergolide treatment resulted in a dose dependent, significant reduction (ranging from 48.5 - 99.9%; $p < 0.02$) in cell colony proliferation across all three UM cell lines. In vivo, in zebrafish OMM2.5 xenograft models, 2.5 μM Ergolide treatment averaged a 56% regression ($p < 0.0001$) of normalized primary xenograft fluorescence compared to vehicle controls.

Conclusions: Our findings suggest that Ergolide is capable of preventing UM/MUM cell survival in vitro; and reduces OMM2.5 primary xenograft fluorescence in vivo that needs to be further explored. Future studies will investigate 1) the mechanism of action of Ergolide in vitro through proteome profiling, and 2) changes to the molecular properties of extracellular vesicles isolated from OMM2.5 cells treated with Ergolide.

CONTROL ID: 3713431

SUBMITTER (NAME ONLY): Jessica Lau

TITLE: Comparison of Ocular Parameters and Target Refractive Error in Chinese Subjects Aged 50 and Above using CASIA2 anterior segment optical coherence tomography and Oculus Pentacam AXL

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare differences and agreement for ocular parameters and target refractive error in Chinese emmetropic (AL 22-24 mm), hypermetropic (AL <22 mm) and myopic eyes (> 26 mm) obtained by two optical biometric instruments; the CASIA2 AS-OCT (Tomey, Japan) and Pentacam AXL (Oculus, Germany) using two different IOL power calculation formulae.

Methods: In this random population-based cross-sectional study, 174 consecutive subjects aged 50 and over underwent biometric assessment using the CASIA2 and the Pentacam AXL devices. The right eye of each subject was used for analysis. Ocular parameters and target refractive error were compared between devices using a constant IOL SEQ equal to 19.50. Measurements were expressed as mean and standard deviation. Differences between devices, using Barrett UII and SRK/T formulae, and across emmetropes, hypermetropes and myopes were determined using Wilcoxon signed-rank test and Kruskal-Wallis test. The agreement in ocular biometry and IOL power between the 2 devices was evaluated by the Bland-Altman method.

Results: Overall, 174 eyes of 174 subjects were analyzed. Mean age was 60.49 (± 6.58). Based on axial length and refractive error, 134 were emmetropes, 7 were hypermetropes and 33 were myopes. 66.67% of subjects were female. There were no significant differences in measured ocular parameters between devices and across emmetropes, hypermetropes and myopes. For target refractive error, statistically significant differences between devices were noted for all three groups, with the difference being highest using Barrett UII formula and in myopes (0.31 ± 0.22), followed by emmetropes (0.26 ± 0.27), and then hypermetropes (0.25 ± 0.29). For each device, there were no statistically significant differences in target refractive error between the two formulae.

Conclusions: Despite using different imaging principles, parameters obtained by the CASIA2 and Pentacam AXL devices are comparable. There were statistically significant differences in target refractive error between devices, but would be within a clinically acceptable margin of error. Both devices are comparable across a range of axial lengths.

CONTROL ID: 3713432

SUBMITTER (NAME ONLY): Victor Sendra

TITLE: Leukocyte Function-Associated Antigen-1 (LFA-1) Antagonist Lifitegrast Prevents Corneal Recruitment of Effector T cells (Th1) by Modulating CXCR3 and CCR4 expression During Dry Eye Disease (DED)

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.G. Sendra, F.L. Barbosa, D.L. Harris, P. Hamrah, ophthalmology, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|P. Hamrah, Ophthalmology, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The interaction of ICAM-1/LFA-1 is essential for T cell activation and migration. Intravascular ICAM-1 has been shown to be upregulated during corneal inflammation, such as in dry eye disease (DED). The purpose of this study was to assess if LFA-1 antagonist Lifitegrast can reduce $CD4^+$ T cell migration to the cornea by modulating the expression of chemokine receptors during DED

Methods: DED was induced in 6–8 week-old mice by exposure to the controlled environment chamber and subcutaneous injections of scopolamine. Mice were treated with topical Lifitegrast (or normal saline [NS] control) 3 times daily. Fifteen days later, DED severity was assessed with corneal fluorescein score (CFS) and T cells were quantified by flow cytometry (FC) of corneal single cells for the cytokines IFN-γ (Th1) or IL-17A (Th17). Expression of chemokine receptors on T cells from local draining lymph nodes (dLNs) were assessed by qRT-PCR and FC. $CD4^+$ T cells from DED mice treated with Lifitegrast or NS were sorted and adoptively transferred to RAG knockout (KO) mice. Five days later, DED severity was assessed and T cells were quantified in pooled corneas and dLNs by FC

Results: CFS and tear secretion were significantly increased at day 15 in DED mice treated with Lifitegrast, compared to DED mice treated with NS ($p < 0.001$). Lifitegrast treatment resulted in reduction of $CD4^+$ T cell recruitment (Th1) to the cornea by FC($P<0.05$) with reduction of corneal IFN-γ and TNF-α compared to DED mice treated with NS. $CD4^+$ T cells from dLNs showed reduction on the expression of chemokine receptors CXCR3 and CCR4 by FC in DED-Lifitegrast vs. NS-treated controls mice ($p<0.05$). Interestingly, adoptive transfer of $CD4^+$ T cells from DED mice treated with Lifitegrast resulted in significant reduction of CFS and improved tear secretion ($p<0.05$) with reduction of T cells (Th1) recruitment into the cornea (17% vs. 44%) but no changes in the dLN compared to NS-treated controls

Conclusions: Lifitegrast treatment reduces CFS and improves tear secretion in DED mice, and resulted in significant reduction in corneal effector Th1 cell recruitment and reduction in pro-inflammatory cytokines. Lifitegrast treatment may mediate DED by inhibiting corneal T cell migration through the modulation of CXCR3 and CCR4 expression on $CD4^+$ T cells in dLNs

CONTROL ID: 3713433

SUBMITTER (NAME ONLY): Sharanya Suresh

TITLE: Morphometric analysis of the human retinal pigment epithelium indicates regional susceptibilities to disease

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Suresh, D. Ortolan, R. Sharma, A. Volkov, A. Maminishkis, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|N. Hotaling, National Center for Advancing Translational Sciences, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) is thought to be functionally different in different regions of the eye, implicating its role in regional retinal diseases like age-related macular degeneration (AMD). Recently, we completed a morphometric map of human RPE and defined five concentric rings containing subpopulations with varying cell sizes. Going from the macula to the periphery, these subpopulations were named P1 to P5. Using this map, this study aims to determine if any subpopulation had a higher prevalence of lesions in non-AMD and AMD eyes and to use changes of cell morphometry to predict the initiation of AMD.

Methods: Flatmounts of 17 non-AMD donor eyes and 5 AMD eyes were stained and analyzed with a machine learning based software created to quantify RPE morphometrics. After identifying micro lesions, 3 RPE-retina flatmounts were optically cleared with BABB and stained for RPE borders and photoreceptors.

Results: RPE cells in the lesioned area exhibited weak phalloidin staining, elongated borders, and a larger area. Analysis of lesion prevalence in each subpopulation indicated that P5 (far-periphery) had significantly more lesioned area than P3 (mid-periphery) in non-AMD eyes (24% vs 7%). AMD eyes showed the same pattern, albeit without statistical significance. To understand RPE morphometric changes with age, we divided the eyes into age groups (<65, 65-79, 80-100, and AMD 80-100). We found that, compared to younger donors, the 80-100 age group of non-AMD eyes had more elongated and less hexagonal cells in P1 (macula). AMD 80-100 data presented with more variability but generally showed worse aspect ratio, hexagonality, and an irregular number of neighbors, indicating abnormalities in the RPE.

Conclusions: The findings show that far peripheral RPE presents with more risk for developing sub-RPE deposits as compared to mid-peripheral RPE in non-AMD donors, highlighting the importance of imaging peripheral retina. Changes in RPE morphometry with age are more evident in the macular region and advances in the resolution of adaptive optics could allow analysis of RPE morphometrics in real time and could be a predictive tool for clinicians.

CONTROL ID: 3713434

SUBMITTER (NAME ONLY): Ortal Fogel Tempelhof

TITLE: Comparison of diamond and metal blade for scleral flap dissection in Trabeculectomy, using an anterior segment optical coherence tomography

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Fogel Tempelhof, S. KURTZ, D. ZUR, E. ROSENFELD, D. ZVI LOBERMAN, M. WAISBOURD, ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To evaluate and compare the characteristics of the filtering bleb and scleral flap in trabeculectomy, created with a diamond or metal blade, using an anterior segment optical coherence tomography (AS-OCT).

Methods: We enrolled patients after a first trabeculectomy, in which the scleral flap was created using a diamond or metal blade, and continued follow up in our clinic by a glaucoma specialist. An AS-OCT was done at least 6 months post operation and analyzed for bleb height, bleb-wall thickness and para-scleral drainage route in the anterior and posterior parts of the scleral flap. Operative success was defined as IOP reduction of 30% and bellow 18 mmHg, addition of medication was considered as qualified success.

Results: 32 eyes (of 30 patients) were evaluated, 18 in the diamond blade group (DB) and 14 in the metal blade (MB) group. Success rate was 94.44% and 71.43%, respectively. Preoperative IOP was 23.33±7.09 [range 12-38 mmHg] in the DB group and 23.43±4.97 [range 16-36 mmHg] in the MB group. A mean IOP reduction at last follow up was 11.56±7.42 and 10.43±5.35 mmHg, respectively, with a lower medication rate in the DB group: 0.7 vs 1.7.
AS-OCT analysis showed a mean bleb height and bleb wall thickness of 843.33±357.37 and 685.11±259.35μm in the DB group compared to 651.29±284.17 and 519.5±237.61μm in the MB group, respectively, with $p<0.05$ for bleb wall thickness.

Conclusions: Higher success rate, IOP and medication reduction was seen with a diamond blade used for the scleral flap in trabeculectomy. This may be attributed to a thicker bleb wall associated with higher filtration rate.

CONTROL ID: 3713437

SUBMITTER (NAME ONLY): Michel Michaelides

TITLE: AAV5-RPGR (botaretigene sparoparvovec) gene therapy for X-linked retinitis pigmentosa (XLRP) demonstrates localized improvements in static perimetry

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Michaelides, T. Antonio Cabral de Guimaraes, Y. Yang, J. Bainbridge, UCL Institute of Ophthalmology, London, UNITED KINGDOM|J. Xu, D. Wang, P. Wong, A. Fung, Janssen, New Jersey, UNITED STATES|A. Forbes, S. Naylor, R. Zeldin, MeiraGTx, New York, New York, UNITED STATES|M.A. Parker, R. Weleber, Oregon Health and Science University and Casey Eye Institute, Portland, Oregon, UNITED STATES|C. Besirli, Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Subretinal injection of AAV5-RPGR gene therapy in participants (pts) with XLRP aims to target as much of the structurally intact retina as possible within the posterior pole. We assessed whether the topographically treated area of the retina (within the bleb) functionally improved over time compared to the untreated surrounding area (outside the bleb), as measured by photopic static perimetry of all tested loci.

Methods: Pts in study MGT009 (multicenter open-label Phase 1/2 trial; NCT03252847) were given 0.3-0.8 mL of AAV5-RPGR subretinally at 1 of 3 doses to the worse-seeing eye in the study dose-escalation phase; maximal coverage of structurally intact retina was achieved with >1 retinotomy, if needed. Location/extent of blebs were documented with intraoperative video. Retinal sensitivity (Octopus 900 full-field static perimetry) was compared within/outside the bleb(s) within 30-degree hill-of-vision (V30) at baseline through 12 mo for 2 intermediate dose pts. To create bleb overlay images, the hill-of-vision surface was superimposed onto the color fundus image; bleb locations were outlined by the surgeon.

Results: Pts 005 and 007 (male; 33 & 27 years of age, respectively) were analyzed. Pt 005 received therapy in a single bleb, while Pt 007 received 4 blebs to allow for maximal coverage. At 12 mo compared with baseline, V30 in total in the treated eye improved in Pt 005 (7.56 dB-sr vs 9.50 dB-sr, +25.7% improvement) and in Pt 007 (9.54 dB-sr vs 10.18 dB-sr, +6.7% improvement). Within the bleb area(s) within V30, improvements were demonstrated in both patients (Pt 005: 1.94 dB-sr vs 2.60 dB-sr, +33.8%; Pt 007: 3.85 dB-sr vs 4.06 dB-sr, +5.4%). Outside the bleb area within V30, hill-of-vision also improved in Pt 005 and Pt 007 (22.9%; +7.5%, respectively). These data are consistent with the expression of a functional RPGR protein.

Conclusions: Increases in baseline-subtracted retinal sensitivity at 12 mo (within/outside the bleb area within V30) indicate improvements in photoreceptor function suggesting local efficacy of AAV5-RPGR gene therapy. The treatment effect may extend beyond the margins of the bleb following surgery owing to subretinal extension before retinal reattachment. Further development of this therapy is warranted.

CONTROL ID: 3713440

SUBMITTER (NAME ONLY): Konstancija Kisonaite

TITLE: Age-related loss of minimal cross-sectional surface area of nerve fibers in the optic nerve head

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kisonaite, Z. Yu, P.G. Soderberg, Ophthalmology, Uppsala Universitet Institutionen for kirurgiska vetenskaper, Uppsala, Uppsala, SWEDEN|S. Bendazzoli, C. Wang, Division of Biomedical Imaging, Kungliga Tekniska Hogskolan Sodertalje, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: The axons of retinal ganglion cells in the optic nerve head (ONH) can be visualized and quantified with 3D-OCT. Thickness as well as cross-sectional surface area have been suggested as possible quantification methods to assess pathological loss of axons in glaucoma. Currently, there is no consensus on a preferred method. This study aimed to estimate the minimal cross-sectional surface area in non-glaucomatous subjects with a custom-made computational algorithm. The cross-sectional surface area, Pigment epithelium central limit - Inner limit of the retina Minimal Area (PIMA), was calculated over the circumference of the ONH as PIMA-2π.

Methods: One eye from each of 40 non-glaucomatous subjects aged 20-69 equally stratified according to age group and gender was estimated for minimal cross-sectional surface area. Image volumes were acquired with 3D-OCT Topcon models OCT2000 and Triton, commonly available at the clinic. Confidence intervals and linear regression were used for statistical evaluation.

Results: A 95% confidence interval for PIMA-2π was estimated to 2.03 ± 0.14 mm^2. In each age group, PIMA-2π was estimated to 2.02 ± 0.36 mm^2, 2.35 ± 0.54 mm^2, 2.13 ± 0.26 mm^2, 1.78 ± 0.30 mm^2 and 1.87 ± 0.23 mm^2 for ages [20;29] [30;39] [40;49] [50;59] [60;69] respectively. The correlation coefficient estimated as a 95% CI for k was $-9.48 \pm 9.07 \times 10^{-3}$ mm^2/year (D.f.= 38).

Conclusions: Presented values of cross-sectional surface area are slightly higher but of the same magnitude as measurements done with Heidelberg Spectralis 3D-OCT in similar studies. This can be attributed to our custom computational algorithm which takes undulations of the cross-sectional area into account. Furthermore, the results imply a loss of retinal ganglion cell axons in non-glaucomatous subjects as measured in cross-sectional surface area. Due to a small sample size and large variation among individuals, definite conclusions cannot be drawn on typical loss in non-glaucomatous subjects.

CONTROL ID: 3713442

SUBMITTER (NAME ONLY): Tonia Rex

TITLE: Intraocular sustained release of EPO-R76E mitigates glaucoma pathogenesis by activating the NRF2/ARE pathway in a mouse model of glaucoma

SESSION TITLE: Neuroprotection and neuroregeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.S. Rex, J. Backstrom, E. Artis, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|T.S. Rex, S. Naguib, Ophthalmology & Visual Sciences, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|C. DeJulius, C. Duvall, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To optimize delivery of erythropoietin (EPO) as a treatment for optic neuropathies and investigate mechanisms of action.

Methods: We generated a mutant form of EPO, EPO-R76E, that has attenuated erythropoietic activity. Purified EPO-R76E was loaded into either PLGA particles or PPS microspheres, which scavenge reactive oxygen species (ROS) and injected into the vitreous of mice one day after elevation of intraocular pressure (IOP) by intracameral injection of microbeads. Levels of EPO-R76E, ROS, and antioxidant proteins were quantified. EPO-R76E activated signaling pathways and NRF2 phosphorylation were quantified. Activation of the antioxidant response element (ARE) was quantified using a reporter construct delivered to ganglion cell layer neurons by AAV. Visual function was assessed by electroretinogram (ERG) and visual evoked potentials (VEP). Optic nerves were assessed histologically.

Results: Treatment with PLGA-EPO-R76E increased phosphorylation of NRF2, activation of the ARE, and levels of antioxidant proteins. This response occurred 1-week earlier than the endogenous NRF2 activation that we previously detected after IOP elevation. In addition, EPO-R76E activated a different signaling pathway to phosphorylate Nrf2. We found that EPO-R76E activates the MAPK pathway to induce phosphorylation of Nrf2, which is a different pathway than used by the endogenous response. This also resulted in a different pattern of antioxidant protein expression than the endogenous response. Both PLGA-EPO-R76E and PPS-EPO-R76E particles preserved the amplitude of the photopic negative response of the ERG (PhNR), the VEP, and reduced axon degeneration. The empty PLGA particles showed increased axon degeneration and decreased visual function compared to glaucomatous controls. In contrast, the empty PPS particles showed improved visual function compared to glaucomatous controls.

Conclusions: EPO-R76E activates the NRF2/ARE pathway through a different signaling pathway than the endogenous antioxidant response to elevated IOP. A single injection of EPO-R76E loaded particles provided neuroprotection for several weeks. The PPS microsphere mediated delivery of EPO-R76E may be safer and more efficacious than PLGA-mediated delivery.

CONTROL ID: 3713443

SUBMITTER (NAME ONLY): Mary Anne Garner

TITLE: Intraocular pressure, ocular perfusion pressure, retinal perfusion and electrophysiology in brain-dead organ donors

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.A. Fazio, Hamilton Glaucoma Center, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|M. Garner, M. Hubbard, S. Hubbard, A.K. Gross, Department of Neurobiology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|M.A. Fazio, M. Clark, U. Karuppanan, C.A. Girkin, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|S. Hubbard, Science and Technology Honors Program, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: The relationship between intraocular pressure (IOP), ocular perfusion pressure (OPP), retinal perfusion and retinal electrophysiologic responses have been explored previously only in animal models. These studies have demonstrated that elevated IOP reduces OPP and when this exceeds the autoregulatory capacity of the retina vasculature, retinal perfusion and electrophysiologic responses are reduced. This study aimed to evaluate these interactions for the first time in the living human eye.

Methods: Three research-consented brain-dead organ donors, designated AOC039, AOC040, and AOC041, underwent ocular examination with biometry, fundoscopy, optical coherence tomography angiograph (OCTA; Spectralis, Heidelberg Engineering), and electroretinography (ERG, Diagnosys LLC). Prior to organ procurement, the anterior chamber was cannulated and IOP was directly measured and stepwise elevated at 10, 30 and 50 mmHg. Both eyes were evaluated in two donors (AOC040 and AOC041), and only the right eye in AOC039 due to time constraints. Systemic blood pressure was monitored continuously during testing by their life-support equipment. Photopic ERG and photopic negative response and OCTA-based perfused retinal capillary density were evaluated as OPP was reduced.

Results: Reductions in retinal capillary density and inner retinal function defined by OCTA and photopic ERG were observed in three human brain-dead donors associated with elevation in IOP and concomitant reduction in OPP (Table 1). Reductions in a-wave, b-wave, and PhNR amplitudes and latencies appeared to be correlated to OPP. There were more appreciable changes in perfusion and functional responses in eyes with lower systemic blood pressure (Figure 1).

Conclusions: In the living human eye, retinal perfusion and inner retinal function is acutely impacted by elevation of IOP, and this impact appears related to systemic BP and OPP. This novel approach will provide a viable model to study the autoregulatory responses to IOP elevation in the living human eye.

CONTROL ID: 3713444

SUBMITTER (NAME ONLY): Divya Rao Parthasarathy

TITLE: Performance of an Automated, Deep Learning-Based Tool to Screen for Age-Related Macular Degeneration (AMD)

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Rao Parthasarathy, J. Toh, F. Savoy, Remidio Innovative Solutions Pvt Ltd, Bangalore, INDIA|

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ABSTRACT BODY:

Purpose: AMD is one of the leading causes of blindness in the world. We developed and assessed an automated screening tool for AMD using deep learning (DL) on color fundus images. The model is deployable on-the-edge on the target device, a smartphone based portable fundus camera.

Methods: We trained an AI binary classifier in two steps. We used two distinct datasets with macula centered images: 108,251 images (55% referable AMD) from the Age-related Eye Disease Study (AREDS), and 598 images (26% referable AMD) captured on Asian eyes using the target device. The model was trained to indicate the presence of referable AMD (intermediate and advanced AMD). We first trained a base model using AREDS only, with a validation set (A) of 990 images (45% referable AMD). We then finetuned this model using the target device dataset only. The finetuning validation set (B) comprised 334 images (34% referable AMD) and test set comprised 332 images (33% referable AMD), both from target device. The reference standard for AMD diagnosis on the AREDS dataset was fundus image grading by a central reading center. On the target dataset, it was the consensus image grading of two vitreo-retinal specialists

Results: The DL algorithm had sensitivity of 94.7% (95% CI: 88.9% to 98.0%), specificity of 87.7% (95% CI: 82.7% to 91.8%) and AUC of 0.98 (95% CI: 0.95 to 1.00) in detecting referable AMD on the validation set B. On the test set, sensitivity was 86.2% (95% CI: 78.3% to 92.1%), specificity was 88.8% (95% CI: 83.9% to 92.6%) and AUC 0.95 (95% CI: 0.92 to 0.98). The model before finetuning had a validation set (A) sensitivity of 89.7% (95% CI: 86.5% to 92.4%), specificity of 93.6% (95% CI: 91.6% to 95.3%) and AUC of 0.97 (95% CI: 0.96 to 0.98).

Conclusions: The DL algorithm shows promising results, despite the small size of the target device and population dataset. This is made possible by finetuning a model previously trained for the same task on a much larger dataset. The strategy proved helpful despite AREDS being captured by traditional desktop cameras on a different population. This on-the-edge AI deployable on a portable camera has potential to make AMD screening accessible, affordable, and effective.

CONTROL ID: 3713445

SUBMITTER (NAME ONLY): Hounsh Munshi

TITLE: Preliminary Retrospective Validation of a Novel Virtual Reality Visual Field Standard Testing Algorithm, as Compared to Standard Automated Perimetry

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Munshi, K. Da Silva, E. Savatovsky, E. Bitrian, A.L. Grajewski, T.C. Chang, Ophthalmology, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual field testing is a pillar of glaucoma diagnosis and management, though it requires an in-person patient visit, a designated space, and a skilled technician to administer the test. This study aims to compare a portable VRVF device utilizing a novel algorithm based on relevant physiological retinal nerve bundles to the SITA Standard algorithm used in Standard Automated Perimetry (SAP).

Methods: A retrospective chart review of glaucoma patients seen at a tertiary care clinic between March and July 2021 was conducted. Eligible patients had a VRVF (24-2, Size III) using the VRVF Standard algorithm, and at least 2 previous SAPs (24-2, Size III) using SITA Standard, taken within 4 years of the most recent visit, with good reliability (<30% false positives, false negatives, and fixation losses) on both VRVF and SAP. The mean light sensitivity threshold values from the first eye tested for each patient were compared between the 2 algorithms using an intraclass correlation analysis (ICC) and a Bland-Altman plot.

Results: From the 40 patients identified, 10 were excluded due to poor reliability, or inconsistent stimulus size or testing strategy. Of the remaining 30 patients, an ICC of 0.89 (95 % CI = 0.79 – 0.95; $p < 0.0001$) was calculated from the respective mean sensitivities of the VRVF Standard and the SITA Standard algorithms. A Bland-Altman plot revealed a mean difference of 0.27±3.36, with upper and lower limits of agreement of 6.87 and -6.33, respectively.

Conclusions: ICC showed excellent agreement between VRVF Standard and SITA Standard algorithms, suggesting that this novel algorithm is a promising tool in perimetric testing in glaucoma patients. Although the Bland-Altman plot showed wide limits of agreement, the data was normally distributed around a low mean difference, reflecting the accepted variability of visual field testing. VRVF Standard detects mean sensitivities with significant correlation to SAP SITA Standard and may accurately be used as an alternative to SAP for visual field testing in glaucoma patients.

CONTROL ID: 3713446

SUBMITTER (NAME ONLY): Brett Trombley

TITLE: Ranibizumab and Regulation of Vascular Endothelial Cell Growth Factor Family Members in Patients with Diabetic Macular Edema

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ranibizumab is a well-established treatment for diabetic patients with macular edema. However, very little is known about the effect of ranibizumab on regulation of VEGF (vascular endothelial cell growth factor) family members by pro- and anti-inflammatory signaling pathways, which was the aim of this study.

Methods: Diabetic patients (n=10) aged 18 years with central diabetic macular edema, BCVA >24 and <78, and central macular thickness (CMT) greater than 250 mm were enrolled in this study (ML39638). Following a full eye exam, imaging, and an aqueous tab, patients received ranibizumab (0.3mg/0.05mL) injections at day one and weeks four and eight. At week 12, a full eye exam, imaging, and a second aqueous tab was obtained prior to the last injection of ranibizumab. Pre- and post-treatment aqueous humor samples were then analyzed using Milliplex MAP magnetic bead assays.

Results: As expected, ranibizumab lowered levels of VEGF-A, decreased CMT (central macular thickness), and improved VA (visual acuity). Ranibizumab – induced changes in levels of VEGF-A and VEGF-C strongly correlated with changes in soluble receptors, sgp130 and sIL-6R, which are associated with IL-6 signaling. In contrast, changes in VEGF-D correlated with sIL-1R1 and sIL-1R2, soluble receptors participating in IL-1 signaling. Changes in CMT and VA did not correlate with changes in levels of VEGF family members. However, following ranibizumab treatment for 3 months, post-treatment values of CMT correlated with post-treatment levels of VEGF-C. Post-treatment VA values correlated with a wide variety of potential biomarkers linked to inflammation.

Conclusions: Ranibizumab treatment affected production of individual VEGF family members and altered specific pro-inflammatory signaling pathways that are seemingly linked to these differing VEGFs. Thus, new drug development focusing on targeting specific VEGF family members or, alternatively, the pro-inflammatory pathways connected to these family members could improve treatment of patients with diabetic macular edema and/or allow for a more personalized treatment approach.

CONTROL ID: 3713447

SUBMITTER (NAME ONLY): Giles Hamilton-Fletcher

TITLE: NORDIC de-noising expands brain activation areas while preserving retinotopic organization in functional MRI

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Improving the temporal signal-to-noise ratio (tSNR) of functional magnetic resonance imaging (fMRI) data helps identify task-relevant signals. 'NOise Reduction with Distribution Corrected' (NORDIC) principal component analysis (PMID: 34462435) suppresses thermal noise, showing benefits when analyzing block-based or event-related fMRI designs across visual and auditory modalities. However, it is not known if the more precise spatiotemporal signals required for retinotopic mapping are preserved. Here, we evaluate the effects of NORDIC pre-processing on tSNR as well as retinotopic cluster sizes and cortical organization at equivalent R-thresholds.

Methods: Healthy sighted subjects (n=7) had T1-weighted anatomical and T2*-weighted functional scans (voxel size=2x2x3.24mm^3, repetition time=2000ms, echo time=26ms) over bilateral visual cortices using a 3-Tesla MRI scanner. Subjects were visually presented checkerboard rings (expanding, or contracting) or wedges (rotating clockwise, or counterclockwise). Each image was shown for 2000ms, across 16 positions, with 8 repetitions, and 4 runs, taking 17 min 4 s overall (Fig. 1a). tSNR (mean of 'voxel mean÷SD') was measured on the fMRI data with or without NORDIC pre-processing, and retinotopy was computed using population receptive field mapping (pRF) with BrainVoyager.

Results: With NORDIC pre-processing, the retinotopic maps appeared to show similar cortical delineation points to standard pre-processing without NORDIC, however, NORDIC also expanded brain activation areas at the same correlation threshold of R>0.2 (Fig. 1b). Quantitatively, functional volume tSNR was significantly increased by NORDIC pre-processing [$t(6)=7.784$, $p=.000237$, $d=3.75$] (Fig. 2a). Similarly, the largest cluster sizes (LCS) of activated brain regions surviving at R>0.2 correlation thresholds increased in both hemispheres with NORDIC pre-processing [$t(13)=5.960$, $p=.000047$, $d=1.59$] (Fig. 2b-d). A regression analysis revealed that LCS increased alongside tSNR [$F(1,12)=11.95$, $p=.0048$, $r^2= 0.4989$] (Fig. 2e).

Conclusions: We show that NORDIC pre-processing increases tSNR and cluster sizes while preserving their retinotopy. This suggests NORDIC retains the spatiotemporal precision in fMRI data required for pRF and improves the detection of activated brain areas. Overall, NORDIC may serve as an important pre-processing technique for topographical mapping in fMRI.

CONTROL ID: 3713453

SUBMITTER (NAME ONLY): Yun Li

TITLE: Deep learning (DL) to segment retinal layer disruption on optical coherence tomography (OCT) in neovascular age-related macular degeneration (nAMD)

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, H. Lu, T. Albrecht, A. Maunz, A. Neubert, F. Benmansour, A. Gomariz, F. Hoffmann-La Roche Ltd., Basel, SWITZERLAND|J. Luu, D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accurate segmentation of retinal layers offers a wealth of information to clinicians and scientists in terms of diagnostic and predictive biomarkers. Disruption of certain retinal layers is key to determining visual outcomes for patients with nAMD. Accurate quantification of such features remains a time-consuming task for retinal specialists and is challenging to automate. This work proposes an effective DL solution to segment the external limiting membrane (ELM) and ellipsoid zone (EZ) with and without disruptions on OCT scans in eyes with nAMD.

Methods: Our dataset contains OCT images acquired with Cirrus HD-OCT (Carl Zeiss Meditec) from patients enrolled in the HARBOR clinical trial (NCT00891735). Manual annotations denoting ELM, EZ, retinal pigment epithelium (RPE), and Bruch's membrane (BM) as layer boundary elevation maps were performed on a subset of the dataset (989 B-scans from 170 patients).

A DL model with UNet architecture is trained on 90% of the dataset using generalized Dice loss. Schematic of the end-to-end pipeline is shown in Figure 1. Performance is validated on the test set (10% of dataset) with (1) Chamfer distance (CD) for measuring distance in layer boundary between the ground truth and segmented result, (2) layer Dice coefficients of retinal layers using argmax of the segmented output, and (3) 1-dimensional (1D) disruption Dice coefficients for measuring overlap of the linearized layer disruption area between the ground truth and segmentation results. An example of how 1D disruption Dice score is calculated on a single B-scan is shown in Figure 2. Results are reported in mean ± SD.

Results: Evaluated on the test set, model performances to segment ELM and EZ, respectively, are as follows: CD, 17.67 ± 13.22, 13.00 ± 9.35; layer Dice coefficient, 0.56 ± 0.16, 0.60 ± 0.15; 1D disruption Dice coefficient, 0.62 ± 0.38, 0.62 ± 0.37.

Conclusions: Our proposed end-to-end DL solution segments disruptions in the ELM and EZ with reasonable accuracy. This provides clinicians and scientists with an automated tool to quickly generate layer disruption features, which may benefit patient management. The proposed 1D disruption Dice score presents a metric designed to capture the model’s ability to accurately predict retinal layers with disruption.

CONTROL ID: 3713455

SUBMITTER (NAME ONLY): David Dyer

TITLE: Three Year Outcomes from the PALADIN Phase IV Study: Distribution of Intraocular Pressure Outcomes by Patient Subgroup

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Dyer, Alimera Sciences Inc, Alpharetta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: David Dyer: Commercial Relationship(s);Code E (Employment):Alimera Sciences

ABSTRACT BODY:

Purpose: As a class effect, corticosteroids can increase intraocular pressure in some patients, but few studies have looked at long term outcomes due to the short lifespan of most treatment options. However, the 0.19 mg fluocinolone acetonide (FAc) implant US FDA label mandated steroid challenge is designed to mitigate the risk of uncontrolled IOP. Here, we report the IOP outcomes of the PALADIN phase IV study, including mean IOP and time to IOP elevation, in the 36 months post-FAc treatment to determine the impact of the 0.19 mg FAc implant on IOP and functional outcomes within this population.

Methods: Full analysis population includes 202 eyes from 159 patients enrolled with CI-DME that received FAc and were followed for up to 36 months. Eyes were followed at day 1, day 7, month 2, and quarterly from month 3 up to month 36. IOP and best corrected visual acuity (BCVA) were reported at each visit and used to determine outcomes post-FAc.

Results: In the full population, most eyes had a mean IOP of ≤ 25 mmHg in the 36 months post-FAc which was similar to that of pre-FAc baseline values (96.6%=post-FAc; 99.0%=baseline). A breakdown of the population showed subtle changes in the frequency distribution that was not dramatically affected over the 36 months post-FAc. For those eyes that experienced an IOP elevation > 25 mmHg, > 30 mmHg, or were prescribed IOP lowering medications, median time to these events were 9.1, 13.7, and 11.8 months respectively. To determine which eyes may be more susceptible to IOP events post-FAc, subgroups were created and the incidence of IOP events were compared to the full population. Eyes with the no additional treatment post-FAc and baseline BCVA ≤ 20/40 were all associated with less incidence of IOP events compared to the full population. Finally, BCVA was not significantly impacted in the eyes experiencing an IOP elevation >30 mmHg or requiring IOP lowering therapy.

Conclusions: In the 36 months post-FAc, the IOP distribution was marginally affected with over 96% of eyes showing a mean IOP ≤ 25 mmHg at any study visit. In eyes who had an IOP elevation > 30 mmHg or required IOP lowering therapy, these events did not affect long term vision when compared to baseline. Finally, a lower incidence of IOP events post-FAc were noted in the eyes with better vision and fewer additional treatments.

CONTROL ID: 3713457

SUBMITTER (NAME ONLY): Matias Soifer

TITLE: Epidemiology Of Herpes Zoster Ophthalmicus in context of the SARS-CoV2 (COVID) pandemic

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Soifer, A.A. Jammal, H.M. Mousa, A.J. Snyder, V.L. Perez, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The incidence of herpes zoster ophthalmicus (HZO) may be increasing, however the impact of the SARS-CoV2 pandemic (COVID) on HZO epidemiology is unclear. This study seeks to determine the variation in the incidence of HZO over the past 6 years with a special focus on its correlation with overall systemic herpes zoster (SHZ) incidence and HZO monthly and seasonal changes before and after the onset of COVID.

Methods: This is a hospital-based epidemiology study of patients attending Duke University Hospital System (DUHS) between 01/2016 and 10/2021 via Duke Enterprise Data Unified Content Explorer (DEDUCE) data with corresponding ICD codes for HZO and SHZ diagnosis. The analysis calculated monthly incidence of novel consults of HZO and SHZ with emphasis on demographics, seasonal variation, and the changes in rates with the COVID pandemic (estimated to impact DUHS population starting in 03/2020).

Results: 24896 patients presented with SHZ at DUHS in the study period, of whom 2921 (11.7%) suffered from HZO. The mean age at the incident episode of HZO was 62.8±15.6 years. Most patients were white (78%), female (63.5%), above 50 years old (79.5%) and non-smokers (61.5%). Over the study period SHZ experienced an overall decline in its incidence, however HZO incident cases have been slightly increasing with a mean of 37/month in 2016, 47/month in 2019, and 50/month in 2021. The ratio of monthly incidence HZO/SHZ demonstrates a steady increase from an annual 9% in 2016 to 13.4% in 2019 and 15.5% in 2021. Interestingly, HZO annual peak incidence steadily emerged in the months of November and February throughout all the years. Since COVID onset, the mean monthly incidence of SHZ decreased significantly (373.1 +/- 35 vs 312.1 ± 28, $p<0.0001$). However, the mean monthly incidence of HZO exhibited a statistically significant increase (39.5 ± 10 vs 46.7 ± 16; $p=0.025$). Likewise, the trendlines of HZO/SHZ exhibited a significant increase since COVID (10.6% ± 4.6 to 15.1% ± 2.7; $p<0.0001$).

Conclusions: These study findings point that HZO incidence may be increasing, despite an overall lower SHZ incidence, which may suggest a distinct mechanism for HZO appearance despite vaccination efforts. A specific seasonal variation with winter peaks was observed, which should guide physicians towards early recognition of HZO. COVID, directly or indirectly, may have accelerated the already increasing HZO incidence.

CONTROL ID: 3713459

SUBMITTER (NAME ONLY): James Randleman

TITLE: Comparative Localized Corneal Biomechanical Changes Following Laser Vision Correction Using Brillouin Microscopy

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.B. Randleman, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: James Randleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To identify and compare focal in vivo changes in corneal biomechanical properties after PRK, LASIK, and SMILE using Brillouin microscopy.

Methods: Ongoing prospective, cross-sectional study comparing Brillouin scan data from patients with normal corneas as determined by routine clinical evaluation before and after undergoing PRK, LASIK, or SMILE. The primary endpoint was regional change in Brillouin longitudinal modulus after surgery.

Results: All eyes having PRK, LASIK, and SMILE showed relatively uniform Brillouin modulus preoperatively across the central 6mm of their corneas. All normal corneas had slightly lower Brillouin modulus centrally of 20-50MHz. Following laser vision correction by all three methods, central longitudinal modulus decreased by 30-50 MHz, while there were no significant changes in peripheral modulus. There were no significant differences between procedure centrally or peripherally.

Conclusions: Brillouin microscopy was able to successfully identify a focal reduction in corneal stiffness for all three laser vision correction procedures and thereby provide novel highly specific localized corneal biomechanical data in vivo.

CONTROL ID: 3713461

SUBMITTER (NAME ONLY): Tolulope Fashina

TITLE: Ophthalmic Imaging and Impression Cytology Findings in the Child Health and Mortality Prevention Surveillance (CHAMPS) Network

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kuthyar, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|D. Blau, Centers for Disease Control and Prevention, Atlanta, Georgia, UNITED STATES|M. Garel, Emory University Emory Global Health Institute, Atlanta, Georgia, UNITED STATES|R. Oliech, J. Agaya, K. Otieno, V. Akelo, Kenya Medical Research Institute, Nairobi, KENYA|P. Rao, Retina and Vitreous of Texas, Texas, UNITED STATES|H.E. Grossniklaus, S. Yeh, Emory Eye Center, Atlanta, Georgia, UNITED STATES|R. Breiman, Global Health, Emory University School of Public Health, Atlanta, Georgia, UNITED STATES|J. Shantha, Francis I. Proctor Foundation for Ophthalmic Research, University of California San Francisco, California, UNITED STATES|J. Mwanza, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|T. Fashina, A. Huachun, S. Yeh, University of Nebraska Stanley M Truhlsen Eye Institute, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Under-five mortality (U5M) rate is disproportionately high in Sub-Saharan Africa. Prior studies have revealed an association between childhood blindness and U5M. Employing CHAMPS procedures which includes postmortem minimally invasive tissue sampling and testing, we studied the feasibility for eyes to provide supportive diagnostic information for determining etiologies of U5M.

Methods: Prospective assessment of the feasibility of photography and tissue sampling of postmortem eyes for identifying disease patterns correlating with ophthalmic disease and causes of U5M. Randomly selected cases of stillbirth and under-5 death from Kenya were enrolled. External, anterior, and posterior segment images were obtained with a portable camera, graded by 2 independent ophthalmologists, and adjudicated by a third ophthalmologist. Intra-class correlation coefficients (ICC) were calculated to determine the inter-rater reliability (IRR) of the grading scheme. Conjunctival specimens were obtained for impression cytology and molecular PCR detection of pathogens.

Results: Of 71 subjects (142 eyes) that underwent ophthalmic photography and standardized grading, external photos predominantly showed periorbital edema (16%), skin mottling (14%), ecchymosis (13%), and periorbital erythema (11%). Anterior segment findings were predominantly conjunctival injection (30%), corneal opacity (23%), and conjunctival icterus (16%). Posterior segment findings were predominantly macular whitening (51%), retinal fold (34%), and optic nerve pallor (9%). The ICC for posterior segment findings was 0.68, indicating moderate IRR. The ICC for external and anterior segment findings were < 0.50, indicating poor IRR for both measures.

Of 50 subjects (100 eyes) in which impression cytology was performed, goblet cells (78%), mucin spots (24%) and squamous metaplasia (5%) were observed. Other findings were acute inflammatory cells (4%), viral inclusions (4%), bacteria morphologies (7%), and fungal elements (3%).

Conclusions: In the postmortem assessment of causes of U5M, an ophthalmic surveillance protocol was implemented and feasible with moderate IRR for posterior segment findings on photography and gradable impression cytology specimens in most eyes assessed. Further studies of these diagnostics in relation to time-of-death may provide further

insight into whether ocular findings may contribute to causes of U5M.

CONTROL ID: 3713462

SUBMITTER (NAME ONLY): Oleg Alekseev

TITLE: Retinal and optic nerve inflammatory findings are a common feature in patients with USH2A-associated retinal degeneration

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Alekseev, E. Krauss, M. Kedrov, A. Iannaccone, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|G. Adamus, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the characteristics of inflammatory findings in patients with USH2A-associated retinal degeneration.

Methods: We retrospectively identified 75 subjects (M=38/F=37, age 4-84) with confirmed disease-causing USH2A gene mutations, all of whom had a complete eye exam, including visual acuity (VA), visual fields (VFs), full field electroretinograms, macular (n=75) and optic nerve (n=40) spectral domain optical coherence tomography (SD-OCT), fluorescein angiography (FA) (n=31), and CLIA-certified testing (n=35) for circulating auto-antibodies (AAbs) against retinal and/or retrobulbar optic nerve (ON) antigens by immunoblot, Western blot, and retinal immunohistochemistry (IHC).

Results: Of the 62 tested eyes with FA, 38 eyes had leakage of optic nerve head, vascular arcades, macula, or a combination thereof. The nerve fiber layer (NFL) was thickened on SD-OCT, most often sectorally, in 49 of 80 eyes, and correlated well with FA leakage, helping explain disproportionate VA losses compared to foveal SD-OCT findings. Cystoid macular edema (CME) was seen by SD-OCT in 47 of 150 eyes. Anti-retinal AAbs were found in 32 of the 35 tested patients [most often against carbonic anhydrase II (16/35) and enolase (15/35)]. AAbs recognizing anti-ON antigens were found in 28 of 34 tested patients. Retinal IHC showed positive staining in 28 of 34 cases, labeling predominantly photoreceptors (26/34) and less frequently ganglion cells (GC=11/34) and NFL (8/34). Altogether, 66.7% (50/75) of patients exhibited clinical signs of inflammation, which correlated directly with the presence of circulating AAbs in 25 of them. These patients received intravitreal and/or sub-Tenon steroid injections, with both subjective and measurable increase in vision (VA, VF, or both), associated with improved OCT and FA characteristics in most cases.

Conclusions: Secondary autoimmunity (affecting optic nerve, NFL, and/or GC) and clinical inflammation involving retina and/or optic disc appear to be common yet underdiagnosed features of USH2A-associated retinal degeneration. Clinical inflammatory manifestations that can be readily detected with macular OCT, disc OCT, and FA affected 2/3 of the patients. Clinical suspicion can be further confirmed by AAb/IHC testing. Identification of these complications is clinically and prognostically important, as meaningful vision improvements can be achieved with treatment.

CONTROL ID: 3713463

SUBMITTER (NAME ONLY): Katarzyna Malendowicz

TITLE: Progression of flecks in pediatric patients with ABCA4-related Stargardt disease

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Malendowicz, H. De Bruyn, J. Akula, A.B. Fulton, Opthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|J. Akula, A.B. Fulton, Harvard Medical School, Boston, Massachusetts, UNITED STATES|I. Mihalek, Department of Molecular Medicine and Biotechnology, Sveuciliste u Rijeci, Rijeka, CROATIA|

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ABSTRACT BODY:

Purpose: To describe the progression of flecks temporal to the fovea in young patients with ABCA4-related Stargardt disease.

Methods: From a total of 44 patients, aged 4.7–19 (median 11. 9) years at first visit, having confirmed biallelic pathogenic variants in ABCA4 and serial autofluorescent (AF) Optos imaging, we selected green laser (532 nm) optomap images of 10 eyes from 5 patients to demonstrate the progression of ABCA4-related Stargardt's (STDG1) by genotype. We selected these patients because their genotypes could be sorted according to the putative residual functionality of the combined alleles based on biochemical characterizations available in the literature. We analyzed the AF images using ImageJ. In the analyses, we set the distance between the center of the fovea and the center of the optic nerve, in each respective image, to unity. We then produced a rectangular region of interest (ROI) of size 1×1.5, with the long sides parallel to the fovea-ONH segment and the nasal short side centered on the fovea (such that the ROI extended into temporal macula). We then used the thresholding tool to identify and quantify (%) bright flecks within the ROI for each image. (Fig. 1A.)

Results: We observed the rise and fall in %AF within the ROI with the age of patient, consistent with the disease progression model described in Cideciyan, et al. (2004). Furthermore, severe genotypes, such as double null, peaked earlier in life than did the milder genotypes (e.g., two semi-functional alleles).

Conclusions: The %AF in the temporal macula is a strong indicator of the stage of STDG1 disease progression in young patients. Both the timing and the peak values of %AF within the ROI are indicative of the severity of the genotype; more severe genotypes produce higher %AF at earlier ages.

CONTROL ID: 3713465

SUBMITTER (NAME ONLY): Adeline Suko

TITLE: Comparing methods for quantifying myosin distributions in the avian crystalline lens

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.T. Suko, V. Choh, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|A. Wong, Systems Design Engineering, University of Waterloo, Waterloo, Ontario, CANADA|A. Wong, Waterloo Artificial Intelligence Institute, University of Waterloo, Waterloo, Ontario, CANADA|

Commercial Relationships Disclosure: Adeline Suko: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Wong: Commercial Relationship: Code N (No Commercial Relationship) | Vivian Choh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Disruption of the actomyosin networks in the chicken lens has been shown to affect lenticular biomechanics. This study compares methods of analyzing and quantifying myosin distributions.

Methods: Lenses from 7-day old white leghorn (Gallus gallus domesticus) chickens were labelled for myosin. Nearest neighbour distances (NNDs) for myosin centroids at the posterior surface were determined using three methods on the same image: 1) ImageJ: manual using the Elliptical tool, 2) ImageJ: automatic using the Analyze Particle tool, 3) MATLAB: automatic using custom-coded software. For analyses using ImageJ, the NND plugin was used. First, the Elliptical tool (manual) on ImageJ was used to determine XY centres of ellipses superimposed on the image by the user. Three ellipses were superimposed on each centroid to account for user error. For the automated ImageJ method, the image was converted to a binary format using the program's Make Binary function. The Fill Holes and Eraser tools in ImageJ were used to correct centroids altered by the thresholding process before determining the myosin centres using the Analyze Particles tool. For analysis in MATLAB, the image was opened and the custom-coded script was run to obtain the myosin centres and NNDs. Corrections were made using MATLAB's Brush tool. The three methods of calculating NNDs from the same 135 centroids were compared (repeated measures ANOVA).

Results: The Analyze Particles tool detected the fewest centroids (135) compared to the Elliptical (166) and MATLAB methods (163). Although the elliptical tool allowed for greater detection, the ellipses do not always fit properly, possibly leading to inaccurate NND values. The MATLAB program uses adaptive thresholding to consider variations in illumination, allowing it to detect more centroids with fewer detection errors than the Analyze Particles tool. Ranges and mean NNDs (±SD) for the same 135 centroids are listed in Table 1; no significant differences were found between the three methods (P=0.2754).

Conclusions: The custom MATLAB program is the choice method for mapping out the proten network using confocal images. It is automated, reducing user error compared to the manual elliptical tool. It also recognized more centroids than the ImageJ "Analyze Particles" feature with fewer errors. Future work involves actin detection to measure actin-myosin distances.

CONTROL ID: 3713466

SUBMITTER (NAME ONLY): Federica Poli

TITLE: Correlation between fundus autofluorescence pattern and retinal sensitivity measured by microperimetry in patients with choroideremia

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.E. Poli, I.H. Yusuf, J.K. Jolly, L.J. Taylor, D. Adejoyu, A.S. Josan, J. Cehajic Kapetanovic, R.E. MacLaren, University of Oxford Nuffield Laboratory of Ophthalmology, Oxford, Oxfordshire, UNITED KINGDOM|F.E. Poli, I.H. Yusuf, J.K. Jolly, L.J. Taylor, D. Adejoyu, A.S. Josan, J. Cehajic Kapetanovic, R.E. MacLaren, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|L. da Cruz, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Choroideremia is an X-linked inherited retinal degeneration, characterised by loss of the retinal pigment epithelium (RPE) followed by photoreceptor cell death. Fundus autofluorescence (FAF) imaging reveals three distinct RPE patterns in the early stages: smooth, mottled and atrophic appearances (Figure 1). It is not known how structural RPE patterns on FAF relate to retinal function as measured by microperimetry (MP).

Methods: A retrospective review of patients with choroideremia, who had smooth and mottled regions on FAF imaging in both eyes, was performed. These were selected from patients recruited for clinical trial NCT02407678. The smooth and mottled regions on FAF images at baseline were delineated and superimposed on to the MP plots (MAIA, 10-2 grid with 68 points) ensuring alignment of retinal vessels. Eight age and gender-matched controls were used to determine expected normal sensitivity values for each point on the MP plots. These were then used to calculate mean sensitivities for the zones corresponding to smooth and mottled regions in the participants. Mean changes from expected normal values in smooth and mottled regions were compared with a paired t-test.

Results: 30 patients fulfilled the inclusion criteria for the clinical trial (mean age 32.2±8.8 years). Of these, eight had distinct smooth and mottled regions in both eyes (mean age 32.3±9.8 years). The mean MP sensitivities for the smooth and mottled regions were 26.5±3.2 dB and 21.0±4.1 dB, respectively. The mean change from expected values was significantly higher in the mottled compared to the smooth regions (4.6 dB loss versus 1.7 dB loss; 95% confidence interval 1.2 to 4.5; p=0.002). In areas of RPE loss, there was no detectable sensitivity.

Conclusions: This study identifies a correlation between retinal function on MP and structure on FAF imaging in patients with choroideremia. The smooth region is more likely to contain intact ellipsoid zone and preserved photoreceptor anatomy (Stevanovic et al, 2020). There are therefore three RPE patterns seen on FAF imaging in choroideremia: i) an early stage with smooth reflectance which correlates to normal retinal anatomy and similar to normal function; ii) an intermediate ‘mottled’ stage associated with measurably impaired photoreceptor function; and iii) the late stage in which RPE loss is complete and function as assessed with MP is absent.

CONTROL ID: 3713467

SUBMITTER (NAME ONLY): Alessandro Iannaccone

TITLE: Interim Safety Results in Two Phase 1/2 Open-label, Dose-escalation Clinical Trials of Subretinal Gene Therapy with AGTC-401 (rAAV2tYF-PR1.7-hCNGB3) and AGTC-402 (rAAV2tYF-PR1.7-hCNGA3) in Subjects with Achromatopsia (ACHM)

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report on safety of AGTC-401 and AGTC-402, two gene therapies designed to compensate for the most often mutated genes, CNGB3 and CNGA3, in ACHM, a form of autosomal recessive congenital severe cone photoreceptor dysfunction.

Methods: A macular subretinal injection (≤300 µL) of AGTC-401 (CNGB3, n=31) or AGTC-402 (CNGA3, n=24) was performed in a study eye of 55 subjects, 5-69 years old (37 adults, 18 children). Subjects were sequentially assigned to 1 of 5 (CNGA3) or 6 (CNGB3) dose groups spanning from $4.0e^{10}$ to $3.2e^{12}$vg/ml. Safety results were evaluated by reported ocular and non-ocular adverse events (AEs), functional and microanatomical imaging-based outcome measures, and chemistry parameters.

Results: Across both trials, 3 drug-related serious adverse event (SAE) cases were seen in children at the highest dose level [$3.2e^{12}$vg/mL, CNGA3 (N=2) and CNGB3 (N=1)], which was assessed to be a dose-limiting toxicity (DLT) dose level in children. Uveitis and posterior segment changes were seen clinically and by imaging studies in 3 children, one of whom also developed subretinal fluid in the untreated fellow eye. No DLTs were observed at any dose level in adults.

At dose levels below the DLT in adults and children, both drugs had a favorable safety profile and none of the 3 SAEs were deemed drug-related [macular hole related to subretinal surgery (n=1); steroid-induced elevated IOP resolved after glaucoma surgery (n=2)]. Most AEs were Grade 1 or 2 (except one Grade-3 anterior chamber inflammation). All intraocular inflammatory AEs were controlled with oral, intravenous and/or topical steroids. Steroid-related IOP elevations were seen in 24 subjects (47.1%), and were non-serious and controlled with IOP-lowering agents in 22 (91.7%). Immunological T-cell and antibody tests to AAV and genes CNGA3 or CNGB3 were not associated with safety findings.

Conclusions: AGTC-401/AGTC-402 gene therapy to potentially treat ACHM was safe and well-tolerated in children up to and including second highest dose ($1.1e^{12}$vg/mL), and in adults up to and including the highest dose ($3.2e^{12}$ vg/mL), which was assessed to be a DLT level in children due to intraocular inflammation that responded to adjusted steroid regimens. Imaging studies were very important in characterizing the SAEs.

CONTROL ID: 3713468

SUBMITTER (NAME ONLY): Juan Queiruga Piñeiro

TITLE: Confocal microscopy in vivo in patients diagnosed with fibromyalgia

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To examine the innervation of central corneal subbasal nerve plexus in patients with fibromyalgia and compare to normal values of healthy patients.

Methods: A prospective, observational study was conducted analyzing 15 right eyes of 15 patients with fibromyalgia (12 women and 3 males) aged 49.83 ± 12,55 years (range 34 to 70 years). Nineteen eyes of 19 healthy patients (12 women and 7 males) aged 40.26 ± 10.86 years (range 23 to 54 years) was selected as control group. Subjects underwent microscopy confocal in vivo (IVMC) with the Rodstock cornea Module attached to Heildelberg's HRT3. At least 3 images of each eye were selected and the following subbasal central nervous plexus parameters were measured with ACC Metrics software: corneal nerve fiber density (CNFD), corneal nerve branch density (CNBD), corneal nerve fiber length (CNFL), corneal nerve fiber total branch density (CTBD), corneal nerve fiber area (CNFA), corneal nerve fiber width (CNFW), corneal nerve fractal dimension (CNFrD). Data analysis was performed with SPSS® software for Windows 22.0 (SPSS ® Inc, Chicago, IL.). The normality of the sample was checked with the Saphiro Wilk test and the results were compared to the T test or the Man-Whitney U test based on the distribution of the data. The differences were considered statistically significant for $P<0.05$

Results: The mean and standard deviation were CNFD: (13.407 ± 2.027 fibers/mm2) vs (23.353 ± 1.778 fibers/mm2) ($p<0.05$); CNFL: (10.108 ± 1.016 mm/mm2) vs (13.850 ± 0.768 mm/mm2) ($p<0.05$); CNFrD: (1.440 ± 0.174) vs (1.475 ± 0.007) ($p<0.05$). These values were significantly reduced in patients with fibromyalgia compared to control group.

Conclusions: Patients with fibromyalgia show a significant decrease CNFD and CNFL. CNFrD may be a diagnostically able parameter in fibromyalgia patients as has already been observed in peripheral neuropathies.

CONTROL ID: 3713469

SUBMITTER (NAME ONLY): Abed Makhlouf

TITLE: Gliosis in RPE65-associated inherited retinal degeneration

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Makhlouf, W. Su, S. Sun, H. Lin, B. Tian, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal gliosis, characterized by increased numbers and morphology change of glial cells in the retina has been associated with retinal degeneration. As inherited retinal degeneration, RPE65 gene mutation associated Leber Congenital Amaurosis (LCA) leads to early onset blindness. Nevertheless, the role of gliosis has not been clearly elucidated in this disease. We seek to determine the development of reactive gliosis during the retinal degeneration in RPE65 mutant LCA disease model. In addition, the potential role of gene replacement therapy on the retinal gliosis in this retinal degenerative model was also evaluated.

Methods: The rd12 mice, the naturally occurring animal model of LCA with the homozygous point mutation (C>T) in the RPE65 gene served as the disease model. Rd12 mice were treated by delivering the wild type copy of hRPE65 cDNA vectorized by AAV2 into subretinal space at 14 days of age. The untreated control group of rd12 mice was injected with formulation buffer. One month post injection, the retina tissue from treated rd12 mice, untreated rd12 mice and the wild type of C57BL/6 mice at the same age were harvested and immune-stained with antibodies against Glial fibrillary acidic protein (GFAP) to assess the activation of astrocytes and Müller cells.

Results: The GFAP-positive Müller cell end-feet were observed at the ganglion cell layer in untreated rd12 mouse from 1.5 months of age and gradually increased along with age until 5 months. In contrast, density of Müller cell end-feet in the AAV2.hRPE65 treated rd12 mouse showed significantly less by quantification. In addition, astrocyte activation was also evaluated by the number of astrocyte quantitation, exhibiting a significant higher density in untreated rd12 mice than treated counterpart. To be noted, the density of both astrocytes and Müller cell end-feet are significantly higher in treated rd12 than that in wild type C57BL/6 mice.

Conclusions: In the rd12 mouse, the degenerated photoreceptors and RPE cells elicits activation of astrocytes and Müller cell, associated with reactive gliosis. The therapy of gene replacement alleviates gliosis observed in rd12 mice. Here, we present an evaluation of reactive gliosis in LCA model. An expanded understanding of the features of gliosis in other inherited retinal degeneration or retinal injury will advance the therapeutic strategies to prevent the formation of the glial scar during the development of retinal degeneration.

CONTROL ID: 3713470
SUBMITTER (NAME ONLY): Yin-Hsi Chang
TITLE: Photoreceptor Manifestations of Primary Mitochondrial Optic Nerve Disorders
SESSION TITLE: Retinal Degeneration
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: Y. Chang, Y. Kang, L. Yeh, K. Chen, W. Wu, L. Liu, Department of Ophthalmology, Chang Gung Medical Foundation, Taoyuan, TAIWAN|P. Liu, S. Levi, H. Wang, N. Wang, Department of Ophthalmology, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|Y. Tseng, G. Seo, H. Lee, Division of Medical genetics, 3billion Inc., KOREA (THE REPUBLIC OF)|C. Lai, Chang Gung Memorial Hospital Keelung Branch Library, Keelung, TAIWAN|
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ABSTRACT BODY:
Purpose: To compare the photoreceptors' (PRs) manifestations in three hereditary optic neuropathies affected by primary mitochondrial dysfunction and discuss whether the retinal ganglion cells (RGCs) or the PRs are preferentially affected.
Methods: A retrospective analysis of patients with genetically-confirmed diagnoses of optic neuropathies associated with mitochondrial dysfunction was performed. This cohort included Leber's hereditary optic neuropathy (LHON), autosomal dominant optic atrophy type 1 (OPA1), and optic atrophy type 13 (OPA13). Patient chart evaluation included clinical characteristics, best-corrected visual acuity (BCVA), fundus photography, spectral domain-optical coherence tomography (SD-OCT), electroretinogram (ERG), and visual evoked potential (VEP) data.
Results: A total of 7 patients with LHON, 6 with OPA1 and 1 with OPA13 were included from a tertiary medical center. Thirteen of 14 individuals were male. The average BCVA at diagnosis was 20/285 and 20/500 in the right and left eyes, respectively. Five out of 7 patients with LHON, and 3 out of 6 patients with OPA1 also showed a mild amplitude reduction or delayed latency on light-adapted ERG and 30Hz flicker responses; however, SD-OCT imaging did not show correlated PR abnormalities. Notably, a 7-year follow up of a patient with OPA13 revealed degeneration of RGCs prior to the degeneration of PRs. Follow-up data also demonstrated continuous loss of cone outer segment tips on SD-OCT imaging.
Conclusions: RGCs are, in general, affected by mitochondrial dysfunction, whereas variable PR dysfunction exists in patients with LHON and OPA1, especially with respect to the cone responses. Involvement of PRs are particularly evident in OPA13 after RGC degenerations.

CONTROL ID: 3713472

SUBMITTER (NAME ONLY): Sharon DSouza

TITLE: Host factors related to SARS-CoV2 infection in the human eye and prophylaxis thereof

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. DSouza, V. Suresh Babu, T. Panigrahi, S. Sethu, A. Ghosh, Narayana Nethralaya Foundation, Bangalore, INDIA|R. Shetty, P. Khamar, P. B, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: To analyse the expression of human host cell specific attachment, entry and anti-viral response genes to SARS-CoV-2 in various layers of human eyes. To investigate if such host factors may be modulated by eye drops for prophylaxis.

Methods: Donor eyes from healthy controls(n=5), COVID-19 infected(n=5) and COVID-19 recovered(n=2) were studied by immunofluorescence or dissected and analysed for gene expression. Expression of ACE2, TMPRSS2, CTSL, MxA, type-1, 2 and 3 IFNs(interferons) were assessed. Ocular surface impression cytology(IC) and nasal swabs from controls(n=12) before and after trehalose eye drops; and IC from dry eye disease(DED) patients(n=7) and controls(n=8) obtained during pre-pandemic period was used to for gene expression analysis.

Results: Gene expression and immunofluorescence revealed significantly higher distribution of ACE2, TMPRSS2, CTSL and antiviral interferon in ocular surface layers compared to retinal and other layers. Increased ocular surface expression of ACE2 and TMPRSS2; along with decreased expression of type-1 IFNs(IFNalpha) was observed in COVID-19 infected eyes compared to healthy donors and COVID-19 recovered eyes. Similar host factor expression profile was observed from IC of pre-pandemic DED patients. Prophylactic use of trehalose eye drops significantly enhanced Type-1 IFN while reducing ACE2 in ocular surface and nasolacrimal ducts of volunteers which may possibly halt the entry & transmission of COVID-19 through ocular portals.

Conclusions: Consistent expression of ACE2, TMPRSS2 and CTSL were observed in ocular surface tissues highlighting potential for SARS-CoV-2 adhesion & transmission. Pharmacological induction of IFNα-mediated antiviral MxA can possibly protect the ocular surface and nasolacrimal duct from respiratory viral infections.

CONTROL ID: 3713473

SUBMITTER (NAME ONLY): Printha Wijesinghe

TITLE: Can tear fluids' microRNAs predict molecular changes associated with age-related macular degeneration (AMD) at an early stage?

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Wijesinghe, J. Xi, J.Z. Cui, J.A. Matsubara, Ophthalmology & Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: MicroRNAs (miRNAs) are small, non-coding RNAs which comprise a large family of post-transcriptional regulators of gene expression. Several miRNAs (miR-146a, -125b, and -34a) have been associated in the pathogenesis of age-related macular degeneration (AMD). Here, we tested 10 selected candidate miRNAs in tear fluids, eye tissues and 5 different brain regions (neocortex-hippocampus, olfactory bulb, striatum-thalamus-hypothalamus, brainstem, and cerebellum) of a transgenic AMD mouse model and its matched control to see the miRNA expression levels and their direction of regulation over time.

Methods: High-fat diet apolipoprotein E knockout ($ApoE^{-/-}$) and wildtype (WT, C57BL/6J) female mice (n=16, 4 per group) were studied at young, 3-4 months and old, 9-10 months. Expression level of mature miRNAs -101a-3p, -125b-5p, -140-3p, -146a-5p, -15a-5p, 34a-5p, -342-3p, -374c-5p, -302c-3p and -653-5p were determined using TaqMan advanced miRNA assays. Cycle threshold (Ct) values normalized to Cel-miR-39-3p were compared between young $ApoE^{-/-}$ vs. WT and between old $ApoE^{-/-}$ vs. WT mice separately for tear fluids, eye tissues and brain regions. A statistically significant (2-tailed Welch's t-test at a Bonferroni corrected $P < 0.01$) intergroup >2-fold difference was used to determine the differentially expressed miRNAs.

Results: 8 miRNAs were detected at Ct <35.0. miR-146a, a proinflammatory marker was significantly upregulated in the tears of both young (7.8-fold) and old (5.8-fold) $ApoE^{-/-}$ mice compared to its age-matched WT control. miRNAs -34a, -15a and -342 were also significantly upregulated in the tears of old $ApoE^{-/-}$ mice. Between young $ApoE^{-/-}$ vs. WT eyes, miR-374c (2.7-fold), and between old $ApoE^{-/-}$ vs. WT eyes, miR-146a (6.5-fold), -125b (4.1-fold) and -374c (3.6-fold) were significantly upregulated. Regarding different brain regions, all tested miRNAs were significantly downregulated or insignificant in young $ApoE^{-/-}$ mice. In contrast, most of the tested miRNAs were significantly upregulated in old $ApoE^{-/-}$ mice. Notably, miR-146a was upregulated by 62.4, 41, and 32.7 folds in neocortex-hippocampus, olfactory bulb and brainstem, respectively.

Conclusions: Our study has demonstrated the translational potential of tear fluids' miRNAs in a transgenic early stage AMD model and with changes over time. Detailed interpretation and significance of the results will be discussed.

CONTROL ID: 3713474

SUBMITTER (NAME ONLY): Denise Loya-Garcia

TITLE: Analysis of engineered corneal endothelium transplanted in an in vivo model

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Loya-Garcia, J.E. Valdez, Ophthalmology and Visual Sciences Institute, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|D. Loya-Garcia, J. Zavala, M.D. Montalvo-Parra, A. Bustamante-Arias, S. Garza, M. Salan, S. Guevara-Quintanilla, M. Hernandez, J.E. Valdez, School of Medicine and Health Sciences, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: CECs cultured in a two-step approach proliferate and retain hexagonality and molecular markers over a vitrified collagen membrane (VCM) produced in a customizable method. In this work, we aimed to analyze the CECs/VCM construct obtained from transplanted corneas of old White New Zealand rabbits

Methods: Five 18 month-old White New Zealand rabbits were used in accordance with ARVO guidelines and the approval of the Institutional Committee. CECs/VCM constructs of 8mm2 with a 30% cell confluence were produced to determine the ability of CECs to proliferate in vivo. Five male New Zealand rabbits 20 months-old were used. Under general and topical anesthesia a paracentesis was made and an anterior chamber maintainer was introduced, descemethorexis was performed and transplantation of the CECs/VCM constructs was done in 5 eyes. Three eyes were transplanted using only VCM. The transplanted eyes were photo-documented daily for 90 days. The corneas were excised and analyzed for ATPase-1 and ZO-1 molecular markers and CECs confluency evaluation by confocal microscopy and light microscopy

Results: Transplanted corneas with CECs/VCM construct showed transparency beginning in the periphery of the engineered tissue after 3 weeks, albeit central corneal opacity remained. Confocal microscopy showed hexagonal CECs positive to ATPase and ZO-1 mainly in the periphery of VCM and fibrosis was observed with light microscopy in the central cornea, which correlates with the central opacity. Eyes transplanted with VCM showed total corneal opacity, edema and neovascularization after 7 days of transplantation that persisted throughout the follow-up. Confocal microscopy showed no CECs over the VCM, and light microscopy showed fibrosis

Conclusions: Thirty percent confluent CECs/VMC construct partially restore corneal transparency in a preclinical model. However, the fibrotic process might be faster than the healing rate of CECs with 30% confluence, thus preventing full corneal transparency restoration. Increasing cell confluence could potentially be necessary to improve corneal healing.

CONTROL ID: 3713478

SUBMITTER (NAME ONLY): Christina Nicou

TITLE: Characterization of transient and sustained intraocular pressure fluctuations in rats

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.M. Nicou, C.L. Passaglia, Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|

Commercial Relationships Disclosure: Christina Nicou: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Passaglia: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although elevated intraocular pressure (IOP) is a major risk factor for glaucoma, little is known about IOP dynamics on different time scales. Most researchers use tonometry to estimate IOP, which gives only pressure snapshots and was shown to induce a stress response in rats. This study sought to characterize the duration, magnitude, and mechanical energy associated with transient and sustained IOP fluctuations in rats.

Methods: Brown-Norway rats underwent an anterior segment cannulation to record IOP from a wireless backpack pressure transducer. Animals were housed in normal light/dark cycle and IOP was sampled at 0.25 Hz for weeks to months. IOP data was mean filtered and analyzed with a peak detection algorithm in MATLAB to characterize transient IOP fluctuations. Sustained IOP fluctuations were determined by interpolating the local minima between peaks. The IOP-related mechanical energy that the eye experiences over time was found by multiplying the area under the transient or sustained curves by the average eye conductance. IOP data was mean-normalized and subjected to a 1-hr statistical analysis to determine daily IOP trends.

Results: Continuous IOP data collected for 246 days in total across 37 animals were analyzed. Based on autocorrelation analysis, transient events were defined as peaks occurring at least 2 minutes apart with a 1 mmHg minimum prominence. There were approximately 219 transients per day that lasted seconds to minutes with magnitudes up to 60 mmHg. The IOP-related mechanical energy associated with transient events was 77 ± 34 mJ/day as compared to 312 ± 345 mJ/day for slow sustained fluctuations in mean IOP. Much of the sustained energy is attributed to the circadian IOP rhythm. The mechanical energy of mean IOP alone was 3455 ± 2303 mJ/day. Distributions of IOP fluctuations failed normality tests and were better described by a dual Gaussian model with standard deviations of 1.9 and 15.3 mmHg, which presumably corresponds to transient and sustained components.

Conclusions: Our results suggest that transient and sustained IOP fluctuations comprise about 10% of the total IOP-related mechanical energy the eye absorbs daily. This is comparable in total energy impact to a 1 mmHg change in mean IOP. The energy of IOP fluctuations is also concentrated in time and thus has considerably more power, which may have implication for glaucoma.

CONTROL ID: 3713479

SUBMITTER (NAME ONLY): James Germann

TITLE: Nonlinear Susceptibility of Collagen fibers in Ocular Tissue With a New IR Laser Source

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Germann, S. Marcos, Instituto de Optica, Consejo Superior de Investigaciones Cientificas, Madrid, Madrid, SPAIN|G. Sardiello, S. Otero Barros, Fyla, Valencia, SPAIN|S. Marcos, Center for Visual Science, The Institute of Optics, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: James Germann: Commercial Relationship: Code N (No Commercial Relationship) | Gaia Sardiello: Commercial Relationship(s);Code E (Employment):Fyla | Sara Otero Barros: Commercial Relationship(s);Code E (Employment):Fyla | Susana Marcos: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Second Harmonic Generation (SHG) can be used to generate confocal images of the collagen architecture of ocular tissue through the depth of said tissue. Typically, SHG images of collagen are collected with a near infrared (IR) source, but the use of longer IR wavelengths is appealing due to deeper penetration and lower potential for photodamage. However, it is unknown if collagen can efficiently create SHG signal using deeper IR wavelengths. To compare how well collagen can convert deeper IR wavelengths, the magnitude of the nonlinear susceptibility ($|X_2|$) of collagen was measured.

Methods: A sample of porcine cornea (n=1) and sclera (n=1, posterior temporal) was optically cleared with Murray's Clear (2:1 Benzyl Benzoate, Benzyl Alcohol) and placed in a custom built SHG microscope. The laser source was a super-continuum SCHx (Fyla, 18 fs, 80 MHz, 925-1175 nm, 37 mW at sample). Images (160×160 μm, 400×400 pxls, 25 μs dwell time) of collagen fibers were taken at 3 μm steps through the sample. Photons were collected in the forward scattering direction with a 10 μm bandpass filter. Once measurement of the image stack completed, the 10 μm bandpass filter was replaced with another 10 μm bandpass filter and the scan repeated. A total of 12 image stacks of the same tissue volume were taken (emission range 465-585 nm). The total number of photons was counted for each image by summing up the value of the pixels. The number of SHG photons generated was compared to the number of excitation photons and $|X_2|$ was computed.

Results: The values of $|X_2|$ (units of $(eV \times cm^5/photons \times s)^{0.5}$) in the wavelength range of 930-1170 nm ranged from $4.87 \pm 0.37 \times 10^{-16}$ to $7.90 \pm 3.27 \times 10^{-18}$ in the cornea and from $3.01 \pm 0.23 \times 10^{-15}$ to $7.30 \pm 0.43 \times 10^{-17}$ in the sclera. In the cornea and the sclera, the largest $|X_2|$ was located in the 930-950 nm range and the smallest was located in the 1054-1074 nm range.

Conclusions: Collagen was able to generate SHG from 930-1170 nm light. The amount of SHG collected was higher in sclera than in cornea, which in turn indicated a higher $|X_2|$ value. Included in the calculation of $|X_2|$ was the concentration of collagen, which is higher in sclera than in cornea and may explain differences in calculated $|X_2|$. Values of $|X_2|$ measured here are from healthy corneas, but irregularities of $|X_2|$ measurements could be used to determine irregularities in collagen formation and be a biomarker of ocular diseases.

CONTROL ID: 3713481

SUBMITTER (NAME ONLY): Raymond Fang

TITLE: Impact of Neural Crest Derived Foxc2 on the Schlemm's Canal Examined with visible-light Optical Coherence Tomography

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Fang, L. Beckmann, H. Zhang, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|P. Norden, T. Kume, Feinberg Cardiovascular Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

ABSTRACT BODY:

Purpose: Glaucoma, a leading cause of blindness, is associated with increased aqueous outflow resistance. Aqueous outflow primarily occurs through the conventional outflow pathway, which includes the trabecular meshwork and Schlemm's Canal (SC). We investigated the role that neural crest (NC)-derived Foxc2 has on the structural development of SC in vivo.

Methods: $Foxc2^{fl/fl}$ and NC-$Foxc2^{-/-}$ (NC-Foxc2-KO) mice were generated. A TonoLab rebound tonometer measured the intraocular pressure (IOP) of mice under deep anesthesia to establish the baseline IOP level. An anterior segment visible-light optical coherence tomography (vis-OCT) system was used to visualize the SC. Only NC-$Foxc2^{-/-}$ with a mild phenotype, having a visually intact anterior segment under a surgical microscope, were imaged. The anterior chamber was cannulated, and the IOP was adjusted to -10 mmHg, -5 mmHg, 0 mmHg, +5 mmHg, and +10 mmHg relative to the baseline IOP. At each IOP level, the SC volume in a 1.5mm by 1.8mm field of view in the nasal quadrant was measured. Additionally, the average SC height and width were found by fitting an ellipse to the segmented SC for each cross-sectional B-scan image (Fig. 1A-B).

Results: Both $Foxc2^{fl/fl}$ and NC-$Foxc2^{-/-}$ mice had an inverse relationship between IOP and SC volume and height. The SC volume was between 34 and 42% smaller in NC-$Foxc2^{-/-}$ relative to $Foxc2^{fl/fl}$ mice at IOP levels from -10 to +5 mmHg relative to baseline (Fig. 1C). No statistically significant difference in SC volume was found at +10 mmHg. The SC height was between 20 and 23% smaller in NC-$Foxc2^{-/-}$ relative to $Foxc2^{fl/fl}$ mice at IOP levels from -10 to 0 mmHg relative to baseline. The SC width was 17 to 18% smaller in NC-$Foxc2^{-/-}$ relative to $Foxc2^{fl/fl}$ mice at IOP levels of 0 to +5 mmHg relative to baseline.

Conclusions: The decreased SC volume in NC-$Foxc2^{-/-}$ mice relative to $Foxc2^{fl/fl}$ mice suggests that NC-specific deletion of Foxc2 influences the structure of SC and conventional outflow pathway. As SC height is less in NC-$Foxc2^{-/-}$ mice at -10 and -5 mmHg, Foxc2 has a crucial influence on the proper development of the aqueous outflow pathway and trabecular meshwork.

CONTROL ID: 3713482

SUBMITTER (NAME ONLY): Isaac Chay

TITLE: Optical coherence tomography angiography evaluation of the fovea avascular zone.

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Chay, C.S. Tan, National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore, SINGAPORE|C.S. Tan, Fundus Image Reading Center, Tan Tock Seng Hospital, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Isaac Chay: Commercial Relationship: Code N (No Commercial Relationship) | Colin Tan: Commercial Relationship(s);Code R (Recipient):Roche

ABSTRACT BODY:

Purpose: To evaluate the size and characteristics of the foveal avascular zone (FAZ) in the superficial and deep capillary plexus in normal, healthy adults using optical coherence tomography angiography (OCTA).

Methods: In a prospective cohort study of 170 eyes, healthy volunteers underwent OCTA scans. The FAZ from 3mm x 3mm scans was independently graded using the ImageJ software. Circularity represents the degree of resemblance of the area to a perfect circle (a value of 1.0 denotes a perfect circle).

Results: The mean age of participants was 22.7 years (21 – 30, SD± 1.5), with mean spherical equivalent of -4.3 D. Mean superficial FAZ area was 0.25 mm^2 (0.04 mm^2 – 0.48 mm^2) while mean deep FAZ area was 0.38 mm^2 (0.12 mm^2 – 0.66 mm^2). The deep FAZ was significantly larger than the superficial FAZ ($p<0.001$). When the left and right eyes were compared, the superficial and deep FAZ sizes correlated strongly (correlation coefficients of 0.94 and 0.89, respectively), with mean differences between eyes of 0.001 mm^2 ($p=0.720$) and 0.005 mm^2 ($p=0.408$), respectively. The mean circularity index was 0.81 (range 0.54 to 0.95) for the superficial FAZ, and 0.89 (range 0.76 to 0.97) for the deep FAZ. The mean Feret's (maximum) diameter was 0.65 mm for the superficial FAZ and 0.78 mm for the deep FAZ ($p<0.001$), at Feret's angle of 92.3^o for the superficial FAZ and 78.4^o for the deep FAZ.

Conclusions: Both the superficial and deep FAZ size varies significantly among healthy young adults. There is strong correlation between the areas of the superficial and deep FAZ, and between the contralateral eyes. Deep FAZ area and Feret's diameter are significantly larger than the superficial FAZ.

CONTROL ID: 3713484

SUBMITTER (NAME ONLY): Gaurang Patel

TITLE: RNAi BASED APPROACH FOR MYOC-ASSOCIATED GLAUCOMA

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Patel, B. Patel, C. Hunt, S.R. Zaveri, S. Walley, R. wudali, S. Tank, K. Praveen, Y. Hu, C. Romano, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|J. Mcninch, M. Schlegel, A. Castoreno, E. Castellanos-Rizaldos, A. Liebow, V. Jadhav, Alnylam Pharmaceuticals Inc, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in Myocilin (MYOC) are responsible for the most common genetic cause of glaucoma, accounting for 8-10% of autosomal dominant familial Juvenile Open Angle Glaucoma cases, as well as 2-3% of POAG cases. MYOC toxic gain of function mutant proteins aggregate intracellularly, leading to trabecular meshwork (TM) stress, elevated IOP, and glaucoma. In this study, we tested the hypothesis that silencing expression of disease-causing MYOC variants could lead to decreased TM stress and lowered IOP.

Methods: First, we made humanized MYOC mice to screen different siRNA duplexes in vivo. Next, we developed humanized MYOC.Y437H mice over-expressing human mutant MYOC using a CRISPRa approach (SAM-MYOC mice). We also validated the model using IOP lowering drugs (timolol and Rhopressa). We then tested several lead MYOC siRNA duplexes in the SAM-MYOC model to assess the IOP lowering efficacy. In addition, we also used ex vivo human eye perfusion culture model to screen this lead siRNA duplexes

Results: First, we found the several best siRNAs duplexes to lower both MYOC mRNA and protein. To develop animal model, out of several CRISPR guides delivered via AAV or Lentivirus in mouse eye, one guide led to significant upregulation (15-20-fold) of mutant MYOC and high IOP (5-6 mmHg from baseline). We showed that both timolol and Rhopressa lowered IOP in these mice, further validating the model. Next, 5 weeks after virally inducing high IOP in SAM-MYOC, we injected either control or MYOC siRNA intravitreally. While the control siRNA had no effect on IOP, in the MYOC siRNA group IOP was lowered to baseline within a week and this effect persisted for more than 5.5 months, when IOP elevated again gradually. Second, we used the ex vivo human eye perfusion culture system to explore the efficacy of MYOC siRNA to knockdown MYOC mRNA and protein in the TM and MYOC protein levels in the perfusate. Over 90% knockdown of both RNA and protein was achieved.

Conclusions: These results suggest that siRNA based knockdown of MYOC is a feasible therapeutic approach to treat human MYOC based glaucoma.

CONTROL ID: 3713485

SUBMITTER (NAME ONLY): Carl Romano

TITLE: ANGPTL7: A PROMISING TARGET FOR GLAUCOMA THERAPEUTICS

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Romano, K. Praveen, S. Walley, B. Patel, S.R. Zaveri, M. Yuan, H. Yang, J. Rabinowitz, Y. Hu, G. Coppola, G. Patel, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|S. Lefebvre, S. Hyde, S. Waldron, J. Mcninch, V. Jadhav, Alnylam Pharmaceuticals Inc, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: ANGPTL7 is a secreted glycoprotein initially discovered in the cornea. There is evidence that ANGPTL7 levels are elevated in aqueous humor of glaucoma patients and it is highly upregulated upon steroid treatment of trabecular meshwork (TM) cells. We have also shown that in our scRNA-seq data, it is one of the most highly expressed genes in TM. We conducted whole exome sequencing of several large cohorts of individuals and demonstrated an association of the ANGPTL7 gene with both lowered IOP and a reduced risk of glaucoma. Both common and rare variants were identified. To further investigate the relationship of ANGPTL7 to IOP, a series of experiments were performed.

Methods: IOP measurements in wild-type and KO mice using a rebound tonometer (Tonolab). Intravitreal and intracameral injections of several agents.

Results: First, we injected ANGPTL7 protein into the eyes of mice and monitored IOP. Either intravitreal or intracameral injection led to elevated IOP that persisted for more than a 4 days. Next, we made an ANGPTL7 knockout (KO) mouse. There was a gene-dose dependent decrease in IOP, with Het mice exhibiting IOP significantly lower than wt and in homozygous KOs the pressure was further decreased (about 2-3 mm difference between wt and full KO). Ocular anatomy was normal. These results suggest, but do not prove, that ANGPTL7 is involved in the normal physiological maintenance of IOP. To further test this notion, we used an RNAi based approach to test whether a distinct means of acute gene silencing, in an adult animal, will lower IOP. We identified several siRNA duplexes that decreased ANGPTL7 expression, and those that showed >50% mRNA KD also lowered IOP (comparably to the KO). We have also shown that siRNA against ANGPTL7 normalizes IOP in several rodent models of ocular hypertension.

Conclusions: These data strongly indicate that ANGPTL7 contributes to the normal physiological regulation of IOP and that pathological over-expression could lead to potentially damaging elevations in IOP. ANGPTL7 thus is a promising new glaucoma therapeutic target.

CONTROL ID: 3713486
SUBMITTER (NAME ONLY): Wynne Weston-Davies
TITLE: Development of long-acting PAS-nomacopan for treatment of GA and other retinal diseases
SESSION TITLE: AMD and diabetic retinopathy
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: W. Weston-Davies, Medical Affairs, Akari Therapeutics PLC, New York, New York, UNITED STATES|
Commercial Relationships Disclosure: Wynne Weston-Davies: Commercial Relationship(s);Code E (Employment):Akari Therapeutics Plc;Code I (Personal Financial Interest):Akari Therapeutics Plc;Code P (Patent):Akari Therapeutics Plc
ABSTRACT BODY:
Purpose: Studies indicate that complement inhibitors slow the progression of geographic atrophy (GA) but may promote choroidal neovascularisation (CNV).[i] [ii] Treatments that slow the progression of GA whilst inhibiting CNV are needed.
Long-acting 68kda PASylated-nomacopan (PAS-nomacopan) inhibits complement C5 and leukotriene B4 (LTB_4), a potent leukotactic agent that increases retinal VEGF. The addition of a PAS polypeptide tail to nomacopan increases the effective MW to 580kda which may permit a dosing interval of up to 3 months. Inhibition of LTB4 may decrease the risk of CNV seen with avicincaptad and pegcetacoplan.
Here we report 1.) the effect of IVT administered PAS-nomacopan in a mouse model of laser-induced CNV, 2.) the pharmacokinetics (PK) of IVT administered PAS-nomacopan in rabbits.

[i] Liao DS, et al. Ophthalmology. 2020 Feb;127(2)

[ii] Jaffe GJ et al. Ophthalmology. 2021 Apr;128(4)
Methods: For the CNV study, 5 groups of C57BL/6 mice received single or repeat 3µL doses of saline, PAS-nomacopan (20mg/ml) or aflibercept (40mg/ml). CNV was induced by laser in the right eye on Day 0. Retinal angiography was undertaken on Days 7 and 14. CNV volume was measured on Day 16 from flat mount choroid preparations.
To examine PK, pigmented rabbits received a single IVT dose of 50µL PAS-nomacopan on Day 1 to the right eye. Vitreous (V), retina (R) and choroid (CH) were harvested on Days 3, 7, 14, 21, 28 and 56. PAS-nomacopan concentrations in eye tissue were measured using liquid chromatography mass spec to derive half-life and bioavailability.
Results: Single IVT PAS nomacopan significantly ($p = 0.022$) reduced CNV compared to saline and was as effective as multiple IVT aflibercept ($p = 0.019$). Single IVT PAS-nomacopan showed a trend towards reduced leakage on Day 14 ($p = 0.097$). Surprisingly, multiple IVT PAS-nomacopan did not reduce leakage or CNV.
The V and R half-life of PAS-nomacopan in rabbits was shown to be 5-6 days and the concentration of the drug in R was approximately 30% of the concentration in V indicating that PAS enters R.
Conclusions: VEGF is a key driver of CNV and LTB4 inhibition reduces VEGF and CNV.[1] We have shown that nomacopan inhibits retinal VEGF in a uveitis model.[2] Collectively, these data support ongoing development of PAS-nomacopan as therapy for GA and other retinal diseases.

[1] Sasaki F et al. JCI Insight. 2018 Sep 20;3(18)

[2] Eskandarpour M et al. Cells. 2021 Feb 15;10(2)

CONTROL ID: 3713487

SUBMITTER (NAME ONLY): Lupe Villegas

TITLE: Spatial characterization of scleral biomechanics in ex vivo rabbit eyes using multi-meridian Optical Coherence Elastography

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Marcos, Center for Visual Science, Rochester, New York, UNITED STATES|L. Villegas, F. Zvietcovich, A. Varea, J.S. Birkenfeld, S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|

Commercial Relationships Disclosure: Lupe Villegas: Commercial Relationship: Code N (No Commercial Relationship) | Fernando Zvietcovich: Commercial Relationship: Code N (No Commercial Relationship) | Alejandra Varea: Commercial Relationship: Code N (No Commercial Relationship) | Judith Birkenfeld: Commercial Relationship: Code N (No Commercial Relationship) | Susana Marcos: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To quantify biomechanical properties on different scleral locations using Optical Coherence Elastography (OCE), and to evaluate the effects of Rose Bengal-Green Light (RGX) crosslinking in scleral stiffening.

Methods: Five freshly enucleated rabbit eyes (24-48h post-mortem) from adult New Zealand white rabbits were measured at four sclera locations (superior/inferior temporal (ST, IT) and nasal (SN, IN)). Elastic waves were induced in the sclera with a small contact probe (diam. 2mm) vibrating at 2 kHz. Wave propagation speeds (WPS) were calculated from images taken with a phase-sensitive swept source optical coherence tomography system in three meridians, vertical (90°), oblique (135°) and horizontal (180°). Intraocular pressure was fixed at 15 mmHg. RGX (523nm, 0.1W/cm2, 400s) was applied on the temporal side of the sclera. OCE measurements were performed before and after RGX. Subsequently, scleral strips were extracted and used for stress-strain measurements (uniaxial stretcher, CellScale, Canada). Young's modulus (YM) was calculated at 8% strain.

Results: WPS in untreated scleral tissue ranged approximately from 5 to 40 m/s. Mean WPS was calculated per each scleral region. Multi-meridional analysis showed differences in WPS across ST: 25m/s (90°), 22m/s (135°), 19m/s (180°); IT: 21m/s (90°), 22m/s (135°), 21m/s (180°); SN: 21m/s (90°),16m/s (135°), 15m/s (180°); and IN: 18m/s (90°), 26m/s (135°), 11m/s (180°). After RGX, WPS increased in IT region (0.7% (90°), 12% (135°). IN region showed the lowest measured WPS (16m/s (135°), 10m/s (180°)). Uniaxial stretching showed that RGX produced 30% increase in stiffness compared with the contralateral untreated sclera. At 8% strain, the estimated YM of RGX-treated tissue were 11.3±7.0MPa(ST), 11.2±4.4MPa(IT), and of untreated tissue were 7.9±6.7MPa(SN), 7.2±4.1MPa(IN), suggesting a vertical WPS to stiffness ratio of 2 and 3 in temporal and nasal regions, respectively.

Conclusions: Wave propagation speed is dependent on scleral location and direction. Both WPS and YM reveal variations of the scleral properties by Rose-Bengal cross-linking, with regional differences in efficiencies. OCE appears as a promising, non-invasive method to quantify the efficacy of scleral stiffening myopia treatments.

CONTROL ID: 3713489

SUBMITTER (NAME ONLY): Mustafa Al-Asady

TITLE: Telepresence robots in medical education and eye health care delivery

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Al-Asady, H. Peeth, Queen Mary University of London Barts and The London School of Medicine and Dentistry, London, UNITED KINGDOM|A. Gupta, L. Raja, C. Lovegrove, P. Thomas, D. Sim, S. Kang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Mustafa Al-Asady: Commercial Relationship: Code N (No Commercial Relationship) | Hussein Peeth: Commercial Relationship: Code N (No Commercial Relationship) | Amit Gupta: Commercial Relationship: Code N (No Commercial Relationship) | Laxmi Raja: Commercial Relationship: Code N (No Commercial Relationship) | Claire Lovegrove: Commercial Relationship: Code N (No Commercial Relationship) | Peter Thomas: Commercial Relationship: Code N (No Commercial Relationship) | Dawn Sim: Commercial Relationship: Code N (No Commercial Relationship) | Swan Kang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Moorfields Eye Hospital, London, is a centre of excellence for ophthalmic research, education and patient care. During the COVID-19 pandemic, medical students' clinical education exposure and patients' multidisciplinary care were greatly affected.

Telepresence robots have been suggested as a solution to reduce the impact of COVID-19.

We present the results of a trial used to evaluate the capabilities of a telepresence robot in improving clinical education for undergraduate medical students, and the possibility to deliver multidisciplinary clinical patient care via a telepresence robot.

Methods: In a two-day trial period, the telepresence robot was used in four tasks: 1) to livestream an adnexal surgery to students off-site; 2) autonomously navigating patients from clinic to pharmacy; 3) by a clinician to remotely review patients with an ophthalmologist who was consulting the patient face to face; 4) and to deliver a teaching session to medical students.

Feedback was gathered using a questionnaire and in a group discussion together with clinicians, patients, students, robot specialists and IT specialists.

Results: 15 patients of a wide age range and 5 medical students were surveyed. The vast majority of both groups were unaware of telepresence robots. The mean rating given by both groups was 6/10 (with a range of 1-10/10 and 3-8/10) respectively. The groups praised the innovation, felt it could support clinical pressures, and improve their involvement. However, there were concerns about impersonality and technical limitations, and each offered ideas for improvements. All students felt there was potential to improve medical education using the robot. Qualitative feedback during the group discussion highlighted the importance of adapting the currently available hardware and software to enhance its use in education and patient care.

Conclusions: This trial provided a greater understanding into the practicalities of incorporating a telepresence robot, in its current form, to clinical medical care and education. While there are challenges with the technical specification of the telepresence robot, the proposition of using such a device has drawn positive engagement from students, patients and clinicians thus validating further research.

CONTROL ID: 3713490

SUBMITTER (NAME ONLY): Julianni Dar

TITLE: Investigating the effect of dissolved oxygen-assisted corneal cross-linking (CXL) on porcine corneas

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Dar, C. Greene, B. Yang, Engineering, Duquesne University, Pittsburgh, Pennsylvania, UNITED STATES|J.P. Vande Geest, V. Jhanji, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.P. Vande Geest, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Julianni Dar: Commercial Relationship: Code N (No Commercial Relationship) | Caitlin Greene: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Vande Geest: Commercial Relationship: Code N (No Commercial Relationship) | Vishal Jhanji: Commercial Relationship: Code N (No Commercial Relationship) | Bin Yang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The overall treatment time of standard CXL takes around 60 to 120 minutes but risks infection and corneal dehydration. There are two types of CXL pathways, with Type-II CXL requiring oxygen. However, the dissolved oxygen in the cornea has limited quantity, thus limiting the effect from Type-II CXL. To reduce the overall treatment time while maintaining efficacy, we propose to improve the Type-II CXL contribution by introducing dissolved oxygen during the treatment. In this study, we assess the enhancement of the cornea's mechanical properties with oxygen-assisted CXL (O2CXL).

Methods: 12 Porcine eyes were obtained from a slaughterhouse 6-hour postmortem and divided into two groups: standard CXL and O2CXL groups. Riboflavin solution at a concentration of 0.146% was used. The corneal portion of the whole globe was submerged in the riboflavin solution for 30 minutes before the treatment. The riboflavin solution used for O2CXL was saturated with oxygen for 20 minutes prior to cornea staining, and oxygen supply was maintained during the 30 minutes staining process. Before each CXL treatment, two identical cornea strips were dissected along the short axis. Given the large intra-sample variation of mechanical properties, we chose one strip as a reference (no CXL treatment). The other cornea strip underwent CXL treatment. All corneal strips were treated with 365nm UV light at 3 mW/cm^2 for 30 minutes. Uniaxial tensile testing was performed on both reference and treated corneal strips to assess the biomechanical enhancement. We determined the tangential modulus at 10% strain and calculated enhancement for each group.

Results: At 10% strain, the treated corneal strip with O2CXL (σ_{mean}=1.22±0.43MPa) resulted in an average of 69.1%±29.5% increase in tangential modulus compared to the non-treated samples (σ_{mean}=0.70±0.25MPa). The treated samples with standard CXL (σ_{mean}=1.45±0.13MPa) showed an average improvement of 26.1%±9.03% compared to the non-treated samples (σ_{mean}=1.06±0.19MPa). Overall, O2CXL is 1.6 times more effective than the standard CXL.

Conclusions: O2CXL showed a significant increase in biomechanical enhancement compared to the standard CXL. Such enhancement could be attributed to the supplied oxygen, which prolonged the Type-II CXL, thus improving its stiffening effect. O2CXL should be further investigated to optimize the current CXL procedure, such as reducing the overall treatment time.

CONTROL ID: 3713493

SUBMITTER (NAME ONLY): Cullen Moran

TITLE: Comparing educational videos with standard education at the post-op visit

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Moran, S. Groth, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Cullen Moran: Commercial Relationship: Code N (No Commercial Relationship) | Sylvia Groth: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patient education is a critical component of post-surgical care. Adequately educating patients after eye surgery can be time consuming, possibly leading to clinic delays and impacting the care of other patients in the clinic. We performed an exploratory study to determine if educational videos are comparable to face-to-face education in terms of time required for the visit and knowledge retained by the patient.

Methods: This prospective study consisted of 46 patients undergoing their first eye surgery, either cataract removal or glaucoma surgery (trabeculectomy or tube shunt) in a single glaucoma specialist's clinic in a tertiary academic medical center. Patients were enrolled on their first post-operative visit. Patients were randomized to undergo standard post-operative patient education or view an educational video of the surgeon explaining precautions, medications, and expectations for the post-operative period. Patients who viewed the video then received an abbreviated version of the standard patient education during their clinic visit with the glaucoma specialist. The time spent face-to-face with the glaucoma specialist was measured for each patient. A survey containing ten surgery-specific knowledge-based questions was given to a subset of patients to assess patient understanding of the post-operative instructions and returned in a pre-stamped and addressed envelope by mail.

Results: Twenty-one patients were randomized to the standard education group and 25 patients were randomized to the video group. The mean age of patients in this study is 66.5 (56% females). Thirty-six patients underwent cataract surgery, 8 tube shunt, and 2 trabeculectomy. The time required for the face-to-face visit with the glaucoma specialist was 5.31 minutes for the video group, compared to 6.10 minutes for the control group ($p = 0.26$). A subset of 33 patients were given the survey and 16 responded. The average score was 8.3 for the standard education group and 8.6 for the video group ($p = 0.75$).

Conclusions: These results demonstrate that educational videos for post-operative patients are comparable to face-to-face patient education both in terms of time required for the visit and patient retention of the information. This study was limited by a small sample size, and further evaluation of these patient education methods is warranted for wider application.

CONTROL ID: 3713494

SUBMITTER (NAME ONLY): Jan Roelof Polling

TITLE: Effect of high dose atropine for progressive myopia is age-dependent

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Polling, E. Tan, W. Tideman, C.C. Klaver, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Polling, T. van der Meer, Optomtery/Orthoptics, Hogeschool Utrecht, Utrecht, Utrecht, NETHERLANDS|W. Tideman, Ophthalmology, Martini Ziekenhuis, Groningen, Groningen, NETHERLANDS|

Commercial Relationships Disclosure: Jan Roelof Polling: Commercial Relationship(s);Code C (Consultant/Contractor):Essilor;Code C (Consultant/Contractor):Hoya;Code C (Consultant/Contractor):Coopervision | Emily Tan: Commercial Relationship: Code N (No Commercial Relationship) | Willem Tideman: Commercial Relationship: Code N (No Commercial Relationship) | Tamara van der Meer: Commercial Relationship: Code N (No Commercial Relationship) | Caroline Klaver: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Atropine has become standard of care for myopia control in the Netherlands; high dose is recommended for those at risk of high myopia. A risk factor for progression of myopia despite therapy is a young age. In our 3 year follow up study, we evaluated the effect of age on spherical equivalent of refraction (SER) and axial length (AL) change in myopic children receiving atropine 0.5%.

Methods: Children aged 4-16 years with progressive myopia ≥ 1D/year or myopia ≤ -2.5D were prescribed atropine 0.5% at baseline. Children with additional ocular pathology were excluded. Examination including cycloplegic refraction and AL measurement was performed at baseline and follow-up. Outcome measures were AL and SER; annual progression of Al and SER were compared between age groups 4-6, 7-9, and 10-16 years. Differences in progression of AL and SER between age groups were calculated with linear regression adjusted for gender. Correlation of progression rates between first year and second or third year was calculated with the Pearson's correlation.

Results: A total of 116 patients were enrolled in the study (mean age: 9.26 ±2.2 years). At baseline, mean SER was -3.47 ±1.73D; mean AL was 24.92 ±0.90mm. 90 (78%) children continued therapy throughout the 3-year follow-up. Mean AL annual progression was 0.41mm ±0.23 (SER -0.75D ±0.08) for 4-6 year-olds; 0.15mm ±0.12 (-0.22D ±0.35) and for 7-9 year-olds and 0.08 mm ±0.08 (-0.14D±0.23) for 10-16 year-olds. Children aged 4-6 years progressed faster in AL than those aged 7-9 years (P=0.001) or 10-16 years (P<0.001), for SER faster progression was found between 4-6 and 10-16 year old's (P=0.04). Children with higher AL progression in the first year of therapy were also the faster progressors in the second and third year of therapy (r=0.40 and r=0.40 1^{st} vs 3^{rd}). Due to the hyperopic shift of SER in the first year of therapy only the 2^{nd} and 3^{rd} year of therapy was a predictor of response to therapy (r=0.14 and r=0.24 1^{st} vs 3^{rd}).

Conclusions: Despite 0.5% atropine, children younger than 7 years of age for progressive myopia progressed up to three times faster in both SER and AL than older children. The latter also had a more consistent protection by this concentration of atropine during the 3 year regimen. Myopia progression in young children may need more stringent control, such as atropine 1% or combination therapy, in particular since they are at risk for the more extreme values of myopia.

CONTROL ID: 3713497

SUBMITTER (NAME ONLY): Joshua So

TITLE: Quality of Life Analysis in Patients with Inherited Macular Dystrophies

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. So, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|S.M. Duff, S. Grover, J. Chen, University of Florida Department of Ophthalmology, Gainesville, Florida, UNITED STATES|Y. Song, Department of Epidemiology, Indiana University, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Joshua So: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Duff: Commercial Relationship: Code N (No Commercial Relationship) | Yiqing Song: Commercial Relationship: Code N (No Commercial Relationship) | Sandeep Grover: Commercial Relationship: Code N (No Commercial Relationship) | Jinghua Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Inherited macular dystrophies are a subset of inherited retinal diseases (IRD) that affect central vision over time. Visual impairment can have significant socioeconomic implications. The purpose of our study is to assess the quality of life of patients with inherited macular dystrophy.

Methods: This questionnaire study included 34 patients who were diagnosed with inherited macular dystrophies. The sample population came from the University of Florida Department of Ophthalmology patient base. Each patient was called over the phone to participate the survey. Data on education, employment, and medical care status were collected. Each of their responses were then analyzed collectively with other patients' responses.

Results: A total of 34 patients (13 males, 21 females) with a mean age of 49.9 +/- 18.3 years (range, 21-78 years) were assessed. 47% of our sample population started having visual difficulties under the age of 18. 12% of participants noticed visual impairments at 19-34 years of age. 21% of participants noticed visual impairments at 35-44 years of age and 17% reported visual losses starting at 45-54 years. At the time of data collection, one patient was still attending school. Of those who have finished school, 36% (12 of 33) only have a high school diploma and 64% (21 of 33) have completed college. 6 of the 12 patients who only finished high school education (50%) reported that it was due to visual difficulties. 30% (10 of 33) of those who were out of school were unemployed (6 females, 4 males). Of the patients who were no longer attending school and unemployed, 60% (6 of 10) stated that they did not have a job due to low vision. 33 out of the 34 patients were insured. Of those who were insured, 12% (4/33) were not fully satisfied with their insurance. In addition, 6% of these patients were reported to have financial or visual difficulties, or both reasons, obtaining vision aids and only 32% had disability insurance.

Conclusions: The results of our study show that inherited macular dystrophy may contribute to lower levels of education, employment rate, and limited access to medical care. Further studies and statistical analysis, such as obtaining vision and visual field data as well as comparing our results to normal population, are required to confirm the contributing factors of the quality of life of patients with inherited macular dystrophy.

CONTROL ID: 3713499

SUBMITTER (NAME ONLY): Akihiro Ikeda

TITLE: Transmembrane protein 135 regulates lipid metabolism in mouse eyecup

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Ikeda, M. Landowski, V. Bhute, T. Takimoto, S. Grindel, S. Ikeda, Medical Genetics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|A. Ikeda, M. Landowski, P.K. Shahi, B.R. Pattnaik, S. Ikeda, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|V. Bhute, Chemical Engineering, Imperial College London, London, London, UNITED KINGDOM|P.K. Shahi, B.R. Pattnaik, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is a significant factor in the development of age-related diseases but how aging disrupts cellular homeostasis to cause age-related retinal disease is unknown. We identified transmembrane protein 135 (Tmem135) as a regulator of retinal aging and its impairment results in age-related disease phenotypes. Notably, the RPE is sensitive to changes of Tmem135 function. Homozygous Tmem135 mutant ($Tmem135^{FUN025/FUN025}$) mice display thickened RPE, and this layer is postulated as the primary site affected by the $Tmem135^{FUN025}$ mutation. Here, we further our studies on Tmem135 in the RPE by performing RNA sequencing on posterior eyecups from $Tmem135^{FUN025/FUN025}$ mice.

Methods: Pooled posterior eyecups from individual 2.5-month-old male and female WT, $Tmem135^{FUN025/+}$, $Tmem135^{FUN025/FUN025}$ mice were collected for RNA sequencing. Analysis was performed using routine methods and focused on genes with more than twofold changes from wild-type (WT) controls. Genes with twofold differences were compared with two transcriptomic datasets of AMD-afflicted RPE/choroid complexes (GSE135092 and GSE29801) to determine common gene expression changes between these mouse models and AMD. Additional eyecups as well as neural retinas were collected from WT and $Tmem135^{FUN025/FUN025}$ mice for lipid measurements and quantitation of lipid synthesis gene expression.

Results: We found significant gene expression changes in $Tmem135^{FUN025/FUN025}$ mouse eyecups relative to WT controls. Many of the significantly-altered genes with greater than twofold differences in the $Tmem135^{FUN025/FUN025}$ mouse eyecups were involved in lipid metabolism. We confirmed these expression changes occur in the eyecup and not in the neural retina. Consistent with these changes, we found increased cholesterol and neutral lipid accumulation in mutant Tmem135 eyecup samples. We found similar changes in genes involved in lipid metabolism between $Tmem135^{FUN025/FUN025}$ eyecups and AMD donor eyes.

Conclusions: Our study suggests that the Tmem135 mutation affects lipid metabolism as similarly observed in human AMD eyes. Thus, Tmem135 mutant mice can serve as a good model for the role of dysregulated lipid metabolism in AMD.

CONTROL ID: 3713500
SUBMITTER (NAME ONLY): Esther Groeneveld-van Beek
TITLE: Laser-assisted Bowman layer graft preparation
SESSION TITLE: Refractive and non-refractive corneal surgeries
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: E. Groeneveld-van Beek, J. van der Wees, V. Kocaba, Amnitrans Eyebank Rotterdam, Netherlands Institute for Innovative Ocular Surgery (NIIOS), Rotterdam, NETHERLANDS|J. de Leeuw, S. Oellerich, G.R. Melles, Netherlands Institute for Innovative Ocular Surgery (NIIOS), Rotterdam, NETHERLANDS|I. Dapena, G.R. Melles, V. Kocaba, Melles Cornea Clinic, Netherlands Institute for Innovative Ocular Surgery (NIIOS), Rotterdam, NETHERLANDS|
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ABSTRACT BODY:

Purpose: To evaluate the results of three different Bowman layer (BL) graft preparation methods: manually (m-BL), femtosecond laser-assisted (fs-BL), and by femtosecond laser followed by excimer laser (fs/ex-BL).
Methods: Descemet membrane-denuded donor corneas (n=41) were used for this study, 2 corneas for m-BL graft, 18 corneas for fs-BL graft and 21 corneas for fs/ex-BL. For fs-BL, the corneas were placed on an artificial anterior chamber and different depth cuts were performed with decreasing increments starting from 30 µm, diameter 9.0 mm. For fs/ex-BL graft preparation, a superficial flap thickness of 80 µm was created by the femtosecond laser (FEMTO LDV Z8, Ziemer). Subsequently, the graft was placed stromal side up and the residual stroma was ablated by the excimer laser (Schwind Amaris 750S) with increasing increments starting from 40 µm. Grafts were analyzed visually and graft thickness regularity was evaluated by histological analysis.
Results: Fs-BL preparation was successful using 30, 20, 15 and 14 µm cuts (success rate: 12 out of 14, 86%). Fs/ex-BL graft preparation was most successful after an 80 µm cut by femtosecond laser with subsequent 60 µm ablation by excimer laser (success rate: 15 out of 21, 71%). Immediately after the femtosecond laser flap, stripes were visible on the treated surface of the flap which were sometimes still visible after excimer laser ablation. Fs/ex-BL grafts were more transparent and less visible in fluid compared to fs-BL or m-BL.
Fs-BL grafts prepared at 14 µm depth were smoother and seem to resemble the thickness of m-BL grafts based on histological analysis. Compared to fs-BL and fs/ex-BL grafts, m-BL grafts showed long fibers protruding from the graft. Macroscopically, laser prepared grafts resembled manually prepared grafts.
Conclusions: It is feasible to prepare thin, regular BL grafts by femtosecond and by femtosecond followed by excimer laser and these grafts were smoother than m-BL grafts. Fs and fs/ex-BL preparation may therefore be an alternative to manual BL graft preparation.

CONTROL ID: 3713501

SUBMITTER (NAME ONLY): Sami Al-Nawaiseh

TITLE: Short-term follow up after Large-Area RPE Removal by Microsecond Laser followed by hiPS-RPE suspension transplantation in rabbits

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Al-Nawaiseh, A. Schulz, P. Wakili, G. Farese, P. Szurman, B.V. Stanzel, opthalmology, Eye clinic sulzbach, Sulzbach, Saarland, GERMANY|S. Al-Nawaiseh, opthalmology, University of Muenster, Münster, North Rhine-Westphalia, GERMANY|C. Burri, M. Frenz, Institute of Applied Physics, Universitat Bern, Bern, Bern, SWITZERLAND|A. Schulz, P. Szurman, B.V. Stanzel, Klaus Heimann Eye Research Institute, Sulzbach, Saarland, GERMANY|C. Kroetz, Fraunhofer IBMT, Sulzbach, Saarland, GERMANY|C. Burri, S. Salzmann, B. Povazay, Institute for Human Centered Engineering, Berner Fachhochschule, Bern, Bern, SWITZERLAND|B. Ralf, Medical Laser Center Lübeck, Lübeck, GERMANY|B. Ralf, Institute of Biomedical Optics, Universitat zu Lubeck Sektion Medizin, Lubeck, Schleswig-Holstein, GERMANY|S.J. Gasparini, M. Ader, DFG Center for Regenerative Therapies Dresden, Technische Universitat Dresden, Dresden, Sachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Cell therapy is a promising treatment for retinal pigment epithelium (RPE)-associated eye diseases. Herein, microsecond laser irradiation targeting RPE cells was used for large-area RPE removal followed by subretinal injection of human induced pluripotent stem cell derived RPE (hiPS-RPE).

Methods: 19 immunosuppressed pigmented rabbits (Chinchilla bastard hybrid) underwent a large area RPE removal using an infrared reflectance (IR) confocal scanning laser ophthalmoscope (cSLO) with spectral-domain optical coherence tomography (SD-OCT) system (Heidelberg Engineering) extended with a prototype laser (modified Merilas 532 shortpulse ophthalmic laser photocoagulator, Meridian Medical) (wavelength, 532 nm; pulse duration, 8 µs), followed by a 25G vitrectomy. Subsequently, a suspension of hiPS-RPE (1000 cells/ µl) was grafted subretinally into the RPE laser lesion under real-time intraoperative OCT imaging (RESCAN 700, Zeiss) by manual injection via a 25/38G cannula connected to a 100µl Hamilton syringe. 5 rabbits served as a control with hiPS-RPE injected subretinally over healthy RPE. The rabbits were followed with in vivo multimodal retinal imaging at baseline after laser and then for 7 days including fluorescein (FA) and indocyanine angiography (ICGA), aw well as SD-OCT (Spectralis ®, Heidelberg Engineering).

Results: Baseline imaging of RPE laser wounds showed mild late phase FA/ICGA leakage, with normal outer retinal and choroidal reflectivity on OCT, without signs of coagulation. The size of the RPE wounds was typically 10-12mm^2. Real time iOCT showed a directed spread of the bleb retinal detachment (bRD) within the lasered zone, in contrast to a circular spread in controls. Subretinal injection ranged from 5-20µl, with lesser volumes/ larger bRD areas over lasered regions. At 7 days, implanted regions showed FA/ICGA leakage, blockage due to hyperpigmentation was observed mostly at the edges of the lasered zone; OCT showed hyperreflectivity of the outer retina with RPE irregularities. Control implantation sites showed hyperreflectivity in all retinal layers and a variably thickened RPE band suggesting clumping.

Conclusions: Microsecond laser irradiation to the RPE seems to accelerate the subretinal integration of hiPS-RPE, when compared to subretinal injection over intact RPE. Future work will address correlation of multimodal imaging and histology.

CONTROL ID: 3713502

SUBMITTER (NAME ONLY): Yashan Bu

TITLE: Probiotics pretreatment attenuates impaired corneal re-epithelialization in diabetic mice through amelioration of T cell immunity and remodulation of the intestinal microbiome

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Bu, S. Xu, Y. Chan, A.C. Lo, J. Ho, K.C. Shih, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Yashan Bu: Commercial Relationship: Code N (No Commercial Relationship) | Sheng Xu: Commercial Relationship: Code N (No Commercial Relationship) | Yau Kei Chan: Commercial Relationship: Code N (No Commercial Relationship) | Amy Lo: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Wing-Kei Ho: Commercial Relationship: Code N (No Commercial Relationship) | Kendrick Shih: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: 1) To compare corneal re-epithelialization rates, ocular surface and systemic T cell immunity after corneal alkali burn injury between probiotics- or vehicle (PBS) -pretreated Akita (diabetic) and wild type (WT) mice.
2) To compare gut microbiota between probiotics- or PBS-pretreated diabetic and WT mice at baseline and 72 hours after corneal alkaline burn injury and to correlate this with the findings of systemic and ocular surface immunity

Methods: Heterozygous $Ins2^{Akita}$ mice were used as a mouse model of Type I diabetes, with WT C57Bl6/J mice serving as controls. Probiotics IRT5 or PBS was administered to the mice by oral gavage continuously for 14 days before the corneal alkaline burn injury. At day 15, alkaline burn was induced on the right eye of mice under general anesthesia. Immediately after injury and on post-injury day 3, the cornea was examined with slit lamp with fluorescein stain under cobalt blue light. T cell profiles on the ocular surface and in the peripheral blood were analyzed by flow cytometry. Intestinal microbiome was characterized by shotgun metagenomics sequencing.

Results: Probiotics pretreatment has restored the delayed corneal wound healing in diabetic mice. In the peripheral blood and on the ocular surface, significantly elevated levels of CD4+ T cells were seen in PBS-pretreated WT mice and probiotics-pretreated WT and diabetic mice, but were not seen in PBS-pretreated diabetic mice. On post-injury day 3, the gut microbiome of diabetic mice had higher alpha diversity in the PBS-pretreated groups but not in the probiotics-pretreated groups. In the probiotics-pretreated diabetic mice, we observed increased Muribaculaceae and Enterococcus faecalis, and reduced Lactobacillus johnsonii and Bacteroides at baseline compared to vehicle pretreated ones. The baseline and post-injury differences in gut microbiome are potentially linked to the altered T cell immunity in diabetic mice, suggesting the immunomodulatory effects of probiotics.

Conclusions: Probiotics pretreatment attenuated the impaired corneal wound healing response after injury in diabetic mice. The ameliorated T cell immunity and remodulated gut microbial composition with probiotics-pretreatment suggest that probiotics is a promising therapeutic agent in the management of diabetic keratopathy.

CONTROL ID: 3713503

SUBMITTER (NAME ONLY): Linda Lundstrom

TITLE: Compact telescopic system for subjective evaluation of intraocular lens designs

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lundstrom, P. Unsbo, C. Börjeson, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN|D. Romashchenko, M. van der Mooren, C. Canovas, R&D, Johnson & Johnson Surgical Vision, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Evaluation of the subjective visual experience through intraocular lenses (IOL) prior to implantation is important both for patient satisfaction and for optimizing the optical design of the IOL. In this work we have designed a compact see-through IOL telescope (Type 2, IOL-T2) that can transfer the scattering as well as other optical properties of the IOL correctly into the pupil plane of the eye.

Methods: The objective of the IOL-T2 consists of a +45 D camera objective and the +20 D IOL in a water cuvette that together have an effective power of +40 D. The intermediate image can then be viewed by a +40 D eyepiece, thus generating a telescope with angular magnification of -1. The eyepiece also serves the purpose to, together with the cornea of the observer, image the IOL into the pupil plane with both the angular and the transverse magnification equal to -1. As a proof of concept, the IOL-T2 was used to evaluate the foveal contrast sensitivity (CS) with and without a glare source for one monofocal and two multifocal IOLs in three subjects. The glare source was located in the 2.5° nasal visual field of the right eye and gave 1 lux at the level of the IOL telescope. The average luminance of the screen was 50 cd/m^2.

Results: The grating resolution CS at 7.5 cycles/degree was reduced with the multifocal IOLs compared to the monofocal design. No statistically significant difference was found between the +2.75 D and the +4.00 D addition. The glare source induced additional decrease in CS, but the reduction varied between individuals and was larger for the monofocal design than the multifocal designs.

Conclusions: The new IOL-T2 has a compact design and transfer all optical properties of the IOL correctly into the pupil plane of the eye. It is thereby a useful tool to compare the subjective (and the objective, see separate abstract) experience through different IOL designs prior to implantation as well as to develop new IOL designs.

CONTROL ID: 3713504

SUBMITTER (NAME ONLY): Molly John

TITLE: Charactering Y79 Cells as a Model of Human Photoreceptor Differentiation

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. John, A. Kantor, M.E. McClements, R.E. MacLaren, K. Xue, Nuffield Department of Clinical Neuroscience, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Model systems for the study of human photoreceptor differentiation are limited. These include retinal organoids and a limited number of cell lines which vary in their states of differentiation. Y79 cells are derived from a retinoblastoma in a 2.5-year-old Caucasian female and grow as multicellular clusters in suspension. Here, we aim to determine the pattern of expression of photoreceptor-specific genes in Y79 cells to determine their suitability as a model for studying human cone versus rod fate determination in vitro.

Methods: Y79 cells were cultured in RPMI 1640 medium supplemented with 10% foetal bovine serum, 1% L-glutamine, 1% Pen-Strep in 5% CO_2 at 35C. Cells were harvested at passage number 15 for total RNA extraction. The expression of a panel of cone-specific, rod-specific, and pan-photoreceptor genes were analysed by RT-PCR and RT-qPCR (n=3).

Results: Y79 cells demonstrated consistent (n=3) and clear expression of rod-specific (NR2E3, NRL, PDE6A, GNAT1) and cone-specific (ARR3, GNAT2, GNTG2) genes, as well as the pan-photoreceptor transcription factor, CRX. While rhodopsin expression was absent, cone photopigment expression was limited, with minimal expression of medium- and long-wavelength opsins and no detectable short-wavelength opsin by both RT-PCR and qPCR.

Conclusions: Retinoblastomas are generally thought to arise from post-mitotic cone precursors and that cone-related gene circuitry sensitises the cells to the oncogenic effects of RB1 mutations. Our results show that Y79 cells express M/L-cone-specific markers, but also a range of distinct rod markers, which could indicate their origin from a precursor stage during cone/rod fate divergence or a degree of trans-differentiation during oncogenic transformation. Further studies will evaluate the use of Y79 cells as a model system for studying photoreceptor differentiation.

CONTROL ID: 3713505

SUBMITTER (NAME ONLY): Ramaraj Kannan

TITLE: Novel genes and variants associated with inflammation identified in Keratoconus families

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Kannan, A. Ghosh, GROW Research Laboratory, Narayana Nethralaya Foundation, Bangalore, Karnataka, INDIA|R. Shetty, P. Khamar, Cornea and Refractive surgery, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: Keratoconus (KC) is a multi-factorial disease with the involvement of genetic and environmental factors. The current study aims to explore the genetic heterogeneity and gene variant identification by high-throughput sequencing.

Methods: Blood samples were collected from 9 KC families(24 KC subjects and 17 healthy first-degree relatives) at Narayana Nethralaya hospital post IEC approval and written informed consent, followed by Whole Exome Sequencing (WES). Variants in protein coding regions with loss of function were identified using SIFT and Polyphen-2. Allele frequency of variants were analysed using gnomAD.

Results: WES revealed variations in the genes involved in regulation of inflammation, a major pathologic driver in KC patients. 485 variants in 57 genes were identified with diverse inheritance patterns. Within these, 28 variants were nonsynonymous with predicted deleterious effects. Further, the variants present in 2 or more families with allele frequency less than $1X10^{-5}$ were identified. Variations in novel genes involved in regulation of inflammatory signalling including ADAMTS18, ANKRD36B/C, CTBP2, FAM104B, KIR2DL1, etc were present in KC subjects. Network analysis revealed their interaction with 138 genes associated with major signalling pathways including inflammation, of which 131 genes showed differential expression in KC epithelium.

Conclusions: Chronic inflammation in KC may be due to mutations in proteins that regulate inflammatory signalling pathways. Our data reveal novel genes including metalloproteinases with possible immunomodulatory roles which may be useful for genomic diagnostics as well as serve as therapeutic targets for KC. Together, our findings provide novel insights into plausible mechanisms underlying the pathogenesis of KC.

CONTROL ID: 3713506

SUBMITTER (NAME ONLY): Sjoukje Loudon

TITLE: Botulinum toxin as adjuvant to rectus muscle surgery in high myopia

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Loudon, H.J. Simonsz, Ophthalmology, Erasmus MC University Medical Center, Rotterdam, NETHERLANDS|G. Holtslag, Deventer Ziekenhuis, Deventer, Overijssel, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Botulinum Toxin (BTX) offers the possibility to temporarily release the contracture of the muscle enabling a far greater effect of surgery. We report on a novel application for BTX in 2 patients with esotropia-associated high myopia (EAHM) to increase effectiveness and long-term stability after surgery.

Methods: The first patient had long standing slowly progressive esotropia of 61 degrees with limited abduction in both eyes: 40 degrees abduction in the RE, 35 degrees abduction in the LE. High myopia was present in both eyes: RE S-14, and LE S-13 with an axial length of 30.88mm and 29.34mm, respectively. Visual acuity was 20/20 in both eyes. He was given 2.5 units of BOTOX^{TM} in the Medial Rectus of the LE followed by 8mm resection of the Lateral Rectus of the LE 2 weeks later. A second surgery was conducted 3 months later on the other eye: 2.5 units of BOTOX^{TM} in the Medial Rectus of the RE followed by an 8mm resection of the Lateral Rectus of the RE 2 weeks later. The second patient had an esotropia of 30 degrees. Abduction was limited in both eyes to 30 degrees. She had undergone previous strabismus surgery at the age of 44 years on the RE (5mm recession of the Medial Rectus and 3.5mm resection of the Lateral Rectus). High myopia was present in the RE of S-17 with an axial length of 33.06mm. Myopia in the LE was S-9 with an axial length of 27.19mm. Visual acuity in the RE was poor: counting fingers. Visual acuity in the LE was 20/20. She was given 2.5 units of BOTOX^{TM} in the Medial Rectus of the RE followed by 7.5mm resection of the Lateral Rectus of the RE 2 weeks later. All procedures in both patients were performed under general anesthesia.

Results: In the first patient we found an overall reduction of esotropia of 57 degrees: post-op results after the first surgery showed a remaining esotropia of 27 degrees in primary position. Six months after the second surgery there was a minimal angle of esotropia of 4 degrees with minimal abduction limitation. In the second patient the esotropia had improved with 18 degrees, to a remaining 12 degrees of esotropia with an improved abduction 6 months later.

Conclusions: We found a large reduction in esotropia using BTX as adjuvant to a resection of the rectus muscle in patients with EAHM. So in addition to the reported applications for BTX, it can also have an important role in increasing the success of surgery in patients with high myopia.

CONTROL ID: 3713507

SUBMITTER (NAME ONLY): Vanessa Collao

TITLE: Lipidome analysis of pseudoexfoliation and other forms of glaucoma, and control aqueous humor

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Collao, J. Morris, M.Z. Chauhan, L. Abdelrahman, S.K. Bhattacharya, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|V. Collao, J. Morris, L. Abdelrahman, S.K. Bhattacharya, Miami Integrative Metabolomics Research Center, University of Miami, Miami, Florida, UNITED STATES|M.Z. Chauhan, Department of Ophthalmology, Jones Eye Institute, University of Arkansas for Medical Sciences, Little Rock, Arkansas, UNITED STATES|J.M. Martinez-de-la-Casa, B. Vidal-Villegas, B. Burgos, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Comprehensive lipid profiling of the aqueous humor (AH) in patients with pseudoexfoliation glaucoma (PEXG) and primary open angle glaucoma (POAG) compared to controls with the aim of determining lipidome based disease group predictability.

Methods: The AH samples were collected from human donors following tenets of the declaration of Helsinki, under IRB exempted protocols. The following samples were collected 23 non-glaucomatous control, 19 POAG, 9 pseudoexfoliation syndrome but without glaucoma (PEX), and 14 PEXG AH. The samples were subjected to Bligh and Dyer lipid extraction. Untargeted lipidomic analysis was performed with 13 deuterated lipid internal standards for normalization among the lipid classes. Machine learning prediction was performed using three supervised logistic regression binary classification tasks stratified by patients: 1) POAG vs control, 2) PEXG vs control, and 3) PEX vs control vectors. Data are presented as mean peak intensity ± standard deviation.

Results: Lipidomic analysis resulted in the combined identification of 489 lipid species within 26 lipid classes across PEX, PEXG, POAG, and control AH. The mean total lipid content demonstrated lipid content to be highest among control AH (13.54±56.1) compared to the remaining PEX (4.21±10.90), PEXG (9.08±25.97), and POAG (5.66±15.75) samples. Notably, multiple cholesterol esters (ChE), phosphatidylcholines (PC), triglycerides (TG), and ceramides (Cer) were present in higher concentrations for the PEXG AH samples: ChE(16:0), ChE(20:3), ChE(18:1), ChE(18:3), ChE(22:6), ChE(18:2), ChE(20:4), PC(16:0/16:0), PC(16:0/18:2), TG(18:1/18:1/20:4), and Cer(t18:0/24:0). The PC (18:0/18:2), PC (36:2), and PC (34:1e) lipid clases are in low concentrations for PEX AH but highly concentrated in PEXG AH samples. Machine learning prediction yielded accuracy as follows: 1) POAG vs control, with 86% accuracy 2) PEXG vs control, with 71% accuracy and 3) PEX vs control, with 86% accuracy.

Conclusions: Despite the similarity in material deposition, several PC species were found in low concentration in PEX AH samples and found in high concentration in PEXG AH samples, suggesting the composition of the materials are fundamentally different in composition. These differences in lipid composition may help to distinguish them. Machine learning prediction has demonstrated the ability to differentiate all three groups and control, mostly with 86% accuracy.

CONTROL ID: 3713508

SUBMITTER (NAME ONLY): Judith Birkenfeld

TITLE: Corneal biomechanical parameters in healthy and early-stage keratoconus eyes from cross-meridian air-puff deformation OCT

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Birkenfeld, A. Varea, A.M. Gonzalez, E. Martinez-Enriquez, S. Marcos, Consejo Superior de Investigaciones Cientificas, Madrid, Madrid, SPAIN|A. Curatolo, International Centre for Translational Eye Research and Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, POLAND|A. Eliasy, A. Abass, B. Lopes, A. Elsheikh, University of Liverpool Faculty of Science and Engineering, Liverpool, Liverpool, UNITED KINGDOM|A. Elsheikh, Beihang University, Beijing, CHINA|J. Merayo-Lloves, Instituto Universitario Fernandez-Vega, Universidad de Oviedo, SPAIN|S. Marcos, Center for Visual Science, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The detection of localized biomechanical alterations in early keratoconus (KC) may open new pathways for diagnosis and customized treatment options. Cross-meridian air-puff deformation Optical Coherence Tomography (OCT) was applied to healthy and early KC subjects. Deformation parameters, cross-meridian symmetry and estimated corneal biomechanical properties were evaluated as potential biomarkers for KC detection.

Methods: Corneal air-puff deformation images from 8 eyes of 8 subclinical/early-stage KC patients (mean age 35yo), and 5 eyes from 3 control (C) subjects (mean age 28yo) were captured along the horizontal (H) and vertical (V) meridian using a novel OCT device (ImTOPScanner, Curatolo, 2020). Custom-built routines were used for image segmentation and quantification at maximum deformation for H and V: 1) Distance between the two peaks of deformed cornea (PD); 2) Asymmetry in Deformation Area (ADefA), i.e. difference between nasal/temporal and superior/inferior deformation area; 3) Deformation Amplitude (DA) Ratios (Vinciguerra, 2016) at distances n=1; 1.5; 2 mm from the corneal apex. Patient-specific eye models were generated using a second-order Ogden material model. Inverse analysis was performed to quantify biomechanical variations. For KC corneas, a custom-built algorithm detected the boundary of the region of pathology, to which distinct material parameters were allocated.

Results: KC corneas showed lower PD (mean PD_{KC}=4.70±0.03 mm) than C corneas (mean PD_{C}=5.13±0.02 mm). In KC corneas $|ADefA_{V}-ADefA_{H}|$ was 0.12±0.15 mm^2, compared to 0.08±0.06 mm^2 in C corneas. The DA ratio was higher in KC than in C corneas for all n (mean increase 0.10±0.04 (H) and 0.14±0.06 (V) for n=1 mm; 0.28±1.11 (H) and 0.44±0.23 (V) for n=1.5 mm; 0.79±0.31 (H) and 1.71±1.17 (V) for n=2 mm). $|DARatio_{V}-DARatio_{H}|$ was higher in KC than in C corneas (2.2, 2.7, and 6.6-fold for n=1; 1.5; 2 mm, respectively). Inverse analysis revealed a tangent modulus at 2% strain of 1.75±0.29 MPa for KC corneas; 1.20±0.37 MPa for KC areas of pathology and 1.43±0.18 MPa for C corneas.

Conclusions: Cross-meridian air-puff corneal deformation OCT reveals differences between healthy and early-stage KC patients. Parameters comparing different deformations in horizontal and vertical meridians seem a well-suited biomarker, independent of intraocular pressure. Results of inverse analysis complement these parameters.

CONTROL ID: 3713510

SUBMITTER (NAME ONLY): Catherine Liu

TITLE: Utility of Removal of Vitreous Cortex Remnants during Vitrectomy for Primary Rhegmatogenous Retinal Detachment Repair

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.K. Liu, H. Anderson, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|T. Wakabayashi, R. Mahmoudzadeh, M. Salabati, S. Garg, A.C. Ho, M. Spirn, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the prevalence of vitreous cortex remnants (VCR) and the utility of VCR removal using a diamond-dusted membrane scrapers (DDMS) on visual and anatomic outcomes after pars plana vitrectomy (PPV) for primary rhegmatogenous retinal detachment (RRD) repair.

Methods: We evaluated the prevalence of VCR in eyes that underwent PPV for primary RRD between July 2014 and February 2021. The presence or absence of VCR on the retinal surface extending from the macula to outside the vascular arcade was identified during PPV using triamcinolone acetonide. The VCR outside the vascular arcade was completely removed using a DDMS under a wide-viewing system. In some cases, the VCR at the fovea was also removed, though not always systematically assessed. Preoperative factors and outcomes were compared between eyes with VCR removed intraoperatively to those without VCR.

Results: VCR was present and removed (VCR+) in 86 (46%) eyes and absent (VCR-) in 101 (54%) eyes. Patients with VCR were significantly older than those without (P=0.006). The preoperative BCVA (logarithm of the minimum angle of resolution) tended to be worse in VCR+ (1.23±0.92 [Snellen equivalent, 20/340]) than in VCR- (1.03±0.89 [20/214]), however, the difference was not statistically significant (P=0.095). There were no between-group differences in postoperative BCVA (VCR+ 0.44±0.54 [20/55]; VCR- 0.42±0.50 [20/53]; P=0.38) or visual improvement (+0.79±0.91, VCR+; +0.61±0.81, VCR-; P=0.31). SSAS was also comparable between the groups (90%, VCR+; 91%, VCR-; P=0.573). The incidence of postoperative PVR (9%, VCR+; 6%, VCR-; P=0.554) and postoperative ERM (28%, VCR+; 29%, VCR-; P=0.97) were comparable between the groups during mean follow-up period of 28.2 months.

Conclusions: Nearly half of the patients with RRD had VCR, which was more likely to occur in older patients. VCR removal resulted in favorable functional and anatomical outcomes comparable to those in eyes without any VCR in patients with RRD.

CONTROL ID: 3713511

SUBMITTER (NAME ONLY): Mark Krebs

TITLE: BLamD-like lesions of tvrm5 mice accumulate in a dorsotemporal streak

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.P. Krebs, J. Peterson, L. Stone, J. Naggert, P.M. Nishina, The Jackson Laboratory, Bar Harbor, Maine, UNITED STATES|D.C. Sterratt, The University of Edinburgh, Edinburgh, Scotland, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Bright-spot lesions in the tvrm5 mouse model of CTNNA1-associated butterfly-shaped pigment (or pattern) dystrophy consist of raised inclusions in the retinal pigment epithelium (RPE). The purpose is to test the hypothesis that these lesions share features with basal laminar deposits (BLamD) and are confined to a dorsotemporal streak.

Methods: C57BL6/J control and tvrm5 eyes were assessed by color fundus imaging, optical coherence tomography (OCT), light and fluorescence microscopy, and transmission electron microscopy (TEM). To map bright-spot lesions, color fundus and OCT images were aligned and transformed to a uniform geometry using choroidal vessels as landmarks. To assess the full posterior eye, eyecups stained to reveal RPE cell boundaries and nuclei were surveyed by tiled z-stack fluorescence microscopy. Stitched tissue layers and surface models were generated by a custom program (OMorph), fit to a cut-sphere geometry by a new version of a retina-morphing software (Retistruct), and oriented using vessel landmarks.

Results: Bright-spot lesions were detected by noninvasive imaging in homozygous tvrm5 mice at one month of age and in older heterozygous tvrm5 mice. Lesions were distributed reproducibly within a 1 x 0.5 mm dorsotemporal streak ~0.5 mm from the optic nerve head. This distribution was confirmed in eyecups surveys analyzed by Retistruct. Lesions consisted of eosinophilic mounds within the RPE and exhibited internal lamination. TEM of lesions showed debris below a thinned layer of RPE cells, accompanied by vacuolization of neighboring RPE cells and collagen fiber accumulation in underlying choroidal pillars. Bruch's membrane appeared intact below debris, suggesting that the lesions were similar to BLamD.

Conclusions: BLamD-like lesions in tvrm5 mice are confined to a dorsotemporal streak near the optic nerve head. This distribution may define a chorioretinal structure related to the non-primate visual streak and area centralis, which may be relevant for modeling macular disease in mice.

CONTROL ID: 3713512

SUBMITTER (NAME ONLY): Paula Sepulveda Beltran

TITLE: Comparison of Molecular and Antifungal Profiles of Fusarium species recovered from patients Treated with Rose Bengal Photodynamic Antimicrobial Therapy vs Antifungal Therapy.

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Sepulveda Beltran, K. Leviste, H. Durkee, J. Parel, G. Amescua, Ophthalmic Biophysics Center, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Maestre-Mesa, D. Miller, Ocular Microbiology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|G. Amescua, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare species diversity, antifungal susceptibility and mycotoxin profiles of Fusarium isolates recovered from patients subjected to RB-PDAT plus antifungal therapy vs those treated with antifungal therapy alone.

Methods: We used a combination of PCR and DNA sequencing to confirm and classify 25 fusarium isolates (5 PDAT-treated; 20 non-PDAT treated) recovered from patients presenting at BPEI with fungal keratitis between July 2016 and November 2021. Primer specific PCR and DNA sequencing were used to screen for the presence of Fumonisin and Trichothecene mycotoxins. Etests were used to evaluate antifungal susceptibility profiles for amphotericin B and voriconazole in accordance with CLSI standards in 21 isolates.

Results: Isolates: In general, 60% (n=15) of isolates belonged to the Fusarium solani species complex (FSSC), of which Fusarium falciforme (20%, n=5) was the most common species. 36% (n=9) belonged to the Fusarium chlamydosporum species complex (FCSC), and 4% (n=1) to the Fusarium dimerum species complex (FDSC), namely Fusarium delphinoides. Of the five PDAT isolates included, 60% (n=3) belonged to the Fusarium solani species complex; one being Fusarium falciforme. The remaining two isolates belonged to the FCSC and FDSC, respectively.

Mycotoxins: At least one mycotoxin was identified in all isolates. Fumonisin toxins were documented in 44% (n=11) of all isolates and in 60% (n=3) of the PDAT-treated species. Trichothecenes were documented in 68% (n=17) of isolates and in all PDAT-treated species.

Antifungal susceptibility testing: None of the isolates demonstrated in vitro susceptibility to voriconazole and amphotericin B with $MICs_{90}$ of >32 µg/ml (R) at 72 hours, respectively. Mean MICs for voriconazole were similar in the non-PDAT treated group (28.8 µg/mL/R) compared to the PDAT-treated group (27.2 µg/ml/R). Similarly, MICs for amphotericin B in the non-PDAT treated group (14.3 µg/mL/R) showed little variation compared to the PDAT-treated group (14.6 µg/ml/R).

Conclusions: Toxin producing members of the Fusarium solani complex remain the most frequently recovered fusarium species from fungal keratitis in South Florida conferring increased resistance to standard antifungal treatment. Isolates treated with RB-PDAT were more likely to be toxins producers.

CONTROL ID: 3713513

SUBMITTER (NAME ONLY): James Twist

TITLE: β1b chain-containing laminins regulate the regenerative response of Müller glia in the zebrafish retina

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Twist, D. Serjanov, D. Hyde, Biological Sciences, University of Notre Dame, Notre Dame, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of laminins, which are principal components of the extracellular matrix (ECM), has been well-studied in vertebrate retinal development. However, far less is known about their potential roles in neuronal regeneration, which is similar to development but is not a mere recapitulation. Therefore, we expect that laminins, which are critical for development, are also involved in regeneration. Here, we examine the role of β1b chain-containing laminins (CCLs) in the regenerative response of Müller glia (MG) in the zebrafish retina.

Methods: Tg(gfap:eGFP) zebrafish, which express enhanced green fluorescent protein within the MG, were dark-adapted for two weeks and used for in vivo morpholino-mediated gene knockdown of Lamb1b protein expression in the retina. The fish were then exposed to intense light for up to 96 hours, resulting in photoreceptor death and initiating a regenerative response, which was assessed via immunohistochemistry in retinal cryosections. Cell-fate tracking studies were performed using intraperitoneal injections of EdU (5-Ethynyl-2′-deoxyuridine), a thymidine analogue that is incorporated into proliferating cells. Finally, the role of lamb1b in the expression of other laminins and cell-surface receptors was assessed via qRT-PCR.

Results: Expression of lamb1b is upregulated in the regenerating retina after 48 hours of light damage (4-fold increase) and remains highly expressed throughout the regeneration process. Morpholino-mediated knockdown of Lamb1b expression results in a significant decrease in the number of proliferating MG and neuronal progenitor cells (NPC) during retinal regeneration at 36 (decreased by 60%; $p \leq 0.01$) and 72 hours (decreased by 30%; $p \leq 0.0001$) of light treatment. Lamb1b protein knockdown also results in significantly fewer EdU+ cells within the outer nuclear layer (decreased by 30%; $p \leq 0.01$). Moreover, the expression of other laminin chains and several integrin receptors is downregulated in the lamb1b morphant.

Conclusions: These data illustrate that β1b CCLs regulate the regenerative response in the zebrafish retina. Specifically, MG and NPC proliferation, as well as the expression of other laminins and their receptors, are both disrupted in response to reduced β1b CCL expression. These results suggest that the ECM plays a crucial role in regeneration and begin to uncover the molecular mechanisms of these processes.

CONTROL ID: 3713514

SUBMITTER (NAME ONLY): Jennifer Faralli

TITLE: αvβ3 Integrin Expression in the Human Trabecular Meshwork/Schlemm's Canal Pathway (TM/SC) is Age Dependent and Segmental

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Faralli, M. Filla, H. Khan, D.M. Peters, Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|K.E. Keller, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D.M. Peters, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies have shown that changes in αvβ3 integrin expression/activity in TM cells can induce a glaucomatous phenotype. This study was to determine if there were age-dependent differences in αvβ3 integrin expression in human anterior segments and TM cell cultures.

Methods: Immunohistochemistry of paraffin embedded human anterior segments was performed by co-labeling with antibodies against αvβ3 integrin and fibronectin. Images were acquired with a Zeiss Z2 epifluorescence microscope. Image J was used to quantify the levels of αvβ3 integrin and fibronectin in the TM/SC. TM cells were cultured in low glucose DME with 10% FBS. One week post confluency, total RNA was isolated and relative levels of the β3 integrin subunit and TGFβ2 were determined using qPCR. An adenovirus vector expressing either wildtype or constitutively active αvβ3 integrin tagged with mCherry was used to determine if its expression in TM cells affected TGFβ2 expression.

Results: Immunolabeling studies showed that αvβ3 integrin levels varied between age-matched donor eyes while fibronectin levels were more uniform. Both αvβ3 integrin and fibronectin could be found on the trabecular beams, in the juxtacanalicular (JCT) region, and both the inner (IW) and outer wall (OW) of SC. Quantification showed there was more αvβ3 integrin in the OW of SC than the beams or JCT/IW of SC. In contrast, there was more fibronectin in the JCT/IW of SC than the beams or OW of SC. Interestingly, the amount of αvβ3 integrin and fibronectin varied from quadrant to quadrant within the same donor eye indicating expression was segmental. Analysis of mRNA levels of isolated cells from normal donor eyes showed an age-dependent loss in αvβ3 integrin and TGFβ2 expression. In contrast, cells isolated from glaucomatous tissue showed an increase in αvβ3 integrin and TGFβ2 expression compared to age matched controls. TM cells overexpressing a constitutively active αvβ3 integrin also showed increased TGFβ2 mRNA levels.

Conclusions: These studies show that expression of αvβ3 integrin appears to be segmental suggesting it may play a role in regulating segmental outflow and its expression/activity may be age dependent. These studies also support earlier findings and show that expression of αvβ3 integrin correlates with TGFβ2 expression in vitro and suggest that αvβ3 integrin signaling may be a gain of function that contributes to glaucoma.

CONTROL ID: 3713518

SUBMITTER (NAME ONLY): Jimin Han

TITLE: Investigating photoreceptor outer segment phagocytosis by retinal pigment epithelium in CLN3-Batten

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Han, R. Singh, Cell Biology of Disease, University of Rochester Medical Center, Rochester, New York, UNITED STATES|K.A. White, V. Swier Mosher, T.B. Johnson, J.M. Weimer, Pediatrics & Rare Diseases, Sanford Health, Sioux Falls, South Dakota, UNITED STATES|J. Han, W. Spencer, C.I. Thomas, R. Singh, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|W. Spencer, C.I. Thomas, Biomedical Genetics, University of Rochester Medical Center, Rochester, New York, UNITED STATES|S. Chear, J. Talbot, A.L. Cook, Wicking Dementia Research and Education Centre, University of Tasmania, Hobart, Tasmania, AUSTRALIA|A.W. Hewitt, Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, AUSTRALIA|J.M. Weimer, Pediatrics, Sanford Health, Sioux Falls, South Dakota, UNITED STATES|

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ABSTRACT BODY:

Purpose: CLN3-Batten disease is a lysosomal storage disorder that leads to retinal degeneration and vision loss. Using induced pluripotent stem cell (iPSC)-based disease modeling studies, we previously showed impairment of a critical retinal pigment epithelium (RPE) cell function, phagocytosis of photoreceptor outer segments (POS) in CLN3-Batten. In this study, our goal was to investigate a direct link between CLN3 mutation and retinal degeneration. Specifically, we introduced a CLN3 mutation (966 bp deletion spanning exons 7 and 8) in an embryonic stem cell line (ESC; H9) and generated a transgenic pig model to study the impact of $CLN3^{\Delta 7/8}$ mutation on POS phagocytosis and retinal homeostasis.

Methods: Isogenic control and mutant ESC lines were generated by CRISPR/Cas9-mediated biallelic deletion of exons 7 and 8. Control and $CLN3^{\Delta 7/8}$ ESC were differentiated to RPE, and parallel cultures were evaluated for morphological and functional characteristics. Yucatan miniswine carrying the orthologous mutation were generated via rAAV-mediated CLN3 editing and somatic cell nuclear transfer; heterozygote offspring were bred to produce homozygote pigs. CLN3-Batten associated retinal phenotypes (reduced RPE lipofuscin, photoreceptor loss) were evaluated by histological analysis of $CLN3^{\Delta 7/8}$ and wild-type (WT) pig eyes at 6-, 36-, and 48-month timepoint. To evaluate POS phagocytosis in ESC-RPE and primary porcine RPE cultures, RPE cells were fed POS (~20 POS/RPE cell) for 2h and rhodopsin (RHO; a POS protein) level was analyzed by Western blotting.

Results: $CLN3^{\Delta 7/8}$ ESC-RPE did not display any disease-associated cellular phenotypes in the absence of POS feeding. However, $CLN3^{\Delta 7/8}$ ESC-RPE showed reduced uptake of POS compared to isogenic control ESC-RPE . Furthermore, compared to POS isolated from WT pigs, POS isolated from $CLN3^{\Delta 7/8}$ pigs was phagocytosed less efficiently by WT primary RPE cells. Consistent with reduced POS phagocytosis, lipofuscin/autofluorescence accumulation was decreased in $CLN3^{\Delta 7/8}$ pig RPE by 36 months, which was followed by significant loss of photoreceptors at 48-month timepoint.

Conclusions: Using in vitro and in vivo models of CLN3-Batten, we show that $CLN3^{\Delta 7/8}$ mutation (that affects ~75% patients) is independently sufficient for promoting both impaired POS phagocytosis and retinal degeneration in CLN3-Batten.

CONTROL ID: 3713520

SUBMITTER (NAME ONLY): Christopher Hammond

TITLE: Association between statin use and retinal layer thicknesses in the UK Biobank

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Statins are one of the most widely prescribed medications, and may be protective for age-related macular degeneration, but studies are not consistent. Retinal thickness is reduced in early AMD; even before AMD develops protective/deleterious AMD polymorphisms may be associated with thicker/thinner retinas respectively. The purpose of this study was to determine if statin use is associated with retinal thickness in a population-based cohort.

Methods: Participants of European ancestry from the UK Biobank were included for analysis. Quantitative OCT data was obtained using the Topcon 3D OCT-1000 Mk2 machine and data for statin use was self-reported. Following quality control (excluding participants with poor image quality, self-reported eye disease or diabetes, reduced vision), 39035 participants were included, with 6796 cases and 32239 controls. Linear regression analyses, adjusted for age and sex, were performed with retinal thickness measures (RNFL, GCL, GC-IPL, ELM-ISOS, ISOS-RPE, photoreceptor layer, RPE and total retinal thickness) used as the outcome variable.

Results: Significant association (after corrections for multiple testing) was identified between statin use and almost all retinal layers. The strongest association was for the total retinal thickness (β=-1.89, p=2.00x10^{-20}). Inner retinal layers were thinner (GCL β=-0.36, p=9.3x10^{-10}, GC-IPL β=-0.51, p=2.3x10^{-9}, and RNFL β=-0.31, p=2.3x10^{-6}), as were outer retinal layers (ELM-ISOS β=-0.081, p=8.9x10^{-4}, ISOS-RPE β=-0.44, p=5.7x10^{-15}, photoreceptor layer β=-0.32, p=8.7x10^{-17}). Statins were not associated with RPE thickness (β=-0.17, p=0.15). Choroidal thickness was not available.

There was no significant difference in the proportion of participants excluded during quality control between statin users and controls (26% vs 25%), indicating that statin use is unlikely to be associated with other retinal abnormalities.

Conclusions: Statin use is strongly associated with a thinner retinal thickness across multiple retinal layers. Mechanisms underlying this association are unclear. Possibilities include direct effects of the medications or of the underlying conditions for which participants were taking the medications.

CONTROL ID: 3713521

SUBMITTER (NAME ONLY): Sonja Simon-Zoula

TITLE: Human retinal pigment epithelium cells can be imaged in vivo with a novel adaptive optics camera using transscleral illumination

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Simon-Zoula, M. Kunzi, T. Laforest, EarlySight SA, Geneva, SWITZERLAND|L. Kowalczuk, R. dornier, C. Moser, Laboratory of Applied Photonic Devices (LAPD), School of Engineering, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, SWITZERLAND|L. Kowalczuk, A. Iskandar, Z. Misutkova, A. Gryczka, A. Navarro, F. Jeunet, I. Mantel, Faculty of Biology and Medicine, University of Lausanne, Lausanne, SWITZERLAND|A. Iskandar, Z. Misutkova, A. Gryczka, A. Navarro, F. Jeunet, I. Mantel, Fondation Asile des aveugles, Jules-Gonin Eye Hospital, Lausanne, SWITZERLAND|F.F. Behar-Cohen, Centre de Recherche des Cordeliers, Université Pierre et Marie Curie - Paris 6, FRANCE|F.F. Behar-Cohen, Ophtalmopôle, Cochin Hospital, FRANCE|

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ABSTRACT BODY:

Purpose: Histopathology studies described morphological changes of the retinal pigment epithelium (RPE) specific to the onset and progression of retinal diseases in human eyes. However to date, no valuable imaging tool is used in the clinic to image RPE cells. Transscleral Optical Imaging (TOI) uses an oblique illumination of the fundus combined with adaptive optics to provide cell-resolution images of the retinal layers up to the RPE, in vivo. A prospective study was carried out to assess safety and repeatability of TOI technology and characterize healthy RPE cells.

Methods: Eyes of subjects above 18 years presenting normal fundus check were examined with Cellularis®, a novel retinal camera prototype for TOI. For each eye, 6 images of the RPE cells were acquired at different locations of the macula (Fig. 1), one of them being imaged 5 times to evaluate the repeatability of the method. Baseline and follow-up ophthalmic exams were performed before and 1-3 weeks after TOI to assess safety. RPE cell features were extracted with a custom software. Spearman test was used for statistical analyses.

Results: 49 eyes (mean axial length (AL): 24±0.9 mm; mean refractive error: -1±1.7) of 29 subjects (mean age: 37±13.3 years; 19 males) were included. No safety issue was reported during the study. RPE cells were characterized by density of 3663±274 cells/mm^2, cell area of 233±17.1µm^2, intercellular distance of 16±0.6µm and number of neighbor cells around 6, in average. Longer AL significantly correlated with decreased cell density (Spearman's correlation coefficient (R)=-0.757; p<0.001), increased cell area (R=0.667; p<0.001) and increased intercellular distance (R=0.763; p<0.001). Similarly, aging significantly correlated with decreased cell density (R=-0.385; p<0.05), increased cell area (R=0.460; p<0.05) and increased intercellular distance (R=0.391; p<0.05). Interestingly, age also correlated with cell morphological features, showing decreasing circularity (R=-0.611; p<0.001) and increasing elongation (R=0.587; p<0.001) with increasing age. Mean coefficient of variation for repeated images was below 4% for each of the features.

Conclusions: TOI allows safe and repeatable in vivo imaging of human RPE cells, consistent with the literature, paving the way for establishing a full RPE normative database.

CONTROL ID: 3713522

SUBMITTER (NAME ONLY): Aaron Beckwith

TITLE: Physiology-informed Transfer Learning Reveals Differences in Optical Coherence Tomography Angiography Vascular Biomarkers

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Nunez, D. Zou, R. Rai, J. Keller, G. Guidoboni, Electrical Engineering Computer Science, University of Missouri, Columbia, Missouri, UNITED STATES|A. Beckwith, M. Lin, G. Guidoboni, Mathematics, University of Missouri, Columbia, Missouri, UNITED STATES|A. Harris, B.A. Siesky, A. Verticchio, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|C. Wikle, Statistics, University of Missouri, Columbia, Missouri, UNITED STATES|E.L. Robinson, School of Social Work, University of Missouri System, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Structural and vascular changes characterize the disease process in glaucoma; yet the interplay between intraocular pressure (IOP), vascular biomarkers, and retinal and optic nerve structure remains uncertain. Currently, utilization of vascular markers in the management of glaucoma is limited by their translation in clinical applications. Here, we use Transfer Learning (TL) applying outcomes from glaucoma progression data to analyze a prospective cross-sectional study in patients with OAG and healthy controls.

Methods: We applied Fuzzy c-Means (FCM) clustering to a progression dataset (Indianapolis Glaucoma Progression Study (IGPS): n=115) enhanced with hemodynamic variables predicted by a validated mathematical model (Guidoboni et al, IOVS, 2014). The model specifically uses intraocular pressure (IOP-Goldmann), blood pressure (BP-automated) and heart rate (HR-automated) as individualized inputs. The 3 clusters identified via FCM on IGPS are then applied to categorize a cross-sectional dataset (n=45 healthy and 11 OAG) based on the mean arterial pressure (MAP) and IOP measured on each subject. Optical coherence tomography angiography (OCTA) biomarkers were measured and analyzed by (i) distinguishing between healthy and OAG subjects, and then (ii) sectioning each group by the 3 FCM-based clusters.

Results: Data categorized via the FCM-based clusters are shown in Fig. 1. The tables display the OCTA marker medians, 25th, and 75th percentiles. The measurements taken on the inside disc image reveal a 3% decrease from healthy to OAG eyes. When further sectioned, there was an increase in the inside disc image in cluster 1 by 3%, but in cluster 3 there was a 4% decrease. All structural markers were worse in OAG than healthy eyes with or without accounting for the clusters.

Conclusions: While one might assume from conglomerated data that measurements of the inside disc image decrease from healthy to OAG eyes, TL reveals a significant increase in a specific cluster of patients. Differential OAG risk may be highlighted by TL and FCM clustering of OCTA and IOP inputs for a combined hemodynamic and pressure model of risk.

CONTROL ID: 3713524
SUBMITTER (NAME ONLY): Larissa Moniz
TITLE: Canadian patient experience with age-related macular degeneration
SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Moniz, Fighting Blindness Canada, Toronto, Ontario, CANADA|C. Andrews, Independent researcher, Hamilton, Ontario, CANADA|J. Pereira, JRL Research & Consulting, Inc, Mississauga, Ontario, CANADA|
Commercial Relationships Disclosure: Larissa Moniz: Commercial Relationship: Code N (No Commercial Relationship) | Chad Andrews: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Pereira: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of vision loss in people over the age of 55. Approximately 2.5 million Canadians have AMD with nearly 180,000 experiencing vision loss. Given Canada's aging population, these numbers will continue to increase. This study aims to understand the physical, psychological and practical challenges faced by those with lived AMD experience and to identify areas of need and reform from a medical, health policy and social care perspective.

Methods: This sequential mixed method study comprised an online survey of Canadians living with AMD. Survey data fields included demographic information, self-reported vision, treatment experiences and goals, and disease impact on social functioning. A subset of respondents also participated in a telephone interviews to more deeply explore the burden of their condition.

Results: Between January to June 2020, 337 individuals (mean age = 63.5; male = 47.5%) participated in our survey. Respondents identified having wet (47.1%), dry (37.7%) or wet and dry (12.8%) AMD. Up to 80% of respondents reported that sight loss resulting from AMD affected their ability to do at least one daily activity. Having AMD placed a significant psychological burden on respondents, most notably through anxiety that their condition would worsen (77%). A significant majority of survey participants (75.4%) received injections as treatment for AMD with 46% being satisfied with their treatment. One-fifth of respondents who received injections either felt they were not beneficial or were unsure. Almost one-third of respondents (32.1%) indicated missing at least one injection appointment in the past year, with barriers including the inability to find someone to accompany them to (39.5%), difficulty travelling to (34.6%) or inability to afford (30.9%) the appointment. A large group of respondents also underscored anxiety about the injection (38.2%) as the most difficult part of the appointment.

Conclusions: This study paints a detailed picture of the experiences of the AMD community in Canada, including its support network, the impact of vision loss on respondents' daily activities and emotional wellbeing and their experience with treatment. This data will help better support patient needs and understand barriers to treatment compliance.

CONTROL ID: 3713527

SUBMITTER (NAME ONLY): Samendra Karkhur

TITLE: Optical coherence tomography angiography based assessment of macular vessel density, retinal layer metrics and subfoveal choroidal thickness in COVID-19 patients.

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Karkhur, B. Sharma, K. Chauhan, D. Soni, N. Yadav, L. Banerjee, Ophthalmology, All India Institute of Medical Science - Bhopal, Bhopal, Madhya Pradesh, INDIA|

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ABSTRACT BODY:

Purpose: OCTA is a non-invasive imaging technique for assessment of retino-choroidal vasculature. It allows for the quantitative assessment of retinal microvasculature. This study evaluates macular vessel density (VD), foveal avascular zone (FAZ) area, subfoveal choroidal thickness (SFCT) and retinal layer metrics by optical coherence tomography angiography (OCTA) in COVID-19 recovered patients. Additionally we studied the correlation of OCTA parameters with severity and duration of COVID-19 disease, steroid administration, and vaccination status.

Methods: It is a case-control study of 180 patients. OCTA parameters namely - superficial and deep VD in various sectors - total, superior, inferior, central, inner, superior-inner, inferior-inner, full; superficial and deep FAZ area; SFCT: central subfield thickness (CST) were measured. Additionally, retinal layer metrics, including nerve fiber layer, ganglion cell layer – inner plexiform complex, inner nuclear layer, outer plexiform layer, and outer nuclear layer were compared between cases and controls. A correlation analysis of OCTA parameters was done with severity and duration of disease.

Results: FAZ area (superficial and deep); retinal layer metrics including ganglion cell layer and inner plexiform layer, outer plexiform layer and outer nuclear layer showed significant reduction while there was a significant increase in SFCT in COVID-19 patients. Corticosteroid treatment resulted in significant decrease in VD. A positive correlation was elicited between FAZ area and disease duration; while VD correlated negatively with the duration of disease. Multivariate analysis showed significant relationship between superficial FAZ area, deep FAZ area and SFCT.

Conclusions: OCTA showed alteration in retinal microvasculature and metrics in COVID-19 patients. Choroid being a highly vascular structure was also affected. There was a resultant alteration in FAZ area and SFCT. Moreover, thrombotic phenomenon associated with COVID could alter retinal layer metrics. Additionally, corticosteroids also appear to alter retinal microvasculature. This study could help understand the wide-spread thrombotic phenomenon often associated with COVID infection and predisposition for the same among specific patients.

CONTROL ID: 3713528

SUBMITTER (NAME ONLY): Yuan Liu

TITLE: Foamy Macrophages Exist in the Scar Area and Clear Lipid Debris after Optic Nerve Injury

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, Z. Hao, M. Khodeiry, R.K. Lee, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tissue damage in the center nervous system elicits a robust inflammatory response, which is partly mediated by infiltrating immune cells including macrophages. Macrophages, as professional phagocytes, initially play an important role in cellular debris clearance. Infiltrating macrophages can uptake lipid debris after spinal cord injury. We investigated if a similar mechanism exists in the optic nerve (ON).

Methods: Col1α1-GFP mouse and C57BL/6 mice underwent optic nerve crush. These mice were sacrificed at different time points (7, 14, and 28 days) after ON injury. Optic nerves were stained for immunohistochemistry and immunofluorescence analysis of macrophage and lipid markers.

Results: Our results demonstrate infiltration of foamy macrophages in the ON after ON crush. Lipid droplets are stained with Oil Red O and engulfed by CD11b labeled foamy macrophages. The peak of Oil Red O staining occurs 14 days after ON crush injury. Those foamy macrophages do not co-localize with GFP-labeled Col1α1 fibroblasts.

Conclusions: The experimental results demonstrate that our model can successfully adapt the prior knowledge learned from the axons and dendrites segmentation of RGC images to the segmentation of vascular structures in OCTA images.

CONTROL ID: 3713529

SUBMITTER (NAME ONLY): Bindu Kodati

TITLE: Endothelin-1 mediated decline in mitophagy in retinal ganglion cells contributes to neurodegeneration during ocular hypertension in rats

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kodati, G.A. Johnson, D.L. Stankowska, R.R. Krishnamoorthy, Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|R. Chaphalkar, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The vasoactive peptide, endothelin-1 (ET-1) has been shown to be elevated both in the aqueous humor and circulation of primary open angle glaucoma patients as well as in animal models of glaucoma. ET-1 administration in rodents has been shown to produce neurodegeneration of retinal ganglion cells (RGCs) and their axons. However, the precise mechanisms underlying these effects are still not completely known. The purpose of the study was to assess mitophagic changes during ET-1 mediated neurodegeneration of RGCs in culture as well as in the Morrison model of ocular hypertension in rats.

Methods: Primary RGCs isolated from rat pups were treated with either vehicle or ET-1 (100 nM) for 24 h. Mitophagic changes were determined by assessing the extent of co-localization of LC3B (a marker of autophagosomes) and TOM20 (mitochondrial marker). Mitophagy was also evaluated in the cultured RGCs by treating with MitoTracker (a label for mitochondria) and LysoTracker (a label for lysosomes in live cells). To confirm these findings in vivo, intraocular pressure (IOP) elevation was carried out in one eye of retired breeder Brown Norway rats. Two weeks following IOP elevation, retina sections from IOP-elevated eyes and contralateral eyes were analyzed for expression of LC3B and TOM20.

Results: ET-1 treatment of primary RGCs for 24 h produced a decrease in co-localization of LC3B and TOM20. A decreased co-localization of MitoTracker and LysoTracker was also found in primary RGCs treated with ET-1, indicative of decreased mitophagy. IOP elevation for 2 weeks in rats, produced a significant decrease in colocalization of LC3B and TOM20 ($n=4$, $p<0.05$) in retinal ganglion cell layer.

Conclusions: A decreased colocalization of TOM20 with LC3B during ET-1 treatment as well as during IOP elevation could be indicative of ET-1 mediated decrease in mitophagy in RGCs. A decline in mitophagy could be one of the mechanisms by which ET-1 promotes neurodegeneration of RGCs in glaucoma.

CONTROL ID: 3713530

SUBMITTER (NAME ONLY): Shrilekha Vedhakrishnan

TITLE: Accommodation with simulated contact lenses in Myopes

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is an association between myopia progression and near work that has led to speculation that the larger accommodative lags reported in myopes may be a factor or an effect in progression. We evaluated the impact of contact lenses design and addition on the accommodative behavior in myopes

Methods: A Hartmann-Shack wavefront sensor in an Adaptive Optics (AO) visual simulator was used to measure the wavefront aberrations in 5 myopic subjects (MS, 27±2yrs; spherical error: -2.25±0.3D) while viewing a stimulus changing between 0-6D (ramdomized,1D steps) through multifocal/bifocal corrections, under natural viewing conditions, measurements were repeated 5times for repeatability. The corrections were simulated with a Spatial Light Modulator or a deformable mirror and the accommodative response was calculated using the defocus term, spherical aberration Z (4,0) of the wavefront aberrations.7 conditions were tested: NoLens (NL) and when viewing through aspheric designs of high (2.50D, HA) and medium add (1.75D, MA), bifocal (4mm central zone, 2.5 D) - center distance (CD), center near (CN) and with inducing positive and negative 1µm spherical aberration (PSA, NSA) using deformable mirror were measured.

Results: There was a systematic decrease in pupil diameter with accommodation, the average slope was -0.19/-0.25/-0.15/-0.11/-0.16/-0.11/-0.15mm/D for NL/PSA/NSA/HA/MA/CN/CD. The average slope of change of spherical aberration with accommodative demand (0-6D) shifted to more negative values for NL/PSA/CD -0.02/-0.07/-0.005µm/D whereas the slope of this change reduced for NSA/HA/MD/CN 0.04/0.01/0.02/0.01µm/D. The accommodative lag computed considering only defocus and 4^{th} order spherical aberration showed higher amount of lag with PSA (0.04D) than NL (0.03D) and the least with MA (0.02D), some conditions caused a lead of accommodation NSA(-0.041D).

Conclusions: AO simulators are useful tools to simulate multifocal contact lenses. The performance and interaction of these lenses are driven by individual presence or absence of high-order aberrations which alters the accommodative response. Near additions in some cases can reduce the accommodative lag and convert them to leads.

CONTROL ID: 3713531

SUBMITTER (NAME ONLY): Archana Nigalye

TITLE: Association Between Macular Pigment Optical Density values and Optical Coherence Tomography Parameters in Age-related Macular Degeneration

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nigalye, R. Katz, V. Douglas, E.S. Lu, G. Tsougranis, I. Lains, M. Kasetty, D. Husain, J.B. Miller, Retina Service, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|T. Elze, S. Pundlik, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A. Nigalye, R. Katz, T. Elze, S. Pundlik, E.S. Lu, G. Tsougranis, I. Lains, D. Husain, J.B. Miller, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dual wavelength autofluorescence (dwAF) method to determine macular pigment optical density (MPOD) is based on absorption of blue wavelength by the yellow macular pigment. Studies show association of MPOD with age-related macular degeneration (AMD) stage. MPOD association with the optical coherence tomography (OCT) parameters is yet to be shown. We studied the association between Heidelberg dwAF MPOD values and OCT structural parameters in AMD.

Methods: Prospective, cross-sectional IRB approved study. Patients with early and intermediate AMD, and controls (> 50 years) underwent dual-wavelength (488 and 514 nm) auto-fluorescence, macula centered 97 line enhanced depth imaging (EDI) OCT (Spectralis, Heidelberg) and color fundus photographs used for Age-related Eye disease study scale staging. The MPOD sum of volume (SoV) values were calculated within the 1° radius circle centered on the fovea relative to the 6° plateau. OCTs graded by two independent graders. Linear mixed-effects regression models were used to determine the association of OCT abnormalities - presence of central drusen, drusenoid pigment epithelial detachment (dPED), hyperreflective foci, ellipsoid zone disruption, and reticular drusen with MPOD, accounting for age, AMD presence, intra-ocular lens (IOL) presence, smoking history, and the use of AREDS supplements.

Results: We included 286 eyes of 161 participants; 201(70%) eyes with AMD (19 early and 182 intermediate), and 85 controls (30%). Mean ± SD participant age was 71±9 years, with majority female (58%), non-smokers (57%), and AREDS users (51%). IOL present in 30% of AMD eyes and 8% of control eyes. OCT abnormalities were not observed in any of the control eyes. In AMD eyes, 29% had dPED, 54% had central drusen, 41% had reticular drusen, 28% had hyperreflective foci, and 53% had ellipsoid zone disruption. Higher MPOD values were significantly associated with age ($\beta = 6.38$, 95% CI: 1.24 – 11.52, $p = 0.015$), IOL presence ($\beta = 364.01$, 95% CI: 268.12 – 459.89, $p < 0.001$), and the presence of dPED ($\beta = 83.66$, 95% CI: 4.93 – 162.39, $p = 0.037$).

Conclusions: The significant association between the MPOD SoV in central 1° radius and the presence of dPED after accounting for confounders, has potential use in determining the role of dual wavelength autofluorescence MPOD as a biomarker in AMD.

CONTROL ID: 3713533

SUBMITTER (NAME ONLY): Susmita Das

TITLE: Drug repurposing identified non-antibiotic drugs for the treatment of Staphylococcal endophthalmitis

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Das, S. Singh, A. Kumar, School of Medicine, Wayne State University, Detroit, Michigan, UNITED STATES|B. Thomas, R. sachdeva, M. bhasin, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gram-positive bacteria, especially staphylococci remain the leading cause of bacterial endophthalmitis. The severe vision loss is attributed, in part, to their increasing resistance to antibiotics, leading to treatment failure. Hence, newer antimicrobials are needed to combat multidrug resistant ocular infections. The aim of this study is to identify non-antibiotic drugs/molecules and test their therapeutic efficacy using experimental models of S. aureus (SA) endophthalmitis.

Methods: Temporal transcriptomic analysis was performed using mouse retina infected with SA. The transcriptomic data was used for systems biology analyses to establish gene signature sets and to identify potential candidate drugs using connectivity map (CMAP). The MIC and cytotoxicity of the predicted drugs were determined. In vitro studies were performed on human Muller glia and retinal pigment epithelial cells to check modulation of inflammatory responses challenged with methicillin-sensitive strain (RN6390) and methicillin-resistant strain (USA300). In vivo efficacy of the drugs was evaluated in mouse model of USA300 endophthalmitis. The effect of drug treatment on SA-induced gene expression was performed by RNAseq of BMDMs.

Results: Our systems biology and CMAP analysis predicted three drugs, Dequalinium chloride (DC), Clofilium tosylate (CT) and Glybenclamide (Glb) which counter regulate the infection signatures of SA endophthalmitis. All predicted drugs exhibited anti-inflammatory properties in cells when challenged with sensitive or resistant strains of SA. Moreover, post drug treatment, a reduction in inflammation was also observed in response to LPS stimuli and heat-killed SA in cultured retinal cells. DC and CT were more effective than Glb in all the cell lines. The RNAseq analyses revealed downregulation of inflammatory signatures in MRSA infected BMDMs. In vivo data showed that while all three drugs reduced intraocular inflammation, DC and CT could reduce the bacterial burden as well.

Conclusions: The predicted three drugs were able to suppress inflammatory mediators during ocular SA and MRSA infection in cells. DC and CT were effective in controlling bacterial burden, while all three efficiently suppressed inflammatory responses in MRSA infected mice eyes.

CONTROL ID: 3713535

SUBMITTER (NAME ONLY): Pawan Shahi

TITLE: A novel Kcnv2 nonsense mutation mouse model of Cone Dystrophy with Supernormal Rod Response

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cone dystrophy with supernormal rod response (CDSRR) is a rare autosomal hereditary retinopathy that affects 1 out of every 100,000 people due to mutations in the KCNV2 gene. This gene encodes for the voltage-gated potassium channel Kv8.2, which is a regulatory component of the delayed rectifier potassium channel in the photoreceptors. Several complete gene knock out mouse models reveal molecular mechanism of the disease. We sought to develop a nonsense mutation, Glu-156-to-Ter (E156X), knock in mouse for disease modeling and therapeutic development.

Methods: A targeted c.466 G>T, p.E156X Kcnv2 mutation was achieved through delivery of CRISPR-Cas9 RNP to the mouse zygote. To confirm the single nucleotide substitution, Sanger sequencing and Restriction Fragment Length Polymorphism (RFLP) were performed on genomic DNA isolated from newly generated mice. We used Espion-E3 system at 6 weeks to record full field electroretinography (ERG) to characterize visual outcome. Standard scotopic and photopic (ISCEV) stimulus was used to record responses to compare a-, and b-wave amplitudes and implicit times. For measurement of c-wave we used a 25 $cd.s/m^2$ flash stimulus. Optical Coherence Tomography (OCT) was used to examine retinal structure, and OptoMotor Response (OMR) to measure visual acuity (VA).

Results: Genotyping validated the expected base change in the target codon, GAG to TAG, resulting in the nonsense mutation in the Kcnv2 gene without any off-target alterations. When compared to wild-type (WT) and het ($E156X^{-/+}$) mice, OCT images revealed the absence of EZ layer in the homozygous ($E156X^{+/+}$) mutant retina. At 6 weeks of age, OMR demonstrated no statistical difference in VA between WT, $E156X^{-/+}$, and $E156X^{+/+}$ mice. In comparison to WT mice, full-field ERG in the $E156X^{+/+}$ mice exhibited a reduced and delayed a-wave amplitude with a flattened peak. The $E156X^{+/+}$ mice had a higher b-wave amplitude at lower flash intensities, but their overall response was delayed at all flash intensities. The c-wave amplitude was noticeably reduced.

Conclusions: The supernormal rod response in the $E156X^{+/+}$ mice revealed by increased amplitude b-wave is consistent with Cone dystrophy caused by clinically relevant KCNV2 nonsense mutation. We report a novel CDSRR mouse model for understanding retinal dystrophy progression and possible therapeutic interventions for clinical translation.

CONTROL ID: 3713536

SUBMITTER (NAME ONLY): Andrea Tornero-Jimenez

TITLE: Intraocular Pressure during Trabeculectomy. Comparison of Intuitive Compression Tonometry versus IC-200 Rebound Tonometry

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tornero-Jimenez, J.A. Paczka, A.M. Ponce Horta, J. Escobedo Espinoza, A. Orozco Garcia, I.F. Vazquez, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara Centro Universitario de Ciencias de la Salud, Guadalajara, Jalisco, MEXICO|A. Tornero-Jimenez, J.A. Paczka, A.M. Ponce Horta, J. Escobedo Espinoza, A. Orozco Garcia, I.F. Vazquez, Research, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Trabeculectomy has been established as a safe and effective surgery to control IOP. An important objective of this technique is to adjust the tightness of the scleral flap to establish a balance between fluid under- and over-filtration in order to achieve the target IOP. Intuitive approximations to get trans-operative IOP values is of common practice besides of observing the exit rate of fluid through the scleral flap edges. IC200-tonometry is an accurate instrument to measure IOP in the supine position. The aim of this study is to compare an intuitive manuever to estimate IOP versus IC-200 rebound tonometry during trabeculectomy.

Methods: In non-consecutive cases in which a trabeculectomy was performed, IOP was measured using an empirical manuever consisting in touching the firmess of the cornea with a cannula by both an experienced glaucoma surgeon (S) and an assisting glaucoma fellow (F). IC-200 rebound tonometry (Icare) was also performed by a third person. IOP estimations were done in random order. IOP guessed values (for the intuitive manuever) and the actual IC-200 (IC) IOP values were verbally manifested at the end of each round of measurements. At least four rounds (R1-R4) of measurements were carried out (one before the paracentesis, two more after the scleral flap was sutured and the anterior chamber was filled with BSS, and one more, prior to the conjunctival closure). Mean value comparisons and correlations were used to analyzed the information. P values of ≤ 0.5 were considered statistically significant.

Results: Sixteen eyes of 15 patients (mean age 54.6±7.7 years; 10 male and 5 female) were included in the study. Mean baseline IOP was 29.1±8.9 mm Hg. Mean trans-operative values were not statistically significant among each other (R1-IC, 11.5±7.7, R1-S, 10.0±5.8, R1-F, 13.3±7.4; R2-IC, 3.9±1.8, R2-S, 4.7±3.5, R2-F, 5.8±4.5; R3-IC, 8.3±5.8, R3-S, 9.5±5.2, R3-F, 10.5±5.1; R4-IC, 6.8±4.3, R4-S, 8.8±5.1, R4-F, 9.3±6.2). Correlations were weak in R1 and R2, but good and statistically significant in the other two rounds (R3-S, r=0.54, p=0.027; R3-F, r=0.80, p=0.0002; R4-S, r=0.54, p=0.027; R4-F, r=0.76, p=0.016).

Conclusions: IC-200 rebound tonometry is a feasible technique to be used trans-operatively during trabeculectomy and has potential to be used in a training process in order to improve surgeon’s ability to estimate IOP in the operating room.

CONTROL ID: 3713537

SUBMITTER (NAME ONLY): Jeffrey O'Callaghan

TITLE: Recombinant Human MMP-3 Increases Outflow Facility In Vivo in Non-Human Primates and Ex Vivo in Human Cadaver Eyes

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We have previously reported that matrix metalloproteinase (MMP-3) increases outflow facility in wildtype mice. Here, we aimed to assess the translatability of MMP-3 in non-human primates (NHP) as well as human donor eyes (HDE) ex vivo.

Methods: Outflow facility was measured in vivo using a modified iPerfusion system. NHPs were anaesthetised with isoflurane, further stabilised by controlling body temperature and were monitored via electrocardiogram. Animals were intracamerally cannulated to iPerfusion, where 5 ng/ml recombinant human MMP-3 (rhMMP-3) was perfused into one eye for 1 hour at 5 mmHg above spontaneous IOP. An outflow reading was then taken while accounting for the time-dependent effect on outflow. Aqueous was sampled immediately after perfusion for ELISA analysis of MMP3 levels. To assess outflow in HDE, we designed eye baths and an incubator to extend the capabilities of the iPerfusion system. Anterior segments were mounted to baths, connected to iPerfusion and cultured for up to 2 weeks. Flow rates were stabilised before a baseline measurement was taken. The anterior chamber was then exchanged with 5 ng/ml rhMMP-3 using syringe pumps and another reading taken after 1 hour.

Results: Outflow facility was successfully measured in vivo in NHP eyes, with an average control facility of 0.45 /ul/min/mmHg. On average, outflow facility was significantly increased in non-human primates by 29 % ($P = 0.006$, $n = 15$) after exposure to rhMMP-3, with a moderate dose-response relationship observed ($R^2 = 0.46$, $P = 0.008$). Heart rate and oxygen consumption were also related to facility using iPerfusion. In human donor anterior segments, outflow facility increased by 56 % on average after treatment ($P = 0.14$, $n = 3$ eyes).

Conclusions: Impaired outflow facility is a key driver of glaucoma pathophysiology, resulting in increased IOP and subsequent loss of glaucomatous degeneration. We successfully adapted the iPerfusion system for use with larger model systems. We have shown the translatability of therapeutic MMP-3-mediated increases in outflow in ex vivo mouse models, NHP in vivo, and post-mortem human donor eyes. Using MMP3 to increase conventional outflow holds promise as a potential new treatment for ocular hypertension and open angle glaucoma.

CONTROL ID: 3713541

SUBMITTER (NAME ONLY): Jacob Dohl

TITLE: Cytoplasmic Hybrids of ARPE-19 Cells and Mitochondria from Patients with Age-related Macular Degeneration Accurately Model Reactive Oxygen Species Hallmarks Found In Vivo

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Dohl, K. Schneider, S. Atilano, A. Bao, M. Kenney, Pathology and Laboratory Medicine, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related Macular Degeneration (AMD) is the leading cause of vision impairment among the elderly in the United States, necessitating novel therapies to prevent vision loss; however, AMD research lacks accessible in vivo and in vitro models. Cytoplasmic hybrids (cybrids), generated through fusing mitochondria-rich platelets from AMD patients with mitochondrially-depleted retinal pigment epithelial cells (ARPE-19), provide a novel and accessible in vitro model for AMD research. A major hallmark of AMD is an increase in reactive oxygen species (ROS). We hypothesized the AMD cybrids would show elevated ROS levels as well as downstream effects of ROS, including mitochondrial DNA (mtDNA) damage, and elevated anti-inflammatory protein expression levels.

Methods: Cybrids from age-, sex-, and mtDNA haplogroup-matched patients with dry AMD (AMD, n=6) and without (Ctrl, n=6) were grown under standard culture conditions. ROS levels were determined using DCFDA fluorescence as well as CellROX Deep Red Reagent intensity (ThermoFisher). mtDNA copy number was determined through qPCR using multiplexed Taqman 18S and ND2assays (ThermoFisher), while fragmentation was qualitatively assessed through long extension PCR (LX-PCR). Western blotting was performed using HSP70 and Actin antibodies (Cell Signaling Technology) at a concentration of 1:1000 and 1:5000, respectively. A two tailed Student’s T test was used for statistical analysis between groups.

Results: AMD cybrids showed a 140% increase in ROS levels ($p<0.05$) and a 3-fold increase in mtDNA copy number compared to controls ($p<0.05$). In addition, LX-PCR demonstrated increased levels of fragmentation across the entire mitochondrial genome. Western blotting showed AMD cybrids had a 1.7-fold increase in HSP70, a key chaperonin which is upregulated during cell stress conditions ($p<0.01$).

Conclusions: Taken together, our findings suggest that AMD cybrids exhibit elevated ROS levels, similar to observations found in vivo, which may contribute to increased antioxidant response and damage to the mitochondrial genome. Further investigations are underway to determine if the cybrid model reflects other in vivo hallmarks of AMD.

CONTROL ID: 3713546

SUBMITTER (NAME ONLY): Oliver Leingang

TITLE: Automated deep learning-based AMD stage detection in real-world OCT datasets

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Leingang, H. Bogunovic, S. Riedl, A. Chakravarty, U. Schmidt-Erfurth, Department of Ophthalmology and Optometry, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|M.J. Menten, R. Holland, D. Rueckert, BioMedIA, Imperial College London, London, London, UNITED KINGDOM|M.J. Menten, D. Rueckert, Institute for AI and Informatics in Medicine, Klinikum rechts der Isar der Technischen Universitat Munchen, Munchen, Bayern, GERMANY|G. Traber, H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel, Basel, Basel-Stadt, SWITZERLAND|L. Fritsche, Department of Biostatistics, University of Michigan, Ann Arbor, Michigan, UNITED STATES|T. Prevost, Department of Population Health Sciences, King's College London, UNITED KINGDOM|H.P. Scholl, Department of Ophthalmology, Universitat Basel, Basel, Basel-Stadt, SWITZERLAND|S. Sivaprasad, NIHR Moorfields Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A.J. Lotery, Clinical and Experimental Sciences, University of Southampton, Southampton, Hampshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To develop an artificial intelligence (AI) method that can classify real-world optical coherence tomography (OCT) volumes and B-scans into different stages of age-related macular degeneration (AMD).

Methods: We trained a two-stage deep learning network to classify macula centered 3D volumes from Topcon OCT images into 4 different categories, i.e. Normal, Drusen, Atrophy and Neovascularization. A 2D ResNet50 was used to identify the disease categories on B-scans while an ensemble of models (ResNet18/Multilayer Perceptron) that uses the concatenated B-scan-wise output of the last hidden layer of the ResNet50 was used to classify the whole volume. Classification uncertainty estimates were generated with Monte-Carlo drop-out at inference time.

A total of 106,892 2D B-scans from a publicly available Spectralis OCT, Heidelberg Engineering, data set, supplemented with slides of atrophy, were used to pre-train a model in a transfer learning setup in order to ultimately classify Topcon OCT images from a data set consisting of 1,964 B-scans from 215 volumes of 189 eyes. The 3D ensemble model was trained on four binary classification problems with 5-fold cross-validation on a total of 1,575 OCT volumes from 1,418 eyes. Performance is reported as a balanced accuracy (ACC), precision (PREC), recall (REC), and specificity (SPEC).

Results: The Topcon scans were acquired from real world retrospective data sets extracted from the University Hospital Southampton and the Moorfields Eye Hospital as part of the PINNACLE study (75%) and supplemented with an internal data set (25%) from the Medical University of Vienna. The B-scan-level classification on a hold-out test set of 336 B-scans reached the performance of ACC/PREC/REC/SPEC: 0.97/0.97/0.96/0.99. The 3D classification of Topcon volumes achieved good performance on all classes on a hold-out test set out of 629 volumes, with high specificity in all classes (at least ACC/PREC/REC/SPEC 0.95/0.95/0.95/0.99) except for drusen (ACC/PREC/REC/SPEC 0.95/0.95/0.95/0.89).

Conclusions: The proposed approach enables the combination of different kinds of data sets into a domain specialized classifier that can reliably identify biomarkers associated with the relevant stages of AMD. Such automated AI tools can then serve to categorise patients by their disease stage, efficiently facilitating subsequent

large-scale data analysis.

CONTROL ID: 3713547

SUBMITTER (NAME ONLY): Tara Balasubramanian

TITLE: Assessment of retinal blood flow in infants with Retinopathy of Prematurity using Fluorescein Angiography and Laser Speckle Contrast Imaging

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the preliminary feasibility of assessing retinal blood flow velocities noninvasively in infants with Retinopathy of Prematurity (ROP) using laser speckle contrast imaging (LSCI) via comparison with intravenous fluorescein angiography (IVFA).

Methods: In this ongoing study, 26 subjects (52 eyes) underwent LSCI using XyCAM RI (Vasoptic Medical, Baltimore, MD) and 6 subjects (6 eyes) received IVFA. Three subjects (3 eyes) aged 3 – 6 months that were diagnosed with ROP received both LCSI and IVFA imaging in quick succession. Perfusion status in 13 arteries and veins of interest was analyzed by determining integrated density and time to peak intensity (TPI) from IVFA data using ImageJ and by computing the mean blood flow velocity index (BFVi) from select vessel segments and in the overall field of view at its peak phase in the cardiac cycle from the LSCI data using the XyCAM software. Time to arterial, laminar, and venous filling was also determined. Arterial-venous transit time (AVTT) and TPI from IVFA was compared to LSCI-based BFVi measurements in subjects with paired imaging data.

Results: Mean peak BFVi for select vessels in subjects who received XyCAM imaging (10 eyes) was 7.2 ± 1.6 (arbitrary units). Mean peak BFVi for overall field of view in subjects who received both imaging modalities was 3.9 ± 1.9. Mean peak BFVi of arteries was significantly different from the peak BFVi of veins ($p < 0.009$). Mean AVTT was 5.4 ± 1.6 seconds and mean TPI was 12.3 ± 0.7 seconds. Among subjects with paired data from IVFA and LSCI, shorter filling times were associated with higher BFVi.

Conclusions: These preliminary findings from a limited cohort of neonates demonstrate the ability to noninvasively assess perfusion using LSCI in a manner that elevated BFVi measurements are associated with faster arterial-venous transit times. Future studies will be needed to establish if noninvasively obtained blood flow information provides insights on ROP severity.

CONTROL ID: 3713548

SUBMITTER (NAME ONLY): Ndidi-Amaka Onyekaba

TITLE: Comparison of Rates of Change in 10-2 and 24-2 Perimetry to Detect Glaucoma Progression

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Onyekaba, A.A. Jammal, T. Estrela, R. Naithani, A. Youssif, H. Tseng, F. Medeiros, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|F. Medeiros, Electrical and Computer Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the performance of rates of change in 10-2 and 24-2 standard automated perimetry (SAP) in detecting glaucoma progression, using rates of structural loss measured by spectral-domain optical coherence tomography (OCT) as an independent reference standard for progression.

Methods: The study included 291 eyes from 185 glaucoma subjects followed for an average of 1.8±1.0 years. Sixty-nine eyes from 39 healthy subjects followed for 1.5±0.9 years were used as control group to estimate age-related losses over time. Rates of change were estimated using linear mixed models. Receiver operating characteristic (ROC) curve regression analysis was used to compare the performance of rates of change of 10-2 and 24-2 SAP mean deviation (MD) over time in discriminating eyes from the control group versus eyes that had different rates of structural progression as measured by OCT. Areas under the ROC curves (AUC) were estimated at rates of global cpRNFL thinning for pre-defined values of -1.0µm/year (slow progression) and -2.0µm/year (fast progression).

Results: Mean rates of change were -0.14±0.18 dB/year and -0.27±0.23 dB/year for 10-2 SAP MD and 24-2 SAP MD, respectively. Rates of change in 24-2 SAP MD performed significantly better than 10-2 SAP MD to discriminate age-related loss from glaucomatous change, as measured by OCT (AUC = 0.808 versus 0.721, respectively; P = 0.011). For discriminating slow progressors from controls, 10-2 SAP had an AUC of 0.715 (95% CI: 0.622-0.808) versus 0.827 (95% CI: 0.763-0.893) for 24-2. For detecting fast progression, the AUCs were 0.707 (95% CI: 0.578-0.836) versus 0.853 (0.767-0.938), respectively.

Conclusions: SAP testing with the 24-2 pattern of points performed better than the 10-2 for detecting eyes with glaucomatous progression as determined by OCT.

CONTROL ID: 3713549

SUBMITTER (NAME ONLY): James Akula

TITLE: Background Adaptation, Stimulus Duration, and the ON and OFF Components of the Full-Field Photopic Flash Rat Electroretinogram

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the impact of light adaptation on the ON and OFF contributions to the amplitude of the photopic b-wave in the rat.

Methods: Electroretinograms (ERGs) were elicited from Long-Evans rats using 4–512 ms (5 durations) stimuli in the presence of 6–500 cd/m^2 (5 intensities) backgrounds. Stimuli were 3–518,240 cd/m^2. In respective sessions covering each of the 25 combinations of duration and background, nine flashes of increasing Weber contrast (0.5–1,036) were presented. To determine if an "equivalent background" could be measured, photopic b-waves were elicited in the dark, 800 ms after a 262 cd.s/m^2 conditioning flash (CF). The respective depolarizing (ON) and hyperpolarizing (OFF) components of each ERG were estimated by optimizing a sum of sigmoidal curves to the stimulus/response (SR) data at multiple timepoints along the ERG traces (Akula et al., 2019). Finally, b-wave amplitude SR data were fit with the Naka-Rushton (NR) equation to estimate the semisaturating intensity (σ).

Results: The b-wave SR function never displayed the "photopic hill" characteristic of the human response. Although it varied by session, across stimulus duration and background intensity, the respective mean maximal derived ON and OFF response was >200 and <40 μV. At fixed stimulus duration, the Weber contrast at σ was stable across background intensity. The "equivalent background" of the CF, assessed from σ, was ~290 cd/m^2.

Conclusions: First, in contrast to the human photopic ERG OFF response, which is of approximately equal amplitude to the ON, in rat the OFF response is <1/5th as large as the ON. This may have important implications for rat daytime vision and likely explains the lack of a rat "photopic hill" (notably, all human conditions characterized by a lack of photopic hill are believed to cause ON pathway deficits). Second, regardless of stimulus duration, amplitudes of the photopic b-wave and its constituent ON and OFF components are mediated by stimulus contrast rather than intensity. Therefore, accurate absolute calibration of photopic stimuli is of secondary importance to internal (i.e., relative) consistency, mitigating issues such as pupil size and instrumentation differences. Third, the value of the NR σ parameter can be used to determine equivalent background, such as for conditioning flashes, which may be of use in designing certain experiments into cone function.

CONTROL ID: 3713551

SUBMITTER (NAME ONLY): Ashley Rowe

TITLE: Ocular Characteristics and Disease Progression in a Preclinical Model of Batten Disease

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rowe, Y. Issioui, K.J. Wert, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|X. Chen, T. Dong, Y. Hu, S. Gray, Pediatrics, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|S. Gray, K.J. Wert, Molecular Biology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Batten Disease is a neurodegenerative genetic condition that presents with impaired vision in children before symptoms progress into motor loss, neurological deficits, and premature death. Recently, phase 1 human clinical trials at UT Southwestern Medical Center have begun to administer AAV9-CLN7 gene therapy to the intrathecal space of pediatric patients (NCT04737460). This gene therapy approach prolongs motor function and extends lifespan in a preclinical mouse model for human CLN7 Batten Disease (MGI:6388452); however, alternative approaches to directly target the retina are likely needed to rescue vision loss. We tracked the progression of vision loss and the overall ocular phenotype in this CLN7 knockout (KO) mouse model. Establishing how this preclinical model compares to the human condition allows it to be used to test preclinical efficacy and safety of gene therapy to address the visual deficits found in Batten Disease patients.

Methods: Retina function and morphology were analyzed in vivo in wild-type, heterozygous, and homozygous CLN7 KO mice. Scotopic and photopic electroretinography (ERG) recordings were taken at 2, 4, and 6 months of age. Ocular coherence tomography (OCT), infrared (IR) and autofluorescent (AF) imaging were analyzed at 3 and 5 months of age. Histological analysis of the eyes and retinal cells were analyzed throughout the study from 1 to 6 months of age.

Results: Live imaging of the CLN7 KO mouse model confirmed that it mimics the human Batten Disease clinical progression, showing a reduction in both a- and b-wave amplitudes by scotopic and photopic ERG and a thinning of the outer nuclear layer of photoreceptor cells along with their inner and outer segments. Both IR and AF imaging showed the vasculature attenuation and accumulation of autofluorescent puncta in the KO mice over time. Histological analysis detected a significant loss of the inner nuclear layer cells by 6 months of age, indicative of bipolar cell death seen in human patients but not previously detected in this preclinical model system.

Conclusions: Overall, our findings establish the clinical progression of vision loss and ocular disease in the CLN7 KO mouse model through 6 months of age, when the mice present with neurological deficits and premature death. These results establish the baseline for preclinical testing of therapeutic vectors to treat vision loss for Batten Disease using this CLN7 KO mouse model.

CONTROL ID: 3713552

SUBMITTER (NAME ONLY): Steffen Künzel

TITLE: Transcriptome analysis of the human choroid qualifies endothelial androgen responses as a disease driver for Central Serous Chorioretinopathy

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.E. Künzel, D.P. Frentzel, D. Pohlmann, L. Zur Bonsen, O. Zeitz, A. Joussen, Ophthalmology, Charite Universitatsmedizin Berlin, Berlin, Berlin, GERMANY|S.E. Künzel, A. Dubrac, Cell Biology, Universite de Montreal, Montreal, Quebec, CANADA|S.H. Künzel, Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Central Serous Chorioretinopathy (CSCR) is a pachychoroidal maculopathy that manifests by fluid accumulation between the neurosensory retina and the RPE. CSCR risk gene loci have been identified and there is clinical and experimental evidence that elevated levels of steroid hormones play a pivotal role in CSCR pathogenesis. Here, we investigate risk and steroid receptor gene expression patterns and their distribution across human choroid/RPE cell types. We aim to decipher potential mechanisms, that might explain the characteristic clinical findings in CSCR patients.

Methods: Query of scRNA seq data from human choroid/RPE: 15,300 sc transcriptomes from 14 samples: macula and peripheral from 7 donors. Unbiased clustering, dimensionality reduction and visualization using PCA, UMAP, tSNE. Counts per million (CPM) comparison: Mann-Whitney U test between donors, paired t-tests for comparison between mac. and perip. Correlation analysis: Pearson R with p-value adjustment by Benjamini-Hochberg. $p<0,05$ considered statistically significant.

Results: Three major results: (1) Expression of the CSCR risk genes PTPRB, CFH, CDH5, TNFRSF10A, ADAMTS9, and NR3C2 is precisely located to the choroidal endothelium, and vascular cell types – not to the RPE. (2) AR (androgen receptor) is significantly higher expressed in the macular endothelium compared to the periphery (expression ratio: er=1,736, p=0,0287). No differential expression was detected for GCCR (glucocorticoid rec.; er=1,317; p=0,0858), MCR (mineralocorticoid rec.; er=0,991; p=0,9172), and PGR (progesterone rec.; er=1,455; p=0,4939). (3) AR expression is positively correlated with CSCR risk gene expression, and with genes coding for VEGF signaling molecules. Among 244 significantly correlated genes, the strongest correlation was detected for RUNX1T1 (Pearson R= 0,096; adjusted p=0,003).

Conclusions: Our findings are a molecular hint that CSCR initially manifests in the choroidal vasculature, not in the RPE – and thus, should be understood as a vascular eye disease. Furthermore, this article puts androgen hormones in the center of the scientific attention. By illuminating a link to VEGF signaling - RUNX1T1 is a strong mediator of VEGF-A initated angiogenesis and permeability - we might also be able to propose a potential mechanistic explanation for this androgen hypothesis.

CONTROL ID: 3713554
SUBMITTER (NAME ONLY): Kuang-mon Ashley Tuan
TITLE: Population Ocular Topography Analysis Using Impression-Based Elevation Data
SESSION TITLE: Contact lens
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K.A. Tuan, Visioneering Technologies Inc, Georgia, UNITED STATES|K.A. Tuan, Mojo Vision, California, UNITED STATES|E. McDonald, C.W. Sindt, EyePrint Prosthetics, Colorado, UNITED STATES|C.W. Sindt, Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|
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ABSTRACT BODY:

Purpose: An ideal scleral lens fit will result a comfortable wear and minimize ocular complications. A successful scleral lens design starts with understanding the ocular topography of the wearer.

Methods: 997 (517 right eyes and 480 left eyes) EyeFit data from EyePrint Pro was analyzed. Ocular topography information was collected using impression-based technology. Scleral elevation data was exported every 10 degrees radially, starting 0.5mm outside of limbus up to 8mm (0.5mm step), which is roughly 30mm in diameter. Data was analyzed via elevation change measured perpendicular to the average limbal plane. Scleral steepness change was then calculated to evaluate the meridional symmetricity and the distribution of this population data is examined. In addition, the potential for successful interpolation and extrapolation of missing data is also assessed.

Results: On average, the eye is steeper at Superior and Temporal, flatter at Inferior and Nasal quadrants (Figure 1). Where Nasal is the flattest quadrant and Temple is the steepest. That means the nasal and temporal sag height differences increases as the chord length increases. As the distance from limbus increases, the range of the population distribution also widens (Table 1, AVG+/- SD). If the slope at adjacent chord length is similar, then a linear extrapolation is possible, but the zone for linear extrapolation is minimal for most eyes. If the slope at adjacent meridian is similar, an interpolation is possible without resulting in localized ridges; however, not all areas can be applied.

Conclusions: Ocular surface is not spherical; the shape becomes more aspheric and asymmetrical as it goes out from the limbus. The ocular shape also deviates from person to person making generalization difficult. A sclera landing zone accounting for the asymmetrical shape of individual eye will have the best outcomes and success.

CONTROL ID: 3713555

SUBMITTER (NAME ONLY): Yogapriya Sundaresan

TITLE: Dual mutational mechanism of the KIZ c.226C>T mutation as the cause of autosomal recessive retinitis pigmentosa

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Sundaresan, E. Banin, D. Sharon, Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|M. Ross, R. Ofri, Koret School of Veterinary Medicine, The Hebrew University, Rehovot, ISRAEL|

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ABSTRACT BODY:

Purpose: Mutations in the Kizuna (KIZ) gene, that encodes the centrosomal protein Kizuna, have been reported to cause autosomal recessive retinitis pigmentosa (ARRP), including a nonsense mutation (c.226C>T, p.R76*), located in exon 3. There is currently no approved treatment for KIZ-associated disease. Our aim is to characterize the expression pattern of KIZ in patient-derived skin fibroblasts as well as in normal mouse and sheep retinas by a novel method of alternative splicing analysis of RNA using next generation sequencing (NGS).

Methods: Skin biopsies were procured from four controls and three RP patients homozygous for KIZ-c.226C>T. In addition, retinas dissected from normal mice (n=6) and sheep (n=1) were included in the analysis. Primers for RT-PCR and NGS amplifying exons 2 to 5 were designed using Primer3. Following NGS, the aligned BAM files were analyzed using Integrative Genomics Viewer (IGV). In addition, potential exonic splicing enhancer (ESEs) sites were determined in WT and mutant human sequence using ESEFinder 3.0.

Results: RT-PCR and NGS-based analyses of RNA isolated from primary fibroblasts of patients and controls revealed the presence of four different transcripts: (i) the full-length transcript, (ii) skipping of exon 3, (iii) skipping of exon 3 and inclusion of an alternative exon, and (iv) skipping of both exons 3 and 4. Subsequent analysis of the expression pattern in the mouse and sheep retinas identified only two transcripts: (i) the full-length transcript and (ii) skipping of exon 4. The analyses revealed a lower expression level of the full-length transcript in patients compared to control (22% versus 58%). ESE analysis identified a 7 bp long sequence that includes the c.226 position with a higher score for the human WT sequence (4.411) compared to the mutant sequence (2.694).

Conclusions: KIZ- c.226C>T is a relatively frequent cause of ARRP in the Jewish population. Our data indicate that this variant might affect a putative ESE, that results in pronounced skipping of exon 3. Therefore, mutation-specific therapies, such as readthrough therapy and RNA editing, might show lower than expected efficacy since many transcripts do not contain this mutation. The KIZ nonsense variant is one of the few IRD mutations reported to affect an ESE, but we predict that ESE-affecting mutations are more common and need RNA-based analyses to be identified.

CONTROL ID: 3713556

SUBMITTER (NAME ONLY): Hongmin Yun

TITLE: SARM1 protects the cornea from sensory nerve degeneration and persistent severe inflammation in murine Herpes Stromal Keratitis (HSK)

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Yun, K.L. Carroll, A. St. Leger, Ophthalmology, Eye and Ear Institute, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: HSK is a blinding corneal disease caused by herpes simplex virus type 1 (HSV-1) infection, which manifests in both humans and mice as corneal opacity, neovascularization, and hypoesthesia. The replacement of corneal sensory nerves with sympathetic nerves in murine HSK plays a central role in maintaining the severe and persistent inflammation in the cornea. Here, we identify sterile apha and TIR motif containing 1 (SARM1) as a host factor that is critical for maintaining corneal nerve homeostasis after HSV-1 infection. Conventionally, SARM1 is expressed in neurons and is responsible for axonal degradation after insult or injury. In this study, we provide evidence that SARM1 acts intrinsically on immune and neuronal cells to prevent HSK.

Methods: SARM1$^{-/-}$ and litter mate wild-type (WT) mice were infected with HSV-1 KOS strain and were monitored for corneal opacity, neovascularization, and blink reflex. SARM1 gene expression in various tissues was assessed by qPCR. At 7dpi and 14 dpi, immune cell infiltration of the cornea was measured by flow cytometry. To assess the intrinsic effect of SARM1 on monocytes, BM derived myeloid cells were infected with HSV-1 KOS and were assayed for inflammatory factors using flow cytometry and metabolic activity using a Seahorse X_{FP}. Differences in nerve architecture were measured using corneal whole mounts and immunohistochemistry.

Results: SARM1$^{-/-}$ mice developed more severe corneal pathology, lost corneal sensitivity, and showed more disrupted corneal nerves compared to WT controls. After HSV-1 infection, SARM1$^{-/-}$ BM derived monocytes were more metabolically active and expressed more vascular endothelial growth factor (VEGF-A) and iNOS compared to WT BM monocytes. Similarly, monocytes from SARM1$^{-/-}$ corneas expressed more VEGF after HSV-1 infection compared to WT corneas. Finally, superior cervical ganglia, the source of sympathetic nerves, were larger in size in SARM1$^{-/-}$ compared to WT mice.

Conclusions: Together, our data reveal that SARM1 is a host factor responsible for suppressing HSK. Specifically, SARM1 appears to act on immune cells by regulating inflammatory mediators in myeloid cells after HSV-1 infection. Additionally, SARM1 also appears to restrict the growth of sympathetic nerves after infection. Therefore, we conclude that due SARM1 may be key factor in determining susceptibility pathology associated with HSK.

CONTROL ID: 3713557

SUBMITTER (NAME ONLY): Cindy Hoppe

TITLE: Targeting the alternative complement pathway as a neuroprotective therapy in glaucoma and optic nerve injury

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hoppe, Y. Guo, M. Shrestha, B. Verma, M.S. Gregory-Ksander, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|C. Hoppe, Y. Guo, M. Shrestha, B. Verma, K.M. Connor, M.S. Gregory-Ksander, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|K.M. Connor, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accumulating evidence from both human and animal models of glaucoma implicates the classical complement pathway as an important mediator of neuroinflammation and glaucomatous neurodegeneration. However, the alternative complement pathway mediates amplification of the complement pathway and has recently been implicated in driving inflammation and propagating injury in experimental models of spinal cord injury and brain injury, where specifically inhibiting the alternative pathway significantly reduced the extent of neurodegeneration. Herein we examine whether specifically inhibiting the alternative pathway is neuroprotective in experimental models of glaucoma and optic nerve injury.

Methods: Intracameral injection of magnetic microbeads (control: saline) was used to elevate the intraocular pressure (IOP) in complement factor B knockout mice ($Fb^{-/-}$, deficient in the alternative complement pathway), complement component 3 knockout mice ($C3^{-/-}$, deficient in all three complement pathways), and wild type (WT) mice. The optic nerve was crushed (ONC) approximately 2mm behind the globe with jeweler's forceps for 10 seconds. Visual acuity was measured by optomotor reflex (OMR). RGC density was quantified in retina whole mounts stained with a RGC-specific anti-Brn3a antibody. The nerve fiber layer (NFL) thickness was analyzed by spectral domain coherence tomography.

Results: IOP was increased equally in microbead injected $Fb^{-/-}$, $C3^{-/-}$ and WT mice as compared to saline controls. At day 35 post-microbead injection, visual acuity was significantly reduced in WT mice (0.37 ± 0.03 cyc/deg to 0.29 ± 0.04 cyc/deg, $p<0.001$) while no significant loss was observed in $Fb^{-/-}$ mice (0.39 ± 0.03 cyc/deg to 0.36 ± 0.03 cyc/deg, $p>0.05$) or $C3^{-/-}$ mice (0.35 ± 0.03 cyc/deg to 0.34 ± 0.04 cyc/deg, $p>0.05$). A significant thinning of the NFL and significant reduction in RGC density was also detected in microbead injected WT mice, but not $Fb^{-/-}$ mice. Similar results were observed following ONC, with $Fb^{-/-}$ mice displaying a significant increase in RGC survival at two weeks post ONC when compared to WT mice.

Conclusions: Our data shows that specifically inhibiting the alternative complement pathway is neuroprotective in mouse models of glaucoma and ONC, revealing the importance of the alternative pathway in the pathogenesis of glaucoma and optic nerve injury and introducing a potential new neuroprotective treatment.

CONTROL ID: 3713558

SUBMITTER (NAME ONLY): Valeria Marigo

TITLE: Molecular analyses of two novel mutations in Rhodopsin causing Congenital Stationary Night Blindness

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Marigo, A. Bighinati, A.N. Felline, F. Fanelli, Life Sciences, Universita degli Studi di Modena e Reggio Emilia, Modena, Emilia-Romagna, ITALY|G. Manes, B. Bocquet, Institut des Neurosciences de Montpellier, INSERM U1051, FRANCE|

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ABSTRACT BODY:

Purpose: Congenital Stationary Night Blindness (CSNB) is a heterogeneous inherited group of retinal disorders characterized by a non-progressive photoreceptor degeneration leading to poor vision at night (nyctalopia), decreased visual acuity, myopia and nystagmus. The inherited causes of CSNB include mutations in the Rhodopsin (RHO) gene. Specifically, the substitution of Gly in position 90 of RHO with Asp was associated to the autosomal dominant form of CSNB. We found two new RHO mutations in patients diagnosed with CSNB. Since dominant mutations in RHO cause also Retinitis Pigmentosa (RP) and are characterized by the retention of the protein in the Endoplasmic Reticulum (ER), we evaluated the structural effects of the two new CSNB mutations and assessed the chaperon effect of retinal.

Methods: The structural effects of the new RHO mutations were investigated by equilibrium and steered molecular dynamics (MD) simulations by the CHARMM force field. In vitro analyses were performed in COS7 cells transiently transfected with cDNA of WT or mutant RHO for subcellular localization of mutant RHO and the potential chaperon-like effect of 11-cis-retinal.

Results: The in vitro analysis in COS7 cells highlighted a different behavior of the two CSNB RHO mutants. One mutation caused some retention in the ER of the opsin protein. Administration of 11-cis-retinal reduced the ER retention to the native opsin levels. The second mutant showed a similar distribution in the cellular compartments compared to the wild type protein. Interestingly, when exposed to 11-cis-retinal a marked reduction of membrane localization and increased ER retention were detected. The computational model could predict the effects of the two mutations on ER retention in the presence of 11-cis-retinal. Moreover, MD analysis highlighted a structural communication between mutation sites and the visual arrestin binding regions.

Conclusions: Consistent with in silico analysis, the two new mutations found in CSNB patients showed a different in vitro behavior in their ER-retention. In this respect, the first mutant could fall in the same cluster, cluster 2, of adRP RHO mutants (Behnen et al, iScience 2018). The second mutant appeared to be destabilized by 11-cis-retinal binding. In their opsin state, both mutants could be affected in visual arrestin binding.

CONTROL ID: 3713561

SUBMITTER (NAME ONLY): Timing Liu

TITLE: Association between retinal fractal dimension and schizophrenia

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Liu, S. Wagner, M. Cortina-Borja, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|E. Trucco, M. Rama Krishnan Mookiah, University of Dundee, Dundee, Dundee, UNITED KINGDOM|A.K. Denniston, University Hospitals Birmingham NHS Foundation Trust, Birmingham, Birmingham, UNITED KINGDOM|S. Wagner, R. Struyven, J. Rahi, A. Petzold, P.A. Keane, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Psychotic disorders, such as schizophrenia, are associated with increased cardiovascular morbidity and, increasingly, neurovascular impairment. Retinal fractal dimension (FD) is a geometric index of complexity associated with neurovascular pathology. In this study, we sought to evaluate the association between schizophrenia and retinal FD and investigate the effect of other comorbidities on this association.

Methods: A hospital-based retrospective cohort study of 96,995 patients, of which 676 had schizophrenia, was run at a tertiary ophthalmic institution in London, United Kingdom. Retinal FD was extracted from macular-centered color fundus photographs using the Vascular Assessment and Measurement Platform for Images of the Retina. Multivariable linear regression evaluated the association between retinal FD and schizophrenia adjusting for age, sex, hypertension and diabetes mellitus.

Results: Patients with schizophrenia were younger (63.2 +/-12.4 versus 68.3 +/- 12.5 years of age, $p<0.001$) and more likely to be diabetic (73.5% versus 47.3%, $p<0.001$) but there was no significant difference in sex or hypertension distribution. Retinal FD was 1.51 +/- 0.03 for both patients with schizophrenia and without. When stratifying by diabetic status, retinal FD was not different ($p=0.11$) between diabetic patients with schizophrenia and those without. However, retinal FD was significantly reduced ($p=0.004$) in non-diabetic patients with schizophrenia. Adjusting for age, sex, hypertension and diabetes mellitus, schizophrenia remained associated with reduced retinal FD (beta coefficient= -0.0034, 95%CI: -0.0057, -0.0012, $p=0.003$). However the main effect was neutralized when incorporating interaction between DM and schizophrenia (schizophrenia $p=0.41$, interaction $p=0.004$).

Conclusions: Retinal FD is reduced in people with schizophrenia but this association was significant only for non-diabetic individuals. This indicates the compound effect of diabetes and schizophrenia on cerebral vasculature. The strong association between retinal FD and schizophrenia indicated the potential utility of using retinal FD as an economic and accessible marker for neurovascular impairment in non-diabetic patients with schizophrenia.

CONTROL ID: 3713562

SUBMITTER (NAME ONLY): Patience Moseley

TITLE: Gene Expression Changes in Two Distinct Rhodopsin Mutant Zebrafish

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Moseley, J.M. Fadool, Program in Neuroscience, Florida State University, Tallahassee, Florida, UNITED STATES|P. Moseley, S.K. Sheikhbahaei, J.H. Dennis, J.M. Fadool, Biological Science, Florida State University, Tallahassee, Florida, UNITED STATES|S.K. Sheikhbahaei, Cell and Molecular Biology Program, Florida State University, Tallahassee, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to characterize retinal gene expression changes that occur in CRISPR-induced rhodopsin zebrafish mutant, rho^{fl9} which contains a non-sense mutation at codon 347 (pS347*), eliminating the conserved VXPX C-terminal targeting signal. (Zelinka et al., 2018). We previously showed that zebrafish heterozygous for the rho^{fl9}allele display opsin mislocalization, rapid rod degeneration but no secondary effect on cones — a similar phenomenon was observed in XOPS-mCFP transgenic zebrafish (Morris et al., 2011). We predicted that the gene expression profile in rho^{fl9} would reflect dramatic downregulation of rod phototransduction genes but upregulation of genes associated with rod regeneration.

Methods: Total RNA was extracted from retinas of age-matched wild-type and rho^{fl9} adult zebrafish. Gene expression profiles produced from RNAseq were used to determine differentially expressed genes, and pathway analysis was used to identify the relevant biological pathways. Cell proliferation was assessed by EdU labeling.

Results: RNAseq counts yielded 15,401 genes; expression of 1,413 genes was significantly different from wild-type. As expected, these data show decreased expression of rod-associated genes, including many disease-associated genes. As anticipated, increased expression of cell cycle-associated genes was observed, but no changes in genes expressed by cones were observed. Initial pathway analyses indicated that significantly down- and upregulated genes are involved in regulating phototransduction, cell mitosis, and photoreceptor specification. When compared to expression data from XOPS-mCFP zebrafish, the pathway outputs were nearly identical. For both mutants, the top downregulated genes consisted of rod-associated genes, while the top upregulated were involved in cell cycle control and neuronal differentiation. EdU immunolabeling on rho^{fl9} adults confirmed the increase of mitosis of rod progenitor cells, but no Müller glia were labeled.

Conclusions: These data characterize gene expression changes that occur in the rho^{fl9} retina. The similarities found between two distinct rod degeneration models suggest that genetic manipulations leading to rod degeneration evoke a predictable pattern of gene expression consistent with a persistent cycle of rod degeneration, regeneration and degeneration. These tools provide genetic models to better understand persistent rod death and degeneration-induced regeneration.

CONTROL ID: 3713565

SUBMITTER (NAME ONLY): Nicole Ross

TITLE: Exploring Smartphone Visual Assistive Applications in Seniors with Low Vision

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ross, J.K. Ho, A.G. Malkin, M. Knizak, B. Peterson, C. Idman-Rait, Specialty and Advanced Care, New England College of Optometry, Boston, Massachusetts, UNITED STATES|M. Estabrook, M. Chun, A.K. Bittner, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|C. Bradley, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Smartphones are becoming increasingly utilized by older adults with low vision, and an increasing number of visual assistive smartphone apps are available at no or little cost. We explored the effect these apps may have on visual ability for seniors with low vision.

Methods: Seniors naïve to the study apps, with a score >20 on the telephone interview of cognitive status (TICS), aged 55+ (mean 72; SD 10 years) and ETDRS visual acuity (VA) better than 1.3 logMAR (n=33, enrollment ongoing) were randomized to one of three study apps (Supervision+ for magnification; SeeingAI for optical character recognition; Aira for remote visual description). Subjects were provided training upon dispense of a loaner iPhone SE with the study app and again at 2-weeks. App proficiency was evaluated, phone use was monitored via Verizon mobile device management and questionnaires were administered at baseline and 3 months post-intervention: activity inventory (AI), Beck depression inventory (BDI), UCLA loneliness scale, and general self-efficacy scale. We applied the method of successive dichotomizations, a polytomous Rasch model, to estimate person measures from the AI pre- and post-intervention, using calibrated item measures and thresholds. Multiple linear regression was used to determine which factors influenced change in AI person measures.

Results: The majority of subjects were white (70%), college graduates (76%), had macular disease (45%) and were male (56%), with a mean (SD) VA of 0.64 (0.33) logMAR, and CS of 1.01 (0.49) logCS. Mean (SD) baseline AI person measures was 0.07 (1.0) logits, and post-intervention the AI change score was 0.41 (0.67) logits. The majority of subjects (69%) showed improvement in visual ability in each of the AI domains: goals, reading, visual motor, visual information and mobility. Baseline BDI score ($p=0.004$), baseline loneliness score ($p=0.007$), and use of the study phone within the past month ($p=0.03$) were significantly associated with greater AI change scores ($R^2=0.50$). Self-efficacy, TICS, VA, app proficiency, and demographics were not significantly related to AI change scores post-intervention (all $p>0.05$).

Conclusions: Use of visual assistive apps may improve visual ability in seniors with low vision. These results indicate that these interventions should be considered as part of the rehabilitation plan.

CONTROL ID: 3713568

SUBMITTER (NAME ONLY): Ankita Kotnala

TITLE: Lipid localization and identification in human retina with subretinal drusenoid deposits (SDD) using LC-MS/MS and MALDI-IMS

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kotnala, D.M. Anderson, K.L. Schey, Vanderbilt University, Nashville, Tennessee, UNITED STATES|A. Kotnala, J. Messinger, C.A. Curcio, Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S. Tortorella, Molecular Horizon Srl, Via Montelino 30, 06084 Bettona, Perugia, ITALY|

Commercial Relationships Disclosure: Ankita Kotnala: Commercial Relationship: Code N (No Commercial Relationship) | David Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Sara Tortorella: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Messinger: Commercial Relationship: Code N (No Commercial Relationship) | Christine Curcio: Commercial Relationship(s);Code F (Financial Support):(CAC) research funding from Genentech/ Hoffman La Roche and Regeneron;Code I (Personal Financial Interest):CAC is a stockholder of MacRegen Inc | Kevin Schey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The molecular characterization of extracellular deposits (drusen, SDD, basal laminar deposit) is crucial for understanding the clinical progression of AMD. Ample evidence supports a role of lipids and associated pathways in forming extracellular deposits, including SDD. Combining powerful analytical tools of Matrix Assisted Laser Desorption Ionization Imaging Mass Spectrometry (MALDI IMS) and liquid chromatography tandem mass spectrometry (LC-MS/MS) provides spatially resolved lipid identifications. The purpose of this study is to localize lipids using imaging mass spectrometry (IMS) and identify them using LC-MS/MS, in human eyes with SDD.

Methods: Fixed retina tissue from two deceased donors (>80 years age) with SDD was sectioned to 12-14 µm thickness and placed on indium-tin-oxide slides for IMS experiments. MALDI matrix was applied by sublimation and images were acquired at 10-15 µm spatial resolution using a Bruker timsTOF Pro instrument. Data were analyzed with FlexImaging and SCiLS software. For nano LC-MS/MS analysis, sections of retina with SDD were manually removed from the slides under a dissecting microscope. Lipids were extracted with MMC (MeOH/MTBE/CHCl3) solvent mixture. In-house packed reverse phase columns (20 cm X 75 µm) were packed with 1.9 µm BEH C18 material. nLC-MS/MS was performed using an EASY-nLC 1000 (Thermo Scientific) coupled to a Q-Exactive HF instrument (Thermo Scientific). LC-MS/MS and MALDI-IMS data were interpreted using MS DIAL-4 and LipostarMSI software.

Results: Five phosphatidic acids (PA (30:0), PA (32:1), PA (32:0), PA (38:6), PA (40:2), 5 phosphatidyl ethanolamines (PE (18:0), PE (40:6), PE (34:1), PE (40:7), PE (38:6), 4 phosphatidylcholines PC(O-32:2), PC (36:3), PC (32:2), PC (40:3), 1 diacylglycerol (DG (38:8) and 1 phosphatidylinositol PI-Cer(38:0) were localized specifically in SDD and tentatively identified using accurate mass measurements from MALDI-IMS in negative ionization mode. Further studies are ongoing to confirm these identities using LC-MS/MS.

Conclusions: Lipid signals were localized to SDD in human retina samples using IMS and are being characterized using LC-MS/MS. Further identifications of lipids in eyes with SDD could help elucidate how lipids are involved in the formation of this extracellular deposit in AMD.

CONTROL ID: 3713569

SUBMITTER (NAME ONLY): SARA AISSATI

TITLE: Investigating the factors limiting visual acuity at different wavelengths.

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. AISSATI, S. Marcos, Instituto de Optica, Consejo Superior de Investigaciones Científicas (IO-CSIC), SPAIN|P. Bharadwaj, E. Slezak, X. Jiang, S. Schleufer, R. Sabesan, Department of Ophthalmology, University of Washington, Washington, UNITED STATES|S. Schleufer, Department of Neuroscience, University of Washington, Seattle, Washington, UNITED STATES|S. Marcos, Center for Visual Science. The Institute of Optics. Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual performance across the visible spectrum is limited by many factors, including monochromatic & chromatic aberrations,differences in spectral sensitivity across cone types, and post-receptoral processing of spatial & chromatic contrast.We sought to investigate the interplay between these factors using a combination of adaptive optics(AO) psychophysics & computational modeling

Methods: Four cyclopleged subjects were measured in a tumbling ‘E-letter’ visual acuity(VA)4AFC experiment under dynamic AO correction.The visual display consisted of a digital micromirror device (DMD) & two LEDs 427±13nm & 630±16nm(luminance for both=5.7cd/m2).Subjects set subjectively the best focus at each tested wavelength.VA was measured under 4 different stimulus conditions with variations in spatial & chromatic contrast: black ‘E’ on either a blue and red background (BKG); red ‘E’ on blue BKG and blue 'E' on red BKG.These conditions were also simulated using ISETBio(Image Systems Engineering Toolbox for Biology)computational pipeline.The simulations incorporated the effects of the calibrated display,human eye’s optics,absorption by the anterior segment of the eye,macular pigment & cone photoisomerizations.To verify the relative contributions of spatial(L+M modulation) & chromatic(L-M modulation) contrast to the visual task, these were calculated from the resultant cone photoisomerizations

Results: VA improved as expected in all conditions after correcting HOAs.The mean LogMAR VA with AO was -0.20±0.04 & -0.06±0.02 for monochromatic red and blue BKG respectively.The mean VA with AO was -0.17±0.05 & 0.03±0.02 for polychromatic targets(red ‘E’ on blue BKG,and vice-versa respectively).The improvement was typically lower for blue letters (11%) compared to red (16%).Simulations verified that once optical aberrations are removed with AO,VA was better under conditions where both spatial & chromatic contrast were high,i.e.the red letters.Conversely,VA was poorer when either of the contrasts were low, for eg.,the monochromatic blue target where the spatial and the chromatic contrast were high(>95%) & low(<10%) respectively

Conclusions: A combination of AO psychophysics experiments and ISETBio simulations enabled us to understand the factors limiting VA at different wavelengths.Similar experimental & modeling platforms,paired with ideal observer analysis,may give insights on the optical,retinal & neural limitations to spatial & chromatic vision

CONTROL ID: 3713570

SUBMITTER (NAME ONLY): Hossein Nazari Khanamiri

TITLE: Evaluation of neurovascular changes in retinal sublayers reveals differentiable retinal degeneration in Alzheimer's disease as compared natural aging

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.K. Nazari Khanamiri, Ophthalmology and Visual Neuroscience, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|M. Montalbano, W. Zhang, M. Motamedi, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retina is a visible extension of the brain that may reflect brain neurodegeneration caused by Alzheimer's disease (AD) and natural senescence. The spatial distributions of neurons, glial, and vasculature, which may be afflicted at different stages of a neurodegenerative process, vary in retinal sublayers. Thus, we aimed to characterize and differentiate the spatial and temporal distribution of AD- versus senescence-induced neuronal and vascular changes of the retina based on immunohistochemistry and optical coherence tomography (OCT) studies in the triple transgenic mouse model of AD (3xTg-AD).

Methods: The retina’s superficial (SVP), middle (MVP), and deep (DVP) vascular plexuses were studied in young (2 months old-M) to middle-aged (14M) and old (18-20M) 3xTg-AD and C57bl/6j mice. Amyloid-β (Aβ) and phosphorylated-tau (ptau) deposition were characterized in retinal and brain samples from 4M, 8M, and 12M animals. Retinal sublayer thicknesses were analyzed in annular OCT scans and retinal ganglion cells (RGCs) were quantified in retina flat-mounts in 2M to 12M transgenic and control mice.

Results: Progressive deposition of Aβ and ptau was detected in the retina (4M) before the brain (8M). Vascular attenuation and RGC loss occurred with AD pathology and natural aging; however, RGC loss was more significant in 8M and 12M 3xTg-AD compared to old controls ($p=0.0426$ and $p=0.0002$, respectively). SVP and DVP, but not MVP, attenuation differentiated old 3xTg-AD from old controls ($P<0.05$). The retinal nerve fiber layer (RNFL), but not ganglion cell layer (GCL), thickness decreased (linear regression, $p=0.0002$) as 3xTg-AD mice aged.

Conclusions: In our animal models, the retina manifests AD pathologies before the brain. Various degrees of AD-induced neurovascular coupling dysfunction within the retina layers can be monitored and quantified as biomarkers of AD progression using noninvasive OCT and OCTA approaches. Retinal neurovascular (NV) biomarkers may differentiate AD-neurodegeneration from neurodegeneration caused by natural aging. More specifically, GCL thickening by neuroinflammation and NV dysfunction (trophic changes) may nullify the thinning effect caused by RGC loss (atrophic changes) in AD but not in natural aging. In contrast, the hypocellular RNFL is less affected by the trophic effects of neuroinflammation and NV dysfunction.

CONTROL ID: 3713572

SUBMITTER (NAME ONLY): Sailie Shirodkar

TITLE: Biomarkers from clinic deployable, multiplex, diagnostic test stratifies ocular surface disease and sub-clinical inflammation in patients.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Shirodkar, R. Shetty, A. Nair, P. Khamar, S. Sethu, A. Ghosh, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: The pathology of most ocular conditions is driven by a number of known molecular pathways. However, targeted management requires tear-based, rapid, multiplexed diagnostic systems in the clinical setting. We deployed such a system that measures 8 soluble factors in the cornea clinic to stratify patients based on correlations between clinical indices and biomarker levels

Methods: We tested tear samples collected from 621 eyes categorised clinically into controls(n=214), dry eye disease(DED; n=107), Keratoconus(KC; n=125) based on slit lamp examination, ocular surface disease index(OSDI) scoring, dry eye evaluation and ocular surface staining. Tear fluid collected using Schirmer's strips were evaluated for soluble factors on a customised multiplex ELISA platform (Bio-M Pathfinder). Another group of clinically healthy subjects were further stratified into – sub-clinical inflammation (SCI) groups 1(n=95) and 2(n=80) based on the level of biomarkers and correlation to clinical indices.

Results: Patients with DED showed significantly higher OSDI scores, MMP9, IL6, TNFα, IL1β, IL17A and sICAM1 levels with reduced Schirmer's test and TBUT values. KC eyes showed significantly higher MMP9 levels. IL10 and VEGF levels remained unchanged across the conditions. SCI-1 and SCI-2 groups had significantly higher inflammatory markers, significantly reduced Schirmer's and TBUT levels which were not low enough to be clinically classified as DED. Inflammatory biomarker detection was successful in all cases with good reproducibility, high sensitivity and specificity.

Conclusions: Clinical usage of a rapid, biomarker platform is feasible and useful to identify subjects with sub-clinical inflammation, helping stratify subjects for customised treatments and surgery.

CONTROL ID: 3713576

SUBMITTER (NAME ONLY): Arshad Khanani

TITLE: Suprachoroidal Delivery of RGX-314 Gene Therapy for Neovascular AMD: The Phase II AAVIATE™ Study

SESSION TITLE: AMD Translational Research

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|A.M. Khanani, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|

Commercial Relationships Disclosure: Arshad Khanani: Commercial Relationship(s);Code F (Financial Support):Adverum, Apellis, Asclepix, Chengdu Kanghong, 4DMT, Dutch Ophthalmic Research Center, Gemini, Genentech, Graybug, Gyroscope, Iveric Bio, Janssen, Kodiak, NGM Bio, Ocular Therapeutics, Oculis, Opthea, Novartis, Recens Medical, Regenxbio, Roche, UNITY Bio;Code C (Consultant/Contractor):Adverum, Allergan, Apellis, Asclepix, Aviceda, Bausch and Lomb, BroadWing Bio, Chengdu Kanghong, Cholgene, 4DMT, Dutch Ophthalmic Research Center, Gemini, Genentech, Glaukos, Graybug, Gyroscope, Iveric Bio, Janssen, Kato Pharma, Kodiak, Oculis, Opthea, Novartis, Polyphotonix, Recens Medical, Regeneron, Retrotope, Regenxbio, Roche, Surrozen, Thea, UNITY Bio;Code S (non-remunerative):Genentech, Allergan, Novartis;Code I (Personal Financial Interest):Aviceda, Gyroscope, Recens Medical, Retrotope, Polyphotonix

ABSTRACT BODY:

Purpose: Intravitreal anti-VEGF injections are approved to treat neovascular age-related macular degeneration (nAMD), yet real world evidence shows patients lose vision over time due to undertreatment. RGX-314 is designed as a single gene therapy intervention utilizing an adeno-associated virus 8 (AAV8) vector, to deliver an anti-VEGF fab transgene, potentially producing continuous anti-VEGF therapy in the eye. Initial data from the AAVIATE trial has provided encouraging evidence of RGX-314 as a potential treatment of nAMD using an in-office, suprachoroidal delivery.

Methods: AAVIATE is an open-label trial that will evaluate the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314 using the SCS Microinjector®. 20 patients in Cohort 1 and 20 patients in Cohort 2 were randomized to receive RGX-314 at a dose level of $2.5x10^{11}$ and $5x10^{11}$ genomic copies per eye (GC/eye), respectively, versus monthly 0.5 mg ranibizumab intravitreal injection at a 3:1 ratio. Cohort 3 is evaluating RGX-314 at the same dose level as Cohort 2 in 20 patients who are neutralizing antibody (NAb) positive. The primary outcome is the mean change in BCVA at 9 months. Secondary outcomes include safety, central retinal thickness (CRT), and additional anti-VEGF injections needed post-RGX-314.

Results: As of November 4, 2021, RGX-314 was well tolerated in 50 patients dosed in Cohorts 1-3. Four serious adverse events were reported in 4 patients, all of which were considered not related to RGX-314. For the total group of Cohorts 1 and 2, all common treatment emergent adverse events (TEAEs) through 6 months in the study eye were mild. Mild intraocular inflammation observed on slit-lamp examination in 7 of 30 patients (23%) was reported at similar incidence across both dose levels, and all cases resolved within days to weeks on topical corticosteroids. Patients dosed with RGX-314 in Cohorts 1 and 2 demonstrated stable BCVA and CRT at 6 months and had a meaningful reduction in anti-VEGF treatment burden (>70%). 4 of 14 patients (29%) and 6 of 15 patients (40%) in Cohorts 1 and 2, respectively, received no anti-VEGF injections over 6 months following RGX-314 administration.

Conclusions: Suprachoroidal RGX-314 has the potential to provide sustained clinical improvements in the treatment of nAMD with a one-time in-office treatment.

CONTROL ID: 3713577

SUBMITTER (NAME ONLY): Jinhai Huang

TITLE: Ultra-small cerium-based metal organic framework for reactive oxygen species scavengings and alleviation of dry eye disease

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, Fudan University, Shanghai, Shanghai, CHINA|Z. Chen, N. Tang, J. Yu, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|

Commercial Relationships Disclosure: Jinhai Huang: Commercial Relationship: Code N (No Commercial Relationship) | Zhongxing Chen: Commercial Relationship: Code N (No Commercial Relationship) | Nana Tang: Commercial Relationship: Code N (No Commercial Relationship) | Jinjin Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to explore the ability of Cerium-based Metal-organic Frameworks (Ce-MOF) nanoparticles to scavenge ROS and its application prospect in dry eye diseases (DED).

Methods: Three kinds of Ce-MOFs with different particle sizes were prepared by hydrothermal method, which were labeled Ce-MOF 1, Ce-MOF 2 and Ce-MOF 3, respectively. The phase structure, functional groups, morphology, particle size, Zeta potential, element composition and ROS scavenging ability of Ce-MOFs were characterized. Subsequently, the CCK-8 and ocular irritation test were used to determine the cytotoxicity. In H_2O_2-induced ROS model, the ability of cleaning out intracellular ROS in human corneal epithelial cell (HCEC) was tested. Finally, the effect of CeMOF 3 on mouse DED was evaluated by slit lamp observation, corneal epithelial staining.

Results: Three kinds of Ce-MOFs were obtained: 500 nm, 50 nm and 3 nm. The phase structure, functional group and thermal stability in Ce-MOFs show no significant difference. CeMOFs showed the concentration-dependent SOD-like and ROS scavenging activities. The cellular and ocular compatibility were confirmed. In HCECs, Ce-MOF 3 show greater antioxidant capacity which reduced ROS level. In the DED treatment, corneal epithelial defect was significantly reduced by Ce-MOF 3.

Conclusions: We had successfully constructed three kinds Ce-MOFs which own antioxidant enzyme and ROS scavenging activity in vitro. Further, the Ce-MOF 3 not only showed good biocompatibility, it also effectively alleviated DED. The new ultra-small Ce-MOF provides a new method for alleviating dry eye disease.

CONTROL ID: 3713578

SUBMITTER (NAME ONLY): Hao Wu

TITLE: Abl kinases regulate the lens vesicle closure

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Wu, Y. Mao, H. yu, X. Zhang, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Hao Wu: Commercial Relationship: Code N (No Commercial Relationship) | Yingyu Mao: Commercial Relationship: Code N (No Commercial Relationship) | honglian yu: Commercial Relationship: Code N (No Commercial Relationship) | Xin Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Incomplete separation of the lens vesicle from the surface ectoderm results in a persistent lens stalk between the lens and cornea, which clinically presents as adhesion between the cornea and the iris and/or lens in Peters anomaly (PA). This study aims to elucidate the Abl-Crk cellular signal network that regulates lens vesicle closure.

Methods: Mouse lines carrying floxed genes of interest were crossed with the lens-specific Le-Cre (Tg/-) to generate conditional knockouts. Embryos carrying expected genes were harvested and sectioned for histochemical analysis. Immunoprecipitation and immunoblotting were carried out using primary mouse embryonic fibroblasts (MEFs) and lens epithelium cells.

Results: Abelson murine leukemia viral oncogene homolog (Abl) and Abl related gene (Arg) mutants (Le-Cre;$Abl^{F/F}$;$Arg^{F/F}$, AblCKO) presented incomplete separation of the lens vesicle from the surface ectoderm as early as embryonic day 10. In vitro, viral expression of Cre recombinase caused $Abl^{F/F}Arg^{F/F}$ lens epithelium cells to scatter, losing their typical hexagon shape and adherens junctions. Heterozygous deletion of Abl substrates Crk adaptor proteins (Crk and its paralog CrkL) in the AblCKO mutants (Le-Cre;$Abl^{F/F}$;$Arg^{F/F}$;$Crk^{F/+}$;$CrkL^{F/+}$) can rescue the lens stalk phenotype in an allele copy-dependent manner, and homozygous deletion of Shp2 was able to rescue the phenotype with partial penetrance. The lens epithelium in AblCKO embryos showed elevated phospho-ERK. But homozygous Abl, Arg, and Erk1/2 quadruple knockout (Le-Cre;$Abl^{F/F}$;$Arg^{F/F}$;$Erk1/2^{F/F}$) embryos still possessed lens stalks. Only homozygous deletion of Rac1 in the AblCKO mutants (Le-Cre;$Abl^{F/F}$;$Arg^{F/F}$;$Rac1^{F/F}$) was able to fully rescue the lens stalk phenotype.

Conclusions: These genetic experimental results suggested that Crk and CrkL, as the direct substrates of Abl, serve as the linkage between Abl and the cell adhesion network. ERK1/2 and Rac1 abolition experiments demonstrated that Rac1, but not ERK, is the downstream effector of Abl in the lens-cornea separation.

CONTROL ID: 3713579

SUBMITTER (NAME ONLY): Benedetto Falsini

TITLE: Pattern Electroretinogram adaptation is abnormal in glaucoma suspect eyes

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Falsini, G. Placidi, T. Salgarello, A. Giudiceandrea, Institute of Ophthalmology, Fondazione Policlinico Universitario A. Gemelli IRCCS - Università Cattolica del Sacro Cuore, Roma, ITALY|M. Sulfaro, S. Paliotta, F. Amore, National Reference Centre Service, Research, Prevention of Blindness and Vision Rehabilitation WHO Collaborating Centre Fondazione Policlinico Universitario A. Gemelli IRCCS Università Cattolica del Sacro Cuore, Roma, ITALY|

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ABSTRACT BODY:

Purpose: A recent study [1] has shown that adaptive changes in the pattern electroretinogram (PERG adaptation) are altered in eyes with early manifest glaucoma, indicating reduced autoregulation and energy budget mechanism in affected eyes. The aim of this study was to evaluate PERG adaptation in glaucoma suspect (GS) eyes and to correlate the results with early anatomical changes in retinal ganglion cells (RGCs) and optic nerve fibers (ONF)

Methods: Twenty-one GS patients and 20 age-matched controls were included in the study. PERGs were recorded in response to 7.5 Hz counterphased horizontal bars (field size 50 x 60 °, 90% contrast) presented in 9 packets of 60 events each and alternated with an unmodulated uniform field. Trends of PERG amplitude and phase changes as a function of stimulus packets were measured with vector response analysis and linear regression statistics for amplitude values[1]. Regression coefficients and phase coherence were determined for each measure

Results: PERG adaptation was detected and significant ($p < 0.05$/$p < 0.01$) in all control subjects, with a mean decline as a function of packets of -3 microV/packet. PERG adaptation had a shallower negative slope in glaucoma suspects, compared to controls, with a mean decline of -0.46 microV/packet ($p < 0.01$). Regression coefficients and phase coherence were also reduced in GS patients compared with controls. No significant correlations were found between PERG adaptation parameters and RCG and ONF thickness of patients

Conclusions: In GS patients, the PERG adaptation is abnormal and not correlated with anatomical changes, suggesting that inner retina autoregulation and energy budget mechanisms are altered early,and independently of anatomical damage, in the disease process

CONTROL ID: 3713580

SUBMITTER (NAME ONLY): Megh Shah

TITLE: Utility of Remote Point-Of-Care Tele-Retinal Imaging for Screening and Diagnosis of Diabetic Retinopathy: A Pilot Study

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Shah, R. Henry, B. Szirth, N. Bhagat, Ophthalmology & Visual Science, New Jersey Medical School Division of Clinical Sciences, Newark, New Jersey, UNITED STATES|R. Henry, Rutgers Robert Wood Johnson Medical School New Brunswick, New Brunswick, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Megh Shah: Commercial Relationship: Code N (No Commercial Relationship) | Roger Henry: Commercial Relationship: Code N (No Commercial Relationship) | Bernard Szirth: Commercial Relationship: Code N (No Commercial Relationship) | Neelakshi Bhagat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the COVID-19 era, tele-retinal technologies are rising to the forefront of contactless ophthalmic care. Point-of-care Optical Coherence Tomography (OCT) and fundus photography remotely analyzed by an off-site retina specialist (tele-R) must be validated for screening retinal disorders. This study assesses the feasibility of tele-R as a screening tool for diabetic retinopathy (DR) in an outpatient clinical setting.

Methods: A retrospective study was conducted on 16 patients (32 eyes, 28 with DR, and 4 controls) presenting to the retina clinic (RC) of an urban academic medical center. Automated OCT-B and 45^0 fundus photographs of the posterior pole were taken using a Topcon Maestro 3D OCT-1 unit, and 3D topographical maps of the macula were generated. Images were transmitted to a remote retina specialist (blinded to patient history and demographics) who assessed severity of DR and diabetic macular edema (DME). Primary outcomes included grading of DR and DME with fundus and OCT-B images, respectively, using the International Clinical Diabetic Retinopathy classification scale. The secondary outcome was identifying the severity grade of DME using the 3D macular map. Concordance was tested between diagnoses obtained from tele-R assessment and in-person examination by the retina specialist (gold standard) using Cohen's Kappa statistic (κ). Eyes that could not be assessed were removed from analysis.

Results: 30 of 32 eyes with sufficient data for analysis were included. The average age was 57.9 (±11.2) years. 37% of patients were male, 69% were Hispanic, and 94% had Type 2 diabetes. The κ±standard error (SE) for DR severity was 0.738±0.099 ($p<0.001$), for DME severity was 0.588±0.122 ($p<0.001$), and for presence of DME was 0.727±0.122 ($p<0.001$). The retina specialist was able to grade the DME severity in only 10/14 (71%) eyes using the 3D macular map alone, but in 93% (13/14) eyes with OCT-B images.

Conclusions: Tele-R is a reliable modality for diagnosis of DR severity; there was substantial agreement on identifying DR severity using tele-R vs in-person examination. There was substantial agreement in discerning DME using tele-R vs in-person while only moderate agreement on determining the severity of DME, which suggests that tele-R may useful in identifying presence of DME but not determining the severity of edema.

CONTROL ID: 3713582

SUBMITTER (NAME ONLY): Mathieu Bakhoum

TITLE: Leveraging DNA methylation to provide accurate prognostication for patients with uveal melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.F. Bakhoum, Yale University, New Haven, Connecticut, UNITED STATES|M.H. Goldbaum, University of California San Diego, La Jolla, California, UNITED STATES|P.S. Mischel, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Mathieu Bakhoum: Commercial Relationship: Code N (No Commercial Relationship) | Michael Goldbaum: Commercial Relationship: Code N (No Commercial Relationship) | Paul Mischel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveal melanoma is the most common primary intraocular cancer in adults. Once uveal melanoma metastasizes, median patient survival is less than 18 months. Primary uveal melanomas with high metastatic tendencies differ from their more indolent counterparts in various ways. They are often monosomic for chromosome 3, frequently harbor mutations in the BAP1 gene and exhibit a distinctive gene expression signature. Single cell RNA sequencing of enucleated primary uveal melanoma tumors revealed that uveal melanomas with different metastatic tendencies are not fundamentally distinct disease subtypes, rather individual tumors harbored cells from both prognostic classes. Hence, prognostic tests that classify UM into two major groups lack the resolution to assess the diversity of an inherently heterogeneous tumor. We then asked whether DNA methylation of the different subclones could be employed to estimate the preponderance of aggressive subclones within an individual tumor, as DNA-methylation of a given genomic locus is a binary state.

Methods: Cell Cutlure, single-cell RNA sequencing, Infinium MethylationEPIC array, pharmacologic and genetic modulation of polycomb repressive complex 1 in uveal melanoma cell lines

Results: Using the Infinium MethylationEPIC array we found that uveal melanoma cells with aggressive features, MP38, had a distinctive methylome than their indolent counterparts, 92.1. We had recently demonstrated that loss of Polycomb Repressive Complex 1 induced a transcriptional and morphological transition from an indolent to an aggressive phenotype. We found that inhibition of Polycomb Repressive Complex 1 ligase activity using a small molecule inhibitor, PRT4165, induced global methylation changes in indolent uveal melanoma cells, 92.1, reminiscent of the methylome of aggressive uveal melanoma cells, MP38. We then sought to determine whether utilizing a methylation panel provides useful prognostic information. We identified the top 200 hypermethylated CpG loci in monosomy vs disomy 3 tumors in The Cancer Genome Atlas uveal melanoma cohort. We found that the higher the methylation values, the worse the prognosis.

Conclusions: In summary, our results indicate that high-risk and low-risk uveal melanoma cells can be distinguished by their methylome. This information can readily be translated into an actionable test to provide accurate prognostication.

CONTROL ID: 3713583

SUBMITTER (NAME ONLY): Helena Filipe

TITLE: Peptide-eluting contact lenses for an improved delivery of dexamethasone to the back of the eye

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To avoid the need of intraocular injections, several strategies have been investigated to improve the permeation of topical drug delivery to posterior segment of the eye, such as the use of peptides as drug carriers. Kyotorphin (L-Tyr-L-Arg) is a small endogenous neuropeptide, whose derivatives (e.g. $KTPNH_2$) were previously designed to increase membrane permeability. Penetratin (a 16-mer peptide) is a known cell penetrating peptide, which have been suggested as a carrier for drug delivery through many tissues, including the ocular membranes. Herein, the possibility of producing therapeutic contact lenses (CLs), loaded with either $KTPNH_2$, Penetratin or a dexamethasone-$KTPNH_2$ complex (Dex-$KTPNH_2$), was evaluated with the aim of increasing the delivery efficiency of dexamethasone to the back of the eye.

Methods: Hydrogels of HEMA-TRIS-NVP were investigated as potential CL backbone. Autodock software was used to model the molecular interactions between the monomers and the peptide and identify potential functional monomers. After polymerization, hydrogel discs ($N \geq 3$) were loaded by soaking in a peptide solution (1mg/mL). The effect of pre-soaking in a solution of vitamin E in ethanol was investigated to prolong the release time. Drug-release was performed in vitro in sink conditions. The swelling behavior and light transmittance of the hydrogels were tested prior and after loading.

Results: Molecular simulation suggested a strong interaction between acrylic acid (AAc) and the peptides. Therefore, AAc was incorporated in the prepolymer mixture as a functional monomer. The light transmittance of the hydrogels resulted higher than 90% at wavelengths above 500 nm. The peptide uptake and the swelling increased with the addition of AAc for all the tested molecules, while the presence of vitamin E was associated to a lower swelling. The pre-soaking in vitamin E and the presence of the functional monomer prolonged the release time of $KTPNH_2$ up to 8h. Unmodified HEMA-TRIS-NVP hydrogels were able to sustain the release of Penetratin or the Dex-$KTPNH_2$ complex for more than 24 hours (Figure 1).

Conclusions: The obtained results shall contribute for the development of new topical treatment forms, able to provide a therapeutic effect in the back of the eye without need of intraocular injections.

CONTROL ID: 3713584

SUBMITTER (NAME ONLY): Yoko Miura

TITLE: Dynamic OCT with retinal pigment epithelium-choroid tissue ex-vivo

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Miura, N. Kubota, M. Ahrens, G. Hüttmann, H. Schulz-Hildebrandt, Institute of Biomedical Optics, University of Lübeck, GERMANY|Y. Miura, Department of Ophthalology, University of Lübeck, GERMANY|T. Kohlfaerber, N. Kubota, Medical Laser Center Lübeck, GERMANY|M. Ahrens, M. Pieper, P. König, G. Hüttmann, H. Schulz-Hildebrandt, Airway Research Center North, Member of the German Center of Lung Research, GERMANY|M. Pieper, P. König, Institute of Anatomy, University of Lübeck, GERMANY|

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ABSTRACT BODY:

Purpose: Cellular and molecular activities in the RPE-Bruch's membrane (BrM)-choriod complex are essential for maintaining retinal function, and their abnormalities may cause the development of diseases such as age-related macular degeneration. Unlike the live-cell imaging of cell cultures, there has been no method to observe this complex in 3D with high temporal resolution. In this study, we observed response of RPE-BrM-choroid tissue to laser irradiation by high-resolution dynamic optical coherence tomography (dmOCT).

Methods: RPE-BrM-choroid explants were prepared from the freshly enucleated porcine eyes. A 577 nm microsecond pulsed laser (100 µm, 200 ms, 180-220 mW, duty cycle 10%) was used to apply very mild coagulation spots on the RPE. The explants were then maintained at 37°C in 5% CO_2. After 24 hours, the tissue was imaged with FD-OCT with microscopic resolution. Using a wavelength range from 580 nm to 930 nm of a supercontinuum light source, a COMS camera with up to 248 kHz line scan rate, and a 10x/0.3 NA microscope objective, 1.8 µm axial and 1.1 µm lateral resolution were achieved. For the dynamic contrast OCT, B-scans were measured at 108 Hz over 1.39 s and the amplitude of the OCT signal was Fourier transformed. The obtained spectra are displayed in RGB colors depending on the frequency band. The tissues were also assessed with the immunohistochemistry with macrophage markers (CD80, CD206).

Results: B-scan imaging with microscopic FD-OCT allowed clear recognition of individual RPE cells, BrM, and choroidal vessels. The volume scan enabled reconstruction of the en face image with dynamic contrast, showing the fast frequency at the wound edge of the laser spots. In the B-scan time series, a number of fast moving signals with diameters of 5-10 µm were observed in the apical space of the RPE as well as in the choroidal vessels. These migratory cell-like signals were particularly concentrated at laser spots and some of them were observed to move from the choroidal vessel to the apical side of the RPE through the RPE cell gap. Immunohistochemistry confirmed the presence of macrophages in the choroidal vessels.

Conclusions: The high-resolution dmOCT allows 4D-analysis of RPE-BrM-choroid tissue at the cellular level with dynamic contrast information. Time-series of B-scan images is useful to observe the tissue dynamic changes over time and the behavior of migratory cells like macrophages at the RPE and surrounding tissues.

CONTROL ID: 3713585

SUBMITTER (NAME ONLY): Frederick Afum Asare

TITLE: Effect of varying levels of optical blur on performance of a Hazard Perception Test for driving

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Appropriate detection of, and reaction to, hazards are important components of safe driving, and for drivers with reduced vision, this skill can become compromised. However, the level of blur that significantly impairs hazard perception performance has not been fully determined. This study examined varying levels of optical blur and their effect on response time to hazards during a computer-based Hazard Perception Test (HPT).

Methods: Five healthy drivers aged 24-56 years with a binocular visual acuity <0.00 LogMAR (range: -0.18 to -0.22 LogMAR) undertook 14 computer-based HPT assessments. These high-quality, first-person CGI video clips require viewers to respond to real-world hazards and are used by the UK Driver and Vehicle Licensing Agency to assess hazard perception performance in learner drivers. The HPT tasks were undertaken with participants being optimally corrected for the viewing distance and with optical blur induced using +1.00, +2.00 and +3.00-diopter spherical lenses. Baseline and blur testing were conducted over four visits with blur levels and video clips being randomized to minimize memorization effects. Participants' response time to hazards was collected with a Cedrus RB540 response box. Data were analysed using a two-factor repeated measures ANOVA and post-hoc pairwise comparisons of means with Holm-Bonferroni correction as appropriate.

Results: The mean visual acuity at baseline, and with +1.00, +2.00 and +3.00-diopter spherical lens was -0.20±0.02, 0.04±0.12, 0.47±0.09 and 0.69±0.1.00 LogMAR respectively. Compared to baseline (1.40±0.16s), response time was significantly ($p<0.001$) delayed by the introduction of a +3.00-diopter lens (mean difference: 0.78s, 95% CI:0.30-1.24). The +2.00-diopter and +1.00-diopter blur lenses delayed responses by 0.40±0.20s (95% CI:-0.06-0.85) and 0.14±0.20s (95% CI:-0.34-0.61) respectively, but these differences were not statistically significant (both $p>0.05$). There was no statistically significant interaction effect of optical blur and hazard perception video type on response time ($p=0.99$).

Conclusions: Simulation of optical blur with a +3.00-diopter spherical lens significantly impairs detection of hazards during hazard perception tests. Lower levels of blur, despite being visually compromising to acuity, did not have a significant effect on HPT.

CONTROL ID: 3713586

SUBMITTER (NAME ONLY): Christina Eckmann-Hansen

TITLE: Ganglion cell-inner plexiform layer thickness in autosomal dominant optic atrophy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Eckmann-Hansen, B.A. Sander, M. Larsen, Department of Ophthalmology, Rigshospitalet, Copenhagen, DENMARK|C. Eckmann-Hansen, M. Larsen, Health and Medical Sciences, Kobenhavns Universitet Sundhedsvidenskabelige Fakultet, Copenhagen, DENMARK|T. Bek, Department of Ophthalmology, Aarhus Universitetshospital, Aarhus, DENMARK|

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ABSTRACT BODY:

Purpose: The aim of this study was to assess the thickness of the ganglion cell-inner plexiform layer complex (GC-IPL) in autosomal dominant optic atrophy (ADOA) and its nasotemporal thickness profile in relation to healthy individuals.

Methods: The study included 145 participants (74 males, 71 females, mean age 44, SD ± 20 years) with various OPA1 mutations, 63 of their first-degree relatives (24 males, 39 females, mean age 38, SD ± 18 years) and 92 unrelated healthy controls (40 males, 52 females, mean age 42, SD ± 19 years). Retinal structure was assessed using optical coherence tomography (OCT) with automated layer segmentation, ETDRS grid pattern thickness analysis (Heidelberg Spectralis, Heidelberg, Germany) and comparison of thickness profiles between groups (RStudio, mixed model, corrected for age and sex with family and eye as a random effect).

Results: For ADOA subjects, first-degree relatives and unrelated controls, mean GC-IPL thickness 3 mm nasal of the foveal center was 43, 98 and 95 µm respectively, whereas 3 mm temporal of the foveal center it was 44, 93 and 89 µm, showing that on a cohort level the nasotemporal thickness ratio is inverted in ADOA, namely 0.98, compared to 1.05 and 1.07 in subjects without ADOA ($p<0.001$). The thickness 6 mm nasal of the fovea center in the three respective groups was 43, 68 and 67 µm and 6 mm temporal of the fovea and 45, 70 and 66 µm, showing that a difference in pattern of ratio reversal was absent at this eccentricity ($p=0.8$ for ADOA versus first-degree relatives). More than half the participants with ADOA had nasotemporal GC-IPL thickness ratios lower than 1.0, which was found in less than 5 % of unrelated healthy subjects.

Conclusions: Half the participants with ADOA in this study were immediately recognizable in that their perifoveal GC-IPL layer was thicker on the temporal than on the nasal side of the fovea, which did only occur in few unrelated healthy controls and relatives without OPA1 mutations. Recognizing this characteristic will often make it possible to make a spot diagnosis of ADOA by comparing the nasal and temporal perifoveal ETDRS field thicknesses.

CONTROL ID: 3713588

SUBMITTER (NAME ONLY): Rahele Kafieh

TITLE: A robust, flexible retinal segmentation algorithm designed to handle neuro-degenerative disease pathology (NDD-SEG)

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Kafieh, D.H. Steel, J. Read, A. Hurlbert, Centre for Transformative Neuroscience and Institute of Biosciences, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|R. Kafieh, S. Rakhshani, School of Advanced Technologies in Medicine, Medical Image and Signal Processing Research Center, Isfahan University of Medical Sciences, Isfahan, Isfahan, IRAN (THE ISLAMIC REPUBLIC OF)|R. Lawson, N. Pavese, Clinical Ageing Research Unit, Newcastle upon Tyne Hospitals NHS Trust and Newcastle University, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|J. Hogg, W. Innes, Royal Victoria Infirmary Eye Department, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|J. Bacardit, School of Computing, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|J. Hogg, R. Lawson, N. Pavese, W. Innes, Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|D.H. Steel, Sunderland Eye Infirmary, Sunderland, Tyne and Wear, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinal Optical Coherence Tomography (OCT) has potential for early detection of neurodegenerative disease (NDD). This requires accurate, automatic segmentation of retinal boundaries despite challenges often pronounced in images from people with NDD, e.g. atrophic layers and indistinct boundaries, media opacity, and movement artefacts. An ideal algorithm would also handle different OCT devices and imaging protocols with diverse resolution, size, artefacts and noise. Our algorithm (NDD-SEG) gives a solution.

Methods: The basic structure is a U-net without pooling and upsampling layers. An initial Retinal Tissue Segmentation Network (RTSN) identifies the retina within the image, even against a noisy background. The Retinal Layer Segmentation Network (RLSN) focuses on fine segmentation of the intra-retinal layers, using the probability map from RTSN cascaded with the original input image. This probability map and texture features are injected into decoder levels of RLSN. The Self-Attention Transformer Block represents higher-level descriptions of the merged data instead of simple concatenation. A new Boundary Preservation Loss (BPL) function is introduced which enables high-precision layer edges to feed into a classification loss function. Together, texture awareness and precision targeting of edges make the network robust to noise.

Results: From 111 OCT volumes from healthy controls and patients with multiple sclerosis (doi:10.1016/j.dib.2018.12.073 and doi:10.1155/2015/259123), 23 are randomly selected for testing and the remainder for training. Reported results are based on two metrics: the mean absolute difference (MAD) for 9 boundaries (in pixels) and Dice's coefficient for 8 layers as distance/similarity between the predicted boundaries/layers and ground truth. The MAD values and Dice scores are presented in Table 1. Size-independence is demonstrated by a < 1% variation in Dice score between segmentation outputs for the original vs. 5 size-distorted images (mean Dice 93.4%). For challenging Parkinson's OCT images (N=44) from an untrained dataset (Newcastle PDD-SRC), NDD-SEG outputs were expert-rated as useable on 54% vs. 1% for a comparator U-net algorithm (Doi:978-3-319-24574-4_28), and more accurate on 100%. See Figure 1 for examples.

Conclusions: Our new method achieves size-independence and robust segmentation even in the presence of image artefacts and pathologies.

CONTROL ID: 3713589

SUBMITTER (NAME ONLY): Tara Salmans

TITLE: Clinical Phenotype and Genetics of Familial Uveal Melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Salmans, A. Ansari, F.H. Davidorf, C.M. Cebulla, M.H. Abdel-Rahman, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|A. Ansari, L. Byrne, M.H. Abdel-Rahman, Human Genetics, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Familial Uveal Melanomas (FUM), defined as more than one case of uveal melanoma within a family, are rare representing less than 1% of all UM patients. The genetic contribution of UM is still largely unknown. This study was performed to better characterize the clinical phenotype and genetics of FUM.

Methods: Germline genetic variants were assessed by whole exome sequencing, a 30-gene cancer panel sequencing and/or BAP1 sequencing in a cohort of 43 FUM presented or referred to the Department of Ophthalmology, The Ohio State University. Patients with detectable germline pathogenic/likely pathogenic (P/LP) variants in BAP1 were not tested for other candidate genes. A systematic review of reported FUM was performed.

Results: Table 1, summarizes the clinical phenotype and genetics of FUM included in the study. Genetic testing of our cohort detected germline BAP1 P/LP variants in 9/43 (21%). Germline P/LP in three established cancer genes (MLH1, PALB2, SMARCE1) were identified in three other families. P/LP variants in five genes possibly associated with cancer predisposition (MMS19, TP53AIP1, DLEC1, RECQL4 and POLI) were identified in five other FUM. Germline P/LP variant in MBD4 was identified in one UM patient with FUM but the variant was not detected in another UM from the family. Except for BAP1, P/LP alteration in other candidate genes were observed in only one patient each. Out of the 121 FUM families reported in the literature, germline testing for BAP1 was carried out on 81 families and P/LP variants were detected in 19%-23%.

Conclusions: BAP1 is the most important cancer predisposition gene in FUM, detected in 19-23% of families. Germline pathogenic variants in other established or possible cancer predisposition genes are detected in ~21% of FUM. Further assessment of the association of other candidate genes with predisposition to FUM and study of other candidate genes are warranted.

CONTROL ID: 3713590

SUBMITTER (NAME ONLY): Catherine Lee

TITLE: A micro-contoured contact lens for delivering 3D-printed ABCB5-positive stem cells for corneal regeneration

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Limbal stem cells (LSC) residing in the limbus continually repopulate the corneal epithelium. Limbal stem cell deficiency (LSCD) occurs when these LSC are damaged or missing. Patients with LSCD are unable to regenerate the corneal epithelium, resulting in blindness due to invasion of the conjunctiva and neovascularization. While tissue from the unaffected eye can be used to treat unilateral LSCD, patients with bilateral LSCD as well as those with inflammation and severe pathologies would greatly benefit from an alternative autologous source of stem cells as allogeneic transplants are associated with poor outcomes and require lifelong immunosuppression. We previously demonstrated that human ABCB5+ LSC were capable of restoration of the corneal epithelium in an NSG mouse model of LSCD. We found that ABCB5 is also expressed by skin stem cells and hypothesized that these dermal cells could provide an alternative source of stem cells for corneal regeneration.

Methods: We first tested the ability of human ABCB5+ dermal stem cells (DSC) expanded in vitro and purified by cell sorting to transform into corneal epithelial cells when cultured in corneal differentiation media. Next, we tested the ability of ABCB5+ DSC to regenerate clear corneas when transplanted onto NSG mice with mechanically induced LSCD. We are currently scaling up to a rabbit model of LSCD and using a 3D bioprinter to seed ABCB5+ DSC on a custom-designed contact lens created from eye impression technology.

Results: Human ABCB5+ DSC were induced in vitro to express significant levels of PAX6 and KRT12. Mice transplanted with human ABCB5+ DSC had clearer corneas compared to controls (Fig 1). Using eye impression technology, we created custom contact lenses modified to accommodate bioprinted ABCB5+ DSCs (Fig 2).

Conclusions: Our results support the use of ABCB5+ DSC as an alternative autologous source of stem cells to regenerate the corneal epithelium. Delivery of these cells using 3D bioprinting and custom contact lenses is promising for robust regeneration of the ocular surface.

CONTROL ID: 3713593

SUBMITTER (NAME ONLY): Prakadeeswari Gopalakrishnan

TITLE:

Relatively Slow Retinal Degeneration Process in a Fam161a Knock-in (KI) Mouse Model for the Human Nonsense Mutation p.Arg 523*

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Gopalakrishnan, C. Matsevich, E. Banin, D. Sharon, A. Beryozkin, A. Obolensky, Molecular Ophthalmology, The Hebrew University Hadassah Medical Center, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: Purpose: The FAM161A-p.Arg523* mutation is the most frequent premature termination codon causing retinitis pigmentosa (RP) in the Israeli Jewish population. Our major aim is to generate and characterize a KI mouse model for this mutation and evaluate its outcome on retinal function and structure.

Methods: Methods: Homozygous knock-in (KI) mice for the p.Arg512* mutation, which corresponds to the human p.Arg523* mutation, were generated by Cyagen Biosciences. Retinal function and structure were examined at the ages of 1 through 21 months (in a 3-months interval) using visual acuity (VA), electroretinography (ERG), optical coherence tomography (OCT), fundus autofluorescence (FAF) imaging, histological and immunohistochemical (IHC) analysis.

Results: Results: Visual acuity analysis showed gradual decrease at the ages 1 to 21 months. Evaluation of retinal function by ERG revealed a progressive decrease in rod and cone amplitudes as compared with WT mice from 1 to 21 months, and a flat response at 21 months. Anatomical structure of the retina, examined by OCT, revealed total loss of outer nuclear layer (ONL) at the age of 21 months, which was first evident at 3 months. Funduscopy examination revealed narrowing of the blood vessels and patchy hyperautofluorescent spots, indicating widespread retinal degeneration. Histological analysis showed progressive loss of photoreceptor nuclei in the ONL but a few nuclei were still evident even in relatively old ages. IHC staining demonstrated reduced and diffused Fam161a expression in the KI comparted to the wildtype retina.

Conclusions: Conclusions: The outcome of the study evidently indicate that the homozygous p.Arg512* mutation has an impact on retinal function and leads to retinal degeneration in the KI mice. Unexpectedly, the rate of photoreceptor loss in the KI model is much slower than in the FAM161A knockout model we previously characterized. In a parallel in vitro study, we provided evidence for the positive significant effect of ataluren on the ability of FAM161A-p.Arg523* patient-derived fibroblasts to grow cilia. Therefore, the KI mouse model can serve as a suitable model to test this therapeutic modality in vivo as well as other modalities such as gene augmentation therapy and RNA editing.

CONTROL ID: 3713594

SUBMITTER (NAME ONLY): Rafael Martínez-Carrasco

TITLE: Muc4 Knockout Disrupts the Ocular Surface Mucosal Barrier in Mice

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Martínez-Carrasco, P. Argueso, M. Fini, New England Eye Center and Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|S. Rachagani, S. Batra, Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: The membrane-associated mucins (MAMs) MUC1, MUC4, MUC16, MUC20, MUC21 and MUC22 project from the apical layer of the ocular surface mucosal epithelia and into the tear film (PMID: 33775913; PMID: 31493487). They are thought to provide a barrier against pathogens and other noxious agents, contribute to hydration, and participate in signal transduction and immune suppression. We investigated the specific role of Muc4 at the ocular surface by characterizing Muc4 knockout (KO) mice.

Methods: Muc4 KO mice were compared to their wildtype (WT) littermates. The ocular surface was imaged using the rodent micron IV with slit-lamp attachment, using white or cobalt blue light after staining with fluorescein (detects epithelial cell damage) or rose bengal (detects mucosal barrier disruption). Staining was scored from 0 to 9 using a scoring system modified from van Bijserveld's. Smoothness was scored from 0-4 considering the alteration of a ring light reflection. The ocular surface was also imaged by scanning electron microscopy (SEM). Gene expression was analyzed by qPCR.

Results: Gross examination revealed no conjunctivitis, blepharitis or other inflammatory disease in KO mice. Fluorescein staining revealed no evidence of epithelial cell damage. In contrast, rose bengal staining was distinctly higher in KO mice than in WT littermates ($n=20$; $P < 0.01$), with a punctate pattern indicative of mucosal barrier disruption. SEM revealed more surface epithelial cells with a lower density of microplicae in KO mice ($n=8$; $P < 0.05$). Pax6 expression was decreased, while K10 expression was increased ($P < 0.05$, $P < 0.01$; respectively), indicating keratinization. In contrast, no increase was detected in expression of cornified envelope genes Sprr1b and Sprr2h. Corneal smoothness was reduced in KO mice ($n=18$; $P < 0.05$), suggesting tear film disruption. No compensatory changes due to Muc4 KO were observed in expression of Muc1 or Muc16, or the secreted mucin Muc5ac ($n=11$).

Conclusions: Cell culture studies have provided evidence that deficiency of a single MAM is sufficient to disrupt the mucosal epithelial barrier at the ocular surface and reduce surface microplicae (PMID: 24968021). This is the first in vivo validation of this finding. We also provide the first evidence that loss of Muc4 results in keratinization, but not cornification of the ocular surface, and leads to tear film disruption.

CONTROL ID: 3713598

SUBMITTER (NAME ONLY): Santiago Sager La Ganga

TITLE: A compact binocular adaptive optics visual simulator for clinical use in highly-aberrated eyes

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sager La Ganga, P.M. Prieto, A.M. Paniagua-Diaz, A. Gambin, P. Artal, Lab. Optica, Universidad de Murcia, Murcia, Murcia, SPAIN|S. Sager La Ganga, Voptica SL, Murcia, Murcia, SPAIN|D. Debnath, S. Goswami, P.K. Vaddavalli, S.R. Bharadwaj, L V Prasad Eye Institute, Hydebarad, INDIA|

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ABSTRACT BODY:

Purpose: Adaptive-optics-based visual simulation is a useful tool in different areas of clinical ophthalmology. However, current commercial instruments are monocular and the most thorough binocular testing can only be performed with bulky laboratory prototypes. In this context, the aim of this work was to develop a compact binocular instrument suitable for clinical environments and able to deal with a wide variety of patients, including those with abnormal eye's optics.

Methods: The new binocular device has been adapted from a commercial monocular version (VAO, Voptica SL, Murcia, Spain). Both eyes' pupils were fit into the Hartmann-Shack (HS) wavefront sensor and liquid crystal on silicon (LCoS) phase modulator, for measurement and manipulation of ocular aberrations. Conversely, the stimulus generator was replaced by two HD screens, one for each eye, for stimulus presentation and psychophysics, including stereo-acuity tests. Additionally, a single intensity modulator was included for generating artificial pupils in both eyes, and a single tunable lens for correction of defocus. A pupil camera monitoring both eyes and a periscopic system allows controlling eye separation and tilt for precise patient's positioning. The whole system is mounted in a relatively compact housing similar to standard ophthalmic equipment. GPU-based processing of the HS images allows for simultaneous measurements in real time for both eyes.

Results: The dynamic range of the device was determined by measuring and inducing aberrations in artificial eyes and in a group of highly-aberrated volunteers, adding trial lenses in some cases to increase ammetropia. By using the tunable lens to roughly compensate for defocus, the instrument successfully copes, both for measuring and correcting, with a range of +/-15D in spherical equivalent, +/-6D in cylinder and at least 1μm in all high-order aberrations over a 4.5-mm diameter pupil. The use of the device was easy both for operators and subjects.

Conclusions: A compact Binocular Visual Adaptive Optics simulator has been developed allowing clinical visual testing under controlled optical conditions in both eyes. The instrument has a high dynamic range much increased with respect to the current commercially available monocular device, and it may be used to better understand the relationship between optics and visual performance in patients with highly aberrated eyes (e.g., keratoconus).

CONTROL ID: 3713603

SUBMITTER (NAME ONLY): Chloe Degre Kendrick

TITLE: The Impact of Pupil Transmission Apodization on Visual Performance at Different Light Levels

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Degre Kendrick, G. Yoon, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|M. Chen, J. Buch, P.F. Jubin, Johnson & Johnson Vision, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: A previous study has shown that pupil transmission apodization can significantly improve through-focus visual performance with spherical aberration by decreasing the impact of peripheral wavefront profiles on retinal image quality. However, this improvement may be limited by the loss of retinal illuminance due to the apodization. The goal of this study is to determine the visual performance benefit of pupil transmission apodization at different luminance levels.

Methods: A liquid crystal spatial light modulator (SLM) was used to generate pupil transmission apodization profiles described by the Gaussian-type function, $e^{-\alpha (r/r_0)^2}$, where r_0 is the pupil radius and α is the apodization coefficient. This profile was relayed on the eye pupil through an optical system, while subjects performed high contrast visual acuity (VA) and contrast sensitivity (CS) tasks. A baseline condition and three Gaussian pupil apodization profiles (α=1, 3, 7) were tested at three stimulus luminance levels (2.5, 250, and 1000 cd/m^2). Each of 16 healthy subjects was dilated with phenylephrine, and a 6 mm artificial pupil was used to maintain a constant retinal illuminance throughout each apodization condition. Visual performance was assessed three times for each condition using a 2AFC QUEST paradigm. A Badal optometer was used to optimize subjects' focus prior to vision testing, but other aberrations were left uncorrected.

Results: VA and CS were improved significantly with increasing stimulus luminance for baseline and each apodization condition. For all luminance levels, VA was improved by the medium and high apodization, more than half a line compared to no apodization. Overall, apodization had a greater benefit for CS at higher spatial frequencies. At 4c/deg, visual benefit was only observed with the low apodization at high luminance. For 8 and 16c/deg, medium and high apodization improved CS by a factor of approximately 2 at medium and high luminance levels. However, the high apodization at low light level did not show any improvement at all spatial frequencies due to significant loss in retinal illuminance.

Conclusions: Gaussian-type pupil transmission apodization was found to be beneficial for VA and CS performance especially at medium and high luminance levels tested in this study. The visual benefit was spatial-frequency dependent, with CS at 4 cpd benefitting the least, and CS at 16 cpd benefitting the most.

CONTROL ID: 3713605

SUBMITTER (NAME ONLY): Eric Ritchey

TITLE: Intra and Inter examiner repeatability of a semi-automated lid wiper epitheliopathy algorithm

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.R. Ritchey, A. Ravikumar, E. Osae, H.M. Queener, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Eric Ritchey: Commercial Relationship(s);Code C (Consultant/Contractor):SightGlass Vision | Ayeswarya Ravikumar: Commercial Relationship: Code N (No Commercial Relationship) | Eugene Osae: Commercial Relationship: Code N (No Commercial Relationship) | Hope Queener: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Lid wiper epitheliopathy (LWE) is a critical clinical marker to identify and track abnormal lid/cornea interaction. We proposed an automated grading algorithm using hue and saturation of LWE staining following manual selection of region of interest. Here we determined the repeatability of this semi-automated algorithm.

Methods: 31 images (15 upper and 16 lower eyelids) representative of LWE staining, observed after instillation of 20 microliters combination solution of 2% sodium fluorescein + 1% lissamine green, were analyzed. Images were processed using a custom MATLAB program that semi-automatically identifies the LWE area using hue and saturation values of the manually delineated lid region. LWE height (mm) was calculated as the average extent of staining perpendicular to the lid wiper curve minus the average Marx line height from images without LWE staining. Two independent examiners (E1 & E2) analyzed the images in a random order twice, with analysis sessions separated by more than a week. Bland-Altman analysis and Intraclass Correlation Coefficient (ICC) were performed to compare the results of height, width and area of the LWE staining.

Results: Intra-examiner variability (E1) between analysis runs for height [-0.003 ± 0.011mm; 95% Limits of Agreement (LoA): -0.025 to 0.019], width [0.094 ± 0.478mm; 95% LoA: -0.843 to 1.031] and area [-0.003 ± 0.012mm^2, 95% LoA: - 0.026 to 0.020] were calculated. Intra-examiner variability (E2) between analysis runs results for height [-0.001 ± 0.021mm; 95% LoA: -0.043 to 0.041], width [0.127 ± 0.670mm; 95% LoA: -1.187 to 1.440] and area [0.058 ± 0.291mm^2, 95% LoA: -0.513 to 0.628] were calculated. The inter-examiner (E1 – E2) variability, using the average value of two analysis runs for each examiner, were calculated for height [0.001 ± 0.012mm; LoA: -0.022 to 0.023; ICC 0.999], width [-0.160 ± 0.395mm; LoA: -0.935 to 0.614; ICC 0.996] and area [0.024 ± 0.148mm^2; LoA: -0.265 to 0.314; ICC 0.997].

Conclusions: Inconsistency in subjective grading methods may prevent detection of changes in LWE staining between observers. This novel hue and saturation method results in highly repeatable measures of height, width and area of LWE staining after subjective delineation of the general lid region between examiners.

CONTROL ID: 3713606

SUBMITTER (NAME ONLY): Vahe Bedian

TITLE: Characterization of VRDN-001, a High Affinity and Potent anti-Insulin-like Growth Factor-1 Receptor (IGF-1R) Inhibitory Antibody for the Treatment of Thyroid Eye Disease (TED)

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Bedian, Viridian Therapeutics Inc, Waltham, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Vahe Bedian: Commercial Relationship(s);Code E (Employment):Viridian Therapeutics;Code C (Consultant/Contractor):Dianthus Therapeutics

ABSTRACT BODY:

Purpose: VRDN-001 is an antagonist antibody to IGF-1R under development by Viridian Therapeutics for treatment of patients with TED, a condition driven by Thyroid Stimulating Hormone Receptor (TSHR) agonistic autoantibodies and crosstalk between TSHR and IGF-1R. TED is characterized by recruitment of fibrocytes that express IGF-1R and TSHR into orbital tissues, where they mediate deposition of hyaluronan and expansion of orbital muscle and fat. Blockade of IGF-1R has been shown to improve TED symptoms in randomized clinical trials. To assess its potential for treating TED, we evaluated the binding characteristics of VRDN-001 to IGF-1R and its potency for inhibition of IGF-1R phosphorylation.

Methods: Binding characteristics of VRDN-001 were investigated using surface plasmon resonance where antibodies were immobilized and recombinant IGF-1R extracellular domain (ECD) was used as analyte. Kinetic parameters and equilibrium dissociation constant were derived by global fitting of data. Binding to cell-surface expressed IGF-1R was assessed by flow cytometry. For cell-based potency testing, IGF-1R expressing primary human ocular choroid fibroblasts (HOCF) and A549 lung carcinoma cells were stimulated with IGF-1, and IGF-1R antibodies were evaluated for inhibition of receptor autophosphorylation using a commercial ELISA kit.

Results: VRDN-001 bound IGF-1R ECD with high affinity (equilibrium dissociation constant K_D = 0.57 nM) and exhibited slow dissociation of IGF-1R (off rate $k_d = 5X10^{-5}\ s^{-1}$). These results were consistent with dose-response of binding to cell surface IGF-1R. In IGF-1 stimulated HOCFs and A549 cells, VRDN-001 inhibited IGF-1R phosphorylation in a dose-dependent manner. VRDN-001 IC50 values were ~0.1 nM and greater than 95% inhibition of phosphorylation was observed with VRDN-001 concentrations in the 1-10 nM range (0.15-1.5 µg/mL).

Conclusions: VRDN-001 bound IGF-1R with high affinity and inhibited IGF-1R signaling with high potency. VRDN-001 shut down IGF-1R signaling at concentrations that can be achieved with moderate clinical doses. The in vitro profile of VRDN-001 suggests favorable efficacy and exposure requirements for treatment of TED patients. A phase 1/2 trial for VRDN-001 in healthy volunteers and TED patients is underway (NCT050176639).

CONTROL ID: 3713607

SUBMITTER (NAME ONLY): Ashley Kramer

TITLE: A comparative analysis of gene and protein expression in a zebrafish model of chronic photoreceptor degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kramer, J. Carthage, T.A. Cook, R. Thummel, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|K. Gurdziel, Genome Sciences Core, Wayne State University, Detroit, Michigan, UNITED STATES|M. Spain, T.A. Cook, Center for Molecular Medicine and Genetics, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Zebrafish are widely utilized to investigate retinal regeneration as they can regenerate photoreceptors (PRs) following acute phototoxic damage. This is mediated by Müller glia (MG), which re-enter the cell cycle to produce retinal progenitors. While this acute model has revealed important MG-dependent regenerative pathways, it may not fully reflect the events underlying human retinopathies, which often follow a chronic pathological timeline. To test this hypothesis, we developed a zebrafish model of chronic low light (CLL) exposure and compared morphological and transcriptomic changes in the CLL damaged retina to our acute light damage model.

Methods: Adult albino zebrafish were exposed to 28 days of CLL and eye tissue was collected at 8 time points. Whole right eyes were collected for immunohistochemistry and whole retinas from the left eyes were used for 3'mRNA-seq.

Results: CLL exposure resulted in the truncation of PR outer segments, and reduced numbers of rod PR nuclei by 28 days post light (dpl) (Fig. 1). Unlike the acute model, MG cell-cycle re-entry was not observed in CLL, suggesting that this damage paradigm is not sufficient to trigger MG-mediated regeneration. Additionally, we did not detect any overt signs of MG gliosis, as is seen early in the acute model. However, we did observe a peak of inflammatory markers (i.e. mpeg1.1, apoeb) by 10dpl, much later than seen in the acute model. This corresponded with a gradual accumulation of microglia at the tips of rod outer segments. Transcriptomic comparisons corresponding to PR differentiation in the acute model vs PR degeneration in the CLL model revealed a set of inversely correlated genes likely representing PR development and maintenance. We detected genes known to be involved in human retinal disease (pdca/b, gnat1/2, grk1a/b, rom1b), and genes not yet characterized in zebrafish regenerative retinal biology (kera, pdca/b).

Conclusions: By comparing the molecular and cellular changes associated with acute vs chronic models of PR degeneration, we identified several candidate genes involved in slow PR degeneration and gliosis. These studies serve as a nexus for future experiments aimed at understanding common retinal degenerative diseases.

CONTROL ID: 3713608
SUBMITTER (NAME ONLY): Jing Xu
TITLE: Hazard Warning Modalities and Timing Thresholds for Drivers with Impaired Contrast Sensitivity
SESSION TITLE: Vision Impairment: Impact on Driving and Mobility
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: J. Xu, A. Hutton, Envision Research Institute, Wichita, Kansas, UNITED STATES|J. Xu, A.R. Bowers, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A.R. Bowers, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: Jing Xu: Commercial Relationship: Code N (No Commercial Relationship) | Abbie Hutton: Commercial Relationship: Code N (No Commercial Relationship) | Alex Bowers: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Impaired contrast sensitivity (ICS) may delay drivers' responses to road hazards. Advanced Driver Assistance Systems that provide hazard warnings can mitigate crash risk; however, the benefits may vary with warning design. We tested 3 collision warning systems with different modalities and timing thresholds and evaluated their impact on the responses of drivers with ICS to pedestrian hazards in a simulator.
Methods: To date, 13 subjects with normal vision (NV) (65–86 y, median CS 1.95) and 9 subjects with ICS (63–84 y, median CS 1.35 log units) participated. They completed 6 city drives with 3 warning conditions: auditory (pulse beeps), directional tactile (pulse vibrations on either left or right side), and non-directional tactile (pulse vibrations on both sides). For each condition, they completed one drive with early and one drive with late warnings, triggered when time-to-collision was 3.5s and 2s, respectively. There were 10 pedestrian hazards per drive that crossed the road from the left or right, requiring a braking response by the driver to avoid a collision.
Results: ICS subjects triggered more early warnings (61 vs 54%) and late warnings (20 vs 7%) than NV subjects and had more collisions (3.8 vs 0%). When warnings were triggered (data pooled across groups), early warnings reduced time to fixate hazards (late 1.8 vs early 1.2s, $p=0.02$), reduced brake response times (2.7 vs 1.7s, $p<0.001$) and reduced collision rates (1.5 vs 0.5%). Brake times did not differ between the groups for early warnings; however, ICS subjects took 0.5 s longer to brake than NV subjects with late warnings ($p=0.02$) and still had a 15.4% collision rate. No collisions occurred for ICS subjects with early warnings. For late warnings, non-directional tactile warnings resulted in the lowest collision rates for ICS subjects (6% vs Auditory 20% vs Directional tactile 19%). For early warnings, modality had no effects on fixation and brake times of ICS subjects. Most subjects preferred early warnings (91%) and the directional tactile modality (73%).
Conclusions: With early warnings, both groups were faster to fixate and brake for hazards and had low collision rates. In events with late warnings, ICS subjects were slow to brake resulting in high collision rates. These results suggest that ICS drivers will benefit more from earlier warnings. Warning modality may be important for late warnings.

CONTROL ID: 3713609

SUBMITTER (NAME ONLY): Ingrid Pan

TITLE: Efficacy and Safety of Tacrolimus for the Treatment of Pediatric Noninfectious Uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Pan, Pharmacy, Children's Hospital Colorado, Aurora, Colorado, UNITED STATES|J. Jung, Pediatric Ophthalmology and Adult Strabismus, Children's Hospital Colorado, Aurora, Colorado, UNITED STATES|C. Lin, Pediatric Rheumatology, Children's Hospital Colorado, Aurora, Colorado, UNITED STATES|A. Palestine, J. Jung, Department of Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaluate the efficacy and safety of tacrolimus for the treatment of pediatric noninfectious uveitis

Methods: Single health system, retrospective review of electronic medical records. A chart review of patients < 18 years old diagnosed with noninfectious uveitis who were intolerant to or failed conventional systemic immunosuppressants seen by Children’s Hospital Colorado Ophthalmology and Rheumatology or University of Colorado Hospital Ophthalmology between January 2014 – January 2021 was completed. The primary outcome was the incidence of improvement in inflammation. Secondary outcomes included incidence of tacrolimus treatment failure and need for dose reduction or discontinuation due to adverse effects. Descriptive statistics were used to analyze the data. This study received IRB approval.

Results: Ten patients (40% female; mean age: 12.9 years) were included. The most common previously failed treatments were methotrexate (n = 10) and biologics (n = 4). Uveitis was secondary to systemic autoimmune diseases in 40% of patients. Tacrolimus was initiated a mean of 3.9 years after onset of uveitis with 9 patients requiring concomitant immunosuppressants. Of the 6 patients with an established goal tacrolimus trough range, 83% reached therapeutic goal at an average of 320.6 ± 205.6 days. Treatment failure requiring alternative therapies occurred in 20% of patients. Laboratory abnormalities were observed in 7 patients; however, dose reduction was only required in 3 patients with no discontinuation of therapy.

Conclusions: In this small cohort of patients who previously failed traditional systemic immunosuppressants, it was effective in reducing inflammation in 80% of patients. Tacrolimus was generally well-tolerated and did not require discontinuation of medication.

CONTROL ID: 3713610

SUBMITTER (NAME ONLY): Vishal Sharma

TITLE: A Deep Autoencoder Model to Denoise Visual Fields in Glaucoma

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Sharma, T. Elze, M. Wang, Schepens Eye Research Institute of Massachusetts Eye and Ear,, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L.Q. Shen, M.V. Boland, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L. Pasquale, Eye and Vision Research Institute, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|S.R. Wellik, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|G. De Moraes, Edward S. Harkness Eye Institute, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J.S. Myers, Wills Eye Hospital, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|S. Yousefi, Hamilton Eye Institute, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To denoise visual fields (VFs) in glaucoma by developing a deep autoencoder model.

Methods: We selected reliable SITA Standard 24-2 VFs from a multi-center dataset excluding Massachusetts Eye and Ear (MEE) data. A 2D convolutional autoencoder was developed to denoise VFs using the multi-center dataset for training. The noise is defined as the difference between the original VFs and the reconstructed (denoised) VFs from our deep autoencoder model. Our autoencoder model was tested on the MEE dataset. To demonstrate the effectiveness of our denoising model, we compared the structure-function relationships between linear regression models using 12 clock-hour retinal nerve fiber layer thickness (RNFLT) from reliable optical coherence tomography (OCT, signal strength at least 6) to predict the 52 TDs of the paired (within 3 months) original VFs and the denoised VFs. Model selection based on Bayesian information criteria (BIC) was applied to remove redundant features from the structure-function linear models. Adjusted r-squared and BIC penalized for linear model complexity were used to measure the structure-function relationship strength.

Results: A total of 419,755 of VFs from 204,619 eyes of 116,288 patients (age: 64.17 ± 15.42 years; mean deviation: -4.93 ± 6.10 dB) in the multi-center dataset excluding MEE data were used to train our deep autoencoder. There were 9,456 OCT-VF pairs from 4,609 eyes of 2,962 patients from MEE (age: 61.76 ± 15.53 years; mean deviation: -5.04 ± 7.01 dB) available to test our denoising autoencoder. Two examples of the original VF and denoised VFs are shown in Figure. 1 (a-d), where we observe extreme values (noise) to be mitigated after being denoised by our autoencoder model. The absolute average VF differences between original and denoised VF were greater in the central sector (Figure. 1 [e]). Smaller absolute denoising amount was correlated with worse TD values and the correlations were greater in inferior paracentral region (Figure. 1 [f]). The denoised VFs (Figure. 2) can be better predicted by the 12 clock-hour RNFLTs than the original VF with R-squared and BIC improvements up to 0.02 and 48 (BIC improvement ≥ 6: strong improvement) in both 3,672 left and 5,784 right eyes, and the improvement is relatively more conspicuous in superior hemifield.

Conclusions: Denoising VFs with our deep autoencoder model can improve structure-function correlation in glaucoma.

CONTROL ID: 3713611

SUBMITTER (NAME ONLY): Rizul Naithani

TITLE: Assessing Gender- and Race-based Differential Item Functioning with the National Eye Institute Visual Functioning Questionnaire for Patients with Glaucoma

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Naithani, A. A. Jammal, T. Estrela, N. Onyekaba, A. Youssif, H. Tseng, F. Medeiros, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|R. Naithani, Campbell University School of Osteopathic Medicine, Buies Creek, North Carolina, UNITED STATES|S. Berchuck, Statistical Science, Duke University, Durham, North Carolina, UNITED STATES|F. Medeiros, Electrical and Computer Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate whether The National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25) can serve as a generic measure for quality-of-life (QoL) assessment in patients with glaucoma across race and gender.

Methods: This was a cross-sectional study of data sourced from the Duke Glaucoma Registry. Patient level diagnosis of glaucoma was classified by the presence and topographic correspondence of functional and structural damage assessed by spectral-domain optical coherence tomography (SDOCT) and standard automated perimetry (SAP) parameters in the worse eye. The NEI VFQ-25 graded scale was collapsed for all items to have three categories going from extreme and moderate difficulty, slight difficulty, to no difficulty. Only items of visual functioning components were studied. Gender evaluated females and males while race studied African Americans and Caucasians as focal and reference subgroups, respectively. The multiple group analysis and differential item functioning (DIF) of the R package, mirt, were used for item-wise analysis. A five-item anchor selection strategy was employed prior to final DIF detection. Expected score standardized differences (ESSD) were calculated and the effect for each item was classified as small (|ESSD| <0.200), moderate (|ESSD| 0.200 to 0.800), or large (|ESSD| ≥0.800).

Results: 258 glaucoma patients were evaluated in the study of which 82 were self-identified as Black or African American and 176 as White or Caucasian. Gender included 138 females and 120 male subjects. Racial DIF was observed for items pertaining to difficulty reading ordinary newspaper print (p=0.008), going downstairs or curbs in low light (p<0.001), seeing how people react to things the patient says (p=0.026), and picking out and matching ones' own clothes (p=0.044). The respective item-level ESSD values were 0.214, -0.672, 0.290, and -0.190. Gender DIF was observed for items pertaining to difficulty in seeing how people react to things patient says (p = 0.033) and driving in difficult conditions (p=0.011) with low to moderate effect (ESSD of 0.196 and -0.484, respectively).

Conclusions: In assessing QoL in glaucoma patients using the NEI VFQ, racial and gender subgroups demonstrated to have different probabilities of endorsing responses for certain activities of daily living with small to moderate effect sizes for clinical utility.

CONTROL ID: 3713612

SUBMITTER (NAME ONLY): Baerbel Rohrer

TITLE: Peptide-based immunotherapy against oxidized elastin ameliorates pathology in mouse model of smoke-induced ocular injury

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Rohrer, N. Parsons, B. Annamalai, C. Nicholson, E. Obert, Ophthalmology, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|B. Rohrer, Research Services, VA Medical Center Ralph H Johnson, Charleston, South Carolina, UNITED STATES|B.W. Jones, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|A.D. Dick, Ophthalmology, University of Bristol, Bristol, Bristol, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of blindness in western populations. It is associated with an overactive complement system, and an increase in circulating antibodies against certain epitopes, including elastin has been reported. Aging and AMD is associated with a loss of the elastin layer of Bruch's membrane (BrM; PMID: 15632016), which can be mimicked in the smoke-induced ocular pathology (SIOP) model in mouse. Of relevance, we previously showed that immunization with elastin peptide oxidatively modified by cigarette smoke (ox-elastin), exacerbated structural and functional damage in SIOP (PMID: 32207814). Here we asked whether ox-elastin peptide-based immunotherapy (PIT) ameliorates damage.

Methods: Mice were exposed to cigarette smoke for 6 months. C57BL/6J mice were injected with ox-elastin peptide at two doses via weekly subcutaneous administration, $FcgR^{-/-}$ and uninjected C57BL/6J mice served as controls. Retinal function was assessed by OKR, morphology by electron microscopy, and complement activation, antibody deposition and mechanisms of immunological tolerance were assessed by Western blotting and ELISA.

Results: Elimination of Fcg receptors, preventing antigen/antibody-dependent cytotoxicity, protected against SIOP. Mice receiving PIT with low dose ox-elastin (LD-PIT) exhibited reduced humoral immunity, reduced complement activation and IgG/IgM deposition in the RPE/choroid, and largely a preserved BrM and improved visual function. LD-PIT reduced IFNg and increased IL-4 within RPE/choroid. In contrast, the high dose PIT was not protective.

Conclusions: Our data further support ox-elastin role in ocular damage in SIOP in part via elastin-specific antibodies, and support the corollary that PIT with ox-elastin attenuates ocular pathology. Overall, damage is associated with complement activation, antibody-dependent cell-mediated cytotoxicity, and altered cytokine signature. Finally, peptide-based immunotherapy might be a suitable strategy for the prevention of AMD.

CONTROL ID: 3713613

SUBMITTER (NAME ONLY): Sarah Nicholas

TITLE: Reversal of TGF-β1 induced fibrosis via inhibition of S1P in the human cornea.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Nicholas, D. Karamichos, North Texas Eye Research Institute, Fort Worth, Texas, UNITED STATES|S.E. Nicholas, D. Karamichos, Pharmaceutical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|S.K. Basu, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|N.A. Mandal, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|N.A. Mandal, Anatomy and Neurobiology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal fibrosis can lead to opacity and may ultimately cause partial or complete vision loss. Currently, the only treatment for severe corneal fibrosis is corneal transplantation. Sphingolipids (SPLs) are known to be associated with fibrosis in various tissues and organs, including the cornea. We previously reported that SPLs are tightly related to both, TGF-β signaling and corneal fibrogenesis. The aim of this study was to elucidate the role of SPLs and TGF-β family members, their crosstalk, and downstream signaling in corneal fibrosis using our previously established 3D in vitro model.

Methods: Healthy human corneal fibroblasts (HCFs) were isolated, plated on polycarbonate membranes, and cultured in EMEM+FBS+VitC (control medium) for 4 weeks. Eight treatment combinations were tested using the following groups in control medium: –0.1ng/mL TGF-β1 (β1), 0.1ng/mL TGF-β3 (β3), 1μM sphingosine-1-phosphate (S1P), and 5μM SPHK I_2 (I_2); the combinations (combo) are abbreviated as: (a) β1/S1P, (b) S1P/β1, (c) β1/I_2, (d) I_2 /β1, (e) β3/S1P, (f) S1P/β3, (g) β3/I_2, and (h) I_2/β3. Each combo was administered for 2 weeks with one group then switched to another group for 2 weeks. Cultures without treatment(s) served as controls (Control/VitC-Only). Using Western Blot analysis, the 3D constructs were examined for the expression of fibrotic markers, SPL and TGF-β signaling pathway members.

Results: Our data revealed that stimulation with β1/I_2 caused significant downregulation in the expression of SMA, Collagen 3, LTBPs 1-4, TGF-βRI, TGF-βRII, SMAD4, pSMAD2, pSMAD3, S1PR3, SphK1 and SphK2. The opposite combo treatment, I_2/β1, lead to significant downregulation of SMA, LTBPs 1-3, TGF-βRII, SMAD4, pSMAD2, S1PR3, and SphK2; and significant upregulation of TGF-βRI. Interestingly, both TGF-β1/S1P and S1P/TGF-β1 combo treatments lead to significant upregulation of Collagen 3 and activation of LTBPs, TGF-βRs, and SMADs. Additionally, LTBPs 1-4, SphK1 and 2, and S1PR3 were all activated by the TGF-β/S1P combos and inhibited by the TGF-β/I_2 combos. When comparing both TGF-β/I_2 treatment groups, we observed that β1/I_2 was more effective in reducing fibrosis compared to I_2 /β1.

Conclusions: Conclusively, using our 3D human corneal in vitro model, we have demonstrated that SPHK I_2 treatment with TGF-β1 induced fibrosis, results in reversal of fibrosis regulated by the inhibition of LTBPs, SphKs, and the downstream SMAD pathway.

CONTROL ID: 3713615

SUBMITTER (NAME ONLY): Erika Ellis

TITLE: Characterization of cone membrane physiology during secondary cone degeneration in the rd10 model of retinitis pigmentosa

SESSION TITLE: Photoreceptors and the OPL

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Ellis, G. Fain, A. Sampath, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Erika Ellis: Commercial Relationship: Code N (No Commercial Relationship) | Gordon Fain: Commercial Relationship: Code N (No Commercial Relationship) | AP Sampath: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In retinitis pigmentosa, secondary degeneration of cones is one of the most debilitating features of the disease. Currently there is little known about how cone membrane physiology changes during secondary cone degeneration. In this study, we sought to characterize cone membrane physiology throughout secondary cone degeneration.

Methods: Using the rd10 mouse model of retinitis pigmentosa, we performed whole-cell patch-clamp recordings from cones in retinal slices. We measured passive membrane properties, recorded light-evoked responses, and measured isolated conductances using voltage-clamp protocols in combination with specific channel-blocking agents. During patch-clamp recordings, cells were filled with a fluorescent dye and cell morphology was imaged after recordings were completed. Experiments were performed in rd10 animals between 3- and 9-weeks old.

Results: Cones in the rd10 mouse showed significantly altered morphology even at the earliest time point, with no outer segment seen on any cells. In line with this, cone membrane capacitance was significantly lower than normal even at the earliest time point and showed no significant change over 9 weeks, with an average membrane capacitance of 2.2pF (n=44). Even at late time points, small light-evoked responses could be elicited from most cones with a bright flash from a 405nm LED. The cone resting membrane potential showed no significant change during degeneration, with an average resting membrane potential of -50mV (n=34), similar to WT cones. Cones maintained a robust HCN1 conductance at all time points. Preliminary recordings of synaptic calcium currents suggest a decrease in the calcium current with age.

Conclusions: Our results show that degenerating cones maintain a depolarized resting membrane potential, even after the loss of the outer segment. The presence of light-evoked responses, although small and desensitized, suggests that cones can maintain ectopic expression of cyclic-nucleotide-gated channels, which with other conductances still present in the membrane may be responsible for maintaining the cell in a depolarized state. There seems to be little change in the HCN1 conductance, but voltage-gated calcium currents appear to be diminished as degeneration progresses.

CONTROL ID: 3713618

SUBMITTER (NAME ONLY): Shaiban Ahmed

TITLE: A deep learning approach for automated dispersion compensation in optical coherence tomography

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ahmed, D. Le, T. Son, T. Adejumo, X. Yao, Department of Biomedical Engineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|X. Yao, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Shaiban Ahmed: Commercial Relationship: Code N (No Commercial Relationship) | David Le: Commercial Relationship: Code N (No Commercial Relationship) | Taeyoon Son: Commercial Relationship: Code N (No Commercial Relationship) | Tobiloba Adejumo: Commercial Relationship: Code N (No Commercial Relationship) | Xincheng Yao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study is to design and validate a fully convolutional network (FCN) architecture to compensate for system dispersion in optical coherence tomography (OCT).

Methods: Our proposed FCN method is based on a modified UNet architecture (Fig. 1A) that uses an encoder-decoder pipeline. The input of the deep leaning pipeline can be single or multiple-channel OCT B-scans. Each B-scan was compensated by different second-order dispersion compensation coefficients to optimize different layers sequentially. The output obtained from the network was a fully compensated OCT B-scan where the dispersion was compensated at all depths. A lab-built SD-OCT system with 840 nm central wavelength was used for the experimental imaging. The axial and lateral pixel resolutions were 1.5 μm and 5 μm, respectively. Nine (7 train and 2 test) different OCT volumes with a field of view 3.5 mm x 3.5 mm were acquired from healthy human subjects. The proposed method was trained and tested using 1, 3, 5, 7, and 9 input channel models. Quantitative analysis was performed using peak signal to noise ratio (PSNR) and structural similarity index metric calculated at multiple scales (MS-SSIM).

Results: High quality all depth compensated OCT B-scans were obtained when the proposed model was implemented using 5, 7, and 9 input channels. Output from the 1 and 3 input channel models also demonstrated better resolution retaining more structural information than a raw uncompensated image. High similarity between the output images and the ground truth was observed and the MS-SSIM score for 5, 7, and 9 input channel models were 0.97 ± 0.016, 0.97 ± 0.014, and 0.97 ± 0.014, respectively. High signal strength compared to the background noise was also observed for these models with PSNR values of 29.95 ± 2.52, 29.91 ± 2.13, and 29.64 ± 2.26 dB for 5,7 and 9 input channel models respectively. Fig. 1B illustrates the ground truth (B1), uncompensated (B2), and output B-scan from 5 input channel model (B3).

Conclusions: The proposed FCN can compensate for the dispersion at all depths and thus provides a feasible solution for fully automated dispersion compensation in OCT.

CONTROL ID: 3713619

SUBMITTER (NAME ONLY): Manon HCA Peeters

TITLE: Assessment of the molecular pathophysiology of central areolar choroidal dystrophy caused by a recurrent mutation (p.Arg142Trp) in PRPH2.

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Peeters, A. Rooijakkers, M. Brullas, A.I. Den Hollander, R.W. Collin, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|Q. Liu, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Central areolar choroidal dystrophy (CACD) is an inherited retinal disease primarily affecting the macula. The disease is strongly linked to mutations in PRPH2. However, the molecular mechanism underlying PRPH2-associated CACD remains largely unknown. This study aims to unravel the pathological mechanism by which a recurrent PRPH2 missense mutation causes CACD.

Methods: HEK293T cells were transiently transfected with plasmids encoding wildtype or Arg142Trp mutant PRPH2. Western blot analysis was used to determine protein levels. Co-transfections of wildtype and mutant Arg142Trp plasmids, followed by co-immunoprecipitation were performed to study PRPH2 homodimer formation. To study subcellular localization, COS-1 cells were transiently transfected with PRPH2-wildtype or PRPH2-Arg142Trp plasmids. In addition, plasmids were stably transfected into IMCD3 cells. Immunocytochemistry (ICC) was used to determine the localization of PRPH2.

Results: No differences in PRPH2 protein levels between PRPH2-wildtype and PRPH2-Arg142Trp conditions were observed. The PRPH2-Arg142Trp protein can still form homodimers with both wildtype and Arg42Trp proteins. In both COS-1 and IMCD3 cells, the wildtype PRPH2 protein spreads into the cytoplasm and partly localizes to the plasma membrane, while the PRPH2-Arg142Trp mutant protein tends to cluster around the nucleus, partially co-localizing with golgi/ER. Moreover, the mutant protein was found only at the base of the cilium, while wildtype protein was observed along the entire cilium.

Conclusions: Our results show no differences in expression levels between PRPH2-wildtype and PRPH2-Arg142Trp proteins. Furthermore, PRPH2 homodimer formation still occurs under PRPH2-Arg142Trp conditions, ruling out aberrant expression levels and erroneous PRPH2 homodimer formation as mechanism underlying CACD. ICC results indicated a difference in subcellular localization between wildtype and mutant PRPH2, with a potential defect in ciliary localization. Further studies are needed to elucidate the mechanism underlying PRPH2-associated CACD.

CONTROL ID: 3713620

SUBMITTER (NAME ONLY): Jeffrey Yu

TITLE: Cost analysis and adherence of over the counter supplements to the AREDS2 protocol

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yu, J.M. Miller, M. Johnson, B. Young, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Jeffrey Yu: Commercial Relationship: Code N (No Commercial Relationship) | Jason Miller: Commercial Relationship: Code N (No Commercial Relationship) | Mark Johnson: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Young: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine "AREDS- and AREDS2-based" supplements available for purchase online, with attention to their cost and adherence to the formulation tested in the AREDS2 protocol.

Methods: “AREDS” and “AREDS2” were used as search terms in Amazon and Google Shopping. The top 30 search results, excluding items marked as promoted ads, were recorded for each search, and each product was checked for compliance with the AREDS2 formula, allowing for both low (25mg) and high (80mg) zinc formulations. The price per daily serving was calculated for each product and prices of “compliant” vs. “non-compliant” formulas were compared using Student’s t-tests.

Results: 120 search results were analyzed across Amazon and Google Shopping. 30.8% (37/120) of the products did not adhere to the AREDS2 formula. 14.2% (17/120) were missing at least one of the ingredients in the AREDS2 formula. 5.8% (7/120) followed the AREDS1 formula. 17.5% (21/120) contained a higher dose of at least one ingredient and 13.3% (16/120) contained less of at least one ingredient than in the AREDS2 formula. 15.8% (19/120) contained at least one extra ingredient beyond those in the AREDS2 formula. The products that deviated in any way from the AREDS2 formulation were 26.0 percent more expensive than those that did not ($0.63 vs. $0.50 per day, $p = 0.0027$). Similarly, products that were missing at least one of the ingredients in the AREDS2 formula were 26.9 percent more expensive than those that were not ($0.66 vs. $0.52, $p = 0.012$).

Conclusions: Our analysis demonstrates that many of the AREDS2 supplements found using popular online shopping marketplaces deviate from the formulations recommended by the AREDS2 clinical trials. Several of the formulations had decreased or missing dosages of vitamin C and vitamin E. Further, some included extra ingredients that have not been shown to be beneficial in AMD but were advertised as such, including bilberry extract, fish oil, and alpha-lipoic acid. Moreover, several of the supplements followed the AREDS1 formula, which is no longer recommended as it imposes increased risk of lung cancer for smokers. Importantly, we also found that products that did not follow the AREDS2 formula were more expensive on average to the consumer. Clinicians may wish to be specific in their recommendation of AREDS2 formulations to avoid inaccurate dosing.

CONTROL ID: 3713621
SUBMITTER (NAME ONLY): Donia Momen
TITLE: 2022 iOS Apps and COVID-19: Can They Help Our Eye Patients?
SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D. Momen, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|G. Wu, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|K. Tien, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|W. Zhao, J. Huynh, University of California Davis, Davis, California, UNITED STATES|A. Xia, Saint Francis High School, Mountain View, California, UNITED STATES|
Commercial Relationships Disclosure: Donia Momen: Commercial Relationship: Code N (No Commercial Relationship) | Gloria Wu: Commercial Relationship: Code N (No Commercial Relationship) | Katherine Tien: Commercial Relationship: Code N (No Commercial Relationship) | Weichen Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Justin Huynh: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Xia: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: 85% of US adults have a smartphone with 87 million people using a health or wellness app monthly in 2020.[1] There are 350,000 eHealth apps.[2] Roughly 33M adults in the US have the chief complaint of vision loss. An estimated 93M are at high risk for serious visual impairment[3]. Only half have visited an eye doctor in the past 12 months, due to COVID 19.[3] American adults over the age of 18 fall into the demographic of mobile app users.

Do free apps help our eye patients during this pandemic?

Methods: We used the search terms “vision test” and “eye exam” in the Apple App Store to compile a list of the top 10 free apps. We looked for how many free apps have eye charts that are “recognized” such as Snellen chart, Landolt C, LogMAR chart, Amsler grid & Visual Field. Control: Inclusion criteria: 1) free; 2) English language; 3) ≥50 reviews, ≥4 star rating in the Apple App store. Exclusion criteria: 1) foreign languages 2) paid apps.

Results: Results: Top 10 iOS apps (from most downloads to least) in the Apple App Store seen in Table 1. For all iOS apps, Snellen vision test: 9/10; Landolt C: 1/10; LogMAR chart: 3/10; Amsler grid: 3/10; Visual field 1/10. Only 1 app connected you with a local optometrist or ophthalmologist. Only 3/10 apps had >1K reviews. iOS apps do not provide a number of downloads.

Conclusions: Although many adults have not received an eye exam over the past 12 months, physicians can still connect with their patients through public education with the use of mobile apps. However, current eHealth apps can improve their content for eye patients.

References:

1. U.S. Department of Health and Human Services. (2016, May 19). Visual impairment, blindness cases in the U.S. are expected to double by 2050. National Institutes of Health. Retrieved January 6, 2022, from https://www.nih.gov/news-events/news-releases/visual-impairment-blindness-cases-us-expected-double-2050
2. 11 surprising Mobile Health Statistics. Mobius MD. (2021, December 21). Retrieved January 6, 2022, from https://mobius.md/2021/10/25/11-mobile-health-statistics. /
3. Facts and Figures on Adults with Vision Loss. The American Foundation for the Blind. (n.d.). Retrieved January 6, 2022, from https://www.afb.org/research-and-initiatives/statistics/adults

CONTROL ID: 3713623

SUBMITTER (NAME ONLY): Julia Stingl

TITLE: Childhood glaucoma or large optic disc? - The Gutenberg Optic Disc Study (GODS)

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.V. Stingl, C. Braun, F. Wagner, A. Schuster, E.M. Hoffmann, Department of Ophthalmology, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, GERMANY|

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ABSTRACT BODY:

Purpose: To compare peripaillary nerve fiber layer (pRNFL) thickness in pediatric large optic discs with pRNFL in adult large optic discs and pediatric normal sized optic discs.

Methods: 107 large optic discs from 70 children aged 5.7 to 17.7 years (LOD-C group), 107 normal optic discs from 60 children (NOD-C group) and 107 large optic discs from 69 adults (LOD-A group) were included. pRNFL was investigated via Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany). Large optic disc was diagnosed if BMO area measured ≥2.5 mm^2. Large optic discs were matched by BMO area, pediatric optic discs by age. pRNFL thickness profiles (circular scan diameter: 4.1 mm) were compared using t-tests and influence of optic disc size on pRNFL was determined with generalized estimating equation (GEE).

Results: Median age was 12.0, 12.1 and 47.3 years and median BMO area was 2.82, 2.02 and 2.80 mm^2 for LOD-C, NOD-C and LOD-A groups, respectively. Pediatric large optic discs showed a larger mean pRNFL thickness than pediatric normal optic discs (85.4µm vs. 82.4±10.1µm, p=0.031) and maxima of pRNFL thickness profile seemed wider and located more nasally. Adult and pediatric large optic discs did not differ significantly in mean pRNFL thickness (84.8±14.0µm vs. 85.4±10.2µm). In GEE regression analysis, pRNFL thickness was positively correlated with age- and sex-adjusted BMO area (β=4.55, p<0.001) in children.

Conclusions: In children, large optic discs were characterized by a larger mean pRNFL thickness with wider and slightly more nasally located pRNFL thickness maxima compared to normal sized optic discs, measured by OCT. pRNFL profiles of adult and pediatric large optic discs showed a similar shape. pRNFL thickness was linked with BMO area in children.

CONTROL ID: 3713625

SUBMITTER (NAME ONLY): Blanche Kuo

TITLE: Association of real-world visual acuity outcomes and number of anti-VEGF injections in patients with diabetic macular edema: 6-year follow-up using the IRIS® Registry

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.L. Kuo, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|B.L. Kuo, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|D. Tabano, V. Garmo, E. Kim, Genentech Inc, South San Francisco, California, UNITED STATES|T. Leng, M. Hatfield, A. LaPrise, Verana Health, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal therapy (IVT) with anti-vascular endothelial growth factor (anti-VEGF) is first line treatment for diabetic macular edema (DME). This study describes anti-VEGF IVT frequency and long-term visual outcomes among DME patients in routine clinical practice in the United States.

Methods: A retrospective analysis was performed among treatment-naïve DME patients (no prior IVT in the past 12 months) initiating anti-VEGF IVT from 1/1/2015-12/31/2019 using de-identified electronic medical records (IRIS® Registry). The change in visual acuity (VA) from baseline and anti-VEGF IVT frequency (average number of injections and intervals) were reported for up to 6 years of follow-up. VA outcomes were further stratified by baseline VA and number of injections (0, 1-2, 3-4, 5-7, 8-10, ≥11) for the given year.

Results: At 1 year, 124,684 eyes received a mean (SD) of 3.9 (2.8) anti-VEGF injections with a mean injection interval of 10.0 (7.9) weeks and gained a mean of +3.2 (16.4) letters. Among patients with six years of follow up, at year 6, 1,235 eyes received a mean of 2.9 (2.1) injections with a mean interval of 12.3 (8.2) weeks and gained a mean of +0.5 (19.7) letters from baseline. Median follow-up time was 2.1 years. When stratified by baseline VA, overall change in VA was negative for eyes starting with VA ≥20/25 and <20/25 to 20/40, and positive for eyes starting with VA <20/40 to 20/80, <20/80 to >20/200, and ≤20/200 at the end of follow-up (Figure 1). When stratified by the average number of received injections in each year, change in VA from baseline was +2.8 in those who received 1-2 injections compared to +4.8 in those who received ≥11 injections in the first year. This trend was consistent in subsequent years (Figure 2).

Conclusions: The number of injections decreased and injection intervals increased year over year up to 6 years regardless of baseline VA. Improvements in VA from baseline were greatest in eyes that received 5 or more injections each year. Results are unadjusted.

CONTROL ID: 3713626

SUBMITTER (NAME ONLY): Paris Margaritis

TITLE: Preparation for a Gene Therapy Trial for LCA5-Associated Retinal Degenerations: Treatment Potential in Patients and Dose-ranging Studies in Non-human Primates

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Margaritis, J. Bennett, S. Chomistek, V. Vasireddy, I. Shpylchak, Z. Wei, A. Luo, J. Sun, S. Zhou, J. Pham, A.M. Maguire, K.E. Uyhazi, T.S. Aleman, Ophthalmology, Center for Advanced Retinal and Ocular Therapeutics (CAROT), University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in LCA5, which encodes lebercilin, account for one of the most severe forms of early-onset blindness, Leber congenital amaurosis (LCA5-LCA). Currently, there are no treatments for this disease. In our previous studies, early delivery of a AAV8-hLCA5 by subretinal injection in knockout mice partially reversed the severe retinal degeneration. In this study we explore the treatment potential of a group of patients with LCA5-LCA and assessed the safety of subretinal delivery of AAV8-hLCA5 in non-human primates (NHPs) in a dose-ranging study.

Methods: Six patients (ages 6-31 years) with LCA5-LCA underwent ophthalmic exams, full-field stimulus testing, and multimodal imaging with fundus autofluorescence and spectral-domain optical coherence tomography over 3- 5 years. In anticipation of Good Laboratory Practices (GLP) studies, we assessed the safety of subretinal injections of two doses (3E10vg and 1E11vg) of AAV8-hLCA5in NHPs. A control animal was injected with excipient. Retinal imaging matching the protocols used in patients was performed prior to euthanasia (d43 post-injection); retina tissue was evaluated for histopathology and LCA5 immunofluorescence.

Results: Visual acuity in the patients ranged from light perception to 20/200 and there was at least ~4 log units of dark-adapted sensitivity loss. Vision declined slightly during the observation period in some patients. Despite the severe retinal dysfunction, patients showed detectable photoreceptors in the pericentral and midperipheral retina. Subretinal delivery of AAV8-hLCA5 at 3E10 or 1E11vg/eye in NHPs was well-tolerated. There were mild injection-related changes in retinal architecture. There were minimal inflammatory cells in the vitreous and mild thinning of the outer nuclear layer in the eye injected with the higher dose (1E11 vg). AAV8-hLCA5 transduces photoreceptors and RPE cells in the exposed area in the NHP retina.

Conclusions: Detectable but severely dysfunctional photoreceptors in the central and midperipheral retina of patients with LCA5-LCA suggest these regions may be targets for gene augmentation. Subretinal delivery of AAV8-hLCA5 was safe at 1E10vg and there was mild inflammation at 1E11vg. The results of this study provide guidance for the doses to be used in a GLP NHP study and ultimately a human clinical trial.

CONTROL ID: 3713627

SUBMITTER (NAME ONLY): Philippe Ortiz

TITLE: Developing a Screening Tool to Predict Diabetic Retinopathy

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Henderer, Y. Zhang, Ophthalmology, Temple University Hospital, Philadelphia, Pennsylvania, UNITED STATES|P. Ortiz, T. Dunn, S. Mcmurtry, E. Manstein, M. Porebski, M. Stelmach, X. Lu, D. Yu, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current AAO Preferred Practice Patterns recommend that all patients with diabetes (DM) undergo an annual screening for diabetic retinopathy (DR). However previous screenings at Temple University have revealed only a 15% prevalence of DR. Performing a comprehensive eye exam on a normal patient serves no purpose except to increase healthcare costs, reduce appointment availability, and waste time for both patients and physicians. Since 85% of exams showed no sign of DR, performing comprehensive eye exams on everyone appears to be a waste of resources. We present a DR screening tool based on biometric parameters available to a primary care physician to identify patients at a low risk of DR who can safely have less frequent screening exams. Use of this tool could eliminate unnecessary exams and reduce healthcare costs.

Methods: 1,927 patients with DM underwent DR screening from 2016-2020. A retrospective chart review recorded 29 biometric variables based on clinical suspicion of predicting DR. 896 patients with unreadable fundus photos or missing variables were eliminated. Univariate and multivariate analysis identified predictive variables in the remaining 1,031 patients. Logistic regression with maximum likelihood estimates was used to create a series of models that resulted in a score representing the likelihood an individual patient has DR on exam. Models were plotted on receiver operating characteristic (ROC) curves to determine model accuracy and to identify a threshold value that optimizes the accuracy of a diabetic screening exam.

Results: Of the 1,031 patients, 217 (21%) were found to have DR in at least one eye. Eight models were created using the biometric variables. The leading model was formulated using the variables seen in Table 1. The area under the curve (AUC) was 0.74 (Figure 1). Closest to (0,1) Criteria determined the optimal cutoff value of 0.375 with sensitivity and specificity of 48.8% and 82.1% respectively and an accuracy of 0.76.

Conclusions: Our best model demonstrated moderate sensitivity and high specificity to identify DR using a cutoff value of 0.375. The next step will be to use this model, created with readily available biometric data, to predict DR in a new cohort of patients. If successful, we hope this model can be used by primary care physicians to better identify patients more likely to have DR and reduce the number of unnecessary eye exams.

CONTROL ID: 3713629

SUBMITTER (NAME ONLY): Nikhil Menon

TITLE: Proteoglycan 4 (PRG4) regulates NF-κB activation in human corneal epithelial cells through suppression of ubiquitin-like modifier: HLA-F Adjacent transcript number 10 (FAT10)

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.G. Menon, Y. Suhail, K. Gupta, T.A. Schmidt, Biomedical Engineering Department, UConn Health, Farmington, Connecticut, UNITED STATES|G. Jay, Emergency Medicine, Brown University, Providence, Rhode Island, UNITED STATES|L. Shapiro, M. Ghosh, Center for Vascular Biology, Department of Cell Biology, UConn Health, Farmington, Connecticut, UNITED STATES|R. Redfern, Ocular Surface Institute, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proteoglycan 4 (PRG4, or lubricin) is a mucin-like glycoprotein present on the ocular surface and in tears. We recently demonstrated ocular surface expression of PRG4 is diminished in a murine dry eye model, and recombinant human PRG4 (rhPRG4) inhibits dry eye inflammation induced chemokine production in human cornea epithelial cells. The ubiquitin like modifier HLA-F Adjacent transcript number 10 (FAT10) is thought to have immune function, and is an important mediator of inflammation with NFκB being a key nodal hub, though its biological role in dry eye remains unexplored. Here, we examined the ability of rhPRG4, to modulate transcriptional and protein expression of the FAT10, as well as NF-κB activation in human corneal epithelial cells.

Methods: Differentiated telomerase-immortalized human corneal epithelial (hTCEpi) cells were cultured in media alone (control) or +TNFα (100ng/ml), ±300μg/ml rhPRG4 (Lubris BioPharma). RNA was collected for RNASeq after 48hr, and cell lysates were collected at 15-60 min for quantitative western blot analysis (N=3).

Results: RNASeq analysis revealed FAT10 was one of the most upregulated genes by TNFα (~8X), and rhPRG4 significantly inhibited this stimulation ($p<0.05$). An increase (~3X) in the proteasomal subunit LMP-2, which is necessary for IκBa degradation and NF-κB activation, stimulated by TNFα was also significantly inhibited by rhPRG4 ($p<0.05$). Quantitative western blotting of hTCEpi cell lysate confirmed both of these findings at the protein level. Finally, immunoblot analysis also indicated reduction of phospho-p65 levels by rhPRG4 followed by TNFa stimulation compared to TNFa alone.

Conclusions: We and others have established rhPRG4's lubricating and anti-inflammatory properties at the ocular surface. rhPRG4 has also been shown to be clinically effective in treating signs and symptoms of dry eye. Here, we demonstrate a novel biological mechanism in which rhPRG4 limits TNFα stimulated NFκB signaling and the production of downstream inflammatory molecules FAT10 and LMP2 in corneal epithelial cells, suggesting a new therapeutic potential for alleviating dry eye inflammation. These findings provide the foundation for further evaluation of rhPRG4's biological mechanism of action on the ocular surface in maintaining homeostasis and effectively treating dry eye disease.

CONTROL ID: 3713630

SUBMITTER (NAME ONLY): Rachel L.W. Hanson

TITLE: EPDev-AI: Early phase development of an AI tool to determine disease activity in nvAMD

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Hanson, A. Airody, C. O'Dwyer, A. White, Academic Unit of Ophthalmology, York and Scarborough Teaching Hospitals NHS Foundation Trust, York, York, UNITED KINGDOM|M. Porteous, R.P. Gale, Research & Development, York and Scarborough Teaching Hospitals NHS Foundation Trust, York, York, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is projected to affect an average of 1.23 million individuals by the 2050. Whilst anti-VEGF treatment for neovascular AMD (nvAMD) is considered the current gold-standard care, this requires regular monitoring and treatment delivery which causes increased capacity challenges. This, along with the current COVID-19 pandemic, have highlighted the need for efficient and safe ways to diagnose and manage nvAMD. The use of artificial intelligence (AI) in medical care has the potential to alleviate some of this projected pressure facing eye clinics. Previous research has shown that AI has comparable sensitivity and specificity to clinicians in identifying ocular disorders from retinal images. The purpose of the current study was to develop and AI model to identify active from inactive nvAMD disease from retinal SD-OCT images.

Methods: Using Google's Vision AutoML software, 1058 Heidelberg SD-OCT images were identified and labelled as either showing nvAMD activity or inactivity. All images were uploaded to Google's cloud storage and automatically assigned two bounding-box labels; 1 label capturing the entire Heidelberg SD-OCT image, including the raster and b-scan, with the second capturing the b-scan only. All labels were automatically allocated to either a train, validate or test group based on an 80:10:10 ratio set by the software.

Results: Of the 1058 images, a total of 2116 labels were assigned, 1012 showing active and 1104 showing inactive nvAMD. Performance of the AI model revealed an area under the precision recall curve (AUPRC) of 0.84 at a threshold of 0.5, specificity of 40.98% and sensitivity of 95.24%. For the active-only images, the specificity was 34.28% with a sensitivity of 97%. For the inactive-only images, the specificity was 51% with a sensitivity of 92.73%.

Conclusions: Utilising Google's AutoML AI software, this model is able to correctly identify active nvAMD from Heidelberg SD-OCT images with a high level of sensitivity and good overall AUPRC.

CONTROL ID: 3713631

SUBMITTER (NAME ONLY): Binxing Li

TITLE: Conditional Knockout of Scavenger Receptor B1 (SR-B1) from RPE Increases Free Cholesterol Accumulation in the RPE of the $Bco2^{-/-}$ Mice

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Li, F. Chang, A. Ranganathan, N. Giauque, Z. Wan, P.S. Bernstein, Department of Ophthalmology and Visual Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Free cholesterol can efflux onto lipid-rich HDL2 particles in the bloodstream from scavenger receptor B1 (SR-B1) on the surface of peripheral cells. SR-B1 has been detected in the retinal pigment epithelium (RPE) of humans and mice. In this work, we investigated if RPE SR-B1 can facilitate free cholesterol efflux from the RPE of $Bco2^{-/-}$ mice.

Methods: To specifically delete SR-B1 from the RPE of the $Bco2^{-/-}$ mice, we bred the Best-Cre mice and the floxed SR-B1 mice ($Srb1^{f/f}$) into the $Bco2^{-/-}$ mice and generated the RPE-specific conditional knockout mice of SR-B1 (Best-Cre;$Srb1^{f/f}$;$Bco2^{-/-}$). SR-B1 expression was examined by western blot and Immunohistochemistry (IHC). Next, to detect the accumulation of free cholesterol in the RPE, we stained the retinal sections of 6-month-old Best-Cre;$Srb1^{f/f}$;$Bco2^{-/-}$ mice (Srb1cKO) and Best-Cre;$Bco2^{-/-}$ mice (control) (3 mice/genotype) using filipin, and cholesterol was imaged with a bright-field microscope under excitation of a 365-nm UV light. We also further quantified the contents of free cholesterol in the RPE of these two mice with gas chromatography-mass spectrometry (GC-MS) (3 mice/genotype).

Results: Western blot and IHC data demonstrate that SR-B1 had been successfully deleted from the RPE of $Bco2^{-/-}$ mice. There was no structural difference between the SR-B1 conditional knockout mice (Srb1cKO) and the control mice. Filipin staining revealed more free cholesterol in the RPE of the retinal sections of the Srb1cKO mice. GC-MS data shows that the accumulation of free cholesterol in the RPE of Srb1cKO mice was increased around 30% relative to the control mice.

Conclusions: Our results demonstrate that specific deletion of RPE SR-BI can increase the accumulation of free cholesterol in the RPE. This finding may enhance our understanding of the metabolism of local RPE lipids.

CONTROL ID: 3713632

SUBMITTER (NAME ONLY): Ciara Shortall

TITLE: Functional assessment of putative splice-altering variants detected in an Irish inherited retinal disease cohort

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Shortall, L. Whelan, E. Kopcic, A. Dockery, P.F. Kenna, G. Farrar, School of Genetics and Microbiology, The University of Dublin Trinity College, Dublin, IRELAND|A. Dockery, Pathology Department, Mater Misericordiae University Hospital, Dublin, IRELAND|E. Duignan, N. Wynne, P.F. Kenna, Department of Ophthalmology, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|J. Zhu, K.A. Stephenson, J. Turner, J.J. O'Byrne, D.J. Keegan, Clinical Genetics Centre for Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|C. Kirk, G. Silvestri, Department of Ophthalmology, Royal Victoria Hospital, Belfast, Belfast, UNITED KINGDOM|C. Kirk, G. Silvestri, Centre for Experimental Medicine, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Aberrant RNA splicing has emerged as a significant cause of inherited retinal diseases (IRDs). Next generation sequencing of IRD patients living in Ireland and utilisation of in silico splice prediction tools have enabled identification of putative splice-altering variants in IRD-associated genes. The aim of this study was to experimentally validate several of these variants using in vitro splice assays.

Methods: Probands underwent target capture sequencing of exons and canonical/noncanonical splice site regions of 254 IRD-associated genes. Putative splice-altering variants were identified and prioritised for further analysis using in silico splice prediction tools, including SpliceAI and Alamut Visual software. Genomic segments containing the variant of interest or wild-type sequence and flanking exons were amplified, cloned into midigene plasmid vectors and transfected into HEK 293 cells. mRNA was isolated 48 hours post-transfection and transcripts were analysed via RT-PCR, gel electrophoresis and Sanger sequencing.

Results: Midigene splice assays were used to evaluate the consequences of OPA1 c.1681+1G>T (NM_130837.2) and FLVCR1 c.1307+5G>T (NM_014053.3), as well as previously unreported variants in TULP1 (NM_003322.4:c.999+5G>T) and CACNA1F (NM_005183.3: c.2576+4_2576+5delAG). Transfection of a wild-type OPA1 midigene resulted in a single mRNA product of expected length while the mutant construct exclusively produced a shorter fragment in which exon 17 was skipped, leading to a frameshift (p.Ile537Glyfs*10). A wild-type FLVCR1 midigene yielded a full-length transcript and an additional product lacking exon 6. In contrast, the mutant FLVCR1 midigene did not produce any detectable full-length transcript and appeared to increase skipping of exon 6, which causes an in-frame deletion of 37 amino acids. The novel TULP1 and CACNA1F variants tested appeared to induce complex aberrant splicing patterns and work is underway to elucidate the precise nature of these defects.

Conclusions: This study characterised splicing defects resulting from canonical and noncanonical splice site mutations in IRD-associated genes – providing new evidence in support of variant pathogenicity. Functional analysis of such variants is vital for accurate classification of pathogenicity and severity, and increasingly important for enabling access to emerging gene therapies.

CONTROL ID: 3713633

SUBMITTER (NAME ONLY): Anil Tiwari

TITLE: Characterization of Rabbit Corneal Ulceration Model for Pre-Clinical Studies.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tiwari, V. Singh Sangwan, Ophthalmology-Cornea and Stem cells, Dr. Shroff's Charity Eye Hospital, New Delhi, Delhi, INDIA|J. Rajput, P. bellur, B. Sangwan, P. Agrawal, M. Ben Thomas, S. Selvam, A. Chandru, T. Bhowmick, V. Singh Sangwan, Pandorum Technologies Pvt. Ltd., Bangalore, Karnataka, INDIA|A. Singh, Opthalmology, Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Here we enumerate hallmarks of corneal fibrosis and ulceration: fibrosis and extracellular deposition (ECM), angiogenesis and inflammation. This study highlights the ophthalmological, clinical and histopathological changes throughout the progression of deep stromal alkali injury in the rabbit cornea.

Methods: Albino New Zealand rabbits were used for the study. Penetrating lamellar keratoplasty was performed on rabbit cornea (n=3) using guarded trephine. 0.75N NaOH was applied followed by irrigating with normal saline. Animals were imaged using the ophthalmological parameters; i) OCT, ii) Slit lamp and iii) Densitometry over the period of 3 weeks. At the end of three weeks animals were sacrificed and eyes were enucleated and further processed for histopathology (H&E, PAS staining) and Immunohistochemistry

Results: The parameters used in clinics for evaluating patients were used to evaluate and grade the scars into nebular, macular and leucomatous. Slit lamp reveled re-epithelization of the wound in first 5-6 days followed by incidences of epithelial defects, inflammation, and opacification. Neovascularization was observed after 14-15 days of alkali burn. OCT: pachymetry wide and raster scans reveled extensive edema and thickening of the central cornea. Densitometry images reveled stable scar formation with the opacity score ≥75, condition of legal blindness. Histology and immunohistochemistry evaluations supported the ophthalmic evaluation results.

Conclusions: The parameters used in clinics for evaluating patients were used to evaluate and grade the scars into nebular, macular and leucomatous. Slit lamp reveled re-epithelization of the wound in first 5-6 days followed by incidences of epithelial defects, inflammation, and opacification. Neovascularization was observed after 14-15 days of alkali burn. OCT: pachymetry wide and raster scans reveled extensive edema and thickening of the central cornea. Densitometry images reveled stable scar formation with the opacity score ≥75, condition of legal blindness. Histology and immunohistochemistry evaluations supported the ophthalmic evaluation results.

CONTROL ID: 3713634

SUBMITTER (NAME ONLY): Cody Moezzi

TITLE: Ultra-widefield Imaging shows significantly increased Retinal Non-perfusion area in Proliferative diabetic retinopathy compared to Diabetic macular edema phenotypes

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Moezzi, E.L. Wolinsky, P.B. Mendivil, A. Cabrera, F. Monickaraj, A. Das, Ophthalmology, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|F. Monickaraj, A. Das, Veterans Health Administration, Albuquerque, New Mexico, UNITED STATES|M.G. nittala, University of California Los Angeles, Los Angeles, California, UNITED STATES|M.G. nittala, Doheny Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) appear to be two distinctive diseases with unique characteristics, including the response to anti-VEGF treatment. Our previous cross-sectional studies showed that these two phenotypes are not always present concurrently. To determine if PDR and DME have distinctive microvasculature status, ultra-widefield fluorescein angiography (UWF-FA) images of patients with “PDR only” or with “DME only” diagnoses were analyzed.

Methods: A retrospective cohort study, of 18 patients, analyzing the UWF-FA images obtained using Optos California imaging system in patients with PDR only (10 eyes) and DME only (8 eyes). “PDR only” cases included those with preretinal or vitreous hemorrhage without any edema by OCT. The “DME only” cases included only center-involving edema with no concurrent neovascularization or vitreous hemorrhage. Three masked examiners graded the angiograms using the Optos Advance software free-hand tool to demarcate the extent of capillary nonperfusion (areas of hypofluorescence). The outcomes included gradable area, area of capillary nonperfusion, and non-perfusion index (NPI; nonperfused/total gradable area). Statistical analyses were performed with a two-sample t-test for unpaired variables.

Results: Quantification of UWF-FA images revealed that patients with a “PDR only” diagnosis had an average area of nonperfusion measuring 329.6 mm^2 (SD±92.9 mm^2) and those with “DME only” diagnosis had an average area of nonperfusion measuring 193.0 mm^2 (SD±27.8 mm^2). Our analysis revealed that the areas of retinal capillary nonperfusion was significantly higher (1.7 fold) for patients with “PDR only” compared to patients with “DME only” ($p<0.005$). The NPI in “PDR only” cases was significantly higher than that observed in “DME only” cases, 0.43 and 0.26, respectively ($p =0.002$).

Conclusions: Ultra-widefield fluorescein angiography demonstrates significantly increased areas of capillary nonperfusion in cases with a “PDR only” diagnosis compared to “DME only” diagnosed cases. The increased severity of nonperfusion in PDR cases may be related to increased production of VEGF and consequent angiogenesis. These preliminary findings show that PDR and DME may be driven by distinct pathological processes and molecular mediators.

CONTROL ID: 3713635

SUBMITTER (NAME ONLY): Amy Nau

TITLE: Use of SPEED Questionnaire for School Based Dry Eye Screening

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Nau, New England College of Optometry, Boston, Massachusetts, UNITED STATES|A.C. Nau, R. Rawal, O. Nau, B. Rawal, R. Rawal, Korb & Associates, PLLC, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) is the most common cause of dry eye, is linked to screen use and can occur in adolescents. The Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire has predictive value for MGD.The purpose of this study was to evaluate the reproducibility of the SPEED questionnaire for determining symptoms of dryness in middle and high school students.

Methods: The SPEED questionnaire was administered online to middle and high school students living in a suburb of Boston, MA USA in May 2020 and June 2021.

Results: The 2020 survey included 462 respondents (male 177, female 276, non binary 5) mean age 14.38 years (range 11-18). 38 nationalities were self-identified: White 49.94%,Asian 27.57%, all others (mixed <3%). The 2021 survey included 288 respondents (male 70, female 111, non-binary 4, preferred not to answer 1; Mean age 15.86 years(range 10-18). 14 nationalities were self-identified: White 51.1%, Asian 28.1%, African American 4.6%, all others <3%). The mean SPEED score in 2020 was 8.325 (SD 4.67; range 0-28) and the mean SPEED score in 2021 was 10.12 (SD 4.78; range 0-23). Data from the 2021 and 2022 plots were compared using the Spearman correlation test and no significant correlation was found between the two timepoints (rho=0.079).

Conclusions: The SPEED reproducibly revealed an alarmingly high prevalence of dry eye symptoms in middle and high school students. The 2021 scores show higher frequency and severity which may be due to an additional year on screens or the one year average age difference. The use of questionnaires is an inexpensive method for dry eye screening to promote early intervention. School districts should administer validated dry eye symptom questionnaires on an annual basis.

CONTROL ID: 3713636

SUBMITTER (NAME ONLY): Joëlle Vergroesen

TITLE: MIND your diet: how to decrease your glaucoma risk with nutrition

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Vergroesen, W.D. Ramdas, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Vergroesen, T. de Crom, T. Voortman, Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|T. Voortman, Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, Gelderland, NETHERLANDS|C.C. Klaver, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|C.C. Klaver, Ophthalmology & Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet is developed as a strategy to promote healthy cognitive ageing. Adherence to the MIND diet has been associated with reduced incidence of Alzheimer's disease and slowed cognitive decline with aging or after stroke. Since open-angleglaucoma (OAG) is also a neurodegenerative disease, it is of interest to study the effect of the MIND diet on the incidence (i) of OAG. To determine whether this diet has a different effect on iOAG risk than diets designed to improve overall health, we also determined the association between iOAG and the Mediterranean diet and Dutch Dietary Guidelines.

Methods: Participants of the Rotterdam Study, a longitudinal population-based cohort study, were regularly monitored for iOAG. Dietary data were collected at baseline using validated food frequency questionnaires. The association between the diet scores and iOAG was analyzed using multivariate logistic regression analyses, adjusted for body mass index, total energy intake, physical activity and follow-up time. Additional adjustment for intraocular pressure (IOP), smoking and education level was also performed. The association between the diet scores and IOP, the main risk factor of OAG, was assessed using multivariate linear regression analyses.

Results: A total of 1020 participants were included in the analyses, among whom 170 developed iOAG over a mean 10.9-year follow-up period. Controls were age (mean 65.8 years) and gender (54.1% female)-matched. As expected, cases had a significantly higher IOP (16.4 vs. 14.2 mmHg). We found that adherence to the MIND diet was associated with a decreased iOAG risk (11% for each 1-point increase in score; Odds Ratio=0.89; 95% confidence interval 0.80-1.00). This association remained even after adjusting for factors that correlate with a healthy lifestyle. Sensitivity analyses, excluding one component of the total MIND score at a time, showed that the protective effect originated especially from the intake of green leafy vegetables, berries and fish. No associations were observed between the Mediterranean diet score or Dutch Dietary Guidelines score and iOAG. Moreover, none of the diet scores were associated with IOP.

Conclusions: A higher adherence to the MIND diet was associated with a lower incidence of OAG. The mechanism is probably not through the IOP. Thus, the MIND diet may also serve as a beneficial dietary pattern for healthy eyes.

CONTROL ID: 3713637

SUBMITTER (NAME ONLY): Collin Goebel

TITLE: Expression of Adenosine Receptors and Their Changes in Age-Related Macular Degeneration

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Goebel, I. Zaitoun, H. Potter, N. Sheibani, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|I. Zaitoun, N. Sheibani, Macpherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Collin Goebel: Commercial Relationship: Code N (No Commercial Relationship) | Ismail Zaitoun: Commercial Relationship: Code N (No Commercial Relationship) | Heather Potter: Commercial Relationship: Code N (No Commercial Relationship) | Nader Sheibani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Adenosine receptors (AR) A1, A2A, A2B, and A3 are known to have important roles in the modulation of inflammatory and neurodegenerative processes. However, much remains unknown about their choroidal expression and their function in ocular neurodegenerative diseases including age-related macular degeneration (AMD). This study tested the hypothesis that AR are expressed in the human choroid and changes in their expression occur in patients with AMD.

Methods: Human ocular samples were obtained from the Lion Gift of Sight Eye Bank at the University of Minnesota. Donor eyes with wet AMD, dry AMD, and no AMD were selected. Each set of donor samples was stained with ADORA1, ADORA2A, ADORA2B, and ADORA3 specific antibodies. Each sample was also stained with collagen IV antibody to label the vasculature and DAPI to visualize cellular organization. Samples were then incubated with secondary antibodies and fluorescence microscopy was used to compare the presence and intensity of AR expression.

Results: Receptor A1 demonstrated expression within the retina, particularly the inner plexiform layer (IPL) and outer plexiform layer (OPL). There was also evidence of expression within the choroidal vasculature. Receptor A2A demonstrated expression within the retinal and choroidal vasculature, and its expression was modestly decreased in samples from patients with wet and dry AMD. Receptor A2B demonstrated expression throughout the retina in all samples, particularly the ganglion cell layer, OPL, and IPL. Receptor A2B was also expressed in the retinal and choroidal vasculature. Receptor A3 was expressed primarily within the inner nuclear layer and outer nuclear layer of the retina.

Conclusions: Our results provide further evidence that AR are widely expressed throughout the human retina and choroid, and receptors A1, A2A, and A2B appear to be strongly expressed within the choroidal vasculature. Furthermore, our results suggest decreased receptor A2A expression in patients with both wet and dry AMD may contribute to the pathophysiology of AMD. Additional studies with a larger sample size will be required to further evaluate the contribution of changes in A2A expression to AMD pathology.

CONTROL ID: 3713640

SUBMITTER (NAME ONLY): Peiluo Xu

TITLE: Cone inner-segment area and circularity in chorioderemia assessed with split-detection adaptive optics scanning light ophthalmoscopy

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Xu, Department of Bioengineering, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|P. Xu, Y. Jiang, J.I. Morgan, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|Y. Jiang, J.I. Morgan, Center for Advanced Retinal and Ocular Therapeutics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Peiluo Xu: Commercial Relationship: Code N (No Commercial Relationship) | Yu You Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Jessica Morgan: Commercial Relationship(s);Code P (Patent):US Patent 8226236, US Patent App. 16/389,942;Code F (Financial Support):AGTC

ABSTRACT BODY:

Purpose: Choroideremia (CHM) is an X-linked inherited retinal degeneration affecting the photoreceptors, retinal pigment epithelium and choriocapillaris. Previous studies have reported local regions of reduced and normal cone density in CHM, but density measurements alone do not fully quantify the cone phenotype. Here, we compare cone inner segment (IS) area and circularity in CHM images to cones in images from normal-sighted controls.

Methods: Nonconfocal split-detection images of the photoreceptor IS mosaic in 13 CHM and 12 normal controls were acquired at 1, 2, and 4° temporal to the fovea using a custom-built, multimodal adaptive optics scanning light ophthalmoscope. Cone centers were manually identified (JIWM) and cone borders segmented (PX). A custom MATLAB script was used to extract perimeter and area for each cone. Cone circularity was calculated as 4π * cone area / cone perimeter^2. Regularities of each metric [defined as mean / standard deviation (stdev)] were calculated for each image. Unbalanced two-way ANOVA and Bonferroni post hoc were used to assess statistical differences between disease states (CHM vs. control) and along retinal eccentricity.

Results: There was an effect of disease [ANOVA; $F(1,65) = 31.88$, $p < 0.001$] and eccentricity [$F(2,65) = 63.23$, $p < 0.001$] on cone area, though there was no significant interaction between disease state and eccentricity [$F(2,65) = 0.02$, $p = 0.981$]. Cones were significantly larger in CHM than control (mean ± stdev: 20.4 ± 8.8 μm^2 vs. 14.5 ± 7.3 μm^2; $p < 0.001$) and larger with eccentricity from the fovea ($p < 0.001$). There was an effect of disease state on cone circularity [$F(1,65) = 4.31$, $p = 0.042$] and circularity regularity [$F(1,65) = 14.72$, $p < 0.001$]. Compared to control, cones in CHM were more circular ($p = 0.042$) and circularity regularity was higher ($p< 0.001$). There was no significant effect of disease state on cone area regularity [$F(1,65) = 1.27$, $p = 0.264$].

Conclusions: Cones are larger and more circular in CHM compared to normal, consistent with the idea that cones expand to form a contiguous mosaic in areas of reduced photoreceptor density. The increase in circularity in CHM was surprising, but one possible explanation may be that the tight packing of normal parafoveal cones result in a lack of intra-cone space and thus adjacent cones' borders abut.

CONTROL ID: 3713644

SUBMITTER (NAME ONLY): Edoardo Villani

TITLE: Dry Eye symptoms during the COVID-19 era

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Villani, F. D'Ancona, L. Marelli, F. Bonsignore, V. Gallo, DISCCO, Universita degli Studi di Milano, Milano, Lombardia, ITALY|E. Villani, F. D'Ancona, L. Marelli, F. Bonsignore, V. Gallo, San Giuseppe Hospital, IRCCS Multimedica, Milano, -- select one --, ITALY|L. Agnifili, Universita degli Studi Gabriele d'Annunzio Chieti Pescara, Chieti, Abruzzo, ITALY|P. Nucci, Biomedical, Surgical and Dental Sciences, Universita degli Studi di Milano, Milano, Lombardia, ITALY|

Commercial Relationships Disclosure: Edoardo Villani: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan, FB Vision, Alcon, Santen, Thea, Visufarma, Fidia;Code F (Financial Support):Allergan, Alfa Intes, Off Health | Fabrizio D'Ancona: Commercial Relationship: Code N (No Commercial Relationship) | Luca Marelli: Commercial Relationship: Code N (No Commercial Relationship) | Francesco Bonsignore: Commercial Relationship: Code N (No Commercial Relationship) | Vanessa Gallo: Commercial Relationship: Code N (No Commercial Relationship) | Luca Agnifili: Commercial Relationship: Code N (No Commercial Relationship) | Paolo Nucci: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Preliminary evidences from the literature, together with our everyday clinical practice and patients reporting, led us to hypothesize that dry eye (DED) symptoms related to some COVID-19 mitigation measures might be a common problem and a relevant issue. We designed this study in order to assess and to monitor DED symptoms' changes from 2019 to 2021, in both DED patients and healthy subjects, and to investigate their relationship with homeworking and facemask wearing.

Methods: We retrospectively reviewed the medical records of patients who, between November and December 2019 (V19), had undergone an eye exam including quantification of Ocular Surface Disease Index (OSDI) score at the Eye Clinic San Giuseppe Hospital, Milan.

Between November and December 2020, we performed a telephone survey (V20) contacting these patients. The survey was repeated between November and December 2021 (V21).

The telephone survey included the OSDI 12-items and a custom-made questionnaire exploring type of job or occupation, home working, screen time, type and average time of face mask-wearing, and recent onset and worsening of DED-related symptoms.

We investigated the difference among V21, V20 and V19 DED symptoms, the rate of subjects with OSDI increase > OSDI minimal clinically important difference (MCID), and associations between DED symptoms, face masks wearing, VDT usage and home working.

Results: Of 120 subjects with V19 OSDI≤12, 43 (36%) and 39 (32%) showed OSDI>12 at V20 and at V21, respectively. OSDI was significantly correlated with duration of face masks use (V20 r= 0.29; P<0.01. V21 r= 0.23; P<0.01) and heavy mask users had a significantly higher OSDI (P<0.05). V20 and V21 OSDI was significantly higher in home-workers (P<0.05) but we did not find a significant correlation between V21 OSDI and referred number of VDT use (r= 0.07; P=0.41).

Of 70 patients with V19 OSDI>12, 18 (26%) and 24 (34%) showed symptoms worsening >MCID at V20 and V21, respectively. The percentage of OSDI worsening >MCID was significantly higher among heavy face masks users (73% vs 12%; P<0.01, Fisher test). The percentage of OSDI worsening >MCID was significantly higher in home workers at V20 but not at V21.

Conclusions: Some COVID-19 mitigation strategies seem to have a significant role in triggering DED symptoms onset or worsening. This issue persisted during the second pandemic year, with weaker correlation to presumed trigger factors.

CONTROL ID: 3713645

SUBMITTER (NAME ONLY): Liancheng Yang

TITLE: Phosphene Mapping to fine-tune local clusters using a paired dots test

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Yang, G. Dagnelie, OPHTHALMOLOGY, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|H. Sun, W. Diaz, K. Sargur, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Intracortical Visual Prosthesis (ICVP) project will implant many (160 – 400) electrodes into a patient's cortex. An accurate phosphene map is needed to present images to ICVP wearers with minimal distortion. As some phosphenes may form closely spaced clusters, this problem becomes significant with absolute mapping methods. Therefore, we created a relative mapping technique presenting pairs of dots for clustered phosphenes.

Methods: Combining the VIVE Pro Eye headset (eye and head tracking) and a Polhemus G4 finger tracker in Unity gaming platform, we tested sighted subjects facing a 36" radius concave sphere cap.

We created a set of 16 randomized dots in the lower left quadrant, representing phosphenes from electrodes in the upper right visual cortex . To limit the number of pairs (which for 160 electrodes would be 12720), we only tested pairs within clusters: Only pairs for which the relative proximity (rp; i.e., pair separation / pair eccentricity) was less than a cut-off value were selected; at rp ≤ 25%, we get 11 pairs (chart 1).

During testing, subjects used the left index finger to indicate the direction between dots in a pair shown in the headset. Subjects performed a practice trial (5 pairs), followed by 3 tests (11 pairs each).

Results: With data sets collected from 23 subjects, we calculate the direction distributions for each pair; as the distance of the dot pair increased, the SD of the distribution decreased, indicating that subjects were able to indicate the direction more precisely. The same relationship was found for relative proximity (box plot size in chart 2). With 5 subjects who were tested twice, we found that subjects improved both accuracy and precision of the direction settings.

Conclusions: The small deviation angles demonstrate that relative direction mapping provides a reliable basis for rearranging phosphenes within local clusters. Limiting pairs to dots within clusters keeps the total number of pairs to be presented to a manageable number compared to the complete combinatorial pairs required for a complete relative mapping. Combined with the absolute mapping techniques we are developing this will allow robust phosphene map construction within a reasonable time frame.

CONTROL ID: 3713646

SUBMITTER (NAME ONLY): Abel Hamdan

TITLE: Imaging-Based Rescue of Uveitis Patients Treated With Injectable Fluocinolone Acetonide

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hamdan, S. Sharma, C. Chen, P. Le, P.M. Kaiser, M. Ramos, J. Bhangu, M.A. McDonald, D. Burton, J. Teter, K. Baynes, S.K. Srivastava, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Abel Hamdan: Commercial Relationship(s);Code R (Recipient):Eyepoint | Sumit Sharma: Commercial Relationship(s);Code C (Consultant/Contractor):AbbVie, Alimera, Bausch & Lomb, Eyepoint, Regeneron, Genentech/Roche, Clearside;Code F (Financial Support):Gilead, Genentech/Roche, Santen, IONIS | Cindy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Phuoc-Hanh Le: Commercial Relationship: Code N (No Commercial Relationship) | Peter Kaiser: Commercial Relationship: Code N (No Commercial Relationship) | Michael Ramos: Commercial Relationship: Code N (No Commercial Relationship) | Jasmin Bhangu: Commercial Relationship: Code N (No Commercial Relationship) | Megan McDonald: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Burton: Commercial Relationship: Code N (No Commercial Relationship) | Jillian Teter: Commercial Relationship: Code N (No Commercial Relationship) | Kimberly Baynes: Commercial Relationship: Code N (No Commercial Relationship) | Sunil Srivastava: Commercial Relationship(s);Code C (Consultant/Contractor):Gilead, Eyevensys, Jcyte, Regeneron, Eyepoint, Zeiss, Bausch, Sanofi, Allergan, Abbvie, Novartis;Code R (Recipient):Gilead, Eyevensys, Eyepoint, Regeneron, Bausch

ABSTRACT BODY:

Purpose: Injectable Fluocinolone Acetonide (FA) was approved in 2018 for treatment of non-infectious uveitis (NIU) affecting the posterior segment. We monitored the incidence of rescue events in a year long prospective investigator initiated study (IIS) evaluating imaging outcomes in patients treated with the FA implant.

Methods: A total of 31 adult NIU patients on FA 0.18mg were initially enrolled in an IIS. 27 NIU patients (13 males; 14 females) (17 white; 10 black) (n=32 eyes) were included in this analysis with a baseline visit and at least one month follow-up. Imaging including OCT and wide field fluorescein angiography were performed at study visits. Criteria for treatment rescue involved the use of additional intravitreal (IV) injections or an increase in immunosuppression to treat resilient and/or worsening leakage on imaging. Patients with bilateral eye disease who received systemic rescue treatment for only one worsening eye had their other eye excluded from primary calculations. 32 different sets of eyes were included for the 1 month, 3 month, and 6 month follow-up data, respectively. 26 eyes were included for 9 month follow-up. 19 eyes were included for 12 month follow-up.

Results: 10 of 32 eyes (9/27 pts) required rescue within one year (31%). Five patients required at least two rescues. On average, 11% of eyes required rescue within 6 months and 16% after 6 months. Three patients with bilateral eye disease received systemic rescue treatment for only one worsening eye (one patient at the 6 month, 9 month, and 12-month follow-up, respectively); the other eye for these patients were excluded. Treatments included NSAID eye drops, steroid eye drops, systemic steroids, dexamethasone intravitreal implants, triamcinolone acetonide injections, repeat FA 0.18mg implants, and FA 0.59mg implants.

Conclusions: About one-third of patients on FA 0.18mg will require rescue treatment within one year. The most likely time for rescue will be around six months to one year following initiation of treatment.

CONTROL ID: 3713647

SUBMITTER (NAME ONLY): Sehar Riaz

TITLE: Regulation of Protocadherin-15 function in the outer retina by alternative splicing of cytoplasmic domain

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Riaz, S. Sethna, S. Riazuddin, Z. Ahmed, University of Maryland Baltimore, Baltimore, Maryland, UNITED STATES|L. Carvalho, Centre for Ophthalmology and Vision Science, Lions Eye Institute, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|

Commercial Relationships Disclosure: Sehar Riaz: Commercial Relationship: Code N (No Commercial Relationship) | Saumil Sethna: Commercial Relationship: Code N (No Commercial Relationship) | Saima Riazuddin: Commercial Relationship: Code N (No Commercial Relationship) | Livia Carvalho: Commercial Relationship: Code N (No Commercial Relationship) | Zubair Ahmed: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Usher syndrome (USH) is a leading cause of deafness-blindness and variants in PCDH15 are responsible for USH type 1F (USH1F). Previous studies showeded three alternative spliced cytoplasmic domains (CD1, CD2 and CD3) of PCDH15., however expression and functional data in the murine retina were lacking. Herein, we investigated the spatiotemporal expression pattern of Pcdh15 isoforms in the developing and mature mouse retina. We evaluated the visual function of three mouse lines, lacking one out of three Pcdh15 cytodomains (Pcdh15-CD1, -CD2, -CD3). Finally, we developed and evaluated the impact of dual-AAV based PCDH15 gene delivery in the mouse retina.

Methods: Immunoblotting and immunofluorescent imaging showed using CD1, CD2 and CD3 domain specific antibodies showed the expression and subcellular distribution of protocadherin-15 isoforms. Mice lacking Pcdh15-CD1, -CD2 or -CD3 isoforms were assessed for structure and function was assessed by optical coherence tomography (OCT) and electroretinography (ERG). Two halves of human PCDH15 were packaged in adeno-associated virus (AAV) and subretinal injection were performed in Pcdh15 mutant and control mice followed by serial ERG analysis.

Results: Both protocadherin-15-CD1 and -CD3 isoforms were detected but no expression of CD2 isoform was found. Consistent with immunoblotting, we also observed expression of protocadherin-15-CD1 and -CD3 isoforms in multiple retinal layers, including photoreceptors, at specific ages from P1 to P42. Consistent with expression data we found intact vision in Pcdh15-CD2 knockout mice at 2-months of age. Currently, we are performing ERG analysis and retinal structural analysis of older mice from each of the mutant lines. In parallel, we also packaged two halves of human PCDH15 in AAV-Anc80L65 capsid and performed subretinal injections in. Finally, Pcdh15 null mice injected with dual AAV at P20-P21 or P30, revealed significant improvement of vision.

Conclusions: Our current findings indicate that although retina expresses multiple isoforms of protocadherin-15, but either not all of them require for normal vision or have functional redundancy. Furthermore, dual AAV based PCDH15 vectors mediated gene replacement therapy revealed promising results and significantly restored vision in Pcdh15 mutant mice.

CONTROL ID: 3713648

SUBMITTER (NAME ONLY): Liwen Lin

TITLE: Signaling through TNFRSF25 using a novel mPTX-35 antibody prolongs corneal allograft survival in mice by in-vivo expansion of regulatory FoxP3$^+$ T cells.

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lin, H.M. Mousa, R.G. Blanco Ortiz, J. Echegaray, V.L. Perez, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|M. Seavey, R.R. Jasuja, Heat Biologics, Inc., Morrisville, North Carolina, UNITED STATES|R. Levy, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: CD4$^+$FoxP3$^+$CD25$^+$ regulatory cells (Tregs) are essential for maintaining self-tolerance and their manipulation is of considerable interest as a strategy to prevent allograft rejection. mPTX-35 is an affinity matured mouse IgG1 anti-Human TNFRSF25 antibody, which can expand Tregs by stimulating the TNFRSF25 receptor. This work tested whether mPTX-35 treatment could prolong allogeneic corneal transplants (CT) in mice accompanied by Tregs expansion.

Methods: Balb/c mice were administered different doses (0.5 ug, 5 ug, 50 ug) of mPTX-35 via subconjunctival (SC) injection and compared to an IgG1 (50ug) control. CD4$^+$FoxP3$^+$CD25$^+$ Tregs in conjunctiva and draining LN were analyzed by flow cytometry 6 and 14 days post-treatment. MHC-mismatched CTs were performed from B6 to Balb/c mice, with the following treatment groups: (1) 1-dose-mPTX-35 (single dose, SC, 5ug, day-3), (2) 2-dose-mPTX-35 (2 doses, SC, 5 ug, day 0 & 7). Data is presented using median survival day post-transplant (MST) comparing mPTX-35 treated to IgG1 controls. Corneal opacity of the graft was scored twice per week using a pre-established scale ranging from 0-4; rejection was defined as a recorded score of ≥3 for two consecutive readings.

Results: In the conjunctiva, Tregs/CD4+ frequency was significantly increased in the mPTX-35 treated mice on day 6 post-treatment at doses of 5 ug mPTX-35 (51.4±3.1%, $p<0.0001$) and 50 ug (48.6±2.5%, $p<0.0001$) vs IgG1 control (16.3±1%). Significant increases were also detected on day 14 in all 3 dose groups. Tregs/CD4+ frequency in the draining LN on day 6 was significantly elevated in the 5 ug mPTX-35 (22.7±2.5%, $p=0.0037$) and 50 ug mPTX-35 (19.8±1.6%, $p=0.0048$), but not in the 0.5 ug mPTX-35 (10.6±1.5%, ns) compared to the control (11.3±2.1%). In contrast to the subconjunctiva, no differences were detected on day 14 in the draining LN. Compared to their IgG1 controls, MST was not prolonged in the 1-dose-mPTX-35 group (27.5 d vs 33d, n=6/group), but significantly prolonged in the 2-dose-mPTX-35 group (39 d vs 21 d, $p=0.0224$, n=6/group).

Conclusions: Local ocular delivery of TNFRSF25 specific mPTX-35 prolongs graft survival day in the allogeneic CT setting in mice. We posit recruiting Treg cells to the local conjunctiva and draining LN inhibits rejection responses. mPTX-35 would be a potential candidate to treat CT rejection in clinic.

CONTROL ID: 3713650

SUBMITTER (NAME ONLY): Scott McPherson

TITLE: Parabiosis Reveals That Recruitment of Circulating Antigen Presenting Cells is Necessary for the Induction of Autoimmune Retinitis

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.W. McPherson, N.D. Heuss, M. Abedin, M. Pierson, H. Roehrich, D.S. Gregerson, Ophthalmology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Characterizing immune cells and conditions that govern their recruitment and function in autoimmune diseases of the nervous system or in neurodegenerative processes is an area of active investigation. We sought to analyze the origin of antigen presenting cells associated with the induction of retinal autoimmunity using a system that relies on spontaneous autoimmunity rather than experimentally induced autoimmunity, avoiding uncertainties associated with immunization with adjuvants at remotes sites or adoptive transfer of in-vitro activated T cells.

Methods: We used R161H TCR transgenic mice (Horai, et. al. J Autoimmunity 44:21, provided by Dr. R. Caspi, B10.R3 background), which spontaneously and rapidly develop severe autoimmune retinitis (AR), in conjunction with $CD11c^{DTR/GFP}$ mice (B6/J background) that allow tracking of activated, antigen presenting microglia within the retina (GFP^{hi} cells). $R161H^{+/-}$ x B6/J F_1 mice were used to analyze the influx/expansion of antigen presenting cells and T cells relative to the course of AR. Parabiosis using $R161H^{+/-}$ x B6/J F_1 mice paired with B10.R3 x B6/J F_1 (wild type recipient) mice was done to explore the origin and phenotype of antigen presenting cells crucial for the induction of autoimmunity. Analysis was done by retinal imaging, flow cytometry, and histology.

Results: Onset of AR in $R161H^{+/-}$ x B6/J F_1 mice was delayed relative to B10.R3-$R161H^{+/-}$ mice revealing a distinct prophase of the disease prior to frank autoimmunity that was characterized by expansion of GFP^{hi} cells within the retina prior to any clinical or histological evidence of autoimmunity. Parabiosis between mice carrying the R161H and $CD11c^{DTR/GFP}$ transgenes and wild type recipients showed that recruitment of circulating GFP^{hi}cells to retinas was required for induction of AR. GFP^{hi} cells were found in 19/30 retinas from wild type recipients with 12 of those recipients developing AR. Conversely, none of the 11 recipients devoid of GFP^{hi}cells developed AR ($p = 0.0006$).

Conclusions: Our results here contrast with our previous findings showing that retinal antigen presenting cells expanding in response to either sterile inflammatory injury or neurodegeneration were derived from myeloid cells within the retina or optic nerve thus highlighting a unique facet of retinal autoimmunity.

CONTROL ID: 3713651

SUBMITTER (NAME ONLY): Rozemarijn Verhoeven

TITLE: Nonclinical Pharmacokinetics and Pharmacodynamics of Brimochol, a Combination Product for the Treatment of Presbyopia

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Verhoeven, Little Creek Research, North Carolina, UNITED STATES|J. Burke, R. Schiffman, Visus Therapeutics, California, UNITED STATES|

Commercial Relationships Disclosure: Rozemarijn Verhoeven: Commercial Relationship(s);Code C (Consultant/Contractor):Visus Therapeutics | James Burke: Commercial Relationship(s);Code E (Employment):Visus Therapeutics;Code P (Patent):Visus Therapeutics | Rhett Schiffman: Commercial Relationship(s);Code E (Employment):Visus Therapeutics;Code P (Patent):Visus Therapeutics

ABSTRACT BODY:

Purpose: Brimochol™ (Visus Therapeutics) is a fixed combination of the cholinergic miotic agent carbachol and the alpha-2 agonist brimonidine that is being developed as a topical ocular product for the treatment of presbyopia. The purpose of these two nonclinical studies was to evaluate ocular distribution and effect on pupil diameter following administration of Brimochol in pigmented rabbits.

Methods: Dutch Belted rabbits (4/group) received a single unilateral administration of 35 µl of Brimochol or carbachol 2.75%, while the contralateral eye received phosphate-buffered saline (PBS). Pupil diameter was measured in conscious animals using a digital pupillometer under scotopic (0 lux), low mesopic (0.3 lux), high mesopic (3 lux), and photopic (669 lux) conditions at baseline and at various time points out to 12 hours postdose. Ophthalmic exams were conducted at 0.25 and 2 hours postdose using the Hackett McDonald scoring system. In a separate study, rabbits received a bilateral administration of Brimochol or carbachol, and concentrations of brimonidine and carbachol were measured in ocular matrices (4 eyes/time point) using liquid chromatography and tandem mass spectrometry.

Results: Brimochol decreased pupil size in all lighting conditions to a greater extent than carbachol alone, and the miotic effect was sustained for up to 12 hours. An improved ocular tolerability profile was observed for Brimochol compared to carbachol alone. The mean maximum concentration (Cmax) for carbachol in the iris ciliary body (ICB) was 32.8 ng/g and the mean area under the curve (AUC) was 223h*ng/g for Brimochol, compared to 17.7 ng/g and 157 h*ng/g, respectively, for carbachol alone, indicating increased exposure to carbachol following Brimochol administration. Time at Cmax (Tmax) was similar between groups.

Conclusions: Brimochol demonstrated effectiveness at reducing pupil size in rabbits for 12 hours and had a greater effect on pupil size than carbachol 2.75% alone. The addition of brimonidine appears to improve the ocular tolerance profile compared to carbachol alone. Perhaps by altering aqueous dynamics, the addition of brimonidine also tends to increase the extent and duration of carbachol exposure in the target tissue.

CONTROL ID: 3713652

SUBMITTER (NAME ONLY): Joanna Kempska

TITLE: Metabolic analysis of serum deprived ARPE-19 cells -implications for cellular metabolic changes in age-related macular degeneration

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kempska, S.R. Sonntag, S. Grisanti, Y. Miura, Ophtalmology, Department of Ophtalmology, University of Lübeck, Lübeck, GERMANY|K. Shima, J. Rupp, Department of Infectious Diseases and Microbiology, Univerity of Lübeck, GERMANY|N. Kubota, R. Brinkmann, Medical Laser Center Lübeck, GERMANY|P. Enzian, Y. Miura, Insitute of Biomedical Optics, University of Lübeck, GERMANY|

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ABSTRACT BODY:

Purpose: Serum deprivation in cultured human retinal pigment epithelial (RPE) cells has been shown to result in cell responses similar to those seen in age-related macular degeneration (AMD). In this study, we investigated the impact of serum deprivation on mitochondrial respiration of cultured ARPE-19 cells. Furthermore, influence of an uncoupler under serum deprivation conditions was also examined.

Methods: ARPE-19 cells were cultured in Dulbecco's modified Eagle's Medium (DMEM, 4.5 g/L glucose) with either normal (10%) or deprived (1%) fetal calf serum (FCS). Under both conditions, some cells were treated with different concentrations of the uncoupling agent carbonyl cyanide 4-(trifluoromethoxy) phenylhydrazone (FCCP) for 24 hours. Cell viability was assessed by cytotoxicity assay with WST-1 (4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate). ARPE-19 cells were pre-treated with sublethal doses of FCCP (0.5 µM and 1 µM) for 24 hours before their mitochondrial respiratory function was analyzed by Mitostress Assay with the Seahorse XFe24 Analyzer.

Results: WST-1 assay results showed FCCP at concentrations up to 1 µM did not affect the viability of ARPE-19 cells after 24 hours of exposure under both normal and serum-deprived conditions. Serum deprivation reduced basal and maximal respiration of ARPE-19 cells by 23% and 21%, respectively, compared to normal serum conditions ($p<0.01$). Pre-treatment with 0.5 µM and 1 µM FCCP for 24 hours significantly reduced basal respiration of RPE cells' under serum deprived condition, while maximum respiration and spare capacity were significantly increased after pre-treatment with 1 µM FCCP. Under normal serum condition, pre-treatment of FCCP showed no significant effect on mitochondrial respiratory functions of ARPE-19 cells.

Conclusions: Results indicate that low doses of mitochondrial uncoupling may enhance potential mitochondrial respiratory function of RPE cells under serum deprived conditions, mimicking the phenotypes of RPE cells in AMD. This suggests that mitochondrial uncoupling of RPE cells may be a potential therapeutic target for degenerative retinal disorders, and further studies are needed to clarify this.

CONTROL ID: 3713654

SUBMITTER (NAME ONLY): Miwa Hara

TITLE: PNPLA2 mobilizes retinyl esters from retinosomes in the retinal pigment epithelium

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hara, Y. Takahashi, J. Ma, G.P. Moiseyev, Biochemistry, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|W. Wu, G.P. Moiseyev, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinyl ester hydrolase (REH) cleaves retinyl esters (RE) to produce retinol. REH has not been identified in the RPE previously. The purpose of this project is to investigate the role of patatin-like phospholipase domain containing 2 (PNPLA2) as REH in the visual cycle.

Methods: PNPLA2 mRNA and protein levels were examined in retinal tissues and sections by real-time (RT)-PCR, western blot analysis and immunofluorescence staining. PNPLA2 knockout ($PNPLA2^{-/-}$) mice were used to examine the retinal function and rhodopsin recovery by electroretinography (ERG). Visual chromophore regeneration was determined by photobleaching mice for 30 min at 5k lux light followed by recovering in the dark for 15 and 40 min. Retinoid profiles were analyzed by HPLC. SiRNA-mediated knock-down was used to analyze the REH activity of endogenous PNPLA2 in HEK293A cells.

Results: Western blot analysis and immunofluorescence staining of the WT mouse retinal tissues and sections confirmed PNPLA2 expression in the RPE and retina. ERG analysis revealed a- and b-wave amplitudes were significantly lower in $PNPLA2^{-/-}$ mice, suggesting impaired retinal function. $PNPLA2^{-/-}$ mice showed lower a-wave recovery after photobleach compared with WT mice. More prominent lipid droplet accumulation along the plasma membrane was observed in RPE cells from $PNPLA2^{-/-}$ mice relative to WT mice. Visual chromophore regeneration was slower in $PNPLA2^{-/-}$ mice compared with WT mice. The content of RE was significantly higher in $PNPLA2^{-/-}$ mouse eyes relative to age-matched WT mice at all tested time points, implying that PNPLA2 hydrolyzes RE from the retinosomes in the RPE, releasing all-trans-retinol (atROL). In cultured cells, siRNA-mediated knock-down increased RE levels, confirming REH activity of PNPLA2.

Conclusions: REH activity of PNPLA2 was required to mobilize retinol from lipid bodies in RPE cells and is an essential component of the visual cycle. The absence of PNPLA 2 expression in the RPE led to declined retinal function and impaired visual chromophore regeneration along with a significant amount of lipid accumulation.

CONTROL ID: 3713655

SUBMITTER (NAME ONLY): Sonal Dalvi

TITLE: E-cigarette vapor extract promotes pro-maculopathy cellular changes in an induced pluripotent stem cell model.

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dalvi, A. Bhogavalli, C.I. Thomas, R. Singh, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|R. Singh, Biomedical Genetics, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Electronic cigarettes (e-cigs), battery-powered devices that produce aerosols by heating e-liquid solution, are a popular alternative to smoking. It is well-established that smoking is a major modifiable risk factor for age-related macular degeneration (AMD). Notably, like cigarette smoke, e-cig vapor exposure stimulates pro-inflammatory and angiogenic responses in the mouse retina. Based on these findings, our purpose in this study was to utilize induced pluripotent stem cell (iPSC)-based disease modeling studies and evaluate the direct relevance of e-cig vapor for AMD pathology development.

Methods: Parallel cultures of control iPSC-derived retinal pigment epithelium (RPE) cells grown as polarized monolayer in transwell inserts were supplemented daily with either varied concentrations of freshly prepared e-cig vapor extract (ECVE, 1%, 5% or 10%) or vehicle (cell culture media;untreated) for 14 days and evaluated longitudinally for cell viability (Calcein AM), and epithelial barrier integrity (transepithelial measurements). At the end of the treatment duration (day 14), quantitative real-time PCR and Western blotting was used to assess expression/levels of inflammation-related genes/proteins (e.g., C3, IL-6). Furthermore, rate of phagocytosis of photoreceptor outer segment (POS) post-feeding of POS (~20 POS/RPE cell) for 2h was determined by measuring levels of RHO, a POS-specific protein, by using Western blotting. Lastly, immunocytochemistry was used to evaluate count and area of TIMP3/NileRed/APOE co-localizing sub-RPE deposits on the transwell membrane.

Results: Chronic exposure (14 days) of control RPE to 1%, 5% and 10% ECVE did not adversely impact cell viability and epithelial barrier integrity. In contrast, compared to untreated iPSC-RPE; ECVE-treated iPSC-RPE showed i) reduced uptake of POS, ii) elevated levels of extracellular HMGB1, a prototypic damage associated molecular pattern (DAMP) molecule, iii) increased levels of sPLA2-IIa, a pro-inflammatory enzyme that promotes inflammation by generation of reactive lipids and iv) increased count and area of sub-RPE TIMP3/Nile Red/APOE- positive drusen-like deposits.

Conclusions: Using iPSC-based disease modeling studies, we show that ECVE exposure promotes sterile inflammation and induces several pro-maculopathy changes in RPE cells, including decreased POS phagocytosis and formation of sub-RPE drusen-like deposits.

CONTROL ID: 3713656

SUBMITTER (NAME ONLY): Frances Silva

TITLE: Cone Contrast Sensitivity and Color Naming: A New Color Vision Test

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Silva, J.C. Rabin, G. Anderson, H. Gillentine, L. Liqing, E. Lee, L. Inclan, N. Trevino, H. Vo, University of the Incarnate Word Rosenberg School of Optometry, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Computer-based color contrast sensitivity (CS) tests diagnose type and severity of hereditary color vision deficiency (CVD) and acquired CVD in various diseases. These tests are predicated on saturation discrimination but provide no information about hue and color naming. Our purpose was to develop a clinically expedient test of cone CS which includes a color naming score (cone contrast naming test; CCNT).

Methods: 26 color vision normals (CVNs, mean age ± SD: 26 ± 5) and 20 hereditary CVDs (CVDs, age 32 ± 12) confirmed by Ishihara, anomaloscope, and cone CS participated after written informed consent. Test distance was 3 ft. in a dark room (Microsoft Surface display). Single letters on a grey background stimulated only L, M or S cones or luminance (Lum). Weber contrast varied from 1%-16% in 2X steps for L, M, Lum; S cones: 8%-128% in 2X steps. On each trial a single letter appeared within a crosshair for 5 sec. Subjects identified the letter and named its color. Letter types (L, M, S, Lum) were presented twice at each of five contrasts and both letter type and contrast were randomized in each session. CS and color naming was based on the number correct using a scale of 100.

Results: CVN CCNT CS correlated with Innova Systems, Inc. cone CS (r^2 = 0.3 $P < .001$) as did CVD CCNT CS (r^2 = 0.8 $P < .001$) validating CCNT CS. Sensitivity of CCNT cone CS for detecting type and severity of hereditary CVD was 100% (mean CVN CS: 84, mean CVD CS: 28, $P < .001$). Specificity in CVDs for confirming normal color vision in the normal cone type was 100% (mean CVN and CVD CS: 84, $P > .89$). Mean CVD CS scores were 6.1 standard deviations below CVD norms ($P < .001$). CVDs showed significant decrements in color naming for the deficient cone, normal cone, and luminance stimulus (mean 39) compared to CVNs (mean 82, $P < .001$). CS alone showed non-repetitive distinct scores in 30% of CVDs and CVNs while a composite score (mean of CS and CN) showed distinct scores in 70% of CVDs ($P < .001$) and in 46% of CVNs ($P < .002$) indicating that the composite score better discriminates between levels of performance in both CVDs and CVNs.

Conclusions: The CCNT combines cone CS with color naming to include both thresholds and color identification in a single, clinically expedient test. The composite score better discriminates levels of color ability important for matching CVDs with occupational needs and identifying the impact of acquired CVD on performance.

CONTROL ID: 3713658

SUBMITTER (NAME ONLY): Timothy A Blenkinsop

TITLE: 3D eye organoids with distinct cornea

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The cornea is a highly specialized tissue, that is crucial for vision. Currently, there is a need for in vitro models of the cornea to study infections, wound healing, drug screening, and as sources for transplant cells. Here, we report on the identification of distinct corneal epithelium as well as other important corneal cells through single cell RNA sequencing (scRNAseq) analysis of a 3D eye organoid.

Methods: 3D eye organoids were grown from H9 ESCs, seeding 3000 cells/well in a 96 ultra-low bind u-bottom plate in mTeSR media supplemented with 2.5% Matrigel and 40nM Thiazovivin (THIA) on day 0. Deafferentation was initiated at day 2 by changing to differentiation media (DM): GMEM with 10% knock out serum replacement, 1mM Sodium pyruvate, 1mM non-essential amino acids, 2mM L-glutamate, 1% penicillin-streptomycin solution and 55μM β-mercapto ethanol. Corneal specification was enhanced at day 32-46 by changing to DM:CnT-PR (1:1) supplemented with 10ng/mL keratinocyte growth factor (KGF) and 40nM THIA, before changing to maintenance media; DMEM:F12, 2% B-27 supplement, 10ng/ml KGF and 2μM THIA at day 48. At day 153, one organoid was digested with 2.5mg/mL collagenase II to form a single cell suspension. The single cell suspension was processed for 10x scRNAseq. The data was clustered by guided clustering using the Seurat package in R, and the resulting clusters were annotated using the Enricher online database and expression of specific gene markers.

Results: scRNAseq data revealed clusters that could be annotated as 11 different cell populations, among which were a corneal epithelium population, corneal stroma, and corneal endothelial like cells. The corneal epithelium had a high expression of corneal keratins (KRT12, KRT5, KRT15) as well as expression of mucus (MUC16), E-cadherin (CDH1) and eye filed marker PAX6. The corneal stroma- and corneal endothelium-like cells had high expression of collagen (e.g. COL8A1), hyaluronan acid synthase (HAS2), KERA, mesenchymal, and hematopoietic markers CD44, CD34 and CD133 (PROM1).

Conclusions: We report on the generation of 3D eye organoids from hESCs that mature to form cells from the cornea. These organoids can be used as tools to study infections, wound healing, and pharmacological screening in a cost-effective way with reduced need for animal experiments.

CONTROL ID: 3713659

SUBMITTER (NAME ONLY): Oana Zeleznik

TITLE: Plasma metabolomics of primary open-angle glaucoma in three prospective US cohorts and the UK Biobank

SESSION TITLE: Epidemiology of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O.A. Zeleznik, J. Kang, J.A. Lasky-Su, B. Rosner, Channing Division of Network Medicine, Brigham and Women's Hospital/Harvard Medical School, Massachusetts, UNITED STATES|C.B. Clish, Broad Institute of Massachusetts Institute of Technology and Harvard, Massachusetts, UNITED STATES|T. Elze, J.L. Wiggs, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Khawaja, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|T. Elze, J.L. Wiggs, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.R. Pasquale, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify plasma metabolites associated with primary open-angle glaucoma (POAG) risk.

Methods: In a case-control study from the Nurses' Health Study (NHS), NHSII and Health Professionals Follow-Up Study (HPFS), 602 incident POAG cases were 1:1 matched to 602 controls. LC-MS/MS metabolomics were measured on plasma samples; 367 metabolites passed quality control analyses. For comparison, in a cross-sectional study in the UK Biobank, 167 NMR metabolites were measured in serum samples from 2238 prevalent glaucoma cases and 44723 controls. Multiple logistic regression was used to identify metabolites associated with POAG in NHS/NHSII/HPFS and glaucoma in UK Biobank. In NHS/NHSII/HPFS, we also used Metabolite Set Enrichment Analysis to identify metabolite classes associated with POAG. All analyses adjusted for established glaucoma risk factors and relevant co-morbidities. False discovery rate (FDR) was used to adjust for multiple comparisons.

Results: Eight metabolite classes were associated (FDR<0.05) with POAG in NHS/NHSII/HPFS: triglycerides (TGs), diglycerides, two lysophospholipids classes [lysophosphatidylcholines and lysophosphatidylethanolamines], and one phospholipid class [phosphatidylethanolamines] were positively associated, while cholesteryl esters, carnitines, and organic acids and derivatives were inversely associated with POAG risk. Interestingly, polyunsaturated TGs with long fatty acyl chains were associated with a lower POAG risk while less unsaturated TGs with shorter fatty acyl chains were positively associated with POAG risk (Figure 1). In the UK Biobank, TGs and phospholipids (from which lysophospholipids are derived through hydrolysis), were positively associated with glaucoma, as found in NHS/NHSII/HPFS. Tyrosine, glucose, and glutamine were positively associated while acetate, 3-hydroxybutyrate, citrate, pyruvate and lactate were inversely associated with glaucoma (FDR<0.2).

Conclusions:

Higher levels of TGs, with potential differences by saturation and fatty acyl chain length, and phospholipids were adversely associated with POAG in both the NHS/NHSII/HPFS and the UK Biobank, suggesting that they play an important and complex role in POAG and may represent new screening and treatment targets.

CONTROL ID: 3713660

SUBMITTER (NAME ONLY): Nergis Khan

TITLE: Predicting systemic health features from retinal fundus images using transfer-learning based AI models

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Khan, C. Perera, E.R. Dow, T. Leng, V.B. Mahajan, P. Mruthyunjaya, D.V. Do, D. Myung, Department of Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|C. Perera, Western Australia Health Networks, Perth, Western Australia, AUSTRALIA|D. Myung, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Whilst color fundus photos are used in routine clinical practice to diagnose ophthalmic conditions, a growing body of evidence suggests that ocular imaging contains valuable information regarding systemic clinical features of patients. These features can be identified through a variety of computer vision techniques including deep learning (DL) AI models. Predictions regarding coronary heart disease, chronic kidney disease, hypertension, current smoking status, and gender have been demonstrated in prior studies. In this study, we aim to both construct a DL model that can predict a variety of systemic features from fundus images and determine the optimal method of DL model construction for this specific task.

Methods: Data were collected from a cohort of patients who had routine fundus imaging for diabetic retinopathy screening between March 2020 and March 2021. This data consisted of matched fundus images and clinical data from chart review. A series of DL models were then created and trained based on the DenseNet201 architecture to predict each of the recorded clinical features. In order to ascertain the optimal method of creating these models, two models were created for each clinical feature - one utilizing transfer learning with images from the ImageNet database, and one without transfer learning.

Results: A total of 1277 fundus images were used to train the DL models to predict various systemic clinical features. Area Under the Receiver Operating Characteristics (AUROC) scores were used to compare the performance of each model. We found that models utilizing transfer learning were superior to those that did not (mean AUROC 0.78 vs 0.63, $p < 0.05$). Models using transfer learning were able to predict the following systemic features Age > 70 (AUROC 0.95), Ethnicity (AUROC 0.93), Gender (AUROC 0.85), ARB Medication use (AUROC 0.81), and ACE Medication use (AUROC 0.81).

Conclusions: Fundus images contain valuable information about the systemic characteristics of a patient. A DL model can predict Age, Ethnicity, Gender and ARB/ACE medication usage with a good degree of accuracy. To optimize DL model performance, we recommend that even domain specific models utilize transfer learning techniques to enhance performance.

CONTROL ID: 3713661

SUBMITTER (NAME ONLY): Jared Tangeman

TITLE: RPE neural competency is restricted by alterations to a homeobox transcription factor regulatory network

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.A. Tangeman, R. Pérez-Estrada, E. Van Zeeland, L. Liu, C. Liang, K. Del Rio-Tsonis, Biology, Miami University, Oxford, Ohio, UNITED STATES|J.A. Tangeman, R. Pérez-Estrada, K. Del Rio-Tsonis, Center for Visual Sciences, Miami University, Oxford, Ohio, UNITED STATES|C. Liang, Computer Science and Software Engineering, Miami University, Oxford, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Embryonic amniotes and some adult salamanders can regenerate neural retina from cells of the retinal pigment epithelium (RPE). Injured embryonic chicken RPE can regenerate neural retina if stimulated with FGF2 at embryonic day 4 (E4), but for reasons that are not understood, this ability is lost by embryonic day 5 (E5). We hypothesize that alterations to transcription factor (TF) networks restrict the neural competency of the developing RPE.

Methods: RPE cells from developing E4 and E5 chickens were collected and subjected to gene expression profiling via bulk and single-nuclei RNA-seq, as well as chromatin accessibility profiling via ATAC-seq. In parallel, RPE was collected at both E4 and E5 at several timepoints following retinectomy in the presence or absence of FGF2 treatment. Changes in gene expression and chromatin accessibility were integrated to assess TF DNA-binding activity and differential behavior of downstream targets.

Results: E4 RPE responds to retinectomy and FGF2 by elevating the expression of genes encoding neural retina TFs, such as PAX6, VSX2, and ASCL1, while simultaneously down-regulating RPE markers OTX2 and MITF. In contrast, the E5 RPE can be induced to express neural retina TFs, but also displays enhanced hallmarks of maturity independent of injury or FGF2 treatment, pertaining to pigmentation, retinoic acid synthesis, extracellular matrix deposition, and reduced proliferative status. Accessibility changes across the E4 to E5 window suggest altered activity of the RPE-determining TF OTX2, which has the potential to regulate downstream targets that enhance RPE fate and block neural retina identity.

Conclusions: RPE lineage commitment is accompanied by widespread shifts in the regulation of RPE maturation genes and neural retina-associated TFs. An altered homeobox TF network at E5 promotes RPE fate and blocks neural retina identity, in part through enhanced OTX2 activity. These findings implicate OTX2 activity as a determinant of RPE lineage commitment and assess several indicators of RPE maturity in relation to neural competence.

CONTROL ID: 3713664

SUBMITTER (NAME ONLY): D Joshua Cameron

TITLE: Zeaxanthin Protects Visual Function from A2E Damage

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Cameron, E.J. Cameron, Optometry, Western University of Health Sciences, Pomona, California, UNITED STATES|

Commercial Relationships Disclosure: D Joshua Cameron: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Cameron: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a devastating eye disease affecting millions of people. One of the compounds that has been shown to contribute to AMD is the vitamin A derivative A2E (N-retinyl-N-retinylidene ethanolamine). Another compound, zeaxanthin, is a carotenoid that naturally accumulates in the retina. Supplements containing zeaxanthin as well as other carotenoids have been shown to improve vision and prevent progression of damage to advanced AMD in some studies. We wanted to see if zeaxanthin alone could protect vision loss associated with A2 in the zebrafish retina.

Methods: Adult zebrafish were maintained using standard conditions. All experiments were approved by our university IACUC. Baseline visual acuity was measured using the optokinetic response as previously described. One eye was injected with 50 μM A2E and the other eye was injected with 0.46 ng/μl zeaxanthin and 50 μM A2E. Visual acuity was assessed at weekly intervals after the injections. Statistical analysis was done using a paired t-test.

Results: Baseline visual acuities were consistent with previously published acuities in adult zebrafish. The average baseline acuity for the right eyes was 49 cycles/degree (c/d) and the left eyes was 47 c/d. A2E caused the visual acuity to slowly decline, whereas zeaxanthin protected the retina from the A2E damage. By the 2^{nd} week post injection, the A2E injected eyes had a nearly 7% decline in the visual acuity on average compared to the original baseline. Zeaxanthin protected the opposite eye. Most eyes even saw an increase in visual acuity relative to baseline.

Conclusions: Zeaxanthin protected visual acuity in zebrafish from A2E damage. Because the zebrafish retina regenerates, longitudinal studies are limited using this testing paradigm, so another model or system may be needed to study the long-term effects of these treatments.

CONTROL ID: 3713668

SUBMITTER (NAME ONLY): Iulen Cabeza

TITLE: Quantification of ciliary muscle movement during accommodation from transscleral OCT images

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I. Cabeza, B. Calvo, Aragón Institute of Engineering Research (i3A), University of Zaragoza, SPAIN|B. Calvo, Centro de Investigacion Biomedica en Red en Bioingenieria, Biomateriales y Nanomedicina (CIBER-BBN), SPAIN|Y. Chang, M. Ruggeri, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Florida, UNITED STATES|Y. Chang, M. Ruggeri, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The accommodative response of the ciliary muscle (CM) is usually quantified from transscleral OCT images using thickness profiles. This approach does not capture the inward movement and change in length of the CM which is observed in real-time ultrasound images. We present a method to quantify the CM movement from transscleral OCT images acquired dynamically during accommodation.

Methods: A transscleral SD-OCT system operating at 1325 nm (Ruggeri et al, Biomed Opt Exp; 2016) was used to acquire OCT image sequences of the CM through the temporal side of the left eye of 3 young subjects (ages: 22, 25, 26 years) and two pre-presbyopic subjects (age: 45 years) during accommodation. The system is combined with an accommodation target to produce a monocular accommodation step stimulus during imaging. Each recording consisted of a sequence of 160 OCT images acquired over 6.2 seconds. The dynamic response of the CM was recorded in response to step stimuli of 2D and 4D for the young subjects, and 2D for the pre-presbyopic subjects. The system is synchronized with an extended depth SD-OCT system that simultaneously acquires images of the crystalline lens during accommodation (Ruggeri et al, Biomed Opt Exp; 2016). In-house software was used to segment the ciliary muscle and lens boundaries in each image. Procrustes analysis was used to register the sequences of CM images assuming that there is no change in CM volume during accommodation. The movement of the CM centroid and apex were then quantified. Changes in lens thickness were also assessed to confirm that all subjects accommodated.

Results: For a 2D stimuli, the change in lens thickness with accommodation ranges from 0.09 to 0.13 mm in the young subjects, and from 0.07 to 0.09 mm in the pre-prebyopic subjects. For a 4D stimulus, the change in lens thickness ranges from 0.13 to 0.20 mm in the young subjects. Figure A shows the change in contour of the ciliary muscle of a young subject (22 y/o) responding to a 4D stimulus. Figures B-F show the dynamic response of the position of the CM apex (left) and the time course of the change in the CM apex position and lens thickness (right) during accommodation.

Conclusions: We demonstrated the feasibility of quantifying the dynamics of the ciliary muscle movement from transscleral OCT images. The results show that the contraction of the cilary muscle in young and pre-presbyopic subjects is comparable.

CONTROL ID: 3713669

SUBMITTER (NAME ONLY): Haoshen Shi

TITLE: Targeted microglial miR-155 inhibition restores homeostatic microglial phenotypes and attenuates vasculopathy in retinas of Alzheimer's models

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Shi, Y. Koronyo, J. Sheyn, D. Fuchs, M. Davis, J. Wilson, K. Black, M. Koronyo-Hamaoui, Cedars-Sinai Medical Center Department of Neurosurgery, Los Angeles, California, UNITED STATES|Z. Yin, O. Butovsky, Brigham and Women's Hospital Center for Neurologic Diseases, Boston, Massachusetts, UNITED STATES|V. Gupta, S.L. Graham, Health and Human Sciences, Macquarie University, Sydney, New South Wales, AUSTRALIA|M. Mirzaei, Molecular Sciences, Macquarie University, Sydney, New South Wales, AUSTRALIA|Z. Yin, O. Butovsky, Harvard Medical School Evergrande Center for Immunologic Diseases, Boston, Massachusetts, UNITED STATES|M. Koronyo-Hamaoui, Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent single cell RNA sequencing studies identified the neurodegeneration-associated microglial phenotype (MGnD/DAM), typically observed surrounding cerebral amyloid plaques in Alzheimer's disease (AD) murine models. Further analyses revealed that the MGnD phenotype expression was regulated by the TREM2/APOE/microRNA-155 (miR-155) signaling pathway. However, this microglial phenotype has never been investigated in any retinal disease, including in the AD-afflicted retina. Mounting evidence demonstrates that the retina mirrors pathological changes that occur in AD brains. Here, we investigated populations of MGnD and their impact on the retinas of double transgenic APP/PS1 mouse models of AD in response to conditional knock-out of microglial miR-155.

Methods: $APP_{SWE}/PS1_{L166P}$, $miR155^{fl/fl}$, and $Cx3cr1Cre^{ERT2}$ mice were crossed to generate an Alzheimer-like mice genotype that can be targeted for conditional knock-out (cKO) of miR-155, specifically in microglia. Mice were sacrificed at 4 and 8 months of age. Retinas or whole eyes were extracted for analyses of retinal flat-mounts, cross-sections, protein homogenates (e.g., MSD, western-blot, mass-spectrometry), and isolated retinal vasculature.

Results: Immunostaining of retinal flat-mounts and cross-sections revealed a substantial population of $clec7a^{+}$ and $galectin\text{-}3^{+}$ MGnD in retinas from APP/PS1 mice. Targeting microglial miR-155 diminished MGnD and upregulated homeostatic microglial marker P2ry12; these findings were associated with anti-inflammatory cytokine profiles. Global proteome analysis by mass spectrometry identified enhanced PI3K-Akt signaling cascades due to microglial miR-155 inhibition. Importantly, such immune intervention protected tight junction integrity and reduced vascular amyloidosis in retinas of APP/PS1 mice.

Conclusions: Targeting neurodegeneration-associated microglia restored the homeostatic retinal-immune milieu in murine models of AD. Our data uncover more complex microglial phenotypes, distinct from the traditional M0, M1 and M2 microglia, and their tight link to the neurovascular unit integrity. The robust protective effects of microglial miR-155 ablation may shed light onto novel innate immune-based treatments for retinal degeneration and AD.

CONTROL ID: 3713672

SUBMITTER (NAME ONLY): Chi Zhang

TITLE: Oxidative stress alters tight junction formation and transcytosis of human retinal microvascular endothelial cells through activation of Wnt signaling

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Zhang, J.J. Zheng, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|C. Zhang, J.J. Zheng, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Chi Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Jie Zheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Abnormal retinal neovascularization associated with various retinopathies can result in irreversible vision loss. Although the mechanisms involved in the occurrence of retinal neovascularization is still under investigation, increasing evidence suggests that aberrant Wnt signaling activated by reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2), participates in the pathogenesis of abnormal neovascularization. We utilized novel small molecule Wnt inhibitors to study the role of ROS regulating Wnt activity affecting tight junction formation and transcytosis of human retinal microvascular endothelial cells (HRMECs) in vitro.

Methods: HRMECs were treated with H_2O_2 for 30 minutes, H_2O_2 together with Wnt inhibitors or vehicle. Quantitative PCR (qPCR) analysis of Axin2 was utilized to assess the inhibitory profile of Wnt inhibitors and the activation profile of Wnt signaling upon H_2O_2 stimulation. Transepithelial endothelial Electrical Resistance (TEER) was used to evaluate cell tight junction formation. Transcytosis assay was used to explore whether Wnt signaling regulates transcytosis of HRMEC in vitro.

Results: Application of H_2O_2 to the HRMECs leads to increased Axin2 mRNA expression. In contrast to this, Wnt inhibitors attenuated H_2O_2 mediated Axin2 mRNA expression. Additionally, HRMECs treated with H_2O_2 presented altered tight junction formation and transcytosis that were regulated by Wnt inhibitors.

Conclusions: We found that increased Wnt signaling activity was detected in H_2O_2 treated HRMECs. The abilities of HRMECs to form tight junction and transcytosis affected by H_2O_2 treatment through upregulation of Wnt signaling in vitro. Moreover, these effects were effectively suppressed by small-molecule Wnt inhibitors.

CONTROL ID: 3713673

SUBMITTER (NAME ONLY): George Ousler

TITLE: Safety and efficacy of ophthalmic mitochondrial reactive oxygen species scavenger Visomitin for the treatment of dry eye disease: findings of VISTA-1 and VISTA-2 studies

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.W. Ousler, M. Watson, Ora Inc, Andover, Massachusetts, UNITED STATES|J.D. Sheppard, Virginia Eye Consultants, Norfolk, Virginia, UNITED STATES|J.D. Sheppard, P. Karpecki, L.T. Friedhoff, A. Petrov, M. Skulachev, Mitotech S.A., LUXEMBOURG|P. Karpecki, Kentucky College of Optometry, University of Pikeville,, Pikeville, Kentucky, UNITED STATES|M. Ngiam, Q. Xue, Essex Bio-Technology Limited, HONG KONG|

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ABSTRACT BODY:

Purpose: Phase 2b/3 study VISTA-1 and Phase 3 study VISTA-2 were designed to identify the optimal dose of mitochondrial reactive oxygen species (mtROS) scavenger Visomitin (SkQ1 ophthalmic solution) in patients diagnosed with dry eye disease (DED) and to identify potential primary endpoints for the pivotal study VISTA-3.

Methods: VISTA-1 and VISTA-2 were multi-center, double-masked, randomized, placebo-controlled studies, each comprising 5 visits over the course of 9 weeks. In VISTA-1, qualified subjects (n=451) were randomized 1:1:1 to receive low or high dose of Visomitin or placebo. In VISTA-2, qualified subjects (n=610) were randomized 1:1 to receive either high dose Visomitin or placebo. In VISTA-1, the co-primary endpoints were change from baseline to Visit 5 (Day 57) in central corneal fluorescein staining (Ora Calibra® Fluorescein Staining Scale) and the change in grittiness (Ora Calibra® 4 Symptom Scale). In VISTA-2, the co-primary endpoints were change from baseline to Day 57 in conjunctival fluorescein staining and in ocular discomfort (Ora Calibra® Ocular Discomfort Scale). Key pre-determined secondary endpoint included the change from baseline to Visit 3 (Day 29) in central corneal fluorescein staining.

Results: The co-primary endpoints of both studies were not met, but in VISTA-2 Visomitin demonstrated statistically significant superiority in the key pre-determined secondary endpoint of change from baseline to Visit 3 (Day 29) in central corneal fluorescein staining ($p<0.05$) relative to vehicle in a large sub-population defined by Schirmer's score. Similar statistically significant improvements in patients treated with Visomitin were observed in the VISTA-1 study. Importantly, in that sub-population both studies demonstrated statistically significant superiority of Visomitin ($p<0.05$) relative to vehicle in clearing of corneal fluorescein staining at Day 29.

Conclusions: Visomitin ophthalmic solution, a drug designed for protecting the ocular surface from oxidative stress at mitochondrial level, demonstrated statistically significant effects on clearing of corneal staining in both VISTA-1 and VISTA-2 studies, which is a highly clinically relevant result. These findings provide support for using clearing of corneal fluorescein staining as the primary endpoint in a forthcoming pivotal study (VISTA-3)."

CONTROL ID: 3713674

SUBMITTER (NAME ONLY): Hongli Wu

TITLE:

Function and therapeutic potential of glutaredoxin (Grx) system in the lens

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Wu, J. Zhang, Y. Yu, K. Lal, M. Au, Pharmaceutical Sciences, University of North Texas System, University of North Texas System, Dallas, TX, US, academic/system, Fort Worth, Texas, UNITED STATES|H. Wu, Y. Liu, North Texas Eye Research Institute, University of North Texas System, University of North Texas System, Dallas, TX, US, academic/system, Fort Worth, Texas, UNITED STATES|K. Green, Department of Chemistry & Biochemistry, Texas Christian University, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the function and therapeutic potential of glutaredoxin (Grx) system, both glutaredoxin 1 (Grx1) and glutaredoxin 2 (Grx2), using Grx1/Grx2 double knockout (DKO) mice and the Grx activators as research models.

Methods: Two-month old Grx1/Grx2 DKO and age-matched wild-type (WT) mice were exposed to 20.6 kJ/m^2 UV radiation for 15 mins to induce cataracts. Mice were euthanized at 4 days post-exposure. The degree of the cataract and lens morphology were evaluated under a dissecting microscope. To further define the crosstalk between the Grx system and nuclear factor erythroid 2-related factor 2 (Nrf2) antioxidant pathway, Nrf2 and its downstream target proteins were examined by using Western blot analysis. Addtionally, we have developed a series of Grx modulators, molecules L1-L4, which are a family of pyridol-containing N-heterocyclic amines. The therapeutic potential of these Grx activators was evaluated using ex-vivo lens organ culture system.

Results: We found that UV radiation caused more severe anterior subcapsular cataract in Grx1/Grx2 DKO than that of WT mice. The opacity of the lenses in DKO mice, appeared to extend deeper into the cortical and even nuclear regions. Lenses of Grx1/Grx2 DKO mice contained significant lower levels of glutathione (GSH) and higher levels of glutathionylated proteins (PSSG), a marker for protein thiol oxidation. Deletion of Grx1 and Grx2 also decreased the expression of antioxidant enzyme transcription factor regulator, Nrf2, and its downstream antioxidant genes, including catalase, superoxide dismutase (SOD), and thioredoxin (Trx). Our ex vivo study showed that L1-L4 dose-dependently protected the lens from H_2O_2-induced opacification.

Conclusions: Grx1 and Grx2 gene deletion impairs Nrf2-dependent antioxidant response, causing elevation of oxidative stress that may increase the lens susceptibility to UV-induced damage. Grx activators can improve the redox homeostasis in the lens and prevent H_2O_2-induced cataract formation.

CONTROL ID: 3713676

SUBMITTER (NAME ONLY): Thomas Strong

TITLE: Characterization of Ephrin Receptor Activation in the Neuropathic Progression of Hereditary and Traumatic Optic Neuropathy Models

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Strong, D. Pelaez, Cell Biology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|T. Strong, H. Wang, D. Pelaez, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Thomas Strong: Commercial Relationship: Code N (No Commercial Relationship) | Hua Wang: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Pelaez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic neuropathies are a major cause of irreversible blindness worldwide. While risk factors are known, the molecular progression that ultimately leads to neuronal apoptosis and blindness has yet to be fully elucidated. Recent studies show ephrin signaling as one of the most dysregulated signaling pathways in the pathophysiology of optic neuropathies. In this study, we hypothesize that neuropathic progression is initiated in part by the anachronic reactivation of repulsive ephrin forward signaling within the neural retina.

Methods: We used two optic neuropathic models, DBA/2J (D2J) mice which develop hereditary glaucomatous defects and the optic nerve crush (ONC) model in C57BL/6 (C57) mice. Semi-quantitative immunoblotting was used to assay the activation of several Eph receptors (Ephs) temporally in the D2J mice (2mo – 23mo) and ONC mice (24-, and 48-hr post-injury). Immunofluorescent (IF) staining was used to confirm the localization of activated Ephs within the retina.

Results: Our results show an age-dependent increase in the activation of several Ephs in the retina of D2J mice, with the majority of Ephs present in a hyperphosphorylated state at age 23mo. Interestingly, results show that EphA1, A3, A6, A7, B1, B2, and B6, are significantly phosphorylated as early as 2mo of age ($p=<0.05$). Additionally, several Ephs are activated within 24hrs of ONC with a significantly greater phosphorylation occurring after 48hrs.

IF images determined the localization of Ephs to the RGC layer. IF analysis further showed that D2J retinas exhibit an age-dependent activation of the EphB1 and B2 receptors throughout the inner retina. IF imaging of the ONC mice shows that EphA2, A3, A4, B1, and B2 become phosphorylated after injury (24hr) and that their spatial distribution is predominately in the inner retina.

Conclusions: These results indicate that Ephs activation and repulsive forward signaling may play a role in the neuropathic progression of both hereditary and traumatic optic neuropathy. These results demonstrate that Ephs can be observed as early as 2mo of age in hereditary optic neuropathy and 24hr in traumatic optic neuropathy. Together these studies underscore the need to explore this repulsive pathway in early optic neuropathies and it provides a glimpse of the number of receptors that are present in the retina of mice, and which are engaged in neuropathic states.

CONTROL ID: 3713680

SUBMITTER (NAME ONLY): Tasnim BEN YACOUB

TITLE: Toward a better understanding of ITM2B pathogenicity in a specific retinal dystrophy, and its potential role in mitochondria

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. BEN YACOUB, C. Letellier, J. Wohlschlegel, C. Michiels, C. Zeitz, I.S. Audo, genetics, Institut de la vision, Paris, Île-de-France, FRANCE|O. Goureau, Institut de la vision, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Our team identified a missense mutation in ITM2B underlying a novel autosomal dominant retinal dystrophy with ganglion cell loss, inner retinal dysfunction and progressive retinal degeneration[1,2] but the function of ITM2B in the retina and physio-pathological mechanisms remains poorly understood. In a previous work, we obtained patient- and control-derived retinal organoids to model the disease recently showed that ITM2B may interact with mitochondrial proteins, implicated in oxidative stress in human retina. This project aims to investigate ITM2B in mitochondrial function and determined if it is altered in the disease.

Methods: Two inducted pluripotent cell lines (iPSC) derived from an affected and unaffected sibling were used. ITM2B mitochondrial immunolocalization in 60 days aged organoids was studied using two mitochondrial markers COX5B and ATP-β. Three sections per conditions were used. Furthermore, IPSC metabolism was analyzed in control and mutant cell lines using a mitostress seahorse assay, using 3 replicates per condition.

Results: ITM2B immuno-localizes with both COX5B and ATB-β mitochondrial markers in retinal organoids sections (figure 1). No difference was noticed between the mutant and the control organoids suggesting that mutant ITM2B does not modify the localization of the protein at this stage. Furthermore, a lower oxygen consumption rate was observed in mutant IPSC compared to control cells (figure 2), which highlight a mitochondrial defect in the mutant cell line, as well as a low capacity to respond to stress.

Conclusions: Our findings suggest a central role of the mitochondria underlying ITM2B pathogenesis in the retina. Further studies on IPSC using biochemical assays, respiratory function using sea-horse and enzyme assays are currently under investigation using as a model fibroblast and iPSC-derived retinal ganglion cells from dissociated mutant organoids and an isogenic control are currently underway and will help determine the function of ITM2B in the retina and elucidate its implications in pathology.

CONTROL ID: 3713681

SUBMITTER (NAME ONLY): Abdallah Abbas

TITLE: Longitudinal analysis of retinal tissue changes in non-converting fellow eyes in neovascular age-related macular degeneration using artificial intelligence

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abbas, University College London Medical School, London, London, UNITED KINGDOM|G. Moraes, R. Struyven, R. Chopra, S. Wagner, K. Balaskas, P. Patel, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|R. Chopra, Google Health, Google Inc, London, UNITED KINGDOM|T.D. Keenan, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Individuals receiving treatment for neovascular age-related macular degeneration (nAMD) can often develop the same pathology in the fellow eye. We describe the changes in volumes of OCT biomarkers for fellow eyes that do not convert to nAMD during treatment by segmenting OCT volume scans using an artificial intelligence (AI) system previously published by De Fauw et al. (2018).

Methods: This study included data from the Moorfields Eye Hospital AMD database for all patients that began treatment for nAMD between June 2012 and June 2017. This included AI-derived segmentation data from Topcon 3D OCT-2000 scans. Only eyes that did not convert by 24 months were used in this analysis. The biomarkers analysed include neurosensory retina (NSR), hyperreflective foci (HRF), retinal pigment epithelium (RPE) and drusen. The median relative change in volume from baseline (month 0) to specified time points of 4, 12, and 24 months was calculated as a percentage.

Results: At baseline our data included a total of 1347 non-converting fellow eyes. The NSR volume remained consistent over the follow-up period, reducing by 0.22% at 4 months and 1.45% by 24 months, relative to baseline. Similarly, RPE volumes reduced by 0.18%, 0.41% and 1.19% from baseline at 4, 12 and 24 months respectively. The volume of HRF changed more considerably, initially increasing by 10.10% and 15.35% at 4 and 12 months respectively, with an overall increase of 51.29% by 24 months. The drusen volume increased by 3.46%, 9.57% and 19.07% at 4, 12 and 24 months, respectively.

Conclusions: The volumes of NSR and RPE tissues in non-converting fellow eyes remained stable over the 24 month follow-up period. In contrast, HRF volume increased considerably, particularly in the second year of follow-up. The drusen volume demonstrated a steady increase over the follow-up period. Longitudinal quantitative analysis of retinal tissue volumes in fellow eyes of patients with nAMD, enabled by AI segmentation, may provide insights into OCT biomarkers that could predict disease progression.

CONTROL ID: 3713682

SUBMITTER (NAME ONLY): Shwetha Mangalesh

TITLE: Short-term treatment effects on retinal microanatomy in preterm infants with severe retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mangalesh, X. Chen, D. Tran-viet, N. Sarin, K. Winter, S.G. Prakalapakorn, S. Freedman, C.A. Toth, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|C.A. Toth, Biomedical Engineering, Duke University Pratt School of Engineering, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: We report optical coherence tomography (OCT)-based retinal microanatomical findings at the posterior pole pre- and post-treatment of retinopathy of prematurity (ROP).

Methods: As part of BabySTEPS (STudy of Eye imaging in Preterm infantS), research OCT volumes from pre-and post-treatment of Type 1 ROP were analyzed. We assessed: vascular dilation and tortuosity from en face retinal vessel maps centered on the optic nerve; presence of extraretinal neovascularization (eNV) from en face and B-scans; and presence of macular edema and retinal layer thicknesses at the foveal center from B-scans.

Results: Of 42 eyes (21 infants) treated for ROP, 34 eyes received intravitreal bevacizumab at 33-37 weeks postmenstrual age (PMA) and 8 laser photocoagulation at 34-44 weeks PMA. OCT images were captured a mean±SD of 1±0.9 days pre- and 5±2 days post-treatment. Of 37 eyes with dilated vessels pre-treatment, 29 improved (narrowed) post-treatment and none worsened. Of 35 eyes with tortuous vessels pre-treatment, 22 improved (tortuosity decreased) and none worsened. eNV was visible in the posterior pole in 6 eyes; all improved post-treatment (Fig 1A,B). Macular edema was present in 12 eyes pre-treatment, persisted in 9 post-treatment, and 7 eyes developed macular edema post-treatment (Fig 1C,D). At the foveal center, the photoreceptor layer (mean difference(MD)= +12.08μm, p=.006) and choroid (MD =+34.12μm, p<.001) were thicker post-treatment (matched-pairs analysis).

Conclusions: This is the first comprehensive evaluation of the short-term effects of ROP treatment on retinal microanatomy. We found an increase in photoreceptor layer and choroidal thickness early post-treatment of Type 1 ROP with either bevacizumab or laser. eNV and vascular dilation and tortuosity predictably improved following treatment. In contrast, macular edema, an inner retinal phenomenon not associated with choroidal thickness [Mangalesh et al Ophth Ret 2020], had a variable response to ROP treatment with improvement, persistence or new-onset after treatment.

CONTROL ID: 3713683

SUBMITTER (NAME ONLY): Elisabeth Artis

TITLE: Development of Tree Shrew Traumatic Optic Neuropathy Model

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Artis, B. Carlson, T.S. Rex, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|B.C. Samuels, Callahan Eye Institute, university of alabama at birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Elisabeth Artis: Commercial Relationship: Code N (No Commercial Relationship) | Brian Carlson: Commercial Relationship: Code N (No Commercial Relationship) | Brian Samuels: Commercial Relationship: Code N (No Commercial Relationship) | Tonia Rex: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Our goal is to translate our published mouse ocular trauma model to a human relevant species, tree shrews.

Methods: We exposed one eye of an anesthetized tree shrew to repeated bursts of overpressure air (20psi). Sham tree shrews were anesthetized and placed into the air blast chamber but were not exposed to the overpressure air. Two, four, or eight weeks post injury visual function was measured and tissue was collected for histology.

Results: We detected some axon degeneration within the optic nerve at the current parameters that appears to be regional. The level of damage was less than that detected in mice likely due to the greater musculature around the eye of the tree shrew and its load-bearing optic nerve head. We are able to measure ERGs and VEPs in this species.

Conclusions: We are able to induce blast-mediated indirect traumatic optic neuropathy in this human-relevant species. We expect that it will be a useful model for testing various therapeutic interventions.

CONTROL ID: 3713685

SUBMITTER (NAME ONLY): Cynthia McAnally

TITLE: Microbial Ingress Risk Evaluation of Novelia Multi-Dose Package for PG/HPG Nano-Emulsion Lubricant Eye Drops

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.L. McAnally, M. Crary, P. Shannon, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Cynthia McAnally: Commercial Relationship(s);Code E (Employment):Alcon Laboratories | Monica Crary: Commercial Relationship(s);Code E (Employment):Alcon Laboratories | Paul Shannon: Commercial Relationship(s);Code E (Employment):Alcon Laboratories

ABSTRACT BODY:

Purpose: Microbial keratitis is a risk for all users of topical ophthalmic solutions due to microbial proliferation within the formulation upon accidental contamination of the product. Historically, preservatives added to the formulation are included to inhibit the growth of microbes introduced from repeated use. Preservative-free products are viable alternatives for individuals who are sensitive or have reservations about using products containing preservatives. To mitigate microbial growth without the use of preservatives, a multi-dose packaging system must present a physical barrier to contamination throughout the use period. This study evaluates the potential of microbial ingress into PG/HPG nano-emulsion (propylene glycol/hydroxypropyl guar preservative-free lubricant eye drop) presented in the NOVELIA® Multi-Dose package over 30 and 90-day use periods.

Methods: Two methods were evaluated per Note for Guidance on In-Use Stability Testing of Human Medicinal Products (CPMP/QWP/2934/99) to simulate consumer use. First, after four days of dispensing, the tip and air intake were submerged in a high level (10^6 CFU/mL) suspension of Brevendamonas diminuta and the tip actuated to simulate routine use of the product followed by a gross contamination event similar to falling into a heavily contaminated liquid. Following the 30-day simulation, the internal contents of replicate samples were evaluated for sterility per USP<71>. Second, after 90 days of dispensing to simulate routine use of the product, the internal contents of replicate samples at T0 and 6-month stability conditions of 25°/40%RH and 30°/75%RH were evaluated per USP<61>. A passing result of no microbial recovery indicates the packaging system prevented microbial ingress into the bottle while a failing result of microbial recovery indicates ingress into the packaging system.

Results: For all microbial challenge simulations, a passing USP<71> sterility result was obtained following the 30-day use simulations of the NOVELIA package. For all 90-day routine use simulations, no microbial recovery was observed over 6 months of monitored stability.

Conclusions: PG/HPG nano-emulsion when presented in the NOVELIA package with the PureFlow^{TM} 200 nozzle remains contaminate-free for up to 90 days. Users who suffer from dry eye disease now have the option of PG/HPG nano-emulsion preservative-free lubricant eye drops in a unique multi-dose package.

CONTROL ID: 3713687

SUBMITTER (NAME ONLY): Philipp Herrmann

TITLE: Multimodal widefield imaging for postoperative monitoring in patients treated with voretigene neparvovec

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Herrmann, B. Lorenz, J.P. Scholz, R. Brinken, K. Küpper, N. Cavriani, L. Wirtz, F.G. Holz, Department of Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M.N. Preising, Department of Ophthalmology, Justus Liebig Universitat Giessen, Giessen, Hessen, GERMANY|

Commercial Relationships Disclosure: Philipp Herrmann: Commercial Relationship(s);Code F (Financial Support):Heidelberg Engineering, Novartis, Zeiss;Code R (Recipient):Novartis, Bayer, Allergan | Birgit Lorenz: Commercial Relationship(s);Code F (Financial Support):Novartis;Code C (Consultant/Contractor):Novartis, Janssen | Johanna Scholz: Commercial Relationship: Code N (No Commercial Relationship) | Ralf Brinken: Commercial Relationship: Code N (No Commercial Relationship) | Markus Preising: Commercial Relationship: Code N (No Commercial Relationship) | Kristina Küpper: Commercial Relationship: Code N (No Commercial Relationship) | Naike Cavriani: Commercial Relationship: Code N (No Commercial Relationship) | Laura Wirtz: Commercial Relationship: Code N (No Commercial Relationship) | Frank Holz: Commercial Relationship(s);Code C (Consultant/Contractor):Acucela, Apellis, Bayer, Boehringer-Ingelheim, Bioeq/Formycon, Roche/Genentech, Geuder, Graybug, Gyroscope, Heidelberg Engineering, IvericBio, Kanghong, LinBioscience, Novartis, Oxurion, Pixium Vision, Stealth BioTherapeutics, Zeiss;Code F (Financial Support):Acucela, Allergan, Apellis, Bayer, Bioeq/Formycon, CenterVue, Ellex, Roche/Genentech, Geuder, Heidelberg Engineering, IvericBio, Kanghong, NightStarX, Novartis, Optos, Pixium Vision, Zeiss;Code O (Owner):GRADE Reading Center

ABSTRACT BODY:

Purpose: Gene augmentation therapy with voretigene neparvovec (VN) has recently been made available for the treatment of patients with RPE65 mutation associated inherited retinal degeneration (RPE65-IRD). In a subset of patients treated with VN, development of atrophy has been previously reported. Here, we identify safety endpoints and imaging modalities that allow assessment of atrophy development following therapy with VN.

Methods: Single center longitudinal analysis of different imaging modalities prior and post treatment with VN in patients treated with VN for RPE65-IRD. Qualitatively analysed imaging modalities included colour fundus photography (CFP, Clarus 700, Zeiss) and confocal scanning laser ophthalmoscopy (Spectralis OCT, Heidelberg Engineering) with 30° and 55° blue light fundus autofluorescence (BAF), 30° and 55° near infrared imaging (IR) as well as spectral-domain optical coherence tomography (SD-OCT) of the macula.

Results: We analysed 18 patients treated with VN (27 eyes treated, 9 fellow eyes untreated). Median age at time of treatment was 28 years (range 7 – 39) and median follow up period was 6 months (range 1-21). Widefield, 55° IR images were available in all patients in good quality and allowed detection of postoperative atrophy development in 7 eyes of 5 patients (26 % of all treated eyes). Acquisition of BAF images was only possible in 3 patients and failed in 15 patients due to low levels of BAF signals. Macular OCT was available in all patients but failed to detect atrophy development sufficiently. Widefield CFP was available and detected atrophy in all patients. However, atrophy development was less obvious in CFP compared with 55° IR and mean time to detect atrophy development with CFP was 4 months (range 1-8) compared to 3.3 months (range 1-8) using 55° IR imaging.

Conclusions: Early detection of atrophy development and progression following VN treatment might be easily missed due to disease specific abnormalities (nystagmus, absent or low levels of BAF, altered retina). Widefield near infrared images appear superior for identification compared with other imaging modalities. Automated detection and quantification of lesion growth based on serial IR images over time is currently explored in order to allow for accurate quantitative analyses.

CONTROL ID: 3713689

SUBMITTER (NAME ONLY): Jose Marcos Sanches

TITLE: Inflammation alters mitochondrial and metabolic homeostasis in corneal epithelial cells

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sanches, W.L. Stuard, N. Mussi, D.M. Robertson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Jose Marcos Sanches: Commercial Relationship: Code N (No Commercial Relationship) | Whitney Stuard: Commercial Relationship: Code N (No Commercial Relationship) | Natalia Mussi: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Robertson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mitochondrial dysfunction is a hallmark of many human diseases. Our laboratory has previously shown that hyperglycemia, as seen in diabetes, and salt-induced hyperosmolarity, as seen in dry eye disease, lead to mitochondrial dysfunction and metabolic abnormalities in corneal (CECs) and conjunctival epithelial cells. We have further found that the insulin-like binding protein-3 (IGFBP-3) plays a key role in mitigating these responses. This study sought to expand on our prior results and investigate the effects of inflammation on mitochondrial and metabolic homeostasis in CECs.

Methods: Telomerase-immortalized human corneal epithelial cells were cultured in serum-free keratinocyte basal media. To establish an inflammatory environment, cells were treated with 50 ng/mL IL-1β for 24 or 48 hours. Metabolism was measured in real time using a Seahorse metabolic flux analyzer. Oxygen consumption rate (OCR), extracellular acidification rate (ECAR), and other metabolic parameters were quantified using a Seahorse XFp Cell Mito Stress Test kit. Total cell number per well was used for normalization. Protein expression for metabolic, mitochondrial and mitophagy-related proteins was assessed using western blot.

Results: At 24 hours, IL-1β had no effect on basal levels of OCR or ECAR. Maximal and spare respiratory were also unchanged. At 48 hours, IL-1β decreased ECAR (P=0.035), while basal OCR was unchanged. This shifted cells towards a more respiratory phenotype. There was a corresponding decrease in spare respiratory capacity (P=0.023). Interestingly, there was a decrease in non-mitochondrial oxygen consumption at 24 hours in the IL-1β group (P=0.003) which was not evident at 48 hours. There were no changes in ATP-linked respiration at either time point. Consistent with the decrease in non-mitochondrial oxygen consumption, IGFBP-3 also showed a drop in intracellular expression levels at 24 hours. This was associated with an observed increased in BNIP3L/NIX. At 48 hours, IGFBP-3 levels were similar in both treated and control groups, BNIP3L/NIX trended downward, while both mTOR and COVI X were increasing. PINK1 was unchanged.

Conclusions: These data confirm that inflammation triggers changes in metabolic and mitochondrial homeostasis in CECs. Further studies are needed to fully define the ability of CECs to respond and adapt to inflammatory stress.

CONTROL ID: 3713690

SUBMITTER (NAME ONLY): Jarrod Harman

TITLE: Multi-omic investigation of metabolic disturbance in a mouse model of retinopathy of prematurity.

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Harman, J. Yang, M. Ko, Z. Fu, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|J.C. Harman, Z. Fu, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. Kinter, Aging & Metabolism Research Program, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Jarrod Harman: Commercial Relationship: Code N (No Commercial Relationship) | Jay Yang: Commercial Relationship: Code N (No Commercial Relationship) | Minji Ko: Commercial Relationship: Code N (No Commercial Relationship) | Michael Kinter: Commercial Relationship: Code N (No Commercial Relationship) | Zhongjie Fu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is the leading cause of blindness in children globally. A key hallmark of ROP is the intricate and underexplored metabolic dysfunction resulting from early hyperglycemia and nutrient/hormone deprivation, which leads to abnormal retinal development. Emerging evidence suggests nutritional interventions may prevent developmental pathology of the retina. However, our knowledge of the metabolic responses occurring during early ROP in premature infants remain very limited. Here we utilized a combination of proteomics and metabolomics to investigate the underlying retinal metabolic shifts in mice with postnatal hyperglycemia-associated retinal vessel growth delay, modeling early ROP.

Methods: Hyperglycemia was induced in neonatal C57BL/6J (WT) pups by intraperitioneal administration of streptozotocin (STZ) on postnatal day (P) 1 to P9. Quantitative mass spectrometry (MS) was utilized to perform proteomic (n=10) and metabolomic (n=12) analyses on pooled retina samples at P10. Bioinformatic analyses were used to determine protein-protein interactions and metabolic overrepresentation enrichment analysis to compare phenotypes. Both male and female mice were used. This work is compliant with ARVO’s Statement for the Use of Animals in Ophthalmic and Vision Research.

Results: In STZ- vs vehicle-control treated WT mice, 63 metabolic enzymes we quantitatively measured and 9 citric acid cycle (TCA) proteins were upregulated (1.2 fold-change [FC]+, $P<0.05$). 147 metabolites were identified with 19 downregulated and 47 upregulated (1.2FC-5FC) resulting from hyperglycemia. Enrichment analysis (Metaboanalyst 5.0) of the differentially expressed metabolites revealed key metabolic pathways including glycolysis/gluconeogenesis ($P<0.003$) and TCA cycle ($P<0.008$), along with purine and pyrimidine metabolism ($P<2.08E-7$, $P<1.47E-4$, respectively) were modulated resulting from postnatal hyperglyemia.

Conclusions: Our data indicate that hyperglycemia induces metabolic shifts in essential pathways necessary for normal retinal development. Further understanding and modulation of these pathways may prevent early ROP.

CONTROL ID: 3713691

SUBMITTER (NAME ONLY): Ujjalkumar Das

TITLE: IDENTIFYING BIO-INTELLIGENCE AT BLOOD-AQUEOUS BARRIER IN PREDICTING AQUEOUS HUMOR PENETRATION USING QSPR APPROACH

SESSION TITLE: Drug delivery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U.S. Das, N. Halder, T. Velpandian, Ocular Pharmacology and Pharmacy Division, Dr. RPC, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|J.S. Titiyal, Department of Ophthalmology, Dr. RPC, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|V. Sreenivas, Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|B.S. Singh, Department of Biophysics, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|B. Jayaram, Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Predicting intraocular penetration after systemic administration is an essential goal in ophthalmic drug discovery. Physicochemical and molecular dynamic properties of xenobiotics are the key elements of bio-intelligence which exist at blood-aqueous barrier. Quantitative structure-property relationship (QSPR) is being used to identify those molecular determinants to define penetration in aqueous humor (AH). Therefore, the proposed study aims to develop QSPR algorithm for penetration of xenobiotics in AH compartment in rabbits.

Methods: New Zealand albino rabbits of either sex weighing (1.5-2 Kg) were divided into five groups (n=12 each) and received intravenous cassette dosage of antifungals (n=8), calcium channel blockers (n=8), beta adrenergic receptor blockers (n=8), statins (n=7) and fluoroquinolones (n=10) at an equimolar dose of 0.1 µM/Kg. Rabbits were sacrificed using carbon dioxide gas followed by AH and blood samples were withdrawn at predetermined time 30, 60 and 120 min post administration. All AH and plasma samples were quantified using validated LC-MS/MS method. Log_{10} aqueous humor-to-plasma (AH/P) ratio were calculated and correlated with molecular descriptors at different time points. Multiple linear regression (MLR) model was derived with best correlated molecular descriptors using Discovery Studio (ver 17.2, Dassault Systemes, BIOVIA).

Results: Differential penetration of xenobiotics in AH compartment was observed. Penetration index (Log_{10} AH/P) was found to be negatively correlated with protein binding ($p<0.0001$), hydrophobicity index ($p=0.022$), and number of double bonds ($p<0.0001$) whereas positively correlated with topological polar surface area ($p=0.001$). MLR algorithm at 60 min generated using parameters viz., protein binding, hydrophobicity index, topological polar surface area and no. of double bonds showed best prediction ($R^2=0.874$, $Q^2=0.823$, RMSE=0.330, n=40, $p<0.001$) as shown in Figure 1.

Conclusions: For the first time, a QSPR algorithm generated based on controlled animal experiment using diverse set of molecules predicted the penetration of drugs in AH. Further the algorithm is under validation using external set to predict the AH penetration in human.

CONTROL ID: 3713693

SUBMITTER (NAME ONLY): Susana del Olmo Aguado

TITLE: Use of plasma rich in growth factors in a macular hole in vivo model

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. del Olmo Aguado, N. de Pablo, M. Persinal Medina, E. Artime, J. Merayo-Lloves, Fundacion de Investigacion Oftalmologica, Oviedo, SPAIN|S. del Olmo Aguado, N. de Pablo, J. Merayo-Lloves, Instituto de Investigacion Sanitaria del Principado de Asturias, Oviedo, Asturias, SPAIN|J. Larrea González, S. Alonso-Alonso, Instituto Oftalmologico Fernandez-Vega, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Plasma rich in growth factors (PRGF) is a novel autologous ophthalmic therapy that contains a large number of biologically active agents that promote tissue regeneration, healing modulation and anti-inflammatory properties, among others. PRGF can be used in diverse formulations and has been tested in some cases of macular hole improving anatomic and visual outcomes. However, the molecular mechanisms of PRGF in the macular treatment is not fully understood. Here, we showed a preliminary study of modulation response of PRGF in a macular hole in vivo model.

Methods: A retinal break in the macula area were performed in New Zealand rabbits with an ACCURUS® Surgical System. At day 7 eyes were treated by injection of saline or PRGF in the macula hole. Electroretinography (ERG) measurements was performed at month of study. After sacrifice, eyes were collected and the sections were analyzed to IL1b, IL6, IL18, MCP1, proliferation and cell death markers.

Results: PRGF reduced cell death in the area around the damage without proliferation detection. The integrity of the retinal structure was better in PRGF-treated eyes. The glial cell response to damage was maintained and no significant differences were observed with PRGF treatment. There was an inflammatory response at the injury area detected by activation of IL1b, IL6 and MCP1. PRGF treatment reduced the expression of these markers. In addition, a reduction of IL18 was observed with respect to uninjured eyes, suggesting a possible activation of autophagy, as previously described.

Conclusions: The use of PRGF could be used as therapy in the surgical repair of macular holes reducing inflammation and maintaining the functionality of cells.

CONTROL ID: 3713694

SUBMITTER (NAME ONLY): Pavlina Tsoka

TITLE: Novel liposomal formulation for sustained release of moxifloxacin; efficacy in experimental bacterial endophthalmitis

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tsoka, M.K. Tsilimbaris, Laboratory of Vision and Optics, University of Crete Medical School, Heraklion, GREECE|E. Scoulica, E. Magkafouraki, Laboratory of Clinical Microbiology and Molecular Microbiology, University of Crete Medical School, GREECE|E. Natsaridis, S. Antimisiaris, Laboratory of Pharmaceutical Technology, Department of Pharmacy, University of Patras, GREECE|E. Natsaridis, S. Antimisiaris, Institute of Chemical Engineering Sciences, Foundation of Research and Technology Hellas, GREECE|M.K. Tsilimbaris, University Eye Clinic, University Hospital of Heraklion, GREECE|

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ABSTRACT BODY:

Purpose: Bacterial endophthalmitis can lead to significant vision loss even after prompt and proper treatment, partially due to the limited time of antibiotics' residence in the vitreous cavity. The purpose of this study was to evaluate the efficacy of a novel drug formulation, which is specifically designed for sustained intraocular release of moxifloxacin, in an experimental model of Escherichia coli (E. coli) – induced endophthalmitis.

Methods: Experimental endophthalmitis was induced in both male and female Sprague-Dawley rats. Animals received an intravitreal injection of approximately 10.000 colony – forming units (CFUs)/eye of the E. coli strain U13, which is susceptible to moxifloxacin. Six hours later, animals received a second intravitreal injection with either free or liposomal moxifloxacin (conventional vs. sustained release delivery respectively). A recently developed novel liposomal formulation of moxifloxacin was used. Clinical scores were evaluated in vivo with slit lamp biomicroscopy and direct ophthalmoscopy and animals were euthanized at 30 hours post treatment, eyes were enucleated and bacterial growth rate was assessed.

Results: An inoculum of 10.000 CFUs/eye of E. coli U13 resulted in conjunctival hyperemia, purulent exudations, iritis and miosed pupils (posterior synechiae) at 30 hours with mild to moderate inflammatory scores and an average bacterial load of 10^5 CFUs/eye. An intravitreal injection of liposomal moxifloxacin (1,6 μg/μl) 6 hours after the bacterial inoculation, resulted in significant reduction of the bacterial load at 30 hours to an average of 200 CFUs/eye.

Conclusions: Escherichia coli – induced endophthalmitis can be achieved in rats and is a highly reproducible model of experimental gram-negative bacterial endophthalmitis. Low inocula of E. coli strain U13 result in mild to moderate progress of the inflammatory signs, thus allowing pharmaceutical intervention. Liposomal moxifloxacin seems as effective as the free antibiotic at early time points. Further experimentation is currently ongoing in order to evaluate the efficacy of the novel moxifloxacin over a longer time frame.

CONTROL ID: 3713696

SUBMITTER (NAME ONLY): Yen-Chiao Wang

TITLE: Keratocyte-specific ablation of Tgfbr1 gene manifests human keratoconus phenotype in mice

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, Indiana University, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Yen-Chiao Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously showed that deletion of Transforming Growth Factor beta (TGF-β) signaling pathway via ablation of its type-2 receptor (TbR2) and Smad4 resulted in thin stroma phenotype similar to the human corneal ectasia disease known as keratoglobus. Herein, we tested the role of Tgfbr1 in the same scenario.

Methods: Transforming growth factor-b type 1 receptor (Tgfbr1) was designed to be conditionally knocked out (Tgfbr1kera-cko) from keratocytes. A novel triple transgenic mice: KerartTA;tetO-Cre;TbR1f/f, were administered with doxycycline (Dox) from postnatal day 1 (P1) to various developing stages including postnatal day 21 (P21), P56. Optical coherence tomography (OCT) was performed to examine corneal thickness and radius of curvature. Bulging appearance was measured and compared to the wild-type littermates (WT). We further compare corneal bulging among Tgfbr1Kera-cko, Smad4Kera-cko and Tgfbr2Kera-cko mice.

Results: The OCT scanning appeared a doom-shaped cornea in the WT but an ectasia cornea with hyper-reflectivity of the corneal stroma was observed in Tgfbr1kera-cko. Moreover, overall corneal thickness in Tgfbr1kera-cko becomes ~60% thinner than that of WT at P21. In the hematoxylin and eosin staining, we observed the uneven thinning and missing stroma in Tgfbr1kera-cko. Unlike Tgfbr2Kera-cko or Smad4Kera-cko which revealed 45-50% thinner stroma throughout the entire cornea, more severe phenotypes including the uneven thinning and disappearing stroma were observed in Tgfbr1kera-cko. Moreover, OCT imaging also revealed corneal bulging suggesting ectasia in Tgfbr1kera-cko mice.

Conclusions: The aforementioned corneal phenotypes in this Tgfbr1kera-cko triple transgenic mouse strain resemble keratoconus in human, which suggest that TGF-ß signaling pathway may play an important role in keratoconus pathophysiology and defect of Tgfbr1 may serve as a potential genetic cause of human keratoconus.

CONTROL ID: 3713697

SUBMITTER (NAME ONLY): Tadeusz Kaczynski

TITLE: Age-Related Macular Degeneration Associated Risk Locus Regulates Apoptosis in Retinal Pigmented Epithelium Cells

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.J. Kaczynski, M.M. DeAngelis, M. Farkas, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|T.J. Kaczynski, M.M. DeAngelis, M. Farkas, Research Service, VA Medical Center, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure: Tadeusz Kaczynski: Commercial Relationship: Code N (No Commercial Relationship) | Margaret DeAngelis: Commercial Relationship: Code N (No Commercial Relationship) | Michael Farkas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Genome-wide association studies have identified a myriad of genetic loci and variants linked to age-related macular degeneration (AMD), yet our understanding of how these loci contribute to AMD is lacking. One such locus contains the coding TNFRSF10A and noncoding AC100861.1 genes. Within AC100861.1 lies a SNP whose minor variant is associated with AMD, but the function of the transcribed long noncoding RNA (lncRNA) and the effect of the SNP are not known. Considering that retinal pigmented epithelium (RPE) cell stress is a major AMD risk factor and that TNFRSF10A is involved in death receptor signaling, we investigated AC100861.1 function through the lens of apoptosis to understand how disruption of this locus may contribute to the RPE death associated with AMD.

Methods: TNFRSF10A and AC100861.1 RNA levels were quantified in donor macular RPE samples and cell line isolates via qPCR. Production of TNFRSF10A and AC100861.1 was manipulated within ARPE-19 cells via transfection of siRNAs or expression vectors. The extent of apoptosis was measured through TUNEL staining followed by flow cytometry. Protein levels were measured through western blot analysis. Transcript localization was assessed in ARPE-19 cells through RNA fluorescent in situ hybridization (RNA-FISH).

Results: Expression from TNFRSF10A and AC100861.1 were found to be downregulated in early-stage AMD, yet in more advanced AMD, expression from both genes was upregulated. TUNEL analysis indicated that knockdown of the AC100861.1 reduced susceptibility to apoptosis in ARPE-19 cells in response to cell stress, while AC100861.1 overexpression had the opposite effect. Conversely, knockdown and overexpression of TNFRSF10A elicited minimal changes in the apoptotic susceptibility. Neither knockdown nor overexpression of AC100861.1 affected TNFRSF10A protein levels. RNA-FISH data identified the AC100861.1 transcript as localized to the cytoplasm.

Conclusions: Our findings reveal an altered expression of TNFRSF10A and AC100861.1 in AMD-affected macular RPE, reflecting a dysregulation of this locus in the disease state. AC100861.1 appears to increase susceptibility to apoptosis, although this does not appear to be mediated through an alteration of TNFRSF10A protein levels. Since the AC100861.1 transcript is primarily localized to the cytoplasm it is more likely to influence processes there, yet the mechanism is not yet known.

CONTROL ID: 3713699

SUBMITTER (NAME ONLY): Ray Enke

TITLE: Temporal and isoform-specific expression analysis of the multiuse CTBP2/RIBEYE locus in the developing chicken and human retina.

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Enke, E. Gage, C. Chenault, K. Washington-Brown, Biology, James Madison University College of Science and Mathematics, Harrisonburg, Virginia, UNITED STATES|D. Agarwal, Bioengineering, University of California San Diego, La Jolla, California, UNITED STATES|S. Szvetecz, N. Jahan, Mathematics & Statistics, James Madison University College of Science and Mathematics, Harrisonburg, Virginia, UNITED STATES|M.K. Jones, K.J. Wahlin, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|D.J. Zack, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Ray Enke: Commercial Relationship: Code N (No Commercial Relationship) | Devansh Agarwal: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Gage: Commercial Relationship: Code N (No Commercial Relationship) | Calvin Chenault: Commercial Relationship: Code N (No Commercial Relationship) | Kameron Washington-Brown: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Szvetecz: Commercial Relationship: Code N (No Commercial Relationship) | Nusrat Jahan: Commercial Relationship: Code N (No Commercial Relationship) | Melissa Jones: Commercial Relationship: Code N (No Commercial Relationship) | Donald Zack: Commercial Relationship: Code N (No Commercial Relationship) | Karl Wahlin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Complex transcriptional gene regulation allows for multifaceted isoform production during retinogenesis. Novel mRNA isoforms transcribed from a single locus can have unlimited potential to code for diverse proteins with different functions. In this study, we explored the CTBP2/RIBEYE gene locus and its unique repertoire of transcripts that are conserved among vertebrates.

Methods: We studied the transcriptional coregulator (CTBP2) and ribbon synapse specific structural protein (RIBEYE) using the developing chicken retina and developing human retinal organoid model systems, as well as in dissected post mortem adult human retina tissue. We performed comprehensive histochemical and multiomics analyses to pinpoint cell and developmental stage-specific expression of CTBP2/RIBEYE isoforms in each of these systems.

Results: We demonstrated that CTBP2 is widely expressed in retinal progenitors beginning in early retinogenesis, but becomes limited to GABAergic amacrine cells in the mature retina. Inversely, RIBEYE is initially epigenetically silenced in progenitors and later expressed in photoreceptor and bipolar cells, where they localize to ribbon synapses. Analysis of previously described ChIP-seq data suggests that differential binding of CRX and OTX2 transcription factors may play a role in isoform-specific expression patterns.

Conclusions: These analyses demonstrate that complex regulation of the multiuse CTBP2/RIBEYE locus is conserved during vertebrate retinal development. Our study also supports a mechanism for epigenetic regulation of this locus by modulating the binding of K50 homeodomain transcription factors.

CONTROL ID: 3713700

SUBMITTER (NAME ONLY): Ping Situ

TITLE: Corneal sensitivity changes in symptomatic neophytes contact lens wearer

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Situ, C.G. Begley, School Of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|T.L. Simpson, School Of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|

Commercial Relationships Disclosure: Ping Situ: Commercial Relationship(s);Code F (Financial Support):CooperVision Inc. | Carolyn Begley: Commercial Relationship(s);Code F (Financial Support):CooperVision Inc. | Trefford Simpson: Commercial Relationship(s);Code F (Financial Support):CooperVision Inc.

ABSTRACT BODY:

Purpose: To understand the neural mechanisms underlying contact lens discomfort (CLD). In Phase 1, the effects of 6-month contact lens (CL) wear on corneal sensitivity in neophytes who became symptomatic (NS) for CLD were investigated. In Phase 2, corneal sensitivity changes in these NS subjects when CL wear was first ceased for 3 months (washout) and then restarted for an additional 3-month period (re-challenge) were studied.

Methods: The NS group were classified based on the Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) scores and comfortable wearing time during Phase 1. A control (C) group of non-CL wearers completed Phase 1 only. Corneal detection thresholds to cooling stimuli (approximately 22°C) were estimated at baseline (BL) by a modified Belmonte esthesiometer at study entry before fitting CLs and repeated at each month over Phase 1 (M1-M6) and during the Phase 2 washout period (WM1-WM3) and re-challenge period (RM1-RM3). Ten NS who completed both phases and 15 C subjects were included in the analysis. Repeated measures ANOVA and post-hoc tests with Bonferroni adjustment were used for data analysis.

Results: Initially, in Phase 1, there was an increase in thresholds (becoming less sensitive) in both groups. The threshold at M4 was significantly different than BL and M1 (both $p \leq 0.041$) for the C group, but the NS group diverged in an opposite direction in M4-6 (Figure 1). In Phase 2, the threshold for the NS subjects increased during the washout period (WM1-WM3) and was significantly higher at WM3 compared to M1, M2 and M4 (all $p \leq 0.046$). Thresholds in Phase 2 tended to decrease (become more sensitive) during the re-challenge period (Figure 2).

Conclusions: Corneal sensitivity in NS wearers tended to increase after an initial reduction and again after restarting CL wear following a washout period. These results demonstrate dynamic sensory responses to CL wear suggesting that altered sensory function may contribute to CLD development in these neophytes.

CONTROL ID: 3713701

SUBMITTER (NAME ONLY): Silvia Han

TITLE: Associations Between Stereoacuity and Vision Characteristics in Children with Uncorrected Refractive Error

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Stereoacuity (stereo) improves monotonically with age during childhood. We investigated vision characteristics that may be associated with stereoacuity in non-strabismic children 3 to 9 years old with uncorrected refractive error.

Methods: Monocular visual acuity (VA, ATS4 Near Acuity Test; logMAR) and stereo (Randot Preschool Stereoacuity Test; arc sec) were assessed. Accommodative accuracy and cycloplegic refraction were measured using the Grand Seiko autorefractor. Accommodative responses were obtained while participants monocularly viewed 20/50 or 20/250 single letters (order counterbalanced) at 33 cm; accuracy was the difference between stimulus and response. Spherical equivalent (SE) measures of accommodation for both letter sizes were averaged for each eye. All sphero-cylindrical measures of cycloplegic autorefraction were converted to Power Vector notation (SE, J0, J45). Cycloplegic SE anisometropia (aniso) was calculated. For analyses, near VA, accommodative accuracy, and cycloplegic refraction from the eye with better near VA (or right eye if equal) were used. Stereo was log transformed for analyses. Associations between log stereo and near VA, interocular difference in near VA (IOD), cycloplegic SE, J0, J45, and SE aniso, and accommodative accuracy were explored using univariate analysis. Variables with significant associations ($p<0.10$) were included in a multivariate regression analysis. We report the log transformed beta-coefficients (β) and 95% confidence interval (CI) for the significant ($P<0.05$) variables from the multivariate analysis.

Results: Poorer log stereo was associated with worse near VA (β = 1.26, 95%CI: 1.02 to 1.50, $P<0.001$), greater IOD (β = 1.01, 95%CI: 0.58 to 1.42, $P<0.001$), greater SE aniso (β = 0.16, 95%CI: 0.08 to 0.25, $P<0.001$), greater J0 (β = 0.18, 95%CI: 0.09 to 0.28, $P<0.001$); and larger accommodative lag (β =0.06, 95%CI: 0.03 to 0.09, $P=0.001$).

Conclusions: Despite stereo improving with age, age itself was not significant after adjustment for other vision characteristics in young children. Of the variables evaluated, worse near VA and greater IOD in near VA had the strongest associations with worse stereo in young children with uncorrected refractive error. Worse stereo was also associated with higher magnitudes of uncorrected astigmatism, anisometropia, and accommodative lag, but to a lesser extent.

CONTROL ID: 3713702

SUBMITTER (NAME ONLY): Nairouz Farah

TITLE: Investigating the survival and function of retinal ganglion cells in an organotypic culture: An in-vitro model for studying synaptogenesis

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Farah, E. Simon, Y. Mandel, Life Sciences, School of Optometry, Bar Ilan University, Ramat Gan, ISRAEL|N. Farah, Y. Mandel, Bar-Ilan Institute for Nanotechnology and Advanced Materials (BINA), Bar Ilan University, Ramat Gan, ISRAEL|E. Simon, The Leslie and Susan Gonda Brain Research Center, Bar Ilan University, Ramat Gan, ISRAEL|

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ABSTRACT BODY:

Purpose: Stem cells replacement therapy is becoming a promising pursued avenue for vision restoration in people with degenerative diseases of the outer retina. However, the integration and survival of the transplanted cells and the formation of fully functioning synapses remain a challenge. Our aim is to develop an in-vitro experimental paradigm which will allow us to address these issues while working under experimentally controlled conditions and avoiding immune system reactions faced in-vivo

Methods: As a first step, we are utilizing organotypic retinal cultures from transgenic rats expressing the calcium indicator GCaMP6f while monitoring the survival of the retinal ganglion cells (RGCs)using both extracellular recordings (multi electrode arrays), and calcium imaging at various time points.

Results: Our calcium imaging revealed robust spontaneous activity of the RGCs up to 72hrs, albeit decreasing throughout culturing period. We observe a decrease in the percentage of spontaneously active RGCs from 4.26% in acute preparations to 2.09% in 96hrs culture. Concurrently with these experiments, we have successfully established the system for extracellular investigation of RGC electrical properties incorporating flexible light pattern stimulation and multiunit analysis of the light induced responses over 60 channels. We were able to observe various RGCs types e.g., ON, OFF, ON-OFF identified by 1sec flashes applied at 0.2Hz. Moreover, through the well-known white gaussian noise stimulus combined with spike triggered averaging we generated RGCs receptive field maps obtaining the expected results both spatial (160μm FWHM) and temporally.

Conclusions: The experimental paradigm presented here can serve as a useful tool for the investigation of stem cell cells integration with the host retina, a main obstacle towards successful cell replacement based vision restoration approaches.

CONTROL ID: 3713704

SUBMITTER (NAME ONLY): Eloy Villegas

TITLE: BINOCULARLY EXTENDED DEPTH OF FOCUS WITH A NEW INVERTED MENISCUS IOL

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Robles, L. Hervella, Voptica SL, Parque Científico de Murcia, Murcia, SPAIN|J.M. Marin, E. Alcon, Clínica Oftalvist Murcia, Murcia, SPAIN|E.A. Villegas, C. Robles, P.M. Prieto, P. Artal, Universidad de Murcia, Laboratorio de Óptica, Campus de Espinardo, Murcia, SPAIN|P. Taña, Clínica Oftalvist Alicante, Alicante, SPAIN|H.S. Ginis, Athens Eye Hospital, Athens, GREECE|

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ABSTRACT BODY:

Purpose: To evaluate the depth of focus induced by a binocular combination of two different models of a new inverted meniscus intraocular lens (IOL), Art40 and Art70 (ArtIOLs, Voptica SL, Murcia, Spain). The two lenses improve the overall off-axis optical quality and induce different amounts of negative spherical aberration.

Methods: Six cataract patients were implanted bilaterally with Art40 and Art70 IOLs to induce low and high values of spherical aberration respectively. The surgery was performed first in the dominant eye with Art40 and a few weeks later in the fellow eye with Art70. As control group, nine patients were bilaterally implanted with a standard monofocal IOL based on aspherical biconvex optics. One month after the last surgery, best-corrected (CDVA) and uncorrected (UDVA) distance visual acuity (LogMAR scale) was measured at 5 m, 66 cm and 40 cm, using trial lenses of -1,5 and -2,5 D and SLOAN charts under photopic lighting conditions.

Results: The monocular CDVA was on average zero in the three groups (eyes implanted with Art40, Art70 models and standard IOLs). In the control group, it decreased rapidly to around 0.25 and 0.43 at intermediate and near distances. In the eyes with Art40, the deterioration was slower to 0.18 and 0.35, while in the eyes with Art70 those values were still better, 0.11 and 0.27. The binocular combination of Art40 and Art70 yielded mean CDVA values of -0.02, 0.01 and 0.12 at far, intermediate and near distances respectively. With the two models of the inverted meniscus lenses, small myopic residual errors were planned (-0.25 and -0.75 D for Art40 and Art70 respectively). As shown in figure, the mean values of binocular UCVA with ArtIOLs were -0.02, 0.01 and 0.06 and in the control group 0.02, 0.17 and 0.39 at 5 m, 66 cm and 40 cm. Inter-subject variability, estimated as standard deviation, ranged between 0.04 and 0.13.

Conclusions: In addition to the optical improvement in the periphery due to the inverted meniscus shape, the binocular combination of the two of ArtIOLs models (Art40 and Art70) improved significantly the useful range of distances. This combination resulted in spectacle independence for the patients without the compromise of halo or disphotopsias.

CONTROL ID: 3713705
SUBMITTER (NAME ONLY): Kierstyn Napier-Dovorany
TITLE: Vigorous exercise in people with vision impairment has positive emotional benefits
SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Napier-Dovorany, Vision Science, Indiana University, Bloomington, Indiana, UNITED STATES|A. Tam, College of Optometry, Western University of Health Sciences, Pomona, California, UNITED STATES|N. Stoehr, Human Physiology, University of Oregon, Eugene, Oregon, UNITED STATES|
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ABSTRACT BODY:

Purpose: People with vision impairment report low levels of health-related quality of life and lower physical activity. Physical activity is associated with improved physical health, decreased symptoms of depression and anxiety and improved quality of life. This pilot study assessed balance confidence and health related quality of life of people with visual impairment who report participating in regular exercise.

Methods: Subjects with self-reported visual impairment completed the International Physical Activity Questionnaires (IPAQ), Activities-specific Balance Confidence (ABC) Scale and SF-36 Health Surveys. The Mann-Whitney U test was utilized to measure differences between participants who participated in vigorous exercise compared to those who participated in moderate exercise.

Results: Sixteen participants had an average age of 50 years old; 75% were female. Visual impairment was reported as reduced visual acuity worse than 20/70 (81%) and/or reduced visual field (87.5%). In the past 6 months 12.5% reported having a fall. All subjects participated in regular physical activity, with 10 subjects participating in vigorous exercise at least 3 days per week, and 6 subjects participating in moderate exercise, including walking, at least 3 days per week.

There were no significant differences in reports of balance confidence between the group that participated in vigorous exercise than those who participated in moderate exercise. Those who participated in vigorous exercise were more likely to feel calm ($p=0.006$), more energetic ($p=0.0234$), and less worn out ($p=0.030$). The group who participated in moderate exercise reported accomplishing less as a result of emotional problems than the group who participated in vigorous exercise ($p=0.036$).

Conclusions: This pilot study of the impact of exercise on people with visual impairment showed improvements in feelings of emotional well being in people who participated in more vigorous exercise. Participants were already exercising regularly, which likely contributed to high balance confidence regardless of the level of exercise.

CONTROL ID: 3713706

SUBMITTER (NAME ONLY): Fabiola Anaya Barragán

TITLE: Microbiological and antimicrobial resistance trends for keratitis and conjunctivitis in a reference center in Mexico City

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Bautista-Hernandez, D.G. Ponce-Ángulo, V.M. Bautista- de Lucio, Microbiology, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|F. Anaya Barragán , C.A. Müller-Morales, A. Ramírez-Miranda, A. Navas, E.O. Graue-Hernandez, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To describe and analyze the frequency and antimicrobial resistance trends of pathogens that cause keratitis and conjunctivitis in a reference center in Mexico City over a period of 8 years.

Methods: A retrospective and observational study was performed with patients diagnosed with infectious keratitis and conjunctivitis through January 2012 - December 2019. The database of the Ocular Microbiology and Proteomics laboratory was analyzed to identify corneal and conjunctival scrapings obtained in this period. Microbiological data, stains and sensitivity/resistance antibiograms of isolated pathogens were analyzed. Mean and deviation were used for continuous variables; percentages for categorical variables. Difference between proportions of pathogens was compared with chi-squared test; resistance patterns were examined with trend analysis.

Results: From 2337 scrapings, a total of 1770 samples were positive cultures (75.7%). 91.5% of positive cultures had bacterial origin. Gram-positive isolates represented 86.4% (n=1399), Staphylococcus epidermidis was the most common pathogen. Gram-negative isolates embodied 13.6% (n=220) with Pseudomonas aeruginosa as the most common species. Fungi represented 7.3% (n=129) of positive isolates, the most frequent was Fusarium sp. Gram-negative bacilli (GNB) and coagulase-negative Staphylococcus (CNS) showed a positive trend throughout the study evaluated by annual percentage change. A significant increase in Kocuria spproportion was evidenced, representing 7.1% of total positive isolates (P=0.01). Resistance to moxifloxacin in S. epidermidis increased significantly (4.1% to 50.6%) along the 8-year study (P=0.02). Pseudomonas sp had an average sensitivity of 97.4% to ceftazidime through the study period.

Conclusions: Most frequently isolated microorganisms were S. epidermidis and P. aeruginosa in the group of gram-positive and gram-negative bacteria, respectively. An increase in the biodiversity of pathogens previously not involved in ocular infections, such as Kocuria sp, was evidenced. A 12-fold increase in resistance to moxifloxacin was noted as previously reported in gram-positive bacteria.

CONTROL ID: 3713707

SUBMITTER (NAME ONLY): Emily Wiecek

TITLE:

Development of Anisometropic Amblyopia in Children treated for Type I Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.K. Wiecek, J. Akula, D. Vanderveen, I. Mantagos, C. Wu, A. Curran, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|E.K. Wiecek, J. Akula, D. Vanderveen, I. Mantagos, C. Wu, A.B. Fulton, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Children with ROP treated with laser tend to have higher incidence of high myopia compared to individuals treated with intravitreal bevacizumab (IVB); however, the incidence of amblyopia and abnormal binocular vision between these two groups has yet to be established. We examined the progression of refractive error and development of anisometropic amblyopia in children treated for ROP with IVB, laser, or IVB followed by laser treatment.

Methods:

We identified premature infants with ROP treated with IVB at Boston Children’s Hospital from 2011-2020 (n =40). We compared cycloplegic refraction and visual acuity data in these individuals to ROP babies treated with laser during the same time frame (n = 48). A subset of individuals treated with IVB also underwent additional treatment with laser (n = 18). We included cycloplegic refraction and visual acuity from 392 cumulative visits (median 3, range 2-13 per individual) over a median of 3.2 (range 0.5-8.5) years. We used a linear mixed effects model to compare risk factors for amblyopia including anisometropic refractive error, astigmatism, and strabismus between groups to determine differences in amblyopia risk and incidence.

Results:

There was a higher incidence of anisometropic amblyopia, as defined by a >0.1 logMAR difference between eyes, in those treated with both IVB and subsequent laser (P = 0.0243). A secondary analysis accounting for differences in ROP characteristics (zone, stage, and number of clock hours of affected retina) and number of laser spots showed ROP zone had a significant effect on anisometropia, with less anisometropia in individuals with zone 2 ROP. There was no effect on incidence of amblyopia. The number of laser spots used for treatment had no significant effect on anisometropia (P = 0.255) or astigmatism.

Conclusions:

Our data provide evidence that a subset of individuals requiring subsequent laser treatment following IVB therapy are more likely to develop anisometropic amblyopia. There was no effect of ROP zone, stage, and area of affected retina on the development of amblyopia in this sample.

CONTROL ID: 3713708

SUBMITTER (NAME ONLY): Aurelie Calabrese

TITLE: A new vessel-based method to estimate automatically the position of the non-functional fovea on altered retinography from maculopathies.

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Calabrese, S. Dours, E. Castet, Laboratory of cognitive psychology, Aix-Marseille University, CNRS, Marseille, FRANCE|V. Fournet, P. Kornprobst, Université Côte d'Azur, Inria, FRANCE|F. Matonti, Centre d'Ophtalmologie Paradis Monticelli, Marseille, FRANCE|

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ABSTRACT BODY:

Purpose: In pathological fundus images with maculopathies, the fovea position is usually located using Normative Anatomical Measures (NAM). This simple method relies on two conditions: that images are acquired under standard testing conditions (primary head position and central fixation) and that the optic disk is entirely visible on the image. However, these two conditions are not always met in the case of maculopathies, especially during fixation tasks. Here, we propose a new Vessel-Based Fovea Localization (VBFL) approach.

Methods: The spatial relationship between fovea location and vessel characteristics (density and direction) is learned from 840 annotated healthy fundus images and then used to predict the precise fovea location in new images. We evaluate our method on three different categories of fundus images: healthy (198 images from 21 eyes, each acquired with the combination of five different head positions and two fixation locations), healthy with simulated lesions (3564 images, with lesions ranging from 20 to 400 deg^2) and 89 pathological fundus images collected in AMD patients.

Results: For normal images taken under standard conditions, the NAM method yields a mean fovea localization error of 1.03° of visual angle (95% CI [0.80, 1.33]), which is slightly, but not significantly reduced by 37% with VBFL. For all conditions where the head is tilted to the side, the NAM estimation error is significantly multiplied by 4.42° (95% CI [3.45, 5.64]) while the VBFL method yields no significant increase in error prediction, with an average value of 1.21° (95% CI [0.93, 1.56]), representing a 73% reduction in prediction error compared to the NAM method. With simulated lesions, performance of the VBFL method decreases significantly as lesion size increases, with a mean error ranging from 0.83° at 20 deg^2 up to 2.3° at 400 deg^2. Overall, performance of VBFL remains better than NAM until lesion size reaches 200 deg^2. For pathological images, the error distribution with VBFL is not higher than for healthy data, suggesting that actual AMD lesions do not negatively affect the method's performance.

Conclusions: The vascular structure provides enough information to precisely locate the fovea in fundus images in a way that is robust to head tilt, eccentric fixation location, missing vessels and actual macular lesions.

CONTROL ID: 3713709

SUBMITTER (NAME ONLY): Vamsi Parimi

TITLE: Variability in visual acuity measured with increasing blur

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Parimi, A.E. Elsner, J.A. Papay, R.N. Gilbert, T.J. Gast, C.A. Clark, S.A. Burns, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Refractive status and the optical quality of the eye impact visual acuity (VA) in a direct manner. Variability of VA measurements is often not provided, so that the confidence limits of the results are unknown. We examined the means and variability in VA measurements by inducing a positive defocus among normal subjects, similar to the defocus with retinal elevation in exudative eye disease.

Methods: Normally sighted adults (n=44, age = 32 +/- 13.01 yr, 21-71 yr) participated in a visual acuity task with refractive correction and three test conditions with the addition of plus lenses (0.75 D, 1.50 D, and 2.25 D). All subjects had best-corrected visual acuity of at least 20/20 and mean spherical error of 1.35 +/- 2.25 D. All subjects were consented and tested in a manner approved by the Indiana University Institutional Review Board, which adhered to the Declaration of Helsinki. Distance VA was measured and analyzed using a 4 alternative forced-choice task with tumbling E's displayed using custom Matlab software on a monitor calibrated for luminance ($85 cd/m^2$) and distance (11.2 feet), with whole pixel increments for the letter size changes. The E was presented in a 1-up-1-down staircase method starting from MAR of 2 arc min, in logMAR steps, providing VA mean and SD both from staircases data and fits to the psychometric function with a cumulative Gaussian distribution.

Results: As expected the subjects had increasingly reduced VA in conditions with higher plus lenses. Mean VA (76% fitted threshold) for refractive correction, +0.75 D, +1.50 D, and +2.25 D were 0.99 +/- 0.45 MAR, 1.75 +/- 0.9 MAR, 3.51 +/- 1.69 MAR, and 5.91 +/- 2.84 MAR, respectively, (paired t-test, $p<0.00331$ for all with Bonferroni correction). The coefficient of variation of all the sizes after the first reversal and the standard deviation of the fitted curve normalized by mean was significantly different across the test conditions (ANOVA, $F= 16.86$; $df=41$; $P<0.0001$ and F $F=73.27$, $df=41$; $P<0.0001$). The confidence limits of VA increased with higher plus lenses, e.g., a subject with no refractive error had a CI for MAR of 0.60 to 0.78 for 0 D but MAR of 3.39 to 4.15 for +2.25 D.

Conclusions: VA measurements in individuals with poor refractive/optical quality of eye have higher variability, leading to inaccurate assessment of visual function in clinical and research environments.

CONTROL ID: 3713710

SUBMITTER (NAME ONLY): Maciej Bartuzel

TITLE: Defocus influence on cones visibility in peripheral macula imaged with non-adaptive optics OCT

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Bartuzel, P. Stremplewski, M. Sylwestrzak, I. Gorczynska, Institute of Physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Torun, POLAND|A. Consejo, Department of Applied Physics, Universidad de Zaragoza, Zaragoza, Aragón, SPAIN|

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ABSTRACT BODY:

Purpose: It is known that in many subjects imaged with OCT systems, the cone photoreceptors can be resolved in the peripheral retina without adaptive optics (AO). However, there are no systematic studies investigating what factors influence the visibility of cones in OCT. We analyze how defocusing of the OCT beam influences the visibility of cones in the peripheral macula when imaged with 5 μm lateral imaging resolution.

Methods: Imaging was performed with SS-OCT in 4 healthy subjects. The accommodation was blocked with Tropicamide. Laser operating at 1.6MHz rate with λ = 1.06μm providing 6μm axial resolution was used. 3D data sets were acquired ~6° nasally from the fovea. The FOV was 5°×5°. Light beam diameter of 6.2mm at the cornea was used providing 5μm nominal lateral resolution at the retina. The beam focus was shifted from the photoreceptor layer in 31 steps over ±312 μm depth. 6 data sets were acquired at each defocus. Cones visibility was calculated from the radially averaged power spectrum (RAPS) of the en face images as the height of a Gaussian peak fitted to the RAPS after subtracting non-periodic component fit. The study was approved by the Bioethics Committee of NCU and adhered to the Declaration of Helsinki.

Results: In all imaged subjects, cones were visible in en face images of the inner/outer photoreceptor segments junction (IS/OS) when the beam was focused at that layer. As expected, the visibility of the cones was decreasing with increasing defocus. Focal shift of ~100μm (~1/3 of the thickness of the retina) causes substantial loss in the cones visibility. Cones visibility is shown as a function of defocus in Fig.

Conclusions: Cone photoreceptors of the peripheral macula can be visualized in non-AO OCT imaging with a nominal transverse imaging resolution of ~5μm provided that the device operator pays attention to the proper focusing of the imaging system. The proposed measure of photoreceptors visibility could be used for determining how much the beam size could be decreased to still resolve photoreceptors within the depth of focus reasonable for the device operator and without paralyzing the accommodation and dilating the pupil.

CONTROL ID: 3713711

SUBMITTER (NAME ONLY): Laura Baqué Vidal

TITLE: Molecular profiling of stem cell-derived retinal pigment epithelial cell differentiation established for clinical translation

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Baqué Vidal, S. Petrus-Reurer, F. Lanner, CLINTEC, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|L. Baqué Vidal, S. Petrus-Reurer, F. Lanner, Division of Obstetrics and Gynecology, Karolinska Universitetssjukhuset, Stockholm, SWEDEN|A.R. Lederer, G. Le Manno, Laboratory of Neurodevelopmental Systems Biology, Ecole polytechnique federale de Lausanne Faculte des sciences de la vie, Lausanne, VD, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Human embryonic stem cell-derived retinal pigment epithelial cells (hESC-RPE) are a promising cell source to treat age-related macular degeneration (AMD). Despite several ongoing clinical studies, a detailed mapping of transient cellular states during in vitro differentiation has not been performed.

Methods: Here we conduct single-cell transcriptomic profiling of a hESC-RPE differentiation protocol that has been developed for clinical use.

Results: Differentiation progressed through a culture diversification recapitulating early embryonic development, in which cells rapidly acquired a rostral embryo patterning signature, before converging towards the RPE lineage. At intermediate steps, we identified and examined the potency of a NCAM1+ retinal progenitor population and showed the ability of the protocol to suppress non-RPE fates. We demonstrated that the method produces a pure RPE pool capable of maturing further after subretinal transplantation in a large-eyed animal model.

Conclusions: Our evaluation of hESC-RPE differentiation supports the development of safe and efficient pluripotent stem cell-based therapies for AMD.

CONTROL ID: 3713712

SUBMITTER (NAME ONLY): Yingkun Cui

TITLE: Systemic hypertension is associated with declined retinal functions via intraocular pressure (IOP)-independent mechanism

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Cui, L. PAN, C. Do, School of Optometry, The Hong Kong Polytechnic University, HONG KONG|C. Wen, The Department of Biomedical Engineering, The Hong Kong Polytechnic University, HONG KONG|C. Wen, C. Do, Research Institute of Smart Ageing, The Hong Kong Polytechnic University, HONG KONG|

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ABSTRACT BODY:

Purpose: Systemic hypertension (HT) is a risk factor for glaucoma, although the precise mechanism remains elusive. Whether or not HT has any effect on intraocular pressure (IOP) as a contributory factor remains controversial. In this preliminary study, we evaluated the cross-sectional changes of blood pressure (BP), IOP changes and functional retinal response in rats with chronic HT.

Methods: Female spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto rats (WKY) aged 4 - 15 months were used. Non-invasive systolic BP and IOP measurements were determined under awake condition by the tail-cuff method and rebound tonometry, respectively. At 7 and 15 months of age, functional retinal response in retinal ganglion cells (RGCs) and cone photoreceptors of both SHR and WKY rats were determined by positive scotopic threshold response (pSTR) and photopic a-wave using full-field electroretinogram (ERG).

Results: SHR showed a sustained BP elevation throughout the studied period when compared with age-matched WKY controls. Interestingly, SHR displayed significantly lower IOP than WKY controls at 4 months (9.0 ± 0.1 vs 10.2 ± 0.1 mmHg), 7 months (9.6 ± 0.1 vs 10.3 ± 0.2 mmHg), and 15 months (9.8 ± 0.1 vs 10.8 ± 0.4 mmHg). At 7 months, pSTR reduced by 27% (N=4, $p<0.01$) in SHR (31.9 ± 1.1 μV) as compared to WKY rats (43.9 ± 2.1 μV). Similarly, a 35% reduction of pSTR was observed at 15 months (SHR: 13.5 ± 1.6 μV vs WKY: 20.9 ± 1.3 μV, N=4-6, $p<0.01$). In contrast, photopic a-wave was only found to be reduced in SHR at 15 months, but no difference was observed at 7 months, when compared with WKY controls.

Conclusions: The ERG data suggest that chronic HT leads to a progressive functional loss in RGCs and cone photoreceptors. In addition, impaired retinal responses observed in SHR may be mediated by an IOP-independent mechanism. Further longitudinal studies are warranted to investigate the precise relationship between IOP and the morphological and functional changes in retina over a prolonged period.

CONTROL ID: 3713713

SUBMITTER (NAME ONLY): Astra Dinculescu

TITLE: The generation and characterization of a large animal model of USH3 disease

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Dinculescu, J. McDowell, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|M.A. McCall, R.G. Gregg, A. Jalligampala, J.M. Noel, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|R. Whiting, University of Missouri School of Medicine, Columbia, Missouri, UNITED STATES|K. Donnelly, University of Missouri Veterinary Health Center, Columbia, Missouri, UNITED STATES|K. Whitworth, R.S. Prather, K.D. Wells, University of Missouri Animal Science Research Center, NSRRC, Columbia, Missouri, UNITED STATES|B. Redel, University of Missouri USDA-ARS, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the clarin-1 (CLRN1) gene cause Usher syndrome type 3 (USH3), an autosomal recessive disorder leading to retinal degeneration, progressive hearing loss, and variable vestibular dysfunction. In our recent study, we showed that CLRN1 transcripts in the human retina are specifically expressed by Müller glia, suggesting that USH3 is a Müller glia-driven disease affecting photoreceptors (Xu et al., 2020). Although mouse models of USH3 display profound hearing loss, they maintain normal vision throughout their lifespan. To address this gap in our ability to study USH3 retinal disease, we successfully generated biallelic mutant CLRN1 pigs.

Methods: We generated CLRN1 mutant swine models at the National Swine Research and Resource Center (NSRRC, University of Missouri), using CRISPR/Cas9 genome editing. We designed two guide RNAs to target exon 1 and the downstream intron to disable the main CLRN1 isoform. mRNAs encoding Cas9 nuclease and the two guide RNAs were injected into zygotes, which were then transferred to surrogate females. The genotypes of the resulting piglets were determined by PCR and evaluated for insertions/deletions (INDELs) by Sanger sequencing. Natural history of disease onset and progression in USH3 pigs is ongoing, and includes fundus imaging, full-field ERG and SD-OCT.

Results: From the first round of embryo transfers we generated one male and one female founder pig with biallelic CLRN1 edits. The male has a 308 bp deletion on one allele and a 307 bp deletion with a 4 bp insertion on the other. The female has a 784 bp deletion and a 5 bp deletion. These edits are predicted to result in premature stop codons in the first extracellular loop of CLRN1, similar to the Y63X mutation found in USH3 patients, creating null alleles. We bred the founders, creating F1 offspring (5 males and 6 females) who inherited edited CLRN1 alleles as expected. Dark-adapted (scotopic) ERG analysis performed in the founders shows a decline in rod function at 6 months of age compared to 3 months.

Conclusions: We have successfully generated the first large animal model for USH3 by zygote injection with CRISPR/Cas9 and guide RNAs. The USH3 pig model represents a novel reagent with tremendous potential to answer basic science questions fundamental to our understanding of Müller glia-photoreceptor interactions, and to evaluate the efficacy of gene-therapy approaches to prevent blindness and deafness in USH3 patients.

CONTROL ID: 3713716

SUBMITTER (NAME ONLY): Elora Vanoni

TITLE: Metabolic defects and circadian clock alterations in Prpf31-mutant mice.

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Vanoni, A. Hamieh, G. Puel, T.D. Leveillard, E.F. Nandrot, Institut de la vision, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Mutations in the ubiquitous Pre-mRNA Processing Factors (PRPF3, 8, 31) constitute the second cause of autosomic dominant retinitis pigmentosa. The retinal pigment epithelium (RPE), crucial for photoreceptors survival, seems to be affected first in the Prpf3, 8 and 31 mutant mice. Indeed, circadian rhythms of photoreceptor outer segments (POS) phagocytosis and retinal adhesion are deregulated, suggesting a possible RPE circadian clock alteration. Moreover, all 3 models share aging RPE structural defects including cytoplasmic vacuoles, a sign of potential cellular stress.

Methods: RPE/choroid and retinal circadian clock gene and protein levels were studied along the light:dark cycle in Prpf31$^{+/-}$ and WT mice using qRT-PCR, immunoblots and immunohistochemistry. Impact of candidates expression silencing by siRNA on POS phagocytosis was explored in RPE-J cells. Oxidative and endoplasmic reticulum (ER) stresses were evaluated either by immunohistochemistry and qRT-PCR/immunoblots up to 18 months. Mitochondrial activity, glycolysis and fatty acids dependency were analyzed using the Seahorse technology on fresh RPE/choroid punches and on primary cultured peritoneal macrophages. Mice were also analyzed on a full body metabolic platform.

Results: Circadian clock activator complex members are overexpressed when phagocytosis starts earlier in mutant RPE/choroids, while repressors expression increases when the peak is attenuated. Strikingly, we confirmed the direct impact of the circadian clock on in vitro POS phagocytosis by RPE cells. Besides, proteins and lipids oxidation as well as proteasome activation, a sign of ER stress, increase with age. We observed mitochondrial respiratory and energy production defects in young mice associated with CoxIV and ATP synthase overexpression. With age, glycolysis and fatty acids dependency are decreased. In contrast and in accordance with the tissue-specificity of the phagocytic defect, no energetic metabolism failure is detected in the mouse body or in peritoneal macrophages.

Conclusions: Our results suggest a deregulated expression of the circadian clock in Prpf31$^{+/-}$ RPE that directly impacts their phagocytic activity. Ongoing studies explore members of the phagocytic and adhesion machineries. We here confirm the tissue-specificity of the pathogenicity, now pointing out global cellular stress and widespread metabolic deficiencies in Prpf31$^{+/-}$ RPE.

CONTROL ID: 3713718

SUBMITTER (NAME ONLY): Stephen Phillips

TITLE: Retinal structure and function changes in the TgF344-AD rat model of Alzheimer's disease

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Phillips, K. Gudapati, A. Feola, K. Bales, K. Hogan, R.S. Allen, Center for Visual and Neurocognitive Rehabilitation, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|C. Galloway, M. Kelberman, R. McCann, D. Weinshenker, Human Genetics, Emory University, Atlanta, Georgia, UNITED STATES|A. Feola, Emory Eye Center, Emory University, Atlanta, Georgia, UNITED STATES|M. Shin, A. Pieper, Harrington Discovery Institute, UH Cleveland Medical Center, Cleveland, Ohio, UNITED STATES|M. Shin, A. Pieper, Department of Psychiatry Case Western Reserve University, Geriatric Research Education and Clinical Centers, Louis Stokes VA Medical Center, Cleveland, Ohio, UNITED STATES|S. Phillips, K. Gudapati, K. Hogan, R.S. Allen, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alzheimer's disease is a neurodegenerative disease where there is an accumulation of amyloid-beta plaques and neurofibrillary tangles of Tau protein within the brain. In this study, we aimed to determine if retinal changes preceded and are associated with cognitive decline in the TgF-344-AD transgenic rat model of Alzheimer's disease.

Methods: In TgF344-AD transgenic rats (n=7-12) and wild type littermate controls (Fischer 344 background, n=5-12), the following parameters were assessed at 3, 6, and/or 15 months: retinal function (electroretinography, ERG), retinal structure (spectral-domain optical coherence tomography, SD-OCT), and spatial memory (Barnes maze). At 16 months, rats were euthanized to acquire the brains and retinas, which were analyzed for amyloid precursor protein (APP) via western blot.

Results: Significant delays in ERG oscillatory potential (OP) implicit times were observed in TgF344-AD rats by 6 months ($p<0.001$), and significant delays in both OP and positive scotopic threshold response (STR) were observed at 15 months ($p<0.01$ for both). TgF344-AD rats also showed significant thinning of the inner and outer segments at 6 months ($p<0.01$), as measured by SD-OCT. Significant cognitive deficits (latency) were observed in TgF344-AD rats at 15 months of age ($p<0.01$). The retinas and brains of TgF-344 AD rats showed an increase in levels of APP.

Conclusions: Retinal function and structure changes were exhibited by the TgF344-AD transgenic rat model prior to an age-related cognitive decline. These results suggest that non-invasive retinal biomarkers may be useful in the diagnosis and staging of Alzheimer's disease. Future research will investigate retinal astrocyte number and morphology.

CONTROL ID: 3713719

SUBMITTER (NAME ONLY): Leonie Flesch

TITLE: Metabolic factors influence CNV activity in neovascular AMD – insights from the BIOMAC study

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Flesch, D. Frentzel, S. Rau, A. Rübsam, S.E. Künzel, S. Wolf, A. Joussen, O. Zeitz, Opthalmology, Charite Universitatsmedizin Berlin, Berlin, Berlin, GERMANY|F. Dreher, M. Schütte, B. Lange, Alacris Theranostics, GERMANY|M. Yaspo, H. Lehrach, Max-Planck-Gesellschaft, Munchen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: To identify candidate systemic metabolic factors which may modulate CNV activity and thereby influence the treatment demand with intravitreal anti-VEGF injections (IAI) in subjects with neovascular AMD.

Methods: Cohort study on 46 patients with neovascular AMD, treated with anti-VEGF injections. The cohort was stratified by treatment need. One group (N=25) received regular IAI at intervals of 6 weeks or less, while still having signs of CNV activity (high frequency group – HF). The second stratum (N=21) included subjects with a treatment interval of 10 weeks or longer and having no signs of CNV activity (low frequency group – LF). Full ophthalmological profiling was performed and EDTA blood samples were collected. Metabolic factors were analyzed using Ultrahigh Performance Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS). Welch's two sample t-test was performed on natural log-transformed data for statistical analysis. Metabolites reaching a $p<0.05$ were considered for further analysis as potential candidates.

Results: Both strata were well balanced regarding age (HF 78.4±8.14; LF 79.7±7.00 years), gender (HF 40% LF 61.9% female) and BCVA (HF 61.4±15.7; LF 65.0±12.4). Due to the group definition, central retinal thickness differed between HF and LF (HF 352.2±98.0 vs. LF 274.8±45.7µm. 34/899 biochemicals were differently regulated between HF and LF. 24 are up- and 10 are down-regulated in HF. Most of the upregulated metabolites belong to the lipid pathway (54%). Key candidates up-regulated in HF: sarcosine (95% CI HF 1.05-1.25; LF 0.74-1.08; ratio LF/HF 0.79; p=0.0024) and retinol (95% CI HF 1.03-2.06; LF 0.58-1.53; ratio LF/HF 0.68; p=0.0494). Key candidates down-regulated in HF: Glutathione, reduced (GSH) (95% CI HF 0.70-1.09; LF 0.99-1.54; ratio LF/HF 1.42; p=0.0296), 2,3-diphosphoglycerate (2,3-BPG) (95% CI HF 0.80-0.98; LF 0.94-1.10; ratio LF/HF 1.15; p=0.0181) and theanine (95% CI HF 0.28-0.47; LF 0.47-1.25; ratio LF/HF 2.29; p=0.0203).

Conclusions: nAMD subjects with higher and lower treatment need differed in several metabolic factors. Metabolites such as sarcosine and retinol, were elevated in the HF group and have pro-angiogenic potential. GSH, 2,3-BPG and theanine were increased in the LF cohort and may inhibit angiogenesis. In summary, systemic metabolic factors may influence treatment need through modulation of CNV activity.

CONTROL ID: 3713720

SUBMITTER (NAME ONLY): Qiuzhi Ji

TITLE: Revealing spectral cone types from structural differences as obtained by AO-OCT imaging in human subjects

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q. Ji, M. Bernucci, Y. Liu, J. Crowell, D.T. Miller, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|D. Miller, Dept of Computer Science, Purdue University, West Lafayette, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human color vision is based on the mixing of neural signals from three types of cone photoreceptors that are sensitive to short (S cone), medium (M cone), and long (L cone) wavelengths of light. Although S, M, and L cones differ primarily in differences of photopigment, other structural differences might be detectable by imaging and potentially useful for distinguishing cone spectral types. To test, we extracted morphological features of thousands of cones from AO-OCT images to classify spectral types and validate against functionally classified results.

Methods: Adaptive optics optical coherence tomography (AO-OCT) volume images of 1°×0.8° at 3.8° temporal retina were acquired in three color normal subjects. Cones were first classified using the cone phase optoretinogram [1]. Morphological features of each cone cell were then extracted from the AO-OCT images: inner segment length (ISL), outer segment length (OSL), and reflectance diameters of the inner-segment-outer-segment junction (ISOS) and cone outer segment tip. We tested for statistical differences in morphological features between cone types and assessed whether these differences could identify spectral cone types using machine learning classifiers (K-nearest neighbors, support vector machine (SVM), and multilayer perceptron). Five-fold cross-validation was performed to evaluate classification performance in terms of precision, recall, and F1 scores.

Results: In the three subjects, 1,986 cones were evaluated (1,328 L cones, 542 M cones, and 116 S cones). The only notable difference we found between M and L cones in all three subjects was the longer (0.46μm) OSL of L cones, which was significant ($p<0.05$) in two of the subjects. Compared to M and L cones, S cones had a longer (3.6μm) ISL, shorter (3.8μm) OSL, and larger (0.71μm) ISOS diameter. These differences were significant for all subjects and consistent with histology [2]. While differences were too small to classify M cones from L cones with any classifier, S cones could be classified effectively using all three classifiers with SVM generating the best performance of 81.2±7.2% precision, 71.4±6.3% recall, and an F1 score of 75.7±5.1%.

Conclusions: Differences in S, M, and L cone structures are revealed in AO-OCT images enabling individual S cones to be distinguished from M and L cones.

[1] Zhang, et al. PNAS 116.16 (2019): 7951-6

[2] Curcio, et al. JCN 312.4 (1991): 610-24

CONTROL ID: 3713721

SUBMITTER (NAME ONLY): Suneel Gupta

TITLE: Evaluations of localized topical tissue-targeted AAV5-Id3 gene delivery to treat

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gupta, N.R. Sinha, L.M. Martin, L. Keele, N.P. Hesemann, P. Sinha, E.A. Giuliano, R. Tripathi, R.R. Mohan, Ophthalmology, Harry S Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|S. Gupta, N.R. Sinha, L.M. Martin, L. Keele, P. Sinha, E.A. Giuliano, R. Tripathi, R.R. Mohan, Ophthalmology, University of Missouri System, Columbia, Missouri, UNITED STATES|N.P. Hesemann, Ophthalmology, MU Health Care Mason Eye Clinic-University Hospital, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inhibitor of differentiation 3 (Id3), a transcriptional repressor gene, over-expression effectively inhibited differentiation of corneal fibroblast to myofibroblast in vitro. This study examined the therapeutic potential of targeted AAV5-Id3 gene delivery into stroma to treat corneal fibrosis using an established rabbit model.

Methods: The study was approved by the institutional animal care and use committee and followed ARVO guidelines. Eighteen New Zealand White rabbits were divided into 3 groups. Only one eye of each rabbit was used. Eyes of group-1 (naïve) received vehicle (n=6); group-2 received AAV5-naked following alkali injury, (n-=6); and group-3 received AAV5-Id3 following alkali injury (n=6). Gene vector into stroma was introduced using an optimized reported topical method. Eyes were periodically examined clinically with the slit lamp microscope, stereomicroscope, pachymetry, tonometry, and in vivo confocal microscopy. Fantes and Modified Hackett-McDonald scores were used to record clinical findings. At the end of 4-weeks, rabbits were humanely euthanized, and corneas were collected for histological, immunofluorescence, and qRT-PCR analyses.

Results: Multimodal clinical imaging and ocular eye examinations revealed that AAV5-Id3 gene delivery significantly reduced corneal fibrosis compared to the AAV5-naked group ($p < 0.01$) without significant ocular manifestations. The qRT-PCR data indicated a significant reduction in mRNA levels of profibrotic genes; αSMA, fibronectin, collagen I, and collagen III (1.4-to-3.2-fold; $p<0.01$ or $p<0.001$) in eyes delivered AAV5-Id3 as compared to the AAV5-naked vector group. Histological and immunofluorescence data (H&E, Cd11b, and α-SMA staining) showed noticeably reduced inflammation and pro-fibrotic proteins levels in AAV5-Id3 therapy group compared to the AAV5-naked vector group. Histological and molecular data corresponds well with masked clinical exams.

Conclusions: Targeted AAV5-Id3 gene transfer into stroma effectively reduces corneal fibrosis in vivo in rabbits without gross clinical toxicity.

CONTROL ID: 3713724

SUBMITTER (NAME ONLY): Ryan Wallace

TITLE: The Use of Ologen Collagen Matrix in Combination with XEN Gel Stent for the Treatment of Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.T. Wallace, C.J. Swiston, I. Danford, C. Chaya, Ophthalmology, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|T.K. Nelson, C. Orr, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|B. Brintz, The University of Utah Division of Epidemiology, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the largest cohort of eyes to undergo simultaneous XEN gel stent +MMC with the addition of Ologen collagen matrix to promote bleb formation and prevent fibrosis.

Methods: Surgical: In addition to ab externo, open-conjunctival XEN + MMC, an Ologen collagen matrix circle was cut in half, with one half positioned below and the other above the XEN stent. Standard post-operative care was followed.
Success Criteria: Success was defined as a >20% drop from preoperative IOP at 12-months without the use of drops, additional procedure (eg. needling), an IOP >21mm Hg at two consecutive visits, or catastrophic events (eg. NLP). Qualified successes were IOPs that met the reduction goal of >20% combined with the use of drops.
Statistics: A linear mixed-effects model was used to estimate change in IOP at each follow-up visit. In this model, age and sex were considered and a patient eye random effect was included for within-eye correlation.

Results: 47 eyes were identified, and 6 were excluded due to insufficient follow up/data or significant compounding factors. After controlling for age and gender, we have strong evidence of a non-zero average change in IOP from baseline and estimate a lower average IOP in all four post-baseline periods (Figure 1 and Table 1). The number of eyes meeting the >20% drop criteria was 82.50% (33/40), 87.80% (36/41), 73.53% (25/34), 70.00% (21/30), and 69.23% (18/26) at 1 month, 3 months, 6 months, 9 months, and 12 months post-operative, respectively. Only one eye required any additional procedures, and no patients had a IOP of >21mm Hg for 2 consecutive clinic visits. No patients had experienced catastrophic events during this time frame.

Conclusions: Some past studies have put the proportion of XEN fibrosis requiring revisions as high as 45%. However, most notably, only 1 eye in this cohort required an additional procedure to control fibrosis. Our numbers also show that the Ologen/XEN gel stent combination resulted in a statistically significant drop in IOP of -7.04 (CI: -9.34, -4.74, $p < 0.001$) from baseline. Thus, the use of Ologen collagen matrix with the XEN gel stent may help prevent bleb fibrosis and the need for revision without affecting XEN efficacy. Further studies with randomization may be required to help determine the true size of this impact in preventing fibrosis and the need for revision.

CONTROL ID: 3713726

SUBMITTER (NAME ONLY): Patricia Fortin

TITLE: The Myopia Management Opportunity in the United States Using the 2020 Census

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Fortin, Nassau University Medical Center, East Meadow, New York, UNITED STATES|J. Kwan, Coopervision Inc, Fairport, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Younger children with myopia benefit most from myopia control treatment(s), which function by slowing myopia progression until eye growth stabilizes. Estimation of myopia prevalence for individuals 5 to 17 years of age in the United States (US) population is of relevance to guide current and future public health responses. Coupling myopia prevalence cross sectional data demographics with the 2020 US Census data offers the opportunity to provide a more up to date estimate of myopia prevalence among children in the US and the subsequent demand on the eye care profession to effectively manage these children.

Methods: The retrospective data set of Kaiser Permanente Southern California pediatric eye exams (Theophanous, 2018) was used to determine the rate of myopia in the 5 to 17 year old age group. This rate was defined as the urban rate of myopia and was then extrapolated to the entire US population, where 80.7% of the US are living in similar urban environments according to the US Census. To estimate the remaining myopia prevalence in rural environments, the myopia odds ratio of 2.61 in urban to rural was applied (Rudnicka, 2016). This gives an estimate of the total myopia prevalence in the US.

Results: The urban myopia prevalence from the Kaiser paper for age 5 to 17 was 41.0%, and the calculated rural prevalence was 15.7%. Extrapolating these myopia prevalence percentage estimations to age-matched US census data, the total number of children with myopia in the US was estimated to be 19,512,708 in 2020 with nationwide myopia prevalence of 36.1%. Holden, 2016 predicted global myopia prevalence of all ages to be 33.9% in the year 2020. Current census data shows Utah, Texas, and Idaho have the largest population proportion of children in this age range; however, the more populous states (California, Texas, Florida, New York, and Illinois) have the greatest number of children, and therefore the greatest numbers of children with myopia.

Conclusions: Estimation of myopia prevalence using the 2020 US Census reveals that 39,025,416 eye exams are required annually across the United States for each child with myopia to be evaluated twice per year. There are approximately 70,000 optometrists and ophthalmologists in the US, and not all provide eye care for children. Each eye care professional would need to provide care to 278 children biannually to meet the current eye care requirements of children with myopia in the US.

CONTROL ID: 3713733
SUBMITTER (NAME ONLY): Ana M. Gonzalez-Ramos
TITLE: OCT-based quantification of multifocal contact lenses on eye
SESSION TITLE: IOLs and Presbyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Gonzalez-Ramos, S. Vedhakrishnan, S. Marcos, E. Martinez-Enriquez, Consejo Superior de Investigaciones Cientificas, Madrid, Madrid, SPAIN|S. Marcos, Center for Visual Science, Rochester, New York, UNITED STATES|
Commercial Relationships Disclosure: Ana M. Gonzalez-Ramos: Commercial Relationship: Code N (No Commercial Relationship) | Shrilekha Vedhakrishnan: Commercial Relationship: Code N (No Commercial Relationship) | Susana Marcos: Commercial Relationship(s);Code P (Patent):WO2012146811A1 | Eduardo Martinez-Enriquez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Multifocal contact lenses (MCLs) are designed to provide near vision functionality in presbyopia. They rely on proper deployment of the multifocal power profile on the cornea and on optical interactions between the MCL and eye. Using custom-developed spectral Anterior Segment Optical Coherence Tomography (OCT) we evaluated the contact lens profile on eye, and potential conformity to the cornea.

Methods: OCT images were obtained on one eye of 13 subjects (age: 35.69 ± 13.83 y/o; Spherical error from -4.75D to +2.50D), with naked eyes and with MCLs on eye. All eyes were tested (5 repetitions) with the same MCLs: 1-Day Acuvue® Moist Brand MCL (Johnson & Johnson® Vision Care; -2.00D distance power; 8.4mm base curve; 14.3mm diameter) and three different additions: +1.25D (Low, L), +1.75D (Mid, M) and +2.50D (High, H). The OCT acquisition speed was 25000 A-Scans/s, the axial range was 7mm in depth, and the axial pixel size 3.4μm. Images were processed using custom routines for segmentation, fan distortion correction, 3D model construction, and surface fitting. The radius of curvature of the external surface of the MCLs (RCL) and the anterior surface of the naked cornea (RC) were obtained from spherical fitting within a 3-mm diameter central area (addition area) and within a 3-6 mm peripheral ring.

Results: RC ranged from 7.5 to 8.2 mm across subjects (8.02±0.22mm, on average). The shift in RCL in the periphery (by 0.55 mm on average) was consistent with the flattening produced by the negative MCL base power, and was constant independently of the corneal power of the subject. RC and RCL were correlated ($p<<0.005$) in the periphery for the three MCL additions ($r=0.87$, 0.84 and 0.82 for L, M and H adds, respectively) and also in the addition area ($p<<0.005$, $r=0.85$, 0.82, 0.78, L, M, H, respectively). The average RCL across subjects in the addition area was 8.37±0.31mm (L), 8.32±0.34mm (M) and 8.30±0.28 mm (H), and in the periphery was 8.59±0.30mm (L), 8.54±0.33mm (M) and 8.53±0.28mm (H), consistent with a relative central steepening, particularly for the higher add.

Conclusions: OCT provided with quantification tools allows to study the fitting of MCLs on eye in vivo. We found that, overall, soft MCLs conform to the underlying cornea, both in the central addition area and the periphery. However, the near central add is provided, as expected.

CONTROL ID: 3713734

SUBMITTER (NAME ONLY): Shawn Gulati

TITLE: Retroprosthetic Membrane Formation Following Glaucoma Procedures with Boston Keratoprosthesis

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gulati, M.S. Cortina, D.P. EDWARD, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Shawn Gulati: Commercial Relationship: Code N (No Commercial Relationship) | Maria Cortina: Commercial Relationship: Code N (No Commercial Relationship) | DEEPAK EDWARD: Commercial Relationship(s);Code S (non-remunerative):Genentech;Code C (Consultant/Contractor):Takeda Pharma

ABSTRACT BODY:

Purpose: To assess features of retroprosthetic membranes (RPM) in Boston Keratoprosthesis (KPro) eyes undergoing diode cyclophotocoagulation (CPC) compared to glaucoma drainage implant (GDI).

Methods: We reviewed records for 193 eyes undergoing KPro surgery from 2007 - 2020. We compared prevalence of RPM, preoperative diagnoses, and visual outcomes following CPC vs. GDI.

Results: 36 eyes met inclusion criteria. 1 eye (3%) had primary CPC, 6 eyes (17%) had both GDI and CPC, and 29 eyes (80%) had GDI without CPC. KPro indication was similar in GDI/CPC group: non-inflammatory (61%, n=22), inflammatory (28%, n=10), and chemical injury (11%, n=4). RPM prevalence was 71% (5/7) in CPC vs. 15% (4/27) in primary GDI ($p<0.01$) (OR:4.8). Mean time from procedure to RPM formation was 3.9 years and similar between groups. At last visit, in CPC eyes, mean VA was 1.8 logMAR (5/7) and no light perception in others (2/7). In primary GDI eyes, mean VA was 1.2 logMAR (24/27) and ≤ light perception in others (3/27).

Conclusions: RPM occurrence in KPro following CPC was significantly higher than after GDI with poor VA outcome. Our data has implications for glaucoma intervention selection with KPro.

CONTROL ID: 3713735
SUBMITTER (NAME ONLY): Debalina Goswami-Sewell
TITLE: Deciphering the Role of bII-spectrin in the Developing Outer Retina
SESSION TITLE: Photoreceptors and the OPL
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: D. Goswami-Sewell, C. Bagnetto, E. Zuniga-Sanchez, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|E. Zuniga-Sanchez, Neuroscience, Baylor College of Medicine, Houston, Texas, UNITED STATES|
Commercial Relationships Disclosure: Debalina Goswami-Sewell: Commercial Relationship: Code N (No Commercial Relationship) | Caitlin Bagnetto: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Zuniga-Sanchez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:
Purpose: Photoreceptors are the main detectors of light that relay visual information to the brain. Establishing proper photoreceptor connectivity during development is critical for proper transmission of visual information. Within the outer retina, photoreceptors synapse selectively to horizontal cells and bipolars. Cone photoreceptors synapse to the dendrites of horizontal cells and cone bipolars, whereas rods connect to the axon terminal of horizontal cells and to the dendrites of rod bipolars. Although the pattern of connections within the retina has been well-described, the molecular mechanisms that guide their selective wiring during development remains unclear.
Methods: We found a member of the Spectrin family, bII-spectrin to be highly expressed in the developing synaptic layer or OPL where photoreceptors are actively making synaptic connections to their respective partners. Based on the timing and location of expression, we set out to determine if bII-spectrin has a role in photoreceptor connectivity during development. To test our hypothesis, we crossed a floxed allele for bII-spectrin to the Chx10cre transgenic mouse line to conditionally remove bII-spectrin throughout the retina. We refer to this cross as bII-spectrin CKO. Next, we examined bII-spectrin CKO retinas for synaptic defects at various developmental ages.
Results: Our initial findings reveal disruption of bII-spectrin leads to synaptic defects in the adult retina. Specifically, rod terminals retract into the nuclear layer (i.e. ONL) and processes from horizontal cells and the dendrites of rod bipolars misproject into the ONL. Surprisingly, cone terminals do not retract nor do the dendrites of cone bipolars misproject into the ONL. Consistent with these findings, we find selective loss of pre- and post-synaptic protein expression in the rod synaptic layer but not the cone synaptic layer. Our data suggests that loss of bII-spectrin mainly affects the rod pathway and not the cone pathway. Developmental analysis of bII-spectrin CKO animals reveals that these synaptic phenotypes arise at early stages (i.e. P7-9) when rod synapse formation begins in the outer retina.
Conclusions: Our work supports a novel role for bII-spectrin in rod photoreceptor connectivity in the developing retina. Future work will focus on deciphering the cellular and molecular mechanisms of how bII-spectrin mediates synapse formation of the rod pathway and not the cone pathway.

CONTROL ID: 3713736

SUBMITTER (NAME ONLY): Marialejandra Diaz Ibarra

TITLE: Automated detection of the spatial location of vitreoretinal instruments from retinal images using Deep Learning methods

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Diaz Ibarra, J.K. To, A. Herekar, B.D. Kuppermann, A. Browne, Ophthalmology, University of California System, Irvine, California, UNITED STATES|J. Liu, S. Abdelkarim, P. Baldi, Computer Science, University of California System, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To create and assess Deep Learning methods for automated detection of locations and depth of vitreoretinal instruments in retinal surgery videos.

Methods: Surgical videos in vitro were recorded using a custom 3D eye model, vitrectomy instrumentation and an ophthalmic surgery microscope. Videos of instrument manipulation throughout the surgical field and at different instrument depths (far, intermediate and near to the retina) were acquired. Video frames (n=26,460) were extracted, labeled for instrument location and used to train Machine learning (ML) employing Convolutional Neural Networks (CNNs) including ResNet-18. The CNN model used was adapted with two outputs predicting the location and depth of surgical instruments.

Results: The resultant algorithm was validated with high reproducibility. The predictability of the algorithm for detecting locations and depth of vitreoretinal instruments in retinal images achieved a 99% accuracy.

Conclusions: Deep Learning methods achieved remarkable accuracy for detecting locations and depth of vitreoretinal instruments in retinal surgical videos and demonstrates the utility of real-time surgical video analysis to aid in vitrectomy. Despite current advances in vitreoretinal (VR) surgery instrumentation and visualization systems, VR surgery remains challenging for trainees and surgeons. Deep learning is an advanced subfield of artificial intelligence that may aid and improve surgical performance.

CONTROL ID: 3713737

SUBMITTER (NAME ONLY): Andrea Naranjo

TITLE: Effect of hepatocyte growth factor-loaded collagen-PEG gels on corneal wound healing.

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Naranjo, G. Fernandes Cunha, D. Myung, Ophthalmology, Stanford Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Andrea Naranjo: Commercial Relationship: Code N (No Commercial Relationship) | Gabriella Maria Fernandes Cunha: Commercial Relationship: Code N (No Commercial Relationship) | David Myung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Corneal injuries can lead to infection, scarring, and significant vision loss. There continues to be a clinical need for better ways to facilitate rapid and phenotypically normal corneal wound healing after injury or disease. Numerous growth factors, including hepatocyte growth factor (HGF), are secreted by the native cornea following injury to facilitate healing. Recently, exogenous HGF has been shown to enhance corneal wound healing. Hydrogel matrices have also been shown to be a promising approach to providing a substrate that supports corneal healing. Here, we evaluate the sustained release of HGF from a collagen gel crosslinked in situ by a multi-functional PEG crosslinker.

Methods: A corneal epithelial cell (CEC) migration essay was performed comparing a negative control (plain medium) and a positive control (10% FBS) with PEG-collagen gel (8-arm PEG-N-hydroxysuccinimide) with and without HGF as well as free, soluble HGF. The cells were monitored for 24 hours and immunofluorescence was performed on the treated cells to evaluate for the expression of phalloidin, Ki-67, CD44, and ZO-1.

Results: CECs with HGF-loaded PEG-collagen gels were able to migrate faster and close wounds at a faster rate than the negative control, PEG-collagen gels alone without HGF, and free HGF. Immunofluorescence demonstrated no alteration in morphology as a result of the PEG crosslinker or HGF. An increase in proliferation markers was detected in the cells treated with the HGF-loaded PEG-collagen gels.

Conclusions: PEG-collagen hydrogels loaded with HGF improves corneal cell migration over collagen gels and HGF alone, and are a promising approach to enhancing corneal wound healing. Further work is merited to study this therapeutic construct in vivo.

CONTROL ID: 3713738

SUBMITTER (NAME ONLY): ROSANNA CALDERON

TITLE: Cross-species comparison of non-canonical Wnt pathway expression in the developing outer plexiform layer

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. CALDERON, A. Nagiel, Developmental, Stem Cell and Regenerative Medicine, University of Southern California, Los Angeles, California, UNITED STATES|R. CALDERON, K. Stepanian, A. Ferrario, A. Nagiel, Ophthalmology, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|G. Fernandez, Cellular Imaging Core, The Saban Research Institute, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptor axons terminate in the outer plexiform layer (OPL) of the retina, where they form synapses with the bipolar cells located in the inner nuclear layer (INL). The purpose of this study is to investigate the developmental expression of non-canonical Wnt signaling components in the OPL as potential mediators of circuit assembly in the outer retina.

Methods: Publicly available single-cell RNA sequencing (scRNAseq) data sets (GSE118614 and GSE138002) were analyzed for expression of non-canonical Wnt mediators, ligands, and receptors at various developmental timepoints in mouse and human retina. To validate expression of candidate genes, mouse (P6-P12 and adult, n=3), human fetal retina (human fetal week (HFW) 12-17, n=1) and human retinal organoid (HRO, n=3) sections were prepared using an RNase-free protocol and mRNA transcripts were detected using fluorescence in situ hybridization (FISH). FISH signal was quantified in the ONL and INL areas using the Find Maxima function on ImageJ. ANOVA analysis was performed to determine statistically significant changes between selected timepoints.

Results: Analysis of scRNAseq for 34 selected non-canonical Wnt pathway genes revealed 6 mediators, 3 Frizzled receptors and 4 Wnt ligands expressed in mouse and human retina during early OPL development. In both mouse and human retina, FISH confirmed expression of non-canonical Wnt mediators Dvl1, Celsr3, and Ryk in all nuclear layers, and of Vangl2 in the INL. The Wnt receptors Fzd3 and Fzd5 were expressed in the INL as early as P6 in mouse retina and GW17.4 in human fetal retina. The Wnt ligand Wnt5a was detected in the INL at P10 and showed a significant decrease in adults ($p<0.001$). Mouse Wnt2b co-localized with the amacrine cell marker ChAT. WNT10A expression was human-specific and restricted to the ONL (scRNAseq shows predominant rod expression).

Conclusions: Non-canonical Wnt signaling pathway components are expressed in the developing mouse and human outer retina during synaptic maturation of the OPL. Importantly, we found previously undescribed expression patterns (e.g., mouse Wnt2b in amacrine cells) and human-specific expression (e.g., Wnt10a in the ONL). This provides the basis for further studies to dissect the functional role of non-canonical Wnt genes in outer retinal development.

CONTROL ID: 3713739

SUBMITTER (NAME ONLY): Brian Leonard

TITLE: Topical application of a novel Harderian-derived nonpolar lipid prolongs tear film break up time in normal Beagle dogs

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.C. Leonard, S. Park, VM: Surgical and Radiological Sciences, University of California Davis, Davis, California, UNITED STATES|D.M. Albert, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D.M. Albert, C.A. O'Neill, T. . Gadek, MCAL Therapeutics, California, UNITED STATES|A.N. Parikh, Department of Biomedical Engineering, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) is a common ophthalmic condition with many underlying causes that are unified by the destabilization of the tear film. Despite current therapeutics, many patients with DED require additional treatments to provide comfort and reduce irritation. We recently identified a novel nonpolar lipid (NPL) isolated from the Harderian gland of the rabbit, not found in human meibum or tears, that increased tear film break up time (TFBUT) and improved ocular surface health in a rabbit model of DED. The purpose of this study was to determine the effect of this novel NPL on TFBUT in normal Beagle dogs.

Methods: In phase 1, a pilot study was performed to determine the dose of the rabbit NPL that prolonged TFBUT from baseline. Dogs (n = 2) were treated with a single dose of NPL (vehicle, 0.1, 0.5, 1, 3 and 10 mg/mL) in both eyes and TFBUT was measured at 1, 3, 6, 12 and 24 hours (h) post-treatment. In phase 2, dogs (n = 5) received one of three treatments (vehicle, 1 mg/mL or 3 mg/mL NPL) once in both eyes and TFBUT was measured at 6 and 24 h post-treatment. In phase 3, dogs (n = 3) received multiple doses (3 mg/mL NPL) over four days and TFBUT was performed at 6 and 80 h post-treatment. Semi-quantitative preclinical ocular toxicology scoring (SPOTS) was performed to document adverse events.

Results: In phase 1, topical treatment with NPL resulted in a dose-dependent increase in TFBUT in healthy Beagle dogs with the most optimal concentration of 3 mg/mL (mean change from baseline [MCB]: 1 h, +9.6 seconds [s]; 3 h, +8.1 s; 6 h, +3.4 s; 12 h, +3.0 s; 24 h, +7.7 s). In phase 2, topical treatment with NPL resulted in an increase in TFBUT with the 1 mg/mL dose (MCB: 6 h, +3.4 s; 24 h, 2.1 s) yet more pronounced increase in MCB TFBUT with the 3 mg/mL dose (6 h, +4.48 s; 24 h, +3.86 s). In phase 3, there was an increase in TFBUT measured at 6 h post-treatment with NPL (6 h, +3.3 s) that returned to baseline levels at 80 h post-treatment (80 h, +0.1 s). The topical NPL was well-tolerated with no pathologic changes detected using the SPOTS system.

Conclusions: Overall, treatment with a single dose of the NPL was well-tolerated at all doses tested and resulted in an increased TFBUT MCB that was most pronounced with the 3 mg/mL dose. Future studies will be focused on determining the effect of this NPL on stabilizing the tear film in murine and canine models of DED.

CONTROL ID: 3713740

SUBMITTER (NAME ONLY): Sierra Schleufer

TITLE: Crystalline arrangement of S-cones in the central human retina

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Schleufer, Graduate Program in Neuroscience, University of Washington, Seattle, Washington, UNITED STATES|S. Schleufer, V. Pandiyan, P. Bharadwaj, R. Sabesan, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The topography of S-cones in the macula sets neural constraints for coding the short-wavelength spectrum of color vision. We aimed to characterize topography of S-cones in the central human cone mosaic and to what extent it deviates from a random arrangement.

Methods: In 2 subjects, cone sub-types were classified via Adaptive Optics Line-scan OCT and a bleaching stimulus of 660±10 nm. Regions of interest (ROIs) were classified at 1.5, ~4, and 10° eccentricity across the 4 cardinal meridians (12 ROIs each). S-cone spacing was quantified in ROIs containing >= 1000 cones using Density Recovery Profile (DRP). DRP measures the density of S-cones at regular intervals within some radius of other S-cones. These were binned by the average nearest-cone distance per ROI, such that DRP was calculated at 1-cone intervals within 18 arcmin. To compare with random arrangement, 1000 Monte Carlo (MC) simulations of each ROI were generated such that cone locations in the mosaic and number of S-cones were maintained, but positions of S-cones within the mosaic were randomized. Crystalline arrangement is indicated by bins at which the DRP for a true S-cone sub-mosaic is significantly lower than the MC distribution.

Results: Mean and std of total cones classified and quantity S-cones per ROI at each eccentricity were 2374±665, 1211±391, and 700±229 at 1.5°, ~4°, and 10° respectively. Density of S-cones decreased with eccentricity while their percentage increased (density (1/deg.2): [1.5°: 152.9 ± 43.3, ~4°: 74.8±22.3, 10°: 61.1±15.9], percent (%): [1.5°: 5.2±0.5, ~4°: 6.2±1.0, 10°: 8.3±2.0]). DRP was calculated for 14/24 ROIs (8, 5, and 1 ROI(s) at 1.5°, ~4°, 10°, respectively, with bin-widths (arcmin) 1.25±0.16, 1.87±0.17, and 2.25).. A low density of S-cones ($p < 0.05$) was observed in 13/14 ROIs within a 1-cone [1.5°: 8/8, ~4°: 5/5; 10°: 0/1] and 2-cone [1.5°: 7/8, ~4°: 5/5, 10°:1/1] radius. Beyond a 2-cone radius, the DRP was indistinguishable from random but for exceptions in two 1.5° ROIs (at a 6-cone and 12-cone radius respectively).

Conclusions: We find that S-cones are arranged with non-random crystallinity in the central human cone mosaic such that they avoid a 2-cone radius of one another. It is unclear whether this crystallinity changes with eccentricity. This finding departs from previous studies, likely due to their limited sampling, and has important implications for retinal development and color-coding retinal circuits.

CONTROL ID: 3713742

SUBMITTER (NAME ONLY): Alfonso Jimenez-Villar

TITLE: Rheological Eye Model to Determine Elastic and Viscoelastic Properties of the Cornea and Crystalline Lens

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Jimenez-Villar, I. Grulkowski, Biofizyka, Uniwersytet Mikolaja Kopernika w Toruniu Wydzial Fizyki Astronomii i Informatyki Stosowanej, Torun, POLAND|B. Kaluzny, Katedra Chorób Oczu, Uniwersytet Mikolaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy, Bydgoszcz, POLAND|

Commercial Relationships Disclosure: Alfonso Jimenez-Villar: Commercial Relationship: Code N (No Commercial Relationship) | Bartlomiej Kaluzny: Commercial Relationship: Code N (No Commercial Relationship) | Ireneusz Grulkowski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To develop a rheological model of the reaction of ocular structures to air-puff stimulation. To determine the relation between Young's modulus and the viscosity modulus according to different IOP values.

Methods: A cross-sectional observational study was performed in 20 healthy eyes from different Caucasian subjects (mean age 27.5 ± 3.5 y.o.; mean spherical equivalent refractive error: -1.1 ± 1.5 D). The reaction of the cornea, crystalline lens and the eyeball to an air jet was recorded by a SS-OCT ocular biometer integrated with an air puff chamber at two different IOP levels. First, in physiological normal IOP conditions and 2 hours after administration of IOP-reducing drops (brimonidine tartrate 0.2%). At the same time, the IOP values were measured with a Goldmann Applanation Tonometer. The displacement of each ocular component was used to design a rheological eye model and to calculate elastic (E) and viscosity (η) moduli from each component after applying an optimization process by a Marquardt-Lavenberg algorithm. Finally, moduli from the cornea were correlated with the IOP measurements.

Results: Fig. 1 demonstrates the rheological model of ocular structures' dynamics during air-puff stimulation. The cornea, crystalline lens and eyeball movement are described by Maxwell and Kelvin submodels to determine the viscoelastic behavior of each component. Moreover, a mass term was included for the lens and for the eye to simulate the lens wobbling and eye retraction. Fig. 2 represents the predicted theoretical deformations based on experimental data. Regarding the mechanical properties of the cornea with the IOP, higher correlation between E and IOP was found although no statistical significance was detected (corneal E: Pearson's R = 0.7097; corneal η: Pearson's R = 0.5869). Additionally, it was observed that η was strongly linearly dependent on the E (Pearson's R = 0.8552).

Conclusions: SS-OCT biometers integrated with air puff subsystems enable to image the dynamics of the cornea, crystalline lens and the whole eye. Therefore, OCT can help to develop rheological eye models which might predict the mechanical behavior of different ocular structures. The determination of the elastic and viscosity moduli from cornea and lens can be used to predict correct IOP values in future studies. In particular, both, E and η from the cornea were linearly dependent on the IOP level.

CONTROL ID: 3713743

SUBMITTER (NAME ONLY): Moksha Laxmi

TITLE: Pharmacological modulation of Toll-like receptor-stimulated downstream inflammatory pathways in an experimental model of uveitis.

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. kumar, R. Chawla, Ophthalmology, Dr RP Centre, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|B.S. Singh, Biophysics, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|M. Laxmi, N. Halder, T. Velpandian, OCULAR PHARMACOLOGY AND PHARMACY DIVISION, RP CENTRE, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Toll-like receptor (TLR) acting as lipopolysaccharide (LPS) sensor is involved in recognition of and response to endotoxin mediated infections. Their activation contributes to uveitis leading to stimulation of signaling events that include expressions of various cytokines such as TNF-α. The mainstay for the treatment is steroids, which are substrates for P-gp transporters, and on topical application, would be effluxed, leading to insufficient therapeutic levels in aqueous humor (AH). Hence, this study evaluated alternative P-gp sparing molecules that act via similar anti-inflammatory pathways to control inflammation.

Methods: Topical dapsone and nimesulide (0.1%) were formulated aseptically and evaluated in endotoxin-induced uveitis (EIU) Wistar rat model in comparison with topical prednisolone (1%). Rats received 0.1 ml saline containing 200 µg LPS through hindpaw, with three times a day (TID) topical instillation of 10 µl vehicle, nimesulide, dapsone and prednisolone (Table 1) in their respective groups. 30 µl of AH was collected for protein extravasation analysis and TNF-α levels.

Results: Results showed topical nimesulide significantly reduced AH TNF-α levels in EIU (Nimesulide) group (14.07±5.36 ng/ml) as compared to EIU (Vehicle) group (40.6±5.51 ng/ml). It also reduced protein leakage in AH of EIU (Nimesulide) group (8.37±2.87 mg/ml) as compared to control (18.48±2.13 mg/ml). The topical dapsone resulted in a significant decrease in total protein concentration of AH in EIU (Dapsone) group (11.44±0.93 mg/ml) when compared to EIU (Vehicle) group (22.5±2.06 mg/ml). Moreover, 0.1% dapsone topical instillation also decreased TNF-α levels in AH of EIU (Dapsone) group (18.4±2.26 ng/ml) when compared to EIU (Vehicle) group (26.49±3.66 ng/ml). While prednisolone administered (TID) in EIU showed non-significant reduction in total protein as well as TNF-α levels in AH.

Conclusions: For the first time, sterile topical nimesulide and dapsone formulations were developed and were found to be effective in modulating TLR by reducing inflammatory markers (TNF-α) and vascular leakage in AH of rats when compared to prednisolone. Therefore, this study showed that molecules that are P-gp sparing could be a better option for targeting TNF-α pathway for their utility in uveitis.

CONTROL ID: 3713745

SUBMITTER (NAME ONLY): Ivan Rebustini

TITLE: Pigment epithelium-derived factor induces CRX alterations in the mouse retina.

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Rebustini, S. Becerra, Section of Protein Structure and Function, LRCMB-NEI-NIH, National Eye Institute, Bethesda, Maryland, UNITED STATES|S.E. Crawford, Dept. Surgery, NorthShore University Research Institute, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Ivan Rebustini: Commercial Relationship: Code N (No Commercial Relationship) | Susan Crawford: Commercial Relationship: Code N (No Commercial Relationship) | S.Patricia Becerra: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The gene Serpinf1 encodes for Pigment Epithelium-Derived Factor (PEDF), which protects photoreceptors from cell death. The Serpinf1 null mouse exhibits normal retinal function; however, PEDF deficiency increases retinal degeneration susceptibility in the rd10 mouse. CRX is a transcription factor that regulates expression of several photoreceptor specific genes, including opsins and phosphodiesterase. This study aims to explore whether regulation of CRX activation is one mechanism by which PEDF exerts photoreceptor survival.

Methods: Serpinf1$^{-/-}$, Serpinf1$^{+/-}$ and Serpinf1$^{+/+}$ mice at 3 months of age were used. Mouse retinal explant cultures we prepared and treated with recombinant human PEDF. Zaprinast (a PDE inhibitor) was added to induce photoreceptor death. Photoreceptor cell death was determined using PSVue-550, a visible fluorescent probe for phosphatidylserine detection on the surface of cells. Subcellular distribution of CRX, PDE6A and pan-acetylation was detected by immunofluorescence. The transcriptional levels of Crx, Pde6a, Rho, Opn1mw and Opn1sw were assessed using qPCR.

Results: PEDF treatment induced the expression of Crx and its regulated genes Pde6a, Opn1mw and Opn1sw. PEDF also enhanced the CRX immunoreactivity in the nuclei of photoreceptors. In contrast, the nuclear CRX immunoreactivity was suppressed in photoreceptors from retinas of Serpinf1$^{-/-}$ mice deficient of PEDF. PDE6A immunoreactivity also decreased in Serpinf1$^{-/-}$ photoreceptors compared to those from Serpinf1$^{+/+}$ mice. Histone acetylation was detected in discrete photoreceptors in Serpinf1$^{+/+}$ but was undetectable in the Serpinf1$^{-/-}$ retinas. Zaprinast-induced photoreceptor death was more pronounced in Serpinf1$^{-/-}$ retinal explants than in wild type controls. PEDF pre-treatment prior to the zaprinast treatment improved photoreceptor survival and enhanced CRX immunoreactivity in both Serpinf1$^{-/-}$ and Serpinf1$^{+/+}$ retinal explants.

Conclusions: The findings imply that PEDF activated the CRX-associated transcription factor network. They provide a novel insight linking extracellular PEDF to nuclear CRX during photoreceptor survival.

CONTROL ID: 3713746

SUBMITTER (NAME ONLY): Shubham Maurya

TITLE: LXB_4 regulation of microglia responses in ocular hypertension induced neuropathy

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Maurya, S. Karnam, L. Yang, J.G. Flanagan, K. Gronert, Herbert Wertheim School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|

Commercial Relationships Disclosure: Shubham Maurya: Commercial Relationship: Code N (No Commercial Relationship) | Shruthi Karnam: Commercial Relationship: Code N (No Commercial Relationship) | Lily Yang: Commercial Relationship: Code N (No Commercial Relationship) | John Flanagan: Commercial Relationship: Code N (No Commercial Relationship) | Karsten Gronert: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The neuroprotective role of specialized pro-resolving mediators such as lipoxins (LXA_4 and LXB_4) are lost during retinal insult, including ocular hypertension (OHT). Using a silicone oil (SO) based model of OHT induced neuropathy and LXB_4 treatment, we aimed to better understand the novel mechanisms involved in LXB_4 mediated neuroprotection.

Methods: To discover novel targets for LXB_4 homeostatic function, we performed single-cell (SC) transcriptomics of retinal cells after treating the healthy C57BL6/J mice (n=4 retina) with LXB_4 by intraperitoneal (IP) injection and topical eye drops. For inducing OHT, we used the established SO model that causes stable and sustained OHT. To validate and explore novel targets of LXB_4 under OHT conditions, mice (n=3) were treated with LXB_4 by IP and topical eye drops every other day from day 7 to day 28. Gene expression of potential targets was analyzed by qPCR.

Results: LXB_4 treatment-induced changes in transcriptomic profile in a limited number of retinal cell types in healthy mice. Unexpectedly, LXB_4 treatment markedly changed gene expression for a distinct pathway in microglia. These selected genes were C5ar1, Clec4a2, Entpd1, Il6ra, and CD37, which are components of the new microglia 'sensome' paradigm, responsible for regulating the microglia phenotype switch in stress/immune responses. LXB_4 treatment downregulated these sensome genes by ≥2-fold ($p < 0.05$). Further, we analyzed the expression of LXB_4-regulated sensome genes under OHT conditions at 4 and 8 weeks. Notably, expression of the microglia sensome gene Clec4a2 was elevated at 4 weeks by 1.63-fold (n=4, $p<0.05$) and at 8 weeks by 1.84-fold (n=3, $p<0.05$). Consistent with scRNA results from healthy mice, LXB_4 treatment in mice with the OHT reduced Clec4a2 expression compared to sham treatment.

Conclusions: Our data identify a novel cellular target and potential mechanism of action for the neuroprotective LXB_4, namely by regulation of microglial sensome gene Clec4a2. The microglia sensome is an essential mechanism for directing microglia activation, an early event in glaucoma pathogenesis. LXB_4 regulation of the microglia sensome is of interest given the homeostatic and protective actions of lipoxins in rat and mouse models of OHT-induced glaucomatous injury.

CONTROL ID: 3713747

SUBMITTER (NAME ONLY): Bilal Haj Najeeb

TITLE: The RAP study, Report 6: Quantification of exudative biomarkers in neovascular age-related macular degeneration (nAMD) using deep learning, a type-based comparative analysis.

SESSION TITLE: AI and Retina 2

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Haj Najeeb, B. Gerendas, H. Bogunovic, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To quantify five exudative biomarkers in eyes with treatment-naïve macular neovascularization type 3 (MNV3) using deep learning and compare the outcomes with those of eyes with MNV 1 and MNV2.

Methods: 34528 optical coherence tomography scans of 457 eyes with nAMD consisting of 281 (250 unifocal, 31 multifocal) eyes with MNV3, 55 eyes with MNV2 and 121 (91 non-polypoidal, 30 polypoidal) eyes with MNV1 were included. The volumes of intraretinal (IRF) and subretinal fluid (SRF), pigment epithelial detachments (PED) and hyperreflective foci (HRF) in nanoliters (nl) and retinal thickness (RT) in micrometers (µm) were quantified by validated deep learning algorithms for each (sub)type of MNV.

Results: The analysis of MNV types shows that MNV3 had the highest mean (± standard deviation) of IRF volume in the central 1, 3 and 6mm: 67±61, 216±196, 291±289nl, and greatest mean of RT 418±104, 391±62, 356±49µm, followed by MNV2 with 31±54, 79±145, 105±216nl (IRF), and 380±80, 372±50, 338±39µm (RT), $p<0.05$. Also, MNV3 presented with the biggest mean of HRF volume 5±5, 32±24, 79±69nl, followed by MNV1 3±3, 22±19, 51±52nl, $p<0.05$. MNV3 revealed the lowest mean of SRF volume 15±35, 72±133, 215±382nl, whereas MNV1 showed the greatest mean of SRF volume 28±38, 168±193, 492±583nl, $p<0.05$, and the biggest mean of PED volume 84±94, 495±583, 667±855nl, $p<0.05$.

The analysis of MNV1 subtypes (polypoidal vs. non-polypoidal) shows that the polypoidal subtype had a significantly higher mean of PED volume in all areas, greater mean of RT in the 3 and 6mm areas, and bigger means of SRF and HRF volumes in the 6mm area only. The mean of IRF volume was not significantly different between both subtypes. In addition, the analysis of MNV3 subtypes (multifocal vs. unifocal) shows that the multifocal subtype revealed significantly higher means of IRF and HRF volumes in all areas and a greater mean of RT in the 3mm area only. No significant mean differences of SRF and PED volumes were observed.

Conclusions: Using deep learning to quantify exudative biomarkers in different MNV types provide clinicians with unprecedented quantitative and topographic details. These pathomorphological differences allow a better understanding of the clinical manifestation, natural course and prognosis of each (sub)type of MNV in nAMD.

CONTROL ID: 3713749

SUBMITTER (NAME ONLY): Jessicca Cho

TITLE: In vivo evaluation of Retinal Ganglion Cells (RGCs) in mice using Temporal Speckle Averaging Optical Coherence Tomography (TSA- OCT).

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cho, P. Zhang, S.J. Karlen, A. La Torre, R.J. Zawadzki, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|J. Cho, N. Marsh-Armstrong, R.J. Zawadzki, Ophthalmology and Vision Science, University of California Davis, Davis, California, UNITED STATES|P. Zhang, School of Optoelectronic Engineering and Instrumentation Science, Dalian University of Technology, Dalian, Liaoning, CHINA|

Commercial Relationships Disclosure: Jessicca Cho: Commercial Relationship: Code N (No Commercial Relationship) | Pengfei Zhang: Commercial Relationship(s);Code P (Patent):US Patent App. 17/168,043, 2021 | Sarah Karlen: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Marsh-Armstrong: Commercial Relationship: Code N (No Commercial Relationship) | Anna La Torre: Commercial Relationship: Code N (No Commercial Relationship) | Robert Zawadzki: Commercial Relationship(s);Code P (Patent):US Patent App. 17/168,043, 2021

ABSTRACT BODY:

Purpose: To present the results of in vivo visualization and quantification of Retinal Ganglion Cells (RGCs) in mice using Temporal Speckle Averaging Optical Coherence Tomography (TSA- OCT).

Methods: We used a custom-built mouse retinal Scanning Laser Ophthalmoscopy / Optical Coherence Tomography (SLO/OCT) system to acquire non-invasive serial OCT volumes with corresponding SLO intensity and fluorescence data to provide input for Temporal Speckle Averaging (TSA) OCT volume processing. The TSA-OCT processing allows reduction of the speckle contrast and enhancement of the cellular retinal morphology probed by OCT. To showcase the performance of this technique, two mouse lines with fluorescently labeled RGC (based on RGCs transcription factor Brn3b-mCherry and Isl2-GFP) were used.

Results: TSA-OCT greatly enhanced the image quality of the Retinal Nerve Fiber Layer (RNFL) and enabled RGCs visualization (see Figure). While a single OCT volume doesn't allow visualization of RGC, the application of TSA-OCT opens the possibility of non-invasive probing of RGCs. Use of mice with fluorescently labeled RGCs allowed mapping of RGC position using a fluorescent SLO system, providing direct comparison with RGC somas visualized by TSA-OCT. Additionally fluorescent labeling of the RGC helped with further validation of TSA-OCT imaging by histology providing one-to-one mapping between in vivo and ex vivo images of RGC.

Conclusions: In these studies, we used a novel TSA-OCT to visualize mouse RGCs in vivo. We did not need Adaptive Optics, suggesting that speckle contrast rather than insufficient lateral resolution is a limiting factor in using OCT for non-invasive in vivo [SJK1] evaluation of cellular retinal morphology in mice. Our ability to visualize and follow RGCs in vivo using non-invasive imaging method should allow a reduction in the number of animals needed in future studies. These results open doors for efficient in vivo monitoring of cellular morphology in animal models of glaucoma during disease progression and therapeutic innervation.

CONTROL ID: 3713750

SUBMITTER (NAME ONLY): Robert Luben

TITLE: Retinal fractal dimension in prevalent dementia: The AlzEye Study

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Luben, S. Wagner, R. Struyven, M. Cortina-Borja, A. Petzold, J. Rahi, P.A. Keane, University College London, London, London, UNITED KINGDOM|R. Luben, S. Wagner, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|E. Trucco, M. Rama Krishnan Mookiah, University of Dundee, Dundee, Dundee, UNITED KINGDOM|A.K. Denniston, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

Commercial Relationships Disclosure: Robert Luben: Commercial Relationship: Code N (No Commercial Relationship) | Siegfried Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Robbert Struyven: Commercial Relationship: Code N (No Commercial Relationship) | Mario Cortina-Borja: Commercial Relationship: Code N (No Commercial Relationship) | Axel Petzold: Commercial Relationship: Code N (No Commercial Relationship) | Emanuele Trucco: Commercial Relationship: Code N (No Commercial Relationship) | Muthu Rama Krishnan Mookiah: Commercial Relationship: Code N (No Commercial Relationship) | Jugnoo Rahi: Commercial Relationship: Code N (No Commercial Relationship) | Alastair Denniston: Commercial Relationship: Code N (No Commercial Relationship) | Pearse Keane: Commercial Relationship(s);Code F (Financial Support):Allergan, Bayer, Heidelberg Engineering, Novartis, Roche, Topcon;Code C (Consultant/Contractor):Apellis, DeepMind;Code I (Personal Financial Interest):Big Picture Medical

ABSTRACT BODY:

Purpose: To analyse the association between retinal fractal dimension (FD) and all-cause dementia in a large ethnically and socioeconomically diverse cohort in London, United Kingdom.

Methods: The AlzEye project is a retrospective cohort study linking ophthalmic imaging of all patients attending Moorfields Eye Hospital aged ≥ 40 years with secondary care Hospital Episodes Statistics Admissions data between January 1st 2008 and March 31st 2018. Dementia diagnoses were coded using the International Classification of Diseases, 10th revision. Retinal fractal dimension was extracted from macular-centered colour fundus photographs using the Vascular Assessment and Measurement Platform for Images of the Retina. Multivariable linear regression was used to examine the association between retinal FD and dementia.

Results: Among 96,995 patients, 4353 had a diagnosis of dementia: 1222 with AD, 885 with VD, 229 with mixed disease and 2017 with unspecified dementia . Compared to those without dementia, patients with dementia were older (79.7 +/- 8.6 vs 67.7+/-12.4), more likely to be women (58.7% vs 50.6%) and more likely to have hypertension (83.3% vs 80.4%, all $p<0.001$). Patients with dementia had reduced retinal FD after adjusting for age, sex, diabetes mellitus and hypertension (beta: -0.0047; 95% CI: -0.005, -0.003; $p<0.001$). No interaction was apparent among covariates.

Conclusions: A strong inverse association was seen between retinal FD and prevalent all-cause dementia after adjustment of known confounders of FD. Subsequent analyses will examine associations between other metrics of retinal morphology, derived from optical coherence tomography and incident disease.

CONTROL ID: 3713751

SUBMITTER (NAME ONLY): Cole Beatty

TITLE: Elucidating neutrophil transcriptomes in meibomian gland dysfunction pathogenesis in mice

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Beatty, S. Littleton, D.R. Saban, Immunology, Duke University, Durham, North Carolina, UNITED STATES|C. Beatty, C. Yu, S. Littleton, R. Mathew, J. Kalnitsky, D.R. Saban, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) is a leading cause of evaporative dry eye disease, yet the mechanism driving pathogenesis remains poorly understood. Recent studies in the Allergic Eye Disease (AED) mouse model have demonstrated the role of a Th17 and neutrophil-driven pathway in MGD pathogenesis. However, the manner by which neutrophils cause MGD in these mice is unclear. We addressed this knowledge gap by performing single cell RNA sequencing on cells, primarily leukocytes, from blood, tears, and conjunctiva collected from the AED mouse model, and compared results against tissues collected from naïve mice.

Methods: AED was induced in 9-week-old female C57Bl/6 mice by immunizing against ovalbumin (OVA) in the presence of pertussis toxin and, following a two-week incubation, OVA was applied to the eye, daily, for one week before collecting tissues, as previously described (Reyes NJ, 2018). Blood, conjunctiva, and tear samples from AED (n=9) and naïve (n=6) mice were harvested and prepared as single cell suspensions. FACS sorting was used to isolate cells from tears (live singlets), neutrophils from blood (live singlets, CD45+, Ly6G+), and leukocytes from conjunctiva (live singlets, CD45+). Sorted cells were pooled by treatment group and by tissue before sequencing. Data was analyzed using Seurat 4 with R version 4.1.

Results: The major immune cell (Ptprc) types identified included neutrophils (S100a8, Cd33), eosinophils (Ccr3, Siglecf), macrophages (Aif1), mast cells (Cd200r3), Th2 αβ T cells (Trac, Gata3), Th17 γδ T cells (Trdc, Rorc), dendritic cells (Flt3, Ccr7), and B cells (Ms4a1). We observed that AED mouse ocular tissues had increased neutrophil abundance and unique neutrophil cluster prevalence relative to naïve ocular tissues. Most notably, of the four identified neutrophil clusters, only a single cluster was associated with disease. This unique population was nearly absent in both the conjunctiva of naïve mice and the blood of either AED or naïve mice.

Conclusions: The notable presence of this disease-associated neutrophil cluster in the conjunctiva and tears of AED mice, but not naïve tissues or AED mouse blood, indicates that this phenotype arises as a result of the local ocular inflammatory environment. Further, it suggests that these neutrophils may be involved in MGD pathogenesis in the AED model.

CONTROL ID: 3713753

SUBMITTER (NAME ONLY): Scott Mooney

TITLE: Quantifying eye movement impairment in children with brain injury

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.W. Mooney, N.M. Alam, G.T. Prusky, Center for Vision Restoration, Burke Neurological Institute, White Plains, New York, UNITED STATES|S.W. Mooney, Brain & Mind Research Institute, Weill Cornell Medicine, New York, New York, UNITED STATES|G.T. Prusky, Department of Physiology and Biophysics, Weill Cornell Medicine, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Scott Mooney: Commercial Relationship(s);Code P (Patent):16/661,596 | Nazia Alam: Commercial Relationship: Code N (No Commercial Relationship) | Glen Prusky: Commercial Relationship(s);Code P (Patent):16/661,596

ABSTRACT BODY:

Purpose: Children with brain injury often exhibit cognitive or communicative deficits that impede conventional vision assessment. Ocular abnormalities in such children can often only be assessed with qualitative or low-resolution techniques. We used a novel vision test powered by eye tracking to determine whether spatial asymmetries in eye movements can be reliably quantified in children with brain injury.

Methods: We measured saccade and pursuit eye movements in 69 children with and 14 children without brain injury (age 3 to 18) during an interactive game-like program called the Visual Ladder, in which the user pops randomly placed/moving virtual bubbles by fixating or tracking them. Mean saccade and pursuit distance for each child were binned into various opposing directional categories to analyze normative asymmetries and identify the children who deviated furthest from the line of best fit (>2 SD) in each comparison.

Results: Both healthy and brain-injured children exhibited significantly longer horizontal saccades/pursuits than vertical and longer downward saccades than upward (all $p < .001$; Fig. 1), in agreement with previously established biases. There were no other significant asymmetries. Children with brain injury did not have shorter saccades than healthy children, but did have significantly shorter pursuits ($p < .001$), which may be partially due to more fragmented pursuit detection from increased noise, and a wider spread for both saccades and pursuits. The 23 outliers detected across the six comparisons (red in Fig. 1) comprised 16 different children with brain injury, revealing how brain injury can manifest in distinct eye movement impairments.

Conclusions: Our results demonstrate that the Visual Ladder can detect and quantify eye movement asymmetries in children with brain injury, including non-verbal children, and suggest that eye movements may be largely healthy in many such children. Further analysis will be needed to relate the distinct impairments apparent in our data to particular disease diagnoses and outcomes.

CONTROL ID: 3713754

SUBMITTER (NAME ONLY): Eleanor Nche

TITLE: Outcomes of descemet membrane endothelial keratoplasty in eyes with glaucoma, maculopathy, and previous corneal transplants

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.N. Nche, T. Batash, A. Katzir, D. Wajnzstajn, K. Safadi, A. Solomon, I. Lavy, Ophthalmology, Hadassah Medical Center Department of Ophthalmology, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: To report and analyze the outcomes of Descemet Membrane Endothelial Keratoplasty (DMEK) in eyes with corneal edema and associated ocular morbidities (glaucoma, maculopathy, and eyes after corneal transplants) in comparison to eyes without.

Methods: A retrospective study of seventy-seven (77) DMEK cases was done. Eyes after combined surgeries, vitrectomy, and eyes with anterior chamber intraocular lenses were excluded. The main outcome measures were best-corrected distance visual acuity (BCDVA) and graft survival. Eyes were separated into six groups as follows and analyzed: glaucoma only (GO), glaucoma and maculopathy (GMC), glaucoma and previous corneal transplant (GCT), previous corneal transplant (CT), maculopathy only (MO), and no associated glaucoma, maculopathy or corneal transplant (N).

Results: Overall, median BCDVA improved from 2.0 [0.2, 3] logMAR before surgery to 0.3 [-0.1, 2.0] logMAR 12 months after DMEK ($p<0.001$) with no difference between the groups at 1month, 3 months, 6 months and 12 months follow up times ($p<0.05$). Median BCDVA logMAR from before surgery improved significantly at 12 months in the N group; 1 [0.4, 3] to 0.2 [-0.1, 0.7] ($p<0.001$), CT group; 2 [0.2, 3] to 0.4 [0.1, 2] ($p<0.01$) and the GCT group; 2 [0.7,3] to 0.4 [0.2, 2] ($p<0.05$) but was not significant in the GO group; 1 [0.3, 3] to 0.3 [0.18, 2] ($p>0.05$), the MO group; 0.6 [0.2, 3] to 0.45 [0.1, 8] ($p>0.05$), and the GMC group; 1.0 [0.3,3] to 0.4 [0.1, 0.6] ($p>0.05$). Overall graft survival rate was 77.9% at 12 months. Highest in the N group (89.5%) and lowest in the GCS group (63.3%) ($p=0.71$).

Conclusions: DMEK offers visual rehabilitation in eyes with associated ocular morbidity. The least improvement in visual acuity is seen in patients with associated glaucoma, or maculopathy, or a combination of glaucoma and maculopathy. Eyes with glaucoma after previous corneal transplantation experience a significant improvement in vision at 12 months, but graft survival is 29% lower than in normal eyes.

CONTROL ID: 3713757

SUBMITTER (NAME ONLY): Gabriella Schmuter

TITLE: Ophthalmology in a virtual world: The impact of the COVID-19 pandemic on specialty conferences

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Schmuter, The City College of New York CUNY School of Medicine, New York, New York, UNITED STATES|L.M. Nijm, Ophthalmology, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|N.N. Kolomeyer, Ophthalmology, Wills Eye Health System, Philadelphia, Pennsylvania, UNITED STATES|J. Tao, Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|P.S. Subramanian, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|T. Kim, Ophthalmology, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|A.V. Rachitskaya, Ophthalmology, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|J.C. Law, Ophthalmology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|A.A. Tooley, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic led to unprecedented cancellation or alteration of healthcare events and medical conferences around the world. Many ophthalmology conferences transitioned to virtual interfaces, and the impact of this transition on the ophthalmology community is unclear. The authors wish to objectively define the impact of the COVID-19 pandemic on subspecialty ophthalmology conferences.

Methods: This study included data from the following five ophthalmology conferences from 2019, 2020, and 2021, as available: American Glaucoma Society (AGS), American Society of Ophthalmic and Plastic Reconstructive Surgery (ASOPRS), American Society of Cataract and Refractive Surgery (ASCRS), North American Neuro-Ophthalmology Society (NANOS), and Women in Ophthalmology (WIO). Data requested from organizations included the following, as available: Number of total conference attendees, number of attendees stratified by level of training, number of attendees stratified by identified gender, and number of research abstracts or presentations (submitted and/or accepted). This study has been approved by the City University of New York Institutional Review Board.

Results: In our study, 60% of organizations demonstrated an increase in number of attendees when using a virtual interface compared to their in-person events. 80% of organizations demonstrated a marked increase in attendance by trainees on their virtual interfaces. 60% of organizations displayed a decrease in number of submitted abstracts when using a virtual interface. 40% of organizations experienced an increase in number of accepted posters and presentations through a virtual platform.

Conclusions: Virtual conference interfaces have the potential to increase overall attendance and research participation within the ophthalmology community. Organizations should consider a hybrid model that incorporates aspects of both virtual and in-person interfaces to potentially maximize attendance, outreach, dissemination of information, opportunity, and minimize costs.

CONTROL ID: 3713761
SUBMITTER (NAME ONLY): Fiona McDonnell
TITLE: Trabecular meshwork exosomes and the extracellular matrix
SESSION TITLE: Aqueous humor dynamics and IOP
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: F.S. McDonnell, B.J. Riddick, H. Roberts, N.P. Skiba, D.W. Stamer, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|
Commercial Relationships Disclosure: Fiona McDonnell: Commercial Relationship: Code N (No Commercial Relationship) | Bre'Ida Riddick: Commercial Relationship: Code N (No Commercial Relationship) | Haven Roberts: Commercial Relationship: Code N (No Commercial Relationship) | Nikolai Skiba: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Stamer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The trabecular meshwork (TM) of the conventional outflow pathway participates in the regulation of outflow resistance, and TM dysfunction is the primary cause of elevated intraocular pressure (IOP) in glaucoma. Specifically, abnormal extracellular matrix (ECM) homeostasis by the TM contributes to outflow dysfunction, leading to a fibrotic/stiffer TM. In contrast, a healthy TM responds to elevated IOPs by remodeling ECM to facilitate increased outflow. We hypothesized that nano-sized extracellular vesicles (EVs) called “exosomes” are key participants in ECM homeostasis.

Methods: Experiments were designed to determine the effect of mechanical stretch and glaucoma on the exosome proteome released from primary human TM cells. TM cells were isolated from glaucomatous (GTM, n=1) and non-glaucomatous (NTM, n=1) donors that were grown to confluence under normal cell culture conditions and then switched to EV-depleted media. NTM cells (n=3) were also subjected to mechanical stretch (20%) for 24 hours. Conditioned cell culture media was collected every 48-72 hours for up to 3 months, or immediately after cell stretch and purified exosomes were isolated using iodixanol buoyant density gradient centrifugation. Fractions (fraction numbers 5-10) were assessed using mass spectrometry, Western blot and nanoparticle tracking analysis (NTA).

Results: Proteomic analysis of exosomes from TM cells showed an abundance of ECM-related proteins, including fibronectin, collagen and the integrin ligand EDIL3, which mediates cell binding and internalization of ECM proteins. Out of the top 20 proteins found across the cell strains, 72% were ECM-related. We validated fibronectin expression by Western blot, and found a 55% decrease in fibronectin binding to exosomes from GTM cells compared to NTM cells. NTM cells subjected to mechanical stretch released exosomes that bind 63% more fibronectin than unstretched controls. NTA demonstrated that the isolated exosomes from GTM cells appear to be larger than those from NTM cells; fractions 5-8: 103±11 vs 123.1±17nm and fractions 9-10: 112±1 vs 149±20nm.

Conclusions: ECM proteins are major components of exosomes released from TM cells. Abundance of these proteins increase with mechanical stretching, suggesting a role in ECM opsonization, degradation and homeostasis. Importantly, our data also suggests that this process may be disrupted in GTM cells due to tissue stiffening or decreased exosome opsonization/binding.

CONTROL ID: 3713762

SUBMITTER (NAME ONLY): Sean McCracken

TITLE: Retinal ganglion cell resilience to injury indicated by cytoplasmic [Ca^{2+}] levels

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. McCracken, P. Williams, Department of Visual Sciences, Washington University in St Louis, St Louis, Missouri, UNITED STATES|S. McCracken, DBBS-Neurosciences, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Sean McCracken: Commercial Relationship: Code N (No Commercial Relationship) | Philip Williams: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal ganglion cells (RGCs) are the sole projection neurons from the retina to the brain, and injury to their axons with an optic nerve crush (ONC) causes significant RGC death over multiple weeks. However, a subset of RGCs survive the injury, and intrinsic characteristics promoting survival remain unclear. Manipulating RGC activity has been shown to increase regeneration after ONC, and as cytoplasmic [Ca^{2+}] levels are influenced by activity, we hypothesized that ground state [Ca^{2+}] levels could predict the survival of RGCs to ONC injury.

Methods: We used two-photon (2p) microscopy to visualize RGCs in-vivo at single-cellular resolution. To label all RGCs, we used an intersectional approach with VGlut2-Cre mice and intravitreal injections of an adeno-associated viral vector (AAV) expressing a Cre-dependent cytoplasmic [Ca^{2+}] biosensor, Twitch-2b. We visualized individual RGCs and quantified their somatic resting [Ca^{2+}] levels in the alive mouse and then performed ONC to assess RGC survival. We also tested two subtypes of RGCs with this paradigm, alpha RGCs (aRGCs; KCNG4-Cre) and intrinsically photosensitive RGCs (ipRGCs; OPN4-Cre).

Results: Baseline [Ca^{2+}] levels varied greatly between RGCs within a single retina (Fig 1). We found that RGCs with high ground state [Ca^{2+}] levels prior to ONC survived 3x better at two weeks post ONC (38 ± 1.2% survival, n=9 retinas, cells(c)=124) than those with low resting [Ca^{2+}] (16 ± .1%, c=136) (p=.018). Cells that survived had significantly higher ground state [Ca^{2+}] levels than those that died (p=4.6E-6). Two subtypes, aRGC and ipRGCs, had much higher ground state [Ca^{2+}] levels compared to all RGCs (p=7.6E-13, p=1.7E-29). Within each subtype, cells with high baseline [Ca^{2+}] had increased survival (aRGC: 63 ± 2%, n=12, c=132; ipRGC: 60 ± 2%, n=9, c=296) compared to those with low [Ca^{2+}] (35 ± 4%, c=63; 47 ± 4%, c=49). Interestingly, for both subtypes, surviving cells had higher baseline [Ca^{2+}] levels than those that died (p=.15, p=1E-4).

Conclusions: Our results for all RGCs and for each subtype, aRGCs and ipRGCs, are consistent with our hypothesis. Thus, we can conclude that high resting cytoplasmic [Ca^{2+}] levels in the RGC soma indicate resilience to axon injury. Future directions include identifying a low resting [Ca^{2+}] level RGC cohort and testing their survival after ONC.

CONTROL ID: 3713764

SUBMITTER (NAME ONLY): Kimberly Stepien

TITLE: Elucidating early cellular retinal structural changes in GUCA1A-related autosomal dominant cone dystrophy

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.E. Stepien, N. Stangel, Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|J. Rogers, Morgridge Institute for Research, Madison, Wisconsin, UNITED STATES|J. Rogers, McPherson Eye Research Institute, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Kimberly Stepien: Commercial Relationship(s);Code C (Consultant/Contractor):Atsena;Code C (Consultant/Contractor):Opsis Therapeutics;Code C (Consultant/Contractor):AGTC;Code S (non-remunerative):Biogen;Code S (non-remunerative):ProQR;Code S (non-remunerative):Foundation Fighting Blindness | Nickie Stangel: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Rogers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mutations in the guanylate cyclase activator A1A(GUCA1A) gene which encodes guanylate cyclase activating protein, GCAP1, have been associated with both autosomal dominant (AD) cone and cone-rod dystrophies. GCAP1 plays a key role in recovery of photoreceptor to the dark-adapted state after light stimulus and its dysfunction is hypothesized to result in apoptosis of photoreceptors. Here we explore earlier cellular retinal structure changes in GUCA1A-related AD cone dystrophy using adaptive optics scanning light ophthalmoscope (AOSLO).

Methods: An asymptomatic 11 year old subject with a known GUCA1A-mediated AD cone dystrophy mutation(c.464A>G, p.(Glu155Gly)) underwent a comprehensive ophthalmic examination and high resolution imaging. Outer retinal structure was assessed using spectral-domain optical coherence tomography (SD-OCT) and the photoreceptor mosaic was imaged using confocal and split-detector AOSLO. AOSLO images were compared to 2 age-matched controls.

Results: Vision was 20/20 and color vision was normal OU. Clinical exam showed mild pigment mottling in the central maculas OU. SD-OCT showed intact but speckled-appearing ellipsoid band in the perifoveal macula. AOSLO demonstrated a disrupted photoreceptor mosaic with significantly decreased cone density when compared to age matched controls (8000 cells/mm^2 vs 23,400 cells/mm^2 at 4 degrees temporal to fovea). Split-detector AOSLO revealed inner segment photoreceptor structure (Figure 1B-arrow) in areas where no waveguiding cones were visualized (Figure 1A-arrow).

Conclusions: Significant cone photoreceptor degeneration occurs before functional loss in GUCA1A-mediated cone dystrophy. Split-detector AOSLO allows for a more precise assessment of retained photoreceptor structure. This highlights the potential utility of AOSLO to increase understanding of retinal degeneration at early asymptomatic stages and to identify ideal candidates with retained photoreceptor structure who may most benefit from emerging gene therapies.

CONTROL ID: 3713767

SUBMITTER (NAME ONLY): Colten Pluff

TITLE: Readability of Online Resources for Diabetic Retinopathy Creates Accessibility Challenges

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Pluff, G.N. Manion, M. Lam, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|B. Young, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Colten Pluff: Commercial Relationship: Code N (No Commercial Relationship) | Garrett Manion: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Lam: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Young: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The leading cause of new cases of blindness in adults is diabetes. Diabetic retinopathy (DR) affects about one-third of adults over 40 years old with diabetes. Patients increasingly seek out online patient educational materials to learn about their health. Given that the American Medical Association (AMA) recommends writing at or below a 6th grade reading level for educational materials, we analyzed the readability of websites about DR found by search engine results to evaluate their accessibility.

Methods: The term “Diabetic Retinopathy” was queried in the Google search engine on November 1st, 2021. The first 10 pages (100 results) were screened and websites with patient-oriented information were analyzed (n=71). They were categorized by search result page number and website organization type: private practice, academic, government organization, informational, or commercial. Flesch Reading Ease, Flesch Kincaid Grade Level, Gunning Fog Score, Coleman Liau Index, and SMOG Index were calculated for each website. Statistical analysis was performed using ANOVA and Student’s T-test.

Results: Private practice websites were the most common (45%). Three sites had Flesch Reading Ease scores of 8th & 9th grade “Plain English”; all other sites were rated “Fairly difficult to read” or worse and averaged college-level difficulty. Only two sites met the 6th grade reading level AMA recommendation by Flesch Kincaid Grade Level; the average was grade 10.5. Average grade level estimation by Gunning Fog Score, Coleman Liau Index, and SMOG Index were 11.4, 11.8, and 12.3 respectively. There was no significant difference in readability between search result pages or website category except for search result page 1 having significantly higher Flesch Reading Ease than pages 5, 6, and 7 ($p<0.009$).

Conclusions: The high reading level of almost all websites in this search exceeds the AMA recommendation, creating difficulty in understanding DR for many patients. Websites that met the recommendation were not listed in the first two pages of search results and are thus less likely to be accessed. These factors could exacerbate disparities in eye health in populations that experience DR more frequently, such as Hispanics and African Americans, or patients with lower health literacy. As search results and website contents are ever-changing, focus on readability may enhance the accessibility of information about DR in the future.

CONTROL ID: 3713768

SUBMITTER (NAME ONLY): Ben Wendel

TITLE: Multimodal high-resolution imaging of retinal function in Retinitis Pigmentosa

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.J. Wendel, V. Pandiyan, X. Jiang, A. Lassoued, E. Slezak, D. Mustafi, J.R. Chao, R. Sabesan, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|W.S. Tuten, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, Washington, UNITED STATES|D. Mustafi, Seattle Children's Hospital, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) is the most common inherited retinal disease and is characterized by progressive photoreceptor degeneration that leads to visual impairment. It remains unknown to what extent the diseased and surviving photoreceptors transduce light and support vision in RP. To address this, we correlated adaptive optics (AO) imaging of cone structure, AO microperimetry with retinally-tracked stimulus delivery, and AO-OCT based optoretinograms (ORGs) in the same RP subjects.

Methods: Three RP subjects (age 25-29) and 3 aged-matched controls were imaged with AO Scanning Laser Ophthalmoscopy (AOSLO) across the four cardinal meridians and the RP transition zone (TZ), which was verified using clinical OCT. Cones were counted in 100 by 100 micrometer regions of interest (ROI) spanning the TZ. Visual sensitivity was assessed by measuring increment thresholds for 543 nm, ½ Goldmann-I stimuli (3 arc-min), that were targeted to predetermined retinal locations via active eye tracking in the AOSLO. ORGs were measured at the same locations with line-field spectral domain AO-OCT to assess cone function. The change in optical path length (ΔOPL) between the cone outer segment tips and inner-outer segment junction reflections in AO-OCT were calculated following a 44% bleach of L/M-cones with 528 nm light stimulus.

Results: Cone density was reduced compared to controls in the majority of ROIs for all three RP subjects ($p<0.05$). Density reduction trended with TZ onset in Subject 1 (S1) and S2, while S3 had patches of reduced density throughout. ΔOPL was reduced in all 3 RP subjects in regions of reduced cone density compared to controls. There was an increased proportion of cones with reduced ΔOPL with increasing eccentricity in all RP subjects ($p<0.05$). Further, we observed a distinct subset (30%) of cones with reduced ΔOPL in a region with otherwise intact OCT outer retinal layers in S3. Interestingly, negative ΔOPLs were observed in the TZ of S1 and S2 (4.9% and 5.2% of cones). Despite significant deficits in cone density and ΔOPL, visual sensitivity to 3 arc-min retinal stimuli targeted to the same areas remained comparable to controls, with the exception of one test site in S1.

Conclusions: Multimodal high-resolution functional imaging enables a complementary picture of disease progression in RP, and shows that deficits in ORG-based measures of retinal function precede the reduction in visual sensitivity.

CONTROL ID: 3713769

SUBMITTER (NAME ONLY): Hannah Wescott

TITLE: Early Experience with the Novel Variable Scanning Speed Optical Coherence Tomography Angiography Imaging

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Wescott, I. Garg, R. Katz, J.B. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|H. Wescott, I. Garg, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Hannah Wescott: Commercial Relationship: Code N (No Commercial Relationship) | Itika Garg: Commercial Relationship: Code N (No Commercial Relationship) | Raviv Katz: Commercial Relationship: Code N (No Commercial Relationship) | John Miller: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon, Allergan, Carl Zeiss, Sunovion and Genentech

ABSTRACT BODY:

Purpose: The ideal tradeoff between A-scan rate, acquisition time and image quality for optical coherence tomography (OCT) and OCT-Angiography (OCTA) is currently unknown. The purpose of this study was to compare the image quality and acquisition time between the variable scanning speed SPECTRALIS® SHIFT technology (spectral domain, 20 kHz, 85 kHz, 125 kHz, and 250 kHz) and 100 kHz swept source OCTA.

Methods: We conducted this cross-sectional observational study from August 2021 to November 2021 at Massachusetts Eye and Ear enrolling 20 healthy eyes. After obtaining written informed consent, patients were imaged on the 100 kHz PLEX® Elite 9000 (Carl Zeiss) using 6 mm x 6 mm angiogram centered on fovea, followed by Heidelberg SPECTRALIS® SHIFT technology (OCTA mode, Scout 20 preset at 85 kHz, 125 kHz, and 250 kHz). The latter gives standard 6.4 mm x 6.4 mm angiogram superimposed on the structural en-face images.

Results: The mean acquisition time were 31.1 seconds for 100 kHz PLEX®, 36 seconds for 85 kHz, 33.8 seconds for 125 kHz and 30.5 seconds for 250 kHz SHIFT technology. The OCTA image resolution was similar for the PLEX® 6 mm x 6 mm image at 1024 x 1024 pixels, while 1016 x 1016 pixels for the 6.4 mm x 6.4 mm image from SHIFT technology. The B-scan image quality and details were comparable between the two devices (Figure 1) but there was better delineation of microvasculature on PLEX® OCTA. Subjectively, there was evidence of higher motion artifacts on all layers and scan speed angiograms from SHIFT technology versus PLEX® due to better iris tracking software in the latter. We also noted progressive decrease in signal to noise ratio with increasing speeds for OCTA images acquired via SHIFT technology (Figure 2).

Conclusions: In this preliminary study we noted that higher scanning speed may not necessarily result in better image quality or significantly shorter scanning time. Although the image resolution was comparable, there were visible difference in capillary details, motion artifacts, etc. between the two devices. Future studies on different scan speed angiograms can open doors to their varied clinical application in patient specific pathology and media opacity status.

CONTROL ID: 3713771

SUBMITTER (NAME ONLY): Heithem El-Hodiri

TITLE: The polycomb repressor complex 2 influences glial reactivity and the formation of Müller glia-derived progenitor cells in the chick retina

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.M. El-Hodiri, W. Campbell, D. Torres, E.C. Hawthorn, L.E. Kelly, L. Volkov, A.J. Fischer, Neuroscience, The Ohio State University College of Medicine, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mammalian retina does not regenerate, while retinas of cold-blooded animals generally have great regenerative capacity. The chick retina falls in between, generating Muller glia-derived progenitor cells (MGPCs) with limited neurogenic capacity. We investigated epigenetic mechanisms underlying MGPC production in the chick retina. We investigated the role of the Polycomb Repressor Complex 2 (PRC2), which catalyzes histone methylation, in damage-induced MGPC production.

Methods: Retinal damage was induced in chicks by intraocular injection of NMDA. PRC2 component activity was inhibited by injection of pharmacological inhibitors into one eye; the other eye (injected with vehicle) served as a control. PRC2 components were inhibited using DZNexp4 (inhibitor of EZH2), Jib04 (inhibitor of JARID2), and EEDi (inhibitor of EED). Eyes were isolated, hemisected, fixed, and processed for immunohistochemistry or single cell RNA or ATAC seq. MGPCs were identified by double labelling for SOX2 and incorporated EdU and counted. Statistical comparisons were performed using Student's t-test.

Results: The PRC2 subunits EZH2, JARID2, and EED displayed increased levels of expression in damaged retinas. Inhibition of EZH2 resulted in decreased MGPC production [control: 121 ± 21.21 MGPCs per retinal section, treated: 12.25 ± 11.40 MGPCs per section, $p < 3.3E-06$ ($n = 8$)]. Similarly, inhibition of JARID2 and EED resulted in significant reductions in MGPCs [66.56 ± 29.64% reduction for JARID2, $p < 1E-07$ ($n = 7$); 51.98 ± 31% reduction for EED, $p < 0.003$ ($n = 15$)]. Analysis of DZNexp4-treated retinas by scRNA-seq revealed changes in differential expression of genes involved in glial and neuronal development and differentiation. Many of these differentially-expressed genes were found to exhibit differential chromatin accessibility by scATAC-seq.

Conclusions: We conclude that the activity of PRC2, in general, and EZH2, in particular, are required for the reprogramming of Müller glia into MGPCs, and that the PRC2 complex and EZH2 normally influence chromatin access to a network of genes associated with glial differentiation.

CONTROL ID: 3713772

SUBMITTER (NAME ONLY): Zongbo WEI

TITLE: Mitotic Activation of Quiescent Lens Epithelial Cells Repairs UVB-Induced Capsular Cataracts

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. WEI, C. Hao, X. Fan, Department of Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Zongbo WEI: Commercial Relationship: Code N (No Commercial Relationship) | Caili Hao: Commercial Relationship: Code N (No Commercial Relationship) | Xingjun Fan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ultraviolet B (UVB) is a significant risk factor to cause lens epithelium damage; however, the mechanism of lens epithelium repair after UVB irradiation is not fully understood. This study aimed to investigate the mechanism of the lens epithelium-mediated repair process after UVB irradiation.

Methods: C57BL/6J mice were irradiated by various doses of UVB. Lens cataracts were examined at different time points by slit lamp, darkfield microscopy, and phase-contrast microscopy. Lens epithelial cell (LEC) mitotic activation and apoptosis was determined by immunofluorescence staining and LECs' ultrastructure was analyzed by TEM.

Results: UVB irradiation above a dose of 2.87 kJ/m^2 triggered LECs apoptosis and subcapsular cataract formation associated with a ring-shaped structure composed of multilayered and irregularly stacked epithelial cells. LECs around wound edges transitioned to mitotically active cells reflected by increased Ki67 expression and BrdU incorporation. These mitotic active LECs performed wound-healing repair through the epithelialization process and removed apoptotic cells via phagocytosis. However, repairs ceased when lens epithelial cells made direct contact, and scar-like tissue in the center of the anterior capsule remained even by six months after UVB irradiation.

Conclusions: Our present study demonstrates that normally quiescent lens epithelial cells can be reactivated for epithelialization repair in response to UV-induced damage.

CONTROL ID: 3713774

SUBMITTER (NAME ONLY): Steven Droho

TITLE: Protein-like polymers containing a thrombospondin-1 agonist are potent, biosafe inhibitors of choroidal angiogenesis

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Droho, D. Swygart, G. Schwartz, J. Lavine, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|W. Choi, M. Fattah, S. Burton, A. Nensel, S. Punekar, N.C. Gianneschi, Chemistry, Northwestern University, Evanston, Illinois, UNITED STATES|N.C. Gianneschi, Materials Science & Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thrombospondin1 (TSP1) is a highly potent anti-angiogenic protein that could be a potential therapy for neovascular age-related macular degeneration (nAMD). Proteins and peptides, however, are poor therapeutics because of rapid degradation and clearance. Our group has pioneered a novel platform wherein therapeutic peptides are packaged as high-density brush polymers called protein-like polymers (PLPs). PLPs display active, functional amino acids, are resistant to proteolysis, and have a high molecular weight, improving pharmacokinetics. ABT898 is an 8 mer bioactive TSP1 peptide that binds the CD36 receptor to inhibit angiogenesis. We created a biostable, nontoxic PLP containing the ABT898 peptide, and tested its ability to inhibit choroidal angiogenesis.

Methods: PLP-ABT898 and PLP-Scramble control were synthesized. PLPs were characterized by size exclusion chromatography-multi-angle light scattering to ensure the molecular weight. PLP binding affinity to CD36 was tested using biolayer interferometry and inhibition of fatty acid uptake in CD36-expressing cells. Toxicity was tested using cell viability assays and by intravitreal injection of PLPs followed by hematoxylin and eosin analysis of retinal morphology. PLP effects upon choroidal angiogenesis were measured using the choroidal sprouting assay and the laser-induced choroidal neovascularization (CNV) model in 10-12 week-old male C57BL6/J mice.

Results: PLP-ABT898 bound CD36 with a KD of 12 nM and inhibited fatty acid update with an IC50 of 184 nM. PLP-ABT898 showed mildly reduced viability at 50 mM in ARPE19 cells. PLP-ABT898 intravitreal injection at 40 μM showed no change in retinal or outer nuclear layer thickness compared to PBS or PLP-Scramble control (N=7-10 per group). In the choroidal sprouting assay, PLP-ABT898 inhibited choroidal angiogenesis by 35% at 5 μM, 68% at 10 μM, and 92% at 20 μM (N=15-22, $p<0.001$ for all) compared to PLP-Scramble. PLP-ABT898 reduced laser-induced CNV area by 2.0-fold (N=19-21, $p<0.05$) on fluorescein angiography and 2.8-fold (N=18-20, $p<0.05$) on immunofluorescence analysis.

Conclusions: PLP-ABT898 was nontoxic and effectively inhibited choroidal angiogenesis. PLP-ABT898 is a potential new therapeutic for nAMD. Additionally, PLP technology is translatable to different peptides or combinations of anti-angiogenic peptides for therapeutic targeting of multiple angiogenesis pathways.

CONTROL ID: 3713775

SUBMITTER (NAME ONLY): Darryl Overby

TITLE: Spatial cluster analysis reveals how segmental outflow patterns change over time in living mice

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.R. Overby, T. Baptiste, D. Duffill, E. Reina-Torres, Bioengineering, Imperial College London, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Darryl Overby: Commercial Relationship: Code N (No Commercial Relationship) | Tiffany Baptiste: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Duffill: Commercial Relationship: Code N (No Commercial Relationship) | Ester Reina-Torres: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aqueous humor outflow through the trabecular meshwork (TM) is non-uniform, or segmental, such that some regions of TM experience higher local outflow than others. Our aims were (i) to develop a quantitative approach to analyze segmental outflow patterns using spatial autocorrelation and cluster analysis, and (ii) to apply these techniques to determine how segmental outflow patterns change over time in living mice.

Methods: Fluorescent tracer microspheres (0.2 μm; 10^{8} μl^{-1}) were infused under anesthesia into the anterior chamber of C57BL/6 mice to label segmental outflow patterns in the TM. To visualize the change in segmental outflow patterns over time within individual eyes, each eye was infused twice with a different tracer color separated by a delay of 2, 7 or 14 days (n=10 mice). Mice were culled 48 hrs after the second infusion. Eyes were enucleated and prepared for flat mount imaging. We analyzed the spatial autocorrelation of tracer intensity patterns within the TM using Moran's I, which yields statistically defined clusters of high, intermediate, and low tracer-labelling (Figure).

Results: The global Moran's I statistic indicated significantly more tracer clustering within the TM than expected by chance (0.67±0.08; mean±SD; N=16 eyes; $p<0.01$). High tracer-labelled clusters were estimated to occupy 26±2% of the TM, while low and intermediate clusters were estimated to occupy 34±6% and 40±7% respectively. There was no change in the total extent of each cluster type over time. However, with increasing delay between the two infusions, the patterns of tracer labelling changed significantly, as indicated by a decreasing spatial correlation coefficient (r=0.69 [0.52,0.86] at 2 days vs. 0.06 [-0.17,0.28] at 14 days; mean [95% CI]; $p<0.01$).

Conclusions: Moran's I provides an objective and reproducible method to identify high, intermediate and low tracer-labelled clusters within the TM. Over 2 weeks in young adult mice, segmental outflow patterns redistribute spatially within the TM. However, despite this redistribution, the TM appears to preserve the overall extent of high, intermediate, and low filtration-active clusters. This suggest that dynamic changes in the spatial distribution of segmental outflow are not random but appear to be regulated by active processes within the outflow pathway.

CONTROL ID: 3713776

SUBMITTER (NAME ONLY): Corinne Beier

TITLE: The role of the vLGN in non-image-forming visual behaviors and its underlying circuit organization

SESSION TITLE: Retinal ganglion cells and central processing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Beier, Z. Zhang, M. Thurman, S. Hattar, 1.Section on Light and Circadian Rhythms, National Institute of Mental Health, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Corinne Beier: Commercial Relationship: Code N (No Commercial Relationship) | Ze Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Martina Thurman: Commercial Relationship: Code N (No Commercial Relationship) | Samer Hattar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The mouse ventral lateral geniculate nucleus (vLGN) receives dense retinal ganglion cell (RGC) innervation but its role in vision remains unclear. We recently showed that the caudal vLGN segregates the visual input of RGCs that drive image-forming vision from the intrinsically photosensitive RGCs (ipRGCs) that drive non-image-forming behaviors. Here, in the context of this newly understood circuit organization, we investigate cell type-specific retina-to-vLGN pathways that drive and modulate non-image-forming behaviors (pupillary light response, circadian photoentrainment, and light-induced sleep).

Methods: Immunohistochemistry of cFos induction was paired with markers for vLGN cell types (Penk and Nos1) following circadian phase shifting light pulses (phase delay, ZT14, or phase advance, ZT22). We mapped afferents of vLGN $Penk^{Cre}$ and $Nos1^{Cre}$ cell types with Cre-dependent helper viruses and monosynaptic G-deleted rabies virus. We used viral chemogenetic strategies to silence (tetanus toxin) or activate (Gq DREADD) vLGN $Penk^{Cre}$ cells to investigate their role in modulating non-image-forming visual behaviors.

Results: cFos induction in the vLGN increases in Penk cells in response to a ZT22 light pulse but not to a ZT14 light pulse compared to dark controls. Light-induced cFos in Nos1 cells is not time-dependent. $Penk^{Cre}$, but not $Nos1^{Cre}$, cells in the vLGN are post-synaptic to ipRGCs. Silencing/activating vLGN $Penk^{Cre}$, but not $Nos1^{Cre}$, cells causes an increase/decrease in pupil constriction during a light step. Preliminary results implicate vLGN $Penk^{Cre}$ cells in phase advancement and sleep; silencing vLGN $Penk^{Cre}$ cells results in deficits to phase advancing light shifts and activating vLGN $Penk^{Cre}$ cells in the late night, but not the early night, induces sleep.

Conclusions: We find that Penk vLGN cells are light-responsive in a circadian time-dependent manner and receive exclusive ipRGC input, which are characteristics thought to be exclusive to the pacemaker, the suprachiasmatic nucleus. In contrast, vLGN Nos1 cells do not share these same features. In agreement with these findings, we show that vLGN Penk cells play a role in modulating non-image-forming visual behaviors. Penk cells modulate the pupillary light response during light steps and play a role in time-dependent visually responsive behaviors: light induced circadian phase advancement and sleep.

CONTROL ID: 3713777

SUBMITTER (NAME ONLY): Vijay Jidigam

TITLE: Neurovascular clock genes in retinal vascular physiology and pathology

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Jidigam, R. Fuller, O.B. Sawant, K. Wilcots, S. Rao, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|R.A. Lang, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mammalian retina contains an autonomous circadian system that regulates various aspects of retinal physiology critical for the processing of visual information and thus optimizing retinal activity with the daily variation in light intensity. The retinal clock can be entrained by light both in vitro and in vivo suggesting that light plays a critical role in the regulation of the retinal clock. Retinal angiogenesis is dependent on the retinal ganglion cells and in mice lacking RGCs, retinal vasculature does not develop thus highlighting the importance of cues that are provided from the underlying neuronal cells. The goal of this study was to test the hypothesis that the light-regulated retinal circadian clock is essential for developmental and pathological angiogenesis.

Methods: To test this hypothesis, we disrupted the light/dark cycle or conditionally deleted the circadian clock genes Bmal1 and Per2 from the retinal progenitor cells (RPCs) and vascular endothelial cells (VECs). Chromatin immunoprecipitation sequencing analysis (ChIP Seq) was used to identify the angiogenic molecular targets of Bmal1 in the neurons. To address the role of the neuronal clock in pathological angiogenesis, oxygen-induced retinopathy (OIR) model was used.

Results: Our results demonstrate that the neuronal clock genes Bmal1 and Per2 are essential regulators of retinal angiogenesis. The clock gene transcripts exhibit circadian rhythmicity in the embryonic retina and this rhythmicity is lost under disrupted light/dark cycles. ChIP analysis indicates that some of the Bmal1 targets within the retinal neurons are angiogenic regulators. Accordingly, deletion of Bmal1 in neuronal cells results in overgrowth of the vasculature while Bmal1 deletion from the endothelial cells causes reduced proliferation, with reduced vessel density. RNA sequencing data from the endothelial cells suggests that pathways primarily related to the cell cycle are altered by the loss of Bmal1. Furthermore, only the neuronal clock is an important mediator of pathological angiogenesis as loss of Bmal1 and Per2 causes a significant reduction of neovascularization.

Conclusions: The data presented here raise an exciting question about the interrelationship between the circadian clock in the neurons and vasculature during retinal angiogenesis. Importantly, a robust circadian clock in the neurons protects the retinal vasculature from oxygen-induced damage.

CONTROL ID: 3713779

SUBMITTER (NAME ONLY): Nicolás Pérez-Llombet Quintana

TITLE: LET Classification of diabetic macular edema: Interobserver agreement between resident doctors and retina specialist ophthalmologists in clinical practice

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pérez-Llombet Quintana, I. Fabelo Hidalgo, M. Alberto Pestano, C. Fernández-Núñez, A. Afonso Rodríguez, G. Quezada-Peralta, M. Gil Hernández, R. Abreu, Ophthalmology, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: To study the interobserver concordance between two resident doctors and two ophthalmologists specializing in retina regarding the detection of characteristics of diabetic macular edema (DME) in optical coherence tomography (OCT) in naïve patients using the LET classification.

Methods: A retrospective consecutive analysis was carried out of patients evaluated in our service who presented DME for 1 year. OCTs were independently analyzed by two residents, on the one hand, as well as by two retinologists on the other hand, determining the characteristics of DME using the LET classification. The data were evaluated using a concordance analysis for each pair of observers.

Results: A total of 95 eyes of 70 patients were analyzed, 67,1% being male and 32,9% female, with a mean age of 66,13 years +/-11,73 years. In the evaluation of the DME characteristics according to the LET classification, the kappa coefficient of interobserver concordance in the resident doctors was: Location (L) 0,36; Extension (E) 0,46; and Traction (T) 0,52. On the other hand, the values obtained among the retinologists observers were: Location (L) 0,709; Extension (E) 0,664; and Traction (T) 0,264. All the results were statistically significant.

Conclusions: Classification of DME by OCT using the LET classification produces an acceptable degree of agreement between different observers, although there are notable differences when it is done by physicians in training and when it is done by retina specialists in clinical practice.

CONTROL ID: 3713781

SUBMITTER (NAME ONLY): Marzia Pendino

TITLE: Evaluating Cannabinoid Receptors as A Therapeutic Target for Uveal Melanoma

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pendino, University College Dublin, Dublin, Dublin 4, IRELAND|M. Pendino, K. Slater, B.N. Kennedy, University College Dublin Conway Institute of Biomolecular and Biomedical Research, Dublin, Dublin 4, IRELAND|S. Garcia Mulero, R. Sanz Pamplona, J. Piulats, Institut Catala de Tecnologia, Barcelona, Catalunya, SPAIN|S. Marcone, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: This research evaluates the disease relevance of cannabinoid receptors in UM patient samples and the therapeutic potential of synthetic cannabinoids in uveal melanoma (UM) cell lines. UM is a rare cancer, but the most common intraocular malignancy in adults that arises from melanocytes within the uveal tract. Unfortunately, up to 50% of patients develop liver metastases that rapidly progress to mortality. There are no effective therapies available for metastatic UM.

Methods: Cannabinoid receptor gene expression in 80 primary UM samples within The Cancer Genome Atlas was analysed for association with disease-free and overall survival. Gene set variation analysis enriched for molecular functions and biological pathways linked to high or low cannabinoid receptor expression. In vitro assays utilised Mel285 and OMM2.5 human UM cell lines derived from a tumour of the eye and a liver metastasis, respectively. Cell viability was examined at 96 hours after treatment with the synthetic cannabinoid HU210 by measuring metabolic activity. Colony formation assays assessed long-term UM cell proliferation. Multiplex ELISA determined the secreted levels of 10 inflammatory factors at 4 and 24 hours after treatment with HU210 in the OMM2.5 cell line. Western Blot analysed expression of CB_1.

Results: Kaplan-Meier survival curves demonstrate a significant corelation between high CB_1 expression and disease-free survival in UM patients. The CB_1/CB_2 agonist HU210 results in a dose-dependent reduction in Mel 285 and OMM2.5 cell viability with 20 μM HU210 reducing cell viability by around 80%, $p < 0.0001$ whereas 150 μM of the more selective CB_2 agonist JWH133 was required to significantly reduced viability by 80%, $p=0.0001$ in both UM cell lines. 10 μM rimonabant hydrochloride and 10 μM SR144528, CB_1 and CB_2 selective antagonists, respectively, were the maximum tolerated concentrations not affecting cell viability. 20 μM HU210 results in a reduction of long-term proliferation of clones in both UM cell lines. Western blot analysis confirmed expression of CB_1 in Mel285, Mel290, OMM2.5 cells.

Conclusions: Significant corelations between high CB_1 expression and disease-free survival in UM patients was identified. HU210 reduces viability and clone proliferation of UM cell lines and modulated inflammatory pathways. Future directions will evaluate the key receptor mediating HU210 effects using antagonists and investigate the mechanism of action.

CONTROL ID: 3713785

SUBMITTER (NAME ONLY): James Jester

TITLE: Characterization of Mouse Meibomian glands by single cell RNA sequencing.

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.V. Jester, S. Lane, D. Brown, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|J. Wiedemann, G. Kashgari, B. Andersen, Department of Medicine and Biological Chemistry, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thus far, our studies using Confetti and the K5-H2B-GFP transgenic mice suggest that there are two stem/progenitor cell populations that independently give rise to the ductal and meibum synthesizing meibocyte populations within the meibomian gland. The purpose of this study was to use single cell RNA sequencing analysis of mouse meibomian glands to further identify/characterize these different cell lineages.

Methods: The tarsal plates from the upper and lower eyelids of 6, 6-month-old, male C57Bl/6 mice divided into two groups were collected and single cells isolated. Cells were then submitted to the UCI Genomics High Throughput Facility and raw sequencing data demultiplexed and processed using Cellranger (10× Genomics version 3.1.0). Preliminary analysis and visualization of the data were performed using R version 4.0.5 and Seurat version 4.0.5. For all datasets, cells with <200 and >6000 genes, and >5% mitochondrial genes detected were removed. We performed integrated analysis of the 2 datasets using SCTransform normalization separately for each dataset, selected 2000 informative features, and performed integration using the FindIntegrationAnchors function. Cells were visualized using UMAP (Uniform Manifold Approximation and Projection). Pseudotemporal ordering of meibocytes and determination of pseudotime dependent transcription factors was performed using Monocle version 2.18.0.

Results: A total of 7259 cells from two different samples were analyzed and 19560 genes detected across all cells. UMAP analysis identified 5 distinct cell clusters, including 1) a Krt 6a positive ductal epithelial cluster, 2) a Krt6a and AWAT2 negative and PPARg positive undifferentiated meibocyte cluster, 3) a AWAT2 positive differentiated meibocyte cluster, 4) a Krt6a and Ki67 positive ductal epithelial progenitor cluster and 5) a Krt6a negative and Ki67 positive meibocyte progenitor cell cluster. Trajectory analysis also identified transcription factors unique to these two different meibomian gland cell lineages.

Conclusions: Our findings support the hypothesis that there are two separate progenitor cell populations that give rise separately to ductal epithelial cells and meibum synthesizing meibocytes. Understanding the regulatory mechanisms that control these separate pathways is needed to establish appropriate cell culture models to evaluate mechanisms that regulate meibum synthesis.

CONTROL ID: 3713786

SUBMITTER (NAME ONLY): Michael Robichaux

TITLE: Maintaining the integrity of the inner segment of rod photoreceptor neurons for intensive immunolabeling and superresolution microscopy

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Robichaux, K.N. Haggerty, Ophthalmology, West Virginia University, Morgantown, West Virginia, UNITED STATES|M.A. Robichaux, S.C. Lyons, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The inner segment (IS) region of rod photoreceptor neurons is a hub for the synthesis and trafficking of visual proteins. These protein “cargoes” are delivered to the basal body (BB) at the apical edge of the IS region prior to their incorporation into the rod outer segment cilium. The study of the localization and dynamics of IS trafficking processes in single rods with superresolution microscopy techniques requires optimized preparation methods with minimal tissue fixation for thorough antibody penetration and immunolabeling. During such rigorous immunolabeling procedures, the IS membrane is susceptible to membrane extraction. The goal of this project was to develop a new methodology for intensive immunolabeling of mouse rods that both preserves the morphology of the IS and is compatible with superresolution imaging.

Methods: We lightly fixed mouse retinas with paraformaldehyde (PFA) before a 3-day primary antibody incubation period in a blocking solution containing saponin, a mild detergent. Primary antibodies used targeted syntaxin-3 and Na,K ATPase (ATP1B2), which are IS membrane markers, and phosducin, a cytoplasmic chaperone protein. After a secondary antibody incubation period, we tested different “post” fixation solutions prior to dehydrating the retinas for resin embedding. We imaged ultra-thin retinal sections with structured illumination microscopy (SIM), stochastic optical reconstruction microscopy (STORM) and conventional transmission electron microscopy (TEM).

Results: We determined that a post-fix solution of 2% PFA and 0.1% glutaraldehyde (w/v) preserved the IS membrane of most rods in immunolabeled retinas as determined by TEM ultrastructure and the SIM/STORM immunolocalization of syntaxin-3 and ATP1B2. We also used STORM to determine that significantly more cytoplasmic phosducin was preserved in the IS of retinas treated with our optimized post-fix solution compared to just PFA alone.

Conclusions: Our optimization of mouse retinal immunolabeling conditions enables future superresolution localization studies focused on the IS. Specifically, by preserving the IS membrane and cytoplasm, we can more accurately test dynamics of visual protein cargoes with trafficking organelles in the IS and the BB region in future studies.

CONTROL ID: 3713787

SUBMITTER (NAME ONLY): Un Chul Park

TITLE: Effects of Human CD34+ Stem Cells and Exosomes from Mesenchymal Stem Cells on Angiogenesis: In vitro Analysis

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Park, P.A. Sieving, S.S. Park, Department of Ophthalmology & Vision Science, University of California Davis Health Eye Center, Sacramento, California, UNITED STATES|Z. Smit-McBride, N. Sun, Vitreoretinal Research Laboratory, Department of Ophthalmology & Vision Science, University of California Davis, Davis, California, UNITED STATES|P. Zhou, J. Anderson, J.A. Nolta, Stem Cell Program, Institute for Regenerative Cures, University of California Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human bone marrow (BM) contains CD34+ stem cells and mesenchymal stem cells (MSCs) that are being explored for tissue regeneration and revascularization. CD34+ cells, which include endothelial progenitor cells, are known to promote angiogenesis which may be impaired by the diabetic state. MSCs, which have paracrine effects via exosomes, reverse the impaired migration of diabetic CD34+ cells in vivo to enhance angiogenesis. This study used an in vitro tube formation assay (angiogenesis assay) to evaluate the angiogenic potential of human CD34+ cells and exosomes from MSCs, alone and in combination, to determine whether the exosomes can enhance the angiogenic potential of CD34+ cells.

Methods: CD34+ cells were harvested from the mononuclear cell fraction of BM of a healthy or diabetic human donor. Exosomes were harvested from MSCs from a healthy BM donor cultured under hypoxic conditions. Tubule formation assay was conducted using HUVEC treated with PBS control, healthy CD34+ cells (50k cells), diabetic CD34+ cells (50k cells), or exosomes (0, 1, 10, and 100 μg) alone or in combination with CD34+ cells. Angiogenesis assay was imaged with ImageXpress Micro system and analyzed using built-in MetaXpress software for angiogenesis.

Results: Healthy CD34+ cells significantly increased HUVECs' tube length, area, and thickness compared to PBS ($p \leq 0.007$). Diabetic CD34+ cells significantly increased tube area compared to PBS ($p = 0.050$), although no significant effect on tube length or thickness was noted. In addition, a significant increase in the number of tube segments, nodes, and branching points was observed in HUVEC treated with either healthy or diabetic CD34+ cells compared to PBS ($p \leq 0.003$). Exosomes (100 ug only) significantly increased tube length, area, and the number of tube segments ($p \leq 0.033$), but its combination with healthy or diabetic CD34+ cells had no additional effect .

Conclusions: Human CD34+ cells from a healthy or diabetic donor both showed an angiogenic effect on HUVEC in vitro, but the angiogenic effect was less robust for diabetic CD34+ cells. Exosomes also had an angiogenic effect in vitro, significant only at the highest dose tested. No additional angiogenic effects were observed when exosomes were added to either healthy or diabetic CD34+ cells. Further studies are ongoing to evaluate the effects of higher doses of exosomes on angiogenesis of CD34+ cells.

CONTROL ID: 3713789

SUBMITTER (NAME ONLY): Xuwen Liu

TITLE: Occludin interaction with dynein required for occludin centrosomal localization and VEGF-induced cell proliferation

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Liu, L. Gao, M. Merlino, D.A. Antonetti, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies suggest that occludin phosphorylation on Ser490 contributes to both VEGF-induced vascular permeability and angiogenesis in cell culture and in transgenic animals. Tight junction, transmembrane protein occludin localizes to centrosomes in a distinct vesicle compartment, required for VEGF-induced endothelial cell proliferation and neovascularization. Dynein motor is solely responsible for minus end trafficking of proteins and vesicles in cells. We hypothesized that dynein trafficks occludin to centrosomes and identified regions of occludin required to bind the dynein light intermedia chain 2 (LIC2).

Methods: Co-immunoprecipitation (Co-IP) studies were performed in bovine retinal endothelial cells (BREC) and human osteosarcoma U2OS cells that have well-characterized centrosomes. A series of occludin mutants were generated to test centrosomal localization in U2OS cells by immunofluorescence (IF) confocal microscopy and VEGF-induced proliferation in BREC.

Results: Accumulation of dynein and pS490 occludin on microtubules was observed in BREC treated with dynein inhibitor dynapyrazole A suggesting a requirement for dynein in trafficking. Co-IP and Western blotting from U2OS cells and BREC revealed that occludin and dynein interact. Mutational analysis of occludin revealed that the occludin coiled-coil domain and specifically the Ser490 phosphorylation site was required for centrosomal localization and VEGF-induced BREC proliferation. The occludin coiled-coil contained homology to the LIC2 binding adapter BICD, CC1 domain and additional mutational analysis and co-IP studies revealed an interaction site between the occludin coiled-coil and the dynein LIC2 with Ser471 contributing an essential role to binding while Ser490 was not required for this interaction but was required for centrosomal localization. Mutation of 7 amino acids in the occludin coiled-coil with homology to the CC1 domain completely blocked LIC2 binding.

Conclusions: These results reveal a novel role for occludin interaction with dynein LIC2 and begin to provide an explanation for the role of occludin in both VEGF-induced vascular permeability and angiogenesis and suggest occludin may serve to link cargo to dynein.

CONTROL ID: 3713790

SUBMITTER (NAME ONLY): Sejiro Littleton

TITLE: Nerve Associated Macrophages in the Cornea are Maintained by IL-34 and are Involved in Mechanosensation

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Littleton, D.R. Saban, Immunology, Duke University, Durham, North Carolina, UNITED STATES|S. Littleton, C. Yu, D.R. Saban, Opthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macrophages (MF) play critical roles in innate immunity but are increasingly appreciated for their roles in the maintenance of tissue physiology, particularly with respect to their interactions with nerves. Certain MF populations, including microglia in the central nervous system as well as nerve associated MF (NAM) of the sciatic nerve in the peripheral nervous system, are dependent on IL-34, the alternate ligand for colony stimulating factor 1 receptor (CSF1R), signaling through which sustains these populations locally. However, the presence of these IL-34 dependent NAM populations in the cornea and their function remains unknown. Here we leverage the unique properties of the cornea, which is imbued with the densest sensory innervation in the periphery of the body and possesses a rich network of NAMs, to investigate the functional significance of IL-34 in corneal NAM populations.

Methods: Corneas from wild type (WT) and Il34 deficient ($Il34^{LacZ/LacZ}$) age matched adult mice were dissected and stained for a combination of F480, CD206, or Iba1 and Tuj1 to label MFs and nerves, respectively. Whole mount corneas were visualized using confocal microscopy and z-stacks of the central cornea were acquired. MF counts and nerve volume were calculated by rendering the signal from z-stacks as a surface using Imaris image analysis software. Additionally, corneal mechanosensation was evaluated in WT and Il34 deficient animals using Cochet-Bonnet esthesiometry.

Results: Il34 deficient animals, as compared to WT, yielded significantly reduced MF counts in the central cornea. The central cornea showed a decreased trend in nerve volume when comparing WT to Il34 deficient mice. Moreover, Il34 deficient mice had significantly reduced corneal mechanosensation compared to WT mice.

Conclusions: Collectively, our results suggest that corneal MFs are maintained in part through IL-34 signaling, and that a reduced number of corneal NAMs is correlated with decreased corneal mechanosensation.

CONTROL ID: 3713793

SUBMITTER (NAME ONLY): Donald Brown

TITLE: Immuno Tomography (IT) and Imaging Mass Cytometry (IMC) for Constructing Spatially Resolved, Multiplexed 3D-IMC Data Sets of the Meibomian gland

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Brown, J.V. Jester, University of California Irvine, University of California Irvine, Irvine, CA, US, academic, Irvine, California, UNITED STATES|L. Gheiratmand, D. Sandkuijl, A. Loboda, Fluidigm Canada Inc, Markham, Ontario, CANADA|

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ABSTRACT BODY:

Purpose:

We have previously used Immuno Tomography (IT) to identify label retaining stem cell populations in the cornea and meibomian gland. While this method provides the unique ability to quantify stem cell populations comprised of 1-4 cells, the number of antigens that can be sequentially used to characterize these unique cells is limited by the antigen stability after antibody stripping and re-probing. To address this deficiency, we have evaluated the capability of imaging mass cytometry (IMC) to generate multiplexed images using metal-conjugated antibodies to label IT plastic sections and generate 3-dimensional IMC data sets (3D-IMC).

Methods:

K5-H2B-GFP mice, 56 days after doxycycline chase were sacrificed and eyelid tissue processed for IT. A total of 400 serial, plastic sections, 2 mm thick were then probed using metal tagged antibodies specific for sox9, collagen type I, E-cadherin, Ki67, GFP, aSMA, vimentin and DNA Intercalator. Multiplexed images were then generated using an Imaging Mass Cytometery system (Fluidigm), and 3D reconstructions assembled.

Results:

All 8 metal labeled tags were detected and their images were successfully assembled into 3D-IMC data sets. GFP labeled nuclei were identified within the meibomian glands in comparable numbers to those previously reported for slow cycling, meibomian gland stem cells.

Conclusions: These findings demonstrate that IMC can be used on plastic sections to generate multiplexed, 3D data sets that can be reconstructed to show the spatial localization of meibomian gland stem cells. We propose 3D-IMC might prove valuable in more fully characterizing stem cell populations in different tissues.

CONTROL ID: 3713795

SUBMITTER (NAME ONLY): Subrata Chakrabarti

TITLE: miRNA 9 regulates endothelial to mesenchymal transition in the retina in diabetes

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Chakrabarti, E. Wang, B. Feng, Western University Schulich School of Medicine & Dentistry, London, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a significant cause of visual impairment. Glucose-induced endothelial dysfunction is one of the important early occurrences in DR. Endothelial to mesenchymal transition (EndMT) is a hyperglycemia-inducible, epigenetically regulated process where endothelial cells lose their endothelial characteristics and acquire a mesenchymal phenotype, resulting in dysfunction of the endothelium. microRNA (miR) 9 is a short non-coding RNA that mediates epigenetic regulation, and is significantly inhibited in the retina in DR. We set out to investigate the role of miR-9 in the pathogenesis of EndMT in early DR.

Methods: Human retinal endothelial cells (HRECs) were used to model the behaviour of the retinal endothelium in DR. HRECs were harvested after treatment with normal (5mM) or high (25mM) concentrations of glucose, and RNA and protein expressions of EndMT-related genes were assessed using qPCR and western blot respectively. miR-9 mimic was used to rescue glucose-induced EndMT in HRECs. Mouse models were used to validate the findings in vivo. Diabetes was induced in 8-week-old mice using streptozotocin, age-matched controls were given mock injections. Retinal tissues were harvested after 2 months, and RNA and protein expressions of EndMT-related genes were analyzed using qPCR and ELISA respectively. Specially generated endothelial-specific miR-9 overexpressing mice were used to validate the ability of miR-9 overexpression to prevent EndMT in vivo.

Results: Glucose significantly inhibited miR-9 expression in HRECs. Glucose-induced inhibition of miR-9 in HRECs correlated with the downregulation of endothelial markers and the upregulation of mesenchymal markers. Transfection with miR-9 mimics prevented the aforementioned in HRECs. Similar results were reproduced in animals. EndMT was seen in the retinas of normal diabetic mice, but not in those of miR-9 overexpressing diabetic mice.

Conclusions: These results, taken together, show that miR-9 is an important regulator of EndMT in the retina. We showed that glucose-induced inhibition of miR-9 mediated EndMT, and that miR-9 overexpression prevented EndMT in DR. Thus, miR-9 may represent an avenue for targeted RNA-based gene therapy against EndMT in DR in diabetic patients.

CONTROL ID: 3713796

SUBMITTER (NAME ONLY): Maximiliano Olivera

TITLE: Automated Machine learning models applied to Optical Coherence Tomography Angiography for detection and classification of Diabetic Retinopathy in Diabetes Mellitus type 1

SESSION TITLE: Machine Learning and Big Data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Olivera, C. Bernal-Morales, R. Struyven, M. Batista-Gonçalves, S. Wagner, P.A. Keane, Medical Retina Research, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|M. Olivera, Vitreo Retina, Hospital Universitario Insular de Gran Canaria, Las Palmas de Gran Canaria, Canarias, SPAIN|A. Alé-Chilet, M. Barraso, S. Marin, S. Feu, J. Rosinés, C. Oliva, T. Hernandez, I. Vila, J. Zarranz-Ventura, Hospital Clinic de Barcelona, Barcelona, Catalunya, SPAIN|

ABSTRACT BODY:

Purpose: To evaluate the diagnostic capacity of Automated Machine Learning (AML) algorithms to classify the degree of diabetic retinopathy (DR) from optical coherence tomography (OCT) and OCT angiography (OCTA) images.

Methods: Cross-sectional study on a pseudonymised dataset of images collected during a previous prospective clinical trial (NCT03422965), corresponding to a cohort of 485 patients with type 1 Diabetes Mellitus and 115 healthy controls. The retinal images were labeled with the corresponding demographic and clinical data collected in the clinical trial. The classification models based on Deep Learning and computer vision algorithms were trained hosted in a cloud-based system, under the Vertex AI platform of Google Cloud Platform, which allows the training of algorithms without the need automated fine-tuning of hyperparameters (AML). The performance was compared for superficial and deep capillary plexuses (SCP and DCP, respectively) on 3x3 mm and 6x6 mm captures, following 3 labeling strategies: No DR vs no DR; No DR vs. Mild DR vs. Referable DR, and No RD vs. Non-Proliferative RD vs. Proliferative RD.

Results: The performance of the classification models was evaluated through precision, sensitivity, specificity and f1-score. Overall, despite having good average precision values (ranging between 0.6 to 0.9 for structural OCT and 0.59 to 0.94 for OCTA), the models trained on structural OCT images had consistently a significative lower power of detection on the greater DR grade on each strategy (ranging from 0% to 33%) compared to 30% to 88% for the models trained on OCTA images. Models performance was consistently superior in those trained using SCP images and was greatest using 3x3 mm scanning protocol.

Conclusions: AML algorithms are able to detect the DR status when trained in OCTA images of DM patients, in particular using OCTA images from the SCP and high definition 3x3mm scan field. Unbalanced datasets may give rise to non-significative good performance metrics if not adequatelly analyzed. These preliminary results raise the interesting hypothesis of using OCTA images to investigate the potential ability of AML algorithms to detect systemic microvascular damage elsewhere in the body, by means of exploring existing relationships between OCTA images and quantitative systemic variables through Oculomics.

CONTROL ID: 3713797

SUBMITTER (NAME ONLY): E Valas Teuma

TITLE: Duo-Pulse Width Laser Engine for Femtosecond Laser Assisted Cataract Surgery: Benefits in Corneal Incision and Lens Fragmentation

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Teuma, R&D, LENSAR Inc, Orlando, Florida, UNITED STATES|

Commercial Relationships Disclosure: E Valas Teuma: Commercial Relationship(s);Code E (Employment):LENSAR, Inc

ABSTRACT BODY:

Purpose: A novel system with an integrated duo-pulse engine (Gen-2 ALLY, LENSAR, Orlando, FL) offers the flexibility of operating with either a short (femtosecond) or long (picosecond) pulse laser. The purpose of this study is to evaluate the efficacy of each option in corneal treatment and lens fragmentation.

Methods: Pairs of human donor eyes were utilized. Two full thickness corneal incisions of 2.5mm width each were performed on the eyes 180° apart with each pulse width. Lens fragmentation patterns were generated in each lens using a mask to cover half the lens volume to limit the laser treatment to the exposed half volume for each pulse width. Evaluation of the corneal incisions and lens fragmentation was performed under the surgical microscope.

Results: Following the short pulse laser treatment, the corneal incisions were consistently easier to open and, in, some cases, gaping. In addition, the intrastromal tunnel was generally free of tissue bridges. With the long pulse laser, the incision was characterized by a residual uncut layer beneath the epithelium that needed to be broken to access the incision. Moreover, the occurrence of an opaque bubble layer (OBL) was more frequent and pronounced with the long pulse laser.

For lens fragmentation, larger surface cleavages were observed in the lens volume treated with the long pulse laser. The size of the cleavage was indicative of the laser's generation of incisional cuts /cracks that expanded beyond the point of photodisruption, including in opaque/hard cataract volumes. However, with the short pulse laser, the fragmentation cuts exhibited discontinuities in the posterior lens volume in some cases, indicative of its challenge to be consistently effective in cutting the fibrous posterior plate.

Conclusions: These preliminary data show that a duo-pulse laser offers unique flexibility to use a short pulse laser that is more effective in construction of corneal incisions with the advantages of minimal OBL occurrence, easier opening and absence of tissue-bridges. The long pulse laser is more effective in lens fragmentation with the cuts continued and extended to the posterior lens including the fibrous posterior plate.

CONTROL ID: 3713798

SUBMITTER (NAME ONLY): Louisa Lu

TITLE: Utilizing intra-operative surgical navigation to improve implant positioning in orbital fracture reconstruction

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lu, B. Erickson, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Louisa Lu: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Erickson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Improper orbital implant placement is the most common cause of revision surgery and complications in orbital fracture repair. Ensuring correct orientation of the posterior aspect of the implant in the orbital apex in complex blowout and more extensive craniofacial fractures (ZMC, LeForte) is particularly critical. Once a cantilevered implant is provisionally anchored to the inferior orbital rim, it can also be challenging to adjust implant angulation. We demonstrate a method of intra-operative navigation utilizing a novel instrument that clamps onto a titanium mesh floor/medial wall implant and registers with a surgical navigation system to facilitate optimal positioning with respect to the orbital apex.

Methods: An orbital floor/medial wall titanium mesh implant was positioned into a novel clamping instrument probe that was subsequently registered by the surgical navigation system, into which a CT maxillofacial scan of a man who suffered left ZMC fracture was imported. The navigable instrument was used to manipulate the implant within the orbital floor of the sterolithographic model skull with real-time feedback of the implant's position within the orbital apex via automatic symmetrical visualization with the radiographic overlay (Figures 1-2).

Results: The navigable instrument successfully aided simulated intra-operative positioning of the implant with continuous verification of the implant's exact position within the orbital apex. This demonstration illustrated that instrument-guided navigation facilitates implant manipulation and real-time visualization of placement, allowing the surgeon to assess for deviations and adjust accordingly for optimal placement.

Conclusions: Intra-operative instrument-guided navigation of orbital implants presents a significant advantage in improving implant positioning in orbital fracture reconstructions. This novel instrument facilitates both manipulation of implant angulation and orientation once provisionally placed as well as guidance to ensure optimal orientation.

CONTROL ID: 3713799

SUBMITTER (NAME ONLY): Pankaj Singh

TITLE: The use of intravitreal Brolucizumab 6 mg (Beovu®) in patients with neovascular age related macular degeneration (nAMD) – The safety outcomes from the Goethe-University Hospital, Department of Ophthalmology in Frankfurt am Main, Germany.

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Singh, L. Franziska, M. Mueller, S. Deuchler, C. Lwowski, T. Kohnen, F.H. Koch, Ophthalmology, Goethe-Universitat Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|

Commercial Relationships Disclosure: Pankaj Singh: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera | Loeffler Franziska: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera | Michael Mueller: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera | Svenja Deuchler: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera | Christoph Lwowski: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera | Thomas Kohnen: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera | Frank Koch: Commercial Relationship(s);Code F (Financial Support):Novartis, Bayer, Alimera

ABSTRACT BODY:

Purpose: There are some post-marketing safety case reports of Beovu®, a rare occurrence of intraocular inflammation (IOI) in association with retinal vasculitis and retinal vascular occlusion, published. Data from real-life practice does, however, allow the safety of Beovu®. These findings are presented in the current retrospective case series.

Methods: Monocentric audit involving a pool of 51 patients (58 eyes) with nAMD and treated with Beovu® between April 2020 and April 2021. This data includes only the patients which had 3 or more intravitreal injections of Beovu® and were treated after 3 uploading doses ever 4 weeks further in treat and extend regime. The following parameters were measured in these patients: visual acuity (VA); central retinal thickness (CRT) with Optical coherence tomography (OCT); intraocular inflammation (IOI); and, intraocular pressure (IOP). Values are reported as means throughout.

Results: The mean age of the patients was 76 years and 50 eyes were pseudophakic at baseline. The mean number of the injections Beovu® given was 6. Two eyes experienced (incidence < 4%) their first IOI-related event within 3 months of the first Beovu® injection. The mean (range) number of days from the last injection to the onset of event were 4 (3-5) for IOI, and 10 (10) for vasculitis with retinal vascular occlusion. One of them had only vitreous haze. Another presented with Iritis, both had no retinal vasculitis and retinal vascular occlusion. These Patients were treated immediately after presentation with systemic and topical steroids. The IOI was resolved in a 5-7 days without loss of VA. There was only one case out of 58 eyes (incidence < 2%)of at least visual acuity loss (!15 ETDRS letters) in eye due IOI and vasculitis with retinal artery occlusion. The treatment with Beovu® was stoped in these eyes and was switched to another medication. There were no IOP-related events observed.

Conclusions: Beovu® shows an overall well-tolerated safety and efficacy profile in our real life clinical practice. The incidence of intraocular inflammation (IOI) (iritis and uveitis), is almost similar in our case series as in HAWK and HARRIER Study. Early detection of IOI and immediate treatment with steroids resolves the IOI and shows no loss in VA.

CONTROL ID: 3713800

SUBMITTER (NAME ONLY): John Hulleman

TITLE: Molecular and ocular characterization of R345W EFEMP1 mice reveal new disease-related insights

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hulleman, M. Renwick, S. Daniel, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: John Hulleman: Commercial Relationship: Code N (No Commercial Relationship) | Marian Renwick: Commercial Relationship: Code N (No Commercial Relationship) | Steffi Daniel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The R345W mutation in EFEMP1 (a.k.a. fibulin-3, F3) causes a rare macular dystrophy (Malattia Leventinese/Doyne Honeycomb Retinal Dystrophy, ML/DHRD) resembling an early onset form of age-related macular degeneration (AMD). Studies have demonstrated that R345W knockin mice form basal laminar deposits (BLamDs) and they have also implicated complement activation as a key pathway in disease progression. Yet little additional information on these mice exists. Herein, we sought to thoroughly characterize the R345W EFEMP1 knockin mice with respect to any molecular or physiological differences vs. wild-type mice with the hope of identifying and eventually targeting new pathways for disease intervention.

Methods: Homozygous R345W knockin mice on the C57BL/6 background (and their littermate controls) were aged up to 20 months prior to analysis. Anterior physiology was measured by in vivo confocal microscopy, rebound tonometer and slit lamp. In vivo retinal structure was evaluated by OCT (also by blue AF), and TEM, histology, and RPE flat mounts post euthanasia. Retinal function was assessed by ERG (scotopic [a,b,c-wave], photopic [a-, b-wave]). Molecular evaluation was achieved using IHC and qPCR.

Results: No increase in corneal haze or stromal thickness were observed, contrasting our findings in EFEMP1 knockout mice. Slit lamp and IOP assessment were unremarkable in mutant mice. Total retinal thickness (by OCT) was not significantly different between groups (16 mo), while retinal AF was slightly, but significantly increased in mutant mice. Aged R345W mice (16 mo) formed canonical, thick, continuous BLamDs, consistent with previous observations. Histologically, aged R345W mice (16 mo) appeared to be more prone to photoreceptor/RPE disorganization/disruptions including RPE whorls. Yet, remarkably, no differences in any ERG functional readings were detected in R345W mice (up to 20 mo). At the molecular level, we detected significant increases in C3, casp1, Il1b and Nlrp3 (qPCR) in mutant RPE/choroid (18 mo) and increased staining for Nlrp3 and Iba1 in posterior sections (IHC).

Conclusions: The R345W mice develop ultrastructural defects (BLamDs), disrupted photoreceptor/RPE organization and increased retinal autofluorescence. Molecularly, inflammasome activation may be a triggering event in ML/DHRD. Pharmacological or genetic targeting of Nlrp3 or Casp1 may alter the course of this AMD-like disease.

CONTROL ID: 3713801

SUBMITTER (NAME ONLY): ISMAIL ZAITOUN

TITLE: Visualization of Choroidal Vasculature and Innate Immune Cells in the Eyes from Pigmented Mice

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.S. ZAITOUN, Y. Song, M. El Ragaby, N. Sheibani, Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|I.S. ZAITOUN, Y. Song, C.M. Sorenson, N. Sheibani, McPherson Eye Research Institute, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|C.M. Sorenson, Pediatrics, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: ISMAIL ZAITOUN: Commercial Relationship: Code N (No Commercial Relationship) | Yong-Seok Song: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed El Ragaby: Commercial Relationship: Code N (No Commercial Relationship) | Christine Sorenson: Commercial Relationship: Code N (No Commercial Relationship) | Nader Sheibani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The biochemical and histological examination of choroid and the status of its cellular components have been very challenging due to the presence of the retinal pigmented epithelium (RPE) layer between the choroid and retina. Here we developed methods for labeling and visualization of choroidal macrophages, mast cells, and vasculature in pigmented mice.

Methods: Eyes from three albino lines (FVBN, CD-1, and BALB/c) and one pigmented line (C57BL/6J) of mice were collected, fixed for 1 h in 4% paraformaldehyde, washed 3 times in PBS, and kept in cold PBS until dissected. The wholemount of choroid-sclera complex from the albino and pigmented mice were independently stained with anti-Iba1 and anti-podocalyxin to label the choroidal macrophages and vasculature, respectively. Mast cells were labeled with Avidin-conjugated rhodamine. To eliminate the pigment from RPE cells of C57BL/6J eyes, the stained tissues were fixed again before bleaching; 4-5 h in a 55°C water bath using 1% H_2O_2. Tissues were then washed and incubated with secondary antibodies and Avidin-conjugated rhodamine. Choroidal macrophages, mast cells, and the vasculature were visualized using confocal microscopy.

Results: The novel staining methods described here allowed the successful visualization of choroidal macrophages, mast cells, and the vasculature in both albino and pigmented mice. Choroidal macrophages in all mouse lines were denser around the optic nerve compared with the equator and periphery. Choroidal mast cells were relatively dense around the optic nerve of all mouse lines examined. However, their distribution in the equator and the periphery were different. The FVBN, CD-1 and C57BL/6J mice had fewer mast cells in the equator compared to the periphery. BALB/c mice had more mast cells, which were almost uniformly distributed in the equator as compared to the periphery. The total number of choroidal mast cells was highest in BALB/c and FVBN mice. The structure of the choroid in all four lines of mice was roughly comparable, except albino mice showed signs of hypotrophy.

Conclusions: Staining and bleaching of pigmented eyes allowed the visualization of choroidal macrophages, mast cells, and vasculature in the eyes of pigmented mice. These methods should allow the evaluation of choroid and its various cellular components in transgenic and preclinical mouse models of eye diseases.

CONTROL ID: 3713802

SUBMITTER (NAME ONLY): JANE Gilmore

TITLE: Goniotomy and Direct Viscodilation of the Collector Channels with Cataract Surgery: 5 year results

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Gilmore, ophthalmology, The University of Texas Southwestern Medical Center Medical School, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: JANE Gilmore: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose is to evaluate a hybrid MIGS procedure using Goniotomy and Direct Viscodilation of the collector channels with cataract surgery in all levels of glaucoma. This unique technique not only removes the trabecular meshwork but also directly viscodilates the collector channels.

Methods: After cataract surgery, the Dual Blade removed 180° of trabecular meshwork. Viscoelastic was injected into the exposed ostium of the Collector Channels as the perpendicular viscoelastic cannula was held firmly against the outer wall and dragged through the gutted canal. Moderate to severe glaucoma comprised 58% of the 213 eyes followed at least 2 years. 32% had previous glaucoma surgery. 71% were African American. 44% were diabetics. 50% were on an anticoagulant.

Results: Initial IOP was 19.0mmHg(SD+/-7.1)on 1.7 medications. At 3 months the IOP was 15.5mmHg(SD+/-5.0). Throughout the first year the IOP hovered around 16.0mmHg in 316 eyes. IOP then settled to 16.2mmHg (SD+/-5.1) at 3 years(n=120)and 16(SD+/-4.1)at 4years(n=63). Although the IOP was reduced by 15%, the reduction in medications hovered around 70% over 5yrs. All eyes had ≤15mmHg AND no meds in 37% (1yr), 30% (2yr) 37%(3yr), and 32% (4yr). Even the moderate to severe group had ≤15mmHg AND no meds 38% (1yr), 30% (2yr), 36% (3yr), and 32% (4yr). Medications were reduced by 1.5 drops per eye over the course of 5 years. Reduction of drops in this group of 316 eyes resulted in a savings of $240,000 in the first year alone.

Conclusions: The synergy of Goniotomy and Viscodilation markedly reduces drops even in advanced glaucoma with at least 50% of eyes achieving IOP ≤15mmHg, thus improving compliance and reducing the associated financial burden. The Goniotomy-Viscodilation-Cataract technique addresses both trabecular outflow resistance and salvages the collapsed collector channels.

CONTROL ID: 3713804

SUBMITTER (NAME ONLY): Mayur Choudhary

TITLE: Identification of disease associated endpoints in a mouse model exhibiting AMD-like pathology with age
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SESSION TITLE: Lipid signaling and homeostasis in retinal health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Choudhary, G. Malek, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|G. Malek, Pathology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Mayur Choudhary: Commercial Relationship: Code N (No Commercial Relationship) | Goldis Malek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is an unmet need for discovering effective treatments and creating animal models of the most prevalent neurodegenerative form of blindness in the elderly, called age-related macular generation (AMD). We performed extensive ocular characterization of an animal model exhibiting AMD-like pathology, the liver-X-receptor alpha knockout mice ($LXR\alpha^{-/-}$, $Nr1h3^{-/-}$), as a function of age and identified multiple endpoints, which may serve as valuable tools in drug discovery.

Methods: $Nr1h3^{-/-}$ mice were divided into three age groups: group 1 (10-14 month old), group 2 (18-22 month old) and group 3 (24-28 month old), and imaged by Micron IV to obtain fundus and optical coherence tomography (OCT) images (n=5/group). Electroretinograms (ERG) were recorded to measure dark-adapted and rod-saturated responses. Retinal morphology and ultrastructure was assessed (n=5/group). RPE-choroid flatmounts (n=4/group) were stained with phalloidin and probed with an antibody to F4/80 and CD68 to evaluate RPE structure and immune cells. Cytokine levels were measured in retinal and RPE/choroid protein lysates as a function of age (n=4/group).

Results: In vivo, $Nr1h3^{-/-}$ mice exhibited inner and outer retinal hyper-reflective spots and localized deposits by OCT. The frequency of outer retinal hyper reflective spots was higher in group 2 (6/10 eyes) and group 3 (4/10 eyes) cohorts as compared to group 1 (1/10 eyes). Also, a significant decline in scotopic-a (Mean ± SEM, group 1: 183 ± 13 µV, group 2: 103 ± 12 µV, group 3: 47 ± 11 µV, group 1 vs 2: $p<0.05$, group 1 vs 3: $p<0.01$), scotopic-b (group 1: 378 ± 36 µV, group 2: 215 ± 23 µV, group 3: 110 ± 8.15, group 1 vs 2: $p<0.05$, group 1 vs 3: $p<0.05$), and photopic-b (group 1: 92 ± 6 µV, group 2: 60 ± 178 µV, group 3: 32 ± 14 µV, group 1 vs 3: $p<0.05$) wave amplitudes were measured with age. Morphologically, the area of RPE dystrophy quantified from RPE/choroid flatmounts increase significantly with age (group 1: 6.2 ± 0.4%, group 2: 8.4 ± 0.8%, group 3:11.5 ± 0.9%, group 1 vs 2: $p<0.05$, group 1 vs 3: $p<0.01$).

Conclusions: $Nr1h3^{-/-}$ mice exhibit an age-related decline in retinal function and compromised RPE morphology, with the oldest cohort showing the most severe phenotype. End-points evaluated in the study can be employed in preventive (younger age; 4-8 months) and interventional pre-clinical studies (older age;14-18 months), testing potential experimental therapies.

CONTROL ID: 3713805

SUBMITTER (NAME ONLY): Jami Gurley

TITLE: Endothelial cell (EC) Caveolin-1 depletion affects whole retinal metabolism and retinal microvascular EC Notch receptor expression

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Gurley, E.H. Hargis, E.N. Enyong, M.H. Elliott, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|A. pranay, A. batushansky, T. Griffin, Aging and Metabolism, Oklahoma Medical Research Foundation Arthritis and Clinical Immunology Research Program, Oklahoma City, Oklahoma, UNITED STATES|C. schafer, C. griffin, Cardiovascular Biology, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Jami Gurley: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Hargis: Commercial Relationship: Code N (No Commercial Relationship) | atul pranay: Commercial Relationship: Code N (No Commercial Relationship) | albert batushansky: Commercial Relationship: Code N (No Commercial Relationship) | christopher schafer: Commercial Relationship: Code N (No Commercial Relationship) | Eric Enyong: Commercial Relationship: Code N (No Commercial Relationship) | courtney griffin: Commercial Relationship: Code N (No Commercial Relationship) | Tim Griffin: Commercial Relationship: Code N (No Commercial Relationship) | Michael Elliott: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aging and diabetes are associated with retinal vascular disease and vision loss. Vascular remodeling that results in retinal endothelial cell (EC) loss of mural coverage has been implicated in early pathogenesis of diabetic retinopathy (DR). We previously observed specific loss of smooth muscle cell (SMC) coverage along superficial arterioles in aged murine and human retinas. Additionally, global-Cav1 (Caveolin-1) knockout in young mice also reduces SMC coverage, and we previously presented data suggesting that EC-specific Cav1 supports SMC preservation. The purpose of this study is to investigate potential EC-Cav1-dependent EC/SMC pathways important for SMC maintenance. As ECs play a role in SMC nutrient availability and EC/SMC communication, our hypothesis is that EC-Cav1 is important for micorvascular SMC maintenance in the adult retina.

Methods: We used Tie2-Cre recombination of the Cav1-floxed gene (Tie2-Cre/Cav1$^{f/f}$) to generate EC-Cav1 KO mice. GC/MS was used to assess changes in whole retinal metabolites from 13-week old male and female EC-Cav1 KO animals. We used shRNA-mediated Cav1 knockdown in human retinal ECs (hRECs) to assess Cav1-dependent effects on Notch receptor expression via Western blot.

Results: EC-Cav1 KO mice showed an overall reduction in retinal glycolytic and amino acid metabolic intermediates. We also show shRNA-mediated Cav1 knockdown reduces hREC Notch1 and Notch4 protein expression. Future metabolic studies will assess EC-Cav1 KO effects on various metabolic pathways in ECs, SMCs, and whole retina tissue. Ongoing studies regarding EC-Cav1 effects on Notch ligand expression, as well as human retinal vascular SMC (hVSMC) receptor and ligand expression, are currently underway.

Conclusions: Our data suggest that EC-Cav1 has a broad impact on the overall retinal tissue metabolic profile, suggesting that Cav1-dependent functions originating from the relatively small proportion of ECs in the retina may have the capacity to significantly alter whole tissue nutrient handling. Additionally, our data showing EC-Cav1 depletion in cultured ECs reduces Notch receptor expression suggests that EC-Cav1 may play an important role in maintenance of EC/EC and/or EC/SMC communication in adult retinal vasculature.

CONTROL ID: 3713806

SUBMITTER (NAME ONLY): Arnold Leigh

TITLE: CRISPR -Cas9-mediated gene correction in Induced Pluripotent Stem Cells derived from Oculocutaneous Albinism Type 2 patients rescues pigmentation defect in Retinal Pigment Epithelium

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Leigh, T. Pfister, A. George, R. Sharma, M. Abu-Asab, K. Bharti, B.P. Brooks, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oculocutaneous albinism type 2 (OCA2) is a rare genetic condition due to recessive mutations in OCA2 gene and results in pigmentation defects of the skin, hair, and eyes. We have previously shown that induced pluripotent stem cells (iPSCs) derived from OCA2 patients successfully recapitulate pigmentation defects when differentiated in vitro into retinal pigment epithelium (RPE). We used CRISPR-Cas9-based homology-dependent repair of a mutant allele in iPSCs derived from an OCA2 patient. The purpose of our study was to create an isogenic pair of iPSCs for studying OCA2 related pigmentation defects in the human RPE.

Methods: All human iPSC work was approved by the NIH Institutional Review Board, protocol # 11-E1-0245 (NCT01432847). iPSCs were derived from OCA2 patients with compound heterozygous mutations. Two sgRNAs were designed, targeting chromosome 15 (NG_009846.1). The donor template used for HDR replaced the mutation c.1211C>T (NM_000275.3) in exon 12. The OCA2_iPSC colonies were transfected using Lipofectamine ™ followed by single-cell cloning in the presence of Puromycin to positively select GFP+ colonies. Selected iPSC clones were transfected with a Cre recombinase-expressing plasmid followed by treatment with Geneticin to select for GFP-negative colonies resulting from recombination and excision of the cassette containing GFP and neomycin. The GFP-negative iPSC colonies were then expanded and analyzed using flow-cytometry to confirm the complete lack of GFP expression. Sanger sequencing was performed on GFP-negative iPSC colonies to confirm correction of the mutation (OCA2-IC_iPSC).

Results: We successfully replaced the c.1211C>T mutation in exon 12 of OCA2 with the wild type sequence as confirmed by Sanger sequencing. The isogenic iPSC pair exhibited normal human karyotype and expression of pluripotency markers like NANOG, OCT4, SOX-2, SSEA4, TRA-1-60, and TRA-1-81. The OCA2-IC_iPSC when differentiated towards RPE exhibited normal pigmentation whereas the OCA2_iPSC derived RPE exhibited partial pigmentation.

Conclusions: Our work establishes proof of principle for CRISPR-mediated gene editing as a strategy for pigment rescue in OCA2. Furthermore, we introduce OCA2 patients and corrected isogenic cell lines as valuable tools for in vitro disease investigation and drug discovery.

CONTROL ID: 3713807

SUBMITTER (NAME ONLY): Veronica Romero Morales

TITLE: Correlation of Paravascular Inner Retinal Defects with Posterior Vitreous Detachment Using En Face OCT

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Romero Morales, E. Bousquet, S. somisetty, A. Santina, N. Abraham, A. Lu, M. Fogel Levin, T.J. Peiris, B. Lee, D. Sarraf, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|V. Romero Morales, Retina, Instituto Mexicano de Oftalmologia I.A.P., Queretaro, Queretaro, MEXICO|

Commercial Relationships Disclosure: Veronica Romero Morales: Commercial Relationship: Code N (No Commercial Relationship) | Elodie Bousquet: Commercial Relationship: Code N (No Commercial Relationship) | swathi somisetty: Commercial Relationship: Code N (No Commercial Relationship) | Ahmad Santina: Commercial Relationship: Code N (No Commercial Relationship) | Neda Abraham: Commercial Relationship: Code N (No Commercial Relationship) | Anthony Lu: Commercial Relationship: Code N (No Commercial Relationship) | Meira Fogel Levin: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Peiris: Commercial Relationship: Code N (No Commercial Relationship) | Brian Lee: Commercial Relationship: Code N (No Commercial Relationship) | David Sarraf: Commercial Relationship(s);Code C (Consultant/Contractor):Optovue

ABSTRACT BODY:

Purpose: Paravascular inner retinal defects (PIRD) are a well-known association of myopia and epiretinal membranes (ERM). We aimed to determine if PIRD can also be correlated with the presence and stage of posterior vitreous detachment (PVD) using en face optical coherence tomography (OCT).

Methods: This was a retrospective cross-sectional, observational, single center study. 9x9 mm and 12x12 mm en face optical coherence tomography (OCT) images (Solix Full Range OCT, Optovue) were reviewed from an OCT angiography database from a single medical retina office (DS) at the Stein Eye Institute at UCLA. PIRD were confirmed with analysis of both the en face OCT and the corresponding B scan. PVD was graded according to the corresponding OCT B scan. PIRD were classified as paravascular retinal cysts (without communication to the vitreous cavity) versus paravascular lamellar holes (with communication to the vitreous cavity) and according to the number of PIRD a) one PIRD versus b) 2 or more PIRD.

Results: En face OCT datasets from 1137 patients were reviewed. A total of 272 eyes from 176 patients (15.49%) showed evidence of at least one PIRD in one eye. The mean age of this cohort was 70.5 ±13.5 years and 100 (57%) were female. In eyes with PIRD, grade 0 PVD was noted in 25 eyes (13%), grade 1 PVD in 32 eyes (16%), grade 2 PVD in 15 eyes (8%), grade 3 PVD in 22 eyes (11%), and grade 4 PVD in 178 eyes (71%).

Of the 272 eyes, 153 (56.25%) displayed paravascular retinal cysts and 119 (43.75%) displayed paravascular lamellar holes. Paravascular lamellar holes were observed in 3 eyes (12%) without PVD, 34 eyes (49.3%) with partial PVD (stage 1 to 3), and 82 eyes (46.1%) with complete PVD (p=0.003). Two or more PIRD were found in 9 eyes (36%) without PVD and in 171 eyes (69%) with partial or complete PVD (stage 1 to 4) (p=0.001).

Conclusions: PIRD are a well-known complication of myopia and ERM. This study correlated the presence and grade of PVD with the development of PIRD. PIRD likely develop as a result of chronic vitreoretinal traction, especially in areas of increased traction as occurs along the major retinal vessels. En face OCT is an effective tool to detect PIRD.

CONTROL ID: 3713809

SUBMITTER (NAME ONLY): Yun-Zheng Le

TITLE: VEGF as a direct regulator of photoreceptor function and a major contributing factor for altering photoreceptor function in diabetes and hypoxia

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Le, J. Hu, M. Zhu, D. Li, Medicine, University of Oklahoma Health Sciences Center, Oklahoma city, Oklahoma, UNITED STATES|J. Hu, Q. Wu, Ophthalmology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, CHINA|D. Li, School of Optometry, Hubei University of Science and Technology, Xianning, CHINA|

Commercial Relationships Disclosure: Yun-Zheng Le: Commercial Relationship: Code N (No Commercial Relationship) | Jianyan Hu: Commercial Relationship: Code N (No Commercial Relationship) | Meili Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Dai Li: Commercial Relationship: Code N (No Commercial Relationship) | Qiang Wu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Vascular endothelial growth factor (VEGF or VEGF-A), a major therapeutic target for blood-retina barrier breakdown (BRB) in diabetic retinopathy (DR) and neovascular age-related macular degeneration (AMD), has been shown to act as a direct functional regulator for peripheral and central nervous system (CNS) neurons. The purpose of this study was to determine whether VEGF is a direct regulator of photoreceptor function and its potential role in altering vision during the progression of DR, AMD, and other hypoxic retinal BRB diseases.

Methods: For this study, we developed a procedure to measure the direct effect of VEGF on photoreceptor function with electroretinography (ERG). Overnight dark-adapted wild-type (WT) mice were injected with recombinant VEGF (rVEGF) intravitreally under long-wavelength illumination. Retinal function in these mice was examined with scotopic and photopic electroretinography ERG immediately after intravitreal rVEGF delivery. Diabetes- or hypoxia-induced alteration of photoreceptor function was examined with Akita diabetic mice or hypoxic mice immediately after injected with rVEGF or vehicle.

Results: In dark-adapted WT mice, rVEGF caused a significant reduction of scotopic ERG a-wave and b-wave amplitudes and photopic ERG b-wave amplitudes in a dose-dependent manner. However, the effect of rVEGF on the alteration of ERG amplitudes was nullified in 5-mo-old Akita diabetic mice in which a higher level of VEGF was present in photoreceptors. A similar result was also observed in 1.5 mo-old hypoxic mice generated by placing the animals with 7% oxygen for 5 days.

Conclusions: Our results suggest that VEGF is a direct functional regulator for photoreceptors and a contributing factor to the loss of photoreceptor function in diabetes and hypoxia (retinal environment in AMD). As VEGF is a major therapeutic target for BRB breakdown in DR, AMD, and other hypoxic retinal BRB diseases, our work provides the mechanistic insights for the therapeutic effects on visual acuity and for the care of anti-VEGF drug treated patients.

CONTROL ID: 3713810

SUBMITTER (NAME ONLY): Mikhail Tsaritsyn

TITLE: Automatic detection of cone photoreceptors in the fovea using confocal AOSLO imaging

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tsaritsyn, A. Jacot-Guillarmod, J. Potic, T. Wolfensberger, C. Bergin, M. Tomasoni, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|A.M. Dubis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A.M. Dubis, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) can be used to image photoreceptors, in vivo. Recently, several algorithms for cone characterisation have exploited the specificity of split dector to robustly image cone inner segements. The high packing density of cones within the fovea, impedes split dector efficacity[1]. We present a novel algorithm for automated cone detector in confocal images: the Automatic Adaptive Thresholding and Maxima Search (ATMS).

[1] (Morgan, J. I. W., Vergilio, G. K., Hsu, J., Dubra, A., & Cooper, R. F. (2018). The reliability of cone density measurements in the presence of rods. Translational Vision Science and Technology, 7(3), 1–11. https://doi.org/10.1167/tvst.7.3.21).

Methods: ATMS first detects darker areas by adaptive local filtering. Those correspond to blood vessels where cones cannot be reliably counted, so they are excluded from further analysis. The image is then split into Regions Of Interest (ROIs) and contrast enhancement is performed separately in each ROI, normalizing by brightness and subtracting its the second derivative. This enhances the bright spots corresponding to cones. Based on the local distribution of luminosity in each ROI, the image was then segmented using adaprive thresholding, and the cones are identified via a local maxima search. Finally, the output was refined by adjusting the threshold probability based on Veronoi properties of the cell mosaic. From this output, cell densities were calculated.

Results: Results were validated on 53 images from 10 subjects. Each image was annotated by 2 graders: the overall mean Dice’s coefficient was 0.96 (Precision = 0.97, Recall = 0.95).

Conclusions: This paper presented a novel, fully automated labelling method which is suitable for analysis of central foveal regions (0° to 3°) in confocal images. Our method was integrated with existing tools that operate in more peripherical regions (4° to 10°), thus building a cell density estimation pipeline which works across the full range of retinal eccentricities.

CONTROL ID: 3713811

SUBMITTER (NAME ONLY): Swati Jain

TITLE: Apoptosis and necroptosis is induced in cone photoreceptor cells subjected to cold storage and rewarming

SESSION TITLE: Blood flow and ischemia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Jain, D. Yoeli, N. Khatter, A. Su, C. Huang, K. Washington, A. Jani, University of Colorado, Denver, Colorado, UNITED STATES|E. Farkash, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blindness afflicts 39 million people worldwide. Retinal ganglion cells are unable to regenerate, making this condition irreversible in many cases. Whole-eye transplantation (WET) may be a viable treatment option. To further enhance our knowledge of WET, individual cell types response to the transplant must be studied. 661W cone photoreceptor cells, derived from mouse, have been widely used as a model for studying macular degeneration. Here, we characterize the 661W cell line for studying the effect of cold ischemia/warm reperfusion injury that is relevant to WET.

Methods: To understand the phenotype of injury during in-vivo cold ischemia/warm reperfusion injury, 661w cells were subjected to cold storage and rewarming (CS/REW). First, cells were subjected to cold storage (CS) in cold saline solution for 24 h at 4°C. Next, cells were rewarmed (REW) in normal growth media at 37°C for 24 h. Control cells were kept at 37°C. A dose response analysis was performed to determine the optimal concentration of pan-caspase inhibitor (Q-VD-OPh) and necroptosis inhibitor (Necrostatin-1) to completely inhibit aoptosis and necroptosis.

Results: Cell death percentage, measured as Annexin V positive and/or PI positive cells by flow cytometry was significantly increased in the 661w cells subjected to CS/REW compared to control cells (Figure 1). We looked for the expression of key integrators of signaling pathways that mediate apoptosis and necroptosis. 661w cells subjected to CS/REW have activation of apoptosis as determined by increased expression of cleaved caspase-3 and increased TUNEL staining. Moreover 661w cells exposed to CS/REW also showed activation of necroptosis as determined by increased expression of RIP3 and pMLKL. The effect of Q-VD-OPh and Necrostatin-1 on caspase-3 protein expression and pMLKL was dose-dependent. Q-VD-OPh treatment at 50 μM inhibit the apoptosis, whereas Necrostatin-1 treatmnet at 100 μM inhibit the necroptosis.

Conclusions: Our results suggest that the inclusion of cold storage followed by warm reperfusion during WET will likely induce cell death by both apoptosis and pnecroptosis. Apoptotic cell death and necroptosis can be successfully prevented using a pan-caspase I inhibitor and Necrostatin-1. Future studies: We will also study the collective effect of inhibiting apoptosis and necroptosis in 661w cells after CS/REW by using a cocktail of Q-VD-OPh and Necrostatin-1.

CONTROL ID: 3713812

SUBMITTER (NAME ONLY): Kelly Klimo

TITLE: Characterizing the structure and the function of the inner retina in non-athletes with multiple traumatic brain injuries

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.R. Klimo, E.A. Stern-Green, E. Day, E. Shelton, L. Jordan, M. Robich, C.E. McDaniel, D.A. VanNasdale, P.T. Yuhas, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Racine, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: As an accessible component of the central nervous system, the retina may be a site to objectively detect TBI-related neurodegeneration. We studied whether multiple TBIs alter the structure or the function of retinal ganglion cells in human subjects.

Methods: Adult case subjects with a history of at least two mild or moderate TBIs (n = 25, mean age ± SD = 32.2 ± 11.8 yrs, 52% female) and age- and sex-matched control subjects with no TBI history (n = 25, 32.5 ± 12.0 yrs, 52% female) were prospectively recruited from an optometry clinic. Full-field flash electroretinography recordings of the photopic negative response (PhNR) were made in accordance with the International Society for Clinical Electrophysiology of Vision. As a structural correlate, the thickness of the retinal nerve fiber layer (RNFL) was quantified using scanning laser polarimetry (SLP) and optical coherence tomography (OCT). All measurements were averaged between both eyes of each subject. Comparisons between the two groups were made using paired t-tests (significance threshold $p < 0.05$). Pearson correlation coefficient tests assessed linear relationships between RNFL thicknesses and PhNR parameters.

Results: Case subjects reported 4.1 ± 2.8 TBIs over a range of 0-41 years. The PhNR amplitude was not significantly different ($p = 0.11$) between the case (24.1 ± 5.1 μV) and the control (27.8 ± 9.1 μV) cohorts, and neither was the PhNR peak time (case: 69.9 ± 6.9 ms; control: 70.1 ± 8.9 ms; $p = 0.95$). Likewise, there was no significant difference between the two cohorts for global RNFL thickness measured by OCT (case: 96.6 ± 9.4 μm; control: 94.9 ± 7.0 μm; $p = 0.42$) or by SLP (case: 57.9 ± 5.7 nm; control: 58.2 ± 4.6 nm; $p = 0.80$). Within the case cohort, there were no significant correlations between OCT thickness and PhNR amplitude ($r = -0.15$, $p = 0.52$), OCT thickness and PhNR peak time ($r = -0.29$, $p = 0.19$), SLP thickness and PhNR amplitude ($r = -0.06$, $p = 0.80$), or SLP thickness and PhNR peak time ($r = -0.36$, $p = 0.10$).

Conclusions: There were no differences in PhNR parameters or in RNFL thicknesses between the case and the control cohorts. Previous works have shown that multiple TBIs elicit RNFL thickness changes in athletes, but our results showed no changes in a general population that suffered multiple TBIs. Future work will evaluate the structure and the function of the outer retina after multiple TBIs.

CONTROL ID: 3713814

SUBMITTER (NAME ONLY): John Gelles

TITLE: Correlation of Scleral Lens Parameters with Scheimpflug Tomography Metrics

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Gelles, D. Chung, S. Greenstein, B. Su, J. Nguyen, A. Singh, P. Hersh, The Cornea and Laser Eye Institute - CLEI Center for Keratoconus, Teaneck, New Jersey, UNITED STATES|J.D. Gelles, S. Greenstein, P. Hersh, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the relationship between base curve (BC) and sagittal depth (Sag) of scleral lenses (SL) with various tomography metrics in patients successfully fit with SL.

Methods: A retrospective chart review of patients successfully fit with SL (Zenlens, 16mm and 17mm, Bausch + Lomb SVP, Lancaster, NY and CustomStable, 17.8 and 16.8mm, Valley Contax, Springfield, OR) was performed. 76 eyes of 44 patients were included in the study. The average age was 45.92 ± 12.31. Of the 76 eyes, 74 were fit for irregular corneal conditions and 2 were fit for ocular surface disease. Final prescribed SL parameters, BC and Sag, and scheimpflug tomography (Pentacam HR, Oculus, Germany) metrics, including maximum keratometry (Kmax), mean keratometry (Kmean), flat keratometry (Kflat), steep keratometry (Ksteep), anterior chamber depth (ACD), white-to-white horizontal corneal diameter (WTW), and the inferior-superior (IS) ratio at the 6 mm zone, were obtained. To account for differences in labeled Sag between the SL designs, the lowest lens Sag was subtracted from the other lenses in their respective SL design cohort. The difference in μ was then consistent across SL designs for direct comparison. Statistical analysis for correlation of tomography metrics and final SL parameters was performed (SPSS, IBM Corporation, Armonk, NY).

Results: A positive correlation was found between the final prescribed Sag and ACD (R=0.70, p<.001), Kmax (R=0.61, p<.001), Kmean (R=0.54, p<.001), Kflat (R=0.45, p<.001), Ksteep (R=0.59, p<.001), and IS ratio (R=0.25, P=.03). No correlation was found between Sag and WTW (R=0.08, p=.5). No correlation was found between BC and ACD (R=0.14, p=.24), Kmax (R=0.11, p=.34), Kmean (R=0.12, p=.29), Kflat (R=0.06, p=.61), Ksteep (R= 0.1, p=.39), IS ratio (R=0.18, p=.12), or WTW (R=0.04, p=.73).

Conclusions: Of the tomographic metrics analyzed, ACD was most strongly correlated with SL Sag followed by a correlation with Ksteep and Kmax. Tomographic metrics were not correlated with SL BC, indicating BC is an independent variable. This data suggests ACD may be the best metric to aid in selecting diagnostic SL during the SL fitting process.

CONTROL ID: 3713815

SUBMITTER (NAME ONLY): Vahid Pourreza ghoushchi

TITLE: Effect of periodic defocus oscillations on contrast sensitivity

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Pourreza ghoushchi, J. Mompeán, P.M. Prieto, P. Artal, Laboratorio de Óptica, Universidad de Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To explore the resilience of the visual system to the blurring effect induced by defocus oscillations. This is determined by the loss in contrast sensitivity produced by sinusoidal oscillations in defocus with a range of amplitudes and temporal frequencies. The aim is to compare with natural conditions of accommodation microfluctuations.

Methods: Contrast sensitivity at 12 c/deg was measured monocularly in 5 young healthy emmetropic subjects through a tunable lens introducing sinusoidal oscillations of defocus around 0 D at 5, 15, and 25 Hz. Peak-to-peak oscillation amplitude varied from 0.15 D to 3 D. The visual stimulus was a Gabor patch at 3 m and a two-choice forced-choice protocol was used. Target presentations were randomized through temporal frequency, amplitude, and contrast (5 contrast values around and adjustment threshold determined in advance). The tunable lens was attached to an open-view Hartmann-Shack wave-front sensor (V. P. Ghoushchi et al., Biomed. Opt. Express 12, 3282-3295, 2021) measuring in real time, thus allowing a) verification of the subject's accommodative state, and b) confirmation of the amplitude and frequency of defocus oscillations generated by the lens.

Results: The figure illustrates the average contrast threshold as a function of amplitude for all subjects. Although there was some variability between subjects, contrast sensitivity was fairly constant despite the defocus oscillations introduced. Only for the fastest oscillations (25 Hz) and highest amplitude (+/-1.5 D) contrast sensitivity appears to suffer a significant degradation.

Conclusions: Our results show that the visual system is resilient to fluctuations in defocus, at least concerning contrast sensitivity tasks. The fact that contrast sensitivity only appears to fall for fast and large oscillations in defocus, suggests that the eye does not average blur and a short time with the image in or around focus is enough to detect the target. These results may have some implications in myopia control and in visual simulators based on oscillating defocus.

CONTROL ID: 3713816

SUBMITTER (NAME ONLY): Melina Cavichini Cordeiro

TITLE: Evaluating the durability of extended aflibercept treatment regimens in patients with resistant CNVs.

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Cavichini Cordeiro, V. Alex, F.P. Kalaw, S. Singh, L. Cheng, W.R. Freeman, Jacobs Retina Center at Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evaluating the efficacy of every 6-or-8-week aflibercept extension regimen in resistant Choroidal Neovascularization (CNV)s requiring monthly treatment.

Methods: This was a retrospective, cross-sectional study. Patients who visited the Retina clinic with a diagnosis of CNV due to AMD requiring escalating regimen and needing monthly aflibercept to control disease were reviewed. There were total of 60 eyes which were included. Subjects received either regular (low) dose aflibercept (A/L- 2 mg) or high dose aflibercept (A/H- 4 mg) injections every 4 weeks initially, until their macular Optical Coherence Tomography (OCT)s were dry, and they were then extended to either every 6-or-8-week injections. The durability of extended intervals was monitored by the reappearance of Intra- or Sub- Retinal Fluid (IRF/SRF) in OCTs which had completely dry macula at the start. Statistical analysis was done using Cox regression model.

Results: Analysis performed using dose regimen as a stratum, after adjusting for age and sex, revealed that the dose regimen (High Vs Regular) prior to extension was a significant predictor with high dose (4 mg) showing a longer time to relapse, $p < 0.04$. There was reduced hazard of recurrence (OR A/H vs. A/L = 0.507, $p= 0.0305$). Also, the longer the duration of monthly aflibercept before extension, the shorter the time to relapse, $p=0.0023$.

Conclusions: Resistant CNV requiring monthly aflibercept therapy could be successfully extended to every 6 - 8 weeks. Eyes which received high dose aflibercept injections as the extension regimen took longer to fail and had less disease relapse than the eyes on regular dose.

CONTROL ID: 3713817

SUBMITTER (NAME ONLY): Viet Nguyen-Minh

TITLE: The regulation of persistent activity in intrinsically photosensitive retinal ganglion cells

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.T. Nguyen-Minh, A.J. Emanuel, E.S. Milner, M.H. Do, Neurology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|V.T. Nguyen-Minh, A.J. Emanuel, E.S. Milner, M.H. Do, F.M. Kirby Neurobiology Center, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Persistent activity in the nervous system supports tasks that range from working memory to the encoding of eye position. Within the retina, it is a prominent feature of intrinsically photosensitive retinal ganglion cells (ipRGCs), which are vital for processes that include the regulation of circadian rhythms and sleep. IpRGCs respond directly to light using a receptor called melanopsin. Melanopsin's active state is stable and drives phototransduction for minutes even after illumination ceases. Thus, successive periods of illumination can increment the number of activated melanopsin molecules and the rate of persistent spike firing. Because small currents have large impacts on ipRGCs, the existence of graded persistent firing suggests a mechanism of precise control. We tested the hypothesis that persistent activity is controlled by negative feedback in melanopsin phototransduction.

Methods: We focused on ipRGCs of the M1 type, which are principal regulators of the master circadian clock and exhibit large, melanopsin-driven responses that are amenable to quantitative analysis. We identified these neurons in the ex vivo mouse retina using a fluorescent reporter and isolated their intrinsic responses with antagonists of synaptic transmission. We made patch-clamp electrophysiological recordings in voltage clamp and current clamp to examine the melanopsin-driven photocurrent and voltage change, respectively. We delivered optical stimuli to probe persistent responses and negative feedback. We altered negative feedback by manipulating Ca^{2+}, one of its mediators.

Results: We found that persistent photocurrent drove negative feedback, which was evident in response desensitization. When we suppressed the persistent photocurrent, by delivering light that depopulates melanopsin's active state, sensitivity increased for a subset of M1 ipRGCs. Acute removal of extracellular Ca^{2+}, which reduces negative feedback, increased the persistent photocurrent in a reversible manner.

Conclusions: Collectively, our experiments indicate that persistent activity in M1 ipRGC phototransduction recruits and is subject to negative feedback. The latter is mediated in part by Ca^{2+} influx. The balance of persistent activation and negative feedback varies across cells. In some cells, delivering light to suppress persistent activation produces a net increase in sensitivity, despite negative feedback produced by the light itself.

CONTROL ID: 3713818

SUBMITTER (NAME ONLY): Clare Bailey

TITLE: The impact of COVID-19 on visual acuity for nAMD patients treated with aflibercept in the UK

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bailey, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, Bristol, UNITED KINGDOM|M.H. Gruszka-Goh, P.H. Scanlon, Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, Gloucestershire, UNITED KINGDOM|A.J. Lotery, University Hospital Southampton NHS Foundation Trust, Southampton, Southampton, UNITED KINGDOM|R. Chhabra, Manchester Royal Eye Hospital, Manchester, Manchester, UNITED KINGDOM|H. Eleftheriadis, King's College London, London, London, UNITED KINGDOM|F. Ghanchi, Bradford Teaching Hospitals NHS Foundation Trust, Bradford, Bradford, UNITED KINGDOM|C. Jones, Norfolk and Norwich University Hospital, Norwich, Norfolk, UNITED KINGDOM|

Commercial Relationships Disclosure: Clare Bailey: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis;Code R (Recipient):Janssen;Code R (Recipient):Roche;Code R (Recipient):Boehringer;Code R (Recipient):Alimera Sciences | Marta Gruszka-Goh: Commercial Relationship(s);Code F (Financial Support):Bayer PLC | Andrew Lotery: Commercial Relationship: Code N (No Commercial Relationship) | Romi Chhabra: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis | Haralabos Eleftheriadis: Commercial Relationship(s);Code F (Financial Support):Bayer PLC;Code R (Recipient):Bayer PLC | Faruque Ghanchi: Commercial Relationship(s);Code R (Recipient):Bayer PLC;Code R (Recipient):Novartis;Code R (Recipient):Allergan;Code R (Recipient):Alimera;Code R (Recipient):Alcon;Code R (Recipient):Roche | Colin Jones: Commercial Relationship: Code N (No Commercial Relationship) | Peter Scanlon: Commercial Relationship(s);Code F (Financial Support):Bayer PLC;Code R (Recipient):Bayer PLC;Code R (Recipient):Topcon

ABSTRACT BODY:

Purpose: To assess the impact of COVID-19 on eyes treated for neovascular AMD.

Methods: Anonymized data from 21 UK centers were extracted from Medisoft for patients receiving treatment with aflibercept and VA data in the pre-covid baseline (01/10/19 to 31/03/20 n=8,313). Comparisons were made for period 1 (01/04/20 to 30/09/20 n=4,011) - lockdown following RCOphth Medical Retinal Management Plan during COVID-19, period 2 (01/10/20 to 31/03/21 n=4,551) - intermittent lockdown following updated RCOphth COVID-19 guidelines, and period 3 (01/04/21 to 30/09/21 n=2,630) -easing COVID-19 restrictions.

VA change was compared for baseline VA, <7 vs. ≥7 injections before period 1 and for eyes losing ≥5 letter in period 1.

Results: The mean change in VA for eyes with a baseline VA of ≤35 ETDRS letters was +0.7, +0.1 and -1.6 letters, 36-55 letters was -3.0, -1.2 and -1.3 letters, 56-75 letters was -2.1, -1.1 and -1.5, and >75 letters was -4.3, -0.7 and -0.4 letters in periods 1, 2 and 3 respectively.

The median VA change was zero letters for all baseline VA groups and time periods except for the >75 letter group in period 1 (median 2 letter loss).

The mean change in VA from baseline for eyes with <7 injections before period 1, was -2.0, -0.6 and -1.2 letters from 2,083, 2,465 and 1,420 eyes in periods 1, 2 and 3, and ≥7 injections before period 1, was -2.9 from 1,928 eyes in period 1 and -1.3 letters from 2,086 and 1,210 eyes in periods 2 and 3. For both groups and time periods the median VA change was zero letters.

For eyes that lost ≥5 ETDRS letters before period 1 the mean change in VA for eyes receiving no injections was +2.3 letters (n=155) and -3.5 letters (n=107), 1-3 injections was +1.4 letters (n=740) and -1.3 letters (n=340), and >3 injections was +2.3 letters (n=199) and -0.8 letters (n=122) in periods 2 & 3 respectively.

The median VA change was zero letters for all time periods and injection number groups except for >3 injection eyes in period 2 (median 3 letter gain) and no injection eyes in period 3 (median 1 letter loss).

Conclusions: In period 1, a small VA loss was experienced by many eyes dependent on baseline VA. Similar VA changes were present for eyes receiving <7 and ≥7 injections before period 1. For eyes that lost ≥5 ETDRS letters during period 1, many had visual gain with more improvement linked to receiving more injections in period 2, falling back in period 3.

CONTROL ID: 3713819

SUBMITTER (NAME ONLY): Brent Dickinson

TITLE: VRDN-002, A Second-Generation Insulin Like Growth Factor-1 Receptor (IGF-1R) Inhibitory Antibody for Thyroid Eye Disease: Preclinical Pharmacokinetics and Clinical Promise

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Dickinson, Viridian Therapeutics Inc, Waltham, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Brent Dickinson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: VRDN-002 is a novel anti-IGF-1R monoclonal antibody intended for treatment of Thyroid Eye Disease (TED). It is engineered to incorporate Fc modifications for half-life extension to enable convenient dosing. TED is most prevalent in patients with Graves' Disease and is driven by Thyroid Stimulating Hormone Receptor (TSHR) agonistic autoantibodies and crosstalk between TSHR and IGF-1R. We sought to compare the pharmacokinetic (PK) parameters of VRDN-002 in cynomolgus monkeys to the marketed IGF-1R antibody, teprotumumab, and to estimate potential human exposures for various dosing paradigms.

Methods: VRDN-002 was administered to cynomolgus monkeys by 30 min intravenous (IV) infusion at 2, 10, and 50 mg/kg, and by subcutaneous (SC) injection at 2 and 10 mg/kg. Teprotumumab 10 mg/kg was also administered by 30 min IV infusion. PK samples were collected at 30 min, 2 and 8 hrs, and 1, 3, 7, 10, 14, 21, 28, 35, 42, 49, and 56 days. VRDN-002 and Teprotumumab levels in serum were measured using a human IgG specific ELISA. Data were analyzed using the WinNonlin non-compartmental model. In addition, a semi-mechanistic model incorporating target-mediated drug disposition (TMDD) was constructed based on a population pharmacokinetic model of teprotumumab in TED patients, as well as VRDN-002 and teprotumumab PK in NHPs. The model was used to estimate human PK for VRDN-002.

Results: VRDN-002 PK administered by IV infusion was approximately linear between 10 and 50 mg/kg doses, suggesting TMDD was saturated at these doses. At 10 mg/kg, VRDN-002 half-life and AUC_{inf} were 14 ± 4 days and 2,300 ± 312 µg.day/mL, respectively, vs. 6.4 ± 0.3 days and 779 ± 79 µg.day/mL for teprotumumab. Bioavailability of VRDN-002 administered via SC injection was 62%. Human exposure estimates of VRDN-002 for various dosing regimens were generated from the semi-mechanistic model.

Conclusions: VRDN-002 demonstrated a desirable PK profile in non-human primates, suggesting potential as a novel therapeutic monoclonal antibody for the treatment of TED. The prolonged half-life of VRDN-002 may enable lower frequency of IV infusion and/or low-volume SC injection; each possibility awaits clinical confirmation.

CONTROL ID: 3713823

SUBMITTER (NAME ONLY): Betul Bayraktutar

TITLE: Efficacy of Intravenous Immunoglobulin (IVIG) Treatment in Patients with Neuropathic Corneal Pain

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Bayraktutar, P. Hamrah, Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|K. Farhad, Department of Neurology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|O. Soto, Department of Neurology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neuropathic pain is caused by an injury to the somatosensorial nervous system and can affect the cornea. Immune-mediated mechanisms have been defined in the pathophysiology and intravenous immunoglobulin (IVIG) has been reported to be an efficient treatment in immune-mediated small fiber neuropathy (SFN) patients. We aimed to evaluate the efficacy of IVIG treatment in patients with neuropathic corneal pain (NCP).

Methods: Medical records of patients who were diagnosed with NCP and SFN based on clinical, in vivo corneal confocal microscopic, and positive skin biopsy findings, and were initiated with IVIG treatment were evaluated. All patients underwent detailed serological evaluation for auto-/dyimmune antibodies (Abs). Demographic features of patients, corneal fluorescein staining (CFS) scores (Oxford scale), ocular pain assessment survey (OPAS) scores, and ocular surface disease index (OSDI) scores were reviewed at baseline and 6-months treatment follow-up.

Results: Fourteen NCP patients who were refractory to topical and systemic therapies were included. The mean age of patients was 43.2±13.3 years. Twelve patients had at least one positive auto-/dysimmne Ab. Two patients had negative results for Ab screening while presenting strong clinical suspicion for potential underlying autoimmunity. Ocular surface staining was not detected in 13 of the patients, 1 had +3 CFS. Four patients discontinued the treatment before 6 months (2 patients after 1month and 2 patients after 3 months) due to side effects (headache (n=2) and systemic Staphylococcal infection (n=1)) or insurance denial (n=1). In the remaining 10 patients, the mean pain intensity score (scale 0-10) in the last 24 hours and in the last 2 weeks improved from 5.4±0.8 to 3.6±0.9 (p=0.004) and from 5.0±0.9 to 3.7±0.9 (p=0.02), respectively. The impact of pain on quality of life reduced significantly in the follow-up visit (from 6.0±2.9 to 4.3±2.9, p=0.03). Overall, patients reported a mean of 32.5% eye pain relief compared to their baseline visit. The mean OSDI score (0-100) did not show significant changes between visits (58.3±25.6 vs 56.2±24.0, p=0.46).

Conclusions: IVIG treatment provides significant pain relief and improves the quality of life in NCP patients. Therefore, in selected cases, IVIG treatment seems to be promising in NCP management, when refractory to other therapies.

CONTROL ID: 3713824

SUBMITTER (NAME ONLY): Nihar Bhattacharyya

TITLE: CTG18.1-mediated Fuchs endothelial corneal dystrophy: characterizing biomarkers of pathogenicity in patients with rare intermediate triplet repeat expansions

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Bhattacharyya, A. Sadan, C. Zarouchlioti, N.J. Hafford-Tear, K. Muthusamy, A.J. Hardcastle, S. Tuft, A.E. Davidson, Institute of Ophthalmology, University College London Faculty of Brain Sciences, London, London, UNITED KINGDOM|K. Muthusamy, S. Tuft, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|P. Skalicka, P. Liskova, Univerzita Karlova, Praha, CZECHIA|

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ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is a degenerative disease commonly associated with a CTG repeat expansion (termed CTG18.1) situated within an intron of the transcription factor encoding gene TCF4. CTG18.1 typically comprises <30 repeats in unaffected or non-CTG18.1-mediated FECD individuals, whereas the majority of FECD patients have a repeat length of ≥50 copies. It is unknown why repeat lengths within the 30-49 range are so rarely detected and if expansions within this range induce defined biomarkers of CTG18.1-expansion mediated FECD (e.g. RNA foci). Here we aim to describe FECD patients within our updated FECD cohort with intermediate repeat lengths (30-49) and, when possible, investigate biomarkers of disease within their corneal endothelial cells (CECs).

Methods: Genomic DNA was extracted from blood samples taken from FECD patients in the UK and the Czech Republic (n=930) and genotyped for CTG18.1-repeat length using short tandem repeat PCR and triplet-primed PCR. Concurrently, primary CECs were cultured following Descemet membrane endothelial keratoplasty (DMEK) in select FECD patients. CECs were probed for repeat containing RNA foci via fluorescence in situ hybridization (FISH) and foci distributions were quantified.

Results: Out of 930 FECD patients, 730 were expansion positive with a CTG18.1 repeat length ≥50 while 186 patients had a repeat length <30 (Figure 1). CTG18.1 repeat length displays a bimodal distribution with only 14 patients with a repeat length between 30-49 (mean age = 65; 9/5 female/male ratio). Primary CECs cultured from a FECD patient within this group expressed RNA foci, but with atypical distribution.

Conclusions: Only 1.5% (14/930) of FECD patients in our cohort have an intermediate CTG18.1 repeat genotype. All cases investigated within this group to date display biomarkers of CTG18.1 expansion-mediated disease within their CECs. However, RNA foci distribution appears abnormal when compared to FECD patients with ≥50 repeats. This suggests a CTG18.1 founder allele length of between 30-49 repeats is sufficient for foci formation but can influence the frequency of RNA foci in CECs and their likely downstream pathogenic effects.

CONTROL ID: 3713826

SUBMITTER (NAME ONLY): Jesse Ward

TITLE: Deep Learning Assisted Quantification of Neovascular Lesions with Optical Coherence Tomography Angiography (OCT-A)

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Ward, R. Slater, J. Pak, R. Linderman, R. Voland, R. Channa, B.A. Blodi, A. Domalpally, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: OCT-A is a relatively new imaging modality allowing noninvasive visualization of macular neovascularization (MNV) in neovascular age-related macular degeneration (nAMD). Grader assessment of MNV area includes annotations on the angiogram using properly segmented OCT-A scans within defined slabs. MNV area is delineated after a comprehensive examination of the cube scan and visualization of flow in areas of retinal pigment epithelial detachment with or without a visible network on the angiogram. To reduce burden on human resources and improve efficiency, we developed an automated, deep learning (DL) algorithm for quantitative assessment of MNV area from OCT-A.

Methods: Training dataset included planimetry annotations of MNV area by multiple graders from 6x6mm OCT-A scans of 44 eyes generating a total of 104 lesion annotations. Screenshots of the annotated angiograms were used for training a U-Net DL model with a ResNet backbone for binary image segmentation. Predictions made by the algorithm were fitted with a binary mask to define borders and area measurements. As the images were of a fixed sized, pixel counts of mask sizes were used to measure predicted masked area. Validation dataset included 28 OCT-A for comparison of grader annotation with DL predictions using area measurements and Dice Similarity Coefficient (DSC).

Results: Mean difference in MNV area between graders was $0mm^2$ (95% CI -1.12 to 1.12). Mean difference in MNV area between the DL algorithm and grader was $0mm^2$ (95% CI -4.07 to 4.07) with an intra-class correlation of 0.731. Mean DSC between DL algorithm and grader was 0.45 +/- 0.26. Examination of OCT-A annotations with DSC < 0.6 (16 images) showed quilting artifacts and absence of MNV network on the angiogram.

Conclusions: There is a moderate correlation between DL quantification of MNV lesions and graders' area measurements using OCTA. It is important to note that the algorithm's decision is limited by the angiogram whereas the grader has access to structural b-scans and flow data. This study shows a very promising trajectory for the use of DL in the quantitative analysis of MNV lesions.

CONTROL ID: 3713827

SUBMITTER (NAME ONLY): Alyssa Spiller

TITLE: Refractive outcomes after primary bevacizumab followed by laser versus primary laser alone for Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Spiller, L. Verkuil, B. Forbes, G. Binenbaum, Ophthalmology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|Y. Yu, G. Ying, G. Binenbaum, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Children with severe retinopathy of prematurity (ROP) commonly develop myopia or high myopia. One proposed benefit of intravitreal bevacizumab (IVB) over laser is decreased myopia; however, many IVB eyes are later treated with laser. We sought to compare prevalence of myopia and high myopia after primary IVB followed by laser photocoagulation (VEGF/LASER) to primary laser (LASER).

Methods: Retrospective cohort of infants who had VEGF/LASER or LASER for Type 1 ROP and cycloplegic refraction at age 6-30 months. Primary outcomes were prevalence of myopic (minimum -1D) and highly myopic (minimum -5D) spherical equivalent refractive error by eye.

Results: 28 eyes (15 infants) had VEGF/LASER at mean PMA weeks 33.8/45.2), 297 eyes (151 infants) had LASER at PMA 37.7; Refractions were at mean 19 months post-treatment. Two groups were similar in myopia (46.4% VEGF/LASER, 43.8% LASER,p=0.23) and high myopia (14.3% VEGF/LASER, 16.2% LASER eyes,p=0.29). Subgroup analysis for zone I at first treatment also showed no difference (myopia 64.3% VEGF/LASER, 67.9% LASER, p=0.73); high myopia (14.3% VEGF/LASER, 37.5% LASER, p=0.22). Among all eyes, total laser spots was associated with myopia (aOR 1.07 per100 spots increase, 95% CI 1.03-1.12) and high myopia (aOR 1.06, 95% CI 1.01-1.12), but spots did not differ among treatment groups (mean 2044 VEGF/LASER, 1857 LASER, p=0.60).

Conclusions: The prevalence of myopia and high myopia did not differ between VEGF/LASER and LASER. Though more laser spots are associated with higher risk of myopia, spot counts were not lower when laser followed primary IVB.

CONTROL ID: 3713830

SUBMITTER (NAME ONLY): SHRUTHI KARNAM

TITLE: Dysregulation of Neuroprotective Lipoxin Pathways in the Mouse Retina Following Silicon Oil-Induced Ocular Hypertension

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. KARNAM, S. Maurya, E. Ng, L. Yang, E. Wang, K. Gronert, J.G. Flanagan, Herbert Wertheim School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently proposed that lipoxins are synthesized in the inner retina, are downregulated following acute and chronic injury, and that restoring their function is neuroprotective. In this study, we characterize the cell-specific regulation and functional expression of lipoxin pathways in response to ocular hypertension (OHT) induced injury to the retina.

Methods: OHT was induced in the C57BL/6J mice by injection of silicone oil (SO) in the anterior chamber of the eye. In the contralateral eye, sterile PBS was injected and served as the control. Intraocular pressure (IOP) was measured weekly in both eyes and mice were maintained for 10 weeks (n=48). At weeks 4, 8, and 10, mice were euthanized, and the retina from both eyes was harvested for qRT-PCR and HPLC/LC/MS/MS-based lipidomic analysis. For cell-specific gene expression of Alox5, Alox15, and lipoxin receptors (Fpr2 and Fpr3), RNAscope in-situ hybridization was performed. GFAP and RBPMS expression were assessed by immunofluorescence of cryosections.

Results: Lipidomic analysis of 4-week retinas showed changes in the activity of the 15-LOX pathway (15HETE and 17HDHA) in the SO injected group when compared with the PBS injected group and age-matched controls. qRT-PCR analysis revealed a significant up-regulation of Alox15, Fpr1, Fpr2, and Fpr3 genes (>2.5-fold induction) at 4, 8, and 10 weeks and a significant down-regulation of Alox5 gene ($p<0.05$) at 8 weeks after SO injection when compared with the PBS injected eyes. Interestingly, this upregulation of Alox15 (~2-fold, $p<0.05$), Fpr1, Fpr2, and Fpr3 genes were also observed in 8-week IOP-induced Alox5 KO mice. RNAscope data showed that Alox5, Alox15, Fpr2, and Fpr3 were localized in GCL along with INL and ONL of the retina and expressed in the optic nerve. At 10 weeks, loss of RGCs was observed as indicated by the expression of RBPMS, and induced GFAP expression was seen in the SO induced retinal sections (including muller glial activation) when compared with the control.

Conclusions: We demonstrate profound dysregulation of the lipoxin pathway in response to induced OHT, further confirming our earlier findings of a potential and novel mechanism for RGC death. Moreover, the lipoxin pathway is expressed in the optic nerve, which provides evidence that this neuroprotective pathway role extends beyond the retina.

CONTROL ID: 3713832

SUBMITTER (NAME ONLY): Mohammed Rigi

TITLE: Keratoconic eyes have reduced collagen XII in Bowman's layer

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Rigi, H. Son, A.S. Jun, C. Eberhart, U. Soiberman, Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal biomechanical failure is the hallmark of keratoconus, a common corneal ectasia, however the cause of this failure remains elusive. Collagen type XII (COL12A1), which localizes to Bowman's layer (BL), is thought to interact with collagen type I and function in stress bearing areas, such as BL. A recent genome-wide association study of keratoconus patients has identified a unique missense mutation in COL12A1. Similarly, proteomic, transcriptomic and immunihistochemical studies of COL12A1 in keratoconus suggest reduced expression at the level of the corneal epithelium and its basement membrane. This study aims to better characterize collagen XII expression in keratoconus corneas compared to non-keratoconus controls.

Methods: Full-thickness corneas obtained from 61 keratoconus cases during keratoplasty and 18 non-keratoconus autopsy were used. Tissue microarrays were constructed from corneal keratoconus and non-keratoconus cases and stained with an antibody to collagen XII alpha 1 (Novus Biologicals, Centennial, CO) at a 1:50 dilution. Four skilled observers (MR, HSS, CGE, USS) analyzed collagen XII stained samples and scores were reached by consensus. Corneal epithelium and stroma were evaluated for extent (in percentages by decile; i.e. 0%, 10%, 20%) and intensity (0-3) of staining, with an overall score obtained by multiplying the two. The epithelial basement membrane (BM) and Bowman's layer were scored for intensity (0-3) of staining alone. A two-tailed Mann-Whitney test was used to compare keratoconus staining scores to controls and a p-value≤0.05 was considered statistically significant.

Results: Median (and interquartile range) staining score in BL was 1 (0.25-1) in controls and 0 (0-0) in keratoconus ($p<0.0001$). Median BM staining score was 2 (1-2.75) in controls and 0 (0-1) in keratoconus ($p<0.0001$). Median epithelial staining score was 1.2 (0.7-2.1) in controls and 0.8 (0.2-1.4) in keratoconus ($p<0.06$). Finally, median stromal staining score was 0.8 (0.75-1.6) in controls and 0.1 (0.1-0.3) in keratoconus ($p<0.0001$).

Conclusions: Collagen type XII expression is reduced in BL, corneal BM and stroma in keratoconus. This loss of expression suggests a role in the pathogenesis of keratoconus, given the putative protective role of collagen XII in stress bearing areas. Further studies are necessary to investigate the mechanisms that lead to collagen type XII dysregulation in keratoconus.

CONTROL ID: 3713833

SUBMITTER (NAME ONLY): David Salom

TITLE: Rhodopsin's Meta-I conformation is stabilized by nanobody binding to its intradiscal side

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Salom, A. Wu, P.D. Kiser, K. Palczewski, C. Sander, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|K. Palczewski, Physiology and Biophysics2, University of California Irvine, Irvine, California, UNITED STATES|E. Pardon, J. Steyaert, Structural Biology Brussels, Vrije Universiteit Brussel, Brussels, BELGIUM|E. Pardon, J. Steyaert, VIB-VUB Center for Structural Biology, Brussels, BELGIUM|

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ABSTRACT BODY:

Purpose: Rhodopsin is the class A archetypical G-protein-coupled receptor (GPCR). Despite the progress in biophysical characterization of rhodopsin at different points of the photo-activation process, the first stages of this process are still poorly understood at the structural level. We have developed several llama antibodies (nanobodies, Nbs) as tools to facilitate the structural characterization of rhodopsin, especially in its early activation state, Meta-I.

Methods: Several nanobodies that bind rhodopsin were obtained upon immunization of llamas with bovine rod outer segments. UV-visible spectroscopy was used to characterize the conformational/spectral changes of rhodopsin upon binding of Nbs. Finally, we performed trials for the co-crystallization of several nanobodies with ground state rhodopsin, activated rhodopsin and apo-rhodopsin (opsin).

Results: Here we present the crystal structures of a nanobody (Nb2) in complex with ground-state bovine rhodopsin, as well as Nb2 in complex with opsin. The binding site of Nb2 includes rhodopsin's N-terminus and extracellular loops, ECL2 and ECL3. Whereas rhodopsin's structure in the ground-state rhodopsin/Nb2 complex is virtually identical to that of rhodopsin by itself, Nb2 binding induces a dramatic structural change in opsin, trapping it in a conformation similar to that of ground-state rhodopsin. The crystal lattice is maintained by Nb2/bRho, bRho/bRho and Nb2/Nb2 protein contacts that allow the small conformational changes required by rhodopsin to transition from the ground state to Meta-I. In solution, several of these nanobodies bind to photoactivated, deprotonated rhodopsin (Meta-II), shifting the equilibrium towards a protonated Schiff base state corresponding to the Meta-I conformation.

Conclusions: We have developed several nanobodies that shift the equilibrium of photoactivated rhodopsin towards the elusive Meta-I state. These nanobodies might be a useful tool to facilitate the crystallization of wild type rhodopsin in different conformational states, and/or bound to different ligands. Current efforts include solving the crystal structure of the Meta-I rhodopsin/Nb2 complex.

CONTROL ID: 3713836

SUBMITTER (NAME ONLY): Michael Dennis

TITLE: REDD1 promotes diabetes-induced retinal inflammation by sustaining GSK3β-dependent NF-κB activation

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.D. Dennis, S. Sunilkumar, A. Toro, C. McCurry, W. Miller, Cellular and Molecular Physiology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|M.D. Dennis, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Clinical studies support a role for the stress response protein regulated in DNA damage 1 (REDD1) in diabetes-induced visual dysfunction. REDD1 was recently shown to directly promote inflammatory signaling in myeloid cells. Retinal inflammation is a significant contributor to the development and progression of diabetic retinopathy (DR). Thus, we investigated the role of REDD1 in development of retinal inflammation in diabetes.

Methods: $REDD1^{+/+}$ and $REDD1^{-/-}$ mice were administered streptozotocin to induce diabetes. Retinas were isolated after 16 weeks of diabetes and analyzed for protein and RNA expression by western blot and qPCR, respectively. Macrophages were visualized in retinal sections by immunofluorescence. Activity of the transcription factor nuclear factor-kappa B (NF-κB) was measured by luciferase assay. Similar analyses were performed on wild-type and REDD1 knockout human MIO-M1 retinal cell cultures after exposure to hyperglycemic conditions, inflammatory cytokines, or genetic REDD1 induction.

Results: Enhanced REDD1 expression was observed in the retina of diabetic $REDD1^{+/+}$ mice in association with increased pro-inflammatory gene expression and macrophage infiltration of the inner retina. Compared to diabetic $REDD1^{+/+}$ mice, inflammatory markers and macrophage infiltration were attenuated in the retina of diabetic $REDD1^{-/-}$ mice. In retinal cell cultures, REDD1 deletion prevented hyperglycemia- and TNFα-induced pro-inflammatory gene expression. REDD1 was not sufficient to promote inflammation, but rather sustained activation of NF-κB in cells exposed to either hyperglycemic conditions or TNFα. In REDD1-deficient cells, GSK3β phosphorylation and Nrf2 activation was observed in association with NF-κB suppression. Consistent with prior studies, REDD1 deletion prevented the development of oxidative stress in cells exposed to hyperglycemic conditions, and Nrf2 knockdown prevented the effect. However, Nrf2 knockdown was not sufficient to restore NF-κB signaling in REDD1-deficient cells exposed to hyperglycemic conditions. In contrast, inhibition of GSK3β suppressed NF-κB activation in cells exposed to hyperglycemic conditions.

Conclusions: The findings provide new insight into how diabetes promotes retinal inflammation and support that REDD1 acts independently of Nrf2 to suppress inflammatory signaling via GSK3β-dependent activation of NF-κB.

CONTROL ID: 3713837

SUBMITTER (NAME ONLY): Miao Zhang

TITLE: A hierarchical optical coherence tomography annotation workflow with crowds and medical experts

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhang, M. Tehrani, N. Movva, M. Hejrati, Early Clinical Development Informatics, Genentech Inc, South San Francisco, California, UNITED STATES|S.S. Gao, S. Mirsharif, Clinical Imaging Group, Genentech Inc, South San Francisco, California, UNITED STATES|V. Steffen, Data and Statistical Sciences, Genentech Inc, South San Francisco, California, UNITED STATES|Z. Wu, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|Z. Wu, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|T. Leng, Byers Eye Institute at Stanford, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|H. Chen, Early Clinical Development, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a heavy burden to annotate clinical images due to the cost and availability of medical experts. To address this problem, we proposed a hierarchical annotation workflow in which medical experts review aggregated crowdsourced annotations, using dense annotation of optical coherence tomography (OCT) images from age-related macular degeneration (AMD) patients as an example.

Methods: Annotation was performed on a cloud-based platform (Labelbox) which distributed images to remote crowds and medical experts. OCT B-scans with ≥ 9 averages from 20x20° volume scans of AMD patients were randomly selected. Two medical experts annotated 25 representative B-scans with rich pathology. In a training session, 27 labellers read through an annotation guideline and practiced on 15 of the B-scans. B-scans with color-coded agreements and disagreements were presented to the crowd, visualizing their discrepancy to the expert annotations. Performance, compared to the medical experts' annotations, was measured quantitatively by a weighted and adaptively normalized mean intersection over union (IOU) for each of the annotated structures (WANI). The top 10 performers on the remaining 10 OCT B-scans (test session, Fig. 1. Left) were selected for larger batches of annotation work. Additional 897 B-scans were labeled by 5 labellers each. Simultaneous truth and performance level estimation (STAPLE) was applied to aggregate the 5 copies of crowd labels. Medical experts qualitatively reviewed the STAPLE result to identify common mistakes to further train the crowd. The crowd and experts annotated another 8 representative B-scans in a follow-up analysis session (Fig. 1. Right).

Results: STAPLE results show above average IOU in individual anatomic structures, while outperforming all crowd labellers in WANI, though lower than experts. On average, it took experts 13.5 minutes to annotate one B-scan in contrast to 23.8 seconds to review one STAPLE result. Improvements in STAPLE WANI were observed in the follow-up session, as the crowd gained experience and further trained on the feedback from experts.

Conclusions: The proposed hierarchical annotation workflow with crowds and medical experts could reduce the burden on medical experts in extensive clinical annotation tasks.

CONTROL ID: 3713838

SUBMITTER (NAME ONLY): Soohyun Kim

TITLE: Comparison of longitudinal changes in chromatic pupillometry in normal dogs and dogs with sudden acquired retinal degeneration syndrome

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kim, A.E. Cooper, D.J. Maggs, A. Marangakis, T. Nguyen, M.J. Motta, S.M. Thomasy, Department of Veterinary Surgical and Radiological Science, School of Veterinary Medicine, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine chromatic pupillary light reflex (PLR) parameters in dogs with and without sudden acquired retinal degeneration syndrome (SARDS) over time.

Methods: Five dogs with acute vision loss within the previous 6 months, a normal fundus, and a flat-line electroretinogram (ERG) were diagnosed with SARDS; 5 age-matched sighted dogs with a normal fundus and ERG served as controls. Both groups underwent red (630nm), blue (480nm), and white light stimulation using a chromatic light source (Melan-100®) adapted for video pupillometry. The tests were repeated for the SARDS-affected dogs at 6 months (6m) and 1 year (1y) post-diagnosis. Pupil size was estimated using ImageJ software, and degree, latency, and velocity of pupil constriction were calculated.

Results: SARDS-affected dogs had significantly reduced ($P<0.001$) pupil constriction in response to red (8.6±7.1% at 6m and 5.7±6.3% at 1y) and white (37.2±21.3% at 6m and 32.1±7.5% at 1y) light vs. control dogs [red: 70.9±14.5% ($P<0.001$); white: 62.7±11.7%], but no difference in response to blue light (77.1±6.8% at 6m and 77.3±9.3% at 1y of SARDS-affected dogs vs. 88.5±5.0% of control dogs; $P=0.666$). Pupil constriction latency in response to red (5.8±4.9s at 6m and 9.1±2.2s at 1y) and white light (0.7±0.4s at 6m and 3.2±3.7s at 1y) was significantly longer in SARDS-affected dogs compared to controls [red: 0.5±0.1s, $P<0.001$ and white: 0.4±0.1s, $P=0.17$], but both groups responded similarly to blue light. SARDS-affected dogs >1 year from diagnosis responded more slowly to white light than did controls or those SARDS-affected dogs within 6 months of diagnosis. Velocity of pupil constriction did not significantly differ between affected dogs and controls for blue ($P=0.946$), or white ($P=0.292$) light at any of the time points tested. Velocity of pupil constriction in response to red light (0.00016±0.0002mm/ms) was significantly slower in SARDS-affected dogs at 6-month post-diagnosis compared to age-matched controls (0.0013±0.0005mm/ms; $P=0.006$).

Conclusions: The Melan-100® can be adapted for video capture pupillometry in unsedated dogs. When compared to normal age-matched control dogs, SARDS-affected dogs demonstrated a decreased degree and prolonged latency of pupil constriction in response to both red and white light, and these differences became more pronounced with increased time from diagnosis.

CONTROL ID: 3713839

SUBMITTER (NAME ONLY): Chris Bradley

TITLE: Determining the Accuracy of Rates of RNFL Loss Measured by Peripapillary OCT

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bradley, J. Yohannan, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|K. Hou, P. Herbert, M. Unberath, Malone Center of Engineering in Healthcare, Johns Hopkins University, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the rates of retinal nerve fiber layer (RNFL) loss in a large population of glaucoma patients and to understand how the accuracy of detecting certain rates of RNFL loss varies based on the frequency and temporal spacing on OCT exams.

Methods: Measurements of RNFL thickness using Zeiss OCT were obtained at a tertiary glaucoma practice from glaucoma and glaucoma suspect patients who were 18 years or older from April 1st, 2013 to July 30th, 2021. Only eyes with at least 5 measurements of superior and inferior RNFL thickness ≥ 50 m and signal strength (SS) ≥ 6 were included in the analysis.

Linear regression was performed on data from each eye and population level rates of RNFL change were computed. Simulated data were then generated from the regression slopes and residuals. The i th simulated data point from the k th eye had the form $y_{i,k} = \beta_k + \varepsilon_{i,k}$ where $\varepsilon_{i,k}$ was randomly chosen from the residuals of all eyes whose rates of worsening were within 0.25 µm/yr of β_k. For each eye, M data points were generated within time period T under two conditions: in the "evenly spread" condition, simulated data were evenly spread out over time; in the "clustered" condition they were clustered (half and half) at the endpoints. The percentage of cases where the true slope was at or below the observed slope was calculated for different M and T.

Results: 12,150 eyes from 7,392 patients satisfied our inclusion criteria. The mean (SD) time between measurements was 403 (180) days. Figure 1 shows the rates of worsening, SS, and baseline RNFL thickness of our sample. The median, 75th and 90th percentile rates of worsening are –0.39, –1.09, and –2.35 µm/yr; the mean (SD) SS is 8.0 (1.0); and the mean (SD) baseline RNFL thickness is 87.50 (32.08) µm. Figure 2 shows the percentage of cases (y-axis) where an observed rate of worsening (x-axis) came from an eye whose actual rate of worsening was at least as severe as the observed rate. Clustering measurements and expanding the time interval between measurements improved accuracy, with the lowest accuracy in the [–3, –2] µm/yr range.

Conclusions: Our analysis shows that detecting rapid worsening (90th percentile) on OCT at 70% correct requires ~13 measurements clustered at the endpoints of a 2-year period. Current clinical practice is 1-2 OCT scans per year.

CONTROL ID: 3713840

SUBMITTER (NAME ONLY): Meenakshi Maurya

TITLE: REV-ERBα deficiency accelerates age-related synaptic remodeling in mouse retina

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Maurya, C. Liu, S. Huang, F. Yemanyi, K. Bora, A.K. Blomfield, J. Chen, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Synaptic remodeling occurs during aging in both humans and mice, leading to neuronal dysfunction. Age-related alterations in the outer retinal synapses have been investigated as a model system to study age-dependent neuronal and synaptic modifications such as in AMD. The role of REV-ERBα has been reported in synaptic strengthening in mice model of Alzheimer's disease. REV-ERBα, a nuclear receptor and transcription factor, regulates multiple biological processes including circadian rhythm, metabolism and neuronal function. The present study aimed to explore whether REV-ERBα regulates age-related retinal synaptic alterations using REV-ERBα knockout (KO) mice as a model.

Methods: 5- and 11- month-old wild-type (WT) and systemic REV-ERBα KO mice were used. Retinal cross sections were immunostained with rod bipolar cell marker Protein kinase C (PKC-α) and pre-synaptic protein synaptophysin antibody to assess synaptic alterations. The number and length of ectopic rod bipolar cell dendrite sprouts were quantified. REV-ERBα localization was analyzed with REV-ERBα antibody immunostaining in WT retinas and with β-Gal reporter staining in REV-ERBα KO retinas. Expression of REV-ERBα in retinal cells was assessed using an online single cell RNA sequencing (scRNA seq) database. RT-qPCR was performed in WT and REV-ERBα KO retinas to evaluate expression of genes involved in cellular energy homeostasis and axonal growth.

Results: REV-ERBα was localized in both outer and inner nuclear layer with REV-ERBα immunostaining and β-Gal reporter staining. scRNA seq analysis indicated expression of REV-ERBα in both rod photoreceptors and bipolar cells. Compared with WT, aging REV-ERBα KO retinas showed an accelerated retraction of rod axons accompanied with aberrant bipolar cell processes extending into the photoreceptor layer by synaptophysin and PKC-α co-localization. Both the number and length of ectopic rod bipolar cell dendrite sprouts in REV-ERBα KO retinas were significantly increased compared to WT in 5- and 11-months old mice. REV-ERBα KO retinas exhibited significantly decreased expression of multiple genes involved in cellular energy and metabolic regulation.

Conclusions: Our findings suggest that genetic loss of REV-ERBα accelerates age-related synaptic remodeling in the outer retina, possibly through modulating expression of genes controlling cellular energy and metabolism to mediate axonal retraction and dendrite growth.

CONTROL ID: 3713842
SUBMITTER (NAME ONLY): Vincent Siu
TITLE: COVID-19 and SARS-CoV-2 Detection in the Conjunctiva: Meta Analysis
SESSION TITLE: Ocular surface health and conjunctiva
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: V. Siu, Washington University in St Louis, St Louis, Missouri, UNITED STATES|J. Alanzalon, University of California Santa Cruz, Santa Cruz, California, UNITED STATES|D. Chien, University of California Los Angeles, Los Angeles, California, UNITED STATES|W. Zhao, University of California Davis, Davis, California, UNITED STATES|G. Wu, UCSF School of Medicine, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: 10% of COVID patients have eye symptoms[1]. Conjunctivitis is the most reported ocular symptom, being reported in 88.8% of all pts with eye symptoms[1].

Literature search for SARS-CoV-2 presence in the conjunctiva of COVID patients with conjunctivitis.
Methods: Review of articles dated 2020-2021 for conjunctival swabs in COVID-19 positive conjunctivitis patients using search terms: “COVID conjunctival swabs,” “COVID conjunctivitis,” and “COVID and eyes”. Search was done on Google Scholar and PubMed. Cases were excluded if patients did not have conjunctivitis or if a positive conjunctival swab was found in a patient with no clinical or lab-confirmed COVID diagnosis.
Results: 27 articles published February 2020-December 2021 were found with 223 conjunctivitis patients. We found that conjunctival swabs tested for SARS-CoV-2 using RT-PCR returned positive 54.4% of the time in COVID-19 patients with conjunctivitis. We also found that 18 patients with no conjunctivitis tested positive on conjunctival swabs.
Conclusions: Further research is needed to study the pathophysiology of SARS-CoV-2 in the eyes and its presence on the ocular surface. As we begin our third year of the pandemic, we expect more case reports and clinical studies on COVID conjunctivitis.

References:
Nasiri N, Sharifi H, Bazrafshan A, Noori A, Karamouzian M, Sharifi A. Ocular Manifestations of COVID-19: A Systematic Review and Meta-analysis. J Ophthalmic Vis Res. 2021 Jan 20;16(1):103–12.

CONTROL ID: 3713843

SUBMITTER (NAME ONLY): Kevin Zhang

TITLE: Conditional knockout of hephaestin in the neural retina disrupts retinal iron homeostasis

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.R. Zhang, B. Baumann, Y. Song, J. Sterling, S. Guttha, J.L. Dunaief, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|Z. Kozmik, Institute of Molecular Genetics, Akademie ved Ceske republiky, Praha, CZECHIA|

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ABSTRACT BODY:

Purpose: Intracellular iron can catalyze Fenton chemistry, causing oxidative stress in iron-loaded tissues. The retina is particularly vulnerable to oxidative assault, and iron accumulation has been implicated in retinal degenerative disease. Thus, it is important to understand retinal iron regulation. In mice, systemic knockout of the multi-copper ferroxidases (MCOs), ceruloplasmin (Cp) and hephaestin (Heph), which facilitate cellular iron export, results in retinal iron accumulation and degeneration. However, the role of MCOs within the neural retina is not clear.

Methods: A neural retina-specific Heph knockout model was generated, using previously developed mRx-Cre and Heph-flox lines, on a background of systemic Cp knockout. qPCR was used to verify Heph KO. Immunohistochemistry for ferritin-L (FtL), ferritin-H (FtH), and transferrin receptor (TfR) were used to determine retinal iron accumulation. Retinal morphology and function were assessed using in vivo retinal photography, optical coherence tomography (OCT), and electroretinography (ERG).

Results: Conditional KO of Heph in the neural retina in mice with systemic Cp KO resulted in age-dependent neural retina iron accumulation in amacrine cells and photoreceptors. Interestingly, retinal ganglion cells became iron depleted. However, unlike the systemic Cp/Heph double knockout model, there was no retinal degeneration or loss of retinal function.

Conclusions: MCOs have a local role in regulating neural retina iron homeostasis, with neural retina-specific deletion of MCOs leading to neural retina iron accumulation. Since neural retina-specific KO of Heph does not cause retinal degeneration, such as that observed in systemic double KO mice, preserved Heph function in either the RPE or systemically mitigates the phenotype in the retina-specific Heph KO.

CONTROL ID: 3713846

SUBMITTER (NAME ONLY): Bernard Rosner

TITLE: Incidence of and Risk Factors for Cataract in Anterior Uveitis

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Rosner, G.N. Papaliodis, C. Foster, J.H. Kempen, Harvard Medical School, Boston, Massachusetts, UNITED STATES|B. Rosner, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|G.N. Papaliodis, J.H. Kempen, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|K. Dreger, J.E. Thorne, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|T. Fitzgerald, N.P. Bhatt, Penn Medicine, Philadelphia, Pennsylvania, UNITED STATES|J.T. Rosenbaum, Oregon Health & Science University, Portland, Oregon, UNITED STATES|C. Foster, Massachusetts Eye Research and Surgery Institution, Waltham, Massachusetts, UNITED STATES|G. Levy-Clarke, National Institutes of Health, Bethesda, Maryland, UNITED STATES|G. Levy-Clarke, The Tampa Bay Uveitis Center, St. Petersburg, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To estimate the incidence and risk factors for cataract in anterior uveitis

Methods: Data were harvested by trained expert reviewers using protocol-driven chart review. Cataract incidence—newly reduced visual acuity worse than 20/40 attributed to cataract or incident cataract surgery—was studied in 4105 eyes of 2645 patients with anterior uveitis.

Results: Cataract developed in 558 eyes (13.6%, 0.043/eye-year). Time-updated risk factors associated with cataract included: older age (over 65 vs. <18 years: adjusted hazard ratio (aHR)=4.79; 95%CI, 2.95- 7.77); higher anterior chamber cell grade (P(trend)=0.0006), prior incisional glaucoma surgery (aHR=1.70; 95%CI, 1.03-2.80), band keratopathy (aHR=2.16; 95%CI, 1.42-3.27), posterior synechiae (aHR=3.43; 95%CI, 2.65-4.43), elevated intraocular pressure (IOP)≥30 vs 6-20 mmHg: aHR=2.27; 95%CI, 1.18-4.37). Higher dose topical corticosteroid use (≥2 drops/day) was associated with 2-to 3-fold higher cataract risk in eyes with anterior chamber cell grades of 0 or 0.5+, but was not associated with higher cataract risk in the presence of ≥grade 1+ anterior chamber cells. Primary (aHR=0.61; 95%CI, 0.32-1.14) and recurrent (aHR=0.72; 95%CI, 0.55-0.94) had lower cataract risk than chronic anterior uveitis.

Conclusions: Cataract complicates a large minority of anterior uveitis cases. Several fixed and modifiable risk factors were identified and a point system developed to guide cataract risk minimization. Topical corticosteroids only were associated with increased cataract risk when anterior chamber cells were absent or minimally present, suggesting their use to treat active inflammation (which itself is cataractogenic) does not cause a net increase in cataract incidence.

CONTROL ID: 3713847

SUBMITTER (NAME ONLY): Michael Heiferman

TITLE: Loss of Cilia in Uveal Melanoma: Implications for Diagnosis

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Heiferman, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|M. Heiferman, K. Ning, E. Song, T. Kowal, I. Dryden, M. Tran, R. Dalal, P. Chu, P. Mruthyunjaya, J. Lin, Y. Sun, Department of Ophthalmology, Stanford University, Palo Alto, California, UNITED STATES|I. Dryden, R. Dalal, P. Chu, J. Lin, Department of Pathology, Stanford University, Stanford, California, UNITED STATES|Y. Sun, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The primary cilium is a microtubule-based, finger-like projection on the surface of most cells in the human body. This organelle plays an important role in both cellular proliferation and division. In most mammalian cells, primary cilia are dynamically regulated in the cell cycle by disassembly at the G2/M phase and reassembly after cell division. Previous studies have found depleted or defective cilia in multiple types of cancer cells, including pancreatic and renal cancers. Although there is more focus on the crosstalk between cilia and cancer development, studies about primary cilia in uveal melanoma (UM) remain scarce. The goal of this study was to investigate the ciliation of human UM tissue and cell lines.

Methods: In the present study, we assessed primary cilia in UM (n=3 patients) and basal cell carcinoma (BCC, n=2 patients) paraffin tissue sections by employing two classic ciliary antibodies: Arl13b and IFT88. These antibodies detect the ciliary axonemes and basal bodies respectively. Unstained paraffin-based slides were deparaffinized and boiled in 1mM EDTA +0.05% Tween 20 prior to immunostaining. UM cell lines (UM 92-1 and UM 202) were cultured until confluent and then serum starved for 48 hours before staining with ciliary antibodies. Arl13b signal was counted as a cilium if one end of the signal was adjacent to the IFT88 signal. Statistical analysis was performed using Student's t-test. $p < 0.05$ was considered statistically significant.

Results: Quantification of immunofluorescently labeled primary cilia indicated that 45 ± 12% of cells were ciliated in BCC tissue (n=658 cells). The ciliation in UM tissue was 0.8 ± 1.2% (n=651 cells), which was significantly reduced compared to BCC tissue ($p < 0.001$). Quantitative analysis showed that ciliary length is significantly shorter in UM samples compared with BCC samples ($p < 0.001$). In cultured human UM cell lines, we found similar ciliation compared to UM tissue samples.

Conclusions: This is the first report of loss of cilia in UM tissue in contrast to BCC which more often retain their cilia. These data provide insight into ocular tumor diagnosis and potential cilia-based therapeutic strategies against UM.

CONTROL ID: 3713848

SUBMITTER (NAME ONLY): Yavuz Cakir

TITLE: The Impact of Volumetric Intraretinal Fluid Lability in the VISTA Clinical Trial on Functional Outcomes

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Cakir, S. Yordi, L. Lunasco, K. Wise, H. Cetin, G. Kalra, C.J. Mugnaini, C. Calabrise, K.E. Talcott, S.K. Srivastava, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of intraretinal fluid (IRF) lability in diabetic macular edema (DME) on anatomic and functional outcomes in the Phase III VISTA Clinical Trial in eyes treated with intravitreal aflibercept injection (IAI).

Methods: A post-hoc higher order image analysis was performed on eyes in the Phase III VISTA DME study. Patients were randomized to receive 2mg IAI injection every 4 weeks (2q4), IAI every 8 weeks following 5 initial monthly doses (2q8), or laser photocoagulation. This analysis focused on the 2q8 group for assessment of fluid lability, defined as a 30% increase in IRF central subfield volume (CSV) above the threshold value at week 16 (i.e., last monthly injection administration) at any timepoint between week 20 and week 52. OCT images were evaluated using a machine learning-augmented platform that extracts retinal fluid features, including volumetric characterization and compartmental retinal features, such as ellipsoid zone (EZ) integrity. Groups were compared for baseline variables and final functional outcomes.

Results: For this assessment, 139 of 148 eyes were included from the 2q8 group. There were 71 eyes (51%) that demonstrated IRF volume lability after Week 16, compared to 68 eyes (49%) that did not. Baseline comparative assessment of the 2 groups did not show a significant difference in mean IRF CSV compared to those without lability (0.15 ± 0.10 mm^3 vs 0.14 ± 0.12 mm^3, respectively; p=0.79) or a difference in BCVA (ETDRS: 58.2 ± 11.2 vs 61.16 ± 10.0, p=0.105). However, eyes with subsequent IRF CSV lability demonstrated greater baseline EZ attenuation [i.e. reduced EZ-RPE central subfield thickness (24.2 ± 16.0 µm vs 30.6 ± 14.8 µm, p=0.017)].

The IRF CSV lability group demonstrated significantly worse mean BCVA at Week 52 (ETDRS: 68.3±13.2 v 73.2±11.09, p=0.027) and Week 100 (68.9±14.1 v 74±11.7, p= 0.035) compared to eyes that had more stable fluid dynamics.

Conclusions: DME eyes with volumetric IRF lability exhibited worse BCVA outcomes compared to those eyes with more stable fluid dynamics. Decreased baseline EZ integrity was more significant in eyes that ultimately developed fluid lability.

CONTROL ID: 3713851

SUBMITTER (NAME ONLY): Rupalatha Maddala

TITLE: Novel molecular mechanisms regulating actin cytoskeletal reorganization in dexamethasone treated trabecular meshwork cells

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Maddala, W. Backman, C. Eldawy, N.P. Skiba, V. Rao, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|V. Rao, Pharmacology, Duke University School of Medicine, Duke University School of Medicine, Durham, NC, US, academic/medsch, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glucocorticoid-induced actin cytoskeletal reorganization in the trabecular meshwork (TM) cells is thought to participate in increased resistance to aqueous humor outflow through the trabecular pathway. However, our understanding of the molecular mechanisms regulating actin cytoskeletal organization in TM cells remains incomplete. Here, we report identification of several molecules known to directly regulate actin cytoskeletal crosslinking whose levels are upregulated in dexamethasone (Dex) treated human TM cells.

Methods: To identify proteins, whose levels were dysregulated in response to Dex treatment of human TM cells, we analyzed the cytoskeletome and nuclear protein fractions derived from Dex-treated (0.5 μM for 7 days) and control TM cells using non-label quantitative proteomics analyses. The findings from these proteomics analyses were independently validated by immunoblot and immunofluorescence analyses in different (donor) strains of human TM cells.

Results: Human TM cells treated with Dex consistently revealed a preferential and significant increase in the levels of proteins regulating actin cytoskeletal organization, cell adhesion and fibrogenic activity in both the cytoskeletome and nuclear protein fractions. Proteins including ArgBP2 (SORBS2), CAP/Ponsin (SORBS1), LIMCH1 (LIM and calponin homology domains 1), palladin, septin 11, calponin-3, FAT1, SIPA1L1, Phospholipid phosphatase 3, DIAPH2 and CTGF which are directly involved in actin cytoskeletal organization, cell adhesion, contraction, Rho GTPase activation and fibrogenic activity exhibited significantly increased levels in Dex treated cells. Several of these proteins exhibit colocalization with actin stress fibers and focal adhesions in TM cells.

Conclusions: The unbiased and global proteomics approach we utilized in this study to determine dexamethasone-induced changes in proteins of the cytoskeletal enriched and nuclear protein fractions of human TM cells identified several proteins directly involved in actin cytoskeletal crosslinking and cell adhesive interactions. Collectively, these findings provide not only novel insights into the molecular basis for glucocorticoid-induced actin cytoskeletal organization in TM cells but also identify novel potential therapeutic targets for lowering ocular hypertension in glaucoma.

CONTROL ID: 3713853

SUBMITTER (NAME ONLY): Jesson Martin

TITLE: Remote monitoring of device-eye distance and ambience illumination in children using Vision App in smart devices.

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Martin, A. Richmond, J. Reed, Kentucky College of Optometry, University of Pikeville, Pikeville, Kentucky, UNITED STATES|N. Lopez-Gill, Universidad de Murcia, Murcia, Murcia, SPAIN|M. Jaskulski, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using Vision App to remotely monitor the habitual usage of the smart device in children to understand the device- eye distance usage and ambience illumination usage.

Methods: Children aged 6 – 13 yrs old were recruited in this study for three months to continuously monitor the working distance (near work) and the face illumination level of the children (ambience light level). The remote monitoring device (Amazon Fire HD 8) was installed with Myopia App (Vision App ©). The App measured the face-device distance (near work) and the illumination level (ambience) in which the children used the devices at home. The subjects were split into two groups; intervention and non-intervention. In the intervention group, the device's screen would turn dark forcing the subject to maintain the distance at least 30 cm from the device, while in the non-intervention group the device just recorded the time, illumination and distance data without any warning. Refraction and axial lengths were measured during the entire period of study (3 months) in two-week frequency.

Results: In the non-intervention group, about 80% of the subjects viewed the devices from the distance < 30 cm, and 87% were working in an ambience light under 100 lux, with an average of only 40 lux. In the intervention group, about 80% of the subjects had a working distance of > 30 cm from the eye, and about 57% were working in an ambience light under 100 lux. The accommodative demand difference between the non-intervention and the intervention group was about 0.75 D. Measurements of axial length over three-month period shows marginal increase in subjects but magnitude varies from subject to subject.

Conclusions: Remote monitoring of the children for three months shows clearly that intervention group's working distance was greater than 30 cm. Vision App intervention might potentially aid in the delay of onset of myopia in children. Ambience light was found to be less than 100 lux for both non-intervention and intervention groups. This long-term study will continue to focus on the measurements of near work and illumination, and its impact on the myopia progression in children.

CONTROL ID: 3713855

SUBMITTER (NAME ONLY): Katharine Bunch

TITLE: Systemic Pegylated-Arginase 1 Treatment of db/db mice Attenuates Diabetic Retinopathy Progression

SESSION TITLE: New drugs, anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The arginase isoforms (A1 & A2) are involved in the pathogenesis of diabetic retinopathy (DR) through a complex relationship with the endothelial and inducible forms of nitric oxide synthase (eNOS & iNOS), which compete with arginase for L-arginine, their common substrate. While eNOS produces nitric oxide to mediate vasodilation, iNOS is expressed under conditions of stress, mediating immune activation that perpetuates inflammation and oxidative stress. With the type 2 diabetic db/db mouse model, we investigated our hypothesis that administration of A1 will halt DR progression by reducing iNOS activity through depletion of L-arginine, thus limiting oxidative stress and inflammation.

Methods: Pegylated arginase-1 (PEG-A1) or PEG-5000 (control) was given via intraperitoneal injection thrice weekly for two weeks (25 mg/kg/dose) in db/db mice between the ages of 16 and 24 weeks (n=11/group). Visual acuity and contrast sensitivity were assessed via Optokinetic tracking. Whole eyes, retinas, and plasma were collected, and globes sectioned for immunofluorescence (IF). IF was performed for A1, markers of inflammation and oxidative stress including IL-6, 3-nitrotyrosine (3-NT), and 4HNE, and for vascular tight junction protein ZO-1. Retina lysates were used to western blot for inflammasome proteins, oxidative stress products, inflammation, and hypoxia, including A1, A2, iNOS, IL-1β, TNF-α, and 4-HNE. Data was analyzed via unpaired t-tests and values of $p<0.05$ were considered significant.

Results: Untreated db/db mice exhibited impaired visual acuity ($p<0.01$), higher visual contrast sensitivity thresholds ($p<0.05$), marked elevation in retinal A1 ($p<0.001$), iNOS ($p<0.05$), IL-1β ($p<0.05$), and 4HNE ($p<0.01$), and increased retinal albumin extravasation ($p<0.0001$) compared to lean controls. PEG-A1 treatment significantly improved visual acuity ($p<0.01$), visual contrast sensitivity ($p<0.05$), and reduced iNOS ($p<0.01$), 3-NT ($p<0.05$), 4HNE ($p<0.01$), IL-1β ($p<0.01$), and TNF-α expression ($p<0.05$) in db/db mice compared to controls. Additionally, ZO-1 integrity was increased ($p<0.05$) and albumin leakage decreased ($p<0.05$) in retinas of PEG-A1 treated db/db mice.

Conclusions: Systemic PEG-A1 administration in db/db mice resulted in improved visual function, increased blood-retinal-barrier integrity, and reduced inflammation and oxidative stress compared to PEG-5000 controls.

CONTROL ID: 3713856

SUBMITTER (NAME ONLY): Kathleen Chirco

TITLE: Using human LCA7 retinal organoids to establish allele-specific editing as a therapy

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.R. Chirco, M. Neuringer, Neuroscience Division, Oregon Health & Science University Oregon National Primate Research Center, Beaverton, Oregon, UNITED STATES|K.R. Chirco, R.C. Ryals, M. Neuringer, Department of Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S. Chew, A.T. Moore, J.L. Duncan, D.A. Lamba, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dominant CRX-associated Leber congenital amaurosis (LCA7) is a severe retinal degenerative disease for which no treatments exist. Disease-causing variants in CRX typically result in production of a dominant negative form of the protein which disrupts normal photoreceptor maturation. We used an in vitro human retinal organoid model to evaluate gene editing of mutant CRX as a therapy for LCA7.

Methods: We utilized CRISPR/Cas9 tools to (a) correct the $CRX^{K88Q/+}$ mutation in a patient-derived iPSC line, and (b) eliminate the mutant CRX allele, leaving the wildtype CRX allele intact. Rescue of LCA7 phenotypes was then compared in retinal organoids for both editing methods using brightfield images of the outer segments (OS), immunofluorescence (IF) staining, and qPCR.

Results: Successful editing of patient iPSCs ($CRX^{K88Q/+}$) to generate a corrected ($CRX^{+/+}$) and an allelic knockout ($CRX^{+/-}$) line was confirmed via Sanger sequencing. Retinal organoids were successfully generated for each of the three iPSC lines, and they exhibited comparable retinal tissue thickness and photoreceptor numbers throughout differentiation. Morphologically, all organoids remained identical until 180 days (D180), when differences in OS morphogenesis emerged. The $CRX^{+/+}$ organoids produced longer OS-like projections by D180, compared to CRX $^{K88Q/+}$ organoids, while $CRX^{+/-}$ organoids produced OS of intermediate length. mRNA (n=14 organoids per line) and protein (n=8 organoids per line) levels for early photoreceptor markers were comparable between $CRX^{+/+}$ and CRX $^{+/-}$ lines, revealing a similar level of rescue at the cellular level. Morphological differences became less apparent by D240.

Conclusions: Here, we established that both gene correction ($CRX^{+/+}$) and an allele-specific gene knockout strategy ($CRX^{+/-}$) can rescue LCA7 phenotypes. Although there was a mild delay in OS morphogenesis for the $CRX^{+/-}$ line, this may be advantageous for therapy, since gene correction has lower efficiency compared to targeted mutagenesis. This work will guide future experiments focused on treating photoreceptor cells within growing retinal organoids.

CONTROL ID: 3713857

SUBMITTER (NAME ONLY): Li Chen

TITLE: Auto-centration on a Femtosecond Laser for Refractive Corneal Lenticule Extraction Treatment

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chen, A.P. Voorhees, Y.S. Yu, H. Fu, Johnson and Johnson Vision, Milpitas, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evalutate the performance of auto-centration for corneal lenticule extraction treatment on a femtosecond laser.

Methods: Eye images from 9 human eyes were collected on a new femtosecond laser. Before imaging on the femtosecond laser, 3 peripheral marks were created on the nasal, temporal, and inferior cornea of which the nasal and temporal marks were aligned to the horizontal axis when the subject was at upright position. When the subject was under the femetosecond laser at supine postion, one infrared (IR) image and one visible image were captured nearly simultaneously when the eye was about 40mm away from the patient interface viewing a coaxial fixation target. Pupil center was detected from the IR image and the 3 peripheral marks were detected from the visible image before applanation. Another visible image was captured right after the eye was applanated which detected the peripheral marks. Then a transformation matrix was created with the detected mark positions in the visible images before and after applanation. The pupil center detected in the pre-applanated IR image was transformed by the transformation matrix to the visible image under applanation and used as the lenticule treatment center. The rotation angle calculated from the detected nasal and temporal marks in the visible image under applanation was used to correct cyclotorsion axis for lenticule treatment.

Results: Pupil centers were detected correctly in the IR images captured on the femetosecond laser before applanation. Peripheral marks were detected in the visible images before applanation and after applanation from the 9 eyes. On average, the lenticule treatment was automatically adjusted 421.756±173.337μm (range from 136.641 to 692.903μm) from the applanated image center. The cyclotorsion axis was corrected -3.94±5.28° (range from -11.85 to 4.66°). The corrected lenticule treatment center was offset 230.014±179.147μm (range from 57.673 to 648.079μm) from the pupil center in the visible images under applanation.

Conclusions: Auto-centration improves the accuracy of treatment centration by placing the treatment center on the corneal position corresponding to the pupil center of the eye before applanation.

CONTROL ID: 3713858

SUBMITTER (NAME ONLY): Julia Arciero

TITLE: Analyzing diameter artifacts in oximetry measures of retinal oxygen saturation

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Arciero, B.C. Shoemaker, Indiana University Purdue University Indianapolis, Indianapolis, Indiana, UNITED STATES|J. Beach, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|A. Verticchio, B.A. Siesky, A. Harris, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Metabolic assessment in ophthalmic diseases is an important, yet largely unrealized, target due to limitations of imaging and tissue target acquisition. Dual-wavelength photographic retinal oximetry measures have identified possible deficits of oxygen metabolism in glaucoma, yet often they yield non-physiological high values of retinal oxygen saturation in small vessels. This study highlights the possible contribution of single and double pass light transmission to the observed diameter artifacts.

Methods: Retinal photographic oximetry images of healthy subjects (N = 10) were obtained with the Oxymap T1 retinal oximeter (Oxymap Analyzer, Iceland). Saturation, optical density (OD), optical density ratio (ODR), and vessel diameter (D) were obtained from arteriolar and venular segments (>30 pixel length) covering a diameter range of 30-200 μm. A conceptual model of light returned from vessels by single and double pass transmission was developed based on optical properties of blood and retinal reflectance to predict their potential contribution to the diameter artifact.

Results: In Fig. 1A, venular saturation showed a greater dependence on D (slope of -0.18) than arteriolar saturation (slope of -0.03). The artifact was more pronounced in small diameter vessels (slope was -0.22 for D <100 μm and -0.07 for D>100 μm, green). The conceptual model predicted that both single and double pass light paths contribute to the steep decrease in ODR with decreasing diameter (Fig. 1B, black).

Conclusions: The widespread adoption of photographic retinal oximetry is currently limited by a lack of precision in measurements that produce non-physiological artifacts. In this analysis, the diameter artifact is manifested most strongly in venules and is predicted to depend on both double and single pass light transmission. Our data suggests improved understanding of the relationships between vessel saturation and diameter are needed to accurately characterize the error in photographic retinal oximetry.

CONTROL ID: 3713859

SUBMITTER (NAME ONLY): Catherine Wang

TITLE: An Association between Large Optic Cupping and Total and Regional Brain Volume: The Women's Health Initiative (WHI)

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Wang, S. Kravets, A. Sethi, J. Hallak, T.S. Vajaranant, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|C. Wang, A. Sethi, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|S. Kravets, University of Illinois at Chicago Division of Epidemiology and Biostatistics, Chicago, Illinois, UNITED STATES|M.A. Espeland, Wake Forest University Department of Internal Medicine, Winston-Salem, North Carolina, UNITED STATES|M.A. Espeland, Wake Forest University Department of Biostatistics and Data Science, North Carolina, UNITED STATES|L. Pasquale, Icahn School of Medicine at Mount Sinai Department of Ophthalmology, New York, New York, UNITED STATES|S.R. Rapp, Psychiatry and Behavioural Medicine, Wake Forest University Health Sciences, North Carolina, UNITED STATES|B. Klein, S. Meuer, Department of Ophthalmology and Visual Sciences, University of Wisconsin, Wisconsin, UNITED STATES|M.N. Haan, Department of Epidemiology and Biostatistics, University of California at San Francisco, California, UNITED STATES|P.M. Maki, University of Illinois at Chicago Department of Psychiatry, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the relationships between optic nerve cupping and total and regional brain volumes.

Methods: This is a secondary data analysis of women, aged 65 to 79, enrolled in a randomized clinical trial of postmenopausal hormone therapy. Women, aged 65+ without glaucoma in the WHI Sight Examination Study with cup-to-disc ratio (CDR) measurements and MRI-based total and regional brain volumes from the WHI Memory Study were included. Large CDR was defined as 0.6 or greater in either eye. Generalized estimating equation (GEE) models were used to account for intra-brain correlations between within right and left sides. Final analysis was adjusted for demographic, clinical characteristics, and the total brain volume (for regional analyses).

Results: Final analyses included 474 women: the mean age ± SD was 69.2 ± 3.6 years; 92.6% of subjects were white. 34 of 474 (7.2%) women had large CDR. With control for total brain volume, demographic, and clinical characteristics, lateral ventricle volume was 3.00 cc larger for those with large CDR compared to those without large CDR (95% CI: (0.02, 5.98), p-value=0.048) (Table 1). Controlling for demographic and clinical characteristics and excluding total brain volume, frontal lobe volume was 4.77 cc lower for those with large CDR compared to those without (95% CI: (-8.70, -0.85), p-value=0.017), and occipital lobe volume was 1.84 cc lower for those with large CDR compared to those without (95% CI: (-3.36, -0.32), p-value=0.018) (Table 2).

Conclusions: Our analysis suggests that in women aged 65+, large CDR is associated with lower relative total brain volume and absolute regional volume in the frontal and occipital lobes. Enlarged CDR in individuals without glaucoma may represent a sign of aging in the optic nerve and the brain.

CONTROL ID: 3713861

SUBMITTER (NAME ONLY): Mahmoud KhalafAllah

TITLE: Longitudinal thickness changes of peripapillary tissues during high myopia development in juvenile tree shrews

SESSION TITLE: Myopia: Structural Changes from Retina to Sclera

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.T. KhalafAllah, Vision Science Graduate Program, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|P.A. Fuchs, F. Nugen, M. El Hamdaoui, B.C. Samuels, R. Grytz, Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|A. levy, Department of Biomedical Engineering, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate thickness changes of the peripapillary tissues during high myopia development in juvenile tree shrews.

Methods: Juvenile tree shrews were randomly assigned to two groups: normal visual experience (n=9) and monocular -10D lens treatment to induce high myopia, where the other eye served as a control (n=12). Lens treatment started at 24 days of visual experience (DVE). Refractive and biometric measurements were obtained daily. Optical coherence tomography (OCT) of optic nerve head was performed weekly (Spectralis, Heidelberg Engineering). A deep learning algorithm was used for auto-segmentation of sclera, choroid-retinal pigment epithelium complex (Ch-RPE), retinal nerve fiber layer (RNFL) and remaining retinal layers (RRL) after nonlinear distortion correction. Thickness values were obtained from 3D reconstructed tissues, and quantified over a 50-μm band starting at 1000 μm from anterior scleral canal opening centroid.

Results: The thickness of all tissues significantly decreased during high myopia development. Using one-way ANOVA with post hoc Tuckey test, relative thickness changes from baseline were significantly different in myopic eyes compared to control and normal eyes at 59 DVE for the sclera (2.6±5.1%, 4.4±6.4% and -9.2±4.9% in normal, control and myopic eyes, respectively; $P<0.05$), Ch-RPE (-3.5±5.3%, -4.01±9.8% and -13.4±8.3% in normal, control and myopic eyes, respectively; $P<0.05$), RRL (-3.3±2.7%, -2.3±2.7% and -6.2±1.9% in normal, control and myopic eyes, respectively; $p<0.05$), and compared to control eyes only for RNFL (-4.9±2.2%, -2.2±3.7%, -5.9±1.8% in normal, control and myopic eyes, respectively; $P<0.05$). In myopic eyes, significant time-thickness interactions were found for all tissues (repeated measures ANOVA, $P<0.001$). Post hoc analysis with Bonferroni adjustment revealed significant thinning from baseline to 31 DVE for all tissues, and from 31 to 38 DVE for RRL only, but not from 38 DVE to any subsequent follow-up while refractive changes were progressing until 59 DVE.

Conclusions: Juvenile high myopia is associated with simultaneous but heterogeneous thinning of peripapillary tissues, with scleral and Ch-RPE thinning were more pronounced than retinal thinning. Peripapillary tissue thinning occurrs early during high myopia development and may contribute to increased risk for glaucoma later in life prompting early screening of myopic eyes.

CONTROL ID: 3713863

SUBMITTER (NAME ONLY): Silvia Aparicio Domingo

TITLE: Establishing a novel preclinical laser-induced model for regenerative therapies of the outer retina

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Aparicio Domingo, K. Li, R. Koley, H. Nguyen, A. Lisker, M. Flores-Bellver, C. Chen, M. Mathias, V. Canto Soler, CellSight Ocular Stem Cell and Regeneration Program, Department of Ophthalmology, Sue Anschutz-Rodgers Eye Center, School of Medicine, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|S. Kim, M. Carlson, S. Mohanty, Nanoscope Technologies LLC, Bedford, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Degenerative conditions affecting the outer retina, such as geographic atrophy (GA) and laser-induced retinal injury, involve death of photoreceptor and retinal pigmented epithelium (RPE) cells leading to vision loss. Models aimed at mimicking these conditions either do not fully reproduce the complete RPE and outer retinal atrophy (cRORA) or involve damage to additional structures of the retina such as inner retinal layers and choroid. To overcome these limitations, we have developed and characterized a novel laser-induced swine model that mimics the anatomical defects of GA and laser injury and provides a preclinical model amenable to cell and gene-based regenerative therapies.

Methods: Optical coherence tomography (OCT) guided micro-focal laser (532nm) beam was applied in 10 Yucatan pigs to induce targeted focal areas of degeneration affecting the RPE and photoreceptors. Laser damage was targeted to the visual streak which contains the highest cone density resembling the human macula. Different laser conditions were tested to define the optimal parameters. Evaluation of structural laser damage was performed weekly by fundus photography, OCT and dye angiography up to one-month post-laser and correlated with functional assessment by multifocal electroretinogram (mfERG). Cellular changes were further evaluated by immunofluorescence analysis.

Results: Optimization of laser parameters using the new laser system achieved focal areas of degeneration affecting both RPE and photoreceptor cells, with no overt abnormal changes in inner retinal layers. Following optimized laser time exposure (120 mW, 88 sec") full ablation of the photoreceptor and RPE layers was achieved at 2 weeks post-laser, while the rest of the retinal layers were preserved and showed no obvious signs of inflammation or remodeling. Importantly, laser injury did not lead to neovascularization, significant choroidal damage, hemorrhage, anomalies of the retinal arterial vasculature, or retinal holes. Furthermore, degeneration of RPE and photoreceptor layers correlated with a decrease in mfERG response.

Conclusions: We have established and characterized a Yucatan minipig model of laser-induced retinal degeneration that mimics the anatomical defects of GA and laser injury. This model provides new opportunities for pre-clinical assessment of regenerative therapies for patients affected by GA and laser-induced retinal trauma.

CONTROL ID: 3713864

SUBMITTER (NAME ONLY): Deepti Sharma

TITLE: IL-33/ST2L Signaling Regulate Blood-Retinal Barrier Integrity via Affecting Cadherin-Catenin Adherens Junction Complex

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Sharma, S. Bisen, G. Kaur, N.K. Singh, Department of Ophthalmology Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiogenesis, neovascularization and vascular remodeling are highly dynamic processes, where endothelial cell-cell adhesion within the vessel wall controls a range of physiological processes, such as growth, integrity and barrier function. The cadherin–catenin adhesion complex is a key contributor to blood-retinal barrier (BRB) integrity and dynamic cell movements. However, the pre-eminent role of cadherins and their associated catenins in adherens junction structure and function is not fully understood. Also, the role of IL33/ST2L signaling in regulating BRB integrity is not known.

Methods: Using a murine model of oxygen-induced retinopathy (OIR) and human retinal microvascular endothelial cells (HRMVECs), we are trying to understand the significance of IL-33/ST2L-signaling on endothelial barrier disruption, leading to abnormal angiogenesis and enhanced vascular permeability.

Results: Our in vivo genetic deletion studies revealed that deletion of IL-33 resulted in reduced vascular tufts and vascular leakage. Therefore, in order to understand the molecular mechanism by which IL-33 regulates the BRB integrity, we performed some in vitro studies using HRMVECs. The electric cell-substrate impedance sensing (ECIS) analysis showed that IL-33 (20 ng/ml) induce endothelial barrier disruption in HRMVECs. Likewise, FITC-dextran permeability assay also showed that IL-33 stimulate the endothelial dysfunction in HRMVECs. As we know, tight junctions (TJs) and adherens junctions (AJs) form the adhesion structure and maintain the BRB integrity, therefore we look for the junctional proteins involved in the IL-33/ST2L mediated endothelial dysfunction. Furthermore, we found that IL-33 mediates the phosphorylation of VE-cadherin and a-catenin in HRMVECs. Furthermore, mass-spectroscopy (MS) analysis revealed the phosphorylation of specific Ser^{439} residue of a-catenin upon IL-33 inducement in HRMVECs. Consequently, mutation of a-catenin at Ser^{439} residue restores the BRB integrity disrupted by IL-33. In addition, we have observed that IL-33 induce the generation of reactive oxygen species (ROS), thereby destabilize adherens junctions in HRMVECs.

Conclusions: We conclude that IL-33/ST2L signaling plays a significant role in angiogenesis and neovascularization by regulating endothelial permeability and BRB integrity.

CONTROL ID: 3713865

SUBMITTER (NAME ONLY): Seema Sajjan

TITLE: Evaluating clinical severity of Ocular Graft vs Host Disease in Three Murine Models using a Novel Scoring System

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sajjan, E. Tibbs, L. Wu, S. Sunshine, X. Cao, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Development of mouse models and corresponding grading systems is imperative to studying the pathophysiology of human disease. Ocular graft versus host disease (oGvHD) affects 40-60% of patients after allogeneic hematopoietic stem cell transplant (HSCT) characterized by decreased vision, pain, fibrosis, and severe dry eye disease. We have developed a novel grading scale for murine models of oGvHD and tested it in three oGvHD murine models.

Methods: We evaluated 3 different murine models of oGVHD (N=5/group), including major histocompatability (MHC) mismatched (C57Bl/6 donor and Balbc/J host), haploidentical (C57Bl/6 donor and B6D2F1 host), and MHC matched but minor histocompatibility antigen-mismatched (129 donor and C57Bl/6 host). Mice underwent total body irradiation followed by donor T and B cell depleted bone marrow +/- splenocyte from donor mice injected via tail vein at day 1 post radiation. The control mice did not receive splenocytes. GvHD and oGvHD scoring was performed weekly. The novel grading system consisted of categories such as eyelid changes (erythema and edema), periocular fur loss, corneal clarity (corneal haze and visualization of intraocular structures), and corneal fluorescein staining (punctate keratopathy and ulceration) with a grade of 0 (normal) to 3 or 4 (most severe) in each category. The overall score for oGvHD at each time-point is the individual scores for each category per mouse summed and then averaged within the groups.

Results: The MHC mismatched mice experienced higher oGvHD score as compared to the control at days 8, 14, 22, 28 and 42 were p= <0.0001 at all timepoints. The haploidentical mice oGvHD score as compared to control at days 6, 13, 19 and 26 were p= 0.20, p= 0.47, p= 0.051, and p= 0.01, respectively. In the MHC matched but minor histocompatibility antigen-mismatched mice, the oGvHD score as compared to the control at days 6, 13, 19, and 26 were p= 0.49, p= 0.n09, p= 0.06, and p= 0.69, respectively.

Conclusions: This is the first study to directly compare and evaluate the timing and severity of 3 different murine models of oGVHD. Utilizing our novel grading system, we identified clinically significant differences between the splenocyte treated and control groups in all 3 models of oGVHD, ultimately enabling us to use varying genetic backgrounds and treatment modalities to find novel targets for oGVHD.

CONTROL ID: 3713867

SUBMITTER (NAME ONLY): Elliott Milner

TITLE: The Summation of Diverse Synaptic and Intrinsic Drives across M1 Ganglion Cell Photoreceptors

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Milner, H. Blume, M.C. Brown, T. Anthony, M.H. Do, F.M. Kirby Neurobiology Center, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|M.H. Do, Neurology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Elliott Milner: Commercial Relationship: Code N (No Commercial Relationship) | Hannah Blume: Commercial Relationship: Code N (No Commercial Relationship) | Michael Brown: Commercial Relationship: Code N (No Commercial Relationship) | Todd Anthony: Commercial Relationship: Code N (No Commercial Relationship) | Michael Tri Do: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intrinsically photosensitive retinal ganglion cells (ipRGCs) of the M1 type are principal regulators of the circadian clock and other non-image visual functions. These cells diversify their intrinsic light responses to encode a broad range of environmental irradiances as a population. Here, we test the hypothesis that this intrinsic, functional diversity combines with circuit influences to produce effective irradiance encoding.

Methods: We recorded electrophysiologically from M1 ipRGCs in the dark-adapted, isolated retinas of adult, transgenic mice. These cells were labeled genetically or retrogradely from their projections in the suprachiasmatic nucleus, the master circadian clock. We used optical stimulation and pharmacological manipulation to characterize the contributions of intrinsic and synaptic drives to cellular activity.

Results: Our experiments indicate that the synaptic input to M1 ipRGCs is highly diverse in both sensitivity and dynamics. The most sensitive response in all M1 ipRGCs examined was synaptic in origin. This synaptic input was required for spike firing of some cells but dispensable for that of many others. This spike firing exhibits features that are advantageous for irradiance encoding. In particular, it encodes the total photon count with fidelity over an orders-of-magnitude variation in time scale. This integrative ability is evident for indivual cells that have varying balances of synaptic and intrinsic drive, and is more precise at the population level.

Conclusions: Synaptic and intrinsic drives vary across M1 ipRGCs to produce population activity that is suitable for representing irradiance. Temporal integration, a hallmark of circadian photoregulation, is already present in the set of cells that carry light information to the clock.

CONTROL ID: 3713868

SUBMITTER (NAME ONLY): Amrita Rajesh

TITLE: Vitreoretinal interface macrophages include microglia and perivascular macrophages at steady-state

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rajesh, S. Droho, J. Lavine, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Amrita Rajesh: Commercial Relationship: Code N (No Commercial Relationship) | Steven Droho: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Lavine: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mobile, ramified macrophage-like cells (MLCs) are detectable at the vitreoretinal interface (VRI) by optical coherence tomography (OCT) imaging in humans. Macrophages (Macs) are heterogeneous cells and MLC identity is unknown. MLCs could include microglia (yolk sac-derived retinal Macs), perivascular Macs (long-lived Macs supporting healthy vasculature), or monocyte-derived Macs (inflammatory Macs derived from blood). The goal of this study was to characterize VRI Macs.

Methods: OCT and OCT-angiography were performed on C57BL6/J mice. Confocal immunofluorescence (IF) for CD31 (endothelial cells, EC) and IBA1 (pan-Mac marker) were performed at the retinal surface on wholemounts. OCT-angiography and CD31 staining were used to match IF images and en face OCT slabs. $Cx3cr1^{CreER}$ x $Rosa26^{zsGreen}$ (Mac^{GFP}) mice were used to fate map Macs 1 week and 1 month post-tamoxifen treatment. IF staining of frozen sections was performed using IBA1, CD31, and/or Tmem119 to delineate microglia. $Tmem119^{GFP}$ mice were used to quantitate GFP^{+} microglia and $Mrc1^{+}$ perivascular Macs by multi-parameter flow cytometry.

Results: En face OCT slabs above the VRI revealed cellular structures. These cells were $IBA1^{+}$ and showed either a ramified morphology or were colocalized to EC. Fate mapping in Mac^{GFP} mice showed that VRI Macs were 84% GFP^{+} and plexiform Macs were 98% GFP^{+} at Week 1 ($p<0.05$). At Month 1, VRI and plexiform layer Macs were equally GFP^{+} compared to Week 1 (82% vs 96%, $p<0.05$ between groups). VRI Macs were 72% $Tmem119^{+}$ or 21% $Tmem119^{neg}EC^{adjacent}$ ($p<0.001$). Macs from $Tmem119^{GFP}$ retinas were 90% $GFP^{+}Mrc1^{neg}$ microglia or 10% $GFP^{neg}Mrc1^{+}$ perivascular Macs ($p<0.05$) by flow cytometry.

Conclusions: VRI Macs are an emerging disease biomarker. At steady-state, VRI Macs are ~70% microglia and ~20% perivascular Macs without any monocyte-derived Mac component. These findings are potentially important for diseases like multiple sclerosis and Alzheimer's, where microglia and perivascular Macs have been implicated respectively.

CONTROL ID: 3713869

SUBMITTER (NAME ONLY): Magdalena Niestrata

TITLE: ATHENA Study Protocol - Optical Coherence Tomography Angiography Analysis for the detection of Neovascular Age-related Macular Degeneration: a Comprehensive Multi-Centre, Prospective, Randomised Diagnostic Accuracy and Non-Inferiority Study

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Niestrata, Imperial College London, London, London, UNITED KINGDOM|P.A. Keane, P. Patel, S. Sivaprasad, T. Peto, S. Madhusudhan, A.K. Denniston, R.P. Gale, K. Balaskas, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Despite optical coherence tomography (OCTA) being available in many ophthalmology units, there is controversy regarding whether it can replace fluorescent angiography (FA) in the diagnosis of wet age-related macular degeneration (wAMD). The main aim of this study is to determine whether the sensitivity and specificity of OCTA combined with Optical Coherence Tomography (OCT) is non-inferior to that of FA combined with OCT for the detection of wAMD.

Methods: This is a non-inferiority, prospective, randomised diagnostic accuracy study. Participants are patients with a suspicion of wAMD who present to an NHS secondary care ophthalmology unit in the UK. They will be randomised to OCT+FA or OCT+OCTA trial arms. Following random allocation using a secure online randomisation system, a clinician will review the OCT with either FA or OCTA first and make an initial diagnosis (wAMD: yes/no). Then the remaining test will be reviewed to further confirm or exclude wAMD. Comparison of the two clinical diagnoses in each arm will provide evidence concerning the added value of OCTA vs FA in patients with an OCT suspicious of wAMD. According to the sample size calculation, allowing for 10% withdrawal of consent, missing data and inconclusive test results, we will aim to recruit 1,067 patients. The non-inferiority of OCTA vs FA will be evaluated with two-sided 95% confidence intervals for the differences in sensitivity and specificity.

Results: The primary outcome of the study will be the difference in sensitivity and specificity between OCT+OCTA and OCT+FA for wAMD detection. Secondary outcomes will include sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of OCTA alone and FFA alone and PPV of OCT for the detection of wAMD. We will also evaluate the intra- and inter-rater variation and perform an economic analysis of the incremental cost per true positive detected and incremental cost per correct diagnosis for wAMD.

Conclusions: This study will provide clinically significant information on the diagnostic suitability of OCTA vs FA for the diagnosis of wAMD and validated criteria for OCTA-based diagnosis of wAMD, which can provide evidence to change the goldstandard imaging guidelines.

CONTROL ID: 3713870

SUBMITTER (NAME ONLY): Xuejuan Jiang

TITLE: Glycemic control and diabetic retinopathy among older African American females with sickle cell trait and G6PD deficiency

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Jiang, V. Yu, R. McKean-Cowdin, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|X. Jiang, R. McKean-Cowdin, Population and Public Health Sciences, University of Southern California, Los Angeles, California, UNITED STATES|M. Torres, R. Varma, Southern California Eye Institute, CHA Hollywood Presbyterian Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evidence suggests that glycated hemoglobin (HbA1c) levels may be systematically underestimating past blood glucose levels among individuals with sickle cell trait (SCT) and those with glucose-6-phosphate dehydrogenase (G6PD) deficiency, leading to an underdiagnosis of diabetes and diabetes control. However, it is unclear how these genotypes may affect the risk of having diabetic retinopathy (DR). The objective of this study is to evaluate the impact of SCT and G6PD deficiency on HbA1c levels and having DR among a sample of African American females.

Methods: The African American Eye Disease Study is a population-based, cross-sectional study of 40+ years old African Americans in Los Angeles, CA. HbA1c and random blood glucose were measured using a DCA 2000 Analyzer and HemoCue B-Glucose System. DR was graded according to ETDRS grading of DR based on photography of 7 standard fields of the fundus of each eye. From 1,789 females, DNAs were extracted. Genotype data were obtained for rs334, encoding the sickle cell mutation, and for rs5030868, encoding the G6PD deficiency mutation. Demographic and clinical data including DR severity were compared statistically between those with and without the rs334 and those with and without G6PD deficiency mutation.

Results: Compared with individuals without SCT (Table 1), individuals with SCT had a higher HbA1c level (6.1 vs. 5.9, $P<0.05$) and prevalence of diabetes (25.5% vs. 18.2%, $P<0.05$), despite similar levels of random glucose ($P=0.42$). The odds of having diabetes in SCT individuals were 1.58 times those of individuals without SCT. The prevalence of DR was lower in SCT individuals (30%) than in individuals without SCT (48%); however, this difference was not statistically significant ($P=0.69$). For G6PD deficiency, the mean HbA1c level was lower in carriers and deficient individuals than normal individuals ($p < 0.001$), despite a similar random glucose level ($P=0.37$). There was no significant difference in the prevalence of diabetes and DR by G6PD genotype ($Ps=0.29$ and 0.64, respectively).

Conclusions: Among older African American females, SCT is associated with a higher HbA1c level and prevalence of diabetes but a lower prevalence of DR. G6PD deficiency is associated with a lower level of HbA1c but did not appear to affect the prevalence of diabetes and DR. Further studies with larger sample sizes are needed to confirm these findings.

CONTROL ID: 3713871

SUBMITTER (NAME ONLY): Jennifer Patnaik

TITLE: Characteristics of babies with unstable clinical course screened for retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Patnaik, J. Stutzman, A.M. Lynch, E. McCourt, Ophthalmology, University of Colorado Health, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Jennifer Patnaik: Commercial Relationship: Code N (No Commercial Relationship) | Jenae Stutzman: Commercial Relationship: Code N (No Commercial Relationship) | Anne Lynch: Commercial Relationship: Code N (No Commercial Relationship) | Emily McCourt: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) screening examinations are recommended for infants with a birth weight (BW) of less than 1500 grams and/or a gestational age (GA) of less than 30 weeks and select infants who do not meet these criteria but have an unstable clinical course. We conducted this study to investigate and characterize babies who met the unstable clinical course criteria at one academic institution.

Methods: A retrospective chart review was performed on the medical records of infants screened for ROP at our hospitals between January 2006 and December 2020. Unstable clinical course was defined as babies screened for ROP who did not meet the birthweight or gestational age screening criteria. Chi-square tests were used to compare infants with unstable clinical course to other infants screened for ROP.

Results: Among 2,328 infants screened for ROP, 144 (6.2%) were defined as unstable clinical course. Infants with unstable clinical course were similar to babies meeting the BW and GA criteria in terms of gender, race/ethnicity and singleton/multiple birth. Four of the unstable clinical course babies (2.8%) developed low grade ROP and none developed type 1 or type 2 ROP or needed treatment for ROP. Rates of ROP were much higher among babies meeting the BW and GA criteria in which 6.7% developed type 1, 5.9% type 2, and 22.3% low grade ($p<0.0001$). Two of the four unstable clinical course infants who developed low grade ROP were born at GA 31 weeks (BW 1800 and 2200 grams), and two were born at GA 32 weeks (BW 1510 and 1695 grams).

Conclusions: At our academic institution, infants defined as unstable clinical course and screened for ROP did not develop ROP to the level that required treatment. Further investigations at other institutions are warranted to determine if the unstable clinical course criteria is indeed capturing infants at risk for ROP.

CONTROL ID: 3713875

SUBMITTER (NAME ONLY): Kristyn Huffman

TITLE: Spatial Sequencing in a Model of Early Onset Retinal Degeneration

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Huffman, S. Borooah, Department of Ophthalmology at the Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|R. Sasik, Center for Computational Biology and Bioinformatics, University of California San Diego, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure: Kristyn Huffman: Commercial Relationship: Code N (No Commercial Relationship) | Roman Sasik: Commercial Relationship: Code N (No Commercial Relationship) | Shyamanga Borooah: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: RNA sequencing has already identified transcriptional signatures associated with retinal degeneration (RD) in various disease models but provides limited spatial data. In this study, we use spatial sequencing in a well characterized model of early onset degeneration resulting from loss of function of Mouse Frizzled Receptor Protein, to better understand the spatial changes associated with RD.

Methods: Eyes from 10–12-week-old RD6 mice (n=6) and C57BL/6 (WT)(n=7) mice were fresh frozen in OCT. 10 µm sections were placed on 10X Genomics Visium Spatial slides. Spatial gene expression was performed, creating a cDNA library mapped to specific tissue locations (Fig 1).

Gene set enrichment analysis identified pathways involved in RD. Pathway analysis of the differentially expressed genes was carried out using WebGestalt.org with Kyoto Encyclopedia of Genes and Genomes as a mapping database.

Results: Uniform Manifold Approximation and Projection clustering identified distinct expression signatures from the ganglion cell layer(GCL), inner nuclear layer(INL), retinal pigment epithelium (RPE)/choroid/sclera, optic nerve, and ciliary body (Fig, 1) but not the outer nuclear layer(ONL) which was contaminated with expression from other layers. Our findings highlight Clu, C4b, Apoe, and C1qa genes (z-score 3.0, 2.4, 2.3, and 2.2) as potential markers of disease in the RPE.

Gene Set Enrichment analysis between rd6 and WT eyes showed upregulation of glycolysis and carbon metabolism pathways in the GCL and Rap1, Hippo and lysosome pathways in the RPE/Choroid/sclera. The ribosomal pathway was downregulated in these layers. No significant pathways were found in the INL, ciliary body or optic nerve.

Conclusions: Our study demonstrates that spatial sequencing can be used to identify differentially expressed genes in most layers in mouse retina, although further optimization is required for ONL. Analysis of differentially expressed genes highlighted potential disease associated targets.

Overall gene set enrichment showed that Rap1 and Hippo pathways are perturbed in rd6 mice. These pathways have previously been implicated in RD. However, further validation with RNAscope will likely confirm their association in this model and as potential targets for treatment.

CONTROL ID: 3713876

SUBMITTER (NAME ONLY): Alecia Gross

TITLE: The cytoskeletal network and cellular function in rod and cone photoreceptors are disrupted in the absence of NUDC expression

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Gross, M. Garner, E. Boitet, A. Gade, N.J. Reish, M. Hubbard, Department of Neurobiology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|G. Ying, W. Baehr, Ophthalmology and Visual Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|N.J. Reish, Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|A. Gade, The University of Alabama at Birmingham School of Public Health, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have shown Nuclear Distribution Protein C (NUDC) has a critical role in the maintenance of rod photoreceptors by regulating outer segment (OS) disk size, likely through actin regulation. We propose that NUDC influences cytoskeletal elements such as microtubule structure and the trafficking of mitochondria or proteins destined for the OS. Here we expand our understanding of the role of NUDC in photoreceptors by testing the hypothesis that NUDC regulation of the cytoskeleton is critical both in rods and cones.

Methods: We generated a NudC floxed mouse and bred it with the rod-cell specific iCre75 or the cone-cell specific HRGP Cre recombinase mouse to produce $NudC^{+/-}$ or $NudC^{-/-}$ in rod or cone photoreceptors, respectively. Retinal function was analyzed using electroretinography (ERG) at P21 and P42, and retinas were isolated and examined by transmission electron microscopy (TEM), immunohistochemistry (IHC), and Western blotting (WB).

Results: ERG analysis uncovered low a- and b-wave amplitudes in P21 rod $NudC^{-/-}$ ($rNudC^{-/-}$) mice under scotopic conditions. IHC staining of retinal cryosections from $rNudC^{-/-}$ mice demonstrate disorganized microtubules in the inner segment (IS) of rod photoreceptor cells along with rhodopsin mislocalization in the IS, outer nuclear layer and synapse. IHC and WB for GFAP also show an increase in gliosis in the $rNudC^{-/-}$ retinas compared with $rNudC^{+/+}$. WB of $rNudC^{-/-}$ retinal lysates show a decrease in rhodopsin, cofilin, and transducin, an increase in LIS1 and Rab11a while ARR1 levels were unchanged compared with $rNudC^{+/+}$. TEM taken from ultrathin sections of $rNudC^{-/-}$ retina show disorganized disk formation and striking morphological changes in the IS. In mice lacking NUDC in cones ($cNudC^{-/-}$), the scotopic ERG response at P21 displays a normal a-wave and a diminished b-wave that is further reduced at 6 wks. The photopic ERG is decreased at P21 and is absent at P42.

Conclusions: NUDC is critical in rod photoreceptor OS disk formation and in localization of mitochondria and phototransduction proteins. Our data are consistent with the hypothesis that NUDC governs disk dimension through actin regulation, stressing the importance of this protein in the cytoskeleton of photoreceptors in development and during homeostasis. Similar to rods, we have found that NUDC is critical for proper cone cell function.

CONTROL ID: 3713877

SUBMITTER (NAME ONLY): Kevin Schey

TITLE: Mechanism of AQP5 trafficking in lens fiber cells

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.L. Schey, R.B. Gletten, Biochemistry, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Kevin Schey: Commercial Relationship: Code N (No Commercial Relationship) | Romell Gletten: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aquaporin-5 (AQP5) is the second most abundant aquaporin in ocular lens fiber cells and its localization and thus fiber cell permeability can be regulated. Previously we have shown that in bovine outer cortical lens fiber cells, AQP5 localizes to cytoplasmic spheroidal, tubular structures that co-stain with autophagosomal and mitochondrial markers. The purpose of this work is to define the mechanism that trafficks AQP5 from cytoplasmic structures to the plasma membrane.

Methods: High resolution immunofluorescence (IF) was conducted on cryosections from cultured bovine lenses with zonules intact and treated with or without bafilomycin A1, an autophagosome/lysosome fusion inhibitor. AQP5, autophagosome marker LC3B, and lysosome marker LIMP2 were imaged by confocal microscopy. Quantitation of cytoplasmic and plasma membrane localized AQP5 was carried by image segmentation and assessing fluorescence intensity in subcellular regions using Nikon NIS Elements software. Transmission electron microscopy was also used to characterize subcellular structures and fusion of cytoplasmic structures to plasma membranes.

Results: In the bovine lens outer cortex, AQP5 was entirely localized to cytoplasmic structures that were mitochondrial marker TOMM20-positive. Little overlap between LC3B or LIMP2 signals and these AQP5-containing structures was observed in this region. In the transition region between the outer cortex and inner cortex, AQP5 structures co-stained with autophagosomal marker LC3B and LIMP2 and appeared to fuse with the plasma membrane. In the inner cortex, AQP5 was completely localized to the plasma membrane. LIMP2 was detected in the plasma membrane in the inner cortex as well. Upon treatment with bafilomycin A1, plasma membrane AQP5 signal was reduced in the outer cortex/inner cortex transition region and cytoplasmic AQP5 structures appear to increase in number.

Conclusions: Bovine AQP5 appears to traffic to the plasma membrane in the outer cortex/inner cortex transition region via an unconventional lysosomal trafficking mechanism that involves fusion of autolysosomes with the plasma membrane. Future experiments will focus on defining the signals that regulate AQP5 trafficking.

CONTROL ID: 3713879

SUBMITTER (NAME ONLY): Elinor Laws

TITLE:

The relationship between retinal ganglion cell degeneration and retinal perfusion after acute traumatic brain injury

SESSION TITLE: Endophthalmitis & Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Laws, N. Saliman, R.J. Blanch, NIHR Surgical Reconstruction and Microbiology Centre, University Hospitals Birmingham NHS Foundation Trust, Birmingham, Birmingham, UNITED KINGDOM|E. Laws, J. Hepschke, N. Saliman, Neuro-ophthalmology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, Birmingham, UNITED KINGDOM|R.J. Blanch, Academic Department of Military Surgery and Trauma, Royal Centre for Defence Medicine, Birmingham, Birmingham, UNITED KINGDOM|A. Belli, Birmingham Neurosurgery, University Hospitals Birmingham NHS Foundation Trust, Birmingham, Birmingham, UNITED KINGDOM|A. Belli, Neuroscience and Ophthalmology, Institute of Inflammation and Ageing, University of Birmingham College of Medical and Dental Sciences, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinal blood flow, measured by optical coherence tomography angiography (OCTA) may be reduced by systemic disease and local ocular ischaemia, but also in association with retinal neurodegeneration. Traumatic brain injury (TBI) impairs the structure and function of the visual pathway. Retinal ganglion cell (RGC) layer degeneration and retinal perfusion loss can occur after TBI, even in absence of visual symptoms, with neurodegeneration delayed by several weeks. It is not clear whether reductions in retinal blood flow associated with neurodegeneration are caused by changes in retinal function (occurring at the time of injury) or simply reflect retinal structural changes (occurring only after neurodegeneration).

Methods: Retrospective case series. Patients attending for moderate to severe TBI assessment at a tertiary referral centre were included. Clinical examination, OCT, OCTA and Humphrey visual field (HVF) analysis were performed for each patient acutely and at follow-up. Data were extracted using manufacturer's software with blood flow assessed as skeletonized vascular density, large vessel masked flow probability and vessel enhanced perfusion density and compared to corresponding retinal ganglion cell layer (GCL) thicknesses.

Results: Sixteen patients aged 20-65 years were included, 12 males and four females. Patients were examined within nine days of TBI and then after 2-6 months. GCL thinning preceded superficial vascular plexus perfusion loss. The strongest association was GCL thickness and skeletonized vascular density (adjusted R squared 0.86; $p<0.0001$). The degree of GCL thinning and perfusion loss correlated to baseline visual function on HVF.

Conclusions: Reduced retinal perfusion is association traumatic RGC degeneration, mirroring, rather than preceding, structural changes.

CONTROL ID: 3713880

SUBMITTER (NAME ONLY): Brandon Anderson

TITLE: Low dose sodium iodate: a potential avenue for testing a wider range of retina-protective therapies

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Anderson, B.A. Bell, Y. Song, J. Dunaief, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sodium iodate causes oxidative stress to the retina and is commonly used by vision scientists to test therapeutics intended to treat disorders like age-related macular degeneration (AMD). An important difference, however, between sodium iodate and AMD is the time it takes to damage the retina. While AMD is a chronic disease that develops over years, sodium iodate damages the retina within a week. Because of this, it is possible that some therapeutics that protect against a slower developing disease such as AMD would be unable to protect against the fast-acting sodium iodate; this may lead to incorrectly discarding these therapies. Decreasing the severity of sodium iodate's damage by dropping the dose is a potential solution to this issue, but this also leads to more variability in the severity of retinal degeneration. To explore this, we hypothesized that a low dose of sodium iodate (20 mg/kg or 25 mg/kg IP) would cause different degeneration severity in males vs. females and old vs. young mice.

Methods: To test our hypothesis, 1% sodium iodate was intraperitoneally injected in male and female mice either 3 months old or 22 months old. Damage was assessed in vivo using confocal scanning laser ophthalmoscope (cSLO) and optical coherence tomography (OCT) 1 and 4 weeks after injection. Image analysis quantified the average thickness of the retina and the total area damaged.

Results: Mice injected with 25 mg/kg sodium iodate had more consistent damage than those injected with 20 mg/kg. Females at the 25 mg/kg dose had less (but still consistent) damage than male mice at the same dose. Older mice had more severe pathology than younger mice.

Conclusions: These results suggest that using 25 mg/kg sodium iodate in 3-month-old female mice may be an effective way to use the sodium iodate model when testing potential therapies for retinal disease such as AMD.

CONTROL ID: 3713882

SUBMITTER (NAME ONLY): Maximilian Garcia

TITLE: More than meets the eye: comparing risk factor associations between PDR and DME.

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Garcia, A. Pan, Vanderbilt University, Nashville, Tennessee, UNITED STATES|R. Zhou, S. Angaramo, R. Haliyur, D.A. Padovani-Claudio, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|M. Artis, Meharry Medical College School of Medicine, Nashville, Tennessee, UNITED STATES|D.A. Padovani-Claudio, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Associations between microvascular complications of diabetes mellitus (DM), including diabetic nephropathy (DNeph), neuropathy (DNeu) and retinopathy (DR) have been reported, particularly for proliferative DR (PDR). Less is known specifically about their relationship with diabetic macular edema (DME), despite it being the leading cause of vision loss in patients with DM type-2 (DM2) and DR. The contributions of tobacco exposure to PDR and DME are also controversial. We further explore these associations using manually phenotyped cohorts of patients with progressive DR stages.

Methods: Vanderbilt's deidentified health record database, the Synthetic Derivative, was used to obtain clinical data from cohorts of patients with DM and no DR (N=239), no DME (N=365), DME (N=213), no PDR (N=341), and PDR (N=237). Continuous variables for multivariate logistic regression analysis included: DM duration (days) and Max HbA1c (%, A1c/glycated hemoglobin). Categorical variables included: hypertension, DNeu, DNeph, PDR, and DME (absent vs present), DM type (Type 1 vs Type 2), vital status (living vs deceased), race (black, vs. white, vs. other), and tobacco use (never vs remote {>5yrs from last exam or death} or current {within 5yr}). A two-sided T-test with $p<0.05$ was used for statistical significance.

Results: Max A1c and DM duration were significantly associated with PDR (p=0.029 and p=0.002, respectively) and DME (p=5.96e-05 and p=0.003, respectively). However, vital status, DNeu and DNeph were only significantly associated with PDR (p=0.013, p=0.001, and p=0.001, respectively) but not with DME. DM1 was significantly associated with PDR (p=3.30e-11) as DM2 was with DME (p=0.013). Relative to no tobacco exposure, remote (p=0.007), but NOT current tobacco use was significantly associated with increased odds of DME (Varma 2014), but neither was significantly associated with PDR. White race was significantly associated with a decreased presence of PDR relative to black race (p=0.037) but not to "other" race (p=0.109) and no association was found between race and DME.

Conclusions: Our results suggest that, although DME and PDR both represent progression in DR and are managed similarly, the factors that affect their development and their pathophysiology are likely significantly different. Exploring these differences may lead to the development of more effective therapies for these potentially blinding conditions.

CONTROL ID: 3713883

SUBMITTER (NAME ONLY): Andrew Benos

TITLE: Hepatic HIF-1 stabilization increases retinal and brain serine/1-carbon metabolism

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Benos, G. Hoppe, D. Hanna, A.B. Grenell, B. Anand-Apte, J. Sears, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|W. Song, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|A.B. Grenell, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|J. Sears, Lerner Research Institute, Cardiovascular and Metabolic Sciences, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|B. Anand-Apte, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stabilization of hepatic hypoxia inducible factor-1 (HIF-1) by dimethyl oxaloylglycine (DMOG) protects both retina and brain from oxygen induced retinopathy (OIR) and oxygen induced periventricular leukomalacia (OPVL), respectively. We have previously demonstrated that hepatic HIF-1 stabilization upregulates serine/1-carbon metabolism (serine/1CM) and that this pathway is essential to HIF induced protection against OIR. In this study, we measured the metabolism of [U-$^{13}C_3$] serine in liver and brain extracts from mouse pups with and without DMOG induced hepatic HIF-1 stabilization.

Methods: C57BL/6J mouse pups were injected with 0.9% NaCl or DMOG 200 µg/g bodyweight intraperitoneally (IP) on P3, P5, and P7. After the third injection, pups were fasted for 4 hrs then injected IP with 80 µL [U-$^{13}C_3$] serine (10 mg/ml), and 1 hr later, brain and liver samples were dissected and snap-frozen. Metabolites were extracted by methanol/chloroform/water and were assayed using gas chromatography mass spectrometry.

Results: DMOG treatment induced a 2-fold increase in both relative abundance and fractional enrichments of M3 serine and M2 glycine in liver. In brain, DMOG treatment increased the fractional enrichment of M3 serine 2.5-fold with no statistiscally significant increase in relative abundance. Brain glycine increased by 50% whereas fractional enrichment increases of M2 glycine was statistically insignificant in brain. There was a trend toward increased M2 hypotaurine in both brain and liver, but hypotaurine levels were decreased in both tissues under DMOG stimulus. Taurine levels were unchanged in both tissues with and without DMOG treatment. M3 Lactate:pyruvate ratios were stable and close to 1.0 in all conditions.

Conclusions: These data demonstrate that exogenous serine (and hence liver derived serine) is able to cross the blood-brain barrier as would be expected for neutral amino acids via their respective carriers. However, DMOG induced increases in M2 hepatic down-stream metabolites of serine/1CM such as M2 glycine in both brain and liver suggesting that hepatic HIF-1 stabilization provides 1C metabolites for brain via liver derived serine, at least in neonatal mouse pups at P7. Serine is a key component of myelin, necessary to glycosphingolipid synthesis, providing a potential mechanism for how hepatic stabilization of HIF-1 (remote protection) could increase CNS myelination.

CONTROL ID: 3713884

SUBMITTER (NAME ONLY): Isabel Fabelo Hidalgo

TITLE: Evaluating the European School for Advanced Studies in Ophthalmology classification for diabetic macular edema in clinical practice

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Fabelo Hidalgo, C. Fernández-Núñez, N. Pérez-Llombet Quintana, G. Quezada-Peralta, O. Durán Carrasco, M. Alberto Pestano, M. Alonso Plasencia, M. Gil Hernández, R. Abreu, Ophthalmology, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the utility of the European School for Advanced Studies in Ophthalmology classification for diabetic macular edema (DME) assessing the interobserver agreement for the staging using optical coherence tomography (OCT) in naïve patients. Secondly to assess the staging problems that may arise.

Methods: We performed a consecutive retrospective analysis of all DME naïve patients who came to our service for 1 year. Two specialist retinal evaluators analyzed independently the OCT images and determined the DME stage using the European School for Advanced Studies in Ophthalmology (ESASO) classification. An interobserver agreement analysis was performed. In cases where staging could not be performed, we evaluated and categorized the cause for no-staging and an interobserver agreement analysis was also performed.

Results: We analyzed 93 eyes of 65 patients (64.6% male and 35.4% female) with a mean age of 66.2 +/- 12.1 years old. Observer 1 staged 60 out of 93 eyes (64.5%). Observer 2 staged 61 out of 93 eyes (65.6%). The Kappa analysis of intra-observer concordance for the staging was 0.508.

Out of 93 cases, observers 1 and 2 could not stage 33(35.5%) and 34 (34.4%) cases respectively as the OCT features of the DME in these cases did not correspond to any of the options provided in the ESASO classification. These findings were statistically significant (p=0.000)

The causes for no-staging were edema with very low thickness that does not alter the ellipsoid zone (T0C1E0/E1), edema with low thickness that does not alter the ellipsoid zone with disorganization of the inner retinal layers (T1C1/2E0D1), edema with increased thickness without cysts (T1-3C0) and Edema with low thickness and severe cysts (T1C3). The Kappa analysis of intra-observer concordance for causes of no-staging was 0.869.

Conclusions: We may conclude that the EMD OCT ESASO classification constitutes a modern and thorough classification for the DME but in our experience does not englobe the totality of DME cases that you may find in clinical practice.

CONTROL ID: 3713886

SUBMITTER (NAME ONLY): Elizabeth Whitcomb

TITLE: Lamin phosphorylation directs nuclear condensation and nuclear envelope reorganization during lens differentiation

SESSION TITLE: Lens Physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.A. Whitcomb, G. Perini-Villanueva, S. Francisco, A. Taylor, Tufts University HNRCA, Boston, Massachusetts, UNITED STATES|M. Kantorow, L.A. Brennan, Florida Atlantic University, Boca Raton, Florida, UNITED STATES|P.G. FitzGerald, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The removal of lens organelles from lens fiber cells is critical for lens clarity. Multiple congenital cataract models show retention of nuclei in the purported organelle free zone, indicating that nuclear breakdown is among essential processes in establishing and maintaining lens clarity. Documentation of processes involved in nuclear envelope breakdown is limited. Identifying the steps of nuclear envelope breakdown in lens denucleation may provide insight into mechanisms of cataract development.

Methods: Nuclear morphology and localization of nuclear Lamins, nuclear pore complexes and inner and outer nuclear membrane proteins were examined during differentiation in chick and mouse lenses using immunofluorescence. Nuclear structure was examined in WT mice using electron microscopy.

Results: Phosphorylation of Lamin is associated with nuclear envelope breakdown. In chick lenses, phosphorylation of Lamin A immediately precedes nuclear condensation. Additionally, after Lamin phosphorylation, nuclear Lamin staining becomes discontinuous in the nuclear membrane. The nuclear pore complex also becomes discontinuous in the nuclear membrane after Lamin phosphorylation and no longer localizes with Lamins. Analysis of nuclear membrane structure by electron microscopy shows nuclear envelope breakdown in areas devoid of nuclear pore complexes.

Conclusions: These data suggest that as in mammalian lenses, phosphorylation of Lamin is an important step in nuclear envelope breakdown during lens fiber cell denucleation in the chick. Furthermore, reorganization of nuclear membrane proteins precedes denucleation.

CONTROL ID: 3713887

SUBMITTER (NAME ONLY): Christina Zarouchlioti

TITLE: A refined amplification-free long-read sequencing method to interrogate TCF4 triplet repeats associated with Fuchs endothelial corneal dystrophy

SESSION TITLE: Application of multi-omics to inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Zarouchlioti, N.J. Hafford-Tear, A. Szabo, N. Bhattacharyya, A. Sadan, A.J. Hardcastle, N. Pontikos, S. Tuft, A.E. Davidson, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|Y. Tsai, Pacific Biosciences Inc, Menlo Park, California, UNITED STATES|P. Liskova, Department of Ophthalmology, Univerzita Karlova, Praha, CZECHIA|P. Liskova, Department of Paediatrics and Adolescent Medicine, Univerzita Karlova, Praha, CZECHIA|N. Pontikos, S. Tuft, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: We have previously demonstrated the application and utility of an amplification-free long-read sequencing method to characterize the Fuchs endothelial corneal dystrophy (FECD)-associated intronic TCF4 triplet repeat (termed CTG18.1). Here we aim to improve on our previously published method to characterise CTG18.1 in a FECD patient cohort using a dual cutter CRISPR/Cas9 enrichment approach in combination with PacBio single molecule real-time (SMRT) long-read sequencing.

Methods: An amplification-free method using a dual CRISPR/Cas9 system, in combination with PacBio SMRT long-read sequencing on a Sequel II platform, was applied to target CTG18.1. FECD patient-derived gDNA samples comprising a diverse range of CTG18.1 allele lengths were analysed. A robust data analysis pipeline was devised and applied to effectively filter, align and interrogate CTG18.1 specific reads.

Results: Dual CRISPR/Cas9-guided SMRT sequencing of CTG18.1 provided accurate genotyping information and enabled us to characterise the levels of somatic mosaicism present for all samples analysed. Advantages of this refined protocol, when compared to our previous method, include the enrichment and sequencing of a larger region of genomic DNA flanking CTG18.1 to enhance the likelihood of encompassing informative polymorphic markers to phase CTG18.1 reads. Furthermore, the dual cutter CRISPR/Cas9-guided design, in combination with sequencing on the PacBio Sequel II System, also enabled enhanced multiplexing capacity and reduced genomic DNA input requirements compared with our original protocol.

Conclusions: CRISPR-guided SMRT sequencing provides a powerful approach to accurately interrogate disease-associated tandem repeat expansions at a nucleotide level and detect levels of instability that are often prevalent within somatic tissues. The refined method presented here offers enhanced phasing capabilities, reduction of the amount of DNA required and increased multiplexing capacity compared to previously published methods.

CONTROL ID: 3713888

SUBMITTER (NAME ONLY): LE HAN

TITLE: Correcting Chromatic Aberrations and Spatial-Spectral Crosstalking in Broadband Line-Scanning SD-OCT

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. HAN, K.K. Bizheva, University of Waterloo, Waterloo, Ontario, CANADA|

Commercial Relationships Disclosure: LE HAN: Commercial Relationship: Code N (No Commercial Relationship) | Kostadinka Bizheva: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In broadband Line-scanning SD-OCT, chromatic aberrations and spatial-spectral crosstalking prevent diffraction limit imaging. We demonstrate these two problems can be resolved by dividing the original broadband spectrum into sub-bands, digital refocusing separately, and registering them afterward.

Methods: The LS SD-OCT system is based on a Michelson interferometer that is powered by a supercontinuum laser (SuperK, NKT Photonics, Birkerød, Denmark). A custom band-pass filter was utilized to select a spectral range of 600 nm – 980 nm. The spectrum after digital filtering is centered at 800 nm, and the effective FWMH bandwidth is 160 nm. The interference signal is detected by a 2D CMOS camera (Dimax S4, PCO, Germany) with a detection aera of 1920 * 500 pixels (spectral-spatial) at a 2.95 kHz frame rate. Volumetric (500 A-scans × 500 B-scans × 1920 pixels) images were acquired, with a field of view (FOV) ~ 0.5 mm × 0.8 mm (x × y) and depth scanning range 1.2 mm (z). The 3 micrometer diameter microbeads were imbedded in transparent agar-based gel. Cucumbers were cut into thin slice and covered by cover glasses. The rat cornea was ex-vivo imaged within 2h after sacrifice.

Results: Fig. 1A shows the images of enface microbeads images. From left to right, the image corresponds to the original OCT signal, refocused OCT signal using the full spectrum, and the registered sub-bands method. The line profiles comparison in (B) suggests that both the x- and y- resolution are improved using the proposed method. (C) and (D) show the original and corrected tilted projection images of cucumber seeds. (E) and (F) show the original and corrected enface image of the middle stroma in the rat cornea. Both the keratocytes and nerves are refocused. (G) and (H) show the original and corrected endothelium cells of the rat cornea.

Conclusions: Our proposed method was successfully used to refocus the microbeads, cucumber, and rat cornea LS-OCT images. The chromatic aberrations and spatial-spectral crosstalking in broadband LS SD-OCT have been reduced which makes broadband LS SD-OCT suitable for cellular resolution imaging.

CONTROL ID: 3713890

SUBMITTER (NAME ONLY): Boyden Myers

TITLE: Dual Palmitoylation of PRCD, a Photoreceptor-Specific Protein Linked to RP, Alters Protein Stability and Subcellular Localization

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Myers, E. Sechrest, G. Hamner, J. Murphy, S. Motipally, S. Kolandaivelu, Ophthalmology, West Virginia University, Morgantown, West Virginia, UNITED STATES|S. Kolandaivelu, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Progressive rod-cone degeneration (PRCD) is a photoreceptor-specific protein essential for maintaining photoreceptor outer segment (OS) structure and rhodopsin packaging densities into disc membranes. Previously, we have shown that PRCD undergoing protein palmitoylation at the second amino acid (Cys2) is crucial for protein stability and proper trafficking to photoreceptor OS. PRCD has several predicted structural domains with unknown significance, with one of the mutations being located in the polybasic region (PBR). This mutation, an arginine to cysteine at the 17th position (R17C), is linked with retinitis pigmentosa (RP). The goal of our study is to determine the structural importance of the PBR in PRCD and to characterize the R17C mutated protein.

Methods: Constructs expressing R17C and a double mutant (C2Y/R17C) were cloned in a pCAG-IRES-EGFP vector with an HA-tag and transiently transfected in hRPE1 cells. Protein stability, membrane association, and subcellular localization were determined by western blot and immunocytochemistry. Palmitoylation status was determined via Acyl-RAC and Acyl-PEG exchange. Localization of R17C and C2Y/R17C was also studied in vivo by subretinal injection in the murine retina.

Results: Protein stability of mutant R17C is significantly reduced by 50% compared to WT, despite having strong membrane association and palmitoylation observed by Acyl-RAC. Interestingly, we distinguished palmitoylation at the Cys17 position with the loss of endogenous palmitoylation (C2Y/R17C), which enhances the protein stability compared to the C2Y protein. Subretinal injection followed by electroporation in murine retina shows C2Y, R17C, and C2Y/R17C double mutant proteins are mislocalized to the subcellular compartment. Immunolocalization in the RPE cell line expressing R17C shows similar phenotypes to WT, and C2Y/R17C shows similarities to the C2Y protein.

Conclusions: Despite being palmitoylated twice and demonstrating strong membrane association, the mutation in the PBR (R17C) affects protein stability and trafficking from the IS. Furthermore, palmitoylation within the PBR alone (C2Y/R17C) does not compensate for protein stability or trafficking. Overall, we demonstrate that the PBR domain in PRCD is indispensable for its function and any defects of the area lead to dysregulation of PRCD protein associated with blinding diseases.

CONTROL ID: 3713891

SUBMITTER (NAME ONLY): Hailey Robles-Holmes

TITLE: Risk Factors for Persistent Avascular Retina Following Bevacizumab Therapy for Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.K. Robles-Holmes, University of Miami School of Medicine, Miami, Florida, UNITED STATES|J. Campbell, Oregon Health & Science University, Portland, Oregon, UNITED STATES|E. Nudleman, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|E. Nudleman, Rady Children's Hospital San Diego, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Peripheral retinal vascularization continues following treatment with bevacizumab (IVB) for type 1 Retinopathy of Prematurity (ROP). However, many eyes have persistent avascular retina (PAR) despite therapy, which may lead to late reactivation, retinal detachment, and blindness. We aimed to identify risk factors for PAR following bevacizumab therapy for type 1 ROP.

Methods: We conducted a retrospective series of 106 eyes from 53 infants with type 1 ROP. 74 eyes from 37 infants received IVB with subsequent laser of PAR at an average of 49.5 weeks postmenstrual age (PMA) 95% CI [45.7, 53.2] (Group 1). 20 eyes from 10 infants were treated with IVB and did not receive subsequent laser (Group 2). Fundus photos were available for 52 eyes of 26 infants in Group 1 and from 14 eyes of 7 infants in Group 2. We compared the patient demographics, timing of treatment, and the fundus photographs at the time of IVB and laser photocoagulation. Length and rate of vascular growth after IVB were measured. In addition, we measured changes in vascular severity score (VSS) following IVB, which provides an objective assessment of disease severity.

Results: The average length of vascular growth following IVB was 100.7 millimeters (mm), 95% CI [86.2, 115.1] over an average of 80.4 days, 95% CI [70.3, 90.4]. Group 2 had higher birthweight (BW) ($p<0.05$), greater extent of retinal vascularization at time of IVB ($p<0.001$), and lower VSS at time of IVB ($p<0.01$) than Group 1. Zone/Stage, gestational age (GA), and post-menstrual age (PMA) at time of IVB did not differ significantly between Group 1 and Group 2. The overall mean VSS decreased significantly following IVB in all Group 1 eyes ($p<0.001$). The amount of VSS change from time of IVB to time of laser was positively correlated with the extent of vascular growth following IVB ($p<0.05$), providing a potential biomarker for PAR.

Conclusions: The presence of PAR requiring laser after IVB was associated with lower BW, more posterior disease, and higher VSS at the time of IVB. In addition, a larger VSS change following IVB was significantly associated with increased vascular growth. VSS may provide a tool for predicting PAR and monitoring for arrest of vascularization.

CONTROL ID: 3713892

SUBMITTER (NAME ONLY): Sezen Karakus

TITLE: The Effect of Topical Recombinant Human Nerve Growth Factor on Tear Production

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Karakus, X. Dai, X. Zhu, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect of the topical recombinant human nerve growth factor (rhNGF) on tear production in patients with severe, refractory dry eye with neurotrophic features.

Methods: A retrospective chart review was conducted on patients treated with topical rhNGF for severe, refractory dry eye with neurotrophic features, defined as refractory corneal staining with minimal or no ocular discomfort that has failed multiple rounds of conventional treatment. Data regarding patient demographics and ocular/systemic past medical history was extracted from patient charts. Tear production as measured by Schirmer test without topical anesthesia was recorded for the worst eye at baseline and subsequent follow-up visits after treatment. Appropriate statistical tests were applied to identify changes in Schirmer test values before and after treatment and the proportion of patients with an increase in tear production reflected by Schirmer test value.

Results: We included 7 patients meeting criteria for severe, refractory dry eye with neurotrophic features with Schirmer values recorded before and after treatment. After an 8-week course of treatment with rhNGF, the median value of the Schirmer test increased from 9 to 16 mm compared to baseline. A meaningful increase was observed in three patients (more than 7 mm). One patient had Sjogren's syndrome and prior LASIK surgery (Schirmer increased from 7 to 27 mm), and the other two patients had prior LASIK surgery (Schirmer increased from 14 to 29 mm and 9 to 16 mm) as a risk factor to have refractory epithelial keratopathy with neurotrophic features. All tolerated the treatment well, reporting eye pain and eyelid sensitivity from drop application that all resolved after completion of treatment.

Conclusions: Treatment with topical rhNGF has shown promising results in our small case series in increasing tear production in patients with severe, refractory dry eye with neurotrophic features with minimum side effects. Further studies should be pursued to determine longer-term treatment effects as well as optimum treatment dose and duration based on underlying etiology.

CONTROL ID: 3713893

SUBMITTER (NAME ONLY): Cassandra Barnes

TITLE: Amphibian Arrestin 1 forms dimers using a novel interaction interface

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Knutson, M. Cosgrove, Biochemistry and Molecular Biology, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|C.L. Barnes, P.D. Calvert, Ophthalmology and Visual Sciences, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|

Commercial Relationships Disclosure: Cassandra Barnes: Commercial Relationship: Code N (No Commercial Relationship) | Bruce Knutson: Commercial Relationship: Code N (No Commercial Relationship) | Michael Cosgrove: Commercial Relationship: Code N (No Commercial Relationship) | Peter Calvert: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Photoreceptor arrestin 1 (Arr1) from mammalian species self-associates into dimers and tetramers. We have shown that amphibian Arr1 oligomerization is limited to dimers – higher order oligomers are not detected at the highest experimental concentrations examined, nor projected to form at millimolar, physiological concentrations. We thus examined if the mechanism of amphibian Arr1 dimer formation differed from that of mammalian.

Methods: Recombinant Arr1s from the African clawed frog, Xenopus laevis (xArr1), and the tiger salamander, Ambystoma tigrinum (salArr1), were expressed in E. coli, purified, and subjected to analytical ultracentrifugation (AUC). AUC results were analyzed in SEDFIT, plotted in GUSSI and fitted in MATLAB to determine oligomer formation and dissociation constants. 3D structure of xArr1 was estimated using Modeler in Chimera, using bovine Arr1 crystal (PDB: 1CF1 chain A) as template. Regions of greatest sequence divergence among Arr1s were found using MegAlign. Lysine crosslinking - Mass Spectrometry and Patchdock were used to identify potential dimer interfaces and create 3D models of xArr1 dimers. Small angle x-ray scattering (SAXS) was performed and analyzed using Raw to estimate dimer shape. xArr1 dimer structure was predicted by visualizing SAXS envelopes and comparing to 3D models from Patchdock using Chimera.

Results: Arr1 from X. lavis and A. tigrinim self-associate in a concentration-dependent manner, however, oligomerization of both species was limited to dimers. AUC analysis of recombinant and endogenous bovine Arr1 supports previously published results that are interpreted to show the formation of tetramers at physiological concentrations. SAXS envelopes of xArr1 are consistent with dimer formation, without indication of larger oligomers. Inositol-hexakisphosphate (IP6) inhibits xArr1 self-association, but not as effectively as for mammalian Arr1. Mutations in xArr1 residues analogous to key residues in mammalian Arr1 that are essential for their tetramerization and in which mutations increase the Kd of dimerization tenfold, had no impact on the affinity of xArr1 dimers. Homology modeling and circular dichroism spectra suggest a similar fold for xArr1 and bovine Arr1.

Conclusions: Together, these results suggest that amphibian Arr1s have a similar structure to that of mammals but use a dimerization interface that differs from those found in mammalian Arr1s.

CONTROL ID: 3713894

SUBMITTER (NAME ONLY): Brandon Lien

TITLE: Comparison of manual versus semi-automated analysis methods for pterygium surface area determination

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lien, O.L. Lee, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|Y. Shin, Doheny Image Reading Center, Doheny Eye Institute Doheny Image Reading Center, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Brandon Lien: Commercial Relationship: Code N (No Commercial Relationship) | Ye Jin Shin: Commercial Relationship: Code N (No Commercial Relationship) | Olivia Lee: Commercial Relationship(s);Code C (Consultant/Contractor):Cloudbreak Therapeutics

ABSTRACT BODY:

Purpose: To describe and validate methodology to assess the pterygium surface area extending beyond the corneal limbus expressed as a percentage of the corneal surface area. To apply and compare the analysis methodology to color photographs of eyes with pterygia using manual grading versus using computer vision techniques.

Methods: The study included 25 photos of 21 eyes of 19 patients with nasal pterygium. The primary gaze images were taken by a single lens reflex camera system (Canfield Scientific, Inc., Fairfield, NJ), using fixed parameters. In both the manual and semi-automated methods, the corneal limbus was identified and demarcated 360 degrees. The extension of the pterygium head, seen as fibrovascular growth extending past the corneal limbus, was identified and demarcated. The pterygium is expressed as a percentage of its surface area over the corneal surface area. Manual analysis was performed by reading center graders using Image J (NIH, Bethesda, MD). The semi-automated method was created using the Python coding language (Python Software Foundation, Fredericksburg, VA) and the OpenCV library (Intel Corporation, Santa Clara, CA). Each method was independently performed and repeated on all 25 images. Intraclass correlation coefficient (ICC) was calculated for inter- and intra- grading agreement.

Results: All 25 images were analyzed using the methodologies described above. The manual and semi-automated method's mean pterygium surface area covered was 11.61% (± 7.21) and 13.08% (± 19.39) of the corneal surface area, respectively. The t-value was 0.354 and the p-value was 0.362. The manual intragrader ICC for percentage of pterygium to corneal surface area was 0.961. The intragrader ICC for the semi-automated pterygium grading methodology was 0.994. When the semi-automated method was compared to the manual method of grading pterygium, the intergrader ICCs ranged from 0.603 to 0.666.

Conclusions: A methodology for measuring pterygium surface area relative to corneal surface area is described and validated using both manual grading and semi-automated computer vision analysis. The reproducibility of this method is high between manual and semi-automated methods. Both methods may be used for standardized evaluation of pterygia in clinical research and clinical trials. The semi-automated quantification allows for reduction in grading speed, while maintaining good reliability.

CONTROL ID: 3713895

SUBMITTER (NAME ONLY): Amrita Saha

TITLE: Potential role of high mobility group box 1 in formation of corneal subepithelial infiltrates in adenovirus keratitis

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saha, M. Islam, A. Ismail, X. Zhou, J. Chodosh, J. Rajaiya, Department of Ophthalmology, Massachusetts Eye and Ear/Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular surface infection by human adenovirus species D (HAdV-D) causes epidemic keratoconjunctivitis (EKC). The most significant long-term complication of EKC is subepithelial infiltrate (SEI) formation, occurring in about one-third of cases. However, the mechanism of SEI formation after adenoviral infection of the cornea remains uncertain. High-mobility group box protein 1 (HMGB1) is an important late inflammatory mediator; extracellular HMGB1 variably regulates inflammatory responses and leukocyte infiltration. In this study, we aimed to define a potential role for HMGB1 in progression to SEI formation.

Methods: Primary human corneal epithelial (PHCE) cells, hTERT-immortalized human corneal epithelial (THE) cells, and primary human corneal fibroblasts (HCFs) were infected with HAdV-D37 or HAdV-C5 at MOI = 5, and cell supernatants were collected through 48 hours post infection. Mass spectrometry (LC-MS/MS) analysis was performed on cell lysates. Immunoblotting was performed on infected cell supernatants, and on cytoplasmic and nuclear cellular fractions, using acetylated HMGB1 antibody. ELISA for secreted HMGB1 was conducted on cell-free supernatants, and HMGB1 gene expression was studied using real-time qPCR. Confocal microscopy was performed to visualize HMGB1 translocation. Cytokine expression by HCFs treated with recombinant HMGB1 was analyzed using human cytokine protein arrays.

Results: HAdV-D37 infection resulted in HMGB1 translocation from the nucleus to the cytoplasm and then to the extracellular space in THE cells, but not in HCF. HAdV-C5, a virus not associated with EKC, did not induce secretion of HMGB1 from any of the cell types tested. Finally, treatment of HCF with recombinant HMGB1 triggered expression of pro-inflammatory mediators.

Conclusions: Our data suggest that HMGB1 is specifically released by adenovirus infected corneal epithelial cells and also provides insights into possible mechanism of corneal SEI formation in EKC. HMGB1 expressed by adenovirus infected corneal epithelial cells could induce underlying stromal cells to express pro-inflammatory mediators, leading indirectly to the development of SEI. HMGB1 may be a viable therapeutic target for preventing the corneal stromal complications of EKC.

CONTROL ID: 3713897

SUBMITTER (NAME ONLY): Kyungsoo Shin

TITLE: Mechanistic insight into the role of vitronectin in age-related macular degeneration

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Shin, J. Kent, F. Marassi, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California, UNITED STATES|R. Thompson, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Kyungsoo Shin: Commercial Relationship(s);Code F (Financial Support):Neuroptika | James Kent: Commercial Relationship(s);Code F (Financial Support):Neuroptika | Richard Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Francesca Marassi: Commercial Relationship(s);Code F (Financial Support):Neuroptika

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a devastating disease characterized by the ectopic accumulation of calcified protein-lipid deposits. Understanding the molecular basis for deposit formation is key for developing diagnostic, preventive, and therapeutic approaches. Using biophysical methods with purified proteins and lipids, we characterized the role of vitronectin (Vn) in mediating hydroxyapatite (HAP) mineralization on lipid surfaces. Vn is a calcium-binding protein and a major component of the AMD proteome with a potential role in HAP deposition; Vn is known to interact with the complement system and variants have been identified as AMD risk factors.

Methods: Using mammalian and E. coli expression systems, we purified full-length Vn and a shorter construct encompassing its hemopexin domain (Vn-HX). The purified proteins were labeled with fluorescent tags for microscopy and characterized structurally by NMR and crystallography. Their interactions with lipids and HAP were determined using thermal shift assays. To examine the effects of Vn on deposit formation, HAP mineralization was initiated from chemically-defined solutions of calcium and phosphate ions, and monitored in the presence of lipids by fluorescence techniques with HAP-specific dyes. A two-tailed Student’s t-test was used for statistical analysis.

Results: Vn and Vn-HX bind HAP, with HAP association significantly increasing their melting temperatures by ~6 °C (Vn $p<0.01$; Vn-HX $p<0.01$). Both promoted HAP mineralization on lipid vesicles leading to the formation of concentric lipid-HAP-protein micro-spheres, ranging in size from 3-10 μm and similar to those observed in AMD pathology. Surface coating of Vn and Vn-HX could be visualized with fluorescently labeled proteins. Addition of Vn ($p<0.01$) and Vn-HX ($p<0.01$) significantly increased HAP mineralization measured by fluorescence with the HAP-specific stains Xylenol Orange, OsteoSense and Alizarin Red S.

Conclusions: Our results demonstrate that Vn can strongly interact with HAP using the calcium-binding site in its hemopexin domain. The Vn-dependent, HAP-specific fluorescence enhancement suggests that Vn plays a role in regulating HAP deposition on lipid surfaces. Our in vitro assays identify Vn as a promising target for AMD diagnosis and treatment, and future work will focus on translation to cellular and in vivo models.

CONTROL ID: 3713898

SUBMITTER (NAME ONLY): Carlos Carpena Torres

TITLE: Effect of artificial tears based on an extract of Artemia salina containing dinucleotides in a rabbit dry eye model

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Carpena Torres, A. Martin, C. Rodríguez Pomar, G. Carracedo, Optometry and Vision, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|F. Huete, A. Martinez Aguila, Biochemistry and Molecular Biology, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|

Commercial Relationships Disclosure: Carlos Carpena Torres: Commercial Relationship: Code N (No Commercial Relationship) | Fernando Huete: Commercial Relationship(s);Code P (Patent):WO2018015582A1 | Alba Martin: Commercial Relationship: Code N (No Commercial Relationship) | Candela Rodríguez Pomar: Commercial Relationship: Code N (No Commercial Relationship) | Alejandro Martinez Aguila: Commercial Relationship: Code N (No Commercial Relationship) | Gonzalo Carracedo: Commercial Relationship(s);Code P (Patent):WO2018015582A1

ABSTRACT BODY:

Purpose: To evaluate the effect of artificial tears based on an extract of Artemia salina, a brine shrimp containing high concentrations of dinucleotides, in a rabbit dry eye model.

Methods: An experimental, prospective, and randomized study was carried out on 20 New Zealand white rabbits divided into 4 different groups (n = 5, each group): healthy rabbits, dry eye rabbits, dry eye rabbits treated with hypromellose, and dry eye rabbits treated with Artemia salina. The dry eye model was induced by the topical instillation of 0.2% benzalkonium chloride. Measurements of tear film quality and damage and inflammation of the ocular surface were performed before and after the topical instillation of the different treatments for 5 consecutive days.

Results: Compared with the dry eye rabbits non treated and treated with hypromellose, the treatment with the artificial tears based on Artemia salina manifested beneficial effects on tears secretion (increased 64.38 ± 18.41%), tear break-up time, corneal staining, density of Goblet cells, height of mucin cloud secreted by Goblet cells, and mRNA levels of IL-1β y MMP9 in conjunctival cells ($P < 0.05$).

Conclusions: The topical instillation of artificial tears based on an extract of Artemia salina was confirmed as a potential secretagogue agent for dry eye treatment, which opened the door for future studies to extrapolate the current findings to dry eye patients.

CONTROL ID: 3713899

SUBMITTER (NAME ONLY): Patricia Sha

TITLE: Evaluation of a combined OCT index in healthy and glaucomatous eyes

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Sha, G.C. Lee, N. Manivannan, S. Magazzeni, Carl Zeiss Meditec, Inc., California, UNITED STATES|A. Bonjean, Centre Ophtalmologique Sorbonne St Michel, FRANCE|L. Moyal, Centre Ophtalmologique Sorbonne St Michel/ Quinze-Vingts Hospital, FRANCE|S. Hammoud, B. Dupas, Centre Ophtalmologique Sorbonne St Michel/ Lariboisière Hospital, FRANCE|M. Lehmann, Centre Ophtalmologique Sorbonne St Michel/ Cochin Hospital, FRANCE|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) provides clinicians with a large number of quantitative parameters that aid in glaucoma diagnosis. The OCT Early Glaucoma Diagnostic Structural Index (EGDSI), was previously proposed and validated in healthy and glaucomatous eyes with no associated disease providing a combined structural index for the detection of early glaucoma[1,2]. In this preliminary, ongoing study, we evaluated the sensitivity and specificity of EGDSI in healthy and in a range of glaucomatous eyes that may include comorbidities.

Methods: Retrospective CIRRUS™ 6000 AngioPlex (ZEISS, Dublin, CA) OCT data were sampled from a glaucoma clinic including 76 eyes of 38 subjects that were clinically diagnosed as healthy, glaucomatous, or having other morbidities (see Table 1). Optic Disc 200x200 and Macular 512x128 cube scans from the first clinical visit were used for analyses. Mean Deviation (MD) from SITA Standard or SITA Fast 24-2 visual field data were collected from non-healthy eyes to gauge severity. Sixteen OCT summary parameters were extracted to calculate EGSDI as previously described. Sensitivity and specificity for EGDSI were calculated using 5% and 1% normative cut-off values determined from the CIRRUS reference database.

Results: For 37 healthy eyes, mean age was 56.3 (standard deviation, SD: 18.4; range: 27.1 to 85.7) years. For 39 eyes with glaucoma or other morbidities, mean age was 65.5 (SD: 13.3; range 30.8 to 85.7) years and mean MD was -5.15 (SD: 8.10; range: -28.79 to 0.35) dB. In the full cohort, sensitivities were 78.8% and 60.6% and specificities were 83.7% and 95.3% at the 5% and 1% cutoffs, respectively (see Table 2). There was an additional false positive (1 of 6) and false negative (1 of 3) due to the additional 9 morbidities.

Conclusions: In this preliminary, ongoing study, EGDSI shows comparable sensitivity to detect glaucoma as previously reported in a range of glaucomatous eyes[3] despite the presence of a limited number of comorbidities, and exhibited additional Type I and II errors. Additional data sampling more comorbidities may help determine their effect on the EGDSI and its clinical utility to aid in detection of glaucoma.

References

[1] Mwanza et al. IOVS 2013; 54(13).

[2] Mwanza et al. TVST 2018; 7(2).

[3] Wilson et al. IOVS 2021; 62(6): Abstract 995.

CONTROL ID: 3713900

SUBMITTER (NAME ONLY): Laura Bohrer

TITLE: cGMP compliant CRISPR correction and retinal differentiation protocol for photoreceptor cell replacement therapy

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.R. Bohrer, N.E. Stone, A.T. Wright, K. Varzavand, M. Devore, R.F. Mullins, E.M. Stone, B.A. Tucker, University of Iowa Institute for Vision Research, Iowa, UNITED STATES|L.R. Bohrer, N.E. Stone, A.T. Wright, K. Varzavand, M. Devore, R.F. Mullins, E.M. Stone, B.A. Tucker, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa, UNITED STATES|S. Han, CellFE, Inc., California, UNITED STATES|T.A. Sulchek, Georgia Institute of Technology, George W. Woodruff School of Mechanical Engineering, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Laura Bohrer: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Stone: Commercial Relationship: Code N (No Commercial Relationship) | Allison Wright: Commercial Relationship: Code N (No Commercial Relationship) | Katayoun Varzavand: Commercial Relationship: Code N (No Commercial Relationship) | Melette Devore: Commercial Relationship: Code N (No Commercial Relationship) | Sewoon Han: Commercial Relationship(s);Code E (Employment):CellFe | Todd Sulchek: Commercial Relationship(s);Code C (Consultant/Contractor):CellFE | Robert Mullins: Commercial Relationship: Code N (No Commercial Relationship) | Edwin Stone: Commercial Relationship: Code N (No Commercial Relationship) | Budd Tucker: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Induced pluripotent stem cell (iPSC)-derived retinal progenitor cells are a promising cell type for restoring vision in patients with retinal degeneration. The purpose of this study was to develop a protocol to generate clinical grade CRISPR-corrected photoreceptor precursor cells for autologous retinal cell replacement.

Methods: IPSCs were generated using dermal fibroblasts isolated from an unaffected control and a patient with NR2E3-associated enhanced S-cone syndrome. CRISPR-Cas9-based homology-dependent repair strategies were designed to correct disease causing NR2E3 mutations. CRISPR reagents were delivered using a microfluidic device, which operates using a reagent-free, convective transport mechanism amenable to the delivery of large molecules under cGMP. Retinal organoids were derived using a stepwise 3D differentiation protocol testing different cGMP compliant reagents and oxygen tension (5-20%) in a cGMP compliant Biospherix cell culture isolator. Organoids were characterized via light and confocal microscopy.

Results: CRISPR reagents were delivered to patient iPSCs using a Zephyr microfluidic transfection system (CellFE). Different gap sizes (7, 9, and 10μm) and flow rates (achieved by applying pressure of 50 or 90PSI to each well) were tested and cell survival and cutting efficiency were evaluated. A 9μm gap size and 90 PSI consistently gave the greatest cutting efficiency (~31%) with lowest cell death. While we previously found that iPSC reprogramming efficiency is highest under 5% oxygen tension, retinal organoid production was inefficient at this oxygen level. Increasing oxygen tension to 20% resulted in decreased pluripotency and increased ectoderm gene expression by day 7 of differentiation. By day 30, laminated retinal organoids were abundant in cultures differentiated under 20% oxygen tension, while they were smaller and less consistent when differentiated at 5% oxygen tension. By 150 days of differentiation retinal organoids generated at 20% oxygen tension under cGMP conditions contain abundant rod and cone photoreceptor precursor cells expressing markers such as NRL and cone arrestin respectively.

Conclusions: We have generated a cGMP compliant protocol incorporating microfluidic transfection and varying oxygen tensions to enable efficient generation, CRISPR correction and differentiation of transplantable photoreceptor cells for autologous cell replacement.

CONTROL ID: 3713901

SUBMITTER (NAME ONLY): Soledad Aguilar Munoa

TITLE: Visual field (VF) progression at 1 year in the prospective observational study of disc haemorrhages (POSH). Association of disc haemorrhage (DH) location and re-bleeding with progression.

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Aguilar Munoa, J. Mohamed-Noriega, P. Praditsuktavorn, D.F. Garway-Heath, NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK, UNITED KINGDOM|J. Mohamed-Noriega, Ophthalmology, Universidad Autonoma de Nuevo Leon, San Nicolas de los Garza, Nuevo Leon, MEXICO|G. Lazaridis, University College London Centre for Medical Image Computing, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To describe VF progression in glaucoma patients 1 year after a DH and explore the correlation with DH location and re-bleeding.

Methods: 30 patients with glaucoma and a DH were recruited at Moorfields Eye Hospital and followed for 5 visits over 1 year (0-1-3-6 and 12 months). In all visits patients had two 24-2 and two 10-2 VF (Humphrey Field Analyzer, Carl Zeiss Meditec, Inc., Dublin, CA), except on month 3 (only one of each). The Glaucoma Progression Analysis (GPA) software was used to establish progression at 1 year. Trend (MD and VFI for 24-2, MD for 10-2, overall and per hemifield (HF)) and event analyses were included. Progression on the HF corresponding to the DH was compared with the opposite HF. Progression rates were compared between ‘re-bleeders’ and ‘non re-bleeders’.

Results: 7 were excluded from analysis: 1 required surgery for progression in the study eye, 3 withdrew before 1 year, and 3 did not attend the last visit within the 1-year window due to COVID-related issues.

16 (70%) of DH were located in the inferior hemi-disc.

3 (13%) cases were labelled ’Possible progression’ on event-based analysis.

Mean MD (SD) at baseline were -3.39 (2.87) for 24-2 and -2.81 (4.22) for 10-2. Progression rates (SD) for MD were: -0.35 (1.6) in the superior HF and -0.27 (1.48) in the inferior HF (p=0.86), on 24-2 VF. On 10-2 VF, the rates were -0.93 (1.44) for the superior HF and -0.23 (0.93) for the inferior HF, p=0.06.

Progression rates in the HF corresponding to the DH vs the opposite HF were: -0.37 (1.74) vs -0.25 (1.32), p=0.79, on 24-2 and -0.82 (1.34) vs -0.34 (1.12), p=0.18, on 10-2.

16 (70%) patients re-bled in either eye during follow-up. Progression rates for re-bleeders vs non re-bleeders were: -0.33 (1.17) vs -0.24 (2.09), p=0.89, for 24-2 MD and -0.69 (1.11) vs -0.28 (0.9), p=0.41, for 10-2 MD.

Conclusions: VF progression was fairly slow in our cohort and most patients remained stable on event analysis. There was a trend towards faster progression in the HF corresponding to the DH, but there was no statistically significant difference over this short observation period. Re-bleeding was common but was not associated with faster progression.

CONTROL ID: 3713903

SUBMITTER (NAME ONLY): Paolo Milella

TITLE: Adaptive optics imaging characteristics of Varicella Zoster Virus retinal segmental periarteritis

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Milella, M. Nassisi, F. Viola, Universita degli Studi di Milano, Milano, Lombardia, ITALY|G. Leone, C. Mapelli, M. Nassisi, F. Viola, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Lombardia, ITALY|G. Ruggi, Ospedale Fatebenefratelli e Oftalmico, Milano, Lombardia, ITALY|A. Scialdone, IRCCS Policlinico San Donato, San Donato Milanese, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: Retinal segmental periarteritis (Kyrieleis plaques) is a rare condition in which white-yellowish exudates are placed in beaded pattern within the retinal arteries. The aim of the study is to report the adaptive optics (AO) imaging characteristics of arterial vasculitis in Varicella Zoster Virus (VZV) related posterior uveitis and correlate it with other imaging modalities.

Methods: Patients diagnosed with VZV posterior uveitis and evidence of retinal segmental periarteritis underwent multimodal imaging including fluorescein angiography (FA), indocyanine green angiography (ICGA), optical coherence tomography (OCT) and AO.

Results: 3 patients (1 female; median age 78 years) were recruited. In all cases, AO images showed arterial wall involvement, perivascular opacification, and focal lumen irregularities. However, the arterial walls were never disrupted. There was no vein involvement. In one case, glistening whitish spots were evident on the surface of the arterial wall, which corresponded to an intense hyperreflectivity on OCT and late focal hypofluorescence on FA and ICGA. In general, arterial plaques showed late iso/hypofluorescence on FA and ICGA. In all cases, arterial plaques modifications were far more evident on AO than angiographic exams.

Conclusions: AO imaging confirms that nodular periarteritis involves arterial walls, but it remains confined within them. Furthermore, AO seems more sensitive to detect vascular inflammation at microscopic level than traditional imaging. Additional studies will be needed to further explore the diagnostic and prognostic value of these findings.

CONTROL ID: 3713904

SUBMITTER (NAME ONLY): Faizah Bhatti

TITLE: Surfactant Protein A Regulates Actin Polymerization and Function in Retinal Endothelial Cells

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.N. Bhatti, Pediatrics and Ophthalmology, The University of Oklahoma College of Medicine, Oklahoma City, Oklahoma, UNITED STATES|W. Chen, J. Fernandes, Pediatrics, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Faizah Bhatti: Commercial Relationship: Code N (No Commercial Relationship) | Wen Chen: Commercial Relationship: Code N (No Commercial Relationship) | Jolyn Fernandes: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Preterm infants are at risk of aberrant angiogenesis and can develop Retinopathy of Prematurity (ROP), a leading cause of acquired visual impairment. Risk factors for ROP are hyperoxia and inflammation. Surfactant protein A (SP-A) is deficient in preterm infants and we previously showed that deficiency of SP-A in mice is associated with decreased retinal vessel growth in early development and in oxygen-induced retinopathy, with abnormal elongation of retinal endothelial cells (EC's). Actin and cytoskeleton function are critical for EC migration and function. We hypothesize that lack of SP-A impairs retinal EC function via decreased actin polymerization, and cytoskeleton dysregulation.

Methods: Gene expression in SP-A$^{-/-}$ and WT P6 mouse retina tissue was evaluated by RNAseq and protein by mass spectroscopy (MS). Confirmation of targets was done by Cytoskeleton PCR Array. Retina flat mounts were evaluated by IHC with staining for actin and cd31 (EC marker). HRECs were treated with control HEPES (HREC+Con) or human SP-A protein (HREC+SPA). Actin expression and organization was analyzed by IHC. Migration and proliferation assays were assessed in HREC's. Data was analyzed by students t-test or one-way ANOVA, with $p< 0.05$.

Results: We show differential expression of factors mapped to signaling pathways and transcriptional regulation of cytoskeleton-dependent functions, including actin polymerization (actin polymerization complex related proteins Arpc2, Arcp4, and WasL), microtubule formation and cell cycle division (Ktn1 and Map4). HRECs+SP-A had more than twice as much cell migration compared to HRECs+Con ($p< 0.0001$) and increased proliferation ($p< 0.0001$). HRECs+SP-A exhibited elongation of actin filaments and protrusion of filopodia compared to HREC+Con, Actin was more peripherally organized in ECs and tip cells of blood vessels in WT compared to SP-A$^{-/-}$ mice.

Conclusions: Deficiency of SP-A alters expression of genes related to actin filament interactions, organization & biogenesis, microtubules, cell shape and size. Furthermore, HREC's exposed to purified SP-A exhibit morphological changes including elongation of cells and migration of actin to endothelial cell borders with an increase in migration and proliferation. Future studies will determine underlying mechanisms of these observed findings which will allow for development of therapy targeting aberrant vessel growth in ROP.

CONTROL ID: 3713905

SUBMITTER (NAME ONLY): ZEESHAN AHMAD

TITLE: Lipid peroxidation and iron accumulation induced ferroptosis in bacterial endophthalmitis

SESSION TITLE: Pathobiology of Microbial Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. AHMAD, S. Singh, X. Walker, R. Wright, A. Kumar, Ophthalmology, Vision and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ferroptosis is a recently discovered non-apoptotic mode of cell death triggered by downregulation of antioxidant enzyme glutathione peroxidase 4 (GPX4). In this study, we sought to determine the role of GPX4 signaling in regulating retinal ferroptosis in bacterial endophthalmitis

Methods: In vivo (C57BL/6 mouse) and in vitro (BMDMs, retinal Muller glia) studies were performed by infecting with S. aureus (SA). Ferroptosis induced cell death and its regulation by GPX4 was assessed by pharmacological inhibition and activation approaches. In mice, disease progression was assessed by both non-invasive (ERG and fundus exam) and invasive (bacterial burden, cytokine levels) methods. Bacterial induced downregulation of GPX4 signaling was assessed by Western blot and immunofluorescence (IFA) whereas qPCR and ELISA assays were used to check the expression of inflammatory mediators in retinal tissue or cell lysates.

Results: Our metabolomics and transcriptomic analysis of S. aureus infected mouse retinal tissues showed a time-dependent increase in mediators of ferroptosis. SA infection was found to increase labial iron pool (LIP) and lipid peroxidation (LPO) in infected mouse retinas and bone marrow derived macrophages (BMDM). This coincided with decreased GPX4 and increased ACSL4 expression. Supplementation of iron quencher, deferiprone (DFP) along with glutathione (GSH) exerted protective effects by reducing SA induced ferroptosis cell death and inflammation both in vivo and in vitro

Conclusions: Our study demonstrate the role of antioxidant signaling GSH-GPX4 in regulating cell death and inflammation in bacterial endophthalmitis. Thus, GPX4 activation and reducing labial iron can be used as new therapeutic approaches to ameliorate bacterial endophthalmitis

CONTROL ID: 3713906

SUBMITTER (NAME ONLY): James Burke

TITLE: Histatin Improves Corneal Wound Healing in a Rabbit Model of Surgical Keratectomy

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Burke, R. Schiffman, Visus Therapeutics, California, UNITED STATES|R.S. Verhoeven, Little Creek Research, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: James Burke: Commercial Relationship(s);Code E (Employment):Visus Therapeutics;Code P (Patent):Visus Therapeutics | Rozemarijn Verhoeven: Commercial Relationship(s);Code C (Consultant/Contractor):Visus Therapeutics | Rhett Schiffman: Commercial Relationship(s);Code E (Employment):Visus Therapeutics;Code P (Patent):Visus Therapeutics

ABSTRACT BODY:

Purpose: Histatins are low molecular weight salivary and lacrimal peptides that have diverse wound healing, anti-inflammatory, anti-apoptotic, and antimicrobial properties. Wounds that are exposed to histatins, such as in the mouth, heal faster with less scarification and inflammation. The purpose of this study was to evaluate the effects of topical ocular administration of histatin-1 on corneal wound healing endpoints in a surgical keratectomy model in the rabbit.

Methods: New Zealand White rabbits (8/group) were anesthetized, and a partial keratectomy was performed in the right eye only using an 8 mm corneal vacuum trephine. The trephined section of the cornea was removed, leaving a central corneal defect of 10-25% of stromal depth (~100 µm). Following the procedure, dose administration was initiated. Animals received a 35 µl topical ocular instillation of histatin-1 or saline in the study eye three times daily for 28 days. Endpoints included fluorescein staining, confocal microscopy, and corneal wholemount immunohistochemistry with Tuj1.

Results: The rate of corneal epithelial healing as measured by area of fluorescein staining (Image J Software) was significantly increased by histatin-1 administration on Days 1-3 ($p<0.05$ and $p<0.01$), with time to healing reduced from 5 to 3 days compared to control. Evaluation of confocal microscopy indicated that histatin-1 inhibited loss of both stromal keratocytes and corneal endothelial cells following keratectomy compared to control and restored cells counts to baseline levels by Day 28 while the control eyes remained reduced by ~40% and ~20%, respectively. The surgical keratectomy resulted in a reduction of corneal nerves as a percentage of initial lesion size by as much as 70% on Day 28, as noted during immunohistochemistry. Histatin-1 administration inhibited this loss of corneal nerves by 20%.

Conclusions: These data demonstrate that topical ocular application of histatin-1 reduced time to corneal wound healing after surgical keratectomy in rabbits from 5 to 3 days, reduced keratocyte dropout and recovery of keratocyte density, decreased corneal endothelial cell loss, and augmented recovery of the keratocytes, endothelial cells and nerves in sub-Bowman’s plexus, suggesting broad utility across a range of corneal and ocular surface indications.

CONTROL ID: 3713909

SUBMITTER (NAME ONLY): Krista Beach

TITLE: Intraocular pressure in infant Rhesus monkeys: diurnal curves and awake versus sedated measurements

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.M. Beach, L. Hung, L. Lou, L.A. Ostrin, Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Krista Beach: Commercial Relationship: Code N (No Commercial Relationship) | Li-Fang Hung: Commercial Relationship: Code N (No Commercial Relationship) | Linjiang Lou: Commercial Relationship: Code N (No Commercial Relationship) | Lisa Ostrin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Measurement of intraocular pressure (IOP) in young Rhesus monkeys is important for the study of numerous ocular conditions, including eye growth and myopia. Recent studies show that select ocular hypotensive agents may protect against experimental myopia. In young monkeys, IOP is traditionally measured under anesthesia, which may confound the findings. This study aimed to establish a method for awake IOP measurement in young monkeys, assess the effects of dilation and sedation, and determine diurnal variation.

Methods: Subjects were infant Rhesus monkeys (Macaca mulatta, n = 11) undergoing lens-treatment for a refractive study. IOP was measured with a rebound tonometer (iCare TonoVet). At three weeks of age, awake IOP was measured every two hours from 7:30 am to 5:30 pm to determine potential diurnal variations. Beginning the following day, awake IOP, awake and dilated IOP (tropicamide 0.05%), and sedated (ketamine 20 mg/kg + acepromazine 0.2 mg/kg) and dilated IOP was measured biweekly from ages 3-15 weeks. Intraclass correlation coefficient (ICC) was used to determine intersession repeatability for IOP measurement on 2 consecutive days at 3 weeks of age.

Results: At age 3 weeks, mean (±SEM) awake IOP was 15.4±0.6 and 15.2±0.7 mmHg for right and left eyes, respectively (P=.59). The ICC between sessions was .63[-.5 to .9], with a mean difference of 2.2±0.3 mmHg between days. Diurnal IOP measurement from 7:30 am to 5:30 pm showed no significant variation (P=.67). For all ages, IOP while awake and undilated was 17.2±0.5 mmHg, awake and dilated was 18.5±0.5 mmHg, and sedated and dilated was 11.1±0.9 mmHg. There was a significant effect of age (P=.01) and condition (P<.001), with no interaction between age and condition (P=.46).

Conclusions: Awake IOP measurement is feasible in young Rhesus monkeys with moderate repeatability. There was no significant diurnal fluctuation in IOP between 7:30 am and 5:30 pm. IOP measured under sedation was significantly lower than IOP measured in awake monkeys, while topical administration of tropicamide did not affect IOP. Findings show that ketamine/acepromazine anesthesia affects IOP in young Rhesus monkeys, suggesting that measurement should be performed before sedation.

CONTROL ID: 3713910

SUBMITTER (NAME ONLY): Tatiana Perepelkina

TITLE: Progression analysis of Stargardt (STGD) disease in children cohort with biallelic ABCA4

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Perepelkina, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|T. Perepelkina, Ophthalmology, LSU Health Shreveport, Shreveport, Louisiana, UNITED STATES|E. Kegeles, A. Naumov, E. Karpulevich, P. Volchkov, Moscow Institute of Physics and Technology, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: Stargardt disease is the most common inherited macular dystrophy caused by the ABCA4 gene's mutations, with an estimated prevalence of 1/8000–1/10000. With its high phenotypic and genotypic heterogeneity, STGD typically causes severe progressive vision loss in children and young adults, incurring a substantial socioeconomic and psychological burden. The typical course of STGD exhibits progressive acuity loss during the school years, yet quantitative assessment of progression remains limited. Any information about natural progression of early disease is essential for anticipatory guidance, as well as for new therapy development.

Methods: We performed a longitudinal retrospective study on a patients' cohort observed at Medical Retina Service, Boston Children's Hospital. Our study group includes 33 children with genetically confirmed biallelic ABCA4 disease whose ages at presentation range from 3 to 18 yr, and age of symptoms onset falls within 7-10 yr range. Genetic variants in the younger group included many with double nulls mutations. We were primarily focusing on studying the STGD progression measuring retinal thicknesses on OCT. Every included patient had at least two longitudinal observations with OCT scan and visual acuity measurements. OCT scans were manually annotated to measure retinal thickness at the fovea, at 1mm and 3 mm away using Label Studio software. In total, 202 OCT images were used in the analysis. Further processing and statistical analysis were performed in Python using Pandas, Numpy, Scipy, and Sklearn packages.

Results: We observed two different modes of the disease progression in the observed patients: a drastic reduction in retinal thickness in the young age (before 8 yr) and changes with low magnitude in older kids. Reduction in ONL thickness for patients < 8 years old was: -38±5 um/yr at the fovea, -23±3 um/yr at 1mm nasal, and -20±3 um/yr at 1mm temporal retina. In older patients, the progression rate was strikingly lower: -1.3±0.6 um/yr at the fovea, 0.8±0.5 um/yr at 1mm nasal, and 0.3±0.5 um/yr at 1mm temporal retinas. Calculations were performed based on N=20 scans from six young patients and N=180 scans from 29 older kids.

Conclusions: Our findings are indicative of the rapid progression of the disease in patients before 8 years old. Studies on STGD progression and early intervention will require the observation of very young children.

CONTROL ID: 3713911

SUBMITTER (NAME ONLY): Erick Palacios

TITLE: Sirtuin 6 regulates endothelin 1 expression in retinal neuronal cells

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Palacios, S. Shi, F. Xia, W. Zhang, H. Liu, Department of Ophthalmology and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|W. Zhang, Department of Neuroscience, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endothelin 1 (Edn1) is a 21-amino acid peptide that potently induces vasoconstriction and plays a key role in retinal neuronal and vascular degeneration in glaucoma and diabetic retinopathy. Yet mechanisms that regulate Edn1 expression in retinal cells remain to be elucidated. Given that Edn1 production is associated with aging or cell senescence, we reasoned that molecules that regulate aging process may be involved in the regulation of Edn1 expression. Sirtuin (Sirt) 1 and Sirt6 are evolutionarily conserved nicotinamide adenine dinucleotide (NAD)-dependent histone deacetylases and share homolog with yeast Sir2 protein that critically regulates lifespan of yeast. This study aims to test whether Sirt1 and Sirt6 can regulate Edn1 expression in retinal neuronal cells.

Methods: Localization of Sirt1 and Sirt6 was determined by immunohistochemistry in mouse retinal sections. Differentiated R28 cells were transfected with siRNA to knockdown Sirt1 or Sirt6, with a non-targeting siRNA as control. Edn1 expression was assessed by quantitative PCR (qPCR).

Results: Sirt6 was abundantly expressed in cells in the ganglion cell layer although weak immunoreactivity of Sirt6 was also noted in the inner nuclear layer and outer nuclear layer of the retina. In contrast, Sirt1 immunoreactivity was universally expressed in all cells. In differentiated R28 cells, Sirt1 siRNA reduced Sirt1 expression by 60.7% and 76.7% at 24 and 48 hours respectively, and raised Edn1 expression by 11.2% and 98.7%. Sirt6 siRNA reduced Sirt6 expression by 59.1% and 72.1% at 24 and 48 hours respectively, and resulted in the elevations of Edn1 by 130.2% and 306.6%.

Conclusions: Although knockdown of either Sirt1 or Sirt6 induced Edn1 expression, Sirt6 siRNA had a much more pronounced effect on Edn1 expression, suggesting that Sirt6 had the primary role in regulating Edn1 expression in retinal neuronal cells. Considering Sirt6 but not Sirt1 was predominantly expressed in retinal ganglion cells (RGCs), our study suggests that Sirt6 may be potentially involved in maintaining RGC health by inhibiting Edn1 expression.

CONTROL ID: 3713913

SUBMITTER (NAME ONLY): Oktay Uzun

TITLE: Pharmacokinetics of a Hydrogel-based Nepafenac Intracanalicular Insert in Canines

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Uzun, A. Desai, S. Ray, C. Patel, C.D. Blizzard, P.K. Jarrett, M. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are often prescribed following ophthalmic surgery to reduce ocular pain and modulate inflammation. Sustained-release drug delivery of NSAIDs may overcome some limitations of topical therapy such as patient self-dosing and nonadherence. Here we evaluate the pharmacokinetics of nepafenac delivered from a biodegradable hydrogel intracanalicular insert in a canine model.

Methods: A hydrogel-based intracanalicular insert containing a low dose of nepafenac was placed bilaterally into the inferior canaliculus of 20 beagle dogs on Day 0. After presence of the insert in the canaliculus was confirmed visually, tear fluid was collected from n=10 eyes with pre-cut 10 mm Schirmer test strips at 2 hours, and 1, 3, 7, 10, 14, 17, 21, 24 and 28 days post-insertion. Aqueous humor (0.1 mL, n=6 eyes) was collected 7, 14, 21, and 28 days post-insertion. Tear fluid and aqueous humor samples were analyzed for nepafenac (prodrug) and amfenac (active metabolite) by liquid chromatography tandem mass spectrometry.

Results: Maximum mean concentration of nepafenac (671 ng/mL) and amfenac (153 ng/mL) in the tear fluid was measured at 2 hours post-insertion indicating rapid dissolution of drug from the insert soon after placement. Mean nepafenac and amfenac levels in tear fluid samples over time showed drug levels gradually tapered over time. Nepafenac and amfenac levels were cleared from the tear fluid by 10-14 days. Both the prodrug and active metabolite were found in the tear fluid in an 85:15 ratio, however, only amfenac was detected in aqueous humor samples. Amfenac concentration in the aqueous humor was highest on Day 7 at 18.3 ng/mL and decreased to 2.6 ng/mL at Day 14. Levels of amfenac in the aqueous humor were 41-fold above the half maximal inhibitory concentration of cyclooxygenase-2 for amfenac (COX-2 IC_{50} = 0.45 ng/mL) indicating potential therapeutic benefit at these concentrations.

Conclusions: A hydrogel-based intracanalicular insert containing nepafenac quickly released drug at therapeutic levels to the ocular surface and continued for 10-14 days. Ocular pharmacokinetic studies of inserts with higher drug doses are needed to further characterize the release profile of nepafenac intracanalicular insert.

CONTROL ID: 3713914

SUBMITTER (NAME ONLY): Zhanhan Tu

TITLE: Pediatric Circumpapillary Retinal Nerve Fiber Layer Development in Healthy Infants and Children Using Hand-Held Spectral-Domain Optical Coherence Tomography

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Tu, S.D. Shah, V. Sheth, S.N. Teli, B.S. Edawaji, H. Kuht, M. Hisaund, A. Patel, R. McLean, M. Thomas, I. Gottlob, F.A. Proudlock, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|I. Gottlob, Cooper University Hospital, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the development of 3-dimensional full circumpapillary retinal nerve fiber layer (cpRNFL) in full-term infants and young children without sedation and dilation using handheld spectral-domain optical coherence tomography (HH-SDOCT) and also to establish normative age-adjusted values.

Methods: OCT images collected from 375 eyes from 231 infants and children aged between 1 day and 14.5 years using an HH-SDOCT (Leica Microsystems, Envisu C2300, Wetzlar, Germany) system were analyzed semi-automatically using GDx Nerve Fiber Analyzer protocol. The developmental trajectories against log post-menstrual age (logPMA) for cpRNFL thickness (at 6° from the disc center) in four quadrants and ONH parameters mostly approximated to linear changes and were modelled using linear mixed models. Several parameters showed non-linear changes and were modelled using fractional polynomials.

Results: The thickness of superior, inferior and nasal cpRNFL quadrants did not significantly change between birth and 14.5 years old. The 1st quartile (Q1), median (Q2) and 3rd quartile (Q3) were 100 μm, 110 μm and 120 μm for the superior cpRNFL quadrant; 99 μm, 110 μm and 120 μm for the inferior cpRNFL quadrant; and 60 μm, 68 μm and 75 μm for the nasal cpRNFL quadrant, respectively. In contrast, the temporal cpRNFL quadrant demonstrated a significant decrease between birth and approximately 18 months of age and then remained relatively constant up to the age of 14.5 years (Q1 = 57 μm; Q2 = 62 μm; Q3 = 70 μm over 18 months of age).

Conclusions: We describe, for the first time, the development of the full cpRNFL from birth to 14 years using 3-dimensional HH-SDOCT imaging. Interestingly, the temporal cpRNFL quadrant shows a different developmental trajectory to the superior and inferior cpRNFL quadrants despite all three quadrants comprising of fibres projecting from the macular region. Our findings also provide normative data during these critical early years of visual maturation for use in clinical diagnosis, monitoring ocular development and understanding further ocular abnormalities.

CONTROL ID: 3713916

SUBMITTER (NAME ONLY): Budd Tucker

TITLE: Automated production of patient derived iPSCs for autologous photoreceptor cell replacement.

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.A. Tucker, L.R. Bohrer, N.E. Stone, K.R. Anfinson, C.M. Schaffer, M.A. Luse, R.F. Mullins, E.M. Stone, Institute for Vision Research, Iowa City, Iowa, UNITED STATES|B.A. Tucker, L.R. Bohrer, N.E. Stone, K.R. Anfinson, C.M. Schaffer, M.A. Luse, R.F. Mullins, E.M. Stone, Ophthalmology and Visual Science, University of Iowa, Iowa City, Iowa, UNITED STATES|B.A. Hittle, K.A. Powell, Biomedical Informatics, The Ohio State University, Columbus, Ohio, UNITED STATES|G.F. Muschler, Biomedical Engineering, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this study we describe the use of custom designed robotics and ISO Class 5 cGMP cell culture atmospheric isolators for the high throughput production of clinical grade patient specific iPSCs and retinal organoids containing transplantable photoreceptor cells.

Methods: Patient derived fibroblast were isolated from 27 individuals, ranging from 6 to 92 years of age, with molecularly confirmed inherited retinal degenerative blindness. Cells were used for iPSC generation using Sendai virus. Oxygen tension was dropped from 20-10% and cultures are subsequently fed daily with E8 media and passaged onto laminin 521 coated 6 well culture plates. Over the next 21 days cultures were fed daily, imaged every 3-5 days, picked, and clonally expanded using the CellX robot. IPSCs were subjected to karyotyping and score card analysis prior to being differentiated using a cGMP compliant 3D differentiation protocol. Differentiated organoids were subjected to immunohistochemistry and single cell RNA sequencing.

Results: Robot generated iPSCs were determined to be pluripotent via score card analysis and no significant difference in the rate of karyotypic abnormalities was detected between iPSCs generated under manual or automated conditions ($P>0.05$). Robot generated iPSCs gave rise to retinal organoids that were indistinguishable from their manually generated counterparts as determined via immunostaining and confocal microscopy using antibodies targeted against NRL, rhodopsin, cone opsin, cone arrestin and recoverin. At 120 days, retinal organoids were dissociated and subjected to single cell RNA sequencing and were compared to cells generated in the Reh laboratory (scRNAseq comparison dataset PMID 32023475). Clustering analysis demonstrated that cells generated on the robotic platform were comparable to those generated under manual conditions in a separate laboratory. Specifically, each of the expected retinal cell types were present in roughly the same proportions between those generated in both groups.

Conclusions: We successfully developed a high throughput robot iPSC generation platform and standard operating procedures for production of high-quality photoreceptor precursor cells that are compatible with current good manufacturing practices. This system will enable clinical grade production of iPSCs for autologous retinal cell replacement.

CONTROL ID: 3713917

SUBMITTER (NAME ONLY): Pallavi Gorijavolu

TITLE: Role of Septins in Regulation of Actin Cytoskeletal Organization in Trabecular Meshwork Cells

SESSION TITLE: Aqueous humor dynamics & Trabecular Meshwork

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Gorijavolu, R. Maddala, W. Bachman, N.P. Skiba, V. Rao, Opthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|R.K. Singh, Obstetrics and Gynecology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|V. Rao, Pharmacology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Actin cytoskeletal organization and cell adhesive interactions of the trabecular meshwork (TM) are recognized to influence aqueous humor outflow and intraocular pressure in humans. However, the molecular mechanisms regulating such cellular characteristics of TM cells remain poorly understood. This study describes for the first time the role of septins, conserved GTP-binding cytoskeletal proteins that polymerize into filaments, in the regulation of actin cytoskeletal organization in human TM cells.

Methods: The presence and distribution of septin isoforms in human TM cells were evaluated by mass spectrometry, immunoblot, and immunofluorescence analyses. The septin interactome of human TM cells was determined using SEPT9 antibody and proteomics analyses. Septin levels in dexamethasone and TGF-β2 treated TM cells were evaluated by immunoblotting. The effects of actin cytoskeleton and microtubule depolymerizing agents as well as inhibitors of septin and Rho kinase on septin and actin cytoskeletal organization were studied in TM cells by immunofluorescence.

Results: Proteomics and immunoblot analyses readily identified the presence of various septin isoforms (Septin 2, 7, 9, 10, 11, 8 and 5) in human TM cells. Several of these septins revealed filamentous organization, co-localization with actin and microtubule networks, as well as distribution to the TM cell cortical, nuclear, and membrane regions. Dexamethasone and TGF-β2 treatments significantly increased SEPT9 and 11 levels in TM cells. Analysis of the human TM cell SEPT9 interactome identified regulatory proteins of the Rho GTPase, actin cytoskeleton, and cell adhesion pathways, in addition to the expected presence of several septins. Pharmacological inhibition of septin oligomerization decreased septin filaments and actin stress fibers in TM cells. While treatment with a Rho kinase inhibitor and latrunculin decreased septin filaments, nocodazole led to an increase in septin filament organization in human TM cells.

Conclusions: This study reveals not only the presence of septin cytoskeleton but also its direct role in regulation of actin cytoskeletal organization, cell shape, and adhesion in TM cells. Based on the effects of the septin inhibitor on actin cytoskeletal organization in TM cells, we posit that septins are potential therapeutic targets for lowering intraocular pressure in glaucoma.

CONTROL ID: 3713919

SUBMITTER (NAME ONLY): Mustapha El Hamdaoui

TITLE: Scleral Crosslinking Using Genipin Can Compromise Retinal Structure and Function in Tree Shrew Eyes

SESSION TITLE: Myopia: Structure-Function Relationship

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. El Hamdaoui, A. Stuber, C.A. Girkin, B.C. Samuels, R. Grytz, Ophthalmology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|T. Kraft, Optometry and Vision Science, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|A.M. Levy, Biomedical Engineering, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the safety of scleral crosslinking (SXL) using genipin at doses that were effective in slowing myopia progression in juvenile tree shrews as shown in our previously published work (El Hamdaoui et al. Transl Vis Sci Technol 2021;10(5):1).

Methods: Three or five retrobulbar injections of genipin at 0 mM (sham), 10 mM, or 20 mM were performed in one eye every other day. Form deprivation (FD) myopia was induced in the injected eye. Retinal thinning, structural integrity, and function were assessed using optical coherence tomography, histology, and ERG, respectively. Differences between treated and control eyes (Treated – Control) were computed and used to test for significant differences across groups (independent samples t-test). The normal and FD groups served as reference groups and the significance level was set to 0.05.

Results: The peripapillary retinal nerve fiber layer (RNFL) thinned significantly in all genipin treated groups compared to the normal and FD groups. Inducing FD alone and in combination with sham injections caused no RNFL thinning suggesting that the observed RNFL thinning was caused by genipin treatment (Fig. 1A). Thickness of the remaining retinal layers (RRL) was significantly thinner in all injected groups, including the sham group, compared to the normal but not to the FD group suggesting that RRL thinning was primarily caused by axial elongation and not by genipin treatment (Fig. 1B). ERG results showed a significant desensitizing shift of the b-wave semi-saturation constant in the sham group and the second highest genipin dose group (Fig. 1C) and a significant reduction in b-wave maxima in the two highest dose groups (Fig. 1D). Histology analysis revealed noticeable degeneration of photoreceptors and retinal pigment epithelium in the highest genipin dose group (Fig. 2).

Conclusions: SXL using genipin may be a feasible treatment for myopia control. However, our results suggest that repeated retrobulbar injections of genipin above 10mM may not be safe in the tree shrew model of myopia. An adequate and sustained delivery strategy of genipin at lower concentrations will be needed to achieve a safe and effective SXL treatment for myopia control in tree shrew eyes. Caution should be used if the proposed treatment approach is translated to humans.

CONTROL ID: 3713920

SUBMITTER (NAME ONLY): John Rodriguez

TITLE: Ora Vanishing Optotypes Reading Test™ in Non-Advanced Age-Related Macular Degeneration: Results Of 1-Year Follow-Up

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Rodriguez, K. Dieter, E. bensinger, G. De Moraes, D.L. Welch, M.B. Abelson, Ora, Inc., Massachusetts, UNITED STATES|G. Wallstrom, SDC, Inc., Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: In a previous study, a reading test based on vanishing optotype characters (Ora Vanishing Optotypes Reading Test™) was used to assess visual function impairment in early AMD patients compared to age-matched controls. The current study aims to investigate the usefulness of this test after one-year follow-up testing of the previously investigated early AMD cohort.

Methods: In the initial study, subjects with non-advanced AMD: N = 11 (grade 1 to 4 on AREDS simplified scale) and normal controls N = 24 (AREDS grade 0) with best visual acuity (VA) 20/25 or better (in both groups) were included. In the one-year follow-up, 9 non-advanced AMD subjects and 16 control subjects were again tested. All testing procedures used in the initial study were repeated in the follow-up. The reading test was administered monocularly with best correction in place. All subjects were asked to read nine passages of pepper words at successively lower contrast levels with a maximum contrast passage as baseline. Reading speed in words per minute (wpm) was recorded for each passage. The primary outcome was reduction of reading speed relative to baseline. Only subjects that participated in both trials were included in the comparison.

Results: At the initial visit, there was no difference in reading speed between groups at maximum contrast [102.0 ± 16.7 wpm (AMD) and 96.2 ± 18.9 wpm (control) ($p = 0.2$)]. These findings were replicated at 1-year follow-up: [97.6 ± 15.2 wpm (AMD) and 95.9 ± 17.2 wpm (control) ($p = 0.8$)]. Although reading speed relative to subject baseline tested lower for the AMD group at reduced contrast levels during the initial visit, this did not achieve significance. However, after one year, reading performance was found to be significantly impaired in AMD subjects compared to controls at 7 out of the 9 tested contrast levels ($p < 0.02$).

Conclusions: Results of the one-year follow-up showed good reproducibility and a potential utility of this technique as a novel functional endpoint in non-advanced AMD clinical trials.

CONTROL ID: 3713921

SUBMITTER (NAME ONLY): Peng Lu

TITLE: Intravitreal Injection of PACAP Attenuates Acute Ocular Hypertension-Induced Retinal Injury via Anti-Apoptosis and Anti-Inflammation in Mice

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Lu, Y. Shi, Y. Xu, J. Huang, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Pituitary adenylate cyclase activating polypeptide (PACAP) has been shown to exert potent neuroprotective effects in central nervous system and retina disorders. However, whether PACAP could attenuate retinal neurodegeneration induced by acute ocular hypertension (AOH) and the precise mechanisms remain unknown. In this study, we aim to investigate the effects of PACAP on retinal ganglion cells (RGCs) survival, apoptosis, retinal reactive gliosis and vascular inflammation in mouse model of AOH injury.

Methods: PACAP was injected into the vitreous body immediately after inducing the AOH injury. Hematoxylin & eosin staining and optical coherence tomography were used to evaluate the loss of retina tissue. Electroretinogram was used to evaluate the visual function of retina. TUNEL assay was used to detect the apoptotic cells. Immunofluorescence and western blot were employed to evaluate the protein expression level.

Results: PACAP treatment significantly attenuated the losses of retina thickness and RGCs, and improved the b-wave amplitudes of scotopic electroretinogram after AOH injury. Additionally, PACAP treatment remarkably reduced the number of apoptotic cells in AOH injury, and inhibited the upregulation of Bax, cleaved caspase3 and downregulation of Bcl-xL induced by AOH injury. Moreover, PACAP markedly abrogated retinal reactive gliosis and vascular inflammation, as demonstrated by the downregulation of GFAP, Iba-1, CD68 and CD45 in PACAP-treated mice. Furthermore, upregulated expression of NF-κB and phosphorylated NF-κB induced by AOH injury were attenuated by PACAP treatment.

Conclusions: These results demonstrated that PACAP could attenuate retinal injury by inhibiting the Bax-Caspase3 dependent apoptotic pathway and NF-κB dependent inflammatory pathway.

CONTROL ID: 3713922

SUBMITTER (NAME ONLY): Juan Angueyra

TITLE: Transcription factors involved in determination of photoreceptor fate

SESSION TITLE: Retinal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Angueyra, V.P. Kunze, L.K. Patak, H. Kim, W. Li, National Eye Institute, Bethesda, Maryland, UNITED STATES|K. Kindt, National Institute on Deafness and Other Communication Disorders, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Juan Angueyra: Commercial Relationship: Code N (No Commercial Relationship) | Vincent Kunze: Commercial Relationship: Code N (No Commercial Relationship) | Laura Patak: Commercial Relationship: Code N (No Commercial Relationship) | Hailey Kim: Commercial Relationship: Code N (No Commercial Relationship) | Katie Kindt: Commercial Relationship: Code N (No Commercial Relationship) | Wei Li: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Cell specification is a fundamental process that underlies the formation of tissues and organs. In the retina, photoreceptor specification must coordinate with development of other retinal cells and eyecup formation. Photoreceptors have defined subtypes which differ in spectral sensitivity, morphology, wiring, and gene expression. Transcription factors (TFs) modulate genetic programs to specify each photoreceptor subtype. Seminal work in mice identified key TFs required for the determination of rods (Mears, 2001, Cheng, 2006) and L cones (Ng, 2001, Roberts, 2005) but work in other species has highlighted that photoreceptor fate is complex and our understanding is still incomplete (Oel et al., 2020; Ochi et al., 2004, Alvarez-Delfin, 2009; Duval et al., 2018; Ogawa at al., 2019). The purpose of our research is to identify mechanisms that control photoreceptor fate during development.

Methods: We performed deep transcriptomic profiling (RNAseq) of photoreceptors—by manually collecting pools of the five photoreceptor subtypes of the adult zebrafish retina—to determine which transcription factors are differentially expressed. Then we developed a platform to perform CRISPR-based reverse-genetic screens to identify which transcription factors control photoreceptor fate determination.

Results: We identified Tbx2 as a critical TF for photoreceptor fate determination. In zebrafish, tbx2b is implicated in UV-cone specification (Alvarez-Delfin, 2009): mutations in this gene lead to loss of UV cone progenitors, which are routed to become rods. tbx2 was duplicated in teleosts, and RNAseq revealed that tbx2b is expressed by UV and S cones, and tbx2a is expressed by UV and L cones. TBX2 is highly conserved across vertebrates and is highly expressed by S cones in primate (Peng, 2019) and by UV cones in chicken (Yamagata, 2021). Using FØ-CRISPR screening techniques (Hojishima, 2019), we generated tbx2b mutant zebrafish larvae that recapitulate the known phenotype. Surprisingly, tbx2a mutants display the same phenotype, suggesting that tbx2b and tbx2a act independently and are both required for UV-cone specification. Furthermore, we found that tbx2a acts in L cones to represses M-cone fate (Sandkam et al., 2020) and that tbx2b acts in S cones to also repress M-cone fate.

Conclusions: This early success substantiate these methods as an efficient and flexible platform to study mechanisms of fate determination in photoreceptors.

CONTROL ID: 3713923

SUBMITTER (NAME ONLY): Richard Grambergs

TITLE: Retinal Characterization of Sphingosine-1-Phosphate Receptor 2 Knockout Mice

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Grambergs, A.P. Shrestha, K. Mondal, T. Hollingsworth, T. Vaithianathan, N.A. Mandal, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|D.M. Sherry, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sphingosine-1-phosphate (S1P) is a bioactive sphingolipid that acts through G protein-coupled S1P receptors (S1PR1-5) to participate in a variety of signaling pathways, but its role in the neural retina has not been studied extensively. We previously showed that S1PR2 is expressed in mouse and rat retinas, primarily in photoreceptors and bipolar cells, and expression is altered by conditions of retinal stress. In this study, we developed S1PR2 knockout (KO) mice on an albino background and performed structural and functional characterizations of their retinas under normal conditions and after intense light-induced retinal degeneration (LIRD) treatment.

Methods: Albino S1PR2 KO and wild-type (WT) littermate mice were raised under similar conditions and underwent retinal assessments at various matched age-points between 3 and 6 months. Retinal function was assessed by electroretinography (ERG), and structural differences by electron microscopy (EM) and optical coherence tomography (OCT). Immunohistochemical (IHC) labeling was used to visualize differences in neuronal and synaptic markers in light- and dark-adapted mice. Mice underwent similar assessments after LIRD (1500 lux for 6 hours) to evaluate their sensitivity to retinal stress.

Results: We found significantly elevated A- and B-wave responses at ERG flash intensities between 4-2000 cd.s/m^2 in S1PR2 KO mice compared to WT at baseline (n = 12 and n = 8, respectively) and after LIRD (n = 10 and n = 11; $P < 0.05$). OCT further showed that KO mice (n = 8) had significantly increased retinal nerve fiber layer (RNFL) (14.8 ± 0.3μm vs 13.3 ± 0.5μm) and outer plexiform layer (OPL) (12.5 ± 0.4μm vs 11.6 ± 0.2μm) thickness compared to WT (n = 10; mean ± SE; $P < 0.05$). EM likewise showed differences in inner neuronal layers and OPL, and reduced synapses between rod terminal and bipolar cells in KO mice. IHC also showed differential labeling of synaptic markers and dendritic arborization of secondary neurons in KO mice compared to WT.

Conclusions: Our findings show that S1PR2 knockout alters murine retinal structural and functional characteristics, suggesting an important role of S1PR2 in the mammalian retina.

CONTROL ID: 3713924

SUBMITTER (NAME ONLY): Chih-Chiun Chang

TITLE: Topical glaucoma therapy is associated with alterations of the ocular surface microbiome

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Preserved topical medications used in the management of glaucoma are associated with ocular surface inflammation. The purpose of this cross-sectional study was to describe the ocular surface microbiome of patients treated with preserved topical ophthalmic medications as compared to that of healthy controls and to determine if microbial community changes were related to measures of ocular surface disease.

Methods: V3-V4 16S rRNA sequencing was conducted on ocular surface swabs collected from both eyes of 17 subjects: 10 patients with asymmetric/unilateral glaucoma using preserved topical glaucoma therapy on only one eye and 7 age-matched, healthy controls with no history of ocular disease or eyedrop use. Air swabs were used as negative controls. Samples were categorized into three groups: patients' glaucomatous eye treated with eyedrops, patients' contralateral eye without eyedrops, and healthy control eyes. Comparisons were made for microbial diversity and composition, with differences in composition tested for association with ocular surface disease measures including tear meniscus height (TMH), tear break-up time (TBUT), and Dry Eye Questionnaire scores (DEQ-5). The Columbia University Institutional Review Board approved this study.

Results: Samples obtained from treated and untreated patient eyes both had greater alpha-diversity (Shannon Diversity; Figure 1A, 1C) and distinct microbial composition (Bray Curtis Distance; Figure 1B, 1D) compared to controls. Patient samples had an increased relative abundance of gram-negative organisms dominated by Akkermansia compared to gram-positive commensals in controls (Figure 2). The microbial composition of patient eyes was associated with decreased TMH and TBUT, while metagenomic predictions based on 16S rRNA data suggested increased synthesis of the inflammatory endotoxin lipopolysaccharide.

Conclusions: The ocular surface microbiome of patients taking unilateral preserved glaucoma drops is characterized by a diverse array of gram-negative bacteria that is significantly different from the predominantly gram-positive microbes detected on healthy control eyes. These compositional differences were associated with decreased tear film measures and distinct inferred protein synthesis pathways, suggesting a potential link between microbial alterations and ocular surface inflammation.

CONTROL ID: 3713926

SUBMITTER (NAME ONLY): Jasmine Mahajan

TITLE: Utility of Three-Dimensional Macular Topography for Non-Ophthalmologist Screening of Diabetic Macular Edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mahajan, B. Zhou, R.K. Henry, M.K. Shah, B. Szirth, N. Bhagat, Rutgers New Jersey Medical School Institute of Ophthalmology and Visual Science, Newark, New Jersey, UNITED STATES|R.K. Henry, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Triage of patients with visual complications of Diabetic Retinopathy (DR) in the emergency department (ED), urgent care centers, or primary care offices can be challenging due to limited availability of ophthalmic specialists. In this pilot study, we deployed non-mydriatic automated Ocular Coherence Tomography (OCT) technology (or tele-OCT-B) in conjunction with 3D macular mapping software to assess the ability of non-ophthalmologists to triage posterior pole OCT-B images for Diabetic Macular Edema (DME).

Methods: Macular OCT-B scans of 41 eyes (21 patients with mean age 56.5 years and male to female ratio of 3:4) were captured in an academic retina clinic using Topcon Maestro 3D OCT-1. 3D topographical maps were rendered. A retinal physician assessed each OCT-B image and 3D map for the presence of DME and the severity level as described by the International Clinical DME Severity Scale. The fundus photo images from Topcon OCT camera were reviewed for DR. Two third-year medical students independently reviewed the topographic maps for the presence of DME. Cohen's kappa (κ) was used to test concordance between student and retina specialist (gold standard) for identifying DME. Statistical analysis was performed using IBM SPSS software version 25.

Results: 38/41 eyes were included in the final analysis. Non-ophthalmologist graders had an average sensitivity of 70% (SD 4.71) and specificity of 80% (SD 3.08) in detecting DME (Table 1). Inter-grader concordance between non-ophthalmologists was substantial ($\kappa=0.78$, $p<0.00001$). Between non-ophthalmologists and the retina specialist, average concordance in detecting any DME was $\kappa=0.50$ (SD 0.008). When stratified by clinical DME severity, on average, non-ophthalmologists correctly classified 8/9 (90%) eyes with moderate to severe DME, 1/5 (20%) eyes with mild DME, and 14.5/15 (97%) eyes with no DME.

Conclusions: While concordance between non-ophthalmologists and the retinal specialist was modest for detection of DME, non-ophthalmologists correctly identified most moderate to severe DME cases on OCT-B with high agreement. OCT-B 3D map may be an invaluable tool to use with non-mydriatic fundus camera in the ED or primary care offices in screening diabetic patients for vision threatening DME who need urgent ophthalmic referral, especially during a pandemic.

CONTROL ID: 3713927

SUBMITTER (NAME ONLY): Nakul Singh

TITLE: Differences in Cataract Surgery Outcomes by Race and Primary Language Spoken

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Singh, S. Bal, T. Ta, A.C. Lorch, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess differences in cataract surgery outcomes by race and primary language spoken in order to better understand delivery of surgical care to diverse patient populations.

Methods: Massachusetts Eye and Ear surgical outcomes were assessed between January 1, 2020 and December 31, 2020. Patient's self-identified race/ethnicity were extracted from the medical record and collapsed into broader categories of White, Black, Hispanic, Asian, declined/unavailable, and other for race. Cataract surgery outcomes were loss to follow up, final refractive error within 0.5 diopter of target refraction and hyperopic final refractive error. Logistic regression was performed to estimate the odds ratios between categories.

Results: A total of 2,166 patients underwent cataract surgery and were included in the analysis (White=1,605, Asian=118, Black=157, Other = 127, Decline/Unavailable = 129) (English speaking = 1,895, Non-English speaking = 248). There were no differences by race or language in final refractive error within 0.5 diopters of target refraction or hyperopic final refractive error. There were no differences by race or primary language spoken for loss of follow up.

Conclusions: There were no racial or language disparities in cataract surgery outcomes, both in final refractive error or loss to follow up during 2020. Hopefully this represents equitable care delivered to patients, but 2020 was an anomalous year in many ways, which may confound identification of structural inequities.

CONTROL ID: 3713929
SUBMITTER (NAME ONLY): Ruolin Wang
TITLE: Identifying Eyes at Risk for Glaucoma Surgery with Deep Learning
SESSION TITLE: Data science, machine learning, and AI
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Wang, P. Herbert, K. Hou, C. Bradley, M. Unberath, J. Yohannan, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|
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ABSTRACT BODY:
Purpose: To develop and evaluate a deep learning model (DLM) to predict eyes at high risk for future incisional glaucoma surgery from observations early in the disease course.
Methods: We used the DLM architecture depicted in Figure 1. A vision transformer (VIT) is used for feature extraction. The input of the transformer consists of 3 channels consisting of spatially aligned VF and OCT data. After VIT-based feature extraction, the latent representation of VF and OCT data is concatenated with the normalized clinical data and fed into a linear classifier predicting the occurrence of glaucoma surgery within the pre-specified time horizon. Data were split at the patient level into 76%, 12%, and 12% for training, validation, and testing, respectively.
Results: DLM performance was evaluated and compared using Area Under the Receiver Operating Characteristic Curve (AUC). Additionally, sensitivity, specificity, and positive predictive value were calculated using an optimal threshold selected using Youden's J index.

Between 1788 and 2893 eyes were included in the analysis depending on the time horizon of interest. In the test set, the DLM achieved an AUC of 0.92 (95% CI: 0.86, 0.98), a sensitivity of 0.74, and a specificity of 0.92 for predicting glaucoma surgery within 2 years from baseline (Table 1). The predictions for other time intervals achieved clinically useful AUC values (>0.8) except for the 5-year time interval with an AUC of 0.78 (95% CI: 0.71, 0.87).
Conclusions: It is possible to identify eyes in need of glaucoma surgery with very high sensitivity and specificity. Implementing such prediction models in the clinical setting may help stratify high and low-risk patients. Future studies will need to assess the performance of such models prospectively in a varied clinical setting.

CONTROL ID: 3713930

SUBMITTER (NAME ONLY): Yan Zhang

TITLE: TGF-β2 Gene Expression in Chick RPE is Differentially Regulated by Retinal Simultaneous Competing Defocus of Opposite Sign

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhang, C.F. Wildsoet, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|W. Song, Department of Ophthalmology, the 2nd Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, CHINA|M.J. Collins, School of Optometry & Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: This study investigated the effects of competing imposed optical defocus on gene expression of TGF-βs in chick retinal pigment epithelium (RPE).

Methods: 14-day old White-Leghorn chicks wore monocular Fresnel lenses incorporating various optical power combinations (plano/-10D, +5D/-10D, +10D/-10D, +10D/-5D, +10D/plano) for 15 min, 2 h, 2 d and 4 d. qPCR was used to quantify differential gene expression in chick RPE for TGF-β1, 2, and 3.

Results: Gene expression of TGF-β2 was up-regulated after short periods (2 h or 2 d) with all lenses. Notably, TGF-β2 gene expression was up-regulated 266 ± 43% (+5D/-10D), 321 ± 106% (+10D/-10D), 200 ± 35% (+10D/-5D), and 221 ± 41% (+10D/plano), respectively after 2 h exposure. The plano/-10D lens also induced up-regulation of TGF-β2 gene expression, but only after 2 days. Significant up-regulation of TGF-β3 expression, albeit much smaller in magnitude, was also recorded with the +5D/-10D lens, and only after 2 h.

Conclusions: Expression of TGF-β2 genes in chick RPE is sensitive to imposed competing retinal defocus, i.e., of opposite sign. That TGF-β2 gene expression was consistently up-regulated with inclusion of myopic defocus (positive power) is consistent with previous results with single vision lens treatment. The results also further support the targeting of RPE TGF-β2 for myopia control.

CONTROL ID: 3713931

SUBMITTER (NAME ONLY): Alberto de Castro

TITLE: Effect of fixational eye movements on OCT corneal topography measurements with raster and meridional scan patterns

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. de Castro, P. Urizar, E. Martinez-Enriquez, S. Marcos, Instituto de Óptica-CSIC, Madrid, SPAIN|P. Urizar, 2EyesVision, Madrid, SPAIN|S. Marcos, Center for Visual Science. The Institute of Optics. Flaum Eye Institute. University of Rochester., New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal surface elevation can be obtained three-dimensionally with anterior segment Optical Coherence Tomography (OCT). However, its accuracy is subject to fixational eye movements during the acquisition. We developed a model to simulate corneal elevation measurements to study the quality of the reconstruction achieved with different scanning patterns.

Methods: A custom spectral domain OCT (25K A-scans/s) was used to obtain videos (N=10, 22 Hz) of the corneal central meridian in 4 eyes from 2 subjects. The anterior corneal surface in each frame was segmented and fitted by conics. The apex movement was compared with simulations of fixational lateral/axial eye movements from MATLAB Image System Engineering Toolbox for Biology (ISETBIO) fixational eye movement generator with/without saccades. The results were used to simulate 3D-OCT acquisition of a cornea using either a raster or a meridional scan pattern with 300x50 A-scans. The 3-mm central data were fitted by a sphere (radius R) and the residuals fitted with up to 6^{th} order Zernike polynomials (zC). Standard deviations (std) of the fitting parameters of repeated simulated adquisitions for different scan patterns were compared.

Results: The mean amplitude of the cornea movement found experimentally was 119 in the lateral and 142 μm in the axial direction. The mean amplitude of the eye movement generator was 88 and 73 μm with and without microsaccades. Amplitude factors 1.32 and 1.95 were then applied to match lateral and axial movements respectively, which reduced the rms error between simulated and average experimental zC std from 3.7 to 0.9 μm. For raster scan, R std was 0.13 mm and mean zC std was 1.3 μm being highest for astigmatism and coma oriented with the slow scan direction. For meridional scan, R std was 0.01 mm and mean zC std was 2.0 μm being highest for astigmatism and trefoil terms. When all meridians were registered in the center, R std was 0.01 and mean zC std was reduced to 0.3 μm.

Conclusions: Simulations of OCT corneal topography measurements with fixational eye movements predict a high influence of the scanning pattern on the measurement variability, particularly on specific Zernike modes. While eye rotations or scan position inaccuracies were not considered, these simulations can serve to determine the variability with different scan patterns and to evaluate the effectivity of motion correction algorithms.

CONTROL ID: 3713932

SUBMITTER (NAME ONLY): Subrata Batabyal

TITLE: AAV-carried MCO Optogenetic Therapy for the Treatment of Inherited Retinal Disorders

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Batabyal, A. Dibas, H. Al-Saad, S. Kim, M. Carlson, S. Mohanty, Nanoscope Technologies LLC, Bedford, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited Retinal Disorders (IRDs) such as Stargardt disease (SD) or Leber congenital amaurosis (LCA) are rare, and sight-threatening with significant unmet needs. In these IRDs, dysfunction or degeneration of photoreceptors leads to loss of light sensitivity. Optogenetics offers a unique opportunity to treat IRDs of varied genetic origins with a universal therapeutic strategy. The purpose of the study is to evaluate the therapeutic efficacy of intravitreally delivered AAV2-carried gene encoding for ambient light-activatable Multi-Characteristic Opsin (MCO) in animal models of SD and LCA.

Methods: To evaluate the therapeutic efficacy, AAV2-MCO (vMCO) was intravitreally delivered in mice models of SD (Abca4tm1Ght/J) and LCA (B6(A)-Rpe65rd12/J). OCT imaging of the retina, behavioral assay (water maze), and ERG were performed longitudinally up to 24 weeks to evaluate the safety and efficacy of the treatment. Immunohistochemistry of the retina sample was also performed to visualize the expression of MCO in the retina (Visualized by mCherry expression).

Results: Our results demonstrated that intravitreal delivery of vMCO to Stargardt and LCA mice arrests further retinal degeneration (measured by retina thickness using OCT) and restores visual function, quantified by electrophysiology of retina (ERG) and visual cortex (VEP). The visually- guided water maze assessment on vMCO-treated mice showed significant improvement (measured by latency to reach platform) as compared to the vehicle-injected control mice group.

Conclusions: vMCO is potentially a restorative treatment that can be used irrespective of the underlying gene mutation. Intravitreal delivery of vMCO in the Stargardt and LCA mice model was effective in restoring vision and arresting further retinal degeneration. While the efficacy of MCO optogenetic monotherapy is now being evaluated in a multicenter trial on advanced Retinitis Pigmentosa patients, clinical evaluation of vMCO for other IRDs will establish it as an outer retinal degenerative disease-agnostic therapy.

CONTROL ID: 3713934

SUBMITTER (NAME ONLY): Yi Hua

TITLE: Mechanical anisotropy of the equatorial sclera does not concur with its preferred fiber orientation

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Hua, M. Quinn, F. Ji, I.A. Sigal, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|F. Ji, I.A. Sigal, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|S. Salinas, R. Amini, Bioengineering, Northeastern University, Boston, Massachusetts, UNITED STATES|R. Amini, Mechanical and Industrial Engineering, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The equatorial sclera is central to overall globe mechanics. However, compared to the front or back of the eye, little is known about equatorial sclera mechanics and its underlying microstructure. Our goal was to quantify equatorial sclera mechanical behavior and collagen fiber architecture, focusing on anisotropy and fiber preferred orientation.

Methods: Five porcine eyes were obtained from a slaughterhouse within 24 h postmortem. Equatorial sclera samples (11 mm × 11 mm) were excised from each of four anatomical quadrants: nasal, superior, temporal, and inferior. Each sample was mounted on a custom-built biaxial mechanical testing system, with the loading axes aligned with the equatorial and meridional directions of the sample. Four submillimeter glass markers were attached to the surface of the sample for optical tracking of tissue deformation (strain). The sample was then loaded under equal-biaxial stress control, with the maximum stress of 120 kPa. Each test consisted of ten loading/unloading cycles, and only data from the tenth cycle was used in our analysis. The sample was immersed in PBS during the test. After testing, the samples were fixed overnight in 10% formalin. Four samples from three eyes were cryosectioned into 30-μm-thick sections. Sections were imaged using polarized light microscopy, and collagen fiber orientations determined using a previously reported technique. Orientation maps were registered and quantified to determine fiber orientation distributions and the preferred orientation of each sample.

Results: The superior and inferior quadrants had the highest anisotropy, with the stiffness along the equatorial direction much larger than that along the meridional direction. The preferred fiber orientation in all four quadrants was in the meridional direction.

Conclusions: A sclera that is softer in the meridional direction may steer the eye to respond to loads by elongating longitudinally, without increasing equatorial diameter. This may reduce optical distortions and insult to the delicate neural and vascular tissues. Surprisingly, the higher equatorial sclera mechanical stiffness did not concur with the preferred meridional collagen fiber orientations. The origin of this discrepancy remains unknown. It is possible that not all fibers are equally stiff. Ongoing efforts are to analyze the collagen architecture of more samples.

CONTROL ID: 3713935

SUBMITTER (NAME ONLY): Eric Weh

TITLE: Delivery of a hydrophobic small molecule LXR agonist via sHDL nanoparticles in a preclinical model of dry AMD

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Weh, C. Lin, A.T. Fahim, C. Besirli, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|L. Mei, M. Yi, A. Schwendeman, Pharmaceutical Sciences, University of Michigan College of Pharmacy, Ann Arbor, Michigan, UNITED STATES|L. Walsh, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: AMD is a blinding disorder characterized by the accumulation of lipids beneath the Bruch's membrane (drusen) and the invasion of immune cells into the retina. Activating the Liver X receptor (LXR) pathway can promote efflux of cholesterol from atherosclerotic plaques and inhibit pro-inflammatory cytokine production. Here, we evaluated the delivery of the hydrophobic LXR agonist (T0) complexed within a synthetic HDL (sHDL) molecule via intravitreal treatment (IVT) in a dry AMD animal model.

Methods: Mice or rats were injected with sodium iodate ($NaIO_3$, 40mg/kg) via the femoral vein. Either vehicle (PBS or DMSO) or drug (sHDL, T0, or sHDL-T0) was given via IVT immediately before $NaIO_3$ injection. A subset of animals were treated with vehicle or drug only. Retina and eye cups containing RPE/Choroid were collected for qRT-PCR and Western blotting. In vivo OCT and ex vivo histology were performed to assess retinal thickness and photoreceptor viability. Retinal immune cell invasion was assessed via flow cytometry. Human iPSC-RPE cells grown on trans-well inserts were used to determine cholesterol efflux.

Results: T0-sHDL or T0 alone significantly increased expression of both Abca1 and Abcg1 in retina and RPE/choroid. Cholesterol efflux studies in iPSC-RPE cells showed significant increase in both apical and basolateral directions with basal efflux being 3.5-4.7 fold higher than apical efflux. We saw significant decreases in IL-6, Tnfα, Nlrp3, and Nf-κb expression via qRT-PCR. Flow cytometry showed sHDL-T0 induced a significant decrease in microglia and macrophage activity (CD45, Ly6C, IBA1) in retinas from $NaIO_3$ treated animals. OCT analysis did not show any difference in retinal thickness at 7-days post $NaIO_3$ treatment. We also did not detect any differences between vehicle or drug treated eyes at days 1-5 post $NaIO_3$ administration.

Conclusions: Activating the LXR pathway enhances expression of cholesterol transporters in the retina/RPE while significantly increasing basal transport of cholesterol in human iPSC-RPE cells. We found significant decreases in pro-inflammatory signaling and immune cell activation in the $NaIO_3$ model of dry AMD after T0-sHDL treatment. Severe and rapid degeneration associated with $NaIO_3$ treatment prevented our ability to detect any neuroprotection in animals treated with the LXR agonist.

CONTROL ID: 3713939

SUBMITTER (NAME ONLY): Eleni Konstantinou

TITLE: Long-term Visual Outcomes of juxta-papillary retinal hemangioblastoma in Von Hippel-Lindau Disease

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Konstantinou, S. Bhandari, E. Agron, T.D. Keenan, C.A. Cukras, A. Thavikulwat, H. Wiley, E.Y. Chew, Retina, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the features and the visual outcomes of retinal hemangioblastomas arising in proximity to the optic disc in Von Hippel Lindau Disease (VHL) at the National Institutes of Health Clinical Center

Methods: Retrospective longitudinal analysis of patients with ONRH associated with VHL. Data were collected on the duration of follow-up, visual acuities (VA), characteristics of RH on multimodal imaging including color fundus photography, ultra-widefield photography, optical coherence tomography, and autofluorescence imaging. Ocular and lesion characteristics at last follow up were compared with baseline, and response to any treatment was assessed.

Results: A total of 59 patients (53% females) with VHL first examined between 2003 - 2020 had ONRH in at least 1 eye. Of these, 10 (17%) patients were examined only once and exclude from further analysis. The total cohort's mean (SD) age at baseline was 37 (16) years. Twenty-six (44%) patients had ONRH in the right eye while bilateral ONRH was found in 5 (8%) patients. The presence or absence of ONRH could not be confirmed in 7 prosthetic eyes (1 right and 6 left). The mean (SD) VA at baseline in eyes with ONRH was 62.9 (27.9) letters (Snellen equivalent 20/60) and 80.4 (18.5) letters (20/25) in eyes that did not have ONRH. Patients were followed for a median (Q1, Q3) of 6.05 (2.09, 10.3) years and the mean VA in the eye with ONRH dropped to 52.85 (31.7) letters (Snellen equivalent of 20/100) at the time of last follow-up.

Conclusions: This longitudinal case series demonstrates progressive loss of visual acuity in this subset of VHL-associated retinal hemangioblastomas, for which treatment options are limited. New treatments, such as systemic hypoxia inducible factor (HIF)-2α inhibitors, hold promise for management of these vision-threatening tumors.

CONTROL ID: 3713940

SUBMITTER (NAME ONLY): Buse Guneri Beser

TITLE: Retinoblastoma (RB) response assessment after intra-arterial chemotherapy (IAC) according to the RB-RECIST guidelines

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Response Evaluation Criteria In Solid Tumors (RECIST) provide radiological standards for solid tumor assessment. However, RECIST is not sufficiently compatible with the evaluation of RB. In May 2021, Berry JL et al. presented a new guideline about response criteria for retinoblastoma (RB-RECIST). We considered the clinical outcomes of RB patients treated with IAC according to the RB-RECIST recommendations.

Methods: A retrospective analysis of all RB patients treated with IAC (melphalan with additional topotecan and/or carboplatin) at Kellogg Eye Center between 2015 and 2021 was performed. Patients who had at least 6 months of follow-up after cessation of first- and/or second-line plus consolidation therapy were included.

Results: 21 eyes of 18 patients (72% females) were analyzed. The eyes were classified according to the International Classification of Retinoblastoma as group B (n=2), C (n=7), D (n=6), or E (n=6). The mean age at IAC was 21 months. Each eye received a mean of 5.6 ± 1.4 IAC sessions (range, 3-9). Consolidation therapy (cryotherapy or transpupillary thermotherapy) was applied in 76%, and intravitreal chemotherapy was injected in 57%. After IAC with a mean follow-up time of 33 months, globe salvage was achieved in 16 eyes(76%). Tumor recurrence (n=1, group C), vitreous hemorrhage (n=1, group D), and neovascular glaucoma (n=3, group E) were the reasons for enucleation. The ocular findings in the last follow-up exam or the exam before enucleation were assessed according to RB-RECIST. Tumor and vitreous seeds regression patterns were demonstrated in Table 1. A complete response(CR) in the tumor was seen 100% in group B, 86% in C, 100% in D, 50% in E. 1 eye(14%) in group C showed progressive disease(PD), and 3 eyes(50%) in group E had a partial response(PR) in the tumor. There was no stable disease(SD). During the study, vitreous seeds were observed in 14 eyes(67%) and subretinal seeds in 12 eyes(57%). CR in vitreous seeds was noted 50% in Group C, 83% in D, 67% in E; CR in subretinal seeding was established 100% in C, 83% in D, 60 % in E (Table 2).

Conclusions: Reporting of outcomes in RB is not standardized. These RB-RECIST guidelines may provide a standardized assessment for tumor response in studies of RB therapy.

CONTROL ID: 3713942

SUBMITTER (NAME ONLY): Sandra Block

TITLE: Prevalence of abnormal corneas in the United States based on Scheimpflug tomography analytics of a pediatric population

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The goal of this study was to determine prevalence of abnormal corneas in pediatric subjects in the US.

Methods: Children aged 3-18 yrs at a school-based vision clinic were enrolled in an IRB approved, prospective, observational, single center (Illinois Eye Institute at Princeton, Chicago) study. Scheimpflug tomography (Pentacam HR, OCULUS Optikgrate GmbH, Germany) was acquired on each eye during comprehensive exams after obtaining consent. Automated multimetric analysis (Belin/Ambrosio Enhanced Ectasia BAD3, OCULUS Optikgrate GmbH, Germany) was run on each scan and the Final BAD-D (Final D) was derived. There is limited reference to prevalence of keratoconus (KC) as determined by tomography in children, and none in a US based population. The prevalence of KC in the generation 2 Raine Study is 1.2% (1 in 84) using a Final D score >2.6 (derived from Scheimpflug imaging). The BAD3 was designed to separate normal from abnormal corneas using a Final D > 2.69. A Final D of > 2.70 was used to calculate prevalence of abnormal corneas for this study.

The following criteria were used to differentiate normal from abnormal corneas (Table 1): Normal, Final D < 2.00 in both eyes, KC Suspect, Final D = or > 2.00 - < 2.70 in at least one eye, and KC, Final D = or > 2.70 in at least one eye. Statistical analysis was performed with SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results: 2212 eyes were screened for this analysis. Subjects > 18 yrs of age or subjects missing data on the Final D measurements were excluded. Among those included, 96.3% (n=2131) were identified as Black or LatinX. (61.9% (n=1369) were Black and 34.4% (n=762) LatinX).

7.7% (n=165) of the total eyes screened, 8.3% (n=114) of the Black and 6.0% (n=46) of the LatinX subjects had a Final D between 2.00 – 2.69 in at least one eye and were assumed KC suspect. 2.3% (n=50) of the total eyes, 2.5% (n=34) of the Black and 1.4% (n=11) of the LatinX population had a Final D = or > 2.70 in at least one eye and were considered keratoconic.

Conclusions: In a primarily Black and LatinX pediatric cohort the prevalence of KC was found to be 2.3% (1 in 50), higher than what has been reported. Patients who are considered keratoconus suspect are important to identify as they require close monitoring. Corneal tomography may be a vital component of pediatric eye exams for early diagnosis and treatment of keratoconus.

CONTROL ID: 3713943
SUBMITTER (NAME ONLY): Cristian Cartes
TITLE: International survey on dry eye diagnosis in experts' clinical practice
SESSION TITLE: Dry Eye, Clinical
SESSION TYPE: Poster Session
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ABSTRACT BODY:

Purpose: To evaluate the practice patterns and opinion from international dry eye experts with respect to dry eye disease (DED) diagnosis in clinical practice.
Methods: An online survey was distributed to DED experts all over the world. The use of diagnosis tests was evaluated in categories including: symptoms questionnaires, functional tests, tear film stability, tear volume, tear composition, ocular surface damage, ocular surface inflammation and eyelid assessment. After, the subjective importance of symptoms, tear break up time (TBUT), non-invasive TBUT, Schirmer test, tear meniscus height, osmolarity, metalloproteinase 9 (MMP9), blepharitis assessment and non-contact Meibography was evaluated according to Likert scale (never, rarely, sometime frequently and always).
Results: The survey was sent to 110 experts, and 77 respondents completed the questionnaire (rate of response=70%). The majority of the experts were from North America (27%) and Europe (40%). Sixty-four participants (83%) had more than 15 years of clinical experience in managing DED. A majority of respondents (73%) diagnose DED using clinical signs and symptoms, but not fulfilling the DEWS II criteria. Seventy-six participants (98.7%) use symptoms questionnaires, being OSDI the most popular (83%), followed by DEQ-5 (30%). All participants evaluate damage to ocular surface, and fluorescein staining is the most frequent method used (92%). In addition, all the respondents perform meibomian gland and blepharitis assessment. Moreover, most of the respondents (78%, n= 60) use finger compression to evaluate meibomian gland function, and 84% utilize non-contact meibography. Furthermore, ocular surface inflammation, tear volume and tear film stability are evaluated by 82%, 98.7% and 96% of the experts, respectively. On the other hand, only 69.8% evaluate tear composition, being osmolarity the most common test (66.2%), and functional tests are performed by 70% of the respondents. With respect to the importance of different tests for DED diagnosis, TBUT ($p= 0.002$) and Schirmer's (0.021) were found to be more important to experts from Europe than North America. No differences were found in any other test. (Fisher exact test $p>0.05$).
Conclusions: This survey offers updated and day-to-day clinical practices by DED worldwide experts, including DED diagnosis. The results highlight the importance of symptoms and clinical signs, but not necessarily following a strict criteria.

CONTROL ID: 3713944

SUBMITTER (NAME ONLY): Jonathan Siktberg

TITLE: Assessing vessel density variability in OCT-A scans as a means of differentiating papilledema from pseudopapilledema

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Siktberg, B. Sean, G. Nashed, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|M. Fard, R. Kaifeh, V. Shah, Aravind Eye Hospital Coimbatore, Coimbatore, Tamil Nadu, INDIA|

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ABSTRACT BODY:

Purpose: In cases of optic disc edema, it is often difficult for the clinician to assess ophthalmoscopically whether the nerve appearance is due to elevated intracranial pressure (ICP) (i.e. papilledema) or due to some other cause (i.e. pseudopapilledema). The differentiation between true papilledema and pseudopapilledema is critically important because of the different implications each diagnosis carries, including prognosis and management. Optical coherence tomography angiography (OCT-A) has recently gained attention as a promising tool to help in the differentiation between papilledema and pseudopapilledema by revealing differences in the pattern of vasculature around the optic nerve between the two conditions. In this retrospective case control study, we compare OCT-A images of patients with true papilledema and patients with pseudopapilledema to test our hypothesis that vascular density variability around the optic nerve is more homogenous in papilledema than in pseudopapilledema.

Methods: Patients who were underwent an OCT-A scan at Aravind Eye Hospital in Coimbatore, India were eligible for the study. Scans which did not meet a useable quality threshold were excluded. The absolute difference between vessel densities in adjacent quadrants were calculated and averaged for the control, papilledema, and pseudopapilledema groups. One-tailed t-tests of the differences were performed among the respective groups to test the hypothesis.

Results: 32 patients qualified for the study including 28 papilledema scans, and 15 pseudopapilledema scans, and 17 control scans. As shown in Table 1, the average adjacent difference in vessel density was significantly higher in pseudopapilledema scans than in papilledema scans ($p=0.02$) or control scans ($p=0.04$). There was no significant difference between papilledema scans and control scans ($p=0.33$).

Conclusions: OCT-A vessel density variability was greater in pseudopapilledema scans than papilledema and control scans in this study.

CONTROL ID: 3713945

SUBMITTER (NAME ONLY): Mariana Aidar

TITLE: Interocular retinal nerve fiber layer thickness in Parkinson disease

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.N. Aidar, D.C. Madeira, Y.T. Boppre, R.A. Saba, E.P. Andrade, Ophthalmology, Iamspe, Sao Paulo, São Paulo, BRAZIL|C.M. Endo, P.I. Kanas, L. Morimoto, A.C. Kara-José, H.B. Ferraz, R.A. Saba, E.P. Andrade, I.M. Tavares, Ophthalmology, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: According to Sheir et al. and Satue et al., some OCT studies demonstrated asymmetrical involvement of the retina in Parkinson's disease (PD).

Satue et al., correlated both macular and RNFL thickness with PD severity using the Hoehn and Yahr scale.

This study aims to compare the thickness of the RNFL between the eyes of patients with PD.

Methods: A prospective cross-sectional observational study was conducted to evaluate the RNFL thickness, global and sectorial (superior, inferior, nasal and temporal quadrants), of both eyes in patients with PD. The study protocol was approved by the Committee of Ethics in Research.

A group of 28 patients with PD, consisting of 16 men (57.14%) and 12 women (42.86%), was evaluated.

The recruitment of patients was carried out at the movement disorders clinic, according to the clinical criteria and Hoehn and Yahr scale.

All patients underwent a comprehensive ophthalmologic examination previously to the OCT exam.

The statistical analyses were performed using the paired t-test. A probability (p) value of ≤0.05 with a two-tailed rejection region was considered statistically significant.

Results: A group of 28 patients with PD, consisting of 16 men (57.14%) and 12 women (42.86%), was evaluated. The mean age of the patients was 63.8±12.1 (median 63; range, 42-88) years - table 1.

The mean RNFL thickness in the right eye of those patients, was 121±23 (median 123) μm at the superior quadrant, 125±25 (median 125) μm at the inferior quadrant, 71±15 (median 69) μm at the temporal quadrant, and 78±21 (median 80) μm at the nasal quadrant; and in the left eye, there was a mean RNFL thickness of 123±21 (median 121) μm at the superior quadrant, 127±23 (median 128) μm at the inferior quadrant, 70±13 (median 71) μm at the temporal quadrant, and 77±13 (median 79) μm at nasal quadrant - table 2.

No statistically significant differences ($p>0.90$) were found when comparing the RNFL thickness, in all quadrants, between right and left eyes.

Three patients in the present study had stage 1.5 on the Hoehn and Yahr scale, while 21 patients had stage 2 and four patients had stage 2.5, meaning that only patients in mild to moderate degrees were evaluated.

Conclusions: The present study demonstrated that in mild to moderate stages of the Hoehn and Yahr scale there are no asymmetry in RNFL thickness between eyes of patients with PD.

CONTROL ID: 3713946

SUBMITTER (NAME ONLY): Stacy Partin

TITLE: Readability, Suitability, and Quality of Online Health Information for Retinitis Pigmentosa & Retinitis Pigmentosa Treatment Options

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: New therapies for Retinitis Pigmentosa (RP) have led to patients desiring more information about the disease and treatment options. Because patients rely heavily on the internet to acquire health information, this cross sectional study was developed to assess the readability, suitability, and quality of online health information for RP and it's associated treatment options.

Methods: We performed two distinct searches of freely available online information: one pertaining to RP and another pertaining to treatments for RP. To assess available information for RP we used the search term "Retinitis Pigmentosa" and evaluated the top 8 search hits. To assess the online information for RP treatment options, we used the search terms "Retinitis Pigmentosa Treatment", "Retinitis Pigmentosa Cure", and "Retinitis Pigmentosa Gene Therapy." 10 websites were evaluated from these three search terms.

A readability analysis was conducted for all sources using Readable (Added Bytes; Horsham, PA). Five readability algorithms were used to produce an average reading grade level for each source. A suitability analysis was conducted to evaluate whether the sources contained content deemed significant for patient knowledge. To assess the quality of the sources, JAMA website quality benchmarks were used.

Results: The readability assessment of RP webpages showed a mean reading grade level of 11.99 (SD=3.15, 95% CI=10.98-12.99). For the RP Treatment sources, the mean reading grade level was found to be 12.53 (SD=3.08, 95% CI=11.65-13.40). The mean suitability score for RP sites was 21.25 of 32 possible points (SD=4.12, 95% CI: 19.51-22.99). The mean suitability score for RP treatment sites was 5.50 out of 16 possible points (SD=3.69 , 95% CI: 4.12-6.88). The interrater reliability was 0.973 (Chronbach's alpha). For the RP sites, the average quality score was 2.63 out of 4 possible points (SD=0.92, 95% CI=1.86-3.39). For the RP Treatment sites, the average quality score was 2 out of 4 possible points (SD=0.86, 95% CI=1.42-2.58).

Conclusions: Our data suggest that the online information made available to patients regarding RP and RP treatment options exceeds the USDHHS recommended 6th grade reading level and contains gaps in content relevant to patients.

CONTROL ID: 3713947

SUBMITTER (NAME ONLY): Alexander Chang

TITLE: Gaze Dependence for Blink Rate Measured with Ora EyeCup Phone

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chang, E. bensinger, J.D. Rodriguez, M. Dusharm, M.B. Abelson, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The rate of blinks provides important insights into the severity of dry eye disease. Without blinking the tear film over the ocular surface will break up and visual acuity will decay, so understanding blink rate is critical to determining the source of ocular discomfort from dry eye. Here we evaluated blink rate at different gaze positions to help determine what gaze prevents blinks or increases blink rates.

Methods: Videos of 4 subjects were acquired from one eye at 3 different gaze positions: up, straight ahead, and down, with 3 one-minute recordings at each gaze position. Patients were instructed to look up approximately 10 degrees from the front position and down approximately 15 degrees from the front position. Videos were recorded using the Ora EyeCup phone with the flash on in 4k and then blinks were counted from each video.

Results: When averaging the whole group across all views the mean blink rate was 15 (standard deviation (stdev) 7.9) blinks per minute. Upward and front facing gaze both led to a similar number of blinks 16 (stdev 6.1) blinks per minute and 16.25 (stdev 8.2) blinks per minute respectively, while a downward gaze subjects averaged 12.2 blinks per minute. A downward gaze showed only trending significance compared to the front gaze ($p=0.069$) and upward gaze ($p=0.1$).

Conclusions: Gaze is a critical factor in blink rate with a downward gaze leading to a lower average number of blinks. This result is in line with the fact that as our gaze lowers so does the interpalpebral fissure height, leading to less exposure of the ocular surface.

CONTROL ID: 3713949

SUBMITTER (NAME ONLY): Gerardo Farese

TITLE: Choroidal Volume Quantification Using Swept-Source Optical Coherence Tomography in Patients Undergoing Photodynamic Therapy

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Farese, P. Szurman, B.V. Stanzel, Eye Clinic Sulzbach, Knappschaftsklinikum Saar GmbH Krankenhaus Sulzbach, Sulzbach, Saarland, GERMANY|P. Szurman, B.V. Stanzel, Klaus Heimann Eye Research Institute, Sulzbach, Saarland, GERMANY|B. Sandhoefner, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Swept-Source Optical Coherence Angiography (SS-OCTA) allows wide-field imaging for visualization of choroidal structures. In patients undergoing verteporfin photodynamic therapy (vPDT) for central serous chorioretinopathy (CSCR), the choroid is the main treatment target. Change in subfoveal choroidal thickness (SCT) on spectral domain OCT (SD-OCT) is an accepted quantitative biomarker for vPDT treatment success. We hypothesized that the punctual nature of this read out may underestimate treatment response. Here we evaluate the effect of vPDT on choroidal volume (CV) with a novel algorithm within the Zeiss Advanced Retinal Imaging (ARI) Network.

Methods: Retrospective case series of chronic CSCR patients with or without secondary MNV undergoing a single half-dose vPDT treatment in one eye. The fellow eye served as control. Inclusion criteria were availability of high signal to noise ratio 12x12mm SS-OCTA (Plex Elite 9000, Zeiss) with minimal artefacts at baseline prior to PDT and at 6-8 weeks (range: 4 -12) follow up in both eyes. CV was calculated using the choroid quantification v1.2 algorithm (ARI Network). Central macular thickness (CMT, ETDRS) and SCT data were extracted from corresponding SD-OCTs (Spectralis, Heidelberg Engineering). Primary outcome parameters were the change in CV and SCT, secondary outcome parameters were CMT and best corrected visual acuity (BCVA).

Results: A total of 16 patients (13 male, 3 female, mean age 53 years) with an average of 53 days between vPDT and follow-up examination were included. In all treated eyes, the mean CV was 49.1 mm^3 prior to PDT, compared to 44.7 mm^3 at follow-up (9.6% reduction) – correspondingly, mean SCT decreased from 426.4 to 381.9 µm (10.4%). In control eyes, mean CV and SCT were similar at vPDT and follow-up examination (45.2 vs. 45.3 mm^3 and 361.6 vs. 366.0 µm, respectively). Mean CMT decreased from 351.4 to 295.4 µm (15.9%) in treated eyes, opposed by a slight increase in mean CMT in reference eyes (314.7 to 343.5 µm). Visual acuity changed from 0.31 to 0.24 logMAR in vPDT eyes.

Conclusions: vPDT treated CSCR eyes showed similar changes in CV using wide-field SS-OCTAand SD-OCT B-scan based SCT, whereas no change was observed in control eyes. Future work will analyze regional characteristics of CV and average CT change, as well as correlation of CV and average CT change with SCT and CMT.

CONTROL ID: 3713950

SUBMITTER (NAME ONLY): Per Soderberg

TITLE: Glaucoma detection based on the waist of nerve fiber layer at the optic nerve head, average thickness or cross-sectional area?

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.G. Soderberg, Z. Yu, K. Kisonaite, Surgical sciences, Uppsala Universitet, Uppsala, SWEDEN|

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ABSTRACT BODY:

Purpose: The waist of the nerve fiber layer at the optic nerve head (ONH) may be expressed as cross-sectional thickness or surface area averaged over the circumference of the ONH. The purpose of the current work was to establish if there is a difference in efficiency between the two quantities for detection of glaucoma.

Methods: A 3D-volume of the optic nerve head was captured with OCT-2000 or OCT-Triton (Topcon, Japan) in one eye without glaucoma in each of 2 groups of 20 subjects aged [20;69]. Each group had a similar age distribution and a gender ratio of 1/1. The waist of the nerve fiber layer at the optic nerve head (ONH) was segmented fully automatically in the OCT volume.

In one group, minimal cross-sectional area was estimated over the circumference of the ONH (PIMA-2π) and in the other group minimal cross-sectional thickness was estimated over the circumference of the ONH (PIMD-2π). On the assumption that both quantities are normal distributed for subjects, a threshold for glaucoma was defined as the probability, α, to classify an eye as glaucoma although it is normal. 1-α then expresses the specificity for detection of glaucoma. The threshold for glaucoma, defined as a fraction below the expected mean of not glaucomatous eyes, is then directly proportional to the variation coefficient with the inverse of the cumulated normal distribution at 1-α as a proportionality constant. A 95% confidence interval for the difference between thresholds for glaucoma estimated as PIMA-2π and PIMD-2π was estimated by iteration based on the estimated mean and standard deviation for PIMA-2π and PIMD-2π, respectively using the t-distribution with d.f. =19.

Results: The estimated mean and standard devation, respectively, for PIMA-2π was 2.01 mm^2 and 0.54 mm^2 (c.v. = 0.26) and for PIMD-2π 350 and 62 μm (c.v. = 0.18). A 95 % confidence interval for the difference between the fraction of PIMA-2π below the expected mean and the fraction of PIMD-2π below the expected mean at specificity 0.95 was estimated to [-4;31] $x10^{-2}$ rel. (D.f 38).

Conclusions: If the threshold for detection is based on variability among subjects and specificity is set to 0.95, there is no difference in efficiency to detect glaucoma between PIMA-2π and PIMD-2π. The lack of difference is probably due to substantial variability among subjects.

CONTROL ID: 3713953

SUBMITTER (NAME ONLY): Deepti Anand

TITLE: High-throughput single-cell RNA sequencing of the developing lens

SESSION TITLE: Lens development and differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Anand, S.A. Lachke, Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|A. Kakrana, S.A. Lachke, Center for Bioinformatics and Computational Biology, University of Delaware, Newark, Delaware, UNITED STATES|R. Skinner, C. Bloomer, I. Saadi, Department of Anatomy and Cell Biology, University of Kansas Medical Center Bookstore, Kansas City, Kansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The eye lens contains anteriorly localized epithelial cells (anterior epithelium of lens, AEL) and posteriorly localized fiber cells (FCs). Cells in the AEL are further distinguished based on their proliferative indexes, while FCs can be distinguished based on their differentiation stages. Thus far, lens transcriptomics has focused on whole lens tissue samples or entire populations of AEL or FCs, and has provided key insights into lens pathobiology. Now, with recent advances, single-cell RNA-sequencing (scRNA-seq) can inform on cell-specific transcript heterogeneity and lead to new insights into pathological changes in individual cells that may contribute toward cataract. To make this approach practicable for wide applicability, we developed a working protocol for lens scRNA-seq that can be applied to tissue samples subjected to short-term storage, and used it to characterize embryonic and newborn mouse lens

Methods: Mouse lenses were micro-dissected at embryonic day (E) 16.5 and postnatal day (P) 0 followed by dissociation with Collagenase/Dispase and TrypLE to obtain a single-cell suspension, followed by cell viability/counts estimates. The cell suspension was frozen for transport and thawed and further processed prior to scRNA-seq library preparation and automated sequencing. Data was analyzed using 10x Genomics data-analysis and Seurat tools

Results: We established a protocol to enzymatically dissociate E16.5 and P0 lenses to obtain a viable cell suspension that can be frozen and thawed and yet be amenable for making scRNA-seq libraries that can yield high-quality RNA for RNA-seq. 10x Genomics tools were used to assign unique molecular identifiers to the expressed transcripts and identify established lens markers. We detected 21,031 cells with total 17,689 genes for E16.5 and 14,108 cells with 17,986 genes for P0. Based on expression profiling and clustering analysis, several distinct cell populations could be distinguished. In addition to known AEL and FC genes, several novel genes in these distinct cell populations were identified

Conclusions: This high-throughput approach to study the lens at single-cell resolution suggests that AEL and FCs can be distinguished further into subsets based on distinct expression profiles. Applying this new approach to lens knockout mouse models will help identify disease-specific cell populations and expedite gene discovery, and thus may find wide applicability in lens studies

CONTROL ID: 3713954
SUBMITTER (NAME ONLY): Dorothy Tung
TITLE: GPR143 Signaling Alters Intracellular Trafficking of POS
SESSION TITLE: Photoreceptor Biology, Protection and Degeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D. Tung, B. Good, A. Figueroa, N. Congrove, B.S. McKay, Ophthalmology and Vision Science, The University of Arizona Department of Ophthalmology and Vision Science, Tucson, Arizona, UNITED STATES|D. Tung, B.S. McKay, Physiology, The University of Arizona Department of Physiology, Tucson, Arizona, UNITED STATES|
Commercial Relationships Disclosure: Dorothy Tung: Commercial Relationship: Code N (No Commercial Relationship) | Brandon Good: Commercial Relationship: Code N (No Commercial Relationship) | Anna Figueroa: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Congrove: Commercial Relationship: Code N (No Commercial Relationship) | Brian McKay: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Photoreceptors undergo a daily renewal process by shedding the distal 10% of their outer segments (POS), which are phagocytosed and degraded by the retinal pigment epithelium (RPE). Inefficient digestion of POS may lead to buildup of lipids and proteins within the RPE and play a role in retinopathies such as age-related macular degeneration (AMD). L-DOPA, a drug that appears to delay onset of AMD, is the ligand of a receptor in the pigmentation pathway involved in vesicular trafficking, GPR143. Here we test whether GPR143 signaling alters the rate of POS degradation by the RPE.
Methods: We isolated POS from bovine retinas via differential ultracentrifugation and sucrose gradient sedimentation. POS were labelled with a pH sensitive dye that increases fluorescence intensity as pH decreases, such that the POS are only visible in the acidic lysosomal compartment. Primary porcine RPE was challenged with POS for 4 hours to allow endocytosis with and without L-DOPA. We removed the excess POS, then added fresh DMEM with dialyzed FBS ± 1μM L-DOPA. Phase-contrast and fluorescent images were captured every 8 hours for 28 hours. 6 experiments were conducted with multiple replicates in each. The number and area of fluorescent POS were analyzed using ImageJ and statistical analysis was performed using Prism Graph.
Results: 4 hours after POS introduction, the number of fluorescent particles and the area they occupied were similar regardless of L-DOPA treatment. At 12 hours, RPE treated with L-DOPA had significantly fewer fluorescent particles (79.1 ± 4.36% of control, $p<0.001$, $n=58$) that occupied a significantly smaller area (79.5 ± 5.03% of control, $p<0.001$, $n=58$). This trend continued at 20 hours, where RPE treated with L-DOPA had significantly fewer fluorescent particles (78.6 ± 5.09% of control, $p<0.001$, $n=58$) that occupied a significantly smaller area (77.7 ± 5.20% of control, $p<0.001$, $n=58$) than the control.
Conclusions: Our results indicate that L-DOPA had no effect on POS phagocytosis measured at 4 hours. Our data also showed that once the POS were in the lysosomal compartment, L-DOPA had no effect on the rate of degradation past 12 hours. However, the reduced number and area of POS in the RPE after 12 hours suggest L-DOPA had a significant effect between hours 4 and 12, which most likely relates to more efficient endosomal trafficking to the lysosomal compartment. These findings may highlight a mechanism by which L-DOPA protects from AMD.

CONTROL ID: 3713956

SUBMITTER (NAME ONLY): Rishabh Hirday

TITLE: Derivation of iPSC monocyte to study immune reaction of early AMD using isogenic 3D choroid/RPE model

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Hirday, T. Park, R. Quinn, A. Ali, E. Nguyen, K. Bharti, OGVFB, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is thought to be caused by atrophy of retinal pigmented epithelial (RPE) cells leading to photoreceptor degeneration, and in advanced disease stages, neovascularization in the choroid. We have developed 3D models of AMD that include cell types found in both choroid and RPE including endothelial cells, pericytes, fibroblasts, RPE, and monocytes. With the goal to make an AMD patient-specific disease model, the purpose of this work is to make a fully isogenic tissue. Here, we aim to derive monocytes from iPSCs and compare them to primary monocytes to advance the development of a fully isogenic 3D AMD model.

Methods: iPSC derived monocytes were generated in vitro by treating attached embryoid bodies with m-CSF and IL-3. Monocytes were repeatedly harvested every 3-4 days over two weeks and were compared to primary monocytes via flow cytometry analysis. Monocytes were stained with CD45 and CD14 to indicate true monocyte phenotype, CD11b for overall macrophages, CD86/CD206 for polarized macrophage subtypes. Monocytes were differentiated into polarized macrophages via solutions with gm-CSF for M1-like or m-CSF for M2-like. Macrophages were analyzed with the same panel of surface markers.

Results: iPSC derived monocytes showed compatible surface marker between experiments, harvests, and cell lines demonstrating reproducibility. Batches of monocytes were then compared to primary monocytes. Primary sources showed >95% CD45 and CD14 co-expression while iPSC monocytes showed CD14 expression at an average 82% from 4 harvests and 85% from 4 different iPSC lines. CD11b expression was observed at 0-4% in both populations indicating monocytes did not undergo spontaneous macrophage differentiation. When differentiated into activated macrophages, both primary and iPSC cells demonstrated M1 or M2 appropriate morphologies with CD86/CD206 protein expression.

Conclusions: Our protocol to generate monocytes from iPSCs confirmed consistency across multiple differentiation batches by surface protein expression. This characterization also shows that our monocytes do not spontaneously differentiate into macrophages. Primary monocytes and iPSC derived monocytes showed similar marker expression, indicating the potential to replace their primary counterpart in our 3D-printed iPSC based AMD model.

CONTROL ID: 3713958
SUBMITTER (NAME ONLY): Salavat Aglyamov
TITLE: Viscous and Elastic Properties of Rabbit Lenses as a Function of Age
SESSION TITLE: IOLs and Presbyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Aglyamov, Mechanical Engineering, University of Houston, Houston, Texas, UNITED STATES|H. Zhang, M. Singh, F. Zvietcovich, K. Larin, Biomedical Engineering, University of Houston, Houston, Texas, UNITED STATES|K. Larin, Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, UNITED STATES|
Commercial Relationships Disclosure: Salavat Aglyamov: Commercial Relationship: Code N (No Commercial Relationship) | Hongqiu Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Manmohan Singh: Commercial Relationship: Code N (No Commercial Relationship) | Fernando Zvietcovich: Commercial Relationship: Code N (No Commercial Relationship) | Kirill Larin: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: The viscoelastic properties of the crystalline lens play an important role in vision health. There is strong evidence that the development of presbyopia and cataract in the lens correlates with the age-related changes in lens biomechanical properties. In this work, we used dynamic optical coherence elastography (OCE) to measure the surface wave dispersion in the lens inside the eyeball ex-vivo and to evaluate age-related changes in both the elasticity and viscosity of the rabbit lens.
Methods: Fifteen fresh rabbit eyes (Pel-Freez Biologicals, LLC, Rogers, AR) were separated into two groups: young (from two to three months old, N=5) and mature (over six months old, N=10). The OCE system colmbined a single-element ultrasound transducer (model ISO 304HP; CTS Valpey Corporation, Hopkinton, MA) with a spectral-domain optical coherence tomography system. The ultrasound transducer had a focal length of about 19 mm and a central frequency of 3.5 MHz. Five single-tone acoustic radiation force bursts ranging from 500 Hz to 2500 Hz were focused on the lens surface. A Kelvin-Voigt viscoelastic model and Scholte wave model were used to quantify the lens elastic and viscous shear moduli.
Results: The average dispersion curves (i.e., phase velocity vs. frequency) for the young rabbit group and mature group and their respective fitting to the model are presented in Fig. 1. As seen in Fig. 1, the surface wave in mature lenses demonstrates higher speed in comparison with young lenses in the whole frequency range. Figure 2 shows the estimations of Young's modulus and the shear viscosity coefficient for two age groups calculated based on the theoretical model. The results demonstrated that the young lenses are softer and less viscous than the mature lenses.
Conclusions: In this study, the dispersion of the surface waves in rabbit lenses was measured inside the eyeball. Based on these measurements, the elasticity and viscosity of the lenses were quantified for young and mature rabbits. The results demonstrate an increase in both stiffness and viscosity of the lenses with age. In our future work, we will use dynamic OCE to measure lens biomechanical properties as a function of age in vivo.
This work was supported by grant NIH R01EY030063 from the NationalInstitute of Health, Bethesda, MD, USA.

CONTROL ID: 3713960

SUBMITTER (NAME ONLY): Vasantha Rao

TITLE: Activation of Glypican-4 regulated Wnt5/PCP pathway in dexamethasone treated trabecular meshwork cells

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Rao, C. Eldawy, W. Backman, N.P. Skiba, R. Maddala, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|V. Rao, Pharmacology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glucocorticoids induce ocular hypertension by increasing resistance to aqueous humor outflow through the trabecular pathway however, the molecular basis for this etiology remains poorly understood. Here we report the activation of glypican-4-regulated Wnt5/PCP pathway in dexamethasone (Dex) treated trabecular meshwork cells, which offers a novel insight into glucocorticoid induced cytoskeletal changes in the trabecular meshwork.

Methods: Dex treated (0.5 μM for 7 days) and control cells from three different human TM cell strains were used to prepare nuclear protein and cytoskeletal-enriched fractions. These fractions were then subjected to label free quantitative proteomics analysis. The effects of Dex and TGF-β2 on glypican-4 (GPC4) protein levels were determined by immunoblot and immunofluorescence analysis, while levels of Wnt5A and phospho-JNK were evaluated by immunoblot analysis.

Results: Using a 2-fold change relative to corresponding controls and a significance of $P<0.05$ as criteria, we identified differentially expressed proteins in both the nuclear protein and cytoskeletome fractions of Dex treated cells. The levels of GPC4, a cell surface heparan sulfate proteoglycan, and regulator of Wnt signaling were significantly elevated in both cytoskeletome and nuclear protein fractions of Dex treated TM cells compared to control cells. Both immunoblot and immunofluorescence analyses revealed distribution of GPC4 to the cytosol and nuclear fractions of TM cells. Additionally, significant increases in the levels of GPC4 were noted in the total cell lysates of human TM cells treated with Dex and TGF-β2 relative to control cells. Intriguingly, the cytoskeletome fraction of human TM cells revealed the presence of only Wnt5A, Wnt5B, Wnt9A and WLS, and relatively high levels of DAAM2, Frizzled-7, PTK7, and Scribble, which are key regulators of the Wnt/RhoA/PCP pathway. Moreover, Dex treatment also resulted in increased levels of Wnt5A and JNK phosphorylation (indicators of activation of the Wnt/PCP pathway) in TM cells.

Conclusions: This study identifies the Glypican-4/Wnt5/RhoA induced PCP pathway as one of the predominant upstream signaling pathways regulating actin cytoskeletal reorganization and cell adhesive changes in glucocorticoid treated TM cells, unravelling a new molecular target for management of IOP in glaucoma.

CONTROL ID: 3713962

SUBMITTER (NAME ONLY): Robert Slater

TITLE:

Improving Reliability of Retinal Vessel Caliber Measurement Using Deep Convolutional Autoencoder

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Slater, J.W. Pak, S. Meuer, R. Voland, J.A. Mares, R. Channa, B.A. Blodi, A. Domalpally, Ophthamology and Visual Science, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|R. Slater, J.W. Pak, S. Meuer, R. Voland, J.A. Mares, R. Channa, B.A. Blodi, A. Domalpally, Wisconsin Reading Center, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Retinal microvasculature can be viewed and measured using color fundus photographs (CFP) and is predictive of systemic microvascular damage. Integrative Vessel Analysis (IVAN) is a semi-automated vessel measurement software that has been used in multiple epidemiological studies. Good focus and clarity of vessels is essential for reliable measurements. Poor image quality accounts for about 10 – 25% data loss using IVAN. This study represents a deep learning autoencoder approach to images and restoring the structural details required for IVAN.

Methods:

The dataset included de-identified CFP (field 1) with vessel measurements in IVAN from the Carotenoids in Age Related Macular Degeneration Study 2 (CAREDS2), an ancillary study of the Women's Health Initiative. The training data was 511 images with reliable vessel measurements, as established by the IVAN software and approved by a human grader using defined criteria. Training images were intentionally degraded by shrinking their original resolution by a factor of 20 and then bringing back to their original size. A U-net based autoencoder was used to reconstruct the original images in 400x400 segments. The trained network was then applied to 12 images IVAN was originally unable to measure. Outcomes included (1) the percent of ungradable images that were considered gradable after autoencoder enhancement and (2) the mean differences between vessel measurements, and 3) sigma, a reliability index between original and enhanced cohorts, to identify any systematic bias.

Results:

Of the 12 images that were considered unreliable by IVAN, autoencoder could retrieve vessel caliber measures in 9 (75%). Two were ungradable due to intrinsic vascular structure and one continued to have poor focus. In the second dataset of gradable images (n = 10) vessel caliber pre and post autoencoder showed a mean difference of 6.03 microns (p = 0.41) for central retinal artery equivalent (CRAE) and 1.12 (p = 0.90) for central retinal vein equivalent (CRVE). The mean sigma for CRAE and CRVE was 3.26 and 3.83 respectively in the original dataset and 4.13 and 4.76 in the autoencoder datase

Conclusions:

A deep convolutional autoencoder improves the vascular details on retinal images and enables IVAN measurements, reducing data loss due to inferior quality photographs. Vessel diameter is not altered due to autoencoder enhancement and can be reliably used in longitudinal data.

CONTROL ID: 3713964

SUBMITTER (NAME ONLY): Hua Yang

TITLE: HIF-inhibitor 64B induces necrosis and suppresses proliferation, metastasis and YAP1 expression in mouse model of uveal melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yang, H.E. Grossniklaus, Y. Yan, Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|M. Offermann, OncoSpherix, Inc, Georgia, UNITED STATES|E. Van Meir, University of Alabama at Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our previous studies have demonstrated the importance of hypoxia in uveal melanoma (UM) growth and have identified that a hypoxia-inducible factor (HIF) inhibitor 64B reduces primary tumor growth and metastasis in an intraocular melanoma mouse model. Here, we further observe the longitudinal growth of UM in a heterotopic UM animal model treated by 64B and identify a potential new mechanism of action.

Methods: The HIF inhibitor 64B was provided by OncoSpherix, Inc. MTT and crystal violet assays were performed to determine cell viability in response to varying concentrations of 64B in cultured human UM cell lines 92.1 and Mel202. Athymic nude mice (Jackson laboratory) implanted with human UM cells 92.1 subcutaneously were divided to the vehicle control and 64B group (10 mice per group). 120 mg/kg 64B by intraperitoneal injection, once per day, started at a tumor size larger than 80 mm^3. Tumor size and mice weight were monitored weekly. Tumor necrosis and liver metastases were quantitated by histology. Immunohistochemistry of Ki67/MIB1 and Yes-associated protein (YAP1) were performed.

Results: Cell viability assays demonstrated that 64B killed 92.1 and Mel202 cells after 3 days of 64B treatment when 64B was at or exceeded the concentration of 2μM. In mouse studies, 64B regressed s.c. 92.1 UM with clear evidence of necrosis and decreased numbers and sizes of liver metastasis compared to the control group. Furthermore, there was a reduction in the percentage of mice that had detectable lung metastasis from 50% in the control group to 20% in mice treated with 64B. The tumor proliferation marker Ki67/MIB1 expression in the 64B groups was significantly less than the control group in the primary tumors, and YAP1 expression associated with hypoxia was suppressed by 64B.

Conclusions: The HIF inhibitor 64B inhibits primary UM growth as well as liver and lung metastasis in a heterotopic mouse model. In addition to the inhibition of HIF function by 64B, the inhibition of the expression of the transcription factor YAP1 might contribute to the antitumor effect of 64B by blocking the ability of YAP1 to promote cancer cell proliferation, chemoresistance, and invasion.

CONTROL ID: 3713965

SUBMITTER (NAME ONLY): Denes Szekeres

TITLE: Risk factors associated with diabetic retinopathy and vision diagnosed by a teleophthalmology program

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Szekeres, E. Sabogal, H. Sadhra, University of Rochester School of Medicine and Dentistry, Rochester, New York, UNITED STATES|J. Basant, K. Wind, R. Warrington, R.S. Ramchandran, Dept. of Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|D. Guo, S. McIntosh, D. Ossip, M. Quick, M. Kaur, Dept. of Public Health Sciences, University of Rochester Medical Center, Rochester, New York, UNITED STATES|R. Fortuna, K. Hazen, Dept. of Internal Medicine, University of Rochester Medical Center, Rochester, New York, UNITED STATES|M. Devine, S. Sridhar, Dept. of Family Medicine, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report on the level of and associated demographic and systemic health factors for diabetic retinopathy (DR) and distance visual acuity (VA) as determined in a primary care based teleophthalmology program for an underserved urban population.

Methods: A retrospective review was performed of prospectively collected, cross-sectional data from a teleophthalmology program to evaluate patients with a diagnosis of diabetes who had not had a documented eye exam in the last year. The analysis used data from six urban primary care sites within a single health system between 2015-2021. Demographic factors, including age, race, ethnicity, and sex and systemic health related information, including blood pressure, smoking status, last HbA1c, and health insurance were associated with VA level and presence and level of DR using single and multivariate linear and logistic regressions with significance set at a p-value less than 0.05.

Results: 1,232 patients were evaluated for DR, 166 (13.5%) had DR and, of those, 82 (49.4%) cases were deemed vision threatening (VTDR) due to presence of diabetic macular edema (macular hard exudates) and/or severe non-proliferative DR or worse. No variables were identified as multicollinear with DR or VA outcome for multiple regression analysis. HbA1c greater than 7.0 ($p<0.005$), increased age ($p<0.014$), and African American race ($p<0.005$) were correlated with worse VA. No other variable was significantly associated with VA. A 1.0 unit increase in HbA1c increased the odds for DR by 1.24 ($p<0.005$; 95% CI 1.20, 1.29) times while only patients under dual Medicare/Medicaid insurance appeared to be 1.96 ($p=0.051$; 95% CI 1.00, 3.87) times as likely of having DR than commercial payors, controlling for other variables. VTDR was 2.93 ($p<0.005$; 95% CI 1.89, 4.53) times as likely with elevated HbA1c. Neither age, sex, smoking status, race nor level of blood pressure control appeared to confer a significantly higher odds ratio for DR or VTDR.

Conclusions: HbA1c remains a key variable associated with worsening VA and DR in patients evaluated via teleophthalmology with demographic factors such as age and being a minority as well as having certain health insurances correlating with worse VA and increased risk of DR, respectively. Further research is needed to clarify these relationships and their impacts on long-term health outcomes in a safety-net population with diabetes.

CONTROL ID: 3713967

SUBMITTER (NAME ONLY): Paul Zhou

TITLE: Test-Retest Reliability of the noel Quantitative Contrast Sensitivity Function Test

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zhou, F. Vingopoulos, A. Bannerman, Z. Hassan, J.B. Miller, N.A. Patel, D.M. Wu, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|P. Zhou, J.B. Miller, N.A. Patel, D.M. Wu, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the test-retest agreement and reliability of the novel active-learning quantitative contrast sensitivity function (qCSF) device.

Methods: Seventy-nine (79) eyes of 57 retina clinic patients with various vitreo-retinal disorders were prospectively tested and subsequently retested on the same day at Massachusetts Eye and Ear using the novel qCSF Manifold Contrast Vision Meter (Adaptive Sensory Technology). Contrast sensitivity outcomes included: area under the log contrast sensitivity function (AULCSF), and contrast thresholds at 1, 1.5, 3, 6, 12, and 18 cycles per degree (cpd). Agreement between test and retest measurements was assessed using Bland Alman (BA) plots. Test-retest reliability was assessed using the intraclass correlation coefficient (ICC).

Results: Bland-Altman plots showed a mean bias of nearly zero for all contrast sensitivity outcomes of the qCSF device. The lower to upper limit of agreement was approximately −0.1 to + 0.1 for AULCSF and −0.1 to + 0.1, −0.075 to + 0.075, −0.13 to + 0.19, −0.25 to + 0.25, −0.7 to + 0.6 and −0.5 to + 0.55 for contrast thresholds at 1, 1.5, 3, 6, 12 and 18 cpd, respectively. ICC demonstrated excellent test-retest reliability (>0.9) for all qCSF outcome metrics, with the exception of the contrast threshold at 18 cpd. The ICC for AULCSF was 0.901 with 95% Confidence Intervals (CI) for ICC population values of 0.85 to 0.936. The ICC for the contrast thresholds at 1, 1.5, 3, 6, 12 and 18 cpd were 0.821 (95% CI for ICC population values: 0.735 to 0.882), 0.924 (95% CI for ICC population values: 0.884 to 0.951), 0.943 (95% CI for ICC population values: 0.912 to 0.963), 0.948 (95% CI for ICC population values: 0.92 to 0.966), 0.949 (95% CI for ICC population values: 0.922 to0.967), and 0.831 (95% CI for ICC population values: 0.707 to 0.906), respectively.

Conclusions: Test-retest agreement and test-retest reliability were excellent for all contrast outcomes derived from the qCSF device, including AULCSF and contrast thresholds at 1 to 18cpd. Incorporating functional outcomes with excellent test-retest agreement and reliability such as the qCSF device in the clinical practice and clinical trials offers the clinicians and researchers good perspectives on whether measured changes in contrast sensitivity can be attributed to the test-retest variability of the device or whether they represent a real change in visual performance.

CONTROL ID: 3713969

SUBMITTER (NAME ONLY): Marcell Paguaga

TITLE: Development of an optical imaging probe for targeted visualization of NLRP3 inflammasome in a mouse model of age-related macular degeneration (AMD)

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Bone marrow-derived macrophages (BMDM) migrate to the site of choroidal neovascularization (CNV) in age-related macular degeneration (AMD). The exact role of these migratory cells in the pathogenesis of CNV remains largely unknown. Inflammation might play a key regulatory role in the pathogenesis of AMD progression. In vivo molecular imaging of inflammasomes could predict the onset and progression of AMD. We report here the development of a novel optical imaging probe, MI-142, that specifically targets NLRP3 and enables the detection and visualization of NLRP3 inflammasomes in retinal cells and ocular tissues.

Methods: MI-142 was synthesized by conjugating a selective NLRP3 inhibitor (CY-09) to a fluorescent dye for optical imaging of inflammasomes. To verify MI-142's ability to target NLRP3, its inhibitory effects were compared to those of CY-09. Following an established protocol, LPS-primed BMDM's were treated with MI-142 or CY-09 and stimulated with nigericin to induce NLRP3 activation. Cell culture supernatants were assayed for mouse IL-1β and TNF-α using enzyme-linked immunosorbent assay (ELISA). To visualize activated NLRP3, LPS-primed BMDM's were stained with MI-142, stimulated with nigericin, fixed with 4% NBF, and imaged through confocal microscopy. In addition, in vivo imaging of inflammasomes was performed in a mouse model of AMD, laser-induced choroidal neovascularization (LCNV).

Results: In comparison to CY-09, MI-142 showed statistically similar inhibitory effects on NLRP3-mediated production of IL-1β at 1 μM, 5 μM, and 10 μM in a dose-dependent manner. In general, neither MI-142 nor CY-09 significantly affected the production of TNF-α. These results suggest that MI-142 retains the inhibitory abilities of its parent compound that enable it to function effectively as a targeted NLRP3 imaging probe. In an in vitro fluorescence imaging experiment, nigericin-induced BMDM's displayed bright MI-142 dependent fluorescence in the cytosol, while untreated cells showed no remarkable fluorescence. In vivo imaging of inflammasomes was achieved in a mouse LCNV model.

Conclusions: This study showed that our novel imaging probe, MI-142, enables visualization of activated NLRP3 inflammasomes in BMDM's and LCNV. Therefore, we propose that MI-142 may be useful to study the onset, progression, and therapeutic response of AMD.

CONTROL ID: 3713972

SUBMITTER (NAME ONLY): Donita Garland

TITLE: Proteome analysis of choroidal aging in wild type and L-ORD mouse models

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Dagar, P. Biswas, R. Ayyagari, Department of Ophthalmolgy, University of California San Diego, San Diego, California, UNITED STATES|D. Garland, Harnly LLC, Bethesda, Maryland, UNITED STATES|A.K. Chekuri, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is a major factor in the development and progression of macular disease whether age-related or heritable. The choroid contributes to the homeostasis of the retina, and age-related changes in choroid structure and function are thought to contribute to these diseases. The purpose of this study was to identify the major effects of age on the choroid in wild type (Wt) mice and in mouse models of late onset retinal degeneration (L-ORD) due to mutations in C1qtnf5/Ctrp5.

Methods: The proteomes of the choroids of wild type C57BL6 and Ctrp5^{S163R} mutant mice were determined at 4.5 and 19 mo and at 4.5 and 18 mo, respectively. The choroid/Bruch's membrane was dissected, proteins solubilized and separated on SDS gels. After in-gel trypsin digestion, peptides were separated and peptide masses analyzed using mass spectrometry. MaxQuant software was used for database searching, peptide and protein identification and quantification. Principal component analysis (PCA) was done using SOLO, Eigen Vector. IHC was used to localize specific proteins.

Results: PCA showed strong clustering by age for both genotypes. About 24% of the 3700 proteins identified were significantly altered with age in Wt mice. Specific markers for mast cells, endothelial cells and melanocytes showed statistically significant changes in each cell type with age. The decrease in plasmalemma vesicle-associated protein, the major component in fenestrae, an endothelial substructure, suggested structural changes in the choriocapillaris. Tyrosinase, the rate limiting enzyme in melanin synthesis decreased 3 fold. These age-related changes occurred to the same extent in Wt and mutant mice. Of the 250 proteins of the innate immune system 60 underwent changes with age. The most remarkable changes were the 4 mast cell proteases which were increased over 3-4 fold in Wt and 10-12 fold in Ctrp5^{S163R} mutant mice, the 5 fold increase in the carboxypeptidase A inhibitor, latexin, in mutant mice and cathepsin S which was increased 5 fold in Wt and 15 fold in mutant mice.

Conclusions: Each of the aging changes identified correlate with processes that are reported to be factors in macular disease. Loss of melanin, changes in choriocapillaris function and immune activation with age will negatively impact retinal homeostasis in both genotypes. The excess immune system activation in Ctrp5^{S163R} mutant mice may be a major factor in the pathobiology of L-ORD.

CONTROL ID: 3713976

SUBMITTER (NAME ONLY): Mircea Mujat

TITLE: Phase imaging in the inner retina

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Mujat, A. Patel, J. Grimble, N. Iftimia, Biomedical Optics Technologies, Physical Sciences Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of the current study was to identify new contrast mechanisms that can reveal retinal structures not visible with other methods. Simultaneous multi-channels offset AO-SLO imaging provides isotropic images of retinal microstructures free of directionality artifacts and enables phase imaging in the living eye with enhanced visualization contrast.

Methods: We developed a new detection scheme with an arrangement of light collecting fibers that provides isotropic imaging while retaining all the advantages of offset aperture and split-detector imaging. Four optical fibers are arranged as a compact bundle and all offset images are collected simultaneously with the confocal image. The two orthogonal offset pairs provide the split-detector imaging in orthogonal directions removing the directionality disadvantage of other techniques. Oblique back-illumination has been used in microscopy to reveal phase objects that are not visible in confocal microscopy. Split-detection analysis, sometimes called differential phase contrast, is interpreted as phase derivative. One can reconstruct the phase from orthogonal phase derivatives or directly calculate the phase gradient.

Results: Split-detection analysis is performed using multiple combinations of the four offset images. Two orthogonal split images are generated for orthogonal fiber pairs 1-3 and 2-4 (A and B in Fig. 1). Two additional split images (C and D) are obtained by adding first adjacent fibers (for example 1+2 and 3+4) and then performing subtraction divided by sum of the two sums. Therefore we obtain four split images: horizontal, vertical, and two diagonal (+/-45deg). They highlight structural edges such as blood vessel walls along different directions given the directionality associated with the split direction. The phase (P) and the phase gradient (PG) images are obtained from either one of these two pairs of split images. In addition, the mean of the four split standard deviation images (STD) isotropically highlights the blood flow vasculature. Circled areas in Fig. 1 highlight local microstructures that have no blood flow associated with them (not visible in the STD image). They could potentially be microglia based on their location in the proximity of the blood vessels.

Conclusions: The multi-aperture AO-SLO imaging based on simultaneous acquisition of multiple offset aperture images provides an improved, isotropic image in the inner retina free of single offset-axis directionality artifacts.

CONTROL ID: 3713979

SUBMITTER (NAME ONLY): Johanna Pfeil

TITLE: Re-treatments after laser coagulation or anti-VEGF injections in infants treated for retinopathy of prematurity – data from the German ROP registry

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Pfeil, A. Stahl, Department of Ophthalmology, Universitatsmedizin Greifswald, Greifswald, Mecklenburg-Vorpommern, GERMANY|T. Barth, Department of Ophthalmology, Universitat Regensburg, Regensburg, Bayern, GERMANY|W. Lagrèze, Department of Ophthalmology, Albert-Ludwigs-Universitat Freiburg, Freiburg im Breisgau, Baden-Württemberg, GERMANY|B. Lorenz, Department of Ophthalmology, Justus Liebig Universitat Giessen, Giessen, Hessen, GERMANY|K. Hufendiek, Department of Ophthalmology, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|R. Liegl, Department of Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|H. Breuss, Department of Ophthalmology, HELIOS Klinikum Berlin-Buch, Berlin, Berlin, GERMANY|S. Bemme, Department of Ophthalmology, Georg-August-Universitat Gottingen, Gottingen, Niedersachsen, GERMANY|J.F. Meyer, Department of Ophthalmology, Vivantes Klinikum Neukolln, Berlin, Berlin, GERMANY|B. Glitz, Department of Ophthalmology, University of Munster Medical Center, Muenster, GERMANY|D. Suesskind, Department of Ophthalmology, Eberhard Karls Universitat Tubingen, Tubingen, Baden-Württemberg, GERMANY|A. Gabel-Pfisterer, Department of Ophthalmology, Klinikum Ernst von Bergmann gGmbH, Potsdam, Brandenburg, GERMANY|C. Skevas, Department of Ophthalmology, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|T.U. Krohne, Department of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|V. Kakkassery, Department of Ophthalmology, Universitat zu Lubeck Sektion Medizin, Lubeck, Schleswig-Holstein, GERMANY|

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ABSTRACT BODY:

Purpose: The German ROP registry collects real-life data on infants treated for retinopathy of prematurity (ROP). This is of particular importance in light of the new treatment option of anti-VEGF for ROP. This abstract compares the re-treatment rates of anti-VEGF versus laser in ROP.

Methods: We analyzed data from 353 infants (692 treated eyes) born between 2011 and 2020. Descriptive statistics were used to analyze the percentage of eyes needing at least one re-treatment. Infants with a need for re-treatment were compared to infants without need for re-treatment regarding demographics (birthweight, gestational age (GA) at birth, postnatal age (PNA) as well as postmenstrual age (PMA) at treatment; t-tests). The interval between initial treatment and re-treatment was compared between different treatment groups (laser, bevacizumab (bvz), ranibizumab (rbz)).

Results: Of the 692 treated eyes 108 eyes (15.6%) needed at least one re-treatment. Re-treatment rates varied between 11.6 and 30.6% during the observation period. Of eyes initially treated with laser (396) 14% were re-treated

compared to 12% of eyes treated with bevacizumab (117) and 24.5% of eyes treated with ranibizumab (159). Laser treated eyes were re-treated after a mean of 22 days, which was significantly shorter than after bvz (mean 53; p=0.0004) or rbz (mean 55; p<0.0001). A second re-treatment was conducted in a total of 28 eyes after a mean of 40 days after the first re-treatment in the laser group, 61 days in the bvz group and 47 days in the rbz group. Infants who needed at least one re-treatment were significantly lighter at birth (614g vs. 709g; p=0.0021), were born with a lower GA (24.8 vs. 25.5 weeks; p=0.0128), had lower PMA at treatment (36.3 vs. 38 weeks; p<0.0001) and lower PNA at treatment (11.5 vs. 12.6 weeks; p=0.0086) compared to infants who did not require re-treatment.

Conclusions: Among the group of infants with treatment requiring ROP, infants with lower GA and birth weight have the highest risk for requiring more than one ROP treatment. Re-treatment rates were higher after initial treatment with rbz and occurred later with rbz or bvz compared to laser. Real life data from registries can help adjusting treatment decisions and follow-up regimens in ROP. Our data collection will be continued as part of the newly established European ROP registry EU-ROP (www.eu-rop.org).

CONTROL ID: 3713980

SUBMITTER (NAME ONLY): Viral Kansara

TITLE: Targeting, Compartmentalization and Durability of Suprachoroidally Injected Small Molecule Suspensions in Multiple Preclinical Models

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess targeting, compartmentalization, and durability potential of suprachoroidal injection of small molecules via microneedle in multiple preclinical models and multiple drug candidates.

Methods: Suprachoroidal injection of multiple small molecule drug candidates (tyrosine kinase inhibitor (TKI), complement factor inhibitor, steroid, kallikrein inhibitor) via a proprietary microneedle were performed in multiple preclinical species (rabbit, porcine, monkey and dogs) to evaluate safety and tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and/or bioavailability in posterior segment ocular tissues including the macula region. Multimodal imaging methods were employed ex vivo and in vivo to evaluate delivery efficiency, flow dynamics, and spread of injectate in the suprachoroidal space (SCS).

Results: Suprachoroidal injections via proprietary microneedle customized for each species were successfully employed in multiple animal models and well-tolerated across species and multiple disease models. In total, over 1000 injections have been performed with free needle lengths between 300 and 1100 µm dependent on species-specific ocular anatomy characteristics. Injections into the SCS demonstrated circumferential and posterior spread of injectate immediately following the injection, confirmed in ex vivo porcine models. In multiple in vivo rabbit studies, an opening of the SCS in the posterior segment was observed. Suprachoroidal delivery of small molecule suspensions exhibited compartmentalization of a dose depot into posterior tissues with high drug levels in the chorioretina, including therapeutic drug levels as far as posteriorly to the optic nerve. In contrast, drug levels in the aqueous humor were 3-5 log orders lower, and negligible systemic drug exposure was observed. Ocular PK studies in rabbits and monkeys showed durability of multiple drug candidates. Specifically, one small molecule drug candidate showed sustained presence at 6 months (last time point evaluated). Suprachoroidally injected steroid and TKI drug candidates exhibited PD effects in in vivo porcine models of ocular inflammation and neovascularization, respectively.

Conclusions: Suprachoroidally injected small molecule suspensions consistently exhibit targeting, compartmentalization, and durability in multiple preclinical models.

CONTROL ID: 3713981

SUBMITTER (NAME ONLY): Steven Newman

TITLE: Posterior Fixation Sutures Expand Binocularity in Patients with Persistent Paretic or Restrictive Pathology

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Newman, Ophthalmology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Steven Newman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To obtain binocularity in primary and down reading gaze, weakening (recession) or strengthening (advancement or resection) procedures are often adequate. To maximize the area of binocular single vision, more aggressive weakening procedures may be necessary. The use of posterior fixation sutures functionally limits the excursion of an otherwise normal muscle. When combined with a recession procedure and applied to the contralateral synergist to a paralyzed muscle, or to the contralateral antagonist to a restricted muscle the area of binocularity can be substantially improved.

Methods: This is a retrospective review of 33 patients treated with posterior fixation sutures at the University of Virginia over a 10 year period. Patients were assessed for alignment in primary and down reading gaze, but also for increase in binocularity as measured by binocular single vision fields and for equalization based on Hess screen analysis.

Results: A total of 33 patients were treated with posterior fixation suture procedures. Sixteen patients were treated with medial rectus recession and Faden procedure for long standing stable abduction deficits (most commonly VI nerve dysfunction). Nine patients were treated with lateral rectus recession and posterior fixation sutures for contralateral adduction deficits usually related to III nerve dysfunction. One patient was treated with a contralateral superior rectus recession and Faden procedure for a surgically induced Brown syndrome following a tuck procedure for a IV nerve palsy. Seven patients had inferior rectus recession for problems with down gaze.

Conclusions: Posterior fixation sutures by limiting excursion of the better moving eye are an effective way of expanding binocularity. This is applicable to both paretic and restrictive syndromes. The area of binocularity and alignment can be fine tuned by additional surgery on the worse moving eye following the initial recession and Faden procedure. The use of the Hess screen and binocular single vision fields is instrumental in guiding surgery.

CONTROL ID: 3713984

SUBMITTER (NAME ONLY): Ryan Anderson

TITLE: Prevalence of Cardiac Sarcoidosis in Patients with Ocular Sarcoidosis

SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Anderson, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|E. Hawkins, J. Van Swol, E. Joseph, Medical University of South Carolina College of Medicine, Charleston, South Carolina, UNITED STATES|L. Perry, Ophthalmology, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|W. Wang, H.A. Sandhu, Ophthalmology and Visual Sciences, University of Louisville, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Some uveitis specialists eschew further differentiation of non-infectious uveitis, even though specific uveitic syndromes may have consequences for systemic health. Sarcoidosis is a multisystem inflammatory disease that is a regionally common cause of non-infectious ocular inflammation. The objective of this study was to determine the prevalence and manifestations of cardiac sarcoidosis in patients with ocular sarcoidosis.

Methods: This was a retrospective cohort study of patients diagnosed with ocular sarcoidosis as defined by the International Workshop on Ocular Sarcoidosis (IWOS) at the University of Louisville from 2017-2020 and the Medical University of South Carolina from 2005-2020. Medical records were first searched for at least a suspected diagnosis of sarcoidosis, then for ocular manifestations of sarcoidosis, and finally for an electrocardiogram (EKG). Patients lacking any of these three components were excluded. Cardiac past medical histories and EKG findings consistent with a sarcoidosis diagnosis were also obtained, including ventricular arrythmias, heart blocks, and paroxysmal ventricular contractions.

Results: Of the 232 patients with sarcoid uveitis, 20 (8.6%) had known cardiac involvement at the time of ocular diagnosis. Sixteen patients (6.9%) had EKG abnormalities consistent with cardiac sarcoidosis. Eight patients had known histories of cardiac sarcoidosis and three had confounding cardiac histories that explained their EKG findings, leaving five patients (2.2%) with ocular sarcoidosis whose cardiac disease was only identified after a diagnosis of possible, probable, presumed, or definite ocular sarcoidosis had been made. Four patients with relevant EKG findings had this study done within 6 months of their diagnosis of sarcoidosis.

Conclusions: Nearly 10% of patients with ocular sarcoidosis have manifestations of cardiac sarcoidosis, some of whom were diagnosed only after presentation to an ophthalmologist with uveitis. Our results suggest that EKG is a reasonable test to include for patients with signs of ocular sarcoidosis to screen for cardiac issues, which are potentially life-threatening. This work suggests that further differentiation of non-infectious uveitis can have important implications for systemic health. Further research is needed to see if EKG abnormalities can be detected before other cardiac manifestations in this patient population.

CONTROL ID: 3713987

SUBMITTER (NAME ONLY): Ahmed ALNAHRAWY

TITLE: Comparison of biometry measurements using Anterion and Lenstar biometers

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. ALNAHRAWY, M. Niestrata, P. Sousa, Y. Gad El, M. Bizrah, A. Aziz, Western Eye Hospital, London, London, UNITED KINGDOM|S. Bazeer, North Middlesex University Hospital NHS Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The purpose was to compare biometry readings between Anterion (Heidelberg Engineering) and Lenstar (Haag-Streit) for patients undergoing cataract surgery and to identify any discrepancies and their significance for surgical planning.

Methods: Biometry measurements were performed on patients in Imperial College London between November'21 and January'22, using Lenstar and Anterion. Measurements of axial length (AL), K1, K2 in diopters (D), anterior chamber depth (ACD), lens thickness and white-to-white (WTW) were compared. The mean differences in measurements were evaluated using standard deviation (SD), 95% confidence intervals (CI) and p values. Statistical analysis was performed using Excel and Python.

Results: A total of 15 patients, 30 eyes, was included. The mean age was 71 (SD 3.2). The majority (10 patients, i.e. 67%) were females and 5 (33%) males. Out of 30 AL measurements, 3 were excluded due to inability to obtain measurement with Anterion in dense cataracts. The mean difference in AL was 0.006mm (SD 0.01mm; CI +/- 0.004) (p=0.039). The mean differences in K1 and K2 were 0.046D (SD 0.388D; CI +/- 0.145) (p=0.049) and 0.256D (SD 0.456; CI +/- 0.170) (p=0.454), respectively. The mean ACD difference was 0.451mm (SD 0.157mm; CI 0.059) (p=0.496). One eye was excluded from the lens thickness analysis due to inability to obtain a measurement with Anterion. The mean lens thickness difference was 0.166mm (SD 0.4195mm; CI 0.1596), statistically very significant (p=0.0001). The mean WTW difference was 0.146mm (SD 1.151mm; CI 0.4299) (p=0.0857).

Conclusions: Both Lenstar and Anterion produce very similar AL readings. Anterion seemed unable to produce measurements in some dense cataracts, which should be further assessed on a larger patient cohort. There was a notable difference in ACD, which may be explained by Lenstar reading being taken from the corneal epithelium to lens epithelium vs Anterion one from corneal endothelium to lens epithelium. There was a statistically very significant difference in lens thickness, however, with a large SD. There was a relatively large difference in white-to-white readings, which may be of relevance in anterior chamber intraocular lense selection. Future studies are needed to assess the differences on a larger patient cohort and in extremes of AL, in short and long eyes, to determine any difference in suitability of the different biometry machines in such circumstances.

CONTROL ID: 3713989

SUBMITTER (NAME ONLY): Rafael Correia Barão

TITLE: Magnetic Resonance Imaging of Glaucoma Drainage Devices

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Filtering blebs from glaucoma drainage devices (GDD) form too posteriorly for direct observation. The purpose of this study was to evaluate magnetic resonance imaging (MRI) features of different GDD and explore clinical correlations.

Methods: Cross-sectional study of ocular, GDD and bleb morphology using a 3-Tesla MRI scanner (Philips Medical Systems, Netherlands) with an 8-channel head coil in consecutive glaucoma patients implanted with one of 4 distinct GDD: Ahmed Glaucoma Valve FP7 (AGV) and Ahmed ClearPath 350mm^2 (ACP; both New World Medical, USA), Baerveldt Glaucoma Implant 350mm^2 (BGI; Abbott Medical Optics, USA) and Paul Glaucoma Implant (PGI; Advanced Ophthalmic Innovations, Singapore). Forty-four patients were recruited but 13 were excluded due to inability to undergo quality MRI. Clinical data was retrieved from patient files. Statistical analysis was performed with Prism 8 (GraphPad Software, San Diego, CA).

Results: A total of 36 eyes from 30 patients aged 57±20 years (mean±SD) were included in this study. Seven eyes had been implanted with the AGV (19%), 8 with ACP (22%), 5 with BGI (14%) and 16 with PGI (44%). Orbital MRI was performed 2,4±2,1 months after GDD implantation. Average total bleb volume was 563±390mm^3, with no significant difference among different GDD (p=0,1223). Bleb volume did not correlate with intraocular pressure (IOP) at any timepoint (pre-operative, time of MRI, last follow-up; p>0,1524, all comparisons), with time from surgery to MRI (p=0,5590) or with axial length (p=0,3398). A double-layered bleb was observed in 94% of eyes (n=34), the layers separated by the GDD endplate. Inferior blebs (between the sclera and the endplate undersurface) were significantly larger with the PGI than with the remaining GDD (380±205 vs. 193±161mm^3; p=0,0043) and also larger with non-valved GDD (BGI, PGI and ACP, collectively) versus the AGV (318±202 vs. 101±64mm^3; p=0,0086). Flattening of the scleral bed underneath the endplate was a common finding in eyes with non-valved GDD (n=15, 52%; absent in all AGV patients) and was associated with larger blebs (observed in 78% of blebs in volume quartile 75-100; p=0,0049).

Conclusions: Double-layered blebs are a common finding with GDD filtering blebs. Bleb morphology seems to be independent of IOP or time from surgery, but dependent on the type of GDD, with non-valved devices (particularly the PGI) forming larger inferior blebs which commonly flatten the underlying sclera.

CONTROL ID: 3713990

SUBMITTER (NAME ONLY): Dietmar Link

TITLE: Application of a novel pneumatic intraocular pressure modulator: technical confounding of the tonographic effect

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: From several studies in occulopression, repeated tonometry or ophthalmodynamometry we have knowledge that the intraocular pressure (IOP) decreases during an artificial IOP increase. This phenomenon is known as the tonographic effect. In healthy eyes an IOP drop of 2–3 mmHg/min was reported. However, there are studies that show a reduced decrease of the IOP drop for instance in glaucoma patients. In this work we determine the tonographic effect in healthy eyes by utilizing a novel pneumatic pressure modulator and validate the modulator technically in order to determine the technical confounding of the tonographic effect.

Methods: For technical validation and in vivo application, a pneumatic intraocular modulator (IOPstim, Imedos Systems GmbH, Jena, Germany) was used. A force sensor (KD34s, ME-Meßsysteme GmbH, Hennigsdorf, Germany) was placed in front of the balloon. Pressure stability was analyzed for 2 minutes. The force values were recorded for five different device target pressures from 50 mmHg to 250 mmHg in steps of 50 mmHg, and this sequence was repeated 10 times. A new balloon was used for each sequence. In the subject study, the IOP of 10 healthy subjects (6 male, 4 female, aged 28.8 ± 6.64 years) was modulated and increased linearly to at least 40 mmHg. At this point, the pressure inside the balloon was kept constant for 2 minutes, with IOP measurements taken every 40 seconds using a rebound tonometer (Icare PRO, Icare Finland Oy, Helsinki, Finland).

Results: The technical setup led to an IOP decrease of 0.7 mmHg within 2 minutes at an operating point of 40 mmHg IOP. In the subject study, the IOP could be increased up to 42.8 ± 3.6 mmHg for all subjects (n = 10), whereby a mean pressure decrease of 4.8 mmHg within 2 minutes was determined, which seems to be caused mainly by physiological processes.

Conclusions: With the new pneumatically based setup, a targeted modulation in terms of level and constancy of the IOP can be realized. Technical validation showed that the purely technical influence on the tonographic effect, i.e. the drop in IOP, carried 0.3 mmHg/min with a total effect of 2.4 mmHg/min. The technical confounding of the tonographic effect is clearly less than the physiological effect itself.

CONTROL ID: 3713992

SUBMITTER (NAME ONLY): Evan Bilsbury

TITLE: AAV-mediated anti-VEGF therapeutics increase corneal allograft survival-rate in a model of high-risk corneal transplantation

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Bilsbury, W. Su, S. Sun, S. Doherty, E. Wood, H. Lin, B. Tian, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|P.W. Tai, G. Gao, Horae Gene Therapy Center, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|W. Su, Ophthalmology, Tianjin Medical University General Hospital, Tianjin, CHINA|S. Sun, Retina, Tianjin Medical University Eye Hospital, Tianjin, CHINA|X. Ke, Q. Zheng, Chengdu Kanghong Pharmaceuticals Group Co Ltd, Chengdu, CHINA|

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ABSTRACT BODY:

Purpose: Previous studies have shown that pharmacological blockade of vascular endothelial growth factor (VEGF) or VEGF-Receptors (VEGF-Rs) can ameliorate corneal neovascularization and improve allograft survival rates in high-risk keratoplasties. However, repeated injections are required because rejection can occur even years after transplantation. In this study, we aim to determine if a single dose of AAV-mediated anti-VEGF treatment can increase the survival rate of corneal grafts in a model of high-risk keratoplasty.

Methods: The corneal suture paradigm was used to produce a rat model of high-risk keratoplasty. Sutures were placed 14-days prior to keratoplasty. At 5 days prior to keratoplasty, sutures were removed and either an anti-VEGF AAV (5×10^9 genome copies/12µl) or PBS (12µl) was introduced to the cornea via intrastromal injection. CoNV and corneal opacity were assessed post-operatively using slit-lamp microscopy weekly and graft thickness was measured post-operatively using optical coherence tomography (OCT). Corneal graft rejection was defined as moderate stromal opacity with only the pupil margin visible and neovascularization around the peripheral graft. Additionally, intraocular pressure (IOP), as one of ocular safety indicators, was measured once a week. Potential inflammation induced by intrastromal injection of AAV-antiVEGF was also analyzed by measuring the percentage of F4/80+ and CD11b+ cells in the cornea.

Results: We observed a significant reduction in CoNV, corneal opacity, and to a lesser extent, corneal thickness in AAV-treated rats (N=6) compared with the control group (N=6). The survival-rate of the allograft was increased in AAV-anti-VEGF treated animals and the incidence of corneal graft rejection was decreased. IOP remained normal in both groups and no inflammation was noted at 2 weeks post-intrastromal injection at this dosage of AAV ($5x\ 10^9$ genome copies), indicating the treatment of AAV vectored anti-VEGF does not elicit IOP change and inflammation.

Conclusions: Anti-VEGF molecules delivered by AAV vectors are safe and efficacious for the long-term inhibition of corneal neovascularization which increases the survival rate of corneal allografts in high-risk keratoplasty.

CONTROL ID: 3713993

SUBMITTER (NAME ONLY): Lisa Nijm

TITLE: Efficacy and Safety of OTX-DED Dexamethasone Intracanalicular Insert in Subjects with Dry Eye Disease: A Multicenter, Randomized, Vehicle-Controlled Phase 2 Study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Gillick, R. Gurses-Ozden, M. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|L. Nijm, University of Illinois Hospital and Health Sciences System, Chicago, Illinois, UNITED STATES|J. Tauber, Tauber Eye Center, Kansas City, Missouri, UNITED STATES|D.G. Evans, Total Eye Care, P.A., Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many patients with dry eye disease (DED) suffer from episodic flare-ups that require an effective short-term treatment. OTX-DED is a physician-administered, biodegradable, preservative-free, hydrogel-based insert that is placed into the canaliculus and releases dexamethasone to the ocular surface for 2-3 weeks. In this study, we evaluated the efficacy and safety of OTX-DED in subjects with dry eye disease.

Methods: Prospective, randomized, double-masked, vehicle-controlled Phase 2 study at 15 US sites. Adult subjects diagnosed with DED in both eyes for >6 months, eye dryness severity score ≥30 and bulbar conjunctival hyperemia grade ≥2 were randomized 1:1:1 to receive either OTX-DED 0.2 mg, OTX-DED 0.3 mg or hydrogel-vehicle (HV) insert. Subjects (N=166) received the same treatment bilaterally on Day 0 and were followed for 8 weeks. The primary endpoint was photographic assessment of bulbar conjunctival hyperemia in the worst zone on Day 15 evaluated by a central reading center and graded using the Cornea and Contact Lens Research Unit grading scale (0 to 4 scale for each zone [nasal, temporal, frontal]). Adverse events (AEs) were collected.

Results: Both 0.2 mg and 0.3 mg groups met the primary endpoint of a statistically significant difference in conjunctival hyperemia in the worst zone compared to HV on Day 15 (P=0.004 and P=0.028, respectively). Change from baseline in mean conjunctival hyperemia grade in the 0.2 mg, 0.3 mg and HV group was -0.51, -0.43, and -0.21 respectively. Statistically significant differences in conjunctival hyperemia compared to HV were also observed for total, nasal, temporal and frontal zones in the 0.2 mg group and total, nasal, and temporal zones in the 0.3 mg group (all P<0.05). No serious ocular AEs were reported. The most common ocular AEs reported by subjects treated with OTX-DED (both 0.2 and 0.3 mg pooled; n=111) were increased lacrimation (8.1%), and intraocular pressure elevation (3.6%).

Conclusions: OTX-DED 0.2 mg and 0.3 mg dexamethasone intracanalicular insert significantly improved bulbar conjunctival hyperemia compared to hydrogel-vehicle in subjects with dry eye disease. Both insert doses were generally safe and well-tolerated.

CONTROL ID: 3713994

SUBMITTER (NAME ONLY): Alexandra Bernardo- Colón

TITLE: Ablation of pigment epithelium-derived factor receptor, PEDF-R, causes photoreceptor degeneration

Alexandra Bernardo-Colón[1], Lijin Dong[2], Mones Abu-Asab[3], and S. Patricia Becerra[1]

1. Section of Protein Structure and Function, LRCMB; 2. Genetic Engineering Core; 3. Section of Histopathology, NEI-NIH

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bernardo- Colón, L. Dong, M. Abu-Asab, S. Becerra, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptor cells produce a receptor protein for pigment epithelium-derived factor (PEDF-R), which is encoded by the PNPLA2 gene of the patatin-like phospholipase domain-containing 2 family. PEDF-R is a membrane-linked lipase detected in the inner segments of photoreceptors. We aim to reveal the physiological role of PEDF-R in photoreceptors by characterizing CRISPR Pnpla2 knock-out mouse lines.

Methods: CRISPR-derived Pnpla2 knock-out mouse lines were generated in a C57BL/6 and rd8 free background. RT-PCR was performed from dissected retinas. Mice were evaluated for fundoscopy, electroretinography and angiography. Organs of the thorax were harvested and imaged using a LEICA microscope. Plasma was collected for lipid analyses. Eyes were enucleated and processed for histology, immunofluorescence, confocal microscopy, and transmission electron microscopy.

Results: Pnpla2$^{-/-}$ mice had undetectable retinal Pnpla2 expression levels, enlarged whiter hearts, and lower plasma free fatty acids and triglycerides levels than their Pnpla2$^{+/+}$ littermate controls. Their retinal pigment epithelial cells accumulated lipid droplets and their photoreceptors were deformed. Fundi of Pnpla2$^{+/-}$ eyes had white spots. The optic nerve area of Pnpla2$^{-/-}$ and Pnpla2$^{+/-}$ mice had an excess of pigment. The a-wave in Pnpla2$^{-/-}$ and Pnpla2$^{+/-}$ mice, and b-wave in Pnpla2$^{+/-}$ mice were attenuated relative to controls. Retinal rhodopsin and opsin gene expression of Pnpla2$^{-/-}$ and Pnpla2$^{+/-}$ were lower than in controls. The immunofluorescent intensities of rhodopsin and opsin antibodies decreased in Pnpla2$^{+/-}$ and Pnpla2$^{-/-}$ photoreceptors relative to controls. The immunofluorescence of PKCα and synaptophysin antibodies (markers for bipolar cells and ribbon synapse) in the Pnpla2$^{+/-}$ retinas were lower than in controls.

Conclusions: Ablation of Pnpla2 in mice causes malformation of photoreceptors and affects photoreceptor performance, identifying PEDF-R as an important component for photoreceptor structure and function. These findings suggest that the absence of PEDF-R in photoreceptor cells interrupts PEDF neurotrophic action, thereby heightening degeneration in the mice.

CONTROL ID: 3713995

SUBMITTER (NAME ONLY): Marisa OBrien

TITLE: Longer-Term Outcomes of Trans-scleral Sutured Intraocular Lens Implantation in Children

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. OBrien, L. Tychsen, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Marisa OBrien: Commercial Relationship: Code N (No Commercial Relationship) | Lawrence Tychsen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report longer-term safety and efficacy outcomes after implantation of trans-scleral sutured posterior chamber intraocular lenses (TSS-IOLs) in children lacking capsular support. Comparison was made between children with ectopia lentis, congenital cataract, or traumatic cataract as well those implanted using 9-0 vs. 10-0 Prolene sutures.

Methods: Outcomes were collated retrospectively for 48 children (61 eyes) implanted with TSS-IOLs. All of the children had a history of lensectomy-vitrectomy with primary or secondary extensive or complete capsulectomy. Main outcome variables were final corrected distance visual acuity (CDVA) and occurrence of IOL-related adverse events (AE). The cause of the initial lenticular abnormality was ectopia lentis in 10 children (19 eyes), congenital cataract in 13 children (16 eyes), and traumatic cataract in 16 children (16 eyes). Mean follow-up for the 3 groups was 10.7, 10.6, and 7.5 years respectively. 39 eyes were implanted using 10-0 Prolene and 9 eyes using 9-0 Prolene.

Results: CDVA (mean 0.4 ± 0.3 logMAR) at last follow-up was best for those with ectopia lentis; mean age at initial surgery 7.8 yrs. CDVA (mean 1.25 ± 0.9) was worst for those with congenital cataract-related deprivation amblyopia; mean age at initial surgery 2.1 ± 0.4 months. The major AE encountered was suture breakage and TSS-IOL dislocation, which occurred in 68% of children with ectopia lentis, 23% with traumatic cataract, and 19% with congenital cataract. The IOL dislocation rate for eyes implanted using the thinner 10-0 Prolene suture was 37%, compared to 0% using the thicker 9-0 Prolene suture.

Conclusions: The TSS-IOL remains a useful option for correction of aphakia in pediatric eyes lacking capsular support. The major determinants of outcome success are lack of deprivation amblyopia (older age at first surgery) and use of thicker, breakage-resistant suture.

CONTROL ID: 3713996

SUBMITTER (NAME ONLY): Ram Prasad

TITLE: Maintenance of intestinal ACE2 minimizes the risk of developing diabetic retinopathy in type 1 diabetes

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Prasad, J. Floyd, B. Asare-Bediako, D. Chakraborty, Y. Adu-Agyeiwaah, A. Harbour, M.B. Grant, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|Q. Li, Ophthalmology Research, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously, we showed that the loss of angiotensin converting enzyme 2 (ACE2) results in disturbed gut-retina axis and contributes to developing diabetic retinopathy (DR). However, the mechanisms responsible for causing DR phenotype are poorly understood. Here, we examined the impact of maintained levels of enteral ACE2 on gut barrier defects, glucose homeostasis, and the development of DR in type 1 diabetic (T1D) mice.

Methods: Two approaches were employed to maintain enteral ACE2 levels in the Akita mice. 1) overexpression of human Ace2 in Akita mice (Vil-Cre.Ace2KI-Akita) by genetic manipulation, and 2) oral administration of an engineered probiotic (Lactobacillus paracasei; LP) which expressed and secreted humanized ACE2 into the intestinal lumen. After nine months of T1D, enteral and retinal endpoints were assessed, including expression of local RAS components, gut barrier integrity, visual function, and histological features of DR.

Results: Despite the presence of nine months of diabetes, Vil-Cre.Ace2KI-Akita and LP-ACE2-Akita mice exhibit sustained intestinal Ang 1-7 levels, preserved junctional proteins (ZO-1, p120-catenin, β-catenin), and maintained gut barrier integrity as demonstrated by lower levels of gut microbial products in the systemic circulation. Increased ACE2 activity leads to Ang-II degradation, resulting in higher Ang1-7 levels. Ang1-7, through activation of the Mas receptor, increases intestinal glucose transporters (SGLT1 and GLUT2). Furthermore, enteral ACE2 forms a heterodimer with the tryptophan transporter B^0AT1, as observed by IHC, which increased incretin (GLP-1 and GIP) secretion. These act in combination to control glucose homeostasis, which, within the retina, reduced acellular capillaries in Vil-Cre.Ace2KI-Akita ($p<0.001$) and LP-ACE2 treated Akita mice ($p<0.0001$) compared with untreated diabetic mice. Sustained enteral ACE2 expression also significantly improved retinal electrical response and visual acuity as measured by ERG (scotopic a wave, $p<0.003$; scotopic b wave, $p<0.01$; photopic a wave, ns; photopic b wave, $p<0.002$) and OKN ($p<0.0001$), respectively.

Conclusions: Taken together, our study demonstrates that sustained enteral ACE2 expression in T1D prevents DR by maintaining intestinal barrier integrity and improving glucose homeostasis.

CONTROL ID: 3713997

SUBMITTER (NAME ONLY): Timothy Domashevich

TITLE: Extracellular vesicles enrichment from postmortem human retina and RPE tissue

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Domashevich, V. Canto Soler, M. Flores-Bellver, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus in Aurora, Colorado., Colorado, UNITED STATES|S. Redenti, Biochemistry Doctoral Program, Lehman College of CUNY Division of Natural and Social Science, Bronx, New York, UNITED STATES|

Commercial Relationships Disclosure: Timothy Domashevich: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Redenti: Commercial Relationship: Code N (No Commercial Relationship) | Valeria Canto Soler: Commercial Relationship: Code N (No Commercial Relationship) | Miguel Flores-Bellver: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Extracellular Vesicles (EVs) are a heterogeneous group of lipid bilayer membrane structures released by all cells. EVs contain specific sets of lipids, proteins, DNA and RNA and are being recognized as key players in cell signaling, homeostasis, and the pathology of various diseases. Most EVs studies have been accomplished by using cell supernatants or different body fluids, but the number of studies on tissue derived EVs is still limited. To characterize and gain insight on the role of EVs derived from the retina and RPE tissue, it is important to establish practical and efficient protocols for their isolation. Here we describe a step-by-step procedure of a novel, optimized and efficient method to isolate EVs directly from both human retina and RPE tissues.

Methods: Our protocol includes enzymatic treatment of dissociated postmortem retina and RPE tissues followed by differential ultracentrifugation and density separation. The isolated EVs were characterized by transmission electron microscopy (TEM), Nanosight (NTA) and Exoview analysis. In addition, western blot against well-known EV specific markers and non-EV markers was used to determine the quality and purity of EV preparations. Furthermore, we analyzed the proteomic cargo of retina- and RPE tissue-derived EVs and validated the proteins found by western.

Results: EVs trapped within the retina and the RPE were successfully isolated while maintaining the integrity of the vesicles and their cargo. The presence of EVs during each isolation step was confirmed via NTA with additional Exoview analysis after final recovery. Characteristic clear rounded membrane vesicles within a size range of 30–170 nm was observed by TEM. The physical characteristics of the vesicle preparations (ultrastructural morphology and size), and their biochemical composition (presence of Syntenin, CD63, and absence of GM130) confirmed that they fulfill the criteria for EVs. Furthermore, proteomic profiling of tissue-derived EV cargo revealed that EVs were enriched in proteins involved in biological processes associated with retina physiology.

Conclusions: This study represents the first human retina and RPE EV isolation protocol to date. This method will enable researchers to gain insight on EV populations in the eye, explore their role in cell-to-cell communication and, provide a novel approach for elucidating mechanisms behind ocular pathogenic conditions.

CONTROL ID: 3714000

SUBMITTER (NAME ONLY): Ryang Hwa Lee

TITLE: Mesenchymal stem cell-derived extracellular vesicles ameliorate experimental autoimmune uveoretinitis in mice via suppressing autoreactive T cell Infiltration

SESSION TITLE: Uveitis: Translational and Pre-clinical Studies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lee, G. Kaur, H. Barreda, E. Kim, Molecular and Cellular Medicine, Texas A&M University, College Station, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accumulating evidence shows that extracellular vesicles (EVs) produced by mesenchymal stem/stromal cells (MSCs) exert their therapeutic effects in several disease models. Previously, we also demonstrated that MSC-derived EVs (MSC-EVs) prevent onset of autoimmune disease in murine models including experimental autoimmune uveoretinitis (EAU). In addition, we found that 3D microcarrier culture conditions increased the expression levels of immunomodulators in MSC-EVs such as TGF-β1, let-7b and TSG-6, enhancing the immunomodulatory function of MSC-EVs. Building on these findings, we herein further investigated if MSC-EVs produced under 3D microcarrier culture conditions (3D MSC-EVs) can be used to treat autoimmune uveitis after the onset of the disease.

Methods: To examine the therapeutic potency of MSC-EVs in the management of EAU after disease onset, MSC-EVs were systemically treated in EAU mice on day 14 after immunization and the severity of EAU in mice was assessed on day 28. To examine if MSC-EVs can directly suppress the infiltration of retina-specific autoreactive T cells, an adoptive transfer model of EAU was induced in mice with or without MSC-EV treatment and the disease progress was evaluated in recipient mice. Also, an in vitro chemotaxis assay was used to demonstrate the inhibitory effect of MSC-EVs on T cell migration.

Results: We found that the treatment of 3D MSC-EVs on day 14 after EAU induction effectively suppressed the disease progress in EAU mice compared to those from control monolayer cultures. Also, 3D MSC-EVs were more effective in preventing the development of EAU in an adoptive transfer model of EAU. Consistent with the findings, MSC-EVs effectively suppressed the migration of retinal reactive T cells under an in vitro chemotaxis setting.

Conclusions: Our results suggest that MSC-EVs directly inhibit the infiltration of retinal reactive T cells toward the eyes, thereby halting the disease progress in EUA mice. The data strongly support the therapeutic potency of MSC-EVs for the treatment of autoimmune uveitis.

CONTROL ID: 3714002

SUBMITTER (NAME ONLY): Geetika Kaur

TITLE: VCAM1 regulates Fra1/JunB mediated IL-8 expression and pathological retinal neovascularization in a murine model of oxygen-induced retinopathy

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Kaur, S. Bisen, D. Sharma, N.K. Singh, Department of Ophthalmology Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pathological retinal neovascularization is a clinical manifestation of various proliferative retinopathies, including retinopathy of prematurity (ROP), diabetic retinopathy, and the wet form of macular degeneration. Over the last decade, numerous studies have reported an increased infiltration of hematopoietic stem cells (HSCs), macrophage/microglia in patients with intraocular angiogenic diseases.

Methods: Using a murine model of oxygen-induced retinopathy (OIR) and human retinal microvascular endothelial cells (HRMVECs), we are trying to understand the significance of IL-33/Hypoxic induced VCAM1 expression in retinal neovascularization.

Results: Here, using a murine model of oxygen-induced retinopathy, we found that NFkB and VCAM1 levels were highly up regulated in retina when new vessels were developing in the retina. Genetic deletion of IL-33 resulted in reduced NFkB activation and VCAM1 levels in hypoxic retina, resulting in reduced neovascularization. These findings suggest a role for IL-33-NFkB-VCAM1 signaling in pathological neovascularization. Our results demonstrate that IL-33 induce tube formation in human retinal microvascular endothelial cells and depletion of VCAM1 levels significantly blocked it. Protein profiler analysis showed that IL-33 regulates VCAM1 dependent IL-8 expression in HRMVECs. In order, to understand how IL-33 induced VCAM1 regulates the expression of IL-8, we did sequence analysis of IL-8 promoter and observed that IL-8 promoter has AP1 binding site. We observed that IL-33 induced the expression of Fra1 and JunB significantly in HRMVECs. Cloning and site directed mutagenesis of IL-8 promoter revealed that the AP1 binds to IL-8 promoter in response to IL-33 and regulate the expression of IL-8 in HRMVECs. Consequently, down regulation of VCAM1 levels significantly reduced IL-33 induced Fra1 and JunB expression as well as IL-8 expression.

Conclusions: These results strongly suggest that IL-33/ST2L-NFkB-VCAM1-AP1 regulates IL-8 expression, playing a key role in retinal neovascularization and thus represents a new pharmacological target for the treatment of diseases where excessive neovascularization is the underlying pathology.

CONTROL ID: 3714003

SUBMITTER (NAME ONLY): Daisy Shu

TITLE: Dimethyl fumarate blocks TNFα-driven inflammation and metabolic rewiring in retinal pigment epithelial cells

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.Y. Shu, T.C. Fitch, S.I. Frank, E.R. Butcher, M. Karg, S. Cai, R. Shah, D. Gollapalli, M. Saint-Geniez, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D.Y. Shu, M. Karg, M. Saint-Geniez, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative damage and inflammatory activation of retinal pigment epithelial cells (RPE) are key contributors to age-related macular degeneration (AMD) pathogenesis. Metabolic reprogramming and oxidative stress are known to drive immune cell activation. However, the existence of such interplay between inflammation and metabolism in RPE remains elusive. This study examines the effects of tumor necrosis factor-α (TNFα), a pro-inflammatory cytokine involved in AMD, on RPE metabolism and investigates the metabolic drug, dimethyl fumarate, as a new regulator of RPE immunometabolism.

Methods: Matured primary human RPE cells were treated with TNFα (10 ng/ml) and/or pre-treated with dimethyl fumarate (DMFu, 80 μM) for 2 hours. Glycolytic and oxidative (OXPHOS) metabolic profiles were determined by Seahorse XFe96. Gene expression of metabolic markers was assessed using qPCR. IL-6 secretion was quantified by ELISA. Cellular ATP content was measured by bioluminescence. Reactive oxygen species (ROS) was measured using a fluorometric mitochondrial superoxide detection kit. Ultrastructural features of mitochondria were imaged by transmission electron microscopy (TEM).

Results: TNFα-induced upregulation of IL-6 secretion ($p<0.0001$, $n=6$) in RPE was accompanied by increased basal and maximal OXPHOS on Seahorse Mito Stress Test ($p<0.0001$, $n=10$). TNFα increased ATP production, mitochondrial ROS production ($p<0.0001$, $n=8$) and gene expression of the mitochondrial antioxidant SOD2 ($p<0.0001$, $n=6$). TEM revealed defects in mitochondrial morphology with engorged mitochondria and loss of cristae integrity with TNFα. DMFu suppressed TNFα-induced IL-6 secretion ($p<0.0001$, $n=6$) and maintained mitochondrial OXPHOS and ATP production at control levels ($p>0.05$, $n=6$). DMFu increased PFKFB3 gene expression ($p<0.0001$, $n=6$) and correspondingly, restored TNFα-induced suppression of glycolysis to control levels ($p>0.05$, $n=6$).

Conclusions: The pro-inflammatory effects of TNFα on RPE are accompanied by defects in mitochondrial morphology and a profound metabolic shift promoting OXPHOS and ROS accumulation. Treatment with the fumaric acid precursor, DMFu, efficiently blocks TNFα-induced pro-inflammatory activation and bioenergetic reprograming of RPE. These results reveal a critical interplay between inflammation and metabolic dysfunction in RPE, identifying DMFu as a potent immunoregulatory drug against AMD progression.

CONTROL ID: 3714005

SUBMITTER (NAME ONLY): Wayne Tschetter

TITLE: Isolating the mechanisms of photoreceptor protection elicited by a ketogenic & low protein diet.

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Tschetter, D. Wafai, I. Fries, M. Six, R.C. Ryals, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Wayne Tschetter: Commercial Relationship: Code N (No Commercial Relationship) | Dahlia Wafai: Commercial Relationship: Code N (No Commercial Relationship) | Ian Fries: Commercial Relationship: Code N (No Commercial Relationship) | Makayla Six: Commercial Relationship: Code N (No Commercial Relationship) | Renee Ryals: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously showed that a ketogenic & low protein (KLP) diet slows photoreceptor degeneration in early weaned rd10 mice but the neuroprotective mechanism remains unclear. We performed a proteomics analysis to determine which proteins the KLP diet modulate in the retina as a way to isolate targets that slow retinal degeneration.

Methods: C57BL6 mice were early weaned and placed on the KLP diet starting at P15. After 30 days of continuous diet administration, ERGs were recorded, serum albumin was measured and retinas were harvested for tandem mass tag (TMT) mass spectrometry to compare differentially expressed proteins. To investigate the effect of dietary protein restriction, a separate group of rd10 mice were early weaned and placed on a low protein diet containing 8% protein. At P23, P30, P40 and P50 weight and blood b-hydroxybutyrate levels were recorded and retinal thickness was measured with optical coherence tomography (OCT). At P30 and P50, serum albumin levels were measured.

Results: TMT analysis quantified a total of 6247 proteins. Of these, 58 proteins were differentially expressed in the retina due to the KLP diet. Only one of these plays a role in phototransduction (SWOPN1). Of interest was an upregulation of antioxidant (GST, APOA4), lipid metabolism (SCP2) and DNA repair (XRCC4) proteins and a downregulation of markers for neuronal damage (GFAP, NFMP). Mice on the low protein diet weighed an average of 30% less than those on standard chow (SC), but blood albumin concentrations were not significantly different from the SC group (~1300pg/mL). Photoreceptor layer thickness decreased from 60.4uM at P23 to 18.3uM at P50, mimicking the rate of degeneration in the SC group.

Conclusions: We previously published that the KLP diet reduces phototransduction, which may serve as the protective mechanism of the KLP diet. However, our data show that these changes are not due to a significant change in phototransduction protein expression but rather activation and suppression of key proteins for neuroprotective pathways. The low protein diet results further support the hypothesis that reduced phototransduction and serum albumin are required to elicit photoreceptor protection in the rd10 mice. These data generate novel therapeutic targets for inherited retinal degeneration.

CONTROL ID: 3714007

SUBMITTER (NAME ONLY): Jeremy Lavine

TITLE: Single cell RNA sequencing reveals a subtype of pro-angiogenic classical monocyte-derived macrophages during experimental choroidal neovascularization

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Lavine, S. Droho, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|C.M. Cuda, H. Perlman, Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Jeremy Lavine: Commercial Relationship: Code N (No Commercial Relationship) | Steven Droho: Commercial Relationship: Code N (No Commercial Relationship) | Carla Cuda: Commercial Relationship: Code N (No Commercial Relationship) | Harris Perlman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Macrophages are key pathogenic cells in neovascular age-related macular degeneration. However, macrophages are heterogeneous cells whose function depends upon their microenvironment and/or origin. Choroidal macrophages are derived from blood monocytes, and classical monocyte-derived macrophages (MDMs) are necessary for laser-induced choroidal neovascularization (CNV). We hypothesized that a subtype of classical MDMs stimulates angiogenesis during laser-induced CNV.

Methods: Female wildtype (WT) and $Ccr2^{-/-}$ mice underwent no treatment or laser injury. On Day 3, eyes were harvested, digested into single cell suspensions, and $CD45^{+}$ cells were isolated by fluorescence-activated cell sorting for single cell RNA-sequencing. Cell Ranger was used for genome alignment and empty droplet exclusion. The data were loaded into Seurat v3 for quality control metrics and cell clustering. Hypergeometric distribution analysis determined which genotype and treatment contributed to each cluster. Differential expression (DE) analysis was performed between each macrophage cluster and all other clusters. GOrilla gene ontology analysis was used to determine the function of each macrophage cluster.

Results: We sequenced 34,215 cells with an average 36,890 reads per cell. We identified 12 total macrophage clusters, including 6 microglia subtypes and 6 macrophage subsets. DE and GO analysis found that only one cluster was enriched for positive regulation of angiogenesis (6.3-fold, $q<0.05$). DE genes contributing to positive regulation of angiogenesis included Vegfa (vascular endothelial growth factor), Anxa1/2/4/5 (annexins), Il1b (interleukin-1 beta), Fn1 (fibronectin), Mmp12/14 (metalloproteinases), and Spp1 (osteopontin). This $Spp1^{+}$ cluster was specifically derived from the WT + laser group. In addition, $Spp1^{+}$ MDMs were enriched for glycolysis and lipid catabolism GO terms, two processes implicated in macrophage-driven angiogenesis. Finally, $Spp1^{+}$ MDMs specifically express the CD11c receptor.

Conclusions: $Spp1^{+}$ MDMs express a transcriptome including VEGF and cytokine signaling, matrix metalloproteinases that degrade basement membranes, annexins to increase endothelial sprouting, and fibronectin for scaffolding that stimulates angiogenesis by multiple pathways. $Spp1^{+}$ MDMs express specific cell surface markers like CD11c, which can be used for therapeutic ablation.

CONTROL ID: 3714009

SUBMITTER (NAME ONLY): Michelle Zhang

TITLE: Carboplatin Chemoresistance in Retinoblastoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhang, J. Kuznetsoff, D. Pelaez, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|M. Zhang, K. Kalahasty, University of Miami School of Medicine, Miami, Florida, UNITED STATES|J. Harbour, Department of Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Michelle Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Jeffim Kuznetsoff: Commercial Relationship: Code N (No Commercial Relationship) | Karthik Kalahasty: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Pelaez: Commercial Relationship: Code N (No Commercial Relationship) | J. William Harbour: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinoblastoma (RB) is the most common intraocular eye cancer in children. Although intra-arterial chemotherapy is effective, there is a strong propensity for therapeutic escape in retinoblastoma and limited second-line treatment options. Characterizing RB cancer progression is essential for discovering novel targeted therapies. Here, we developed different techniques for characterizing RB in vitro and generated a new chemoresistant retinoblastoma cell line.

Methods: A naïve retinoblastoma cell line (RB028) and a treated retinoblastoma cell line (RB006) were transduced with a constitutively expressing GFP system as a surrogate readout of viability using the Incucyte Imaging System. The sensitivity of the GFP signal in retinoblastoma cell lines was validated using DMSO. This system was then used to generate kill curves with clinically relevant chemotherapy agents (carboplatin, melphalan, and topotecan). RB028 was treated with repeated sublethal dosages of 1uM melphalan and 1uM carboplatin and was monitored for the development of chemoresistance after recovery. We characterized the recovered cell lines' invasiveness and clonogenicity in Cultrex and in HyStem matrices.

Results: GFP signals in both RB006 and RB028 were quenched within 4 hours of 50% DMSO treatment and were sufficiently sensitive for generating a cost-effective viability assay. Baseline corrected AUCs of kill curve assays for RB006 is higher than RB028 for carboplatin (1-10uM) and for melphalan (5-20uM), highlighting the preservation of clinically-relevant chemoresistance mechanisms in RB cells using our culturing system. Treated naïve RB028 recovered within two weeks for carboplatin and within three weeks for melphalan. RB028 was treated up to four times with carboplatin (RB028-4XC). Compared with Naïve RB028, RB028-4XC had higher baseline-corrected AUCs for carboplatin (10-40uM) and demonstrated a greater propensity for remaining viable as small clusters in preliminary characterization assays.

Conclusions: We generated a new carboplatin chemoresistant retinoblastoma cell line useful for downstream molecular analysis of chemotherapy resistance mechanisms. Though further in vitro characterization is still necessary, preliminary findings reveal traits associated with more clinically aggressive phenotype.

CONTROL ID: 3714011

SUBMITTER (NAME ONLY): Kevin Frick

TITLE: Differences in Serious Difficulty Seeing and Utilization of Eye Exams by Sexual Orientation (2016-2020)

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.D. Frick, Carey Business School, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Kevin Frick: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Challenges with access to some types of health care that result in health differences have been documented for individuals with sexual orientation other than straight. There is little evidence as to whether these occur in eye care and translate into vision impairment.

Methods: Data from the Behavioral Risk Factor Surveillance System (BRFSS) from 2016-2019 and the National Health Interview Survey (NHIS) from 2016-2020 were used. Both surveys employ complex sampling. Analyses accounting for study design were conducted using R. In both studies sexual orientation was coded to compare those who responded straight with lesbian or gay, bisexual, or other. Only BRFSS data from Virginia and Wisconsin were used; these states included the sexual orientation and diabetes modules (including the eye exam question) each year. Respondents were asked "Are you blind or do you have serious difficulty seeing, even with glasses?" Individuals who reported diabetes were grouped into having had an eye exam in the past year and having had one longer ago or never. For vision, in the NHIS, respondents were grouped into those who indicated no trouble or a little trouble seeing even when wearing glasses and those who indicated a lot of trouble or cannot see even with glasses. Accounting for survey design, the association between sexual orientation and outcomes of interest was assessed using chi-squared tests.

Results: In Virginia (Wisconsin), among individuals indicating straight sexual orientation the prevalence of receiving an eye exam in the past year ranged from 72.2-73.8% (71.0-79.7%); these ranged from 11.5% less likely to 23.1% more likely (14.4% less likely to 8.3% more likely) than those of other sexual orientations. In Virginia (Wisconsin) among individuals indicating a straight sexual orientation, prevalence of serious difficulty seeing ranged from 3.9-4.4% (2.3-3.1%), with differences ranging from 0.1% more to 2.7% less (1.4% to 3.2% less) than those of other sexual orientation. In the NHIS, the prevalence of a lot of trouble seeing for those who indicated straight sexual orientation ranged from 1.2-1.7% and the prevalence ranged from 0.1-1.0% less than that for individuals of other sexual orientation. No p-value was ≤0.05.

Conclusions: There is no association between sexual orientation and use of timely eye exams among those with diabetes or the prevalence of serious difficulty seeing.

CONTROL ID: 3714012

SUBMITTER (NAME ONLY): Whitney Thiel

TITLE: Compensatory phagocytic function and Müller glia reactivity in the absence of microglia

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Thiel, Z.I. Blume, D. Mitchell, Biological Sciences, University of Idaho, Moscow, Idaho, UNITED STATES|

Commercial Relationships Disclosure: Whitney Thiel: Commercial Relationship: Code N (No Commercial Relationship) | Zachary Blume: Commercial Relationship: Code N (No Commercial Relationship) | Diana Mitchell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Models of microglia deficiency are used to probe their functions in the retina. In these microglia-deficient tissues, phagocytosis may be compensated by other glial cell types. We found Müller glia (MG) increase phagocytic load in microglia deficient retinas (Mitchell et al. IOVS 2021). We further use a microglia-deficient genetic zebrafish mutant to investigate MG phagocytic activity and determine downstream effects on MG. We hypothesized increased phagocytic load leads to MG reactivity.

Methods: Developing whole eyes and retinal cryosections from microglia-deficient and sufficient siblings were analyzed. We used confocal microscopy to visualize apoptotic cells (TUNEL), MG, and lysosomes (LAMP1). We visualized apoptotic cell engulfment in live, transient transgenic zebrafish expressing TP1:mcherry-CAAX stained with acridine orange and 3D image rendering (n=4). To see if phagocytosis induced apoptosis in MG, we correlated phagocytosis to MG cell death using cleaved caspase 3 staining (n=8-20/group). To examine MG reactivity, we measured gfap transcripts in individual pairs of eyes by qPCR (n=10-20/group), and GFAP intensity from stained retinal cryosections (n=3-4). To inhibit MG phagocytosis, we used L-SOP treatment (n=8-20/group). We used a transgenic reporter to quantify reactive MG (gfap:nGFP, Bernardos et al., 2007; n=5-8). To examine possible cell cycle re-entry by post-mitotic MG, we used EdU immersion and quantified EdU+MG (n=8-9/group). We also examined id2a and ascl1a transcripts in eyes using qPCR (n=5-9 & n=9-19/group, respectively).

Results: MG increase their phagocytic load to engulf dying cells in the absence of microglia, from ~15% in wt to ~50% TUNEL+ cell engulfment in mutants ($p<0.0001$). LAMP1 staining of MG increased in the absence of microglia. Correlation analysis of engulfment to MG cell death is ongoing. Increased expression of gfap in microglia-deficient eyes ($p=0.01$) was detected but lost after L-SOP treatment. In the absence of microglia, we found increased gfap:nGFP+ MG compared to wt siblings ($p=0.007$). We detected no increased incorporation of EdU by MG in the absence of microglia, or differences in expression of id2a or ascl1a.

Conclusions: MG compensate phagocytic function in the absence of microglia, leading to signs of MG reactivity. However, increased MG phagocytic activity alone does not trigger cell cycle re-entry of differentiated MG in the absence of tissue damage.

CONTROL ID: 3714016

SUBMITTER (NAME ONLY): Katherine Wert

TITLE: Dysregulation of Tricarboxylic Acid (TCA) Cycle Activity and Lipid Metabolism in Preclinical Models of Retinitis Pigmentosa

SESSION TITLE: Retinal metabolism

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.J. Wert, A. Rowe, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|K.J. Wert, Molecular Biology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|R. Gordillo, Internal Medicine, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|R. Gordillo, Touchstone Diabetes Center, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Katherine Wert: Commercial Relationship: Code N (No Commercial Relationship) | Ashley Rowe: Commercial Relationship: Code N (No Commercial Relationship) | Ruth Gordillo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal degenerative diseases, such as retinitis pigmentosa (RP), have complex genetic causes but are characterized by the loss of the photoreceptor neurons. For the majority of these diseases, treatment is unavailable. Previously, we found that cellular metabolic pathways were disrupted in the neural retina at RP disease onset in an autosomal recessive (ar) preclinical mouse model, and that replenishing TCA cycle intermediates provided resilience to the photoreceptors against cell death and delayed vision loss in both the arRP and an autosomal dominant (ad) RP preclinical model. Investigation into the duration of photoreceptor resilience and the mechanism underlying the supplementation effect will provide insight into potential treatment targets for patients with RP disease, regardless of the causal genetic mutation.

Methods: The $Rho^{P23H/+}$ adRP preclinical mouse model was treated orally with single TCA cycle intermediates (alpha-ketoglutarate, succinate, and citrate) and followed via live imaging and histological analysis through 7 months of age. Additionally, as cells with high metabolic demand and mitochondrial dysfunction have been shown to favor reductive carboxylation to increase lipid metabolism, we profiled hundreds of individual lipids via mass spectrometry analysis from neural retinas of wild-type, arRP, and arRP mice treated with TCA cycle intermediates (alpha-ketoglutarate and citrate).

Results: We found that replenishment of TCA cycle intermediates in the adRP preclinical mouse model was able to prolong visual function and provide resilience to the photoreceptor neurons against cell death through at least 7 months of age. Furthermore, we detected an altered lipid profile in the neural retinas of mice with RP disease compared to healthy controls, and that supplementation with TCA cycle intermediates restored many of the lipid pathways in the neural retina to levels seen in wild-type controls.

Conclusions: Enhancement of TCA cycle activity toward altering lipid metabolism provides resilience to the photoreceptor cells against cell death and prolongs visual function in preclinical models of RP, regardless of the causal genetic mutation. Understanding this balance of photoreceptor cell metabolism and its dysregulation during disease can lead to more effective clinical treatments for patients with RP and other forms of retinal degenerative disease.

CONTROL ID: 3714018

SUBMITTER (NAME ONLY): Nicholas Stone

TITLE: A novel perfusion system for modeling the outer retina-RPE-choriocapillaris unit in vitro

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.E. Stone, A. Shrestha, K. Mulfaul, R.F. Mullins, B.A. Tucker, University of Iowa Institute for Vision Research, Iowa City, Iowa, UNITED STATES|N.E. Stone, A. Shrestha, K. Mulfaul, R.F. Mullins, B.A. Tucker, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

Commercial Relationships Disclosure: Nicholas Stone: Commercial Relationship: Code N (No Commercial Relationship) | Arwin Shrestha: Commercial Relationship: Code N (No Commercial Relationship) | Kelly Mulfaul: Commercial Relationship: Code N (No Commercial Relationship) | Robert Mullins: Commercial Relationship: Code N (No Commercial Relationship) | Budd Tucker: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to develop a novel culture system capable of providing tightly controlled uniaxial flow to cells cultured on the bottom of a transwell insert to replicate the mechanical stresses applied to choroidal endothelial cells in vivo. In addition to providing a platform capable of elucidating the connection between applied fluidic shear with the molecular and morphological maturity of endothelial cells, by placing patient-matched iPSC-derived retinal pigment epithelium (RPE) and fully differentiated iPSC-derived neural retina on top of the transwell, this system will constitute an in vitro model of the outer human retina.

Methods: Our disposable, single use transwell perfusion system was printed using an Object30 Prime 3D printer (Stratasys). After printing the device, cells from a human choroidal endothelial cell line were seeded on transwell inserts, after which the culture system was assembled by placing the transwell inserts into the device, which in turn was placed in a six well plate. A peristaltic pump was then used to provide controlled fluid flow across the seeded endothelial cells. After the conclusion of a perfusion experiment, the transwell membrane can be recovered from the system, allowing observation of cell morphology via microscopy as well as analysis of the molecular characteristics of the perfused cells.

Results: As per Figure 1, the perfusion device was designed with rectangular flow channels to induce uniaxial flow. Cells perfused using this system remained viable for 72 hours post-perfusion (417µl/hour) and remained attached to the surface of the transwell insert following removal from the perfusion device. Now that we have established that the system can apply controllable fluidic shear stress for days while keeping perfused cells viable, we will proceed to investigate the effect of increasing rates of shear stress on the morphological, molecular, and functional maturity of choroidal endothelial cells with and without RPE plated above.

Conclusions: We have used modern rapid-prototyping techniques to develop a perfusion system capable of testing the effect of fluidic shear on the phenotype and behavior of choroidal endothelial cells in vitro. Further, we believe that this system can be extended to serve as an in vitro model of the entire retina and used to determine the causes of and evaluate treatments for inherited blindness.

CONTROL ID: 3714019

SUBMITTER (NAME ONLY): Tatiana Rosenblatt

TITLE: Gender Disparities in the American Association for Pediatric Ophthalmology and Strabismus

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Rosenblatt, A.D. Azad, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T. Rosenblatt, A.D. Azad, A. Kossler, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Tatiana Rosenblatt: Commercial Relationship: Code N (No Commercial Relationship) | Amee Azad: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Lora Kossler: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Despite increasing numbers of women entering the field of ophthalmology, many subspecialties still lack gender parity among their society membership, and significant disparities persist among leadership positions and in the upper ranks of academia. We aim to evaluate male and female representation as members, awardees, executive committee members, and presidents of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) to understand recent trends in gender diversity within pediatric ophthalmology.

Methods: A retrospective, longitudinal study using publicly available data from AAPOS online archives and member directories from 2000 – 2020. Primary outcomes included percentage of women as new members, award winners, and leadership positions (executive committee, president). Secondary outcomes included total membership and the proportional representation of men and women, calculated by dividing the number of men and women at a given benchmark by the total number of men and women in the organization.

Results: Over the past two decades, AAPOS achieved total membership parity with 52.0% women and 48.0% men, $p=0.087$ (Figure 1). Furthermore, AAPOS demonstrated significant growth in the representation of women as new members (50.1% to 59.8%, $p=0.001$) and in the percent of female award winners between the two decades (23.1% to 39.9%, $p=0.005$), but no significant difference in the percent of female executive committee members or presidents (Table 1). Moreover, the proportion of women who won awards by 2020 was significantly less than that of male awardees (8.6% vs. 19.3%, $p<0.001$), and the proportion of female executive committee members was less than that of men holding such roles (7.7% vs. 15.4%, $p=0.004$). There was no significant difference between the proportion of men and women as presidents (0.6% vs. 1.6%, $p=0.070$) (Figure 1).

Conclusions: AAPOS has demonstrated significant growth in female membership and award recognition over the last 20 years; however, gaps still exist between men and women as award winners and executive committee members. This phenomenon demonstrates that the “wait and watch” approach to diversity is not sufficient to achieve gender parity at all levels of an organization. Targeted interventions such as addressing implicit bias, amending promotion criteria to recognize more varied achievements, and diverse nomination slates are needed to close this gender gap.

CONTROL ID: 3714020

SUBMITTER (NAME ONLY): Ahmed Sayed

TITLE: Repeatability assessment of monocular and binocular visual field measurements with a head mounted display

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sayed, Biomedical Engineering, Helwan University, Helwan, Cairo, EGYPT|A. Sayed, EECS, Milwaukee School of Engineering, Milwaukee, Wisconsin, UNITED STATES|V. Roongpoovapatr, M. Abou Shousha, R.K. Parrish II, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|T. Eleiwa, Benha University, Benha, EGYPT|

Commercial Relationships Disclosure: Ahmed Sayed: Commercial Relationship: Code N (No Commercial Relationship) | Vatookarn Roongpoovapatr: Commercial Relationship: Code N (No Commercial Relationship) | Taher Eleiwa: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Abou Shousha: Commercial Relationship(s);Code P (Patent):10386645;Code I (Personal Financial Interest):Heru Inc. | Richard Parrish II: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the visual field (VF) measurement repeatability using a portable VF quantification tool for both monocular and simultaneous binocular measurements.

Methods: In a previous work, we designed and implemented a virtual reality head mounted display (VRHMD) to measure VF. The measurement covered the central 80 degrees diameter area, in both monocular and binocular testing modes. In this study, we examined the repeatability of our devices VF measurements by repeating the VF test two times in two different groups of patients. The first group included 10 patients (10 eyes) with known monocular VF losses. We compared the VRHMD VF monocular testing outcomes with the standard of care: standard automated perimetric (SAP), which we used as the reference measurement. In the second group, another 10 patients (20 eyes) with binocular glaucomatous and neurological VF losses, participants were VF tested binocularly (simultaneous VF measurement for the two eyes). Binocular test outcomes were compared with the integrated monocular SAP tests for both eyes of the participants. We compared the VRHMD VF and SAP VF reproducibility tests qualitatively using paired VF images, and quantitatively with Intraclass correlation coefficient statistical metric.

Results: The VRHMD VF outcomes were qualitatively comparable to their matching references in the monocular and binocular groups of patients, as visual results show. The VRHMD VF quantitative repeatability metric for repeated testing with the ICC metric was found to be significant in the two groups (0.83 for the first test monocular group, 0.73 for the second binocular testing group) indicating excellent agreement for VRHMD monocular measurements and good agreement for the binocular measurements, respectively.

Conclusions: Monocular and binocular VRHMD VF measurements were found to be repeatable and statistically reproducible.

CONTROL ID: 3714021

SUBMITTER (NAME ONLY): Courtney Liang

TITLE: Effect of Low Dose Atropine Eye Drops on Ocular Structure and Function

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Liang, A. Jnawali, S. Curtin, F.A. Vera-Diaz, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Courtney Liang: Commercial Relationship: Code N (No Commercial Relationship) | Ashutosh Jnawali: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Curtin: Commercial Relationship: Code N (No Commercial Relationship) | Fuensanta Vera-Diaz: Commercial Relationship(s);Code C (Consultant/Contractor):Essilor International

ABSTRACT BODY:

Purpose: Myopia is associated with abnormal scleral constitution and remodeling. We investigated the effect of low dose atropine eye drops on scleral thickness and pressure to evaluate ocular rigidity, and other visual parameters in emmetropes and myopes.

Methods: Young adults (N=19, 24.4±1.2yrs) with emmetropia (SE +0.4±0.3D) or myopia (SE -2.4±1.7D) were enrolled. Lenstar LS900 was used to measure axial length (AXL), corneal thickness (CCT), anterior chamber depth (ACD) and lens thickness (LT); Spectralis SD-OCT anterior segment module to evaluate anterior scleral thickness, and wide-field posterior module to evaluate retinal and choroidal thickness. IOP was measured with GAT and iCare in the central cornea and with iCare at four scleral locations: 4mm nasal, 4mm temporal, 5mm superior and 5mm inferior from the limbus. Other tests included pupil sizes under dim, bright and near conditions, dynamic retinoscopy (MEM) and contrast sensitivity (CS, Rubin). Subjects used 1 drop of 0.05% atropine in each eye every night for 7 days. All measurements were taken: twice during Visit-1 (before and 30mins after instillation of atropine), and once during Visit-2 (1 week later, at a similar time: ±2 hours).

Results: Pupils became significantly larger after instillation of atropine (Dim: 1.5±0.7mm, Near: 2.1±0.7mm, Bright: 2.2±0.8mm, $p<0.01$ all). Accommodation lags increased (0.4±0.7D, $p=0.05$) and CS decreased (-0.2±0.3LogCS,$p=0.02$) in Visit-2. Corneal IOP decreased (1.6±2.7mmHg, $p=0.02$), but scleral IOPs significantly increased at 5mm superior (7.2±2.7mmHg, $p=0.04$) and 4mm temporal (3.6±2.7mmHg, $p=0.04$) in Visit-2. ACD was deeper in Visit-2 (0.1±0.1mm, $p=0.02$), and a trend was noted for longer AXL, thicker CCT and thinner LT. Those subjects for whom temporal sclera thickened with atropine, tended to also have higher IOPs temporally ($R=0.4$, $p=0.06$). No significant effect of atropine on retinal or choroid thickness was noted for any eccentricity.

Conclusions: Although short-term use of 0.05% atropine eye drops significantly increased pupil sizes, more variability was noted on accommodation and other visual parameters. Corneal IOP significantly decreased after 1 week use of atropine, whereas superior and temporal scleral IOP increased. Higher IOP in anterior sclera and trend for thickening in the same area with atropine use may be associated with the mechanism of atropine in myopia management.

CONTROL ID: 3714022

SUBMITTER (NAME ONLY): Kiran Vupparaboina

TITLE: Deep-learning based diagnostic quality assessment of choroid layer in OCT scans

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.K. Vupparaboina, J.A. Sahel, J. Chhablani, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|S. Manne, S.P. Koidala, S. Jana, Electrical Engineering, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|A. Mohammed, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|K. Ozimba, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|S.B. BASHAR, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

Commercial Relationships Disclosure: Kiran Vupparaboina: Commercial Relationship: Code N (No Commercial Relationship) | Shanmukh Reddy Manne: Commercial Relationship: Code N (No Commercial Relationship) | Surya Koidala: Commercial Relationship: Code N (No Commercial Relationship) | Kalah Ozimba: Commercial Relationship: Code N (No Commercial Relationship) | Abdul Rasheed Mohammed: Commercial Relationship: Code N (No Commercial Relationship) | SARFORAZ BASHAR: Commercial Relationship: Code N (No Commercial Relationship) | Jose Sahel: Commercial Relationship(s);Code I (Personal Financial Interest):, GenSight Biologics (S, I), SparingVision (S, I); Prophesee (I), Chronolife (I) | Soumya Jana: Commercial Relationship: Code N (No Commercial Relationship) | Jay Chhablani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Various vision-related ailments including age-related macular degeneration (AMD) and central serous chorioretinopathy (CSCR) are caused due to the dysfunctions manifested in the highly vascular choroid layer of the posterior segment of the eye. Accurate detection of choroidal structural changes plays a crucial role in disease diagnosis. Optical Coherence Tomography (OCT) imaging enabled clinicians to visualize choroid layer. Consequently, many methods have been developed to assist clinicians in diagnosis. However, the performance of these algorithms is largely constrained by the quality of the OCT scan. This study aims to achieve automated quality assessment of choroidal features (CQA) in OCT scans. We examine deep learning architectures to discriminate between good and bad quality OCT scans and also generate corresponding visual explanations via Grad-CAM.

Methods: A retrospective dataset of 1094 healthy and 3080 diseased OCT B-scans taken from Heidelberg Retina Angiography (HRA) Spectralis OCT machine was used in this experiment. The images were graded subjectively into two classes `good' and `bad' by a trained expert (K. Ozimba) based on various parameters including visibility of the choroid, the contrast between choroidal luminal (vessel) and stromal regions, contrast between the choroid and sclera, especially at choroid sclera interface. Inspired by the efficacy of deep learning features in image quality assessment, we employed variants of two ubiquitous architectures: residual networks (ResNets) and EfficientNet. We evaluated the model performance via stratified 5-fold cross-validation and demonstrated the model's discriminative ability through visual explanations generated by Grad-CAM.

Results: The average accuracy over 5-folds was found to be 97.69%, 96.99%, and 97.92%, respectively, for ResNet18, EfficientNet B0, and EfficientNet B3. Grad-CAM-generated visual explanations on representative images also demonstrate the superiority of EfficientNet B3 over the other models.

Conclusions: We have demonstrated the efficacy of transfer learning in CQA-OCT images by deploying and comparing the performance of state-of-the-art deep learning models, namely, ResNet18 and EfficientNet (B0 & B3). Further, we have also provided explainable visual feedback using Grad-CAM that corroborates closely with clinicians.

CONTROL ID: 3714023

SUBMITTER (NAME ONLY): Mitchell Jacobs

TITLE: Effect of caffeine on vessel density in healthy subjects assessed with optical coherence tomography angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jacobs, C. Turski, N. Fowler, V. Kupper, K. Acharya, J. Chadwell, A. Dupont, N. Demas, R. Maldonado, Ophthalmology and Visual Sciences, University of Kentucky College of Medicine, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Caffeine is a readily available and regularly used neurostimulant with effects on systemic vasculature. There is limited data on the effects on retinal vasculature with some reports indicating vessel constriction. We aim to evaluate if caffeine alters the macular vascular density of the superficial capillary plexus (SCP) on optical coherence tomography angiography (OCTA).

Methods: This IRB-approved study prospectively recruited healthy, low caffeine users who consumed, on average, less than 136 mg of caffeine daily. We analyzed 22 eyes from 11 individuals between the ages of 18 and 40, with no preexisting ocular conditions. Baseline 3x3mm and 6x6mm OCTA scans centered on the fovea as well as 6x6mm scans centered on the optic nerve head (ONH) were obtained. Participants were then given a 200mg caffeine pill. Scans were repeated at 60 and 120 minutes after caffeine administration. All images were analyzed with the Advanced Retina Imaging (ARI) network software (Carl Zeiss Meditec, Dublin, CA) superficial perfusion density algorithm for vascular density (VD) defined as the total area of perfused vasculature in a region of measurement. Ordinary one-way ANOVA of each group was performed using GraphPad Prism Version 9.3.0.

Results: Mean age was 24.6 +/- 4.6 years and 82.2% were females. For the 3x3 mm scans, the VD was 31.55%, 31.57%, and 32.06% at baseline, 60, and 120 minutes respectively (p=0.9993 and p=0.7933). For the 6x6 mm scans, the VD was 38.16%, 39.09%, and 39.04% at baseline, 60, and 120 minutes respectively (p=0.7300 and p=0.7546). For the ONH scans, the VD was 41.06%, 39.74%, and 41.44% at baseline, 60, and 120 minutes respectively (p=0.5649 and p=0.9498).

Conclusions: Our results indicate no change in the SCP vessel density after 200 mg caffeine. Larger placebo-controlled studies are needed to confirm this finding.

CONTROL ID: 3714024

SUBMITTER (NAME ONLY): Alexandra Warter

TITLE: Adjuvant use of long-acting intravitreal steroids and anti-VEGF agents in monotherapy resistant chronic Wet-Age Related Macular Degeneration.

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Warter, M. Cavichini, C. Galang, F.P. Kalaw, A. Heinke, D.G. Bartsch, L. Cheng, W.R. Freeman, Jacobs Retina Center, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Controversy exists regarding the therapeutic use of concomitant intravitreal steroids with anti-VEGF (inhibitory vascular endothelial growth factor) in choroidal neovascularization (CNV) resistant to mainstay treatment. We performed a retrospective observational clinical study in a consecutive cohort of patients' eyes with persistent CNV anatomically unresponsive to aggressive high-dose high-frequency (HDHF) monotherapy (i.e.: monthly 4 mg aflibercept). We evaluated anatomic and visual changes proceeding a simultaneous intervention in a long-cohort designed to study the therapeutic safety and efficacy of adjuvant steroids with anti-VEGF in resistant chronic Wet-Age Related Macular Degeneration (Wet-AMD).

Methods: A total of 12 eyes with unresponsive CNV despite treatment with alternating anti-VEGF agents (mean: 43.75±SD23.08) was studied. Resistance was considered persistent retinal fluid following HDHF treatment. Combination consisted in the simultaneous administration of anti-VEGF and steroids followed by 2 weeks of prophylactic topical antiglaucoma medication (Timolol 0.5%/Dorzolamide 2%). Slit-lamp, Visual Acuity (BCVA), Intraocular-pressure (IOP), and Optical Coherence Tomography (Heidelberg Spectralis HRA+Spectral Domain (Heidelberg Engineering, Heidelberg, Germany)) measurements of central retinal thickness (CRT) were recorded every 4 weeks for 4 consecutive months. Baseline predictors relating treatment efficacy were evaluated. Outcomes included changes in BCVA, IOP, and reduction in CRT.

Results: Initial analysis showed no safety data complications. Anatomic outcomes were statistically significant evincing a reduction in CRT ($p<0.0001$) compared to baseline; paired analysis showed an average CRT reduction of 50.90 µm ($p<0.05$) at 1 month, 76.5 µm ($p=0.0336$) at 2 months, and 86.33 µm ($p=0.0340$) at month 3. Association between CNV types and CRT reduction was significant (least-square means: type 1=-81.77, type 2=42.49, RAP/type 3=137.71, $p=0.022$).

Conclusions: We found combination of steroids and anti-VEGF produces clear anatomic improvement in recalcitrant CNV. Although other studies evidenced visual and anatomic changes consequent of combination, these were not in chronic monotherapy resistant eyes. In such eyes, we found overall disease improvement. Therefore, combination therapy may be useful in treating resistant Wet-AMD.

CONTROL ID: 3714025

SUBMITTER (NAME ONLY): Tejasvi Kakani

TITLE: Predicting future falls for glaucoma patients based on retrospectively vs. prospectively-collected fall and near fall data from prior years

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kakani, G. Xiao, A. Mihailovic, P.Y. Ramulu, Wilmer Eye Institute/Glaucoma, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the association between prospectively recorded and retrospectively self-reported fall data with the likelihood of subsequent falls in a cohort of glaucoma patients.

Methods: Participants recorded falls and near falls prospectively daily over a 2-year period. In addition, at the baseline visit participants were asked if they experienced a fall in the year prior to study baseline. Based on these data participants had their faller/near faller status classified for every study year. Logistic regressions were applied to assess whether self-reported falls or prospectively-evaluated falls/near falls over the prior year were associated with falls in the subsequent year. Models controlled for age, gender, race, degree of visual filed (VF) loss, comorbidities and polypharmacy. Models also included interaction between the VF severity and faller/near faller status in the prior year to examine if prediction of a fall in the subsequent year differed by the level of VF severity.

Results: 244 glaucoma patients were included in this study. Average participant age was 71 years (SD=7.6), about half were female and third were Black. Self-report of a fall in the year preceding the study baseline did not predict falls in the first study year. Those who fell in the first year of the study were 2.4 times (Odds Ratio (OR)=2.41, p=0.003) more likely to report a fall in the second year as compared to those who did not fall in the first study year. In addition, near falls in the first year of the study were associated with higher odds of falls in both the first (concurrent) study year (OR=3.49, p<0.001) and the subsequent second year (OR=3.14, p<0.001). However, individuals with more severe VF loss were not disproportionately more likely to fall in subsequent years if they experienced fall or near falls in prior years.

Conclusions: Prospectively recorded falls and near falls for glaucoma patients are predictive of falls in subsequent years, while self-reported falls based on memory do not predict falls in the subsequent years. This highlights the importance of prospective collection of fall data to accurately judge the association of visual impairment and/or fall prevention strategies with fall rates.

CONTROL ID: 3714026

SUBMITTER (NAME ONLY): Emma Youhnovska

TITLE: Immunohistochemical analysis of RPE cell viability atop drusen in enucleation and evisceration specimens

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Youhnovska, A.A. Goyeneche, E.B. Nassrallah, S. Bergeron, A.S. Dias, M.N. Burnier, MUHC – McGill University Ocular Pathology & Translational Research Laboratory, McGill University Faculty of Medicine and Health Sciences, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Drusen are lipoproteinaceous deposits found between the retinal pigmented epithelium (RPE) and Bruch's membrane. Soft drusen are amorphous, granular, large (>125) and are associated with age-related macular degeneration leading to vision loss. As drusen grow, they disrupt the RPE by pushing against the cells. The aim of this study is to evaluate RPE viability atop drusen in histopathological sections obtained from enucleated and eviscerated eyes.

Methods: A total of 158 eyes were obtained from the MUHC-McGill University Ocular Pathology and Translational Laboratory, Montreal, Canada (2013-2019); 79 were enucleated (50%) and 79 eviscerated (50%). The eyes were embedded in paraffin and histopathological sections were obtained. Initial studies were done to identify the eyes with drusen. These were stained using an immunohistochemical panel aimed at RPE identification and viability assessment. The panel includes HMB-45, MelanA (melanocyte markers) and Cytokeratin 8/18 (CK8/18) (epithelial cell marker) for RPE identification. It also includes the polyclonal cytoplasmic stain Ki-67 (Cell proliferation marker), and monoclonal intranuclear stains p53 (cell damage marker), p21 (cell cycle arrest marker), caspase-3 (apoptosis marker), and lipofuscin for viability. Histopathological analysis was done in scanned sections (Zeiss AxioScan.Z1) in eyes with drusen. RPE atop the drusen were compared to normal RPE cells surrounding it.

Results: Histopathological analysis was performed. The prevalence of drusen was comparable in enucleated (45.6%) and eviscerated (48.1%) eyes and increased with age. Of the 158 eyes, 53 (33.7%) were found to have soft drusen of which we studied 20 (10 enucleated; 10 eviscerated). The cells atop the drusen expressed positivity for CK 8/18 and HMB-45 but were negative for MelanA. Similar results were observed in the undisturbed RPE. As for viability, the intranuclear and cytoplasmic stain positivity reflected the degree of damage to the RPE above the drusen in concordance with the presence of lipofuscin.

Conclusions: The histopathological study of drusen and RPE is possible in enucleation and evisceration patient samples. Our immunohistochemical panel identified the cells overlying drusen as RPE cells. Damage to the RPE overlying drusen was quantified and qualified by intranuclear and cytoplasmic stain positivity and compared to the state of the undisturbed RPE.

CONTROL ID: 3714027

SUBMITTER (NAME ONLY): Johann Pacheco

TITLE: Asymptomatic Optic Nerve Enhancement in Myelin Oligodendrocyte Glycoprotein Associated Disease

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Pacheco, D. Tajfirouz, K. Fautsch, M.T. Bhatti, J.J. Chen, Ophthalmology, Mayo Clinic Research Minnesota, Rochester, Minnesota, UNITED STATES|A. Madhavan, Neuroradiology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|S.J. Pittock, E. Flanagan, Neurology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been reported that the rate of asymptomatic magnetic resonance imaging (MRI) optic nerve enhancement is as high as 51% in neuromyelitis optica; however, this has yet to be investigated in patients with myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD). We performed a multicenter retrospective study to determine the frequency of asymptomatic optic nerve enhancement in MOGAD patients.

Methods: This was a multicenter retrospective study of MRI's of patients with MOGAD. Study inclusion included positive serum MOG-IgG by a cell-based assay, MOGAD phenotype, and availability of post contrast orbital MRI sequences. The MRI studies were reviewed by a blinded, expert neuroradiologist. Medical records were reviewed for demographic information, details of ON attacks, and outcomes. Scans performed within 30 days of ON attack were classified as attack scans. Images obtained prior to ON attack or at time of non-ON attack were classified as inter-attack scans.

Results: 172 MRIs and 102 sequences (21 unique patients, 48% female) met study inclusion. Inter-attack MRIs represented 59% (60/102) of sequences (median 105 days post ON, range 35-1897). Of the inter-attack scans, 22% (13/60) of scans or 6 unique patients, showed optic nerve enhancement. This enhancement was located at prior sites of ON in 71% (10/13) of scans. Three patients showed enhancement without obvious clinical symptoms of ON, but two had ADEM without an eye examination at that time of the MRI, and one had a preceding MRI without enhancement, but did have a prior MRI with enhancement in that area. Long term visual outcomes were not significantly different between patients with asymptomatic enhancement and those without, with most patients in both groups improving to 20/20.

Conclusions: Asymptomatic optic nerve enhancement occurred in 22% of inter-attack MRIs, the majority in patients with evidence of prior optic neuritis and occurring at prior sites of ON attack. New asymptomatic optic nerve enhancement in areas without prior optic neuritis was rare. These findings are important for understanding the natural history of MOGAD, the interpretation of symptoms or response to treatment, and the adjudication of attacks in upcoming MOGAD clinical trials.

CONTROL ID: 3714028

SUBMITTER (NAME ONLY): Andreas Hartwig

TITLE: Special spectacle lenses for driving and their spectral effects

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hartwig, Hartwig Research Center, Heikendorf, GERMANY|A. Hartwig, Aston University, Birmingham, Birmingham, UNITED KINGDOM|

Commercial Relationships Disclosure: Andreas Hartwig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Spectacle lenses for improvement of vision during night time driving have been introduced to the market a few years ago. The main purpose of those lenses is to reduce glare. Three options to achieve a reduction of glare are currently used: spectral manipulation especially of shorter wavelengths, purpose-adapted anti reflexion coatings or a combination of the afore mentioned approaches.

To enhance the knowledge, how driving lenses achieve their purpose, the spectral irradiance was compared.

Methods: Four spectacle lenses for driving (refractive power of 0 D, refractive index 1.6) were evaluated (DriveSave, Zeiss, Germany; EnRoute PRO, Hoya, Japan; Formula Drive, Optovision, Germany and Streetlife, Essilor, France). A plano standard lens (refractive index 1.6) was measured as control. The spectral irradiance, within the wavelength range of 380 to 780 nm (step size = 5 nm), was measured using the Mavospec Base spectrometer (Gossen, Germany). The measurements were performed for three different conditions: a filament bulb, a white LED (peak at 455 nm) and a blue LED (peak at 410 nm) in a dark environment.

Results: From the spectrograms it is visible that manufacturers use different approaches to reduce glare whilst driving.

For the filament bulb condition, no significant change of the spectral irradiance was observed for the DriveSave and Streetlife lenses. The EnRoute and Formluar Drive lenses appear as edge filters and start transmittance from 420 nm onwards. The standard lens appears similar, but transmittance starts at 410 nm.

For the white LED condition, no significant change of the spectral irradiance was observed throughout all lenses, except a reduction of the blue peak by about 5 mW/m^2 for the DriveSafe, EnRoute and Formula Drive lenses.

For the blue LED condition, the blue peak was reduced by 82 mW/m^2 by the Streetlife lens. The DriveSafe and standard lenses reduce the peak by 276 mW/m^2 and 455 mW/m^2, respectively. The EnRoute and Formula Drive lenses, however, nearly eliminate the blue peak (2,24 mW/m^2 and 7,95 mW/m^2, respectively).

Conclusions: From the spectrograms of different lenses under different illumination conditions it is evident that various approaches are used to reduce glare whilst driving. As different approaches exist, it is important during patient consultations to test various lenses for driving and allow the patient to choose the lenses, which shows the best effect for each individual.

CONTROL ID: 3714030

SUBMITTER (NAME ONLY): Monica Diaz Coranguez

TITLE: Disheveled interacts with claudin-5 and contributes to norrin-induced BRB restoration.

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Diaz Coranguez, D.A. Antonetti, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Monica Diaz Coranguez: Commercial Relationship: Code N (No Commercial Relationship) | David Antonetti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previous studies reveal that norrin reverses VEGF-induced permeability in a β-catenin dependent pathway. Here, we explored the contribution of disheveled-1 (Dvl1) in norrin-induced blood-retinal barrier (BRB) restoration. We hypothesized that Dvl1 promotes tight junction (TJ) stabilization through both canonical and non-canonical signaling pathways.

Methods: BRB properties in primary bovine retinal endothelial cells (BREC) were determined by measurements of transendothelial electrical resistence (TEER) or solute flux of 70kDa RITC-dextran. The knockdown of Dvl1 using siRNAs was confirmed by qRT-PCR and Axin2 mRNA content was used as a measure of β-catenin signaling activity. Dvl1 localization at the TJ was observed by immunofluorescence confocal microscopy and the interaction between Dvl1 and claudin-5 or ZO-1, was analyzed by co-immunoprecipitation assays in BREC or in HEK293 cells co-transfected with Dvl1 mutants and claudin-5 or ZO-1.

Results: Analysis of BRB properties in BREC demonstrated that norrin was able to completely restore TEER after VEGF. The knockdown of Dvl1 using siRNAs specifically reduced basal barrier properties and ablated norrin-induced barrier restoration, despite increased b-catenin signaling in knockdown samples. Similar results were found in flux assays of a 70 kDa RITC-dextran molecule, suggesting that Dvl1 is required for norrin-induced BRB restoration. Dvl immunofluorescence staining showed co-localization of Dvl1 with ZO-1 and claudin-5 at the TJ complex. Dvl1 and TJ proteins interaction analysis by co-immunoprecipitation of endogenous protein in BREC, demonstrated that Dvl1 interacts with both claudin-5 and ZO-1 and this interaction was most abundant in the presence of VEGF/norrin co-stimulation. Studies in HEK293 cells co-transfected with Dvl1 mutants and claudin-5 or ZO-1, reveal a requirement of the Dvl1 PDZ domain for this interaction. Transfection of the C-terminal fragment of Dvl1, containing the PDZ binding motif but not the DIX, PDZ or DEP domains, blocked Dvl1/claudin-5 interaction, increased basal permeability and prevented norrin-induced BRB restoration.

Conclusions: Together, these results demonstrate that norrin signals though Dvl1 to stimulate barrier properties and suggest a non-canonical signaling role of Dvl1 in regulation of barrier properties through direct binding to claudin-5 and ZO-1.

CONTROL ID: 3714033

SUBMITTER (NAME ONLY): Uzoamaka Nwagbo

TITLE: Elovl4b Ablation in Zebrafish Leads to Loss of Ocular C30 to C34 Very-Long-Chain Polyunsaturated Fatty Acids

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Nwagbo, P.S. Bernstein, Pharmacology & Toxicology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|U. Nwagbo, P.S. Bernstein, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Uzoamaka Nwagbo: Commercial Relationship: Code N (No Commercial Relationship) | Paul Bernstein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Very-long-chain polyunsaturated fatty acids (VLC-PUFAs) are a distinct class of lipids with chain lengths greater than 24 carbons found in the retina and a few other tissues in vertebrates. ELOVL4 is a member of the ELOVL elongase family responsible for the rate-limiting step of VLC-PUFA biosynthesis. Patients with autosomal dominant Stargardt-3 disease, a juvenile form of macular degeneration, have genetic mutations in ELOVL4 leading to the formation of a non-catalytically active protein and loss of retinal VLC-PUFAs. Interestingly, low retinal VLC-PUFAs are also characteristic of age-related macular degeneration. Moreover, retinas isolated from patients with age-related macular degeneration are reported to have low omega-3 (n-3) to omega-6 (n-6) fatty acid ratios compared to healthy controls.

The retinal pathology caused by VLC-PUFA depletion has historically been difficult to study because homozygous Elovl4 mutations cause skin and neurological disorders in humans and neonatal lethality in mice. Mice with homozygous Elovl4 mutations are susceptible to catastrophic drying from losing their protective skin barrier. Thus, we created and examined a zebrafish model of Elovl4 deficiency and haploinsufficiency.

Methods: We created a deletion mutation in exon 2 of the Elovl4b gene using CRISPR-Cas9. F0 mosaic mutant zebrafish were screened and outcrossed with wild-type fish over two generations to generate a stable line. At ~4 months post-fertilization, their eyes were isolated, total fatty acids extracted, and the quantity of n-3 and n-6 VLC-PUFAs was determined through gas chromatography and mass spectrometry.

Results: We found that homozygous Elovl4b mutant zebrafish eyes had no detectable C30 to C34 VLC-PUFAs in their eyes, in contrast to age-matched wild-type controls. Heterozygous fish with one functional copy of Elovl4b had intermediate lipid profiles.

Conclusions: Our data indicate that the loss of Elovl4b in zebrafish alters ocular biochemistry in a way that is comparable to macular degeneration. We expect diminished ERG amplitudes and visual function in the homozygous and heterozygous fish and altered retinal histology. We plan to correct such abnormalities by feeding synthetic VLC-PUFAs.

CONTROL ID: 3714034

SUBMITTER (NAME ONLY): Jan Skerswetat

TITLE: Disability Glare Quantified Rapidly with AIM (Angular Indication Measurement) Glare Acuity

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Skerswetat, A. Boruta, P.J. Bex, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Jan Skerswetat: Commercial Relationship(s);Code I (Personal Financial Interest):PerZeption Inc.;Code P (Patent):Northeastern University, Boston | Anna Boruta: Commercial Relationship: Code N (No Commercial Relationship) | Peter Bex: Commercial Relationship(s);Code I (Personal Financial Interest):PerZeption Inc.;Code P (Patent):Northeastern University, Boston

ABSTRACT BODY:

Purpose: Disability glare is a consequence of straylight that causes discomfort and an objective perceptual deficit. The novel computer-based AIM Glare Acuity method was used to measure subjective and objective performance under standard and simulated straylight conditions.

Methods: AIM Acuity(Figure 1) entailed a sequence of 2 trials, each containing a 4*4 grid of 6° cells displayed on a 32” 4K monitor, using a gray background(3.4 cd/m2). Each cell contained a dark Landolt-type C surrounded by either a 0.1° thin dark(0.2 cd/m2; Baseline), 1° thick dark(Mask control), or 1° thick light(195 cd/m2; Glare) ring. Each C was randomly rotated and varied in size, spanning easy to difficult sizes. An adaptive algorithm updated the sizes in the 2nd trial based on the participant’s responses during trial 1. Participants indicated the location of each C’s gap via mouse click on the surrounding ring. The angle between the true and reported C orientation as a function of stimulus size that was fit with a cumulative gaussian function, from which ETDRS-equivalent acuity was also calculated(Figure 1). After each trial, participants indicated their subjective glare experience via continuous sliders, ranging from “No glare” to “Strong glare”. After 5 min dark adaptation, 18 normally-sighted participants(18 years median age) performed the task using their dominant eye without(control) or with a Bangerter 0.3 filter(simulated straylight condition) at 60cm distance. ANOVAs and planned comparisons determined effects between conditions.

Results: AIM Glare Acuity took 39sec(SD=17sec) to complete. Visual acuity was significantly lower with Glare rings for both control and simulated straylight conditions, but with a much stronger effect for the latter(Figure 2). No significant differences were found between Baseline and Mask dark rings for any condition. Subjective experiences of glare were significantly higher in glare than control ring conditions.

Conclusions: Visual acuity and subjective discomfort reports were significantly impaired by AIM Glare rings and the effects were amplified by stimulated straylight. Dark mask control rings did not affect acuity or discomfort, suggesting that performance was impaired by disability glare rather than contrast masking. AIM Glare Acuity may therefore be suitable to investigate disability glare in <40 sec in clinical populations, e.g. patients pre-/post- refractive or cataract surgery.

CONTROL ID: 3714036

SUBMITTER (NAME ONLY): Jana Zernant

TITLE: A common haplotype in the PRPH2 gene modifies Stargardt/ABCA4 disease.

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure: Jana Zernant: Commercial Relationship: Code N (No Commercial Relationship) | Winston Lee: Commercial Relationship: Code N (No Commercial Relationship) | Jun Wang: Commercial Relationship: Code N (No Commercial Relationship) | KERRY GOETZ: Commercial Relationship: Code N (No Commercial Relationship) | Ehsan Ullah: Commercial Relationship: Code N (No Commercial Relationship) | Takayuki Nagasaki: Commercial Relationship: Code N (No Commercial Relationship) | PEI-YIN SU: Commercial Relationship: Code N (No Commercial Relationship) | Gerald Fishman: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Tsang: Commercial Relationship: Code N (No Commercial Relationship) | Santa Tumminia: Commercial Relationship: Code N (No Commercial Relationship) | Brian Brooks: Commercial Relationship: Code N (No Commercial Relationship) | Robert Hufnagel: Commercial Relationship: Code N (No Commercial Relationship) | Rui Chen: Commercial Relationship: Code N (No Commercial Relationship) | Rando Allikmets: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: ABCA4/Stargardt disease is the most prevalent Mendelian eye disorder, with over 1,500 causal variants reported in the ABCA4 locus. The vast clinical variability, ranging from early onset fast progressing cone-rod dystrophy to late-onset macular disease, is mostly explained by extensive heterogeneity in the ABCA4 locus, including several cis-modifier alleles. While comprehensively studied, the penetrance of several causal variants and variant combinations is still not completely understood. We hypothesized that variants in unlinked loci influence the ABCA4 disease penetrance and tested if variation in the PRPH2 gene – known to most often clinically phenocopy ABCA4 disease – may play a modifying role.

Methods: We performed exome sequencing in 622 confirmed and well characterized Stargardt/ABCA4 disease patients and compared variation in the PRPH2 gene to cohorts of ethnically matched controls and between genetically determined subgroups of ABCA4 disease.

Results: The frequent haplotype in the 3' end of PRPH2, including common variants c.910G>C (p.Glu304Gln), c.929A>G (p.Lys310Arg) and c.1013G>A (p.Gly338Asp), and tagged by the p.Asp338 variant with MAF=0.21 in the general population, was significantly increased in the patient cohort, MAF 0.25, p=0.0014. Significant differences were also observed between ABCA4 disease subgroups. In the late-onset subgroup, defined by the hypomorphic p.Asn1868Ile variant, the allele frequency for the PRPH2 p.Asp338 variant was 0.16 vs 0.26 in the remaining cohort, p=0.0065. Known functional data allows suggesting a mechanism by which the PRPH2 haplotype influences the ABCA4 disease penetrance. These associations were replicated in an independent cohort of 408 patients. The association was highly statistically significant in the combined cohorts of 1030 cases, p=4.00E-05 for all patients and p=0.00014 for the hypomorph subgroup.

Conclusions: We suggest that the common haplotype in PRPH2 gene plays substantial trans-modifying role in ABCA4 disease overall, and specifically in the disease subgroup defined by the hypomorphic p.Asn1868Ile allele.

CONTROL ID: 3714037
SUBMITTER (NAME ONLY): Jordan Safran
TITLE: The application of collagen matrix to reverse hypotony following trabeculectomy with mitomycin C
SESSION TITLE: Surgery & Wound Healing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Safran, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|J. Wong, D. Lee, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|
Commercial Relationships Disclosure: Jordan Safran: Commercial Relationship: Code N (No Commercial Relationship) | Jae-Chiang Wong: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the role of collagen matrix in reversing ocular hypotony following trabeculectomy.
Methods: This retrospective cohort study included patients who required surgical revision due to hypotony following trabeculectomy from January 2019 to October 2021. Patients with at least 3 months of follow-up post-surgery were included. Demographic and clinical data were collected at the pre-operative and post-operative visits for up to 6 months. Post-operative complications were recorded at each visit.

Surgical Technique: The conjunctiva was horizontally incised approximately 8-mm posterior to the limbus. Conjunctiva and tenon were dissected anteriorly to the limbus. The collagen matrix was placed overlying the prior trabeculectomy site. The incision was closed using an 8-0 Vicryl suture in a running fashion. All surgeries were performed by a single surgeon (DL).
Results: Of the 18 patients identified, 11 eyes of 11 patients met inclusion criteria. Mean patient age was 71.3±7.5 years and mean follow-up duration was 110.8±78.6 days (range 22-247). Eight (73%) eyes had hypotony associated with an over-filtering bleb and three (27%) were associated with cystic bleb leaks. Four (36%) eyes had prior bleb revisions which included bleb needling (2) which led to over-filtration and conjunctival advancement (1) and thermocautery (1) for cystic bleb leak. 12x1mm implants were used in five (45%) eyes and 6x2mm implants were used in six (55%) eyes. Mean IOP at the pre-operative visit, and 1-day, 1-week, 1-month, 3-month, and 6-month postoperative visits were 3.3±2.1 (n=11), 6.6±4.7 (n=11), 7.8±3.2 (n=11), 8.5±4.0 (n=10), 7.6±2.5 (n=7), 11.0±6.5 (n=4) mmHg, respectively ($p<0.05$ at all time points). All three bleb leak patients were noted to be seidel negative by postoperative week 1. One patient required lamellar keratoplasty for persistent corneal edema, but no additional glaucoma surgeries or medications were indicated during the follow-up period.
Conclusions: Our initial experience with collagen matrix shows promise as an effective method of reversing hypotony while maintaining therapeutic IOP levels. Additionally, it was also effective in reversing leaks associated with thin-walled cystic blebs without the need for additional tissue manipulation. No surgical failures were recorded. Our findings are consistent with previously published literature.

CONTROL ID: 3714040

SUBMITTER (NAME ONLY): Samuel Koller

TITLE: X-linked retinitis pigmentosa caused by a non-canonical splice variant in RPGR

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Variants in RPGR are associated with severe forms of retinitis pigmentosa (RP) and usually found within the purine rich exon ORF15. Pathogenic variants can also be found in non-canonical splice sites (NCSS), but may be classified as VUS (variant of unknown significance) by ACMG (American College of Medical Genetics) guidelines. We investigated the effect of an NCCS variant 9 nucleotides in front of RPGR exon 12 on splicing by mini-gene assay and whole-blood RNA analysis.

Methods: Clinical diagnosis was established by comprehensive ophthalmic exam and multi-modal imaging of the patient and his mother.

Patient DNA was analyzed by whole exome sequencing. Segregation analysis was performed by Sanger sequencing. Effects of a potential splice variant was analyzed by cDNA derived from a mini-gene assay and a whole-blood sample from the patient and his mother.

Results: A rare NCSS variant was found in a patient with X-linked retinitis pigmentosa (RP) in front of RPGR exon 12, which was predicted to create a novel splice acceptor site 8 nucleotides upstream of exon 12.

Sanger sequencing confirmed the carrier status of the patient’s mother, who showed a tapetal-like fundus reflex as assessed by multi-modal imaging.

Analysis of cDNA form a mini gene assay, designed to study this variant, confirmed the predicted novel acceptor site. This specific acceptor site was not active in the control mini-gene construct which contained the reference sequence. The novel acceptor site was confirmed by the analysis of cDNA generated from a whole blood samples of the proband and his mother, who is a confirmed carrier of the variant.

Conclusions: Care has to be taken by the interpretation of non-canonical splice site variants by ACMG guidelines, as they could be pathogenic. Only a functional assay can classify NCSS as likely pathogenic. It has been suggested that contribution of NCSS variants is underestimated by 35%-40%.

If no blood sample for RNA extraction is available, a mini-gene experiment/approach may be a reliable and a fast assay to characterize NCSS variants in RPGR.

We have shown that NCSS variants can contribute to the diagnostic yield in (RPGR) X-linked RP. These variants should be analyzed on transcript level in order to identify a splicing effect but also for designing therapeutic approaches in the future.

CONTROL ID: 3714041

SUBMITTER (NAME ONLY): Ashley Farre

TITLE: Control of selected transcripts in LWS1 vs LWS2 cones by thyroid hormone in zebrafish

SESSION TITLE: Retinal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.A. Farre, A. Duncan, D.L. Stenkamp, University of Idaho, Moscow, Idaho, UNITED STATES|S. Hunter, University of California Davis, Davis, California, UNITED STATES|M. Starostik, L. Gieser, M. English, A. Swaroop, National Eye Institute, Bethesda, Maryland, UNITED STATES|C. SUN, Washington University in St Louis, St Louis, Missouri, UNITED STATES|A. Santhanam, E. Shihabeddin, J. O'Brien, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In humans, the long and middle wavelength-sensing cone opsins (LWS/MWS) are encoded in a tandemly replicated array. Zebrafish possess a tandemly replicated long wavelength-sensitive (lws) array; the zebrafish lws genes and human LWS and MWS genes share a common ancestor. The differential regulation of human LWS vs. MWS is viewed as a stochastic mechanism, while there is evidence for trans-regulatory mechanisms in zebrafish. Our lab demonstrated thyroid hormone (TH) promotes lws1 at the expense of lws2 (Mackin et al., 2019, PNAS). The present work aims to identify additional transcriptional differences in the LWS1 vs. LWS2 cone populations, toward elucidating the genetic mechanisms underlying the differential regulation of LWS cone opsin expression.

Methods: We isolated GFP+ (LWS1) cones and RFP+ (LWS2) cones from adult male lws:PAC(H) zebrafish using established FACS methods (Sun et al., 2018, Exp Eye Res). Bulk RNA-Seq was used to identify differentially expressed (DE) transcripts of interest in these two cone populations. A separate, single cell RNA-Seq dataset was used to complement this DE list with transcripts enriched in lws1- or lws2-expressing cones. Larval zebrafish were treated with TH, and qPCR and multiplex in situ hybridization (HCR) of DE transcripts were performed.

Results: Based on a false discovery rate (FDR)<0.05, ~130 transcripts were enriched in LWS1 cones (~1.6 % of LWS1 transcriptome), and ~93 transcripts were enriched in LWS2 cones (1.2% of LWS2 transcriptome), suggesting that these cone types are highly similar yet with a subset of distinct transcripts. Among the DE transcripts were those encoding phototransduction components [gngt2b], nuclear receptors [nr2f2], extracellular proteins [si:busm1-57f23.1], transcription factors [vax2], and regulators of circadian rhythm [cry1ba, aanat2]. qPCR and HCR data show some transcripts are DE in control vs TH-treated larvae, including gngt2b (qPCR: $p<0.05$, $n=6$). For some transcripts such as si-busm1, HCR was able to detect expression domain changes in the eye upon TH treatment.

Conclusions: This study identified several transcripts that were DE in LWS1 vs. LWS2 cones, which have been presumed identical aside from opsin expression. Some of those DE transcripts are regulated by TH. This dataset provides foundations to investigate the mechanism by which lws1 and lws2 are differentially regulated, including candidates for functional testing.

CONTROL ID: 3714042

SUBMITTER (NAME ONLY): Kimberly Edwards

TITLE: Robust generation of retinal organoids from porcine induced pluripotent stem cells.

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.L. Edwards, Department of Cellular and Molecular Pathology, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|K.L. Edwards, D.M. Gamm, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|L. Chu, Department of Comparative Biology and Experimental Medicine, University of Calgary, Calgary, Alberta, CANADA|D.M. Gamm, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|Y.C. Martin, Waisman Center, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|J.A. Thomson, Morgridge Insitute for Research, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tremendous advances have been made in human pluripotent stem cell (PSC)-derived retinal cell transplantation in mammalian model species, but evolutionary divergence in synaptic proteins may limit what can be learned from xenogeneic transplants. Allografts with species-specific PSC-derived retinal cells from pigs, a popular large animal pre-clinical model, can provide valuable anatomic, functional, and safety data for future cell replacement trials. We optimized the timeline of our established human retinal organoid (RO) differentiation protocol to align with porcine development and generated a retinal differentiation protocol that produces an abundance of porcine induced pluripotent stem cell (piPSC)-derived ROs containing a high percentage of photoreceptors.

Methods: To generate piPSC-ROs, we shortened the timing of our human PSC-RO protocol (Capowski et al., Development 2019) to better align with pig gestation. Embryoid bodies (EBs) were weaned into Neural Induction Media (NIM) over 24 hours for pig cultures vs. 4 days for human cultures, then treated with NIM + BMP4 for retinal specification and plating on Matrigel on d2 for pig vs. d6-7 for human. Pig cultures were switched to Retinal Differentiation Medium (RDM) with daily feeding on d5 (vs. d16 for human) until manual lifting of 3D ROs on d11-13 (vs. d25-30 for human). ROs were maintained with twice-weekly feeding of 3D-RDM. Differentiation of ROs was assessed by brightfield microscopy for morphology and structural organization and immunocytochemistry (ICC) for cell type-specific protein expression and localization.

Results: Light microscopic images demonstrated the phase-bright outer rim characteristic of ROs. ICC of piPSC-ROs revealed highly organized outer laminae with an abundant photoreceptor population evidenced by RECOVERIN+ and CRX+ cells, including both rods (NRL+ and RHODOPSIN+) and cones (RP-1+). As expected, piPSC-ROs contained additional retinal cell types such as CRALBP+ muller glia and G0alpha+ bipolar cells.

Conclusions: We present a robust and reproducible protocol for generating retinal organoids from pig iPSCs in a manner that parallels production of human PSC-derived ROs and photoreceptors. We anticipate that piPSC-ROs will provide a highly useful, conspecific donor cell source for assessing the potential for synaptic connectivity and functional responses to photoreceptor transplantation in pig preclinical models.

CONTROL ID: 3714045

SUBMITTER (NAME ONLY): Changrim Lee

TITLE: Conjunctival Goblet Cells Stimulated with an Allergic Mediator Secrete Extracellular Vesicles that Exhibit Autocrine Secretagogue Activity

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lee, D.A. Dartt, Schepens Eye Research Institute, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|C. Lee, D.A. Dartt, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Goblet cell functions especially secretion of mucins are relatively well studied owing to their protective role on the ocular surface; however, little attention is given to the other secretory products, such as extracellular vesicles (EVs). The purpose of this study is to examine the function of goblet cell secreted EVs, especially their secretagogue activity, and test whether EVs produced by vehicle (health) or inflammatory stimuli (disease) will cause distinct actions on recipient goblet cells.

Methods: Serum starved primary human conjunctival goblet cells (HCGCs) grown from conjunctiva explants were incubated for 4 h either with the allergic mediator histamine (His, 10^{-5} M) to induce inflammation or HBSS (non-treated control) to indicate normal cells. EVs isolated from collected media using Total Exosome Isolation Reagent (Invitrogen) were denoted as EVs-His and EVs-NT, respectively. To examine secretagogue activity, first passage cells (trypsinized and passaged primary cells) were treated with EVs diluted to 1, 10, 100, 1000 ng/mL) for 4 h in HBSS. The amount of secreted high molecular weight proteins (HMWP) in the cell culture supernatants was measured using an enzyme-linked lectin assay (ELLA).

Results: HCGCs stimulated with His secreted 4-fold higher amount of total EV proteins into the media compared to that of the untreated cells, which confirmed that the primary cells are effectively stimulated with His. For secretagogue activity of EVs, addition of 10 ng/mL EVs-His to HCGCs induced secretion of HMWP by 4.8-fold. The same concentration of EVs-NT caused a 1.6-fold increase. For both EV-His and EV-NT, an increase of 1.0~1.9-fold was observed at the other four concentrations; however, all lower than the activity seen at 10 ng/mL. Fold-change of secretion in His treated (positive cntl) and untreated cells (negative cntl) was 2.2 and 1.0, respectively.

Conclusions: We conclude that HCGCs EVs have differential secretagogue activity when stimulated with inflammatory mediator compared to under control (healthy). EVs have an indispensable role in regulating goblet cell secretion at the extracellular level, which warrants in-depth investigation into their molecular properties and mechanism of action.

CONTROL ID: 3714047

SUBMITTER (NAME ONLY): Diana Do

TITLE: Development of a New Patient-Reported Outcome Instrument to Assess Diabetic Retinopathy Treatment Experiences

SESSION TITLE: Epidemiology of Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.V. Do, Byers Eye Institute, Palo Alto, California, UNITED STATES|A. Levine, P. Marquis, Modus Outcomes LLP, Cambridge, Massachusetts, UNITED STATES|S. Sherman, C. Hartford, R. Rao, D. Rofail, Regeneron Pharmaceuticals Inc., Tarrytown, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a de novo patient-reported outcome (PRO) questionnaire for assessing the impact of treatment with anti-vascular endothelial growth factors (VEGFs) versus panretinal photocoagulation (PRP) on patients' experience of living with proliferative diabetic retinopathy (PDR).

Methods: A review of literature and online resources was conducted to develop a conceptual model of the PDR patient experience and to identify existing PROs used in PDR and other ophthalmic conditions. Concept-to-item mapping of the identified PROs was conducted to identify items relevant to the patient disease and treatment experiences. This formed the initial PRO instrument, which was further refined using insights gained from adult patients treated with aflibercept and/or PRP. Two rounds of in-depth, semi-structured interviews were conducted to elicit patients' feedback on living with PDR and treatment experiences and to assess their ability to interpret the PRO content and its relevance to their experience.

Results: Forty patients treated with aflibercept (n=23) and/or PRP (n=34) for PDR were interviewed during Round 1 and of these, 30 were later interviewed in Round 2. An initial list of 72 items with conceptual coverage across symptoms and impact domains was drafted based from existing instruments relevant for PDR. Patients' feedback led to refinement of instructions, items, and response options to improve clarity and comprehension, remove overlap, and increase relevance. A new scale was added to enable assessment of concepts proximal to experience of PRP or anti-VEGF treatment. The revised PRO measure and preliminary conceptual framework includes 85 items across four scales: Daily activities (54), Emotional impact (5), Vision problems (15), and Treatment experience (11).

Conclusions: A robust and comprehensive PRO instrument was developed to evaluate the effects experienced by patients who are treated for their PDR. A validation study in a larger sample is warranted to confirm scoring, item reduction opportunities, and psychometric properties.

CONTROL ID: 3714048

SUBMITTER (NAME ONLY): Gary Mikaelian

TITLE: Quality of vision improvements with decentered multifocal optics in scleral contact lenses

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Mikaelian, R&D, NIDEK Inc, San Jose, California, UNITED STATES|P. Caroline, College of Optometry, Pacific University College of Health Professions, Forest Grove, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Decentered contact lens optics can potentially reduce the quality of vision by introduction of unwanted low and higher order aberrations. It is well known that scleral lenses commonly decenter inferiorly and temporarily. Yet, many of the commercially available scleral lenses center the optics at the geometrical center of the lens, which is rarely aligned with the visual axis. A number of scleral lens designs now allow for the offset in the optic zone alignment. In most cases this feature can be used to align the lens optics with respect to the visual axis. However, in some patients with small pupils and large angle kappa (the distance between the visual axis and pupillary axis), the effect of the multifocal design may be diminished due to the misalignment between the pupil and the “add zone” on the lens. The purpose of this study is to evaluate the use of a conventional optometric instrumentation, which provides angle alpha and angle kappa measurement in order to predict which patients may benefit from a decentered multifocal lens design and provide the eyecare practitioner with the tools to quantitatively define the amount of decentration needed for a specific patient.

Methods: Both eyes of three normal eye subjects were measured with the NIDEK OPD Scan III. The subjects LDist and RMS were recorded. Both eyes were fitted with standard scleral lenses and OPD Scan III measurement was performed over the scleral lens. The LDist determines the amount and location of the decentered optics. A custom scleral lens (with displaced optics) was ordered. The custom scleral lenses were placed on the subjects’ eyes and allowed to equilibrate for 30 minutes. OPD Scan III measurement was performed over the lenses and the LDist and RMS was recorded.

Results: Preliminary results demonstrate that the RMS values of the wavefront and quality of vision are both dependent on the optics alignment with respect to the visual axis.

Conclusions: Multifocal scleral contact lenses are a promising modality for presbyopia management. There is a clear need in being able to address the reduction in the quality of vision due to the lens decentration on the eye. This study provides insights on how optometric instrumentation may be used to determine which patients may benefit from multifocal scleral lenses with off-centered optics and provide a pathway for automating the decision of the amount of decentration for a particular patient.

CONTROL ID: 3714049

SUBMITTER (NAME ONLY): Rohan Gupta

TITLE: Automatic retinal layer segmentation in OCT images of a laser induced porcine model for retinal injury

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gupta, F. BARONE, A. Maminishkis, J. Amaral, I. Bunea, K. Creel, M. Farnoodian, K. Bharti, Ocular and Stem Cell Translational Research Section, National Eye Institute, Bethesda, Maryland, UNITED STATES|S. Heaps, B. Alvisio, OSIO Bioinformatics Core, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) provides useful assessment of retinal health, but OCT image analysis is often qualitative. Machine learning segmentation methods have been shown to be effective in quantifying changes seen in OCT images. However, there are no automatic segmentation tools for preclinical porcine models. We propose a novel computational pipeline using supervised deep learning methods to automatically segment porcine retinal layers in OCT B-scans in a laser-induced model for retinal injury.

Methods: B-scans were acquired in Yucatan pigs using the Spectralis (Heidelberg, Germany) spectral domain OCT and were exported with a corresponding infrared reflectance fundus image that specifies the scan location. B-scans and fundus images were manually segmented by an experienced observer using LabelMe, a Python based annotation tool (Wada, 2018). The healthy and laser-treated datasets consist of 12 B-scans (6 eyes, 3 pigs) and 12 B-scans (7 eyes, 4 pigs), respectively.

Our proposed pipeline is primarily composed of three U-Net semantic convolutional neural networks. The first U-Net was trained to segment 7 retinal layers under healthy conditions. Due to the destructive effects of the laser in the retinal outer segments, a separate set of models (trained with a laser-treated dataset) is required to accurately segment damaged regions. To automatically identify regions of laser ablation within the OCT, a second U-Net is tasked to perform binary segmentation on the fundus image. Image processing techniques utilize relationships between the two image types, outputting predicted boundaries of lasered regions on B-scans. Using this B-scan input, a third U-Net is trained to segment damaged retinal layers.

Results: Model outputs were compared to manual segmentation and were evaluated using mean dice coefficient (MDC), a measure of similarity between two samples. The first U-Net displayed an average MDC of 0.916 (SD=0.062) and the second U-Net presented an MDC of 0.995. Subsequent computations predict boundaries of the laser ablated regions with a mean absolute pixel error of 7.50 (SD=7.33).

Conclusions: Initial results suggest potential of this framework to be used as an effective evaluative tool for researchers using porcine models for retinal degeneration. Future work includes retraining models with larger datasets and developing algorithms for layer quantification by varied metrics.

CONTROL ID: 3714051

SUBMITTER (NAME ONLY): Pia Klobučar

TITLE: The Use of Virtual Reality Glasses with Biometry to Study Eye Movements and Visual Function in Patients with Retinitis Pigmentosa

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Klobučar, N. Vidović Valentinčič, A. Fakin, Univerzitetni klinicny Center Ljubljana, Ljubljana, SLOVENIA|

Commercial Relationships Disclosure: Pia Klobučar: Commercial Relationship: Code N (No Commercial Relationship) | Nataša Vidović Valentinčič: Commercial Relationship: Code N (No Commercial Relationship) | Ana Fakin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the characteristics of saccadic eye movements of patients with retinitis pigmentosa (RP) and to what extent they help improve peripheral visual stimuli detection.

Methods: Study included 6 patients with RP (median age 40, 19-56; 3 male) and 8 healthy controls (median age 37, 28-55; 1 male). The median of best-corrected visual acuity (BCVA) on the better eye was 0.8 (0.5-1.0) in patients with RP and 1.0 in controls. Patients with RP had a concentrically narrowed visual field between 10-35° radius measured by II/4 isopter on Goldmann perimetry. Participants underwent visual field examination (IC test) using the HP Omnicept Reverb G2 virtual reality headset with eye-tracking sensors. The test consisted of 24 static and 23 moving targets (size Goldmann V, duration 1.5 s), presented in a repeatable random sequence at 10°, 20°, and 30° distances from the central fixation point. Each participant performed the test twice, first (IC-fixed) with central fixation, and second (IC-mobile) with free eye movements. The number of saccades, average speed, amplitude number, and the average duration were determined using the accompanying IC software (Fusion) and compared between patients with RP and healthy participants. Macro-saccades were defined as the eye movements reaching at least 50°/s with the amplitude at least 1.2°.

Results: All healthy participants detected 100% of stimuli on IC-fixed and median 100% (94-100%) on IC-mobile, while RP patients detected median 30% (0-98%) stimuli on IC-fixed and 84% (11-100%) on IC-mobile ($p=0.18$). On the IC-mobile test, the RP patients had a significantly higher number of macro-saccades than controls (median 547 vs 250; $p<0.01$), which were also significantly faster (median speed 1187 °/s vs 951 °/s, $p< 0.05$), and of larger amplitude (median 9.9° vs 7.9°, $p<0.05$); whereas their duration did not differ significantly (73 ms vs 58 ms, $p=0.11$).

Conclusions: Patients with RP increased the likelihood of peripheral stimuli detection with saccadic eye movements. Interestingly, while the number, speed, and amplitude of their macro-saccades during scanning were higher than in controls, the duration of saccades was relatively similar. VR with biometry is a novel modality that can be used to measure visual function and adaptive mechanisms in patients with visual loss.

CONTROL ID: 3714052

SUBMITTER (NAME ONLY): Stephanie Hartouni

TITLE: Identification of pericyte biomarkers in aqueous and vitreous humor reflecting diabetic retinopathy severity

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hartouni, I. Tom, M. Chang, Genentech Inc, South San Francisco, California, UNITED STATES|D. Yang, R. Lamy, J. Wu, J.M. Stewart, University of California San Francisco, San Francisco, California, UNITED STATES|D. Yang, R. Lamy, J. Wu, J.M. Stewart, Department of Ophthalmology, Zuckerberg San Francisco General Hospital and Trauma Center, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pericyte dropout is an early pathologic hallmark of diabetic retinopathy (DR) and may contribute to vascular instability and disease progression. Aqueous humor (AH) and vitreous humor (VH) biomarkers reflecting pericyte status within the retina may therefore be prognostic for progression to more severe, vision-threatening forms of DR, including proliferative DR (PDR) and diabetic macular edema (DME) and may help guide treatment decisions. In this study, putative pericyte-selective markers were evaluated in AH, VH, and plasma for their ability to reflect DR severity.

Methods: AH, VH, and plasma specimens (n=181) were collected during ocular surgery or injection procedures from the study population (n=98) spanning nondiabetic, diabetes mellitus without DR (DM), non-proliferative DR without DME (NPDR), PDR without DME, and DME patients. 24 patients from the total study population had matched VH, AH and plasma. Concentrations of Regulator of G-protein signaling 5 (RGS5), Pigment epithelium-derived factor (PEDF), and Pyruvate dehydrogenase kinase isozyme 4 (PDK4) were measured in samples via enzyme-linked immunosorbent assay. Kruskal-Wallis ANOVA test was used to compare biomarker levels across cohorts, Dunn's multiple comparison test was used for pairwise comparison to DM population, and a Spearman correlation evaluated the relationship between matrices.

Results: In VH, RGS5 was significantly increased in PDR and DME cohorts relative to DM (p=0.0019, p=0.0253 respectively), PEDF was significantly increased in PDR and DME cohorts (p=0.0004, p=0.0157 respectively), and PDK4 was significantly increased in the PDR cohort (p=0.0271). RGS5, PEDF, and PDK4 demonstrated significant correlation between matched AH and VH samples (r=0.8798 p=<0.0001, r=0.6650 p=0.0005, and r=0.5774 p=0.002 respectively). AH had similar significant elevations in advanced disease cohorts over DM for RGS5 and PDK4. None of the markers showed statistically significant elevations over the DM population in plasma across the DR cohorts.

Conclusions: These preliminary results demonstrate that multiple pericyte-selective biomarkers change with disease severity in diabetic retinopathy. This change with disease progression supports further investigation into their utility as prognostic biomarkers.

CONTROL ID: 3714053

SUBMITTER (NAME ONLY): Abhishek Vats

TITLE: Pharmacological chaperones improve rhodopsin homeostasis and protects photoreceptors in the RHO P23H mouse model of retinitis pigmentosa

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mutations in RHODOPSIN (RHO) accounts for ~25-30% of autosomal dominant retinitis pigmentosa (adRP). No pharmacological treatments are available for RP. Many RHO mutants are structurally unstable and trigger dominant negative effects including disrupted proteostasis and rod cell death, which cause vision loss. We hypothesize that small molecule chaperones can stabilize the native folding and homeostasis RHO, which in turn will rescue rods in RHO-associated adRP. We previously discovered non-retinoid chaperones of RHO (such as YC-001). The purpose of this study is to test this hypothesis using in vitro, ex vivo and in vivo models and to develop new drug candidates for RP treatment.

Methods: We used high content imaging to profile the chaperone activities of two non-retinal chaperones towards 27 RP-causing human RHO mutants by quantifying cell-surface level of these RHO mutants in NIH3T3 cells. AutodockVina was used for docking calculation of chaperones. Two chaperone molecules were treated to the $Rho^{P23H/+}$ knock-in mouse retinal explants to evaluate their chaperon activities to RHO. Intravitreal injections of two compounds were performed to $Rho^{P23H/+}$ knock-in mice and efficacies were evaluated by OCT, ERG, and retinal histology.

Results: The in vitro high-content imaging assay showed that YC-001 and the other chaperone molecule rescued the transport of 9 and 11 mutants, respectively, in NIH3T3 cells. Docking calculations indicate that YC-001 binds in the β-ionone ring pocket with ΔG=-7.9 kCal/mol while the other chaperone molecule fills in a larger space of chromophore pocket with ΔG=-5.5 kCal/mol. Further, YC-001 treatment led to improved RHO homeostasis in the $Rho^{P23H/+}$ retinal explants. Interestingly, YC-001 also reduces the number of residential macrophages (microglia) in the retinal explants. Finally, single, or double intravitreal injections of chaperones microparticles increased photoreceptor function and ONL thickness in $Rho^{P23H/+}$ mice.

Conclusions: We showed that the YC-001 and the other non retinal chaperones increased RHO transport, improved RHO homeostasis and protected photoreceptors in $Rho^{P23H/+}$ adRP mouse model. Collectively, here we provide a strong proof-of-principle that non-retinoid chaperones are promising drug candidates in treating RHO-associated RP.

CONTROL ID: 3714054

SUBMITTER (NAME ONLY): Shanmukh Reddy Manne

TITLE: Automatic identification and quantification of retinal cysts in optical coherence tomography images using deep residual encoder-decoder architecture.

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal cysts or fluid spaces accumulated between different layers of eye are key signatures of diseases like age-related macular degeneration (AMD) and macular edema (ME). Accordingly, for accurate screening and disease management, clinicians seek to quantify these lesions using ubiquitous optical coherence tomography (OCT) scans. However, manual delineation is tedious and may induce errors. In response, attempts were made towards automated quantification based on imag processing and machine learning approaches. However, the detection accuracy is still sub-optimal and has scope for improvement. Against this backdrop, we attempt to build a robust fluid segmentation tool leveraging a pre-trained encoder-decoder architecture with residual network (ResNet) at the encoder that was proven to be effective in other segmentation tasks by preserving features across layers.

Methods: This is a retrospective study consisting of 3175 OCT scans (1048 with fluid/cysts and 2127 without any lesions) taken from wide-field swept-source optical coherence tomography (OCT) device (Carl Zeiss Plex Elite 9000) with a resolution of 12mm×3mm. The presence of fluid was detected based on our previously validated XGBoost algorithm. We employed ResUNet deep-learning architecture which uses residual network at the encoder (see Fig. 1). Masks required to train the model were obtained by manually labeling fluid regions by a trained expert using the ImageJ tool. Dataset is randomly partitioned into training and testing (unseen) sets with a split-ratio of 90:10. Finally, the OCT scans were resized to (256, 256) and the model was trained using Dice coefficient as loss function (epochs: 80, batch size: 16).

Results: The proposed method achieves an averaged Dice score of 91.47% against ground truth segmentations and outperforms the existing UNet based approaches as well. Fig. 2 depicts representative test OCT images with both manual as well as algorithmic segmentation and also provides volumetric quantification of cysts in 3D volume for a subject.

Conclusions: The proposed approach achieves segmentation accuracy close to trained optometrists. Next, we are working towards extending this to identify different types of fluids and also perform voxel-level segmentation that enables volumetric quantification of retinal cysts.

CONTROL ID: 3714055

SUBMITTER (NAME ONLY): Yang Liu

TITLE: Transcriptome profiling of mechanically stretched mouse optic nerve head astrocytes

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, North Texas Eye Research Institute, Pharmacology & Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|H. Wu, North Texas Eye Research Institute, Pharmaceutical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|Z. Zhou, Biostatistics & Epidemiology, School of Public Health, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Astrocytes are the major glia cell type within the optic nerve head (ONH). During glaucoma pathogenesis, elevated intraocular pressure (IOP) deforms the ONH and activates astrocytes relevant to their mechanosensing mechanisms. In this study, we performed RNA sequencing (RNA-seq) to investigate the mechanisms underlying astrocyte activation.

Methods: Primary mouse ONH astrocytes were derived from C57BL/6J mice and subjected to mechanical stretch of 12% strain for 24 hours using a FlexCell Tension System. Total RNA was extracted from astrocytes and RNA-seq libraries were prepared and sequenced on an Illumina Miseq2000. RNA-seq analysis was performed to identify significant differentially expressed genes, which were further investigated in pathway enrichment analysis. The Egl1 mouse strain was obtained from the Jackson Laboratory and intraocular pressure (IOP) was measured non-invasively using the TonoLab tonometer. Immunofluorescent staining was performed to validate the gene of interest in the ONH of glaucomatous mice.

Results: RNA-seq identified 2197 significantly up-regulated and 2092 significantly down-regulated genes (FDR<0.05) in mechanically stretched ONH astrocytes. Based on gene ontology enrichment results, identified genes are associated with a variety of cellular components (pigment granule, preribosome, et al.), biological processes (ATP hydrolysis coupled cation transmembrane transport, protein folding, et al.) and molecular functions (structural constituent of cytoskeleton, tRNA binding, et al.). Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis show that differentially regulated genes are involved in phagosome, carbon metabolism, and Aminoacyl-tRNA biosynthesis, et al. There was an increased expression of Iba1 in the ONH of glaucomatous mice.

Conclusions: Mechanical stretch regulates the expression levels of genes that may be responsible for ONH astrocyte activation during the pathogenesis of glaucoma. This study provides new insights into mechanisms of astrocyte activation induced by mechanical stimulation. These new insights will lead to novel therapeutic targets for glaucoma.

CONTROL ID: 3714057

SUBMITTER (NAME ONLY): Stephanie Duret

TITLE: Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) Measures in MERTK-Related Retinal Degenerations

SESSION TITLE: Advanced Imaging of Retinal Structure and Function in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Duret, J. Wong, J.L. Duncan, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|H. Zhou, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|A. Roorda, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the MERTK gene cause autosomal recessive rod-cone degeneration that results in impaired outer segment phagocytosis followed by photoreceptor death. We measured the area of cone coverage and cone density in patients with MERTK-related rod-cone degeneration using adaptive optics scanning laser ophthalmoscopy (AOSLO), a non-invasive method to visualize cones with high resolution.

Methods: Seven eyes of four patients with MERTK-related rod-cone degeneration were studied with visual acuity, optical coherence tomography (OCT), fundus autofluorescence (FAF), OCT angiography (OCTA) and AOSLO. AOSLO images were obtained from six eyes with stable fixation. Twelve-month follow up images were taken in four eyes of two patients and density was calculated at one region in each eye at baseline and at month twelve. The area of cone coverage was measured by tracing the visible and contiguous cones in and around the fovea using ImageJ. Cone density was measured in one region near the fovea by a single grader. AOSLO cone spacing was converted to Z-scores, or standard deviations from the normal mean. We analyzed choriocapillaris flow deficit percent (CC FD%) from 6x6mm OCTA scans in the better eye of each patient. CC FD% was the ratio of area with FD, defined as greater than one standard deviation below mean values from a normal database. Average CC FD% was compared between subjects and controls.

Results: Visual acuity ranged from 0.5 to bare hand motion. At twelve months, the area with visible and contiguous cone mosaics decreased from 3.7 deg^2 ± 1.9 to 1.0 deg^2 ± 0.52 (mean ± std dev). Mean cone density near the fovea decreased from 1391.7 cones/deg^2 to 922.2 cones/deg^2 and spacing increased from 1.7 arcmin to 2.1 arcmin. Cone spacing Z-scores were abnormal (23.2 ± 9.7). For three of four patients, the CC FD% was within normal limits (9.9 ± 3.8). The patient with the most advanced disease showed abnormally increased mean CC FD % (21.7 ± 12.9).

Conclusions: Cones persist at the fovea but the area with contiguous cones decreases over time in MERTK-related rod-cone degeneration. Cone density is reduced below normal and decreases over time. Choriocapillaris flow is preserved even in regions with increased cone spacing until advanced stages of rod-cone degeneration. AOSLO and OCTA may provide sensitive measures of disease progression over one year in patients with MERTK-related rod-cone degeneration.

CONTROL ID: 3714059

SUBMITTER (NAME ONLY): Ethan Osias

TITLE: Changes in Buccal Fat Pad Volume in Thyroid-Eye Disease: An Imaging Study

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Osias, M. Cale, P. saffari, S. Diniz, D. Rootman, Orbital and Ophthalmic Plastic Surgery, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thyroid Eye Disease (TED) is currently considered primarily a disease of the orbit; however, there is a growing body of evidence to suggest that periorbital facial tissue, such as the buccal fat pad (BFP) can also be affected. In some cases, surgeons remove buccal fat during orbital decompression in order to improve cosmesis. We performed this retrospective cohort study in order to determine whether TED is associated with changes in BFP volume.

Methods: Computed Topography (CT) scans and charts of adult patients with and without TED were collected from a database of patients who were seen at Stein Eye Institute. Inclusion criteria for the TED group included presence of TED and availability of adequate scans. The control group consisted of patients presenting for non-thyroid related reasons, who had CT scans done for other orbital pathologies. Exclusion criteria included history of orbitofacial trauma or facial surgery, poor quality scans, scans with a slice interval greater than 2mm, or scans without clear buccal fat pad limits. The collected patients were compiled in a spreadsheet in random order, and three independent, blinded observers then measured buccal fat pad volume, proptosis, and maximal skull width using Horos, a free, open-source medical image viewing software. The primary outcome was buccal fat pad volume, measured in cubic centimeters.

Results: A total of 69 scans were included in our study, 29 TED patients and 40 controls. Our analysis consisted of an analysis of covariance that included TED diagnosis, age, and proptosis as covariates. The difference in BFP volume between TED patients and controls was 0.317cc (p-value = 0.374). In our study, TED was not associated with a statistically significant change in BFP when controlling for relevant patient factors like age and proptosis.

Conclusions: We found that TED did not significantly impact BFP volume. These findings suggest that there may not be a compelling reason to extract buccal fat from these patients during orbital decompression surgery. However further analysis is needed to assess the impact of other factors such as sex and presence of comorbidities on the buccal fat pat volume in TED.

CONTROL ID: 3714060

SUBMITTER (NAME ONLY): Breanne Christie

TITLE: Evaluating the influence of stimulation parameters on phosphene detectability for epiretinal prostheses

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Traditional, non-adaptive methods for estimating detection threshold of electrically-evoked phosphenes have not permitted a systematic characterization of stimulation parameters. Instead, the Bayesian adaptive method can accurately estimate thresholds with fewer trials, making it ideal for studies with human subjects. In this study, we implemented the Bayesian method to gain a better understanding of how stimulation parameters influence the thresholds of phosphenes evoked by epiretinal electrodes. Our results will be used to develop advanced stimulation paradigms that increase resolution and minimize perceptual adaptation of visual feedback provided by epiretinal prostheses.

Methods: Three people with Argus II devices participated in this study. 12 electrodes for subject S1 and 6 electrodes for S2 and S3 were selected. Each electrode's threshold was estimated using a Bayesian adaptive method in a yes/no experiment, in which subjects reported if they observed a phosphene after hearing an auditory cue. Using the collected responses, the next stimuli were presented at the amplitude level that maximized the entropy for the threshold and the slope of the Weibull psychometric function. The process continued until the thresholds of all selected electrodes stabilized (the differences between 3 consecutive estimations were smaller than 3 μA) or exceeded 30 trials. Thresholds were estimated for pulse train frequencies of 6, 20, and 60 Hz, each tested with 2 and 4 pulses within a train. We also estimated the thresholds of pulse trains with a fixed train duration of 250 ms at 6, 20, and 60 Hz.

Results: A paired Wilcoxon sum rank test for all pairs of estimated thresholds with different pulse parameters within-subjects showed no significant differences ($p>0.05$) for two out of three subjects. For S2, the estimated threshold at 60 Hz was unexpectedly greater than the threshold at 20 Hz with 250 ms pulse trains ($p=0.02$), with root mean square differences of 128 μA.

Conclusions: We investigated the effect of pulse train duration and frequency on estimated detection thresholds using Argus II electrodes. We interpret the results as showing effects of sensory adaptation at high frequencies, causing the thresholds to not decrease as expected. We, therefore, conclude that higher pulse frequencies do not necessarily enable a broader dynamic range of stimulation parameters for Argus II users.

CONTROL ID: 3714061

SUBMITTER (NAME ONLY): Devika Bose

TITLE: DEVELOPMENT OF AN RPE-SPECIFIC IN VITRO STARGARDT DISEASE MODEL

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Bose, M. Farnoodian, K. Bharti, Opthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) is a polarized tissue that has important functions like supporting photoreceptors of the eye, transporting nutrients and secreting growth factors and cytokines. Our lab studied the surface proteome of RPE by cell surface capturing technology which revealed the presence of ABCA4 on the surface of RPE. We focused on the role of the ABCA4 protein as mutations in ABCA4 gene have been associated with various retinal degenerative diseases including the Stargardt disease. To specifically understand the function of ABCA4 protein in RPE, we developed an in-vitro Stargardt disease model using ABCA4$^{-/-}$ induced pluripotent stem cells (iPSC)-derived RPE and Stargardt patient iRPE.

Methods: We used CRISPR/Cas9 technology to generate iPSCs with a knockout of the ABCA4 gene targeting exon 1 of the ABCA4 gene. Resultant targeted clones were screened and two independent clones (C1 and C2) that resulted in out-of-frame deletions on both alleles were selected. For the Stargardt patient, fibroblasts were isolated from skin biopsy which were reprogrammed to form iPSCs. ABCA4$^{-/-}$ iPSCs and Stargardt patient iPSCs were differentiated to form Stargardt iRPE. ABCA4 knockout was confirmed by qRT-PCR, dd PCR, immunostaining and Sanger sequencing. Cells were evaluated for RPE-specific morphology by Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) and functions such as electrophysiological response.

Results: Stargardt iRPE and the corresponding isogenic control iPSCs displayed normal karyotype and expressed similar levels of developmental and mature RPE markers. Immunostaining of iRPE monolayers for maturity markers RPE65 and EZRIN further confirmed qRT-PCR observation. TEM of iRPE monolayers showed normal polarized RPE features like abundant apical processes and tight junctions between neighboring cells in Stargardt iRPE. SEM also suggested the formation of normal and fully confluent apical processes in Stargardt iRPE compared to isogenic Control iRPE. In addition, Stargardt-iRPE showed similar electrophysiological response compared to the Control iRPE.

Conclusions: We generated an in vitro Stargardt disease model using ABCA4$^{-/-}$ and Stargardt patient iRPE. We found that the genetic profile, cell morphology and structural features of patient and ABCA4$^{-/-}$ iRPE behaved like Control iRPE suggesting there are no developmental defects in RPE due to ABCA4 loss of function.

CONTROL ID: 3714063

SUBMITTER (NAME ONLY): Iona Raymond

TITLE: A multi kinase inhibitor (MKI) biodegradable intravitreal implant is well tolerated and inhibits retinal vascular leakage in the DL-AAA rabbit model for up to 12 months

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.D. Raymond, J. Yang, C. Vangyi, C. Maheshwari, S. Das, C. Panwala, G. Szekely, T. Navratil, Research and Development, Glaukos Corp, Laguna Hills, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: MKIs have been shown to inhibit vascular leakage clinically in the treatment of wAMD, RVO and DME. The approved anti-VEGFs are effective; however, their short duration a creates burden on the practice and patient. Our goal is to develop a long-acting intravitreal biodegradable implant that would be effective in managing the disease for ~6-12 months. We investigated the tolerability and efficacy of MKI biodegradable intravitreal implant, to inhibit retinal vascular leakage in the DL-AAA Dutch-Belted rabbit model.

Methods: Several biodegradable implant formulations were developed and tested in-vitro for drug release kinetics. The lead formulation was selected based on in-vitro release data to be tested in the rabbit model. DL-AAA rabbits were induced 8 weeks prior to study start. Seven DL-AAA female rabbits received 1 GLC-009 implant OD and 1 placebo implant OS, and 3 received 2 GLC-009 implants OU. Eyes were monitored using fluorescein angiography (FA), aide Angle (55°) IR imaging, and slit lamp ophthalmic exams including McDonald-Shadduck scoring at Days 1, 8 and monthly thereafter for 12 months. To assess tolerability, 3 naïve female Dutch Belted rabbits received 1 GLC-009 implant OD and sham injection OS, and 3 rabbits received 2 GLC-009 implants OD and 2 placebo implants OS. Plasma was collected to monitor systemic drug exposure.

Results: Administration of 1 and 2 GLC-009 implants showed significant inhibition of retinal vascular leakage compared to placebo on FAs beginning at Day 8 and continuing for 12 months. Both 1 and 2 GLC-009 implants provided maximal inhibition of vascular leakage. Observations consistent with intravitreal injections were observed and fully resolved. Systemic exposure was minimal, with values near or below the lower limit of quantitation. Initial signs of implant biodegradation were observed beginning on Day 210.

Conclusions: An MKI biodegradable intravitreal implant, was well tolerated in naïve DB rabbit eyes and significantly inhibited retinal vascular leakage in the DL-AAA rabbit model for 12 months. If confirmed clinically, such MKI long lasting implant could offer a long duration therapeutic alternative in the treatment of wAMD, RVO and DME.

CONTROL ID: 3714065

SUBMITTER (NAME ONLY): Raymond Wong

TITLE: Berberine rescues corneal endothelial cell loss in Fuchs dystrophy

SESSION TITLE: Corneal Endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Wong, N. Deshpande, V. Kumar, U.V. Jurkunas, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|R. Wong, N. Deshpande, V. Kumar, U.V. Jurkunas, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is a degenerative disease of the corneal endothelium (CE) with multiple and poorly understood etiologies. Hallmarks of FECD are corneal endothelial cell (CEnC) loss and endothelial guttata. Previously, we have reported that loss of antioxidant enzyme NQO1, which is transcriptionally regulated by Nrf2, and upregulation of estrogen metabolizing enzyme CYP1B1 contribute to increased susceptibility of CEnCs to ultraviolet-A (UVA) light, a physiologic stressor of CE. The purpose of this study is to test the protective effect of a naturally occurring Nrf2 agonist and CYP1B1 inhibitor, berberine, against CEnC loss after UVA exposure in vivo.

Methods: 10-week-old C57BL/6 female mice corneas were irradiated with UVA light (500 J/cm^2). Post-irradiation, 2 cohorts of mice (N=5 each) were intraperitoneally injected with 10 mg/kg berberine or vehicle once a week up to 1 month. CEnCs were imaged before and at 1 week, 2 weeks, and 1-month post-UVA using Heidelberg Retinal Imaging Rostock Corneal Module (HRT-RCM). Cell counting was performed using ImageJ and statistical analyses of computed cell density were performed using a one-way analysis of variance (ANOVA) and post-hoc Tukey's HSD.

Results: At 1-week post-UVA, the vehicle-treated group showed a 25.3±2.7% decrease (1760±23 vs. 2362±42 cells/mm^2 at baseline; $p<0.001$), while the berberine-treated group showed only a 12.7±1.4% decrease (1970±28 vs. 2263±64 cells/mm^2 at baseline; $p<0.001$) in CEnC density, thus exhibiting 49% protection with drug compared to no treatment ($p<0.01$). At 2 weeks, the vehicle-treated group showed a 37.5±2.7% decrease (1474±49 vs. 2362±42 cells/mm^2 at baseline; $p<0.001$), whereas the berberine-treated group showed only a 19.4±1.4% decrease (1822±27 vs. 2263±64 cells/mm^2 at baseline; $p<0.001$) in CEnC density, indicating a continued 48% protection with drug compared to no treatment ($p<0.001$) at this time-point.

Conclusions: We demonstrate that treatment with berberine can rescue UVA-mediated CEnC loss at an early time-point in FECD. This study provides a potential line of treatment to rescue a deficient antioxidant system in FECD. Further investigation into the long term effect is warranted.

CONTROL ID: 3714067

SUBMITTER (NAME ONLY): Justis Ehlers

TITLE: The Impact of Compartmental Exudative Volatility on Visual Acuity Outcomes in Neovascular AMD

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.P. Ehlers, L. Lunasco, S. Yordi, H. Cetin, K. Sarici, T.K. Le, K.E. Talcott, P.K. Kaiser, S.K. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R. Zahid, J. Hu, X. Meng, Novartis AG, Basel, Basel-Stadt, SWITZERLAND|A.M. Khanani, Sierra Eye Associates, Nevada, UNITED STATES|

Commercial Relationships Disclosure: Justis Ehlers: Commercial Relationship(s);Code C (Consultant/Contractor):Aerpio, Alcon, Allegro, Allergan, Genentech/Roche, Novartis, Thrombogenics/Oxurion, Leica, Zeiss, Regeneron, Santen, Stealth, Adverum, IvericBIO, Apellis, Boehringer-Ingelheim, RegenxBIO;Code F (Financial Support):Aerpio, Alcon, Thrombogenics/Oxurion, Regeneron, Genentech, Novartis, Allergan, Boehringer-Ingelheim, IvericBio, Adverum;Code P (Patent):Leica | Leina Lunasco: Commercial Relationship: Code N (No Commercial Relationship) | Sari Yordi: Commercial Relationship: Code N (No Commercial Relationship) | Hasan Cetin: Commercial Relationship: Code N (No Commercial Relationship) | Kubra Sarici: Commercial Relationship: Code N (No Commercial Relationship) | Thuy Le: Commercial Relationship: Code N (No Commercial Relationship) | Katherine Talcott: Commercial Relationship(s);Code F (Financial Support): Zeiss, Novartis, RegenxBio | Robert Zahid: Commercial Relationship(s);Code E (Employment):Novartis | Joanne Hu: Commercial Relationship(s);Code E (Employment):Novartis | Xiangyi Meng: Commercial Relationship(s);Code E (Employment):Novartis | Peter Kaiser: Commercial Relationship(s);Code C (Consultant/Contractor):Aerie, Allegro, Allergan, Allgenesis, Alzheon, Annexon Biosciences, AsclepiX, Aviceda, Bayer, Bausch and Lomb, BIogen Idec, Bionic Vision Technologies, Boehringer Ingelheim, Zeiss, Clearside, DelSiTech, DTx Pharma, Duet Therapeutics, Eyevensys, Galecto Biotech, Galimedix, Gemini, Glaukos, Innovent, iRenix, Iveric Bio, jCyte, Kanaph Therapeutics, Kanghong, Kodiak, LensGen, NGM Biopharamaceuticals, Novartis, Ocugenix, Oculis, Ocuphire, OcuTerra Therapeutics, Omeros, Ophthea, Oxurion, Palatin, Regeneron, Retinal Sciences, Retrope, Roivant, Samsung, Sandoz, Santen, Stealth, Sustained Nano Systems, Takeda, Thea, 2020 Onsite | Arshad Khanani: Commercial Relationship(s);Code C (Consultant/Contractor):4DMT, Adverum, Aerpio, Alcon, Allergan, Apellis, Broadwing Bio, DORC, Gemini, Genentech, Graybug, Gyroscope, Iveric Bio, Kato, Kodiak, Novartis, Opthea, Oxurion, PolyPhotonix, Recens Medical, Regenxbio, Surrozen;Code F (Financial Support):Adverum, Alkahest, Allergan, Annexon, Gemini Genentech, Gyroscope, Iveric Bio, Kodiak, NGM Pharmaceuticals, Novartis, Opthea, Ophthotech, Oxurion, Recens Medical, Regenxbio | Sunil Srivastava: Commercial Relationship(s);Code C (Consultant/Contractor):Bausch and Lomb, Adverum, Novartis, and Regeneron. ;Code F (Financial Support):Regeneron, Allergan, and Gilead;

ABSTRACT BODY:

Purpose: Greater volatility of retinal thickness during anti-VEGF therapy has been associated with poorer visual acuity outcomes in eyes with neovascular age-related macular degeneration (nAMD). This post hoc analysis of the HAWK study examined whether specific exudative compartmental volatility (e.g., intraretinal fluid [IRF], subretinal fluid [SRF], and subretinal hyperreflective material [SHRM]) was associated with visual outcomes.

Methods: The HAWK study was a randomized phase 3 study in patients with nAMD (NCT02307682). Six hundred fifty-two eyes in the brolucizumab 6 mg and aflibercept 2 mg arms were included in the post hoc analysis. IRF, SRF, and SHRM volume was measured using a machine-learning enhanced feature-extraction platform with manual correction, as needed. For each eye, the standard deviation (SD) of the volume of each exudative compartment (IRF, SRF, and SHRM) was calculated from Week 12 to Week 56 (i.e., following the initial loading phase and representing the visit-to-visit variability). For each exudative compartment, eyes with SDs ≤25th percentile and ≥75th percentile were considered to have low and high volatility, respectively. The effect of volatility on mean change in best corrected visual acuity (BCVA) was examined from Week 12 at Week 56.

Results: Eyes with high SRF volatility demonstrated significantly worse visual outcomes compared to eyes with low SRF volatility (n=163, mean change=-2.18 letters vs n=314, mean change=+1.35 letters, respectively; P=0.0044). Similarly, eyes with high IRF volatility (n=163, mean change=-2.63 letters; P<0.0001) and eyes with low IRF volatility (n=367, mean change=+2.30 letters) had significant differences in change in visual acuity. Finally, there was also a significant difference in change in BCVA between eyes with high SHRM volatility (n=163, mean change=-2.47 letters; P=0.0001) and eyes with low SHRM volatility (n=166, mean change=+1.97 letters).

Conclusions: High volatility of each exudative parameter, including SRF, was associated with poorer visual outcomes. This suggests that identifying exudative fluctuation and potentially stabilizing that volatility may be important in maximizing visual acuity outcomes.

CONTROL ID: 3714068

SUBMITTER (NAME ONLY): Cindy Chen

TITLE: Identification of Retinal Fluid Accumulation in Uveitis Patients with Normal Foveal Contour on OCT and Retinal Vascular Leakage on Ultra-Widefield Fluorescein Angiography

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Chen, S. Sharma, D. Mammo, K. Baynes, J.P. Ehlers, S.K. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Cindy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Sumit Sharma: Commercial Relationship(s);Code C (Consultant/Contractor):Alimera, Allergan, Eyepoint, Genentech, Regeneron, Bausch and Lomb, Clearside | Danny Mammo: Commercial Relationship: Code N (No Commercial Relationship) | Kimberly Baynes: Commercial Relationship: Code N (No Commercial Relationship) | Justis Ehlers: Commercial Relationship(s);Code C (Consultant/Contractor):Aerpio, Genetech, Novartis, Allegro, Leica, Zeiss, Alcon, Allergan, Regeneron, Oxurion, Roche, Santen | Sunil Srivastava: Commercial Relationship(s);Code C (Consultant/Contractor):Gilead, Eyevensys, Jcyte, Regeneron, Eyepoint, Zeiss, Bausch, Sanofi, Allergan, Abbvie, Novartis;Code R (Recipient):Gilead, Eyevensys, Eyepoint, Regeneron, Bausch

ABSTRACT BODY:

Purpose: Patients with active uveitis with retinal vascular leakage (RL) on ultra-widefield fluorescein angiography (UWFA) may have normal foveal contour on spectral domain optical coherence tomography (OCT). In this study, we evaluate changes in fluorescein leakage on UWFA and changes in retinal thickness measures on OCT to determine the layers of retinal fluid accumulation on OCT in patients with uveitis.

Methods: This is a retrospective IRB approved study. Patients were imaged with UWFA and OCT on the same day at baseline and follow-up visit. Patients included all had active uveitis with significant RL on UWFA and normal foveal contour with absence of macular edema on OCT scans at baseline and significant improvement of RL on UWFA post-treatment. OCT analysis software with manual expert reader-correction was used to segment the ILM, ONL, EZ, RPE, and Bruch's membrane. Segmentation metrics for retinal volume (RV) and mean central subfield thickness (CST) on OCT were obtained. UWFA metrics of leakage area using 3, 6, 9-disc diameter areas centered on the macula were quantified using a fully automated customized software.

Results: A total of 27 eyes from 21 patients (14 females, 7 males) were included in the study. At baseline, the average total RL on UWFA was 8.5%. After treatment, the average total RL decreased to 5.1%. The most significant improvement in RL on UWFA was seen within 3-disc diameters centered on the macula with an average change of 96% pre- and post-treatment. At baseline on OCT, the average total, outer (EZ-RPE), middle (ONL-EZ), and inner (ILM-ONL) RV was 11, 1, 3, and 7 mm^3. On follow-up after treatment, the average total, outer, middle, and inner RV was 10, 1, 3, and 6 mm^3.The average total, outer, middle, and inner CST at baseline was 290, 38, 126, and 127 µm. After treatment, the average total, outer, middle, and inner CST was 267, 37, 110, 120 µm. The most significant decrease in average CST occurred within the middle retinal layer.

Conclusions: In uveitis patients with active RL and normal retinal contour, reduction in leakage leads to decrease in retinal thickness on OCT. The majority of improvement occurs in the middle retinal layer (ONL-EZ). Despite "normal" retinal contour, eyes with active RL have retinal edema. Normal retinal contour and thickness on OCT does not rule out active RL.

CONTROL ID: 3714073

SUBMITTER (NAME ONLY): Sujay Shah

TITLE: Epigenetic Regulation of Neural Progenitor Multipotency

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shah, A. Fernandes, P. Mattar, Cellular and Molecular Medicine, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|S. Shah, A. Fernandes, P. Mattar, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|

Commercial Relationships Disclosure: Sujay Shah: Commercial Relationship: Code N (No Commercial Relationship) | Alex Fernandes: Commercial Relationship: Code N (No Commercial Relationship) | Pierre Mattar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Heterochromatic epigenetic modifications such as DNA and histone methylation have previously been shown to restrict the potential of neural stem cells, but it has remained unclear how these processes are controlled. Using retina as a model system, our lab identified that transcription factor Casz1 interacts with Mi2/NuRD chromatin remodelling complex to regulate the potential of retinal progenitor cells (RPCs) during development. We hypothesize that the Mi2/NuRD complex regulates RPC potential by restricting the epigenome. Our objective is to determine whether and how the Mi2/NuRD complex regulates RPC potential.

Methods: We focused on the key Mi2/NuRD subunit Chd4, which imparts the nucleosome remodelling enzymatic activity exhibited by the complex. We obtained a floxed Chd4 allele, that was cross-bred with a retina-specific Chx10-Cre allele to excise an essential region of the Chd4 gene specifically in the developing retina. We first performed phenotypic analysis to identify the role of Chd4 during retinal development and follwed up with "omic" studies to identify the mechanisms that might regulate RPC potential.

Results: Phenotypic analysis of adult retinas showed that conditional knock-out (cKO) of Chd4 lead to an atypical retinal architecture, where the retinal layers were highly distorted as compared to control. Using cell-specific markers we ascertained that Chd4 cKO lead to a skewed generation of different retinal cell-fates, where early cell types such as retinal ganglion cells were overproduced at the expense of late-born cell-fates such as rod photoreceptors. To determine how Chd4 affects gene expression, we performed single-cell RNA-seq on control and cKO RPCs. While our analysis of this dataset is still preliminary, we have been able to identify many genes that are differentially expressed in cKO RPCs and are currently in the process of validating these data. Furthermore, we performed ATAC-seq on control and cKO P0 RPCs to determine how Chd4 regulates gene accessibility to modulate RPC potential. Through the preliminary analysis, we observed that Chd4 cKO lead to an increase in genomic accessibility.

Conclusions: In future work, we propose to perform a systematic review of the "omic" datasets we have obtained in order to identify how the Mi2/NuRD complex regulates RPC potential.

CONTROL ID: 3714076

SUBMITTER (NAME ONLY): Hsuan-Yeh Pan

TITLE: Regulation of inflammatory cytokine expression by the NFAT signaling pathway in retinal pigment epithelial cells (RPE)

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Pan, M. Valapala, Indiana University, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Hsuan-Yeh Pan: Commercial Relationship: Code N (No Commercial Relationship) | Mallika Valapala: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Nuclear factor activated in T cells (NFAT) has been known to regulate the expression of a wide variety of inflammatory cytokines. The NFAT family of proteins possess five different isoforms (NFAT1-5). NFAT1-4 isoforms are dephosphorylated and activated by calcineurin. Activated NFAT proteins translocate to the nucleus and enhance the expression of several inflammatory cytokines including interferon gamma (IFNγ), interleukin (IL)-2, IL-4, and IL-17, granulocyte-macrophage colony-stimulating factor (GM- CSF). We investigated the involvement of NFAT proteins on lipopolysaccharide (LPS)-mediated expression of inflammatory cytokines in the retinal pigment epithelial cells (RPE).

Methods: We treated ARPE-19 cells with NFAT inhibitor, MAGPHPVIVITGPHEE (VIVIT), for 4-6 hrs followed by 10 μM LPS for 24 hrs to analyze whether NFAT is involved in the regulation of LPS-induced expression of inflammatory cytokines in the RPE. Human cytokine antibody array was used to examine several cytokines expression in the cells treated with LPS and LPS in combination with the NFAT inhibitor, VIVIT. Quantitative real time PCR (qRT-PCR) analysis was performed to evaluate the expression of LPS-induced cytokines in the RPE.

Results: In ARPE-19 cells treated with 10 μM LPS, human cytokine antibody array showed an induction in the expression of several cytokines including IL-6, IL-8, IL-7, Monocyte Chemoattractant Protein-1 (MCP-1), GM-CSF, growth-related oncogene (GRO) and growth-related oncogene alpha (GRO alpha). The cytokine array revealed that LPS-induced expression of IL-6, IL-8 and growth-related oncogene alpha (GRO alpha) was decreased in the presence of 10 and 20 μM of the NFAT inhibitor, VIVIT. qRT-PCR analysis showed an induction in the expression of IL-7, CCL3, GM-CSF, and MCP-1 upon LPS treatment and LPS-induced expression of MCP-1 and GM- CSF was decreased in the presence of the NFAT inhibitor, VIVIT. qRT-PCR analysis also revealed that the expression of tumour necrosis factor alpha (TNF- α) was decreased upon treatment with LPS and VIVIT.

Conclusions: These results suggest NFAT proteins play an important role in regulation of inflammatory cytokine expression in the RPE. Furthermore, these studies suggest that suppression of NFAT activity by a peptide inhibitor can inhibit inflammatory cytokine expression

CONTROL ID: 3714077

SUBMITTER (NAME ONLY): fangfang lu

TITLE: Phenotypic screening for pro-regenerative genes in retinal pigment epithelium via CRISPR Cas9 mediated F0 knockouts

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. lu, L. Leach, J.M. Gross, Department of Ophthalmology, Louis J. Fox Center for Vision Restoration, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|L. Leach, Department of Developmental Biology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.M. Gross, Department of Molecular Biosciences, The University of Texas at Austin, Austin, Texas, UNITED STATES|F. lu, Department of Ophthalmology, The Second Xiangya Hospital, Central South University, Changsha, Hunan, CHINA|

Commercial Relationships Disclosure: fangfang lu: Commercial Relationship: Code N (No Commercial Relationship) | Lyndsay Leach: Commercial Relationship(s);Code P (Patent):#9458428 | Jeffrey Gross: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Zebrafish retinal pigment epithelium (RPE) are able to regenerate after genetic ablation and our previous work has identified several critical regulators of RPE regeneration, including Wnt signaling, mTOR signaling, and immune response factors. Despite these advances, our understanding of the mechanisms driving intrinsic RPE regeneration remains limited. To address this, we conducted a rapid in vivo functional screen of candidate regenerative loci to determine a requirement for RPE regeneration.

Methods: Target genes were selected based on upregulation in regenerating RPE identified from bulk RNA-sequencing data generated from FACS-sorted $eGFP^{+}$ RPE cells. Synthetic guide RNAs (gRNAs) targeting three non-overlapping regions of each candidate gene were generated. Each gRNA was injected, followed by headloop (HL) PCR to confirm mutagenesis efficacy. Having validated each gRNA set, one-cell stage embryos derived from rpe65a:nfsB-eGFP transgenic crosses were then injected with the three synthetic gRNAs-cas9 protein complex (RNP) per gene. Control embryos were injected with a set of scrambled RNPs. At 5 days post-fertilization (dpf), RNP injected larvae carrying the rpe65a:nfsB-eGFP transgene were exposed to 10mM metronidazole (MTZ) for 24 hours to ablate the RPE. At 4 days post-injury (dpi), genotyping of individual embryos was performed to confirm mutagenesis. RPE-specific immunostaining with ZPR2 was performed on ablated RNP injected and control larvae at 4dpi. RPE pigment recovery between injected and control groups was quantified using a MATLAB-based script to assess effects on RPE regeneration.

Results: Mutagenesis rates were high for gRNAs, supporting the efficacy of this approach. Preliminary MATLAB-based quantification data showed significant pigment recovery differences ($p<0.05$) between il11a and scrambled RNP injected groups, as well as between ptgs2a and scrambled RNP injected groups.

Conclusions: il11a and ptgs2a are putative pro-regeneration genes required for RPE regeneration and screening of additional candidate regenerative loci are underway.

CONTROL ID: 3714078

SUBMITTER (NAME ONLY): Rajat Rai

TITLE: Physiology-enhanced data analysis of the Thessaloniki Eye Study: relationship between intraocular pressure and venous resistance

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Rai, G. Guidoboni, J. Keller, D. Zou, R. Nunez, Electrical Engineering and Computer Science, University of Missouri System, Columbia, Missouri, UNITED STATES|B.A. Siesky, A. Verticchio, A. Harris, Opthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|C. Wikle, Statistics, University of Missouri System, Columbia, Missouri, UNITED STATES|E.L. Robinson, School of Social Work, University of Missouri System, Columbia, Missouri, UNITED STATES|M. Lin, Mathematics, University of Missouri System, Columbia, Missouri, UNITED STATES|B.M. Wirostko, Opthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|D. Giannoulis, V. Kilintzis, F. Topouzis, Department of Ophthalmology, Aristotle University of Thessaloniki, Thessaloniki, GREECE|

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ABSTRACT BODY:

Purpose:

Physiology-enhanced data analytics provide a platform to quantify the contributions of various risk factors to primary open angle glaucoma (POAG) pathogenesis, a requirement for personalized disease management. Here, physiology-enhanced data analytics is used to estimate intraocular pressure (IOP) and its relationship to vascular resistance in the retinal venules and central retinal vein (CRV) in participants of the Thessaloniki Eye Study (TES).

Methods:

TES involved 3136 eyes including 98 POAG eyes and 423 eyes suspected of POAG. Structural and vascular assessments were conducted via Heidelberg Retinal Tomography (HRT) and Flowmetry (HRF). IOP and systolic and diastolic blood pressures (SBP, DBP) were used as individualized input data for a validated mathematical model (Guidoboni et al 2014), providing hemodynamic outputs based on fundamental mechanisms of vascular physiology. The enhanced dataset is made by the combination of collected and simulated data.

Results:

OAG eyes had higher IOP and lower DBP compared to healthy eyes and POAG suspects. Diastolic CRV resistance was significantly higher (5-fold) in POAG eyes compared to healthy eyes. In glaucoma suspects compared to healthy, median CRV resistance was similar, while the 75^{th} percentile was much higher (Table 1). The differences in the venous resistances are also accompanied by significant differences in structural and vascular biomarkers (Table 1).

Conclusions:

Hemodynamic alterations in the venous circulation may influence the relationship between IOP and glaucoma and alter risk. In addition, increased vascular resistances of the retinal veins are indicative of higher susceptibility to vessel collapse in patients with POAG.

CONTROL ID: 3714079

SUBMITTER (NAME ONLY): Gabriella Szekely

TITLE: A novel Pilocarpine Ophthalmic Topical Cream formulation applied to eyelids is well tolerated, supporting its clinical evaluation for the treatment of dry eye disease and presbyopia

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Szekely, I.D. Raymond, C. Vangyi, J. Shiah, V. Akunuri, C. Panwala, T. Navratil, Research and Development, Glaukos Corp, San Clemente, California, UNITED STATES|T. Koritz, Global Commercial Development, Glaukos Corp, San Clemente, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cream-based formulations applied to the eyelid offer a novel approach for the delivery of pharmaceutically active compounds for the treatment of ocular disorders. We performed studies to investigate the tolerability and toxicity of a pilocarpine ophthalmic topical cream applied to the eyelids of Hanford minipigs.

Methods: Male Hanford minipigs (N=16; 3-5/group) were administered sterile Pilocarpine Ophthalmic Topical Cream (low, mid and high dose) or its vehicle (Pilocarpine Ophthalmic Topical Cream, 0%) to the upper eyelids of both eyes for 28 days with a 14-day recovery period. Parameters evaluated included viability, clinical signs, dermal and ocular irritation, ophthalmic examinations, intraocular pressure (IOP), pupillometry, body weight, food consumption, toxicokinetics, clinical pathology (hematology, coagulation and serum chemistry), organ weights, macroscopic and ocular and systemic microscopic observations.

Results: There were no vehicle- or drug-related effects on mortality, clinical signs, eyelid dermal and ocular irritation scores, ophthalmic examinations, IOP, pupil size, body weights, clinical pathology, organ weights, or macroscopic observations. There were no vehicle- or drug-related microscopic findings in ocular tissues and extraocular tissues including eyelids and lacrimal glands. Toxicokinetic evaluation at a local dose 2.1 times higher than the highest planned clinical dose showed lower systemic exposures than those observed following a single dose of 10 mg pilocarpine hydrochloride tablets in human. Pilocarpine concentrations in target tissues, including main and accessory lacrimal glands and ciliary body, were at levels deemed likely to be effective.

Conclusions: A novel sterile Pilocarpine Ophthalmic Topical Cream was well tolerated with low systemic exposures after application to the eyelids. Concentrations achieved in the target tissues support the eyelid route of administration. Therefore, local and systemic safety concerns of Pilocarpine Ophthalmic Topical Cream are low and support the evaluation of the efficacy and safety in the Phase 2 clinical trials for the indications of dry eye disease and presbyopia.

CONTROL ID: 3714081

SUBMITTER (NAME ONLY): Isabel Pinilla Lozano

TITLE: Changes in retinal and choroidal capillary plexus evaluated by OCTA in type 1 diabetic patients without diabetic retinopathy

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Pinilla Lozano, M. Diaz-Barreda, A. Boned-Murillo, I. Bartolome, Ophthalmology, Hospital Clinico Universitario Lozano Blesa, Zaragoza, Aragón, SPAIN|I. Pinilla Lozano, M. Sopeña, G. Fernandez-Espinosa, E. Orduna-Hospital, Universidad de Zaragoza, Zaragoza, Aragón, SPAIN|N. Cuenca, Universitat d'Alacant, Alacant, Comunitat Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: To study anatomical and vascular changes in the superficial capillary (SCP) and deep capillary (DCP) plexuses in the retina, as well as changes in the choriocapillaris (CC) and foveal avascular zone (FAZ) using optical coherence tomography angiography (OCTA) (DRI-Triton SS-OCT) in type 1 diabetic (DM1) patients without diabetic retinopathy (DR).

Methods: We performed a single-center cross-sectional descriptive study including 40 eyes of well-controlled DM1 patients who had been diagnosed at least 10 years prior, and 72 eyes of 72 healthy subjects. All participants underwent a full ophthalmic examination including OCTA using Deep Range Imaging (DRI)-Triton swept source (SS)-OCT.

Results: Mean age was 41.70±11.48 and 42.78±13.70 years in DM1 group and in the control group respectively. There were no differences in VA, EE, AL nor IOP. Statistical differences were found in all areas of the SCP, with lower values in DM1 patients. There were differences in all quadrants except the central zone in the DCP. In the CC there were only significant blood flow changes in the central area. We did not find significant differences in the FAZ in neither of the plexuses, but the horizontal FAZ SCP diameter was found significantly different. The anatomical evaluation frequently showed abnormalities such as microaneurysms in both plexuses, FAZ modifications and areas with lack of blood perfusion.

Conclusions: DM1 patients without DR present microvascular abnormalities with lack of retinal and CC blood perfusion, as well as anatomical changes in retinal blood vessels.

CONTROL ID: 3714083

SUBMITTER (NAME ONLY): Tina Govindarajan

TITLE: Accuracy of Laser-Generated Partial Thickness Corneal Incisions Using an Integrated Femtosecond Laser Phacoemulsification System

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Govindarajan, E. Teuma, LENSAR Inc, Orlando, Florida, UNITED STATES|

Commercial Relationships Disclosure: Tina Govindarajan: Commercial Relationship(s);Code E (Employment):LENSAR | E Valas Teuma: Commercial Relationship(s);Code E (Employment):LENSAR

ABSTRACT BODY:

Purpose: Corneal incisions created during cataract surgery include full thickness incisions (FTIs) used to access the anterior chamber and partial thickness incisions (PTIs) used to correct corneal astigmatism. Laser-generated corneal incisions demonstrate increased accuracy, predictability and reproducibility compared to standard, manual incisions. This study assessed the accuracy of partial thickness corneal incisions constructed in the porcine eye model by an integrated femtosecond laser phacoemulsification system (ALLY System, LENSAR, Orlando, FL).

Methods: Paired corneal PTIs, 180° apart, were generated on 36 porcine eyes at 3 incision depth modes and 3 arc lengths (30°, 60°, and 90°). The 3 incision depth modes were Fixed Depth, Fixed Residual Stroma and Percentage Depth. Incision depths were measured with a Fourier Domain OCT system. Incision arc lengths captured from the laser system and from a laboratory microscope were analyzed using a MATLAB algorithm.

Results: For Fixed Depth PTIs, the mean achieved depths were 407µm ± 30µm and 628µm ± 30µm for intended depths of 400µm and 600µm, respectively. In the Fixed Residual Stroma group, the mean achieved residuals were 181µm ± 23µm and 276µm ± 33µm for intended residual depths of 150µm and 250µm, respectively. For the Fixed Percentage Depths group, the mean achieved percentages were 75% ± 4% and 86% ± 4% for intended percentage depths of 75% and 85%, respectively. Arc lengths measured from microscope images for intended arc lengths of 30°, 60° and 90°, were 30.20° ± 0.44°, 60.32° ± 0.56° and 89.56° ± 0.28°. Similarly, arc lengths measured from laser system images were 30.38° ± 0.54°, 60.19° ± 0.61° and 89.55° ± 0.34°, for intended corresponding arc lengths of 30°, 60° and 90°.

Conclusions: The LENSAR ALLY System constructs accurate, predictable, and reproducible PTIs at selected parameters and incision modes. Additionally, incision arc length measurements are consistent between images acquired by the laser system during the procedure and images acquired via microscopy after laser treatment. The consistency and regularity associated with the PTIs created using the ALLY system may help minimize the incidence of undesirable refractive surprises, thus providing an advantage compared to manual PTIs.

CONTROL ID: 3714085

SUBMITTER (NAME ONLY): Qitong Gao

TITLE: An end-to-end deep learning method for predicting retinal layer thickness from Optical Coherence Tomography (OCT) images in patients with clinical progression of Age-related Macular Degeneration (AMD)

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop a fully-automated, end-to-end system that can capture and predict changes in retinal layer thickness from OCT scans.

Methods: We used 1308 OCT images (496 x 768 resolution) collected from 118 patients with AMD that progressed over time. Each patient dataset contained a consecutive sequence of OCT images obtained from multiple follow-up visits over at least two years (mean follow-up time 11.08 years ± 8.53). The region between the retinal pigment epithelium (RPE) and outer plexiform layer (OPL) was initially segmented by experts, and its thickness was presented by averaging the number of pixels between the two layers over the horizontal axis. Then, a Convolutional-Neural Network (CNN) was trained to capture the thicknesses from the longitudinal OCT scans, formulating thicknesses time-series for each patient. At last, a long-short term memory (LSTM) model was trained to process the time series and predict the thickness change in the future.

Results: OCT sequences in the dataset are split by 8:2 ratio to constitute training and testing dataset. In the test set, images obtained from t=0 to t=T-1 were used to evaluate the performance of the CNN, while t=T was left for evaluating the LSTM. The CNN achieved 13.0% mean absolute error (MAE) between the predicted thicknesses and the measurements extracted from segmentations. The LSTM achieved 21.46% MAE in predicting the RPE-OPL layer thickness at t=T, using the thickness time-series (t=0 toT-1) extrapolated by the CNN.

Conclusions: Our learning-based approach can facilitate predictions of retinal layer thickness changes directly from the OCT scans that could be used to predict AMD progression or response to treatment.

CONTROL ID: 3714086

SUBMITTER (NAME ONLY): Pedram Hamrah

TITLE: Trigeminal Ganglia Sensory Neurons Alter the Expression of Vascular Adhesion Molecules on Endothelial Cells in a Neuropeptide-dependent Fashion

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Vascular adhesion molecules on endothelial cells (ECs) are key players in immune cell recruitment during inflammation. We have recently shown that limbal vessels are in close proximity with sensory nerves and that ciliary nerve axotomy results in upregulation of adhesion molecules on the vascular endothelium. The purpose of this study is to dissect the molecular mechanism involved in the neuronal modulation of vascular adhesion molecules by trigeminal ganglia (TG) sensory neuron.

Methods: $CD31^{+}CD45^{-}Lyve\text{-}1^{-}$ blood ECs and $CD31^{+}CD45^{-}Lyve\text{-}1^{+}$ lymphatic ECs were sorted by flow cytometry (FC) from normal corneal limbus and assessed for the expression of neuropeptide receptors (NP-Rs): NK1R, VIP-R1, VIP-R2, CRLR by qRT-PCR. TG sensory neurons were obtained from C57BL/6 mice pups and HUVECs were purchased from ATCC. Co-cultures were performed by seeding TG neurons in a transwell plate with HUVECs in presence of recombinant TNF-α. The antagonist for NP-Rs for VIP, SP and CGRP were used to block neuropeptides. HUVECs were then assessed for adhesion molecule expression by qRT-PCR or FC

Results: Sorted limbal blood ECs showed high expression levels of NK1R, VIP-R1, VIP-R2 and CRLR compared to lymphatic ECs (800-, 7400-, 6200- and 69-fold change respectively ($P<0.05$). mRNA Expression of adhesion molecules (MadCAM-1, and E-selectin) on HUVECs was reduced with TG neuron in presence of recombinant TNF-α by 94% and 90% respectively ($P<0.05$). qRT-PCR showed that MadCAM-1 and E-selectin inhibition by TG neurons was reversed in the presence of SP and VIP antagonists ($P<0.05$). Similarly, FC histograms confirmed the reversal of the inhibitory effect of TG neurons on MadCAM-1 by using VIP and SP antagonists. Additionally, E-selectin inhibition by TG neurons was reversed by VIP and CGRP antagonists ($P<0.05$) by qRT-PCR.

Conclusions: Corneal limbal blood ECs show high levels of NP-Rs expression, suggesting the potential role of NPs on regulating their functions. We observed that the expression of adhesion molecules was inhibited in co-cultures with TG neurons. Moreover, this inhibitory effect could be reversed blocking NPs, demonstrating a selective NP effect on regulating the expression of adhesion molecules. Collectively, these findings suggest that TG sensory neurons regulates the expression of adhesion molecules on ECs through NPs during inflammation.

CONTROL ID: 3714088

SUBMITTER (NAME ONLY): Karen Chang

TITLE: A bioengineering strategy mimicking electrical stimulation to promote neurite outgrowth of retinal ganglion cells through glutamate signaling

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Being a part of the central nervous system, retinal and optic nerve injuries caused by trauma or diseases often lead to progressive degeneration of retinal ganglion cells (RGCs) and permanent vision loss that cannot be restored. The purpose of this study is to develop a biocompatible polyelectrolyte scaffold that supports RGC survival and directs axon growth to promote optic nerve regeneration.

Methods: Retinal explants or primary RGCs were isolated from postnatal day 0-3 C57BL/6 mouse pups and cultured in the presence or absence of glutamate blockers targeting ionotropic or metabotropic glutamate receptors, respectively. Cultures were treated with or without electrical stimulation (ES) at 20 Hz, 50 μA for 15 min or plated on top of polyelectrolyte scaffolds that were fabricated by electrospinning and incubated for 1-5 days. The rate of cell survival, neurite outgrowth, neurite lengths, and angles of neurite extensions were quantified by immunocytochemistry. Statistical significance was calculated using Student's t-test or one-way analysis of variance (ANOVA), and a value of $p < 0.05$ was considered statistically significant.

Results: We found ES significantly promoted the number and lengths of RGC neurites. This effect of ES was largely diminished in the presence of glutamate receptor blockers targeting ionotropic N-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)/kainate receptors, or metabotropic receptors. Glutamate-conjugated polyelectrolyte biomimetic isotropic or aligned electrospun scaffolds were thus generated, featuring similar 3D fibrous structures and physical properties, to mimic continuous glutamate stimulation. The glutamate-containing polyelectrolyte scaffolds supported RGCs survival and promoted robust growth of long neurites in both retinal explants and dissociated cell cultures ($p<0.01$). The aligned scaffolds also drove directed nerve elongations along the direction of the fibers, guiding neurites growing towards the same orientation.

Conclusions: ES enhances RGCs growing long neurites through glutamate signaling. By constructing a glutamate-rich polymer scaffold, it presents a permissive biomaterial that drives robust and directed axon growth in primary cultured RGCs as well as retinal explants. Such polyelectrolyte scaffolds can be beneficial for future nerve repair and regeneration.

CONTROL ID: 3714089

SUBMITTER (NAME ONLY): Carolina Gandara

TITLE: Comparison of multiple batches of human iPSC-derived retinal organoids produced at large scale

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Gandara, W. Atkin, H. Steward, M. Kay, G. Buchanan, L. Armstrong, V. Chichagova, Newcells Biotech, UNITED KINGDOM|L. Armstrong, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Due to well-known limitations of current retinal models, an in vitro 3D model of the human retina that is reproducible and accurately predicts in vivo outcomes is highly desirable. In this study, we have compared the gene and protein expression profile in several batches of human iPSC-derived retinal organoids (ROs) to understand the level of variability found in ROs produced at large scale.

Methods: Gene expression of 20 known retinal genes and representative markers of key cell types were quantified every 30 days by real-time PCR and immunofluorescence, respectively. RNA and 10 µm-cryosections were extracted from pools of ROs selected at random at different stages of differentiation and maturation from at least 4 biological replicates. iPSCs were used as a baseline control for relative quantification of gene expression. Quantification of Z-stack sum projections for marker expression was done using Fiji. One-way ANOVA and Turkey's multiple comparison test of gene and protein expression data was performed.

Results: Expression of photoreceptors (PRs), bipolar cells, müller glia, retinal ganglion cells (RGCs), horizontal cells (HCs), amacrine (AC) and retinal pigmented epithelium cells was increased in all ROs compared to iPSCs. The expression of different cell types fluctuates across RO development, which resembles in vivo development. Interestingly, the expression of RGC markers (MATH5 and BRN3) peaked at day 60, whereas cone (OPN1SW, OPN1MW and OPN1LW) and rod (RHO) PR genes are expressed from day 120 achieving highest expression at day 210 in culture. In terms of cell populations, RCVRN was observed on average in 20% of the cells in day 150 ROs. This average was consistent across different batches of ROs ($p>0.05$). This expression level plateaus at day 210 with nearly 30% RCVRN positive cells present in several ROs.

Conclusions: We have analysed the gene and protein expression profile of several batches of human iPSC-derived ROs across different stages of development. We observed that some key retinal cell types, such as PR, HC and AC, appear at consistent levels between batches. This data set provides crucial information for pre-clinical studies in ROs with application in drug discovery, disease modelling and gene therapy.

CONTROL ID: 3714090

SUBMITTER (NAME ONLY): Paul Cullen

TITLE: Changes in Optic Nerve Glia Induced by Astrocyte-specific Deletion of STAT3

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.F. Cullen, D. Sun, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optic nerve head, where retinal ganglion cell axons emerge from the eye, is a region dominated by astrocytes and a site of early glaucomatous damage, yet much remains unknown about the reactive changes these glia undergo during disease progression and how reactivity influences neuronal survival and the preservation of vision. Although astrocyte reactivity is heterogeneous, many conserved elements are mediated through the transcriptional activator STAT3, and our group has previously shown that astrocyte-specific deletion (KO) of this gene worsens progression in a murine model of ocular hypertension. Here we present additional evidence of changes induced by this targeted deletion, both in astrocytes themselves as well as microglia, in order to better understand the protective roles mediated by this key pathway.

Methods: Optic nerves were isolated from mice with astrocyte-specific STAT3 KO - both constitutive & tamoxifen-induced – and investigated with immunostaining techniques to assess changes in protein expression and morphology in both astrocytes and microglia; as well as astrocyte density.

Results: Astrocyte specific KO of STAT3 was accompanied by diminished expression of cytoskeletal elements – including GFAP & Nestin – in both constitutive and induced animals, with the greatest changes colocalizing with a region of altered astrocyte morphology and reduced density (mean density 10.5 [SD +/- 3.7] per 10,000 μm^2 in KO, 17.2 [SD +/- 3.1] per 10,000 μm^2 in controls, N=3) in the constitutive knock outs. Additional markers seen in control astrocytes, such as Cxcl10 and ApoE, were entirely absent in STAT3 KO astrocytes. Finally, major changes in microglial morphology were observed in the optic nerves of KO animals, including realignment of cellular processes parallel to axonal orientation.

Conclusions: Astrocyte specific deletion of STAT3 results in major changes to astrocytes of the optic nerve – in terms of marker expression, morphology, and overall numbers – as well as resident microglia. That many of these changes are also found in tamoxifen induced knock outs suggests that astrocytic STAT3 is required for normal interactions of these glial cell types in the adult animal, rather than resulting from developmental changes induced by constitutive deletion.

CONTROL ID: 3714092

SUBMITTER (NAME ONLY): Zander Esh

TITLE: Cellular transformation and polarization in differentiating iPSC-derived retinal pigment epithelium

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Esh, D. Ortolan, J. Montford, M. Nimmagadda, R. Sharma, K. Bharti, Unit on Ocular Stem Cells and Translational Research, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Since the advent of induced pluripotent stem cell (iPSC) technology over a decade ago, scientists have harnessed it to develop differentiation processes that can be applied to clinical therapeutics for better patient outcomes. To that end, we have developed a protocol to differentiate iPSCs into fully polarized and functional retinal pigment epithelium (RPE) cells in a way that recapitulates endogenous biological development of RPE. Verifying that our protocol mirrors natural differentiation is a vital step towards developing next-generation therapeutics for diseases that affect RPE.

Methods: iPSC lines were acquired from Allen Institute with GFP tags for TUBA1B and F-ACTIN. Dual SMAD inhibition was used to generate neuroectoderm which was then directed towards RPE progenitors. Inhibition of the FGF and TGF pathways with addition of activin-A then induced the RPE progenitors into committed RPE cells. This differentiation was staged on iBidi chamber slides and lines were fixed at critical stages of differentiation and maturation. The fixed lines were then stained with antibodies for marker proteins critical for development and imaged for fluorescence analysis.

Results: TRA-1-81 and SOX2, proteins expressed most in pluripotent stem cells, decreased during the differentiation process, confirming the cells' transformation from a pluripotent to a non-pluripotent state. Randomly organized intracellular actin filaments in differentiating cells rearranged into polygonal shapes to provide the hexagonal architecture characteristic of mature RPE cells. Cilia, another sign of RPE maturity, was observed with the TUBA1B GFP tag during the start of RPE maturation. MITF expression increased during differentiation, marking RPE lineage. Concomitantly, expression of TYRP1, needed for melanosome formation also increased. Absorbance of light by the cells also increased with maturation, suggesting increasing pigmentation. Additionally, PAX6, OTX2 and RPE65, which are marker proteins for RPE, increase with time.

Conclusions: Our differentiation protocol is successful in developing RPE cells from human-derived iPSC lines. These cells recapitulate the hallmark features and expression patterns characteristic of human RPE cells. This study has provided a more robust understanding of RPE differentiation process and advances us towards a biologically capable clinical therapeutic for RPE disease.

CONTROL ID: 3714094

SUBMITTER (NAME ONLY): Lyubomyr Lytvynchuk

TITLE: MODIFIED SURGICAL IMPLANTATION TECHNIQUE OF SCLERAL-FIXATED ITRAOCULAR CARLEVALE IOL WITH FORMATION OF "SCLERAL POCKETS"

SESSION TITLE: Cataract surgery: techniques and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Lytvynchuk, M. Ponomarov, E. Carlos Reyna, M. Rehak, Ophthalmology, Justus Liebig Universitat Giessen Fachbereich Medizin, Giessen, Hessen, GERMANY|L. Lytvynchuk, Ophthalmology, Karl Landsteiner Gesellschaft Institut fur Krankenhausorganisation, Vienna, AUSTRIA|

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ABSTRACT BODY:

Purpose: To evaluate the refractive results of the modified surgical implantation technique of intraocular acrylic posterior chamber lenses (IOL) with intrascleral fixation Carlevale IOL (FIL SSF, Soleko, Italy).

Methods: 71 patients (72 eyes) were included in this non-randomized retrospective study. Carlevale IOL implantation with intrascleral fixation was performed in all cases. In 29 patients (29 eyes) the standard implantation technique with scleral flaps was preformed (group 1), while in 42 patients (43 eyes) a modified "scleral pocket" technique was used (group2). Standard examinations were carried out after 1, 4, 8 weeks and after 12 months. The modified technique consisted of the formation of 2.5 x 2.5 mm "scleral pockets" of ½ the scleral depth, in the meridian of 3 and 9 o'clock with an opening away from the limbus. Next, sclerotomies were performed with a 23G trocar inside the pockets 1.5 mm from the limbus. Then, Carlevale IOL was implanted through a sclero-corneal tunnel, followed by fixation in the intrascleral space of the "scleral pockets". Postoperative mean refractive error was analyzed in both groups.

Results: The mean follow-up time was 11.8 months (1-30 months). The mean age of the 71 patients (72 eyes) was 75.7 years (28-95 years). The mean refractive error in group 1 was 0.47 (-2.39 - +3.11), while in group 2 it was 0.021 (-2.64 - +1.98). The minimum dioptric power of the implanted Carlevale IOL was +9.0 D, the maximum +25.5 D. The mean axial length was 23.76 mm (21.55-25.92 mm). The complications of the early postoperative period included fluctuations in intraocular pressure (IOP): 11 patients with a history of glaucoma developed an intraocular hypertension (30 to 45 mmHg) and 1 patient developed a transient hypotension. Mild corneal edema was observed in 30 patients. There were no complications associated with Carlevale IOL implantation within 12 months follow-up period.

Conclusions: The new technique makes it possible to minimize the manipulation on the sclera by simplifying access to the sclera, reducing operating time and postoperative rehabilitation through more reliable sealing of sclerotomies. In all cases the correct and centered position of the IOL was achieved. The IOP fluctuation remains one of the most common complications in the postoperative period.

CONTROL ID: 3714095

SUBMITTER (NAME ONLY): Riccardo Sacco

TITLE:

Theoretical investigation of Na+/K+-ATPase activity regulation on aqueous humor production

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Na+/K+-ATPase plays a major role in the electrochemical equilibrium across the ciliary epithelium (CE). Clinical data demonstrate reducing pump activity through Na+/K+-ATPase inhibitors such as nitric oxide-donating prostaglandin may help reduce intraocular pressure (IOP), an established risk factor for glaucoma. In this investigation we estimate optimal levels of Na+/K+-ATPase inhibitors using a mathematical model of the impact of Na+/K+-ATPase activity regulation on aqueous humor production (AHP).

Methods:

AHP is described by the iterative solution of the coupled interaction between electrodiffusion of Na+, Cl- and K+ and AH fluid motion through a compartment scheme of the CE including ciliary capillary (CC), stroma, pigmented (PE) and nonpigmented (NPE) cells, lateral intercellular spaces (LIS) and posterior and anterior chambers connected to the episcleral vein (EV) through an outflow facility conductance. A gap junction separates PE and NPE and a tight junction separates the two LIS. Ion transport is modeled by passive membrane transporters and active Na+/K+-ATPase pump. Cell electroneutrality is enforced by a fixed intracellular negative charge. Simulations are performed under short circuit conditions and hydrostatic pressures of 25 and 8 mmHg in CC and EV.

Results:

Fig. 1 shows the predicted AH volumetric flow rate Q_{AH} (VFR) as a function of the adimensional ratio $\gamma = [ATP]/Ksat$, [ATP] being the intracellular ATP concentration and Ksat=1μM the half-saturation constant, for several values of the maximum activation pump flux density Jmax. Results indicate that for sufficiently high Jmax, there exists a (different) range of γ for which Q_{AH} decreases with respect to the reference value 2.5 μL/min. Fig. 2 shows the percent variation ΔQ_{AH} with respect to baseline conditions (γ=0, '*') as a function of Jmax, for several values of γ. Results indicate that maximum Na+/K+-ATPase impact on VFR reduction is of 8%.

Conclusions:

Model predictions suggest that a marked inhibition of ATPase activity ($\gamma << 1$) does not significantly reduce AHP. Conversely, modeling demonstrates that allowing an intermediate level of pump activity (for [ATP]=5Ksat) maximizes AHP reduction. These results demonstrate potential ability of mathematical virtual laboratories to assist clinicians in optimizing IOP lowering medications.

CONTROL ID: 3714097

SUBMITTER (NAME ONLY): Carlos Mendez Mangana

TITLE: Detection of graft failure in post-keratoplasty patients by Automated Deep Learning

SESSION TITLE: Machine Learning and Big Data

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The overall aim of the study is to explore the capability of detection using algorithms trained in Automated Deep Learning (AutoML) of graft failure from a proprietary dataset of post-keratoplasty patients from a case series published in the literature.

Methods: Observational cross-sectional study, for which Automated Deep Learning algorithms were trained following the success/failure labeling strategy based on clinical notes, on a cohort corresponding to 220 images of post-keratoplasty anterior pole eyes. Once the image quality criteria were analyzed and the dataset was pseudo-anonymized, it was transferred to the Google Cloud platform, where using the Vertex AI- AutoML API, cloud and edge-based algorithms were trained, following expert recommendations on dataset splitting (80% training, 10% test, 10% validation).

Results: The metrics obtained in the cloud-based and edge models have been similar, but we chose to analyze the edge model as it is an exportable model, lighter and cheaper to train. The initial results of the model presented an average accuracy of 0.995, with a Specificity of 95.8% and a Sensitivity of 95.8%. For the label "Graft Failure" the algorithm presented a Specificity of 92.3% and a Sensitivity of 100%. Other metrics such as F1-score, AUC, confusion matrix and activation map development were contemplated.

Conclusions: The initial results of our study indicate that it is possible to train algorithms in an automated fashion for the detection of Graft Failure in patients undergoing penetrating keratoplasty surgery. These algorithms, especially the edge type, are very lightweight tools and easily integrated into mobile or desktop applications, potentially allowing every corneal transplant patient to have access to the best knowledge to enable the correct and timely diagnosis and treatment of this condition.

The metrics obtained in our training process are very good, but since it is a relatively small dataset, it is possible that we have some tendency to overfitting.

The use of Automated Machine Learning opens the possibility of working in the field of artificial intelligence by computer vision to professionals with little experience of programming and is a growing field.

In the next stages of our research line we will seek to expand the working dataset, train algorithms in a traditional way using the Tensorflow library and open ourselves to collaborations to increase the impact of our work.

CONTROL ID: 3714100

SUBMITTER (NAME ONLY): Sam Cooler

TITLE: Automated identification of ganglion and amacrine cell types in a large primate retina dataset

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Recent advances in the analysis of large-scale 512-electrode array recordings have revealed 10+ novel retinal ganglion cell (RGC) and amacrine cell types in the primate retina. To better understand the function of these cell types and the way they vary across retinas and experimental conditions, we are developing methods to automatically identify both the known and novel cell types in a large archival dataset.

Methods: We analyzed 182 ex vivo recordings (89k cells) from peripheral macaque retina. The spatial, temporal, and spectral properties of each cell's visual response were parameterized from the spike triggered average obtained with random checkerboard visual stimuli (Fig. 1A). To classify novel cell types with atypically sparse spiking and inhomogeneous receptive fields (RFs), we used a multi-stage process, iteratively identifying known and then novel types. We compensated for the variation of light response properties across the visual field and across retinas by using the parameters of known RGC types as benchmarks.

Results: The automated classification methods reliably identified the ON & OFF parasol and ON & OFF midget RGC types, achieving 0.96±0.06 accuracy (mean±SD), with 49% of experiments reaching >0.98 accuracy (≈1 error/type/recording) relative to manual supervised labels. Normalizing for spatial and temporal variability using ON & OFF parasol RGCs increased classification accuracy from 0.70±0.13 (Fig. 1B) by reducing across-dataset parameter variance (Fig. 1C). Measures of RF properties, such as the RF solidity (fill fraction of convex hull), enabled classification of a novel type with 0.92±0.12 accuracy in 8 recordings (6k cells; Fig. 1D).

Conclusions: Automated classification applied to a large primate retina dataset, using iterative analysis and variability normalization, provides a broad, objective overview of the functional properties of numerous known and novel cell types.

CONTROL ID: 3714102

SUBMITTER (NAME ONLY): Steven Trinh

TITLE: Macrophage phenotypes differentially modulate profibrotic pathways in corneal and conjunctival fibroblasts

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Trinh, A. Corpuz, S. Alfuraih, J. Weng, A. Sharma, School of Pharmacy, Chapman University, Orange, California, UNITED STATES|S. Alfuraih, School of Pharmacy, Nova Eastern University, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macrophages exhibit a spectrum of phenotypes with differential biological functions including phagocytic, proinflammatory or wound healing, profibrotic. Cornea and conjunctiva contain a significant resident macrophage population. Injury to the cornea and systemic diseases such as graft-versus-host disease can cause ocular surface fibrosis and myofibroblast formation. The present study was designed to investigate whether macrophage polarization can modulate profibrotic signaling in corneal and conjunctival fibroblasts.

Methods: Bone marrow-derived macrophages (M0) were cultured from femur and tibia bone marrow cells of BALB/c mice in the presence of macrophage colony stimulating factor (m-CSF). Macrophage polarization was induced by adding LPS + IFN-γ (M1 spectrum) or IL-4 (M2 spectrum). Flow cytometry was used to characterize the macrophage subtypes by staining for CD11b, F4/80 (Pan markers), CD86 (M1) and CD206 (M2) markers. Cultured murine corneal and conjunctival fibroblasts were exposed to M0, M1 or M2 macrophage supernatants. Immunostaining and real-time PCR were performed to quantify alpha-smooth muscle actin (α-SMA) as a marker for transdifferentiation of the fibroblast to myofibroblasts. The cDNA of supernatant exposed fibroblasts was used to quantify gene expression changes in profibrotic cytokines (TGF-β1, PDGF, CTGF), renin angiotensin system (RAS) components (angiotensin converting enzyme (ACE) and angiotensinogen), and the macrophage proliferation cytokine (m-CSF) using real-time PCR.

Results: Supernatants from M0 and M2 macrophages caused a 2- to 4-fold increase in expression of α-SMA in corneal and conjunctival fibroblasts. Further, > 60% fibroblasts exposed to supernatant of M0 and M2 macrophages showed α-SMA staining. Supernatant from all the three macrophage phenotypes significantly increased the expression of cytokines (TGF-β1 and PDGF), RAS components (ACE and angiotensinogen), and m-CSF and the changes were phenotype specific. Supernatant of M1 macrophages had more prominent effect on RAS components whereas cytokine expression was increased more robustly by supernatant of M0 and M2 macrophage subtypes.

Conclusions: Polarized macrophages cause transdifferentiation of corneal/conjunctival fibroblasts to myofibroblasts and increase the expression of profibrotic mediators in the fibroblasts in a phenotype-specific manner.

CONTROL ID: 3714103

SUBMITTER (NAME ONLY): Chaerim Kang

TITLE: Publication Outcomes for Retina Abstracts Presented at Global Ophthalmology Conferences

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kang, J.C. Lin, P.B. Greenberg, Brown University, Providence, Rhode Island, UNITED STATES|N. Janigian, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Chaerim Kang: Commercial Relationship: Code N (No Commercial Relationship) | John Lin: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Janigian: Commercial Relationship: Code N (No Commercial Relationship) | Paul Greenberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Publication outcomes for retina conference presentations are not well-described. The objective of this study was to characterize publication outcomes and predictors of publication for publicly available retina abstracts presented at global ophthalmology conferences.

Methods: We included all publicly available, English-language retina abstracts from 2016 meeting archives for conferences in World Health Organization (WHO) regions. We searched PubMed, Medline, and Google Scholar from January 1, 2014 to May 1, 2021 to identify whether each abstract was published within five years. Descriptive statistics, χ^2 tests, and t-tests were used to compare abstracts by conference and publication. Univariate and multivariate logistic regression were used to identify predictors of publication.

Results: Among the 11 included conferences, 900 retina abstracts were presented; 60% (539/900) were published in a peer-reviewed journal within five years. Author affiliation with an academic institution [OR=1.93, 95% CI=1.00–3.71] and positive results [OR=1.85, 95% CI=1.10–3.12] were significant predictors of publication in multivariate analysis.

Conclusions: This study provides a comprehensive evaluation of publication outcomes from retina abstracts. Author affiliation with an academic institution and reporting positive results predicted publication.

CONTROL ID: 3714104

SUBMITTER (NAME ONLY): Filippos Vingopoulos

TITLE: Structure-Function Associations between Contrast Sensitivity (CS) and Vascular Metrics on Wide Field Swept Source Optical Coherence Tomography Angiography (WF SS OCTA) across stages of Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Vingopoulos, G. Baldwin, R. Katz, I. Garg, Y. Cui, J.Y. Moon, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|F. Vingopoulos, G. Baldwin, I. Garg, J.Y. Moon, N.A. Patel, D.M. Wu, D. Husain, J.W. Miller, L.A. Kim, D.G. Vavvas, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|Y. Cui, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences,, Guangzhou, CHINA|

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ABSTRACT BODY:

Purpose: To investigate structure-function associations between CS and vascular metrics on WF SS OCTA across stages of non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR), in the absence of diabetic macular edema (DME).

Methods: This prospective observational study included 95 eyes of 78 patients, including 20 mild NPDR eyes, 12 moderate/severe NPDR, 22 PDR, 14 diabetic eyes without DR (DMnoDR), and 27 control eyes. LogMAR Visual Acuity (VA) was measured. CS was measured with the active learning quantitative CS function (qCSF) Manifold Contrast Vision Meter (Adaptive Sensory Technology) and outcomes included Area under the Log CSF (AULCSF) and contrast sensitivity (CS) thresholds at 1-18 cycles per degree (cpd). All eyes were imaged using WF SS OCTA (Plex Elite 9000, Carl Zeiss Meditec). The ARI Network (Zeiss Portal v5.4) delivered vascular metrics, including vessel density (VD) and vessel skeletonized density (VSD) in the superficial and deep capillary plexus (SCP, DCP) on 6x6 mm images. Mixed-effects multivariate regression models were used to evaluate associations between CS functional outcomes and WF SS OCTA structural outcomes across DR stages.

Results: Controlling for age and lens status in the whole cohort, VD in the SCP was significantly associated with LogMAR VA (β= -0.02, P<0.001), AULCSF (β= 0.03, P<0.001), and CS thresholds at 1cpd (β= 0.02, P=0.004), 1.5cpd

(β= 0.02, P=0.005), 3cpd (β= 0.03, P=0.009), 6cpd (β= 0.04, P=0.002), 12cpd (β= 0.04, P= 0.002) and 18cpd (β= 0.01, P= 0.044).VSD in the SCP was associated with LogMAR (β= -1.19, P= 0.010), AULCSF (β= 1.18, P= 0.010), and CS at 1cpd (β= 1.00, P=0.008), 1.5cpd (β= 0.91, P=0.016), 3cpd (β= 0.89, P= 0.039), 6cpd (β= 1.5, P= 0.011) and 12cpd (β= 1.44, P= 0.008); VD in the DCP was associated with LogMAR (β= -0.01, P=0.008), AULCSF (β= 0.01, P= 0.066) and 12cpd (β=0.18, P=0.013) and VSD in the DCP with LogMAR (β= -0.49, P=0.013), AULCSF (β= 0.47, P= 0.099), 12cpd (β=0.82, P=0.021).

Conclusions: We present novel structure-function associations across stages of DR without DME, leveraging WF SS OCTA imaging and CS metrics. The progressive decline in the OCTA vascular metrics across DR stages seems to be associated with equally large changes in contrast sensitivity metrics as in VA.

CONTROL ID: 3714105

SUBMITTER (NAME ONLY): Marcelle Morcos

TITLE: Impact of Micropulse Laser Trabeculoplasty: A 2-Year Retrospective Analysis

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Morcos, J. Klenda, P. Fortin, A. Pansick, C. Draper, Ophthalmology, Nassau University Medical Center, East Meadow, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate change in intraocular pressure (IOP) after micropulse laser trabeculoplasty (MLT).

Methods: A retrospective cohort study was conducted at an ophthalmology clinic at a public hospital in New York. 71 eyes with open-angle glaucoma and no history of incisional surgery treated with MLT were followed. An Iridex IQ 532 laser with MicroPulse technology at 532 nm was used to treat 360° of the trabecular meshwork. Follow-up IOP measurements were obtained at two years. Number of topical glaucoma medications before and after MLT were recorded. Paired t-tests compared baseline to follow-up.

Results: Significant IOP reduction occurred at 2-year follow-up ($p=0.001$) from pre- ($M=18.19$, $SD=4.30$) to post-MLT ($M=15.86$, $SD=3.65$). Stratifying by baseline IOP showed significant IOP reduction for IOP>19,(<p=0.001): pre- ($M=22.39$, $SD=2.99$), post-MLT ($M=17.29$, $SD=4.09$). No significant change occurred for baseline IOP<19 ($p=0.44$). No significant change of number of medications occurred ($p=0.57$).

Conclusions: MLT appears to be a long-lasting beneficial adjunct therapy in patients with uncontrolled IOP on topical medications. Prospective randomized controlled studies would further document the utility of this treatment modality.

CONTROL ID: 3714106

SUBMITTER (NAME ONLY): Nan Zhang

TITLE: Systemic Nicotinamide Riboside Treatment Protects Retinal Ganglion Cells in an Aged Optic Nerve Crush Mouse Model

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Zhang, Y. Li, X. Zhang, M. Chrenek, J. Wang, E.E. Geisert, J.M. Nickerson, J.H. Boatright, Emory Eye Cneter, Emory University, Atlanta, Georgia, UNITED STATES|N. Zhang, Y. Li, X. Zhang, J.H. Boatright, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|B. Charles, Department of Diabetes & Cancer Metabolism, City of Hope Beckman Research Institute, Duarte, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously demonstrated that systemic treatment with nicotinamide riboside (NR), a nicotinamide adenine dinucleotide (NAD^+) precursor, elevated retinal NAD^+ levels and protected retinal ganglion cells (RGCs) in a young mouse model of optic nerve crush (ONC). Because NAD^+ levels decline in age and disease, we now compare neuroprotective effects of systemic NR treatment on young and aged mice subjected to ONC.

Methods: Young (3-6 months old) and aged (18-24 months old) C57BL/6J mice were intraperitoneally (i.p.) injected with NR (1000mg/kg) for 5 consecutive days. PBS was injected as vehicle. Two weeks later, unilateral ONC was conducted. Pattern electroretinography (PERG) was conducted 3 days after ONC. In separate cohorts, young and aged mice were injected with NR or PBS; no crush surgery was conducted. Retinas were harvested for whole-mount immunofluorescence staining with RGC marker Brn3a or NAD^+ concentration measurement (Fig.1)

Results: Systemic NR treatment significantly elevated retinal NAD^+ concentrations in both young(young-PBS+no crush vs young-NR+no crush:100±3vs193±10, $p<0.05$, n=10) and aged C57BL/6J mice(aged-PBS+no crush vs aged-NR+no crush:106±6vs192±10, $p<0.05$, n=10) , and also in eyes of young mice following ONC(young-naïve vs young-NR+ONC 100±3 vs. 142±9, $p<0.01$, n=6), but not in aged mice following ONC(aged-naïve vs aged-NR+ONC:110.2±5 vs 122.6±8, $p>0.05$, n=6). In both young and aged mice, PERG responses and numbers of Brn3a-positive cells from crushed retina were diminished compared with non-crushed(Table.2). NR treatment significantly preserved Brn3a-positive RGC numbers in both young and aged mice following ONC(young-PBS+ONC vs young-NR+ONC:1120±72vs1389±72 cells/field, $p<0.05$, n=7-9; aged-PBS+ONC vs aged-NR+ONC:1004±34vs1193±49 cells/field, $p<0.05$, n=7-8) and preserved PERG responses in young(young-PBS+ONC vs young-NR+ONC: P1:5.43±0.7vs8.91±0.8μV, $p<0.01$; N2:-8.02±0.9vs -12.2± 1.0μV, $p<0.01$, n=15) but not in aged mice following ONC(aged-PBS+ONC vs aged-NR+ONC:P1:2.42±0.4vs3.70±0.5μV; N2:-4.15±0.5 vs -6.03± 0.7μV, $p>0.05$, n=14).

Conclusions: NR treatment significantly protected against ONC-induced RGC death in both young and aged mice and significantly protected against ONC-induced RGC dysfunction in young but not in aged mice. It may be that ONC in aged mice partially suppresses NR-induced elevation of NAD^+, preserving RGC survival but not RGC function.

CONTROL ID: 3714107

SUBMITTER (NAME ONLY): Dmitri Serjanov

TITLE: Regulation of Retinal Regeneration by the Extracellular Matrix Protein Nephronectin

SESSION TITLE: Non-neuronal control of retinal neuron regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Serjanov, J. Twist, M. Swantkowski, D. Hyde, University of Notre Dame, Notre Dame, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Dmitri Serjanov: Commercial Relationship: Code N (No Commercial Relationship) | James Twist: Commercial Relationship: Code N (No Commercial Relationship) | Meghan Swantkowski: Commercial Relationship: Code N (No Commercial Relationship) | David Hyde: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Extracellular matrices (ECMs) are an important source of developmental and homeostatic molecular cues. Although much is known regarding the molecular mechanisms of retinal regeneration, our understanding of the ECM's role in this context remains unclear. This study investigates the role of the ECM molecule nephronectin (Npnt) in regulating Müller glia (MG) and neural progenitor cell (NPC) proliferation and retinal neuron survival in the light-damaged adult zebrafish retina.

Methods: We used in vivo morpholino-mediated gene knockdown to repress Npnt expression in the adult zebrafish dorsal retina. Anti-PCNA immunolabeling of Tg(gfap:egfp) zebrafish retinal sections was used to visualize proliferating MG and NPCs. TUNEL labeling was used to assess cell death. qRT-PCR was used to examine expression of target genes. Protein expression levels and subcellular distribution were assessed using protein immunoblotting of samples enriched for either cytosolic or nuclear proteins from dorsal retinas.

Results: Npnt is present in the adult zebrafish retina and exhibits increased expression 48h after intense light treatment. Knockdown of Npnt results in decreased NPC proliferation and GDNF expression, leading to a significant increase in the death of inner retinal neurons. Protein immunoblotting revealed a novel pattern on Npnt processing and translocation. Under normal conditions, Npnt is observed as a 60 kDa protein, with a portion being cleaved into 20 and 40 kDa fragments. Upon light damage, the entire population is cleaved into the two fragments. Furthermore, our data suggest that one of these fragments is translocated into the nucleus, suggesting that it may directly regulate expression of target. Indeed, Npnt knockdown results in decreased expression of integrins α3b, α4, α11a, and β1, as well as ECM components, such as laminins α1 and α5. Knockdown of these genes also results in decreased MG and NPC proliferation.

Conclusions: These findings demonstrate that the ECM provides regulatory cues guiding zebrafish retinal regeneration. Npnt appears to regulate retinal neuron survival and NPC proliferation. Interestingly, our data suggest that upon damage, Npnt is transported into the nucleus, where it may directly regulate expression of several ECM-related genes that govern the regeneration response. These findings suggest a novel role for Npnt, and expand our understanding of the role of the ECM in retinal regeneration.

CONTROL ID: 3714109

SUBMITTER (NAME ONLY): Sonali Nashine

TITLE: Effects OF CRISPR knockout of the Humanin trimeric CNTFR/gp130/WSX-1 receptor in AMD

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.R. Nashine, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Sonali Nashine: Commercial Relationship: Code N (No Commercial Relationship) | M.Cristina Kenney: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the AMD (Age-related Macular Degeneration) RPE transmitochondrial cell lines, the protective effects of Humanin G (HNG) mitochondrial derived peptide are mediated through the extracellular trimeric CNTFR/gp130/WSX-1 receptor. Binding of Humanin to this receptor leads to the activation of downstream signaling factors, phosphorylation of JAK2 and STAT3, and transcription of genes that confer cytoprotection in AMD.

Methods: We created a novel CRISPR-edited triple knock-out (KO) cell pool of the extracellular trimeric CNTFR/gp130/WSX-1 receptor genes in a wet AMD RPE transmitochondrial cybrid cell line by sequential knock-out of these genes and performed Sanger sequencing to confirm the knockout. HNG was exogenously added to AMD RPE transmitochondrial cybrid cells, which had identical nuclei from the mitochondria-deficient ARPE-19 cells but differed in mitochondrial DNA (mtDNA) content which was derived from a clinically characterized AMD patient. Cell viability and apoptotic cell death were compared between AMD wild-type (WT) vs. AMD KO cells using the MTT assay and Caspase- 3/7/ NucLight IncuCyte® live-cell imaging.

Results: Sanger sequencing of the KO cell pool results: (1) CNTFR gene: KO score=88 %; Indel=94 %; (2) gp130 gene: KO score=62 %; Indel=64 %; (3) WSX-1 gene: KO score=94 %; Indel=99 %. These results demonstrate successful CRISPR editing of the trimeric receptor genes. There was decreased ($P = 0.02$) cellular metabolic activity that reflects cell viability in AMD KO untreated cells (0.88 ± 0.03) compared to AMD WT untreated cells (1 ± 0.04). Higher viable cell number (IncuCyte live-cell imaging) was observed in HNG-treated AMD WT cells (1.14 ± 0.02) compared with untreated AMD WT cells (1 ± 0.04, $P = 0.03$). We found significant reduction ($P<0.01$) in cell number in untreated AMD KO vs. untreated AMD WT cells. HNG-induced rescue was reduced significantly in AMD KO cells compared to that in AMD WT cells ($P<0.05$).

Conclusions: The CRISPR-Cas9 knockout (CRISPR-KO) of the CNTFR/gp130/WSX-1 receptor reduces cell survival in AMD KO cybrids in vitro and blunts the protective effects of exogenous HNG, demonstrating the crucial role of this receptor in HNG-mediated cytoprotection.

CONTROL ID: 3714112

SUBMITTER (NAME ONLY): Emma Lessieur

TITLE: Partial deletion of Lrat inhibits prodromal characteristics of diabetic retinopathy

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Lessieur, Y. Du, A. Saadane, J. Kiser, T.S. Kern, Center for Translational Vision Research, University of California Irvine, Irvine, California, UNITED STATES|H. Liu, Department of Biology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|T.S. Kern, Veterans Health Administration, Long Beach, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evidence suggests that cells from the outer retina play an important role in the pathogenesis of diabetic retinopathy (DR), but whether or not the visual cycle activity is subnormal in diabetes, and whether decreasing or not that activity is a therapeutic approach to inhibit DR is controversial. Here we used the Lecithin:retinol acyltransferase (Lrat) knockout mice to investigate the effects of visual cycle inhibition on the development of early DR.

Methods: Diabetes was induced in male C57Bl/6J (WT) and Lrat heterozygous ($Lrat^{+/-}$) and homozygous ($Lrat^{-/-}$) mice using streptozotocin. Retinoid metabolism, and biochemical and physiological abnormalities in the retina were evaluated at 2 months of diabetes using published methods. Vascular histopathology, permeability and retinal thickness were evaluated at 8 months of diabetes. Non-retinal effects of inhibition of the visual cycle were examined in leukocytes ex vivo at 2- and 8-months of diabetes.

Results: At 2-months of diabetes visual function assessed by OKT and ERG was not significantly affected by diabetes or $Lrat^{+/-}$ whereas in $Lrat^{-/-}$ was severely attenuated. Rhodopsin levels in WT and $Lrat^{+/-}$ diabetics were similar to corresponding values of 11-cis-retinal as determined by retinoid analyses when compared to WT nondiabetics. $Lrat^{+/-}$ mice differed in their level of all-trans-retinyl esters by 50% less when compared to WT and diabetes had no influence in the total levels. No all-trans-retinyl esters were detected in the $Lrat^{-/-}$ groups. Diabetes-induced increase in retinal superoxide was significantly inhibited in $Lrat^{+/-}$ and $Lrat^{-/-}$ diabetic mice when compared to WT diabetics. At 8-months of diabetes, thickness of the ONL by OCT was similar between WT and $Lrat^{+/-}$ but $Lrat^{-/-}$ showed total loss of photoreceptors. Degeneration of retinal capillaries was significantly inhibited in $Lrat^{+/-}$. Similar trends were apparent in diabetic $Lrat^{-/-}$ mice, but mortality in this group precluded further evaluation. The diabetes-induced increase in retinal vascular permeability was inhibited in the inner plexiform and inner nuclear layers of $Lrat^{+/-}$mice, but not in the outer plexiform layer. The leukocyte-mediated cytotoxicity against retinal endothelial cells at 2- and 8-months of diabetes was inhibited in $Lrat^{+/-}$ and $Lrat^{-/-}$ mice when compared to WT diabetic mice.

Conclusions: $Lrat^{+/-}$ diabetic mice are protected from the development of retinal vascular pathology in early DR.

CONTROL ID: 3714115

SUBMITTER (NAME ONLY): Neha Pondicherry

TITLE: A Low-Cost Alternative for Screening Infectious Trachoma in Resource-Limited Settings

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pondicherry, SOM, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|J.D. Keenan, L. Della Santina, T. Lietman, M. Deiner, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Trachoma, an eye disease caused by Chlamydia trachomatis, is responsible for severe visual impairment/blindness of 1.9 million people worldwide. To treat this disease, WHO recommends community-wide prevalence surveys with trained health workers - a challenge in many resource-limited countries. One possible solution aims to use deep learning (DL), a subsect of artifical intelligence (AI) machine learning. Researchers from the Proctor Foundation at UCSF have developed a DL algorithm to identify trachoma from conjunctival photographs, but the algorithm has only been trained on photographs from Ethiopia - which limits its diagnostic accuracy in other populations. After further training with conjunctival photographs from the Peruvian Amazon, we hypothesize the overall diagnostic accuracy of the algorithm will improve.

Methods: For the present study, 700 conjunctival photographs were selected from a de-identified photo repository of 0–9-year-old kids from the Peruvian Amazon taken during routine trachoma monitoring. The Peruvian photographs were split into a training set (n=600) and a testing set (n=100), and all 700 photos were manually graded and given follicular annotations based on the WHO simplified grading scale for trachomatous inflammation. To test the sensitivity and specificity, the algorithm provided a grade of trachoma (i.e., presence or absence of TF) for each photograph in the test set, and sensitivity and specificity of the algorithm was calculated twice, both pre- and post-exposure to the Peruvian pictures.

Results: When the existing algorithm (trained only on Ethiopian photographs) was run on the 100-photograph Peruvian test set before training with Peruvian photographs, the overall accuracy was 0.50, with a sensitivity of 4% and specificity of 96%. After the addition of the Peruvian training set, the algorithm’s accuracy for the same Peruvian test set improved to 0.82, with a sensitivity of 88% and specificity of 76%.

Conclusions: Our results are consistent with our hypothesis that with increased amounts of diverse population photos, the AI DL algorithm would consolidate and more accurately diagnose follicular trachoma overall. Using a diverse range of populations to improve machine learning for trachoma screening is important to accommodate for the diversity of populations affected by trachoma globally.

CONTROL ID: 3714117

SUBMITTER (NAME ONLY): Mark Simcoe

TITLE: Exploring the p.Gly863Ala variant in ABCA4: the complex allele with p.Asn1868Ile is enriched in ABCA4-retinopathy patients compared to the general population

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Simcoe, S. Vermeirsch, N. Pontikos, M. Michaelides, O.A. Mahroo, A.R. Webster, G. Arno, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|C.J. Hammond, P.G. Hysi, Ophthalmology, King's College London, London, London, UNITED KINGDOM|M. Simcoe, S. Vermeirsch, N. Pontikos, M. Michaelides, O.A. Mahroo, A.R. Webster, G. Arno, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|J. Chiang, Molecular Vision Laboratory, Hillsboro, Oregon, UNITED STATES|C.J. Hammond, P.G. Hysi, Department of Twin Research, King's College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The p.Gly863Ala missense variant in ABCA4 is associated with ABCA4-retinopathy (Stargardt disease). It has been previously noted that this variant often occurs in cis with another missense variant, p.Asn1868Ile. The purpose of this study was to assess the co-segregation of these variants in a large population-based cohort (UK Biobank) and a single centre ABCA4-retinopathy patient cohort.

Methods: Whole exome sequencing data was available for 37586 participants of European ancestry in the UK Biobank for the population-based cohort. The haplotypic structure of this ABCA4 region was determined from pairwise linkage disequilibrium calculations. The patient cohort included 96 ABCA4-retinopathy patients carrying p.Gly863Ala variant recruited at Moorfields Eye Hospital.

Results: In the UK Biobank cohort 924 participants carried the p.Gly863Ala variant. Only 265 (29%) of these participants also carried the p.Asn1868Ile variant. Haplotypic analysis identified three haplotypes containing the p.Gly863Ala variant, with the p.Asn1868Ile present on one. ICD10 codes indicated that six participants carrying the p.Gly863Ala variant had been diagnosed with retinal disease that may be ABCA4-retinopathy (degeneration of macula and posterior pole), two of whom were also carrying the p.Asn1868Ile variant. In the patient cohort that had received a diagnosis with p.Gly863Ala as one allele, 63/96 had data available for p.Asn1868Ile genotype and 53/63 (84%) also carried the p.Asn1868Ile variant. Therefore, the odds ratio for ABCA4 retinopathy for carriers of both variants compared to p.Gly863Ala only is 9.8 (95% CI: 5.3-17.9, $p=6.7x10^{-14}$).

Conclusions: There is a significant ($p=6.7x10^{-14}$) association of the p.[Gly863Ala;Asn1868Ile] allele in ABCA4-retinopathy cases compared to the p.Gly863Ala variant alone. Thus, the p.Gly863Ala variant is present on several haplotypes with a haplotype carrying both this variant and the p.Asn1868Ile variant being highly enriched in disease. This suggests that a modifying effect of the haplotype may exist (possibly due to the p.Asn1868Ile variant that has recently been shown to act as a low penetrant pathogenic allele in its own right). Further investigation is needed to determine additional factors that may influence the penetrance of disease in carriers of p.Gly863Ala, such as cis modifiers and the severity of trans alleles.

CONTROL ID: 3714118

SUBMITTER (NAME ONLY): Jody Summers

TITLE: Emmetropization is Associated with a Modified Inflammatory Response in the Eye

SESSION TITLE: Myopia: Mechanism of Emmetropization and Eye Growth

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.A. Summers, D. Soriano, E. Martinez, Cell Biology, University of Oklahoma Health Science Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Jody Summers: Commercial Relationship(s);Code C (Consultant/Contractor):Plex Pharmaceuticals;Code F (Financial Support):Plex Pharmaceuticals | Diana Soriano: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Martinez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Visually regulated eye growth (emmetropization) is associated with some choroidal changes consistent with that of inflammation. In response to imposed myopic defocus the choroid thickens, exhibits increased vascular permeability, and increases the synthesis of a number of proteins associated with the acute phase response, including ovotransferrin, apolipoprotein A-1 and interleukin 6 (IL6). This study was undertaken to determine whether treatment with the anti-inflammatory drug, dexamethasone (DEX), could alter the emmetropization process.

Methods: DEX or vehicle was administered daily to chicks during the development of monocular form deprivation myopia during the last 7 days of a 17 day deprivation period (4 mg/kg, IP). On the last day of treatment, occluders were removed and chicks were allowed to experience unrestricted vision for ≈20 hrs ("recovery"). Choroids and sclera were isolated from recovering and fellow control eyes. Gene expression of Il6 was quantified using Taqman™ PCR and normalized to GAPDH. Scleral proteoglycan synthesis (an indicator of eye growth in chicks) was evaluated by CPC-precipitation of $^{35}SO_4$-labelled glycosaminoglycans.

Results: DEX treatment resulted in a significant decrease in choroidal IL6 gene expression in recovering eyes, compared to recovering eyes of vehicle treated chicks (↓85%; p = 0.0029, Mann Whitney Test). No significant differences were detected in IL6 gene expression in choroids from control eyes between DEX and vehicle treated chicks (p = 0.4958, Mann Whitney Test). DEX treatment resulted in a significant decrease in scleral proteoglycan synthesis in control eyes, compared to control eyes of vehicle treated chicks (↓59%, p =0.0001, t-test). Despite the suppression of scleral proteoglycan synthesis observed in control eyes of DEX-treated chicks, DEX treatment resulted in a significant increase in scleral proteoglycan synthesis in recovering eyes relative to fellow controls (↑185%, p= 0.0028, paired t-test). No differences were detected in scleral proteoglycan synthesis between recovering and control eyes of vehicle treated chicks (p=0.1374, paired t-test).

Conclusions: DEX treatment reduced choroidal gene expression of IL6 in recovering eyes, resulting in a disinhibition of scleral proteoglycan synthesis during recovery from induced myopia. These results provide additional support for a role of inflammation in visually regulated eye growth.

CONTROL ID: 3714119

SUBMITTER (NAME ONLY): Gabriella Moraes

TITLE: Automatic segmentation of anatomical parameters in fellow eyes of patients starting anti-VEGF injections for neovascular age-related macular degeneration

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Moraes, R. Struyven, A. Abbas, R. Chopra, S. Wagner, K. Balaskas, P. Patel, P.A. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|T.D. Keenan, National Institutes of Health, Bethesda, Maryland, UNITED STATES|R. Chopra, Google Health, UNITED KINGDOM|

Commercial Relationships Disclosure: Gabriella Moraes: Commercial Relationship: Code N (No Commercial Relationship) | Robbert Struyven: Commercial Relationship: Code N (No Commercial Relationship) | Abdallah Abbas: Commercial Relationship: Code N (No Commercial Relationship) | Reena Chopra: Commercial Relationship(s);Code E (Employment):Google Health | Siegfried Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Konstantinos Balaskas: Commercial Relationship(s);Code R (Recipient):Novartis, Topcon, Allergan, Bayer, Heidelberg-Engineering, Alimera | Praveen Patel: Commercial Relationship(s);Code C (Consultant/Contractor):Bayer, Genentech, Novartis | Tiarnan Keenan: Commercial Relationship: Code N (No Commercial Relationship) | Pearse Keane: Commercial Relationship(s);Code R (Recipient):Topcon, Allergan, Bayer, Haag-Streit, Carl Zeiss Meditec, Heidelberg-Engineering;Code C (Consultant/Contractor):Deep Mind;Code C (Consultant/Contractor):Roche;Code C (Consultant/Contractor):Apellis;Code I (Personal Financial Interest):Big Picture Medical

ABSTRACT BODY:

Purpose: Individuals with neovascular age-related macular degeneration (nAMD) are at considerable risk of developing the same condition in their fellow eye. We analysed the relationship between volumes of OCT biomarkers at baseline with groups of fellow eyes converting to nAMD during a 2-year follow-up period. Biomarkers were quantified using an artificial intelligence (AI) system (De Fauw et al. 2018).

Methods: Fellow eyes of individuals who started treatment for nAMD between June 2012 and June 2017 in the Moorfields Eye Hospital AMD database were included. AI-derived volumes of neurosensory retina (NSR), retinal pigment epithelium (RPE), drusen and hyperreflective foci (HRF) were compared at baseline (the visit the first eye started treatment) between fellow eyes that did and did not convert within 2 years.

Results: A total of 1578 fellow eye scans at baseline were analysed. Of these, 231 eyes converted to nAMD during the 2 year follow-up period and 1347 eyes did not. At baseline, fellow eyes that converted presented with a mean (standard deviation) volume of 0.107mm3 (0.096) and 0.001mm3 (0.001) of drusen and HRF respectively, and were significantly greater (p-values ≤0.05, Mann-Whitney U test]) than the non-converting group (0.068mm3 of drusen and 0.000mm3 of HRF). Baseline RPE volume in eyes that converted was 0.803mm3 (0.097), which was significantly less than in the non-converters (0.835mm3, p-value ≤0.05). NSR volume was 9.211mm3 (0.727) and 9.260mm3 (0.767) in converting and non-converting groups respectively.

Conclusions: Baseline drusen and HRF volumes appear to be important OCT biomarkers for fellow eye disease progression to nAMD. Automated OCT qualification of retinal structures in fellow eyes may suggest new management protocols with a personalised prediction of AMD progression.

CONTROL ID: 3714120

SUBMITTER (NAME ONLY): Ditta Zobor

TITLE: Central Visual Function and Genotype-Phenotype Correlations in PDE6A-Associated Retinitis Pigmentosa in Preparation for a Gene Supplemental Trial

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Zobor, T. Strasser, K. Stingl, M. Fischer, B. Wilhelm, E. Zrenner, B. Wissinger, S. Kohl, N. Weisschuh, L. Kuehlewein, Universitatsklinikum Tubingen Forschungsinstitut fur Augenheilkunde, Tubingen, Baden-Württemberg, GERMANY|D. Zobor, Semmelweis Egyetem Szemeszeti Klinika, Budapest, Budapest, HUNGARY|G. Blumenstock, Department of Clinical Epidemiology, Eberhard Karls University Tuebingen, Tübingen, GERMANY|E. Zrenner, Werner Reichardt Centre for Integrative Neuroscience (CIN), Eberhard Karls University Tuebingen, GERMANY|

Commercial Relationships Disclosure: Ditta Zobor: Commercial Relationship: Code N (No Commercial Relationship) | Torsten Strasser: Commercial Relationship: Code N (No Commercial Relationship) | Gunnar Blumenstock: Commercial Relationship: Code N (No Commercial Relationship) | Katarina Stingl: Commercial Relationship: Code N (No Commercial Relationship) | M. Dominik Fischer: Commercial Relationship: Code N (No Commercial Relationship) | Barbara Wilhelm: Commercial Relationship: Code N (No Commercial Relationship) | Eberhart Zrenner: Commercial Relationship: Code N (No Commercial Relationship) | Bernd Wissinger: Commercial Relationship: Code N (No Commercial Relationship) | Susanne Kohl: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Weisschuh: Commercial Relationship: Code N (No Commercial Relationship) | Laura Kuehlewein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Autosomal recessive RP (arRP) can be caused by mutations in the phosphodiesterase 6A (PDE6A) gene. Here, we describe the natural course of disease progression with respect to central retinal function, i.e., visual acuity, contrast sensitivity, and color vision and establish a detailed genotype-phenotype correlation.

Methods: 44 patients (26 females; mean ± SD age 43 ± 13 years) with a confirmed genetic diagnosis of PDE6A-associated arRP underwent comprehensive ophthalmological examination and follow-ups including best corrected visual acuity (BCVA) with ETDRS charts, contrast sensitivity (CS) with Pelli-Robson charts at 3 m and 1 m distance, and color vision testing using Roth 28 Hue and Panel D15 saturated color cups. Mean ± SD duration between baseline and last follow-up was 28 ± 12 months.

Results: The most frequently observed variants were c.998+1G>A/p.?, c.304C>A/p., and c.2053G>A/p. In general, symmetry between right and left eyes was high (r = 0.89). Central retinal function in patients homozygous for variant p.R102S was better when compared to patients homozygous for variant c.998+1G>A/p.?, although the former were older at baseline. Central retinal function was similar in patients homozygous for variant p.R102S and patients heterozygous for variants c.304C>A/p.R102S and c.2053G>A/p.V685M, although the latter were younger at baseline. Annual decline rates in central retinal function were small (0.015 logMAR/year).

Conclusions: We conclude that the severity of the different disease-causing PDE6A mutations in humans with respect to central visual function may be ranked as follows: c.2053G>A/p.V685M in homozygous state (most severe) > c.998+1G>A/p.? in homozygous state > c.304C>A/p.R102S and c.2053G>A/p.V685M in compound-heterozygous state > c.304C>A/p.R102S in homozygous state (mildest). The assessment of treatment efficacy in interventional trials will remain challenging due to small annual decline rates in central retinal function.

CONTROL ID: 3714121

SUBMITTER (NAME ONLY): Ioannis Pallikaris

TITLE: Intraocular Lens Stabilisation with a novel implant: One year follow up in a cohort of 120 patients

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.G. Pallikaris, O. Sahin, L. Leonidou, M. Modatsos, D. Liakopoulos, G. Louca, H. Ginis, EYEPCR B.V., GREECE|A. Elmassry, Alexandria University Faculty of Medicine, Alexandria, EGYPT|I.G. Pallikaris, Panepistemio Kretes Iatrike Schole, Heraklion, Crete, GREECE|

Commercial Relationships Disclosure: Ioannis Pallikaris: Commercial Relationship(s);Code C (Consultant/Contractor):EYEPCR B.V.;Code P (Patent):EYEPCR B.V.;Code F (Financial Support):EYEPCR B.V. | Ahmed Elmassry: Commercial Relationship(s);Code F (Financial Support):EYEPCR B.V. | Onurcan Sahin: Commercial Relationship(s);Code C (Consultant/Contractor):EYEPCR B.V.;Code P (Patent):EYEPCR B.V. | Loukia Leonidou: Commercial Relationship(s);Code C (Consultant/Contractor):EYEPCR B.V. | Manolis Modatsos: Commercial Relationship(s);Code E (Employment):EYEPCR | Dimitris Liakopoulos: Commercial Relationship: Code N (No Commercial Relationship) | Georgios Louca: Commercial Relationship: Code N (No Commercial Relationship) | Harilaos Ginis: Commercial Relationship(s);Code C (Consultant/Contractor):EYEPCR B.V.;Code P (Patent):EYEPCR B.V.

ABSTRACT BODY:

Purpose: To present safety and efficacy, clinical and surgical observations regarding a novel intracapsular implant

Methods: Ongoing prospective study of 120 patients with 12 months follow-up. The novel implant (fixOflex, EYE-PCR, Netherlands) is a hydrophilic acrylic ring (9.8mm diameter, 1.7mm thickens) injected through a 2.4mm incision prior to the intraocular lens (IOL) implantation. The optic of the IOL is secured in the ring's retainers. Patients were recruited following randomization at Alexandria El nour Eye Hospital. All patient received the same type of IOL (Tecnis ZCB00, J&J, NJ).

Results: Mean best corrected visual acuity and spherical equivalent was 0.92 ± 0.15 and -0.76 ± 0.86 respectively, 6 months postoperatively.

Mean postoperative anterior chamber depth was 4.26 ± 0.53 mm at six months follow up. Endothelial cell dencity at six months postoperatively was within normal limits (2268±432) after cataract surgery. No anterior chamber reaction or IOP changes were observed. Mean time for ring implantation was 1 min and 9 sec. No serious adverse events were observed. No Posterior Capsule Opacification (PCO) was observed (120 cases 6 months follow-up, 59 patients 1 year follow-up).

Conclusions: FixOflex provides an open capsule space for fast and safe IOL implantation providing postoperative stabilisation. The ring and IOL positioning is easy to control while additional minor manipulations are rarely needed.

CONTROL ID: 3714122

SUBMITTER (NAME ONLY): Jan Peterson

TITLE: Terminal e-Beam sterilization of Densomeres™ retains structural integrity and sustained bioactivity of bevacizumab in rabbit cornea model

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Peterson, W. Chen, B.M. Libin, Sustained Nano Systems LLC, Hollywood, Florida, UNITED STATES|P.K. Kaiser, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|J.M. Liebmann, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Jan Peterson: Commercial Relationship(s);Code C (Consultant/Contractor):Sustained Nano Systems LLC | WeiLiam Chen: Commercial Relationship(s);Code O (Owner):Sustained Nano Systems, EndoMedix | Peter Kaiser: Commercial Relationship(s);Code C (Consultant/Contractor):Sustained Nano Systems LLC | Barry Libin: Commercial Relationship(s);Code O (Owner):Sustained Nano Systems LLC | Jeffrey Liebmann: Commercial Relationship(s);Code O (Owner):Sustained Nano Systems LLC;Code C (Consultant/Contractor):Thea, Allergan, Genentech

ABSTRACT BODY:

Purpose: Terminal sterilization could reduce production time and costs for anti-angiogenic monoclonal antibodies (mAbs) needed for sustained ocular delivery in retinal diseases if they retain molecular integrity and prolonged in vivo bioactivity. After observing up to 12 months of sustained release and bioactivity in previous in vitro and in vivo tests, highly densified poly(lactic-co-glycolic acid) (PLGA) microspheres (Densomeres™) incorporating bevacizumab were tested again following e-Beam terminal sterilization for their integrity and sustained bioactivity using a rabbit corneal injury model.

Methods: Bevacizumab was incorporated into Densomeres that were resuspended in saline for injection through a 28-ga needle. Control Densomeres contained no active drug. Terminally sterilized doses using e-Beam were assessed for molecular integrity by SEC-HPLC and functional bevacizumab bioactivity in vivo. Six adult male New Zealand white rabbits (3 active, 3 control) were anesthetized and a 9-0 silk suture placed in one cornea of each animal to induce neovascular encroachment from the limbus. A single 0.5 mL subconjunctival injection with Densomeres was made at the same meridian. External photographs taken over 60 days to documented neovascularization were scored on a 0-5 scale by trained observers. If sutures came out during follow-up, they were replaced to maintain the neovascularization stimulus.

Results: Bevacizumab extracted from Densomere samples for SEC-HPLC before and after e-Beam sterilization matched the authentic reference bevacizumab [Fig. 1]. For e-Beam sterilized Densomeres, anti-angiogenic bioactivity persisted after the single injection through Day 60. Comparing controls to eyes receiving Densomeres with bevacizumab, the average difference in scores from Day 7 to Day 60 was 3.2 ± 0.5 [Fig. 2]. This difference matched the sustained effects observed for up to 12 months after a single injection using traditional Densomere preparations.

Conclusions: Compared to controls, e-Beam sterilized Densomeres™ containing the mAb bevacizumab exhibited both structural integrity and prolonged anti-VEGF bioactivity in vivo following a single injection in the rabbit corneal neovascularization model.

CONTROL ID: 3714124
SUBMITTER (NAME ONLY): Runjie Bill Shi
TITLE: Eye-Hand Movement Latency for Grasping Objects under Crowded Conditions in Early Glaucoma
SESSION TITLE: Visual Fields and Psychophysics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: R. Shi, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA| R. Shi, University of Toronto Institute of Biomedical Engineering, Toronto, Ontario, CANADA|G.E. Trope, Z. Butty, Department of Ophthalmology and Vision Sciences, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|G. Issashar Leibovitzh, L. Tarita-Nistor, Donald K Johnson Eye Institute, Krembil Research Institute, Toronto, Ontario, CANADA|E. Niechwiej-Szwedo, Department of Kinesiology and Health Sciences, University of Waterloo, Waterloo, Ontario, CANADA|
Commercial Relationships Disclosure: Runjie Bill Shi: Commercial Relationship: Code N (No Commercial Relationship) | Ewa Niechwiej-Szwedo: Commercial Relationship: Code N (No Commercial Relationship) | Graham Trope: Commercial Relationship: Code N (No Commercial Relationship) | Galia Issashar Leibovitzh: Commercial Relationship: Code N (No Commercial Relationship) | Ziad Butty: Commercial Relationship: Code N (No Commercial Relationship) | Luminita Tarita-Nistor: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: To investigate whether patients with pre-perimetric glaucoma have different eye-hand latency in grasping tasks under crowding. Hypotheses: 1) These patients have longer latencies than controls and 2) crowding affects latency.
Methods: 4 patients from the Glaucoma Clinic (age: 53–75 years) and 3 healthy controls (age: 41–55 years) participated. For patients, their visual fields' mean deviation, average retinal nerve fiber thickness, and vertical cup-to-disc ratio ranged from −0.89 to +3.3 dB, 64 to 94 μm and 0.52 to 0.80 (mean: +0.86 dB; 81 μm; 0.67), respectively. Participants performed an object gasping task with eye and hand movement tracking (EyeLink and Leap). The better eye with at least 20/50 near-distance visual acuity was tracked. A vertical whiteboard was placed with only one white target object (control condition), or the white target surrounded by four colored objects along the azimuth. The crowding objects were set up either 5° (narrow crowding) or 10° apart (wide crowding). The target object was placed at the center or at the ±5° (or ±10°) position. At start of each trial, a board with a fixation target hid the whiteboard. After 3 seconds, this board was removed rapidly by the experimenter. The participant grasped the white target object and moved it to a marked target location as quickly and accurately as possible. Each crowding condition was repeated 12 times to obtain mean eye latency (first reported saccade by EyeLink after revealing the whiteboard) and reach latency (when hand velocity exceeded 10 mm/s). The difference between the two was defined as the eye-hand latency.
Results: Glaucoma subjects had on average (±standard error) +105±89 ms longer eye-hand latency than controls across all conditions. This difference was +116±92, +111±93, and +88±84 ms in control, wide, and narrow conditions, respectively. However, crowding had no effect on latency: the averages were 237±70, 256±41, and 272±35 ms in controls, and 354±65, 366±73, 360±66 ms in glaucoma subjects. Latency did not correlate with age (r=0.09, p=0.85).
Conclusions: Patients with early glaucoma have longer eye-hand latency (i.e., they initiate hand movement slower) than controls in grasping tasks. Crowding appears to have no effect on latency. Further limb kinematic parameters will be investigated.

CONTROL ID: 3714125

SUBMITTER (NAME ONLY): Mile Brujic

TITLE: Corneal Permeability of Pilocarpine HCl 1.25% with Varying pH Formulations

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Brujic, Premier Vision Group, Bowling Green, Ohio, UNITED STATES|J. Giyanani, W. Chang, V. Waknis, W. Pack, Y. Shabaik, J. Seal, A. Gore, Allergan, an AbbVie company, Irvine, California, UNITED STATES|K.K. Nichols, University of Alabama at Birmingham, School of Optometry, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Mile Brujic: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan (an AbbVie company), Abb Optical, Alcon, Art Optical, Bausch + Lomb, Blephex, Contamac, CooperVision, CSEye, Euclid, Eyevance, Horizon, Johnson & Johnson, Kala, Luneau, Novartis, Optovue, Oyster Point, RVL, Sight Science, Sun Pharma, Tarsus, Tangible Science, Walman Optical, Zea Vision | Jaya Giyanani: Commercial Relationship(s);Code E (Employment):AbbVie Inc | William Chang: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Vrushali Waknis: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Weston Pack: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Yumna Shabaik: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Jennifer Seal: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Anu V Gore: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Kelly Nichols: Commercial Relationship(s);Code F (Financial Support):Allergan (an AbbVie company), Kala, Tear Science;Code C (Consultant/Contractor):Allergan (an AbbVie company), Alcon, Aerie, Axim, Bruder, Dompe, HanAll Bio, Kala, Novartis, Osmotica, Oyster Point, Sight Sciences, Tear Film Innovations, Thea, Tarsus and Visionology

ABSTRACT BODY:

Purpose: Evaluate the in vitro corneal permeability of Pilocarpine HCl 1.25% with varying pH formulations.

Methods: Cornea permeability was assessed using Lonza Human Corneal Epithelial Cells (HCEC) grown in a 24-well Transwell cell culture insert. The permeability of 5 formulations of Pilocarpine HCl 1.25% topical solution with varying pH levels (pH = 4.3, 5.1, 6.06, 7.16, and 7.96) were examined.

Results: Mean Apparent Permeability (P_{app}) increased as pH increased (0.330, 0.431, 1.19, 0.670, 5.03, 7.02 x 10^{-6} cm/s) with a dramatic increase in pH above 7 (Figure 1). A significant decrease in Transepithelial Electrical Resistance (TEER) values at 120 minutes was observed compared with baseline for all tested formulations except mannitol control. Despite this decrease, limited permeability of the lower pH formulations suggest that the barrier function of the cell layers was not compromised during the study.

Conclusions: The increase in permeability from pH 4.3 to pH 7.96 may be attributed to increasing un-ionized form of pilocarpine (~0.07% un-ionized at pH 4.3 vs. ~87.6% un-ionized at pH 7.96) in the formulation, as permeability across corneal epithelial layers favor un-ionized molecules. Increased permeability could translate into higher levels of pilocarpine in the anterior chamber and greater or longer activation of the iris sphincter and/or ciliary muscle, the target tissues of Pilocarpine HCl 1.25% to induce the pinhole effect and increase depth of focus.

CONTROL ID: 3714126

SUBMITTER (NAME ONLY): Brittany Tsou

TITLE: Prevalence of falls and fall-related outcomes in older adults with diagnoses of ocular disease

SESSION TITLE: Vision Function, Aging Outcomes, and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Tsou, D. Huh, P.Y. Ramulu, F. Woreta, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Brittany Tsou: Commercial Relationship: Code N (No Commercial Relationship) | Dana Huh: Commercial Relationship: Code N (No Commercial Relationship) | Pradeep Ramulu: Commercial Relationship: Code N (No Commercial Relationship) | Fasika Woreta: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To provide nationally-representative epidemiological data on falls and fall-related outcomes among older Americans with ocular disease.

Methods: Cross-sectional analysis of National Health and Aging Trends Study (NHATS) data from 2011 to 2017. Observations were obtained from annual interviews of participants. Ocular disease, falls, and fall-related injuries were identified through International Classification of Diseases (ICD) codes. Diagnoses of ocular disease included age-related macular degeneration (AMD), diabetic eye disease, retinal vascular occlusions, cataract, corneal disease, glaucoma, disorders of refraction and accommodation, and visual disturbance and blindness. Risk factors for falls and fall-related outcomes were identified through multivariable analysis.

Results: A total of 24,479 observations were contributed by 7,423 participants with an average number of 3.3 observations per person. There were 9,900 (40.4%) observations from participants with a diagnosis of ocular disease. Of 7,423 participants, 1,379 (18.6%) had >1 fall in the past year, 1,023 (13.8%) had any fall in the past month, 2,578 (34.7%) reported fear of falling (FoF), 1,047 (14.1%) reported FoF limiting activity, and 1,051 (14.2%) suffered fall-related injuries. Risk factors associated with falls and fall-related outcomes included being older, white, requiring a proxy correspondent, and having a higher body mass index or medical comorbidities. AMD was associated with fall-related injuries (OR 1.33; 95% CI, 1.08-1.63, p=0.007). Diabetic eye disease was associated with >1 fall in the past year (OR 1.62; 95% CI, 1.04-2.51, p=0.031), FoF (OR 1.77; 95% CI, 1.28-2.44, p=0.001), FoF limiting activity (OR 1.82; 95% CI, 1.23-2.67, p=0.002), and fall-related injuries (OR 1.64; 95% CI, 1.11-2.42, p=0.014). Visual disturbance and blindness were associated with >1 fall in the past year (OR 1.91; 95% CI, 1.01-3.64, p=0.048), any fall in the past month (OR 1.97; 95% CI, 1.11-3.49, p=0.020), FoF (OR 2.08; 95% CI, 1.13-3.81, p=0.018), and fall-related injuries (OR 2.95; 95% CI, 1.66-5.25, p<0.001).

Conclusions: Various diagnoses of ocular disease including AMD, diabetic eye disease, and visual disturbance and blindness were associated with falls, FoF, FoF limiting activity, and fall-related outcomes.

CONTROL ID: 3714128

SUBMITTER (NAME ONLY): Molly Naylor

TITLE: CNG Channel Trafficking to the Rod Outer Segment is Dependent upon Peripherin-2

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Naylor, J. Martínez-Márquez, J.N. Pearring, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Molly Naylor: Commercial Relationship: Code N (No Commercial Relationship) | Jorge Martínez-Márquez: Commercial Relationship: Code N (No Commercial Relationship) | Jillian Pearring: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The outer segment of rod photoreceptors is composed of two distinct membrane subdomains: discs and plasma membrane. We are interested in understanding how membrane proteins are trafficked to these two subdomains. One resident outer segment plasma membrane protein is the cyclic nucleotide-gated (CNG) channel. It was previously reported that in peripherin-2 knockout (Rds) mice the CNGβ1 subunit is absent from rods, suggesting that CNGβ1 stability or trafficking to the outer segment requires peripherin-2 (Prph2). We recently showed that the CNG channel travels by a conventional pathway through the Golgi, while it is established that Prph2 uses an unconventional pathway bypassing the Golgi. Together, these data suggest that either Prph2 and CNGβ1 interact before segregating into separate pathways or the Prph2/Rom-1 complex known to traffic through the Golgi facilitates CNGβ1 delivery. We investigated both possibilities to understand how Prph2 is engaged in CNG channel delivery to the outer segment.

Methods: Rds, Rom1$^{-/-}$, and C57Bl6J mice were analyzed. DNA constructs were introduced in Rds rods by standard in vivo electroporation. Fixed agarose retinal sections were immunofluorescently stained and imaged by confocal microscopy. Retinal lysates were deglycosylated using PNGase F and EndoH enzymes and analyzed by Western blot

Results: We overexpressed a MYC-tagged CNGβ1 in Rds rods and found it was trapped in internal membranes, but CNGβ1 localization was restored to the outer segment when full-length FLAG-tagged Prph2 was expressed. These data are consistent with a trafficking defect and not protein instability. To determine whether the CNG channel is trafficked with the Prph2/Rom1 complex, we stained Rom1$^{-/-}$ retinas and found the CNG channel was properly localized in the outer segment. This suggests CNGβ1 and Prph2 are engaged before pathway segregation, leading us to investigate which molecular feature of Prph2 is required for CNGβ1 delivery. We expressed Prph2/Rhodopsin chimeras containing either the Prph2 C-terminus or tetraspanin core and show that both Prph2 chimeras are capable of trafficking CNG to the outer segment.

Conclusions: We conclude that Prph2, and not the Prph2/Rom1 complex, is necessary and sufficient for CNGβ1 trafficking to the outer segment. Additionally, we determine that both the Prph2 tetraspanin core and C-terminus can facilitate CNGβ1 outer segment delivery.

CONTROL ID: 3714130

SUBMITTER (NAME ONLY): Hangjing Wu

TITLE: Optic neuropathy associated with TGFβ dysregulation in mice with a glaucoma-causative mutation of Adamts10

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Wu, R.W. Kuchtey, J. Kuchtey, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Hangjing Wu: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Kuchtey: Commercial Relationship: Code N (No Commercial Relationship) | John Kuchtey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Beagle dogs homozygous for a G661R mutation in ADAMTS10 develop primary open angle glaucoma. ADAMTS10 is a secreted matrix metalloproteinase that interacts with fibrillin-1 and is thought to promote formation of fibrillin microfibrils in the extracellular matrix. Here, we established a mouse model carrying the G661R mutation of Adamts10 (Adamts10$^{G661R/G661R}$) to investigate its ocular phenotypes related to glaucoma and to explore possible functions of ADAMTS10.

Methods: ADAMTS10 and fibrillin-1 expression were examined by immunohistochemistry. Retinal ganglion cell (RGC) function was assessed by positive scotopic threshold response (pSTR) in flash electroretinogram (ERG). Cross-sections of the optic nerves from mice at 3, 6 and 24 months of age were stained with PPD for manual axon quantification using ImageJ. Retinal apoptotic cells at postnatal day 10 were examined by TUNEL assay.

Results: ADAMTS10 immunostaining labeled the retinal nerve fiber layer and RGC axons in the optic nerve where fibrillin-1 was not detected, suggesting fibrillin-independent function for ADAMTS10 in these structures. Adamts10$^{G661R/G661R}$ mice had reduced pSTR amplitude, indicating RGC dysfunction. The reduced RGC function in Adamts10$^{G661R/G661R}$ mice coincided with RGC axon structural changes manifested as smaller optic nerves and fewer optic nerve axons, which may contribute to glaucoma. The reduced number of optic nerve axons for Adamts10$^{G661R/G661R}$ mice occurred early, suggesting developmental deficits. Subsequent experiments found increased apoptosis in the retina of Adamts10$^{G661R/G661R}$ mice during postnatal development, which could result in fewer RGCs produced, accounting for fewer optic nerve axons in adulthood. Consistent with a protective effect of TGFβ signaling against apoptosis during retinal development as shown previously by others, we found increased apoptosis accompanied by decreased TGFβ signaling in the developing retina of Adamts10$^{G661R/G661R}$ mice.

Conclusions: The G661R mutation of Adamts10 causes glaucoma-related phenotypes at early age and decreased TGFβ signaling in the developing retina, implying a role of ADAMTS10 in retinal development via regulation of TGFβ signaling.

CONTROL ID: 3714131

SUBMITTER (NAME ONLY): Salwah Rehman

TITLE: Correlation of hyperautofluorescent ring with outer retinal anatomy in rod-cone dystrophy

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rehman, R.E. MacLaren, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|S. Rehman, R.E. MacLaren, University of Oxford Nuffield Laboratory of Ophthalmology, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure: Salwah Rehman: Commercial Relationship: Code N (No Commercial Relationship) | Robert MacLaren: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Rod cone dystrophies typically result in progressive concentric loss of visual field which correlates closely to the photoreceptor degeneration as it progresses from the periphery. A recent study noted that photoreceptors at the edge of the degeneration may regrow outer segment processes following successful gene therapy, resulting in some reversal of field loss (Cehajic-Kapetanovic et al., 2020). Within this zone, photoreceptors exist in the outer nuclear layer but without defined inner or outer segment processes. On imaging with fundus autofluorescence (FAF), this zone of partially degenerate photoreceptors can be identified by a fluorescent ring. We, therefore, explored this ring sign further in order to understand its anatomical relationship to outer retinal degeneration.

Methods: We identified 59 patients who had rod-cone dystrophy and fluorescent rings on FAF retrospectively from our clinical database and categorised the rings according to disease progression. The images were analysed using measurements of horizontal fluorescent ring radius from fovea along with ellipsoid zone (EZ) and external limiting membrane (ELM) line width from spectral domain optical coherence tomography (OCT).

Results: The majority of patients had mutations in RPGR (18) or USH2A (18) and the remainder had identified mutations in RHO (5), RP1 (5), SNRNP200 (4), PRPF8 (2), EYS (2), FLVCR1 (2), RP2 (1) and PRPF31 (1). Three distinct stages of ring were evident: early-stage large irregular ring involving the optic disc,10(17%), mid-stage circumferential fluorescent ring around the fovea, 19(32%), and late-stage pattern of diffuse irregular hyperautofluorescence in the central macula, 30 (51%). A high correlation between internal ring radius to EZ width (r=0.94) and external ring radius to ELM width (r=0.97) in all 29 patients with early-mid stage of disease was evident. Fluorescent ring thickness was also strongly correlated with loss of EZ on OCT (r=0.92) in these patients.

Conclusions: Our results suggest that patients with rod-cone dystrophy may exhibit a pattern of fluorescent rings on FAF. Early and mid-stage rings correlated with inner and outer segment loss and got smaller as the degeneration progressed. This may represent a useful biomarker with which to assess the progression of retinitis pigmentosa and may represent a zone in which reversal of visual field loss is most likely to be seen following gene therapy.

CONTROL ID: 3714132

SUBMITTER (NAME ONLY): Megan Priem

TITLE: Pharmacokinetics of a Hydrogel-based Besifloxacin Intracanalicular Insert in Canines

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Priem, A. Desai, C. Patel, C.D. Blizzard, P.K. Jarrett, M. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Megan Priem: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Ankita Desai: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Chintan Patel: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Charles Blizzard: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Peter Jarrett: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix | Michael Goldstein: Commercial Relationship(s);Code E (Employment):Ocular Therapeutix

ABSTRACT BODY:

Purpose: Topical ocular antibiotics are often prescribed for antimicrobial prophylaxis following ophthalmic surgery or for the treatment of bacterial conjunctivitis. Sustained-release delivery of antibiotics may overcome some limitations of topical therapy such as reliance on patient self-dosing. Here we evaluate the pharmacokinetics of besifloxacin delivered from a biodegradable hydrogel intracanalicular insert in a canine model.

Methods: A hydrogel besifloxacin intracanalicular insert was placed bilaterally into the inferior canaliculus of 20 beagle dogs on day 0. After presence of the insert in the canaliculus was confirmed visually, tear fluid was collected from n=10 eyes with pre-cut 10 mm Schirmer test strips at 0.5, 1, 2, 4, 8 hours, and 1, 3, 7, 10, 14, 21, 28, 35, and 42 days post-insertion. Tear fluid samples were analyzed for besifloxacin by liquid chromatography tandem mass spectrometry.

Results: Mean besifloxacin levels in tear fluid samples post-insertion are presented in Figure 1. Mean besifloxacin levels in tear fluid samples demonstrated gradual tapering over time and clearance from the tear fluid by 35-42 days. All $AUC_{0\text{-}24}/MIC_{90}$ values were above 100 for 21 days for H. influenzae, S. aureus, S. epidermis, and S. pneumoniae suggesting the insert produced bactericidal levels of besifloxacin for common ocular isolates of conjunctivitis.

Conclusions: A hydrogel-based intracanalicular insert with besifloxacin produced clinically effective drug levels capable of killing the most common isolates of bacterial conjunctivitis for 21 days. A single dose besifloxacin intracanalicular insert may reduce the need for patients to self-administer antimicrobial therapy.

CONTROL ID: 3714133

SUBMITTER (NAME ONLY): Sally Ong

TITLE: Intranasally Administered Insulin Reaches the Retina and Choriocapillaris in Rats

SESSION TITLE: Neuron rescue and regeneration in the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Ong, J.R. Gustafson, J. Konstantopoulos, R.M. Sappington, Ophthalmology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|S. Craft, Gerontology and Geriatric Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Sally Ong: Commercial Relationship: Code N (No Commercial Relationship) | Jenna Gustafson: Commercial Relationship: Code N (No Commercial Relationship) | Joanne Konstantopoulos: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Craft: Commercial Relationship: Code N (No Commercial Relationship) | Rebecca Sappington: Commercial Relationship(s);Code C (Consultant/Contractor):SAJE Pharma LLC

ABSTRACT BODY:

Purpose: Insulin treatment decreases neurodegeneration associated with diabetes. Unfortunately, the risks of hypoglycemia and infection limit the use of systemic insulin as a neuroprotective agent in early diabetic retinopathy. Recent evidence suggests that intranasal delivery of insulin penetrates the brain. Here we examined whether intranasal delivery could serve as a non-invasive route of administration for insulin to the retina and choroid.

Methods: Female Sprague Dawley rats were deprived of food for 12-18 hours and anesthetized with IP ketamine/xylazine. Rats (n = 4) were placed in the supine position on a heating pad (37 degrees Celcius) and one 20ul drop of FITC-insulin (total dose 6 Units/40ul saline) was pipetted into each naris 5 minutes apart. The control group (n = 4) received equivalent doses of saline. One hour after the first drop was intranasally given, rats were sacrificed, enucleated, and the brain was removed. The presence of FITC insulin was examined in cryosections of brain and whole eye, using confocal microscopy. Deposition of FITC-insulin in neural retina and choroid was further characterized by immunohistochemical co-localization studies.

Results: Sixty minutes after intranasal administration of FITC-insulin, fluorescent signal was evident in both ocular and brain tissue. Ocular and brain tissue from the control group was negative for FITC signal. FITC patterning indicated deposition of insulin predominantly in the retinal pigment epithelium and near outer segments of rods and cones. Lower intensity deposition was observed in the choriocapillaris, the inner and outer plexiform layers, and the nerve fiber layer. Brain sections, which served as positive controls, confirmed the deposition of intranasal insulin in the hippocampus, cortex, and hypothalamus.

Conclusions: To the best of our knowledge, this is the first study to demonstrate that intranasal insulin is delivered to the retina and choriocapillaris within one hour of administration. These data suggest that intranasal delivery could be a lower risk alternative for early or supplemental insulin therapy in diabetic retinopathy.

CONTROL ID: 3714135

SUBMITTER (NAME ONLY): Naren G Kumar

TITLE: Transcriptional adaptations of Pseudomonas aeruginosa upon exposure to human tear fluid

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. G Kumar, S. Abboud, L. Tabor, M. Grosser, Y. Wu, M. Mettrucio, D.J. Evans, S.M. Fleiszig, Herbert Wertheim School of Optometry and Vision Sciences, University of California Berkeley, Berkeley, California, UNITED STATES|D.J. Evans, Touro University California, Touro University California, Vallejo, CA, US, academic/campus, Vallejo, California, UNITED STATES|

Commercial Relationships Disclosure: Naren G Kumar: Commercial Relationship: Code N (No Commercial Relationship) | Sara Abboud: Commercial Relationship: Code N (No Commercial Relationship) | Lauren Tabor: Commercial Relationship: Code N (No Commercial Relationship) | Melinda Grosser: Commercial Relationship: Code N (No Commercial Relationship) | Yvonne Wu: Commercial Relationship: Code N (No Commercial Relationship) | Matteo Mettrucio: Commercial Relationship: Code N (No Commercial Relationship) | David Evans: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Fleiszig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The healthy cornea is usually resistant to infection. While the tear film covering the ocular surface contains a multitude of antimicrobial factors, the common corneal pathogen Pseudomonas aeruginosa can survive and replicate in human tear fluid in vitro. RNA-sequencing studies performed in our laboratory have shown numerous alterations to gene expression in P. aeruginosa when exposed to human tear fluid, and many suggest changes to the bacterial outer membrane. Here, we sought to identify P. aeruginosa genes required for survival in tear fluid by characterizing genes whose lack of function resulted in bacterial cell death in tear fluid.

Methods: A Tn-Sequencing experiment was designed, in which a pool of transposon mutants with mutations in non-essential genes, was sequentially passaged in tear fluid for 96 h at 24 h intervals. 701 genes were identified to be conditionally essential for survival in tear fluid. Those genes were overlayed onto the RNA-sequencing dataset containing 331 differentially-expressed genes to identify only those genes that were important for survival in tear fluid and differentially-expressed ($p < 0.05$, Log_2 fold-change > 8). Enrichment analysis was performed to furhter identify groups of similarly acting bacterial genes required for survival in tear fluid.

Results: This approach yielded 75 candidate genes with potential involvement in the mechanisms underlying P. aeruginosasurvival in tear fluid. These conditionally-essential genes were associated with cell wall remodeling (arn operon, 14-fold enrichment), glycerol uptake (glp operon, 30-fold enrichment), dicarboxylate transport (dct operon, 31-fold enrichment), 5 two-component systems that regulate bacterial motility (cheY), cell wall biosynthesis and biofilm formation, and include a novel putative two-component sensor histidine kinase.

Conclusions: These data suggest that P. aeruginosaovercomes the antimicrobial activity of tear fluid by altering the expression of genes involved in the remodeling of the bacterial cell wall, overcoming nutritional limitation via uptake of alternative metabolites, and likely other adaptive responses.Targeting these adaptive changes could facilitate development of novel strategies to manage P. aeruginosa infections at the ocular surface and beyond.

CONTROL ID: 3714136

SUBMITTER (NAME ONLY): Sanghoon Kim

TITLE: OCT-guided variable-spot ERG enabled spatially resolved measurements to assess retinal function in a selected and integrated region

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Kim, M. Carlson, S. Batabyal, S. Mohanty, Nanoscope Instruments, Inc, Bedford, Texas, UNITED STATES|S. Aparicio-Domingo, K. Li, V. Canto Soler, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited retinal disorders and dry age-related macular degeneration undergo the progressive dysfunction and death of photoreceptors at different rate and locations. However, isolated functional characterization of specific regions of the retina, as for example geographic atrophy lesions or therapeutically treated areas, is often challenged by the lack of spatial targetability, and collateral bleed-through responses of nearby cells. Further, different cell and gene therapy approaches may target discrete regions of the retina and photoreceptor types. Therefore, we developed optical coherence tomography (OCT) guided variable-spot electroretinogram (vsERG) platform to enable spatially resolved and isolated measurement of retina function with minimal response from unintended region(s).

Methods: In the novel Nanoscope Instruments' NS-NEEL OCT guided vsERG platform, the stimulation light path for ERG and OCT are combined such that the tunable lens can deliver stimulation spot sizes ranging from 30 μm to 4 mm. Also, the precise scanning optics enable unrestricted placement of the stimulation spot on the retina. ERG responses from normal and photoreceptor-lacking areas of the rat and pig retina were measured. Different stimulation spot sizes were used with pre-selected wavelengths (455, 530 and 630 nm) at various intensities to determine functional responses from rods and the different types of cones.

Results: VsERG measurement showed reduced ERG response from regions lacking photoreceptors compared to normal retinal regions. Both, cone and rod response (detected with photopic and scotopic stimulation respectively), exhibited lower ERG-signals in the photoreceptor-degenerated retinal regions. In addition, vsERG recording from different types of cones produced unique characteristic responses based on stimulation wavelength (blue, green and red), which decreased concomitantly with decreased size of the stimulated retinal area.

Conclusions: Our results demonstrate that OCT-guided vsERG with selected stimulation wavelengths is suitable for functional evaluation of different types of photoreceptors in normal and diseased retina in a highly defined region with minimal contribution from adjacent areas. OCT guided vsERG based monitoring of physiological function will enable improved characterization of retinal degenerative diseases and evaluation of therapeutic interventions.

CONTROL ID: 3714137

SUBMITTER (NAME ONLY): Varalakshmi Wuyyuru

TITLE: Vitreous Flow Rate of 25-Gauge and 27-Gauge Dual-Cutting 20,000CPM Beveled Vitrectomy Probes during Vitreous Removal

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Wuyyuru, K. Phan, Y. Zhu, C. Garufis, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Varalakshmi Wuyyuru: Commercial Relationship(s);Code E (Employment):Alcon | Kevin Phan: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon | Ying Zhu: Commercial Relationship(s);Code E (Employment):Alcon | Carrie Garufis: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: 1) To evaluate the vitreous flow rate of the 25+® Gauge (GA) and 27+® GA dual cutting, 20,000 cuts per minute (cpm) beveled vitrectomy probes under various system settings; 2) Compare the performance of the 20K beveled probes with previous generation 10K beveled probes.

Methods: The 25+ GA and 27+ GA HYPERVIT® beveled20K vitrectomy probes were driven by the CONSTELLATION® Vision System (Alcon Vision, LLC.) to aspirate porcine vitreous. A precision balance (Mettler Toledo, XS) was used to chart and record mass change during aspiration over 1 min.

Flow rates were evaluated ranging from 2.5K to 20K cpm. Three duty cycles were evaluated for each cut rate: core, 50/50, and shave. Vacuum was kept constant at 650 mmHg. For each probe gauge, 6 probes were used to measure flow rate and each duty cycles' cut rate was tested at least 3 times. Average flow rate was calculated for each setting and statistical analysis was performed using Welch's T-Test with a statistical significance level of $p<0.05$.

Results: At the maximum cut rate for the three duty cycles of core, 50/50, and shave, the 25+®GA probe flow rates were 3.52±0.26, 3.47±0.26, and 3.64±0.15 cc/min, respectively. Corresponding flow rates for the 27+®GA probes were 2.17±0.16, 2.09±0.18, and 2.07±0.22 cc/min, respectively. Statistical analysis indicated significant differences in flow rate for cut rates less than 7.5K cpm compared to the maximum cut rate under same duty cycles and vacuum ($p<0.05$) and no significant difference was shown between each duty cycle ($p<0.05$) for both probe gauges.

When operating at maximum cut rate of 20K cpm at core duty cycle, the 25+®GA and 27+®GA HYPERVIT® beveled achieved flow rates 23.61% and 19.63%, respectively, higher than the previous generation 25GA and 27GA Advanced ULTRAVIT® probe flow rates at maximum cut rate of 10K cpm, ($p<0.05$).

Conclusions: The aspiration flow rate did not significantly change by duty cycle for all cut rates for both 25+®GA and 27+®GA HYPERVIT® beveled 20K vitrectomy probes. In addition, for all probes, aspiration flow rates increased as cut rate increased. In comparison with previous generation Advanced ULTRAVIT® probes, the HYPERVIT® beveled vitrectomy probes achieved higher flow rates.

CONTROL ID: 3714138

SUBMITTER (NAME ONLY): Zer Keen Chia

TITLE: Comparison of a virtual reality-based visual field test to conventional perimetry and OCT

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Chia, A.W. Kong, M.L. Turner, M. Deiner, Y. Ou, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|B.T. Backus, Vivid Vision, Inc., San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Zer Keen Chia: Commercial Relationship: Code N (No Commercial Relationship) | Alan Kong: Commercial Relationship: Code N (No Commercial Relationship) | Marcus Turner: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Backus: Commercial Relationship(s);Code E (Employment):Vivid Vision, Inc.;Code P (Patent):Vivid Vision, Inc.;Code I (Personal Financial Interest):Vivid Vision, Inc. | Michael Deiner: Commercial Relationship: Code N (No Commercial Relationship) | Yvonne Ou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To 1) assess the correlation between a new virtual reality visual field test, Vivid Vision Perimetry (VVP-10), and standard automated perimetry (SAP) in a global, sector-, and pointwise manner; 2) assess the structure-function relationship between VVP-10 and OCT; and 3) assess the test-retest variability of VVP-10

Methods: Subjects with glaucomatous visual field defects were remotely trained to take the VVP-10 test and proceeded to take 10 tests over 14 days. VVP-10 response rate (fraction seen) at each point and SAP results including mean deviation (MD) and mean sensitivity (MS) at each point were recorded. Retinal nerve fiber layer thickness (RNFLT) at the optic nerve head was also recorded for each subject. Pearson correlation coefficients and the 95% confidence intervals were calculated for VVP-10 overall fraction seen vs SAP MD. Similar correlation coefficients were calculated for sector- and pointwise comparisons of VVP-10 average fraction seen vs SAP MS and structure-function analyses of RNFLT vs SAP MS and VVP-10 average fraction seen by sector. Test-retest variability was assessed with the intraclass correlation coefficient and a Bland-Altman plot of odd- vs even-numbered tests.

Results: A total of 36 eyes from 19 subjects were included in the study. However, one subject who was unable to take the test properly and reproduce accurate results was identified as an outlier and excluded. The global correlation of VVP-10 overall fraction seen vs SAP MD was 0.90 (95% CI [0.80 – 0.96]). Sector-wise correlations between VVP-10 average fraction seen vs SAP MS ranged from 0.31 – 0.95; pointwise correlations ranged from 0.11 – 0.92. The correlation between RNFLT vs VVP-10 overall fraction seen was 0.49 [0.22 – 0.73] with sector-wise correlations ranging from 0.12 – 0.65. The correlation between RNFLT vs SAP MD was 0.57 [0.36 – 0.76], and sector-wise correlations of RNFLT vs SAP MS ranged from -0.14 – 0.62. The ICC was 0.97 [0.95 – 0.98] and one eye fell outside of the lower level of agreement in the Bland-Altman plot.

Conclusions: Strong concordance exists between VVP-10 and SAP in a global, sector-, and pointwise manner. VVP-10 also demonstrates similar correlation with RNFLT compared to SAP. Finally, VVP-10 exhibits excellent test-retest variability, and its portable nature allows for remote testing and monitoring of glaucomatous field progression.

CONTROL ID: 3714140

SUBMITTER (NAME ONLY): William Bachman

TITLE: Role of Brg1/SMARCA4 chromatin remodeling protein in the expression of genes involved in actin cytoskeletal organization and cell adhesion in the trabecular meshwork cells.

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Bachman, R. Maddala, C. Eldawy, N.P. Skiba, V. Rao, Opthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|V. Rao, Pharmacology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: William Bachman: Commercial Relationship: Code N (No Commercial Relationship) | Rupalatha Maddala: Commercial Relationship: Code N (No Commercial Relationship) | Camelia Eldawy: Commercial Relationship: Code N (No Commercial Relationship) | Nikolai Skiba: Commercial Relationship: Code N (No Commercial Relationship) | Vasantha Rao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To understand how dexamethasone influences the expression of actin cytoskeletal, contractile, and fibrogenic proteins in trabecular meshwork cells, in this study we focused on identifying the upstream regulators of gene expression in dexamethasone treated cells.

Methods: Human TM cells treated with dexamethasone (Dex, 0.5 μM) for 24 hrs, 5 and 7 days along with their respective controls were extracted for the nuclear protein fraction and analyzed for the differential profile of proteins by non-label quantitative LC-MS-MS proteomics. Distribution and changes in Brg1 levels in TM cells treated with Dex were evaluated by immunofluorescence and immunoblot analyses. Effects of Brg1 inhibition and deficiency on the levels of client proteins in TM cells were determined using a chemical inhibitor (PFI-3) and siRNA of Brg1, respectively.

Results: The protein levels of Brg1/SMARCA4, the catalytic subunit of the SWI/SNF family of chromatin remodeling complex, were significantly increased in the Dex treated TM cell nuclear protein fraction compared to control cells based on mass spec and immunoblot analyses. Brg1, an actin binding nuclear protein was distributed predominantly in the nucleus. Brg1 and several of other components of the SWI/SNF complex were readily detectable in the cytoskeletome fraction of the human TM cells indicating an association between the SWI/SNF chromatin-remodeling complex and nucleoskeletal actin and actin related proteins. Inhibition of Brg1 activity and suppression of Brg1 expression significantly decreased the protein levels of cell adhesion proteins (ArgBP2, CAP/ponsin), contractile protein (CNN3), fibrogenic protein (CTGF) and MICAL2 (regulator of SRF/MRTF-A transcriptional activity) and glypican-4 (regulator of Wnt signaling) in human TM cells.

Conclusions: This study identifies Brg1, a catalytic subunit of the SWI/SNF family chromatin-remodeling complex as one of the upstream regulators of the expression of actin cytoskeletal, contractile and cell adhesion proteins in dexamethasone treated human TM cells. Thus, Brg1 and the SWI/SNF chromatin-remodeling complex may be promising targets to lower intraocular pressure in steroid-induced glaucoma.

CONTROL ID: 3714141

SUBMITTER (NAME ONLY): Mengyu Wang

TITLE: Improving Circumpapillary Retinal Nerve Fiber Layer Thickness (RNFLT) Norms with Retinal Anatomy

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wang, T. Elze, K. Wirkner, J. Thiery, M. Loeffler, C. Engel, T. Kirsten, F.G. Rauscher, Leipzig Research Centre for Civilization Diseases (LIFE), Leipzig University, Leipzig, Saxony, GERMANY|M. Wang, T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|T. Peschel, K. Wirkner, M. Loeffler, C. Engel, F.G. Rauscher, Institute for Medical Informatics, Statistics, and Epidemiology (IMISE), Leipzig University, Leipzig, Saxony, GERMANY|L.R. Pasquale, Eye and Vision Research Institute, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|L.Q. Shen, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Thiery, Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Leipzig University Medical Center, Leipzig, Saxony, GERMANY|T. Kirsten, Medical Informatics Center - Department of Medical Data Science, Leipzig University Medical Center, Leipzig, Saxony, GERMANY|

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ABSTRACT BODY:

Purpose: Current circumpapillary RNFLT norms only adjust for age, gender and ocular magnification. We aim to improve the circumpillary RNFLT norms with retina anatomy.

Methods: From the population-based Leipzig Research Center for Civilization Diseases (LIFE) adult study, we include data with: (a) no retinal pathological findings on fundus images; (b) image quality ≥ 20 dB, average number of B-scans ≥ 50, and no more than 5% missing or unreliable RNFLT measurements among the 768 locations of Spectralis optical coherence tomography (OCT) scans. The retinal anatomy was represented by the 2D inner limiting membrane (ILM) contour map and scanning laser ophthalmoscopy (SLO) fundus photo at the optic nerve head. Feature exaction was performed by principal component analysis followed by uniform manifold approximation and projection. Linear regression was applied to associate the ILM and SLO features with pointwise RNFLTs adjusting for age, gender and ocular magnification. One eye per subject was randomly selected for regression analyses. Model selection based on Bayesian information criteria (BIC) was used to remove redundant features from the linear models. Adjusted r-squared and BIC values penalized for linear model complexity were used to measure the linear models' accuracies.

Results: 7,285 eyes from 7,285 subjects (56.1 ± 12.2 years; 53.3% are female) were included. Figure 1 (a) and (b) shows the R^2 improvement by using ILM and SLO features on top of age, gender and ocular magnification, respectively. Additionally using ILM and SLO features strongly (BIC improvement ≥ 6) improved RNFLT norms at 85.4% and 96.5% of the 768 locations with average R^2 improvement of 0.026 (max: 0.051) and 0.029 (max: 0.065) compared with average R^2 of 0.042 (max: 0.082) using age, gender and ocular magnification alone, respectively. Combining ILM and SLO features (Figure 2) provided more accurate personal norms than using SLO and ILM separately, which was supported by RNFLT norm improvement (BIC improvement ≥ 6) at 79.9% and 93.2% of the 768 locations with average R^2 improvement of 0.017 (max: 0.032) and 0.020 (max: 0.049).

Conclusions: Adjusting for retinal anatomy represented by ILM and SLO imaging features substantially improved personal circumpapillary RNFLT norms. Our new norms may improve the diagnostic accuracy of OCT for glaucoma patients, although further validation is needed in patient population.

CONTROL ID: 3714142

SUBMITTER (NAME ONLY): Luke Mein

TITLE: Use of dexamethasone to mitigate occurence of intraocular inflammation associated with brolucizumab intravitreal injections

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mein, M. Singer, Retina, Medical Center Ophthalmology Association, San Antonio, Texas, UNITED STATES|M. Singer, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure: Luke Mein: Commercial Relationship: Code N (No Commercial Relationship) | Michael Singer: Commercial Relationship(s);Code C (Consultant/Contractor):Aerie, Allegro, Allergan, DRCR, Genentech, Icon, Ionis, Kalvista, Kodiak, Novartis, Opthea, Optos, Regeneron, Santen, Senju, Sydnexis, Ribomic, Eyepoint;Code I (Personal Financial Interest):Aviceda, Nanoscope, Inflammasome

ABSTRACT BODY:

Purpose: Brolucizumab has been plagued by a higher percentage of intraocular inflammation (IOI) than other anti-VEGF agents currently being used today. In the HAWK and HARRIER studies, the incidence of IOI was 4.4% overall, with 3.3 % of patients demonstrating retinal vasculitis (RV) and 2.1% of patients demonstrating retinal artery occlusion (RO). In this retrospective study, we hypothesize that with concurrent injection of dexamethasone this rate of inflammatory reaction can be mitigated.

Methods: In this series of nine patients, eleven eyes, dexamethasone 0.4mg/0.1mL was injected at the same visit as brolucizumab 6mg/0.05mL, with the intent of assessing the therapeutic effect of decreasing macular thickness/volume on OCT as well as following the patient for potential pressure spikes or IOI events. Each eye was determined to have an absence of any active IOI prior to brolucizumab injection. Patients were followed via the parameters of visual acuity, IOP, presence of inflammation, and OCT via macular volume (MV) and central subretinal thickness (CST). An OCT RNFL was used to compare the treated eye vs the fellow eye to look for any damage due to IOP spike relative to the fellow eye, as well as absolute damage.

Results: Of the fifty-two brolucizumab/dexamethasone injections performed, there were no reported IOP spikes or instances of white-out after injection. Additionally, there were no reported instances of inflammation after injection. These patients had improved CST and MV results on OCT compared to previous treatments with other anti-VEGF medications. There were no significant changes in OCT RNFL values after injections.

Conclusions: Our results are consistent with the hypothesis that dexamethasone is a potential adjunct treatment with brolucizumab as a possibility to decrease intraocular inflammatory events without side effects relating to pressure spikes or RNFL changes. Further analysis will need to be performed with an increased number of patients and eyes to extrapolate the efficacy of this data due to the initial low frequency of intraocular inflammation.

CONTROL ID: 3714143

SUBMITTER (NAME ONLY): Carrie Garufis

TITLE: Intraocular Pressure (IOP) Performance of Vitreous Removal With 27-Gauge Dual-Cutting 20,000 cpm Beveled Vitrectomy Probes

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Garufis, Y. Zhu, V. Wuyyuru, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure: Carrie Garufis: Commercial Relationship(s);Code E (Employment):Alcon | Ying Zhu: Commercial Relationship(s);Code E (Employment):Alcon | Vara Wuyyuru: Commercial Relationship(s);Code E (Employment):Alcon

ABSTRACT BODY:

Purpose: This study aims to 1) understand IOP stability during vitreous removal with 27+Gauge (Ga) dual-cutting, 20K cuts per minute (cpm) beveled vitrectomy probes; 2) understand the operation time of vitreous removal during a vitrectomy.

Methods: 27+® HYPERVIT® beveled 20K cpm vitrectomy probes were driven by a CONSTELLATION® Vision System (Alcon Vision, LLC.) to aspirate porcine vitreous in a hollow acrylic eye model. A digital transducer (OMEGA, PX409-001GUSBH) was connected to the bottom of eye model to detect IOP change during aspiration. For each testing, 4cc of fresh porcine vitreous was filled into the eye model. Six samples were tested under core duty cycle, vacuums of 250mmHg, 450mmHg and at 650mmHg and cut rate of 20,000cpm. Both system IOP compensation enabled and disabled were used with 30mmHg as the initial infusion pressure. Average IOP fluctuation during aspiration, final stable IOP and average operation time of vitreous removal were calculated for each test setting. Statistical analyses were performed on average IOP fluctuation rate using Welch's t- test with $p<0.05$.

Results: Without IOP compensation, the average fluctuation rate for vacuums of 250, 450 and 650 mmHg were -0.018 ± 0.003, -0.049 ± 0.007 and -0.094 ± 0.009 mmHg/s, respectively, demonstrating significant fluctuation rate differences between each vacuum setting ($p<0.05$). With IOP compensation, average IOP fluctuation rates significantly decreased to 0.004 ± 0.003, 0.010 ± 0.007, and 0.011 ± 0.010 mmHg/s for the same vacuums compared with IOP off ($p<0.05$). No significant difference of IOP fluctuation rate was shown between each vacuum setting ($p>0.05$).

Without IOP compensation, the final stable IOP after removing vitreous at vacuums of 250, 450, and 650 mmHg were 23.14 ± 0.50, 16.05 ± 0.79, and 8.49 ± 0. 44 mmHg, respectively. With IOP compensation, IOP maintained at 31.32 ± 0.93, 31.33 ± 1.01, and 31.46 ± 1.09 mmHg for the same vacuums. Corresponding operation times of complete removal of 4cc vitreous were 366s, 289s, and 230s, respectively.

Conclusions: At maximum cut rate, 27+® Ga 20K cpm probe with IOP compensation provides stable IOP and less fluctuation during vitrectomy for different vacuum levels compared to no compensation. IOP compensation is an essential feature for surgeons to efficiently control the fluidics environment during posterior segment procedures.

CONTROL ID: 3714144

SUBMITTER (NAME ONLY): Matthew Lawrence

TITLE: Safety and Tolerability of AAV in the Anterior Chamber: A Platform for Gene Therapy

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lawrence, M. O'Connor, Virscio, New Haven, Connecticut, UNITED STATES|J. O'Callaghan, M. Campbell, Genetics, The University of Dublin Trinity College, Dublin, IRELAND|T. Chalberg, A. Keravala, Exhaura, Dublin, IRELAND|

Commercial Relationships Disclosure: Matthew Lawrence: Commercial Relationship(s);Code E (Employment):Virscio | Jeffrey O'Callaghan: Commercial Relationship(s);Code E (Employment):Exhaura | Merissa O'Connor: Commercial Relationship(s);Code E (Employment):Virscio | Tom Chalberg: Commercial Relationship(s);Code I (Personal Financial Interest):Exhaura | Annahita Keravala: Commercial Relationship(s);Code I (Personal Financial Interest):Exhaura | Matthew Campbell: Commercial Relationship(s);Code I (Personal Financial Interest):Exhaura

ABSTRACT BODY:

Purpose: To evaluate the safety and tolerability of intracameral recombinant AAV as a gene therapy vector in nonhuman primates. The anterior segment is an attractive target for genetic intervention due to its accessibility, relative immune privilege, and ease of monitoring through aqueous sampling, and in vivo imaging techniques. We demonstrate that intracameral delivery of AAV9 vector is well tolerated and has a unique transduction profile in the nonhuman primate.

Methods: In an initial experiment, 8 primate eyes were intracamerally injected with 50 ml of 5E11 vg or 9E11 vg (vector genomes) of AAV9-expressing eGFP. In a second experiment, 7 primate eyes were intracamerally injected with 50 ml of 5E12 vg of AAV9 encoding a secreted protein. At 2-week intervals for 4 months, ophthalmic examinations were performed using specular microscopy, pachymetry, tonometry, slit lamp biomicroscopy, anterior segment imaging, and anterior segment OCT. Clinical observations were performed routinely. Serum and aqueous samples were also collected as part of routine examinations. Immunohistochemistry (IHC) was performed on the anterior chamber of the eye at study termination.

Results: Intraocular pressure was maintained within normal ranges at all timepoints following treatment. Corneal thickness, endothelial cell area and cell density measurements were not significantly different at any time point between AAV9 vector and vehicle injected eyes. No significant change in body weight or food consumption was observed. No evidence of increased inflammation was detected compared to contralateral vehicle control eyes. IHC revealed an open iridocorneal angle and no evidence of inflammation or cellular damage. Eyes injected with AAV encoding GFP revealed efficient transduction of the corneal endothelium, and eyes injected with AAV encoding a soluble secreted protein demonstrated high aqueous levels by ELISA.

Conclusions: We have observed sufficient tolerability of the anterior chamber to intracamerally delivered AAV vector in the nonhuman primate. This study did not reveal clinical signs indicative of localised or systemic side effects. Transduction was found unique to the corneal. This pre-clinical data demonstrates the potential of genetic intervention in the corneal endothelium of the anterior chamber to treat corneal diseases or to generate a “protein factory” for the treatment of other anterior segment conditions such as glaucoma.

CONTROL ID: 3714145

SUBMITTER (NAME ONLY): Augustine Nti

TITLE: Residual fit error of multifocal contact lenses as a function of increasing Zernike coefficients

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Nti, D.A. Berntsen, The Ocular Surface Institute, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Augustine Nti: Commercial Relationship: Code N (No Commercial Relationship) | David Berntsen: Commercial Relationship(s);Code C (Consultant/Contractor):Visioneering Technologies;Code F (Financial Support):Bausch + Lomb

ABSTRACT BODY:

Purpose: Complex optical designs such as multifocal lenses are being utilized for myopia control. Zernike polynomials are used to calculate metrics of image quality to predict visual performance. We determined if Zernike polynomials can adequately fit zonally reconstructed wavefront maps of multifocal contact lenses.

Methods: Three center-distance multifocal lenses (Biofinity “D” +2.50 add, Proclear “D” +2.50 add, NaturalVue) were studied. The Biofinity and Proclear lenses have a gradual radial increase in plus power from the lens center, while the NaturalVue Multifocal has an extended depth of focus design. Two lenses of each power ranging from -1.00 to -6.00D in 1D steps were measured for each lens design. Wavefront aberrations of each lens were measured in a wet cell with the SHSOphthalmic aberrometer and used to reconstruct zonal wavefront error maps. The wavefront error maps were then fitted with Zernike polynomials through the 6^{th}, 7^{th}, 10^{th}, 15^{th}, 20^{th}, 25^{th} and 30^{th} radial orders for a 6mm diameter pupil. The accuracy of each Zernike fit was calculated as the root-mean-square (in microns) of the difference between the zonal wavefront error map and the modal wavefront error map reconstructed from each Zernike fit. A repeated-measures ANOVA was used to determine the effect of lens design and Zernike radial order on the residual fit error.

Results: Root-mean-square of the residual fit error wavefront map (RMSFE) depended on both the lens design and radial order of the Zernike fit (lens x order interaction; $p < 0.0001$). RMSFE decreased for all three lenses with increasing radial order. For a 6^{th} order fit, RMSFE was less than 0.1μm for the Biofinity and Proclear lenses and 0.22μm for the NaturalVue. RMSFE reduced to less than 0.05 μm for all three lenses with the 15^{th} order polynomial fit. There was little additional improvement in the RMSFE (< 0.005μm) between the 20^{th} and 30^{th} order fits for both Biofinity and Proclear, but there was an additional 0.014μm reduction in RMSFE for the NaturalVue design. There was no difference in RMSFE between all three lens designs with the 30^{th} order fit.

Conclusions: Zernike fits were able to describe the multifocal optics of the lenses studied, but the number of radial orders needed depended on the complexity of the multifocal lens design, requiring through the 25^{th} radial order for one design.

CONTROL ID: 3714146

SUBMITTER (NAME ONLY): Robert Mackin

TITLE: Dopaminergic amacrine cell diversity is regulated by the liver kinase LKB1.

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Mackin, J. Liang, C. Burger, M. Samuel, Neuroscience, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Robert Mackin: Commercial Relationship: Code N (No Commercial Relationship) | Justine Liang: Commercial Relationship: Code N (No Commercial Relationship) | Courtney Burger: Commercial Relationship: Code N (No Commercial Relationship) | Melanie Samuel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To unlock the full potential of regenerative medicine requires a more complete understanding of the molecular determinants that influence cellular migration, proliferation, identity, and fate. Out of the diverse neuronal subtypes exemplified in the neural retina, the dopaminergic amacrine cells (DACs) have an outsized importance given that they are the primary source of retinal dopamine while making up just one percent of the total amacrine cell population. The focus of our investigation was to identify factors that influence DAC placement, number, and connectivity. Through this screen we uncovered a candidate signaling pathway controlled by the serine-threonine kinase LKB1 that is critical for DAC fate.

Methods: We leveraged Cre recombinase technology to selectively knock out LKB1 from either retina or amacrine cell precursors. In concert with transgenic mice that allow for visualization of DACs by the expression of GFP driven by the promoter for tyrosine hydroxylase we were able to analyze the effects of the absence of LKB1 on the fate of the dopaminergic amacrine cells. Using cross sections and whole flat-mounted retinas we analyzed DACs in the first, second, and third post-natal weeks.

Results: We observed an approximate doubling of DACs early in development that persisted into adulthood. Surprisingly, in addition to the increase of DACs in their endogenous location in the Inner Nuclear Layer (INL) we observed a substantial number of DACs displaced into the ganglion cell layer (GCL). These cells retained expression of the amacrine cell marker Ap2 but projected their neurites to the Inner Plexiform Layer (IPL) from the opposite side from their inner nuclear layer counterparts. We also observed DAC stratification in layer S2 of the IPL in addition to layers S1 and S3 observed in controls. Similar results were observed in mice that had LKB1 selectively deleted from amacrine cell precursors.

Conclusions: These results suggest that LKB1 signaling is required cell intrinsically within amacrine cell precursors to restrict the total population of DACS, migration of DACS to the INL, and stratification of DAC processes to S1 and S3 layers of the IPL. These findings contribute to our understanding of signaling pathways that influence important attributes of DAC fate in murine retina.

CONTROL ID: 3714147
SUBMITTER (NAME ONLY): Karthik Kalahasty
TITLE: OCULAR MARKERS ASSOCIATED WITH GULF WAR ILLNESS SYMPTOMS
SESSION TITLE: Neuro-ophthalmology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: K. Kalahasty, Y. Lee, K. Cabrera, A. Galor, VA Miami Healthcare System, Miami, Florida, UNITED STATES|K. Kalahasty, Y. Lee, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Abreu, K. Aenlle, N. Klimas, Nova Southeastern University, Fort Lauderdale, Florida, UNITED STATES|A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|
Commercial Relationships Disclosure: Karthik Kalahasty: Commercial Relationship: Code N (No Commercial Relationship) | Yonghoon Lee: Commercial Relationship: Code N (No Commercial Relationship) | Kimberly Cabrera: Commercial Relationship: Code N (No Commercial Relationship) | Maria Abreu: Commercial Relationship: Code N (No Commercial Relationship) | Kristina Aenlle: Commercial Relationship: Code N (No Commercial Relationship) | Nancy Klimas: Commercial Relationship: Code N (No Commercial Relationship) | Anat Galor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Gulf War Illness (GWI) is a chronic, multisystem disease diagnosed in Gulf War Era (GWE) veterans associated with manifestations of ocular disease including dry eye symptoms, photophobia and convergence insufficiency. Given the ability to image peripheral and central nerves within the eye and detect ocular surface inflammation, the eye may serve as a biomarker for GWI, assisting with diagnosis and the understanding of disease pathophysiology. In this study, we examine whether individuals presenting with GWI symptoms have differences in ocular imaging and inflammatory cytokine profiles compared to their GWE counterparts.

Methods: This is a prospective case-control study of 94 individuals who served during the GWE. Individuals were split into 2 groups: those with GWI symptoms (cases, identified by Kansas criteria) and those without GWI symptoms (controls). Information on demographics, co-morbidities, and diagnoses of eye diseases were captured. In addition, all individuals underwent optical coherence tomography (OCT) imaging (retinal nerve fiber layer (NFL), ganglion cell layer-inner plexiform layer, and macular maps) and provided a blood sample. Blood was analyzed for inflammatory cytokines using a custom ELISA-based chemiluminescent assay. Statistical analyses were performed using SPSS 28.0. Predictors of GWI symptoms were analyzed using forward stepwise binary logistic regression and receiver operating characteristic (ROC) curves.

Results: The mean patient age was 55±5, 90.3% self-identified as male, 55.9% as white, and 53.8% as Hispanic. After confirming non-collinearity between predictors, the binary logistic analysis model revealed that inferior temporal ganglion cell thickness (odds ratio; OR=0.66, 95% confidence interval; CI=0.49-0.88), superior temporal ganglion cell thickness (OR=1.34, 95% CI=1.03-1.75), temporal NFL thickness (OR=1.08, 95% CI=1.01-1.16), IL1 beta levels (OR=0.86, 95% CI=0.73-1.01), IL2 levels (OR=0.71, 95% CI=0.55-0.91), and IL17 levels (OR=1.03, 95% CI=1.01-1.04) all predicted GWI symptoms. ROC analysis demonstrated an area under the curve of 0.83 (95% CI=0.74-0.93, $p<0.001$) for this model. As determined by Youden's index (top left point on the ROC curve), the best cut-of value for the prediction model was associated with a sensitivity of 90% and a specificity of 65%.

Conclusions: These results elucidate differences in OCT and systemic inflammatory markers in individuals with versus without GWI symptoms.

CONTROL ID: 3714148

SUBMITTER (NAME ONLY): Sudha Swamynathan

TITLE: Secreted Ly-6/uPAR Related Protein-1 (SLURP1) Suppresses Canonical TGF-b Signaling in Corneal Epithelial Cells

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Swamynathan, S.K. Swamynathan, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Sudha Swamynathan: Commercial Relationship(s);Code P (Patent):University of Pittsburgh, patent number-9731014 | Shivalingappa Swamynathan: Commercial Relationship(s);Code P (Patent):University of Pittsburgh, patent number-9731014

ABSTRACT BODY:

Purpose: Secreted Ly-6/uPAR Related Protein-1 (SLURP1), abundantly expressed by the corneal epithelium (CE) and secreted to the tear film, is an anti-inflammatory protein with anti-tumor properties. TGF-b pathway has diverse roles in tissue homeostasis as well as pathological conditions including epithelial-mesenchymal transition (EMT) during tumor metastasis. Here, we studied the influence of SLURP1 on canonical TGF-b signaling using Slurp1X-/- mouse cornea and human corneal limbal epithelial (HCLE) cells.

Methods: The effect of Slurp1 ablation on TGF-b signaling was studied by comparing TGF-b Receptor 2 (TGFBR2), Smad4, and phospho-Smad2/3 expression in wild type (WT) and Slurp1X-/- mouse corneas by immunoblots and immunofluorescent staining. The effect SLURP1 on TGF-b signaling was analyzed by comparing the TGF-b-induced Smad2/3 phosphorylation and E-cadherin expression in HCLE and HCLE-SLURP1 cells engineered to over-express SLURP1.

Results: Slurp1X-/- mouse corneas displayed elevated expression (127% of WT) and prominent nuclear localization of TGFBR2, coupled with elevated expression of Smad4, and phospho-Smad2/3. Upon stimulation with 5ng/ml TGF-b, HCLE-SLURP1 displayed decreased SMAD2/3 phosphorylation compared with that in HCLE cells. After 1h of TGF-b addition, the phospho-SMAD2/Total SMAD2 ratio was 20% lower in HCLE-SLURP1 compared with HCLE cells. Upon TGF-b treatment, E-cadherin expression decreased to a greater extent in HCLE compared with HCLE-SLURP1 cells. Confluent HCLE-SLURP1 cells retained E-cadherin in their cell membranes more efficiently than HCLE cells at 24h and 48h after TGF-b addition.

Conclusions: Increased expression of TGFBR2, Smad4 and pSmad2/3 indicate higher canonical TGF-b signaling activity in Slurp1X-/- corneas. SLURP1 suppresses canonical TGF-b signaling in HCLE cells and protects E-cadherin from TGF-b induced disintegration, consistent with a role for SLURP1 in protecting the CE cells from TGF-b-induced EMT.

CONTROL ID: 3714149

SUBMITTER (NAME ONLY): VIRGINIA MARES

TITLE: Artificial intelligence to identify conventional treatment patterns in neovascular age-related macular degeneration in a real-world population

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.D. MARES, Ophthalmology, Universidade Federal de Minas Gerais, Belo Horizonte, MG, BRAZIL|V.D. MARES, H. Bogunovic, O. Leingang, G.S. Reiter, U. Schmidt-Erfurth, Ophthalmology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|D. Barthelmes, UniversitatsSpital Zurich, Zurich, SWITZERLAND|

Commercial Relationships Disclosure: VIRGINIA MARES: Commercial Relationship: Code N (No Commercial Relationship) | Hrvoje Bogunovic: Commercial Relationship: Code N (No Commercial Relationship) | Oliver Leingang: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Barthelmes: Commercial Relationship: Code N (No Commercial Relationship) | Gregor Reiter: Commercial Relationship(s);Code F (Financial Support):RetInSight | Ursula Schmidt-Erfurth: Commercial Relationship(s);Code F (Financial Support):RetInSight

ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) is the main diagnostic tool to detect and monitor progression of neovascular age related macular degeneration (nAMD). The purpose of this study is to predict anti-VEGF treatment requirements in nAMD using artificial intelligence (AI) based on OCT images for identifying fluid biomarkers in a real-world cohort.

Methods: OCT (Spectralis, Heidelberg Engineering) data of treatment-naïve patients with nAMD from the Fight Retinal Blindness! in Zürich were processed at baseline, and the end of the loading dose (2 months after the first anti-VEGF injection), to predict subsequent one year treatment needs. First, intraretinal (IRF), subretinal fluid (SRF) and pigment epithelial detachment (PED) were segmented using a deep learning convolutional neural network (Vienna Fluid Monitor, RetInSight, Vienna, Austria). Second, a set of quantitative features from the segmented layers and fluid regions were computed across the three central subfields at 1mm, 3mm, and 6mm, to describe retinal pathomorphology both quantitatively and spatially. Finally, using the computed set of features, a predictive model of future treatment requirements was built using machine learning and was evaluated with a ten-fold patient-level cross-validation.

Results: Two hundred and nine eyes from 164 patients were evaluated for a one year period following the loading dose. The treatment intervals ranged from 0 to 13 weeks. 100/209 eyes had lower median (≤7) and 109/209 eyes had an upper median (≥8) number of injections. The model identified the two groups (lower and upper median) based on number of injections with a mean accuracy of 0.74 (CI) area under the curve (AUC). The amount of SRF after the loading dose and at baseline in the central-3mm area were found to be the most important predictive features (Figure 1).

Conclusions: We used AI to predict treatment requirements in nAMD by correlating fluid biomarkers with resulting therapeutical patterns based on OCT images. The potential of a personalized anti-VEGF therapy for minimizing the risk of undertreatment while improving resource management and avoiding overtreatment will have to be evaluated in respect to this current state-of-the-art concept in a prospective manner.

CONTROL ID: 3714152

SUBMITTER (NAME ONLY): Qianlan Xu

TITLE: Stress accelerates age related changes in mammalian vision

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Xu, C. Rydz, I. Lee, D. Skowronska-Krawczyk, Physiology & Biophysics, UC Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Qianlan Xu: Commercial Relationship: Code N (No Commercial Relationship) | Cezary Rydz: Commercial Relationship: Code N (No Commercial Relationship) | Irene Lee: Commercial Relationship: Code N (No Commercial Relationship) | Dorota Skowronska-Krawczyk: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age and elevated intraocular pressure (IOP) are major risk factors for glaucoma. We aim to learn how aging contributes to loss of vision in response to stress caused by elevated IOP.

Methods: 3 and 18-month-old mice were treated with mild IOP (30mmHg). Phenotype and molecular changes in young and old retina upon IOP stress assessed included: RGC cell body survival by Brn3a immunostaining; Visual path in optic nerve neurofilament by NF68 staining; RGC function measured by pattern electroretinography (PERG); Transcriptomic and epigenomic analyses.

Results: Both RGC counting statistics and PERG assays showed significant decreases in old retina upon 1hr of 30mmHg IOP elevation but barely changed in young ones. Optic nerve analysis showed dramatically reduced NF68 immunoreactivity in aged eye. RNA-Seq analysis with FDR<0.05 and two-fold expression change cutoff revealed 156 activated genes and none repressed upon stress in young retina. In old retina, there were more stress dysregulated genes including 257 up- and 24 down-regulated. And a large portion of the stress-activated genes showed higher fold changes in old versus young retina. Pre-ranked gene set enrichment analysis and heatmaps showed multiple curated aging related pathways such as inflammatory/immune response, senescence and p53 pathways. ATAC-Seq analysis revealed that chromatin accessibility changes played a necessary regulatory role in many susceptible genes against stress like Fgf2 and Bcl3.

Conclusions: RGC/axonal loss and deterioration of vision correlated with age. Transcriptomic response to IOP stress revealed ontology enrichment in pathways associated with aging and senescence and showed higher vulnerability in old versus young retinae. Our data suggests that stress accelerates aging of the visual system. Current glaucoma treatment paradigm limits to lowering eye pressure. Elucidating pathways involved in accelerated aging may lead novel therapeutic targets for glaucoma treatment and prevention in the future.

CONTROL ID: 3714154

SUBMITTER (NAME ONLY): Shreya Banerjee

TITLE: Characterization of behavioral abnormalities in zebrafish vps16 mutants as a potential model of genetic leukoencephalopathy

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Banerjee, S. Bongu, S. Hughes, D. Bessert, X. Luo, R. Thummel, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Shreya Banerjee: Commercial Relationship: Code N (No Commercial Relationship) | Shivani Bongu: Commercial Relationship: Code N (No Commercial Relationship) | Sidney Hughes: Commercial Relationship: Code N (No Commercial Relationship) | Denise Bessert: Commercial Relationship: Code N (No Commercial Relationship) | Xixia Luo: Commercial Relationship: Code N (No Commercial Relationship) | Ryan Thummel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Genetic Leukoencephalopathies (gLEs) are white matter disorders affecting the central nervous system, causing progressive abnormalities in visual and motor systems. A mutation in Vacuolar Protein Sorting 11 (VPS11) has been identified in humans as a causative allele of gLE. Functioning with VPS11, VPS16 forms membrane-tethering complexes that control crucial cellular processes in the endolysosomal pathway. However, the role of VPS16 in gLE is unknown. Here, we are characterizing the behavioral responses of a zebrafish vps16 mutant line as potential model for gLE.

Methods: Immunohistochemistry and TUNEL were used to assess retinal and brain pathology and hypomyelination at 7 days post-fertilization (dpf). Behavioral assays were used at 5 and 7dpf to assess evoked visuomotor responses, short-term memory (habituation), and long-term memory (using various time periods between two habituation stimuli). Appropriate statistical analyses were used to determine differences between wild-type and mutant animals.

Results: Immunohistochemical and TUNEL analysis indicated that vps16 mutant larva showed retinal and brain pathology, including hypomyelination and increased apoptosis. Behavioral analysis showed that mutants could visualize changes in light/dark backgrounds but showed a progressive loss of distance moved and velocity from 5-7dpf. Mutants showed signs of short-term memory (habituation to 10 consecutive tap stimuli) but habituated faster than wild-type siblings. Finally, in response to two sets of multiple taps with 2min, 5min or 30min rest periods in between, both wild-type and mutant larva “remembered” the first habituation response after a 2min rest. After 5min, wild-type animals still “remembered” the first response, but mutant animals did not. Finally, after 30min, neither group “remembered” the first habituation event and responded to the second set as a novel habituation stimulus. Together, these results suggest that loss of Vps16 function has a progressive adverse effect on larval zebrafish visual, motor, and cognitive systems, which is consistent with their hypomyelination phenotype.

Conclusions: Our findings support the use of zebrafish to further characterize behavioral defects associated with gLE and provide the first insights into impaired Vps16 function.

CONTROL ID: 3714157

SUBMITTER (NAME ONLY): Yuval Cohen

TITLE: The Association between Refraction and Conners' parent rating scale in Children between 6-12 Years of Age

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Cohen, A. Vidan, O. Chassid, Medicines, Bar-Ilan University, Ramat Gan, Tel Aviv, ISRAEL|M. Mahajnah, M. Idel, Pediatric Neurology and Child Development Institute, Hillel Yaffe Medical Center, Hadera, Haifa, ISRAEL|M. Mahajnah, Technion Israel Institute of Technology The Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Haifa, ISRAEL|Y. Cohen, Y. Greenberger, A. Vidan, O. Chassid, Ophthalmology, Ziv Medical Center, Safed, Northern, ISRAEL|

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ABSTRACT BODY:

Purpose: To associate between the child behavioral problem as determined by the Conners' parent rating scale (CPRS) to cycloplegic refraction and ocular biometry.

Methods: Children, between the age 6-12 years, visiting the pediatric ophthalmology clinic for suspected ammetropia were recruited to the study. A complete eye exam, cycloplegic refraction and ocular biometry using Lenstar ocular biometry were performed. For each child, CPRS was completed and scored for seven behavioral problems and three attention deficit hyperactivity disorder (ADHD) subtypes. Correlation was performed between CPRS reports to refraction and ocular biometry.

Results: Children with emmetropia (N-21) and hyperopia (N-132) were included. CPRS for ADHD was positive 27.2% of the hyperopic children, as compared to 9.5% among emmetropes. Hyperopic children had significantly high cognitive problems and oppositional behavior that present in 24.6% and 21.5%, respectively. Hyperopic children with positive and negative CPRS for ADHD had similar spherical power of +3.2±2.1 D and +3.7±2.7 D (p=0.52), however the cylinder was significantly higher in the positive CPRS for ADHD (p=0.02).

Conclusions: Conners' parental scoring for ADHD was positive three times more in hyperopes than emmetropes. Astigmatism in a hyperopic child was associated with positive CPRS for ADHD.

CONTROL ID: 3714158

SUBMITTER (NAME ONLY): Conan Chen

TITLE: Characterization of miRNA cargo in extracellular vesicles released by polarized human retinal pigment epithelium cells

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Chen, S. Aparicio-Domingo, K. Li, T. Domashevich, V. Canto Soler, M. Flores-Bellver, CellSight Ocular Stem Cell and Regeneration Program, Department of Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|R. Dubin, Center for Epigenomics, Computational Genomics Core, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|S. Redenti, Biology Doctoral Program, The Graduate School and University Center, Lehman College, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) plays an essential physiological role between the photoreceptor cell layer and the choroid. This interaction is critical in the maintenance of an internal equilibrium within the retina. Several retinal diseases occur as a consequence of RPE dysfunction. Our team has established a differentiation protocol that is efficient in producing pure populations of fully differentiated, functionally mature RPE cells from human induced pluripotent stem cells (hiPSC). The purpose of this study was to analyze and characterize the population of extracellular vesicles (EVs) released by hiPSC-derived RPE cells. EVs are cell-derived nanoscale particles containing a range of molecular cargo including small RNA with emerging roles as essential mediators of cell-to-cell communication in developmental processes.

Methods: We established a differentiation protocol that is efficient in producing functionally mature RPE cells from hiPSC. To characterize EVs secreted by hiPSC-RPE cells, we analyzed the release rate, concentration, morphology and miRNAs content of EVs obtained from hiPSC-RPE. Transcriptomic analysis of miRNA EV cargo provided a comprehensive analysis of this signaling system, including miRNA cargo-predicted targetome correlated with Gene Ontology pathways.

Results: Characteristic EV morphology and size (30-170 nm) was observed by TEM. The average concentration of released EVs corresponded to 7.76×10^{10} particles/ml (apical) and 5.40×10^{10} particles/ml (basal). Transcriptomic analysis identified a total of 208 high confidence miRNAs; 17 detected only in RPE-EVs (1 only found in apical and 5 only in basal). Target gene prediction of differentially expressed miRNAs was carried out against a retinal and choroid database. To gain functional insight on RPE-EV transcriptomic cargo, we conducted over representation analysis and determined several biological processes enricheded in EV-associated miRNAs, including mechanisms of cell communication, signal transduction, cell growth and maintenance, metabolism, oxidative stress, immune response, inflammation, neurogenesis and phagocytosis.

Conclusions: This study represents the first transcriptomic profile from EVs released by hiPSC-derived RPE. EV content provides a snapshot of the originating cell's phenotype by revealing molecular cargo associated with mechanisms regulating human retinal physiology.

CONTROL ID: 3714159

SUBMITTER (NAME ONLY): Aysha Kinakool

TITLE: Visual hallucinations caused by Charles Bonnet Syndrome are not impacted by the psychosocial factors resulting from COVID-19 restrictions

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Kinakool, S.S. Moro, J.K. Steeves, Centre for Vision Research and Psychology, York University, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Charles Bonnet Syndrome (CBS) is a poorly understood, debilitating phenomenon following vision loss from common diseases such as age-related macular degeneration and currently has no treatment. Individuals with CBS often experience visual hallucinations in the form of images such as people, landscapes, or patterns that do not exist. This experience is the result of an imbalance between the loss of vision and the active visual brain but is often misdiagnosed as dementia or a mental health condition. Psychosocial factors have been suggested to exacerbate CBS visual hallucinations. The ongoing COVID-19 pandemic has resulted in the implementation of public health safety measures including extended periods of total or partial lockdowns to reduce virus transmission. To date, Canadians have undergone several waves of restrictions that may increase the risk of pervasive psychosocial issues from social isolation. The goal of this research is to assess how the social constraints of the current COVID-19 pandemic may affect CBS visual hallucinations.

Methods: We surveyed 39 individuals (M: 69 years, SD: 16 years) with CBS from the CNIB Foundation. Visual hallucinations, anxiety, social isolation, loneliness, and QoL were assessed using: The Specific Psychotic Experiences Questionnaire and modified versions of the Generalized Anxiety Disorder 7 scale, Steptoe Social Isolation Index, DeJong Gierveld Loneliness scale, and the World Health Organization QoL scale, respectively.

Results: 90.6% of patients reported no change (increase: 6.3%; decrease: 3.1%) in average duration and 62.2% reported no change (increase: 21.6%; decrease: 16.2%) in frequency of CBS hallucinations. No significant differences were observed in anxiety ($p= 0.514$); QoL ($p= 0.155$); social isolation ($p= 0.835$); and loneliness ($p= 0.296$) between participants who reported experiencing a change compared no change in hallucinations.

Conclusions: The social constraints of the current COVID-19 pandemic measured through anxiety, social isolation, loneliness, and QoL do not affect visual hallucinations caused by CBS. This is consistent with the notion that CBS hallucinations are associated with an active visual cortex following vision loss.

CONTROL ID: 3714160

SUBMITTER (NAME ONLY): Fangyuan Gao

TITLE: Essential role of ELOVL2 in maintenance of membrane structure in ARPE19 cells

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Gao, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|E. Tom, Q. Xu, D. Skowronska-Krawczyk, Dept. of Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: ELOVL2 encodes an enzyme that elongates polyunsaturated fatty acids (LC-PUFAs). It's crucial for synthesis of omega-3 docosahexaenoic acid (DHA) and VLC-PUFAs, all playing critical role in retina biology as integral parts of photoreceptor disk membranes. The RPE cells are important in regulation and delivery of LC-PUFAs to the adjacent photoreceptors. However, the practical role of ELOVL2 in RPE structure and function remain unclear.

Methods: To understand the biological role of ELOVL2 in RPE, we used siRNAs directed against ELOVL2 in ARPE19 cells and investigated the effect of ELOVL2 in ARPE19 cells morphology and biology functions. Fluorescently labeled WGA was used to visualize cell membranes. Mass spectrometry-based lipidomic and proteomic analyses were used to understand the molecular role of ELOVL2 in ARPE19 cells.

Results: WGA staining of normal ARPE19 cells reveals a highly ordered pattern of cells, with cell boundaries strongly stained and sharply demarcated. In ELOVL2 KD ARPE19 cells, the staining becomes more diffuse, stronger in cytoplasm and staining perinuclear regions in the cell. Moreover, the borders of ELOVL2 KD ARPE19 cells are disordered and there are more discontinuities between cells. The quantitative results of the fatty acid composition of membrane lipidsshowed that there was a significant decrease of FA 22:4, 22:5 and 26:4 in ELOVL2 KD ARPE19 cells. Among them, FA22:4 and FA22:5 are substrates of ELOVL2, and FA26:4 are elongation products of FA24:4, which is a product of ELOVL2. Therefore, the lack of ELOVL2 leads to a decline in VLC-PUFA synthesis. Then the molecular mechanisms of the role of ELOVL2 in cell membrane were assessed by proteomics,revealing that among all the 153 significantly changed proteins (out of 2381 proteins in total, (|Fold change|≥1.5, P-Value < 0.05), 48 proteins were identified as membrane proteins (DAVID database), including membrane magnesium transporter 1 (MMGT1, up-regulated, p=0.01), caveolin 2 (CAV2, down-regulated, p=0.02), platelet derived growth factor receptor beta (PDGFRB, down-regulated, p=0.004), et al.

Conclusions: Our data revealed that ELOVL2 depletion disrupted membrane compositions on lipid and protein levels and may further alter the membrane structural and functional properties. These changes of the cell membrane will most probably affect transmembrane transport, transmembrane receptors' activity and other membrane related biological functions.

CONTROL ID: 3714161

SUBMITTER (NAME ONLY): J. Peter Campbell

TITLE: Effectiveness of an artificial-intelligence based single-exam retinopathy of prematurity prediction model in three Asian populations

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Campbell, A.S. Coyner, M. Oh, S.R. Ostmo, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Shah, Aravind Eye Care System, Coimbatore, Tamil Nadu, INDIA|P. Singh, J. Kalpathy-Cramer, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|N. Valikodath, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|E. Cole, T. Al-Khaled, R. Chan, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|S. Bajimaya, Tilganga Institute of Ophthalmology, Kathmandu, NEPAL|S. KC, Helen Keller International, New York, New York, UNITED STATES|T. Chuluunbat, B. Munkhuu, National Center for Maternal and Child Health of Mongolia, Ulaanbaatar, Ulaanbaatar, MONGOLIA|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous work has demonstrated that an artificial-intelligence (AI) based retinopathy of prematurity (ROP) risk model could provide both early prediction of treatment-requiring (TR) ROP and reduce the overall number of examinations in a US population. However, significant demographic differences exist between US and low and middle income countries (LMIC), which may limit translation of risk models based on demographics to other populations. In this work, we evaluate whether a modified AI-based risk model could perform with high sensitivity despite demographic differences in 3 LMICs.

Methods: Retinal fundus images were collected from 2351 subjects as part of an Indian ROP telemedicine screening program. A VSS was derived from the first exam after 30 weeks postmenstrual age. Using five-fold cross-validation, logistic regression models were trained and validated on 2 variables (gestational age at birth and VSS at first exam) for the eventual outcome of TR-ROP. Sensitivity, specificity, and respective 95% confidence intervals (CIs) were evaluated on test datasets acquired from Indian (n = 762 subjects, 27 TR-ROP), Nepalese (n = 330 subjects, 3 TR-ROP), and Mongolian babies (n = 319 subjects, 53 TR-ROP). All 3 test sets were consecutive population-based cohorts imaged as part of ROP telescreening programs.

Results: For the Indian, Nepalese, and Mongolian test datasets, the model had sensitivity [95% CI] equal to 100.0% [87.2%, 100.0%], 100.0% [29.2%, 100.0%], and 100.0% [93.3%, 100.0%], respectively. Specificity was 63.3% [59.7%, 66.8%], 77.1% [72.27%, 81.6%], and 45.8% [39.7%, 52.1%]. The mean ± standard deviation weeks subjects were identified prior to TR-ROP diagnosis was 2.1 ± 2.5, 0.7 ± 1.2, and 4.7 ± 5.1 weeks. Post-hoc analysis of the Indian dataset determined that, if those who screened negative were to never be screened again, the total number of examinations could be reduced by 45.0%.

Conclusions: We found 100% sensitivity and moderate specificity of a modified AI-based ROP risk model in 3 LMIC populations. There are two potential advantages to implementation of this risk model in ROP telescreening programs: (1) high-risk infants could be identified well before TR-ROP diagnosis, potentially reducing the risk of late treatment, and (2) the number of exams required to effectively screen a population could be significantly reduced.

CONTROL ID: 3714163

SUBMITTER (NAME ONLY): Assel Talaspayeva

TITLE: The diagnostic accuracy of wearable binocular high-speed pupillometer in subjects with a different eye pathology and normal subjects.

SESSION TITLE: Retina imaging and pupillometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Talaspayeva, M. Harooni, Brooklyn Eye Center, New York, UNITED STATES|

Commercial Relationships Disclosure: Assel Talaspayeva: Commercial Relationship: Code N (No Commercial Relationship) | Mark Harooni: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To test and identify diagnostic accuracy of a single binocular, lightweight pupillometer device, that measures the pupillary light reflex (PLR) and to determine the asymmetry of the PLR (afferent pupillary defect, APD) among normal subjects and subjects with various eye pathology.

Methods: Data from subjects (N=150) with confirmed various ocular pathology (retinal diseases, optic nerve disease, refractive errors, amblyopia) and healthy subjects age 18 -70 yr were collected.

Patients with cloudy corneas and dense cataracts affecting the measurement of APD were excluded from the study. Visual acuity (Snellen visual acuity chart), autorefraction (Auto-Ref-Keratometer), intraocular pressure (IOP) was measured using Goldman tonometry, slit lamp and fundus examination were obtained. The optic nerve and retina were measured with OCTA (Optovue Inc.).

The pupillary light reflex (PLR) of the right and left eye concurrently was measured and analyzed with binocular wearable pupillometer in all patients. Parameters included relative APD, APD in superior and inferior fields, amplitude, latency, time to max constriction.

Pupillometer images interpretation with a single-page report were exported and analyzed, according to a specified grading protocol.

Results: All subjects were divided into 4 groups.

1.Patients who have asymmetric vision from either retinal or optic nerve disease without any other eye pathology.

2. Patients with significant asymmetric refractive errors without any other eye pathology.

3. Patients with monocular amblyopia without any other eye pathology.

4. Control groups with subjects with normal eye exam and normal pupillography test.

All groups had APD and pupillary abnormal parameters when compared with controls ($p<0.03$) with high sensitivity and specificity.

Conclusions: The binocular pupillometer demonstrated good diagnostic accuracy in its ability to help diagnose afferent and efferent pupillary defects (including relative afferent pupillary defects) in a retinal and optic nerve pathologies, refractive errors and amblyopia. This findings demonstrates that pupillometer is a valuable adjunctive tool to assist in diagnosis and may provide a method for monitoring disease progression.

The device does not require a darkened room and requires minimal patient cooperation which makes test easy and accurate.

CONTROL ID: 3714164

SUBMITTER (NAME ONLY): Zhongjie Fu

TITLE: Single-cell analysis reveals decreased metabolism in mice with phase I ROP

SESSION TITLE: Single cell analysis in retinal research in health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Fu, J.C. Harman, W. Allen, E. Bull, J. Yang, M. Ko, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|Z. Fu, J.C. Harman, Ophthalmology, Harvard Medical School, Völklingen, GERMANY|W. Yan, Center for Brain Science and Department of Molecular and Cellular Biology, Harvard University, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Delayed retinal vascularization of immature retinas (phase I) is the driving force of late-stage retinopathy of prematurity (ROP), a leading cause of blindness in children. Postnatal hyperglycemia within the first few weeks of life is a significant risk factor for ROP. We aim to examine retinal metabolic responses in mice modeling hyperglycemia-associated phase I ROP.

Methods: Hyperglycemia was induced with intraperitoneal (i.p.) injection of streptozotocin (STZ) in mice from postnatal (P) day 1 to 9. At P10, reteinal vessel growth was delayed. Single-cell suspensions were prepared from mouse retinas by using Worthington papain dissociation system (n=3 mice per group). A retinal cell barcoded library was prepared at the Single Cell Core at Harvard Medical School (HMS), sequenced at Biopolymer Facility at HMS, and aligned to the mouse genome at Harvard Chan Bioinformatics core. The downstream clustering analysis was performed using R package ‘Seurat’ (version 3.2.2), genes and cells were filtered so only cells with more than 300 genes detected or genes expressed in more than 10 cells were kept. The gene enrichment analysis was performed using ‘enrichGO’ function from R package ‘clusterProfiler’ and mouse annotation database ‘EnsDb.Mmusculus.v79’. The p-value was adjusted using Benjamini & Hochberg method with a cutoff of 0.05 on the enrichment tests.

Results: In mice with phase I ROP, there was a robust down-regulation of genes involved in metabolic pathways in rod, cone, bipolar and amacrine cell clusters. The major metabolic pathways involved are generation of precursor metabolites and energy, ATP metabolic process, cellular respiration, and oxidative phosphorylation ($p<0.001$). There was an up-regulation in genes involved in visual development, such as visual perception, eye development, axon development, and synapse organization related gene-ontology terms in rod, cone, bipolar and amacrine cell clusters of phase I ROP retinas. In Müller glia, genes involved in energy production-related pathways were downregulated, while genes involved in gliogenesis, axon development and angiogenesis-related pathways were upregulated.

Conclusions: We found that mice with phase I ROP experienced metabolic stress in retinal neurons and glia. Retinal remodeling may occur as compensatory responses. Modulating metabolic pathways may restore cellular homeostasis and prevent progression to severe ROP in premature infants.

CONTROL ID: 3714165

SUBMITTER (NAME ONLY): Travis Harding

TITLE: Sodium Potassium ATPase β2 Subunit (ATP1B2) is Indispensable for Cone Photoreceptor Function and Survival

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Harding, E. Sechrest, B. Myers, M.A. Robichaux, S. Kolandaivelu, Ophthalmology, West Virginia University, Morgantown, West Virginia, UNITED STATES|M.A. Robichaux, S. Kolandaivelu, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|T.G. Wensel, Biochemistry, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The photocurrent is an ion gradient that retinal photoreceptors rely on for conversion of light into electrical impulses. This gradient is largely mediated by Na^+/K^+-ATPase pumps, which are localized in the photoreceptor inner segment, where they exist as a heterodimer (a catalytic α3 and a non-catalytic β2 subunits). Previous studies have shown that the mouse lacking ATP1B2 results in rapid photoreceptor degeneration, but the specific importance of ATP1B2 in cones remains unstudied. The goal of this study is to elucidate the role of ATP1B2 in the overall function and health of cone photoreceptors.

Methods: Using CRISPR/Cas9, our lab generated a floxed Atp1b2 mouse model, which was then crossed with a cone-specific Cre to make a conditional knockout of Atp1b2 in cones. Visual function and retinal thickness were assessed using electroretinography (ERG) and optical coherence tomography. Morphology, protein localization, and protein expression were analyzed by immunohistochemistry and immunoblotting. Na^+ concentrations were analyzed using CoroNa$^+$ Green probes. Ultrastructural analysis was completed using transmission electron microscopy (TEM).

Results: Mice with the conditional deletion of Atp1b2 in cones display progressive cone degeneration and severe loss of cone function compared to control littermates. A significant decrease and mislocalization of cone specific proteins, such as PDE6α', and GNAT2, and accumulation of Na^+ ions were observed in these mice. The ultrastructure of Atp1b2$^{-/-}$ cones at P60 showed a dysmorphic cone outer segment structure with abnormal swelling and holes. No major defects were observed in the cone IS, where the Na^+/K^+-ATPase is primarily localized. Interestingly, despite the normal expression of rod-specific proteins and only minor abnormalities to rod ultrastructure in cone Atpb2$^{-/-}$ retinas, a significant reduction of the scotopic ERG response was recorded in these mice at P60.

Conclusions: Our data demonstrate that ATP1B2 is critical for cone photoreceptor function and survival. Loss of ATP1B2 from cones leads to accumulation of Na^+ ions, which we hypothesize is likely the reason we observed abnormal ultrastructure of the cone OS and cone degeneration. Furthermore, our data suggest that alterations to the Na^+ gradient in cones can also have a harmful effect on other retinal neurons such as rods, contributing to changes in overall retinal function and health.

CONTROL ID: 3714166

SUBMITTER (NAME ONLY): Yesha Raval

TITLE: Clinical Validation of the Mobile Allergen BioCube (mABC) in Subjects with Seasonal Allergic Conjunctivitis or Rhinoconjunctivitis

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Raval, P.J. Gomes, K. Quealy, M.B. Abelson, Ora, inc., Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Yesha Raval: Commercial Relationship(s);Code E (Employment):Ora | Paul Gomes: Commercial Relationship(s);Code E (Employment):Ora | Kara Quealy: Commercial Relationship(s);Code E (Employment):Ora | Mark Abelson: Commercial Relationship(s);Code E (Employment):Ora

ABSTRACT BODY:

Purpose: The purpose of this study was to show that subjects with allergic conjunctivitis (AC) or allergic rhinoconjunctivitis (ARC) develop moderate to severe ocular allergic signs and symptoms following 90 minutes of exposure to ragweed or timothy grass pollen in a mobile Allergen BioCube (mABC).

The clinical validation of the mobile Allergen BioCube (mABC) was performed in this study. A stationary version of the ABC was previously validated and used to conduct studies assessing the efficacy of drugs in the treatment of allergic rhinitis.

Methods: Subjects with a self-reported history of ocular allergic symptoms for the last 2 consecutive years during the ragweed or timothy grass seasons who had a positive skin test reaction to ragweed or timothy grass pollen within 24 months of Visit 1 were screened for this study. Subjects were exposed to either ragweed or timothy grass pollen in the mABC for 90 minutes and assessments were made at specified intervals (0, 10, 30, 60, and 90 minutes). A qualifying score was defined as a bilateral score of 2 or greater for both ocular itching and redness using standardized 0-4 severity scales at 90 minutes post-exposure.

Results: All subjects were asymptomatic prior to entering the mABC. All subjects experienced an increase in severity of ocular and nasal symptoms upon pollen exposure. Sixty (60%) percent of patients developed qualifying levels of bilateral ocular itching (mean score 2.7) and redness (mean score 3.1) at 90 minutes post-exposure. These subjects had a clinically (>1) and statistically ($P<0.05$) meaningful increase from baseline in all ocular and nasal allergic parameters at 90 minutes.

Conclusions: The mABC was effective in inducing ocular allergic signs and symptoms in subjects with a history of AC/ARC over a 90-minute exposure period. The mABC will be an important tool for evaluating allergy therapeutics in clinical studies requiring an environmental allergy model across multiple ophthalmology/allergy centers.

CONTROL ID: 3714167

SUBMITTER (NAME ONLY): Shahid Husain

TITLE: Role of DNA Methylation in RGC Death during Glaucoma Progression

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Husain, S. Singh, W. Guzman, Ophthalmology, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|

Commercial Relationships Disclosure: Shahid Husain: Commercial Relationship: Code N (No Commercial Relationship) | Sudha Singh: Commercial Relationship: Code N (No Commercial Relationship) | Wendy Guzman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The objective of this study is to determine the role of DNA methylation in RGC death during glaucoma pathology. We administered a selective DNA methylation inhibitor (Decitabine) or delta-opioid receptor agonist (SNC-121) to regulate the DNA methylation and methyltransferases activities in a rat glaucoma model and measured changes in biochemical and functional outcomes.

Methods: We used male and female Brown Norway rats (3-4 months old) to elevate intraocular pressure (IOP) by 2.0 M hypertonic saline injections in limbal veins. The changes in global DNA methylation were measured using the ELISA-based 5-methylcytosine (5mC) DNA Quantification Kit (# P-1030, EpiGenetek, Farmingdale, NY) according to manufacturer instructions. The activity of DNA methyltransferases (DNMTs) were measured by Enzyme Assay Kit from EpiGentek (Cat # P-3139, Farmingdale, NY), and changes in the expression pattern of DNMT-1, -3a, and -3b were determined by RT-PCR, WB, and immunohistochemistry.

Results: A significant RGC neuroprotection was offered by Decitabine and SNC-121 treatment at day 42, post glaucomatous injury as measured by Pattern ERGs. We also find an increase in genome-wide DNA methylation in the retina samples of ocular hypertensive animals at day 42, post glaucomatous injury, which was significantly inhibited with SNC-121 treatment. Additionally, we found an overall increase in the DNA methyltransferases (DNMTs) activity, mRNA, and protein expression of DNMT1, DNMT3a, and DNMT3b in the retina sections of ocular hypertensive animals at day 7 and 42, post glaucomatous injury.

Conclusions: Our novel data demonstrate that mRNA and protein expression of DNA methyltransferases (DNMTs) and global DNA methylation were increased in the retina of ocular hypertensive animals. Based on these findings it appears that Inhibition of DNA methylation may provide RGC neuroprotection in glaucoma.

CONTROL ID: 3714168

SUBMITTER (NAME ONLY): Mikiko Nagashima

TITLE: Microglial dynamics during photoreceptor death and regeneration in zebrafish

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nagashima, P.F. Hitchcock, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Mikiko Nagashima: Commercial Relationship: Code N (No Commercial Relationship) | Peter Hitchcock: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Microglia are the innate immune cells of the central nervous system and govern injury-induced inflammation by secreting pro- and anti-inflammatory cytokines and chemokines. In mammalian retinas, microglia reside in the retinal parenchyma, nerve fiber/ganglion cell layers and inner and outer plexiform layers. We have identified a novel population of microglia, unique to zebrafish, which reside among the retinal pigment epithelial cells. In this study, we compared the response of subretinal microglia with that of parenchymal microglia following death of photoreceptors. We then assay regeneration of photoreceptors in the csf1ra^{j4e1} mutant, where the number of parenchymal microglia, but not subretinal microglia, is diminished.

Methods: Photolytic lesions were used to selectively kill photoreceptors. The transgenic reporter line, Tg(mpeg:eGFP) and 4C4 antibody were used to visualize microglia. PCNA immunocytochemistry and TUNEL staining was used to assay proliferation and cell death, respectively.

Results: At 1 day post lesion (dpl), the number of microglia in the damaged outer retina increases by two-fold, whereas the number of microglia in the inner plexiform layer decreases significantly. This is accompanied by subretinal microglia descending toward the site of photoreceptor death. At 1 dpl, a small subset of microglia is co-labeled with TUNEL and the number of phagocytic microglia increases by 2 dpl. At 2 dpl, more than half of microglia in the subretinal space become PCNA+. By 14 dpl, the subretinal and parenchymal microglia resume their normal distribution, suggesting resolution of inflammation. In the csf1ra^{j4e1} mutants, the number of parenchymal microglia was significantly reduced, whereas the number of subretinal microglia matched that of wildtype animals. The diminished number of parenchymal microglia in the mutants did not affect the photoreceptor regeneration.

Conclusions: This study establishes the common and distinct responses of microglia populations that reside in retinal parenchyma and subretinal space in response to the selective death of photoreceptors. Activation, migration, and phagocytosis universally occur among microglia, whereas activated microglia proliferate predominantly in the subretinal space. The normal regeneration of photoreceptors in csf1ra^{j4e1} mutants suggests that subretinal microglia are sufficient to trigger the acute inflammation that governs photoreceptor generation.

CONTROL ID: 3714169

SUBMITTER (NAME ONLY): Sushil Dubey

TITLE: IL6 dysregulation in retinal pigment epithelium of global Cas9 expressing mouse strain

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The therapeutic potential of the CRISPR/Cas9 mediated gene editing in ophthalmic diseases is uncertain due to the lack of a comprehensive understanding of the toxicity and immune responses associated with the exogenous expression of Cas9. The purpose of this study is to evaluate for signatures of off-target immune responses and cytotoxicity associated with long-term Cas9 expression in the retina and retinal pigment epithelium (RPE).

Methods: Rosa26-Cas9 knock-in mice (RD8 negative), that constitutively express Cas9, were evaluated using color fundoscopy, spectral-domain optical coherence tomography (SD-OCT), and full-field electroretinography (ERG) across different age groups and compared to age-matched wild-type (WT) controls. RPE integrity was examined using ZO-1 immunofluorescence of RPE/choroid flat-mounts. In vitro evaluation of Cas9 toxicity in RPE cells was performed using MTT and annexin/PI assays. A panel of 84 genes associated with mouse innate and adaptive immunity was screened in neural retina and RPE/choroid of Cas9 and WT mice using Taqman PCR arrays. Statistical tests used included Mann-Whitney U, ANOVA, and Fisher's exact.

Results: Cas9 was expressed abundantly in the retina of Rosa26-Cas9 mice compared to WT mice, and fundus imaging revealed a normal-appearing posterior segment in young and aged (up to 12 months) mice. Full-field ERG responses were largely normal, but significant reduction was observed at the highest flash intensity in both a-wave and b-wave amplitudes of Cas9 mice compared to that of controls (p-value = 0.008). ZO-1 staining reveals intact RPE with regular hexagonal tiling even in the aged mice. Plasmid enforced expression of Cas9 in ARPE-19 cells demonstrated no loss of cell viability. Of the 84 genes tested in RPE/choroid of Cas9 and WT mice, IL6 was significantly upregulated (17.20 fold, p=0.0012) in Cas9 mice.

Conclusions: The Rosa-26 Cas9 knock-in mice appear phenotypically normal even up to 1 year. Mildly reduced full-field bright-flash ERG recordings were observed. Overall, long-term Cas9 expression does not appear to significantly reduce retinal cell viability. The altered expression of IL6 observed in the RPE/choroid of Cas9 mice implies the unexpected consequences and off-targeting events that CRISPR/Cas9 might cause. Further investigations of the mechanism by which IL6 is upregulated are underway and should be fully considered before employing this technology.

CONTROL ID: 3714171

SUBMITTER (NAME ONLY): Andrea Viczian

TITLE: A new mouse model for familial exudative vitreoretinopathy

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Viczian, M.E. Zuber, Ophthalmology, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|A.M. Moon, Molecular and Functional Genomics, Geisinger Medical Center, Danville, Pennsylvania, UNITED STATES|A.M. Moon, Pediatrics and Human Genetics, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Andrea Viczian: Commercial Relationship: Code N (No Commercial Relationship) | Anne Moon: Commercial Relationship: Code N (No Commercial Relationship) | Michael Zuber: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Familial exudative vitreoretinopathy (FEVR) is a genetic disorder in which the retinal vasculature fails to form fully (hypovascular). We discovered that loss of the T-box transcription factor, Tbx3, in mouse embryonic retinal progenitor cells results in a hypovascular retina. This study aimed to characterize this phenotype and determine how the loss of Tbx3 affects angiogenesis.

Methods: To remove Tbx3, we crossed the validated Tbx3-floxed mice with the optic cup-Cre recombinase driver, BAC-Dkk3-CRE, and confirmed loss of retinal protein by western blot. Cryostat retinal sections and flat mounts were immunostained, imaged, and cells counted using standard techniques. Statistical analysis was performed using Prism v9.3. ImageJ (v1.52q) and Volocity (v6.3) software were used for analysis.

Results: Blood vessels failed to extend to the edge of the P9 Tbx3 conditional knockout (cKO) retina and occupied significantly less of the total retinal surface area than wildtype siblings (WT, 0.489 ± 0.019; cKO, 0.230 ± 0.023). We also observed that the hyaloid artery failed to regress. At P30, we observed fewer branch points, decreased vascular density, and incomplete formation of the superficial plexus in mutant mice compared to controls. The astrocytic lattice was similarly stunted in the mutants, primarily in the dorsal region. Previous studies have shown that melanopsin-positive intrinsically photosensitive retinal ganglion (ipRGCs) and dopaminergic amacrine cells control retinal angiogenesis. At one month of age, we found a significant loss of ipRGCs (~30%) throughout the retina, with an even more substantial loss (~50%) in the dorsal region. In addition, we failed to detect the expression of tyrosine hydroxylase-positive amacrine cells in the Tbx3 cKO retina (3 litters: n=6 WT; n=5 cKO).

Conclusions: The loss of Tbx3 in retinal progenitors inhibits retinal angiogenesis in a pattern consistent with previous mouse models of FEVR. Our working hypothesis is that defects in angiogenesis are caused by a loss of ipRGCs and the absence of dopaminergic amacrine cells. Future studies will determine the molecular mechanism driving this defect in the Tbx3 cKO retina.

CONTROL ID: 3714172

SUBMITTER (NAME ONLY): Seth Hubbard

TITLE: The role of cofilin1 in cytoskeletal regulation of rod photoreceptors

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hubbard, Science and Technology Honors Program, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S. Hubbard, M. Garner, M. Hubbard, H.J. Levi, A.K. Gross, Department of Neurobiology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nuclear distribution protein C (NUDC) has been shown to regulate actin equilibrium through the stabilization of the F-actin severing protein cofilin1 (CFL1). Previously, we have shown NUDC is crucial for the development and maintenance of rod photoreceptors in X. laevis tadpoles and mice. We hypothesize NUDC modulates F-actin dynamics within photoreceptors through CFL1. Since CFL1 is further regulated by phosphorylation (pCFL1), we hypothesize the phospho-mimetic and phospho-null mutants of CFL1 will alter actin equilibrium within rods, thereby affecting outer segment (OS) disk formation. Here, we investigate the biochemical processes underlying F-actin architecture in the rod OS through transgenic expression of CFL1 mutants and shRNAs against Cfl1 in X. laevis.

Methods: We utilized immunohistochemistry (IHC) on X. laevis, mouse and human retinal sections to uncover the presence and localization of CFL in photoreceptors. We have expressed transgenic wild type CFL1 (CFL1), constitutively active phosphonull CFL1 ($CFL1^{S3A}$), dominant negative phosphomimetic CFL1 ($CFL1^{S3D}$), or shRNAs against Cfl1 in X. laevis tadpoles under the rod opsin promoter. Western dot blots, IHC, and protein proximity ligation assay (PLA) with fluorescent confocal microscopy will be employed to visualize the localization of key proteins within the rod cell at 2 and 4 weeks post-fertilization. We will utilize transmission electron microscopy to image ultrathin sections of 2wk old X. laevis to uncover photoreceptor OS ultrastructure in the presence of endogenous CFL1, its knock-down, or the mutant CFLs.

Results: We found CFL1 and pCFL1 both expressed in the inner segment (IS) of X. laevis, mouse, and human photoreceptors. PLA indicates that CFL1 is in close proximity (< 40nm) to NUDC in the IS and at the base of the OS in rods of mouse and X. laevis. Initial IHC staining shows transgenic overexpression of WT CFL1 in X. laevis does not affect photoreceptor development or maintenance while $CFL1^{S3D}$ produces actin and cytoskeletal disruptions.

Conclusions: We show CFL1 is expressed and colocalizes with NUDC at the base of the rod OS. Additionally, transgenic expression of $CFL1^{S3D}$ results in cytoskeletal dysregulation, supporting our hypothesis that NUDC governs the interactions between CFL1 and F-actin. Further analysis is ongoing. This work is critical for furthering our understanding of the molecular mechanisms behind OS disk regulation and formation.

CONTROL ID: 3714174

SUBMITTER (NAME ONLY): Alice Kitay

TITLE: The role of cumulative dosage on retinal structural changes in patients with HCQ retinopathy

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Albeit the introduction of spectral-domain optical coherence tomography (SD-OCT) modified screening facilities of Hydroxychloroquine (HCQ) retinopathy, the investigation of risk factors suggesting an early identification of retinal changes due to the drug is pivotal.

Methods: In a retrospective observational manner a dataset of 27 eyes with clinical hydroxychloroquine toxicity were analyzed and compared to an age-, gender-, ethnicity-matched control group with no toxicity. However, both groups had a significant difference in means of cumulative HCQ dosage in gram. SD-OCT scans (Heidelberg Engineering, Heidelberg Germany) were analyzed and automatic retinal-layer segmentation performed. Subsequently, mean thickness values subdivided in full retina, ganglion cell layer (GCL), outer nuclear layer (ONL), photoreceptor layer, retinal pigment epithelium (RPE) and outer retinal layer (photoreceptor layer + ONL) were calculated and compared. Additionally, layers were categorized in center, middle ring and outer ring according to the ETDRS grid.

Results: The conducted study highlights changes of retinal thickness in patients with clinical toxicity. When comparing full retina layer in the central subfield, results revealed significant difference between eyes with toxicity to control eyes (250.8 ± 26.1 versus 272.1 ± 23.6, p=0.011), while the categorical variable including the percentage of eyes with reduced retinal thickness did not outline any significance (7.4% vs. 0%, p=0.554). However, comparing middle and outer ring of the full retina layer did show significant difference in both calculations (292.3 ± 27 versus 332.8 ± 16.6, p <0.001 respectively 59.3% versus 7.4%, p=0.013 and 265.8 ± 31.6 versus 292.0 ± 14.9 respectively 57.7% versus 0%, p=0.011). Similar results were detected for the middle ring of GCL and ONL. The GCL showed a highly significant difference of retinal thickness in eyes with toxicity compared to control eyes (35.3 ± 15.2 versus 49.6 ± 3.9, p=0.001) which resulted in a GCL thinning of 51.9% in toxicity eyes compared to reference data.

Conclusions: Our data elucidate the impact of the cumulative dosage in regard of retinal changes. We emphasize the importance of OCT imaging as a screening tool to quantify structural changes in the different retinal layers that might help to identify early changes for patients with HCQ retinopathy with no clinical manifestation at an early stage.

CONTROL ID: 3714176

SUBMITTER (NAME ONLY): Altan Rentsendorj

TITLE: Synaptic loss correlates with pTau accumulation and decreased UCH-L1 expression in the retinas of MCI and Alzheimer's patients

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rentsendorj, T. Torbati, D. Fuchs, J. Sheyn, M. Davis, N. Mirzaei, K. Black, Y. Koronyo, M. Koronyo-Hamaoui, Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|M. Koronyo-Hamaoui, Department of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cerebral hallmarks of Alzheimer's disease (AD) manifest in the neurosensory retina at early disease stages. However, synaptic loss that tightly predicts cognitive decline has never been described in the AD retina. The ubiquitin-proteasome system (UPS), a major degradation pathway for damaged proteins, has been implicated in AD pathogenesis. A vital component of UPS, ubiquitin hydrolase (UCH-L1), exhibits a neuroprotective role and is required for normal synaptic function. Since low levels of brain UCH-L1 were linked with cerebral Aβ accumulation in AD, we explored its expression in AD patients' retina.

Methods: Using various histological approaches, we assessed synaptic integrity, tauopathy, apoptosis and UCH-L1 levels in post-mortem retinas of patients with confirmed mild cognitive impairment (MCI) due to AD or AD dementia, compared to age- and sex-matched subjects with normal cognition (NC). We visualized and quantified synaptic density by analysis of pre- and post-synaptic markers (e.g., VGlut1, PSD95, Synaptophysin) and determined their spatial and cell layer distribution.

Results: We detected extensive (1.6- to 3-fold) pre- and post-synaptic losses in the IPL and OPL of MCI and AD patients, whereas early synaptic loss was mostly detected in the far peripheral regions. Along with marked synaptic loss, the retinal layers of MCI and AD patients demonstrated 2- to 4-fold decreases in levels of UCH-L1 as compared to NC. Notably, decreased levels of retinal UCH-L1 directly correlated with pre-synaptic loss ($p<0.0001$), especially in the far periphery of AD patients. The pre-synaptic VGluT1 marker also inversely correlated with pTau (e.g., AT8) accumulation, colocalizing at sites of synaptic loss, in the IPL and OPL layers in MCI and AD patients. These changes were accompanied by significant 1.8-4.2-fold increases in apoptotic cell death in the retinas of these patients ($p< 0.05–0.001$).

Conclusions: Our results reveal a substantial retinal synaptic loss at sites of pTau accumulation in prodromal and clinical AD patients. Retinal UCH-L1 expression was significantly deficient in MCI and AD patients, and due to its part in the UPS protein degradation pathway and tight correlation with retinal synaptic loss in AD, this study suggests its importance in retinal synaptic protection against AD-related stress.

CONTROL ID: 3714177

SUBMITTER (NAME ONLY): Ethan bensinger

TITLE: Capturing Tear Film Stability with the Ocular Protection Index (OPI) acquired with Ora EyeCup Phone

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. bensinger, J.D. Rodriguez, M. Marquis, K. Dieter, I. Sinyak, M.B. Abelson, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with dry eye disease experience greater tear film instability and more rapid rates of tear film break-up post blinks. The Ora EyeCup Phone is able to measure tear film stability utilizing the Ocular Protection Index (OPI) scale. OPI not only looks at the time for the tear film to break up but also allows the assessment of the break up area.

Methods: We tested 15 patients (12 female; mean age 62 yo) with a reported history of dry eye disease and a tear film break up time less than 5 seconds. Fluorescein was instilled via micropipette in both eyes 3 minutes prior to video recording. The EyeCup was fitted with led lights to activate the fluorescein and a filter was placed in front of the camera. Patients were instructed to hold their gaze on a crosshair positioned straight ahead of the subject while a 1-minute 4k 60 frames per second video on each eye was recorded using the google Pixel 5. Patients were asked to blink normally while the video was acquired to provide a natural interblink interval (IBI) and tear film break up time (TFBUT). Videos were processed using a custom semi-automated algorithm previously described.

Results: Video acquisition with the Ora EyeCup Phone was successful in all patients and took five minutes or less from instruction to successful recording of both eyes. Video quality was similar to videos previously measured using a DSLR camera in a slit lamp exam. In all patients the OPI was below 1, indicating they had an unprotected ocular surface. The average OPI was 0.090 (standard deviation 0.027).

Conclusions: This study demonstrated the feasibility of performing real-time, home-based assessment of tear film stability and ocular surface protection using a novel technology. This proof-of-concept study suggests the usefulness of this technology in clinical trials investigating the effect of different treatment modalities for dry eye disease outside the laboratory setting.

CONTROL ID: 3714178

SUBMITTER (NAME ONLY): Michael Shelton

TITLE: Time course of artificial tear efficacy in dry eye disease revealed by inter-blink interval visual acuity decay (IVAD) test

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shelton, E. Besinger, J.D. Rodriguez, M.B. Abelson, K. Dieter, M. Dusharm, G. Wallstrom, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with dry eye disease experience greater tear film instability and more rapid rates of tear film break-up. This faster decay of ocular surface protection can impact visual function, as a smooth, regular tear film is critical to maintaining best corrected visual acuity (BCVA). Using an enhanced version of the inter-blink interval visual acuity decay (IVAD) test (1), we examined the impact of an artificial tear compound (Systane Ultra, Alcon, Inc.) on visual function between blinks.

Methods: We tested 15 patients (12 female; mean age 62 yo) with a reported history of dry eye disease. To examine how visual acuity changed between blinks for these patients, we used an upgraded version of the IVAD test (1). In this test, patients are instructed to blink three times and then hold their eye open. While holding their eye open, patients identify rotated Landolt C images presented at their distance BCVA for each eye, with time to visual acuity decay determined by patients' accuracy at this task at various time points between blinks. We repeated the test for each qualifying eye at 5 time points (prior to the administration of the artificial tear, and again at 5, 15, 45, and 90 minutes post-administration).

Results: Our findings revealed that prior to the administration of the artificial tear, patients maintained BCVA for 12.3±2.3 seconds before experiencing decay. Soon after the drop was administered, time increased by more than 50% at both the +5-minute (18.8±3.3 seconds; $p=0.0008$) and +15-minute (22.1±2.5 seconds; $p=0.0449$) timepoints before returning to baseline (12.9±1.7 and 12.6±2.1 seconds at +45- and +90-minute time points respectively; both $p > 0.85$).

Conclusions: Our new version of a technique to assess visual function in dry eye disease revealed that a commercially available artificial tear can help significantly prolong the duration of BCVA in patients with dry eye disease. This effect is transient across the time course, with a larger effect soon after the drop is administered (+5 and +15 minutes) and returning to baseline by the 45-minute time point. These results add further evidence demonstrating how tear film stability impacts visual function in patients with dry eye disease (1) and support the usefulness of the IVAD test as a novel end point for assessing visual function in new therapies developed for the treatment of dry eye disease.

CONTROL ID: 3714179

SUBMITTER (NAME ONLY): Sree Indrani Motipally

TITLE: Palmitoylation in PRCD protein plays an indispensable role in conferring protein stability by preventing protein ubiquitination

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Motipally, S. Kolandaivelu, Department of Ophthalmology, West Virginia University Eye Institute, Morgantown, West Virginia, UNITED STATES|S. Motipally, Department of Neuroscience, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|S. Kolandaivelu, Department of Biochemistry, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|

Commercial Relationships Disclosure: Sree Indrani Motipally: Commercial Relationship: Code N (No Commercial Relationship) | Saravanan Kolandaivelu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Progressive rod-cone degeneration (PRCD) is an integral membrane protein strongly associated with photoreceptor disc membranes that is crucial for maintaining the structural and functional integrity of photoreceptor outer segments (POS). Previously we showed that the sole cysteine (Cys2) in PRCD is palmitoylated, a post translational lipid modification that is essential for protein stability and trafficking to the OS. However, the precise role of palmitoylation in PRCD remains obscure. The focus of this study is to define how palmitoylation in PRCD supports protein stability and trafficking to the OS using multiple PRCD mice models and cell culture studies.

Methods: We evaluated visual function by electroretinogram (ERG) at various ages in the PRCD-C2Y animals and littermate controls. To investigate the role of palmitoylation, we made plasmid construct changing palmitoylation to myristoylation (PRCD-C2G) and analyzed protein stability and trafficking by western blotting and immunohistochemistry. Furthermore, PRCD aggregation into mitochondrial membranes and proteasomal insufficiency was investigated in various PRCD-C2Y models. Next, mitochondrial function is analyzed in age matched WT, and PRCD mutant retinas using seahorse flux analyzer. Ultrastructure of PRCD-C2Y retina was performed by transmission electron microscopy.

Results: Our ERG and ultrastructure studies in PRCD-C2Y animal models show attenuated visual responses, lamellar disorientation, and vesicular profiles in the photoreceptor OS like canine models. Furthermore, substituting myristoylation (PRCD-C2G) for palmitoylation neither alleviated the protein stability nor restored PRCD trafficking to the OS. Interestingly, mutating C-terminal ubiquitin sites (K50R/K54R) enhanced the stability in PRCD-C2Y mutant protein. Also, our data shows dysregulated mitochondrial metabolism in PRCD-C2Y retina.

Conclusions: Our studies demonstrate that palmitoylation in PRCD is indispensable for PRCD protein stability and trafficking to POS. Substituting myristoylation for palmitoylation does not rescue protein stability or trafficking of PRCD-C2Y mutant. However, mutating ubiquitin signal in palmitoylation deficient PRCD-C2Y led to enhanced protein stability suggesting that both palmitoylation and ubiquitination coordinate to maintain PRCD protein homeostasis.

CONTROL ID: 3714182

SUBMITTER (NAME ONLY): Asad Loya

TITLE: Association of Lifetime Major Depressive Episode with Significant Visual Impairment or Blindness

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Loya, Baylor College of Medicine Department of Ophthalmology, Houston, Texas, UNITED STATES|Z.S. Hussain, University of Medicine & Health Sciences, Basseterre, SAINT KITTS AND NEVIS|J. Andoh, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|B.J. Harvey, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Very recent empirical estimates of Americans living with visual acuity loss or blindness have significantly superseded prior benchmarks. Previously published literature demonstrates a strong association between vision loss and psychiatric disease. This US national database analysis utilizes the latest edition of the NSDUH to characterize the odds of lifetime episode of major depression associated with significant visual impairment or blindness in the United States.

Methods: The latest edition of the National Survey of Drug Use and Health (NSDUH) database was executed for procurement of nationally de-identified cases of major depressive episode (MDE) and significant visual impairment or blindness. Significant visual impairment or blindness (despite refractive correction) is defined using interview-generated responses. Patients with unknown incidence of visual impairment or MDE were excluded. Univariable and multivariable logistic regression yielded odds ratios (ORs) and standard error of mean (SEM) with 95% confidence intervals (95% CI). Statistical significance was achieved at $p<0.05$.

Results: Of 42,179 patients, 7543 (17.9%) experienced a lifetime MDE. Of the lifetime MDE cohort, 481 (6.3%) cases experienced significant vision loss or blindness (Table 1). Of the cohort with no lifetime MDE, 1,338 (3.8%) experienced vision loss/blindness. Univariable logistic regression highlights increased odds of lifetime MDE for patients afflicted with significant visual impairment or blindness (OR=1.695, 95% CI: 1.523-1.887, $p<0.001$) (Table 2). Multivariable analysis adjusting for psychosocial factors and chronic diseases supported this finding (OR=1.561, 95% CI: 1.379-1.767, $p<0.001$).

Conclusions: Within the US national population, significant visual impairment or blindness prognosticates significantly increased odds of lifetime development of major depressive episode. Recent advances in our understanding of the heightened prevalence of vision loss and blindness in America acts as provision for highlighting current associations related to psychiatric disease, including major depressive episode. Clinical decision-making should reconcile efforts to maintain quality of life in ophthalmologic patients with low vision through multidisciplinary approaches.

CONTROL ID: 3714183

SUBMITTER (NAME ONLY): Yi Zhang

TITLE: Widefield optical coherence tomography angiography imaging with distortion correction

SESSION TITLE: Innovations in image processing and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Zhang, Q. Zhang, H. Zhou, X. Zhou, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R.K. Wang, Opthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop widefield OCT angiography (OCTA) imaging with distortion free, a field-of-view (FOV) of at least 100 degrees, and an ability to quantify retinal flow.

Methods: OCTA images were acquired by a swept-source optical coherence tomography (SS-OCT) with a central wavelength of 1060 nm (PLEX® Elite 9000; ZEISS, Dublin, CA) running at 100 kHz with a 6×6 mm scan pattern. Widefield images were obtained by automatic stitching of the OCTA scans acquired at nine fixation spatial positions guided by the system. A phantom eye was used to develop, validate and test the developed distortion correction method. The en face images of retinal flow were first generated for individual scans, and then distortion was corrected by modeling the beam propagation in the eye. The final widefield image was formed by montaging distortion-corrected spatial scans together through an algorithm based on the Distinctive Image Features from Scale-Invariant Keypoints. Measurements of retinal flow impairment zone, vessel density, vessel skeleton density were compared before and after distortion correction.

Results: Normal eyes (N=5) and eyes with diabetic retinopathy (DR) (N=5) were recruited in this study. Results from phantom eye demonstrated successful correction of distortion during scanning. Clinically, the proposed method was shown capable of successfully achieving a FOV as large as 100 degrees on both normal eyes (Figure 1 A) and eyes with DR (Figure 1 B). The distortion-corrected images demonstrated continuous vessel connections across the whole montaged image. The statistical analyses showed a significant difference ($p<0.05$) in retinal flow impairment zone measurements before and after distortion correction.

Conclusions: Distortion correction is clinically important in the visualization and quantification of the widefield OCTA image with a FOV up to 100 degrees, which provides a more accurate assessment of microvascular involvement in eye diseases, particularly for the diseases that require the inspection of peripheral regions, such as DR.

CONTROL ID: 3714184

SUBMITTER (NAME ONLY): Leyla Yavuz Saricay

TITLE: The Refractive Errors in Patients with Bardet-Biedl Syndrome (BBS)

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Yavuz Saricay, E. Moulton, E. Gonzalez, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|L. Yavuz Saricay, E. Moulton, E. Gonzalez, A.B. Fulton, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Leyla Yavuz Saricay: Commercial Relationship: Code N (No Commercial Relationship) | Eric Moulton: Commercial Relationship: Code N (No Commercial Relationship) | Efren Gonzalez: Commercial Relationship: Code N (No Commercial Relationship) | Anne Fulton: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study corneal astigmatism in BBS. The ciliopathy associated with BBS may contribute to increased proliferation and vertical migration of corneal epithelial basal-layer cells, thus consequent astigmatism.

Methods: We studied the cycloplegic refraction and results of keratometry in 48 patients (96 eyes) with biallelic diagnosis of a form of BBS (BBS1, BBS2, BBS6, BBS7, BBS10, BBS12, or MKS1) seen at Boston Children’s Hospital from February 2011–August 2021.

Results: The mean age of patients was 16.3 (± 8.0) years. The mean best-corrected visual acuity was 20/60, the mean keratometry value at the steepest axis was 48.05 D (±9.50) at 89 degrees, and the mean keratometry value at the flattest axis was 43.46 D (±6.35) at 168 degrees. Average corneal astigmatism was 4.59D (>4D = extreme range), mean spheric refractive error was -2.75 D (±3.88), and mean cylindric refractive error was -2.62 D (±1.39).

Conclusions: Genetically diagnosed BBS patients demonstrated high corneal astigmatism. BBS is a member of the ciliopathy family, and corneal microtubule-based protrusion and corneal development/remodeling dysfunction can be linked. We suggest that these patients should be screened by corneal topographic evaluation and that the primary cilium should be considered a target in disease management.

CONTROL ID: 3714185

SUBMITTER (NAME ONLY): Jennifer Kang-Mieler

TITLE: Initial Treatment Efficacy of Aflibercept-loaded Microparticle-hydrogel Drug Delivery System in a Laser-induced Choroidal Nonhuman Primate Model

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Kang-Mieler, K. Rudeen, Biomedical Engineering, Illinois Institute of Technology, Chicago, Illinois, UNITED STATES|K.P. Roszak, S. Park, B.D. Story, S.M. Thomasy, Surgical and Radiological Sciences, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|G. Yiu, S.M. Thomasy, Ophthalmology and Vision Science, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|W.F. Mieler, Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Jennifer Kang-Mieler: Commercial Relationship(s);Code P (Patent):Patent No 10,980,882 | Kayla Rudeen: Commercial Relationship: Code N (No Commercial Relationship) | Karolina Roszak: Commercial Relationship: Code N (No Commercial Relationship) | Sangwan Park: Commercial Relationship: Code N (No Commercial Relationship) | Brett Story: Commercial Relationship: Code N (No Commercial Relationship) | Glenn Yiu: Commercial Relationship(s);Code C (Consultant/Contractor):Abbvie, Alimera, Anlong, Clearside, Endogena, Genentech, Gyroscope, Intergalactic, Iridex, NGM Biopharmaceutical, Regeneron, Thea, Topcon, Zeiss | William Mieler: Commercial Relationship: Code N (No Commercial Relationship) | Sara Thomasy: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intravitreal injections of anti-vascular endothelial growth factor (VEGF) has become the gold standard of treatment for wet age-related macular degeneration. However, this treatment is limited by the need for repeated injections due to the rapid clearance and short half-life of anti-VEGFs. Recently, we developed a drug delivery system (DDS) that releases bioactive aflibercept (AFL) for six months. This system showed treatment efficacy in a laser induced choroidal neovascularization (CNV) rodent model. The purpose of this study was to determine the treatment efficacy of AFL-DDS in a laser-induced CNV nonhuman primate model.

Methods: AFL-loaded poly(lactic-co-glycolic acid) microparticles were created using a modified double emulsion technique. Then, microparticles were embedded into a biodegradable, thermoresponsive poly(ethylene glycol)-co-(L-lactic-acid) diacrylate/N-isopropylacrylamide hydrogel to create AFL-DDS. Eight CNV lesions were created by laser photocoagulation (50 µm, 150 ms, 750 mW) in each eye of rhesus macaques. For all animals, OD was treated with AFL-DDS (50 µl, 15 ug) and OS was used as control. At Week 0 (14 days after the laser induction), AFL-DDS treatment was administered. Fluorescein angiography (FA) and spectral domain optical coherence tomography (OCT) was obtained at Weeks 0, 2, and 4. Lesion size was measured using the multi-Otsu thresholding (MOT) analysis and normalized to the measurements at Week 0.

Results: Before the AFL-DDS treatment, FA and OCT confirmed that CNV lesions were fully developed. No complications observed due to the CNV induction or AFL-DDS intravitreal injection. At Week 0, average lesion area was 0.38 ± 0.01 mm^2 for the AFL-DDS treated eyes. Two weeks after AFL-DDS treatment administration, average lesion area was 0.78 ± 0.05 mm^2. When normalized to Week 0, the lesion increased by 136.7 ± 16.6%. By 1-month post-treatment, average lesion size was 0.38 ± 0.01 mm^2. When normalized to the Week 0, an increase of 9.7 ± 3.6% was still observed.

Conclusions: Current results show that AFL-DDS treatment had a positive effect on reducing CNV lesions in a short-term treatment study. Based on the positive effects of AFL-DDS, a longer duration of CNV evaluation will be conducted.

CONTROL ID: 3714186

SUBMITTER (NAME ONLY): Steven Mansberger

TITLE: Patient Reported Outcome Measures while using a device to objectively measure eye drop adherence

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.L. Mansberger, F.G. Sanchez, J.P. Rees, S.K. Gardiner, V. Klei, J. Duvdevany, M.L. Kobak, R.M. Kinast, Devers Eye Institute, Legacy Health System, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Steven Mansberger: Commercial Relationship(s);Code C (Consultant/Contractor):Thea;Code C (Consultant/Contractor):Nicox;Code O (Owner):Nicox;Code F (Financial Support):AbbVie;Code O (Owner):Universal Adherence | Facundo Sanchez: Commercial Relationship: Code N (No Commercial Relationship) | Jack Rees: Commercial Relationship: Code N (No Commercial Relationship) | Stuart Gardiner: Commercial Relationship: Code N (No Commercial Relationship) | Viridian Klei: Commercial Relationship: Code N (No Commercial Relationship) | Julie Duvdevany: Commercial Relationship: Code N (No Commercial Relationship) | Max Kobak: Commercial Relationship: Code N (No Commercial Relationship) | Robert Kinast: Commercial Relationship(s);Code O (Owner):Universal Adherence

ABSTRACT BODY:

Purpose: The Devers Drop Device (D3) is a first-generation eye cap monitor (Figure) to objectively measure eye drop adherence and eye drop-taking behavior. It includes local and cloud storage of adherence data, wireless communication, visual and auditory alerts, and a universal fit, which allows it to attach onto any FDA-approved eye drop bottle cap. We were interested in patient reported outcome measures (PROM) using the D3.

Methods: We enrolled research subjects with a diagnosis of glaucoma or glaucoma suspect who own an Android smartphone or iPhone, and use latanoprost eye drops at bedtime. The study included two stages: Stage 1) a 25-day period (±3 days) evaluating baseline patient adherence with the D3 device; and Stage 2) a subsequent 25-day (±3 days) period to determine the effect of the D3 device with no reminder versus a daily alert from the D3 device. At enrollment and at the last visit, we administered a questionnaire and the Glaucoma Treatment Compliance Assessment Tool (GTCAT) to determine attitudes about adherence and satisfaction with the D3. We defined adherence as the proportion of eye drops administered within +/-3 hours of the expected dosing time. We used linear regression to determine the association of adherence with sociodemographic factors, and questionnaire responses.

Results: We enrolled 53 participants with 50 completing Stage 1 (1 patient withdrew, 1 patient had a latanoprost-related adverse event, and 1 device failure). Adherence was 90.2% ± 18% (range 32-100%). Lower adherence was associated with lack of insurance coverage for prescription medications (p=.05), higher total number of eye drop bottles used per day (p=.06), higher number of eye drops per day (p=.10), and 4 GTCAT questions (p<=.14 for each). Ninety-six percent (96%) of the subjects were able to use the device; and 98% reported that the device stayed attached to the cap. However, only 49% were able to connect the device to their home wifi network. We received several recommendations for improvement including decreasing its size and improving its connectivity.

Conclusions: We have developed a D3 prototype for research in glaucoma adherence with good patient satisfaction. Future developments should include a smaller, consumer-ready version that is easy to connect.

CONTROL ID: 3714187

SUBMITTER (NAME ONLY): Sunil Bellur

TITLE: Racial Differences in the Rates of Pseudophakic Cystoid Macular Edema after Routine Phacoemulsification Cataract Surgery

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bellur, H. Sen, National Eye Institute, Bethesda, Maryland, UNITED STATES|H. Pakhchanian, M. Asahi, M. Dalal, H. Sen, The George Washington University, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Black patients are prone to prolonged inflammation after cataract surgery, but there is a lack of data on whether rates of pseudophakic cystoid macular edema (PCME) is higher in black patients compared to white patients. This retrospective study aimed to assess if race is an independent risk factor in the development of post-operative PCME after routine phacoemulsification cataract surgery (PCS).

Methods: A retrospective cohort study was conducted using TrinetX, a federated multicenter database with over 80 million patient records across 57 healthcare organizations. Patients who underwent routine PCS were included. Exclusion criteria included complex PCS, history of macular edema, diabetic retinopathy, iridocyclitis, and/or panuveitis. Primary and secondary outcome measures were the incidence and prevalence of PCME and iridocyclitis, respectively, from post-operative day(d) 1 to 180. The cohort was stratified into black and white groups and underwent 1:1 propensity score matching (PSM) for age, gender, and medical comorbidities to calculate adjusted Risk Ratios (aRR) with 95% confidence intervals. Diabetes mellitus (DM) was analyzed in a subgroup analysis.

Results: The study included 24,324 black and 24,324 white patients after PSM. Over the 1-180d post-operative interval, the black cohort had a significantly higher prevalence and risk (aRR [95%CI]) of PCME (0.7% vs 0.4%, aRR 1.98 [1.53,2.56], p<0.001) and iridocyclitis (1.6% vs 0.3%, aRR 5.35 [4.16,6.89], p<0.001). Incidence of PCME peaked between 45-90d in the black cohort (0.3%) and 1-45d in the white cohort (0.2%). Incidence of PCME was higher in the black cohort vs white cohort in the 45-90d (0.3% vs 0.1%, aRR 2.65 [1.69,4.16], p<0.001) and 91-135d interval (0.2% vs 0.1%, aRR 2.93 [1.6,5.38], p<0.001). Incidence of iridocyclitis was higher in the black cohort in the 1-45d (0.5% vs 0.1%, aRR 3.81 [2.58,5.63], p<0.001), 45-90d (0.5% vs 0.1%, aRR 6.19 [3.76, 10.18], p<0.001), and 91-180d intervals (0.6% vs 0.1%, aRR 7.05 [4.47,11.14], p<0.001). A subgroup analysis excluding DM included 15,523 black and 15,523 white patients; prevalence of PCME over 1-180d was higher in black vs. white patients (0.8% vs 0.4%, aRR 1.98 [1.45,2.7], p<0.001), as was iridocyclitis (1.5% vs 0.3%, RR 5.09 [3.7, 7.0], p<0.001).

Conclusions: In this study, race was shown to be an independent risk factor in developing PCME after routine PCS.

CONTROL ID: 3714189

SUBMITTER (NAME ONLY): Aicha Saadane

TITLE: Deficiency in classical monocytes prevents superoxide, inflammation and retinal vascular lesions in diabetic mice

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saadane, A.A. Veenstra, M. Minns, Y. Du, E. Lessieur, T.S. Kern, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accumulating evidence suggests that leukocytes play a critical role in diabetes-induced vascular lesions and other abnormalities that characterize the early stages of diabetic retinopathy (DR). However, it is not clear which subset of leukocytes is involved in this process, here we used $Ccr2^{-/-}$ mice to study the role of $CCR2^{+}$ monocytes in the pathogenesis of the retinopathy.

Methods: Experimental diabetes was induced in wild-type (WT) and $Ccr2^{-/-}$ mice using streptozotocin. After 2 months of diabetes, superoxide levels, expression of inflammatory proteins, leukostasis, leukocyte- and monocyte-mediated cytotoxicity against retinal endothelial cell (EC) death, retinal thickness, and visual function were evaluated using published techniques. Retinal capillary degeneration was determined after 8 months of diabetes. Flow cytometry of peripheral blood for differential expression of CCR2 in monocytes was determined.

Results: In nondiabetic mice, CCR2 was highly expressed on monocytes, and $Ccr2^{-/-}$ mice lack $Ccr2^{+}$ monocytes in the peripheral blood. The diabetes-induced retinal superoxide, expression of pro-inflammatory proteins (iNOS and ICAM-1), leukostasis, and leukocyte-mediated cytotoxicity against retinal EC were inhibited in diabetic Ccr2-deficient mice and in chimeric mice lacking Ccr2 only from myeloid cells. In order to focus on monocytes, these cells were immuno-isolated after 2 months of diabetes, and they significantly increased monocyte-mediated EC cytotoxicity ex vivo. Monocytes from Ccr2-deficient mice caused significantly less EC death. The diabetes-induced retinal capillary degeneration was inhibited in $Ccr2^{-/-}$ mice and in chimeric mice lacking Ccr2 only from myeloid cells.

Conclusions: Ccr2-deletion inhibits the development of retinal vascular lesions (presumably via the population of monocytes that express the Ccr2 protein). Thus, $Ccr2^{+}$ myeloid cells (mainly monocytes) contribute to the pathogenesis of early lesions of DR.

CONTROL ID: 3714190

SUBMITTER (NAME ONLY): Yoon Jeon Kim

TITLE: Restoration of translocator protein dysfunction alleviates oxidative stress induced by A2E in human retinal pigment epithelial cells

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kim, S. Kim, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|J. Choi, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Yoon Jeon Kim: Commercial Relationship: Code N (No Commercial Relationship) | Sang A Kim: Commercial Relationship: Code N (No Commercial Relationship) | Jeong A Choi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We investigated the effects of translocator protein (TSPO) on the functional regulation of retinal pigment epithelium (RPE) using an A2E (N-retinylidene-N-retinylethanolamine) induced cellular stress model, mimicking lipofuscin accumulation in degenerative RPE cells.

Methods: We examined A2E-induced changes of TSPO mRNA level in a human RPE cell line (ARPE19). To figure out the function of TSPO in RPE cells, we treated TSPO siRNA for 24 hours and compared their viabilities and oxidative stress levels with the negative control group. Cellular functions following TSPO ligand treatment were investigated.

Results: Four hours after A2E treatment, A2E-exposed ARPE19 exhibited significant induction of oxidative stress and increase in mRNA of TSPO accompanied with intracellular A2E accumulation. Knock-down of TSPO with siRNA exhibited increased intracellular accumulation of A2E and aggravated oxidative stress without significant changes in cell viability. Treatment with TSPO ligand reduced A2E accumulation and restored oxidative stress response.

Conclusions: Our results support the possibility that restoration of TSPO homeostasis may help overcome A2E-induced cellular stress in ARPE19 cells, serving as a potential therapeutic strategy of AMD.

CONTROL ID: 3714191

SUBMITTER (NAME ONLY): Maurice Marquis

TITLE: Patient self acquired photos with the Ora Eyephone compared to self reported eye redness in mobile biocube

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Marquis, M.B. Abelson, J.D. Rodriguez, E. bensinger, I. Sinyak, Ora Inc, Andover, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Maurice Marquis: Commercial Relationship(s);Code E (Employment):Ora Inc | Mark Abelson: Commercial Relationship(s);Code E (Employment):Ora Inc | John Rodriguez: Commercial Relationship(s);Code E (Employment):Ora Inc | Ethan bensinger: Commercial Relationship(s);Code E (Employment):Ora Inc | Igor Sinyak: Commercial Relationship(s);Code E (Employment):Ora Inc

ABSTRACT BODY:

Purpose: Objective measures of conjunctival redness while inside an environmental chamber has til now not measured. With the use of the Ora EyeCup phone we are able to get objective images of ocular redness and obtain patient self assessed redness and itching.

Methods: During exposure in Ora's Biocube 15 patients were given the Ora EyeCup Phone to take photos at 90 minutes into exposure. Patients were prompted to take photos by the EyeCup Phones custom software at multiple timepoints. Patients took photos of their own eye with the Ora EyeCup attached looking straight head and looking upwards while holding down their lower lid. After photos were taken at each timepoint subjects were sent to a e-diary to assess allergic symptoms including eye redness evaluated while using a mirror. Photos were then evaluated using a custom grading software on the same scale that the patient was given.

Results: The mean patient reported redness was 3.1 on a scale from 0 to 4 with only whole integers. Mean redness from photo grading was 3.25 with the average difference between patient reported redness and photo graded redness was 0.3.

Conclusions: These results indicate that patient self-reported redness was in good agreement with expert graders indicating that these experienced allergy patients are able to correctly assess their symptoms. Patients were successfully able to acquire high quality gradable images alleviating the need for a photo technician in the chamber and illustrating the ease of use for the Ora EyeCup phone.

CONTROL ID: 3714193

SUBMITTER (NAME ONLY): Hongyuan Zhang

TITLE: In-vivo human corneal biomechanical screening fulfilled by motion-tracking Brillouin microscopy

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zhang, L. Asroui, J.B. Randleman, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|G. Scarcelli, University of Maryland at College Park, College Park, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Hongyuan Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Lara Asroui: Commercial Relationship: Code N (No Commercial Relationship) | Giuliano Scarcelli: Commercial Relationship: Code N (No Commercial Relationship) | James Randleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Overcome motion artifact during slow Brillouin acquisition by introducing 3-dimensional tracking. Demonstrate that motion-tracking Brillouin microscopy can distinguish keratoconus, post-LASIK or post-PRK from the control based on the different distribution of Brillouin shifts.

Methods: Optical coherence tomography and pupil tracking were combined with a traditional Brillouin microscope to reduce motion blur caused by patient movement during slow Brillouin scan. Positioning errors were corrected in 3 dimensions by combing axial information from OCT and lateral information from pupil tracking. Tracking accuracy was tested in advance using enucleated porcine eyes. During in-vivo human measurement, 30 axial scans were applied to discrete points on each cornea. An axial scan took 5 seconds with a step size of 15 μm. 2-dimensional interpolation was used to connect the measured discrete points to generate a map of Brillouin shifts of the cornea.

Results: Data from tests on porcine eyes showed that axial positioning errors were within 5 μm along a movement of 1 mm with a step size of 100 μm. Meanwhile, lateral positioning errors were within 3 μm over a 9 mm movement. In-vivo Brillouin results showed that a normal cornea, a subtle keratoconus, a post-LASIK and a post-PRK shared similar Brillouin shifts of around 5.7 GHz at the periphery. The difference mainly existed in the center region. The Brillouin shift at the center was about 5.69 GHz for the normal cornea, 5.67 GHz for the post-LASIK cornea and the post-PRK cornea. For the subtle keratoconus cornea, the Brillouin shift at the cone was about 5.65 GHz.

Conclusions: Patient movement can be tracked precisely by pupil tracking and OCT. Brillouin shifts at different depths can be reaccommodated properly after motion compensation. Maps of Brillouin shifts across the cornea can show weak regions and help keratoconus diagnosis.

CONTROL ID: 3714194

SUBMITTER (NAME ONLY): Chris Schulz

TITLE: Automated video assessment of the eyelids

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Schulz, H. Clarke, S. Makuloluwe, Eye Department, Portsmouth Hospitals University NHS Trust, Portsmouth, Portsmouth, UNITED KINGDOM|S. Kang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Chris Schulz: Commercial Relationship: Code N (No Commercial Relationship) | Holly Clarke: Commercial Relationship: Code N (No Commercial Relationship) | Sarith Makuloluwe: Commercial Relationship: Code N (No Commercial Relationship) | Swan Kang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Advances in artificial intelligence might allow automated video assessment of the ocular adnexa. This study aimed to develop and test a program to automate assessment of eyelid position (MRD1 & MRD2), blink lagophthalmos (bLag) and average ocular surface area exposure (OSAE) from videos.

Methods: A custom program was designed to analyse each frame from a video of a person's face (fig 1). A neural network was trained to label periocular anatomy using 7101 annotated images with 98.2% accuracy. Using this program, MRD1, MRD2, bLag and OSAE were determined for 77 videos of individuals with acute onset facial nerve palsy (FNP), 33 with ptosis, 33 with thyroid eye disease (TED) and compared with 65 controls. For 31 individuals with FNP, videos were assessed prior to onset of FNP, at onset and at 6 months. Test-retest reliability was evaluated by Bland-Altmann analysis of separate videos taken within 48 hours of each other for both controls (n=34) and FNP (n=33).

Results: Comparison of automated measures in each group is seen in figure 2. MRD1 (mm) was 3.6 in controls, vs 2.2 in ptosis ($p<0.001$), 3.9 in FNP ($p=0.049$) and 4.1 in TED ($p=0.038$). MRD2 (mm) was 5.9 in controls vs 6.4 in TED ($p<0.001$). Median bLag (mm) was 0.0 in controls vs 3.7 in FNP ($p<0.001$). OSAE (mm2) was 13.1 in controls vs 12.2 in ptosis ($p<0.001$), 13.3 in FNP ($p=0.50$) and 13.7 in TED ($p=0.002$). At an individual level, OSAE and bLag increased after the onset of FNP ($p=0.002$ & $p<0.001$, respectively) with a subsequent decrease after 6 months ($p=0.035$ & $p=0.004$, respectively). Regarding test-retest reliability, 95% limits of agreement MRD1, MRD2, bLag and OSAE were 1.1mm, 1.0mm, 3.7mm and 1.6mm^2, respectively.

Conclusions: Automated video assessment of the adnexa is feasible, demonstrating promising validity and reliability. Such technology might facilitate remote clinical assessment and self-monitoring. It might also facilitate the measurement of novel, sensitive and clinically meaningful clinical markers e.g. blink lagophthalmos and ocular surface exposure.

CONTROL ID: 3714195

SUBMITTER (NAME ONLY): Mahsa Darvishzadeh Varcheie

TITLE: Personalized patient interface for optimal alignment with ophthalmic devices for remote monitoring

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Darvishzadeh Varcheie, S.A. Bello, G. Zacks, K. Arianta, J. Straub, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patient alignment is a crucial step to obtain acceptable image quality using ophthalmic devices. Alignment is traditionally done by an ophthalmic technician or by an automated system, which requires operator training and can be expensive to manufacture. In this work, we explore the feasibility of a repeatable and easy-to-use self-alignment solution.

Methods: An iPhone X (Apple, Cupertino, CA) was used to acquire a point cloud of participants' faces, which served as the basis for a 3D printed, personalized patient interface (PPI). The PPI was installed on a low-cost OCT prototype system [Zacks et al. IOVS 2021; 62(8):2135] with self-triggered scan acquisition (ZEISS, Dublin, CA). The PPI creates a comfortable face-rest that restricts the subject's motion while yielding repeatable positioning of the eye in relationship to the system. A fixation target was used to guide the subject's gaze. Initial alignment of the system to the subject's pupil was executed by an experienced technician, after which, the optical system's lateral coordinates, reference arm position and refractive error correction were locked. Subsequently, subjects were asked to self-acquire 3 OCT scans on each eye, retracting from the PPI between images. The system captured 5.78 x 5.78 mm OCT volumes with 512 A-scans/B-scan, 128 B-scans and 2.77 mm of depth. A subject matter expert evaluated the OCT cubes and quality maps [Bello et al. IOVS 2021; 62(8):1881] of all acquired scans to determine the PPI self-alignment success rate. Subjects with a range of ocular pathologies, including age-related macular degeneration were recruited under IRB.

Results: A total of 96 OCT scans from 32 eyes (19 subjects) were self-acquired. In 15 scans misalignment in one or more directions caused image quality to be compromised, resulting in a 0.1562 (0.0901, 0.2445) proportion with 95% confidence. 6 cases out of the 15 failed cases were from 2 eyes whose patients had trouble fixating. The other 30 eyes had at least 1 successful scan. A summary of the results and reasons for self-scan failures are shown in Table 1 and Figure 1.

Conclusions: We introduced a novel approach suitable for self-alignment using a PPI. Results show that good OCT image quality can be obtained using this approach, which could pave the way for personalized ophthalmic imaging and facilitate use cases where expert technicians are not available, such as home monitoring.

CONTROL ID: 3714196

SUBMITTER (NAME ONLY): Brett King

TITLE: Investigating the Impact of Blur on Virtual Reality Perimetry

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. King, W.H. Swanson, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Brett King: Commercial Relationship(s);Code F (Financial Support):Olleyes, inc. | William Swanson: Commercial Relationship(s);Code F (Financial Support):Olleyes, inc

ABSTRACT BODY:

Purpose: Virtual reality perimetry is an evolving diagnostic option for clinicians, yet there is little known on the effect of blur. As some of the devices utilize existing spectacles for distance correction that may have a bifocal or progressive lens design, this could impact the overall results of the test. Furthermore, from previous reports we would expect to see a modest decline in sensitivity with 3.00 diopters (D) of blur for a Size III stimulus and less effect with a Gaussian Blob. This study was aimed at determining the effect of blur in a virtual reality perimeter.

Methods: A virtual reality (VR) headset driven perimeter (Olleyes, Inc. Summit, NJ) was modified to allow the choice of a Gaussian Blob (SD=0.25°) or a standard Size III stimulus. 12 control subjects aged 21-31 years-old were tested using the Normal Threshold 10-2 pattern with different levels of introduced blur for both stimuli (0.00D, +1.50D, +3.00D, +4.50D). For interleaving, the subjects were divided into four groups with either ascending or descending sequences of blur and either starting with the Size III stimulus or the Gaussian Blob. Mean sensitivities (MS) were calculated and a two-way ANOVA was generated.

Results: The Gaussian Blob had a range in median MS from 32.8 decibels(dB) at 0 blur to 32.0dB at +4.50D. The Size III stimulus had a mean MS range from 32.5dB to 31.5dB. The ANOVA found that the effects of blur and stimulus were statistically significant ($p<0.01$) while there did not appear to be a significant interaction ($p=0.85$).

Conclusions: The effects of blur and stimulus may be statistically significant, but the small effect may not have a clinical significance. The results here are unexpected and differ from what has been reported for bowl-style perimeters. A possible reason for the discrepancy could be a slight blur to the stimulus secondary to diffraction from the internal Fresnel lens in the VR headset. Another plausible cause could be the use of a mesopic background allowing for larger summation area that reduces the impact of blur.

CONTROL ID: 3714197

SUBMITTER (NAME ONLY): Arvind Chandna

TITLE: Decoupling of accommodation by monocular viewing of a midline target

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Riddell, A. Horwood, School of Psychology and Clinical Language Sciences, University of Reading, Reading, Berkshire, UNITED KINGDOM|A. Chandna, D. Singh, S. Heinen, Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|J. Badler, Psychology, Philipps-Universitat Marburg, Marburg, Hessen, GERMANY|

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ABSTRACT BODY:

Purpose: Chandna et al. (2021) recently showed that during monocular pursuit of a midline target, the covered eye usually did not execute a normal vergence response. Rather, it tended to make a conjugate eye movement while accommodation showed a symmetric response. Although accommodation, driven by blur and proximity, and through vergence by disparity cues, is normally thought to be yoked, there is some evidence for decoupling; e.g. aniso-accommodation reported in anisometropic amblyopia in children (Toor et al., 2018) and experimentally lens-induced in adults (Marran & Schor, 1998). We investigated whether manipulating cues driving accommodation and vergence in a binocular or monocular midline ocular tracking task can decouple accommodation responses in the two eyes and provide clues to the underlying mechanism.

Methods: The data from an earlier study of midline vergence that did test blur and proximity, along with disparity (Horwood and Riddell, 2008) were re-examined. 22 typical participants (age range 19-25 years) with normal visual acuity and binocular status were included. Subjects were naïve to the task and inexperienced with vision experiments, and instructed to observe a midline target (clown image or Gabor patch) under eight different paradigms. Each of these paradigms involved the manipulation of the target to add or remove cues for blur, proximity or disparity.

Results: In paradigms where there was no disparity cue (i.e., monocular viewing) the covered eye still executed predominantly conjugate rather than vergence movements (Horwood et al., 2001; Chandna et al., 2021). There was also evidence of decoupled accommodation for monocular viewing. The covered eye had a significantly lower accommodation amplitude than the viewing eye ($p < 0.01$; Friedman test, Tukey-Kramer correction). The asymmetric accommodation was not present with binocular viewing even when blur and proximity cues were removed ($p > 0.01$; Friedman test, Tukey-Kramer correction).

Conclusions: The results suggest that the accommodation response is not as strongly yoked as previously believed. Absence of the disparity cue results in asymmetric accommodation and decoupling of the accommodative response as well as the vergence response. This may explain the asymmetric accommodation observed in previous studies as well as that observed in anisometropia, in addition to variability in AC/A ratios in certain types of strabismus.

CONTROL ID: 3714198

SUBMITTER (NAME ONLY): Srinivasa Sripathi

TITLE: High content screen for small molecules that inhibit epithelial to mesenchymal transition in human stem cell-derived RPE cells

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sripathi, C. Berlinicke, X. Chamling, R. Mikeasky, Y. Duan, C. Bell, M. Hu, J. Qian, N. Esumi, D.J. Zack, Ophthalmology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|J. Maruotti, Phenocell, Grasse, FRANCE|K.J. Wahlin, Shiley Eye Institute, University of California, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Epithelial to mesenchymal transition (EMT) of the RPE, which can leads to RPE dysfunction and retinal degeneration, has been implicated in diseases such as PVR and AMD. As a possible therapeutic approach to these diseases, we have been pursuing in vitro high content screening (HCS) to identify molecules that inhibit RPE-EMT.

Methods: Based on gene and protein expression studies using human stem cell-derived models of RPE EMT, we found that within 3 hours after EMT induction there are significant increases in SNAI1 and decreases in BEST1 expression. Utilizing CRISPR/Cas9 engineering, we are generating a dual knock-in fluorescent reporter stem cell line for SNAI1(GFP) and BEST1 (tdTomato). Both reporters are preceded by a 2A self-cleaving peptide (P2A) sequence, so the endogenous proteins are expressed without alteration. After differentiating the reporter line to RPE monolayers, RPE-EMT is induced by 1) dissociation followed by re-plating into 1536-well plates or 2) treatment of RPE monolayers in 384-well plates with TGF-β/TNF-α. Twelve hours prior to EMT induction, compound libraries to be screened were dispensed using an acoustic liquid handler. After 72 hours, images were acquired and analyzed to determine the percentage of cells that express the reporter fluorescent proteins, the intensity of the reporters' fluorescence per cell, and other morphological characteristics.

Results: With the BEST1-tdTomato line that we generated, dissociation and TGF-β/TNF-α induced RPE EMT show decreased tdTomato expression at 24-72 hrs. In an initial screen for inhibitors of RPE EMT, 19 hits were identified, and these hits are being characterized in a secondary screen by qPCR to assess their effects on a variety of other EMT and RPE markers. One of the active molecules we identified is BAY 65-1942, an inhibitor of IKKβ. Expression of a core set of down-regulated visual cycle genes was significantly restored by BAY 65-1942 treatment, and elevation of EMT regulators was significantly suppressed.

Conclusions: Our initial screen has identified bioactive compounds that can inhibit EMT in hRPE cells and maintain their "RPE-ness." We hope that this new dual reporter screening system will provide a robust platform for the discovery of novel inhibitors of RPE EMT, and aid in the understanding and treatment of RPE EMT.

CONTROL ID: 3714199

SUBMITTER (NAME ONLY): Mellisa Clemons

TITLE: Mitochondria as an Interface for Retinal Development and Disease

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Clemons, Biological Sciences, University of Idaho, Moscow, Idaho, UNITED STATES|P. Fuerst, WWAMI Medical Education Program, University of Washington School of Medicine, Moscow, Idaho, UNITED STATES|M. Clemons, D. Eisenbrandt, H. Griffin, Natural Sciences, North Idaho College, Coeur d'Alene, Idaho, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mitochondrial dysfunction is linked to retinal degeneration and dysfunction, but basic organization of mitochondria on a cellular and ultrastructural level remains poorly characterized. The mitochondria are critical organelles with roles in energy production, intracellular calcium regulation, and developmental cell death. In this study we complement a basic analysis of mitochondrial organization and ultrastructure with additional comparisons in mutant mouse models.

Methods: Using ImageJ and serial electron micrographs of mouse retina, we performed ultrafine 3D reconstructions of mitochondria in rods and rod bipolar cells (RBCs). We characterized the volume distribution and morphological complexity of individual mitochondria within wild type (WT) retinas. We used One-way ANOVAs with a Tukey Kramer post hoc to compare WT mitochondria with two additional genetic models that both regulate developmental cell death; Bcl2 associated x-protein ($Bax^{-/-}$) and Down Syndrome Cell Adhesion Molecule – Like 1 ($Dscaml1^{-/-}$) mutant mice.

Results: Data show that WT and $Bax^{-/-}$ individual mitochondria have larger volumes than $Dscaml1^{-/-}$ mitochondria ($p=0.00014$) and ($p<10^{-6}$). $Bax^{-/-}$ mitochondria show increased morphological complexity when compared to $Dscaml1^{-/-}$ mitochondria ($p<10^{-7}$), with WT mitochondria being more complex than both $Bax^{-/-}$ and $Dscaml1^{-/-}$ mitochondria ($p<10^{-7}$) and ($p<10^{-6}$).

Conclusions: Our results provide a characterization of normal mitochondria in the RBCs of WT retinas. This information is essential in further understanding of mitochondrial function in developing and degenerating models. The comparison between WT and $Bax^{-/-}$ show that loss of Bax contributes to the morphological complexity of mitochondria. Initial comparison of $Dscaml1^{-/-}$, a gene implicated in retinal developmental and degenerative diseases, shows that mitochondrial morphology and volume relies on Dscaml1 expression. Additional studies focused on proteins that interact with Dscaml1 will need to be completed to determine the possible pathways responsible for mitochondrial differences and how these contribute to disease pathology.

CONTROL ID: 3714200

SUBMITTER (NAME ONLY): Lizzie Anne Aquino

TITLE: Comparison of 2-Field and 5-Field Mydriatic Handheld Retinal Imaging in a Community-Based Diabetic Retinopathy Screening Program

SESSION TITLE: Using Technology for Care Delivery and Improvement

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To compare 2-field (2F) and 5-field (5F) mydriatic handheld retinal imaging for the assessment of diabetic retinopathy (DR) in a community-based teleophthalmology DR screening program (DRSP)

Methods: Following a validated standard imaging protocol, 5F imaging [macula, disc, superior, inferior and temporal] was acquired using a handheld retinal camera (Aurora, Optomed plc) through dilated pupils. 2F (disc and macula) and 5F images were independently assessed by masked graders using the International DR classification at a centralized reading center. Simple (K) and weighted (Kw) kappa statistics were derived for DR/DME. Sensitivity and specificity for referable DR [refDR (moderate nonproliferative DR (NPDR) or worse or ungradable images] and vision threatening DR [(vtDR) severe NPDR or worse] for 2F compared to 5F imaging were calculated.

Results: Images of 805 eyes from 407 consecutive patients with diabetes from a community-based teleophthalmology DRSP were evaluated. Distribution of DR severity by 2F/5F images (%): no DR 66.0/61.7, mild NPDR 10.7/14.4, moderate NPDR 7.9/8.1, severe NPDR 3.3/5.6, PDR 5.6/4.6, ungradable 6.5/5.6. Table 1 presents the cross-tabulation of DR severity by 2F and 5F with ungradable eyes excluded from the analysis. Exact agreement of DR grading between 2F and 5F photos was 81.7%, within 1-step 97.1%, K 0.64, Kw 0.78. Sensitivity/specificity for 2F compared 5F was refDR 0.80/0.97, vtDR 0.73/0.98. Figure 1 presents a sample comparison of 2F and 5F images. The rate of ungradable images with 2F was 16.1% higher than with 5F (6.5% vs 5.6%).

Conclusions: Mydriatic 2F and 5F handheld imaging have substantial agreement for DR severity grading. Mydriatic 2F handheld imaging achieves the sensitivity and specificity thresholds (0.80/0.95) for refDR (0.80/0.97) but not for vtDR (0.73/0.98) suggesting that lower thresholds for referral must be used when using 2F handheld imaging in a community-based teleophthalmology DRSP. Without the addition of peripheral fields included in 5F handheld imaging, the sensitivity threshold when using vtDR for referrals will not be achieved and would limit its use in DRSP.

CONTROL ID: 3714201

SUBMITTER (NAME ONLY): TANU PARMAR

TITLE: Morphological and functional effects of nicotinamide on primary RPE cells derived from old donors

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. PARMAR, G. Malek, OPHTHALMOLOGY, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|G. Malek, PATHOLOGY, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelial (RPE) cells act as metabolic gatekeepers adjusting the exchange of nutrients between the neural retina and the choroid. They are vulnerable in several retinal diseases including age-related macular degeneration and there is great interest in identifying methods to improve their morphology and function. Nicotinamide adenine dinucleotide (NAD+) is a coenzyme common to most metabolic pathways. Previously an association between NAD+ levels and the development and progression of several age-related diseases has been shown. Herein we investigated the effects of NAD+ on the integrity and function of primary human RPE cells derived from old donors.

Methods: Primary RPE from old donors (n=4; ages 71-93) were treated with nic+MEM or DMEM. Bright-field and confocal microscopy (ZO-1 and phalloidin staining) were used to assess RPE morphology. Gene expression of RPE markers including MERTK, MITF, PEDF, OXTR, TYR, VEGF and others was measured by RT-PCR. Mitochondrial function and glycolysis were measured on XFe24 Extracellular Flux Analyzer. Phagocytosis assay was done using pHrodo Red E. coli BioParticles Conjugates. Data analyzed included a minimum of three biological and experimental replicates. Statistical methods for analysis included two-tailed Student’s t-test and two-way ANOVA

Results: Supplementation with NAD+ promoted a significant improvement in RPE cell morphology and cytoskeletal organization, resulting in a more cuboidal cobblestone pattern with defined ZO-1 borders and organized phalloidin. Nic+MEM resulted in a significant increase in the expression of MERTK, MITF, OXTR, and TYR and a decrease in PEDF and VEGF. RPE-related function of phagocytosis also increased by approximately 2 fold in the presence of nicotinamide. A shift in the two metabolic pathways of glycolysis and oxidative phosphorylation was also observed in the presence of nicotinamide.

Conclusions: In line with previous studies, nicotinamide supplementation improves the morphology and function of RPE cells isolated from aged donor eyes. The metabolic shift promoted by nicotinamide in primary RPE cells indicates a potential strategy for improving the health of aged/diseased cells as seen in AMD. Future studies are focused on evaluating the impact of NAD+ on cells isolated from young donors

CONTROL ID: 3714203

SUBMITTER (NAME ONLY): Janet Sparrow

TITLE: A high fat diet increases bisretinoid levels in mouse retina

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.R. Sparrow, H. Kim, J. Zhao, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J.R. Sparrow, Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J.L. Walewski, Medicine, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bisretinoid lipofuscin accumulates in retina with age. Bisretinoids form due to unchecked reactivity of vitamin A aldehyde and levels are known to reflect visual cycle kinetics; the difference between formation vs. photodegradative loss; and conditions underlying some forms of retinal disease. Otherwise modulators are little known. Here we sought to determine whether dysregulation of vitamin A in an experimental model of obesity associated with a high fat diet (HFD) can lead to increased formation of bisretinoids.

Methods: Black (C57BL/6J) and albino (C57BL/6J^{2cj}) wild type mice (all male) were raised either on a HFD (fat: 60% kcal from fat; from age 6 weeks) or a control diet (CD) (fat: 10% kcal from fat). Retinoids and bisretinoids were quantified by HPLC and UPLC with reference to authentic standards and non-invasive measurement of short wavelength fundus autofluorescence (488 nm; quantitative fundus autofluorescence, qAF) was performed. Rbp4 levels in mouse plasma were measured by ELISA.

Results: In albino C57BL/6J^{c2j} mice fed a HFD from age 6 weeks to 12 months, final body weight was 30% higher than in mice fed a CD. At age 6 months, black C57BL/6J mice fed a HFD weighed 37% more than mice given a CD. In C57BL/6J mice receiving the HFD there was a 2.2-fold increase in plasma all-trans-retinol (vitamin A) at age 14 weeks, a 17% increase in glucose and a 29% increase in retinol-binding protein 4 (Rbp4) relative to CD mice. In the plasma of HFD-fed C57BL/6J^{2cj} mice (age 1 year), Rbp4 and retinol were also elevated relative to the CD. Non-invasive measurement of bisretinoid by qAF revealed a 35% increase in the HFD-fed C57BL/6J^{c2j} mice (1.10.12, meanSD) as compared to CD-fed mice (0.80.1). The levels of A2E in the C57BL/6J^{c2j} HFD-fed mice were more than 2-fold greater than in the mice fed the CD and similar increases in A2GPE and A2DHPPE were also measured (for A2GPE, HFD: 11.42.8; control: 4.72.3). Quantitation of bisretinoids revealed that in 6 month old C57BL/6J mice the bisretinoids A2E, A2-DHP-PE and A2GPE were increased 44%, 36% and 3-fold, respectively. Diet-induced obese C57BL/6J mice at age 3 years also exhibited a 1.9 and 2.5-fold increase in A2E and A2-DHP-PE, respectively, relative to CD mice.

Conclusions: A HFD leading to obesity in mice is associated with elevated plasma RBP4 and retinol, and elevated levels of bisretinoid lipofuscin in retina.

CONTROL ID: 3714204

SUBMITTER (NAME ONLY): Pawan Shrestha

TITLE: Monocarboxylate transporters: Role and Regulation in Corneal Diabetes

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Shrestha, S.E. Nicholas, D. Karamichos, Pharmaceutical Science, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|A. Whelchel, Department of Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|J. Ma, Department of Biochemistry, Wake Forest University School of Medicine, Winston-Salem, North Carolina, UNITED STATES|P. Shrestha, S.E. Nicholas, D. Karamichos, North Texas Eye Research Institute, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes Mellitus (DM) is a group of metabolic disorders that can cause structural and functional changes in the human cornea, including nerve and stromal defects. Monocarboxylate transporters (MCTs) are a family of proton-linked plasma membrane transporters that carry monocarboxylates (i.e. molecules with one carboxylate group) across plasma membranes. In the context of corneal health and disease, their role, presence, and functions are undetermined and solely focused on the most common MCT isoforms 1 through 4. The aim of this study is to investigate the role of MCTs 1 through -5, -8, and -10, in the context of corneal diabetes.

Methods: Primary stromal corneal fibroblasts were isolated from Healthy (HCFs), as well as Type I (T1DMs), and Type II (T2DMs) diabetic subjects. Mono-cultures: Cells were cultured for three weeks on 6-well transwell plates and stimulated with stable Vitamin C, to promote ECM assembly. Co-cultures: SH-SY5Y neurons were seeded at a density of 12k and 500k on top of the 3D stromal constructs after three weeks, to create the stroma-neuron co-culture, followed by an additional week in culture. Cultures without neurons served as controls. At four-weeks, all constructs were processed for RNA isolation and Real-Time Quantitative Reverse Transcription PCR (qRT- PCR). Furthermore, expression of MCTs was also investigated, using immunofluorescence.

Results: No significant modulation of MCTs was observed for any of the cell types tested at the low cell density of 12k. Co-cultures with 500k neuron cell densities showed upregulation of MCT1, MCT8 and MCT10 in HCFs, T1DMs and T2DMs. The cells were stained with different MCT isoforms for immunofluorescence. Data showed bright red signal within the cytoplasm, indicating the presence of MCTs, but no obvious changes between conditions.

Conclusions: By utilizing two 3D in vitro models, this study reveals the existence and modulation of MCTs in the diabetic cornea. The changes observed, due to neuronal density, suggest that MCTs are potentially critical to neuronal degeneration and pathology seen in diabetic keratopathy/neuropathy. Further studies are needed, in order to fully delineate the role of MCTs in corneal diabetes.

CONTROL ID: 3714205

SUBMITTER (NAME ONLY): SUDIPTA PANJA

TITLE: A Novel Method to Improve Protein Solubility and Elasticity in Aged Human Lenses

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. PANJA, R.B. Nahomi, J. Rankenberg, M. Nam, R.H. Nagaraj, Sue Anschutz-Rodgers Eye Center, Department of Ophthalmology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|C.R. Michel, H. Gaikwad, R.H. Nagaraj, Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Presbyopia is a progressive, age-related visual impairment characterized by the lens's lack of ability to focus on nearby objects. During presbyopia, proteins in the lens become increasingly insoluble and aggregated, contributing to the loss of elasticity and accommodation. This study reports the development of a small molecule that improves protein solubility and elasticity in aged lenses.

Methods: Aggrelyte-2 (S,N-Diacetyl-L-cysteine methyl ester) or the control compound (N-Acetyl-L-cysteine methyl ester, aggrelyte-2C) was incubated (at 500 μM) with a suspension of 5 mg/ mL of water-insoluble protein (WI) of aged human lenses (65-75 years) for 24 or 48 h. The mixture was centrifuged, and the protein concentration in the supernatant was measured, N^{ε}-acetyllysine (AcK) in proteins was measured by western blotting and LC-MS/MS (in enzyme digested samples). The protein thiol content was estimated by a fluorescence method. Human (60-70 years) and mouse lenses (C57BL/6J, 5-8 months) were incubated with aggrelyte-2 at 2.5- or 2-mM concentration for 3 days to determine effects on the elasticity of lenses, using a coverslip method.

Results: Upon incubation of aggrelyte-2 with aged human lens WI, we measured 1.0-1.3 μg/μL of soluble proteins after 24 h and 1.0-1.5 μg/μL after 48 h. Incubation of aggrelyte-2C (that lacked the lysine acetylation capacity), we observed 0.7-0.9 μg/μL of soluble proteins after 24 h and 0.7-1.1 μg/μL after 48 h, which were ~1.35-fold lower efficient than aggrelyte-2. The AcK content in the solubilized proteins increased in the samples incubated with aggrelyte-2 but not with aggrelyte-2C. The LC-MS/MS results revealed AcK levels of 1.5–2.1 nmoles/mg protein in the aggrelyte-2 treated samples, compared to 0.6–0.9 nmoles/mg protein in the samples treated with aggrelyte-2C. Western blotting revealed a significant increase ($p<0.01$) in the αA-crystallin content in the solubilized protein. The protein-thiol content in the WI treated with aggrelyte-2 and aggrelyte-2C increased by 1.93- and 5.07-fold over untreated controls. The elasticity of lenses treated with aggreltyte-2 significantly improved ($p<0.01$ and $p<0.001$ for mouse, and human lenses, respectively) with a concomitant increase in the AcK levels.

Conclusions: Aggrelyte-2 solubilizes WI through acetylation and disulfide reduction and decreases stiffness in aged human lenses. It could be developed as a therapy against presbyopia.

CONTROL ID: 3714206

SUBMITTER (NAME ONLY): Abeir Baltmr

TITLE: Impact of COVID-19 pandemic on patients with nAMD: Assessing clinical outcomes of patients who underwent four and eight weekly anti-VEGF treatment with no clinic review

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Baltmr, M. Farag, P. Vouzounis, S. Alkhalili, E. Ahmed, M. Eldakkak, S. Khandhadia, R. Borbara, C. Rennie, G. DeSalvo, A.J. Lotery, University Hospital Southampton NHS Foundation Trust, Southampton, Southampton, UNITED KINGDOM|A.J. Lotery, Division of Clinical Neurosciences, Clinical and Experimental Sciences,, Faculty of Medicine, University of Southampton, Southampton, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: During the COVID-19 pandemic, in line with the UK Royal College of Ophthalmologists' (RCOphth) guidelines, anti-VEGF treatment regimens for Neovascular Age Related Macular degeneration (nAMD) were adjusted to 8 weekly Aflibercept injections with no clinic review. New patients and those who mentioned a significant drop of vision during their injection visits had OCT and their management adjusted to 4 weekly injections. This work audits our practice at a tertiary university hospital during the 2020 pandemic.

Methods: Retrospective electronic data was collected from the Medisoft ophthalmology database for patients with nAMD, who received Aflibercept over a 5 month period from 01.03.2020 to 01.08.2020.

Best Corrected Visual Acuity (BCVA), Central Macular Thickness (CRT), and number of injections were collected, and compared with our previously published year one data of 225 treatment naïve eyes of 223 patients with nAMD, treated with 8 weekly Aflibercept with mean BCVA of 61 letters & mean CRT of 235 µm at month 5 of therapy. We also assessed the clinical outcomes of our patients who received 4 weekly Aflibercept injections.

Statistical analysis was done using SPSS version 24.

Results: 1778 eyes of 1427 patients met the inclusion criteria and were included in the study. 1338 patients (93.8%) received 8 weekly injections, their mean BCVA ± SD was 59.7 ± 17.3 with CRT of 239.3 µm ± 67.2 SD at baseline and their latest BCVA ± SD was 59.3 ± 17.4, with CRT of 231.8 µm ± 73.8 SD. More than one third of them 618 (43.3%) received three injections during that period.

89 of our patients (6.2%) received 4 weekly injections during our study period. Their mean BCVA ± SD was 60.5 ± 17.6 with CRT of 276.1 µm ± 96.4 SD at baseline and their latest BCVA ± SD was 62.3 ± 15.1, with CRT of 247.8 µm ± 49.0 SD.

Conclusions: Reassuringly, during the COVID-19 pandemic, patients on a fixed 8 weekly Aflibercept pathway maintained their vision. Their mean BCVA & CRT were comparable to our pre-COVID audit outcomes with a treat and extend protocol. Patients on 4 weekly injections also maintained their vision during the pandemic. RCOphth COVID guidelines allowed AMD patients to receive effective therapy whilst minimizing time in hospitals and permitted ophthalmologists to do other COVID related tasks.

CONTROL ID: 3714207

SUBMITTER (NAME ONLY): Dawn DeCarlo

TITLE: Factors Influencing Reading Speed in Pediatric Vision Impairment

SESSION TITLE: Visual Function Assessment and Quality of Life Outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.K. DeCarlo, A. Durena, L. Gao, Ophthalmology & Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|M. Kwon, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine factors contributing to maximum reading rate in children with low vision.

Methods: Thirty-one children with vision impairment of ocular origin aged 7 to 16 performed a variety of tasks including best-corrected visual acuity (VA), WISC verbal comprehension and working memory testing, Woodcock Johnson IV Broad Reading Cluster (WJ-BRC) which is derived from Letter-Word Identification, Passage Comprehension and Sentence Reading Fluency subtests, RAN/RAS rapid automatized naming tasks and MNREAD testing using the iPad based test and scoring algorithm. Additionally, visual span profiles (range of letters that can be recognized reliably without moving the eyes) were determined using a trigram task. Data was analyzed first looking at univariate associations. A model predicting reading speed was developed using backward stepwise regression. Significance was set at p=.05, 2-tailed.

Results: Mean participant age was 11.5 ± 2.7 years and mean VA was 0.67 ± 0.2 logMAR (range 0.2-1.02). More girls (55%) than boys (45%) participated. Most participants had nystagmus (81%). The mean maximum reading rate (MRR) was 117 ± 38 words per minute. Visual span size averaged 24.7 ± 9.8 bits (range 7.0 to 39.7). Mean standard score was 93.5 ± 12.1 on the WJ-BRC and 105 ± 9 on the RAN/RAS. Visual span size was significantly correlated with MRR (p=.03; R^2=0.16) and age (p=.002; R^2=0.28) but not with VA (p=.5), automaticity (p=.7) or WJ-BRC (p=.7). MRR was not significantly correlated with any demographic or visual factors; it was also not correlated with the WISC verbal comprehension or working memory indices or the WJ-BRC. In addition to visual span size, MRR is significantly correlated with age (p=.003; R^2=0.27), and automaticity (p=.01; R^2=0.2). The final regression model included VA, automaticity, WJ- BRC, age and visual span size as well interactions between visual span and the other variables. The model explained 80% of the variance in reading speed. (R^2 = 0.80, F (10,20) = 7.97, p = < .0001).

Conclusions: Consistent with the literature, reading speeds vary from child to child, and increase over time as they mature. Although visual acuity alone is not significantly associated with reading speed, it does contribute. The visual span contributes to and interacts with other factors associated with reading speed suggesting a significant role for early visual processing in the development of reading speed.

CONTROL ID: 3714208

SUBMITTER (NAME ONLY): Earnest Kim

TITLE: Decrease in Returning Pediatric Amblyopia Patients and Potential Impact on Visual Outcomes

SESSION TITLE: Amblyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Prompt treatment of amblyopia, the leading cause of vision loss in children, is imperative for preserving vision. One of the primary barriers to successful amblyopia treatment is failure to follow up. Previous research has identified socioeconomic status as a significant risk factor for predicting whether patients are lost to follow up after the initial visit (23% of patients). In this retrospective study, we investigate patient follow up for their prescribed appointments and the potential impact on visual outcomes.

Methods: We performed a retrospective data study on pediatric patients aged 0-9 years who were first diagnosed with amblyopia in 2018 at Oregon Health & Science University. We analyzed each patient's consecutive office visits during 1/1/2018 – 12/31/2019, calculating interocular visual acuity for the subset of patients that had recorded subjective visual acuities with optotypes.

Results: There were 904 patients in our study; they had an average of 4.1 completed (SD: ± 3.8), 2.4 canceled (SD: ± 1.4), and 1.4 no-show appointments (SD: ± 0.7). Out of 904 pediatric patients, there was a 46% decline in returning patients by the 5^{th} visit resulting in 488 remaining patients. For the patients who had subjective visual acuity values, we measured visual improvement with the interocular visual acuity (IVA). The IVA improved from the 1^{st} and 5^{th} visits (mean 1^{st} visit, ± SD, 0.277 ± .344 vs. mean 5^{th} visit, 0.178 ± .282 , P<.001).

Conclusions: The number of returning patients decreased with each subsequent visit, but for those patients who returned for 5 visits, they had a significant improvement in visual acuity. However, close to half of patients did not return for 5 visits and may not have experienced an improvement in vision. Further studies need to investigate the factors that contribute to appointment adherence to promote successful treatment in amblyopia patients.

CONTROL ID: 3714211

SUBMITTER (NAME ONLY): Pingping Zhao

TITLE: The Impact of Race on the Relationship Between Cup-To-Disc Ratio and Glaucomatous Visual Field Loss

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zhao, Y. Li, M. Eslami, S. Kazeminasab, M. Fazli, V. Sharma, M. Wang, T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|O. Halawa, N. Zebardast, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the impact of patient race on the association between cup-to-disc ratio (CDR) and glaucomatous visual field (VF) loss.

Methods: From all patients from Mass. Eye and Ear glaucoma service, the most recent pairs of reliable Humphrey 24-2 VFs (false positives/negatives ≤ 15%, fixation losses ≤ 20%) and vertical CDR measurements obtained from peripapillary optical coherence tomography volume scans (Cirrus HD-OCT, signal strength ≥ 6) were selected if the patient self-identified as either Asian, Black or White on an electronic medical record questionnaire. Model selection by Bayes Factors (BF), estimated by Bayesian Information Criterion, was performed to identify the association between VF mean deviation (MD) and CDR with age and race as covariates. Additionally, the MD vs. CDR relationship was compared between the separate race groups.

Results: 16,198 eyes of 9,597 patients (56.1% female) were selected. 909 patients identified as Asian, 1,561 as Black and 7,127 as White. There was a significant main effect of race (ANOVA, $p<0.001$) vs. age, MD and CDR. Although White patients where the oldest group, their MD was highest and their CDR lowest among all races (Fig. 1A-C). The Bayesian model comparison identified CDR as the best single parameter model and the model consisting of age, race and CDR as the best overall model for MD (Fig. 1D), with higher age, higher CDR, and Asian and Black race significantly associated with lower MD (each $p<0.001$). CDR and MD are negatively correlated; the correlation strength substantially differs by race (Pearson's r in the entire population: -0.28, Asians: -0.23, Blacks: -0.32, Whites: -0.27, each $p<0.001$). Fig. 2 shows a scatterplot of MD vs. CDR colored by patient race, together with the respective three linear regression fits, which considerably differ between the race groups, with the largest negative slope for Black patients.

Conclusions: Based on the most recent measurements of all patients of a large glaucoma clinic, our results confirm larger CDR to be related to more severe glaucomatous VF loss. The strength of this association considerably varies by patient race, with the strongest relationship observed for Black patients. As CDR is an important clinical parameter to diagnose glaucoma, our results suggest to include patient race when interpreting CDR in the context of glaucoma severity.

CONTROL ID: 3714212

SUBMITTER (NAME ONLY): Kai Seely

TITLE: Integration of multidimensional data from bedside optical coherence tomography imaging for retinopathy of prematurity examination.

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Seely, S. Mangalesh, V. Tai, D. Tran-viet, K. Winter, S.J. Chiu, C.A. Toth, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|C. Viehland, C.A. Toth, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe a method for rapid optical coherence tomography (OCT) image capture and multidimensional visualization of retinopathy of prematurity (ROP) in preterm infants in BabySTEPS2.

Methods: We developed retinal OCT imaging protocols for use with an investigational 400kHz, 1060nm swept-source system with a 700g handheld, noncontact probe in preterm infants at risk for ROP. Two imaging protocols were used at the bedside, the day of clinical ROP screening, without sedation or use of an eyelid speculum: Scan 1 (0.7 sec, 1900 A-scans/B-scan, 128 B-scans per 10x10mm volume, with pairs of adjacent A-scans summed producing 950 A-scans/B-scan) for cross-sectional assessment of retinal layers; and Scan 2 (1.4 sec, 640 A-scans/B-scan and 640 B-scans per 10x10mm isodense volume) for en face retinal vascular assessment. For multidimensional visualization, we developed infant-specific software (DOCTRAP v66.2) to optimize automatic segmentation of OCT volumes from Scan 1 and generate total retina thickness maps. We extracted en face retinal vessel maps from maximum pixel intensity at each A-scan position from Scan 2. With auto-montaging software (i2k Retina; DualAlign, Inc.), we created a single posterior pole vessel map per eye and overlaid corresponding thickness maps for comparison to color fundus photos.

Results: We were able to capture, integrate, and visualize multidimensional data from high-speed investigational bedside OCT imaging of preterm infant retinas. This included: depth-resolved analysis of retinal microanatomy at locations of interest (e.g., at the foveal center and vascular-avascular junction); intensity maps of total retinal layer thicknesses; and retinal vessel maps (Figure 1). These data demonstrated important ROP pathology (e.g., retinal neovascularization and plus disease) and in contrast to color photographs, enabled integrated assessment of the developing preterm retina (e.g., retinal layer thicknesses and presence of macular edema).

Conclusions: This method for multidimensional data analysis will be used by human graders and analyzed by semi-automated software (i.e., ROPtool) in BabySTEPS2, and may be integrated into future artificial intelligence-based ROP screening methods.

CONTROL ID: 3714214

SUBMITTER (NAME ONLY): Amber Wilkerson

TITLE: Pathophysiological consequences of Soat1/SOAT1 inactivation for the ocular surface and Meibomian gland homeostasis

SESSION TITLE: Dry eye regulators: lacrimal gland, meibomian gland, basic mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Wilkerson, I.A. Butovich, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Amber Wilkerson: Commercial Relationship: Code N (No Commercial Relationship) | Igor Butovich: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The gene/enzyme pair Soat1/SOAT1 was previously shown to be critical for making cholesteryl esters (CEs) in the mouse Meibomian glands (MGs) as the loss of its function in MGs led to arrest of CE production, accumulation of free cholesterol in meibum, and major changes in its rheological properties. The purpose of this study was to investigate the role of Soat1/SOAT1 in meibogenesis and ocular surface (patho)physiology using Soat1 knockout ($Soat1^{-/-}$) mice as animal models of human MG dysfunction (MGD).

Methods: Age matched male and female $Soat1^{-/-}$ mice and their wild type (WT) littermates were used in this study. Ocular surface (OS) damage was assessed via fluorescein staining using a slit lamp. Freshly harvested tarsal plates (TPs) were used for RNA extraction or processed for histology and histochemistry. TP transcriptomes were analyzed using Clariom D microarrays and RNA expression data was processed in the Expression Console software package and transcriptome analysis console. Mouse TPs and corneas were evaluated by H&E, Oil Red O, and/or LipidTox staining.

Results: Slit lamp examination of $Soat1^{-/-}$ mice demonstrated an increase in fluorescein staining ($P<0.001$) of the OS in comparison with WT mice. After 5 months of age, about half of $Soat1^{-/-}$ mice developed corneal ulcers. Lipid staining of knockout MGs revealed minimal lipid accumulation in the acini with most of the lipid staining within the central ducts compared to the robust staining throughout the acini and central ducts of WT mice. Comparative transcriptomic analysis of $Soat1^{-/-}$ vs. WT mice demonstrated upregulation of about 980 coding genes and downregulation of >1,400 genes ($p<0.05$; $2<$Fold Change<-2). The major significantly upregulated pathways included cholesterol and bile acid metabolism, formation of the cornified envelope, keratinization, inflammation, and apoptosis. Among suppressed pathways were lipid metabolism, muscle contraction, Ca(II) signaling, creatine-phosphate metabolism, signal transduction, immune response, and others.

Conclusions: Inactivation of Soat1/SOAT1 leads to severe changes in the OS physiology, and MG biochemistry and morphology that resemble certain types of human MGD. The transcriptomic data were consistent with the $Soat1^{-/-}$ mouse phenotype and biochemical changes in their meibum. The $Soat1^{-/-}$ mice can be used as a useful model of human MGD.

CONTROL ID: 3714217

SUBMITTER (NAME ONLY): Fabio Lavinsky

TITLE: Optic Nerve Head, Choroidal Thickness and Individual Macular Layers Measurements with Optical Coherence Tomography in Normal and Glaucoma Eyes with Distinct Peripapillary Atrophy Areas

SESSION TITLE: Imaging in glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Lavinsky, V.M. Lubisco, H. Bohn, A.T. Barros, L.P. Bellini, School of Medicine, Universidade do Vale do Rio dos Sinos, Sao Leopoldo, RS, BRAZIL|F. Lavinsky, R.L. Lindenmeyer, H.M. Pakter, J. Lavinsky, D. Lavinsky, Ophthalmology, Hospital de Clinicas de Porto Alegre, Porto Alegre, RS, BRAZIL|F.M. Fujihara, J. Lavinsky, P.D. Mello, Ophthalmology, Universidade Federal de Sao Paulo Escola Paulista de Medicina, Sao Paulo, SP, BRAZIL|H.M. Pakter, D. Lavinsky, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, BRAZIL|E. Picetti, Hospital Conceicao, Porto Alegre, Rio Grande do Sul, BRAZIL|

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ABSTRACT BODY:

Purpose: The aim of this study is to evaluate the differences in optic nerve head (ONH), choroidal thickness and individual macular layers measurements in normal and glaucoma eyes in groups divided by the area of their peripapillary atrophy (PPA).

Methods: Subjects with glaucoma presenting typical ONH findings, high intraocular pressure with or without visual field (VF) damage and normal controls were included. Patients underwent 24-2 perimetry (SITA standard;Humphrey Field Analyzer; Zeiss) and Spectral Domain Optical Coherence Tomography (SD-OCT) (Spectralis;Heidelberg Engineering). Manual measurements of the temporal and superior and inferior-temporal PPA area observing the infrared image and the B-scans were manually performed by a trained examiner. Eyes were divided in four groups based on the PPA area. SD-OCT parameters analyzed were average circumpapillary retinal nerve fiber layer (cRNFL), average circumpapillary choroidal thickness (cChoroid), the hypotenuse of the vertical optic nerve head cupping (HVOC) and the individual macular layers obtained automatically from the device. For calculating HVOC we used the length and depth of the optic nerve cupping as the sides of a right triangle. The mean deviation (MD) of the VF was evaluated. Statistical analysis was performed using generalized estimated equations.

Results: 89 eyes (57 subjects) qualified for the study. The mean age was 65.72±12.47 years. The number of eyes was 81 in the glaucoma and 8 in the control group. Four groups were divided by the quartiles of the PPA area: 1: ≤ 0.44 mm^2 (n=24); 2: 0.44-0.69 mm^2 (n=21); 3: 0.69-0.92 mm^2 (n=22) and 4: ≥ 0.92 mm^2 (n=22). The control eyes distribution was: 6 eyes in group 1, 2 in group 2 and none in groups 3 and 4. cRNFL, HVOC and inner macular layers demonstrated overall significant differences between groups (table 1). VF MD, additional macular layers and cChoroid differences weren't significant, except for the outer plexiform layer (OPL) in the outer circle of the grid (table 2).

Conclusions: Eyes with distinct PPA areas demonstrated differences in ONH and macular parameters related to glaucoma. Longitudinal studies evaluating PPA area and the associated change in other structural and functional parameters may provide additional information about the clinical course of glaucomatous eyes with PPA.

CONTROL ID: 3714218

SUBMITTER (NAME ONLY): WEILIANG Wang

TITLE: Quantitative comparison of retinal vascular changes by quadrants after treatment of retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wang, Duke-NUS Medical School, SINGAPORE|S. Freedman, S.G. Prakalapakorn, Department of Ophthalmology, Duke University Medical Center, Durham, North Carolina, UNITED STATES|S. Freedman, S.G. Prakalapakorn, Department of Pediatrics, Duke University Medical Center, Durham, North Carolina, UNITED STATES|D. Wallace, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Plus disease, i.e. retinal vascular dilation and tortuosity in the posterior pole, is usually present in type 1 retinopathy of prematurity (ROP), and typically improves after treatment. However, it is unknown if vessels in certain quadrants respond to treatment quicker. The purpose of this study is to quantitatively compare posterior pole vascular changes between temporal vs. nasal and superior vs. inferior quadrants after treatment.

Methods: This retrospective study used prospectively-collected narrow-field retinal images from infants treated for ROP. We included images acquired in the session just prior to and ≤6 weeks post-treatment. We used ROPtool (a semiautomated vessel analysis program) to trace and analyze ≤2 vessels/quadrant, following the same vessels over time. The following ROPtool indices of vessel characteristics were calculated: dilation index (DI), tortuosity index (TI), and combination dilation/tortuosity indices: sum of adjusted indices (SAI) and tortuosity-weighted plus (TWP). Using the Wilcoxon signed-rank test, ROPtool indices pre- and post-treatment were compared between temporal vs. nasal and superior vs. inferior quadrants.

Results: Fifteen eyes (8 infants) were treated for ROP. Among 80 eligible imaging sessions, 627/640 (98.0%) vessels were traceable by ROPtool. Temporal quadrant values were higher than nasal quadrant values for all ROPtool indices pre-treatment, for DI at weeks 1-5 post-treatment, and for SAI at week 1 post-treatment (Table 1). Post-treatment, the temporal quadrant values decreased faster than nasal quadrants for all indices week 1 post-treatment [median weekly rates: DI (-1.2 vs. -0.6, p=0.02), TI (-1.4 vs. -0.8, p=0.003), SAI (-1.0 vs. -0.5, p=0.01), TWP (-1.0 vs. -0.5, p=0.04)] (Fig 1A, 1C).

There were no statistically significant differences in ROPtool indices between superior and inferior quadrants pre- and ≤6 weeks post-treatment.

Conclusions: Among eyes treated for ROP, temporal vessels were more dilated and tortuous pre-treatment, remained more dilated post-treatment, and had faster regression of dilation and tortuosity than nasal vessels in the first week post-treatment.

CONTROL ID: 3714219

SUBMITTER (NAME ONLY): Emilee Rickabaugh

TITLE: Hagfish slime protein membranes as in vitro models of Bruch's membrane in the subretinal tissue

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Rickabaugh, D. Weatherston, E. Vargis, Biological Engineering, Utah State University, Logan, Utah, UNITED STATES|T. Harris, J. Jones, Biology, Utah State University, Logan, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bruch's membrane resides in the subretinal tissue and helps to regulate the flow of nutrients and waste between the retinal pigmented epithelial (RPE) and vascular cell layers of the eye. Bruch's membrane plays a key role in the development of subretinal diseases such as Age-Related Macular Degeneration. Age-Related Macular Degeneration, or AMD, is the degradation of the RPE cell layer, leading to progressive vision loss. Bruch's membrane plays an active role in the development of AMD. The thickness, brittleness, and permeability of Bruch's membrane all have a significant impact on the degradation of the RPE cell layer. As the interactions between Bruch's membrane, the RPE layer, and the vascular layer play a pivotal role in AMD, modeling these layers is a key step in researching potential therapies for AMD and other retinal diseases.

An accurate model of Bruch's membrane must be proteinaceous, semi-permeable, and nonporous with similar mechanical properties to in vivo Bruch's membrane while also being able to support both RPE and vascular cell cultures. Many current models of the subretinal tissue utilize inferior models of Bruch's membrane called Transwells, which are porous, nonpermeable, plastic membranes that are much thicker than a healthy Bruch's membrane.

Methods: To create a more accurate model, artificial membranes were synthesized using solubilized hagfish slime proteins. The characteristics of the hagfish membranes were evaluated using mechanical stress testing, permeability assays, and brightfield microscopy. The capacity of the membranes to support ARPE-19 and Human Retinal Microvascular Endothelial Cell cultures was determined using cell staining with brightfield microscopy, fluorescent microscopy, immunocytochemical imaging, and enzyme-linked immunosorbent assays.

Results: The tests demonstrate the potential of these hagfish protein membranes to accurately replicate Bruch's membrane in an in vitro model of the subretinal tissue. When compared to existing models of the subretinal tissue, the hagfish membranes demonstrate more mimetic geometric properties, mechanical properties, and permeability characteristics to those of a natural Bruch's membrane, as well as the ability to support relevant cell cultures.

Conclusions: The verification of this model will create an opportunity for more comprehensive and accelerated initial testing for potential retinal disease therapies.

CONTROL ID: 3714221

SUBMITTER (NAME ONLY): Mojtaba Fazli

TITLE: The Impact of Inflammatory Markers on the Ganglion Cell Complex in Non-Glaucoma Subjects

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Fazli, F.G. Rauscher, K. Wirkner, C. Engel, T. Kirsten, M. Loeffler, J. Thiery, T. Elze, M. Wang, Leipzig Research Centre for Civilization Diseases (LIFE), Leipzig University, Leipzig, Saxony, GERMANY| M. Fazli, T. Elze, M. Wang, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|F.G. Rauscher, K. Wirkner, C. Engel, M. Loeffler, Institute for Medical Informatics, Statistics, and Epidemiology (IMISE), Leipzig University, Leipzig, GERMANY|T. Kirsten, Medical Informatics Center - Department of Medical Data Science, Leipzig University Medical Center, Leipzig, Saxony, GERMANY|J. Thiery, Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Leipzig University Medical Center, Leipzig, Saxony, GERMANY|T. Ebert, Medical Department III – Endocrinology, Nephrology, Rheumatology, Leipzig University Medical Center, Leipzig, Saxony, GERMANY|T. Ebert, Department of Clinical Science, Intervention and Technology, Division of Renal Medicine, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: Prior studies suggest that inflammation is associated with glaucoma, and glaucoma is known to damage the ganglion cell complex (GCC), defined as the three innermost retinal layers, including the nerve fiber layer, the ganglion cell layer, and the inner plexiform layer. Here, we study the impact of inflammation on GCC thickness in non-glaucoma subjects.

Methods: From the large population-based LIFE-Adult study (Leipzig Research Centre for Civilization Diseases), we extracted the machine-segmented GCC thickness map from Heidelberg Spectralis macular optical coherence tomography (OCT) scans. Subjects with glaucomatous findings on fundus photos, self-reported glaucoma, or glaucoma medication intake were excluded from data analyses. Inflammatory status was assessed by high-sensitivity C-reactive protein (hsCRP) and interleukin 6 (IL-6). The two inflammatory markers were separately associated with the global, sectoral and pointwise GCC thickness by partial correlations adjusted for age, sex, and scan focus. P values were corrected for multiple comparisons. One eye per subject was selected randomly if both eyes were available.

Results: 7,521 eyes from 7,521 subjects (age: 56.7 ± 12.5 years; 52.0% female) were included. Higher IL-6 (partial correlation [r]: -0.02, $p = 0.01$) but not hs-CRP ($p = 0.79$) was significantly associated with thinner global average GCC. Figure 1 shows the pointwise partial correlations between inflammatory markers and GCC thickness. Higher hs-CRP and IL-6 were particularly associated with thinner GCC thickness in the parafoveal ring-shaped region significantly affecting 20.9% and 20.4% of the scan region, respectively. Figure 2 shows the sectoral partial correlations between the inflammatory markers and GCC thickness using Early Treatment Diabetic Retinopathy Study based sectors. Both hsCRP (each $p \leq 0.049$) and IL-6 (each $p \leq 0.001$) were significantly associated with thinner GCC in the four inner sectors. In addition, hsCRP had significant associations ($p = 0.049$) with thicker GCC in the superior outer sector, and IL-6 had significant associations ($p = 0.02$) with thinner GCC in the nasal outer sector.

Conclusions: Our results suggest that higher levels of inflammatory markers are specifically linked with thinner GCC in the parafoveal ring-shaped region in non-glaucoma subjects, which may help better understand the inflammatory pathway in the pathogenesis of glaucoma.

CONTROL ID: 3714222

SUBMITTER (NAME ONLY): Sixian Song

TITLE: Stxbp1b is essential for synaptic expression of Stx3 in zebrafish retina

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Song, J.M. Fadool, Biological Science, Florida State University, Tallahassee, Florida, UNITED STATES|

Commercial Relationships Disclosure: Sixian Song: Commercial Relationship: Code N (No Commercial Relationship) | James Fadool: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The SNARE complex facilitates fusion of vesicular cargo to a target membrane. Syntaxin 3 (Stx3) has been implicated in trafficking of proteins to the photoreceptor outer segment and exocytosis of synaptic vesicles. Previously, we found that stxbp1b and stx3 were essential for photoreceptor morphogenesis and survival in zebrafish. The purpose of this study was to further investigate the roles of Stx3 and Stxbp1b in retina development.

Methods: An ENU-induced mutation of stxbp1b and a CRISPR-targeted allele of stx3 were used in this study. For rescue experiments, in vitro transcribed mRNA encoding wildtype stxbp1b, phosphomimetic mutant Y474D, non-phosphorylatable mutant Y474F, and wildtype stx3 were injected into 1-2 cell stage embryos. The optokinetic response (OKR) assay was used to screen for visual responses after 5 dpf. Immunolabeling was performed for photoreceptor-specific and synaptic markers. Fluorescence intensity was quantified using ImageJ.

Results: Zebrafish contain two paralogues of STX3, stx3 and stx3a. In situ hybridization of embryos at 48 hours post-fertilization (hpf) shows stx3 expression in the outer nuclear layer of the retina, and stx3a is expressed in the inner retina. Immunolabeling with an antibody to rat Stx3 detected both paralogues with signal on photoreceptors, the outer plexiform layer (OPL) and inner plexiform layer (IPL). In $stx3^{-/-}$ retinas, labeling for Stx3 was largely restricted to the IPL. Quantitative immunolabeling revealed that expression of Stx3 was significantly downregulated in the photoreceptor layer and IPL of stxbp1b mutant retinas. Labeling for other synaptic makers were not altered in the IPL of either mutant retina. All Stxbp1b mRNA injections were enough to rescue photoreceptor morphology. However injected-larvae failed to display an OKR, and the Stx3 immunolabeling of the OPL and IPL remained significantly reduced.

Conclusions: These data indicate that Stxbp1b is essential for Stx3 expression in photoreceptor and Stx3a expression in IPL, suggesting that Stxbp1b acts as a chaperon protein for both Stx3 paralogues. But phosphorylation of Y474 of stxbp1b is dispensable for formation of the outer segment.

CONTROL ID: 3714223

SUBMITTER (NAME ONLY): Asher Khan

TITLE: Early Lifetime Substance Use and Development of Significant Visual Impairment or Blindness: An Analysis of the National Survey on Drug Use and Health

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Khan, K. Riaz, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|K. Shah, Psychiatry, Griffin Memorial Hospital, Norman, Oklahoma, UNITED STATES|Z.S. Hussain, University of Medicine and Health Sciences, SAINT KITTS AND NEVIS|A. Loya, Baylor College of Medicine Department of Ophthalmology, Houston, Texas, UNITED STATES|K. Shah, Psychiatry and Behavioral Sciences, Oklahoma State University, Tulsa, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Asher Khan: Commercial Relationship: Code N (No Commercial Relationship) | Zain Hussain: Commercial Relationship: Code N (No Commercial Relationship) | Asad Loya: Commercial Relationship: Code N (No Commercial Relationship) | Kaushal Shah: Commercial Relationship: Code N (No Commercial Relationship) | Kamran Riaz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent research has highlighted a significantly high prevalence of visual impairment among Americans with a history of early lifetime substance abuse. The purpose of this study is to further investigate the effects of early lifetime substance use on the eventual onset of severe visual acuity impairment or blindness in this patient population.

Methods: The National Survey on Drug Use and Health was queried to identify all cases of substance use before 21 years of age as well as all cases of significant visual impairment with refraction correction or blindness. Any cases with unknown or arbitrary visual outcomes were eliminated from analysis. Univariable and multivariable binary logistic regression with time-dependency was performed to evaluate odds of visual impairment influenced by 16 individual substances or classes. Adjusted variables of interest included gender, marital status, age bracket, race, level of education, total family income, poverty level, population density, and lifetime history of chronic disease.

Results: After elimination of 312 arbitrary cases, 55824 total cases were considered for analysis with 2577 (4.6%) cases of blindness or significant visual impairment despite refraction correction. Interviewees reporting illicit substance use prior to 21 years of age experienced significantly enhanced odds of eventual vision loss/blindness (OR=1.252, CI 1.175-1.322, $p<0.001$). Specifically, the use of cigarettes, alcohol, marijuana, cocaine, hallucinogens, lysergic acid diethylamide, phencyclidine, ecstasy, inhalants, methamphetamine, and tranquilizers significantly enhanced odds of permanent vision loss. Interviewee-reported substance use yielding borderline/no significance in relation to eventual vision loss/blindness included crack, heroin, pain relievers, stimulants, and sedatives.

Conclusions: Multivariate analysis demonstrated substantially enhanced odds of eventual significant visual impairment with refraction correction or blindness in relation to substance use prior to 21 years of age. A number of commonly abused substances have greater risk for permanent vision impairment. These findings may further help clinicians and public health agencies in mitigation efforts including education, prevention and rehabilitation.

CONTROL ID: 3714224

SUBMITTER (NAME ONLY): Rayne Lim

TITLE: Complement dysregulation in an iPSC-RPE model with CFH/FHL-1 haploinsufficiency.

SESSION TITLE: Stem cell models of retinogenesis and retinal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Lim, S. Shirali, J. Rowlan, A. Engel, M. Nazario, M. Neitz, J. Neitz, J.R. Chao, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|J. Du, Ophthalmology and Visual Sciences, West Virginia University, Morgantown, West Virginia, UNITED STATES|J. Du, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early onset macular drusen (EOMD) is an inherited retinal degeneration where patients develop clinical features similar to AMD early in life. This rare condition is associated with high penetrance genetic variants in the complement factor H (CFH) gene which result in loss of CFH and factor H-like protein 1 (FHL-1) expression. We identified an EOMD family with a novel c.351-2A>G variant in the conserved 3' splice site of exon 4. Induced pluripotent stem cells (iPSC)-derived retinal pigment epithelium (RPE) generated from two EOMD patients heterozygous for the mutation showed significantly reduced (~ 50%) CFH and FHL-1 expression, consistent with haploinsufficiency. This study will examine the effects of CFH/FHL-1 haploinsufficiency on complement inhibition and regulators of complement activators (RCA) in RPE.

Methods: iPSC-RPE derived from healthy controls and EOMD subjects were seeded on Matrigel coated dishes and transwell filters. Media CFH/FHL-1 levels were quantified by WB and ELISA, and an in situ C3b breakdown was performed to assay CFH/FHL-1 function. Expression of soluble complement components were evaluated via real-time PCR and WB. Expression of RCA members were also assessed with real-time PCR and immunostaining. RPE cultured on chamber slides were treated with 10% NHS and stained for C5b-9 to visualize MAC deposition.

Results: EOMD RPE cells had a significantly decreased CFH protein secretion per cell and reduced in situ C3b cleavage activity. In naïve conditions, EOMD RPE had elevated levels of soluble C3bα, C3bβ, and C3bα fragments, consistent with higher C3 turnover. No differences in C5 and CFI protein expression was found. Transcript levels of CD46 (membrane cofactor protein; MCP), CD55 (decay accelerating factor; DAF) and clusterin (CLU) were unchanged, while CD59 and vitronectin (VTN) were significantly increased. On immunostaining, VTN and CLU-positive deposits were found only in EOMD RPE and increased basal localization of CD55 was observed. In response to treatment with 10% NHS, MAC deposition was significantly increased in EOMD RPE compared to controls.

Conclusions: These findings indicate that reduction in CFH and FHL-1 expression contributes to complement dysregulation, suggesting that the RPE cells derived from EOMD patients could be more susceptible to complement-mediated stress.

CONTROL ID: 3714225

SUBMITTER (NAME ONLY): Andrés Vásquez Quintero

TITLE: Smart contact lens with dynamic artificial iris: simulated visual performance in keratoconus

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vásquez Quintero, P. Pérez-Merino, H. De Smet, Centre for Microsystems Technology (CMST), Universiteit Gent, Gent, BELGIUM|

Commercial Relationships Disclosure: Andrés Vásquez Quintero: Commercial Relationship(s);Code O (Owner):Azalea Vision;Code C (Consultant/Contractor):Azalea Vision | Pablo Pérez-Merino: Commercial Relationship: Code N (No Commercial Relationship) | Herbert De Smet: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

To evaluate the effect of pupil decentration and visual performance of an active artificial iris smart contact lens design using realistic eye models of keratoconus.

Methods: The artificial iris is based on guest–host liquid crystal cells (GH-LCD) in order to actively modify the transmittance of the lens and effective pupil size. Experimental validation of the GH-LCD spectrum and iris contrast (determined to be 1:2.1) enabled the development of patient-specific eye models for virtual ray tracing analysis in ZEMAX (Focus Software, Tucson, Arizona, USA). A custom methodology was developed to find the optimum pupil centration of the smart contact lens with dynamic artificial iris (6-mm, 4-mm and 2-mm pupil diameters) that produce best optical quality. The optical quality was calculated from simulated wave aberrations in terms of Visual Strehl Ratio (VSR), for 6-mm pupils, and estimated for decentrations ranging from -2 to +2 mm in 0.1 mm steps in horizontal and vertical meridians, referred to the pupil center. The methodology was applied to four keratoconic corneas.

Results: Customized pupil centration resulted in improvements in the image quality when compared with centered pupil positions for all the analyzed cases. On average, optimized pupil position produced a range of 12% to 35% increase in the Visual Strehl, with greater benefit for corneas with higher magnitude of high-order aberrations; i.e., eyes with low visual quality have most to gain with an optimized pupil centration. The visual modelling also suggests an extra increase in the maximum depth-of-focus value for a 4-mm (0.25 D) and 2-mm (0.75 D) pupil diameter for the estimated optimal pupil centration.

Conclusions: Numerical simulations show that the active control of pupil size and centration enhanced the visual function in keratoconus, especially in highly aberrated eyes. This correction could be implemented in practice using customized smart contact lenses with GH-LCD.

CONTROL ID: 3714227

SUBMITTER (NAME ONLY): Apoorva Karsolia

TITLE: Comparing spatial patterns of fixation preference in strabismus during visual and memory-guided saccades

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Karsolia, V.E. Das, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Apoorva Karsolia: Commercial Relationship: Code N (No Commercial Relationship) | Vallabh Das: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In individuals with strabismus, fixation preference when making a saccade to an eccentric visual target is thought to be driven by regional visual suppression of the peripheral retina. Here, we compare spatial patterns of fixation preference during visual and memory-guided saccades to understand the potential temporal persistence of visual suppression following the disappearance of a visual target.

Methods: Eye movements were recorded in one exotropic monkey (~25°) while performing visual and memory saccade tasks during binocular viewing. Stimuli consisted of eccentric visual targets presented at random locations within ±30 deg horizontally and ±10 deg vertically. During the memory paradigm, the animal fixated centrally while an eccentric target was flashed for 200ms. Following a variable delay period of 200, 400 or 800ms during which the animal continued to maintain central fixation, the central target was extinguished and the animal made a saccade to the remembered location of the target in darkness. The frequency of an eye acquiring the target at a particular location was calculated to develop fixation preference maps that were then compared between visually-guided and memory-guided saccades.

Results: Alternating and non-alternating saccadic eye movements were detected during both visual and memory paradigms indicating that fixation preference was a property of strabismus irrespective of the continued presence of visual information. Spatial patterns of fixation preference, where targets in the far right visual field were acquired by the right eye and targets in the far left visual field were acquired by the left eye, were observed for both visual and memory-guided saccades. Irrespective of which eye fixated centrally, the border for fixation switch occurred between the lines of fixation (~7°) and was influenced by visual suppression. The area between left and right fixation zones was similar for memory-guided saccades at all delay periods (200, 400 and 800ms) as compared to visually-guided saccades.

Conclusions: Visual suppression in individuals with strabismus influences eye choice behavior for both visually-guided and memory-guided saccades. Temporal dynamics of visual suppression deduced via patterns of fixation preference during memory-guided saccades suggest that effects of visual suppression persists even upto 800ms after the disappearance of visual information.

CONTROL ID: 3714230

SUBMITTER (NAME ONLY): Kazuya Oikawa

TITLE: Early neuroinflammatory responses in the visual pathway in a feline inherited glaucoma model

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Oikawa, J. Kiland, V. Mathu, O. Torne, G.J. McLellan, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|K. Oikawa, O. Torne, G.J. McLellan, Surgical Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myeloid cell activation has been implicated in glaucoma pathogenesis in humans and animal models. The purpose of the study is to delineate early myeloid cell activation in an inherited feline model of glaucoma.

Methods: Retinal, optic nerve head (ONH) and distal optic nerve (ON) tissues from 8 juvenile 10-12 week-old cats (4 males and 4 females) with feline congenital glaucoma (FCG) and 5 age-matched normal control cats (3 males and 2 females) were used. Data for weekly intraocular pressure (IOP) and optic nerve axon counts were available for all subjects. Protein and gene expression in tissue cryosections were examined by immunofluorescence labeling (IF) and RNAscope in situ hybridization (ISH), respectively. Retinal tissue was IF labeled for myeloid cell marker, IBA-1 and flat-mounted. ISH for markers of infiltrating monocytes/macrophages (CCR2) and proinflammatory cytokines (IL1A, C1QA, TNF) was performed. Microglia were identified by IF of homeostatic microglial marker, P2RY12. Microscopy images wereanalyzed using Image J, QuPath and Imaris. Two-tailed unpaired t-test or Mann-Whitney test or ANOVA were used for between-group comparisons ($p<0.05$ considered significant).

Results: Mean IOP [SEM] was higher in FCG (19.4 mmHg [3.1]) than age-matched controls (13.5 mmHg [1.8]) ($p<0.001$). Profound microgliosis was observed in the retina and ONH in juvenile FCG cats (no detectable axon damage) compared to age-matched controls ($p<0.01$) whereas ON myeloid cell density was not significantly different between groups. The density of $CCR2^{+}$ infiltrating monocytes was increased in ONHs in FCG relative to controls. While C1QAwas ubiquitously expressed in myeloid cells, only small subsets expressed IL1A or TNF in FCG. The majority of IBA1+ myeloid cells in the retina, ON and prelaminar ONH are positive for P2RY12 in cats, but loss of P2RY12 expression was identified in the retrolaminar region of the ONH in FCG. Myeloid cells in the FCG retina were more morphologically heterogeneous than normal, ranging from ameboid to hypertrophic, with reduced complexity of myeloid cell processes.

Conclusions: Activation of myeloid cells in early-stage FCG is characterized by a subset of proinflammatory myeloid cells, infiltrating monocytes and morphological remodeling in the retina and ONH.

CONTROL ID: 3714231

SUBMITTER (NAME ONLY): Lara Carroll

TITLE: Retinal HtrA1 upregulates inflammatory factors in response to hypoxia in vivo

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Carroll, B. Wood, G. Pandey, L. Owen, Dept Ophthalmology and Visual Sciences, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|M.M. DeAngelis, Dept Ophthalmology and Ira G. Ross Eye Institute, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure: Lara Carroll: Commercial Relationship: Code N (No Commercial Relationship) | Blair Wood: Commercial Relationship: Code N (No Commercial Relationship) | Gaurav Pandey: Commercial Relationship: Code N (No Commercial Relationship) | Margaret DeAngelis: Commercial Relationship: Code N (No Commercial Relationship) | Leah Owen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated HTRA1 is significantly associated with retinopathy of prematurity (ROP) in human disease and animal models. Mechanisms for this association are not clear. We hypothesize that HTRA1 modulates ocular inflammatory gene expression during hypoxia.

Methods: HtrA1 and inflammatory factors with predicted roles in ROP disease were measured using RT-PCR in murine retinal or retinal pigment epithelial (RPE) cells. ΔΔCt values were compared among P14 transgenic HtrA1 overexpression ($HtrA1^{TG}$) pups and wildtype (WT) C57Bl6J littermate controls under normoxic or hypoxic oxygen induced retinopathy (OIR) conditions (N=3/group). Following humane euthanasia and enucleation, retinal tissue was isolated using microdissection. RPE cells were isolated from choroid via mechanical dissociation in RNAprotect solution for RNA extraction. HtrA1, IL-1ß, TNFα, IL6, and Iba1 cDNA was amplified in triplicate, and Ct values normalized to ß2M. Statistical significance was assessed using one-way ANOVA followed by Bonferroni-corrected two tailed t-tests for multiple comparisons.

Results: Baseline HtrA1 expression in normoxia-reared $HtrA1^{TG}$ pups was 3.3-fold and 19-fold higher in retinal and RPE tissues, respectively ($p<0.0001$) compared with WT littermates. Under OIR conditions, WT retinal HtrA1 levels decreased significantly (2-fold; $p<0.001$), whereas RPE levels did not change. In contrast, OIR conditions in $HtrA1^{TG}$ pups increased HtrA1 expression significantly in both retina (1.5-fold; $p<0.005$) and RPE (2-fold; $p=0.005$). Compared to normoxic conditions, OIR increased $HtrA1^{TG}$ retinal expression of IL-1ß (4.5 fold; $p<0.001$), TNFα (23 fold; $p<0.0001$), and IL6 (4.3-fold; $p<0.005$). In WT retinas, a more moderate hypoxia-induced increase of IL-1ß (3 fold; $p<0.005$) and TNFα (12-fold; $p<0.0001$), but not IL6 were observed. We found no statistically significant expression changes for any inflammatory gene within the RPE.

Conclusions: We demonstrated that inflammatory gene expression was upregulated in hypoxic P14 retinae, further amplified by HtrA1 overexpression. In contrast to previous reports, hypoxia did not increase inflammatory gene expression in RPE cells. However, our study isolated RPE cells from the underlying choroid to prevent contamination from macrophages/monocytes within the choroidal vasculature. Our data suggest that HtrA1-mediated inflammatory activity specific to the retina rather than the RPE can exacerbate ROP.

CONTROL ID: 3714232

SUBMITTER (NAME ONLY): Igor Sinyak

TITLE: Reliability of Redness Imaging with the Ora EyeCup Phone

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Sinyak, E. bensinger, M. Marquis, J.D. Rodriguez, M.B. Abelson, Ora Inc, Andover, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Igor Sinyak: Commercial Relationship(s);Code E (Employment):Ora Inc | Ethan bensinger: Commercial Relationship(s);Code E (Employment):Ora Inc | Maurice Marquis: Commercial Relationship(s);Code E (Employment):Ora Inc | John Rodriguez: Commercial Relationship(s);Code E (Employment):Ora Inc | Mark Abelson: Commercial Relationship(s);Code E (Employment):Ora Inc;Code I (Personal Financial Interest):Ora Inc

ABSTRACT BODY:

Purpose: Object measures of symptoms of dry eye are difficult to measure without an expert evaluating the eye in a slit lamp real time. In this study we assess the ability for the Ora EyeCup Phone to consistently capture eye redness in a large patient population. To obtain variations in eye redness patients were exposed to Ora's Controlled Adverse Environment (CAE) with images acquired in the CAE.

Methods: A custom android application on the pixel 5 was used to capture nasal and temporal images from 600 subjects with dry eye disease. Images were captured 29 times during the study, each time collecting a nasal and temporal view of each eye. Images were automatically uploaded from the phones and automatically downloaded onto expert graders computers. Using a custom grading software, graders evaluated each eye with the images with the nasal and temporal images on the screen. If the image was too blurry, the eye was closed or did not reach a sufficient interpalpebral fissure height, or patients gaze was off from the target that eye at that timepoint was marked as ungradable. Some timepoints images did not make it to the grading program either from issues in the upload or image acquisition issues at that timepoint.

Results: Grading of the images is currently still ongoing, but to date total of 133,396 images, or 66,698 sets of nasal and temporal images, have been evaluated by an expert grader. Of these sets only 970 or 1.45% were marked as ungradable. However, some images that were supposed to be acquired and graded did not make it to the graders for reasons listed above. This accounted for an additional 764 missing image sets or 1.15%.

Conclusions: The very low percentage of ungradable sets of images indicates the Ora EyeCup phone provides consistent quality for measuring ocular redness during clinical trials.

CONTROL ID: 3714233

SUBMITTER (NAME ONLY): Sneha Singh

TITLE: Differential innate immune response and replication of SARS-CoV-2 in human diabetic corneal epithelial cells

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Singh, A. Kumar, Ophthalmology, Visual and Anatomical Sciences (OVAS), Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|G. Garcia, V. Arumugaswami, University of California Los Angeles, Los Angeles, California, UNITED STATES|R. Shah, A.A. Kramerov, A.V. Ljubimov, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|A. Jha, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes predisposes an individual to severe COVID-19. Diabetic cornea is also known to have impaired wound healing, increasing the chances of infection. Earlier, we reported the ability of SARS-CoV-2 to infect conjunctival cells, and the presence of viral RNA and proteins was also detected in the corneas of COVID-19 donors. In this study, we evaluated the effect of diabetes on corneal innate immune response during SARS-CoV-2 infection and sought to determine the underlying mechanisms.

Methods: Human primary corneolimbal epithelial cells (HCECs) were isolated from the corneas of three diabetic and three non-diabetic donors. In vitro studies were performed by infecting HCECs with SARS-CoV-2 – USA-WA1/2020 strain at MOI 0.5. Viral replication was assessed by viral genome copy number. RNAseq analysis was performed to determine genes/pathways altered by diabetic vs non-diabetic HCECs. qPCR was used to assess the expression of innate inflammatory and antiviral genes. Western blot was performed to detect the protein expression of antiviral signaling molecules.

Results: The primary HCECs were found permissive to SARS-CoV-2 infection, as evidenced by increased viral replication which peaked at day 3 p.i. along with an induction of p-STAT1. Interestingly, HCECs from diabetic cornea had higher viral RNA on all three days post-infection. SARS-CoV-2 infected HCECs exhibited induced expression of inflammatory genes and their levels were relatively higher in diabetic cells. RNA-seq analysis revealed significant differences in diabetic vs. non-diabetic SARS-CoV-2 infected cells with alteration in genes regulating viral response, inflammation, and injury. The most affected down-regulated genes are related to lipid metabolism, ferroptosis, and oxidative stress.

Conclusions: Our study demonstrates increased SARS-CoV-2 replication and differential innate antiviral and inflammatory response in HCECs from diabetic corneas. These results indicate that diabetes is a potential risk for enhanced infectivity of SARS-CoV-2 for the ocular surface.

CONTROL ID: 3714235

SUBMITTER (NAME ONLY): Pengxiao Zang

TITLE: Generative-adversarial-learning-based biomarker activation map for improving the interpretability of deep-learning-aided diabetic retinopathy screening

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zang, T. Hormel, J. Wang, S.T. Bailey, C.J. Flaxel, D. Huang, T.S. Hwang, Y. Jia, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Zang, J. Wang, Y. Jia, Department of Biomedical Engineering, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Deep learning (DL) can assist the diagnosis of diabetic retinopathy (DR) based on optical coherence tomography angiography. However, it is unclear how deep learning classification models arrive at their results, limiting discovery of DR biomarkers. To improve interpretability, a novel biomarker activation map (BAM) generation framework based on generative adversarial learning (GAL) is proposed.

Methods: 50 healthy participants and 305 patients with diabetes were recruited in this study. Masked trained retina specialists graded each eye based on 7-field fundus photography using early treatment of diabetic retinopathy study (ETDRS) criteria as either non-referable (nrDR; ETDRS score < 35) or referable (rDR; ETDRS score ≥ 35 or macular edema). Macular 3×3-mm scans for one or both eyes of each participant were acquired using a commercial 70-kHz spectral-domain OCT system. 456 superficial vascular complex (SVC) en face OCTA images were collected. The data set was divided into training (60%), validation (20%), and testing (20%) sets and used to train a referable/non-referable DR classifier that used the en face SVC angiograms as input. Two U-shaped networks were also trained as generators. The main generator was trained to produce an angiogram that the classifier would classify as nrDR from an input angiogram, while the assistant generator produces angiograms that would be classified as rDR (Fig. 1). The BAM was finally constructed as the absolute difference image between the input angiogram and output of the main generator.

Results: The diagnosis of rDR achieved an overall accuracy of 92%. Compared to the traditional class activation maps (CAMs) (Fig. 2B), the generated BAMs explicitly highlighted most of the pathological nonperfusion area, which represents the most important DR biomarker visible in the input angiogram (Fig. 2E). Unlike traditional CAMs, the BAMs ignored non-pathological features like the foveal avascular zone while emphasizing real pathological features that contribute the diagnostic decision making.

Conclusions: The generated BAMs using GAL method could provide sufficient interpretability to help clinicians utilize DL-aided referable DR screening, and help to quickly discern the DR-related pathologies. This innovation may also facilitate the new biomarker discovery on OCTA used for diagnosis of retinal vascular diseases.

CONTROL ID: 3714236

SUBMITTER (NAME ONLY): Moloy Goswami

TITLE: Glutaminase deficiency disrupts metabolic homeostasis of photoreceptors to induce rapid degeneration

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Goswami, E. Weh, S. Subramanya, N. Miller, S. Chaudhury, H. HAGER, C. Besirli, T.J. Wubben, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|H.B. Durumulta, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|C.A. Lyssiotis, University of Michigan Department of Internal Medicine, Ann Arbor, Michigan, UNITED STATES|A. Andren, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptors (PRs) have prodigious energy and biosynthetic demands. Most of the glucose delivered to PRs is converted to lactate, instead of pyruvate, via aerobic glycolysis. Due to this limited pyruvate, PRs need to utilize alternative fuels to supply tricarboxylic acid (TCA) cycle metabolites and support energy production and biomass. Glutamine (Gln) contributes to biosynthesis, energetics, and redox balance in other bioenergetically demanding cells. This study assessed the contribution of Gln catabolism to PR metabolism, function, and survival.

Methods: To study the role of Gln catabolism in vivo in PRs, we generated a rod PR-specific glutaminase (Gls) conditional knockout ($Gls^{fl/fl}$: Rho-Cre; Gls cKO) and a rod PR-specific tamoxifen inducible Gls conditional knockout ($Gls^{fl/fl}$:Pde6g-Cre^{ERT2}). Immunohistochemistry (IHC) and western blot analysis addressed the abundance and location of GLS. The function and survival of PRs was examined using OCT, ERG, and histology. Targeted metabolomics assessed the metabolic state in cKO and control retinas. RT-PCR analyzed the expression of genes involved in glutaminolysis, redox balance, and cell death.

Results: Rod PR-specific knockdown of GLS (Gls cKO) was validated with IHC and western blot, and metabolomics confirmed the substrate of GLS, Gln, was increased, and its product, glutamate, reduced. Gls cKO retinal metabolomics at P14 demonstrated decreased pyruvate, lactate, and aspartate. Correspondingly, the expression of genes involved in pyruvate metabolism, Pdha/b and Pcx, were increased while Pdk was decreased. The expression of transaminase Bcat1 and TCA cycle genes were also increased. Oxidative defense genes, Sod1/2, were upregulated as were markers of apoptosis, necroptosis, and ferroptosis. These molecular changes resulted in the Gls cKO mouse demonstrating comparable outer nuclear layer (ONL) thickness to controls at P14 with rapid and complete PR degeneration thereafter. Increased TUNEL staining in the ONL and GFAP staining was noted at P21. In accordance with these anatomic findings, Gls cKO mice showed significant decreases in scotopic amplitudes via ERG. Inducing knockdown of GLS in mature rod PRs with tamoxifen at P45 also resulted in significant degeneration.

Conclusions: This study demonstrates that GLS-mediated Gln catabolism is essential for PR metabolism, function, and survival.

CONTROL ID: 3714237

SUBMITTER (NAME ONLY): Katarzyna Komar

TITLE: Effect of stimulating beam diameter on two-photon visual thresholds

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Two-photon vision is the perception of short-pulsed near-infrared laser radiation (800-1200 nm) focused on the retina as having color as 400-600 nm, their half-wavelength counterparts. It is due to a nonlinear optical phenomenon - the two-photon absorption occurring in visual pigments (PNAS 111(50), E5445, 2014). To date, the effect of different beam sizes on the cornea on the two-photon thresholds has not been investigated. The present work provides experimental data to address this issue.

Methods: The two-photon (1040 nm, laser pulse duration 200 fs and repetition frequency 76 MHz) and one-photon (520 nm) visual thresholds of 4 dark-adapted healthy volunteers (2 women, 2 men, 32-43 y.o.) were determined by using 4-2-1 staircase strategy with a custom-build optical system. The stimulus was a circumference of 0.5 deg diameter, centered at fovea, obtained by fast scanning the retina with laser beams. The measurements were performed for 3 diameters of stimulating beam at cornea: 0.36 mm, 0.6 mm, and 1.2 mm for each wavelength. For each diameter, 5-7 various degree of defocus was applied around the best correction position found subjectively by each volunteer. The pupils of subjects were dilated, and accommodation was blocked by using 1% Tropicamide. The study was approved by the Ethics Committee of the Collegium Medicum, NCU.

Results: The mean two-photon thresholds calculated for all participants lie on 3 parabolas corresponding to the beam diameters at the cornea, each with a minimum located near (less than 0.3 D) the position of best correction. The parabolas became tighter and the mean threshold value (±1SD) at minimum decreases with increasing the size of the beam on the cornea: 18.1±3.4 μW, 9.8±1.6 μW, and 5.1±1.4 μW for 0.36 mm, 0.6 mm, and 1.2 mm diameter, respectively.

For one-photon stimulus, the discrepancies between individuals were greater and a significant difference between visual thresholds was observed only for 0.36 mm and 0.6 mm beam: the mean minimal visual thresholds were equal to 36±15 fW and 21±6 fW, respectively. The thresholds for the 1.2 mm diameter beam were roughly similar to the minimum found for 0.6 beam: 20±12 fW.

Conclusions: The data show that the size of the beam on the cornea significantly affects the two-photon visual threshold. The lack of difference between the 1.2 mm and 0.6 mm beams for single-photon (520 nm) vision may be due to more significant aberrations in the eye for this wavelength.

CONTROL ID: 3714238

SUBMITTER (NAME ONLY): Sanjaya Shrestha

TITLE: Deficiency of the transcription elongation factor Ell2, a downstream target of the cataract-linked RNA-binding protein Celf1, causes eye defects

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shrestha, S. Aryal, A. Siddam, F. Hernandez, S.A. Lachke, Department of Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently showed that the cataract-associated RNA-binding protein (RBP) Celf1 post-transcriptionally controls the key transcription factors Pax6 and Prox1 in the lens. To further understand the regulatory relationship between RBPs and the factors that control transcription in the lens, we focused on Ell2 (Elongation factor for RNA Polymerase II 2), which we found to be abnormally over-expressed in the lens in Celf1 lens-specific conditional knockout ($Celf1^{cKO}$) mice and which was independently identified by iSyTE as a high-priority candidate gene in the lens.

Methods: Ell2 expression in lens development was evaluated by RT-PCR, in situ hybridization (ISH), Western blotting (WB) and immunostaining (IF). Germline ($Ell2^{-/-}$) and lens-specific conditional KO mice ($Ell2^{cKO}$) were generated by crossing mice carrying Ell2 floxed alleles with CMVCre and Pax6GFPCre mouse lines, respectively.

Results: Ell2 overexpression in $Celf1^{cKO}$ mouse lens as suggested by microarrays and RNA-sequencing was independently validated by RT-qPCR. Further, RNA-immunoprecipitation (RIP) using Celf1 antibody indicated that Celf1 protein directly binds Ell2 RNA in lens cells. These data, along with iSyTE-based lens-enriched expression analysis, identified Ell2 to be a high-priority target in the lens. RT-PCR confirmed robust Ell2 RNA expression in mouse lens at various stages and ISH showed that Ell2 RNA is present in fiber cells near the transition zone at E16.5. WB confirmed Ell2 protein (~72 kDa) in mouse lens and immunostaining showed Ell2 protein levels in lens fiber cell nuclei at embryonic and postnatal stages. In agreement with Ell2's robust expression in the lens, $Ell2^{-/-}$ and $Ell2^{cKO}$ mice showed ocular defects, including small eye and lens abnormalities.

Conclusions: Ell2 has been shown to interact with RNA polymerase II and increase its elongation rate along template DNA by relieving the transient "pause" in the early stages of transcription. While Ell2 has been associated with cancer and other defects, its role in eye development has not been examined. This study identifies Ell2 as a novel downstream target of the cataract-linked gene Celf1 and validates its robust expression at the RNA and protein levels in the lens. Further, $Ell2^{-/-}$ and $Ell2^{cKO}$ mice exhibit ocular defects indicating its important role in the eye and lens.

CONTROL ID: 3714239

SUBMITTER (NAME ONLY): Tyler Heisler-Taylor

TITLE: MIF inhibition improves retinal function in NMDA mediated excitotoxic damage

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Inhibition of macrophage migration inhibitory factor (MIF) has shown promise protecting retinal neurons in excitotoxic retinal damage models. We evaluated the ability of three MIF inhibitors (MIFi) to improve electroretinography (ERG) function in the chick excitotoxic retinal damage model.

Methods: Experiments were performed under an IACUC approved protocol. White leghorn chicks (n=3/group) were given intravitreal injections with NMDA (500nmol) at day 0 (D0) plus one of three different MIFi: ibudilast, AV1013, or CPSI-1306 at 1.0 mg/ml or vehicle (sterile water). Injections of MIFi and vehicle was performed on D-1, and D0. ERG waveforms were captured between D10-D14 with the Celeris ERG system. Light adapted ERGs and oscillatory potentials were captured with flash intensities between 0.05 and 25 cd*s/m^2. Additionally, 20Hz flicker and long flash ERGs were recorded. Statistics were calculated in Graphpad PRISM using ANOVA with Tukey and Dunnett multiple comparison testing. A p-value ≤ 0.05 was considered statistically significant.

Results: ERG measurements resulted in no significant differences between MIFi-treated and vehicle-treated NMDA-damaged eyes in the CPSI-1306 and AV1013 groups. Ibudilast treatment resulted in significant improvement in two groups: the ERG b-wave and the long flash ERG bipolar-ON wave. NMDA-damaged eyes treated with ibudilast were found to have significantly higher b-wave amplitudes at 3, 8, and 13 cd*s/m^2 (177.24±47.04 μV vs 278.60±61.78 μV, p=0.0049; 192.08±64.39 μV vs 279.90±40.62 μV, p=0.0173; 183.16±66.67 μV vs 265.00±27.23 μV, p=0.0288; NMDA+vehicle vs NMDA+ibudilast, respectively). The ON waves were also improved due to statistically higher amplitudes (11.09±5.26 μV vs 35.54±22.68 μV, p=0.0170; NMDA+vehicle vs NMDA+ibudlast). Both of these waveform groups correspond to inner retinal neurons, which are most susceptible to excitotoxic damage caused by NMDA.

Conclusions: Ibudilast is approved in Japan for neurologic and inflammatory indications and is in clinical trials for multiple sclerosis in the US. Preliminary results show ibudilast is promising for excitotoxic retinal damage prevalent in many retinal disorders like blast injury, diabetic retinopathy, vein occlusion and retinal ischemia.

CONTROL ID: 3714240

SUBMITTER (NAME ONLY): Ramkailash Gujar

TITLE: Choroidal Vascularity Profile in Diabetic Eyes Using Wide Field Optical Coherence Tomography

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report the wide-field choroidal vascularity up to the mid-equator area in diabetic retinopathy (DR) subjects using wide-field optical coherence tomography (WF-OCT).

Methods: This is an observational, cross-sectional study. WF-OCT images (55 degrees) were obtained using Spectralis HRA+OCT (Heidelberg Engineering, Germany) in extremes of gazes in all quadrants and manual montages were created to obtain wide field images up to mid equator. A previously reported semi-automated algorithm was used to calculate choroidal vascularity profile (CVI). Regression analysis was performed to identify the factors influencing CVI.

Results: Forty-seven eyes from 25 patients were enrolled in the study. The mean age was 68.4±10.6 years. The refractive error (spherical equivalent) ranged from -2.25 to +3.75 diopters. Most common DR grade among study subjects was moderate NPDR (29.41%) and 74.5% eyes had diabetic macular edema (DME). The mean CVI in the macular area (58.29±3.63) was significantly lower than in any of the other fundus areas (all $p \leq 0.01$). The maximum CVI was seen in the nasal region (66.60 ± 5.61), followed by temporal (65.69 ± 3.81), superior (65.01 ± 4.87), and inferior (63.80 ± 5.42). The vertical macular area had the least coefficient of variation (CV) of CVI (0.06) while the inferior quadrant had the highest CV (0.08).

Conclusions: The current study describes the CVI profile on WF-OCT in DR eyes upto mid-equator. The significant increase of the CVI compared to healthy subjects and its significant regional variations introduce this novel quantitative parameter as a reliable biomarker of the diabetes-induced choroidal microangiopathy.

CONTROL ID: 3714242

SUBMITTER (NAME ONLY): Mohamed Ashraf

TITLE: Clinical utility of navigated ultrawide field optical coherence tomography in differentiating nonproliferative and proliferative diabetic retinopathy

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ashraf, J.K. Sun, L.P. Aiello, P.S. Silva, Ophthalmology, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|M. Ashraf, J.K. Sun, L.P. Aiello, P.S. Silva, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate whether ultrawide field integrated SS-OCT can be used to distinguish between nonproliferative features such as intraretinal microvascular abnormalities(IRMA) from proliferative features such new vessels(NV).

Methods: This cross-sectional study evaluated patients with severe nonproliferative diabetic retinopathy (NPDR)who presented to a single MD retina clinic (MA) at the Beetham Eye Institute from July 1 to Dec 15, 2021.Patients were imaged on a device combining UWF color imaging(CI) and navigated SS-OCT (Silverstone,Optos). A 12-mm raster protocol (macula, optic nerve head and superotemporal to inferotemporal arcades) and mid-peripheral volume scans in all four quadrants were performed. Any area with suspected NV or large IRMA (>8A) were imaged. A clinical assessment and UWF stereoscopic CI grading by the MD providing clinical care was performed. Lesions were considered to be NV if they were seen to break through the internal limiting membrane on SS-OCT.

Results: The study included 14 eyes of 8 patients with diabetes mellitus. 25.0 % were female, mean age of 51.5±7.97 years,42.9% had type 1 DM, with a mean duration of 23.4±9.3 years, and an average A1c of 8.4±1.9%. A total of 24 IRMAs were suspicious for NVE on UWF-CI grading. 21 (87.5%) were captured on navigated OCT with 3(12.5%) located outside the imaged area. Among IRMA imaged(N=21), evaluation of SS-OCT image determined that 5 lesions(23.8 %) were NVE and not IRMA. Of these, 3 were flat and confined to the posterior hyaloid face and 3 had forward extension and vitreous invasion. In one eye an additional NVE was detected that was not previously flagged as a suspicious NVE. The NVE identified resulted in a change in the DR grading from severe NPDR to PDR in 4 eyes(21.4%).

Conclusions: This pilot study explores the possible clinical utility of navigated SS-OCT in assessment of IRMA in subjects with severe NPDR. Initial findings suggest a substantial portion of eyes may have undetected proliferative disease that can be identified using this modality and thus further investigation is warranted. Future studies will include a larger cohort of patients to compare between OCT/UWF-CI grading, UWF-CI grading alone and UWF-FA to establish whether this approach provides benefit to existing imaging modalities with regard to IRMA as well as all other important diabetic retinopathy lesions.

CONTROL ID: 3714244

SUBMITTER (NAME ONLY): Benjamin Sivyer

TITLE: Functional diversity of intrinsically photosensitive retinal ganglion cells in the mouse retina.

SESSION TITLE: Retinal ganglion cells and central processing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Sivyer, M. Berry, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Benjamin Sivyer: Commercial Relationship: Code N (No Commercial Relationship) | Michael Berry: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There are six main ‘types’ of melanopsin expressing intrinsically photosensitive retinal ganglion cells (ipRGCs) in the rodent retina (M1-M6). Recent studies indicate there is likely an increased diversity within these groups but this functional diversity remains uncertain. We have recently identified a subtype of M1 ipRGCs coding for reflected luminance which forms the primary projection to the supraoptic nucleus (SON) of the hypothalamus. These results illustrate at least two distinct anatomical subtypes of M1s in the dorsal retina. Our hypothesis for the present study is that M1 ipRGCs comprise multiple functional subtypes in the dorsal retina.

Methods: To test this hypothesis, we combined multielectrode array (MEA) recordings (256 channels) with optogenetics to ‘Opto-tag’ channelrhodopsin-expressing ipRGCs. The dorsal retina of dark-adapted GlyT2Cre::Ai32 mice (n = 4 retinas from 3 mice) was dissected and maintained in a recording chamber at 32 C. Light responses to scotopic, mesopic, and photopic (=visual stimuli included luminance steps, chirp stimuli, UV/green color stimuli, and 1 minute long steps. Spike data was sorted and ipRGCs were functionally classified using unbiased clustering methods.

Results: We found 8 functional clusters of ipRGCs (n = 282 ipRGCs) that differed in their sensitivity, response latency, and maintained spiking. Two of the most sensitive functional clusters (clusters 3 and 5) had profoundly different light responses. Cluster 3 had transient responses to illumination (response duration 15.92 ± SEM 3.1s; n = 18 ipRGCs p <0.0001) and apparent depolarization block to sustained visual stimuli and/or high light intensities. This group fired only transiently to a 60-second visual stimulus (response duration 1.47 ± SEM 0.15; n = 18 p< 0.0001). Cluster 5 had sustained responses to all light intensities (response duration 75.39 ± 1.5s; n = 32 ipRGCs; p<0.0001) and was able to spike continuously during the 60s stimuli. The majority of the Opto-tagged cells fell into cluster 5 (n = 17 of 32) while none were found in cluster 3 (n = 0 of 18).

Conclusions: The mouse retina has 8 functional clusters of ipRGCs and the two most sensitive (presumptive M1 ipRGCs) fall into two distinct functional groups. Our data suggest that a unique population of M1 ipRGCs projecting the SON of the hypothalamus encodes sustained luminance information.

CONTROL ID: 3714245

SUBMITTER (NAME ONLY): Cleophace Akitegetse

TITLE: Assessment and reproducibility of ocular oximetry in tissues of the eye fundus

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Akitegetse, N. Lapointe, M. Picard, N. Dargis, P. Sauvageau, D. Sauvageau, Zilia Inc., Québec, Quebec, CANADA|D. Sauvageau, Chemical and Materials Engineering, University of Alberta, Edmonton, Alberta, CANADA|

Commercial Relationships Disclosure: Cleophace Akitegetse: Commercial Relationship(s);Code E (Employment):Zilia Inc. | Nicolas Lapointe: Commercial Relationship(s);Code E (Employment):Zilia Inc. | Maxime Picard: Commercial Relationship(s);Code E (Employment):Zilia Inc. | Natasha Dargis: Commercial Relationship(s);Code E (Employment):Zilia Inc. | Patrick Sauvageau: Commercial Relationship(s);Code O (Owner):Zilia Inc.;Code E (Employment):Zilia Inc. | Dominic Sauvageau: Commercial Relationship(s);Code O (Owner):Zilia Inc.;Code E (Employment):Zilia Inc.

ABSTRACT BODY:

Purpose: Oxygen plays a central role in multiple physiological and pathophysiological processes, and retinal oxygen supply has been found to be an important factor in many ocular diseases. Zilia has developed an oximetry technology that allows oxygen saturation (StO2) measurements in targeted locations of the retinal tissue. The objectives of the study were to evaluate the stability of StO2 measurements over the period of acquisition, the repeatability of measurements at a given location, establish preliminary normative data, compare oximetry levels in individuals in different regions of the eye fundus.

Methods: 24 subjects (16 females, 8 males, age ranging from 19 to 83) were enrolled for this study. Acquisitions consisted of 10-sec measurements in 3 locations of the eye fundus: inferotemporal optic nerve head (ONH), macula and nasal retina. Four subjects were randomly selected for repeated measurements at the same locations in the same eye after 15-30-min breaks.

The minimum period of acquisition required to obtain reliable StO2 measurements was established. Paired T-tests were performed to assess repeatability and compare StO2 variations in the different regions of the fundus.

Results: No significant difference was observed between 2 successive measurements at the same location (separated by 15-30 min breaks). Mean StO2 was 67.3%±5.57% in the ONH, 62.1%±4.69% in the nasal retina and 43.63%±10.97% in the macula. Significant differences in StO2 measurements were observed between the ONH tissue and the nasal retina ($p<0.025$), the ONH and the macula ($p<0.0001$), and the nasal retina and the macula ($p<0.0001$)

Conclusions: Ocular oximetry offers a unique window into the retina and systemic health by means of examining hemodynamics. Until now, retinal oximeters have offered semi-quantitative information about the oxygenation in large superficial retinal blood vessels. However, to become useful in clinical settings, a technology enabling reproducible quantitative oxygenation measurements, both in the superficial blood vessels and the underlying capillaries present in the intervessel tissues, is desirable. The present study demonstrates the efficacy and reproducibility of the Zilia ocular oximetry technology towards measuring StO2 of the microcapillary network within the retina and the ONH.

CONTROL ID: 3714246

SUBMITTER (NAME ONLY): Stephanie Trejo Corona

TITLE: Randomized Trial of Treat-and-Extend Intravitreal Aflibercept for Radiation Retinopathy: 1-Year Outcomes

SESSION TITLE: If the eye is a camera, the retina is the film - Retinal pathologic insights

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Trejo Corona, C. Villanueva Boone, C. Moore, A. Brown, J. Munoz, A.C. Schefler, Retina Consultants of Texas, Houston, Texas, UNITED STATES|T. Aaberg Jr., Retina Specialists of Michigan, Michigan, UNITED STATES|A.C. Schefler, Blanton Eye Institute, Houston Methodist Hospital, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Radiation retinopathy (RR) commonly causes poor, long-term visual acuity outcomes in patients previously treated with radiation plaque, proton beam, or orbital radiation therapy. Current treatments are not FDA-approved and prior studies have had variable outcomes with small sample sizes. We performed a multi-center, prospective, randomized clinical trial to assess the safety and efficacy of 2 mg intravitreal aflibercept injections (IAI) given in a treat-and-extend regimen for radiation retinopathy and optic neuropathy.

Methods: Thirty-nine eyes in 39 patients with RR were assigned randomly to cohorts (1:1 ratio) in which patients either did or did not receive a loading dose of 3 IAI followed by a treat-and-extend regimen. The primary outcome measure was the mean Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) change from baseline. Statistical analyses were performed using Student’s t-tests for comparison of groups.

Results: At baseline, mean patient age was 58.18 years (range, 23-81), 53.85% of patients were female, mean ETDRS BCVA was 58 letters (range, 20 - 83), and mean central retinal thickness (CRT) was 472 µm (range, 294 – 927) at baseline. Thirty-six patients completed the Month 12 visit (92.3%). There was a significant difference in the overall mean BCVA change between cohorts, with 2.8 letters and 7.5 letters gained in cohorts 1 and 2, respectively ($p < 0.01$). Additionally, there was a significant difference in CRT from baseline to week 52 overall (472.92 µm to 314.47 µm) and within cohorts 1 (442.6 µm to 295.4 µm) and 2 (504.8 µm to 333.6 µm), respectively ($p < 0.001$). 97.2% of patients had visual acuity of 20/200 or better, and 30.56% improved 10 or more ETDRS letters.

Conclusions: In this cohort of patients, aflibercept improved vision and CRT in patients with radiation retinopathy using a treat-and-extend regimen compared to historical controls.

CONTROL ID: 3714247

SUBMITTER (NAME ONLY): Renee Ryals

TITLE: Lipid nanoparticles transfect multiple retinal cell types in the non-human primate.

SESSION TITLE: Gene therapy and other novel therapeutics in ophthalmic diseases 2

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Our lab has generated novel lipid nanoparticles (LNPs) for delivery of gene editors to the retina and demonstrated robust transfection of the rodent retina. The goal of this study was to evaluate retinal transfection efficiency in a more clinically relevant model, the non-human primate (NHP).

Methods: Novel LNP variants were prepared via rapid microfluidic mixing of an organic phase containing the lipids (ionizable lipid, DSPC, sterols, and PEG) and aqueous phase containing GFP mRNA. LNPs were characterized for hydrodynamic radius, polydispersity index (PDI), encapsulation efficiency and zeta potential (ZP). LNPs were transfected into NHP iPSC-derived RPE cells at multiple doses ranging from 500 ng to 10 µg. Rhesus macaques received baseline optical coherence tomography (OCT), fundus autofluorescence (FAF) and ultra-wide-field imaging. Subretinal surgery was performed by a skilled retinal surgeon using an Alcon Constellation vitrectomy machine to deliver 100 µl (50 µg total) of LNPs to each bleb per eye. No systemic immune suppression was used. At 48 hours post-injection, in vivo retinal imaging was performed and eyes were then harvested for histology and immunohistochemistry (IHC). LNPs were also subretinally delivered to WT C57BL6 mice. In vivo retinal imaging and IHC of retinal sections were performed to characterize intracellular gene expression.

Results: All LNPs had a diameter <85 nm, with a PDI <0.10. The ZP of the particles varied from -1.1 to -5.3 and encapsulation efficiency ranged from 98-99%. GFP expression was observed in NHP iPSC-derived RPE cells at 48 hours post-LNP transfection at all doses tested. Baseline imaging confirmed that all macaques had normal retinal morphology prior to surgery. At 48 hours post-injection, in vivo retinal FAF imaging showed robust GFP expression in the subretinal blebs. IHC demonstrated GFP expression localized to photoreceptors, RPE and Müller glia (Figure 1). Evaluation of the same particles in WT mice on the same day confirmed GFP expression and localization.

Conclusions: LNPs successfully transfected many retinal cells in the NHP including photoreceptors, RPE and Müller glia post-subretinal delivery. These data demonstrate the translatability of LNP-mediated gene delivery to retinal cells across species and support their development as delivery systems for retinal disease therapies.

CONTROL ID: 3714248

SUBMITTER (NAME ONLY): Mandkhai Molomjamts

TITLE: The impact of unconjugated hyperbilirubinemia on angiogenic and oxidative stress genes in the neonatal rat retina exposed to LPS.

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Molomjamts, K. Satrom, T. Gisslen, E.C. Ingolfsland, Pediatrics, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) and unconjugated hyperbilirubinemia are common comorbidities found in preterm infants. As a potent antioxidant, low dose unconjugated bilirubin (UCB) may have a protective effect against the development of ROP, particularly in conditions of oxidative stress such as sepsis, yet it has not been tested in a preclinical study. We hypothesize that key oxidant stress factors and endothelial cell angiogenic factors are upregulated in retinas of jaundiced pups when exposed to lipopolysaccharide (LPS).

Methods: The Gunn rat model of neonatal jaundice was used in this study. Homozygous jaundiced pups (jj) and littermate non-jaundiced heterozygous (Jj) controls received intraperitoneal saline or LPS on postnatal day (P)5 and were euthanized on P7. Whole retinal dissection was performed. Retinas from 3-6 pups/group underwent RNA extraction, cDNA synthesis, and quantitative polymerase chain reaction (qPCR) with Vegfa, Ang2, Slit2, Birc5, p53, and GPX4 probes and normalized against PPIA. Outliers were identified by ROUT test (Q=1%) and comparisons were made by two-way ANOVA ($P<0.05$) (GraphPad Prism 8).

Results: LPS upregulated mRNA expression of angiogenic factors, Vegfa by threefold, Ang-2 by threefold, and Birc5, downstream target of Ang-2, by fourfold compared to saline groups at P7 ($p<0.05$). Antioxidant GPX4 and pro-oxidant P53 mRNA expression were upregulated threefold and twofold respectively in LPS groups compared to saline groups. There were no significant differences in any tested genes between Jj and jj groups.

Conclusions: LPS increased gene expression of key angiogenic molecules and had a mixed effect on pro-and anti-oxidant factors in the neonatal rat retina. These effects were not altered by the presence of unconjugated hyperbilirubinemia, despite previous evidence from our group describing the heightened antioxidant effects of unconjugated hyperbilirubinemia in the brain, which may suggest a differential effect from the blood-retina barrier. The induction of angiogenic factors by LPS in the retina validate published findings but further study is needed to determine if increased GPX4 by LPS may ameliorate its pathogenic role in ROP.

CONTROL ID: 3714249

SUBMITTER (NAME ONLY): Jennifer Sun

TITLE: Updating the Diabetic Retinal Disease Staging System through the Restoring Vision Moonshot™

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.K. Sun, L.P. Aiello, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|J.K. Sun, L.P. Aiello, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|T.W. Gardner, Ophthalmology, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|M.D. Abramoff, Ophthalmology and Visual Sciences, Iowa State University, Ames, Iowa, UNITED STATES|A.R. Glassman, Jaeb Center for Health Research, Tampa, Florida, UNITED STATES|H. Colhoun, The University of Edinburgh Division of Health Sciences, Edinburgh, Edinburgh, UNITED KINGDOM|S. Vujosevic, San Giuseppe Hospital, Arezzo, Toscana, ITALY|S. Dutta, JDRF, New York, New York, UNITED STATES|T. Tan, T. Wong, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|S. Levine, Mary Tyler Moore and S. Robert Levine, MD Charitable Foundation, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite advances in treatment, diabetic retinal disease (DRD) is a leading cause of vision loss for working-age adults worldwide. The development of novel, more effective therapies to preserve and restore vision is limited by current staging systems for DRD. These do not evaluate the neurosensory or peripheral retina, systemic health or molecular targets, and do not directly address impact of DRD on visual function or quality of life. The goal of this work was to define promising variables for a revised DRD staging system to better define DRD, stage risk of disease worsening and predict treatment response.

Methods: Six working groups conducted narrative reviews in the areas of: vascular retina, neural retina, visual function, quality of life, basic and cellular mechanisms, and systemic health to identify promising biomarkers for DRD risk, disease progression, and treatment response. Targeted reviews of the literature were conducted by a total of 50 experts in DRD from 12 countries, who used standardized evidence grids to collect information about each parameter.

Results: Selected tests and variables of interest included “traditional” ETDRS lesions, predominantly peripheral lesions on ultrawide field imaging, electroretinography, spectral domain optical coherence tomography, hemoglobin A1c, diabetes duration, and multiple molecular pathways. Visual function tests included best corrected visual acuity, contrast sensitivity, low luminance visual acuity and static automated perimetry. Quality of life instruments ranged from paper-pencil questionnaires to the RetCAT computerized adaptive testing system. Key information will be presented in each working group area to define the current level of evidence for promising parameters and to identify major gaps in knowledge that need to be addressed in future clinical and translational studies.

Conclusions: The DRD Staging System Update initiative is the first step in a Restoring Vision Moonshot™ which will expand access to data sharing and collaboration platforms to enable restoration and preservation of visual function in persons with diabetes. The second step is the establishment of a human eye tissue and the third step is development of a curated retinal image bank. The ultimate goal of this “Moonshot” is to create a world without visual loss from diabetes, a mission inspired by the late Mary Tyler Moore.

CONTROL ID: 3714251

SUBMITTER (NAME ONLY): Amrit Sehmi

TITLE: Exploring digital exclusion for patients using remote consultations at Moorfields Eye Hospital.

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Sehmi, S. Kang, D. Sim, R. Mathew, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The use of video consultations was scaled urgently at Moorfields Eye Hospital due the COVID-19 pandemic, and has been sustained within the Trust. This provision was much needed and initiated without the usual stakeholder engagement. Digital exclusion will drive health inequalities in our patients, unless we fully understand it and create solutions to make our services accessible for all. The aim of the project is to understand the reasons why patients failed to utilise digital services during the pandemic.

Methods: A retrospective analysis of all patient-initiated video consultation cancellations from December 2020 to November 2021 was undertaken. All rebooked appointments were excluded from analysis. Reasons for cancellation were extracted from the Patient Appointment System (PAS) to identify those who were digitally excluded. Patients who had opted out of data sharing or cancelled their video consultation but had attended another subsequent appointment were excluded from the analysis for digital exclusion.

Results: Over a 1-year period, 10,457 video consultations were undertaken at Moorfields Eye Hospital. 5% (535) of appointments were cancelled by patients. Of these, 14% (73 patients) were digitally excluded. Digital exclusion was due to 3 main factors; lack of resources (53%), lack of skills (19%), lack of trust in the video consultation model (19%), or a combination of these factors (9%).

The age range of digitally excluded patients was 9 to 89 years old. Those most digitally excluded were the 70-79 year olds (26%, 19 patients). The least digitally excluded age group were the 20-29 years olds (1%, 1 patient).

In terms of sub-speciality, 52% (38 patients) were from the adnexal service, 27% (20 patients) from general ophthalmology, 12% (9 patients) from paediatric ophthalmology, and the remainder from ocular oncology (4%), strabismus (3%) and medical retina (1%).

Conclusions: The reasons for digital exclusion are complex, but need to be understood and addressed, if we are to continue to scale digital services in the health sector and without widening health inequalities. Our work identified 3 main factors, with lack of resources being the overarching reason. Further implementation research in the fields of digital resource provision coupled with education may enable greater inclusion of this group of patients and enhance digital healthcare provision equality.

CONTROL ID: 3714252

SUBMITTER (NAME ONLY): Collynn Woeller

TITLE: Activation of the aryl hydrocarbon receptor inhibits IGF1R and TSHR-mediated signaling in thyroid eye disease

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Woeller, S.E. Feldon, E. Roztocil, Department of Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thyroid eye disease (TED) is an autoimmune disorder that can lead to proptosis, optic neuropathy and vision loss. In TED, the connective tissue behind the eye becomes inflamed, remodeled and enlarged. Thyroid stimulatory hormone receptor (TSHR) and insulin-like growth factor 1 receptor (IGF1R) signaling are central mediators of TED pathology. Teprotumumab, an IGF1R blocking antibody, recently became the first disease-specific treatment for TED. While teprotumumab represents a major advance and reveals TED specific treatments are feasible, there are limitations with the therapy including: incomplete patient response, patient relapse after therapy, undesirable side effects and cost. Therefore, additional therapies are needed. The objective of this research was to investigate the ability of the aryl hydrocarbon receptor (AHR) to block IGF1R and TSHR signaling in TED orbital fibroblasts.

Methods: Primary human orbital fibroblasts from TED patients and non-TED patients and HEK293FT cells were cultured under standard conditions. HEK293FT cells were transfected with TSHR cDNA and a cyclic-AMP response element (CRE) dependent luciferase reporter construct. Orbital fibroblasts or reporter cells were treated with IGF1, TSH or TED patient specific antibodies in the presence or absence of the AHR activating compounds, FICZ or esomeprazole (a proton pump inhibitor). Cells were collected and analyzed using luciferase reporter assays and quantification of phosphorylation of downstream cell signaling proteins (AKT and CREB). Cell migration was measured using scratch assays in cells treated with or without IGF1.

Results: Activation of TSHR by TSH or TED patient antibodies led to a robust increase in CREB phosphorylation and CREB-dependent luciferase activity in TSHR-expressing reporter cells. Activation of the AHR by FICZ or esomeprazole inhibited TSHR-induced CREB signaling. In TED orbital fibroblasts, IGF1R signaling induced phosphorylation of AKT and increased cell migration. Esomeprazole and FICZ mitigated IGF1-induced AKT phosphorylation and fibroblast migration in a dose-dependent manner.

Conclusions: These data show that activation of the AHR by FICZ or esomeprazole inhibit TSHR and IGF1R signaling. Given that both IGF1R and TSHR pathways are key mediators of TED pathology, these studies reveal that AHR activation may be a novel mechanism to treat TED.

CONTROL ID: 3714253

SUBMITTER (NAME ONLY): Arun Govindaiah

TITLE: A Validation Study of An Automated Artificial Intelligence-based Detection Model for Disc Hemorrhage Using Color Fundus Imaging

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Govindaiah, A. Bhuiyan, iHealthscreen Inc., New York, UNITED STATES|O. Otero-Marquez, L. Pasquale, A.C. Brown, R. Smith, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: An external validation of an automated Artificial Intelligence AI- and color fundus image-based model for detection of disc hemorrhage, a significant risk factor in glaucoma progression.

Methods: A deep machine learning architecture named “EfficientNet B5”, pre-trained with the “ImageNet” dataset, was implemented to train a network to detect the disc hemorrhages in fundus images. For this, 150 images with disc hemorrhages and 650 normal or without disc hemorrhages were used to train and test the model. Full-color fundus images were first cropped using automated AI to get only the optic disc area of the retina. These images were then resized to 100x100 pixels. This helps in reducing the number of retinal features that the network encounters, given the relatively small size of training data. The image sets were randomly augmented at each epoch for variation with rotation, translation and sheering with noise addition that resulted in newly generated images upto 35 times the original number. An early stopping mechanism was employed wherein the training is stopped if no improvement in training loss is seen in 25 consecutive epochs. The network weights with the best training loss were saved. For external validation, we have used another dataset obtained from the Department of Ophthalmology at Icahn School of Medicine at Mount Sinai. This dataset consisted of 144 images with disc hemorrhage and 831 normal or without disc hemorrhages.

Results: For detection of disc hemorrhage on the external validation dataset, we achieved 93.13% accuracy (95% CI: 91.35% to 94.64%) with a sensitivity of 71.53% (95% CI: 63.42% to 78.73%), a specificity of 96.87% (95% CI: 95.45% to 97.95%) and a kappa score of 0.71 (95% CI: 0.65 to 0.78).

Conclusions: We have performed an external validation study of the automated disc hemorrhage detection from a color fundus image. In the future, we aim to improve the sensitivity by adding more data and study the tool prospectively with deployment in clinical settings.

CONTROL ID: 3714254

SUBMITTER (NAME ONLY): Jinli Wang

TITLE: Overexpression of NADPH Oxidase 4 Induces Endothelial Senescence by Impairing Mitochondrial Biogenesis and ATF4 Activation

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, X. Tang, J.J. Wang, S.X. Zhang, Department of Ophthalmology and Ross Eye Institute, University at Buffalo, Buffalo, New York, UNITED STATES|X. Tang, Department of Endocrinology and Metabolism, VIP Medical Service Center, The Third Affiliated Hospital, Sun Yat-sen University, Guangdong Provincial Key Laboratory of Diabetology, Guangzhou, Guangdong, CHINA|S.X. Zhang, Department of Biochemistry, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: NADPH oxidase 4 (Nox4) is the major source of oxidative stress in endothelial cells (ECs) and is upregulated in diabetic retinopathy (DR). Increased cellular senescence has been observed in retinal blood vessels and contributes to DR pathogenesis. In this study, we investigated the role and mechanism of Nox4 in inducing retinal endothelial and vascular senescence in DR.

Methods: Primary brain microvascular endothelial cells (BMECs) and retinal microvessels (RMVs) were isolated from wild-type (WT) and humanized EC-specific Nox4 transgenic ($hNox4^{EC\text{-}Tg}$, referred to as TG) mice. Cellular senescence was evaluated by (1) senescence-associate β-galactosidase activity (SA-β-GAL); (2) expression of senescence-related genes quantified by quantitative real-time RT-PCR (qPCR); (3) senescence-associated secretory phenotype by measuring the secretion of IL-1β and hydrogen peroxide (H_2O_2) by ELISA or a H_2O_2 Assay Kit, respectively.

Results: TG-BMECs demonstrated a significantly increased number of SA-β-GAL positive cells compared with WT-BMECs. Consistently, expression of senescence markers including p21, Cdk6, Cdkn2a (p16) increased drastically in BMECs, and in RMVs, isolated from TG mice. Moreover, the levels of IL-1β and H_2O_2 secreted from TG-BMECs were significantly higher than that from WT-BMECs. To determine the mechanism of Nox4-mediated cellular senescence in ECs and retinal vessels, we examined mitochondrial biogenesis and the activating transcription factor 4 (ATF4)/p16 pathway, which have been linked to premature senescence in ECs and diabetic microvascular complications. We found that the expression of genes involved in mitochondrial biogenesis, including Opa1, Mfn2, Nrf1, Ppargc1β, and Tfam, was substantially decreased by 40-60% in TG-BMECs. A significant reduction in Mfn2 expression was also observed in RMVs from TG mice. Furthermore, overexpression of Nox4 led to an increased activation of the ATF4/p16 pathway. Inhibition of H_2O_2 by catalase or reducing oxidative damage by a potent radical-trapping antioxidant largely abolished Nox4-induced ATF4 activation and ameliorated senescent cells in TG-BMECs.

Conclusions: Overexpression of Nox4 induces endothelial and vascular senescence in the retina in part through impairing mitochondrial biogenesis and activation of the ATF4/p16 pathway, which may contribute to the development of DR.

CONTROL ID: 3714255

SUBMITTER (NAME ONLY): Gonzalo Quezada Peralta

TITLE: Usefulness of ultra-wide field retinography using confocal scanning laser ophthalmoscopy (cSLO) in patients with retinal tears and retinal detachments

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.E. Quezada Peralta, I. Fabelo Hidalgo, N. Pérez-Llombet Quintana, C. Fernández-Núñez, O. Durán Carrasco, R. Rodríguez Gil, M. Gil Hernández, R. Abreu, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|M. Campos Nazer, Universidad Catolica del Norte Sede Coquimbo, Coquimbo, CHILE|

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ABSTRACT BODY:

Purpose: We present a descriptive study based on a series of cases where we measured the detection capacity and its characteristics using ultra-wide field retinography in patients with retinal tears and retinal detachments.

Methods: Ultra-wide-field retinographies were performed using confocal laser ophthalmoscopy Mirante (Nidek, Gmagori Japan) during the course of 1 month in all patients with a clinical diagnosis of retinal tear or retinal detachment who came to our ophthalmology department in the emergency department. We analyzed the demographic characteristics obtained in the clinical history, location of the tear and if it was visible, it is position 1 of the gaze using the tools of the Mirante platform and the area of detachment of the total retina with the ImageJ application (open source).

Results: A total of 14 patients were recruited; the average age was 65 years with a male / female ratio of 1.8 / 1. 43% (6) correspond to retinal tears and 57% (8) to retinal detachments (RD). In only 1 patient with RD, retinography could not be obtained due to media opacity. Both eyes were equally affected in a 1: 1 ratio. In 17% (1) of the tears it was possible to see them in the primary gaze position while 100% were visible in the secondary and tertiary gaze position, 100% of RDs could be seen in primary gaze position. 50% (3) of the retinal tears presented peri-tear fluid. On average, the tears were found 56° from the fovea, with the upper and lower temporal quadrants being the most affected, both 40% of the time and the upper nasal the remaining 20%. No primary lesions were found in the lower nasal quadrant. The average area of the detached retina with respect to the total retina seen in ultra-wide field retinography, in RD cases, was 68%. All the tears (100%) were treated by laser photocoagulation and 38% of the RDs (3) were treated by pars plana vitrectomy (PPV) plus silicone injection and the remaining 62% (5) by PPV and gas tamponade.

Conclusions: Ultra-wide-field retinography using cSLO is an excellent tool for detecting and characterize retinal tears and retinal detachments in clinical practice.

CONTROL ID: 3714256

SUBMITTER (NAME ONLY): Shulamit Schwartz

TITLE: Epiretinal Membrane in Patients with Diabetic Macular Edema: To Peel or not to Peel?

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Schwartz, A. Loewenstein, G. Rabina, ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|S. Schwartz, Tel Aviv University, Tel Aviv, ISRAEL|A. Loewenstein, Tel Aviv University, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To compare anatomical and functional outcomes of pars plana vitrectomy (PPV) with epiretinal membrane (ERM) peeling in diabetes mellitus (DM) patients with and without diabetic macular edema (DME).

Methods: A retrospective interventional case series of consecutive patients who underwent PPV with ERM peeling. Patients were divided into two groups: With and without preoperative DME. Visual acuity (VA) and optical coherence tomography (OCT) parameters were evaluated before surgery and during 12 months follow-up.

Results: A total of 354 patients underwent PPV with ERM peeling, of which 81 met the inclusion criteria. Twenty-three were diagnosed with DME and were younger (66.3±9.6 vs 75.1±8.5years, $p<0.001$), had longer DM duration (18.9±7.1 vs 14.3±11.4 years, $p=0.04$) and higher HbA1C% (7.6±1.4 vs. 7.0±1.1, $p=0.01$). VA improved from 20/105 to 20/60 Snellen ($p=0.004$) and central macular thickness (CMT) decreased from 469.3±64.9μm to 331.1±92.2μm ($p<0.001$) in the DME group and from 20/80 to 20/45 Snellen ($p<0.001$) and from 478.9±77.4μm to 353.1±64.1μm ($p<0.001$) in the non DME group. Yearly intravitreal injections rate decreased from 5.9±2.5 to 2.9±3.0 ($p<0.001$) injections in the DME group.

Conclusions: DME patients with ERM, experience significant improvement in VA, macular thickness and yearly intravitreal injections after PPV with ERM peeling. DME patients are younger, with lower VA, longer duration of DM and higher HbA1C% levels at presentation in comparison to diabetic ERM patients without DME.

CONTROL ID: 3714257

SUBMITTER (NAME ONLY): Almudena Moreno Martínez

TITLE: Functional results and biomarkers after dexamethasone intravitreal implant in diabetic macular edema patients according to new ESASO Classification.

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Moreno Martínez, C. Blanco Marchite, F. López Martínez, A. Donate Tercero, E. González Aquino, C. Cava Valenciano, S. Copete Piqueras, Complejo Hospitalario Universitario de Albacete, Albacete, Castilla-La Mancha, SPAIN|

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ABSTRACT BODY:

Purpose: To assess functional outcomes and biomarkers changes after intravitreal dexamethasone implant (DEXI) in eyes with diabetic macular edema (DME), naïve and non-responders to vascular endothelial growth factor inhibitors (antiVEGF).

Methods: Retrospective real-world study conducted on consecutive DME patients with DEXI and were controlled at 2, 6 and 12 months. Subjects were divided in groups: naïve patients and non-responders to previously treated eyes with ≤3 antiVEGF injections (early switch) or >3 antiVEGF injections (late switch). Outcomes were best-corrected visual acuity (BCVA) and biomarkers with spectral domain optical coherence tomography (OCT) according to The European School for Advanced Studies in Ophthalmology (ESASO) classification and retreatments after DEXI.

Results: A total of 112 eyes were finally included in the study. At baseline, there were no statistically significant differences between gender, BCVA, CRT, type of diabetes mellitus, DME subtype and state of the lens. At month 2, the BCVA (logMAR) changed from 0.4 ± 0.52 to 0.35 ± 0.30, 0.52 ± 0.46 to 0.40 ± 0.52 and 0.70 ± 0.35 to 0.52 ± 0.44 in naïve, early and late switch group, respectively ($p<0.001$ between all groups). BCVA decreased at 6 and 12-month visit in naïve and early switch group and was stable in late switch from 6 month to final visit. Retinal thickness (T) improved at month 2, 6 and 12 in all groups ($p<0.001$). There was similar size cyst (C) reduction in all groups with statistically significant differences at 2 and 6-months ($p<0.001$ and $p=0.003$, respectively, between all groups). Presence of disorganization of the inner retinal layers (D) and subretinal fluid (F) improved at 12-month visit from baseline in all groups ($p=0.04$ at 6-month visit in both biomarkers). Hyperreflective foci (H) decreased in all groups over the study period ($p< 0.01$ at final visit). We found better results in D, F and H biomarkers over study period in late switch group. We did not found differences in the ellipsoid zone and/or external limiting membrane (E) and vitreoretinal relationship (V) alterations between groups in all time investigated. 89 (79.46%) eyes received additional treatment after first DEXI.

Conclusions: There were similar results in BCVA and biomarkers after DEXI in all groups with better findings in late switch group.

CONTROL ID: 3714261

SUBMITTER (NAME ONLY): Alejandro Arboleda

TITLE: Biocompatibility of photoactivated collagen-riboflavin hydrogels for corneal regeneration

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Arboleda, G. Fernandes Cunha, A. Manche, Y. Seo, C. Logan, D. Myung, Ophthalmology, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|D. Myung, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|S.C. Heilshorn, Department of Materials Science and Engineering, Stanford University, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal trauma and infections have high morbidity requiring urgent intervention and close follow-up. Novel techniques are needed to improve patient outcomes, decrease surgical burden, and prevent blindness. Here we study the in vitro and ex vivo biocompatibility and regenerative capacity of a collagen-riboflavin hydrogel crosslinked by UV light.

Methods: We have developed a hydrogel consisting of collagen type I and 0.25 mM riboflavin-5-phosphate photo-crosslinked by UV (365nm) light. Epithelial and stromal integration was assessed by admixing cultured stromal cells within the hydrogel pre-cursor solution, exposing the complex to UV light, and seeding epithelial cells on the formed hydrogels. Confocal microscopy was used to visualize adherence and identify immunohistochemical markers associated with normal morphology. Epithelial wound healing over the hydrogel was also tested in ex vivo rabbit corneas. A 5mm anterior keratectomy was performed and a photo-crosslinked collagen-riboflavin hydrogel was placed in the defect. The organ culture specimen was then incubated for 72 hours and analyzed with confocal microscopy. All procedures were conducted on physically crosslinked collagen hydrogels without photo-crosslinking.

Results: Microscopy of the in vitro tissue showed adherence of epithelial cells to the hydrogel-stromal interface. Immunohistochemical staining was positive for IL-1β and TNF-α in epithelial and stromal layers. The epithelial cells also expressed Ki67, CD44 receptors, ZO-1, and CK12. In the organ culture model, the hydrogel was visualized in the keratectomy wound with overlying re-epithelialization after 72 hours. The corneal epithelium demonstrated a multi-layered epithelium as well as ZO-1 staining. The photo-crosslinked hydrogel showed faster epithelial growth in the in vitro model and both faster and morphologically superior re-epithelialization in the organ culture model compared to the physically crosslinked hydrogel.

Conclusions: Collagen hydrogels photo-crosslinked using riboflavin and UV light support epithelial cell growth in vitro and in ex vivo organ culture. Upon immunohistochemical analysis, corneal epithelial cells in the in vitro model expressed markers of epithelial phenotype and, in organ culture, exhibited multi-layered morphology. The photo-crosslinked hydrogel was superior in its ability to support epithelial cell growth compared to the physically crosslinked hydrogel.

CONTROL ID: 3714265

SUBMITTER (NAME ONLY): Vanessa Rozo

TITLE: Role of TgWIP on the migration of Toxoplasma gondii into the eye

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Rozo, S. Park, S.M. Thomasy, B.C. Leonard, Department of Surgical and Radiological Sciences, University of California Davis, Davis, California, UNITED STATES|L.O. Sangare, D.A. Solis, J. Saeij, Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine, University of California Davis, Davis, California, UNITED STATES|S.M. Thomasy, Department of Ophthalmology & Vision Science, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular involvement occurs in about 70-90% of patients infected with Toxoplasma gondii. The genetic determinants of T. gondii that allow the parasite to migrate across the blood-retinal-barrier are poorly understood. Identification of genetic factors are critical to understanding the pathogenesis of T. gondii and may provide novel strategies for therapeutic intervention. A previous large-scale screen identified the parasite secreted effector TgWIP as a potential candidate gene that influences parasitic migration to the eye. Upon invasion, T. gondii secretes TgWIP into the host cytosol and enhances dendritic cell motility and transmigration, potentially turning them into shuttling vectors of T. gondii to the eye.

Methods: CRISPR-Cas9 was used to generate T. gondii parasites lacking TgWIP (△TgWIP). CD-1 mice were infected with 200,000 parasites/mouse in 4 groups: wildtype (WT) intravenously (IV) (n=5), WT intraperitoneally (IP) (n=5), △TgWIP IV (n=5), △TgWIP IP (n=5). Mice were sedated, examined, and imaged at baseline and at 7 days post-infection (pi) using slit-lamp biomicroscopy, indirect fundoscopy, posterior segment optical coherence tomography (OCT), color fundus photography, and fluorescein angiography (FA). Animals were euthanized on day 7, globes were fixed and processed for histologic analysis and immunohistochemistry for identification of parasites.

Results: All animals survived to day 7 pi, however one mouse died from the WT IV group during imaging. Fundic photography demonstrated marked vasodilation pi in all treatment groups with △TgWIP IV infected mice having the greatest degree of retinal vessel dilation from baseline to day 7, followed by △TgWIP IP, WT IV, and WT IP. FA revealed poorly delineated vasculature at day 7 compared to baseline, indicative of increased vascular permeability. Moderate thickening of the choroid was evident on OCT at day 7 pi with △TgWIP infected animals demonstrating a significantly more pronounced thickening when compared with WT infected controls. Histopathologic analysis and immunolocalization of T. gondii are currently being performed.

Conclusions: All mice infected with T. gondii demonstrated vascular dilation and increased vascular permeability with a subjectively more significant effect in animals infected with △TgWIP irrespective of infection route. The role of TgWIP in parasite migration and inflammatory changes to the eye requires further investigation.

CONTROL ID: 3714267

SUBMITTER (NAME ONLY): Maria Grant

TITLE: Intravitreal administration of AAV2-SIRT1 reverses diabetic retinopathy (DR) in a murine model of type 2 diabetes (T2D)

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.B. Grant, Y. Adu-Agyeiwaah, C.P. Vieira, B. Asare-Bediako, S. Li Calzi, Ophthalmology and Visual Sciences, University of Alabama at Birmingham, BIRMINGHAM, Alabama, UNITED STATES|S.S. Hammer, J.V. Busik, Physiology, Michigan State University, East Lansing, MI, US, academic, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: SIRT1, a nutrient-sensing deacetylase, regulates various cellular stress responses. Loss of SIRT1 in the diabetic retina causes inflammation, neurovascular degeneration and visual impairment. Here, we investigated the effect of intravitreal administration of AAV2-SIRT1 on DR in a model of T2D, the db/db mouse.

Methods: After 6-months of diabetes, db/db mice were injected intravitreally with either AAV2-SIRT1 (AAV2-SIRT1-db/db) or control virus (AAV2-GFP-db/db) and euthanized three months later. SIRT1 upregulation was confirmed by RT-PCR and IHC. Caspase-3, Iba1, and GFAP expression were examined using IHC. Hypoxia Green reagent, a membrane-permeant, fluorogenic probe that can detect cells that are adapting to a hypoxic environment, and specific retinal cell surface markers were used for flow cytometry. ERG and OKN response measurements were undertaken to determine changes in retinal neural function and visual response, respectively.

Results: Retina of AAV2-SIRT1-db/db mice showed increased SIRT1 expression at mRNA (3.0±0.9 vs. 0.5±0.1, $p<0.05$) and protein (28.4±6.0 vs. 13.9±2.0, $p<0.05$) level compared to AAV2 GFP-db/db mice. $Iba1^+$ microglia were reduced in AAV2-SIRT1-db/db mice (4.0±1.0 vs. 9.0±2.0; $p<0.05$) compared to AAV2-GFP-db/db. GFAP reactivity in retinal macroglia of AAV2-SIRT1-db/db (869.9±30.0) was reduced compared to AAV2 GFP-db/db mice (1258±30.0; $p<0.01$). Caspase-3 positive cells were reduced in AAV2-SIRT1-db/db mice (15.0±5) compared to AAV2 GFP-db/db mice (8.0±3.0; $p<0.05$). Simultaneous detection of hypoxia and cell surface markers demonstrated that AAV2-SIRT1 administration reduced the number of hypoxic endothelial cells, bipolar cells, and photoreceptors compared to AAV2-GFP as assessed by flow cytometery. The scotopic b-wave (326.0±43.0) was significantly improved in AAV-SIRT1-db/db compared to AAV2 GFP-db/db mice (188.0±39; $p<0.05$). OKN responses were also enhanced in AAV2-SIRT1-db/db mice (0.39±0.01 vs. 0.28±0.02; $p<0.05$).

Conclusions: Intravitreal administration AAV2-SIRT1 reversed DR through inhibiting retinal inflammation and apoptosis, reducing the number of hypoxic retinal cells, and improving the function of retinal neural cells and visual responses.

CONTROL ID: 3714268

SUBMITTER (NAME ONLY): Michael Farkas

TITLE: Random integration of AAV plasmid into the mouse genome following sub-retinal delivery

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Farkas, E.D. Au, University at Buffalo, Buffalo, New York, UNITED STATES|L. Carroll, L.A. Owen, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adeno-associated virus (AAV) mediated gene augmentation therapy is the gold standard for treating inherited retinal dystrophies (IRDs). While, wild-type AAV integrates into a specific location in the human genome, other studies have shown extensive integration of recombinant AAV in other organs, but little is known about integration into the retinal genome. Due to the potential consequences of integration and increasing interest in AAV-mediated gene therapy, we used a high-throughput base-resolution approach to investigate this phenomenon.

Methods: Eyes of four one-month old mice were injected with 1×10^9 viral particles of pAAV-AcGFP. At 30 days, fluorescent fundus imaging was performed, mice sacrificed, eyes enucleated, and retinas removed and flash frozen. Retinal DNA was isolated and subject to the Agilent SureSelect XT HS2 DNA System using custom baits for the pAAV-AcGFP. Libraries were prepared and 2 x 150 bp sequenced on an Illumina HiSeq4000. Reads were aligned to the mm39 mouse genome with BWA-MEM, and integration sites were identified from discordant and split reads with at least 20 soft-clipped bases. Integration sites were RT-PCR validated.

Results: On average, 60 million reads were generated per sample, with 2.5 million discordant or split. We found 904 to 8,195 unique integration sites per animal, with 327 to 5,290 sites unique to an individual eye in one animal. In all, 105 exons and 1,072 introns contained AAV plasmid sequence, with the remaining sites intergenic; integrated plasmid sequence was typically a few hundred bases. Aside from suspected homologous recombination of the plasmid's β-globin intron in mouse hemoglobin genes, no other region was over-represented in integration sites, though we identified sequence fragments from the entire plasmid. Pathway analysis revealed various significant pathways among genes with plasmid integration, but none related to cell-cycle or other cancer-related pathways.

Conclusions: There is little overlap between integration sites in different animals, or between eyes of the same animal, suggesting AAV integration is largely random. Random integration opens the possibility that sites may occur in deleterious regions. Further, this raises concerns regarding multiple injections in IRD patients. Finally, we do not know the consequence of intragenic integration on expression or translation, though exonic integration likely causes frameshifts.

CONTROL ID: 3714269

SUBMITTER (NAME ONLY): Vikram Paranjpe

TITLE: Understanding Motivations and Barriers to the Use of Tele-Ophthalmology for Clinic-Based Visits Early in the COVID-19 Crisis

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Paranjpe, S. Massa, L.A. Al-Aswad, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|L.A. Al-Aswad, Department of Population Health, NYU Langone Health, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Vikram Paranjpe: Commercial Relationship: Code N (No Commercial Relationship) | Scott Massa: Commercial Relationship: Code N (No Commercial Relationship) | Lama Al-Aswad: Commercial Relationship(s);Code O (Owner):GlobeCheck;Code C (Consultant/Contractor):AI Optics, Topcon Medical Systems Inc, Aerie Pharmaceuticals Inc, Zeiss;Code F (Financial Support):New World Medical, Save Vision Foundation, Topcon Medical Systems Inc

ABSTRACT BODY:

Purpose: While tele-ophthalmology has existed in various forms as an adjunct tool in screening, diagnosis, and remote management, its adoption as a primary means of eye care delivery has been limited. The COVID-19 pandemic led to limited ability to provide in-person eye care and accelerated the need for tele-ophthalmology. This ongoing study seeks to understand patients' attitudes, motivations, and barriers to the use of tele-ophthalmology in lieu of in-person visits.

Methods: From March – October, 2020, in-person visits to a single university-based eye clinic were restricted to urgent ocular complaints. All routine visits were offered as video visits (VV) through the electronic medical record (EMR). 800 patients who completed a VV during this period, as well as a random selection of 800 patients who completed an in-office visit 6 months prior but no VV during this period, were sent an online survey. Data collected included demographic information, use of and comfort with digital devices, knowledge of the VV option, and reasons for use/non-use of the VV option.

Results: 35 individuals (54% male, 46% female; 80% White, 9% Black, 3% Asian, 9% other; mean age 63 ± 15 years) have participated in the study to date. 15 (43%) did not have a VV and 20 (57%) completed a VV. There were no significant differences in demographic factors between groups. 80% without vs 75% with a VV ($p>0.05$) felt somewhat or very comfortable using digital devices. 100% without vs 90% ($p>0.05$) with a VV were registered for the EMR patient portal prior to March 2020. Of the individuals who did not complete a VV, 25% did not want a VV for eye care, 25% were unaware of the VV option, 19% did not feel follow up was needed, 25% felt VV were insufficient for their eye care needs, and 1% reported lack of insurance coverage of VV as reasons for not choosing to complete a VV. Binomial logistic regression showed that demographic factors, comfort with digital device use, and prior access to the patient portal did not influence use/non-use of a VV.

Conclusions: The importance of tele-ophthalmology continues to increase as the COVID-19 pandemic threatens to limit feasibility of or patient willingness for in-person visits. An understanding of patients' attitudes towards and barriers to accepting video visits may help minimize disruptions in necessary eye care in case of future limitations in access to in-person services.

CONTROL ID: 3714270

SUBMITTER (NAME ONLY): Michelle Dowell

TITLE: Referral Patterns for Pediatric Eye Care within the Public Sector of Barbados

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Da Silva, H. Munshi, E. Savatovsky, A.L. Grajewski, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Dowell, K. Da Silva, D. Callender, D. Grosvenor, Ophthalmology, The Queen Elizabeth Hospital, Barbados, Bridgetown, BARBADOS|M. Campbell, I. Hambleton, D. Grosvenor, Ophthalmology, The University of the West Indies at Cave Hill, Bridgetown, Saint Michael, BARBADOS|

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ABSTRACT BODY:

Purpose: Utilizing this unique opportunity to evaluate the majority of all children who seek eye care in Barbados, this study aims to determine the origin of referrals and age at first presentation to pediatric eye care centers in the public sector.

Methods: A retrospective, cross-sectional chart review of all patients under 18 years who sought eye care between Jan 1st and Dec 31st, 2019 at the two public eye care clinics in Barbados: Winston Scott Polyclinic, a primary care center (PCC) and Queen Elizabeth Hospital, a tertiary care center (TCC) in Barbados. Records with illegible handwriting or missing notes were excluded. The origin of referrals, age at the first visit to an eye care provider and relevant diagnoses were documented.

Results: Preliminary data was collected from 1,112 charts: 514 from TCC (10 months) and 598 from PCC (3 months). There was a statistically significant difference ($p<0.0001$) between the mean age of referral to TCC (3.6 ± 3.2 years) and PCC (8 ± 4.6 years) (Figure 1). 43% of the TCC referrals were initiated by interdepartmental referrals; 33% were referred from local polyclinics. School screenings constituted 69.2% of referrals to PCC (Figure 2). Referrals for retinopathy of prematurity (ROP) screening all occur at TCC between the ages of 1 and 7 months, with a mean of 2.2 months.

Conclusions: The pediatric population in Barbados has access to two public eye care centers, one PCC and one TCC. The difference between referral ages to the primary and tertiary care centers may be accounted for by the nature of visits. The TCC tends to see younger patients for conditions that may require immediate intervention (e.g., cataract management or ROP screening/management), while the PCC mainly receives referrals for refractive error assessment initiated by teachers' observations of students' behavior (e.g., difficulty seeing the board). The mean age of referral to PCC is 8 years, higher than recommended by the Guidelines for Development of Eye Care Programs and Services in the Caribbean, and the US Preventative Services Task Force, which emphasize the importance of eye screening at an early age. Further investigations should assess whether the later age of screening in Barbados negatively impacts visual outcomes.

CONTROL ID: 3714273

SUBMITTER (NAME ONLY): Marcos Crespo

TITLE: In vivo determination of the human corneal elastic modulus by VOCT

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Crespo, C.J. Rapuano, Z.A. Syed, Cornea Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|T. Deshmukh, F.H. Silver, OptoVibronex, LLC., Allentown, Pennsylvania, UNITED STATES|D. Benedetto, Center for Advanced Eye Care, Vero Beach, Florida, UNITED STATES|H. Jimenez, J.S. Pulido, Department of Ophthalmology, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vibrational optical coherence tomography (VOCT) supplements traditional optical coherence tomography with soundwaves to obtain the resonant frequency (RF) and the elastic modulus of anatomical structures. In this prospective study, we used VOCT to determine the in vivo elastic modulus of the human cornea.

Methods: Central corneal thickness measurements obtained from VOCT were correlated with those of Pentacam® (Oculus; Wentzler, Germany) pachymetry. VOCT measurements were performed at two different locations [central cornea (CC) and inferior cornea (IC)] in 32 normal eyes from 16 subjects. The RF and thickness values obtained from VOCT were employed in a calibration equation to calculate the corresponding modulus value. Repeated measurements were obtained in a subset of 10 eyes to assess the effect of anesthetic drops on the agreement of measurements.

Results: VOCT thickness values demonstrated a positive (r^2=0.97) and linear correlation (y = 0.939x - 13.92) to those of Pentacam. Five peaks (#1-5) were identified on the weighted displacement vs. frequency plots, although their presence was variable across eyes. The mean RF values for peaks #1-5 on the CC were 73.5±4.9, 120.4±2.0, 148.7±8.0, 207±7, and 239±3 Hz, respectively. The mean RF values for peaks #1-5 on the IC were 72.1±6.3, 120.3±1.8, 147.2±6.7, 205±7, and 238±4 Hz. Based on the corresponding RF, the calculated elastic modulus for peaks #1-5 on the CC were 1.023±0.104, 2.05±0.16, 2.94±0.40, 5.31±0.37, and 6.87±0.33 MPa, respectively. The IC elastic modulus for peak #1-5 were 0.975±0.150, 1.991±0.236, 2.76±0.28, 5.08±0.73, and 6.52±0.79 MPa. The effect of topical anesthesia in elastic modulus values for each peak was not significant ($p>0.05$), except for peak #2 in the CC ($p<0.05$).

Conclusions: This pilot study demonstrates the utility of VOCT as an in vivo, non-invasive technology to measure the elastic modulus in human corneas. The structural origin of the various moduli obtained can be hypothesized based upon reported in vitro studies, but further analyses are necessary for confirmation.

CONTROL ID: 3714274

SUBMITTER (NAME ONLY): Jie Cheng

TITLE: Histone Deacetylase and Myosin Inhibitors Promote Neurite Outgrowth in Injured Retinal Ganglion Cells Derived from Human Pluripotent Stem Cells

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cheng, S. Li, C. Berlinicke, P. Zhang, X. Chang, D.J. Zack, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|D.S. Welsbie, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inhibition of dual leucine zipper kinase (DLK) and leucine zipper-bearing kinase (LZK) pathways promotes retinal ganglion cell (RGC) survival both in vitro and in vivo, but has limited effect on, and may even inhibit axonal regeneration. With the goal of finding ways to promote axonal regeneration of RGCs treated with DLK/LZK inhibitors, we investigated the effect of histone deacetylase inhibition and myosin inhibition on the neurite outgrowth of injured RGCs.

Methods: Human pluripotent stem cell-derived RGCs (hRGCs) were challenged with the microtubule-destabilizing agent colchicine and treated with a DLK/LZK inhibitor (tozasertib), an HDAC inhibitor (trichostatin A, TSA), and/or a myosin inhibitor (blebbistatin). After seventy-two hours, the viability of hRGCs was evaluated using a live cell stain (Calcein-AM), a dead cell stain (ethidium homodimer), and the ATP-based CellTiter-Glo assay. Neurite length and branchpoint number were quantified by high content screening. In addition to testing a wild-type stem cell line, a CRISPR-generated DLK/LZK knock-out hRGC line was also tested. The expression levels of genes of interest were determined by quantitative PCR.

Results: Although colchicine-induced hRGC cell death was inhibited by DLK/LZK inhibitor, tozasertib, the neurite length and the number of branchpoint were greatly reduced. The addition of the HDAC inhibitor TSA or the myosin inhibitor blebbistatin to colchicine/tozasertib treated hRGCs led to increases in neurite length and branchpoint number compared with colchicine/ tozasertib treatment alone. Combined treatment with TSA and blebbistatin led to further increases in neurite length and the number of branchpoint. Similar results were obtained in an hRGC line in which both DLK and LZK were knocked out. Furthermore, colchicine-induced reduction of expression of the RGC-specific genes BRN3A, RBN3B, THY1, and SOX11 was partially reversed by treatment with tozasertib, tozasertib/TSA, or tozasertib/blebbistatin.

Conclusions: In this study, we found that treatment with HDAC and myosin inhibitors increased neurite outgrowth in injured hRGCs which were concurrently treated with a DLK/LZK inhibitor. The effect of TSA and blebbistatin was additive. The combined inhibition of DLK/LZK, HDAC, and myosin suggests a possible therapeutic approach to repair injured RGCs.

CONTROL ID: 3714276

SUBMITTER (NAME ONLY): Yutaka Kaneko

TITLE: The Utility and Safety of Liquid-Based Cytology in the Diagnosis of Intraocular Lymphoma

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kaneko, K. Nishitsuka, Department of Ophthalmology and Visual Sciences, Yamagata University Faculty of Medicine, Yamagata, JAPAN|R. Ohe, M. Futakuchi, Department of Pathological Diagnostics, Yamagata University Faculty of Medicine, Yamagata, Yamagata, JAPAN|

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ABSTRACT BODY:

Purpose: In the diagnosis of intraocular lymphoma, cytology with vitreous body samples has a low diagnosis rate because of the sparse number of cells and the destruction of cells during specimen preparation with conventional direct smear methods. Attempts have been made to improve the diagnosis rate by preparing cell block specimens. However, these are often difficult to prepare due to the availability of small quantities of samples. Liquid-based cytology (LBC) can increase cell accumulation by adsorbing atypical cells on the slide after fixation with a special fixation fluid. This can reduce cell destruction. We investigated the utility and safety of LBC for vitreous biopsy under perfusion in intraocular lymphoma.

Methods: Vitreous biopsy was performed on intraocular lymphoma (19 eyes in 15 patients) between 2015 and 2021 at Yamagata University Hospital. Vitreous body samples were obtained with 25-gauge vitrectomy under perfusion using a cut-rate of 8,000 rotations/min, and LBC specimens were prepared (BD SurePath, USA). After the vitreous biopsy, cell block specimens were prepared with the samples obtained from the perfusion pack.

Results: Atypical lymphocytes were identified in 14 of 19 eyes (73.7%) using LBC and in 13 of 19 eyes (68.4%) using cell block specimens. These atypical cells were also immunohistochemically positive for CD20 and Ki67. There were no complications during the vitreous biopsy under perfusion.

Conclusions: In diagnosing intraocular lymphoma, LBC for vitreous biopsy under perfusion is a useful and safe method that can achieve pathological diagnosis at a level comparable to cell-block specimens.

CONTROL ID: 3714277

SUBMITTER (NAME ONLY): Sophia DiCesare

TITLE: HiBiT tagging of endogenously expressed retinal degeneration-associated proteins enables sensitive, unbiased chemical and genetic modulator screens.

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. DiCesare, S. Daniel, J. Hulleman, Opthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|M. McCoy, B. Posner, HTS, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Until now, methods for identifying compounds or genetic manipulations that alter the homeostasis of retinal proteins of interest (POI) have been limited mainly to non-physiologic constitutive overexpression of large fluorescent/luminescent reporter tags fused to that POI. Here we describe an attractive alternative strategy that allows for easy monitoring endogenously expressed POIs from retinal cells for unbiased drug/gene discovery.

Methods: As an initial proof-of-principle, we used a CRISPR/Cas9 ribonucleoprotein and ssODN HDR template to genome engineer immortalized RPE cells to express a 2xFLAG HiBiT tag (29 total residues) on fibulin-3 (F3, EFEMP1), a protein associated with Malattia Leventinese/Doyne Honeycomb Retinal Dystrophy and glaucoma. To detect the HiBiT tag, conditioned media or lysates were supplemented with LgBiT and substrate to generate NanoBiT (HiBiT + LgBiT), a bright and stable luciferase. Cells were used to efficiently screen ~10,000 compounds from the UT Southwestern chemical library. Toxic compounds and NanoBiT inhibitors were identified in counterscreens. Hit compounds were verified in dose-response, repurchased, and validated in differentiated/polarized primary porcine RPE cells to confirm their activity on F3 secretion/intracellular levels.

Results: Genome engineering of F3 resulted in the formation of a single 2xFLAG-tagged HiBiT species as detected by western blotting. LgBiT complementation of 2xFLAG HiBiT F3 in media enabled detection in sub-microliter volumes. Compound screening identified both F3 enhancers and reducers. Surprisingly, a series of drugs typically used for treatment of glaucoma significantly increased F3 expression whereas a set of compounds that can regulate epithelial to mesenchymal transition (EMT) signaling significantly reduced both secreted and intracellular F3.

Conclusions: These findings support the use of the versatile 2xFLAG HiBiT tag in retinal drug discovery. Such an approach can also be used to enrich (via the 2xFLAG peptide) endogenous POI interacting partners. We speculate that this same general approach can also be applied to other retinal degeneration genes and may ultimately be useful in identifying mutant-specific drugs or genetic manipulators.

CONTROL ID: 3714278
SUBMITTER (NAME ONLY): Alexis O'Neil
TITLE: Systemic and Ocular Manifestations of Anti-MOG
SESSION TITLE: Neuro-ophthalmology
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. O'Neil, H. Nguyen, R. Karanjia, Ophthalmology, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|H. Nguyen, Vision Research Centre, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|C. Rush, Neurology, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|R. Karanjia, Dohney Eye Institute, California, UNITED STATES|
Commercial Relationships Disclosure: Alexis O'Neil: Commercial Relationship: Code N (No Commercial Relationship) | Hong-An Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Carolina Rush: Commercial Relationship: Code N (No Commercial Relationship) | Rustum Karanjia: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is limited data available for the Canadian adult population diagnosed with anti-MOG. The goal of this study was to increase the understanding of the ophthalmic and neurological manifestations of anti-MOG disease in adults living in a Canadian setting through a retrospective/prospective chart review. With more information on the disease, clinicians can better identify these patients, understand the disease progression, and manage treatment options.

Methods: Data from standard of care ophthalmic and neurological assessments was collected over a 1-year period for patients who were diagnosed with Anti-MOG disease. Data collected includes patient demographics, ophthalmic assessment, neurological assessment, MRI and bloodwork results.

Correlation analysis was made between titer of MOG antibody and objective quantified ophthalmic findings, including electro-diagnostic results, MRI imaging, OCT imaging, and ophthalmic and neurological examination results.

Results: Five patients who were diagnosed with Anti-MOG have been tested. Of these, 60% were female and 40% were male, with ages ranging from 18 to 63 years old. On ocular examination the majority of eyes had normal visual acuity (60%). The remaining eyes had, 20/30, 20/50, hand motion and light perception vision (one eye each, 3 patients). On fundus examination, half the eyes showed signs of optic atrophy on RNFL testing. Vision loss was asymmetric as evidence by a relative afferent pupillary defect in the two patients with decreased vision. In patients affected with Anti-MOG with decreased visual acuity, pattern Visual Evoked Potentials were significantly reduced in amplitude. Other than the initial optic neuritis, one patient experienced no additional neurological effects, while the others experienced scintillating scotomas, recurrent mild paresthesia of both legs, and seizures. The MRIs displayed hyperintense T2 abnormalities in all patients.

Conclusions: The initial results of this study match existing literature for anti-MOG disease. Optic nerve atrophy is a commonly found ocular sign in patients with anti-MOG. Interestingly, patients were found to have decreased VEP amplitudes but normal inner and outer retinal function. The study recruitment is ongoing.

CONTROL ID: 3714279

SUBMITTER (NAME ONLY): Ying Zheng

TITLE: Sustained release of EOBO rewetting agent from a new silicone hydrogel contact lens material

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zheng, J. Dou, J. Wu, Alcon Laboratories Inc, Johns Creek, Georgia, UNITED STATES|Y. Kim, C.J. Radke, Chemical and Biomolecular Engineering, University of California Berkeley, Berkeley, California, UNITED STATES|Y. Kim, C.J. Radke, Herbert Wertheim School of Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A newly designed surface wettable silicone hydrogel (SiHy) contact lens material was studied based on sustained release of amphiphilic rewetting agent, EOBO [poly(oxyethylene)-co-poly(oxybutylene)]. The purpose of this study was to evaluate the uptake and release profiles of EOBO from the SiHy lens material.

Methods: The EOBO uptake profile into the lens matrix was evaluated with a fluorescence microscope using a fluorescent EOBO (Figure 1). EOBO release from the lens to a fixed volume of phosphate buffered saline (PBS) was measured with high-performance liquid chromatography (HPLC) at various times (Figure 2). Fick's second law and EOBO concentration measurements at equilibrium were used to obtain the diffusion coefficient and the partition coefficient of EOBO.

Results: Diffusion coefficient of EOBO measured was ~10^{-11} cm^2/s, which is about three to four magnitudes less than that of polymers with similar hydrodynamic radius. In addition, the lens partition coefficient of over 100 for EOBO indicated strong favorable interactions between EOBO and the hydrogel lens matrix. Lower molecular weight or more hydrophilic portion of EOBO preferentially released, whereas higher molecular weight or less hydrophilic EOBO practically retained within the bulk material. The unique interaction between the lens material and the rewetting agent contributed to the prolonged release of EOBO from the SiHy material. Results showed that EOBO released continuously from the bulk material for more than 7 days (Figure 2).

Conclusions: An in-vitro study and theoretical modeling were conducted on a new surface wettable SiHy contact lens material with a sustained release rewetting agent EOBO to demonstrate the feasibility of an enhanced re-wettable contact lens material. The unique interaction between the lens material and the rewetting agent contributed to the sustained release of EOBO from the SiHy lens material for more than 7 days.

CONTROL ID: 3714280

SUBMITTER (NAME ONLY): Aminat Adama

TITLE: Generation Of A Transcriptional Signature Describing Neuroprotective Lipoxin Activity

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Adama, A. Tuccitto, J.M. Sivak, Krembil Research Institute, Toronto, Ontario, CANADA|J.M. Sivak, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|A.S. Adama, A. Tuccitto, University of Toronto Department of Laboratory Medicine and Pathobiology, Toronto, Ontario, CANADA|K.G. Wigg, University Health Network, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: We previously reported on the neuroprotective activity of the lipid mediators, lipoxin A_4 and B_4 (LXA_4 and LXB_4). However, the downstream signaling cascades induced by these molecules in neuronal cells are still unclear. Here we aimed to develop a preliminary molecular signature describing LXA_4 and LXB_4 transcriptomic changes following treatment in neuronal cells.

Methods: Using next-generation sequencing, 4 treatment groups were analyzed: LXA_4, LXB_4,15-HETE (an inactive LXB_4 precursor) and Vehicle. The 15-HETE and Vehicle groups served as controls to identify genes specifically induced by each lipoxin treatment. HT22 neuronal cells were plated at $1x10^6$ cells per well in supplemented high glucose DMEM media and seeded overnight at 37°C. The following day, cells were treated with LXB_4, LXA_4, 15-HETE and Vehicle at 1µM in 4 biological replicates. Cell lysates were collected 1 hour after treatment, and total RNA was purified and seqeunced using an Illumina platform. Following sequencing, the data was bioinformatically sorted for differential gene expression analysis. Treatment groups were then fruther comparatively analyzed in R to identify lipoxin-specific transcripts.

Results: In comparison to vehicle 242 genes were identified specific to LXB_4 treatment, 539 for LXA_4, and 440 genes for 15-HETE treatment ($p<0.01$). Interestingly, only 23 genes were common between LXA_4 and LXB_4. In further analyses 15-HETE-specific genes were matched against LXA_4 and LXB_4 and common reads were removed to generate a molecular signature specific to each lipoxin treatment. The final unique gene counts were 185 and 315 genes with altered expression for LXB_4 and LXA_4 treatment, respectively.

Conclusions: A preliminary neuronal molecular signature for LXA_4 and LXB_4 signaling was identified, consisting of altered transcripts unique to each treatment. Next steps include ongoing characterization of the top hits under a variety of conditions and timepoints.

CONTROL ID: 3714283

SUBMITTER (NAME ONLY): Loh-Shan Leung

TITLE: Correlated Changes in Retinal Thickness and Visuomotor Function in Asymptomatic Hydroxychloroquine Toxicity Patients

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.B. Leung, B. Hwang, A.R. Berneshawi, R.T. Chang, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|R. Goel, T. Tyson, L.S. Stone, NASA Ames Research Center, Moffett Field, California, UNITED STATES|R. Goel, San Jose State University, San Jose, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously shown that a 5-min eye-movement test can capture many largely independent “oculometric” parameters of human visual/visuomotor function (Liston & Stone, 2014). This test has been successfully used to characterize mild neural impairment due to traumatic brain injury, sleep and circadian disruption, and alcohol consumption (Liston et al., 2017; Stone et al, 2019; Tyson et al, 2021). Here, we extend this approach to study patients at risk of progressive posterior-segment illness to see how oculometrics relate to standard clinical ophthalmological measures.

Methods: Five female patients (≥20/40 BCVA, 34-60 years old) undergoing hydroxychloroquine treatment (2-7mg/kg/day for 10-23 years for rheumatologic illness) have participated thus far. Under monocular viewing conditions in randomized order, they tracked a moving spot undergoing radial step-ramp motion in 90 randomized directions, at 5 randomized speeds, starting at random times (see Stone et al, 2019). We computed nine independent oculometrics (latency, initial acceleration, steady-state gain, proportion smooth, saccadic rate, saccadic amplitude, direction noise, speed responsiveness, and speed noise). Spectral-domain optical coherence tomography (Zeiss, Dublin, CA) was used to measure the average thickness of the nine Early Treatment Diabetic Retinopathy Study macular sectors from the internal limiting membrane to the retinal pigmented epithelium. We used Pearson’s correlation between retinal thickness and our oculometrics with t-statistics to test separate one-sided hypotheses across 10 retinae.

Results: We found significant changes in different aspects of visuomotor performance. Most notably, latency increased, initial acceleration decreased, and steady-state pursuit gain decreased as retinal thickness decreased (r^2 = 0.364, 0.579, & 0.692; one-tailed P = 0.032, 0.005, & 0.001, respectively). Speed responsiveness appeared to decrease although marginally for our current sample (r^2 = 0.253, P = 0.069). Lastly, direction discrimination and saccadic behavior appeared unchanged.

Conclusions: Oculometrics may provide sensitive measures of changes in retinal thickness. More importantly, they have the potential to detect impairment before it becomes evident with standard clinical imaging, while also providing insight into the behavioral implications of any resulting deficits in visual/visuomotor function.

CONTROL ID: 3714284

SUBMITTER (NAME ONLY): Cristhian Ildefonso

TITLE: Photoreceptor and RPE co-expression of a dominant mutant polymerase gamma subunit 1 leads to accelerated retinal degeneration in wild type mice

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Ildefonso, R. Ridley, E. Walsh, A.S. Lewin, Ophthalmology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|C.J. Ildefonso, A.S. Lewin, Molecular Genetics & Microbiology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: AMD patients accumulate RPE mitochondrial DNA mutations. Furthermore, mitochondrial haplotypes, (e.g., haplotype J) are linked to AMD. In mice, increased expression of a dominant mutant polymerase gamma-subunit 1 ($PolG1^{D1134A}$) causes accelerated skin aging. We have reported that this mutant PolG1 increases mitochondrial DNA mutations, decreases mitochondrial genomes copies, lowers expression of antioxidant genes in ARPE-19 cells. Herein, we define the effects of mutant PolG1 expression in photoreceptors and RPE in C57BL6/J mice.

Methods: We injected C57BL6/J mice subretinally with 10^{10} vector genome copies of rAAV5, delivering either GFP or $PolG1^{D1134A}$ under the control of the small CBA promoter. We evaluated these mice's retina at one, two, and four months. We use electroretinography (ERG), spectral-domain optical coherence tomography (SD-OCT), and fundoscopy for each evaluation. After the final assessment, we euthanized these mice harvested their eyes. We used immunofluorescence to detect DNA damage (8-OHdG), changes in RPE65, and tight junctions (ZO-1). Finally, we used ultra-thin plastic sections to identify morphological changes within the retina.

Results: Mutant PolG1 expression in the retina decreased the a-, b-, and c-wave amplitude by 50% compared to GFP treated eyes beginning at one month after injection. The ONL of these mice was also significantly thinner when measured in SD-OCT images. Retinas cross-sections showed an abnormal distribution of RPE65 in mutant PolG1 treated mice. Flat-mounts co-stained with ZO-1 and 8-OHdG showed localized increase in oxidized DNA in animals treated with mutant PolG1. Ultra-thin retina sections of mutant PolG1 treated eyes showed accumulation of toluidine positive material under the Bruch's membrane, and death of RPE cells.

Conclusions: Our studies suggest that dominant mutant PolG1 expression in both photoreceptors and RPE cells results in accelerated retinal degeneration. This degeneration was characterized by a substantial decrease in retinal function (ERG response) and structure (SD-OCT, immunofluorescence, and ultra-thin sections). Future studies will elucidate the RPE and photoreceptors individual contribution to retinal degeneration due to mutant PolG1 expression, while also identifying changes in markers of accelerated aging in the retina.

CONTROL ID: 3714285

SUBMITTER (NAME ONLY): NIKOLAS PONTIKOS

TITLE: Eye2Gene: prediction of causal inherited retinal disease gene from multimodal imaging using AI

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. PONTIKOS, W. Woof, G. Arno, M. Daich Varela, B. Liefers, T. Guimaraes, K. Balaskas, O.A. Mahroo, M. Michaelides, A.R. Webster, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|K. Hess, F.G. Holz, Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|P. Krawitz, Institute for Genomic Statistics and Bioinformatics, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|N. PONTIKOS, W. Woof, G. Arno, O.A. Mahroo, M. Michaelides, A.R. Webster, Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Shah, S.M. Downes, University of Oxford Nuffield Department of Clinical Neurosciences, Oxford, Oxfordshire, UNITED KINGDOM|S. Madhusudhan, Ophthalmology, Liverpool University Hospitals NHS Foundation Trust, Liverpool, Liverpool, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRDs) are single-gene disorders caused by genetic mutations in any one of over 270 genes. Identifying the causative gene through genetic testing is crucial for gene targeted treatments, recruitment to clinical trials, prognosis and family planning. However the prescription and interpretation of genetic results requires phenotype-genotype recognition that only few IRD experts can provide. Therefore we aimed to develop Eye2Gene, an AI algorithm, to predict the probable IRD causative gene from the retinal scans of suspected IRD patients.

Methods: Eye2Gene was trained and tested on retinal scans of IRD patients with a known genetic diagnosis from Moorfields Eye Hospital (MEH). Following quality control, the MEH training dataset consisted of 44,817 images from 1,907 IRD patients from MEH, covering 3 modalities: Fundus Auto-Flourescence (FAF), Infrared (IR), and Spectral-Domain Optical Coherence Tomography (SD-OCT). For each of the 3 modalities, five distinct InceptionV3 convolutional neural networks (CNNs) were trained on different subsets of the training data using 5-fold cross validation to identify up to 36 gene classes. This resulted in Eye2Gene, an ensemble of 15 CNNs. Generalisability was assessed on a held-out dataset consisting of 264 patients from MEH and an external cohort of 37 patients from University Hospital of Bonn (UHB). To benchmark Eye2Gene against human performance, a subset 50 FAF scans were evaluated by 8 ophthalmologists.

Results: Eye2Gene yields a top-5 accuracy of 88% in the MEH held-out dataset and 83% in the external validation UHB dataset. On the human benchmarking dataset, Eye2Gene achieved a top-5 accuracy of 72% compared to 78% for ophthalmologists.

Conclusions: Eye2Gene is an AI algorithm capable of predicting the 36 top most common IRD genes to a top-5 accuracy of >80%. Eye2Gene achieves performance similar to a consensus of human experts on an external dataset. Eye2Gene can eventually enable democratisation of IRD expertise, currently only available in a few centres around the world.

CONTROL ID: 3714286

SUBMITTER (NAME ONLY): QING WANG

TITLE: Defective Microtubule-Based Transporters Alter Basal mTORC1 And Akt Signaling in Lowe Syndrome Patient-Derived Cells

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. WANG, B. Wang, T. Kowal, Y. Hu, Y. Sun, ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lowe syndrome is a rare congenital disease that presents with renal failure, developmental delays, congenital cataracts, and glaucoma. The coordination between endocytosis dysfunction and the Akt/ mTORC1 signaling in Lowe syndrome patient cells is unclear. The present study tests the hypothesis that microtubule-based transport proteins are involved in the trafficking of lysosomes and maintenance of subsequent basal mTORC1 and Akt signaling. The relationship between endocytosis dysfunction and mTORC1/Akt signaling was also examined.

Methods: We examined mTORC1 and Akt signaling in normal human fibroblasts (NHF558) treated with nocodazole, which blocks microtubule polymerization, in complete culture medium. Activation of mTORC1signaling was assayed by the phosphorylation of p70 S6 Kinase (Thr389); activation of Akt signaling, by the p-ser473 Akt level. We also examined lysosome distribution in noncancerous cells in which Arl8a, Arl8b, SKIP, Rab7a or RLIP was knockdown by siRNA. Lysosome distribution was quantified by using average LAMP1 intensity.

Results: Knockdown of anterograde transport proteins small GTPase Arl8 or SKIP in normal human fibroblasts leads to perinuclear lysosome positioning and decreased mTORC1 signaling. However, Arl8 or SKIP knockdown in Lowe 1676 cells did not cause perinuclear lysosome accumulation and decreased mTORC1-mediated phosphorylation of p70 S6 Kinase (Thr389). Furthermore, we found that knockdown of retrograde transport proteins caused lysosomes to be scattered throughout the cytoplasm and decreased the perinuclear lysosome accumulation in normal human fibroblasts. However, we did not observe similar disruption in Lowe patient-derived fibroblasts with Rab7 or RLIP knockdown. Thus, these experiments show that mTORC1 and AKT signaling is sensitive to lysosome dynamics and that OCRL plays a role in the crosstalk between these pathways.

Conclusions: Whereas previous studies mainly focused on how transporters such as the kinesins and dynein motors regulate lysosome positioning, here we showed that the microtubule and actin systems themselves also play important roles in the transporting of lysosomes. These data suggested that under pathological conditions (e.g. congenital glaucoma), there are alternative pathways to regulate the mTORC1 and Akt signaling response to nutrient stimulus.

CONTROL ID: 3714287

SUBMITTER (NAME ONLY): Yin Shan Eric Ng

TITLE: Therapeutic effect of hindered phenol compound in a solid lipid nanoparticle formulation in mouse models of dry AMD

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Ng, Z. Ji, A. Arta, Y. Su, P.A. D'Amore, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Z. Ji, Y. Su, Wuhan University Renmin Hospital, Wuhan, Hubei, CHINA|A. Arta, A.J. Urquhart, Department for Micro- and Nanotechnology, Danmarks Tekniske Universitet, Lyngby, DENMARK|

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ABSTRACT BODY:

Purpose: We have previously shown that hindered phenol compounds have potent cytoprotective activity against oxidized low-density lipoprotein-induced death of retinal pigment epithelial cells (RPE) in vitro. The goal of this work was to determine the ocular pharmacokinetics (PK) as well as the therapeutic effect of a sustained-release solid lipid nanoparticle (SLN) formulation of the hindered phenol pentamethyl-6-chromanol (PMC) in two mouse models, in which characteristics of AMD are induced by aging and high fat diet.

Methods: PMC-loaded SLNs (SLN:PMC) were prepared by high-shear homogenization and delivered by periocular injection.For the PK study, total PMC in cornea/lens, retina, and RPE/choroid was determined by LC/MS analysis at 24 hours post-injection. For the efficacy study, 12-month-old wildtype C57BL/6J and APOE4-TR mice were fed with high fat diets (HFD) and treated weekly with SLN:PMC or empty SLN for five to six months. The eyes were then subjected to transmission electron microscopic analysis, or the RPE/choroid complex were used for gene expression analysis by semi-quantitative real-time PCR.

Results: A single periocular injection of PMC (969 ng in 5 ul) either as SLN:PMC or free drug achieved therapeutic levels of total PMC (~100 ng/tissue, 17 uM) in both the retina and RPE/choroid complex at 24 hours (n = 3-4 eyes/group). Five to six months of HFD in aged C57BL/6J and APOE4-TR mice resulted in significant sub-retinal deposits of drusen-like material, thickening and sometimes disruption of the Bruch’s membrane, and frequent signs of RPE degeneration. Weekly treatment with SLN:PMC (1 mM of PMC) resulted in reduction of sub-retinal deposits, preservation of the normal morphology of the Bruch’s membrane and RPE. Analysis of gene expression of the RPE/choroid did not reveal any significant changes to genes that are involved in RPE function comparing aged C57BL/6J mice with and without HFD and comparing HFD fed C57BL/6J mice without and without PMC treatment.

Conclusions: We have developed a sustained release SLN:PMC formulation which upon periocular injection achieved therapeutic levels of PMC in the back of the eye in the mouse. Preliminary experiments based on ultrastructural analysis suggested that SLN:PMC treatment was effective in reducing dry AMD-like pathologies in mouse models. These data support SLN:PMC as a potential therapeutic formulation for dry AMD.

CONTROL ID: 3714288
SUBMITTER (NAME ONLY): Vimal Prabhu Pandiyan
TITLE: Cone spectral composition in the fovea
SESSION TITLE: Functional imaging and wavefront correction
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: V. Pandiyan, S. Schleufer, P. Bharadwaj, R. Sabesan, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|
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ABSTRACT BODY:

Purpose: The fovea subserves high acuity vision by virtue of its densest packing of cone photoreceptors in the retina. Recent advances in high-resolution adaptive optics (AO) imaging have enabled detailing the distribution of foveal cones in humans, but their differentiation by spectral type has remained elusive. While it is known from anti-S-opsin staining that the proportion of short-wavelength (S-) cones decreases towards the foveal pit, the lack of immunostains for differentiating long and middle-wavelength (LM-) cones has made it impossible to ascertain their foveal distribution. Here we explore the spectral composition of the human fovea using an AO line-scan OCT-based optoretinogram.

Methods: A reflective mirror-based line-scan AO-OCT was used to image the fovea in two subjects. Volumes were recorded after 1-3 minutes of dark adaptation and a 660±10 nm bleach. The B-scan rate was 12 kHz and the field of view ranged from 1-1.6°. The volumes were reconstructed and registered. The optical phase change between the two reflections encasing the outer segment - the inner-outer segment junction, and outer segment tips - was calculated for each cone, and converted to optical path length (OPL). The change in OPL due to bleach was subjected to clustering analysis to distinguish cone spectral types. L:M-cone ratios and percent S-cones were calculated in the steps of 0.2° by 0.7° rectangular regions-of-interest in the range between 0.3° to 0.9° eccentricity along the 4 cardinal meridians.

Results:

The resolution was sufficient to visualize and spectrally classify cones 0.3° from the foveal center. Within 1° eccentricity, 9253 and 9115 cones were typed for subjects S1 and S2 respectively, with high accuracy. The proportion of S-cones increased with eccentricity; S1 : 2.2 to 6% and S2 : 3 to 8.9%. The rate of increase in S-cone proportion was the same in both, equal to 2.5 % per deg. The L:M cone ratio remained relatively stable within 1° eccentricity; S1 : 1.8 to 2.4 (Mean= 2.0), and S2: 1.2 to 2.0 (Mean = 1.5). No systematic difference was observed across the 4 cardinal meridians.

Conclusions: The first view of the human trichromatic cone mosaic in the fovea reveals an increasing S-cone proportion in line with prior reports, and a relatively stable L:M cone ratio. This has important implications for understanding the genetic mechanisms that control the photopigment expressed in cones and cell migration processes that occur during foveal development.

CONTROL ID: 3714290

SUBMITTER (NAME ONLY): Lara Asroui

TITLE: Comparison of Brillouin Shifts Between Keratoconus, Post-LASIK, and Normal Control Corneas

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Asroui, H. Zhang, J.B. Randleman, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|G. Scarcelli, University of Maryland at College Park, College Park, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the difference in Brillouin shifts between keratoconus patients, post-LASIK patients, and normal control patients.

Methods: Patients with keratoconus, post-LASIK patients, and normal control patients underwent imaging with Brillouin microscopy. The Brillouin shift was measured at multiple different points within the central 8mm of the cornea. Brillouin maps were then constructed for each cornea imaged using the data obtained. Comparisons between keratoconus and normal corneas, post-LASIK and normal corneas, and keratoconus and post-LASIK corneas were made.

Results: In the central 2mm, normal control corneas had a Brillouin shift of 5.7 GHz, which was higher than that of keratoconus corneas (5.6 GHz, p=0.001) and post-LASIK corneas (5.68 GHz, p=0.001). In addition, keratoconus corneas had lower Brillouin shifts than post-LASIK corneas (p=0.005). In keratoconus corneas, the difference in Brillouin shifts between the region of the cone and the peripheral “normal” regions was 60 MHz. In post-LASIK corneas, the difference in Brillouin shifts between the region of the ablation zone and the peripheral unaltered regions was 40 MHz. In normal control corneas, the difference in Brillouin shifts between the central 2mm and the peripheral cornea was less than 20 MHz.

Conclusions: Brillouin microscopy can effectively distinguish between keratoconus corneas, post-LASIK corneas, and normal control corneas.

CONTROL ID: 3714294

SUBMITTER (NAME ONLY): Giovanni Gregori

TITLE: The Importance of Bruch's Membrane Segmentation in Choriocapillaris Measurements Underlying Drusen in Eyes with Age-Related Macular Degeneration

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Gregori, J. Li, M. Shen, Y. Shi, R. Laiginhas, J. Liu, P.J. Rosenfeld, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|H. Zhou, Q. Zhang, Y. Cheng, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate how the properties of choriocapillaris (CC) flow deficits (FDs) measurements in regions underlying drusen are affected by Bruch's membrane (BM) segmentation.

Methods: Swept-source optical coherence tomography angiography (SS-OCTA) imaging (PLEX® Elite 9000; Carl Zeiss Meditec, Inc, Dublin, CA) of eyes with age-related macular degeneration (AMD) were acquired using a 6x6 mm scan pattern. For a given OCTA scan, a reference surface corresponding to the location of BM was generated in several different ways, manually as well as using semi-automated and fully automated layer segmentation algorithms on B-scans. A completely automated algorithm used the OCTA scan and an associated BM surface as inputs to generate compensated CC slabs and binarized FDs maps, as described in several prior studies. Maps of local agreement between different FD maps of the same scan were generated by computing the absolute difference between the FD% within a small window centered at each pixel (Fig. 1C).

Results: Two graders manually segmented the full BM in 4 eyes with large confluent drusen. The mean absolute distance was 5.4μm between these surfaces over the regions where drusen were present. The FDs maps produced by the graders were qualitatively and quantitatively different, see Fig.1. On an additional set of 5 eyes, the graders manually corrected the BM in the regions under drusen. The resulting mean CC FD% under the drusen were significantly different between the graders. However, a well-trained, experienced grader can generate consistent measurements on different images of the same eye. When such a grader manually corrected the BM in the central region (1mm diameter) of 28 eyes with drusen, each imaged three separate times, the mean standard deviation of the CC FD% measurements was 2.3%.

Conclusions: CC FD maps can be strongly dependent on the exact shape and position of the BM surface used to segment them. In regions where the retinal pigment epithelium (RPE) geometry and its relation to BM are affected by an underlying pathology, as when drusen are present, the variability associated the BM surface segmentation and the resulting CC FDs maps can be substantial. In these cases, great care needs to be exercised in both the measurement process and the interpretation of results.

CONTROL ID: 3714295

SUBMITTER (NAME ONLY): Miguel Miron Mendoza

TITLE: The effects of vimentin knockout on corneal fibroblast mechanical behavior in 3D collagen matrices

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Miron Mendoza, E. Nakahara, M.P. Bhatt, J. Hulleman, M. Petroll, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The intermediate filament vimentin has been linked to myofibroblast transformation of corneal keratocytes and the development of fibrosis during wound healing. Studies in other systems suggest it can also regulate key aspects of cell mechanical activity such as polarization, mechanosensing and focal adhesion dynamics. In this study, we investigate the role of vimentin on corneal fibroblast spreading in 3D culture.

Methods: A CRISPR/Cas9 RNP targeting vimentin was electroporated into human corneal fibroblasts, followed by screening to identify vimentin KO cell lines. Vimentin KO was verified by Western blotting and immunostaining. To assess cell spreading and mechanical activity, cells were embedded in 3D fibrillar collagen matrices. Samples were cultured for 4h or 24h in defined serum-free media (S-) or S- supplemented with PDGF BB (to stimulate cell spreading). 3D and 4D DIC imaging were used to assess cell mechanical behavior, global matrix contraction and live cell spreading. F-actin labeling was used to assess cytoskeletal organization and morphological changes.

Results: Both control (clone F11) and vimentin KO (clones F5 and G12) cells were able to spread and elongate within 3D collagen matrices in response to PDGF. Vimentin KO cells produced a similar percentage of matrix contraction as control cells (PDGF control = 33.3 ± 9.8; and PDGF KO = 37.2 ± 6.4; $P = 0.89$), and this was significantly higher than in S- media (S- control = 15.2 ± 3.0, $P = 0.049$ compared to PDGF; and S- KO = 11.4 ± 12.3, $P < 0.01$ compared to PDGF). Live cell imaging showed that during initial cell spreading in PDGF, all cell lines formed dendritic cell extensions that generated localized tractional forces by displacing collagen fibers. While the number of dendritic cell processes was similar (control = 15.3 ± 1.0; and KO = 13.2 ± 3.0, $P = 0.08$), motility and turnover of dendritic cell processes was more rapid in KO cells.

Conclusions: Corneal fibroblasts are able to spread, elongate and generate tractional forces in response to PDGF in the absence of vimentin within 3D collagen matrices. However, the increased activity and turnover of dendritic processes suggest underlying differences in the mechanics of cell spreading. The KO cell lines developed here should allow the role of vimentin in modulating corneal fibroblast behavior to be further assessed using a range of culture conditions and mechanical assays.

CONTROL ID: 3714296

SUBMITTER (NAME ONLY): Kristyn Hake

TITLE: The regulatory role of LOXL1-AS1 in gene expression

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hake, H. Schmitt, M.F. Suarez, K.M. Perkumas, M.A. Hauser, W.D. Stamer, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: LOXL1-AS1 is a long non-coding RNA associated with pseudoexfoliation glaucoma (PEXG). PEXG is characterized by the disrupted regulation of aqueous outflow and increased intraocular pressure. LOXL1-AS1 responds to mechanical stress, controls transcription, and patients with PEXG display fibrillary deposits in the eye; thus, we hypothesized that LOXL1-AS1 regulates genes involved in extracellular matrix (ECM) remodeling, cell adhesion, and mechanotransduction pathways in outflow cells.

Methods: LOXL1-AS1 was knocked down in primary cultures of human trabecular meshwork (TM) and Schlemm's Canal (SC) cells (4 strains each) using targeted Ad-shRNA in cells, and in human lens epithelial cells (HLE-B3) cells by transfection with a targeted siRNA. Knockdown (KD) verification and ECM gene expression were determined using qPCR or RNAseq. Genes with significant expression differences were further investigated using western blots, as were the mechanotransduction hub proteins, FAK, MAPK, pMLC, and AKT.

Results: Only data from experiments with >50% of LOXL1-AS1 knocked down was analyzed. In HLE-B3 cells with LOXL1-AS1 KD, 7 genes were significantly altered ($p<.05$). Thrombospondin 2 and Tenascin C were upregulated by 2-fold ($p<.05$) while TIMP1 decreased by 50% ($p<.05$). After KD of LOXL1-AS1 in TM cells, the expression of 7 ECM genes were significantly altered ($p<.05$). Of these, col11α1 showed a 50% decrease in expression and integrinβ3's expression doubled ($p<.05$). Genes affected by LOXL1-AS1 KD in TM were Col6α6 (4-fold increase, n=3, p=.04) and Col3α1 (1.5 fold increase, n=3, p=.001). When LOXL1-AS1 was KD in SC cells, 13 genes showed significantly altered RNA expression. Of these, integrinα2 was upregulated by 2.5-fold and lamininλ1 decreased by 50% ($p<.05$), but protein validation did not show a significant change. Of the mechanotransduction proteins analyzed, the phosphorylation of AKT was significantly elevated in SC cells (n=4, p =.008), and trending toward elevation in TM cells (n=4, p=.056).

Conclusions: LOXL1-AS1 regulates many genes in a cell type-dependent manner. For outflow cells, LOXL1-AS1 controls the expression of key ECM components and AKT, a central mechanotransduction protein. Thus, polymorphisms in LOXL1-AS1 may contribute to fibrillary deposits, cell signaling, and/or ECM homeostasis in the conventional outflow pathway of the eye of PEXG patients.

CONTROL ID: 3714297

SUBMITTER (NAME ONLY): Emily Lawrence

TITLE: Topical and systemic administration of FDA-approved GLP-1R Agonists rescue retinal ganglion cells in hypertensive glaucoma

SESSION TITLE: Pharmacology/cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Lawrence, M. Guo, J. Wong, T. Schwartz, J. Wu, J. Lu, J. Sterling, J.L. Dunaief, Q.N. Cui, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The centrally-acting GLP-1R agonist NLY01 reduces microglial/macrophage activation and rescues retinal ganglion cells (RGCs) in a mouse model of hypertensive glaucoma (PMID33147455). Clinically-available GLP-1R agonists are also associated with a reduced risk for glaucoma in diabetic patients (PMID34413054). In this study, we examined whether FDA-approved GLP1R agonists, administered either topically or systemically, prevent RGC loss and decrease neuroinflammation in an mouse model of hypertensive glaucoma.

Methods: Three-month old C57BL/6J mice were injected with either microbeads or BSS. IOP was measured weekly and remained elevated in bead-injected eyes for 7 weeks. GLP-1R agonists were initiated within 3 days of ocular injection and administered either twice daily topical (lixisenatide 20µg/kg/day or liragutide 400µg/kg/day) or twice weekly subcutaneous (liraglutide 400µg/kg/day or NLY01 5mg/kg/injection). At the end of 7 weeks, retina flatmounts were immunolabeled for RBPMS and Iba1 to quantify RGC and myeloid cell density, respectively. Quantitative PCR assessed pro-inflammatory cytokine expression in cellular populations enriched for either macrophage/microglia or astrocytes. Microelectrode array recording of dark and light-adapted retinas functioned to characterize RGC function. RGC axons were quantified using optic nerve cross sections.

Results: Compared to bead-injected eyes treated with topical liraglutide, RGC density was 24% lower in bead-injected untreated eyes ($p=0.0048$). Similarly, topical lixisenatide was associated with 29% RGC rescue following IOP elevation ($p=0.0096$). Subcutaneous liraglutide and NLY01 injections resulted in complete RGC rescue after IOP elevation. While myeloid cellular density trended up following microbead injections, differences were not significant and remained comparable before and after treatment with topical and systemic agents. Pro-inflammatory cytokine expression, RGC function, and axon quantifications are pending.

Conclusions: Topically and systemically administered GLP-1R agonists improved RGC survival following IOP elevation. The number of activated myeloid cells in the retina were not significantly affected by GLP-1R agonist treatment in this experiment.

CONTROL ID: 3714298

SUBMITTER (NAME ONLY): John Bladen

TITLE: Multidisciplinary pathway for orbital lymphoma

SESSION TITLE: Ocular tumors sans uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bladen, Z. Sultan, Orbital, Kings College Hospital NHS Foundation Trust, UNITED KINGDOM|J. Brady, G. Mikhaeel, Clinical Oncology, St Thomas' Hospital, London, London, UNITED KINGDOM|J. Salisbury, Histopathology, Kings College Hospital NHS Trust, UNITED KINGDOM|S. Connor, Neuroimaging, Kings College NHS Foundation Trust, UNITED KINGDOM|S. Bowcock, Haematology Chartwell Unit, Kings College NHS Foundation Trust, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Evaluating a new, comprehensive orbital lymphoma service. A prospective case series was carried out to evaluate the pathway and to identify common themes in orbital lymphoma

Methods: 20 patients (mean age 67 SD14.4; M:F 1:1). presented to ophthalmology over 2 years, were managed on a pathway involving MDT care across ophthalmology, haematology, pathology, oncology and radiotherapy. Baseline investigations included MRI orbits, half-body PET-CT scan, FBC, U&E, Calcium, LDH LFT, ESR, HIV, Hepatitis B&C, open orbital biopsy and bone marrow biopsy. Patients were recorded under AJCC v8 TNM for ocular adnexal lymphoma and Ann-Arbor (AA) staging systems. All patients were discussed at the weekly haematology-oncology MDT on confirmation of histological diagnosis. Those undergoing radiotherapy have an imaging response assessment at 3 months with subsequent long-term follow-up under joint haematology-ophthalmic care

Results: The pathway was completed by 16 cases, 1 case was palliated prior to biopsy, 1 had a diagnostic pancreatic biopsy, 2 followed up elsewhere. Commonest presentation was ptosis (5), palpable mass (4), proptosis (3), conjunctival lesion (2) and epiphora (2). Two had contiguous, bilateral orbital disease. Histology: 11 EMZL, 4 DLBCL, 1 SLL. Bone marrow involvement in 1 EMZL and 1 DLBCL. Doxycycline had no effect on 2 conjunctival lesions. Mean time from biopsy to treatment (radiotherapy or chemotherapy) 61 days. Radiotherapy was given to 11 (4-30Gy). DBCL received 3 cycles of R-CHOP. 15 had radiologic remission with 1 contracted lesion considered remission

Conclusions: A multi-disciplinary approach is essential in managing orbital lymphoma. Doxyxycline had no effect and higher doses of radiotherapy was required in some EMZL. Bone marrow biopsy is essential for staging. Having expertise within each area provides a comprehensive patient experience, however coordination between multiple sites and locations can pose difficulties in running a smooth and timely pathway

CONTROL ID: 3714299

SUBMITTER (NAME ONLY): Mariela Aguilar

TITLE: Automated Assessment of Visual Photosensitivity in Healthy and Traumatic Brain Injury Study Participants

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.C. Aguilar, R. Mittal, A. Gonzalez, V. Graham, P.A. Sepulveda Beltran, K. Leviste, E. Arrieta, B. Maceo Heilman, J. Parel, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Maceo Heilman, B. Hurwitz, Department of Biomedical Engineering, College of Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|W.J. Feuer, B.L. Lam, A. Galor, Anne Bates Leach Eye Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|G. Alvarez, E. Felix, Department of Physical Medicine and Rehabilitation, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Hurwitz, Department of Psychology, University of Miami, Coral Gables, Florida, UNITED STATES|E. Felix, A. Galor, VA Miami Healthcare System, Miami, Florida, UNITED STATES|J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Traumatic brain injury (TBI) is a condition with devastating lifelong consequences. Visual photosensitivity is a common and incapacitating symptom associated with TBI. The purpose of our study was to assess visual photosensitivity in healthy and TBI study participants using the Ocular Photosensitivity Analyzer (OPA, Aguilar et al. BOE 2018, 9(11): 5583-5596).

Methods: Twenty-five healthy study participants (13 females and 12 males, age = 32.5±13.3) and nine TBI study participants (2 females and 7 males, age = 35.7±14.5) were tested using the OPA under an IRB approved protocol. The automated OPA produces light stimuli of varying intensities utilizing unequal ascending and descending steps. Each stimulus is presented for 2 seconds, followed by a rest period of 4 seconds. The subject is instructed to indicate whether the light stimulus is “uncomfortable” by pressing a hand-held button. The visual photosensitivity threshold (VPT) is calculated from the mean of 10 response reversals. A higher VPT indicates more tolerance to light while a lower VPT indicates less tolerance to light. Additionally, study participants were administered the Visual Light Sensitivity Questionnaire-8 (VLSQ-8), prior to being tested with the OPA, to assess the presence and severity of visual photosensitivity symptoms. The VPT and VLSQ-8 scores of healthy and TBI study participants were compared.

Results: The VPT of healthy and TBI study participants were 2.5±0.8 and 1.6±0.9 log lux, respectively, $p<0.05$. VLSQ-8 scores of healthy and TBI study participants were 11.6±3.3 and 20.7±8.9, respectively, $p<0.05$. VPT scores were negatively correlated with VLSQ-8 scores ($r=-0.56$, $p<0.01$).

Conclusions: Visual photosensitivity was assessed in healthy and TBI study participants using the OPA. Healthy study participants had higher VPT and lower VLSQ-8 scores compared to TBI study participants. Quantitative clinical outcome measures are needed in TBI to better characterize disease severity, monitor progression, and evaluate efficacy of emerging treatments.

CONTROL ID: 3714303

SUBMITTER (NAME ONLY): Michael O'Hare

TITLE: The role of Notch 3 in maintaining retinal vascular stability during aging

SESSION TITLE: Molecular events in diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. O'Hare, J. Arboleda-Velasquez, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M. O'Hare, J. Arboleda-Velasquez, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Notch signaling plays a critical role in vascular development, regulating fundamental processes such as angiogenesis, arterial/venous differentiation, and mural cell investment. However, aberrant Notch signaling can result in severe vascular phenotypes as observed in cerebral arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and has been implicated in pericyte loss during diabetic retinopathy. An interesting question remains regarding the changing requirement for Notch signaling during aging. It is evident that Notch 3 signaling plays an important role in the differentiation of mural cells during development, yet it remains unclear how these interactions are affected during aging and how this affects retinal vascular stability.

Methods: Two knockin mouse lines were generated expressing human Notch 3 with or without the C455R CADASIL mutation expressed under an SM22-cre in a Notch 3 knockout (N3KO) background and aged to 24 months. Fluorescein angiography was carried out at 6, 12 and 24 months. Immunolabelling was carried out on cryosections and flat-mounted retinas assessing changes in the vascular, glial and neuronal retinal components. Transmission election microscopy (TEM) was used to assess changes in microvascular structure.

Results: We report that the C455R mutation in Notch 3 causes a significant reduction in retinal vascular stability in an age dependent and dominant negative manner. C455R mutant mice displayed increased vasopermeability and retinal vascular caliber at 24 months ($P<0.05$). Interestingly, we also report that N3KO mice develop retinal vascular aneurysms at 24 months of age, this phenotype can be rescued through the expression of wild type Notch 3 in mural cells.

Conclusions: These data have shown for the first time a requirement for Notch 3 in the aging vasculature and that the expression of the C455R mutation results in an increase in vasopermeability in the retina at 24 months. Whereas, mice expressing wild type Notch 3 rescued the phenotype of N3KO mice. These findings may hold importance for retinal vascular diseases such as diabetic retinopathy in which alternations in Notch 3 expression have been reported and warrants further investigation.

CONTROL ID: 3714307

SUBMITTER (NAME ONLY): Dominic Brown

TITLE: Agreement Between Functional History and Plan of Care in Low Vision Rehabilitation

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.L. Brown, C. Bradley, R.W. Massof, G. Dagnelie, J.E. Goldstein, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: For successful low vision rehabilitation (LVR), the clinician's plan of care (POC) should agree with the patient's functional visual goals. A retrospective review of patient records tests this premise by determining the level of agreement between patients' functional histories (FH) and their POCs. Further, this study aims to explore the application of functional domain classifications as a method of classifying elements in the FH of the patient, and estimating how well the provider's POC addresses those elements.

Methods: As a feasibility study, we analyzed the FH and POC of 20 consecutive new patients at the Wilmer Eye Institute Lions Vision Rehabilitation Service. The FH was reviewed and each element assigned to one of 11 functional domains, 10 from the Dutch Activity Inventory (PMID: 21090911) and an 11th (glare) that we created. The proportion of the domains identified in the FH that were addressed in the POC was calculated and served as the dependent variable. Pearson correlations between the dependent variable and age, best-corrected visual acuity of the better seeing eye (BCVA), and contrast sensitivity (CS) were estimated for the sample of patients.

Results: Of the 20 records included in this feasibility study, 50% of patients had 100% agreement between functional domains identified in the FH and POC. The other half had levels of functional domain agreement uniformly distributed from 18%-91%. The overall mean (SD) level of functional domain agreement was 78% (28%). The correlation between the level of agreement and age in our sample was -0.38. The most common domains documented in the FH were learning and applying knowledge (90%), mobility (50%) and glare (50%). The least common were self-care (0%), general tasks and demands (10%), and community/social/civic life (30%).

Conclusions: The distribution of the levels of functional domain agreement found in this study demonstrates the feasibility of the described approach in determining how thoroughly clinicians address the needs of patients. Our method provides a means of retrospectively determining the level of functional agreement between FH and POC that otherwise cannot be done in the absence of structured questionnaires. This is an ongoing study, which will expand towards evaluating various methods of retrospectively categorizing elements in the FH and POC.

CONTROL ID: 3714308

SUBMITTER (NAME ONLY): Nolan Adams

TITLE: The Effect of Blue-light-blocking Intraocular Lenses on Sleep, Mood, and Circadian Rhythm in Diabetic Patients

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Adams, O. Iqbal, J. McDonnell, Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|R. Hakim, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|M. Wesolowski, Clinical Research Office, Loyola University Health System, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to investigate the effect of blue-light-blocking intraocular lens (IOL) versus non-blue-light-blocking IOL placement during cataract surgery on sleep, mood, and Circadian rhythm in diabetic patients. Placement of a blue-light-blocking IOL may reduce exposure of the intrinsically photosensitive retinal ganglion cells to blue light, inhibiting the ability of these cells to synchronize the body's Circadian rhythm, which may in turn affect sleep patterns and mood.

Methods: We recruited 20 patients diagnosed with diabetes mellitus type 2 who were scheduled to undergo bilateral cataract surgery. Patients filled out the SCRAM (Sleep, Circadian Rhythms And Mood) Questionnaire before cataract surgery and again 1-3 months after cataract surgery. Changes in SCRAM Questionnaire answers before and after surgery were assessed to estimate the effect of IOL type.

Results: In diabetic patients undergoing bilateral cataract surgery, across all types of IOL, SCRAM Questionnaire scores for Good Sleep increased by 3.39 (P = 0.45), Morningness increased by 0.08 (P = 0.98), and Depressed Mood decreased by 3.61 (P = 0.21). When patients receiving ultraviolet-light-blocking IOLs were compared to those receiving blue-light-blocking IOLs, their scores for Good Sleep increased by 7.99 less (P = 0.11), Morningness increased by 10.70 more (P = 0.17), and Depressed Mood decreased by 0.82 less (P = 0.72).

Conclusions: These results suggest that cataract surgery may result in subjectively improved sleep quality and mood regardless of the type of IOL placed, although results were not statistically significant. No statistically significant improvement in sleep quality, Circadian rhythm, and mood was shown in patients receiving blue-light-blocking IOLs as compared to those receiving ultraviolet-light-blocking IOLs.

CONTROL ID: 3714309

SUBMITTER (NAME ONLY): Shintaro Shirahama

TITLE: MHC class II positive retinal microglia exacerbate uveitis by activating infiltrating T cells

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Shirahama, M.S. Gregory-Ksander, B. Ksander, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Shirahama, M.Y. Lee, Y. Okunuki, K.M. Connor, M.S. Gregory-Ksander, B. Ksander, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M.Y. Lee, Y. Okunuki, K.M. Connor, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Understanding the function of MHC class II positive (MHC-II+) antigen-presenting cells (APCs) is critical in understanding the pathogenesis of uveitis, which has two potential sources of APCs, retinal microglia and systemic macrophages. We previously published evidence that MHC-II+ microglia are not required for the induction of uveitic specific T cells. In the current study, we determine whether MHC-II+ microglia exacerbate uveitis by activating retina-infiltrating T cells.

Methods: EAU was induced by IRBP immunization of C57BL/6 mice, and the clinical score was determined by the standard method. FACS analysis was used to determine MHC-II expression on microglia (TMEM119 and P2RY12 antibodies). Knock-down of MHC-II specifically on microglia and not on systemic macrophages was achieved using an inducible knockout mouse (Tmem119-CreERT2 x MHC-II$^{flox/flox}$ B6 mice; Tmem119-Cre KO mice) in which deletion of MHC-II was induced by tamoxifen and confirmed by FACS analysis. Adoptive transfer EAU was induced by harvesting T cells from the spleen and lymph nodes of donor mice at 14 days post-IRBP immunization and injecting i.p. (5×10^7 cells/mouse) into naïve recipients.

Results: During the first 10 days after induction of EAU, there was no increase in MHC-II+ retinal microglia (1.1 +/- 0.3%) as compared with retinas of naïve mice (0.7 +/- 0.3%). By contrast, in the later stage of EAU (day 20), there was a significant increase in the number of MHC-II+ Tmem119+ microglia (56.8 +/- 1.0%) within the retina. Similar results were obtained using P2RY12, another microglia specific antibody. Removal of MHC-II specifically from these retinal microglia and not from macrophages using inducible Tmem119-Cre KO mice significantly reduced the severity of the disease when the clinical score was compared with the frequency of MHC-II+ microglia ($r=0.78$, $p=0.0036$). To further confirm this, uveitic T cells from IRBP immunized WT mice were adoptively transferred into either MHC-II$^{flox/flox}$ or Tmem119-Cre KO mice, resulting in a significant delay in the development of uveitis ($p=0.03$).

Conclusions: Our data indicate that MHC-II+ retinal microglia do not participate in the induction of uveitis but are important in the later stages where they exacerbate disease by activating retina-infiltrating T cells.

CONTROL ID: 3714310

SUBMITTER (NAME ONLY): Stavroula Almpanidou

TITLE: Color Perception in patients with Diabetic Macular Edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate color perception in patients with diabetic macular edema (DME) assessed with a new digital color test and with pseudoisochromatic plates and explore the correlation with optical coherence tomography (OCT) parameters.

Methods: Twenty-nine patients (n=29 eyes) with DME and mean age of 70.2 years (SD=6.8) were retrospectively included. Color vision was evaluated in all subjects using the H-R-R, the Ishihara Test (38 plates) and the digital color test. The total number of correct plates was measured for each test and assessed in correlation with OCT parameters: Central Macular Thickness (CMT), Volume Cube (VC) and Total Average Thickness (TAC). The new color test records the level of brightness needed to detect color targets of red, green and blue hues and results were also correlated with these OCT parameters. Spearman correlation coefficient was computed for estimating correlations among CMT values and results of the color tests.

Results: The mean visual acuity was 0.60 (SD 0.30) logMAR and the mean CMT, VC and TAC values were 429.5 μm (SD 129.9), 11.9 mm^3 (SD 3) and 330.1 μm (SD 82.9), respectively. All participants demonstrated color vision defects in all color tests; in the Ishihara (Mdn=3.0 plates, IQR: 1.0-20.0), in the H-R-R (Mdn=2.0 plates, IQR: 0.0-4.8). Regarding the new digital color test, increased needs for brightness in red (Mdn=28.0%, IQR: 24.0-31.0), green (Mdn=20.0%, IQR: 15.5-25.0) and blue (Mdn=26.0%, IQR: 21.5-31.0) colored targets were also detected. The CMT values were significantly ($p<0.05$) correlated with the brightness values in the blue targets. Specifically, more brightness was required for the detection of the blue targets in individuals with increased values of CMT.

Conclusions: Color vision was found to be affected in patients with DME and should be evaluated as a useful part of a comprehensive ophthalmological examination. Furthermore, this study presents preliminary evidence of the efficacy of a new digital color test to detect deficits in patients with diabetic macular edema.

CONTROL ID: 3714311

SUBMITTER (NAME ONLY): Samantha Bradford

TITLE: Transepithelial Crosslinking Using Femtosecond Laser Machined Epithelial Microchannels for Riboflavin Delivery

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bradford, R. Joshi, Y. xie, D. Brown, T. Juhasz, J.V. Jester, S.B. Han, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|R. Joshi, T. Juhasz, J.V. Jester, Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultraviolet corneal collagen crosslinking (UVA CXL) via photoactivation of riboflavin (Rf) is an effective treatment for Keratoconus, and in development as a refractive procedure. A drawback of UVA-CXL is the need for epithelial debridement to achieve adequate stromal Rf concentrations, leading to discomfort, delayed recovery, and risk of infection. Transepithelial (TE) CXL using chemical disruption of the corneal epithelial barrier has been shown to have limited success in addressing these concerns. Also an intact epithelium could act as a barrier to irradiation, preventing effective TE UVA-CXL. This study describes a femtosecond laser (FS) approach to machine corneal epithelial microchannels (MC) for enhanced stromal Rf penetration combined with nonlinear optical (NLO) CXL to avoid both epithelial damage and shielding of irradiation.

Methods: Using a 1030nm FS laser with 5μJ pulses, 2μm diameter by 25μm long MC were machined into the epithelium of ex vivo rabbit corneas at a density of 100 MC/mm^2. Rf penetration through the MC was then determined by applying 1% Rf in PBS with osmolarity ranging from 200-450 mOsm for 30 minutes followed by removal of the cornea and extraction from the central stromal button. Stromal Rf concentrations were compared between osmolarity groups. Eyes treated with MC UVA-CXL were compared to eyes treated with BAK UVA-CXL using collagen autofluorescence (CAF) to determine the effect of CXL. CXL was performed both with and without continuing drops of Rf solution to determine the shielding effect of the solution on the surface of the eye.

Results: Rf levels were highest in eyes treated with 250 mOsm solution. No eyes treated with TE UVA CXL with continued dripping produced measurable CAF in either group. Eyes without further dripping after the start of CXL did produce CAF. Additionally organ culture showed a normal corneal epithelium following both MC alone and MC NLO CXL, while BAK alone, BAK UVA CXL, and MC UVA CXL treated corneas all showed extensive epithelial and stromal damage at 24 hours post treatment.

Conclusions: FS epithelial MC enhance stromal penetration of Rf for corneal CXL, but both the epithelium and a layer of Rf solution shield the cornea from UVA irradiation, inhibiting CXL. Data suggests that combining MC with NLO CXL minimizes damage, avoids shielding, could lessen patient discomfort, speed recovery, and decrease risk of infection.

CONTROL ID: 3714312
SUBMITTER (NAME ONLY): Pablo De Gracia
TITLE: Fixation Stability for Emmetropic and Myopic Patients as a Function of the Target's Frequency Content
SESSION TITLE: Myopia and refractive error development
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: P. De Gracia, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|A. Wazir, Z. Goodman, E. Ong, Midwestern University Chicago College of Osteopathic Medicine, Downers Grove, Illinois, UNITED STATES|
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ABSTRACT BODY:
Purpose: To describe fixation stability in emmetropic and myopic subjects through focus as a function of the frequency content of targets.
Methods: In order to identify the patterns of FEMs (microsaccades) of emmetropic, myopic, and hyperopic subjects, we measured the binocular fixational eye movements of 35 subjects (7 emmetropic or low hyperopes, 28 myopic) with an eye tracker (EyeLink 1000). We did this for three targets: natural image (NI), Maltese cross (MC), and 20/40 letter E (LE). And 11 levels of blur (+5D and -5D in 1 D steps). A total of 33 trials were recorded per subject. Each complete session of measurements for one subject lasted between two and three hours. The order of the conditions was randomized across subjects.
The optical system is formed by an Eye Tracker attached to an optical system that allows representing different vergence levels (without introducing magnification) through two motorized Badal systems with a precision of 0.01D. Also, this optical system also allows to precisely control pupil sizes. Pupil sizes were set to 4 mm by controlling a physical aperture placed in a conjugated plane to the eye’s pupil plane: this allowed for constant retinal illumination across subjects. For each trial, the EyeLink recorded binocular eye movements during two minutes at a rate of 1,000 measurements per second. If needed, subjects were corrected for their natural refractive error using contact lenses to standardize the baseline level of blur at 0 D.
Results: Microsaccades were identified and analyzed following the Engbert and Kliegl model (2003). More than 150,239 binocular microsaccades were recorded. Emmetropes modulate peak velocity and magnitude as a function of the level of blur imposed, obtaining larger peak velocities and magnitudes than myopes when experiencing both myopic and accommodation inducing blur. This was seen across all three target stimuli, each stimulus possessing different ranges of spatial frequency content. Natural image and Letter E targets shown larger differences between emmetropes and myopes than the Maltesse Cross target. Microsaccade frequency was a 20% higher on average in myopes than emmetropes (23.15 % LE, 21.74% MC, and 15.83% NI) .
Conclusions: Through the presented data, we provide initial evidence on the characteristics of microsaccades in myopes and emmetropic/hyperopic subjects for different levels of blur and frequency contents in the target.

CONTROL ID: 3714314

SUBMITTER (NAME ONLY): Shreya Nagri

TITLE: Efficacy of various glaucoma drop adherence techniques on glaucoma medication compliance

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Nagri, P. Janardhana, UMass Memorial Health, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The most common barriers to patient compliance in glaucoma treatment are lack of self-confidence in patients in administering medicine properly and difficulty of drop administration. This prospective survey study will compare different techniques to increase compliance by increasing patient confidence and competency in administering their glaucoma medications. The techniques that will be tested here are giving a glaucoma dropper-aid device vs showing an instructional glaucoma drop administration video.

Methods: In this study, we will conduct a pre and post-survey of glaucoma adherence questions, using the Morisky Medication Adherence Scale (MMAS-8) and the Quality of Life and Glaucoma 17-item questionnaire (GlauQoL-17). We grouped these individuals into either a control group with no intervention, a group given a glaucoma drop applicator with instructions on proper use, or another group showing a patient-provider education video on how to administer the drops properly at the clinic visit.

Patients will be given a post-glaucoma adherence survey questionnaire/satisfaction questionnaire 4 weeks post-intervention. Included are patients who are actively being treated for Primary Open Angle Glaucoma (POAG) at the UMass Memorial Eye clinic. Non-English speaking patients will be included only if their primary language is either Spanish or Portuguese because instructional videos were only provided in English, Spanish, and Portuguese.

Exclusion criteria include the following:

- Individuals <18 years old
- Prisoners
- Adults unable to provide consent (adults lacking consent, nonverbal)
- Non-English speaking patients, besides Spanish and Portuguese
- First-time glaucoma drop users

Our target recruitment is 50 participants.

Outcomes:

1. Improvement in medication compliance based on patient responses to Morisky Medication Adherence Scale and the Quality of Life and Glaucoma 17-item questionnaire

Results: Preliminary results are implying that patients who received video instruction or dropper-aid had an increase in adherence to glaucoma drops.

Conclusions: We hope to show that intervention with technology such as dropper-aids or video instruction, helps increase patient compliance with glaucoma drop treatment. With limited physician-patient interactions, it is important to understand what the optimal tools are that will help patients increase medication compliance.

CONTROL ID: 3714315

SUBMITTER (NAME ONLY): Naomi Wijesingha

TITLE: Cataract surgery outcomes in patients with amblyopia

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.S. Wijesingha, Bedford Hospital NHS Trust, Bedford, Bedford, UNITED KINGDOM|A. Sharma, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|J. Bradbury, West Suffolk NHS Foundation Trust, Bury Saint Edmunds, Suffolk, UNITED KINGDOM|S. Balal, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Cataract surgery associated with amblyopia can be challenging as there is an increased risk of operative complications and postoperative refractive surprise (as amblyopic eyes may be smaller or larger than other eyes), uncertain visual potential in the amblyopic eye and there is a risk of postoperative diplopia reported in the literature. Several factors may contribute to fixation switch diplopia, including surgical eye sequence, delay between surgeries and target refraction. The aim of this study was to review one year of cataract surgery in amblyopic patients at Moorfields Eye Hospital, Bedford, to assess visual potential and complications in this patient group.

Methods: Data from 42 consecutive patients who underwent bilateral phacoemulsification with known amblyopia was extracted retrospectively for cases between March 2018 and March 2019 with target refraction of emmetropia for both eyes. Parameters analysed included: preoperative and postoperative refractive status, preoperative and postoperative visual acuity (logMAR, best corrected and pinhole), presence/absence of diplopia, type of amblyopia (anisometropic, strabismic, visual deprivation), need for extra intervention/surgery, interval between surgery to fellow eye and eye sequence (dominant vs non-dominant first).

Results: The amblyopic eye was operated on first in 72% of cases, and no cases of postoperative diplopia were identified.

Conclusions: This study found no evidence for an increased risk of diplopia postoperatively. Visual acuity in the amblyopic eye can improve considerably after cataract surgery which is often delayed leading to an increased risk of complications associated with dense cataract. Operating earlier would relieve symptoms such as blur and avoid potentially difficult surgery.

CONTROL ID: 3714317

SUBMITTER (NAME ONLY): Praveer Singh

TITLE: Can the eye be a window to the lungs? AI predicts Bronchopulmonary Dysplasia through Retinal Fundus Photographs

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Singh, J. Kalpathy-Cramer, Radiology, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|P. Singh, J. Kalpathy-Cramer, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A.S. Coyner, K. Sonmez, Medical Informatics & Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|R.V. Chan, Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|B.K. Jordan, C. McEvoy, Neonatology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S.R. Ostmo, J. Campbell, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D. Erdogmus, Electrical and Computer Engineering, Northeastern University, Boston, Massachusetts, UNITED STATES|M.F. Chiang, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bronchopulmonary Dysplasia (BPD) is the leading cause of serious pulmonary morbidity in premature infants. Recent work has found that retinal fundus photos (RFPs) can contain information relevant to systemic health in adults. In this study, we evaluated the hypothesis that RFPs obtained as part of ROP screening may predict a future diagnosis of BPD.

Methods: 5255 RFPs were collected from 871 patients as part of a multi-institutional Imaging and Informatics in Retinopathy of Prematurity (i-ROP) study. Apart from clinical information, the dataset comprised of Reference Standard diagnoses for Plus disease for all patients. All RFPs corresponding to either patients without a diagnosis of BPD or captured at PMA>=34 weeks were removed (since BPD is diagnosed at 36 weeks PMA), leaving 477 patients /1284 RFPs (Post Menstrual Age [PMA]- mean:32.43, std:0.88), which were then divided into Train, Val, and TestSets via 80:10:10 splits on patient level. A Deep Learning (DL) model was trained to predict BPD at 36 weeks using the TrainSet (1006 RFPs; BPD:429, Normal:577; Plus:13, Pre-Plus:23, Normal:970; [PMA]- mean:32.48, std:0.89). The best performing model with the highest AUC-ROC score on the ValSet (137 RFPs; BPD:61, Normal:76) was finally evaluated on the TestSet (141 RFPs; BPD:47, Normal:94; Plus:4, Pre-Plus:4, Normal:133; [PMA]- mean:32.27, std:0.74). To avoid the DL model learning any common biomarkers with ROP disease, a secondary model was trained with only Non- Plus/Pre-Plus images using a pruned TrainSet (970 RFPs; BPD:403, Normal:567; Plus:0, Pre-Plus:0, Normal:970; [PMA]- mean:32.47, std:0.89) and ValSet (127 RFPs; BPD:55, Normal:72), though the performance was reported on the original TestSet.

Results: The model trained with original TrainSet, performs with an overall AUC-ROC of 0.82 (image-level) and 0.86 (patient-level) on the TestSet (Fig.1). Performance improves to 0.84 (image-level) and 0.87 (patient-level) when the model is trained on a pruned TrainSet with only Non- Plus/Pre-plus images (Fig.2).

Conclusions: We found that a DL model trained on RFPs could predict a future diagnosis of BPD, even in babies with no clinical signs of ROP. In other words, the model isn't just learning that BPD and ROP often occur in the same babies. Early identification of babies at high risk for BPD may facilitate interventional trials to reduce morbidity from

BPD in the future.

CONTROL ID: 3714318

SUBMITTER (NAME ONLY): Maria Fernanda Suarez

TITLE: Characterization of Loxl1-knockout-induced elastosis in mice with different genetic backgrounds

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Suarez, H. Schmitt, K. Hake, M. Kuhn, T. Watkins, M.A. Hauser, D.W. Stamer, Ophthalmology, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|M.H. Elliott, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pseudoexfoliation syndrome (PEX) is a systemic, age-related disorder characterized by the deposition of fibrillar material in body tissues. Pseudoexfoliation glaucoma (PEXG), the ocular manifestation of PEX, is the most common identifiable secondary form of open angle glaucoma. PEXG is characterized by greater IOP elevation, advanced loss of visual field upon diagnosis, and resistance to IOP therapies. Polymorphisms in lysyl oxidase-like 1 (LOXL1), an enzyme that crosslinks collagen/elastin and is critical for ECM formation and repair, significantly associates with PEX. Since LOXL1 levels appear lower and elastosis higher in people with PEX, the aim of the study was to characterize the ocular and non-ocular elastosis phenotypes associated with Loxl1$^{-/-}$ mice

Methods: 129S.C57Bl/6 Loxl1$^{+/-}$ mice were backcrossed onto C57Bl/6 or 129S background and aged for 2 months. Early onset and high prevalence of spontaneous anal prolapse in C57Bl/6 background mice necessitated the study of younger animals. Skin elastic recovery measurements, histology and western blots were performed to analyze systemic organ changes. For ocular studies, outflow facility was measured by iPerfusion, Schlemm's canal (SC) perimeter was quantified using ImageJ in semi thin histology sections, and the presence of extracellular matrix accumulation below inner wall of SC was documented by transmission electron microscopy

Results: Skin elastic recovery was significantly lower in Loxl1$^{-/-}$ N6 C57Bl/6 mice (23.18%) compared to Loxl1$^{-/-}$ from 129S.C57Bl/6 mice (48.67%) (p=0.0015). N6 C57Bl/6 Loxl1$^{-/-}$ mice showed qualitatively enlarged luminal spaces of lung and lax elastin orientation in both systemic and in ocular tissues. Densitometric analysis of western blots from lung tissue displayed increased tropoelastin expression in Loxl1$^{-/-}$ respect to Loxl1$^{+/+}$ for N6 C57Bl/6 mice (1.56-fold) and for 129S.C57Bl/6 mice (1.50-fold) ($p<0.05$). No changes were observed in outflow facility for both mice backgrounds, except between Loxl1$^{+/-}$ and Loxl1$^{-/-}$ (2.54 vs 4.48 nl/min/ mmHg) for the mixed background (p= 0.042). By TEM we observed increased ECM accumulation in the SC inner wall in Loxl1$^{+/-}$ and Loxl1$^{-/-}$ mice from both backgrounds

Conclusions: Results show that genetic background significantly influences the elastosis phenotype at both the systemic and ocular levels, providing an opportunity to identify the genes associated with genetic susceptibility

CONTROL ID: 3714319

SUBMITTER (NAME ONLY): Raji Shyam

TITLE: Mitochondrial ROS in Slc4a11 KO corneal endothelial cells lead to ER stress

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Shyam, D.G. Ogando, J.A. Bonanno, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Raji Shyam: Commercial Relationship: Code N (No Commercial Relationship) | Diego Ogando: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Bonanno: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent studies from Slc4a11$^{-/-}$ mice have identified glutamine-induced mitochondrial dysfunction[BJA1] as a significant contributor toward oxidative stress, impaired lysosomal function, aberrant autophagy, and cell death in this Congenital Hereditary Endothelial Dystrophy (CHED) model. Because lysosomes are derived from the endoplasmic reticulum (ER) – Golgi, we asked whether ER function is affected by the lack of Slc4a11.

Methods: All experiments were conducted in 8 week old Slc4a11 WT and KO mice or in immortalized mouse WT and KO cell lines. Protein expressions were determined using the Simple Protein Wes® system. Real Time PCR analysis was conducted to amplify the transcripts of XBP1, unspliced-XBP1, spliced-XBP1, and β-actin. Fura-2AM was used to measure cytosolic calcium levels, and aggresomes were measured using a Proteostat Aggresome detection kit. In order to quench mitochondrial ROS, cells were treated with 2μM MitoQ for 16 hours.

Results: In mouse Slc4a11$^{-/-}$ corneal endothelial tissue, we observed the presence of dilated ER and elevated expression of ER stress markers BIP and CHOP. Slc4a11 KO mouse corneal endothelial cells incubated with glutamine showed increased aggresome formation, BIP, and GADD, as well as less ER Ca^{2+} release as compared to WT. Treatment of Slc4a11 KO cells with the mitochondrial ROS quencher MitoQ restored ER Ca^{2+} release and relieved ER stress markers indicating that mitochondrial ROS induces ER stress in corneal endothelial cells.

Conclusions: This study shows that in the presence of glutamine (in vivo or in vitro) the loss of Slc4a11 leads to ER stress that can be reversed by quenching mitochondrial ROS. Mitochondrial ROS also triggers lysosomal dysfunction with autophagy impairment in Slc4a11$^{-/-}$ corneal endothelial cells. Since lysosomes are derived from ER-Golgi, our findings suggest that ROS-induced ER stress is an important trigger for cellular dysfunction in the Slc4a11 KO model.

CONTROL ID: 3714320

SUBMITTER (NAME ONLY): Jean Moon

TITLE: Genetic dissection of the delivery pathways for vitamin A to ocular tissues in mice

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Moon, R. Srinivasagan, J. von Lintig, Pharmacology, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Jean Moon: Commercial Relationship: Code N (No Commercial Relationship) | Ramkumar Srinivasagan: Commercial Relationship: Code N (No Commercial Relationship) | Johannes von Lintig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The eyes acquire vitamin A derived from either the extrinsic or intrinsic pathway, distributing vitamin A from intestinal enterocytes or from hepatic stores. Vitamin A deficiency or excess are commonly associated with blinding and inflammatory diseases. However, we have a limited understanding of mechanisms controlling the distribution pathways. We used a genetic dissection approach in transgenic mice to investigate how ocular homeostasis is perturbed under different dietary supply conditions.

Methods: We utilized mice with mutations in intestine-specific transcription factor (ISX) or stimulated by retinoic acid gene 6 (STRA6) which have been identified as gatekeepers of the extrinsic and intrinsic pathways, respectively. Mice were supplemented with preformed vitamin A (4,000 IU/kg) or β-carotene (25 mg/kg) for 7 wks. Scotopic and photopic responses were then recorded from mice that were dark adapted overnight using ERG. Retinoid concentrations were measured by HPLC, and retinoid-dependent processes were evaluated by gene and protein expression analyses. Rhodopsin and M-opsin levels were evaluated by immunohistochemistry in retinal cross sections and whole mounts.

Results: We observed $Isx^{-/-}$ mice possessed normal ocular vitamin A concentrations but acquired high levels of retinoids in peripheral tissues in a STRA6-dependent manner. Ocular retinoid levels were significantly lower in $Stra6^{-/-}$ compared to WT and $Isx^{-/-}$ mice. $Stra6^{-/-}$ mice displayed significant reduced photopic responses and M-opsin staining. Interestingly, genetic deletion of ISX partially rescued ocular vitamin A deficiency in $Isx^{-/-}$/$Stra6^{-/-}$ mice. Remarkably, photopic ERG responses were significantly improved in $Isx^{-/-}$/$Stra6^{-/-}$ double-knockout mice compared to that of the $Stra6^{-/-}$ counterparts. The double-knockout mice displayed a significant recovery of cone photoreceptors. However, the rescue of vision came at the expense of a massive accumulation of vitamin A in other tissues, demonstrating that vitamin A is randomly distributed when present in excessive amounts.

Conclusions: Our analysis in different genotypes revealed STRA6 is critical for maintaining ocular vitamin A homeostasis and cone photoreceptor function. The partial rescue of vision in $Isx^{-/-}$/$Stra6^{-/-}$ double-knockout mice was associated with hyper-vitaminosis A in most peripheral tissues, demonstrating the requirement of an eye-specific delivery pathway of the essential nutrient.

CONTROL ID: 3714323

SUBMITTER (NAME ONLY): Binapani Mahaling

TITLE: Mustard Gas Exposure causes Retinal Muller Cell Gliosis via Caspase 1-dependent NLRP3 Pyroptosis

SESSION TITLE: Novel animal models and neuroprotection in the retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Mahaling, S.S. Chaurasia, Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|R.R. Mohan, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|S.S. Chaurasia, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sulfur mustard is a chemical weapon threat, and its exposure to the eye causes severe eye pain, photophobia, excessive lacrimation, anterior segment defects and blindness. This study aims to evaluate the possible effects of mustard gas toxicity on retinal Muller glial cells.

Methods: Muller glial cells (MIO-M1) were cultured in DMEM and exposed to nitrogen mustard at different concentrations (50-1000μM) for 3h, 24h and 72h. Real-time cellular integrity and morphological evaluation were done using the xCELLigence system. Cellular toxicity and viability were performed using TUNEL and Prestoblue assays. The intracellular oxidative stress was measured by DCFDA, and DHE staining and antioxidant gene expression was determined by qPCR. The effect of nitrogen mustard on glial cell activation was determined by GFAP and vimentin antibody staining and by qPCR of inflammatory markers. AO/PI and DAPI staining further evaluated cell death, apoptosis, necrosis, and DNA damage. We assessed the pyroptosis mechanism by measuring caspase-1, caspase-3, and ASC and NLRP3 inflammasome using immunoassays.

Results: The cellular and morphological evaluation revealed hyperactivation of Muller glial cells after nitrogen mustard exposure in a dose- and time-dependent manner. Nitrogen mustard significantly increased oxidative stress up to 24h with enhanced cell death in 72 h. We found a significant increase in antioxidant enzymes at lower concentrations of nitrogen mustard. Increased oxidative stress and inflammatory milieu caused activation of NLRP3 inflammsome resulting in Muller cell gliosis. NM-induced cell death was mainly driven by caspase-1 and NLRP-3 pyroptosis and was less dependent on caspase-3.

Conclusions: In conclusion, the nitrogen mustard caused retinal Muller glial cell gliosis with increased oxidative stress, inflammation, and cell death primarily driven by caspase-1/NLRP3 pyroptosis.

CONTROL ID: 3714324

SUBMITTER (NAME ONLY): Lyna Azzouz

TITLE: Adjunctive nondamaging focal retinal laser therapy reduces intravitreal injection burden in diabetic macular edema.

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Azzouz, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|A.F. Durrani, Y. Zhou, Y.M. Paulus, Ophthalmology, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is a leading cause of vision loss in patients with diabetes mellitus. Current treatment for DME requires frequent intravitreal injections, resulting in a significant burden on patients. Nondamaging focal laser is a newer therapy designed to treat DME without permanently damaging the retina. This study aims to assess the impact of adjunctive laser therapy on the injection burden and on visual acuity in patients with DME.

Methods: A retrospective analysis of 18 eyes of 14 patients with DME treated with the Pascal 532nm Endpoint Management (Synthesis Photocoagulator, Iridex, USA) was conducted. Demographic data, visual acuity, laser treatment parameters, and anti-VEGF injection burden six months before and after treatment were collected. Wilcoxon Signed-rank tests were used to assess changes in visual acuity and injection burden before and after treatment.

Results: Eighteen eyes of 14 patients were included in this study. Mean age at time of treatment was 62.6 +/- 17.1 years. Twelve patients had type 2 diabetes and two had type 1 diabetes. Eight patients had proliferative diabetic retinopathy, two had mild non-proliferative diabetic retinopathy (NPDR), two had moderate NPDR, and two had severe NPDR. All patients were followed for a minimum of six months following the laser treatment. All patients were treated with 30% of threshold laser with landmarks off and laser spot size of 200 micrometers, pulse duration of 15 milliseconds, and spacing of 0.25 Φ apart. Mean number of spots was 655.6 +/- 160.5. Mean number of intravitreal injections in the six-month period prior to laser treatment was 3.39+/- 2.57 injections compared to 2.33 +/- 2.40 injections in the six months following laser treatment (p=0.02). There was no significant difference between mean visual acuity on the day of treatment compared to visual acuity on the most recent follow-up (p=0.34), logMAR VA of 0.38 +/- 0.27 (approx. Snellen equivalent 20/50) and logMAR VA of 0.35 +/- 0.32 (approx. Snellen equivalent 20/40), respectively.

Conclusions: Subthreshold focal retinal laser therapy is associated with a statistically and clinically significant decrease in the number of intravitreal injections required in the six-month period immediately following treatment, without compromising visual acuity. This laser has the potential to alleviate the burden of injections on both patients and clinics.

CONTROL ID: 3714325

SUBMITTER (NAME ONLY): Kirsten Da Silva

TITLE: Patterns of Pediatric Visual Impairment in the Public Sector of Barbados

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Da Silva, E. Savatovsky, H. Munshi, A.L. Grajewski, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|K. Da Silva, M. Dowell, D. Grosvenor, Ophthalmology, Queen Elizabeth Hospital, Bridgetown, BARBADOS|M. Campbell, Psychology, The University of the West Indies at Cave Hill, Bridgetown, Saint Michael, BARBADOS|D. Callender, D. Grosvenor, Ophthalmology, The University of the West Indies at Cave Hill, Bridgetown, Saint Michael, BARBADOS|I. Hambleton, Biostatistics, The University of the West Indies at Cave Hill, Bridgetown, Saint Michael, BARBADOS|

ABSTRACT BODY:

Purpose: This study describes the patterns and causes of visual impairment in Barbadian children.

Methods: A retrospective chart review of all patients 18 years and younger who presented to the sole public pediatric ophthalmology clinics in Barbados at Queen Elizabeth Hospital (QEH) and Winston Scott Polyclinic (WSPC) between Jan 1st and Dec 31st, 2019 was conducted. Age at the first visit to an eye care provider (A_0) and final visit in 2019, sex, visual acuity and clinical diagnoses were obtained and stored using a REDCap data collection tool.

Results: 955 patient charts were collected from QEH (Jul to Dec) and WSPC (Nov to Dec) with a male: female ratio of 1:1. 11.5% of patients met the WHO criteria for visual impairment (4.5% binocular and 7.0% monocular), with an A_0 of 4.0 years. Refractive error (59.4%) and strabismus (36.9%) were the most common diagnoses among this group (Fig. 1), of which 79.4% had amblyopia. Overall, refractive error was the most common ocular disorder seen in the study population (39.6%), followed by allergic eye disease (35.2%), and strabismus (14%). Children aged 5 to 11 years old comprised the largest group of patients seen in 2019 with an A_0 of 5.9 years.

Conclusions: The burden of eye disease in the Barbadian adult population was described in the Barbados Eye Study over 20 years ago. However, no such studies have been conducted on the pediatric population. Causes of visual impairment in the Barbadian population are treatable and preventable. This preliminary data revealed that refractive error and strabismus were the leading causes of visual impairment in children. These results are comparable with trends observed in epidemiological studies conducted in the United States. On average, Barbadian children are first seen by an eye care provider when they are almost 6 years old. This is later than the US Preventative Services Task Force's recommended age for pre-school vision screening of 3-5 years. The causes of visual impairment observed in this study can be detected and treated with earlier vision screening. This study only reflects those children whose caregivers actively sought ophthalmic attention through the public sector. Implementation of a nation-wide vision screening program can identify children who do not receive eye care and improvements can be made in the approach to pediatric eye disease in Barbados.

CONTROL ID: 3714326

SUBMITTER (NAME ONLY): Goldis Malek

TITLE: Nuclear Receptor Atlas of the Choroid: Implications for Disease

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Malek, V. Parmar, J. Peavey, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|G. Malek, Pathology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Goldis Malek: Commercial Relationship: Code N (No Commercial Relationship) | Vipul Parmar: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Peavey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mechanisms underlying abnormal choriocapillaris vascular changes, seen in wet age-related macular degeneration, are unknown. Nuclear receptors (NR) are a family of transcription factors responsible for various cellular homeostatic mechanisms and vascular changes during development/disease. We created a NR atlas of human choroidal endothelial cells (CEC), freshly isolated choroid (FI), and choroid from a wet AMD mouse model, to identify candidate receptors that may play a role in vascular stability and/or disease.

Methods: Samples: (a) CECs isolated from human donor eyes (n=6 males and 2 females, ages 47-90, normal ophthalmic history), through positive enrichment by VE-cadherin cell sorting; b) FI human choroid (n=3 males and 3 females, ages 61-90) and (c) choroid from aged laser induced CNV and control C57BL/6J mice (n=2-3 females and 11 males/cohort). CECs were plated on gelatin/fibronectin til confluence, dissociated, and sorted with a CD31 antibody to ensure a pure cell population. RNA was isolated (n=3 passages up to passage 5), integrity evaluated with an Agilent Bioanalyzer, and cDNA synthesized. Expression of all 48 NRs plus the aryl-hydrocarbon receptor (AhR) and AhR translocator (ARNT), in human CECs and FI, were determined by relative absolute qRT-PCR (arbitrary expression ratio=arbitrary mass of housekeeping gene/NR±SEM) and by PCR array for mouse samples.

Results: The highest expressed NRs came from the thyroid hormone receptor-like subfamily [LXRβ (CEC: 1.22±0.02; FI: 1.04±0.02), PPARβ/δ1 (CEC: 1.01±0.02; FI: 1.02±0.05), PPARβ/δ2 (FI: 1.09±0.08), RARα (CEC: 1.03±0.04; FI: 1.15±0.05), RARβ (CEC: 1.47±0.05; FI: 1.80±0.12), RARγ (CEC: 1.34±0.07; FI: 1.15±0.05), Rev-ErbAβ (CEC: 1.14±0.03; FI: 1.04±0.07), RORα (FI: 1.15±0.04), RORβ (FI: 1.15±0.06), and RORγ (FI: 1.15±0.06)]. Highly expressed RXR-like NRs included RXRγ (FI: 1.44±0.04), COUP-TFII (CEC: 1.02±0.02), V-erbA-related (CEC: 1.17±0.03), and TR4 (CEC: 1.01±0.01; FI: 1.10±0.05). AhR (CEC: 1.41±0.04; FI: 1.33±0.12) and ARNT (FI: 1.00±0.02) were also highly expressed. Remaining NRs were categorized into intermediate (CEC, n=12 NRs; FI, n=10 NRs), low (CEC, n=13 NRs; FI, n=17 NRs), and absent (CEC, n=15 NRs; FI, n=12 NRs) expression bins.

Conclusions: With this atlas we identified candidate receptors (e.g. LXR, AHR, RARα, RARβ, RARγ, COUP-TFII, REV-ERBAα, REV-ERBAβ, PPARβ/δ1, PPARβ/δ2, RORα, and RXRγ) as potential regulators in vasculature homeostasis/disease.

CONTROL ID: 3714329

SUBMITTER (NAME ONLY): Minhaj Nur Alam

TITLE: Contrastive learning improves representation and transferability of diabetic retinopathy classification models

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Alam, D. Rubin, Biomedical Data Science, Stanford University School of Medicine, Stanford, California, UNITED STATES|M. Alam, J. Hallak, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|T. Leng, Stanford University School of Medicine, Stanford, California, UNITED STATES|J. Hallak, AbbVie Inc, North Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect of contrastive learning (CL)-based pre-training on the performance of diabetic retinopathy (DR) classification

Methods: We have developed a CL-based method to produce models with better representations and initializations for the detection of DR in color fundus images. Our model takes in image data, uses two-step data augmentation (neural style transfer + random geometric augmentation) to create a pair of augmented images, and then uses contrastive loss to maximize similarity of the two images in encoded space. The contrastive learning framework contains a Resnet50 encoder (CNN, ReLU, maxpool, and dense layers) with a projection head that maps the representation. The CL training utilizes a high batch size of 2048 and is trained for 100 epochs. Once the model is trained, the encoder(Resnet50) is used as a pre-trained model for a DR classification task (non-referrable vs referable DR). We compare our model with a model pre-trained with Imagenet weights. The model is trained and validated on a Kaggle dataset (35,126 fundus data) with 10–fold cross validation (split as training and validation set) and tested independently on real-life data (2,500 fundus data) from the University of Illinois (UI) Retina Clinic. For the DR classification, a learning rate of 1e-5 with gradual decay, batch size of 64, dropout rate of 0.4, and ADAM optimizer are used as hyperparameters

Results: The CL trained model performed significantly better compared to the Imagenet trained model (AUC of 0.94(CI 0.90-0.99, $p<0.001$) vs 0.82(0.75-0.85, $p<0.001$) on Kaggle data and 0.91(0.88-0.96, $p<0.001$) vs 0.8(0.74-0.85, $p<0.001$) on UI data). We reduced the training data size to 10% of the total data. At 10% training data, the AUC was 0.84(0.8-0.87, $p<0.05$) for CL model vs 0.69(0.59-0.75, $p<0.05$) on Imagenet model (Kaggle data) and 0.81(0.79-0.86, $p<0.05$) vs 0.65(0.6-0.75, $p<0.05$) for UI data. The results reflect that the model generalized well(transferable from Kaggle to UI data) and CL based training allowed to utilize a small number of annotated data(10%) while still generating good diagnostic accuracy

Conclusions: CL based pre-training with neural style transfer significantly improves DL classification performance and allows training with small, annotated datasets,therefore reducing ground truth annotation burden of the clinicians

CONTROL ID: 3714333
SUBMITTER (NAME ONLY): João Heitor Marques
TITLE: Role of the vitreous in ocular biomechanics
SESSION TITLE: Novel animal models and neuroprotection in the retina
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Marques, P. Baptista, J. Coelho, M. Menéres, A. Meireles, J. Melo Beirão, Centro Hospitalar Universitario do Porto EPE, Porto, PORTUGAL|
Commercial Relationships Disclosure: João Heitor Marques: Commercial Relationship: Code N (No Commercial Relationship) | Pedro Manuel Baptista: Commercial Relationship: Code N (No Commercial Relationship) | João Miguel Coelho: Commercial Relationship: Code N (No Commercial Relationship) | Maria João Menéres: Commercial Relationship: Code N (No Commercial Relationship) | Angelina Meireles: Commercial Relationship: Code N (No Commercial Relationship) | João Melo Beirão: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:
Purpose: To analyze, for the first time in vivo, the role of the vitreous in ocular biomechanics.
Methods: Prospective longitudinal study that included 24 patients submitted to unilateral pars plana vitrectomy (PPV) for vitreous opacities or epiretinal membrane. Ocular biomechanics were analyzed with Oculus Corvis ST one week before and one month after surgery. The whole eye movement (WEM) was analyzed separately as a function of posterior segment compression. Posterior vitreous detachment (PVD) was access optical coherence tomography. The fellow non-operated eyes were used as control
Results: After PPV, we observed changes in biomechanics towards a softer corneal behavior, namely a reduction in SP-A1 (p=0.009). However, intraocular pressure (IOP) was also lower (p=0.034). WEM distance decreased after vitrectomy (p=0.020). There were no significant differences in fellow non-operated eyes. A cross-sectional comparison before PPV showed that eyes with PVD at the macula also have a shorter WEM distance (p=0.047). There were no significant differences according to the reason for PPV (vitreous opacities in 16 eyes or epiretinal membrane in 8 eyes).
Conclusions: This study shows changes in response to an air pulse after PPV, which suggest a role of the vitreous in ocular biomechanics. Due to the lower IOP after surgery, no definite conclusions may be drawn regarding corneal measurements and indexes. More importantly, we observed changes that relate to the posterior segment of the eye, namely the vitreous. A decrease in WEM distance conveys a reduction in anterior-posterior deflection and reduced compression of the posterior segment. Lower IOP alone would produce the opposite effect. Eyes with PVD may also have reduced WEM. Together these findings demonstrate, for the first time in vivo, that the attached vitreous exerts a centripetal force on the globe.

CONTROL ID: 3714336

SUBMITTER (NAME ONLY): Ravirajsinh Jadeja

TITLE: HBI-002 treatment improves retinal ischemia-reperfusion injury in mice

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Jadeja, M. Jones, P.M. Martin, Biochemistry and Molecular Biology, Augusta University, Augusta, Georgia, UNITED STATES|E. Gomperts, H. Levy, M. Young, A. Gomperts, Hillhurst Biopharmaceuticals Inc, Montrose, California, UNITED STATES|L. Otterbein, Surgery, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. Thounaojam, M. Bartoli, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ischemia is a major cause of vision loss in a number of degenerative retinal diseases, including diabetic retinopathy (DR). The up-regulation of heme oxygenase (HO-1) has shown to be protective. The precise mechanism(s) by which HO-1 confers protection against cellular stress and tissue injury has not been defined, however, overwhelming evidence in the literature points to carbon monoxide (CO) generation. Low doses of CO have shown the potential for benefit in numerous disease paradigms. The impact of low dose CO therapy on conditions of the retina has not been widely evaluated. HBI-002 is an oral drug product containing precise amounts of CO. In the present study, we evaluated the therapeutic efficacy of HBI-002 in regulating retinal ischemia-reperfusion (I/R) in mice.

Methods: Male C57BL/6J mice (8-10 weeks old) were anesthetized and subjected to retinal ischemia by inserting a 32-gauge needle in the anterior chamber of the right eye to infuse sterile saline. The intraocular pressure was raised to 110 mm Hg and maintained for 40 min, after which reperfusion was begun by removing the needle. HBI-002 or vehicle (2 mg/kg) was orally administered to mice 60 minutes before I/R and then dosed daily for 7, 14, or 28 days with two doses of 2 mg/kg 60 min apart. Endpoint analyses included optokinetic tracking and electroretinogram (ERG) analysis as well as monitoring for changes in oxidative stress, inflammation, morphometric changes, and neurodegeneration by immunohistochemistry and Western blotting analysis.

Results: Oral treatment with HBI-002 significantly induced HO-1 expression thereby inducing a significant antioxidant response in the retinas of HBI-002 treated mice. The thickness of the total retina and of the inner nuclear layer was preserved as were ganglion cells in I/R-injured eyes of HBI-002 treated mice. Importantly, visual function was significantly better as evidenced by increases in spatial frequency threshold and improved ERG responses in I/R-injured eyes in HBI-002 treated mice.

Conclusions: Collectively, our proof-of-concept studies provide significant evidence for the therapeutic potential of HBI-002 in improving retinal I/R injury in mice. HBI-002 will enter Phase I testing in healthy subjects in early 2022, and rapid clinical evaluation in retinal disease could follow.

CONTROL ID: 3714337

SUBMITTER (NAME ONLY): Anna Matynia

TITLE: Optic Nerve-Independent Light Perception in Mouse Models of Photoallodynia

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Matynia, S. Parikh, M.B. Gorin, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|A. Matynia, S. Parikh, J. Suwanwanitch, M.B. Gorin, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Light mediates reflexive behavior via optic nerve pathways such as the pupillary light reflex and trigeminal pathways such as the photic corneal blink reflex. Photoallodynia is a painful response induced or enhanced by light, common to many distinct ocular conditions from cone-dominant dystrophies to corneal injury to migraine. The contributions of the optic and trigeminal nerves to light and pain perception using light aversion, a surrogate for photoallodynia, was investigated.

Methods: Light aversion behavior at 1000 lux was quantitated as an aversion index (AI: 0=no aversion; 1=complete aversion) in wild type (WT) mice and mice lacking rod and cone photoreceptors (Usher 1B, USH), in combination with optic nerve lesions (Optic Nerve Only – ONO, Trigeminal and Optic nerve, Artery and Sheath Transection – TOAST) or bilateral enucleation (BiLat). Nitroglycerin (NTG), a model for migraine, and morphine (MOR) were used to unmask light aversion. Acoustic startle was used to evaluate drug-induced acoustic hypersensitivity. Immunohistochemistry was used to evaluate retinal ganglion cells.

Results: All mice with surgical lesions or enucleation exhibited minimal-to-no light aversion with vehicle. NTG-induced and MOR-induced light aversion in wild-type mice was highest in sham (NTG=0.81±0.06, n=12; MOR=0.88±0.06, n=14), and reduced after ONO (NTG=0.51±0.09, n=13; MOR=0.12±0.06, n=13), TOAST (NTG =0.22±0.13, n=8; MOR=0.63±0.13, n=8) and BiLat (NTG =0.01±0.04, n=6; MOR=0.55±0.12, n=6). USH mice have intact melanopsin-expressing retinal ganglion cells and normal drug-induced light aversion (NTG =0.87±0.04, n=20; MOR=0.78±0.06, n=20) that is significantly reduced after BiLat (NTG =0.25±0.08, n=10; MOR=0.22±0.09, n=10). NTG and MOR do not affect acoustic startle responses.

Conclusions: Retinal-optic nerve pathways mediate light aversion in disease- and injury-free states. Trigeminal pathways are recruited in pathophysiological states and may represent a major component that signals light-induced or -enhanced pain. Acoustic stimuli do not further enhance light aversion, indicating distinct pathways from acoustic blink reflexes. NTG and MOR provide useful tools for identifying the neural circuit(s) underlying this latent light perception. Melanopsin expression has been observed in trigeminal ganglion neurons that respond to light ex vivo, providing a potential alternative circuit to influence light aversion.

CONTROL ID: 3714339

SUBMITTER (NAME ONLY): Ayesha Sultan

TITLE: Proenkephalin-derived BAM8-22 peptide analogue alleviates neuropathic corneal pain in mice

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sultan, B. Bayraktutar, S. Puri, D.L. Harris, P. Hamrah, Center for Translational Ocular Immunology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|A. Sultan, B. Bayraktutar, S. Puri, D.L. Harris, P. Hamrah, Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|R. Patil, G.S. Jacob, OKYO Pharma Ltd., New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Damage to the corneal sensory nerve endings contributes to the emergence of refractory pain in neuropathic corneal pain (NCP), for which there are currently no approved therapies available. Proenkephalin-derived endogenous peptide, BAM8-22, has been attributed with generating analgesia. In this study, we evaluated the effect of topical ophthalmic therapy with BAM8-22 peptide analogues on NCP, in a murine model of ciliary nerve ligation.

Methods: Eye-wipe response to topical hyperosmolar saline (HOS) was used as the primary outcome measure. Following the establishment of a baseline eye-wipe response to HOS [5M], 10–12 week-old male mice underwent ciliary nerve ligation for induction of NCP. Post-surgery, corneal fluorescein staining (CFS) and Cochet-Bonnet esthesiometry were used to assess ocular epithelial integrity and corneal sensitivity in operated mice that had a positive corneal pain outcome. Animals were randomized in treatment groups (n=5) and topically treated with lipidated BAM8-22, non-lipidated BAM8-22, and vehicle for 11 days. Systemic gabapentin was used as the positive control. Excised corneal whole mounts were immunostained for ßIII-Tubulin and CD45 to assess nerve and immune cell density alterations.

Results: NCP induction surgery generated a sustained pain response in all mice (24.46±1.32 vs.12.62±1.25 eye wipes/30 sec, $p<0.05$). Corneal sensitivity amongst all the treatment groups remained intact and no corneal epithelial defects were observed post-surgery. Topical application of both lipidated BAM8-22 analogue (24.2±1.59 vs.12.6±0.98, $p=0.045$) and non-lipidated BAM8-22 (25.17±1.66 vs.13.18±0.7, $p=0.018$) resulted in a decrease in pain response compared to vehicle treatment. Systemic gabapentin treated mice were used as the positive control and showed a lowered pain response (25.5±2.25 vs.12.5±2.6, $p=0.011$). Corneal nerve density decreased in all the NCP mice compared to sham (64884.53±4353.51 vs. 152348.87±6344.17 mm/mm^2, $p<0.0001$). Among all the different NCP treatment groups, significantly higher corneal nerve density was detected in non-lipidated BAM8-22 treated mice as compared to vehicle (104188.79±5622.31 vs. 54429.42±6343.29 mm/mm^2, $p<0.0001$) while no significant differences were observed in the $CD45^+$ cell density among groups ($P>0.05$).

Conclusions: BAM8-22 analogues, administered topically, were effective in alleviating neuropathic corneal pain in our murine model of NCP.

CONTROL ID: 3714341

SUBMITTER (NAME ONLY): Masoud Norouzi Darabad

TITLE: A mathematical model to understand the formation of the outer retinal corrugations

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Norouzi Darabad, A. Ramachandran, Department of Chemical Engineering and Applied Chemistry, University of Toronto, Toronto, Ontario, CANADA|P. Oquendo, H. Hamli, W. Lee, F. Nagel, A. Bansal, I.M. Melo, R.H. Muni, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

ABSTRACT BODY:

Purpose: Outer retinal corrugations (ORCs) can often result in outer retinal folds (ORFs) and poor vision in patients with rhegmatogenous retinal detachment (RRD). However, the pathophysiology of ORCs is not well understood. We have developed a mathematical model to further understand the mechanical aspects of the formation of ORCs. In particular, we are interested in the changes in mechanical properties of the retina that result in the formation of ORCs.

Methods: We have modeled the retina as a composite material consisting of the outer retinal layer (photoreceptor layer) and the inner retinal layer (the part of the retina that excludes the photoreceptor layer) with thicknesses T_o and T_i and elastic modulus E_o and E_i respectively. We selected optical coherence tomography (OCT) images of 8 RRD patients with visible ORCs and no cystoid macular edema (CME). The thickness of the outer and inner retinal layers, and the relative increase in the length of the outer retinal layer (γ) is measured from OCT images. This information is used along with the mathematical model to find the values of E_o / E_i resulting in corrugations with frequency similar to OCT imaging.

Results: Measurements from OCT images of patients with RRD show that there is approximately 30% increase (γ=0.3) in the length of the outer retinal layer and a 400% increase in the thickness of the outer retinal layer (T_o). Using our mathematical model, we found that in order to form corrugations with a frequency similar to what is observed on OCT imaging E_o / E_i should be 0.1 or smaller. In other words the outer retinal layer should become 10 times softer compared to inner retinal layer. It is noteworthy that this trend is the opposite of that observed in an attached retina, i.e. the outer retina is stiffer than the inner retina. This indicates that the outer retina could be undergoing significant structural changes and softening relative to the inner retina when detached from the RPE.

Conclusions: We compared predictions from a mathematical model with measurements from OCT images to make inference about the mechanical conditions required for the formation of ORCs. Our results show that the outer retina should undergo structural changes that reduces the elastic modulus of the outer retinal layer such that $E_o / E_i \leq 0.1$. These results have significant implications on how best to achieve retinal reattachment to reduce abnormalities such as outer retinal folds.

CONTROL ID: 3714343

SUBMITTER (NAME ONLY): Ratheesh Meleppat

TITLE: Age-dependent changes in the retinal pigment epithelium cells using ex vivo confocal fluorescence imaging

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.K. Meleppat, M.E. Burns, R.J. Zawadzki, Ophthalmology & Vision Science, University of California Davis, Davis, California, UNITED STATES|K. Ronning, M.E. Burns, Center for Neuroscience, University of California Davis, Davis, California, UNITED STATES|S.J. Karlen, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure: Ratheesh Meleppat: Commercial Relationship: Code N (No Commercial Relationship) | Kaitryn Ronning: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Karlen: Commercial Relationship: Code N (No Commercial Relationship) | Marie Burns: Commercial Relationship: Code N (No Commercial Relationship) | Robert Zawadzki: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate age-dependent changes in mouse retinal epithelium (RPE) cells, including cell number, cell size, and the concentration of the pigmented granules and their emission spectra, using multicolor confocal fluorescent microscopy (MCFM). These changes were compared between a mouse model of Stargardt disease ($Abca4^{-/-}$ [129S4]) and agouti wild-type (WT) controls.

Methods: We performed in situ live tissue imaging of RPE flat-mounts from agouti $Abca4^{-/-}$ and agouti WT (129S1/SvlmJ) controls at multiple ages (1.5 months, 4 months, 8 months and 13 months) using a Nikon A1 confocal microscope. High-resolution confocal image z-stacks of the RPE cell mosaic were acquired with four different excitation wavelengths (405nm, 488nm, 561nm, and 640nm). The autofluorescence images of RPE, including voxel-by-voxel emission spectra, were acquired and processed with Nikon NIS-AR Elements software.

Results: An enhanced visualization of the RPE cell mosaic as well as pigmented granules (melanosomes and lipofuscin) with an unprecedented resolution and contrast were generated using MCFM for both mouse strains at all ages. The changes in RPE cell number, cell volume, concentration of the lipofuscin and melanosomes (per cells), the emission spectra from the lipofuscin granules, and the total emission spectra from the RPE volume were quantified and compared over time between strains. We found the concentration of lipofuscin consistently increased with age whereas the number of melanosomes decreased proportionally in both mouse strains. At all ages there was an increased number of lipofuscin granules in $Abca4^{-/-}$ compared to WT.

Conclusions: A systematic and comprehensive investigation of the age-dependent changes in RPE cells and pigmented granules was possible with MCFM. An increased number of lipofuscin and decreased number of melanosomes with age is common in both mouse strain, albeit, more rapid in $Abca4^{-/-}$. The reduction in melanosomes could be linked with the formation of melanolipofuscin, which requires additional investigations. The changes in the RPE with age and $Abca4^{-/-}$ deficiency could be linked the pathological condition associated with a Stargardt disease.

CONTROL ID: 3714345

SUBMITTER (NAME ONLY): Stephanie Campbell

TITLE: Real world feasibility of home-monitoring application in macular degeneration

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Campbell, OKKO Health, Bristol, UK, UNITED KINGDOM|S. Campbell, Aneurin Bevan University Health Board, NHS Wales Primary Care Services, Pontypool, Gwent, Wales, UNITED KINGDOM|J. Antoun, A. John, A. Foss, Ophthalmology, Queens Medical Centre, Nottingham University Hospitals NHS Trust, Nottingham, England, UNITED KINGDOM|A. Foss, University of Nottingham, Nottingham, England, UNITED KINGDOM|

Commercial Relationships Disclosure: Stephanie Campbell: Commercial Relationship(s);Code O (Owner):OKKO Health | Joe Antoun: Commercial Relationship(s);Code E (Employment):OKKO Health | Anita John: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Foss: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The ability to safely and reliably monitor visual function at home can help to facilitate the reduction of the personal, economic and environmental burdens of AMD through early identification of deterioration. A critical success factor is real-world patient acceptability and ease of use. Therefore, this study aimed to: 1) evaluate the clinical validity of the OKKO Health visual acuity data versus in clinic measures of visual acuity; and 2) explore the usability and acceptability of home vision monitoring.

Methods: Participants undergoing regular anti-VEGF injections in an NHS macular clinic were invited to participate. Patients were trained in the use of the OKKO Health app by the nurse practitioner and instructed to play three times weekly, between their scheduled monthly clinic visits. Participants were followed up for three months and a total of four clinic visits, during which chart LogMAR visual acuity was measured using a ETDRS eye chart. This was compared to the app visual acuity data in the week preceding the clinic appointment. Usability of the OKKO Health app was determined through the use of the system usability scale.

Results: Data presented are from a larger ongoing study. Of the 50 adults consented (Age range: 79 ± 7 years; range: 65 - 88), 72% (n = 36) initially downloaded and registered the app. Of these, 44% (n = 16) played consistently three times per week for three months. Bland-Altman analysis was carried out on a total of 60 sessions showing good agreement with the OKKO Health app. On average, the OKKO visual acuity score was 0.077 logMAR ± 0.23 logMAR better than in-clinic measurements using an ETDRS eye chart. The average score on the system usability scale was 83 ± 13, suggesting excellent usability in those who downloaded the app.

Conclusions: The OKKO Health app provides a feasible (usable and valid) means of monitoring visual function at home and was well-accepted with good adherence by patients who initially downloaded and registered on the app.

CONTROL ID: 3714346

SUBMITTER (NAME ONLY): Joana Andoh

TITLE: Participatory Evaluation of Framework Outlining Barriers to and Facilitators of Diabetic Retinopathy Screening Utilization in a High-Risk Population

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Andoh, A. Norcott, K.H. Nwanyanwu, Ophthalmology and Visual Science, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|E. Fairless, Ophthalmology, The University of Oklahoma, Norman, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Joana Andoh: Commercial Relationship: Code N (No Commercial Relationship) | Althea Norcott: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Fairless: Commercial Relationship: Code N (No Commercial Relationship) | Kristen Nwanyanwu: Commercial Relationship(s);Code O (Owner):Eyefull, LLC

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of blindness in working-age people in the US. DR is more prevalent and diagnosed at more severe stages in racial and ethnic minorities and low resource communities. Our group developed a framework to organize determinants of DR screening in a high-risk population. The purpose of this study was to evaluate this framework to identify additional barriers to and facilitators of DR screening applicable to those with severe disease.

Methods: We conducted individual semi-structured, qualitative interviews of participants with a history of laser or surgery for DR at an urban, academic health center. We recorded select demographic information of each participant. After the interview, participants were compensated with a monetary gift card. Interviews were recorded, analyzed, and organized in comparison to the initial framework based on grounded theory. To conduct a participatory evaluation, we recruited and trained a community stakeholder to analyze four transcripts. The study authors discussed evaluation findings, synthesized poignant themes, and proposed interventions.

Results: A total of 28 participants were included in the final analysis. Four additional participants were required for the severe disease cohort to reach theoretical saturation. Eleven participants identified as female and 17 identified as male. Participants identified as Black (17), White (4), Hispanic/Latinx (4), and other/no answer (3). The original coding framework themes remained relevant (Figure 1). Themes were organized into two categories: individual (vision status, competing concerns, emotional context) and structural factors (resource availability, cues to action, knowledge-creating experiences, and in-clinic experience). The patient-doctor relationship was an additional theme present in the severe cohort analysis. During the participatory evaluation, the community stakeholder highlighted examples of select themes, in addition to possible interventions (Figure 2).

Conclusions: We present participatory evaluation as a means of reviewing a framework to identify barriers and facilitators to diabetic retinopathy screening in a high-risk population. The emergence of poignant themes and possible interventions emphasize the importance of participatory research in understanding social determinants of diabetic retinopathy.

CONTROL ID: 3714349

SUBMITTER (NAME ONLY): Kristen Kerber

TITLE: Effect of Stimuli Depth on Static and Dynamic Accommodation Responses in Young Children

SESSION TITLE: Myopia and refractive error development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.L. Kerber, A. Jnawali, F.A. Vera-Diaz, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Kristen Kerber: Commercial Relationship: Code N (No Commercial Relationship) | Ashutosh Jnawali: Commercial Relationship: Code N (No Commercial Relationship) | Fuensanta Vera-Diaz: Commercial Relationship(s);Code C (Consultant/Contractor):Essilor International

ABSTRACT BODY:

Purpose: Inaccurate accommodation responses to blur may be associated with myopia. Conflicting results in previous studies may be a result of varied stimuli characteristics. We sought to compare static and dynamic accommodation responses (AR) and associated pupil constriction to two different stimuli in children.

Methods: Static and dynamic AR and pupil sizes were measured on the right eyes of young children (N=97, 7.58±0.96yrs) with functional emmetropia (SE OD +0.95±0.54D; AXL OD 22.79±0.75mm) using a WAM-5500 open-field binocular autorefractor WMT-2 Moving System (Ait, Luneau). Two targets of 'dead leaves' stimuli which capture spatial characteristics of natural images were used: the real object (3D), and a flat, 2D picture of the same object. Static AR were measured for a 2.5D demand. Dynamic AR were measured for a sinusoidally moving stimuli (27 seconds, 1-4D demand, 9 second-cycles) and results fitted with sinusoidal functions. Children were classified into High Risk (HR) or Low Risk (LR) for myopia based on their parental myopia and baseline refractive error.

Results: Static AR for a 2.5D demand did not differ significantly between the 2D (1.79±0.45D) and 3D (1.75±0.51D) stimuli ($p>0.05$). Pupil sizes were also not significantly different (2D: 5.89±0.89mm, 3D: 5.97±0.85mm; $p>0.05$). Children at LR for myopia accommodated significantly more accurately than those at HR when viewing both static 2D (LR: 1.89±0.48D, HR: 1.68±0.38D; $p=0.006$) and 3D stimuli (LR: 1.83±0.62D, HR: 1.65±0.34D; $p=0.007$). Dynamic accommodation amplitudes were larger for the 2D (1.27±0.21D) than the 3D (1.24±0.23D, $p=0.025$) stimuli, and latencies longer for the 3D stimuli (2D: 0.34±0.22msec, 3D: 0.42±0.28msec; $p=0.008$). AR amplitudes were significantly larger for children at LR compared to those at HR for myopia (2D - LR: 1.31±0.17D, HR: 1.22±0.19D; $p=0.037$; 3D - LR: 1.32±0.18D, HR: 1.15±0.23D; $p<0.001$) stimuli.

Conclusions: No overall differences were found between the 2D and 3D stimuli for static responses, but the dynamic amplitudes and latencies were more accurate with the 2D compared to the 3D stimuli. Children with LR for myopia showed more accurate static and dynamic responses than those at HR for myopia. Differences in AR in young children may predict the development of myopia.

CONTROL ID: 3714351

SUBMITTER (NAME ONLY): Richard Thompson

TITLE: Two-Photon Fluorescence Excitation of Tetracyclines for Imaging Retinal Minerals

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Thompson, H. Zeng, A. Puche, K. Ray, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|K.R. Hegde, Coppin State University, Baltimore, Maryland, UNITED STATES|I. Lengyel, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

Commercial Relationships Disclosure: Richard Thompson: Commercial Relationship: Code N (No Commercial Relationship) | Hui Hui Zeng: Commercial Relationship: Code N (No Commercial Relationship) | Kavita Hegde: Commercial Relationship: Code N (No Commercial Relationship) | Adam Puche: Commercial Relationship: Code N (No Commercial Relationship) | Krishanu Ray: Commercial Relationship: Code N (No Commercial Relationship) | Imre Lengyel: Commercial Relationship(s);Code F (Financial Support):Optos, F. Hofmann La Roche

ABSTRACT BODY:

Purpose: Calcium phosphate minerals are ubiquitous constituents of retinal drusen (PMID 25605911) and the presence of larger hydroxyapatite (HAP) deposits termed nodules is predictive of progression to advanced AMD within one year (odds ratio 6.4 : 1)(PMID 30404862). HAP can be imaged by fluorescence lifetime imaging microscope (FLIM) following staining with common tetracycline antibiotics (PMID 32319262). These results and others suggested that imaging HAP deposition in the retina might prove a useful biomarker for the early detection and monitoring progression of AMD and other diseases. However, some of the best performing tetracyclines are best excited at wavelengths near 400 nm, which raises safety issues and where background fluorescence particularly in the vitreous and lens is strongly excited. Since multiphoton excitation occurs only at the focal point, such imaging is effectively confocal and background fluorescence in the excitation path is minimized. In addition, there are minimal safety concerns with the excitation wavelength used by the two photon system (780 nm in this experiment) as it is similar to the wavelengths widely and safely used for OCT. Here we tested multiphoton excitation for imaging HAP in a FLIM using an ultrafast laser in the near-infrared for fluorescence excitation of HAP-bound tetracyclines.

Methods: Donors provided consent under ethical standards. Cadaver eyes were dissected, flat-mounted, and stained with chlortetracycline or solutions essentially as previously described (PMID 32319262) and imaged in an ISS Alba FLIM with excitation at 780 nm, 90 fsec pulse duration, and 12 mW average power through a 20 X 0.7 NA objective. The instrument was calibrated with standards of known lifetimes.

Results: Both HAP-bound doxycycline and chlortetracycline were efficiently excited by focused 780 nm pulses; measured average lifetime values were similar (3.6 and 1.9 nsec, respectively) to those measured previously for HAP-bound tetracyclines with one photon excitation (3.8 and 1.7 nsec, respectively); and both distinct from the typical average lifetime of the retinal background fluorescence (0.2 – 0.4 nsec; reviewed in PMID 28673870).

Conclusions: Based on these results we propose that in vivo imaging of tetracycline-labelled HAP in the outer retina could become a useful tool to monitor mineralization using a fluorescence lifetime ophthalmoscope with multiphoton excitation.

CONTROL ID: 3714352

SUBMITTER (NAME ONLY): Resya Sastry

TITLE: Quantification of Fluid Compartment Changes in Patients with Limited Response to Anti-VEGF Treatment for Diabetic Macular Edema using a Machine Learning Algorithm in Routine Clinical Practice

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.C. Sastry, R.P. Singh, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|S.W. Perkins, Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Resya Sastry: Commercial Relationship: Code N (No Commercial Relationship) | Scott Perkins: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Singh: Commercial Relationship(s);Code C (Consultant/Contractor):Novartis, Genentech, Regeneron, Alcon, Bausch and Lomb, 41 Gyroscope;Code F (Financial Support):Aerie, Apellis, Graybug

ABSTRACT BODY:

Purpose: Anti-VEGF treatment response is assessed anatomically by changes in the central retinal thickness (CRT) and by BCVA outcomes at 3 months after initial monthly injection. This study aims to characterize treatment outcomes of DME patients with limited early response to anti-VEGF at month (M) 3 using a machine learning (ML) algorithm to quantify fluid on optical coherence tomography (OCT) and analyze features of patients within subcategories.

Methods: A retrospective chart review of treatment naive patients ≥ 18 years diagnosed with DME was conducted. All patients had ≥ 12 months of follow-up after initial anti-VEGF treatment and available OCT scans at baseline (M0), M3, M6, and M12. A ML algorithm, Notal OCT Analyzer, quantified fluid volumes on OCTs of subretinal (SRF), intraretinal (IRF), and total retinal fluid (TRF) at each time point. Patients were categorized as limited early responders (LER) if they had ≤ 10% CST reduction and/or < 5 ETDRS letter gain at M3; the other were early responders (ER). BVA, CST, and fluid change at M12 and M0 were compared between groups. Analysis included the Welch's t-test, Welch's ANOVA, and one-way analysis of means.

Results: The study included 220 eyes (162 LER, 58 ER) then divided into those who satisfied the anatomic criteria (113 aLER, 107 aER), or VA criteria (134 vLER, 86 vER). At M12, BVA and CST outcomes were significant for aLER and aER. The aLER mean letter gain was 1.32 ETDRS and aER was 9.14. The aLER mean CST reduction was 24.94 mm and aER was 129.51 mm. There was no BVA, TRF, and IRF variance across time for LER ($p > 0.1$), while all ER groups varied between M0 and M3 ($p < 0.001$). SRF varied across time for all ER, vLER, and LER. CST had high variance across all groups ($p = 0.008$) except aLER with a low significance ($p < 0.01$).

Conclusions: The M12 outcomes between the LER and ER groups showed significant difference between the aLER and aER indicating worse BVA and CST outcomes for those with ≤ 10% CST reduction at M3. Furthermore, limited BVA improvement after M3 for all LER groups indicates vision is unlikely to improve after M3. Similarly, all ER groups showed minimal fluid, BVA, and CST changes after M3. Thus, the characterization of response type at 3 months of monthly anti-VEGF injections can predict anti-VEGF treatment outcomes in DME patients.

CONTROL ID: 3714354

SUBMITTER (NAME ONLY): Manas Biswal

TITLE: Impact of prolonged oxidative stress in the retinal pigment epithelium (RPE) on the photoreceptors in an animal model of dry-AMD.

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.R. Biswal, R.J. Paulson, Pharmaceutical Sciences, University of South Florida College of Pharmacy, Tampa, Florida, UNITED STATES|G.P. Lobo, Ophthalmology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|M. Valapala, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|A.S. Lewin, Ophthalmology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|M.R. Biswal, Ophthalmology, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|A.S. Lewin, Molecular Genetics and Microbiology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|

Commercial Relationships Disclosure: Manas Biswal: Commercial Relationship: Code N (No Commercial Relationship) | Glenn Lobo: Commercial Relationship: Code N (No Commercial Relationship) | Mallika Valapala: Commercial Relationship: Code N (No Commercial Relationship) | Ryan Paulson: Commercial Relationship: Code N (No Commercial Relationship) | Alfred Lewin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Prolonged oxidative stress in the retinal pigment epithelium (RPE) can cause the death of RPE and photoreceptor cells, leading to vision loss in patients with dry-AMD. However, the molecular mechanism(s) of how oxidative stress in the RPE contributes to human retinal cell degeneration is poorly understood. The study aims to investigate the crosstalk between RPE and the retina while RPE is under prolonged oxidative stress.

Methods: We used a mouse model of RPE oxidative stress (Sod2flox/flox/VMD2-cre mice), which were generated by RPE-specific deletion of Sod2, the mitochondrial isoform MnSoD, an oxidative stress response protein. These mice showed progressive retinal degeneration that recapitulates some of the features of dry AMD. To identify a possible mechanism for these pathologies, we harvested eyes from Sod2flox/flox/VMD2-cre mice and age-matched littermate control Sod2flox/flox mice and performed histological, biochemical, and visual function analysis.

Results: Histological and electron microscopic analysis provided important information related to photoreceptor outer segments recycling, structure, and health, where progressive degeneration of the outer photoreceptor segments was observed. However, no changes in the expression of phototransduction proteins were detected. A modest increase in oxidative stress markers was noted. Oxidative stress in the RPE induced the expression of TFEB, one of the key transcription factors that determine the effective lysosomal clearance.

Conclusions: This study establishes a connection between RPE oxidative stress and the induction of lysosomal biogenesis via TFEB. It has broad implications in understanding human inherited retinal degeneration and will help develop novel therapeutics to treat vision loss.

CONTROL ID: 3714356

SUBMITTER (NAME ONLY): Robbert R. Struyven

TITLE: Deep learning-based detection of Plus disease of Retinopathy of Prematurity

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.R. Struyven, S. Wagner, B. Liefers, G. Zhang, S. Glinton, M. Kelly, M. Radia, J. Than, S. Balal, C. Hennings, P. Pooprasert, N. Pontikos, P.A. Keane, P. Patel, G. Adams, K. Balaskas, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, NIHR Biomedical Research Centre for Ophthalmology, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a proliferative retinal vascular disease, typically affecting preterm low birth weight neonates. In high-income countries, ROP has been identified through screening programmes with paediatric ophthalmologist-led clinical examination for at-risk neonates, yet because of a growing survival rate of premature infants globally, the demand for screening is increasing. We explore if a custom deep learning with coding or an AutoML deep learning model without coding can diagnose ROP Plus disease in fundus images.

Methods: A retrospective cohort study of optic disc-centred retinal photographs, acquired using the Retcam Version 2 device (Natus Medical Incorporated©), from preterm neonates fulfilling Royal College of Ophthalmologists screening criteria for ROP screening at the Homerton University Hospital, London, United Kingdom between January 2008 and January 2018. Two models were trained - a custom model with DenseNet architecture, as well as a Google Cloud AutoML Vision model trained through the online interface without the use of coding. The reference standard was derived from a hierarchical grading system: two juniors, both with three years of ophthalmology experience, labelled images as ungradable, normal, Pre-plus or Plus disease with arbitration by a senior paediatric ophthalmologist on disagreements. Our models were trained on a dataset of 6620 posterior pole images of 1370 patients. Model performance was through a split-sample internal validation on 200 images (100 normal, 49 Pre-Plus and 51 Plus) from 111 patients.

Results: On internal validation, the custom coding model had a sensitivity of 39.7%, specificity of 97.3%, area under the curve (AUC) of 0.941, and 95.2% accuracy for normal versus diseased (Pre-Plus and Plus disease) classification. The AutoML model had a sensitivity of 60.3%, specificity of 98.9%, AUC of 0.95, and 96.7% accuracy for normal versus diseased classification.

Conclusions: We demonstrate that the use of custom models, as well as automated machine learning that does not require coding, have similar performance. External validation comparing the two models with independent human graders is still pending.

CONTROL ID: 3714357

SUBMITTER (NAME ONLY): Salvatore Stella

TITLE: Differential Expression of the Vesicular Inhibitory Amino Acid Transporter (VIAAT)/slc32a Paralogues in Zebrafish Retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Stella, A. Ostman, Neural and Behavioral Sciences, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Salvatore Stella: Commercial Relationship: Code N (No Commercial Relationship) | Alexandria Ostman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the retina, the slc32a1 gene or the vesicular inhibitory amino acid transporter (VIAAT) has been of great interest and is expressed at synaptic terminals of horizontal cells in the outer retina and amacrine cells in the inner retina; with GABA having a significant role in both feedback and feedforward signaling in the outer retina driven by horizontal cells, and GABAergic and glycinergic feedback signaling in the inner retina among amacrine cells. Zebrafish are a widely used model for retinal studies and have undergone a gene duplication event that has resulted in the duplication of ~ 50% of all genes. This duplication event has permitted the partitioning of gene function or expression patterns. The goal of this study is to explore the impact of this duplication event on the expression profile of VIAAT paralogues (slc32a1 and si:dkey-126h10.1) in the adult zebrafish retina.

Methods: Adult zebrafish brains or retinas were used to extract RNA, and generate probes for in situ hybridization as described previously (Grillo et al., Purinergic Signal. 2019). Indirect immunofluorescence and confocal microscopy with antibodies targeted to VIAAT, GABA, glycine, and glutamic acid decarboxylase (GAD) were used to characterize the key components of the inhibitory signaling system in the inner and outer zebrafish retina. Ensembl and BLAST were used to identify slc32a1 members. All sequences were compiled and aligned using BLAST, and evolutionary analysis and the phylogenetic tree creation were completed using MEGA (ver. 11), with the human protein sequence serving as the reference in BLAST.

Results: Unexpectedly, we found that the expression slc32a1, the 1st VIAAT homolog was expressed exclusively in the inner retina at amacrine cells, and si:dkey-126h10.1, the 2nd VIAAT homolog was restricted to horizontal cells in the outer retina. This novel observation may relate to the developmental changes that likely occurred during the gene duplication event in teleosts through the segregation of inner and outer retinal circuitry.

Conclusions: This will also serve as an important tool for the development of gene targeted approaches involving VIAAT in the zebrafish retina. Our data suggest that these VIAAT expression patterns may provide the specificity necessary to dissect the cell type specific roles for VIAAT inhibitory neurotransmission in the outer and inner retina.

CONTROL ID: 3714358

SUBMITTER (NAME ONLY): Sarah Griffin

TITLE: Minimally Invasive Glaucoma Surgery Wet-Lab: A Follow-Up Needs Assessment Survey for Ophthalmology Residents

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Griffin, A. Stefaniak, R. Vasaiwala, M. Chaku, Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Sarah Griffin: Commercial Relationship: Code N (No Commercial Relationship) | Alexis Stefaniak: Commercial Relationship: Code N (No Commercial Relationship) | Roshni Vasaiwala: Commercial Relationship: Code N (No Commercial Relationship) | Meenakshi Chaku: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In 2012 Saheb and Ahmed found that minimally invasive glaucoma surgeries (MIGS) lower intraocular pressure, decrease dependence on medications, and have an excellent safety profile. In 2017 75.5% of glaucoma surgeries performed in the US on Medicare patients 65 years or older in the US were MIGS. A 2020 study surveyed US program directors and found that both didactics and wet labs are used for resident training in MIGS. However, 37% of program directors did not feel that the experience was adequate for independent practice and only 27% felt that MIGS should be an ACGME requirement. Since 2017 Loyola's citywide annual microsurgical wet lab for six Chicago residencies has focused on hands-on training in MIGS to meet the increasing interest amongst residents. During COVID-19, Loyola continued to host our annual wet lab, providing MIGS training virtually. The purpose of this study was to assess residents' perspectives of their current MIGS training and how residents' perspectives have changed since 2017.

Methods: In 2017 and 2020 respectively, 31 and 44 residents of 6 Chicago programs attended our wet lab. Residents were given a pre-wet lab survey regarding their interest in MIGS and training satisfaction. The data collected was anonymous and de-identified. In 2017 data was collected in-person on iPads using RedCap software and in 2020 the data was collected remotely using Qualtrics data collection platform. In both wet labs residents performed various MIGS and intraoperative gonioscopy.

Results: In 2017 and 2020 respectively, 77% and 81% of residents reported that they were interested or very interested in MIGS. In 2017 32% of residents were satisfied by their MIGS training. In 2020, still only 25% of residents were satisfied by their current MIGS training.

Conclusions: Despite widespread use of MIGS in the US and growing interest amongst graduating ophthalmologists, there continues to be a gap between resident interest in MIGS and satisfaction with training during residency. Over the four years, this gap has remained unchanged. A MIGS-based hands-on wet lab experience is one way to improve MIGS training for residents and close the gap between interest and satisfaction with current MIGS resident training.

CONTROL ID: 3714360

SUBMITTER (NAME ONLY): Dusanka Deretic

TITLE: Regulation of Rabin8 during ciliary trafficking of rhodopsin

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Deretic, T. Fresquez, Ophthalmology and Visual Sciences, University of New Mexico Health Sciences Center, Albuquerque, New Mexico, UNITED STATES|B.M. Tam, O.L. Moritz, Ophthalmology, The University of British Columbia, Vancouver, British Columbia, CANADA|

Commercial Relationships Disclosure: Dusanka Deretic: Commercial Relationship: Code N (No Commercial Relationship) | Beatrice Tam: Commercial Relationship: Code N (No Commercial Relationship) | Orson Moritz: Commercial Relationship: Code N (No Commercial Relationship) | Theresa Fresquez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Rabin8, the GEF for the small GTPase Rab8, provides the backbone of the Rab11-Rabin8-Rab8 ciliogenesis complex, which regulates sorting of rhodopsin into transport carriers (RTCs). Membrane association and function of Rabin8 is regulated by NDR2 kinase (aka STK38L), a canine early retinal degeneration (erd) gene. In this study, we continued to investigate the function of the Rab11-Rabin8-Rab8 complex and its control by NDR2 kinase in ciliary trafficking of rhodopsin.

Methods: Human GFP-Rabin8 WT was cloned into the XOP0.8 eGFP-N1 expression vector for the generation of transgenic X. laevis. The following Rabin8 mutants were generated: a phosphomimetic GFP-Rabin8 S272E and the non phosphorylatable GFP-Rabin8 S272A; the Rab8 GEF domain mutants GFP-Rabin8 E192A and F201A; and Rab11 binding mutants GFP-Rabin8 Δ300-305 and GFP-Rabin8 T419A Y423A L428A. The resulting phenotypes were analyzed by confocal microscopy. Interactions of GST-tagged Rabin8 mutants were examined by GST-pulldowns.

Results: Human GFP-Rabin8 WT colocalized with endogenous X. laevis Rabin8. It accumulated at the Golgi exit sites (GES) possibly affecting its own NDR2 phosphorylation and that of the endogenous Rabin8, which accumulated nearby. GFP-Rabin8 WT colocalized with rhodopsin in the Golgi, at the GES and on RTCs. GFP-Rabin8 S272E, a phosphomimetic, colocalized with endogenous Rabin8 at the GES and on RTCs. By contrast, non-phosphorylatable GFP-Rabin8 S272A accumulated at the GES and failed to reach the RTCs. GFP-Rabin8 E192A and F201A, Rab8-GEF mutants, colocalized with rhodopsin in the Golgi, at the GES and on RTCs, which were often enlarged, likely due to the disruption of Rab8 function. GFP-Rabin8 Δ300-305 mutant was cytosolic. GST-pulldowns showed that mutations did not alter the ability of Rabin8 to interact with Rab8 and Rab11. GST-Rabin8 Δ300-305 was likely misfolded, so the cytosolic expression of GFP-Rabin8 Δ300-305 in transgenic rods was likely due to disrupted dimerization, which is essential for its function. We have synthesized GFP-Rabin8 T419A Y423A L428A mutant that disrupts the Rab11 binding but not the Rabin8 dimerization, for immediate transgenesis.

Conclusions: During ciliary targeting, Rabin8 phosphorylation by NDR2 kinase likely occurs at the GES, regulates Golgi exit and directs Rabin8 to the base of the cilium for Rab8 activation. Ongoing experiments will establish the role of Rabin8-Rab11 interaction in rhodopsin ciliary trafficking.

CONTROL ID: 3714361

SUBMITTER (NAME ONLY): Paul Kenna

TITLE: A novel KCNV2 variant in Cone Dystrophy with Supernormal Rod Response (CDSRR) – Evidence for Pathogenicity

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.F. Kenna, Research Foundation, Royal Victoria Eye and Ear Hospital Dublin, IRELAND|E. Duignan, Department of Ophthalmology, Royal Victoria Eye and Ear Hospital Dublin, IRELAND|P.F. Kenna, L. Whelan, C. Shortall, G. Farrar, Department of Genetics, The University of Dublin Trinity College, Dublin, IRELAND|

Commercial Relationships Disclosure: Paul Kenna: Commercial Relationship: Code N (No Commercial Relationship) | Emma Duignan: Commercial Relationship: Code N (No Commercial Relationship) | Laura Whelan: Commercial Relationship: Code N (No Commercial Relationship) | Ciara Shortall: Commercial Relationship: Code N (No Commercial Relationship) | G.Jane Farrar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the phenotypic and genotypic findings in two siblings with a severe cone dystrophy and electroretinogram (ERG) findings characteristic of CDSRR.

Methods: Over 1600 genetic retinopathy patients attending the Genetic Eye Disease Service at the Royal Victoria Eye and Ear Hospital, Dublin, have been recruited prospectively as part of Target 5000. Testing includes: best-corrected visual acuity (BCVA), Goldmann perimetry, Lanthony D15 colour vision, slit-lamp biomicroscopy, ISCEV clinical standard electrodiagnostics, colour and autofluorescence fundus photography and optical coherence tomography. DNA samples undergo exon sequencing of c. 254 candidate genes using target-capture oligo panels or whole exome sequencing in research and/or accredited facilities. Variants of uncertain significance are subjected to in silico analysis.

Results: Two brothers, 15 and 16 years old respectively, reported life-long reduced vision and photophobia. BCVA was 6/48 and each had red/green colour deficits. ERGs showed delayed rod-isolated responses of low-normal amplitudes and dark-adapted rod-dominated maximal responses of unusually high amplitude. Cone-isolated responses were delayed and markedly reduced in amplitudes. This constellation suggested CDSRR as a likely diagnosis. Genotyping revealed compound heterozygosity for KCNV2 c.1381G>A, p.(Gly461Arg), a known pathogenic variant, and c.1354G>C, p.(Ala452Pro), a previously unreported variant. In silico analyses using SIFT, Mutation Taster and Polyphen 2 predicted the latter to be deleterious.

Conclusions: KCNV2 (OMIM *607604), causative of CDSRR, encodes the subunit Kv8.2 of a voltage-gated potassium channel in rods and cones. Activation is enabled by complex formation with other subunits and expression influenced by transcription factors CRX and NRL. KCNV2 variants underlie up to 4.3% of cone dystrophies. c.1381G>A, p.(Gly461Arg) is the most commonly reported variant. c.1354G>C, p.(Ala452Pro), a previously unreported missense variant, is absent from the gnomAD database and has not been reported in ClinVAR or HGMD. It affects a highly conserved amino acid in the ion transport domain. Two missense variants affecting a nearby codon have been reported to cause CDSRR. Further functional studies are underway, however, this report provides, to the best of our knowledge, the first evidence for pathogenicity of KCNV2 c.1354G>C, p.(Ala452Pro).

CONTROL ID: 3714363

SUBMITTER (NAME ONLY): Peter Murphy

TITLE: Optogenetic stimulation and calcium imaging of single ganglion cells in the living macaque fovea

SESSION TITLE: Advances in high resolution imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Murphy, J.E. McGregor, Z. Xu, W. Merigan, D.R. Williams, Center for Visual Science, Rochester, New York, UNITED STATES|P. Murphy, Z. Xu, D.R. Williams, Optics, University of Rochester, Rochester, New York, UNITED STATES|J.E. McGregor, W. Merigan, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: Peter Murphy: Commercial Relationship: Code N (No Commercial Relationship) | Juliette McGregor: Commercial Relationship: Code N (No Commercial Relationship) | Zhengyang Xu: Commercial Relationship: Code N (No Commercial Relationship) | William Merigan: Commercial Relationship(s);Code F (Financial Support):Alcon | David Williams: Commercial Relationship(s);Code P (Patent):University of Rochester;Code F (Financial Support):Warby Parker;Code F (Financial Support):Alcon

ABSTRACT BODY:

Purpose: The perceptual roles of most retinal ganglion cell (RGC) classes are controversial in part because we lack a paradigm for measuring the perceptual consequences of activating cells of only one class in the living primate eye. Recent success in classifying single RGCs with in vivo calcium imaging (McGregor 2018, PLoS One, 13), in vivo optogenetic activation of RGCs en masse (McGregor 2020, Nat. Commun. 11, 1703; Sahel 2021, Nat. Med. 27., 1223), and in vivo targeted excitation of single cones (Harmening 2014, J. Neurosci. 34, 5667) now bring such a paradigm within reach. As a first step, we demonstrate the optogenetic stimulation of single foveal RGCs in the living macaque.

Methods: RGCs in an anesthetized female macaque were stimulated and imaged using adaptive optics scanning light ophthalmoscopy. Co-expression of the optogenetic actuator and calcium indicator was achieved via intravitreal injection of AAV2-CAG-ChrimsonR-tdTomato and AAV2-CAG-GCaMP6s. We selected single RGC somas from those closest to the foveal center because of their large separation from their nearest neighbors (>20 μm). On each trial, the targeted soma was exposed to 12.5 μm diameter flashes (640 nm, 900 μW) of 0.8 second duration. Four consecutive flashes were delivered, each separated by 15s. The GCaMP responses to the flash of both targeted and nearby cells were imaged with a 1° field (488 nm, 25 μW) and the ΔF/F for each soma's response was averaged over the four flashes.

Results: In two cells serving cones at the foveal center, it was possible to record calcium responses in the targeted cell on single trials, a result that was repeatable in the same cells in two sessions one week apart. In the first session, the targeted cell responses showed mean ΔF/F values of 0.314 and 0.177. Nearby cells showed little or no response with a mean of 0.003 (se = 0.008, n = 52, 95% CI [-0.013, 0.018]). In the second session, the same two targeted cells gave values of 0.291 and 0.189. Nearby cells gave a mean value of 0.015 (se = 0.007, n = 66, 95% CI [0.002, 0.028]).

Conclusions: We can directly activate single RGCs in the living eye and measure the resulting calcium signal, the first step toward a method to measure the sensations produced by individual RGCs in the awake behaving monkey. Such a paradigm could also provide valuable information for RGC-based optogenetic or optoelectronic vision restoration therapies.

CONTROL ID: 3714367

SUBMITTER (NAME ONLY): Neena Haider

TITLE: Altered Transcription Kinetics Drives Save or Abort Decision for Retinal Cell fate in Retinitis Pigmentosa: Reset with Modifier Gene Therapy

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.B. Haider, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M.M. DeAngelis, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure: Neena Haider: Commercial Relationship(s);Code C (Consultant/Contractor):Ocugen | Margaret DeAngelis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) are a large group of genetically heterogeneous disorders that result in severe vision loss. Over 150 unique gene mutations in over 100 genes have been associated with RP, with high variability in disease onset, severity, and progression. Our prior and recent Ingenuity Pathway Analysis(IPA) revealed that Nr2e3 regulates several key biological networks that are critical to maintaining homeostasis in the retina including phototransduction, survival, apoptosis, immunity, oxidative stress, ER stress, neuroprotection and metabolism. In this study we determine the expression profiles of the key retinal transcription regulators such as Nr2e3, Nr1d1, neural retinal leucine zipper (Nrl), Cone-rod homeobox (Crx), retinoic acid receptor related orphan receptor alpha (Rora) and thyroid receptor beta (Thrb) in multiple RP models before and after treatment with AAV-Nr2e3 therapy.

Methods: Neonatal and developed rd1$^{-/-}$, Rho $^{-/-}$, rd16$^{-/-}$, Rho^{P23H}, and rd7 $^{-/-}$ AAV-Nr2e3 treated and untreated mice were euthanized and eyes were enucleated according to IACUC guidelines. RNA was isolated from retinas (N=7) at P0, P7, and P30. Gene expression profiling of key regulator genes were carried out by RNA Seq and quantitative real-time PCR.

Results: Overall, there is a significant downregulation in expression of key retina transcription factors in each model. This shift in turn causes misregulation of key homeostasis gene networks as disease progresses in each model. AAV-Nr2e3 therapy attenuates retinal degeneration and results in increased expression of key retinal transcription factors and reset of retina homeostasis.

Conclusions: This is the first report evaluating the impact of transcriptome kinetics on retinal degeneration. The primary mutation causes a shift of transcription kinetics, forcing the retina to make a save or abort decision early in disease, leading to progressive photoreceptor degeneration. This combinatorial mutational load including the primary mutation and key retinal transcription factor modulation determines phenotypic outcome of each disease. This study further shows the profound impact of AAV-Nr2e3 modifier gene therapy in attenuating retinal disease. This study uncovers how altered transcriptome kinetics impacts pathogenesis of retinal degeneration and therapeutic intervention resets these transcriptomes.

CONTROL ID: 3714368

SUBMITTER (NAME ONLY): Corey Lacher

TITLE: Reduced Macular Vessel Density in Glaucoma Suspects correlates with abnormal Pattern Electroretinogram Parameters and Retinal Nerve Fiber Layer Thinning

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.R. Lacher, A. Tirsi, R. Gupta, J. Tsai, V. Gliagias, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|A. Tirsi, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|D. Orshan, C. Tello, New York Institute of Technology, Old Westbury, New York, UNITED STATES|S. Tello, Rye High School, Rye, New York, UNITED STATES|P. Derr, Diopsys Inc., New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Corey Lacher: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Tirsi: Commercial Relationship(s);Code C (Consultant/Contractor):Diopsys Inc. | Derek Orshan: Commercial Relationship: Code N (No Commercial Relationship) | Rohun Gupta: Commercial Relationship: Code N (No Commercial Relationship) | Joby Tsai: Commercial Relationship: Code N (No Commercial Relationship) | Vasiliki Gliagias: Commercial Relationship: Code N (No Commercial Relationship) | Sofia Tello: Commercial Relationship: Code N (No Commercial Relationship) | Peter Derr: Commercial Relationship(s);Code E (Employment):Diopsys Inc. | Celso Tello: Commercial Relationship(s);Code C (Consultant/Contractor):Diopsys Inc.

ABSTRACT BODY:

Purpose: Recent studies have demonstrated the presence of abnormalities in the macular retinal vessels of patients with open-angle glaucoma. We performed a prospective, observational cross-sectional study to determine whether changes in macular retinal vessel density (VD) were associated with steady-state pattern electroretinogram (ssPERG) parameters, retinal nerve fiber layer (RNFL) thickness, and ganglion cell inner plexiform layer (GCL-IPL) thickness measurements in glaucoma suspects (GS).

Methods: 14 patients (19 eyes) with normal Humphrey 24-2 visual field tests, suspicious optic nerve head findings and refractive errors < ± 5.0 Diopters were enrolled in the study conducted at Manhattan Eye Ear and Throat Hospital. Participants underwent ophthalmological examination and tests on Humphrey Field Analyzer (HFA), Diopsys NOVA PERG, SPECTRALIS® OCT, and the Cirrus HD OCT-A Angioplex devices. VD of the retinal arteries was calculated using the vessel analysis plug-in on ImageJ. An inner circular boundary with a diameter of 0.6mm was used to exclude the foveal avascular zone and a 1mm (VD1mm) or 2mm (VD2mm) diameter circle was used as an outer boundary. Correlation analyses were used controlling for age and spherical equivalent.

Results: Results were gathered from 19 eyes of 14 patients aged 59.64 ± 14.16 years of age, with mean IOP 17.29 ± 3.98 and HFA 24-2 mean deviation 0.51 +/- 0.72. VD1mm was negatively correlated with FAZ area ($r=-0.684$, $p<0.01$) and positively correlated with PERG parameters Mag ($r=0.665$, $p<0.01$), MagD ($r= 0.682$, $p<0.01$) and MagD/Mag ratio ($r= 0.599$, $p<0.05$). VD1mm was also positively associated with nasal-inferior RNFL thinning, although the relationship was not significant ($r=.483$, $p=0.068$). VD2mm was positively correlated with nasal-superior RNFL thinning ($r=0.693$, $p<0.01$). No significant associations between VD and GCL-IPL thickness were found.

Conclusions: This study is the first to demonstrate that reductions in macular VD correlate with abnormal ssPERG parameters and RNFL thinning in patients with GS. Macular VD decrease was detected sooner than GCL-ILP thickness changes, which is most likely associated with early stages of disease. Further studies are necessary to determine the interactions between GCL-IPL, PERG and VD across the disease spectrum and by sectors.

CONTROL ID: 3714369

SUBMITTER (NAME ONLY): Melissa Barnett

TITLE: No Impact of Headache or Visual Impairment Adverse Events following AGN-190584 Observed on Patient Reported Outcomes

SESSION TITLE: IOLs and Presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Barnett, University of California, Davis Eye Center, Sacramento, California, UNITED STATES|S. McGee, Precision Vision, Edmond, Oklahoma, UNITED STATES|W. Pack, D. Yuan, J. Campbell, Allergan, an AbbVie company, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Melissa Barnett: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan (an AbbVie company), ABB, Acculens, Azura, Bausch+Lomb, BCLA, Bruder, Contamac, CooperVision, Dompe, EveryDay Contacts, JJVC, Mojo Vision, Novartis, Ocusoft, Oyster Point, Percept, Raayonnova, RVL Pharmaceuticals, Science Based Health, STAPLE Program, Synergeyes, Sun Pharma, Tangible Science, Tarsus, Visus, Vistakon | Selina McGee: Commercial Relationship(s);Code C (Consultant/Contractor):Allergan (an AbbVie company), Cynosure, Dompe, Horizon, Kala, Lumnenis, Novartis, Otpovue, Osmotica, Sun, Tarsus, Versant | Weston Pack: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Daisy Yuan: Commercial Relationship(s);Code E (Employment):AbbVie Inc | Joanna Campbell: Commercial Relationship(s);Code E (Employment):AbbVie Inc

ABSTRACT BODY:

Purpose: Evaluate the impact of headache or visual impairment adverse events (AEs) following active treatment with AGN-190584 on patient reported outcomes (PROs) metrics in the GEMINI 1 and GEMINI 2 phase 3 clinical trials.

Methods: Post hoc analysis of PROs stratified by headache and visual impairment (characterized as dimness of vision or jumping vision) AE occurrence were conducted on pooled data from the identical GEMINI 1 and GEMINI 2 phase 3 studies. Least squares mean (LSM) change from baseline in PRO domain scores for the Presbyopia Impact and Coping Questionnaire (PICQ) and Presbyopia Patient Satisfaction Questionnaire (PPSQ) were compared between study participants in the active treatment group (AGN-190584) who did or did not experience headache or visual impairment of special interest over the course of the 30 day clinical trials. Data were stratified by the number of lines gained (≥1, ≥2, or ≥3) in mesopic Distance Corrected Near Visual Acuity (DCNVA) at hour 3 on day 30.

Results: There were no significant differences in the PICQ and PPSQ domain LSM change scores between study participants who did or did not experience a headache AE regardless of whether the study participants achieved a ≥1, ≥2, or ≥3-line improvement in mesopic DCNVA at hour 3 on day 30. Similarly there were no significant differences in the PICQ and PPSQ domain LSM change scores between study participants who did or did not experience a visual impairment AE regardless of whether the study participants achieved a ≥1, ≥2, or ≥3-line improvement in mesopic DCNVA at hour 3 on day 30. Table 1 shows the PICQ and PPSQ results for the participants who achieved a ≥3-line improvement as that was the primary efficacy endpoint of the studies.

Conclusions: No observed differences in the domain change scores between study participants who did or did not experience AEs of headache or visual impairment suggests that these AEs did not materially impact patient reported benefits in study participants who received AGN-190584.

CONTROL ID: 3714370

SUBMITTER (NAME ONLY): Kelleigh Hogan

TITLE: Long-term levodopa treatment maintains protective effects in retinal and visual function in diabetic rodents

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hogan, R.S. Allen, M.T. Pardue, Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|K. Hogan, R.S. Allen, M.T. Pardue, Center for Visual and Neurocognitive Rehabilitation, VA Medical Center Atlanta, Decatur, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Kelleigh Hogan: Commercial Relationship: Code N (No Commercial Relationship) | Rachael Allen: Commercial Relationship: Code N (No Commercial Relationship) | Machelle Pardue: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Levodopa restores retinal dopamine levels in diabetic retinopathy and ameliorates retinal dysfunction in both rodent models and clinical studies. However, these studies involved short-term treatment prior to the onset of retinal vascular defects. In this study, we evaluated the protective effect of levodopa treatment in later stages of DR in a diabetic rat model when started after detection of early retinal dysfunction.

Methods: Hyperglycemia (≥250 mg/dL) was induced in a subset of 2-month-old male Long Evans rats via streptozotocin (STZ) injection (100 mg/kg). Oral administration of levodopa (10 mg/kg levodopa, 2.5 mg/kg carbidopa, 0.8 g/kg powdered peanut butter dissolved in 1:1 water) or peanut butter vehicle (0.8 g/kg powdered peanut butter in 1:1 water) for 5 days per week began at 6 weeks post-STZ injection and continued until 24 weeks post-STZ injection. Rats were assessed with full-field electroretinogram and optomotor response prior to STZ injection and for every 4 weeks following hyperglycemia. Mixed-effects linear regressions were used to compare the effect of diabetes and levodopa treatment on outcome measures.

Results: Levodopa treatment improved spatial frequency thresholds in diabetic rodents (n=9) relative to vehicle-treated diabetic rodents (n=9) by 30% (at 24 weeks post-STZ injection, 0.390±0.008 vs. 0.298±0.008 c/d, $p<0.001$). Levodopa similarly improved contrast sensitivity thresholds in diabetic rodents by 35% during treatment period (at 24 weeks post-STZ, 5.018±0.217 vs. 3.212±0.139 a.u., $p=0.004$). In response to dim stimuli, dark-adapted, levodopa-treated diabetic rodents had improved oscillatory potential delays compared to vehicle-treated rodents at 24 weeks post-STZ injection (57.72±1.09 vs. 67.50±2.53 ms, $p=0.008$). Oscillatory potential delays in response to dark-adapted bright stimuli were worsened by diabetes but were not improved with levodopa treatment.

Conclusions: Levodopa maintained its protective effect on retinal and visual function to 24 weeks post-STZ when vascular defects are present in the STZ-induced diabetic rat. Future work will look at vascular biomarkers to evaluate the effect of dopaminergic treatment on vascular defects in DR.

CONTROL ID: 3714371

SUBMITTER (NAME ONLY): Emma Stenz

TITLE: Outcomes of Eyes Undergoing Silicone Oil Removal Following Complex Rhegmatogenous Retinal Detachment Repair

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.C. Stenz, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|E.C. Stenz, C.C. Wykoff, S.B. Patel, Retina Consultants of Texas, Houston, Texas, UNITED STATES|C.C. Wykoff, S.B. Patel, Blanton Eye Institute, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Emma Stenz: Commercial Relationship: Code N (No Commercial Relationship) | Charles Wykoff: Commercial Relationship: Code N (No Commercial Relationship) | Sagar Patel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The use of silicone oil (SO) during rhegmatogenous retinal detachment (RRD) surgery allows for prolonged retinal tamponade. While SO removal (SOR) is performed to optimize visual function, there are incompletely defined risks such as re-detachment (re-RD) associated with SOR. The current study characterizes rates of re-RD and functional outcomes following SOR.

Methods: Data was retrospectively collected from an urban retina practice with 14 physicians. Inclusion criteria were SO placement (SOP) during an RRD repair followed by SOR from 2016-2021. Exclusion criteria were vitreoretinal surgery performed outside the practice and post-operative follow-up periods of <3 months. Analyzed parameters included epidemiological data, intraoperative variables, and post-operative outcomes. Statistical analysis included one-way ANOVA with Tukey HSD testing (significance defined as $p<0.05$).

Results: 89 eyes of 88 patients underwent SOR following ≥1 RRD repair with SOP. 77 of 89 eyes (86.5%) did not undergo further RRD surgery following SOR; of this group, 2 eyes did not achieve reattachment due to persistent subretinal fluid (SRF) and 1 eye underwent enucleation due to Proteus spp. panophthalmitis. Additional RRD repairs were required by 12 of 89 eyes (13.5%); of this group, 2 eyes received gas tamponade while 10 eyes received SOP in re-surgeries. 9 of 10 eyes receiving SOP a second time did not undergo further SOR, while 1 eye proceeded successfully with a second SOR (Table 1). Only 1 of 12 eyes experiencing an additional RRD repair remained unattached due to persistent SRF. Visual acuity (VA) among eyes without additional RRD repairs following SOR improved by 0.32logMAR from SOR (baseline VA) to final follow-up ($p<0.05$), while VA among eyes undergoing ≥1 additional RRD repair minimally improved or worsened from baseline (Table 2).

Conclusions: This study characterized re-RD rates and visual outcomes among eyes undergoing SOR after RRD repair. VA improvement was observed among eyes that did not undergo additional surgeries following SOR. Further work comparing the risks of re-RD with the functional benefits following SOR may help guide clinical management.

CONTROL ID: 3714372

SUBMITTER (NAME ONLY): Brian Lemanski

TITLE: Clinical utility of quantitative pupillometry (QP) for the detection of afferent pupillary defects (APDs)

SESSION TITLE: Functional imaging and wavefront correction

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lemanski, N. Lemanski, M. Cheng, Mabel MP Cheng MD PLLC, Schenectady, New York, UNITED STATES|

Commercial Relationships Disclosure: Brian Lemanski: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Lemanski: Commercial Relationship: Code N (No Commercial Relationship) | Mabel Cheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: APDs are a condition when there is an unequal response to a light stimulus, indicating unequal optic nerve / retinal disease. Health care providers screen for APD by performing a swinging flashlight test (SL test). However, SL test can be difficult to execute causing inter-observer variability and quantification of APD, from the author's experience, is seldom done. QP may solve shortcomings of SL test by objectively quantifying pupil responses to a light stimulus, and may have better sensitivity.

Methods: Retrospective review of 456 patients presenting for pre-surgical evaluation in a two physician cataract and refractive practice. Patients over 18 years of age without iris / pupil damage had QP via the EyeKinetix II (Konan Medical) in a room at 35 lux. Values over 0.5 on the Eyekinetix RAPD score (ERS) were considered indicative of an APD. (Note: Konan uses ERS of 0.3 for possible APD; we chose 0.5 based on instrument reproducibility tests). A subset of APD patients were referred out for additional workup with their consult letters read for documented APD.

Results: Of 456 patients, 56 had ERS above 0.5. Attributed causes: glaucoma (28), retinal detachment (5), NAION (3), Thyroid Eye Disease (2), ARMD (2), workup pending (8) and other (8) including CRAO, pituitary tumors, and multiple sclerosis. Of 36 patients referred, 4 had APD detectable by sub-specialists (smallest ERS by sub-specialist was 0.91). Subsequent workup showed all patients had abnormal visual fields, and/or clinically significant thinning of retinal nerve fiber layer and/or ganglion cell layer. Insufficient ERS threshold was observed in 3 patients with pseudotumor, 2 with strokes, and 1 with papilledema.

Conclusions: QP appears to be an indispensable tool for screening patients. While bilateral diseases may not trigger APD, elevated ERS values are strong indicators further workup is needed. QP appears more sensitive to APD detection vs health care provider SL test. Quantification of APDs by QP makes QP a useful adjunct in clinical decision-making processes for further testing (e.g. OCT, Visual Field, etc) and may make QP suitable for progression monitoring. Additional research is needed to study further benefits of QP amongst different patient populations as well as longitudinal evaluations.

CONTROL ID: 3714373

SUBMITTER (NAME ONLY): Jeremy Rogers

TITLE:

In vivo measurement of the light distribution in the focal plane of an AOSLO focused at inner and outer retina

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rogers, Morgridge Institute for Research, Madison, Wisconsin, UNITED STATES|N. Stangel, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|A. Dubra, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Jeremy Rogers: Commercial Relationship: Code N (No Commercial Relationship) | Nickie Stangel: Commercial Relationship: Code N (No Commercial Relationship) | Alfredo Dubra: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

Adaptive Optics Scanning Light Ophthalmoscopy (AOSLO) provides exceptional contrast of cone photoreceptor outer segments using reflectance confocal imaging due to the high reflectivity afforded by the cone geometry. Imaging modalities that provide contrast of other structures is more challenging, but nonconfocal split detection has proven effective at imaging inner segments and vasculature, and has been used to image Retinal Pigment Epithelium and ganglion cells. However, optimizing the detection geometry remains a largely brute force effort of trial and error. We hypothesize that measurement of the distribution of light in the focal plane at different retinal layers would provide valuable guidance for designing detector geometry to optimize contrast in retinal structure of interest.

Methods:

We previously demonstrated a custom microscope using a descanned imaging detector for ex vivo imaging that allowed exploration of image contrast by creating virtual nonconfocal geometries in post processing. While image sensors are far too slow to image the light distribution at each pixel in an AOSLO image in vivo, measurement of the statistical distribution of light is possible. A scientific CMOS operating at 13kHz frame rate (small ROI) was placed at the confocal image plane of an AOSLO using an integration time of 39us. A human subject was imaged with the AOSLO focused on photoreceptors (Fig. 1a) and inner retina (Fig. 1b) at 2 degrees temporal from the fovea. Each frame captured approximately half of the period of the 13kHz resonant scanner. Intensity thresholds were used to select only the frames corresponding to the pixels at the edge of the AOSLO image (Fig. 1c).

Results:

The average intensity (Fig. 1d-e) and coefficient of variation (Fig. 1f) are shown. The mean intensity peak drops when focused at the inner retina as expected and the distribution is broader. Since the the signal must vary as across pixels to produce image contrast, the coefficient of variation is used as an indication of contrast. C.V. is higher at the center when focused on photoreceptors, but when focused on the inner retina, the C.V. is higher at larger detector seperations.

Conclusions:

Measurement of the light distribution at the AOSLO focal plane is possible with a descanned CMOS detector and can provide guidance to optimize detection geometry for improved nonconfocal detection at different retinal layers.

CONTROL ID: 3714375

SUBMITTER (NAME ONLY): Peter Lwigale

TITLE: BMP3 suppresses embryonic corneal myofibroblast phenotype by promoting focal adhesion turnover and αSMA fiber disassembly

SESSION TITLE: Corneal stromal biology, wound healing modulators, and regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Lwigale, J. Spurlin, Biosciences, Rice University, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Peter Lwigale: Commercial Relationship: Code N (No Commercial Relationship) | James Spurlin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Acute damage to the cornea often initiates drastic tissue remodeling, resulting in fibrotic scarring that disrupts light transmission and precedes vision impairment. Very little is known about the factors that can mitigate fibrosis and promote scar-free cornea wound healing. Here, we sought to elucidate the mechanistic regulation of transient myofibroblast differentiation during scar-free embryonic cornea wound healing.

Methods: Wounded embryonic chicken corneas were analyzed for BMP and TGFβ ligand expression by qPCR and in situ hybridization. Signal transduction of these pathways was assessed by immunohistochemical staining for respective pSMADs on histological sections of healing embryonic tissues. Primary chick embryonic keratocytes were stimulated with recombinant BMP and TGFβ ligands to determine induction and turnover of the myofibroblast phenotype.

Results: We found that alpha-smooth muscle actin (αSMA)-positive myofibroblasts are superficial and their presence inversely correlates with wound closure. Expression of TGFβ2 and nuclear localization of pSMAD2 were elevated during myofibroblast induction. BMP3 and BMP7 were localized in the corneal epithelium and corresponded with pSMAD1/5/8 activation and absence of myofibroblasts in the healing stroma. In vitro analyses with primary keratocytes revealed that BMP3 inhibits the persistence of TGFβ2-induced myofibroblasts by promoting disassembly of focal adhesions and αSMA fibers. This was confirmed by the transient expression of vinculin in vivo.

Conclusions: Our data highlight a novel mechanism to inhibit myofibroblast persistence during cornea wound repair. Myofibroblasts are transient in wounded embryonic corneas and correlate with upregulation of pSMAD1/5/8. Stability of αSMA fibers in cultured myofibroblasts requires mature focal adhesions. BMP3 drives the disassembly of αSMA stress fibers by promoting the dissolution of focal adhesion complexes.

CONTROL ID: 3714376

SUBMITTER (NAME ONLY): Kiara Eldred

TITLE: Mechanisms of DNA-methyl aging in trisomy 21 human and mouse retina

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Eldred, T. Reh, Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|S. Horvath, Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Kiara Eldred: Commercial Relationship: Code N (No Commercial Relationship) | Steve Horvath: Commercial Relationship(s);Code E (Employment):UC Regents;Code F (Financial Support):Epigenetic Clock Development Foundation | Thomas Reh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aging is a leading risk factor for retinal degenerative disease. A better understanding of the mechanisms of aging could lead to treatments for age-related retinal disease. When DNA methylation patterns are observed genome wide over the course of an individual's lifetime, these marks change in a predictable way, and can be used to generate a DNA methyl-aging clock (DNAmA Clock) in humans and mice. Trisomy of the 21st chromosome (T21) causes premature aging and early onset of age-related retinal diseases including cataracts, macular degeneration and glaucoma. Adults with T21 have also been shown to have an accelerated DNAmA Clock. We show that age acceleration of T21 tissues already occurs in the fetal retina. If we can better understand the molecular mechanisms of accelerated aging in T21 individuals, we may be able to better understand mechanisms of age-related retinal diseases in both T21 and normal individuals.

Methods: To identify the DNA-methyl age, we extract genomic DNA and profile the CpG methylated regions using the Infinium MethylationEPIC Kit for human samples or the mammalian methylation array developed by Arneson et al., 2021 for mouse samples. We then calculate the DNA-methyl age based on comparison to the Horvath Pan-Tissue clock. We apply this assay to normal and T21 human retina, and normal and T21 mouse retina and other tissues. We use the mouse model of T21 called Ts65Dn.

Results: We observe a robust DNA-methyl age acceleration in T21 fetal human retinal samples when compared to age matched controls. To further understand the region of the 21st chromosome that is important for age acceleration, we perform similar analysis of the retina from the Tn65Dn mouse model of T21, and also observe robust age acceleration in Tn65Dn mice compared to controls. Other tissues in Tn65Dn mice at various ages also show an accelerated aging profile in the Horvath Pan-Tissue clock.

Conclusions: We show that the DNAmA Clock is accelerated in the fetal retina of humans with T21. Additionally, mice with a homologous region of the human 21st chromosome have an accelerated DNAmA Clock. These results indicate that the age-acceleration that occurs in T21 humans is also present in mice and will allow future studies to better understand the molecular basis of age acceleration and potentially develop new approaches to age-related disorders, such as macular degeneration.

CONTROL ID: 3714380

SUBMITTER (NAME ONLY): Laura Moreno Leon

TITLE: A MiniCEP290 gene replacement therapy to treat CEP290-Leber congenital amaurosis (LCA10)

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Moreno Leon, B. Sahu, H. Khanna, Research and Development, Iveric Bio, Cranbury, New Jersey, UNITED STATES|W. Zhang, G. Gao, Gene therapy center, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Laura Moreno Leon: Commercial Relationship(s);Code E (Employment):Iveric Bio | Wei Zhang: Commercial Relationship(s);Code E (Employment):Intergalactic Therapeutics | Bhubanananda Sahu: Commercial Relationship(s);Code E (Employment):Iveric Bio | Guangping Gao: Commercial Relationship: Code N (No Commercial Relationship) | Hemant Khanna: Commercial Relationship(s);Code E (Employment):Iveric Bio

ABSTRACT BODY:

Purpose: Leber congenital amaurosis (LCA) is a debilitating eye disorder and is considered one of the most severe forms of retinal degeneration causing severe vision loss at infancy. Mutations in CEP290 (LCA10) are the most frequent cause of LCA and account for > 26% of all cases. Adeno-associated viral (AAV) vectors are currently the most efficient vectors for gene delivery to the retina. However, the CEP290 gene is too large to be packaged into standard AAV vectors, creating a challenge for the development of a LCA10 gene therapy. We designed a mutation-independent gene therapy delivered with an AAV vector to treat LCA10.

Methods: We designed shorter versions of CEP290 (miniCEP290) under photoreceptor-specific promoters that can be delivered using AAV vectors. Cep290-mutant mice ($Cep290^{rd16}$) were injected in the subretinal space at postnatal 10 days. Photoreceptor response to light was measured by electroretinography (ERG). Retinal structure and protein trafficking were evaluated by immunofluorescence using specific marker antibodies.

Results: After demonstrating the efficiency of a CEP290 minigene [CEP290 amino acid 580-1180 domain] under the control of a ubiquitous promoter to enhance function and survival of photoreceptors in neonatal $Cep290^{rd16}$ only until 5 weeks of age, this current study ‘s goal was to improve the efficacy of the miniCEP290 approach and optimize protein expression. We show that the expression of CEP290-580-1180 under the control of the rhodopsin kinase promoter improved the ERG response for both rod and cone photoreceptors by ~1.5 folds. Further, modification of the miniCEP290 gene construct with different CEP290 domains improved the photoreceptor structural and functional rescue by ~500% in the $Cep290^{rd16}$ mice. We also show that the expression of the new miniCEP290 prolonged the survival and improved the protein trafficking defects, in transduced photoreceptors.

Conclusions: Our preliminary results indicate that miniCEP290 approach with conventional AAV vectors may have the potential for mutation-independent gene therapy in LCA10 patients. These studies may also pave the way to develop new minigene therapies for retinal degenerative diseases caused by mutations in other large genes including Stargardt disease and Usher Syndrome, which are not currently amenable to treatment using conventional AAVs.

CONTROL ID: 3714385

SUBMITTER (NAME ONLY): John Lillvis

TITLE: Evaluation of refractive error in a geographically isolated population may reveal unique risk factors associated with visual disability

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lillvis, C. Zhang, M.M. DeAngelis, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|L. Owen, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|T. Shaikh, Pediatrics, University of Colorado Health, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: John Lillvis: Commercial Relationship: Code N (No Commercial Relationship) | Charles Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Leah Owen: Commercial Relationship: Code N (No Commercial Relationship) | Tamim Shaikh: Commercial Relationship: Code N (No Commercial Relationship) | Margaret DeAngelis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The Democratic Republic of Timor-Leste is a geographically isolated but ethnically diverse population. Prior research has shown that ocular disease in Timor-Leste varies from developed countries. Although uncorrected refractive error is a common cause of low vision in this population, the types and prevalence of refractive error has not been well characterized.

Methods: Individuals ≥40 years were recruited from Timor-Leste via a population-based cross-sectional survey using multistage cluster random sampling described previously. Autorefraction was performed as part of a full eye examination which included magnified examination of the anterior segment and dilated indirect ophthalmoscopy. Data on age, gender, height, weight, and smoking status were obtained. Descriptive statistics were calculated in Excel and regression analyses were performed using R.

Results: Autorefraction was performed on 578 individuals ≥40 years (273 males, median 52 years). After excluding eyes with cornea or lens opacities, refraction data were available for 1051 eyes (526 OD, 525 OS) of 552 individuals. Spherical equivalent (SE) ranged from -7.5 to 10.12 D. Myopia (SE ≤-1.0D), hyperopia (SE ≥ 1.0 D), and astigmatism (|cylinder| ≥ 1.0 D) were present in 236 (22.4%), 120 (11.4%), and 238 (22.6%) eyes, respectively. Anisometropia (≥ 1.0 D) was present in 17.8% of individuals where autorefraction was available for both eyes. Moderate myopia (3-6 D), high myopia (≥6 D), and high hyperopia (≥3 D) were found in 70 (6.6%), 9 (<1%), and 6 (<1%) eyes, respectively. Neither the presence nor degree of myopia were associated with increased education, BMI, or smoking status, but both were associated with increasing age.

Conclusions: Characterization of refractive error in the Timorese shows a lower prevalence of myopia than developed countries such as the United States or Singapore but the prevalence is comparable to similar populations in Southeast Asia/Oceania. Specifically, the observed prevalence of 22% was nearly identical to that found in individuals ≥40 years in a rural population on Sumatra. Similar to the Sumatran population, prevalence of myopia increased with older age in the Timorese, possibly related to cataract formation. Further work is ongoing to determine the contributions of both environmental factors and genetics on the low prevalence of myopia identified in the Timorese.

CONTROL ID: 3714386
SUBMITTER (NAME ONLY): Daniel Chung
TITLE: Neural Adaptation with Wavefront Guided Scleral Lenses for Keratoconus
SESSION TITLE: Functional imaging and wavefront correction
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D. Chung, J.D. Gelles, S. Greenstein, N. Brown, A. Guevara, P. Hersh, Cornea and Laser Eye Institue-Hersh Vision Group, CLEI Center for Keratoconus, Teaneck, New Jersey, UNITED STATES|J.D. Gelles, S. Greenstein, P. Hersh, Rutgers New Jersey Medical School Institute of Ophthalmology and Visual Science, Newark, New Jersey, UNITED STATES|
Commercial Relationships Disclosure: Daniel Chung: Commercial Relationship: Code N (No Commercial Relationship) | John Gelles: Commercial Relationship(s);Code C (Consultant/Contractor):Ovitz, Contamac | Steven Greenstein: Commercial Relationship: Code N (No Commercial Relationship) | Nick Brown: Commercial Relationship(s);Code E (Employment):Ovitz | Andres Guevara: Commercial Relationship(s);Code E (Employment):Ovitz | Peter Hersh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report on visual performance over time with traditional scleral lens (tSL) and wavefront-guided scleral lenses (wfgSL) in patients with keratoconus (KC).
Methods: 11 eyes of 8 patients diagnosed with KC were fit with a tSL. After the tSL was finalized, a comprehensive wavefront aberrometry system (X-Wave, Ovitz, Rochester, NY) was used to create a wfgSL (ARES, Ovitz, Rochester, NY). A crossover was performed, best-corrected lens visual acuity (BCLVA) and total higher-order root mean square (HORMS) were compared between the tSL and wfgSL at dispense and after 1-month of lens wear.
Results: When comparing wfgSL to tSL, at dispense, there was a 0.1 ± 0.1 logMAR ($p < 0.01$) improvement in BCLVA and a 0.58 ± 0.29 μ ($p < 0.01$), a 49 ± 13% improvment in HORMS. At 1-month follow-up there was a 0.2 ± 0.1 logMAR improvement ($p < 0.01$) in BCLVA and a 0.54 ± 0.20 μm ($p < 0.01$), a 48 ± 9% improvement in HORMS. No eyes lost lines of visual acuity at dispense or at the 1-month follow-up.

At dispense of the wfgSL, 3 of 11 eyes showed no improvement in BCLVA. At 1-month follow-up, all 3 eyes showed a 0.1 logMAR improvement without additional improvement in HORMS.

Of note, at the dispense of the wfgSL, 1 of the 11 eyes showed a 0.1 logMar improvement in BCLVA, and at the 1-month follow-up, the same eye showed an additional 0.3 logMar lines and a 0.22 μ, 12% improvement in HORMS. Post analysis of this improvement correlated to lens malposition at dispense and correct positioning at the 1-month follow-up.
Conclusions: When compared with tSL, wfgSL reduced HORMS and improved BCLVA. One month after initiating wfgSL wear, BCLVA continued to improve at the follow-up visit without change in HORMS. This improvement is likely secondary to neural adaptation to wfgSL optics. Further studies are needed to understand the role of neural adaptation in wfgSL.

CONTROL ID: 3714387

SUBMITTER (NAME ONLY): Allison Grenell

TITLE: Sorsby Fundus Dystrophy (SFD)-associated mutations in Tissue Inhibitor of Metalloproteinase 3 (Timp3) leads to metabolic dysfunction in the RPE and Retina.

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.B. Grenell, B. Anand-Apte, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|A.B. Grenell, A.D. Benos, B. Anand-Apte, Ophthalmic Research, Cleveland Clinic, Cleveland Clinic, Cleveland, OH, US, health/system, Cleveland, Ohio, UNITED STATES|C. Singh, Division of Gastroenterology, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|C. Singh, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Du, Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|H. Brunengraber, Nutrition, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although it is well established that photoreceptor death underlies retinal degeneration (RD), the pathological mechanism(s) remain unclear. We hypothesize that aberrant energy metabolism in the retinal pigment epithelial (RPE), results in nutrient deprivation in the retina and contributes to pathology in SFD.

Methods: Proteomic and metabolic analysis of RPE and retinas from mice expressing S179C TIMP3 and age-matched littermate controls was performed. To directly explore metabolic alterations, targeted metabolomics was performed via gas chromatography-mass spectroscopy (GC-MS) with $^{13}C_6$ glucose isotopic tracing on murine SFD RPE and retina. Retina and RPE were isolated and separately incubated in media containing $^{13}C_6$ glucose for 24 hours following which intra and extra cellular metabolites were extracted with 70% methanol. Metabolite abundance and isotopic distribution of metabolites were quantified using GC/MS and Agilent MassHunter. Finally, IsoCor software was used to correct for natural isotopic abundance.

Results: Proteomic analysis identified changes in several metabolic pathways suggesting metabolic dysfunction in TIMP3 S179C RPE.Targeted metabolomics demonstrated an increased abundance of extracellular M3 labeled lactate along with intracellular TCA cycle intermediates, indicative of increased RPE glycolytic flux, suggesting metabolic dysfunction. Mass isotopic distributions reveal minimal changes which suggests that TCA flux (reflective of rate of metabolite production and breakdown) is unperturbed. In the retina, we observed decreased M3 lactate enrichment intracellularly, characteristic of decreased glycolytic flux. A decrease in abundance of retinal intracellular TCA cycle intermediates was also observed with increased enrichment of M4 glutamate, M3 fumarate and M3 malate. This suggests major perturbation of TCA cycle operations.

Conclusions: In mice expressing SFD-associated Timp3 mutations, the RPE and retina both display aberrant energy metabolism. RPE exhibits an increased glycolytic flux while the retina shows a decreased glycolytic flux along with increased TCA cycle flux. This adds to the growing body of evidence implicating metabolic dysfunction in retinal degeneration and opens the door to unique hypotheses of metabolic changes following extracellular matrix disruptions.

CONTROL ID: 3714388

SUBMITTER (NAME ONLY): Samuel Adade

TITLE: Neural recordings of extraocular muscle motoneurons do not show evidence for selective innervation of muscle compartments

SESSION TITLE: Neurophysiology and Treatments of Binocular Vision Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Adade, V.E. Das, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Samuel Adade: Commercial Relationship: Code N (No Commercial Relationship) | Vallabh Das: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Selective innervation of extraocular muscle (EOM) compartments may explain the observation made via MRI that certain horizontal recti compartments may contribute to specific vertical eye movements such as vertical vergence and that not all compartments of the cyclovertical EOMs contribute to all vertical eye movements. We investigated the discharge characteristics of EOM motoneurons (MN) during vertical vergence and vertical smooth-pursuit for evidence of selective innervation of EOM compartments. Our hypothesis was that selective innervation of compartments would manifest as a sub-population of horizontal MN that are modulated during vertical vergence and a sub-population of cyclovertical MNs that are modulated during vertical smooth-pursuit but not vertical vergence.

Methods: We recorded from all EOM MN populations in the abducens, oculomotor and trochlear nuclei as two non-human primates performed vertical vergence and vertical smooth-pursuit. The relationship between MN firing rate and horizontal/vertical eye parameters of the innervated eye during each task was determined using multiple linear regression analysis by fitting the data to the equation FR= K_v*(vert. eye pos.) + K_h*(horiz. eye pos.) + R_v*(vert. eye vel.) + R_h*(horiz. eye vel.) + B. Position (K_h, K_v) and velocity sensitivities (R_h, R_v) were considered significant if the 95% confidence interval did not include zero.

Results: We did not find different subpopulation of EOM MNs with different responses during vertical eye movement tasks where some EOMs compartments have been previously found to contract and relax differentially. Thus 28 of 30 abducens MN recorded showed no significant modulation in relation to vertical eye position during vertical vergence and all 30 cells did not modulate during vertical smooth-pursuit. All 149 cyclovertical MN in our sample discharged in relation to vertical eye position during vertical smooth-pursuit (Mean K_v = 4.7 spk/s/°). 147 out of the 149 cyclovertical MN (35/35 IO, 27/27 SO, 41/41 SR, and 44/46 IR) modulated during vertical vergence with mean K_v of 6.2 spk/s/°. Analysis of medial rectus MNs is ongoing.

Conclusions: Our data suggests that the EOM compartments are not selectively innervated and the observed differential contractility of EOM compartments is due to other mechanisms.

CONTROL ID: 3714389

SUBMITTER (NAME ONLY): Yuanyuan Chen

TITLE: Pharmacological study of retinal degeneration

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|Y. Chen, Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Yuanyuan Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Photoreceptor degeneration leads to acquired blindness, and it is common in conditions such as retinitis pigmentosa, retinal toxicity, and age-related macular degeneration. Drugs that protect the retina from photoreceptor loss are much needed, as most retinal degenerative diseases have no treatment. We aim to seek effective pharmacological treatments to prevent retinal degeneration using target-based and phenotypic strategies.

Methods: Lead compounds were identified using small molecule drug screening targeting rhodopsin homeostasis, and one compound was identified from aging studies in other organs. The leads were tested firstly in immortal mammalian stable cells in vitro, and they were then studied using retinal explant culture. Finally, the most efficacious compounds were studied in vivo using systemic or intraocular administrations to rodent models of retinal degeneration ($Rho^{P23H/+}$ knock-in mice and aged Fischer344 rats). Efficacy and mechanism of actions of compounds were evaluated using combined methods of electroretinogram (ERG), optic coherence tomography (OCT), immunohistochemistry, RNA-seq, and immunoblots.

Results: Three types of retinal protecting agents were identified: 1) non-retinoid chaperones of rhodopsin; 2) selective inducers of misfolded rhodopsin clearance; and 3) anti-aging purine metabolite against age-related photoreceptor degeneration.

Conclusions: We showed proof-of-principle evidence that photoreceptor degeneration due to RHO misfolding mutations can be rescued by restoring proteostasis using small molecule chaperones or inducers of misfolded protein clearance. Age-related photoreceptor loss can be rescued by oral administration of an anti-aging purine metabolite.

CONTROL ID: 3714390

SUBMITTER (NAME ONLY): Steven Maskin

TITLE: Rete Ridge Structures Form Meibomian Gland Distal External Duct Wall and Basal Epithelial Layer

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Maskin, Dry Eye and Cornea Treatment Center, Tampa, Florida, UNITED STATES|

Commercial Relationships Disclosure: Steven Maskin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate potential relationship between lid margin rete ridges (RR) and meibomian gland (MG) external duct wall.

Methods: Retrospective volume evaluations of upper lid margin confocal microscopy (CFM) at 2 micron depth intervals down to 120 um depth to evaluate spatial relationships between above structures. Eight glands from eight lids of eight patients (M:F = 1:7) whose average age was 51.1 (range 26-74 years) were evaluated.

Results: Each confocal evaluation demonstrated typically round RR in peri-orifice position undergoing morphologic differentiation with progressive depth characterized by ovalization and flattening. The dermal – epidermal basement membrane of the RR differentiates into the MG extermal duct wall while the epithelial cell projections of the RR become the basal epithelial layer.

Conclusions: Rete Ridge examination using volume CFM indicates a role of these structures in the development of the MG external duct wall and basal epithelium. As the RR is known to provide stem cell activity in skin, this finding strongly suggests the RR is likely to provide similar activity for MG.

CONTROL ID: 3714394

SUBMITTER (NAME ONLY): Michael Landowski

TITLE: A Novel Function of Transmembrane Protein 135 in Peroxisomal Homeostasis

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Landowski, V. Bhute, S. Grindel, Z. Haugstad, S. Ikeda, A. Ikeda, Department of Medical Genetics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|M. Landowski, S. Ikeda, A. Ikeda, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Michael Landowski: Commercial Relationship: Code N (No Commercial Relationship) | Vijesh Bhute: Commercial Relationship: Code N (No Commercial Relationship) | Samuel Grindel: Commercial Relationship: Code N (No Commercial Relationship) | Zachary Haugstad: Commercial Relationship: Code N (No Commercial Relationship) | Sakae Ikeda: Commercial Relationship: Code N (No Commercial Relationship) | Akihiro Ikeda: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Transmembrane Protein 135 (Tmem135) is critical for controlling retinal aging in mice. For example, Tmem135 mutant mice develop age-dependent photoreceptor pathologies whereas mice overexpressing wild-type Tmem135 (Tmem135 TG) display age-dependent RPE pathologies. Changes in mitochondrial dynamics correlate with the ocular pathologies in Tmem135 mutant and TG retinas, but the molecular mechanism of how Tmem135 maintains mitochondrial dynamics is unknown. It has been shown that peroxisomal changes can affect mitochondrial dynamics. In this study, we investigated whether peroxisomal changes are observed in Tmem135 mutant and TG mice.

Methods: Tissues including the neural retina, eyecup, liver and heart were collected from 10-week-old WT, Tmem135 mutant, and Tmem135 TG mice for Western blot analysis and immunohistochemistry to assess peroxisomal membrane protein 70 (PMP70), an indicator of peroxisome number. Additional tissues were collected for lipidomics to assess peroxisomal function.

Results: We found increased PMP70 in the neural retinas and eyecups of Tmem135 mutant mice. In contrast, PMP70 was decreased in the neural retinas and eyecups of Tmem135 TG mice. We analyzed our retinal lipidomics datasets for lipids derived from peroxisomal products such as those containing long-chain polyunsaturated fatty acids (PUFAs) (i.e. C22:5 and C22:6). Strikingly, 62.5% of the downregulated lipids in the Tmem135 mutant retinas contained either C22:5 or C22:6 PUFAs. In contrast, 46% of the upregulated lipids in the Tmem135 TG retinas contained either C22:5 or C22:6 PUFAs. We confirmed these peroxisomal changes in the livers and hearts of Tmem135 mutant and TG mice.

Conclusions: Our results indicate peroxisome number was inversely-correlated with the amount of functional TMEM135. The changes in peroxisome numbers were associated with global lipidome alterations in Tmem135 mutant and TG retinas. In particular, the concentrations of lipids containing C22:5 or C22:6 PUFAs were correlated with the amount of functional TMEM135, suggesting TMEM135 has a role in peroxisomal PUFA metabolism. Together, our study indicates the importance of TMEM135 in peroxisomal homeostasis that may contribute to retinal mitochondrial dynamics and aging in the murine retina.

CONTROL ID: 3714395

SUBMITTER (NAME ONLY): Ekaterina Lobanova

TITLE: Impaired activity of Sterol Regulatory Element-binding Proteins modifies phospholipid composition of the retina

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Lobanova, Y. Wang, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|M.G. Agbaga, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|J. Ellis, East Carolina University, Greenville, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Ekaterina Lobanova: Commercial Relationship: Code N (No Commercial Relationship) | Jessica Ellis: Commercial Relationship: Code N (No Commercial Relationship) | Yixiao Wang: Commercial Relationship: Code N (No Commercial Relationship) | Martin-Paul Agbaga: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Significant evidence supports the benefits of consuming omega-3 fats, i.e., phospholipids containing DHA (Docosahexaenoic Acid), for human health. DHA is highly concentrated in the brain and retina despite the fact that it cannot be synthesized in these tissues and has to be transported across the blood-brain and blood-retina barrier (BRB). Mechanisms responsible for DHA transport and its retention behind BRB are poorly defined. Previous studies showed that disruption of lysophosphatidylcholine transport leads to DHA depletion, which was accompanied by upregulation of transcriptional factors, the Sterol Regulatory Element-binding Proteins (SREBPs), and might hint at their potential role in the regulation DHA levels. Here, we used mouse genetics to probe the contribution of basal activity of SREBPs in setting the fatty acid composition of phospholipids in the retina.

Methods: To impair SREBPs' activity, we knocked out SREBP cleavage-activating protein (SCAP) specifically in the retina. The phospholipid and fatty acid analysis was performed using mass spectrometry. The retinal health, function, and structure were assessed with Optical Coherence Tomography (OCT), fluorescein angiography, electroretinography (ERG), and immunostaining. RNAseq was used to study transcriptional changes.

Results: Lipidomics analysis of retina-specific SCAP knockout mice showed reduced levels of docosahexaenoic (DHA), arachidonic (AA), and monounsaturated (MUFA) fatty acids, resulting in a simpler fatty acid profile with higher content of saturated fatty acids. Removal of SCAP also led to progressive thinning of the retina and vasculature defects reminiscent of Retinal Angiomatous Proliferation (RAP). Changes in fatty acid composition were different from mice which lack a receptor protein Mfsd2a transporting lysophosphatidylcholine.

Conclusions: We found that the basal activity of SREBPs in the retina contributes to the fatty acid composition of retinal membranes. The lipid profile of membranes is critical for retinal health and maintenance of the vasculature network. The findings support the rationale to study the role of SREBP transcriptional factors in lipid metabolism in the retina.

CONTROL ID: 3714398

SUBMITTER (NAME ONLY): Brenna Hefley

TITLE: Characterization of tear extracellular vesicles in keratoconus

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Hefley, D. Karamichos, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|B. Hefley, D. Karamichos, Pharmaceutical Science, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|A. Khan, K. Riaz, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|C. Deighan, NanoView Biosciences, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Keratoconus (KC) is a progressive, vision-threatening disease that is characterized by the thinning and bulging of the cornea. KC is found in both sexes and presents in second decade of life. Extracellular vesicles (EVs) are membranous structures that are shed from the plasma membrane or originate from the endosomal system. EVs transfer information, such as RNA and proteins, from one cell to another. We sought to describe and investigate morphology and biochemical signatures of EVs in tear film isolates from KC patients.

Methods: Tears were collected from 10 healthy (5 males and 5 females) and 9 KC (4 males and 5 females) subjects. Tear samples were collected passively from the lateral meniscus of the eye using a glass capillary tube. Samples were processed and analyzed using the ExoView^{TM} R100.

Results: Analysis demonstrated that KC tears had higher CD9+ and CD63+ than Healthy tears. KC had lower CD81+ than tears from healthy subjects. KC had higher CD81/CD9 colocalization than healthy. KCs had lower CD63/CD9 colocalization than healthy. KCs have lower CD63/81 when compared to healthy. Healthy and KC samples had the same expression of triple colocalization, CD63/CD81/CD9. Sex stratification revealed both KC males/females having higher CD9+ and CD63+ than healthy males/females. KC females had lower CD81+ than healthy females and KC males had a higher CD81+ populations when compared to healthy males. Our data also showed that KC males/females had higher colocalizations of CD81/CD9 when compared to healthy males/females. KC females also showed lower colocalization of CD63/81 than healthy females. KC males had higher colocalization of CD63/CD81 compared to healthy males. KC males/females had lower CD63/CD9 than healthy males/females. KC females had higher CD63/CD81/CD9 than healthy females and KC males had lower CD63/CD81/CD9 than healthy males. Both Healthy and KC derived EVs had a diameter range of 50 to 200nm, with the majority being between 50 and 80 nm suggesting a majority of exosome population and a minor population of apoptotic vesicles.

Conclusions: For the first time, we were able to isolate and characterize tear EVs from KC subjects. The differences described suggest that there is a distinct phenotype present in KC-derived tear EVs when compared to healthy samples. Knowledge of these EV findings may help researchers and clinicians for future diagnosis and management of KC patients.

CONTROL ID: 3714399

SUBMITTER (NAME ONLY): JOE XING

TITLE: Retinal Task Detection and Image Perception using End-to-end Deep Neural Network (DNN) based Algorithms

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhang, E.A. Rossi, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J. XING, C. Walshe, C.K. Sheehy, C. Light Technologies, Inc., Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: To establish an end-to-end data-driven learning method that detects retinal tasks and image landmarks to determine SLO-based retinal tracking results

Methods: We present a novel method for SLO-based systems to automatically detect eye motion task paradigms and retinal landmarks on image data, such as foveal localization, utilizing a fully data driven, end-to-end DNN based algorithm. Our DNN approaches were tested using a 99-subject concussion/control database collected at the University of Pittsburgh for both fixation and saccade tasks. The task-based detection results aimed to localize the fovea, as well as identify the stimulus target positions of each video sequence to be used for task sorting. These detection results were evaluated and compared with “strip-registration” based approaches to quantify model performance.

Results: Preliminary results of model performances were measured using the IoU (intersection over union) metric by comparing DNN predictions of landmarks on the image with the annotated ground truth. We demonstrate a precision metric of >0.9 and a recall metric of >0.9 for each prediction of certain visual landmarks on the image, which gives an overall mean Average Precision (mAP) >50 for the sorting of retinal motion tasks. This detection approach has a great generalizability for different types of landmark detections following the same supervised training pipeline. We experimented on detecting different types of objects in the image with minimum amounts of training data, on the order of 10 SLO images, by utilizing the concept of “Transfer Learning” with most of the neurons in the DNN pretrained using ImageNet. By doing this, we improved the requirement on training data size and data annotation efforts.

Conclusions: The use of DNN algorithms to extract latent features of SLO videos with supervised training demonstrates exquisite classification and prediction power while alleviating the limitations of manual feature engineering. A generalized data-driven approach to learn the data representation automatically is of the utmost importance to consider the latent features embedded in SLO videos. Future applications of this technique will be applied to quantify saccadic latency to differentiate concussed vs. healthy control subjects.

CONTROL ID: 3714400

SUBMITTER (NAME ONLY): Nickolai Nilsen

TITLE: The diurnal relationship of axial length and choroidal thickness in winter and summer.

SESSION TITLE: Myopia and refractive error development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Nilsen, H. Pedersen, L.A. Hagen, J. Stuart, R.C. Baraas, Department of Optometry, Radiography and Lighting Design, Universitetet i Sorost-Norge, Kongsberg, Viken, NORWAY|

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ABSTRACT BODY:

Purpose: Diurnal and seasonal variations in daylight have been implicated in ocular growth (Hagen, Sci. Rep. 2018, 8(1), 1-10.; Ulaganathan, Exp. Eye Res. 2019. 189). The aim of this study was to explore the diurnal relationship between axial length and choroidal thickness in humans in winter and summer at 60° latitude North.

Methods: Twenty-four ocular healthy participants (age 17-24 yrs, 11 males), with logMAR visual acuity ≤0.00 and stereo acuity of ≤120” were included and measured in Southern Norway during the winter (6 hours of daylight/day) and summer (18 hours of daylight/day). On day 1, an actigraph was handed out to the participants to collect habitual sleep times (HST) over a 7-day period. Individual HST and self-reported habitual wake up time were used to calculate the timing of 9 rounds of measurements on day 8. Each round consisted of accommodation washout (15 min), OCT imaging (Heidelberg Spectralis OCT2 EDI) and axial length (AL) measurements (Zeiss IOLMaster 700). The central 1 mm choroid (CT) was segmented with custom-made software using an active-contour method. A sinusoid, with a period of 24 hours, was fit to the data (AL and CT) with an non-linear mixed effects model to estimate the MESOR, amplitude and phase, and determine the seasonal effect of these parameters.

Results: AL ranged from 21.26 to 27.53 mm and CT ranged from 90 to 659 mm. Increasing AL correlated with thinner CT in winter and summer (R^2=0.42, p<0.0001, R^2=0.38, p<0.0001, respectively). AL and CT underwent significant diurnal variations both in winter and summer (one-way ANOVA, p<0.0001). MESOR AL increased significantly from winter to summer (Δ0.045 mm, p<0.0001) whereas MESOR CT did not change. AL and CT acrophase was 12 hours out-of phase in winter and there was a significant acrophase advance for AL only, about 90 min earlier in the summer (p<0.05).

Conclusions: The results show that the diurnal rhythms of AL and CT are in anti-phase in winter, but because there is no evidence for a seasonal change in the diurnal rhythm of CT between winter and summer, we find instead that there is a shift in the relationship between acrophase of AL and CT in summer related to seasonal changes of AL only.

CONTROL ID: 3714401

SUBMITTER (NAME ONLY): Elias Pavlatos

TITLE: Combining OCT Corneal Topography and Thickness Maps to Diagnose Keratoconus Using a Convolutional Neural Network

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pavlatos, D. Huang, Y. Li, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To design a convolutional neural network (CNN) for keratoconus detection using optical coherence tomography (OCT) corneal topography and thickness maps.

Methods: Normal subjects (n = 52) and patients with either keratoconus (n = 131) or contact lens-related warpage (n = 20) were recruited. Keratoconus eyes were divided into 3 groups: 1) Manifest (n = 89): slit-lamp or topographic signs of keratoconus and corrected distance visual acuity (CDVA) < 20/20, 2) Subclinical (n = 16): topographic signs of keratoconus but CDVA ≥ 20/20, and 3) Forme fruste (n = 26): normal-appearing eye with keratoconus in the contralateral eye. The central 6mm of the cornea was imaged using a radial OCT scan pattern (Avanti, Optovue Inc.), and maps of pachymetry, epithelial thickness, anterior surface mean curvature, and posterior surface mean curvature were generated (Li et al, Ophthalmology, 2012; Pavlatos et al, BOE, 2020; Figure 1). All maps were down-sampled to a size of 16×16 pixels. The 4 map types were each treated as different color channels, and a grid search was used to optimize the network architecture and hyperparameters. Binary classification was performed to separate the keratoconus cases and non-keratoconus cases (normal or contact lens warpage). Repeated 5-fold cross-validation was used to evaluate model performance, and class activation maps were generated.

Results: The average balanced accuracy of the CNN during cross-validation was 94 ± 2%. The precision and recall were 98 ± 3% and 91 ± 4%, respectively. The area under the receiver operating characteristic curve was 0.94 ± 0.02. The network was able to detect 100% of the manifest and subclinical keratoconus cases. The accuracy for the forme fruste keratoconus cases was 56 ± 19%. The network demonstrated good specificity, with 97 ± 6% of normal eyes and 96 ± 9% of warpage eyes being classified as non-keratoconus cases. The class activation maps indicated that the regions of the topography and thickness maps which contained the keratoconic cone were most important to the CNN for disease detection (Figure 2).

Conclusions: OCT mapping of the cornea and CNNs can be used to detect keratoconus with high accuracy. This approach could be expanded to automate the classification of corneal diseases.

CONTROL ID: 3714402

SUBMITTER (NAME ONLY): Caleb Bates

TITLE: Reducing serine and glycine leads to impaired RPE phagocytosis

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bates, R. Fallon, A. Greer, M. Friedlander, M. Gantner, The Lowy Medical Research Institute, California, UNITED STATES|Y. Ideguchi, M. Friedlander, The Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular telangiectasia type II (MacTel) is a macular degenerative disease that causes progressive vision loss. While MacTel is predominantly characterized by macular defects, post-mortem eye studies in MacTel patients reveal pan-retinal changes in the retinal pigmented epithelium (RPE), including reduced phagosomes compared to age-matched controls. We have reported that MacTel patients exhibit low circulating levels of serine and glycine. The impact of these non-essential amino acids on RPE function is unknown. The purpose of this study was to assess the impact of reduced serine and glycine on RPE phagocytic function.

Methods: To assess RPE phagocytic function, we cultured human fetal RPE cells in serine- and glycine-free media, measured expression of endosomal markers, and quantified phagocytic capacity via flow cytometry and imaging. To assess the impact of reduced circulating serine and glycine levels on RPE in vivo we aged mice on a serine- and glycine-free diet and quantified RPE phagosomes using electron microscopy.

Results: We found decreased phagocytic function in human fetal RPE cells after culture in serine- and glycine-free media. Interestingly, these cells also had elevated expression of endosomal markers. Mice aged on a serine and glycine-free diet had fewer phagosomes in their RPE, recapitulating what was observed in MacTel patients.

Conclusions: RPE phagocytic capacity is disrupted when serine and glycine availability is reduced, both in vitro and in vivo. This suggests that the reduced levels of circulating serine and glycine observed in MacTel patients may be a contributing factor to RPE dysfunction and macular disease.

CONTROL ID: 3714403

SUBMITTER (NAME ONLY): Blake Boehm

TITLE: Effect of Bimatoprost Treatment on Lymphangiogenesis in Human Ciliary Body Smooth Muscle Cells

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The presence of uveolymphatic pathways were recently discovered and may contribute to drainage of aqueous humor and regulation of intraocular pressure (IOP). Bimatoprost is a prostaglandin-analog commonly used to reduce IOP. Prior work with topical bimatoprost in monkey demonstrated partially endothelial lined passages within the ciliary body stroma. We hypothesized that these passages are lymphatic in nature and human ciliary body smooth muscle (CBSM) cells are the source of the lymphangiogenic proteins.

Methods: CBSM cells were dissected and cultured from the anterior segment of four human donors ages 60, 62, 73, and 76. CBSM cells were treated with vehicle control (0.001% ethanol), 3.3, 10, 25.7, or 257 nM of bimatoprost or bimatoprost free acid. Immunoblot analysis was performed on cell lysates to determine the effect of drug treatment on protein expression for the lymphatic markers: LYVE-1, PROX-1, TIE-1, ANG-1, ANG-2, and NRP-2. Fold-change as compared to vehicle control was quantified and two-tailed paired t-tests were used for statistical analysis.

Results: Bimatoprost treated CBSM cells demonstrated a 33 ± 7% decrease in NRP-2 expression (n=3; p=0.048) at 10 nM, while no dose-dependent trend was observed for LYVE-1 (n=2), TIE-1 (n=3), or PROX-1 (n=3). ANG-1 (n=2) and ANG-2 (n=1) exhibited a dose-dependent although non-statistically significant increase in protein expression with a maximal increase of 56% and 64% for ANG-1 and ANG-2, respectively. Bimatoprost free acid treated CBSM cells (n=1 for each target) exhibited a dose-dependent decrease in NRP-2, no dose-dependent trend in LYVE-1, PROX-1, or ANG-2, and a dose-dependent increasing trend in TIE-1 and ANG-1.

Conclusions: Our study confirmed the expression of lymphatic markers by human CBSM cells, and that bimatoprost and bimatoprost free acid had differential effects on lymphatic gene expression in CBSM. The significant decrease in NRP-2 at 10 nM of bimatoprost may be due to changes in receptor trafficking since NRP-2 is a co-receptor for VEGFR-3. Increases in TIE-1, ANG-1 and ANG-2 may indicate development of lymphatics in response to drug treatment. Experiments are ongoing to better characterize this trend.

CONTROL ID: 3714409

SUBMITTER (NAME ONLY): Chase Paterson

TITLE: Investigating the effects of RPE detachment on angiogenic factors using micropatterning

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Paterson, J. Cannon, E. Vargis, Biological Engineering, Utah State University, Logan, Utah, UNITED STATES|

Commercial Relationships Disclosure: Chase Paterson: Commercial Relationship: Code N (No Commercial Relationship) | Jamen Cannon: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Vargis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: During age-related macular degeneration (AMD), RPE cell detachment can cause overexpression of proangiogenic factors, such as vascular endothelial growth factor (VEGF). The only approved treatments target VEGF to slow angiogenesis progression in AMD. However, other angiogenic proteins may also be viable targets. Clarifying the relationship between RPE cell detachment and other angiogenic factor secretions could lead to more therapeutics and increase the efficacy of current treatments. Understanding this relationship is difficult with current methods, such as animal models or scratching assays, as they can be costly, time-consuming, or nonrepresentative.

Methods: To better model RPE cell detachment, we use a method called micropatterning to control the spatial arrangement of cells by preventing growth using polydimethylsiloxane stencils. AutoCAD software was used to generate patterns, which were then formed into stencils to mimic 10, 25, and 50% overall detachment of an RPE monolayer. These increasing amounts of detachment correspond to AMD progression. After the stencil areas were verified by comparison to the original CAD drawings, the growth of primary porcine RPE cells was successfully controlled using stencils. Trypan blue exclusion assays were used for cell counts, which were used in an enzyme-linked immunosorbent assay to correlate amounts of angiogenic secretion to levels of RPE detachment.

Results: Morphological changes were seen with a decrease in pigmentation, showing a decline in barrier and light absorption functions as degeneration increased. One day after stencil removal, the degree of change of angiogenic factor secretions correlated to level of detachment. Whereas VEGF concentration was not as affected by varying levels of detachment as anticipated, intriguingly, angiopoietin-2 secretion had some of the most noticeable changes.

Conclusions: Engineering methods can be used to create tunable models of RPE cell-cell detachment and degeneration correlated to AMD pathologies. Angiogenic factor secretion was affected by varying levels of detachment. Immunocytochemical staining and a phagocytosis assay will be used to visualize angiogenic protein expression and see how other crucial functions are affected by detachment. The results of this research will clarify how different levels of degeneration can impact the expression of angiogenic proteins and possibly reveal other therapeutic targets.

CONTROL ID: 3714412

SUBMITTER (NAME ONLY): David Evans

TITLE: Melanocortin agonist PL9643 significantly improves ocular signs and symptoms of moderate to severe dry eye disease (DED), including tear film break up time (TFBUT)

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Evans, E.B. McLaurin, Total Eye Care, Memphis, Tennessee, UNITED STATES|K. Kenyon, Tufts University School of Medicine and New England Eye Center, Boston, Massachusetts, UNITED STATES|G.W. Ousler, M. Watson, Ora Inc, Andover, Massachusetts, UNITED STATES|P. Vollmer, Andover Eye Associates, Andover, Massachusetts, UNITED STATES|G. Torkildsen, Vita Eye Clinic, Shelby, North Carolina, UNITED STATES|J. Winters, J. Dodd, R. Jordan, S. Wills, C. Spana, Palatin Technologies Inc, Cranbury, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: DED is characterized by ocular irritation and potential visual impairment due to inflammation and tear deficiency. Melanocortin agonists may represent a new therapeutic avenue to treat inflammatory ocular diseases. The efficacy and tolerability of the melanocortin receptor pan-agonist PL9643 was examined in a subpopulation of subjects with moderate to severe DED as part of a phase 2 study.

Methods: This was a randomized, placebo-controlled study of subjects with DED. A subpopulation of subjects (n=53) with a duration of DED≥5 years, inferior corneal staining>1, and eye discomfort on a visual analog scale (VAS)≥25 was analyzed. Subjects received placebo solution during a 2-week run-in period and were randomized to either placebo or PL9643 topical solution TID for 12 weeks. The controlled adverse environment (CAE™) model was used to exacerbate signs/symptoms. Endpoints included TFBUT, changes in inferior corneal fluorescein staining and ocular discomfort (Ora Calibra® scales) after 2 and 12 weeks. Other endpoints were changes in additional signs/symptoms of DED, and occurrence of adverse events (AEs).

Results: In these subjects with moderate or severe disease (n=53), PL9643 treatment demonstrated a significant improvement over placebo at week 12 for TFBUT with an LS means treatment difference vs placebo of +0.4058 (P=0.0137). PL9643 treatment also demonstrated a significant improvement over placebo for fluorescein staining with treatment differences of -0.55 (P=0.0097) for inferior corneal staining and -0.93 (P=0.0242) for corneal sum staining (inferior, superior, and central). Ocular discomfort demonstrated significant improvement vs placebo in change from baseline at week 2 (treatment difference -0.4, P=0.0227). In addition, PL9643 treatment demonstrated numerical improvement in conjunctival redness (Ora Calibra® scale) and in VAS symptoms at weeks 2 and 12. Fewer AEs occurred in those receiving PL9643 vs placebo and there were no treatment-related serious or ocular AEs observed.

Conclusions: In subjects with moderate or severe DED, PL9643 led to significant improvement in TFBUT at week 12 and other subjective and objective benefits at 2 weeks which were maintained for 12 weeks vs placebo. PL9643 had a safety profile comparable to placebo. Results support the continued development of PL9643 as a novel therapeutic method for DED.

CONTROL ID: 3714414

SUBMITTER (NAME ONLY): Ayellet Segre

TITLE: Integrating gene regulation and single cell expression with genetic associations identifies genes and cell types contributing to primary open angle glaucoma risk and intraocular pressure

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.V. Segre, A.R. Hamel, J. Wang, J. Rouhana, J.L. Wiggs, Ocular Genomics Institute, Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A.V. Segre, A.R. Hamel, J. Wang, J. Rouhana, J.L. Wiggs, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|T. van Zyl, Department of Ophthalmology and Visual Sciences, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|W. Yan, A. mcadams, A. Monavarfeshani, J.R. Sanes, Department of Molecular and Cellular Biology and Center for Brain Science, Harvard University, Cambridge, Massachusetts, UNITED STATES|Q. Liang, R. Chen, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is no cure for primary open-angle glaucoma (POAG), characterized by progressive optic nerve damage and vision loss, due to limited understanding of the molecular and cellular causes. Here we aimed to identify genes and cell types that may affect POAG risk by integrating known POAG and intraocular pressure (IOP) genetic loci with genetic regulation of gene expression (eQTLs) and splicing (sQTLs), and single cell expression in ocular tissues.

Methods: We developed a method called ECLIPSER, that tests whether expression of genes mapped to genome-wide association study (GWAS) loci of a complex trait, based on e/sQTLs, is enriched in specific cell types. For each trait, tissue, and cell type, a GWAS locus is scored based on the fraction of cell type-specific genes (fold-change>1.3, FDR<0.1). Cell type enrichment of a GWAS loci set is assessed against a null distribution of loci of unrelated traits taken from Open Target Genetics, using a Bayesian Fisher's exact test. We mapped genes to 127 POAG loci and 133 IOP loci found in large GWAS meta-analyses, by applying colocalization methods, eCAVIAR and enloc, to the GWAS loci and overlapping e/sQTLs from 49 GTEx tissues and retina eQTLs (EyeGEx). GeneEnrich was used for gene set enrichment in biological processes.

Results: ≥1 e/sQTL colocalized with 61% (202 loci) of POAG and IOP GWAS loci (Posterior Prob>0.01), with an average of 3-4 genes per locus. POAG genes were enriched in elastic fiber formation and extracellular matrix organization (P<6E-05, FDR<0.01), and IOP genes in vasculature development (P=5E-05, FDR=0.13). Applying ECLIPSER to the mapped genes and single-nucleus RNA-seq of the anterior segment (AS), optic nerve head (ONH) and retina from healthy eyes, identified significant enrichment (P=0.01-4E-04, FDR=0.008-0.16) for POAG in astrocyte and Müller glia in ONH and retina, and ciliary and iris fibroblasts in the aqueous outflow pathway in AS. The IOP genes were enriched in smooth muscle, astrocyte, pericyte, and vascular endothelium in ONH, astrocyte in retina, and trabecular meshwork and ciliary fibroblasts in AS (P=0.001-0.009, FDR=0.02-0.15).

Conclusions: This work suggests hundreds of regulatory mechanisms and genes that may contribute to POAG risk in specific cell types in the front and back of the eye, which could help guide novel therapies.

CONTROL ID: 3714415

SUBMITTER (NAME ONLY): Gislin Dagnelie

TITLE: Comparing alerts in a smart object finder for visual prosthesis wearers

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Dagnelie, A. Kartha, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|R. Sadeghi, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|P. Gibson, Advanced Medical Electronics Corp, Minneapollis, Minnesota, UNITED STATES|R. Chamberlain, L. Barrett, K. Kramer, Minnesota Health Solutions, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual prosthesis wearers' ability to locate people and objects in real-life environments is limited by low resolution and distracting information. Object recognition by a neural net can assist them, provided we can efficiently convey information about the location and nature of a desired object in the visual field.

Methods: Video from a head-worn camera was analyzed for the presence of selected objects by a TensorFlow SSD neural net trained on the COCO dataset, running on a Raspberry Pi processor in a control box worn by the subject. Subjects wore their Argus system and earbuds, and were either shown the raw Argus II video or given one of 3 prompts for objects in view: a flashing icon in the image, icon + binaural tone conveying direction and size/closeness, or icon + spoken object identity. Here we present data collected in Argus II users looking for and walking towards a person in our lab in one of 6 pre-selected random positions. Each position was tested twice, in random order, followed by a return trial to the starting location; a trial ended in reaching the target or time-out/incomplete. Prior to testing, subjects familiarized themselves with the size of the room and were given several practice trials on a person standing nearby, with each modality. Outcomes were success rate, number of steps, and time to completion.

Results: With the native Argus II system, success rates varied from 25–38%; 95–99 s and 27–33 steps were required to reach the target. In the trials with prompts, these values were: 92 – 96%, 26–34 s and 9–17 steps (icon); 83 – 100%, 31–32 s and 12–15 steps (icon+tone); and 92 – 100%, 35–37 s and 9–18 steps (icon+voice). All changes in prompted trials relative to the native system were significant by 2-tailed t-test. Only for one subject was a difference found between prompts: Icon + tone resulted in faster completion than icon alone. Return trials showed a slight, but not significant, improvement over outbound trials. Subjects preferred using the system, but did not express a preference for a particular prompt.

Conclusions: Providing an Argus II user with a system that detects a desired object results in significant improvement of all measured performance aspects, but no evidence was found for advantage of a particular alert system.

CONTROL ID: 3714417

SUBMITTER (NAME ONLY): Holly Wright

TITLE: Investigation of the Nrf2 Pathway in Mitigating Nitrogen Mustard and Chloropicrin Induced Corneal Injury

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Wright, D. Goswami, A. Roney, R. Kerin, K. Liby, N. Tewari-Singh, Pharmacology and Toxicology, Michigan State University, East Lansing, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The eye is one of the most sensitive organs to toxic chemical exposures. Ocular chemical injuries cause corneal damage and the loss of viable corneal epithelial cells, leaving patients with few effective treatment options. Nitrogen mustard (NM), a structural analog of warfare agent sulfur mustard, is a vesicating agent. Chloropicrin (CP), is a broad-spectrum pesticide that is used in agriculture, and is also a warfare agent. NM and CP can have severe toxic effects to the eye including irritation, corneal edema, and long-term ocular injuries but there are no effective therapies available. Our previous studies indicate that eye toxicity from NM and CP exposure can cause activation of signaling pathways related to DNA damage, oxidative stress, and inflammation. Triterpenoids are activators of the nuclear factor-erythroid factor 2-related factor 2 (Nrf2) pathway, which transcriptionally activates genes related to anti-inflammatory responses and cytoprotective effects reducing oxidative stress. Thus, activating Nrf2 pathway can be a targeted approach for the treatment of chemical induced corneal toxicity.

Methods: Human corneal epithelial (HCE) cells were exposed to 60 μM NM for 6 or 24 hours. mRNA was isolated and qPCR analyses were carried out for Nrf2 pathway related genes, inflammatory markers, and cytokines.

Results: NM exposure led to a decrease in Nrf2 mRNA expression at 24h post exposure. Changes in phase II antioxidant enzymes of the Nrf2 pathway NAD(P)H quinone dehydrogenase-1 (NQO-1) and heme oxygenase-1 (HO-1) were observed. NQO-1 mRNA expression decreased at both 6 and 24h post NM-exposure, while HO-1 expression increased at 6h (6.5-fold increase) followed by a decrease at 24 h. NM exposure caused a decrease in the mRNA expression of antioxidant enzymes catalase and glutathione peroxidase-1 at both the time points. An increase in TNF-α mRNA expression (1.8-fold) was observed at 24h post NM exposure.

Conclusions: NM exposure in HCE cells causes increased expression of inflammation, and oxidative stress related markers and decreases the expression of Nrf2 pathway genes. Since CP has similar effects to the vesicating agent NM, we are investigating the involvement of the Nrf2 pathway in CP-induced corneal injury in HCE cells. Based on these studies, we will further evaluate the effect of activating Nrf2 pathway by triterpenoids for the treatment of NM and CP-induced corneal toxicity.

CONTROL ID: 3714420

SUBMITTER (NAME ONLY): Navid Nouri

TITLE: Whole genome sequencing for rare variants and imaging analyses in model organisms identify SLC16A8 as a significant contributor for AMD risk

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Nouri, A. Stockwell, B. Hannon, T. TRUONG, Y. Malato, K. Browder, A. Sene, M. Mccarthy, S.Y. Chaney, H. Jasper, B. Yaspan, Genentech Inc, South San Francisco, California, UNITED STATES|E.Y. Chew, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Polygenic predisposition to advanced age-related macular degeneration (AMD) enables strategies to define the complex pathogenesis of this disease. We combined human genetics and in vivo functional studies in Drosophila melanogaster to identify novel pathways implicated in AMD pathogenesis.

Methods: Whole genome sequencing (WGS) and subsequent rare variant (RV) burden test analyses were performed for 6055 advanced AMD cases and 8294 non-AMD diseased controls. We extracted rare exonic SNPs (minor allele frequency <1%) predicted to alter amino acids or affect functionality of the protein. Since comparison cohorts were comprised of non-AMD clinical trial patients, a reverse regression with a Bayesian spike and slab prior was used to remove non-AMD specific associations. For functional characterization of candidate genes at association signals, we performed RNAi screens using Drosophila models. The impact of whole eye knockdowns of orthologous genes of interest on photoreceptor survival was assessed using deep pseudopupil (DPP) and optic neutralization of cornea imaging approaches that follow ommatidial morphology.

Results: WGS for RV burden tests pinpointed multiple genes, including the top hits CFI (P=3.13E-14; OR=4.57), CFH (P=2.14E-06; OR=2.05), and SLC16A8 (P=1.50E-05; OR=1.78), all from loci previously associated with AMD (Table 1). We focused functional analysis on the proton-coupled monocarboxylate transporter SLC16A8 (solute carrier family 16 member 8) which is expressed only in the retinal pigment epithelia of humans and also rodents. Knockdown of the Drosophila ortholog sln (silnoon) led to progressive loss of retinal homeostasis in the adult fly, as visualized by changes in photoreceptor EGFP expression patterns at day 14 (95% mean loss of DPP), but not by day 1, 7, or in comparison to negative controls (n=10 for each line and timepoint; reproduced in two separate assays).

Conclusions: An unbiased, genome-wide analysis of rare coding variants provided additional support of a causal role for SLC16A8 in protection against AMD when functional. We demonstrate that deletion of the Drosophila ortholog sln disrupts retinal homeostasis, and highlight a potential therapeutic opportunity for the treatment of AMD.

CONTROL ID: 3714421

SUBMITTER (NAME ONLY): Anara Serikbaeva

TITLE: Hyperglycemia promotes mitophagy and thereby mitigates hyperglycemia-induced damage

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Serikbaeva, D. Ogbu, A. Kazlauskas, Department of Physiology and Biophysics, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|A. Serikbaeva, R. Zelkha, Y. Li, A. Kazlauskas, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The fact that diabetic retinopathy (DR) typically takes decades to develop suggests the existence of an endogenous system that protects from diabetes-induced damage. The purpose of this project was to consider if such a system is present in primary human retinal endothelial cells (HRECs).

Methods: HRECs were cultured in endothelial cell-specific media from Lonza containing 5 mM (normal glucose, NG) or 30 mM D-glucose (high glucose, HG). Expression of VCAM1 protein was evaluated by Western blotting. Cell death was measured by Annexin V and propidium iodide staining. Mitochondria functionality was assessed by oximetry (Seahorse analysis of basal respiration, spare respiratory capacity, and the level of ATP) and a novel approach measuring resolution of an acute increase in reactive oxygen species. A fluorescent probe, mtKeima, was used to monitor mitophagy. Mitophagy was suppressed by siRNA-based approaches to reduce the expression of genes required for mitophagy. Endothelial cell barrier integrity was monitored via trans-endothelial electrical resistance (TEER). Two-tailed Student's t-test was used for statistical analysis.

Results: We expected that HG would be deleterious to HRECs, and that prolonging the exposure would increase damage. Instead, we observed that extended exposure to HG was beneficial. While TNFa-induced expression of VCAM1 was similar in HG versus NG after a short exposure to HG, it became lower in HG cells if the exposure to HG was extended. Similarly, oxidative stress-induced death declined in HG cells as the duration of exposure to HG was prolonged. Furthermore, mitochondrial functionality, which was compromised by 1 day of HG, improved in cells that were cultured in HG for 10 days. Prolonged exposure to HG increased clearance of damaged mitochondria (mitophagy), which provides a mechanistic explanation for how HG improved mitochondrial functionality. Finally, antagonizing mitophagy compromised the cells' ability to endure HG; susceptibility to cell death increased and barrier function declined.

Conclusions: HG induces adaptation of HRECs, which enables them to resist cytokine-induced activation and oxidative stress-induced death. The underlying mechanism involves enhanced mitophagy leading to increased mitochondrial functionality. Hyperglycemia-induced mitochondrial adaptation (HIMA) exists in HRECs and is a plausible explanation for the delayed onset of DR.

CONTROL ID: 3714424
SUBMITTER (NAME ONLY): Johannes Birtel
TITLE: The retinal phenotype in primary hyperoxaluria type 2 and 3
SESSION TITLE: Inherited Retinal Disease Genetics II
SESSION TYPE: Poster Session
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ABSTRACT BODY:
Purpose: The primary hyperoxalurias (PH; PH1-3) are three rare inherited disorders of the glyoxylate metabolism characterized by endogenous overproduction of oxalate. As oxalate cannot be metabolized by humans, PH may affect various organs, most notably the kidneys, bones, heart, and eyes. Vision loss and severe oxalate deposition are commonly seen in infantile PH1, whereas non-infantile PH1 usually present with no or mild retinal alterations. If patients with PH2 and PH3 develop retinal disease has not been investigated so far. This is, however, important in light of emerging therapeutic options. Here, the ocular phenotype in patients with PH2 and PH3 and its relation to systemic disease is investigated.
Methods: A renal, molecular and ophthalmic examination including multimodal retinal imaging (OCT, fundus autofluorescence imaging, fundus photography) was performed of each patient.
Results: Thirteen patients (4 with PH2; 9 with PH3) from 11 families were included. Median age at first renal symptoms and diagnosis was 1.5 and 4.5 years in PH2 patients; and 3 and 7 years in PH3 patients. Median age at time of ophthalmic examination was 11 years and median BCVA was 20/20. A 30-years-old patient with PH2 had drusen-like deposits in both eyes that were interpreted as crystallized oxalate. On OCT imaging, these deposits appeared as focal hyperreflective subretinal lesions. At the time of the ophthalmic examination, he was on dialysis and his oxalate level was markedly elevated. The remaining 12 patients showed no retinal oxalate deposits. Out of those 12, only the oldest PH2 patient (59-years-old) had elevated oxalate levels and end-stage kidney failure (ESKF), whereas all other PH2 and PH3 patients had had normal or near-normal plasma oxalate levels.
Conclusions: Retinal disease manifestation in PH2 and PH3 clearly differs from patients with infantile PH1. Age of ESKF-onset might be an important predictor for retinal alterations in PH. A later decline in kidney function associated with increased plasma oxalate levels could also increase the risk of systemic oxalosis with subretinal oxalate deposition. At this mild end of the phenotypic spectrum, additional genetic and/or environmental modifiers might result in variable susceptibility.

CONTROL ID: 3714425

SUBMITTER (NAME ONLY): George Maiti

TITLE: Single cell transcriptomic analyses of human cornea organoids reveal cell lineages of a developing cornea

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We performed scRNA-sequencing of human donor corneas and cornea organoids derived from induced pluripotent stem cells (iPSC) and matured in culture for 4 months to elucidate the transcriptomic cell fate of human cornea organoids.

Methods: Three cornea organoids and 3 healthy donor corneas (Lions Eye Institute for Transplant and Research, FL) were digested with collagenase to prepare single cell suspension. Libraries were generated using Chromium Single Cell 3' Library & Gel Bead Kit v2 (10x Genomics). The libraries were run on an Illumina HiSeq 4000 as 150-bp paired-end reads. The Cell Ranger Single-Cell Software Suite v3.01 was used to perform sample demultiplexing, barcode processing, and quality control filtering and integrating. The integrated dataset has 55,241 cells in the gene-cell-barcode matrix that includes a total 25,885 and 29,356 cells from the 3 organoids and 3 human corneas, respectively.

Results: The transcriptomic data showed high reproducibility within each sample category. Differential gene expression analysis between the two sample categories showed 559 genes to be uniquely expressed in the organoid, 389 in the cornea and 971 genes expressed in common. An integrated analysis of the corneas and the organoids yielded 30 distinct cell clusters (CL). Of these, 14 CL were detected in the cornea and 10 in the organoid samples (Fig.1). The organoids harbor cell clusters representing corneal epithelium (KRT5), stroma (LUM) and endothelium (TJP1) with minor population of myofibroblast-like cells (5%) and immune cells (CCL3). Unlike the cornea, where the largest group consists of stromal cells, the organoid shows almost equal proportion of epithelial (28%), stromal (33%) and endothelial (31%) cell contribution. Interestingly, we also found the organoid cell fates to be consistent with that of a developing cornea that shows high expression of SIX3 and PAX6. The organoids also have low expression of KERA, KRT12, ALDH3A1 and KLF4, known to be expressed in the adult cornea.

Conclusions: Our work, provides for the first time, a transcriptomic map of human cornea organoids at a single cell resolution. The organoids recapitulate epithelial, endothelial and stromal cell fates of the developing cornea. These well characterized organoids offer a 3D platform to investigate corneal development, diseases and cell-based therapies.

CONTROL ID: 3714426

SUBMITTER (NAME ONLY): Atul Jaiswal

TITLE: Impact of COVID-19 on healthcare access for older adults with combined hearing and vision loss: A Canada-wide survey of healthcare workers

SESSION TITLE: Mental Health Outcomes and Vision Rehabilitation Services

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Jaiswal, P. Holzhey, S. Budhiraja, A. Paramasivam, N.R. Boie, W. Wittich, School of Optometry, Universite de Montreal, Montreal, Quebec, CANADA|A. Jaiswal, W. Wittich, CRIR/Institut Nazareth et Louis-Braille du CISSS de la Montérégie-Centre, Longueuil, Quebec, CANADA|S. Santhakumaran, McGill University Faculty of Medicine and Health Sciences, Montreal, Quebec, CANADA|M. Savundranayagam, Western University Faculty of Health Sciences, London, Ontario, CANADA|C. Vincent, CIRRIS/Department of Rehabilitation, Universite Laval, Quebec, Quebec, CANADA|E. Kröger, Faculty of Pharmacy, Universite Laval, Quebec, Quebec, CANADA|E. Kröger, Centre d'excellence sur le vieillissement de Québec, CIUSSSCN, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Older adults with combined hearing and vision loss (dual sensory loss/DSL) are a highly vulnerable population during the COVID-19 pandemic. Although around 1.1 million older Canadians live with DSL, data are scarce on how COVID-19 affected their access to healthcare during the pandemic. Therefore, the present study explored the impact of COVID-19 on healthcare access for older Canadians with DSL.

Methods: We distributed an online survey for healthcare workers who provided services to older adults with DSL during the pandemic. Survey data were collected from 228 Canadian healthcare workers between August and November 2021. Content analysis was used to analyze open-ended qualitative data, whereas descriptive statistics were used for quantitative survey data using SPSS.

Results: Almost all healthcare workers felt that COVID-19 has negatively affected their care delivery to older adults with DSL, especially due to physical distancing and use of Personal Protective Equipment. Moreover, those using telehealth with their older clients reported that COVID-19 related shift to telehealth appointments restricted access to healthcare for their clients. Most respondents (91%) felt that older adults with DSL found it difficult to follow pandemic-related physical distancing guidelines in a clinical or health system setting. While 69% of them believed that the health system was not adapted to match the needs of older adults living DSL, 71 % felt healthcare professionals are not adequately trained to meet the needs of this population in pandemic situations such as COVID-19.

Conclusions: We concluded that the pandemic has negatively impacted healthcare services to older adults with DSL. The pandemic accentuated the need for equitable care for older adults with DSL, considering the unique challenges experienced by them and their healthcare providers. Our study findings underscored the need for training of healthcare professionals on the communication and accessibility needs of older adults living with DSL.

CONTROL ID: 3714427

SUBMITTER (NAME ONLY): Ludovic Zimmerlin

TITLE: Improved generation and long-term engraftment of retinal organoids from Tankyrase/PARP-Inhibitor-Regulated Naïve human pluripotent stem cells (TIRN-hPSC)

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zimmerlin, R. Kanherkar, T. Park, M. Barbato, M. Koldobskiy, E.T. Zambidis, Oncology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|L. Zimmerlin, R. Kanherkar, T. Park, E.T. Zambidis, Institute for Cell Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|I.A. Bhutto, Y. Liu, M. Singh, G.A. Lutty, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Generation of retinal organoids (RO) from conventional, primed hPSCs is inefficient and optimized in only a few ‘permissive’ lines. We recently established naïve epiblast-like TIRN-hPSC with reduced interline variability of differentiation for improved vascular progenitor engraftment. Here, we tested whether TIRN-hPSC-derived ROs also possess improved in vivo development to mature photoreceptors.

Methods: Isogenic primed vs TIRN-hPSC were differentiated with an established 3D RO protocol. Horse-shoe (HS)-shaped domains matured to retinal cups (RC) with laminated layers. Neuroepithelial specification and epigenomic integrity were validated at 4-20 weeks by RT-PCR, immunofluorescence, RNA-Seq, and CpG methylation sequencing. Interline variability of RC differentiation was quantitated to 16 weeks. RC neural sheets were transplanted into the subretinal space of NOG-SCID mice, and human photoreceptor specification and engraftment was evaluated at 6-9 months post-transplant.

Results: Although several conventional hPSC lines failed to differentiate into RCs, all TIRN-reverted hPSC efficiently generated HS domains and well-differentiated RC organoids with efficiencies comparable to “permissive” hPSC lines. Eye field-specific transcripts and photoreceptor progenitor markers (2-20 weeks) were detected in greater quantities in TIRN RCs (e.g., CRX^+RCV^+, HuC/D^+ ganglion/amacrine cells, $PROX1^+$ horizontal cells, $MITF^+$ pigmented epithelium). TIRN-derived RO displayed improved maturation of $rhodopsin^+$ photoreceptors with proper histo-architecture. Confocal microscopic evaluation of NOG eyes transplanted with TIRN-derived RC sheets demonstrated long-term engraftment (10 months) of mature human cells in tabulation-like structures with development of a full repertoire of mature rod/cone photoreceptors (e.g., $rhodopsin^+$, L/M $opsin^+$, $recoverin^+$), astrocytes ($GFAP^+vimentin^-$), and Mueller cells ($GFAP^+vimentin^+$). Transcriptomic and epigenetic studies revealed that chemical PARP inhibition of the TIRN method mediated the improved epigenetic plasticity to retinal lineages.

Conclusions: TIRN reversion of conventional hPSCs abolished interline variability of RO development across genetic background, augmented retinal fate specification, and potentiated long-term survival of transplanted photoreceptors for at least 10 months.

CONTROL ID: 3714428

SUBMITTER (NAME ONLY): Safia Benamar

TITLE: The aftermath of the COVID-19 pandemic on access to corneal transplant procedures in Morocco

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Benamar, M. Belmekki, Ophthalmology, Hopital Universitaire International Cheikh Zaid, Rabat, Rabat-Salé-Kénitra, MOROCCO|I. Hmamouchi, Rheumatology, Hopital Universitaire International Cheikh Zaid, Rabat, Rabat-Salé-Kénitra, MOROCCO|I. TARIB, EyeCare Consultants of New Jersey, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic led to disrupted corneal supply to countries tributary to foreign eye bank donations. The authors carried out the first retrospective, observational study to assess the impact of the pandemic on corneal tissue supply and quality in Morocco, by comparing the surgical patterns during the pre-pandemic time and the first year of the pandemic at the only tertiary eye center performing keratoplasty in Morocco.

Methods: A retrospective analysis comparing the years 2019 and 2020 (January 1^{st} to December 31^{st}) was performed based on electronic health records database from the department of Ophthalmology at Cheikh Zaid International Hospital.Quantitative analysis evaluated the numbers of keratoplasties performed, the number procedures for therapeutic or tectonic purposes, the numbers of delivered corneal tissue, numbers of patients on the waiting list. Quality assessment of the grafts was based on the mean endothelial cell density count provided by the supplier, prior to corneal surgery. The comparison was based on a Chi2 test with $p<0.05$ considered statistically significant. Statistical study was performed using Jamovi (The Jamovi project2021,Version 1.6[Computer Software])

Results: Out of a total of 345 patients registered on the corneal transplant list on 2019, 252 patients underwent keratoplasty (73%) with 4,4 % for tectonic or therapeutic purposes, whereas out of 507 patients on the list on 2020, 160 received keratoplasty (31,55%) with 13,7% in a context of emergency. The waiting list grew from 293 patients in 2019 to 453 in 2020 marking an increase of 21,4 %. A statistically significant decrease in the number of corneal tissue received at our center was noted, with a mean of 4,8 (+/- 4,23) per week in 2019 and 2,9 (+/- 3,02) per week in 2020 (p=0,02).All corneal tissue was exclusively provided by three US eye banks. Mean endothelial cell density count prior to surgery was not statistically different between 2019 (2699 c/mm^3 +- 255) and 2020 (2668 c/mm^3 266),(p= 0,22).

Conclusions: These results reflect the imbalance between corneal demand and supply creating a disruption of the corneal tissue chain in Morocco. Given the exceptional activity of the local Eye bank of Morocco due to numerous challenges, and the scarcity of centers that perform keratoplasty, Morocco witnesses a gap between corneal blindness and access to keratoplasty which was further enlarged during the pandemic.

CONTROL ID: 3714429

SUBMITTER (NAME ONLY): Owen Clinger

TITLE: Potent retinal protection by oral administration of a purine metabolite against age-related retinal degeneration and RHO-associated retinitis pigmentosa

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Clinger, Y. Xi, A. Vats, J.A. Sahel, Y. Chen, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|O. Clinger, Y. Xi, A. Vats, A. Wolf-Johnson, L. Birder, E. Jackson, Y. Chen, Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|A. Wolf-Johnson, L. Birder, Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|J.A. Sahel, Institut de la Vision, Sorbonne Universite, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Retinal degeneration is a common cause of vision loss, and photoreceptor loss is specifically involved in blinding diseases such as age-related macular degeneration and retinitis pigmentosa. Finding an oral agent that prevents retinal degeneration is an ideal goal for treating these diseases. The purpose of this study is to evaluate the efficacy of an oral purine metabolite as a retina protective agent in two rodent models: aged Fischer344 rats and $Rho^{P23H/+}$ knock-in mice.

Methods: Aged Fischer344 rats were treated with the purine compound by supplementing the agent at 5 mg/kg in drinking water. Treatment began at 22 months of age and lasted for 8 weeks. Electroretinogram (ERG) and optical coherence tomography (OCT) were recorded at 0 and 7 weeks of treatment. Retinae were collected at 8 weeks of treatment for purine analyses, RNA-seq, immunoblots, and immunohistochemistry. Non-treated age-matched animals were used as controls. $Rho^{P23H/+}$ mice were treated with 11 mg/kg of the purine metabolite beginning at postnatal day (PND) 15 by daily intraperitoneal (i.p.) injections. Drinking water for the mother of the treated litter, and subsequently the weaned pups, was also supplemented with the agent. Retinal morphology and function were evaluated weekly by ERG and OCT until the mice were sacrificed at 5 and 7 weeks of treatment. Mice treated with PBS by i. p. injections were used as vehicle controls.

Results: Eight weeks of daily oral treatment by a purine metabolite led to potent retinal protection in the Fischer344 rats at 2 years of age. This was demonstrated by thicker retinae and outer segment layers, and a higher number of nuclei in outer nuclear layer and retinal ganglion layer. Higher scotopic ERG responses were observed, suggesting improved retinal function. Rhodopsin level was significantly increased by the treatment, suggesting restored rod photoreceptor homeostasis. Systemic treatment with the same agent in $Rho^{P23H/+}$ mice also showed delayed retinal degeneration and improved retinal function via OCT and ERG, respectively.

Conclusions: We discovered an oral agent that potently protects the retina against degeneration in two rodent models, thus providing a promising direction for drug development against retinal dystrophies.

CONTROL ID: 3714430

SUBMITTER (NAME ONLY): David Corell

TITLE: The proteomic phenotype of the epigenetically conditioned, injury-resilient mouse retina

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Corell, E.E. Broyles, J. Gidday, Ophthalmology, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|M.M. DeAngelis, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: A variety of conditioning treatments share a strong preclinical track record for epigenetically modifying the retina in ways that protect it from injury and disease [1]. Translational relevance is enhanced by the demonstration that repetitive conditioning can extend the disease-resilient phenotype long after treatment [2-4]. In the present study, we performed quantitative mass spectrometry (MS) on retinae from male and female mice following 2 wks of repetitive hypoxic conditioning (RHC) to gain a proteome-wide understanding of the epigenetically modified phenotype induced prior to injury.

Methods: Adult, outbred Swiss-Webster ND4 mice of both sexes were treated with RHC, or served as normoxic controls; whole retinae (without choroid/RPE) were harvested the following week and processed for MS3 analysis on a Fusion Orbitrap MS using TMTpro labels for quantification, with <5% FDR. Differentially expressed proteins (>1.1 fold-change) were analyzed bioinformatically (z-score>2) (IPA, Qiagen).

Results: MS identified and quantified 6253 proteins, 688 of which were differentially expressed in response to RHC across both sexes. The expression of 166 of these proteins changed uniquely in males or females, whereas that of 522 proteins (216 upregulated and 306 downregulated) were sex-independent. Findings in the latter group implicated increased nuclear (MAF, SOX17, TP53, WT1) and mitochondrial (TFB1M, PHB) transcription, enhanced blood-retinal barrier integrity (PTGDS, MAPK7), increased ceramide synthesis (SMPD1), and Akt/mTOR activation (PIP4P1, KRT17). Bioinformatic analyses of these shared proteins predicted RHC-induced changes in the expression of proteins involved in diverse signaling and metabolic pathways consistent with the promotion of cell survival/anti-apoptotic signaling and free radical scavenging, and a reduction in inflammation, microglial reactivity, microtubule dynamics, and cell migration/movement.

Conclusions: RHC induces widespread and sustained changes in the retinal proteome prior to injury/disease. This 'prime-the-pump' phenotype, conserved across sexes, is foundational to understanding innate, epigenetically-induced mechanisms of neuroprotection that could be leveraged for therapeutics.

References: [1] Gidday JM, Cond Med 2018; [2] Zhu Y et al., IOVS 2007; [3] Zhu Y et al., Mol Med 2012; [4] Harman JC et al., IOVS 2020.

CONTROL ID: 3714431

SUBMITTER (NAME ONLY): Yinjie Guo

TITLE: Uncoupling caspase 8-mediated-apotosis from caspase 8-mediated-inflammation in glaucoma

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Guo, M. Shrestha, M.S. Gregory-Ksander, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Guo, M. Shrestha, M.S. Gregory-Ksander, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Marshak-Rothstein, Medicine, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) apoptosis is the common endpoint in glaucoma and both the intrinsic and extrinsic apoptotic pathways have been implicated in human and experimental models of glaucoma. However, caspase 8, which is central to the extrinsic pathway of apoptosis has been linked to both RGC apoptosis, as well as glial activation, and neuroinflammation. The recent development of a caspase 8 mutant mouse ($Casp8^{DA/DA}$) in which a point mutation in the auto-cleavage site blocks caspase 8-mediated apoptosis but does not block caspase 8-mediated inflammation, allows us to uncouple the two pathways and determine the extent to which caspase 8-mediated inflammation and/or apoptosis contributes to the death of RGCs in glaucoma.

Methods: Intracameral injection of magnetic microbeads (control: saline) was used to elevate the intraocular pressure (IOP) in three groups of mice: WT mice (positive control, RGC apoptosis); Fas deficient Fas^{lpr} mice (negative control, no RGC apoptosis); $Casp8^{DA/DA}$ mutant mice (experimental, no extrinsic apoptosis). IOP was monitored by rebound tonometry. At 5 weeks post microbead injection, visual acuity was measured by optomotor reflex (OMR) and RGC function was assessed by pattern ERG (pERG). Retina and optic nerves were processed for RGC and axon quantification.

Results: Rebound tonometry showed equal elevation of IOP in microbead-injected WT, Fas^{lpr}, and $Casp8^{DA/DA}$ mice as compared to saline controls. At 5 weeks post microbead injection, as compared to saline controls, a significant reduction in both visual acuity and pERG was observed in WT mice (pos. control), which correlated with a significant loss of RGCs and axons. By contrast, no significant reduction in visual acuity or pERG, nor loss of RGCs and axons was observed in Fas^{lpr} mice (neg. control). The $Casp8^{DA/DA}$ mice, in which the extrinsic apoptotic pathway is blocked, displayed a significant reduction in visual acuity and pERG equal to that observed in WT mice and, as in WT mice, this loss of function correlated with a significant loss of RGCs and axons.

Conclusions: Our data shows that the caspase 8-mediated extrinsic pathway of apoptosis is not required for the death of RGCs and loss of visual function in a microbead-induced mouse model of glaucoma, indicating that caspase 8-mediated inflammation, but not apoptosis is the driving force in the development of glaucoma.

CONTROL ID: 3714434

SUBMITTER (NAME ONLY): Leah Owen

TITLE: Placental Inflammation Significantly Correlates with Reduced Risk for Retinopathy of Prematurity

SESSION TITLE: Retinopathy of Prematurity

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Owen, B. Wood, L. Carroll, M.M. DeAngelis, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|L. Owen, OB-GYN, University of Utah Health, Salt Lake City, Utah, UNITED STATES|C. Zhang, M.M. DeAngelis, University at Buffalo, Buffalo, New York, UNITED STATES|J. Comstock, Pathology, Primary Children's Hospital, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: The relationship between placental inflammation and retinopathy of prematurity (ROP) is debated. Clarity may provide clues to potential pathomechanisms influencing pre-clinical ROP risk.

Methods: Acute placental inflammation for infants born prior to 32 weeks between 2010-2019 at one institution was characterized using gold-standard Amsterdam histology grading criteria denoting acute maternal versus infant-level inflammation. Relationships between histology, presence or absence of ROP, gestational age (GA), sex and birthweight (BW) were determined by univariate and multivariate analysis; infants were excluded if full clinical data were not available. In parallel, candidate ROP proteins were measured in cord blood specimens from a prospectively collected validation cohort of infants born prior to 31 weeks with (n=11) or without (n=12) acute placental inflammation using ELISA (HTRA1 and IGF1) or Luminex (VEGFA and TGFb-1). Protein values were correlated with histology outcomes using a one-tailed t-test.

Results: 182 infants met inclusion and exclusion criteria; 100 infants demonstrated presence of ROP. Univariate analysis demonstrated significantly positive correlations (p£0.1) between the presence of ROP, BW (p= 5.48e-09) and GA (p=6.56e-12); significant inverse correlations were identified between preeclampsia (p=0.03) and acute histologic placental inflammation (p=0.09). In multivariate analysis GA remained positively correlated with ROP (p=5.34e-09) and acute inflammation inversely correlated (p=0.02). BW and preeclampsia did not remain significant. Further analysis of placental inflammation by severity revealed significant inverse associations for both maternal-level (p=0.01) and infant-level (p=0.005) inflammation with the presence of ROP disease. Candidate proteins HTRA1 (p=0.003) and TGFb-1 (p=0.02) were significantly increased in cord blood from infants born in the setting of acute placental inflammation histology compared to non-inflammatory placental histology. Changes in VEGFA and IGF1 were not significantly associated with ROP development.

Conclusions: Utilizing a systems biology-based approach, that included two independent cohorts, we demonstrate that preeclampsia, and moreover, placental inflammation is protective of ROP development. Data further suggests that protein changes in HTRA1 and TGFb-1 underlie the pathomechanisms between placental inflammation and ROP development.

CONTROL ID: 3714435

SUBMITTER (NAME ONLY): Pooja Biswas

TITLE: Htra1 KO mice develop severe photoreceptor loss and RPE abnormalities.

SESSION TITLE: Molecular Mechanisms Underlying Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Biswas, A. Berry, S. Pachauri, M. Dagar, P. Shaw, R. Ayyagari, Ophthalmology, Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|N.W. Khan, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|D. Garland, Harnly LLC, Bethesda, Maryland, UNITED STATES|M.M. Jablonski, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: High-temperature requirement protein A1 (HTRA1) is a serine protease secreted by a number of tissues including the retinal pigment epithelium (RPE). The purpose of this study was to characterize the retinal phenotype of an Htra1 gene knock-out ($Htra1^{-/-}$) mouse model to understand the role of HTRA1 in retinal pathology.

Methods: The ocular phenotype of these $Htra1^{-/-}$ mice was studied by evaluation of gross morphology, fundus imaging, and electroretinography (ERG) at ages 5 and 19 months. For further evaluation, retinal morphology and expression of relevant marker genes and proteins were evaluated by immunohistochemistry (IHC) and quantitative real time PCR (qRT-PCR) of 19 months old $Htra1^{-/-}$ mice and compared with age matched controls.

Results: ERG responses in the $Htra1^{-/-}$ mice were highly reduced compared to wildtype mice as early as 5 months and progressed until 19 months. A significant loss of short wavelength cones ($p<0.0001$) and medium wavelength cones ($p<0.0001$) was observed in $Htra1^{-/-}$ mice compared to the age-matched controls by IHC at 19 months. A significant reduction in the level of expression of Opn1sw/S-opsin ($p=0.0002$), Opn1mw/M-opsin ($p=0.0002$) and Rho/Rhodopsin ($p=0.0002$) transcripts was noted at 19 months by qRT-PCR. In addition, the expression of HTRA1 protein was not detected in $Htra1^{-/-}$ mice retina. A significant increase in the expression of other macular degeneration (MD) associated genes, C1qtnf5/Ctrp5 ($p=0.0008$), Timp3 ($p<0.0001$) and Efemp1 ($p=0.0008$) were observed in $Htra1^{-/-}$ mouse by qRT and IHC at 19 months. Whereas expression of the RPE markers ZO1 ($p=0.0023$) and MERTK are significantly lower at 19 months. Progressive accumulation of auto-fluorescent spots close to retinal vessels were observed at 5 months and 19 months of age. Evaluation of retinal phenotype including ultrastructure analysis by electron microscopy (EM) at multiple younger ages is in progress.

Conclusions: The $Htra1^{-/-}$ KO mice showed loss of photoreceptors, decrease in the expression of rod, cone, and RPE markers and abnormal photoreceptor function. In addition, accumulation of extra cellular matrix (ECM) components associated with MD phenotype was also noted suggesting a possible role for HTRA1 in retinal and macular degeneration pathology.

CONTROL ID: 3714436

SUBMITTER (NAME ONLY): Kevin Fuller

TITLE: Hypoxia adaptation is essential for Aspergillus fumigatus virulence in the cornea

SESSION TITLE: Modulation of ocular surface immunity during health and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.K. Fuller, E. Adams, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|K.K. Fuller, J.D. Lightfoot, Microbiology & Immunology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure: Kevin Fuller: Commercial Relationship: Code N (No Commercial Relationship) | Emily Adams: Commercial Relationship: Code N (No Commercial Relationship) | Jorge Lightfoot: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: For internal organs, such as the lung, fungal infection drives the development of tissue hypoxia due to inflammation, vascular occlusion and necrosis. It is unknown however whether the cornea –a thin tissue with ostensibly good access to atmospheric oxygen– similarly becomes hypoxic during fungal keratitis (FK). In this study, we tested development of corneal hypoxia, as well as the role of fungal hypoxia adaptation, in the pathogenesis of Aspergillus fumigatus keratitis.

Methods: C57BL/6J mice were immunosuppressed with methylprednisolone on the day preceding inoculation. The next day, corneas were abraded with an algerbrush and topically inoculated with germinated A. fumigatus spores. To measure tissue hypoxia, animals were injected with pimonidazole (Hypoxyprobe) 90 min prior to tissue harvest. Ocular sections were imaged by fluorescence microscopy following staining with anti-hypoxyrprobe or anti-Aspergillus antibodies. The srbA gene of A. fumigatus was deleted via a CRISPR-Cas9 approach. For the virulence studies, animals were inoculated with wild-type (WT) or the ΔsrbA mutant and eyes were imaged daily by slit-lamp and optical coherence tomography (OCT). At 24 and 48 h post-inoculation (p.i.), corneas were isolated for histopathology (PASH stain), fungal burden (CFUs) or flow cytometry.

Results: In corneas infected with A. fumigatus, positive hypoxyprobe staining was observed as early as 12 h p.i. and this signal intensity increased 24 and 48 h p.i. Given these results, we hypothesized that a key regulator of the hypoxic response in A. fumigatus, SrbA, would regulate growth within the infected cornea. We first deleted the srbA gene and, consistent with previous reports, found the mutant was unable to grow in vitro at oxygen levels below 3%. In contrast to corneas infected with WT A. fumigatus, those infected with ΔsrbA failed to develop signs of disease (opacification or ulceration), displayed normal corneal structure by OCT, and did not harbor viable fungus. This corresponded with histopathology and flow cytometry, which revealed a lack of inflammatory cells in ΔsrbA-infected corneas.

Conclusions: Taken together, these results support a model in which fungal antigen rapidly drives the development of corneal hypoxia, thereby rendering SrbA essential for fungal growth and virulence. Consequently, proteins essential for fungal hypoxia adaptation could serve as targets for novel FK therapy.

CONTROL ID: 3714437

SUBMITTER (NAME ONLY): Beatrice Tam

TITLE: Generation of peripherin-2 knock out in Xenopus laevis using Crispr/Cas9

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. Tam, O.L. Moritz, Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

Commercial Relationships Disclosure: Beatrice Tam: Commercial Relationship: Code N (No Commercial Relationship) | Orson Moritz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Peripherin-2 is an integral membrane protein expressed in rod and cone photoreceptors and is involved in disk morphogenesis. It is specifically localized to the highly curved rim regions of the outer segment disks. The purpose of this investigation was to knock out peripherin-2 in X. laevis to aid in the study of the role and functions of this protein.

Methods: Crispr/Cas9 methodology was used to knock out Xenopus peripherin-2 (xrds38). Multiple PAM sites in the DNA sequence were identified and synthetic guide RNA's were designed and generated by in vitro transcription. sgRNA's were coinjected with Cas9 mRNA into fertilized single cell X. laevis embryos. Injected embryos were raised at 18C on a 12:12 light cycle. At 2dpf (days post-fertilization), whole embryos were used to generate genomic DNA. The region surrounding the PAM site was amplified by PCR and DNA sequence analysis was performed to assess the efficiency of editing. At 14dpf, tadpoles were sacrificed and their eyes were enucleated for western blot and immunohistochemical analysis.

Results: Xenopus laevis are pseudo-tetraploid and have two functional genes (and therefore four alleles) that encode xrds38. Several sgRNA's to different PAM sites were investigated and a single sgRNA (sg3) was identified that efficiently edits both genes based on sequencing of genomic DNA. Western blots and antibody labeling of frozen sections confirmed that a subset of animals generated no longer expressed xrds38 in their retinas. Lack of xrds38 expression did not cause retinal degeneration.

Conclusions: We were able to successfully knock out xrds38 expression in photoreceptors. The lack of retinal degeneration observed is likely because X. laevis also express a second peripherin-2 (xrds35/36) which is highly similar in sequence. Xrds35/36 is not however thought to be an orthologue of rom1. The ability to knock out xrds38 will allow us to obtain further insights into the role of peripherin-2 in disk morphogenesis and outer segment homeostasis. Future studies will include simultaneously knock out of both xrds38 and xrds35/36.

CONTROL ID: 3714439

SUBMITTER (NAME ONLY): Todd Appleby

TITLE: Pathways for Local and Global Motion Processing in the Primate Retina

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Appleby, Graduate Program in Neuroscience, University of Washington, Seattle, Washington, UNITED STATES|F. Rieke, Physiology and Biophysics, University of Washington, Seattle, Washington, UNITED STATES|M.B. Manookin, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Todd Appleby: Commercial Relationship: Code N (No Commercial Relationship) | Fred Rieke: Commercial Relationship: Code N (No Commercial Relationship) | Michael Manookin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: During natural viewing, separation of locally moving objects from self-motion-induced global motion is pivotal for safely navigating the world. In many vertebrates, retinal pathways extract local motion from a visual scene. In contrast, no global motion specific pathways in vertebrate retina have been discovered. In primate retina, neither form of motion selectivity has been identified. Here, we recorded from several ganglion cell types in the primate retina, including some of the lesser studied types. In order to test sensitivity to global and local motion, we first assess how global motion affects signal integration, and then measure each cell type's selectivity for local motion relative to global motion.

Methods: Recordings were performed in an intact, in vitro preparation of the macaque monkey retina. Spike responses or whole-cell synaptic currents in ganglion cells were recorded using borosilicate glass electrodes. Neural responses were measured to stimuli that contained local or global motion. Surround-specific motion stimuli were also used to test the effects of motion in the receptive-field surround on cellular responsiveness.

Results: We found pathways in the primate retina that perform computations required for extracting local motion from a visual scene. Additionally, one pathway performs a global motion computation–a novel computation among vertebrate retinas. Further, the receptive field surround was critical in performing these computations. Surround motion shifted sensitivity of responses across cell types, with ganglion cells showing either facilitation or suppression of responses.

Conclusions:

We show here three primate retinal ganglion cells that are selective for local motion, and one that is selective for global motion. We demonstrate that the way in which the receptive field surround affects the receptive field center is key in encoding local and global motion in the primate retina. These results are the first to show that selective processing of local and global motion in the primate visual system begins in the retina.

CONTROL ID: 3714440

SUBMITTER (NAME ONLY): Emily Gower

TITLE: Development of Image Recognition Technology to Identify Individuals with Trachomatous Trichiasis Who Need Surgery

SESSION TITLE: Using Technology for Care Delivery and Improvement

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Gower, J. Weaver, Epidemiology, University of North Carolina at Chapel Hill Gillings School of Global Public Health, Chapel Hill, North Carolina, UNITED STATES|J.C. Prieto, H. Shah, Psychiatry, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|K. Jones, R. Flueckiger, R. Chew, RTI International, Research Triangle Park, North Carolina, UNITED STATES|H. Kana, National Eye Centre, Kaduna, Kaduna, NIGERIA|

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ABSTRACT BODY:

Purpose: Trachomatous trichiasis (TT) is the leading infectious cause of blindness, and an estimated 1.8 million currently need surgery to prevent blindness. The disease primarily affects individuals living in rural parts of developing countries, which can make case identification challenging. Surgery is provided primarily through surgical camps, making it necessary to identify cases in advance. Currently, community members receive a brief training on how to identify TT and then are tasks with going door-to-door to identify potential cases. However, their success is limited, with only 15%-30% of potential cases actually having TT, and many cases are not identified. The goal of this project was to develop an image recognition algorithm that can identify TT with at least 90% accuracy. Ultimately, the goal of this project is to provide local communities with the ability to identify TT with a high rate of accuracy, which will increase the efficiency of TT surgery programs.

Methods: We utilized images from an ongoing TT surgery clinical trial in Ethiopia to develop the algorithm. We designed segmentation and patching software to identify the regions of interest (the upper eyelid) and to indicate areas of the eyelid with and without TT. We trained neural networks to classify each eyelid as having TT present or absent. We then created a smartphone app that incorporates the algorithm that can be used by local community members to identify patients with TT. We conducted a field evaluation in Mozambique to determine how well individuals can take high-quality images using the app.

Results: We utilized over 5,000 images of eyes with and without TT to train and test the algorithm. The algorithm currently has a sensitivity of 92% and specificity of 87%. Six individuals were trained on use of the app and they tested the app over a 5-day period in 2 districts in Mozambique. They took 991 images with the app. The majority of the images were of acceptable quality for the algorithm to process. Over 98% of community members were willing to have their eyelids imaged in order to evaluate the algorithm and app.

Conclusions: This study demonstrated strong potential for machine learning to identify eyelids with TT. Future research should evaluate the effectiveness of this approach across multiple trachoma-endemic countries.

CONTROL ID: 3714442

SUBMITTER (NAME ONLY): Ashwin Badrinath Pothiadia Irungovel

TITLE: Pupil recovery dynamics following melanopsin activation with suprathreshold stimuli

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pothiadia Irungovel, T. Trinh, S. Viswanathan, SUNY College of Optometry, New York, New York, UNITED STATES|A. Hartwick, Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Ashwin Badrinath Pothiadia Irungovel: Commercial Relationship: Code N (No Commercial Relationship) | Toan Trinh: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Hartwick: Commercial Relationship: Code N (No Commercial Relationship) | Suresh Viswanathan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the dynamics of pupil redilation following melanopsin activation with suprathreshold light stimuli.

Methods: Consensual PLR was recorded from normal subjects (n=4, 23-53 years of age) using a custom pupillometer (Diagnosys LLC) to full-field blue (450nm) LED test stimuli of -3.47 log W/sr/cm^2 (14.88 log photons/cm^2/sec) presented to the dilated fellow eye following 5 minutes of dark adaptation. PLR and its recovery was sampled from 3 seconds prior to stimulus onset till 16 minutes after stimulus onset for several durations of the test stimuli in the range of 5 – 120 seconds. Maximal constriction and Post Illumination Pupillary Response (PIPR) at 6 seconds after stimulus offset and for 10 seconds each minute thereafter was calculated. The responses following light offset was fit with an equation of the form $y = a\,(1\text{-}e^{-bx})$ that describes the exponential increase in pupil diameter to the maximum.

Results: Pupil diameter was reduced to 40% (±5) of the pre-stimulus baseline diameter and was similar for all stimulus durations and was sustained for the entire duration for which the test stimuli were presented. The 6s PIPR was 58% (±6%) of the pre-stimulus baseline diameter and PLR recovered to 85% (±3.5) of pre-stimulus baseline diameter by 16 minutes following light onset for all stimulus durations. The time constant b in the equation describing the exponential rise to maximum gradually increased from 0.37 to 0.9 as stimulus duration increased from 5 to 120 seconds.

Conclusions: Suprathreshold test stimuli for melanopsin activation elicit prolonged tonic constriction of the pupil that can take a significant amount of time to recover back to baseline. These preliminary results highlight the importance of allowing adequate inter-stimulus interval durations while performing repetitive testing of PLR with suprathreshold stimuli for melanopsin activation.

CONTROL ID: 3714443

SUBMITTER (NAME ONLY): Haaris Khan

TITLE: Long-term Outcomes of Rehabilitative Surgery in Ocular Cicatricial Pemphigoid and Drug-induced Pseudo-Pemphigoid

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.M. Khan, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|M. Wirth, Department of Ophthalmology, University Hospital Zurich, SWITZERLAND|P.J. Dolman, S. Yeung, A. Iovieno, Department of Ophthalmology, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Ocular Mucous Membrane Pemphigoid (OcMMP) is a chronic autoimmune condition that causes progressive cicatrizing conjunctivitis and shortening of the fornices. Our goal was to investigate the long-term outcomes of fornix reconstruction and cicatricial entropion repair in patients with OcMMP.

Methods: Patients with a diagnosis of OcMMP that underwent fornix reconstruction (with amniotic membrane/buccal mucosal graft) or cicatricial entropion repair by the same surgeon (PJD) between January 1, 2000, to September 1, 2020, were analysed. Patients included in the study had a positive biopsy suggesting OcMMP and/or clinical features of OcMMP or pseudo-pemphigoid. Patients were graded from stages 1 to 4 according to the Foster Classification. The primary outcome was the overall success of fornix reconstruction based on whether there was restoration of a deep fornix at the last follow up appointment. Secondary outcomes included areas of trichiasis, restriction in ocular motility and visual loss from corneal injury.

Results: Ten patients with a diagnosis of OcMMP (80% Foster classification of 3-4) were enrolled (5 males and 5 females, median age: 78) as well as three patients with pseudo-OcMMP (2 females and 1 male, median age: 88). Mean follow up time was 24.9 ± 29.1 months from the initial surgery. Six of the OcMMP patients underwent fornix reconstruction and five underwent entropion repair. In eight OcMMP patients with consistent follow-up, loss of fornix depth or reformation of symblepharon was found on average at 7.1 ± 7.0 months post-operatively. Only one OcMMP patient maintained a deep fornix and half of the patients required an additional corrective surgery. Three patients had an average decrease in visual acuity of 1.75 ± 1.09 logMAR and went on to have evisceration or enucleation surgeries. Recurrence of trichiasis occurred in all but one patient. Eight patients were on systemic immunosuppressive therapy at the time of surgery, but there was no difference in success of outcome between medically treated and non-treated cases. Pseudo-OcMMP patients were noted to have short-term benefit from surgical intervention.

Conclusions: This is the first study reviewing the long-term outcomes of fornix reconstruction and cicatricial entropion repairs in cases of OcMMP, and while initial results are beneficial, these largely reverse an average of 7 months following the interventions.

CONTROL ID: 3714444

SUBMITTER (NAME ONLY): Mary Whitman

TITLE: Investigation of extraocular muscle development in a mouse model of infantile nystagmus syndrome

SESSION TITLE: Nystagmus and Strabismus: Genetics, animal models and imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Whitman, S.K. Vemula, S. Kim, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|M. Whitman, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Mary Whitman: Commercial Relationship: Code N (No Commercial Relationship) | Sampath Vemula: Commercial Relationship: Code N (No Commercial Relationship) | Seoyoung Kim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Infantile nystagmus syndrome (INS) is characterized by involuntary oscillatory eye movements, beginning in infancy. Eye muscle specimens from patients with INS display an increased proportion of slow myosin heavy chain (MyHC) positive muscle fibers and alterations in the neuromuscular junction. It is unknown if these changes are the cause or effect of long-standing nystagmus. Using albino mice as a model of infantile nystagmus, we examined the development of extraocular muscles and their innervating motor neurons during postnatal development.

Methods: We examined the extraocular muscles of postnatal day (P) 0, P10, P14, P21, 6 and 12 week old albino mice and littermate wild-type controls. Balc/c albino mice were crossed to mixed background pigmented mice, and heterozygous mice were crossed to generate experimental litters. Using immunostaining, we compared slow and fast myosin heavy chain (MyHC) composition between control and albino mice extraocular muscles (EOMs) (n=3-6 animals of each genotype at each timepoint). Data were analyzed using unpaired student’s t-test.

Results: In control animals, there is a higher proportion of slow MyHC fibers at P0 (5.28±0.53%), with decreasing expression over time (1.37± 0.12% at 12 weeks), consistent with prior reports. In albino mice, the proportion of slow MyHC fibers is similar to controls at P0 (4.84±1.48%), P10 (4.88±3.14%), and P14 (1.04±0.06%). By P21, there is a higher proportion of slow MyHC fibers in albinos (2.52±0.31%) compared to controls (1.23±0.082%), which persists into adulthood (4.22±1.27% slow MyHC fibers in albinos, 1.37± 0.12% in controls at 12 weeks).

Conclusions: Albino mice, who display nystagmus, have an increase in the proportion of slow MyHC fibers in their extraocular muscles. This is similar to the findings seen in human samples. We see evidence of this difference as early as P21, but not before eye opening (~P12), suggesting that there may be sensory activity-dependent mechanisms that contribute to EOM development.

CONTROL ID: 3714445

SUBMITTER (NAME ONLY): Meraf Wolle

TITLE: A cross-sectional study of gender differences in trachomatous scarring in a formerly trachoma hyperendemic district in Tanzania

SESSION TITLE: Anterior Segment and Trauma Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Wolle, G. Mgboji, B. Munoz, F. Naufal, S.K. West, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M. Saheb Kashaf, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the relationship between gender and the prevalence, and severity, of trachomatous scarring (TS) in a formerly trachoma hyperendemic district.

Methods: A cross-sectional study was conducted amongst adults in Kongwa District, Tanzania. Participants underwent ocular examination. The presence and severity of TS was evaluated in photographs of the everted upper eyelid of each eye. The TS severity was graded using the photographic four step severity scale which goes from S0 (none) to S4 (severe). The analysis was done at the person level; for each participant the more severely affected eye was selected. For the analysis TS was dichotomized; S3 and S4 scars (more severe TS) were grouped together and compared to S0, S1, S2 scars (none to mild TS) which were also grouped together. Logistic regression models were used to examine the association between the age, gender, and TS severity.

Results: A total of 3701 participants were included in this study. We report on a subset of these individuals, 2271 participants. The participants' mean age was 35.8 years (range: 15-94, SD 17.2) and 61% were female. Males and females had similar prevalence of minimal (S1) and mild (S2) TS; females had an increased prevalence of more severe TS. Figure 1 shows the prevalence of more severe TS (S3 and S4 scars) by age and gender. Age was associated with more severe TS; for every year increase in age, there was a 6.6% increase in the odds of having more severe TS (95% CI: 5.8%, 7.4%). More severe TS was seen in females; females were 2.61 times more likely to have more severe TS compared to males (95% CI: 1.95, 3.50).

Conclusions: Gender and age are positively associated with more severe trachomatous scarring. The significantly increased odds of more severe trachomatous scarring in females in this study suggests that focusing on reasons why women develop more severe scarring could yield a pathway by which to reduce the risk of developing downstream potentially blinding trachoma sequalae.

CONTROL ID: 3714447

SUBMITTER (NAME ONLY): Heather Durkee

TITLE: Combined System for Dynamic Refraction and Ocular Biometry During Accommodation

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Changes in ocular power during accommodation are the result of changes in lens shape. Yet, few studies have quantified the relation between ocular biometry and objective accommodative response. These studies typically rely on static measurements repeated at multiple accommodative demands. The goal of this project is to develop an instrument to dynamically measure the relation between changes in refraction and ocular biometry during accommodation.

Methods: The combined system includes a Shack-Hartmann aberrometer to measure refraction, a fixation target to stimulate accommodation, and a previous whole-eye OCT system for biometry (Ruggeri et al, Biomed Opt Exp 2012). The fixation target uses a two-channel Badal system that generates either step and ramp stimuli with vergences ranging from -20 D to +10 D. Refraction and OCT biometry are recorded sequentially by flipping a dichroic mirror. OCT images are processed using a semi-automatic segmentation software to quantify corneal and lens curvatures and intraocular distances. Accuracy of the refraction was assessed by comparing measurements on 23 eyes of 12 subjects (SE range: -9.25 to 2.25 D) with measurements acquired with a commercial autorefractor (KR-800, Topcon). Accommodation responses of three human subjects (ages = 21, 27, 31 years) to three ramp stimuli (2, 4, and 8 D at 0.25 D/s) were recorded in triplicate 25Hz (refraction) and 8.7 Hz (OCT). The responses were analyzed to correlate changes in refraction and biometry.

Results: Bland-Altman analysis shows a mean difference between the clinical autorefractor and custom-made aberrometer of -0.02 D ± 0.9 D (95% confidence limits). The accommodative responses of all three subjects had a similar behavior, with a 6 s latency followed by a linear response with time or accommodative demand up to maximal accommodation.

Conclusions: We demonstrate the feasibility of combined dynamic objective refraction and biometry during accommodation. Dynamic recordings provide faster and more precise quantification of accommodative responses.

CONTROL ID: 3714448

SUBMITTER (NAME ONLY): Ahmad Santina

TITLE: Non-Neovascular Fluid in Age Related Macular Degeneration: Observe and Extend

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Presence of fluid on optical coherence tomography (OCT) in age-related macular degeneration (AMD) is considered a biomarker of neovascular activity. However, recent evidence has shown that fluid does not always indicate neovascularization. Our goal was to describe non-neovascular fluid in AMD and its response to anti-VEGF treatment or observation.

Methods: This observational case series included AMD eyes with macular drusen and/or drusenoid pigment epithelial detachment associated with non-neovascular fluid. OCTA was performed in all eyes to exclude the presence of macular neovascularization at multiple visits. Subretinal fluid (SRF) was tracked and measured to determine the response to anti-VEGF therapy and observation without injections.

Results: 10 eyes of 9 patients with intermediate AMD and SRF were studied over a median period of 54 months (Range: 5.5 months-10 years). Median visual acuity at first visit with documented fluid in logMAR was 0.2 (Snellen equivalent 20/30) with a range of 0-0.4 (20/20–20/50). 6 eyes had a history of anti-VEGF therapy with a median number of 3 injections (Range: 3–27 injections). Median follow-up while receiving injections was 3.5 months (Range: 2–48 months) while median follow-up off injections was 12 months (Range: 4-43 months). None of the eyes responded to anti-VEGF injections except for one eye that showed a response after 1 injection but no response after subsequent injections. SRF thickness remained stable and unchanged during the follow-up off injections in all eyes (n=6) with prior injection and in all eyes (n=4) never injected. 5 out of the 10 eyes developed geographic atrophy and CRORA and one eye developed IRORA and all eyes exhibited at least 2 out of 5 OCT biomarkers of atrophy.

Conclusions: This study provides preliminary data regarding the progression of non-neovascular fluid in AMD with or without anti-VEGF injections. A possible mechanism for fluid development may be related to RPE pump impairment. Distinguishing neovascular versus non-neovascular fluid using multimodal imaging, including OCTA, is essential to avoid unnecessary anti-VEGF injection.

CONTROL ID: 3714451

SUBMITTER (NAME ONLY): Rodrigo Abreu

TITLE: Coherence analysis between an artificial intelligence algorithm and human experts in diabetic retinopathy screening

SESSION TITLE: Machine Learning: Segmentation and Classification

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of this study was to apply an artificial intelligence (AI) algorithm, through deep learning, for the optimized development of an automated diabetic retinopathy (DR) detection algorithm using retinographies and to study the consistency of retina ophthalmologists with the artificial intelligence system in DR screening under routine clinical practice conditions.

Methods: A clinical practice retinographies dataset were used to train an algorithm formed by two component networks which were independently optimized, with the outputs combined to give a single classification for DR. For evaluation, an international standardized retinography dataset in diabetic retinopathy (Messidor-2) was used, which were evaluated by the AI algorithm and two retinal experts with more than 10 years of experience, from different autonomous regions and health systems and diabetic retinopathy screening programs in a blind and independent manner. No prior unification of diagnostic criteria (DR) was performed among the observers to simulate conditions of routine clinical practice, the grades to be used being: absent DR, mild DR, moderate DR, severe DR and proliferative DR. The comparative analysis was performed by grouping DR grades into two groups: Non-derivable (absent DR and mild DR) and Derivable (mild, moderate, severe and proliferative DR).

Results: An image training datsetset of 109,628 images was used for the training phase. Both the AI algorithm and retinal experts analyzed the 1744 images in the evaluation dataset each. The consistency results pitting observer 1 and 2 independently against the AI algorithm were as follows, respectively: a sensitivity of 0.99 and 1; a specificity of 0.74 and 0.71; and an area under the ROC curve of 0.87 and 0.86.

Conclusions: In the current state, our deep learning-based algorithm for retinography-based screening of diabetic retinopathy develops behavior aligned with that of expert retinal ophthalmologists under routine clinical practice conditions. There is the possibility of applying this algorithm in clinical practice with the aim of improving health outcomes compared to the current standard of ophthalmologic management of diabetic patients.

CONTROL ID: 3714452
SUBMITTER (NAME ONLY): Arulita Gupta
TITLE: Time-Driven Activity Based Costing Analysis of Blepharoplasty and Ptosis Repair Surgery
SESSION TITLE: Oculoplastics
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: A. Gupta, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|S. Berkowitz, K.S. Dempsey, S. Patel, L. Mawn, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|
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ABSTRACT BODY:

Purpose: Declining reimbursement and rising costs of labor, operating space, and equipment are threatening the financial health of large academic medical centers. Our goal is to use electronic health record (EHR) time logs and the cost per unit of each resource to calculate the complete cost profile of upper eyelid surgery using time-driven activity based costing (TDABC) analysis. The TDABC analysis uses a bottom up, process based approach to determine resource utilization and estimate cost compared to the level of maximum Medicare reimbursement in the hospital setting.

Methods: Using TDABC analysis, we calculated the cost of healthcare resources consumed for patients undergoing elective upper eyelid surgery (CPT 15822, 15823, 67901, 67903, 67904, 67908) at Vanderbilt University Medical Center (VUMC) in fiscal years 2018-2020. We devised an upper eyelid surgery process flow map and used de-identified time-stamped logs extracted from the EHR, averaged across 154 unique patient encounters, to categorize pre-operative, peri-operative, and post-operative durations. We used cost per minute data for space and equipment, personnel, materials, and overhead provided by the VUMC financial management office for cost allocation. This study was approved by Vanderbilt Institutional Review Board.

Results: TDABC analysis resulted in a total cost of $5393.72 per patient, which is $1706.91 more than the average maximum Medicare reimbursement of $3686.81 for the six upper eyelid procedures studied. Upper eyelid surgery cases do not reach breakeven unless the case duration is less than 39.97 minutes, overhead is reduced by 48.6%, or reimbursement is increased by 46.3%.

Conclusions: The analysis demonstrates that true costs for upper eyelid surgery are significantly greater than the maximum allowable Medicare reimbursement for a hospital setting. Reimbursement is inadequate even under ideal capacity constraints with fully available ORs and full copayment from every patient.

Upper eyelid surgery TDABC analysis can guide surgeons and administrators in providing higher value, lower cost care by optimizing processes, settings of care, and allocating resources judiciously. Ophthalmology departments in academic hospital settings may also benefit from accurately measured upper eyelid surgery costs to inform policy discussion regarding appropriate reimbursement.

CONTROL ID: 3714453

SUBMITTER (NAME ONLY): Alex Pham

TITLE: A comparative study on the efficacy of netarsudil versus brimonidine in eyes already being treated with anti-ocular hypertensive medications

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pham, C. Bradley, C. Casey, J. Yohannan, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of the addition of netarsudil compared to brimonidine in glaucoma patients requiring more than two baseline glaucoma medications for intraocular pressure management.

Methods: A chart review was performed to compare eyes prescribed with netarsudil (n=176) and eyes prescribed with brimonidine (n=193) as a third to fifth agent in the setting of uncontrolled IOP. Five sequential IOP measurements were obtained to determine the mean change in IOP before and after treatment ($\Delta IOP = \text{mean } IOP_{4,5} - \text{mean } IOP_{1,2,3}$). A multilevel linear mixed-effects model assessed the impact of medication (independent variable) on ΔIOP (dependent variable). Additional independent variables of interest included the number of glaucoma medications at baseline, age, sex, glaucoma type and severity, race, and pre-treatment IOP. Multiple linear regression estimated the effect of both medications as a third to fifth agent. Bootstrap analysis was performed to remove sampling bias and equate the distributions of potentially confounding variables for both netarsudil and brimonidine.

Results: The unadjusted mean ΔIOP for netarsudil and brimonidine was −2.20 and 0.60 mmHg respectively ($p < 0.001$). The linear mixed-effects model showed that netarsudil significantly improves IOP by 2.30 mmHg more than brimonidine. However, bootstrap analysis revealed both medications demonstrated statistically similar benefits. Both the mixed-effects model and bootstrap analysis showed diminishing effects of both medications with an increasing number of other glaucoma medications at baseline, albeit this trend was not significant in the mixed-effects model. Specifically, the multiple linear regression model revealed the estimated ΔIOP of netarsudil and brimonidine when added as a third, fourth, and fifth agent is −3.18, −2.49, and −1.79 mmHg; and 0.13, 0.82, and 1.51 mmHg, respectively. Both medications failed to control IOP at similar rates, leading to additional laser and surgical interventions in subsequent follow-up in approximately a third of eyes.

Conclusions: When escalating pharmacologic therapy, netarsudil and brimonidine are comparable options in terms of efficacy. Both medicines have diminishing effectiveness when added in eyes with more glaucoma medications at baseline. Clinicians should consider individual costs and tolerance when deciding the most appropriate treatment.

CONTROL ID: 3714454

SUBMITTER (NAME ONLY): Rachel Downes

TITLE: Proliferative vitreoretinopathy phenotype in the setting of retinal tear without preceding retinal detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) has been defined as a major complication of rhegmatogenous retinal detachments (RRD). We seek to describe the phenomenon of PVR development in patients with horseshoe retinal tears (HST) in the absence of a preceding RRD.

Methods: This is a retrospective case series of patients who initially presented with retinal tears without rhegmatogenous retinal detachment. Patients with history of retina surgery or RRD prior to retinal tear diagnosis were excluded. PVR was defined according to the standard PVR classification. We analyzed the associated risk factors predisposing the patients to PVR development including presence of vitreous hemorrhage, phakic status, patient factors (e.g., myopia, smoking history), and interventional history (laser retinopexy vs. cryotherapy and the number of laser spots).

Results: Eight patients with PVR development following a HST were identified. The median age was 55.5 years old. Five patients were male. Three of 8 patients identified as former smokers. All 8 patients were myopic. Seven of 8 patients are phakic. All 8 patients presented with vitreous hemorrhage at the time of retinal tear diagnosis. Seven patients had 1 HST at the time of diagnosis and one had 2 HSTs. Seven of 8 patients had laser retinopexy and 1 patient had cryo-retinopexy. In the 7 patients with laser retinopexy, 5 of 7 had laser retinopexy with greater than 700 laser spots. Three patients were identified as having Grade B PVR, and 4 patients had Grade C PVR (1 unknown grade). Six out of 8 patients required retinal surgery for PVR retinal detachments. The other 2 patients required surgery for epiretinal membrane.

Conclusions: While proliferative vitreoretinopathy is classically defined as a complication following rhegmatogenous retinal detachment, we describe a series of patients who develop PVR following retinal tear without detachment. Vitreous hemorrhage was a uniting risk factor in this case series. Our case series suggests that PVR can develop within a spectrum from retinal tears to RRD. Awareness of this potential complication of HST may aid in patient education.

CONTROL ID: 3714456

SUBMITTER (NAME ONLY): May Ameri

TITLE: Fallacy of Disease: Equivocation

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ameri, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|D.T. Szynkarski, R. Cortez, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|D.S. Gombos, S.P. Patel, N.S. Al-Zubidi, The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is extremely difficult to clinically differentiate between ocular immune-related adverse events (IrAEs) of immune checkpoint inhibitors (ICIs) and paraneoplastic-associated retinopathy. Although rare, early detection of IrAE retinopathies is essential, given the degree of tissue damage is often disproportionate to the symptoms. The purpose of this study is to exaCancmine and discuss the diagnostic challenge of distinguishing between melanoma-associated retinopathy and immune checkpoint inhibitor (ICI) related retinopathy - which poses a unique diagnostic challenge.

Methods: Dilated fundus exam (DFE), electroretinogram (ERG), MRI, PET scan, cytokine panel, and a literature search were conducted.

Results: A 55-year-old male with a history of metastatic malignant melanoma of left forearm Stage IV (rpT2a, pN0, cM1c) on ipilimumab and nivolumab presented with symptoms of nyctalopia, diminished color contrast and light/dark contrast, abnormal visual phenomena, and constricted visual field OU. The exam showed 20/20 vision OU, bilateral color vision deficiency (9/14 OD and 10/14 OS), and no RAPD OU. The DFE showed no optic nerve swelling, pallor, or retina abnormalities. ERG did not show the classic “electronegative response” which we would expect to see with MAR. Instead, we see a normal b-wave and absent a-wave which denotes pure rod dysfunction. Thus, the patient’s symptoms are likely attributed to an ICI-related adverse event such as bilateral retinal vasculitis.

Conclusions: Although severe and insidious in nature, ocular IrAEs are a lesser-known effect of ICIs in the medical community; moreover, even in specialized oncology clinics, it is still extremely difficult to diagnose due to the ambiguity of the disease. Further, immediate appropriate treatment through discontinuation of ICI and starting a trial of steroids, IVIG, and PLEX is necessary for ocular IrAEs to prevent permanent vision loss. Especially, given that these retinopathies often require further specialized testing such as ERGs or mfERG to differentiate between them and cancer-related retinopathies, recognition by oncologists and early referral to an ophthalmologist is essential.

CONTROL ID: 3714457

SUBMITTER (NAME ONLY): Jennifer Hyuna Kim-Lee

TITLE: Clinical, structural, and functional characteristics of RPE65 mutation related Leber congenital amaurosis in a Mexican cohort

SESSION TITLE: Inherited Retinal Disease Genetics II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To describe the clinical, structural, and functional features of RPE65 mutation related Leber congenital amaurosis (LCA) in a Mexican cohort.

Methods: A descriptive, observational, and transversal study was carried out. Twelve unrelated patients with molecularly and clinically diagnosed RPE65-LCA were included. Visual function studies included best-corrected visual acuity (BCVA), refraction testing, Farnsworth-Munsell D-15 test, full-field electroretinography (ERG), Full Field Stimulus Threshold test (FST), Goldmann kinetic visual field, chromatic perimetry, and microperimetry. In addition, spectral domain optical coherence tomography (SD-OCT) and autofluorescence (AF) imaging (488 nm and 532/633 nm) were performed in all patients. Measures of central tendency were utilized to analyze the data.

Results: Twenty-four eyes of 12 patients (ages 10-32) were analyzed. The BCVA ranged from 20/50 (snellen) to light perception and the average was of 1.09 ± 0.75 (logmar). There were no detectable rod and cone ERGs in all patients. By FST (analyzed in 17 eyes), 82% (n=14) presented a rod- and cone-mediated function while the remaining 18% (n=3) presented only a cone-mediated function. The extent of kinetic fields varied widely regardless of the age and only 25% (n=6) of the eyes detected a III4e stimulus (range of 5-70 degrees of remaining central vision). In the chromatic perimetry, the mean global deficit of rod- and cone-mediated function was of 46.8 ± 9.1 dB and of 31.0 ± 7.1 dB respectively. Absent (n=20) or minimal (n=4) AF was observed in both short and long wavelength AF images. On average, the horizontal extension of the ellipsoid zone (EZ) was of 3366 ± 3047 µm and the subfoveal outer nuclear layer (ONL) thickness was of 53 ± 29 µm. In the microperimetry (evaluated in 8 eyes), the preferred retinal loci were situated mainly in the fovea-parafovea and superior perifovea.

Conclusions: Accurate diagnosis of RPE65-LCA remains the foremost goal since it allows to stage the degree of retinal degeneration, estimate the prognosis, and tailor the treatment addressing the characteristics of each patient. Our study contributes to the understanding of the genotype-phenotype correlations of this disease in the Mexican population and accentuates the importance of undertaking a multimodal evaluation to identify patients who may benefit from gene therapy.

CONTROL ID: 3714458

SUBMITTER (NAME ONLY): Nan Gao

TITLE: The mechanisms underlying ocular pain initiated by blue light stress

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Gao, F. Yu, Ophthalmology, Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Nan Gao: Commercial Relationship: Code N (No Commercial Relationship) | Fu-shin Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular pain (OP) causes significant morbidity and negatively impacts the quality of life for millions in the United States. However, despite an increased recognition of the importance and prevalence of OP, its diagnosis and management remain challenging because of a lack of understanding regarding the mechanisms underlying OP. We sought to establish a blue light exposure animal model that recapitulates the features of human OP.

Methods: Eight-week-old C57BL/6 mice were reared in cycles of 12-hour of blue light (BL) with 420nm wavelength alternating with 12-hour of darkness . Control mice will be maintained in 12 light/12 dark cycle from white light sources. The changes of behavior were assessed by wind, cold, and chemical stimulation. Corneas or trigeminal ganglion were collected, and immunostaining were performed for tunnel staining, β3-tubutin, SP, TRPV4 or TRPV1. Expression of TRPV1, TRPV4, galanin and SP in corneal projecting neurons (CPNs) were assessed using qPCR.

Results: We discovered that BL-exposure induces hypotonic/hypertonic-induced eye-wiping and decrease tear secretion and stability after cycle 1. The cold-stimulated blinking and wind-stimulated eye-closing behaviors required 3 cycles and their intensities further increased between cycle 7 and 9. Whol e mount confocal microscopy revealed that BL exposure reduced the number of branching of stromal nerve fibers and decreased the density of epithelial nerve endings with increased tortuosity and beadlike fibers/endings. Using neuronal retrograde tracer, the CPNs were identified and most CPNs are both TRPV1 and 4 positive. BL exposure increased the TRPV1 (TRPV1^{high}), but not TRPV4 staining intensity, particularly in some TRPV4 positive CPNs. The CPN enriched TG fraction had significantly elevated mRNA expression of TRPV1, but not TRPV4, as well as neuropeptides, substance P (SP), CNTFRα and NGFR. At the protein levels, certain TRPV1^{high} CPNs are also SP positive in the TG and more SP positive nerve endings in the corneas of BL exposed mice.

Conclusions: Taken together, we established a mouse ONP model suitable for studying mechanisms underlying the pathogenesis and chronicity of OP and showed that BL exposure increases TRPV1 and SP expression in the TG and SP secretion, resulting in the sensitization of nociception and ONP.

CONTROL ID: 3714461

SUBMITTER (NAME ONLY): Mahesh Agarwal

TITLE: Role of cytoskeletal dynamics in neutrophil activation and cytotoxicity toward retinal endothelial cells in early diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Differentiated HL-60 (dHL-60; neutrophil-like) cells were treated with the major DR risk factors viz. TNF-α (10ng/ml), IL-1β (10ng/ml), high glucose (HG, 30mM), and precursor of advanced glycation end product-methylglyoxal (MGO, 10μM), for 6 hours. dHL-60 activation was assessed by measuring superoxide level (using dihydroethidium dye, DHE; 5mM) and CD11b expression. The actin cytoskeleton was visualized in TRITC-Phalloidin-labeled cells using an epifluorescence microscope. Cytoskeletal parameters such as F-actin intensity and distribution, and morphological features (cell size and shape) were quantified using ImageJ.

Methods: Differentiated HL-60 (dHL-60; neutrophil-like) cells were treated with the major DR risk factors viz. TNF-α (10ng/ml), IL-1β (10ng/ml), high glucose (HG, 30mM), and precursor of advanced glycation end product-methylglyoxal (MGO, 10μM), for 6 hours. dHL-60 activation assessed by measuring superoxide level using dihydroethidium (DHE;5mM) dye and CD11b expression. The actin cytoskeleton was visualized in TRITC-Phalloidin-labeled cells using an epifluorescence microscope. Cytoskeletal parameters such as F-actin intensity and distribution, and morphological features (cell size and shape) were quantified using ImageJ.

Results: Our findings revealed that, among the aforementioned risk factors and when compared with untreated dHL-60 cells, TNF-α elicits the highest increase in superoxide generation (1.58-fold; $P<0.001$) and CD11b expression (1.26-fold; $P< 0.001$). Further, neutrophil activation by TNF-α correlated with the highest increase (1.12-fold; $p<0.01$) in both cell size and F-actin polarization. In contrast, and rather unexpectedly, HG and MGO treatments caused a reduction in superoxide production, which was consistent with a concomitant reduction in cell size (12%; $P<0.01$) and F-actin polarization (30%; $P<0.001$).

Conclusions: By correlating F-actin changes with superoxide generation, these findings raise the possibility of a potentially novel link between cytoskeletal dynamics and neutrophil activation in early DR. Ongoing studies are aimed at further elucidating the molecular mechanisms by which DR risk factors alter cytoskeletal dynamics in neutrophils and determining whether cytoskeletal modulation in neutrophils is necessary and sufficient to regulate its adhesion to and cytotoxicity toward retinal ECs.

CONTROL ID: 3714462

SUBMITTER (NAME ONLY): Michael Lin

TITLE: Comparison of portable perimetry tests with the Humphrey Field Analyzer

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lin, Y. Zhao, S. Freeman, J. Kang, S. De Arrigunaga, D.S. Friedman, D.L. Liebman, A.M. Roldan, T. Elze, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D. Chang, Genentech Inc, South San Francisco, California, UNITED STATES|D. Chang, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The tablet-based Melbourne Rapid Fields (MRF) visual field (VF) test (M&S Technologies, Niles, IL, USA) and IMOvifa virtual reality (VR) VF test (CREWT Medical Systems, Inc., Tokyo, Japan) are portable VF tests that may allow for at-home monitoring and more frequent testing. We compared MRF and IMOvifa outputs to the Humphrey Field Analyzer (HFA) 24-2 Swedish Interactive Threshold Algorithm Standard program.

Methods: In a pilot observational study, subjects who were glaucoma suspects or had a prior glaucoma diagnosis took IMOvifa and MRF tests. All subjects were reliable, experienced HFA testers. We built density plots of average mean deviation (MD) and pattern standard deviation (PSD) and compared MD and PSD group means of each novel device to the HFA. We used paired t-tests to compare sensitivities of 54 corresponding locations from HFA 24-2 also tested on the new devices.

Results: For 50 subjects with an average age of 61 years (range 30-79), MD and PSD for all three devices were not significantly different (MD: HFA vs. IMOvifa CI=[-0.30 to 1.38], p=0.205; HFA vs. MRF CI=[-0.75 to 0.93], p=0.837; PSD: HFA vs. IMOvifa CI=[-0.05 to 1.18, p=0.070]; HFA vs. MRF CI=[-0.65 to 0.57], p=0.905). MRF sensitivities differed from those of HFA at 28 locations, while 23 locations differed for IMOvifa versus HFA. MRF reported greater point sensitivity in the nasal field versus HFA but lower sensitivity in the temporal field. IMOvifa generally reported lower sensitivity versus HFA.

Conclusions: While average MD similarities between the novel devices and the HFA suggest they provide similar results, point-by-point comparisons indicate significant differences. Peripheral point sensitivity differences between MRF and HFA may be related to MRF's flat tablet format versus HFA's spherical bowl format. The IMOvifa had a small bias throughout the field. The small sample size and calculation of MD as a weighted average toward the VF center may explain the lack of difference in MD despite many mostly peripheral differences in sensitivity between each novel device and the HFA.

CONTROL ID: 3714463

SUBMITTER (NAME ONLY): Anisa Chaudhry

TITLE: Repeatability and correlation of a virtual reality perimeter with standard automated perimetry in glaucoma patients

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.F. Chaudhry, A.R. Berneshawi, J. Liu, A. Shue, D. Chang, R.T. Chang, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|D. Chang, J. Kim, Genentech Inc, South San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Anisa Chaudhry: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Berneshawi: Commercial Relationship: Code N (No Commercial Relationship) | Jocelyn Liu: Commercial Relationship: Code N (No Commercial Relationship) | Ann Shue: Commercial Relationship: Code N (No Commercial Relationship) | Dolly Chang: Commercial Relationship: Code N (No Commercial Relationship) | Julia Kim: Commercial Relationship: Code N (No Commercial Relationship) | Robert Chang: Commercial Relationship(s);Code C (Consultant/Contractor):Genentech, Inc.

ABSTRACT BODY:

Purpose: To determine the repeatability of the head-mounted VisuALL Field Analyzer (vFA; Olleyes Inc., Summit NJ) and visual field parameter output correlation with the Humphrey Field Analyzer (HFA; Carl Zeiss Meditec, Dublin CA).

Methods: 45 experienced visual field test takers with an established glaucoma diagnosis and an HFA visual field (HVF) < 3 months were enrolled at a single institution. Both eyes (N=90) underwent portable vFA testing (virtual reality visual field with calibrated light stimuli meant to mimic HFA) on two separate visits. At the first visit, patients completed two vFA tests and one HVF SITA Standard 24-2 for each eye. The order may have started with HVF first if the patient had already completed it as part of their clinical visit during enrollment. Patients who had not already completed an HVF, started with the vFA first before performing an HVF. The second visit occurred within two months of the first visit, in which the patient completed one additional vFA for both eyes.

Results: The mean age of the cohort was 68 years (range of 31-88). Gender distribution was 25,20 (56% male, 44% female). The two baseline vFA tests showed high intravisit test-retest reliability with Pearson correlation coefficient r=0.94 for mean deviation (MD), and r=0.93 for pattern standard deviation (PSD) values. The average MD and PSD values of the two baseline vFA tests also had high Pearson correlation values of r=0.92 and r=0.87 for MD and PSD, respectively. Lastly, the vFA values also demonstrated high intervisit repeatability when comparing the average of the two baseline MD and PSD with the follow up visit (Pearson r=0.9 for MD, and r=0.87 for PSD).

Conclusions: The vFA has a high intravisit and intervisit test-retest reliability at baseline and follow-up among glaucoma patients experienced with perimetry and correlates well with gold standard HFA. The vFA may be a useful clinical tool to enable remote glaucoma monitoring and potentially allow more frequent visual field testing to assess change over time.

CONTROL ID: 3714466

SUBMITTER (NAME ONLY): Meghana Kalavar

TITLE: Effect of the SARS-CoV-2 (COVID-19) Pandemic on Authorship Gender Disparities in the Ophthalmology Literature

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kalavar, Havener Eye Institute, The Ohio State University, Columbus, Ohio, UNITED STATES|M. Kalavar, A. Watane, P.G. Iyer, K. Cavuoto, J. Sridhar, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Watane, Yale University, New Haven, Connecticut, UNITED STATES|J.A. Haller, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies in several fields of medicine have found that women published less during the COVID-19 pandemic, potentially due to an increase in domestic responsibilities. This study examines whether a similar pattern exists for female authorship in ophthalmology.

In this study, we compared the proportions of female authorship published in high-impact ophthalmology journals before and during the COVID-19 pandemic.

Methods: A cross-sectional study analyzing authorship gender of articles published during the COVID-19 pandemic (between July and September 2020) compared to matched articles published in the same journals before the COVID-19 pandemic (between July and September 2019). Gender of first and last author was analyzed using an online gender determination tool.

Results: A total of 577 articles and 1113 authors were analyzed. There was no significant difference in the average number of publications per male and female author when comparing pre-pandemic to during the COVID-19 pandemic. There was a significant increase in the percentage of female first authorship from pre-pandemic (32%) to during the COVID-19 pandemic (40%, $p=0.01$), but no significant increase in last authorship ($p>0.05$). When analyzing only research articles, a similar increase in female first authorship was noted when comparing pre-pandemic (31%) to during the COVID-19 pandemic (43%, $p=0.02$). No significant differences were noted when analyzing editorials ($p>0.05$).

Conclusions: While disparities continue to exist between male and female authorship, an increase in female first authorship was noted during the COVID-19 pandemic for overall articles as well as research articles.

CONTROL ID: 3714468

SUBMITTER (NAME ONLY): Lina Zelinger

TITLE: Genetic analysis of familial AMD cohort identifies genes associated with disease susceptibility

SESSION TITLE: Molecular genetics of ocular conditions

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Zelinger, J. Advani, M. English, A. Swaroop, NNRL, National Eye Institute, Bethesda, Maryland, UNITED STATES|T.M. Martin, J. Maykoski, M.L. Klein, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|A. Kwong, Department of Biostatistics and Center for Statistical Genetics, University of Michigan, Ann Arbor, Michigan, UNITED STATES|C. Malley, E.Y. Chew, Division of Epidemiology and Clinical Applications, Clinical Trials Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|Y. SERGEEV, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|R.N. Fariss, Biological Imaging Core, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. Kwong, 23andMe, Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) continues to present a major challenge to the vision field. With over 11 million patients in the US and 190 million worldwide, AMD is the third leading cause of vision loss in the world. Despite more than 150 years of research at-least 50% of the heritability of AMD remains unclear. Our goal is to take advantage of familial clustering of AMD to gain a better understanding of the genetic factors contributing to AMD development.

Methods: Patients with familial history of AMD seen at the Casey Eye Institute were recruited for the study. Medical and ophthalmologic data and blood samples were collected. DNA was isolated from blood samples, and whole exome/genome sequencing was performed on 554 AMD patients and controls from 127 families. FASTQ files were aligned against human reference genome GRCh38 using BWA (Version 0.7.17). Variants were called by GATK (Version 3.8-1), and annotated with ANNOVAR. Variant and segregation filters were applied to retain only rare and potentially pathogenic variants segregating within at least one family.

Results: Combining classic genetic approaches and bioinformatic tools, we were able to verify associations in 11 previously reported genes, including well established genes such as complement factors, but also newly identified genes such as DCHS2 and DNAH14. This corresponds to only 13% of our families suggesting that there are other contributing genetic factors within our cohort. Notably, 4 genes were found to segregate in more than one family, while the remaining were each found only in one family, underlining the challenges in identification of rare genetic factors. We then performed systematic analysis of WES data to identify segregating rare variants in genes not previously associated with AMD. This analysis yielded 5869 genes. Next, we filtered the list to genes which segregated in 3 or more families, resulting in 330 genes. To identify high confidence candidates, we investigated if they overlaped known AMD loci or belonged to a distinct pathway. This highlighted 2 pathways previously not associated with AMD, lipid transport and sphingolipids. Additional experiments to validate these findings are underway.

Conclusions: We performed genetic analysis on a large familial AMD cohort. Our results corroborate other familial studies and provide new insights in to the molecular pathways contributing to AMD.

CONTROL ID: 3714470

SUBMITTER (NAME ONLY): Kaitryn Ronning

TITLE: Comparing microglia and monocyte-derived macrophages in the retina after photoreceptor degeneration

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Ronning, M.E. Burns, Center for Neuroscience, University of California Davis, Davis, California, UNITED STATES|S.J. Karlen, M.E. Burns, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure: Kaitryn Ronning: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Karlen: Commercial Relationship: Code N (No Commercial Relationship) | Marie Burns: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: During photoreceptor degeneration monocytes from the periphery can infiltrate the retina and join the resident microglia in the immune response to neuronal loss. After photoreceptor loss is complete ramified macrophages re-tile the retina, but this population remains heterogeneous. Here we compared subtypes of macrophages before and after photoreceptor degeneration.

Methods: Using a light-inducible model of photoreceptor degeneration ($Arr1^{-/-}$ mice), we investigated retinal macrophages before and after photoreceptor degeneration (0 and 20 days of light exposure, respectively). To compare subtypes of macrophages in the retina, we used flow cytometry to quantify cell numbers, immunohistochemistry to quantitatively examine cellular morphologies, and single-cell mRNA sequencing (scRNAseq) to investigate gene expression. All mice were handled according to ARVO, NIH, and UC Davis IACUC guidelines.

Results: After photoreceptor degeneration is complete, the retina contains a heterogeneous population of macrophages. ScRNAseq revealed transcriptionally distinct subpopulations, including one population that highly expressed genes associated with a monocytic lineage in addition to genes similarly expressed by mildly activated microglia, such as Aif1, Lyz2, and Sepp1. Using a fluorescent lineage tracing paradigm to conclusively identify microglia and monocyte-derived macrophages ($Arr1^{-/-}$ $Ai9^{KI/KI}$ $Cx3cr1^{+/YFP\text{-}CreER}$), we find that monocyte-derived macrophages comprise approximately half of all retinal macrophages after photoreceptor degeneration is complete. Additionally, these monocyte-derived macrophages reside alongside bone fide microglia throughout the retina, although they are typically less morphologically complex than the resident microglia.

Conclusions: Following photoreceptor degeneration, a heterogeneous population of macrophages remain in the retina. This population consists of both microglia and monocyte-derived macrophages. The monocyte-derived macrophages adopt a range of microglia-like characteristics, including expression of genes such as Aif1, spatial tiling throughout the retina, and a ramified morphology. However, differences in transcriptional signatures, morphological complexity, and response to further injury suggest these cells with disparate etiologies may remain functionally distinct populations over prolonged periods of time.

CONTROL ID: 3714471

SUBMITTER (NAME ONLY): Kanika Seth

TITLE: CALM: A retrospective registry to characterize clinical outcome data for chronic non-infectious posterior segment uveitis patients treated with a 0.18 mg fluocinolone acetonide intravitreal insert

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Seth, R.P. Singh, S. Sharma, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Kanika Seth: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Singh: Commercial Relationship(s);Code I (Personal Financial Interest):Novartis, Genentech, Regeneron, Alcon, Bausch and Lomb, 41 Gyroscope;Code F (Financial Support):Apellis, Aerie, Graybug | Sumit Sharma: Commercial Relationship(s);Code C (Consultant/Contractor):AbbVie, Alimera, Bausch & Lomb, EyePoint, Regeneron, Genentech/Roche, Clearside;Code F (Financial Support):Gilead, Genentech/Roche, Santen, IONIS

ABSTRACT BODY:

Purpose: Uveitis describes a heterogeneous group of diseases characterized by intraocular inflammation due to either infectious or non-infectious causes. Non-infectious uveitis (NIU) often requires sustained, long-duration therapy, either systemic or local. The fluocinolone acetonide intravitreal (FAi) insert (0.18) is used to treat chronic, non-infectious posterior uveitis by delivering a low-dose, sustained release of FA for up to 36 months. The purpose of this study is to describe the outcomes of the FAi in treating NIU in a real-world database.

Methods: A phase IV, web-based registry system was developed to capture patients treated with the FAi insert from multiple clinical sites, to assess the impact on ocular inflammation using OCT imaging, fluorescein angiography, and visual acuity endpoints. Visual acuity was converted from Snellen equivalent to ETDRS. Safety details, including intraocular pressure and glaucoma interventions, were collected and summarized.

Results: Eight sites have contributed data for 149 eyes of 115 patients with a mean (± standard deviation [SD]) age of 63.7 ± 12.6 (range 19 to 90) to the registry. 60% of the patients are female and 70% are white. The majority of eyes (79.2%) were treated for either posterior or panuveitis. Mean OCT thickness at the time of study entry was 374.1 ± 159.4 microns and average VA was 57.9 ± 25.0 letters. OCT central subfield thickness measurements indicate that 42% of the eyes had a dry central retina at the time of implant. That number increased to 55% at 6 months. 55% of eyes had 20/50 or better visual acuity at baseline and that number increased to 60% at 6 months. Mean baseline IOP was 13.8 ± 4.6 mmHg (range 5 to 30) and increased 1.0 ± 4.9 mm Hg on average at 6 months. The retrospective database will remain open for up to 5 years.

Conclusions: Preliminary data in the CALM registry database indicate effective control of non-infectious uveitis, with improved visual acuity outcomes and without major safety signals. Additional data will be needed to validate these short-term results.

CONTROL ID: 3714472

SUBMITTER (NAME ONLY): Jung Lee

TITLE: Tissue-specific evidence for SARS-CoV-2 within intraocular tissues

SESSION TITLE: Infection and Immunity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, Y. Wang, S. Kodati, C. Chan, H. Sen, National Eye Institute, Bethesda, Maryland, UNITED STATES|S.R. Stein, K.M. Vannella, D.S. Chertow, Emerging Pathogens Section, Critical Care Medicine Department, National Institutes of Health Clinical Center, Bethesda, Maryland, UNITED STATES|S.R. Stein, K.M. Vannella, D.S. Chertow, Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, UNITED STATES|A. Grazioli, Kidney Diseases Branch, Kidney Disease Section, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland, UNITED STATES|D.L. Herr, R Adams Cowley Shock Trauma Center, Department of Medicine and Program in Trauma, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|J. Rabin, R Adams Crowley Shock Trauma Center, Department of Surgery and Program in Trauma, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|K.K. Saharia, Department of Medicine, Division of Infectious Disease, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|S.M. Hewitt, D.E. Kleiner, Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, Bethesda, Maryland, UNITED STATES|P. Perez, B.M. Warner, Salivary Disorders Unit, National Institute of Dental and Craniofacial Research, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To systematically investigate ocular changes in autopsied eyes from fatal cases of Coronavirus disease 2019 (COVID-19) and to investigate the localization of severe acute respiratory syndrome coronavirus (SARS-CoV-2) within ocular structures.

Methods: Macroscopic and microscopic histopathological evaluation was performed and the localization of SARS-CoV-2 RNA within ocular tissues investigated using an in situ hybridization (ISH) technique in 13 eyes. Contralateral eyes were freshly dissected, and droplet digital polymerase chain reaction (ddPCR) assay was performed on ocular fluids and tissues to quantify SARS-CoV-2 RNA.

Results: A total of 21 fatal COVID-19 cases were included (mean age, 60.2 years [range, 27-91 years]; 23.8% female). Histopathological abnormalities include vascular changes (61.9%), cytoid bodies (52.4%), and retinal edema (23.8%) with minimal inflammation (0.09%) were observed. Non-CMV viral inclusions were identified in one eye. No CMV positivity was detected. Of the 21 contralateral eyes tested by ddPCR, 14 tested positive for SARS-CoV-2. Using ddPCR and ISH, SARS-CoV-2 localization was observed in the following ocular tissues and fluid: cornea (27.3%), aqueous (26.3%), lens (54.5%), vitreous (15.0%), retina (22.2%), choroid/sclera (47.4%), and optic nerve (50.0%). The choroid/sclera, optic nerve and lens were the most frequent ocular structures found to be ddPCR positive. Evidence of replication was detected in four cases.

Conclusions: Our results suggest that SARS-CoV-2 localizes to intraocular tissues. However, histological changes observed are likely a secondary hemodynamic change rather than primary effect of the virus.

CONTROL ID: 3714473

SUBMITTER (NAME ONLY): Victor Perez

TITLE: Robust ocular inflammatory response to an immune allergic eye disease challenge in a novel murine IKZF1 transgenic model associated with Steven's Johnson's Syndrome.

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.L. Perez, H.M. Mousa, R. Mathew, L. Lin, R.G. Blanco Ortiz, C. Beatty, S. Littleton, J. Kalnitsky, J. Echegaray, D.R. Saban, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|S. Komai, S. Kinoshita, M. Ueta, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|

Commercial Relationships Disclosure: Victor Perez: Commercial Relationship(s);Code F (Financial Support):Alcon, Heat Biologics, NIH;Code C (Consultant/Contractor):Asclepix, Brill, Dompe, Kala, Kiora, Novartis, Oyster Point Pharma;Code I (Personal Financial Interest):Trefoil | Hazem Mousa: Commercial Relationship: Code N (No Commercial Relationship) | Rose Mathew: Commercial Relationship: Code N (No Commercial Relationship) | Liwen Lin: Commercial Relationship: Code N (No Commercial Relationship) | Ricardo Blanco Ortiz: Commercial Relationship: Code N (No Commercial Relationship) | Cole Beatty: Commercial Relationship: Code N (No Commercial Relationship) | Seitaro Komai: Commercial Relationship: Code N (No Commercial Relationship) | Sejiro Littleton: Commercial Relationship: Code N (No Commercial Relationship) | Joan Kalnitsky: Commercial Relationship: Code N (No Commercial Relationship) | Jose Echegaray: Commercial Relationship: Code N (No Commercial Relationship) | Shigeru Kinoshita: Commercial Relationship: Code N (No Commercial Relationship) | Mayumi Ueta: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Saban: Commercial Relationship(s);Code C (Consultant/Contractor):Roche, AbbVie, Novartis;Code F (Financial Support):Dompe

ABSTRACT BODY:

Purpose: To characterize the ocular phenotype of a novel transgenic mouse strain with a constitutional ocular expression of the IKZF1 isoform, found in humans to be associated with Steven's-Johnson's syndrome (SJS), after immune challenge using the allergic eye disease (AED) model.

Methods: IKZF1 transgenic mice (IK-Tg) were provided by Ueta et al. Experiments were carried out on wild-type (WT) Balb/c and IK-Tg mice aged 8-10 weeks. Both strains underwent immunization followed by a sequential topical challenge using an established model of AED. Clinical eye disease was assessed using (1) an established composite score (2) Meibomian gland plugging, and (3) fluorescein corneal photographs. The challenge-response of each group was compared by calculating the endpoint to baseline change in each score (Δ). Mann-Whitney test was used with a $p<0.05$ cutoff. Molecularly, flow cytometry was used to quantify conjunctival immune cell and submandibular lymph nodes (SMLN) cytokine expression. Fold-increase from unchallenged counterparts was calculated and results of the challenged groups were analyzed descriptively.

Results: After AED challenge, IK-Tg eyes had a significantly larger increase in composite ocular score (Δ ocular score: 5.6 [5.1,6.25] vs 4.8 [4.3,5.25], p=0.001) and Meibomian gland plugging (Δ plugs: 7 [4.25,9] vs 5 [4,6], p=0.01) plus a trend towards higher increase in corneal staining (Δ fluorescein staining: 3.5 [2.25,5] vs 1 [1,3], p=0.06) compared to challenged WT eyes [n=22/group] (Figure 1). In addition, challenged IK-Tg mice had a higher increase in % eosinophilic composition (5.1 vs 4.3-fold increase) and a higher overall % composition of neutrophils (11% vs 2%) in the conjunctival CD45 population compared to challenged WT mice [n=10/group]. Compared to their unchallenged counterparts, both groups experienced increased CD4 cytokine expression in the SMLNs with IK-Tg having a larger increase in IFN-gamma (1.5 vs 1.1 folds), a lower increase in IL-13 (1.9 vs 2.3 folds), and a similar increase in IL-17 (2.8 vs 2.9 folds) % expression change [n=10/group].

Conclusions: IK-Tg mice are characterized by a unique disease phenotype responding distinctly to immune challenge resulting in added exaggeration of ocular disease which can model the hypersensitivity of ocular inflammatory disorders, more specifically, SJS.

CONTROL ID: 3714474

SUBMITTER (NAME ONLY): Lema Noubani

TITLE: Discovering Risk Factors Associated with Open Angle Glaucoma Using a Robust Electronic Health Record (EHR) Database

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Noubani, K.P. Shanmugam, Texas A&M University Health Sciences Center, Bryan, Texas, UNITED STATES|C. Murugesan, M. Raju, Informatics, University of Missouri, Columbia, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Lema Noubani: Commercial Relationship: Code N (No Commercial Relationship) | Krishna Shanmugam: Commercial Relationship: Code N (No Commercial Relationship) | Charunetha Murugesan: Commercial Relationship: Code N (No Commercial Relationship) | Murugesan Raju: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It has been well reported that primary open-angle glaucoma (OAG) is a second leading cause of irreversible blindness across the globe. Identifications of potential risk factors associated with OAG could provide preventive measures to control OAG earlier in the disease progression. In this study, we used a large electronic health record (EHR) database representing a wide demographic to assess risk factors for OAG.

Methods: The OAG study cohort was identified using International Classification of Diseases (ICD) codes. We retrieved a total of 132,504 OAG records from 2001 to 2015 for retrospective analysis using exclusion and inclusion criteria for the study. We assessed the relationship between OAG and selected variables using multivariable logistic regression. Adjusted risk ratios were calculated from fitted logistic models and a p-value of < 0.05 was considered statically significant.

Results: Estimated from the dataset, the overall prevalence of OAG was about 15.3%. The incidence of OAG was higher in African Americans (27.5%) and Asians (13.9%) and a lower incidence was observed among the Hispanic (11.0%) race. When comparing gender, females showed a higher prevalence of glaucoma (16.3%) compared to the male population (15.7%). Furthermore, an adjusted odds ratio analysis from the regression model revealed several potential risk factors including atherosclerosis (1.19; 95% CI 1.13. – 1.51), hypertension (1.32; 95% CI 1.20-1.42) and obesity (1.26; 95% CI 1.1 - 1.40) when compared to the non-glaucoma group.

Conclusions: The results preliminarily suggest that obesity and hypertension may be risk factors for OAG and lead one to believe these disease processes should be explored in further detail. Furthermore, the African American race has a higher risk of developing glaucoma compared to the Caucasian (p <0.05) race. With the use of a massive cohort gathered through the EMR database, the identified risk factors can increase our current understanding of glaucoma risk and can therefore, aid in timely intervention and disease management.

CONTROL ID: 3714476

SUBMITTER (NAME ONLY): Shubha Subramanya

TITLE: Flow cytometry methods to detect markers of outer retinal stress and cell death in a model of acute nutrient stress

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Subramanya, R. Fernando, M. Goswami, E. Weh, H. HAGER, C.G. Besirli, T.J. Wubben, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent data have shown that disruption of nutrient delivery and utilization by photoreceptor cells is a common pathway in regulating cell death in retinal degenerative diseases. Experimental retinal detachment (RD) in rodents is a model of acute outer retinal nutrient stress that leads to photoreceptor apoptosis. The purpose of this study was to optimize flow cytometry markers of outer retinal stress and apoptosis in a rodent model of nutrient stress.

Methods: Methods Experimental RD was created in mice and rats via subretinal injection of 1% hyaluronic acid. 3 days post-RD, retinas were harvested and dissociated into single cells using trypsin. Dissociated cells were either incubated with Annexin-V, propidium iodide (PI), and Phiphi lux (active caspase-8) or fixed and stained with TUNEL and cleaved caspase-8. Z-VAD, a pan-caspase inhibitor, was injected sub-retinally at the time of RD and these markers were assessed 3 days later. Tert-butyl hydroperoxide (TBH) was injected intravitreally (IVT), retinas harvested and dissociated 6 and 24 hours later, and cells incubated with DCFDA, C11-Bodipy, and Calcein-AM to examine oxidative stress using flow cytometry. Cells were gated, and data were analyzed by comparing signals to either isotype controls or unstained cells using FCS Express software (De Novo Software, Ontario, CA).

Results: Statistically significant increases in TUNEL (>17-fold; $p<0.001$) and active Caspase-8 (>17-fold) were observed in RD. Treatment with Z-VAD significantly reduced these markers. To confirm these results, we repeated RD in a previously reported model of photoreceptor neuroprotection, the PKM2 conditional knockout mouse. We confirmed that compared to detached retinas in WT animals, PKM2 cKO mice showed reduced TUNEL staining (>7-fold vs >1.3-fold). In WT mice, TBH-mediated oxidative stress increased DCFDA staining (>2.3 fold) and lipid peroxidation markers (>6.7-fold) as well as reduced viability (>1.7-fold).

Conclusions: Flow cytometry is a sensitive, quantifiable, and reproducible method for measuring apoptosis and oxidative stress in a model of outer retinal nutrient stress. It has the advantage of increased efficiency compared to traditional histologic methods. These flow cytometric methods will be key to assessing novel photoreceptor neuroprotective therapies in a multitude of retinal degeneration models.

CONTROL ID: 3714477

SUBMITTER (NAME ONLY): Runze Li

TITLE: Simultaneous Assessment of the Whole Eye Biomechanics Using High Frequency Ultrasonic Elastography

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Li, X. Qian, C. Gong, J. Zhang, M.S. Humayun, Q. Zhou, Department of Biomedical Engineering, University of Southern California, Los Angeles, California, UNITED STATES|R. Li, X. Qian, Y. Liu, B. Xu, M.S. Humayun, Q. Zhou, Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conventional elastography usually targets and assesses the biomechanical properties of specific ocular structures, for example, the cornea. However, there are some diseases that are broadly impacted by different structures across the entire eye. Glaucomatous optic neuropathy, for example, is associated with increased stiffness in the cornea, sclera, and iris. Therefore, there is a need to develop a tool that can concurrently quantify the biomechanical properties of multiple ocular structures. In this study, we aim to develop a high frequency array based ultrasonic elastography (HFUE) to meet this requirement.

Methods: A 18 MHz linear array was used for imaging and elastic wave acquisition. The rabbit was first anesthetized and positioned, and a shaker tip was brought into contact with the corneal limbus to initiate the elastic wave. An infusion line and intraocular pressure (IOP) sensor were inserted into the posterior segment of the eye through trocars. The height of infusion line was modulated to elevate the IOP. To capture the elastic wave propagation with fine image quality, the acquisition speed was set to 10 KHz. Pulse-width of shaker was set to 1 ms to induce vibrations while maintaining a broad bandwidth of the elastic wave. Raw data was saved for further analysis. Group velocity was calculated to reconstruct the Young's modulus.

Results: Figure 1 shows the elastic wave mapping of the eye and the corresponding B-mode imaging during different levels of IOP. Figure 2 shows the biomechanical response of cornea, lens, iris, parapapillary sclera (PPS), and optic nerve head (ONH) to the different IOPs levels. The Young's modulus of cornea and iris has a linear relation with IOP, PPS and ONH has an second polynomial relation with IOP, while lens is not affected by IOP.

Conclusions: Our elastopgrahy system can concurrently assess the biomechanical properties of multiple ocular structures and detecting the changes in biomechanical properties associated with changes in IOP.

CONTROL ID: 3714478

SUBMITTER (NAME ONLY): Sindhu Velmurugan

TITLE: A new mode of gene therapy to subdue the limitations of the allotopic method: an analytic approach

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Velmurugan, T. Chou, J. Eastwood, D. Alba, V. Porciatti, J. Guy, H. Yu, ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the efficacy of gene therapy using mito-targeted and allotopic expression strategies to treat LHON in mice.

Methods: Adult DBA/1J mice (N=30) were randomly split into three groups and were injected with mitochondria-targeted AAV carrying mutant human ND4 gene (hND4G11778A) to induce LHON. We rescued them at a two-day interval using 1) mito-targeted strategy with MTSAAVs carrying- a) mCherry(n=10), b) wtND4(n=10), naïve (mCherry-mCherry) (n=10) and 2) allotopic strategy (n=20) with MTSAAV carrying a) mCherry (n=10), b) wtND4 (n=10) into both eyes. The rescue of the optic nerve and retina atrophy was evaluated using PERG and TEM.

Results: Our main hypothesis is that the mito-targeted strategy will likely result in a higher delivery efficacy than the allotopic approach making it a quicker and an efficient treatment option for LHON. PERG was performed and mice treated with mito-targeted wildtype hND4 showed a PERG amplitude increase by 34% (p=0.150), 46% (p=0.035), and 83% (p=0.093) respectively at 3, 6, and 12 months after injection, whereas mice treated with allotopic expressed wildtype hND4 increased PERG amplitude by 12% (p=0.594), 21% (p=0.357), 43% (p= 0.012), and 33% (p=0.087).The time course of age-related PERG changes was different between the 2 groups (Interaction age x treatment, P=0.003) (Fig.1A), indicating the efficiency of mito-targeted rescue over allotopic where no significant effect of age (P=0.55) but an overall effect of group on PERG amplitude between the rescued and unrescued mice(P=0.043) was observed (Fig.1B). The significance in amplitude difference (control vs rescue) for mice in mito-targeted strategy (OD, P=0.006; OS, P=0.023) indicates that the rescue efficacy with mito-targeted ND4 compared to allotopic.
TEM revealed that MTND4-rescued mice displayed a shift towards small axons showing that the mito-targeted hND4 efficiently prevented the demise of small axons that are lost in human LHON.

Conclusions: Our data showed that the severe visual loss induced by a mitochondrial disease may be reversed using both mito-targeted and allotopic expressed gene therapy,but mito-targeted therapy likely mediates a quicker and more efficient rescue than the allotopic strategy making it a promising option to treat LHON.

CONTROL ID: 3714479

SUBMITTER (NAME ONLY): Alaina Reagan

TITLE: Introducing a novel Mthfr$^{677C>T}$ mouse to model a common risk variant for glaucoma

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Reagan, M. Sasner, G. Howell, The Jackson Laboratory, Bar Harbor, Maine, UNITED STATES|K. Christensen, R. Rozen, McGill University, Montreal, Quebec, CANADA|T. Bottiglieri, Baylor Scott & White Health, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Methylenetetrahydrofolate reductase (MTHFR) is a critical enzyme in the folate/methionine/homocysteine pathway. Variants in MTHFR, notably 677C>T, have been associated with glaucoma as well as Alzheimer's disease and vascular dementia, suggesting an overlapping mechanism in brain and eye. However, mechanisms driving increased risk are not known, hindering the development of new treatments. Approximately 30% of individuals carry at least one copy of MTHFR$^{677C>T}$, causing a 50% decrease in MTHFR enzyme efficiency. Reduced efficiency can lead to high levels of homocysteine in blood, resulting in vascular inflammation and increased risk for vascular damage. We hypothesize that vascular-specific expression of MTHFR$^{677C>T}$ drives damaging effects in the retinal vasculature, priming the environment for additional risk.

Methods: CRISPR technology was employed to engineer the Mthfr$^{677C>T}$ allele into C57BL/6J (B6) mice. Characterization of the Mthfr$^{677C>T}$ retina includes: RNAscope to determine MTHFR expression, assays to examine MTHFR enzyme activity and relevant metabolite levels, retinal wholemount immunostaining to evaluate vascular abnormalities and inflammatory markers, retinal cross-section immunostaining to examine neuronal layer thickness and glial reactivity, and in vivo OCT and Micron IV imaging as well as pERG to assess retinal morphology and ganglion cell function, respectively.

Results: Previous data show Mthfr$^{677C>T}$ mice phenocopy the human condition — mice show a 50% reduction in MTHFR enzyme activity in liver and brain, elevated levels of plasma homocysteine, altered brain metabolites associated with the methionine cycle, as well as morphological and functional changes in cerebrovasculature. We anticipate similar phenotypes will arise in retinas of our young (6 month) and aged (18 month) cohorts of Mthfr$^{677C>T}$ mice, and are focusing on examining blood retinal barrier integrity using leakage assays and assessing endothelium, vascular smooth muscle, pericytes, basement membrane and tight junctions by immunostaining. Current data support our hypothesis with Mthfr$^{677C>T}$ mice showing evidence of retinal arterial tortuosity.

Conclusions: We have created a novel mouse strain to determine the precise mechanisms by which MTHFR$^{677C>T}$ increases risk for vascular dysfunction with age and in neurodegenerative retinal disease.

CONTROL ID: 3714480

SUBMITTER (NAME ONLY): Katherine Chuang

TITLE: Outcomes of Pseudomonas aeruginosa Keratitis in Patients Using Extended Wear versus Standard Soft Contact Lenses

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chuang, R. Enzor, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|B.M. Perzia, Ophthalmology, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|E. Bowers, Otolaryngology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|R. Enzor, A. Mammen, R.P. Kowalski, V. Jhanji, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pseudomonas aeruginosa is the most common cause of contact lens-related bacterial keratitis; overnight wear is the most important risk factor irrespective of lens type. Silicone hydrogel lenses with high oxygen permeability are FDA-approved for continuous overnight wear, typically for 1 week to 1 month. In this study, we compared outcomes of Pseudomonas aeruginosa keratitis (PAK) between patients wearing extended-wear (EW) versus standard soft contact lenses.

Methods: This retrospective cohort study includes 145 sequential cases of PAK in soft contact lens wearers (SCLW) at a single academic site from 1/2006 to 9/2019; 127 cases occurred in standard SCLW and 18 cases in EW SCLW. P values were calculated using unpaired 2-tailed Student's t-test for continuous variables or chi-squared or Fisher's exact test for binary variables.

Results: Mean age was 36.4 ± 18.1 years in standard SCLW and 56.8 ± 18.9 in EW SCLW ($P<0.0001$), and average time to presentation was 2.66 ± 2.55 days in standard SCLW and 4.22 ± 4.62 days in EW SCLW ($P=0.033$). Overnight wear of contact lenses was reported by 71 (55.9%) of standard SCLW and 17 (94.4%) of EW SCLW ($P=0.0014$). Corneal stromal thinning was present in 59 (46.5%) of standard SCLW and 10 (55.6%) of EW SCLW ($P=0.47$). Maximal stromal thinning was 18.4 ± 29.4% in standard SCLW and 29.4 ± 36.1% in EW SCLW ($P=0.15$), and a procedure (corneal glue, amniotic membrane, or penetrating keratoplasty) was required for progressive stromal thinning in 16 (12.6%) of standard SCLW and 3 (16.7%) of EW SCLW ($P=0.71$). The length of antibiotic treatment was 50.6 ± 67.2 days in standard SCLW and 78.3 ± 97.2 in EW SCLW ($P=0.15$). Final logMAR visual acuity was 0.75 ± 0.83 in standard SCLW and 0.83 ± 0.85 in EW SCLW ($P=0.71$).

Conclusions: Outcomes of PAK were similar between EW and standard SCLW. While not significantly different, a trend existed toward an increased rate of progressive stromal thinning and a longer course of antibiotic treatment in patients wearing EW contact lenses. Final visual acuity and need for a procedure for corneal stromal melting was similar between the two groups.

CONTROL ID: 3714482

SUBMITTER (NAME ONLY): Miaomiao Yu

TITLE: Visuo-motor assessments of eye-brain diseases using infrared oculography

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Yu, M. Shariati, Y.J. Liao, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Miaomiao Yu: Commercial Relationship: Code N (No Commercial Relationship) | Mohammad Ali Shariati: Commercial Relationship: Code N (No Commercial Relationship) | Yaping Liao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Infrared oculography is a noninvasive method of assessing visuo-motor behavior by acquiring time series data. While this technique is widely deployed in eye clinics for improving reliability of visual field attestation and ophthalmic imaging, it is not widely used for diagnostic purposes. The current study aims to curate and analyze a detailed oculography dataset from neuro-ophthalmic patients using novel rapid number reading paradigms. Our goal is to highlight the oculography features associated with each number reading test that best distinguish patient groups with visuo-motor dysfunctions, namely vision loss, eye movement disorder, and Parkinson's disease.

Methods: We performed 1059 recordings using 500-Hz 2-dimensional infrared oculography (RED500, SensoMotoric Instruments (SMI), Germany) in 111 participants (healthy controls and patients with clinically diagnosed eye-brain diseases) who have had careful clinical neuro-ophthalmic assessments. We used regularly and irregularly spaced variations of the King-Devick (KD) rapid number reading test (each one 40 numbers per page, 3 pages total) and extracted time series oculography data using commercial software BeGaze (SMI) and Python scripts. Fixation, saccade and blink parameters were analyzed using biostatistical methods.

Results: Initial power analyses conducted showed regularly spaced number reading paradigms to be good assessments of visuo-motor dysfunction. One-way ANOVAs revealed that significant effects of patient group in 4 out of 13 oculography features. Fixation count, saccade count, total saccade duration and total reading time, were significant for all three KD test variations. Effect sizes were also greater for eye movement disorders (nystagmus and cerebellar ataxia), and Parkinson's disease (most common neurodegenerative disease with ocular-motor manifestations) as compared to those with vision loss (homonymous hemianopia, severe optic neuropathies), highlighting the efficacy of such reading paradigms in diagnosing neuro-ophthalmic diseases associated with visuo-motor dysfunction.

Conclusions: The results indicate fixation count, saccade count, saccade duration and total reading time as reliable features for distinguishing the visuo-motor abnormality in patients with vision loss, ocular motor dysfunction, and Parkinson's disease. Within reading paradigms, regularly spaced paradigms are better indicators of patient group than irregularly spaced.

CONTROL ID: 3714483

SUBMITTER (NAME ONLY): Elena Solli

TITLE: Grading and Quantification of Papilledema from Fundus Photographs Using Convolutional Neural Networks

SESSION TITLE: Machine Learning and Augmented Virtual reality

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Solli, M.J. Kupersmith, Neurology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|W. Jui-Kai, J. Branco, R.H. Kardon, L. Pasquale, M.J. Kupersmith, Ophthalmology, The University of Iowa Hospitals and Clinics Department of Pathology, Iowa City, Iowa, UNITED STATES|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Convolutional neural networks (CNNs) trained on large datasets of fundus photographs differentiate normal from eyes with papilledema but quantifying and grading the papilledema has been limited. Our study investigated if: (1) CNN models can quantify optical coherence tomography measurements for each photo and grade the amount of papilledema in photos using Frisén grading, (2) the CNN model can be adequately trained on a relatively small dataset.

Methods: We used fundus photographs from 165 subjects (330 eyes) in the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT) as input data. Because the IIHTT had few eyes with severe papilledema, we included additional fundus photos from 24 subjects (43 eyes) taken from our clinic for the Frisén grade analysis, and grouped photos showing Frisén grade five papilledema with the Frisén grade four photos. Each photo was labeled according to its Frisén grade (by expert reader), retinal nerve fiber layer thickness (RNFLT), total retinal thickness (TRT), and optic nerve head volume (ONHV) derived from 3D segmentation of corresponding optical coherence tomography images. We trained separate models for quantification of RNFL, TRT, and ONHV, and Frisén grading, using the Densely Connected Convolutional Neural Network “DenseNet161” as the base architecture.

Results: We found a moderate correlation between the true Frisén grades and those predicted by the model (R=0.483, <0.001). We found a strong correlation between the true RNFLT (R=0.793, p<0.001), TRT (R=0.831, p<0.001), and ONHV (R=0.825, <0.001) values and those predicted by the model.

Conclusions: CNN models can identify Frisén grade and provide quantification of OCT-derived RNFLT, TRT, and ONHV values from fundus photographs with moderate success. With supervised learning, it is possible to create reasonable models using relatively small datasets.

CONTROL ID: 3714484

SUBMITTER (NAME ONLY): Scott Oliver

TITLE: Does gene expression profile (GEP) and preferentially expressed melanoma antigen (PRAME) predict metastatic risk in all uveal melanoma, including small tumors and iris melanoma?

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.C. Oliver, Sue Anschutz-Rogers Eye Center, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Scott Oliver: Commercial Relationship(s);Code C (Consultant/Contractor):Castle Bioscience;Code F (Financial Support):Roche/Genentech;Code F (Financial Support):Regeneron

ABSTRACT BODY:

Purpose: To determine whether gene expression profile (GEP) and preferentially expressed melanoma antigen (PRAME) predicts metastatic risk in a variety of uveal melanomas. GEP Class 2 and PRAME+ is known to predict increased risk of metastasis in medium-sized choroidal melanoma.

Methods: Retrospective case series of consecutive patients treated at the University of Colorado for uveal melanoma from 2009-2021. Data included tumor height, diameter, location (iris vs choroidal), American Joint Committee on Cancer (AJCC) stage, cytogenetic GEP, PRAME status, last follow-up, and metastasis onset.

Results: 259 uveal melanomas were treated over an 11-year period (51 iris, 208 choroidal). Mean follow-up was 4.6 years, median = 4.2 years. Of these, GEP results were obtained in 227, and PRAME results in 125 (3 GEP technical failures, PRAME available in 2016). No Class 1B tumors (n=39) metastasized over a mean follow-up of 5 years (range = 0.4-11 years). After 60 months of follow up, GEP class 2 predicted increased metastatic risk in all AJCC TNM Stages I-IV (Stage I: GEP2 = 35% vs GEP 1a = 3% vs GEP 1b = 0%; Stage II: GEP2 = 38% vs GEP1a = 5% vs GEP1b = 0%; Stage III: GEP2 = 62% vs GEP 1a = 0% vs GEP1b = none; Stage IV: GEP2 = 100% vs GEP1a/1b = none).

However, irrespective of GEP status, no choroidal tumors <2 mm in height (n=9, GEP2=0) or <8 mm in greatest linear diameter (n=30, GEP2=5), and no iris tumors (n=30, GEP2 = 7), metastasized. No metastases occurred amongst PRAME negative Class 1a/1b tumors (n=51). PRAME positivity predicted more rapid onset of metastasis in Class 2 tumors (11 months PRAME+ vs 20 months PRAME-).

Conclusions: GEP predicts metastatic risk in medium and large choroidal melanoma but does not predict metastatic risk in choroidal tumors <2 mm in height, choroidal tumors <8 mm diameter, or iris melanoma.

CONTROL ID: 3714485

SUBMITTER (NAME ONLY): Bhim Rai

TITLE: Profile of age-related macular degeneration in Bhutan: Should screening be considered?

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.B. Rai, T. Maddess, Neuroscience, Australian National University The John Curtin School of Medical Research, Canberra, Australian Capital Territory, AUSTRALIA|B.B. Rai, Ophthalmology, JDW National Referral Hospital, Thimphu, Thimphu, BHUTAN|M.G. Morley, Ophthalmology, OCB, Boston, Massachusetts, UNITED STATES|M.G. Morley, Harvard Medical School, Boston, Massachusetts, UNITED STATES|P.S. Bernstein, Ophthalmology, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the severity of age-related macular degeneration (AMD) at first presentation among the Bhutanese patients attending vitreoretinal (VR) clinics and to inform national health policy on the potential benefits of a screening program.

Methods: A retrospective cross-sectional consecutive case series study was conducted on new AMD cases. If a patient presented with asymmetrical AMD, the eye with more severe AMD was considered. If both the eyes had the same severity one eye was chosen randomly. Collection of demographic data and clinical details including diagnostic testing (fundus photography, OCT and fluorescent angiography) and clinical staging were performed.

Results: Of 521 new AMD patients aged 71.9 ± 11.3 years, 306 (58.7%) were males (p=0.005). At their first presentation, 234 patients (44.9%) already had late-stage AMD. Importantly, 69 patients (29.5%), that is half of total neovascular AMD (nAMD) patients, had disciform scars (DS) which were beyond treatment, and 7 (3.0%) had geographic atrophy (GA). Fourteen of nineteen polypoidal choroidal vasculopathy (PCV) patients were younger than 50 years.

Conclusions: Half of total nAMD cases presented as DS not amenable to the treatment. Many potentially treatable patients with nAMD had already lost central vision and were legally blind. Young people with PCV losing vision early in life with longer morbidity-affected life and socio-economic burden was concerning. GA and DS cases need visual rehabilitation to improve their QoL. Incorporating a screening program for AMD with effective health education, and maintaining a national AMD Registry, would potentially lower AMD-related blindness and visual impairment.

CONTROL ID: 3714486
SUBMITTER (NAME ONLY): Saima Khan
TITLE: Readability and Suitability of Online Uveitis Patient Education Materials
SESSION TITLE: Clinical Uveitis & Orbital Inflammation: Etiology, Epidemiology & Clinical Assessment
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Khan, J. Moon, C. Martin, E. Bowden, E. Crowell, Mitchel and Shannon Wong Eye Institute, The University of Texas at Austin Dell Medical School, Austin, Texas, UNITED STATES|E. Tsui, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|J.L. Chen, UC Davis Health Eye Center, University of California Davis, Sacramento, California, UNITED STATES|
Commercial Relationships Disclosure: Saima Khan: Commercial Relationship: Code N (No Commercial Relationship) | Jared Moon: Commercial Relationship: Code N (No Commercial Relationship) | Cole Martin: Commercial Relationship: Code N (No Commercial Relationship) | Eileen Bowden: Commercial Relationship: Code N (No Commercial Relationship) | Judy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Edmund Tsui: Commercial Relationship: Code N (No Commercial Relationship) | Eric Crowell: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose:

Online patient education materials (PEMs) can be difficult for patients to comprehend. With increasing accessibility of online PEMs, it is imperative that healthcare providers understand the quality of such literature so they may direct patients to accurate healthcare information. The purpose of this study is to assess readability, suitability, and accountability of online uveitis PEMs.
Methods: In a cross-sectional analysis, two board-certified ophthalmologists with fellowship training in uveitis analyzed PEMs found on the first ten Google search websites when using the keyword “uveitis”. Readability was assessed using an online calculator; suitability using the Suitability Assessment of Materials (SAM) tool; and accountability using JAMA benchmarks. A review article written for researchers and healthcare professionals was used as a control. Content analysis data were analyzed with the Kruskal-Wallis test and a post hoc Dunn-Bonferroni test. The correlation between accuracy and readability was analyzed using a Spearman correlation test.
Results:

The mean SAM score was 21.05, indicating that the websites were on average adequately suitable to educate patients. The WebMD Uveitis site scored highest with a score of 25.5, while allaboutvision.org scored lowest at 18.0. There was a statistically significant correlation between SAM scores of unique graders ($r=0.8910$, $p<0.0001$).
The average Flesch Reading Ease (FRE) score was 44.0 (95% CI: 34.2, 53.8). The average reading grade score was 11.0 (95% CI: 9.4, 12.6). There was a statistically significant correlation between FRE scores and reading grades ($r= -0.9748$, $p<0.0001$). The difference in average reading grade scores among all websites was statistically significant ($p<0.0001$). The WebMD Uveitis site scored highest on readability.
The average accountability score among the sites was 2.36 out of 4, with statistically significant variation between the sites.
Conclusions: Uveitis websites are only adequately suitable for patient education, and all are above the recommended reading level. We recommend that uveitis specialists be cognizant of the online materials to which they refer their patients. As the average American reads at an eighth grade level, we recommend that authors of online uveitis PEMs use language written at a sixth grade level. This will bridge health literacy gaps and improve access and adherence for all patient populations.

CONTROL ID: 3714489

SUBMITTER (NAME ONLY): Kouros Nouri-Mahdavi

TITLE: Lower Diastolic Blood Pressure: A Risk Factor for Faster GCC Rates of Progression in Patients with Moderate to Advanced Glaucoma

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Nouri-Mahdavi, V. Mohammadzadeh, M. Mohammadi, L. Shi, A.L. Coleman, S.K. Law, J. Caprioli, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|E. Su, R.E. Weiss, Department of Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is scant data in the literature on the association of baseline blood pressure (BP) measures and subsequent structural rates of change in glaucoma. We investigated the influence of various baseline BP measures on change rates of macular ganglion cell complex (GCC) thickness in patients with moderate to advanced glaucoma.

Methods: 105 eyes (105 patients) from the Advanced Glaucoma Progression Study with >4 OCT scans and ≥2 years of follow-up were included. Longitudinal rates of GCC change at superpixels and globally were estimated with a Bayesian hierarchical model with both subject and superpixel-level random effects and residuals. The influence of various baseline BP measures on global GCC rates of change were investigated based on prognostic models adjusting for relevant baseline demographic and clinical measures including gender, ethnicity, age, presence of diabetes, intraocular pressure (IOP), central corneal thickness (CCT), axial length (AL), contrast sensitivity, and 10-2 mean deviation (MD). We report one-sided Bayesian p-values defined as the posterior probability that a given regression coefficient is greater than or less than zero with $p<0.025$ used to identify statistical significance.

Results: The average (SD) 10-2 visual field (VF) MD of the study cohort was –8.3 (5.3) dB. The average (SD) follow-up time and number of OCT images per eye were 3.6 (0.44) years and 7.4 (1.1). On multivariable analyses, female gender ($p=0.003$), higher IOP ($p=0.013$), thicker CCT ($p<0.001$), shorter AL ($p=0.001$), higher contrast sensitivity at 12 cycles per degree ($p=0.02$) and better 10-2 MD ($p=0.019$) at baseline predicted faster macular GCC deterioration (Table 1). Adjusted for the above covariates, a lower diastolic BP (DBP) at baseline predicted worse GCC rates of change ($p<0.001$). Parallel multivariable models incorporating various other BP measures at baseline showed that lower diastolic perfusion pressure, lower mean arterial pressure and lower mean arterial perfusion pressure predicted faster GCC rates of change (all p0.001).

Conclusions: Our newly designed hierarchical Bayesian model properly estimates global and regional macular structural rates of change. A decrease in various DBP measures at baseline predicts faster (worse) macular GCC rates of decline in patients with moderate to advanced glaucoma.

CONTROL ID: 3714490

SUBMITTER (NAME ONLY): Colette Chiu

TITLE: Generation and characterization of RHO knockout Xenopus laevis

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.N. Chiu, B.M. Tam, J. Feehan, O.L. Moritz, Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|J. Feehan, The Sainsbury Laboratory, University of East Anglia, Norwich, Norfolk, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Xenopus laevis frogs are useful for the study of rhodopsin (RHO) variants due to the ease with which transgenic animals can be generated. RHO knockout X. laevis would provide a useful background for the generation of transgenic animals in which the properties of RHO mutants could be studied in the absence of WT RHO. However, generation of knockouts is complicated by the fact that there are three functional X. laevis RHO genes totaling six alleles. Therefore, we have used a multi-generation approach to develop RHO knockouts, using multiple rounds of CRISPR/Cas9-based gene editing.

Methods: Single-cell X. laevis embryos were injected with Cas9 mRNA and sgRNAs designed to target and edit the X. laevis RHO genes. The resulting animals were raised to maturity and bred to identify animals with null RHO alleles caused by frameshift mutations in the first exon. A second round of editing was used to achieve full knockout of remaining functional RHO alleles by editing the second exon. Rod opsin expression was examined by dot blot, and retinal degeneration and photoreceptor morphology were investigated by confocal microscopy.

Results: By characterizing partial RHO knockout; we found that the RHO.L gene was the highest expressed of the three X. laevis RHO genes, and is responsible for 80% of the rod opsin in a tadpole retina. Partial RHO knockouts did not cause extensive retinal degeneration, but resulted in smaller outer segments. Complete RHO knockouts were generated from a background genotype in which RHO.L and RHO.2.L were knocked out and the RHO.S gene carried an in-frame 12 bp deletion that caused retinal degeneration. Editing of the remaining mutant RHO.S gene reduced retinal degeneration. Photoreceptors with complete RHO knockout as assessed by antibody labeling survived to 14 days, and elaborated morphologically abnormal outer segment-like membranes that lacked RHO.

Conclusions: We have generated X. laevis in which a subset of rod photoreceptors lack RHO expression. Further breeding should result in complete RHO knockout lines. Photoreceptors lacking RHO survive to at least 14 days post-fertilization, and elaborate outer segment-like membranes, a result that differs significantly from previous reports in knockout mice. Further characterization of these membranes may demonstrate the role of RHO in outer segment structure; these animals will also be useful for examining the properties of RHO mutants in the absence of wildtype RHO.

CONTROL ID: 3714491

SUBMITTER (NAME ONLY): Anna Camos-Carreras

TITLE: Oral teriflunomide effect on visual function in multiple sclerosis: multifocal electroretinogram responses after 12 months of treatment.

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Camos-Carreras, M. Figueras-Roca, M. Dotti-Boada, B. Sanchez-Dalmau, Ophthalmology Department, Hospital Clinic de Barcelona, Barcelona, Catalunya, SPAIN|S. Alba-Arbalat, S. Llufriu, A. Saiz, P. Villoslada, Neurology Department, Hospital Clinic de Barcelona, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: Development of predictive biomarkers of response to therapy is a priority for therapeutic optimization in multiple sclerosis (MS). The retina represents an ideal model to investigate effects of disease modifying therapies (DMTs) using non-invasive technologies such as multifocal electroretinography (mfERG) and optical coherence tomography (SD-OCT). After DMTs onset, functional changes may precede structural ones, so neurophysiological retinal response deserves further evaluation. The aim of this study was to analyze changes of first kernel mfERG responses after 12 months of oral teriflunomide treatment (14mg/day) in patients with relapsing-remitting MS (RRMS).

Methods: We conducted a prospective open-label study in RRMS patients starting treatment with oral teriflunomide. Patients were assessed at baseline and after 12 months of follow-up. Baseline exploration consisted of monocular 2.5% low contrast letter acuity (2.5% LCLA), SD-OCT (Spectralis, Heidelberg), mfERG (Reti-Port Science, Roland Consult) and Expanded Disability Status Scale (EDSS). At 12 months of teriflunomide treatment, mfERG exam was repeated. mfERG first kernel responses included N1 wave amplitude and peak time as well as P1 wave amplitude and peak time; results were provided as mfERG sum response and sectorial responses by concentric rings (1-5).

Results: 24 subjects (75% females; mean age of 46.8 years), mild disabled (median EDSS=2.0), were included by March 2018 and completed one year of follow-up. mfERG first kernel responses changed over 12 months showing a mean amplitude increase in N1 (+1.19 nV/deg2 [+17.4%], p=0.048) and P1 (+3.55 nV/deg2 [+20.4%], p=0.006) as well as a decreased peak time in N1 wave (-0.002 ms [-6.7%], p=0.006). Considering sectorial (ring) responses, significant increases were found in N1 amplitude (ring 5) and decreases in peak time (ring 1, ring 3 and ring 4) as well as increases in P1 amplitude (ring 3, ring 4 and ring 5).

Conclusions: After 12 months of teriflunomide oral treatment in RRMS patients, we observed significant improvement in retinal function, as revealed by increased wave amplitudes as well as decreased latencies. Considering lack of a control group, the small sample size and the variability of mfERG explorations, these results require further confirmation.

CONTROL ID: 3714492

SUBMITTER (NAME ONLY): Chun-hong Xia

TITLE: Distinct changes of aquaporins in Connexin 50 knockout and MEK1 transgenic lens epithelial cells

SESSION TITLE: Lens Physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Xia, W. Lin, C. Ou, T. Zhang, I. Xu, X. Gong, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the expression of water channel protein aquaporins (Aqps) in the lens epithelial cells of connexin 50 (Cx50, encoded by Gja8) knockout mice with microphthalmia and MEK1(E) transgenic mice with macrophthalmia. To investigate the mechanism about how Cx50 and MEK1 mediated signal transduction pathways regulate water channels and water transport to affect the lens size and homeostasis.

Methods: Single-cell RNA-sequencing (scRNA-seq) analysis was performed to determine the expression levels of genes including aquaporins in lens epithelial cells of Gja8 knockout (Cx50KO) and MEK1(E) transgenic mice. Aqp1 and Aqp5, two major aquaporins expressed in lens epithelial cells, were further characterized for their protein levels and distributions in vivo and in vitro by using western blot analysis and immunostaining.

Results: Altered Aqp1 and/or Aqp5 protein expressions were observed in the epithelial cells of Cx50KO and MEK1(E) lenses. The scRNA-seq data revealed up-regulated Aqp1 in Cx50KO lens epithelial cells while both Aqp5 and Cx46 remained unchanged. Western blot analysis demonstrated Aqp1 protein level was 2.5-fold increased in the Cx50KO lens epithelial cell homogenates compared to wild-type control samples and was 3-fold increased in cultured Cx50KO lens epithelial cells compared to the wild-type control. Immunostaining further confirmed increased Aqp1 expression in cultured lens epithelial cells. Aqp5 protein levels were insignificantly changed in the Cx50KO lens epithelial cells. In contrast, the Aqp5 level was significantly increased in lens epithelial cells of the MEK1(E) mice while Aqp1 remained unchanged.

Conclusions: Upregulated Aqp1 in Cx50KO lens epithelial cells indicates that both Cx50 and Aqp1 likely play important roles in regulating lens water homeostasis. Increased Aqp1 may result from compensatory mechanism for water transport due to a loss of Cx50. Increased Aqp5 in MEK1(E) lens epithelium likely contributes to enlarged lenses leading to macrophthalmia. These data indicate new regulatory mechanisms of Aqp1 and Aqp5 in water transport of lens epithelial cells in Cx50KO and MEK1(E) lenses.

CONTROL ID: 3714493

SUBMITTER (NAME ONLY): Talha Soorma

TITLE: S-cone electroretinograms recorded with a portable device in a series of patients with bi-allelic pathogenic variants in NR2E3

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Soorma, X. Jiang, S. Leo, G. Arno, A.R. Webster, O.A. Mahroo, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|X. Jiang, I. Chow, C.N. Lee, C.J. Hammond, O.A. Mahroo, Ophthalmology, King's College London, London, London, UNITED KINGDOM|C. Valor-Suarez, I. Chow, C.J. Hammond, Guy's and St Thomas' NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Patients with recessive NR2E3-retinopathy can show enhanced S-cone electroretinogram (ERG) responses. We investigated use of a portable ERG device to record S-cone ERGs with skin electrodes in the clinic or office setting from patients and healthy participants.

Methods: Consecutive patients in the retinal genetics clinic with bi-allelic variants in NR2E3 were recruited as well as healthy controls. ERGs were recorded using a portable device (RETeval with Sensor Strip skin electrodes, LKC technologies, Gaithersburg, MD) following pupil dilation. Stimuli were blue flashes (0.25 and 1.0 photopic cd m-2 s) delivered in the presence of a red background (560 cd m-2). Averages from up to 500 responses were analysed.

Results: Recordings were well tolerated (completed in <5 min per eye). Recordings from 5 healthy participants (3 females) and 5 patients (3 females) were analysed. Mean (SD) age of the healthy participants was 32 (6.8) years (median 30). ERGs from healthy participants were similar with small a-wave amplitudes (<3 and <6 microvolts for the two stimuli respectively), and a-wave peak times of approximately 15-18 ms. B-waves were larger than a-waves, usually with 2 or more peaks. Mean (SD) age of the patients was 44 (8.9) years (median 39). In 3 patients, typical “enhanced” S-cone responses were seen, with simplified waveforms. These patients had larger a-waves (typically >4 and >8 microvolts for the two stimuli) than the healthy participants. The b-waves were of similar size to the a-waves (b: a ratio close to 1) and showed single broad peaks at 50 ms or later (delayed compared to controls). In 1 patient, similar ERGs were recorded from one eye, but the fellow eye, which had a dense brunescent cataract, showed attenuated responses. In the 5^{th} patient, responses were severely attenuated; this patient had widespread retinal degeneration (and attenuated responses on conventional recordings).

Conclusions: The characteristic S-cone waveform features were observable using the portable device and skin electrodes in the majority of the patients tested; these were clearly distinct from the waveform obtained in control participants. S-cone ERGs may be more attenuated by brunescent cataract than standard white light ERGs. The technique may be useful in supporting the diagnosis of NR2E3-associated retinopathy when this is suspected.

CONTROL ID: 3714494

SUBMITTER (NAME ONLY): Dipesh Verma

TITLE: Roles of carboxy terminal domains in rhodopsin trafficking to Xenopus laevis rod outer segments

SESSION TITLE: Animal models of human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.K. Verma, T. Woellert, H. Malhotra, P.D. Calvert, Ophthalmology and Visual science, SUNY Upstate Medical University, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cytosolic carboxyl-termini of G-protein coupled receptors (GPCRs) play important roles in dimerization, folding, and membrane transport. Characterized by a small hydrophobic helix and a long flexible tail, C-termini interact with cytosolic partner proteins that couple GPCRs to and modulate signaling pathways. Additionally, GPCRs feature a variety of transport signals within their C-termini, including $E(X)_3LL$, $F(X)_6LL$, and VxPx motifs. However, the mechanism(s) by which these sequences regulate GPCR trafficking remain opaque. Here we examine the functions of C-terminal tail domains in transport of Xenopus laevis rhodopsin to ciliary compartments.

Methods: The role of the rhodopsin C-terminal domains in its localization in the outer segments of photoreceptors was investigated using transgenic X. laevis. Several X. laevis rhodopsin gene mutation and truncation constructs were generated based on multiple sequence alignment and structural information from mammalian rhodopsins and EGFP was appended to the C-termini. Transgenic tadpoles expressing constructs under the Xenopus opsin promoter were generated by REMI and the distribution of gene product was quantified in rods using confocal microscopy.

Results: Contrary to previous reports, truncation of the rhodopsin C-terminus at residue 310 resulted in significant mislocalization of rhodopsin to the photoreceptor cell body, showing that the C-terminus is indeed essential for proper outer segment localization. Addition of VxPx to this truncated construct did not rescue outer segment localization. A previous study of zebrafish rhodopsin showed that methionine 317 (M317), which is conserved across all vertebrate species examined to date except Xenopus which possesses a leucine at this site (L317), results in partial mislocalization of the protein to the cell body. This was completely mitigated by replacing M317 with L. We show here that the reciprocal experiment, generating L317M mutation in Xenopus rhodopsin, results in its partial mislocalization.

Conclusions: Our results show that residue 317 and the VxPx motif are essential for efficient rhodopsin trafficking. L317 allows the most efficient rhodopsin localization to rod outer segments. Remarkably, vertebrates possess rhodopsins with the inefficient M317 and, thus, their rods have chronic, low-level rhodopsin mislocalization.

CONTROL ID: 3714495

SUBMITTER (NAME ONLY): Gaelle Lefevre

TITLE: AAV-mediated hPDE6B gene therapy preserves retinal function in rd10 mice

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: AAV-mediated gene therapy is an attractive option for the treatment of inherited retinal dystrophies. Retinitis Pigmentosa caused by mutations in PDE6B are potentially good candidates for such treatment, and different animal models are available for proof of concept and preclinical investigation. Among them, the rd10 mouse model, which displays a complete deficiency in PDE6B activity, exhibits rapid rod photoreceptor degeneration followed by secondary cone cell death. In this model we evaluated the biological activity of clinical-grade recombinant AAV2/5 vector batches encoding the human PDE6B cDNA (hPDE6B) under transcriptional control of a RK (Rhodopsin Kinase) promoter.

Methods: rd10 mice were reared in dark environment until postnatal (PN) day 28. A volume of 1uL AAV vectors was injected subretinally at PN14 in a single eye. Two cohorts of 6 animals each were treated with two different vector doses: 1.6 x 10e9 and 5 x 10e9 vg/eye. The presence of a bleb after subretinal injection was controlled by OCT examination. At PN35, optical coherence tomographic examination (OCT) and electroretinogram (ERG) were performed. At PN60, OCT, ERG and quantitative optometric response (qOMR) were performed. Mice were sacrificed at PN65, and treated and control eyes were fixed and processed for morphological evaluation as well as immunohistochemistry (IHC).

Results: In the high-dose group, a statistically significant improvement of retinal response to light stimulus (ERG and qOMR) was observed in the treated eye at the earliest time point of evaluation (PN35) and the correction was maintained until sacrifice. Retinal morphology evaluated by OCT was preserved and IHC revealed higher survival of photoreceptors in the treated eye compared to the contralateral eye. In the low-dose group, no statistically significant difference in ERG and qOMR was observed between treated and untreated eyes. However, significant preservation of photoreceptors in treated eyes was observed, mainly at the earliest time point and retinal morphology was partially preserved.

Conclusions: AAV-mediated hPDE6B gene therapy is a valid strategy to prevent photoreceptor degeneration in a PDE6B-related RP model, which further supports the relevance of this approach in the clinic. Therapeutic threshold, however, appears as a critical parameter to achieve clinical benefit.

CONTROL ID: 3714496

SUBMITTER (NAME ONLY): Asmaa Youssif

TITLE: Association of pattern electroretinogram parameters with structural and functional metrics in glaucoma

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the association of steady-state pattern electroretinogram (PERG) with standard automated perimetry (SAP) and optical coherence tomography (OCT) parameters in glaucoma.

Methods: This was a cross-sectional evaluation of glaucoma patients and normal controls included in an observational cohort study. Each patient underwent 24-2 SAP, OCT, and PERG testing with the Diopsys NOVA PERG contrast sensitivity protocol (ConSen protocol) within 7 days. The following PERG parameters were analyzed: MagnitudeD, corresponding to the amplitude of the average signal, and MagD/Mag Ratio, the consistency of the response. For both parameters, lower values indicate an increased likelihood of visual dysfunction. The parameters were tested at high (Hc) and low contrast (Lc). Tests with excessive artifacts or low signal quality were excluded. Linear mixed models nested at the patient and eye levels were used to evaluate the relationship between PERG parameters with SAP MD and RNFL thickness and R^2 was used to measure the strength of the relationship.

Results: The study included 85 visits of 77 eyes of 40 subjects with mean age of 67.5±9.4 years. Eyes had an average SAP MD of -4.97±6.49dB and RNFL thickness of 74.1±18.0µm, with 18% of eyes classified as normal and 82% as glaucoma. The Lc MagnitudeD was 0.014 lower for each 1 MD dB lower (R^2 =0.41; P = 0.001) and 0.040 lower for each 10 µm thinner RNFL (R^2=0.38; P = 0.011), after adjustment for age and gender. For MagD/Mag ratio, RNFL thickness, but not SAP MD, was significantly associated with MagD/Mag ratio at Lc, with 0.03 lower value for each 10µm thinner RNFL (R^2 = 0.39; P = 0.021). Neither RNFL nor SAP MD were significantly associated with PERG Hc parameters in multivariable analyses.

Conclusions: Low contrast stead-state PERG parameters were significantly associated with structural and functional metrics in glaucoma.

CONTROL ID: 3714497

SUBMITTER (NAME ONLY): Jessica Cooke

TITLE: Propensity of patient-derived hiPSCs for retinal differentiation

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Cooke, A.P. Voigt, N.E. Stone, S. Whitmore, A.P. DeLuca, K.R. Anfinson, A.J. Reutzel, H.T. Daggett, J.L. Andorf, E.M. Stone, R.F. Mullins, B.A. Tucker, Institute for Vision Research, Iowa City, Iowa, UNITED STATES|J.A. Cooke, A.P. Voigt, N.E. Stone, S. Whitmore, A.P. DeLuca, K.R. Anfinson, A.J. Reutzel, H.T. Daggett, J.L. Andorf, E.M. Stone, R.F. Mullins, B.A. Tucker, Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|M.A. Collingwood, C.A. Vakulskas, Enzyme Evolution, Integrated DNA Technologies Inc, Coralville, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify a transcriptomic profile in undifferentiated and early differentiating hiPSCs that would predict a given cell line's propensity to generate retinal cells.

Methods: Human iPSCs generated via Sendai virus were validated by scorecard and karyotype analysis prior to differentiation. hiPSC lines were differentiated toward a retinal cell lineage using a stepwise 3D differentiation protocol. RNA was isolated from days 0 and 7 of differentiation and subjected to RNA-sequencing. Transcriptome profiles were determined and validated from a total of 15 independent donors with low vs. high retinal differentiation capacity. Findings were validated in a masked fashion using an additional 16 cell lines.

Results: At 0 and 7 days post-differentiation, cultures were evaluated using RNAseq. Retinal structures were quantified for retinal phenotype microscopically at 16 and 20 days of differentiation. Analysis was focused on identifying genes differentially expressed between good retinal producers (40-80% of organoids showing a retinal phenotype, n=8) and poor retinal producers (<30% of organoids showing retinal phenotype, n =7). Good and poor retinal producer populations demonstrated remarkable gene expression similarity across all lines prior to differentiation (day 0), which was validated via qPCR-based expression analysis. By just 7 days of differentiation, when embryoid bodies all looked the same, significant differences in gene expression could be detected between good vs poor retinal producers. Ingenuity pathway analysis revealed perturbations in both OCT4 and SOX2 effector gene expression, with expression of many of the factors being maintained in poor producers indicating delayed suppression of pluripotency. This pattern of altered genes expression was validated in an additional 16 cell lines in a masked fashion.

Conclusions: There were no discernable differences in pluripotency or other gene expression in undifferentiated hiPSCs. By day 7 of differentiation, a signature gene expression profile, which predicts a given hiPSC line's propensity to generate retinal cells upon further differentiation, could be detected. Specifically, 25+ genes that are differentially expressed between days 0 and day 7 of differentiation were identified. Modulation of these key factors may assist in enhancement of retinal differentiation.

CONTROL ID: 3714500

SUBMITTER (NAME ONLY): kyung sik jung

TITLE: Technique Optimization for Long-term Culture of Human Primary Retinal Pigment Epithelium Cells

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. jung, S.K. Dubey, R. Dubey, M.E. Kleinman, Surgery, East Tennessee State University James H Quillen College of Medicine, Johnson City, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Significant challenges with current techniques to reproducibly grow RPE monolayers remain, and it is unclear which models are the most physiologically relevant. Here, we studied various conditions of long-term primary human RPE (hRPE) culture to optimize techniques for reproducible development of functional, polarized RPE monolayers.

Methods: Early passage (p3-5) hRPE cells (Lonza) were seeded at densities of 0.5, 1, and 2 x 10^5 cells per cm^2 (n=2-4). For media, hRPE were initially fed RPE cell Growth Medium Bullet Kit (RtEGM, Lonza) or RPE culture medium (RPECM, alpha-MEM plus 1% N1 Supplement, 1% Glutamine-Penicillin-Streptomycin, 1% non-essential amino acids, 250 mg/L taurine, 20 mg/L hydrocortisone, 0.013 mg/L triiodo-thyronine) with 1, 5, 10% FBS on transwell plates coated with human fibronectin (2 µg/cm^2). RPE cultures with RtEGM media were either left with same media type or switched to RPECM (1, 5, 10% FBS) at 2d while cells with RPECM were kept in that media. TER, ZO-1 immunofluorescence, and pigmentation were evaluated at various time-points (14d/21d/28d). Statistical analyses were performed with ANOVA and Mann-Whitney U test.

Results: Long-term hRPE cultures with high-density seeding of hRPE isolates (2 x 10^5) yielded the most tightly packed hexagonal arrays with the peak TER values ($P<0.05$) by 21d. Cultures seeded in RtEGM and then switched to 1%, 5%, and 10% FBS in RPECM demonstrated significantly increased TER measurement (> 400 Ω cm^2, $P<0.05$) compared with RtEGM (250 – 350 Ω cm^2) or RPECM (20–50 Ω cm^2). Cultures seeded in RtEGM initially and then switched to RPECM at 2d reproducibly formed monolayers with increased pigmentation (3x) compared to cultures in RPE culture media alone.

Conclusions: Establishing reproducible long-term primary hRPE cultures is critical to experimental designs that propose to study RPE biology. Our data provide an optimized technique for long-term culture of hRPE with high density seeding in growth factor enriched media (RtEGM) followed by feeding with RPECM at 2d. Tight junctions, TER and pigmentation are significantly increased, and monolayers are well-formed by 21d. The utilization of these methods will greatly assist others in the field that are performing long-term RPE culture to achieve reliable models of RPE cell biology and AMD-like RPE degeneration in vitro.

CONTROL ID: 3714501

SUBMITTER (NAME ONLY): Konstantina Sampani

TITLE: Association of capillary plexus vessel density with risk of proliferative diabetic retinopathy in eyes with advanced nonproliferative diabetic retinopathy

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sampani, Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|K. Sampani, M. Ashraf, P.S. Silva, L.P. Aiello, J.K. Sun, Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|M. Ashraf, P.S. Silva, L.P. Aiello, J.K. Sun, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Konstantina Sampani: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Ashraf: Commercial Relationship: Code N (No Commercial Relationship) | Paolo Silva: Commercial Relationship(s);Code F (Financial Support):Optos;Code F (Financial Support):Optomed | Lloyd Aiello: Commercial Relationship(s);Code C (Consultant/Contractor):Kalvista;Code I (Personal Financial Interest):Kalvista;Code C (Consultant/Contractor):Novo Nordisk | Jennifer Sun: Commercial Relationship(s);Code C (Consultant/Contractor):American Medical Association (JAMA Ophthalmology);Code C (Consultant/Contractor):American Diabetes Association ;Code F (Financial Support):Adaptive Sensory Technologies;Code F (Financial Support):Boehringer Ingelheim;Code F (Financial Support):Genentech/Roche;Code F (Financial Support):Janssen;Code F (Financial Support):Physical Sciences, Inc;Code F (Financial Support):Novartis

ABSTRACT BODY:

Purpose: To investigate whether retinal vessel density (VD) of the superficial (SCP), intermediate (ICP) or deep (DCP) capillary plexuses is associated with the risk of progression to proliferative DR (PDR) in eyes with moderate to severe nonproliferative DR (NPDR).

Methods: Treatment-naïve eyes with moderate to severe NPDR within the ETDRS fields on ultrawide field photographs were imaged using 3x3 mm scans on OCTA (AngioVue). DR severity was graded by certified graders. OCTA images were exported to ImageJ (ver 1.51, National Institutes of Health) to manually calculate VD of the parafovea. Clinical data, including treatment history and demographics were reviewed and recorded on standardized forms.

Results: The study group was 75 treatment-naive eyes (70 subjects) with moderate (N=37), moderately severe (N=20) or severe (N=18) NPDR at baseline and a mean follow-up of 2.9±1.3 yrs. Mean±SD age was 49.4±13.4 yrs, 47.2% were female and 61.1% had type 1 diabetes with 26.1±11.8 yrs duration. Eleven eyes, all with baseline severe NPDR, developed PDR within 1.3±1.2 yrs. In the whole cohort, no significant difference was found in mean baseline OCTA SCP, ICP or DCP VD between eyes with or without 2 or more step DR severity worsening or between eyes that did and did not progress to PDR. Time to event analyses of the subgroup with moderately severe or severe NPDR found eyes with decreased DCP VD had higher risk of PDR [point estimate (95% CI): 1.43 (1.1-15.3), p=0.03]. In the subgroup with baseline severe NPDR, time to PDR onset was significantly faster in eyes with increased SCP [1.43 (1.1-15.3), p=0.03], decreased ICP [-0.97 (0.2-0.9), p=0.04] or decreased DCP [-2.51 (0.1-0.6), p=0.02] VD, even after adjusting for age, signal strength index and spherical equivalent.

Conclusions: Subgroup analyses from this study suggest that retinal capillary plexus VD is potentially associated with risk of PDR onset in eyes with moderately severe to severe NPDR. Findings from this cohort are consistent with the hypothesis that eyes with lower DCP, and possibly ICP VD may have faster onset of PDR. The association of higher PDR risk with higher SCP VD could be due to greater SCP perfusion from vascular shunting and capillary remodeling that precedes neovascularization, but additional studies are needed to validate and address this issue.

CONTROL ID: 3714502

SUBMITTER (NAME ONLY): Arianna Tovar

TITLE: Identification and quantification of activated dendritic cells in central cornea in in-vivo confocal microscopy images using artificial intelligence

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tovar, H. Levine, A. Cohen-Karp, A. Galor, B.E. Goldhagen, Miami Veterans Administration Medical Center, Miami, Florida, UNITED STATES|A. Tovar, H. Levine, A. Cohen-Karp, A. Galor, B.E. Goldhagen, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Activated dendritic cells (aDCs) have recently been identified as potential biomarkers indicating the presence of a systemic auto-immune disease in individuals with dry eye (DE). However, their evaluation with in-vivo confocal microscopy (IVCM) is relatively subjective. Therefore, there is a need for a standardized identification method of aDCs to improve generalizability. Our aim was to validate an algorithm that automatically identifies and quantifies aDCs using IVCM images of the central cornea.

Methods: A retrospective analysis of IVCM images obtained from individuals seen at the eye clinic at the Miami Veterans Affairs Hospital was performed. Images from individuals with corneal scarring were excluded due to potential confounding. Artificial intelligence was utilized through the use of an automated aDC counter which was developed using transfer learning with IVCM images. IVCM images used in the development of this algorithm were acquired prior to the start date of this study and did not include any of the same patients. ADCs were manually quantified based on morphology by reviewers that were masked to the algorithm findings, and intra-class correlation (ICC) was used to compare automated and manual counts. Algorithm accuracy was defined as aDC counts within 1 cell compared to manual quantification.

Results: A total of 193 non-overlapping IVCM images from 110 individuals were included. The mean age of individuals included in the study was 55.5±18.4 years; 70.0% were male, 58.2% self-identified as White and 24.5% as Hispanic. There was no statistically significant difference in the mean aDC count between automated and manual quantifications (1.06±1.82 cells/image vs 1.21±1.98 cells/image, p=0.47). The algorithm identified a total of 207 aDCs within the dataset, out of which 184 were manually verified as aDCs. The automated algorithm performed the aDCs count with 87% accuracy and an ICC of 83% ($p<0.01$).

Conclusions: The number of aDCs in the central cornea can be successfully estimated with the use of artificial intelligence with comparable results to manual quantification. Further assessment is needed before the widespread clinical implementation of an automated aDC counter.

CONTROL ID: 3714504

SUBMITTER (NAME ONLY): Alyanna Corpuz

TITLE: Characterization of mechanisms underlying ocular GVHD-associated conjunctival fibrosis

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Corpuz, K. Shamloo, J. Weng, A. Sharma, Chapman University School of Pharmacy, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A significant number of chronic GVHD patients suffer from pathological changes affecting conjunctiva including pseudomembranous conjunctivitis, symblepharon, fornix shortening and bulbar subepithelial conjunctival fibrosis. The purpose of the present study was to investigate the mechanisms underlying GVHD-associated conjunctival fibrosis.

Methods: A mouse model of major histocompatibility-matched and minor histocompatibility-mismatched allogeneic transplantation from B10.D2 donors to BALB/c recipients was used to induce ocular GVHD. Control group was BALB/c to BALB/c syngeneic transplantation. Eyes were harvested at 2 and 4 weeks after the transplant. The tissue sections were stained for alpha-smooth muscle actin (α-SMA) to detect myofibroblast formation as a marker for fibrosis. Nanostring technology based spatial immunostaining was performed for macrophages markers. Gene expression quantification and immunostaining was also performed for profibrotic mediators including TGF-β1, PDGF, and components of renin angiotensin system (RAS).

Results: Prominent α-SMA staining was observed in the bulbar orbital conjunctiva of mice that received allogeneic bone marrow transplantation. Immunophenotyping revealed a concomitant increase in macrophage markers and profibrotic M2 macrophage markers in the conjunctiva of these mice. Allogenic transplantation also caused a 2- to 10-fold increase in the gene expression and protein expression of TGF-β1, PDGF, angiotensinogen and angiotensin converting enzyme in the conjunctiva of these mice.

Conclusions: Results of the present study demonstrate that GVHD-associated conjunctival fibrosis is accompanied by myofibroblast formation, influx of macrophages and an increase in profibrotic mediators.

CONTROL ID: 3714506
SUBMITTER (NAME ONLY): Lindsay Fague
TITLE: DLK is Necessary for Retinal Ganglion Cell Axonal Regeneration in Xenopus laevis
SESSION TITLE: Neuroprotection and Neuroregeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: L. Fague, University of California Davis, Davis, California, UNITED STATES|N. Marsh-Armstrong, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|
Commercial Relationships Disclosure: Lindsay Fague: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Marsh-Armstrong: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Unlike mammalian species, Xenopus laevis can regenerate their retinal ganglion cell (RGC) axons after optic nerve injury. The molecular mechanisms enabling this remain unknown. We performed a pilot CRISPR-screen using a novel moderate-throughput tadpole optic nerve crush (ONC) assay to identify genes necessary for axonal regrowth. Among the genes targeted was Dual leucine zipper kinase (Dlk; i.e. Map3k12).
Methods: For Dlk knockout (KO) line creation, sgRNAs targeting Dlk were injected into eggs within 30 minutes of fertilization. Dlk KO tadpoles were subjected to ONC using bevelled 50-75 um glass needles mounted on micromanipulators at 8 days post-fertilization. Optic nerves and tecta were live imaged over the next 7 days using a Leica fluorescent stereomicroscope. For retrograde tracing, Mitotracker-soaked gelfoam was inserted into the optic tecta at 6 days post-ONC and eyes were dissected out 24 hours later. Degree of reinnervation was assessed from the live imaging data. Phosphorylation of Jun (pJun) and source of tectal innervating axons were assessed in immunolabeled cryosections imaged using a Leica Dragonfly confocal microscope. Custom IPlab scripts were used for all quantifications. All animals were genotyped via sequencing and TIDE analysis.
Results: Dlk full KO animals had 27% of the tectal innnervation seen in wildtype animals 6 days post-ONC, and animals with only 2 copies of an in-frame deletion, Dlk(d56-58), had 60% (X. laevis is allotetraploid with 4 copies of Dlk). In wildtype animals, innervation post-ONC was mainly from central (crushed) RGCs; however, in Dlk KOs, tectal innervation was limited to the most peripheral (newly born) RGCs. ONC significantly increased nuclear pJun selectively in RGCs 2d post-ONC, a response blunted but not absent (40% less than control retinas) in Dlk KOs.
Conclusions: Dlk specifically affects RGC axonal regeneration in a regeneration-capable species. Our assay shows that while new axons are born after injury, most tectal innervation post-ONC comes from preexisting axons, and this innervation is selectively inhibited in the Dlk KO animals. Findings are largely consistent with other literature placing Dlk in a pathway conveying an axonal injury signal to the soma. However, the pJun results show that RGC soma sense axonal injury independent of Dlk. We believe that genes downstream of Dlk in X. laevis offer much promise to promote RGC axonal regeneration in mammals.

CONTROL ID: 3714509
SUBMITTER (NAME ONLY): David Szynkarski
TITLE: Tractional retinal detachment repair: a retrospective study to improve prognostication
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D.T. Szynkarski, R. Cortez, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|D.T. Szynkarski, S. Trejo Corona, R. Cortez, S.B. Patel, T. Wong, D. Garcia, J. Major, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|
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ABSTRACT BODY:
Purpose: Tractional retinal detachment (TRD), the separation of the neurosensory retina from the retinal pigment epithelium (RPE), is a common consequence of proliferative diabetic retinopathy (PDR). TRD cases are complex and have varied surgical outcomes. In this study, we performed a retrospective observational study to observe trends in TRD surgical outcomes with the goal of aiding in preoperative prognostication.
Methods:

Medical records of 193 patients with concurrent diagnoses of PDR and TRD requiring surgery between December 2016 and September 2021 were reviewed. Macula involvement and vitreous hemorrhage at presentation as well as visual acuity (VA) prior to, 1 month after, and 6 months after surgery were recorded. LogMAR VA was used to calculate the mean, standard deviation, and two-tailed t-tests.
Results: Two hundred and seventeen eyes from 193 subjects were studied (n = 217). Mean VA was 1.66 logMAR (~20/900) preoperatively, 1.54 logMAR (~20/700) 1-month post-operatively, and 1.40 logMAR (~20/500) 6-months postoperatively. Of those with a preoperative VA of 20/200 or less, 31% achieved a postoperative VA of 20/70 or better, 12% fell between 20/70 and 20/200, and 57% did not exceed 20/200 at 6-month follow up. Seventy-four percent of TRDs involved the macula. A statistically significant difference in preoperative VA between the macula involving and macula sparing groups ($p > 0.15$) was not observed. However, at 6-month follow-up, 63% of eyes with macula sparing TRDs regained VA of at least 20/70 compared to only 37% of eyes with macula involving TRDs. This suggests that preoperative VA and presence of macula involvement are independent factors that can help prognosticate VA outcome. However, eyes without vitreous hemorrhage (VH) and with preoperative VA of 20/200 or worse were less likely to improve to 20/70 or better versus eyes with VH prior to surgery (14% vs 39%). Therefore, presence of VH may be a confounding factor to consider when using preoperative VA as a prognostication tool.
Conclusions: TRDs are challenging to repair and have a wide array of outcomes, making preoperative prognosis difficult. This study quantifies the prognostic advantage conferred by a preoperative VA of 20/200 or better and by the presence of macula sparing disease. It also demonstrates the effectiveness of TRD repair as a whole. Further analysis will be aimed at elucidating the presence of other confounding variables.

CONTROL ID: 3714510

SUBMITTER (NAME ONLY): Marie Elise Torm

TITLE: Relation between type I diabetes duration and capillary density in the macula

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.W. Torm, J. Hajari, O.N. Klefter, M. Larsen, Department of Ophthalmology, Rigshospitalet, Glostrup, DENMARK|M.W. Torm, J. Johannesen, M. Larsen, Kobenhavns Universitet Sundhedsvidenskabelige Fakultet, Kobenhavn, DENMARK|J. Johannesen, Department of Pediatrics, Herlev Hospital, Herlev, DENMARK|T.W. Gardner, Department of Ophthalmology and Visual Sciences, Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: In patients with diabetes, retinal capillary non-perfusion often precedes ophthalmoscopically visible lesions such as microaneurysms and dot hemorrhages. Signs of capillary perfusion loss have been detected in children and adolescents with a duration of diabetes shorter than 10 years. The purpose of this ongoing study is to map capillary perfusion loss in type I diabetes from early childhood.

Methods: This observational study has currently enrolled 50 participants with type I diabetes and 31 age-matched healthy control subjects. Patient age range was 6-32 (mean 15) years and diabetes duration 14.5-17.5 years (n = 8), 9-11.5 years (n = 14), 4.5-6 years (n = 17), and 0-4 months (n = 11). In healthy controls, the age range was 8-34 (mean 16) years. Exclusion criteria were significant chronic systemic disease other than diabetes and ocular disease other than diabetic retinopathy. Examinations included 3x3 mm macular optical coherence tomography angiography scans (OCTA; Topcon Triton) and fundus photography (Optos). Capillary densities of four different ETDRS grid sectors of the macula were calculated using proprietary software (Topcon ImageNet6) (fig. 1).

Results: Of 50 patients with type I diabetes, seven had very mild and two had mild non-proliferative diabetic retinopathy. Superficial capillary plexus density in patients with diabetes duration 14.5-17.5 years was 44.7 % (mean of temporal sector), compared to patients with shorter diabetes duration and healthy subjects (mean temporal sector densities 47.8 % and 47.6 %, respectively). The numerical deficit in the grid sectors decreased in the order nasal, inferior, temporal, superior. Three of the eight patients with a density below 44.7 % had fundus photographic retinopathy, the rest did not.

Conclusions: Preliminary data from this observational study of patients with type I diabetes suggest that decreased macular capillary density can be detected after a diabetes duration of 15 years and before it can be seen on color fundus photographs. Full enrolment and longer observation time may provide more definite information about these issues.

CONTROL ID: 3714511

SUBMITTER (NAME ONLY): Diana Scavuzzo

TITLE: Clearing up the causes of corneal clouding in aniridia-related keratopathy

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.K. Scavuzzo, J.D. Lauderdale, Cellular Biology, University of Georgia, Athens, Georgia, UNITED STATES|D.K. Scavuzzo, Optometry, University of Pikeville, Pikeville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure: Diana Scavuzzo: Commercial Relationship: Code N (No Commercial Relationship) | James Lauderdale: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aniridia often results in progressive corneal clouding termed aniridia-related keratopathy (ARK), but the causes of this corneal clouding are not well understood. The current study investigates three hypotheses as to the causes of corneal clouding in ARK: decreased ocular surface integrity, increased conjunctivalization, and activation of the pro-fibrotic response. Clinical, histological, and immunofluorescent evaluations were performed in the $Pax6^{+/-}$ mouse model Small Eye (Sey).

Methods: Wild-type ($Pax6^{+/+}$) and Sey ($Pax6^{+/-}$) corneas were assessed at two time points: 17-19 weeks old (mild ARK symptoms) (N=10 wild type, 6 Sey) and 40+ weeks old (severe ARK symptoms)(N=6 wild type, 6 Sey). Clinical assessment was performed by corneal clarity and ocular surface integrity scoring via fluorescein uptake.Histological assessment was performed on one eye of each mouse via paraffin sectioning, hematoxylin and eosin staining and periodic acid-schiff (PAS) staining to assess conjunctivalization. Two-way analysis of variance was performed for statistical analysis of PAS staining. Immunofluorescent evaluation was performed on one eye of each mouse via cryosectioning, blocking with 0.2% Bovine Serum Albumin and 5% goat serum, and incubating in 1:1000 dilution primary antibodies a-SMA (myfibroblast marker) and collagen type III (marker of fibrotic wound healing response).

Results: Consistent with our hypothesis, as corneal clarity decreased, ocular surface integrity decreased in Sey mice at each time point. Two way ANOVA showed average number of conjunctivalization in mouse corneas differed between wild-type and Sey mice ($df=1$, $F=10.367$, $p<0.01$). Conjunctivalization did not differ between 17-19 week old and 40+ week old mice ($df=1$, $F=3.163$, $p=0.106$). As corneal clarity decreased in 40+ week old Sey mice as compared to 17-19 week old Sey and wild type, this finding was contrary to our hypothesis. Our hypothesis of activation of the pro-fibrotic response was confirmed through immunofluorescent evaluation, with expression of a-SMA and collagen type III in the anterior stroma as corneal clouding progressed.

Conclusions: We have furthered the hypotheses of ocular surface integrity and activation of the pro-fibrotic response contributing to progressive corneal clouding in ARK, while our hypothesis of increased conjunctivalization was not supported. The findings of pro-fibrosis could open pathways for potential treatment modalities.

CONTROL ID: 3714513

SUBMITTER (NAME ONLY): Huilan zeng

TITLE: Immune cell- mediated experimental RGC loss is correlated with glaucoma donors' ophthalmic metrics

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. zeng, O.W. Gramlich, D. Wadkins, M.H. Kuehn, Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, Iowa, UNITED STATES|H. zeng, O.W. Gramlich, D. Wadkins, M.H. Kuehn, Veterans Affairs Medical Center, Iowa City, Iowa, UNITED STATES|

Commercial Relationships Disclosure: Huilan zeng: Commercial Relationship: Code N (No Commercial Relationship) | Oliver Gramlich: Commercial Relationship: Code N (No Commercial Relationship) | David Wadkins: Commercial Relationship: Code N (No Commercial Relationship) | Markus Kuehn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously shown that peripheral blood mononuclear cells (PBMC) from glaucoma patients can degrade retinal ganglion cells (RGC) in immune deficient mice. Here we correlate the RGC loss in mice with ophthalmic metrics of donating patient.

Methods: Blood samples were obtained from primary open angle glaucoma (POAG) patients without regard to disease state or rate of vision loss (n=20). In addition, samples were obtained from non-glaucomatous controls (n=10). Exclusion criteria were other retinal diseases (except AMD) autoimmune disease or neurodegenerative diseases. PBMC were isolated from these samples and transferred into immune deficient NOD/scid gamma (NSG) mice by intraperitoneal injection. Each mouse received PBMC from one donor only, creating an immunologic 'avatar' of the patient. After transfer mouse eyes received a microbead injection calibrated to cause mild, transient elevation of intraocular pressure (IOP). 50 days after PBMC transfer, RGC density was determined in retinal flat mounts using cresyl violet staining. Data were compared to clinical findings observed in the patients.

Results: Transfer of human PBMC did not cause significant side effects. However, retinas of mice having received PBMC from POAG donors displayed significantly fewer RGC than those having received PBMC from controls (255±64.8 RGC/field vs. 341±131 RGC/field, p=0.027) in central area. Among donors with POAG, PBMC of those with more advanced disease caused less damage to the recipients' RGC than PBMC with less advanced disease. Avatars of donors with a ganglion cell layer (GCL) thickness above the median displayed 197±60.9 RGC/field whereas those with GCL thickness below the median contained 282 ±75 RGC/field (p:0.017). Likewise, avatar mice of donors with visual field loss above the median displayed 296±62 RGC/field, significantly more than those having received PBMC from donors with more advanced field loss (204±84 RGC/field, p=0.045). Other clinical parameters, including maximum or average IOP of the patient, do not appear to be correlated with RGC loss in recipient mice.

Conclusions: Conclusions: These findings confirm that transfer of PBMC obtained from glaucoma patients causes more damage to RGC in NSG mice than those of controls. Our data also indicate that immune reactions may be more pronounced in POAG patents with moderate disease than in those with advanced disease.

CONTROL ID: 3714514

SUBMITTER (NAME ONLY): John Bryan

TITLE: Development of convolutional neural networks for automated image gradeability assessment in a diabetic retinopathy screening program

SESSION TITLE: AI in the Retina

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Bryan, P. Bryar, R. Mirza, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: John Bryan: Commercial Relationship: Code N (No Commercial Relationship) | Paul Bryar: Commercial Relationship: Code N (No Commercial Relationship) | Rukhsana Mirza: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The standard of care for diabetic patients is to have an eye exam or retinal imaging to assess for diabetic retinopathy (DR). In recent years there has been increased interest in developing artificial intelligence (AI) tools for optimizing screening of ocular imaging. In this retrospective study, we developed an AI-based approach for assessing the gradeability of images in a DR screening program.

Methods: Non-mydriatic retinal images were gathered from diabetic patients who underwent imaging during a primary care or endocrinology visit at Northwestern Medicine from September 1, 2017 to June 1, 2021. The Eidon SLO Confocal Scanner (Centervue Inc., Fremont, CA) was used. Images were interpreted by Northwestern ophthalmologists for gradeability, presence and severity of DR, and the presence of non-DR pathologies. Following image interpretation, the TensorFlow and Keras platforms were utilized to train convolutional neural networks (CNNs) to assess image gradeability. Images were divided into training, test, and validation sets. Inception V3 and Xception V1 network architectures were evaluated, with network weights preinitialized using a network trained on ImageNet, a set of 14 million images used for computer vision research. Networks built with different combinations of hyperparameters (learning rate (LR), dropout rate (DropR), and dense layer output dimensionality (DLOD)) were compared by validation set performance.

Results: 1550 non-mydriatic retinal images from 575 patients (55% female, median age 58) were analyzed in this study. Northwestern ophthalmologists deemed 23.6% (366/1550) of these images to be ungradable. Of gradable images, ophthalmologists found 20.4% (241/1184) had DR of varying degrees and 26.9% (319/1184) had non-DR ocular pathology.

Comparing CNNs, validation set performance was maximized with (LR = 0.001, DropR = 0.3, DLOD = 256) for the Inception V3 network and (LR = 0.0001, DropR = 0.3, DLOD = 256) for the Xception V1 network. On the test set the Inception V3 network exhibited 87.5% accuracy (AUC 0.935) and the Xception V1 network exhibited 86.41% accuracy (AUC 0.929).

Conclusions: It is feasible to develop CNNs that can assess the gradeability of non-mydriatic retinal images with a high degree of accuracy. AI-based frameworks such as these may enable more efficient identification of ungradable images in DR screening programs.

CONTROL ID: 3714517
SUBMITTER (NAME ONLY): Vish Reddy
TITLE: Ophthalmology residents' attitudes toward stress and wellness when fulfilling on-call responsibilities
SESSION TITLE: Vision care training and education
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: V. Reddy, S. Blatt, Loyola University Health System, Maywood, Illinois, UNITED STATES|
Commercial Relationships Disclosure: Vish Reddy: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Blatt: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Trainee wellness and burnout continue to emerge as an ACGME area of focus for resident training. Maslach, et al. define burnout syndrome as a depleted state characterized by emotional exhaustion, depersonalization, and a decreased sense of accomplishment. Ophthalmology residency has its own unique triggers that can lead to burnout, the most stressful of which taking weekend call.

Through knowledge-transfer exercises that impart specific stress-reduction strategies such as breath-control exercises, expressing gratitude, and identifying positive affirmations, we hope to modify Ophthalmology residents' attitudes toward stress and wellness.
Methods: This prospective study was reviewed by our institutional IRB and awarded an exempt status. The aforementioned knowledge transfer exercises were reviewed with first-year Ophthalmology residents through online lectures and discussion sessions in October 2020. Residents were encouraged to use these strategies to combat the stress of taking weekend call. The effectiveness of these strategies was quantified using pre- and post- call questionnaires which measured self-efficacy, stress regulation, and solution-mindedness.
Results: These questionnaires had a response rate of 87% with a completion rate of 91%. In our cohort of first-year Ophthalmology residents, breath-control exercises were identified as the most effective strategy for mitigating the stress of taking weekend call. Breath control exercises were both the most utilized and most effective strategy for in improving self-efficacy, stress regulation, and solution mindedness. Residents responded "moderately true" or "exactly true" in response to breathwork effectiveness questions in 73.9%, 82.9%, and 71.9% of cases respectively. Final biostatistical analysis is pending and will provide further insights.
Conclusions: Teaching ophthalmology residents strategies to combat stress is an effective tool for promoting wellness and preventing physician burnout.

CONTROL ID: 3714518

SUBMITTER (NAME ONLY): Sancy Low

TITLE: Cat-12 Risk Stratification for Conventional and Femtosecond Laser-assisted Cataract Surgery

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report the utility of St. Thomas' Hospital Cataract Risk Stratification Tool (Cat-12) in femtosecond laser assisted cataract surgery (FLACS) research and NHS patients undergoing conventional cataract surgery. Trainees, fellows and consultants were selected into 3 groups to keep complications within national standards for all surgeon grades.

Methods: 609 patients, 338 female (mean age 71y) and 271 male (mean age 69y) treated between November 2017-February 2018 were included. 330 underwent conventional surgery, 279 underwent FLACS. Cat-12 stratifies risk into: low (score<3), moderate (3-6), and high risk (>6). Surgeon selection was any grade for low risk; fellows/ consultants for moderate risk, consultants for high risk cases. Accurate completion of Cat-12 was examined, all complications by surgeon grade, and risk category analysed.

Results: Cat-12 was completed in 98% of all participants. 68% were considered routine (<3 Cat-12 score). 22.5% of these were performed by trainees, due to consultants recruiting routine cases for FLACS research. For moderate risk cases, 40% were performed by trainees/fellows, 60% by consultants. Similarly, 37% high risk cases were performed by trainees/fellows (9%,28%). Our trainees and fellows were exposed to higher complexity cases, with adequate supervision based on Cat-12 stratification. PCR rates were 1.2% in low risk, 1.5% moderate risk and 2.2% in high risk groups, better than UK published standards for cataract surgery. There were more complications in the conventional surgery group (n=22) compared to FLACS (n=9), most commonly iris trauma (n=8) followed by anterior chamber tears (5 manual capsulorhexis, 3 rhexis tags following FLACS). There were no cases of endophthalmitis, one case of suprachoroidal haemorrhage in a high risk case, which was performed by a consultant, with a good final outcome.

Conclusions: Using the Cat-12 Tool, we identified the level of supervision required, and grade of surgeon needed to deliver safe, effective surgery. Trainees and fellows performed higher complexity cases (medium and high risk, while routine cases were recruited into research). We report low complication rates when juniors were supervised by the correct level of surgeon selected at the time of listing. There was no difference in complication rates between our junior and senior surgeons.

CONTROL ID: 3714519

SUBMITTER (NAME ONLY): Bianca Maceo Heilman

TITLE: Age-dependence of the objective optical and mechanical accommodative response measured using a combined dynamic autorefractor and OCT system

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Maceo Heilman, H. Durkee, M. Ruggeri, L. Rohman, A. Ho, J. Parel, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Maceo Heilman, M. Ruggeri, L. Rohman, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|A. Ho, J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To develop approaches to restore accommodation, research has focused on studying the age-related changes leading to presbyopia. Prior studies have quantified changes in lens shape in response to static accommodative demands, but there is limited data on the relation between lens shape and objective accommodation, and the dynamics of lens shape changes. The goal of this study is to quantify the age-dependence of the optical and biometric accommodative response using a custom-built combined autorefractor and OCT system.

Methods: Accommodative responses of 12 subjects aged 20 to 66 years (mean spherical equivalent refraction −1.67 ± 2.30 D, range -6.25 to 1.75 D) were measured using a device that combined a fixation target providing a controlled ramp accommodation stimulus, wavefront-based autorefractor, and an extended-depth OCT system that acquires images of the anterior segment and lens. Subjects were presented with a 12 D ramp stimulus at a speed of 0.5 D/s. Wavefront measurements and cross-sectional OCT images were acquired sequentially in real-time during the ramp at 33 Hz and 4.7 frames/s, respectively. Three runs were performed on each subject. Lens thickness was quantified from the OCT images using a semi-automatic segmentation software. The following parameters were quantified versus age: maximal accommodation, lens thickness change, accommodation response vs stimulus, lens thickness per D stimulus, and the relation between lens thickness change and optical accommodative response.

Results: Refraction and lens thickness varied linearly with stimulus. The optical response to a given stimulus decreased with age at a rate of 0.023 D/D/year. (Figure 1C) There was no statistically significant age-dependence of the change in lens thickness per Diopter of accommodative response in pre-presbyopic eyes (Age <50 years, average: 0.032 mm/D). (Figure 1D)

Conclusions: The decrease in accommodative gain (response/stimulus) combined with constancy of the lens thickness per Diopter response lends further support to the theory that attributes presbyopia to age-related changes in the ability of the lens to change shape.

CONTROL ID: 3714522

SUBMITTER (NAME ONLY): Sujata Rao

TITLE: Loss of melanopsin results in late-onset cone photoreceptor degeneration

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rao, K. Wilcots, R. Fuller, R. singh, I. samuels, M. Yu, J.W. Crabb, Ophthalmic Research, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|K. Wilcots, Chemistry, Cleveland State University, Cleveland, Ohio, UNITED STATES|I. samuels, Louis Stokes VA Medical Center, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Melanopsin (Opsin 4) is a photopigment expressed in the retinal ganglion cells and is critical for non-image forming vision. The goal of this study was to determine the role of melanopsin signaling for maintaining retinal integrity and function.

Methods: $Opn4^{-/-}$ and wild-type littermate control animals were longitudinally assessed from 3 months (M) to 14M using optical coherence tomography (OCT) based measurements. OCT findings were validated using immunofluorescence and protein blots. Transcriptomic (RNA Seq) and proteomic analyses of the retina were carried out at 4M and 12M. Rates of degradation of phagosomes and the diurnal exposure of phosphatidylserine was measured using anti-rhodopsin and Annexin A5.

Results: Loss of melanopsin results in late-onset degeneration of the retina with spatiotemporal differences in the progression of the photoreceptor degeneration. For example, medium opsin (M-opsin) is reduced at 12M in $Opn4^{-/-}$ retinas, with a severe reduction in the dorsal region of the retina. A similar dorsal-ventral gradient in outer nuclear layer thickness was detected. Electroretinography (ERG) analysis failed to detect any changes in the rod photoreceptor responses but cone responses were significantly reduced. A morphometric analysis of the RPE indicates changes in RPE cell size accompanied by an overall reduction in cell junction proteins in the $Opn4^{-/-}$ mutants. Our preliminary assessments suggest that the RPE changes preclude retinal degeneration. Accordingly, the degradation of phagosomes appears to be delayed suggesting that the rhythm of RPE phagocytosis is altered in the $Opn4^{-/-}$ animals. The diurnal exposure of phosphatidylserine is persistent suggesting that the early stages of phagocytosis are affected. The retinal and RPE pathologies are age-related and do not manifest in animals younger than eight months old.

Conclusions: Melanopsin signaling plays an important role during retinal development, however, the contribution of this signaling axis in retinal homeostasis is not well understood. Here we provide evidence that melanopsin signaling plays a critical role in protecting the aging retina from damage. Moreover, our data suggest that melanopsin signaling may play a critical role in the phagocytosis of the photoreceptor outer segment and raises the possibility that melanopsin could function in the RPE.

CONTROL ID: 3714523

SUBMITTER (NAME ONLY): Joel Imventarza

TITLE: Development of a Skin Biopsy-Based Calcification Assay for Detection of Optic Disc Drusen: A Pilot Study

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Imventarza, A. Kumar, Y.J. Liao, Ophthalmology, Stanford University, Palo Alto, California, UNITED STATES|J.A. Imventarza, A. Kumar, Y.J. Liao, Liao Eye-Brain Lab, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optic disc drusen are acellular calcified deposits in the anterior, unmyelinated optic nerve and occur in up to 2.4% of the population. The majority of patients develop vison loss due to optic neuropathy. These ectopic calcifications have been shown to consist of calcified mitochondria, which result from a combination of narrow scleral canal, impaired axoplasmic flow, and local metabolic stress, ischemia and inflammation. Both intra-and extracellular calcium concentrations are highly regulated by biological process, and mitochondria is known to be effective calcium buffering organelle intracellularly. We aimed to assess different conditions that promote calcification in human skin-derived primary human fibroblast cultures.

Methods: We cultured human fibroblasts and treated with different conditions for 21 days: 1-4 mM potassium phosphate, 2-6 mM tri-calcium phosphate, 2-3.2 mM sodium phosphate, 0.4-2 mM ibotenic acid, 1-10 mM 3-nitro-propionic acid, and osteogenic differentiation media (0.01 mM dexamethasone, 10 mM B-glycerophosphate, and 50 mM ascorbic acid). Calcification was evaluated by staining with Alizarin-red S and quantified by measuring optical density at 560nm using a plate reader. To assess cell viability, we performed MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay and absorbance measurement at 570 nm. We performed statistical analysis using one-way ANOVA and unpaired T test, and $p < 0.05$ was considered as statistically significant.

Results: Calcification in normal human fibroblast cultures, indicated by Alizarin-red S staining, was significantly induced by culturing for 21 days in elevated extracellular concentrations of calcium using potassium phosphate, tri-calcium phosphate, and sodium phosphate. This avid calcification did not impact cell viability per MTT assay. Excitotoxic toxins using ibotenic acid and 3-nitro-propionic acid did not induce calcification but did lead to lower cell viability. The highest level of calcification was induced with 4mM potassium phosphate (5.69±1) and 3.2 mM sodium phosphate (5.21±0.4).

Conclusions: Our study determined the optimal concentration of extracellular potassium and sodium phosphate that an induce calcification in primary human fibroblasts after 7 and 21 days in culture. This finding will help us design a novel in vitro assay for assessing increased risk of calcification in patients with optic disc drusen.

CONTROL ID: 3714524

SUBMITTER (NAME ONLY): Miyah Davis

TITLE: Accumulation of abnormal tau in OPL/IPL and within RGCs is linked with early ganglion cell loss in postmortem retinas of MCI and AD patients

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.R. Davis, N. Mirzaei, J. Sheyn, D. Fuchs, A. Rentsendorj, K. Black, Y. Koronyo, M. Koronyo-Hamaoui, Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|C. Miller, Department of Pathology Program in Neuroscience, Keck School of Medicine, University of Southern California, Los Angeles, California, UNITED STATES|M. Koronyo-Hamaoui, Department of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously identified the neuropathological hallmarks of Alzheimer's Disease (AD), amyloid β-protein (Aβ) plaques and neurofibrillary tangles comprised of hyperphosphorylated tau (pTau) protein, in the retina of AD patients. Retinal Aβ deposits were detected in subjects with mild cognitive impairment (MCI) and AD, with variable distribution across cell layers and subregions. Loss of retinal ganglion cells (RGCs) was also documented in these patients. While increased pTau was also reported, there is still a gap in our understanding of retinal tauopathy in AD. Moreover, the topographical distribution of retinal pTau in AD and cell-type vulnerability has never been reported.

Methods: To quantify retinal pS396Tau in different subregions and cell layers and in RGCs, which express the ribonucleic acid binding protein with multiple splicing (RBPMS), we used quantitative immunohistochemical analyses. Manual count and immunoreactive-area of pTau-containing RGCs and RBPMS-positive RGCs were assessed in postmortem retinae of subjects with normal cognition (NC), MCI, or AD.

Results: We find a substantial 45% decrease in RBPMS-expressing RGCs in postmortem retinas of both MCI and AD patients. RBPMS cell loss was accompanied by 2-3-fold pS396Tau increases in prodromal and clinical AD retinae, especially in the superior-temporal mid-periphery region. While pS396Tau is densely observed in the outer plexiform layer (OPL), colocalization of pTau inside RBPMS-RGCs is also pronounced. Elevated pS396Tau in remaining RBPMS-RGCs may drive degeneration and displacement to deeper retinal layers in disease states.

Conclusions: The patterns of abnormal pS396Tau distribution in the human retina are described with increased vulnerability of RBPMS-expressing RGCs to pTau accumulation and loss. Future studies should investigate the susceptibility of other retinal cell types to tauopathy in early stages of AD.

CONTROL ID: 3714528

SUBMITTER (NAME ONLY): Daniel Ferraz

TITLE: Risk of ischaemic stroke following a diagnosis of glaucoma

SESSION TITLE: Biomechanics and ocular blood flow

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Ferraz, S. Wagner, M. Cortina-Borja, J. Rahi, H. Khalid, J. Huemer, P.A. Keane, Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A.K. Denniston, Ophthalmology, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To analyse the incidence rates of ischaemic stroke among patients newly diagnosed with glaucoma at a regional ophthalmic institution in London, United Kingdom.

Methods: We conducted a retrospective cohort study of all patients >= 40 years of age and newly diagnosed with glaucoma between January 1st 2008 and March 31st 2018. Records were linked with national hospital admissions data and ischaemic stroke was defined through the International Classification of Diseases 10th Revision. Incidence rates with 95% confidence intervals were calculated using the Poisson distribution and adjusted hazard ratios (HR) through Cox proportional hazard modelling and Fine-Gray competing risks regression.

Results: Among 31,060 patients with a new diagnosis glaucoma, 16,322 (52.5%) were female, mean age was 64.8 (12.3) years and 512 had an ischaemic stroke with a crude incidence rate of 348.9 (319.5-380.0) per 100,00 person-years at risk. Glaucoma was diagnosed at a younger age in those of Asian (63.9 +/- 11.5) and Black (62.3 +/- 12.1) ethnicity versus those of White ethnicity (67.3 +/- 12.1, p<0.001); also in those at greater levels of socioeconomic deprivation (most deprived 62.5 +/- 12.3 years versus least deprived 66.3 +/- 11.9, p<0.001). On adjusted analysis, male sex (cause-specific HR 1.36, 1.14-1.62) and increasing age (1.08, 1.07-1.08) were associated with greater hazards of stroke; no significant association was seen with ethnicity or socioeconomic deprivation. Estimates from competing risks regression were similar to those from Cox modelling.

Conclusions: An earlier age of glaucoma diagnosis is seen in ethnic minority groups and those from greater levels of socioeconomic deprivation. Following glaucoma diagnosis, incidence of ischaemic stroke is higher in elderly males but does not appear to be associated with ethnicity or socioeconomic deprivation.

CONTROL ID: 3714529

SUBMITTER (NAME ONLY): Rishi Ramessur

TITLE: Outpatient workshops to improve digital health literacy: lessons learned

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ramessur, H. Kandola, A.K. Sehmi, L. Raja, S. Thomas, D. Sim, S. Kang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|C. Gruber, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: 10% of patients invited to Moorfields Eye Hospital Oculoplastic video consultation (VC) clinics decline to participate, and 5% are unable to join on the day. 28% of our patients indicated that they would like to join sessions to improve their digital skills. Amidst growing evidence that some patient groups may be unable to capitalise on the benefits of teleophthalmology, we set up a digital skills workshop at Moorfields Eye Hospital.

Methods: Patients who had previously declined a VC - and those attending parallel clinics who were keen to improve their digital skills - were invited to participate. Delivered by a member of our Video Consultation Team using departmental laptops, tablets and patients' devices, training included using our VC platform, taking a 'selfie' photo of the eye, and sending it via email. Pre- and post-workshop surveys explored patients' confidence with online services, inclination to use VC and perceived utility of the workshop using a 10-point Likert scale (0 'extremely unlikely' to 10 'extremely likely'). Paired T-test was used to assess significance of difference between ratings before and after the workshop. Qualitative feedback was analysed thematically.

Results: Feedback was obtained from 16 patients of 24 patients (67% response rate). 58% were invited to the workshop after declining a VC; 42% attended ad hoc from a parallel clinic, interested in improving their digital skills. Average age was 63 years (69% male, 31% female). Patients reported greater inclination to use a VC after attending the workshop compared to before (mean rating 6.1/10 vs 4.75/10, p=0.02) and felt more comfortable with VCs after the workshop compared to before (mean rating 6.1/10 vs 4.5/10, p=0.005). Patients found the workshop useful (mean rating 7.8/10) and were likely to recommend it to family and friends (mean rating 8/10). The most common suggestion was for an interpreter for patients with limited command of English. Commonly reported barriers to using VCs were lack of: confidence navigating online (63%), awareness that health services could be accessed remotely (38%), and confidence that a VC would adequately address their health problem (38%).

Conclusions: Patients consider digital skills workshops useful to improve confidence and motivation with using online services. Scaling these workshops may help address an increasing issue of exclusion as services become more reliant on teleophthalmology.

CONTROL ID: 3714531

SUBMITTER (NAME ONLY): Shruti Patil

TITLE: Viral delivery approaches for CRISPR/Cas9-based knockdown of the Myocilin gene in Trabecular Meshwork

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.V. Patil, S. Yacoub, B. Kodati, B. Nagarajan, J. Millar, R. Kasetti, S. Curry, C. Kiehlbauch, A.F. Clark, G. Zode, Department of Pharmacology and Neuroscience and the North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|C.C. Searby, Q. Zhang, V.C. Sheffield, Department of Pediatrics, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is a major risk factor for the progression of primary open angle glaucoma (POAG). Damage to the trabecular meshwork (TM) is responsible for increased aqueous humor outflow resistance that raises IOP. Of the factors that are involved in TM dysfunction, mutation of the myocilin gene (MYOC) was the first identified. MYOC mutations contribute to ~4% of POAG cases. Although, the normal role of myocilin is unknown, mutations in MYOC cause a deleterious gain-of-function leading to lack of extracellular secretion and endoplasmic reticulum (ER) stress within TM cells. Our goal is to develop genome editing methods to modify genes associated with TM pathophysiology, which are not addressed by current IOP lowering therapies. We previously demonstrated the feasibility of targeting the mutant (mut)-MYOC gene using CRISPR/Cas9 genome editing in mice and human donor eyes using the adenovirus (Ad)-5 gene transfer system. However, Ad5 is not a suitable vector for clinical use. Therefore, we aim to study the efficacy of adeno-associated virus (AAV) and lenti virus (LV) vectors expressing CRISPR/Cas9 to target the TM and reverse ocular hypertension (OHT) in mut-MYOC associated POAG.

Methods: We compared the TM specific tropism of single-stranded (ss) and self-complimentary (sc) AAV serotypes with the LV vector that express eGFP driven by the CMV promoter. These vectors were injected via intravitreal (IVT) and intracameral (IC) routes to determine expression in ocular tissues. Efficient CRISPR-Cas9 constructs that selectively knockdown MYOC (cr-MYOC) were designed to evaluate the effect on ER stress markers in mut-MYOC expressing transformed TM cells and the effect on IOP in the transgenic (Tg)-MYOC^{Y437H} mouse model of OHT.

Results: Of the AAV serotype tested, Trp-mutant scAAV2 had prominent expression of eGFP in the TM via slow-IC route. However, expression was also observed in other retinal and optic nerve head tissues. In contrast, LV_eGFP expression was more specific to the TM injected via the IVT route. Cr-MYOC transduced cells were shown to have reduced expression of MYOC and ER stress markers GRP78, ATF4 and CHOP. LV_cr-MYOC injected mice show significantly reduced IOP in Tg-MYOC^{Y437H} mice.

Conclusions: LV was found to be more specific and efficient in mediating target gene expression in the TM and facilitate MYOC gene knockdown.

CONTROL ID: 3714535

SUBMITTER (NAME ONLY): Christopher Turski

TITLE: Morphological and Functional Short-Term Outcomes after Bevacizumab Loading Dose in patients with center-involving Diabetic Macular Edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Turski, M. Jacobs, N. Fowler, R. Harpole, E. Altman, G. Kindl, M. Abou-Jaoude, R. Maldonado, Ophthalmology, University of Kentucky College of Medicine, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: A loading dose (LD) of three-monthly intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) is frequently used to determine treatment response. Here, we compare morphological and functional outcomes of bevacizumab on spectral domain-optical coherence tomography (SD-OCT) in eyes with center-involving diabetic macular edema (ciDME) pre- and post- LD.

Methods: IRB approved observational, retrospective chart review of treatment-naïve patients with ciDME who received bevacizumab injections from 01/01/2017 to 01/19/2019 who were identified by ICD-10 code. Exclusion criteria included previous treatment with anti-VEGF or intraocular steroids in the last year, poor quality images, or incomplete chart data/missing imaging. Variables tracked included best corrected visual acuity (BCVA) and central foveal thickness (CFT) before and after LD. Central foveal OCT frames were graded qualitatively using Imagivault software, including for disorganization of retinal inner layers (DRIL) and ellipsoid zone (EZ) disruption. Analysis of variance was conducted using SPSS.

Results: 330 potential subjects were identified, and after applying exclusion criteria 24 eyes from 21 patients (mean age 65.17 ± 7.86 years, 54.2% male) were analyzed. Mean BCVA was 0.31 ± 0.19 logMar (~20/40) at baseline and 0.33 ± 0.33 logMar (~20/40) after LD. Mean CFT decreased from 449 ± 105 µm at baseline to 405 ± 113 µm after LD. Using CFT reduction metrics, 5 (20.8%) of patients were categorized as responders (>20% reduction), 6 (25.0%) as partial responders (10-20% reduction), and 13 (54.2%) as non-responders (<10% reduction). Average change in CFT from baseline in responders was -213 µm; in partial responders -68 µm, and in non-responders +32 µm. DRIL was detected in 100% of responders, 83.3% of partial responders, and 100% of non-responders. EZ disruption was present in 0% of responders, 16.7% of partial responders and 30.8% of non-responders. At baseline, responders had a significantly increased mean CFT in comparison to non-responders ($p = 0.02$).

Conclusions: The response to a LD of bevacizumab in eyes with ciDME was sub-optimal with the majority of patients being non-responders. Factors indicative of a better response were increased baseline CFT and absence of EZ disruption.

CONTROL ID: 3714536

SUBMITTER (NAME ONLY): Kevin Houston

TITLE: In Search of Pathological Suppression of Binocular Vision After Stroke: An Exploratory Study

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Houston, P. Tirandazi, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|K. Houston, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: In a prior prospective study, 74% of stroke survivors with strabismus failed to report diplopia (Rowe, 2010). The possible reasons were investigated hypothesizing that pathological suppression exists and is related to laterally imbalanced attentional networks, and therefore associated with hemispatial neglect (HSN) and/or visual extinction (VE) after controlling for other reasonable factors.

Methods: A 1 year review of all inpatient vision clinic records included comprehensive eye and sensorimotor exam with 2AFC Randot E, Stereobook R+L and Randot Stereopsis, TV trainer, induced strabismus test, covertest, motorfield, motility and NPC. Evaluation for HSN included line bisection, cancellation, and VE. Failed suppression tests were tabulated and the clinician reviewer, considering all information, rated(1-10) the likelihood-certainty of suppression vs. another explanation. Hypothesized association of HSN and VE with likelihood rating and proportion of test failures was analyzed.

Results: There were 113 consecutive records with ≥1 suppression test (median 4, range 1-10). Only 33% passed all suppression tests administered. 47% did not have diplopia with optically induced strabismus. Actual strabismus was present in 50%, of whom 49% denied diplopia. Randot stereopsis was failed in 64%, and stereobook R+L in 23%. Potential confounders reported as most limiting clinician reviewer certainty were homonymous hemianopia (HH), order effects with preceding tests potentially breaking suppression, and generalized reduction of awareness/insight. Multiple regression analysis did not support HH or interocular acuity differences as confounders. Insight and order effects could not be tested. HSN was a significant predictor of suppression certainty P=.001, controlling for age P=.004. Post hoc exploration of other possible factors via forward selection identified VE P<.001 and subsequently parietal lobe involvement P=0.03 as independent predictors, with age, HSN, and VE ultimately dropping out.

Conclusions: Findings support the hypothesis that failure to report diplopia from strabismus after stroke is common and that there is relationship to HSN, or more specifically VE and the associated parietal corticies. Prospective studies would allow for control of potentially confounding order effects and generally reduced insight for impairment in stroke patients, while introducing psychophysical and dichoptic testing paradigms.

CONTROL ID: 3714537

SUBMITTER (NAME ONLY): Pawarissara Osathanugrah

TITLE: The Impact of Race on the Efficacy of Bevacizumab for Macular Edema Secondary to Retinal Vein Occlusions

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Osathanugrah, M. Prasad, N. Sanjiv, S. Ness, N.H. Siegel, X. Chen, M.L. Subramanian, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-VEGF injections are often used for the treatment of macular edema from retinal vein occlusions (RVO). Variable response to intravitreal bevacizumab has been reported for treatment of diabetic macular edema (DME). In this study, we performed a retrospective chart review to examine potential racial variances in treatment response to bevacizumab in patients with macular edema secondary to RVO.

Methods: Intravitreal anti-VEGF naïve patients aged over 18 who received at least one intravitreal bevacizumab injection for central and branch RVO were included. Data were collected before treatment, 1-3 months after the first injection, and 1-3 months after 3 injections. Primary outcome measures were percentage of patients with visual acuity (VA) improvement (defined as >0.1 on logMAR scale), reduction in central macular thickness (CMT), and the presence of systemic disease. Analysis was performed using multivariate regression for percentage change of CMT and logistic regression for percentage of patients with VA improvement.

Results: 156 eyes were included for the single injection analysis and 101 for the 3-injection analysis. There was no significant difference in odds of VA improvement between Black (B) and White (W) patients after one injection (B=51.9%, W=55.7%, OR 1.20, P=0.66) and after 3 injections (B=70.4%, W=68.1%, OR 1.48, P=0.55) after controlling for age, sex, baseline VA, baseline CMT, laser history, injection time course, follow-up delay, and presence of hypertension, diabetes, and hyperlipidemia. Similarly, there were no differences in %CMT reduction among the race groups after one injection (B= -30.8%, W= -27.5%, p=0.78) and after 3 injections (B= -25.8%, W= -32.8%, p=0.52) using the same controls. Among all patients, there were higher rates of hypertension in Black compared to White patients (66% vs 46%, p= 0.02). Rates of diabetes appeared higher in Black compared to White patients but were not statistically significant (B=25%, W=12%, p=0.06).

Conclusions: There were no statistically significant differences in treatment response to a single or a series of 3 bevacizumab injections in patients with macular edema secondary to RVO across different races despite a significant difference in presence of hypertension. These results are in contrast to a prior study done by our group with similar methodology for DME.

CONTROL ID: 3714539
SUBMITTER (NAME ONLY): Samuel Cubillos
TITLE: Impact of Amblyopia Treatment on Visual Outcomes in Pediatric Patients with Optic Nerve Pathology
SESSION TITLE: Amblyopia
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Cubillos, C. Mocan, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|
Commercial Relationships Disclosure: Samuel Cubillos: Commercial Relationship: Code N (No Commercial Relationship) | Cem Mocan: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: There is limited evidence describing the effects of amblyopia treatment in eyes with coexisting optic nerve pathology (ONP). The purpose of the study was to evaluate the visual acuity outcomes following patching treatment of eyes with coexisting ONP.
Methods: Retrospective cohort study undertaken at a single university outpatient clinic setting. Clinical records of pediatric patients with a diagnosis of amblyopia coexisting with ONP were reviewed. Baseline presenting visual acuity (B-VA) and final best corrected visual acuity (F-VA) were recorded using Snellen eye charts and converted to their corresponding logMAR values. Primary outcome was the F-VA attained with ≥1 year patching and refractive correction. Secondary outcome was the prevalence of eyes with F-VA ≥20/40. F-VA was categorized into four groups. Difference between F-VA and B-VA was calculated for each eye (Diff-VA). Wilcoxon signed rank sum test was conducted to evaluate Diff-VA for all subjects that had B-VA and F-VA as measured with Snellen chart. Spearman correlation analysis was conducted to analyze the association between B-VA and F-VA.
Results:
The clinical records of 7 eyes of seven patients with a mean baseline age of 6.8±2.6 years (range: 4-10 years) who had ONP, had patching treatment and had Snellen VA tests recorded were included in this study. Optic nerve hypoplasia, optic nerve atrophy, myelinated nerve fibers, and traumatic optic neuropathy were the various etiologies of ONP included. The mean B-VA and F-VA in logMAR were calculated as 0.976±0.509 and 0.723±0.188, respectively. A final Snellen VA of <20/200 was attained in 0%, 20/200–20/60 in 85.7%, and 20/60–20/40 in 14.3% of the eyes. None of the eyes that received amblyopia treatment achieved a F-VA≥ 20/40. The mean Diff-VA for the 7 eyes that had visual acuity measurements available for analysis was -0.252 ± 0.377 (p=0.156). F-VA was not found to be associated with B-VA (rho=0.593; p=0.161).
Conclusions: Our results suggest that regardless of the underlying pathology, final visual function in amblyopic eyes with coexisting ONP remains between 20/200 and 20/40. Baseline visual function does not appear to be predictive of final visual outcomes in these eyes. Although patching treatment may result in modest increase in visual function, childhood onset ONP appears to confer a poor prognosis for visual function.

CONTROL ID: 3714540

SUBMITTER (NAME ONLY): Stephen Odaibo

TITLE: Clinical Validation of a Multi-Camera Compatible Autonomous Artificial Intelligence System for Diabetic Retinopathy Screening in Primary Care

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Odaibo, A. Courtes, S. Dukor, V. Irekponor, N. Imasogie, G. Duru, O. Oyediran, RETINA-AI Health, inc., Houston, Texas, UNITED STATES|J. Fernandes, G. Rogell, N. Adams, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To perform clinical validation of RETINA-AI Galaxy, a Multi-Camera Compatible Autonomous Artificial Intelligence System for Diabetic Retinopathy Screening in Primary Care

Methods: The study involved 4 U.S. primary care sites from where subjects were recruited. 397 study subjects ages 22 and above who had diabetes and had not been previously diagnosed with more than mild diabetic retinopathy were prospectively enrolled between March 25, 2021 and May 28, 2021. ClinicalTrials.gov ID: NCT04774822. Subjects underwent an AI screening protocol in which one fovea-centered and one optic disc-centered image were taken for each eye for each of the 5 robotic fundus cameras in the study. The images were then transmitted to the cloud-based software-as-a-medical AI device for analysis. 4W-D validation stereoscopic fundus imaging along with optical coherence tomography (OCT) macula cube scanning was also done. Validation imaging was interpreted by three American Board of Ophthalmology-certified retina specialists. Primary endpoints were sensitivity and specificity of detection of more than mild diabetic retinopathy (mtmDR) detection and vision-threatening diabetic retinopathy (vtDR), using double grading with adjudcation on a probabilistic grading schema filter, Certainty Ratio >3/5:=mtmDR. 95% CI shown in Figures was via clustered bootstrap.

Results: On the DRSPlus, Crystalvue, Topcon, DRS, and Nexy cameras respectively: for mtmDR detection, Area Under the ROC curve (AUC) was 0.97, 0.93, 0.95, 0.95, and 0.91 respectively; and (Sensitivity, Specificity near 82.5%) were (94.97%, 82.6%), (89.24%, 82.5%), (87.34%, 83.2%), (88.24%, 85.3%), and (83.65%, 82.6%) respectively. For vtDR, AUCs were 0.97, 0.91, 0.96, 0.97, and 0.93 respectively; and (Sensitivity, Specificity near 82.5%) were (97.06%, 84%), (88.24%, 88.1%), (93.94%, 94.8%), (94.12%, 85%), and (94.12%, 90.9%) respectively. On the Blinded Assessment, (Sensitivity, Specificity) of mtmDR were (90.6%, 90.6%), (87.3%, 84.7%), (81.6%, 93.2%), (83%, 92.8%), and (78.6%, 87%) respectively; and for vtDR were (73.5%, 96.2%), (82.4%, 91.3%), (93.9%, 94.5%), (91.2%, 94%), (91.2%, 92.4%) respectively.

Conclusions: The multi-camera compatible AI system met primary endpoints, demonstrating efficacy and safety in the detection of more than mild diabetic retinopathy and vision threatening diabetic retinopathy in the primary care setting.

CONTROL ID: 3714541

SUBMITTER (NAME ONLY): Gauri Patil

TITLE: Statistical Accuracy of fMRI Retinotopic Mapping in Patients with Altered Neurovascular Function with different Stimulus Presentation

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.L. Schneider, Medical Scientist Training Program, University of Rochester Medical Center, Rochester, New York, UNITED STATES|G. Patil, C.L. Schneider, Brain and Cognitive Science, University of Rochester, Rochester, New York, UNITED STATES|G. Patil, University of Rochester Medical Center, Rochester, New York, UNITED STATES|B.Z. Mahon, Psychology, Carnegie Mellon University, Pittsburgh, Pennsylvania, UNITED STATES|B.Z. Mahon, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure: Gauri Patil: Commercial Relationship: Code N (No Commercial Relationship) | Colleen Schneider: Commercial Relationship: Code N (No Commercial Relationship) | Bradford Mahon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Functional Magnetic Resonance Imaging (fMRI) measures neural activity indirectly by monitoring local changes in blood oxygenation and blood flow. Altered patterns of cerebral blood flow that occur, for instance, in stroke patients, may affect the analysis and interpretation of fMRI data. Here we investigate relations between experimental design and altered hemodynamic responses using computational approaches modeled on the early visual system.

Methods: Population receptive field mapping is used to localize cortical representation of different regions of the visual field. We used computational modeling to determine how the accuracy and precision of population receptive field mapping is affected by altered hemodynamic responses in two conditions: 1) stimuli presented sweeping across the visual field and 2) stimuli presented randomly across the visual field. Hemodynamic response functions for both analyses were modeled using a 2-gamma function with a time-to-peak varying between 0 and 12 repetition times (TRs) from stimulus onset.

Results: We found that the analysis was more robust to an altered hemodynamic response when the stimuli were presented in a random sequence. Sequential stimulus presentation led to systematic errors, that were not present with the random presentation sequence, leading to an increase in Type I errors (false positive). For both stimulus presentation methods, the sensitivity and specificity of the analysis greatly deteriorated if the time-to-peak was delayed by greater than +/- 1 TR.

Conclusions: These results highlight the importance of tailoring the experimental design to altered hemodynamic responses and point to the need for subject- and voxel-specific hemodynamic response functions when analyzing fMRI data in patient populations with neurovascular abnormalities. Without these modifications, researchers run the risk of making incorrect conclusions about retinotopic reorganization.

CONTROL ID: 3714542

SUBMITTER (NAME ONLY): Yan Liu

TITLE: Improving ultrafast ophthalmic adaptive optics by accounting for deformable mirror actuation

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, J. Crowell, M. Bernucci, D.T. Miller, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|K. Kurokawa, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultrafast ophthalmic adaptive optics (AO) outperforms conventional AO in correcting ocular aberrations and improves AO clinical utility [1]. However, the higher loop rate necessitates shorter wavefront sensor exposure durations that are comparable with deformable mirror (DM) response time. Thus, DM actuation may corrupt the sensor measurement and degrade the AO performance. Here, we study this effect and develop a way to minimize it.

Methods: Our AO system [1] consists of (1) a Shack-Hartmann wavefront sensor (SHWS) with 300 lenslets that sample a 6.7 mm eye pupil and a rolling-shutter camera (0.1 ms exposure time) that captures the SHWS images, and (2) a DM (ALPAO high-speed DM97-15) with a 1 ms rise time followed by ringing as specified by the manufacturer. To study the DM actuation effect, we controlled the delay between sending control commands to the DM and start of the SHWS exposure. We compared the power rejection curves (for pink noise applied to the DM) and step responses to fixed aberrations for exposure delays of 0, 1 and 6 ms. 0-ms delay exposes the SHWS to almost the entire DM response and 6-ms delay avoids it entirely. The rows of lenslets affected by DM actuation were determined by comparing the lenslet spot displacements, from which we determined the optimal delay.

Results: Overshoot of the step response to a large aberration (2.7 μm RMS wavefront error) occurred for the 0-ms exposure delay, while no overshoot occurred for the 1- and 6-ms delays. DM actuation affected the top two rows of SHWS lenslets (out of 20) for the 0-ms exposure delay and no rows for the 1-ms delay. Because the rolling shutter exposes rows from top to bottom in 3 ms, 0.3 ms was therefore determined as the optimal exposure delay. Reducing exposure delay from 1 ms to 0.3 ms, AO loop rate increased 17% to 233 Hz; closed-loop bandwidth increased 14% to 37.2 Hz; convergence time to diffraction limit reduced 14% to 4.3 ms; and power rejection curve peak magnitude remained the same. For smaller aberrations (0.32 μm RMS wavefront error, comparable to ocular aberrations after spectacle correction), no overshoot was observed in the step response for 0-ms delay, and closed-loop bandwidth increased 21% to 39.3 Hz compared with 1-ms delay.

Conclusions: DM actuation reduces AO performance when aberrations are large, but this decrease can be greatly reduced with the right exposure delay.

[1] Liu et al., IOVS, 62(8):16 (2021).

CONTROL ID: 3714543

SUBMITTER (NAME ONLY): RENATO LECA

TITLE: Could tear vitamin D be a new biomarker for keratoconus?

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. LECA, F. Scorza, G. Jorge, C. Scorza, A. Hofling-Lima, F.A. Fonseca, Ophthalmology, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|R. LECA, G. Ribeiro, F. Paccini, F. Almeida, F.A. Fonseca, Ophthalmology, Faculdade de Medicina do ABC, Santo Andre, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: The main function of vitamin D3 in the human body is to participate in the metabolism of calcium and phosphate, but, as it is actually a hormone, it also has an important immunomodulating action, presenting important biological activity in the innate and adaptive immune system, and acting in practically all tissues, since various types of cells have receptors and activating enzymes, including in the eye. Studies have shown that serum vitamin D3 deficiency is related to several eye diseases, such as dry eye, uveitis, AMD, glaucoma, diabetic retinopathy, and keratoconus, but very little is said about the relationship between tear levels of this vitamin and eye diseases; In this work, we will study the relationship between tear and serum levels of vitamin D3 in cases of keratoconus and in control cases.

Methods: This study was performed with 71 individuals, being 32 individuals with keratoconus in both eyes (64 eyes),15 men and 17 women, aged between 16 to 27 years (mean 20,5 years), and 39 individuals without eye disease (control group with 78 eyes), 12 men and 27 women, aged between 19 to 27 years old (mean 21,75 years). Serum and tear vitamin D3 were evaluated in all participants.Tears were collected using the Schirmer strip in the all eyes with keratoconus and in the all eyes of the control group; for serum examination, 3 milliliters of venous blood were collected from all participants in this study. All blood and tear samples had their vitamin D3 levels assessed, by their metabolite 25 (OH) vitamin D3, by electrochemiluminescence examination, and statistical analysis was performed by the Chi-square test.

Results: In the group of individuals with keratoconus, the average verified level of vitamin D in the tear was 73.03 ng /ml, ranging from 57.5 to 88.4 ng / ml, whereas in all tear samples in the control group, the levels were above 100 ng /ml, the upper limit of detection of the electrochemiluminescence apparatus, with $p < 0.0001$. In blood samples, the mean found in the group of individuals with keratoconus was 21.36 ng / ml, while in the control group it was 29.95 ng /ml, with $p < 0.05$.

Conclusions: Compared with control eyes, the results of vitamin D3 levels were significantly lower both in plasma and in tears, particularly in tears, thereby demonstrating the important relationship of vitamin D3 levels in keratoconus; these results allow us to suggest that tear vitamin D3 level could be a potential biomarker for keratoconus

CONTROL ID: 3714544

SUBMITTER (NAME ONLY): Anne Vielle

TITLE: Modeling retinal Alzheimer’s disease histopathology with human iPSC-derived retinal organoids

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Alzheimer’s disease (AD) is a complex multifactorial disease that affects 33 to 38 million people worldwide, causing irreversible damage to the central nervous system. In the eye, the retinal phenotype is consistent with the brain histopathology, including the presence of beta-amyloid (Aß) plaques and intracellular neurofibrillary tangles (NFT) of abnormally phosphorylated Tau proteins (pTau). Unfortunately, no treatment exists to cure this disease. Thus, we set out to develop and characterize the first hiPSC-derived organoid model of retinal AD histopathology that can be used for the validation of potential therapeutic drugs.

Methods: hiPSC from 3 wild type (WT) and 2 familial AD (fAD) donors were used to generate retinal organoids (RO) using the Zhong et al. (2014) protocol. The cellular composition and histopathological hallmarks of AD were assessed at 6 months of differentiation by Western blot, immunofluorescence staining for retinal cell type-markers as well as Aβ and pathological pTau forms, and by NIAD-4 staining for amyloid plaques. Quantification was performed using FIJI software for 2D images and 3D-ARQ for whole mount ROs.

Results: AD-ROs are similar to WT-ROs in cellular composition and structure. However, pathological pTau staining and Aß deposits are significantly increased in AD-ROs compared to WT-ROs. Finally, we developed a quantitative, high-throughput assay for plaque detection that is amenable to translational research applications.

Conclusions: Our AD-RO models mimic the histopathology of the human AD retina and constitute valuable tools for the screening and validation of candidate molecules with therapeutic potential.

CONTROL ID: 3714546

SUBMITTER (NAME ONLY): Edgar Espana

TITLE: Latent Transforming Growth Factor-β Binding Protein 1 expression in the corneal stroma

SESSION TITLE: Corneal stromal biology, wound healing modulators, and regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.M. Espana, S. Salvatori, M. Sun, D. Cogswell, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Latent Transforming Growth Factor-β Binding Protein 1 (LTBP1) is poorly characterized in the cornea, and our knowledge of its function is mostly unknown. The aim of the current study was to elucidate the expression and role(s) of LTBP1 in regulating corneal stromal structure and function during homeostasis and following injury. The biological importance of LTBP1 radicates in its property to maintain Transforming Growth Factor (TGF) - β latent.

Methods: Analysis of LTBP1 expression, temporal and spatial, was performed at different postnatal days (P) in wild-type C57BL/6 mouse corneal stromas and after injury. Ltbp1 mRNA expression as well as LTBP1 protein content and locatization with stromal maturation were studied. Total (latent + active) TGF- β was analyzed in vitro using transformed mink lung cells transfected with luciferase cDNA driven by PAI-1 promoter. To test the amount of total TGF-β stored in the stromal matrix at different ages, we measured exactly similar aliquots of stromal extract at different ages.

Results: Ltbp1 mRNA stromal expression, obtained after enymatic removal of corneal epithelium, was present at P4 but decreased with corneal maturation at P10, P30 and P140. There was a signficant decrease in Ltbp1 mRNA expression with corneal maturation. In contrast, Wes protein analysis showed increased deposition of LTBP1 with corneal maturation. Highest levels were noted at P140, the oldest age in which protein expression was investigated. Immunofluorescent microscopy showed LTBP1expresion in all ages studied with expression of LTBP1 localized to the extracellular matrix in the entire stromal thickness. Ltbp1 mRNA was significantly upregulated after injury and LTBP1 expression up-regulated following two different injury models: stromal abrasion and full thickness laceration. Besides, we investigated whether increased LTBP1 expression with corneal maturation correlated with increased TGF- β activity since it is well established that LTBP1 is the main regulator of latent TGF- β. We found a statistically significant increase in total TGF- β stromal corneal with corneal maturation, P30 vs P150, t-test, unpaired, p=0.04.

Conclusions: This study indicates that LTBP1 plays a regulatory role in corneal development and in the function of the adult cornea. LTBP1 deposition and total TGF-β storage increase during stromal maturtion. The expression of LTBP1 is recapitulated during wound healing.

CONTROL ID: 3714547

SUBMITTER (NAME ONLY): Ryan Lamrani

TITLE: Tube Shunt Surgery for Glaucoma Management: 12-year data

SESSION TITLE: Glaucoma epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lamrani, J. Wong, D. Lee, J.S. Myers, Glaucoma, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R. Lamrani, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|J. Wong, Rowan University School of Osteopathic Medicine, Stratford, New Jersey, UNITED STATES|D. Lee, J.S. Myers, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Ryan Lamrani: Commercial Relationship: Code N (No Commercial Relationship) | Jae-Chiang Wong: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Lee: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Myers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the long-term surgical outcomes of tube shunt (TS) surgery in patients with various types of glaucoma.

Methods: This retrospective chart review included patients who underwent TS surgery from 01/2006 to 01/ 2012. Patients with at least 10-years of follow-up data were included. Demographic and clinical data were collected at the pre-operative and post-operative follow-up visits until their latest visit (up to 01/2022). Surgical failures were defined as eyes that required reoperation or progressed to no light perception (NLP).

Results: 30 eyes of 26 patients were included. Mean age was 60.4±10.2 with a mean follow-up of 12.1±1.8 years after their first TS surgery. At the last visit, BCVA in the operated eye declined from 0.9±0.8 to 1.4±0.9 ($p=0.006$), CDR increased from 0.6±0.2 to 0.8±0.2 ($p=0.01$), VF progressed from -11.7±7.4 to -16.4±7.1 ($p=0.53$), IOP lowered from 31.0±11.0 mmHg to 12.5±11.9 mmHg ($p<0.01$) but lowered to 12.6 ±14.5 mmHg among patients with no reoperation ($p<0.01$), and glaucoma medication use reduced from 3.1±1.2 to 2.1±1.6 regardless of need for reoperation ($p=0.013$). 18 eyes (60%) had vision worse than 20/200 at their last visit and 2 eyes (6.7%) progressing to NLP. 6 eyes (20%) required additional TS surgery within 10-years with a mean IOP of 27.6±15.4 before the subsequent TS surgery. Among the 16 eyes with an Ahmed valve, 6 eyes (37.5%) required additional surgical intervention: 3 eyes underwent cyclophotocoagulations (CPC) (18.7%), 1 trabeculectomy (Trab) (6.2%), and 2 needed a second TS (12.5%). Among the 13 eyes with a Baerveldt implant, 4 eyes (31.2%) required additional surgery, 2 (15.6%) of which required two procedures. 1 eye required a new TS, 1 needed a Trab, 1 eye underwent Trab + CPC (7.8%), and 1 eye needed both a TS (switched to Ahmed valve) + CPC (7.8% each). During the follow-up period, 7 eyes (23.3%), 4 eyes (13.3%), and 3 eyes (10%) required one, two, and three TS revisions, respectively.

Conclusions: In this long-term retrospective study, patients undergoing TS surgery overall had maintained a therapeutic IOP and useful vision. However, a significant portion of patients underwent additional procedures with approximately a third of eyes requiring additional surgical interventions.

CONTROL ID: 3714548

SUBMITTER (NAME ONLY): Chloe Guillaume

TITLE: Characterization of retinal morphology in the naturally occurring hypopigmented 13-lined ground squirrel

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Guillaume, P. Summerfelt, J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|C. Yu, H.M. Follett, J. Carroll, Cell Biology, Neurobiology, & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|O. Bowie, School of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D. Merriman, Department of Biology, University of Wisconsin Oshkosh, Oshkosh, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cone-dominant 13 lined ground squirrel (13-LGS) is an emerging model for vision research. Here, we sought to characterize a naturally occurring hypopigmented 13-LGS model using non-invasive imaging.

Methods: Six (5M, 1F) 13-LGS from the same hypopigmented pedigree were anesthetized and underwent non-invasive retinal imaging and axial length measurement. Near infrared reflectance (NIR), Near infrared autofluorescence (NI-AF), and short wavelength autofluorescence (SW-AF) scanning laser ophthalmoscopy (SLO) imaging was used for qualitative assessment. Optical coherence tomography (OCT) scans were obtained to quantify retinal thickness. Adaptive optics scanning light ophthalmoscope (AOSLO) images were acquired along vertical strips from the optic nerve head (ONH) inferior to the visual streak. Regions of interest were then selected at 0.75° increments along this strip to estimate cone density. Quantitative metrics were compared to eccentricity matched data from one-year-old wildtype animals (OCT: n = 12 eyes, AOSLO: n = 6 eyes).

Results: SLO imaging revealed variable choroidal visualization in all animals. Two animals had substantially shorter axial length values (5.87 and 5.90 mm; normal range = 8.53 - 8.9 mm). These two animals had significantly increased total retina, inner retina, outer retina, and choroidal thicknesses, while thickness values for the other 4 animals were within normative ranges (see Figure). AOSLO imaging was not possible in the two short-eyed animals due to poor image quality. In remaining hypopigmented animals, density measurements fell within ± 2 SD of the normative eccentricity matched mean values (c.f., at 6.25 degrees eccentricity, normal mean ± 2SD: 534.98 ± 115.46 cones/deg^2; hypopigmented range: 522.37 – 594.09 cones/deg^2).

Conclusions: While some of the hypopigmented 13-LGS present similarly to wildtype animals, the decreased axial length, abnormal OCT, and altered SLO observed in two of the hypopigmented animals present similarly to that of human albinism patients. This supports continued examination of the hypopigmented 13-LGS pedigree as an emerging model to study human albinism.

CONTROL ID: 3714549

SUBMITTER (NAME ONLY): Ashley Deemer

TITLE: Visual function outcome measures of a comparative trial of low vision enhancement head-mounted display systems (HMD)

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A comparative clinical trial was conducted to evaluate the effectiveness of a virtual bioptic telescope in an HMD vision enhancement system possessing a wide field of view to currently employed specifications in HMD vision enhancement technology through patient reported outcome measures. As HMDs are being developed and implemented into clinical vision rehabilitation, it is important to evaluate the effectiveness of new features as it translates into the functional ability of visually impaired individuals.

Methods: Patients were randomized into two arms with the following HMD specifications: 1. a magnification bubble embedded in an unmagnified 70° field of view (bubble) and 2. full-screen magnification in a 45° field of view (legacy). Participants completed baseline testing then took the device home for a 2-4 week trial period. Participants were encouraged to use the device in their daily activities (excluding mobility). The Activity Inventory (AI) was administered before and after the home trial to measure the effect of system use on self-reported functional ability measures. Baseline and follow-up AI results were analyzed using Rasch analysis.

Results: A total of 88 (n=44 legacy, n=44 bubble) participants with BCVA of <20/60 in the better-seeing eye and at least 70° of peripheral visual field completed the study. There was no difference in age, BCVA, or baseline AI person measures between groups. In the legacy group, improvements were seen in reading (Cohen's d=0.99, p <0.001) and inside-the-home tasks (d=0.44, p=0.04). In the bubble group, improvements were seen in reading (d=0.82, p <0.001) and visual information tasks (d=0.39, p=0.03). There was no improvement in visual motor function or mobility in either group. Between group effects did not reach statistical significance.

Conclusions: Based on the AI results, use of both the legacy and bubble HMD result in improvements in reading, visual information (i.e. seeing faces), and inside-the-home tasks with reading having the strongest effect size. The lack of improvement in mobility and visual motor function is expected and likely due to limited field of view and lack of binocular disparity. There were trends for legacy device users to report better outcomes with reading and in-home tasks and bubble users to report better outcomes with visual information tasks, but there was no significant difference between groups.

CONTROL ID: 3714551

SUBMITTER (NAME ONLY): Isabelle Dortonne

TITLE: Utility of the red reflex test for detecting posterior ophthalmic pathology in the pediatric population

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Dortonne, M. Manrique, S. Rana, W. Madigan, Ophthalmology, Children's National Hospital, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The red reflex test (RRT) continues to be an important part of the ophthalmology screening exam in the pediatric population to ensure early detection of ocular pathologies. Although RRT is considered a reliable examination technique for identifying anterior segment pathology (ASP), significant limitations in accurately detecting posterior segment pathology (PSP) have been reported. Delayed diagnosis of such conditions in children may cause permanent visual impairment leading to morbidity. This study aims to evaluate the utility of RRT for detecting ASP and PSP in the pediatric population. Furthermore, we aim to evaluate the impact of pharmacologic dilation and room illumination on the sensitivity and specificity of RRT.

Methods: After IRB approval, a prospective gathering of data was conducted at our tertiary care institution. Ophthalmology residents/fellows blinded to the patient's ophthalmologic diagnosis, performed a standardized RRT both in a dark room and a room with standard illumination. The RRT was repeated in the same manner after pharmacological pupil dilation. Finally, the patient was examined by a retina specialist to identify any ocular pathology. Analysis was performed using R statistical software.

Results: 34 eyes were analyzed. Mean age was 7.7 ±4.8 years. The RRT showed higher sensitivity and negative predictive value (NPV) for ASP; however, specificity rates and positive predictive value (PPV) were higher for PSP (table 1). There was no significant difference between RRT results in ambient light versus a dark room for both ASP and PSP. Dilation did not produce a statistically significant difference in RRT results (table 2).

Conclusions: Red reflex testing is an economical, effective screening method for children that provides a high sensitivity and negative predictive value for ASP such as cataract and corneal abnormalities. For any symptoms concerning for PSP, patients should be referred for prompt evaluation by an ophthalmologist regardless of their RRT findings. This study also finds that it is appropriate to conduct RRT in both ambient and dark lighting conditions. Furthermore, pediatricians can adequately conduct RRT without the need for dilation drops, which may improve times of consultation during a young child’s visit.

CONTROL ID: 3714552

SUBMITTER (NAME ONLY): Xiaohua Gong

TITLE: Functional interaction between connexin 46 and periaxin in cataractogenesis

SESSION TITLE: Cataractogenesis: pathogenesis, prevention and treatment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Gong, C. Xia, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|V. Rao, Department of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Xiaohua Gong: Commercial Relationship: Code N (No Commercial Relationship) | Vasantha Rao: Commercial Relationship: Code N (No Commercial Relationship) | Chun-hong Xia: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To test a hypothesis that Periaxin (Prx) gene variant of 129 mouse strain background acts as a gain-of-function variant to facilitate severe nuclear cataract in connexin 46 knockout (Cx46KO) lenses by characterizing Prx-Cx46 double knockout (DKO) lens phenotypes. To determine the underlying cellular mechanism for functional association between connexin 46 and periaxin in lens homeostasis, stiffness and cataract formation.

Methods: Biochemical approaches including western blotting and morphological tools including laser confocal microscopic imaging were used to characterize and compare the molecular and cellular changes among lenses of wild-type, Cx46KO at different strain backgrounds and the Prx-Cx46 DKO mice in vivo. Prx gene variances were characterized in cultured cells in vitro.

Results: Severe nuclear cataracts in Cx46KO lenses were associated with the presence of highly expressed 129-periaxin proteins that were colocalized with F-actin in protrusions in lens fiber cells. The presence of 129-periaxin appeared to be associated with increased lens stiffness. Prx-Cx46 DKO at 129 strain background developed mild cataract that was similar to mild cataract in Cx46KO at C57BL/6J background, which expressed a low level of Prx variant in lens fibers.

Conclusions: Mild cataracts in DKO lenses suggest that a loss of periaxin significantly attenuate the development of severe nuclear cataracts in Cx46KO lenses at 129 strain background and 129-Prx gene acts as a gain-of-function variant to facilitate cataractogenesis caused by increased calcium levels in Cx46KO lenses. This result further indicates that both Cx46-mediated cell communication and Prx-mediated membrane-cytoskeletal complex regulate the calcium homeostasis in the lens fibers.

CONTROL ID: 3714553

SUBMITTER (NAME ONLY): Thanh-Tin Nguyen

TITLE: Quantification of fibrovascular ridge thickness in retinopathy of prematurity using swept-source optical coherence tomography

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.P. Nguyen, S. Ni, S. Khan, X. Wei, S.R. Ostmo, Y. Jia, D. Huang, Y. Jian, J. Campbell, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S. Ni, S. Khan, X. Wei, Y. Jia, D. Huang, Y. Jian, Department of Biomedical Engineering, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) stage is classified based on the appearance of the ridge on ophthalmoscopy or imaging. Using ultra-widefield (UWF) optical coherence tomography (OCT) we hypothesized that we could measure the axial thickness of the peripheral ridge, and that there is a positive correlation between stage category and ridge thickness.

Methods: We captured 26 unique ridge portions (showing at least 3 continuous clock hours of disease) in 11 patients with stage 1 to 3 ROP using portable, swept-source OCT with up to a 140° field of view (FOV). Area from the retinal pigment epithelium to the inner ridge surface was manually segmented (Figure 1), and axial thickness was calculated pixel-wise (1 pixel=4.4 μm) along the transverse dimension. A masked grader provided diagnosis of max stage using International Classification of ROP (ICROP) guidelines, as well as a second label representing a continuous spectrum of stage (e.g. 1.5). We compared ridge thickness (mean and standard deviation [SD]) to stage categories (analysis of variance [ANOVA]) and the stage spectrum (linear regression).

Results: The mean (+SD) ridge thickness increased with stage classification, with thickness of 252 (+49), 340 (+77), and 380 (+95) μm for stages 1, 2, and 3, respectively ($p=0.04$ by ANOVA). There was a significant relationship between the max ridge thickness and the continuous stage labels (Figure 2, $R^2=0.566$; $p<0.001$).

Conclusions: UWF OCT measurement of retinal thickness at the peripheral ridge correlated with ICROP stage classification and with continuous approximation of stage labels. These results suggest that OCT may provide objective and quantifiable biomarkers for ROP stage in the future, and that ROP severity overall may be better represented as a spectrum, since it varies both axially and circumferentially in eyes with ROP.

CONTROL ID: 3714554

SUBMITTER (NAME ONLY): Shirin Hassan

TITLE: Both Street Width and Direction of Traffic Flow Contribute to Making Streets Difficult to Cross for Pedestrians

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Hassan, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Shirin Hassan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: My lab has previously shown that young and older pedestrians alike find a two-way street more difficult to cross than either a one lane, one-way street or a roundabout. However, what makes the two-way street more difficult to cross? Is it the greater street width and/or the opposing directions of traffic flow? This study aimed to determine the individual effects of street width and traffic direction on the safety of crossing decisions.

Methods: 30 young, 13 young-old and 19 older-old subjects with normal vision made crossing decisions about whether or not they thought it was safe to cross at three different types of streets; a one lane, one-way street (one-way), a two-way street and a street that had two lanes of one-way traffic. Crossing decisions at each street type were made for a range of vehicular gap times. The percentage of unsafe decisions was calculated for each subject at each street by computing the number of times a subject deemed it was safe to cross when the measured gap time at a particular street was shorter than the subject's measured crossing time at that street. A linear mixed model with repeated measures for subject was used to determine if the percentage of unsafe decisions changed as a function of age and type of street.

Results: We found that all age groups made significantly more unsafe decisions at the wider street of two lanes of one-way traffic compared to the one-way street ($p<0.0001$). When assessing the effect of traffic direction, performance varied as a function of age. Specifically, young subjects made significantly more unsafe decisions at the two-way street compared to the two lanes of one-way traffic ($p<0.0001$). While the young-old subjects made a similar number of unsafe decisions at the two lanes of one-way compared to the two-way street ($p=0.41$), the older-old subjects made significantly more unsafe decisions at the two lanes of one-way traffic compared to the two-way street ($p<0.0001$). All subjects, irrespective of age, made significantly more unsafe decisions at the two-way street compared to the one-way street ($p<0.0001$).

Conclusions: Our data suggests that street width and the direction of traffic flow both increase the level of difficulty of making a safe crossing decision. It appears that with increasing age, pedestrians have more difficulty simultaneously processing information from two lanes compared to just one lane at a time.

CONTROL ID: 3714555

SUBMITTER (NAME ONLY): Viren Govindaraju

TITLE: Difluprednate for the Treatment of Postoperative Hypotony following Complicated Retinal Detachment Surgery.

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Govindaraju, A. Omari, G.A. Williams, T. Hassan, Ophthalmology, Beaumont Health, Royal Oak, Michigan, UNITED STATES|D. Jung, K. Koustas, Z. Saleem, R. Shields, Oakland University, Rochester, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Severe hypotony following successful complex retinal detachment (RD) repair can progress to phthisis bulbi without intervention, even in the setting of long-term postoperative intraocular tamponade with silicone oil. It is also known that the use of periocular and intraocular steroids has been seen to induce an elevated intraocular pressure (IOP) response in some eyes. This study sought to assess the impact of topical difluprednate on raising intraocular pressure in patients with hypotony following surgical repair of a complex-RD.

Methods: A retrospective, consecutive case series was conducted on patients treated with difluprednate after successful complex RD repair at Associated Retinal Consultants (ARC, Royal Oak, Michigan) from January 2013 to June 2021. Patients were identified as having had complex RD repair by Current Procedural Terminology (CPT) code.

Results: Medical records of 230 patients were reviewed and 39 eyes of 39 patients were found to develop hypotony (IOP < 8 mmHg), despite having complete retinal reattachment and not having cyclitic membranes, at least 1 month after their last surgery. The majority of patients were left with long term silicone oil tamponade (26 of 39, 66.6%) and had required a retinectomy at the time of surgical repair (30 of 39, 76.9%). Patients presented with hypotony an average of 41 days after their last surgery (6-167 days). After initiation of topical difluprednate, there was a statistically significant increase in mean IOP (5.6mmHg) and at the patient's final follow up (8.6 mmHg, p=0.032).The average follow-up was 833 days after difluprednate initiation (range 76-2406 days). One patients progressed to phthisis bulbi, and all remained with complete retinal attachment at the last follow-up visit.

Conclusions: Topical difluprednate therapy for hypotony following successful complex RD repair resulted in a statistically significant increase in IOP and prevented phthisis bulbi in a majority of patients.

CONTROL ID: 3714556

SUBMITTER (NAME ONLY): Angela Kim

TITLE: Comparative analysis of wide-field optical coherence tomography angiography to ultra-widefield fluorescein angiography and pseudocolor fundus photos in the detection of diabetic retinopathy

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kim, M. Abou-Jaoude, M. Jacobs, N. Fowler, H. James, C. Turski, S. Reddy, R. Maldonado, Ophthalmology, University of Kentucky, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection of diabetic retinopathy (DR) is vital in preventing poor visual outcomes and is done with ultra-widefield color fundus photos (CFP) and fluorescein angiography (FA). Optical coherence tomography angiography (OCTA) may have a role but limited literature exists. Here we aim to determine the potential utility of OCTA in DR screening.

Methods: This is an IRB-approved retrospective image analysis of subjects with type 1 or 2 diabetes mellitus with or without DR at a single academic center. Subjects received FA and CFP (OPTOS, UK) and OCTA (Plex-Elite, Zeiss, Germany) in the same eye, same day. The arteriovenous and late phase frames were used for FA and 12x12mm vitreo-retinal interface (VRI) and superficial plexus slabs for OCTA. Images were analyzed by three masked graders on Imagivault (Melbourne, Australia). Graders evaluated for enlarged/irregular foveal avascular zone (FAZ), venous beading (VB), intraretinal microvascular abnormalities (IRMA), microaneurysms (MA), nonperfusion (NP), and neovascularization elsewhere (NVE) or disc (NVD). Images with poor quality or artifacts were excluded. We estimated sensitivities and specificities of features against FA as gold standard and Fleiss Kappa for intergrader agreement and reliability.

Results: From 43 total eyes, 36 met inclusion criteria. Mean age was 57 with 14 mild, moderate, or severe NPDR, 19 PDR, and 3 no DR. OCTA sensitivity was 0.94-1.00 for all features and specificity 0.75-1.00 in detection of MA, IRMA, NVE, NVD, NPA, and VB. CFP had sensitivity in detecting VB, MA, NVE, and NVD from 0.89 to 1.00 and specificity in detecting MA, VB, NVE, and NVD from 0.91-1.00. Inter-grader agreement showed FA was highest in detecting MA (89%, kappa 0.53) and NVD (89%, kappa 0.81). CFP had highest agreement in number of IRMA (75%, kappa 0.18); OCTA had highest agreement in IRMA (72%, kappa 0.63), MA (72%, kappa 0.45), and number of NVE (75%, kappa 0.47).

Conclusions: In our study OCTA outperformed FA in sensitivity and repeatability of detecting FAZ enlargement/irregularity and IRMAs. In addition, OCTA had comparable performance in detecting neovascularization. CFP overall was least able to accurately and reliably detect a variety of diabetic lesions. These findings highlight OCTA strengths in the evaluation of DR.

CONTROL ID: 3714557

SUBMITTER (NAME ONLY): Ignacio Alcalde

TITLE: Morphological and functional evidences for TRPM8 expression in the mouse retina

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Alcalde, C. Sánchez-Fernández, E. Artime, S. López, J. Merayo-Lloves, Fundación de Investigación Oftalmológica, Instituto Universitario Fernandez-Vega, Oviedo, SPAIN|I. Alcalde, C. Sánchez-Fernández, C. Martín, J. Merayo-Lloves, Instituto de Investigacion Sanitaria del Principado de Asturias, Oviedo, Asturias, SPAIN|C. Martín, Dept. Biología Funcional, Universidad de Oviedo, Oviedo, Asturias, SPAIN|A. Tejedor, Universidad de Oviedo, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Novel transgenic mice expressing fluorescent reporters associated to TRP channels have improved morphological studies of protein location. Here we report the expression of TRPM8 cold-transducing ion channel in a subset of retinal neurons. This study also aims to study the function of TRPM8 in the retina.

Methods: Retinas from TRPM8-EYFP and TRPM8-KO mice were used to detect by immunofluorescence Calretinin, Calbindin, Parvalbumin, Tyrosine hydroxylase, Choline acetyl transferase, GAD 65/67 and mGluR2. Prior to morphological analysis, WT and KO mice were examined by electroretinography (ERG) and optomotor tests to evaluate the functional role of TRPM8 in the retina. ARVO statements for the use of animals were followed.

Results: We described a population of TRPM8-positive amacrine cells with cell bodies distributed in the internal nuclear layer (INL) and ganglion cell layer (GCL), forming two densely packed neuropil layers coincident with ChAT+ sublayers 2 and 4 of the inner plexiform layer (IPL). Retinal amacrine cells from TRPM8-KO mice did not express TRPM8 protein or mRNA and were less numerous than in WT mice. Electroretinographic analysis showed alterations in oscillatory potentials and b-wave in KO mice. Optomotor test showed impaired movement discrimination in KO mice compared with WT.

Conclusions: A subtype of amacrine cells expressing TRPM8 channels has been identified. It appears unlikely that TRPM8 channels expressed by these neurons are involved in cold detection. In contrast, the expression of ChAT and the alterations in oscillatory potentials strongly suggest that about 60% of these cells may be starburst-like cells and could be involved in directional selectivity.

CONTROL ID: 3714558

SUBMITTER (NAME ONLY): Christopher Fuller

TITLE: Three Year Outcomes from the PALADIN Phase IV Study: Predictive Value of Prior Steroid Challenge and Intraocular Pressure Outcomes

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Fuller, Texas Retina Associates, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Christopher Fuller: Commercial Relationship(s);Code C (Consultant/Contractor):Alimera, Iveric Bio, Novartis;Code I (Personal Financial Interest):Lineage Cell Therapeutics

ABSTRACT BODY:

Purpose: A steroid challenge is mandated prior to the use of the 0.19 mg fluocinolone acetonide implant (FAc), however it is unclear which steroid is superior in identifying intraocular pressure (IOP) risk. Here we looked at the positive predictive value (PPV) of the steroid challenge by quantifying the incidence of IOP response post-FAc. FAc is indicated for the treatment of diabetic macular edema in eyes that have previously been treated with a course of corticosteroids without clinically significant rise in IOP. We computed the PPV of the steroid challenge for the full population but also for eyes that received 1 or > 1 dexamethasone implant (DEX), the most used steroid for challenge. The time course of IOP over 36 months (M) and visual acuity outcomes were also determined.

Methods: Full analysis population includes 202 eyes from 159 patients enrolled with CI-DME that received FAc and were followed for up to 36M. Subjects were followed at day 1, week 1, 2M, and quarterly from 3M up to 36M. PPV was calculated by computing the percentage of eyes whose IOP remained ≤ 25 mmHg at any time (Max PPV) or by the 36M time point (Last-PPV) post-FAc who also passed the steroid challenge (≤ 25 mmHg post challenge) pre-FAc.

Results: The Max PPV of all eyes was 78.0% with the Last PPV being 96.9%. For eyes with 1 DEX or > 1 DEX Max PPV values were 85.7% and 68.3%, and Last PPV values were 98.7% and 96.3% respectively with twice as many eyes receiving only 1 Dex prior to FAc. 20.3% of eyes received IOP lowering medication with a peak mean increase in IOP of 2.12 mmHg at 9M ($p<0.0001$) and 0.88 mmHg (NS) at 36M. Over the course of 36M, 87% of eyes had IOP ≤ 20 mmHg, 97% had IOP ≤ 25 mmHg, and 99% had IOP ≤ 30 mmHg. Eyes that received any prior steroid challenge or prior DEX all gained vision by 36M (+4.5 letters, $p<0.02$; +12.7, NS).

Conclusions: The steroid challenge pre-FAc is highly predictive of the IOP response post-FAc and not dependent on steroid choice or number of Dex. This is evident by the small change in mean IOP of the full population and that 97% of eyes had IOP ≤ 25 mmHg over the 36M post-FAc. Similarly, the steroid choice had little impact on visual acuity gains at 36 months with the full population experiencing significant vision improvement by nearly a line and eyes receiving a DEX challenge were able to maintain vision.

CONTROL ID: 3714559

SUBMITTER (NAME ONLY): Mikhail Tsurkan

TITLE: Creation of Grafts with Bioengineered Descemet Membrane for Corneal Lamellar Keratoplasty

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tsurkan, S. Arndt, S. Tsurkan, TissueGUARD GmbH, Dresden, GERMANY|M. Tsurkan, Leibniz Institute of Polymer Research Dresden, Max Bergmann Center of Biomaterials Dresden,, Dresden, GERMANY|A. Gomez Bedoya, A.L. Sabater, Department of Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Created human corneal endothelial cell (HCEC) layers or sheets aimed for the revaluation of a degenerated corneal endothelium, but mostly failed in the clinical validation due to poor mechanical stability. The immature Descemet membrane in bioengineered grafts is the main obstacle to their clinical transition. Human corneal endothelial cells have poor extracellular deposition properties in vitro. The creation of an artificial Descemet membrane could resolve this issue, but a high collagen and laminin content, as well as 16±3 microns thickness, require advanced bioengineering techniques.

Methods: We utilized peptide-functionalized, fully synthetic “smart” cell culture carriers to culture primary human MSC, which have high ECM deposition properties. Macromolecular crowding with Ficoll was used to enhance ECM secretion. Cells were cultured for ten days and removed by the diluted ammonium hydroxide solution. The formed membrane was reseeded with various cell types to validate cell adhesion and proliferation. After the confluent cell layer formation, the culture carrier was subsequently enzymatically degraded to release free-floating bioengineered Descemet membrane with attached cell layer, which was validated with various DMEK cannulas by mimicking in lab transplantation experiments

Results: The microscopic and cell staining analyses revealed that cell to cell and cell-to-matrix contacts were impaired. We utilized peptide-functionalized, fully synthetic “smart” cell culture carriers to culture primary human MSCs, which have high ECM deposition properties additionally enhanced with Macromolecular crowding. Cells were cultured for 10 days and removed by ammonium hydroxide solution. The formed bioengineered Descemet membrane was reseeded with cell types to validate cell adhesion and proliferation. After the confluent cell layer formation, the culture carrier was subsequently enzymatically degraded to release free-floating bioengineered Descemet membrane with attached cell layer, which was validated with various cannulas by mimicking in lab transplantation experiments has not impacted the implant integrity and cell viability

Conclusions: This proposed bioengineering technique has allowed, for the first time, the formation of endothelial lamella tissue with a bioengineered Descemet membrane which is shown to stabilize surgical implantation in model Descemet membrane endothelial keratoplasty DMEK experiments.

CONTROL ID: 3714560

SUBMITTER (NAME ONLY): Shahin Hallaj

TITLE: Long-term surgical outcomes of Glaucoma Drainage Implants in eyes with preoperative intraocular pressure less than 19

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hallaj, J. Wong, R. Razeghinejad, A. Shukla, N.N. Kolomeyer, J.S. Myers, D. Lee, Glaucoma Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Wong, Rowan University School of Osteopathic Medicine, Stratford, New Jersey, UNITED STATES|R. Razeghinejad, A. Shukla, N.N. Kolomeyer, J.S. Myers, D. Lee, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine long-term surgical outcomes of Glaucoma Drainage Implants for patients with low to normal preoperative intraocular pressures

Methods: The retrospective cohort study included patients requiring Glaucoma Drainage Implants (GDI) with preoperative Intraocular Pressures (IOP) less than 19 mmHg from March 2006 to May 2017. Patients with at least 1-year follow-up in the post-operative period were included. Demographic and clinical data were collected at the preoperative and postoperative visits for up to 7 years. Surgical failures were defined as eyes that required reoperation or progressed to no light perception

Results: 46 eyes of 45 patients met inclusion criteria. Mean patient age was 66.5±13.2 years old, and mean follow-up duration was 37.3±26.5 months (range: 12-84). 9 (18.7%) eyes experienced surgical complications: 3 (33%) inflammation, 3 (33%) flat anterior chamber, 1 (11%) hypotony (without any hypotony maculopathy), 1 (11%) exotropia/hypertropia. Among all 46 eyes included, 13 (28.2%) faced failure, all of which were due to the need for reoperation and revision (n=12, 92.3%) or removal (n=1, 7.6%) of the tube shunt. Unlike SLT, ALT, CPC, vitreoretinal, and corneal surgeries, a history of a previous trabeculectomy was significantly associated with a higher risk of failure (OR:3.938, p=0.046). Moreover, those with a higher MD/year loss rate had greater chances to experience GDI failure (p=0.036). Mean IOP ranged from 13.3±3.2 to 14.9±4.5 mmHg at the preoperative visit and each follow-up visit for up to 5 years (p>0.05 for all), respectively. Humphery 24-2 visual field (VF) mean deviations (n=11) were not significantly different at -11.8±10.2 and -15.9±5.8 (p>0.05) during the most recent preoperative and postoperative visits, respectively. Moreover, the mean annual progression rate was different at -2.6±2.0 and 0.23±0.67 for preoperative and postoperative VF loss (p=0.007), indicating that the intervention slowed down the pace of VF loss at 0.53 ± 1.4 MD/year. Nonetheless, the total number of medications used by the patients significantly reduced from 3.1 ± 3.5 preoperative to 1.7 ± 1.1one year postoperative (p=0.036).

Conclusions: Unchanged IOP, as well as slower postoperative mean VF loss progression rate reported in this study, implies the significant effectiveness of tube shunt placement in controlling glaucoma in patients with low to normal IOP.

CONTROL ID: 3714561

SUBMITTER (NAME ONLY): Aseel Hamoud Bedan

TITLE: Subthreshold Micropulse Laser Treatment in Diabetic Macular Oedema

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bedan, F. Zacharaki, M. Rashsad, S. Morgan, F. Carr, Ashford and Saint Peter's Hospitals NHS Trust, Chertsey, Surrey, UNITED KINGDOM|

Commercial Relationships Disclosure: Aseel Hamoud Bedan: Commercial Relationship: Code N (No Commercial Relationship) | Fani Zacharaki: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Rashsad: Commercial Relationship: Code N (No Commercial Relationship) | Stephen Morgan: Commercial Relationship: Code N (No Commercial Relationship) | Francis Carr: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the effect of micropulse MP laser treatment in patients with diabetic macular oedema DMO over a three months period.

Methods: it's a retrospective study of 80 patients with DMO, these patients are outside the treatment criteria for anti-VEGF injections, that's to say their best corrected visual acuity BCVA is better than 6/12, and/or the central macular thickness CMT is less than 400 micrometre. We measured there BCVA, CMT before and three months after MP laser treatment. We used coloured photographs, fundus autofluorescence FAF, and optical coherent tomography OCT to highlight and marks left on the retina after treatment.

Results: At three months 43 of the patients improved their BCVA, 25 worsened. CMT showed improvement in 43 of the patients and worsened in 36. Retreatment was not done on any of them using the 3 months. No one of the patients had any laser scars or marks detected on biomicroscopy, FAF or OCT scans.

Conclusions: MP laser treatment is an effective, affordable way of treating patients with DMO not meeting the treatment criteria of anti-VEGF injections.

CONTROL ID: 3714564

SUBMITTER (NAME ONLY): Reddikumar Maddipatla

TITLE: Toward longitudinal evaluations of biological processes in transgenic mice models using an integrated cellular-resolution optical coherence microscopy and fluorescence microscopy.

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Maddipatla, C. Liu, P. Tankam, school of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Reddikumar Maddipatla: Commercial Relationship: Code N (No Commercial Relationship) | Chia-Yang Liu: Commercial Relationship: Code N (No Commercial Relationship) | Patrice Tankam: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Nowadays, scientists are equipped with robust tools to induce genetic mutations in animal models to advance the understanding of disease mechanisms. The purpose of this work is to enable the evaluation of the outcomes of these genetic modifications and follow up these processes over time on a single specimen using advanced optical imaging techniques.

Methods: An integrated optical coherence microscopy (OCM) and dual-channel fluorescence microscopy (DCFM) system was developed to simultaneously co-register the reflectance and fluorescence signals from the cornea of transgenic mouse models. OCM was equipped with a broadband source with a central wavelength at 850 nm and FWHM of 165 nm. DCFM was designed with two excitation peaks at 473 nm for Tdtomato and 561 nm for green fluorescent proteins (GFP). A conditional knockout mouse that expresses both tdTomato and GFP in the corneal stroma was engineered to evaluate the system performances. Reflectance and fluorescence signals were registered simultaneously at a given plane of focus in the corneal stroma. However, unlike OCM, DCFM does not possess an intrinsic depth-sectioning capability. Therefore, subsequent acquisitions with DCFM alone were performed by z-scanning the sample with a step size of 2 μm to evaluate the axial resolution of DCFM.

Results: The system achieved the simultaneous co-registration of reflectance and fluorescence signals with a lateral resolution of 2 μm and speed of 250kHz line rate. OCM achieved an axial resolution of ~2 μm in the cornea.

Conclusions: The custom multimodal system was evaluated on corneal imaging of a transgenic mouse. Future work will focus on enhancing the contrast detection and depth-sectioning of DCFM.

CONTROL ID: 3714565

SUBMITTER (NAME ONLY): Hugo Barba

TITLE: Germ-Free Laser-Induced Murine Model Shows The Effect Of The Microbial Organ On Choroidal Neovascularization.

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.A. Barba, J. Zhang, D. Skondra, Ophthalmology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|E. Chang, Medicine. Microbiome Medicine Program, Knapp Center for Biomedical Discovery, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|A. Movahedan, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|M. Spedale, B. Theriault, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|U. Nadeem, Pathology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|N. Deng, Ophthalmology, Aier Eye Hospital Group, Changsha, Hubei, CHINA|

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ABSTRACT BODY:

Purpose: Emerging data link the gut microbiome with neovascular age related macular degeneration (nAMD) and choroidal neovascularization (CNV), its hallmark lesion. Our team has previously described how the microbial organ modulates the retinal expression of genes/pathways associated with nAMD such as vascular endothelial growth factor (VEGF), peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1alpha and hypoxia-inducible factor (HIF) 1 pathway. To further confirm the effects of the gut microbiome on nAMD, we compared the laser-induced CNV formation between germ-free (GF) mice and specific pathogen free mice (SPF).

Methods: Male GF C57Bl/6 mice were bred/kept in sterile isolators in the UChicago Gnotobiotic Facility. Age/gender-matched SPF C57Bl/6 mice were used as control. Around 16 weeks of age, mice underwent laser photocoagulation (power 120mW/duration 0.1 sec/50um spot size, Argon 532 nm, Iridex OcuLight GL) using our specialized sterile protocol for GF mice and conventional protocol for SPF mice. Choroidal flatmounts were immunostained with isolectin IB4 for CNV and IBA-1 for activated microglia. Images were taken using a Leica-SP5 confocal microscope. CNV and IBA-1 signal were analyzed with Image-J software and data were analyzed with R Studio. Sterility of GF mice was checked weekly with cultures and PCR.

Results: PCR and cultures were negative before and after the laser sessions confirming GF sterility. GF group showed decreased CNV size by 35% (12,940.05um^2±5,627um^2, n=9 vs 19,873.39um^2±13,336um^2, n= 20, P= 0.0345) but had similar CNV formation rate compared to SPF group (92% vs 94% respectively). Number of IBA-1 positive activated microglia within 100um outside the lesion was decreased in the GF mice (5.36 and ± 4 vs 9.03 ± 5, P = 0.03). However, IBA-1 signal within CNV lesion was similar between the two groups (55.66 ± 2.79 vs 55.86 ± 6.55, P > 0.05).

Conclusions: These results, together with the RNA-seq data previously obtained, suggest that the microbial organ may have a considerable influence on the development of nAMD lesions. The GF laser-induced CNV model allowed us to eliminate other factors such as antibiotics showing the direct effects of the overall microbiome over the CNV formation. Further studies are needed to determine which microbes, either protective or pathogenic, have the highest impact on the development of nAMD and the mechanisms involved.

CONTROL ID: 3714566

SUBMITTER (NAME ONLY): Yonghong Jiao

TITLE: Association of hyperopia reserve with the severity of parental refractive status in pre-school Chinese children--Beijing Hyperopia reserve study

SESSION TITLE: Refractive Error: Myopia, Hyperopia, vision and models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Jiao, Y. Fang, J. Hu, S. Jin, Beijing Tongren Hospital, Beijing, Beijing, CHINA|J. Pu, W. Chen, X. Liu, L. Wang, J. Feng, H. Tong, S. Xing, Maternal and Child Health Hospital of Haidian District, BEIJING, CHINA|Z. Zhou, School of Biomedical Engineering, Capital Medical University, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: Beijing Hyperopia Reserve Study is a prospective observational study to investigate 3-years trajectory of the hyperopia reserve elimination in a kindergarten-based sample of Chinese children 3 through 6 years of age in an urban city, Beijing. The baseline data was collected in 2020. Parental myopia was associated with a high risk of early-onset myopia. In addition, myopia and high myopia seem to have different patterns of inheritance, and more severe myopia leads to an increased risk of myopia in children aged 12 to 15 years old. Limited data of those associations is shown in children before the onset of myopia. Hyperopia reserve is a refractive status that precedes myopia and attracts wide attention both in parents and clinicians. We conducted this study to explore the impact of severity of parental myopia on hyperopia reserve status in Chinese pre-school children.

Methods: The study enrolled 2111 pre-school children from 22 randomly selected kindergartens including 1011 girls (2022 eyes) and 1100 boys (2200 eyes). Among them, 494, 844, 500, 273 children were 3, 4, 5, 6 years old. All children were taken cycloplegic refraction by using cyclopentolate 1%. Refraction was recorded in spherical equivalent, appreciated as hyperopia reserve. Parents were asked to complete a questionnaire about the severity of refractive status (normal; mild myopia <-3D; moderate myopia ≥-3D and≤-6; high myopia >-6D) and near/outdoor activities time and reading habits.

Results: The mean hyperopia reserve was 1.11±0.97 diopter and the mean axial length was 22.3±0.7mm in all children. In total, 90.7% of children had at least one myopic parent. There was a descending trend of hyperopia reserve and axial length with increasing severity of parental refractive status (Fig a and b). It is noted that the mean axial length in children in mild-high, mod-high, and high-high was beyond the average of the whole population (Fig b). The hyperopia reserve was correlated with neither indoors (P=0.631) nor outdoor activity time (P=0.330).

Conclusions: More severe myopia in parents was associated with less hyperopia reserve in preschool children. The children with highly myopic parents have longer axial lengths and may have higher risks of being myopia.

CONTROL ID: 3714567

SUBMITTER (NAME ONLY): Rishab Majumder

TITLE: Age-Associated Changes in Astrocytes Cilia of Mouse Retina and Optic Nerve

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Majumder, K. Ning, T. Kowal, Q. WANG, M. Tran, B. Wang, Y. Hu, Y.J. Liao, Y. Sun, Spencer Center for Vision Research, Byers Eye Institute, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|R. Majumder, T. Kowal, Y. Sun, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Defects in primary cilia and ciliary signaling are associated with an array of neurodegenerative diseases. Advanced age is a primary risk factor for many neurodegenerative diseases, including age-related macular degeneration and glaucoma. Primary cilia are sensory organelles that transmit and regulate various cellular communication pathways, including Sonic hedgehog and Wnt signal pathways. Astrocytes and neurons are recognized to form primary cilia in the central nervous system (CNS). While many studies have examined cilia in photoreceptors and CNS neurons, there are few studies based on the role of primary cilia in astrocytes in the anterior visual pathway. This study assessed ciliary frequency (ration of ciliated cells) changes in aged astrocytes within the mouse retina and optic nerve.

Methods: Three- and 20-month-old C57/BL6 mice were used in the study. The globes and optic nerve, including the optic chiasm, were collected and immunostained for cilia markers. Retina whole-mounts were immunostained with astrocytes marker (GFAP antibody) and ciliary markers (Arl13b and gamma-tubulin antibody). Confocal images were captured and analyzed per retina (2 central, 2 middle, 2 peripheral) at high magnifications. The anterior optic nerve and optic chiasm in longitudinal frozen sections were obtained and immunostained with an astrocytic nuclear marker (Sox9 antibody), myelin basic protein (MBP) and ciliary marker (Arl13b antibody). Anterior-to-posterior optic nerve sections were quantified, including the optic nerve head, optic lamina, myelinated region, pre-chiasm, chiasm, and post-chiasm. Statistical analysis was performed using One-way ANOVA and the Student’s t-test.

Results: In mouse retina, most astrocyte ciliation is observed in 3-month-old mice among all regions. Aged retinal astrocytes showed a significant reduction in ciliation in each region ($P<0.05$, Student t-test). In the optic nerve, chiasm, and post-chiasm regions displayed higher ciliation rates in Sox9-positive astrocytes compared to anterior optic nerve in 3-month-old mice. Interestingly, ciliation in chiasm region significantly decreased compared to the anterior optic nerve in 20-month-old mice ($P<0.05$, One-way ANOVA).

Conclusions: This novel age-associated alteration was discovered in astrocyte cilium found in the mouse retina and optic nerve. These findings suggest possible involvement of primary cilia in age-associated retinal diseases.

CONTROL ID: 3714568

SUBMITTER (NAME ONLY): Benjamin Zhou

TITLE: An Analysis of Patient Satisfaction after Double Eyelid Surgery using Social Media Reviews

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Zhou, J. Mahajan, C. Tseng, R. Henry, P.D. Langer, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Because double eyelid surgery is often an aesthetic surgery for cosmetic purposes, patient outcomes rely heavily on qualitative measurements of satisfaction. It is important to characterize individual factors that shape patient perspectives about double eyelid surgery, as cosmetic satisfaction may translate to improved body image and self-esteem.

Methods: All reviews under the category “double eyelid surgery” on RealSelf.com were collected using an automated web crawler. Reviews were then characterized as overall positive or overall negative and given a primary categorization that defined the theme of the review and a secondary categorization if there was additional secondary reasoning for being positive or negative. The number of stars for rating different categories on a scale of 1 to 5 was also gathered.

Results: A total of 549 double eyelid surgery reviews were collected. Of the 549 total reviews, 456 (83%) were positive and 93 (17%) were negative. Among the positive reviews, the most frequently cited primary reasons were bedside manner (n=226, 50%) and aesthetic result (n=195, 43%). Among the negative reviews, the most frequently cited primary reasons were aesthetic result (n=67, 72%) and bedside manner (n=18, 19%) (Table 1). Overall, most patients (n=403, 84.3%) gave the highest overall rating of 5 stars for their doctor. The most cited reasons for a 5 out of 5 rating were “staff professionalism and courtesy” (n=220), “answered my questions” (n=216), and after care follow-up (n=210). The most frequently cited reasons for the poorest rating of 1 out of 5 were “after care follow-up” (n=21), “time spent with me” (n=21), and “doctor’s bedside manner” (n=19) (Table 2).

Conclusions: Patient satisfaction is a significant aspect of perceived success and encompasses many components like preoperative encounters, surgery experience, and the postoperative recovery course. In this study, the majority of reviews were positive most commonly due to bedside manner and aesthetic result. Negative reviews were most frequently due to aesthetic results. Our findings emphasize the importance of the multifaceted components of the clinical encounter both inside and outside the operating room. Although operative performance and final appearance are always important, preoperative and postoperative management can play a huge role in overall patient satisfaction.

CONTROL ID: 3714570

SUBMITTER (NAME ONLY): Alessia Tassoni

TITLE: Classical complement initiator C1q mediates synapse and neuronal loss in a light damage model of photoreceptor degeneration

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tassoni, J. Vereen, Y. Andrews-Zwilling, E. Cahir-McFarland, L. Mattheakis, T. Yednock, Annexon Biosciences, Brisbane, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Geographic Atrophy (GA) is an advanced form of age-related macular degeneration leading to photoreceptor death and visual loss. Increased expression of complement components has been observed in retinal tissue from GA patients. The role of C1q and the classical complement pathway in driving disease progression is under investigation. We examined expression and tissue localization of complement proteins in the retina of mice exposed to light damage and determined the potential therapeutic benefit of classical complement inhibition in this model.

Methods: Balb/c mice were exposed to white light to cause retinal damage and observed at Day 1, 3 and 7 post light exposure. Classical complement component levels were measured in retina lysates by ELISA. C1q expression in the tissue was assessed by IHC. Microglia engulfment of synapses was assessed using IMARIS software. To test the role of the classical complement pathway in photoreceptor cell damage, C1q activity was pharmacologically blocked by intravitreal injection of a C1q inhibitory antibody. Retina specimens from GA patients were procured from the San Diego Eye Bank.

Results: There was progressive loss of photoreceptor synapses and cell bodies, as well as an increase in microglial cells across the outer plexiform (OPL, synapses) and outer nuclear layers (ONL, cell bodies) in mice exposed to light damage. C1q expression was induced in microglia and was localized on photoreceptor synapses and cell bodies following light damage. There was a significant correlation between levels of C1q in the OPL and ONL and photoreceptor synapse and cell body loss. C1q-tagged synapses were engulfed by microglial cells upon damage suggesting a causal relationship. Treatment with a C1q inhibitory antibody normalized complement component levels. Preliminary evidence showed reduced photoreceptor synapse and cell body loss, and reduced inflammation. We confirmed C1q deposition on photoreceptor synapses in human GA retina tissue suggesting that this mechanism may be operative in humans.

Conclusions: We provide first evidence of C1q deposition on photoreceptor synapses in a light exposure model of retinal damage in mice and in human GA tissue. Preliminary results suggest that inhibiting C1q protects against photoreceptor neuron damage. A Phase 2 study with a C1q inhibitory antibody is ongoing in GA patients (clinical trials.gov NCT04656561).

CONTROL ID: 3714571

SUBMITTER (NAME ONLY): Himanshu Malhotra

TITLE: sptPALM-based trafficking analysis of GPCRs in primary cilia

SESSION TITLE: Biochemistry and Molecular Biology of the Retina/RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Malhotra, P.D. Calvert, Ophthalmology and visual sciences, SUNY Upstate Medical University Hospital, Syracuse, New York, UNITED STATES|

Commercial Relationships Disclosure: Himanshu Malhotra: Commercial Relationship: Code N (No Commercial Relationship) | Peter Calvert: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Super resolution microcopy techniques have pushed the limits of optical imaging to unprecedented spatial resolution. A frontier in super-resolution microscopy is its utilization in live cells or organisms. A few studies have examined the trafficking of GPCRs in living primary cilia using sparse individual molecule labeling, e.g., with Qdots. However, many questions remain regarding GPCR movement in primary cilia as well as photoreceptor ciliary outer segment that this approach cannot adequately address due to the low numbers of GPCRs observed. We thus are developing live cell sptPALM (single particle tracking photoactivation localization microscopy) approaches for mapping the motion of hundreds to thousands of individual GPCRs within a single cilium.

Methods: Dynamics of the GPCR, somatostatin receptor 3 (SSTR3), was examined in hTERT-RPE1 cell primary cilia by sptPALM. hTERT-RPE1 cells stably expressing SSTR3-mEos4b were generated using lentiviral transduction. Upon starvation, hTERT-RPE1 cells expressing SSTR3-mEos4b generates pocketed cilia where SSTR3-mEos4b is enriched. sptPALM imaging was performed using a Nikon microscope equipped with an iLAS2 ring TIRF illuminator. Sparse photoswitching of mEos4b specifically in the cilium was achieved by dim 405nm laser focused to the diffraction limit and positioned by galvanometer mirrors. Activated molecules were excited with widefield 561nm illumination and videos were acquired on an EMCCD camera at 50 frames per second. Videos were analyzed using TrackMate (Fiji) and MATLAB scripts developed in-house

Results: Hundreds to thousands of individual GPCR molecules were tracked within single cilia using sptPALM. Various parameters of these movements were mapped onto each cilium. Analysis of mean squared displacement as a function of time revealed that GPCR dynamics acquired using sptPALM corresponded to previous results with Qdots. Diffusion coefficients segregated into at least two groups when analyzed by histogram, agreeing with our previous work suggesting that ciliary membranes possess F-actin delimited corrals.

Conclusions: We show that our sptPALM approach is capable of tracking the dynamic of thousands of GPCRs in a single cilium within minutes, at high temporal and spatial resolution. Thus, sptPALM will allow us to map the biophysical properties of membranes and proteins of primary cilia, and photoreceptors, with unprecedented spatial resolution and high throughput.

CONTROL ID: 3714572

SUBMITTER (NAME ONLY): Michael Dorr

TITLE: Modeling the relationship between VA measured with Snellen and ETDRS standards

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Dorr, L.A. Lesmes, Adaptive Sensory Technology, San Diego, California, UNITED STATES|Y. Zhao, Z. Lu, Center for Neuroscience, New York University, New York, New York, UNITED STATES|Z. Lu, Division of Arts and Sciences, New York University Shanghai, Shanghai, Shanghai, CHINA|

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ABSTRACT BODY:

Purpose: Visual acuity (VA) is measured with the ETDRS standard in clinical trials. Snellen remains the real-world standard, although Snellen VA is typically worse by 6 ~ 12 letters (0.12 ~ 0.24 LogMAR). In this study, we modeled ETDRS-Snellen discrepancies for 163 observers from Kaiser (2009) to enable better translation between the VA standards.

Methods: We used a VA behavioral function to simulate VA behavior for 27 observers with VA threshold τ from -0.3 to 2.3 LogMAR and VA-dependent range 0.253 + 0.185 VA LogMAR (Zhao et al. 2021). We scored VA behavior using ETDRS and Snellen rules (Kaiser, 2009). From repeated simulations of each observer, we computed the mean and standard deviation (SD) of VA scores and modeled ETDRS-Snellen score pairs using maximum likelihood.

Results: For the two charts, Figure 1 shows the bias (deviation from identity line) and variability (SD) of VA scores. Small biases observed when τ < 1.0 LogMAR increased significantly as VA worsened: bias > 0.20-0.50 LogMAR as τ > 1.0 LogMAR. Likewise, variability increased for worse VA: SD up to 0.15 for ETDRS and 0.19 for Snellen. Results from each simulated observer were used to construct the probability distributions for ETDRS-Snellen score pairs (Figure 2A). They were used to successfully model all the ETDRS and Snellen scores (Figure 2B) in Kaiser (2009) ($p > .05$ for all differences between observed scores and model predictions).

Conclusions: Using a VA behavioral function, we successfully modeled discrepancies between ETDRS and Snellen scores from a large sample of subjects with a wide range of VA scores. The model can be used to translate between VA measured in trials and real world.

CONTROL ID: 3714573

SUBMITTER (NAME ONLY): Blake Snyder

TITLE: Expansion of a teleophthalmology program for diabetic retinopathy screening during the COVID19 pandemic

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. Snyder, T. Vargas-Ramos, J. Ross, M. Ellis, C. Bacorn, S.C. Lee, M. Lim, G. Yiu, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic prompted efforts to encourage social distancing and minimize non-urgent in-person eye care. Here, we report the outcomes of a teleophthalmology program for diabetic retinopathy screening at an integrated health system in California that was expanded during the pandemic.

Methods: We performed a retrospective review of patients who underwent remote retinal imaging as part of a teleophthalmology program for diabetic retinopathy (DR) screening using Current Procedural Terminology (CPT) codes 92227 and 92228 at the University of California, Davis Health system between May 31st, 2019 and June 8th, 2021. Retinal images were captured at primary care locations using a Topcon NW400, Nikon RetinaStation, or Optos Primary fundus cameras, and image grading were performed by trained ophthalmologists or optometrists using a store-and-forward method. Patient records were reviewed to collect demographic, follow-up, and clinical outcomes information.

Results: During COVID19 pandemic, the teleophthalmology program screened 570 individuals (mean age 63.2 ± 13.7). There was a significant increase in the number of patients screened per month prior to and following the COVID-19 lock-down in March 2020 (5.0 ± 3.1 patients screened per month prior to and 39.1 ± 34.8 patients per month following, P = 0.0004). Among these, 204 patients received a recommendation for in-person eye care referral, of which 127 received a referral to the UC Davis Eye Center, 85 appointments were scheduled, and 82 patients were followed in person, with a median time of 108 days between screening and in-person follow-up. Follow-up rates were generally lower during the initial months after the pandemic and increased over time. Among the patients who followed in person (mean age 63.9 ± 13.8), 10% of eyes had mild non-proliferative DR (NPDR), 5% had moderate NPDR, 3% had severe NPDR, 2% had PDR, and 4% had diabetic macular edema (DME), with similar proportions before and after the COVID-19 lockdown.

Conclusions: Expansion of a teleophthalmology program during the COVID19 pandemic demonstrated improved DR screening rates, increased referrals, and improved follow-up for diabetic eye care at an integrated health system in Northern California.

CONTROL ID: 3714574

SUBMITTER (NAME ONLY): Burak Mergen

TITLE: Intrastromal Aflibercept for the Treatment of Corneal Neovascularization

SESSION TITLE: Corneal Immunology and Neovascularization

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although previous studies have shown a regression in corneal neovascularization (CoNV) after intrastromal bevacizumab injection, more efficient or alternative treatment options are still needed and the effect of intrastromal aflibercept injection on CoNV in humans has not been studied. We performed a retrospective, observational clinical study to investigate the effect of a single intrastromal injection of aflibercept on eyes with CoNV.

Methods: This retrospective study included 17 eyes of 17 patients with CoNV who underwent intrastromal injection of a single dose aflibercept (Eylea 40 mg/mL) at a single institution. 0.1 mL of aflibercept was administered into the stromal areas with apparent neovascularization (NV) by allocating the dose to each quadrant with NV until the observation of stromal whitening (max. 0.025 mL/quadrant). Slit lamp photography, best corrected visual acuity, and intraocular pressure of patients was recorded. The ratio of CoNV area to the entire corneal area was calculated using ImageJ by a masked observer. The examination findings of the patients 30 and 60 days after injection were compared to those at the baseline visit.

Results: Among 17 patients with CoNV, 15 patients (88.2%) were male and 2 (11.8%) were female. Four patients (23.5%) had a history of penetrating keratoplasty. The mean age of the patients was 52.9±12.1 years. The mean CoNV area (37.0±18.1%) decreased significantly 30 days (25.3±14.6%, p=0.0.18) and 60 days after aflibercept injection (21.4±14.3%, p<0.001). No significant systemic or ocular adverse events were observed during the follow-up.

Conclusions: Within the limitation of this retrospective study, a single dose of intrastromal aflibercept injection provided a significant reduction in the CoNV. However, further prospective randomized controlled trials with a longer follow-up period are needed for extending the results of this study.

CONTROL ID: 3714579

SUBMITTER (NAME ONLY): Paul Knepper

TITLE: A Two-Year, Phase 1 Study to Evaluate the Efficacy of Oral Curcumin on Drusen Volume

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Knepper, N.J. Volpe, S. Aman, Z. Zaparackas, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|P.A. Knepper, N. Pfahler, I. Bielskus, Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Advanced age-related macular degeneration (AMD) is a leading cause of vision loss. The presence and size of drusen are risk factors for the development of advanced AMD and loss of central vision. Although the cause of drusen remains unclear, individuals with larger drusen are more likely to develop advanced AMD. In this study, we evaluated the effect of oral curcumin on drusen volume and the development of advanced AMD over two years in AMD patients with drusen ≥125 μm at baseline using a new technique of tracking changes in individual drusen over time.

Methods: AMD participants with drusen ≥125 μm and without geographic atrophy or choroidal neovascularization (n=15) were recruited from the office of Zaparackas and Knepper, Ltd. in Chicago, IL after IRB approval and informed consent. Participants received curcumin orally at a dose of 2660 mg/day for two consecutive years. Optical coherence tomography (OCT) was used to acquire retinal photographs which were analyzed manually using ImageJ software. Drusen volume was measured for all macular drusen ≥63 μm and was recorded in mm^3. Macular regions were defined using the 1, 3, and 6-mm grid. Individual drusen were classified by size at baseline as 63-124 μm, 125-249 μm, or ≥250 μm and tracked over time.

Results: After two years, total drusen volume decreased significantly from 0.0253 (±SD 0.015) to 0.0220 (±0.013) mm^3 (-13.1%, p=0.01). Drusen ≥250 μm at baseline decreased in volume from 0.0117 (±0.0078) to 0.0095 (±0.0073) mm^3 (-18.9%, p=0.004). Drusen 125-249 μm at baseline decreased in volume from 0.0128 (±0.0105) to 0.0110 (±0.0089) mm^3 (-14.6%, p=0.09). All drusen ≥125 μm (AREDS definition of large drusen) decreased from 0.0215 (±0.0142) to 0.0183 (±0.0131) mm^3 (-14.8%, p=0.008). Medium drusen 63-124 μm did not significantly change (-3.4%, p=0.74). None of the 15 participants developed advanced AMD (geographic atrophy or choroidal neovascularization) during the study and no serious adverse events were recorded.

Conclusions: Drusen volume decreased significantly in AMD participants taking curcumin for two years. Larger drusen at baseline exhibited larger decreases in volume. None of the participants developed advanced AMD during the study. These results are the first to identify a change in drusen volume by categorizing and tracking individual drusen over time. Curcumin may be a safe and efficacious method to reduce drusen volume and risk of AMD progression.

CONTROL ID: 3714580

SUBMITTER (NAME ONLY): Steven Stasheff

TITLE: Complex non-tumor retinal ganglion cell-glial interrelationships in neurofibromatosis-optic pathway glioma (NF1-OPG) mice

SESSION TITLE: Retinal circuits

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.F. Stasheff, Y. Zhu, Children's National Hospital Center for Neuroscience and Behavioral Medicine, Washington, District of Columbia, UNITED STATES|S.F. Stasheff, F. Nadal-Nicolas, W. Li, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose:

We report further details of a mouse model for neurofibromatosis type 1 (NF1) and optic pathway glioma (OPG) formation that exhibits developmental abnormalities of retinal electrophysiology distinguishable from OPG formation per se. Underlying mechanisms may help explain variable visual loss among children with NF1 and OPGs and lead to improved diagnosis and treatment methods.

Methods: We refined previous analysis of relationships among visual behavior, anatomic abnormalities, and electrophysiologic activity of retinal ganglion cells (RGCs) recorded by in vitro multielectrodes in transgenic mice with neurofibromin (Nf1)-deficient glial precursors (NF1-OPG) and littermate controls. We focused on 1) early developmental abnormalities (postnatal day 11 (P11), P14, P21, and P35); and 2) retinotopic distribution of RGCs vs. their activity. We emphasized correlations among previously described patterns of RGC loss; retrobulbar hypomyelination; inter-subject and -eye differences; in vivo estimates of vision (optomotor responses, OMR) and retinal/optic nerve anatomy (optical coherence tomography, OCT); and optic nerve/chiasm histology.

Results: Development – Prior to first eye opening, “waves” of spontaneous RGC activity are less robust in NF1-OPG mice. Retinotopic distribution – RGC density partially correlates with electrophysiologic activity, but fewer RGCs are active in NF1-OPG mice, and activity levels do not predict patterns of RGC loss. Declines in OMR-estimated visual acuity and retinal thinning on OCT correlate with RGC survival, but with moderate variability among subjects and eyes.

Conclusions: Our findings support the existence of multiple anatomic and physiologic effects of Nf1-mutant glial precursors, several preceding OPG formation. These features may better explain vision loss in many young NF1-OPG patients that remains incompletely explained by readily observed OPG features. Future longitudinal studies may refine our understanding of the nature and relative pace of these distinct mechanisms, leading to improved identification of patients at higher risk for visual loss and to more targeted treatments.

CONTROL ID: 3714583

SUBMITTER (NAME ONLY): Joseph Holden

TITLE: Retinal Vascular Compromise and Increased Astrocyte Density in GC1 Knockout Mice

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Holden, S. Al-Awamlh, L. Croteau, A. Boal, D.J. Calkins, L. wareham, Ophthalmology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is increasing evidence to support a vascular role in the pathophysiology of glaucoma with one element possibly involving insufficient or erratic blood supply to the proximal optic nerve and retina. The α1 subunit of soluble guanylate cyclase (GC1), an enzyme involved in a major pathway of blood flow regulation, has been implicated through human GWAS studies with glaucoma incidence. Because aged GC1 knockout mice exhibit characteristics common to glaucoma, we sought to investigate whether GC1 signaling affected retinal morphology and integrity of the neurovascular unit, which could contribute to the neurodegeneration observed in the model.

Methods: Age-matched 3- or 15-month GC1-/- and WT mice were utilized throughout the study. Using immunohistological staining and fluorescein angiography, we assessed retinal vasculature and astrocytic morphology. We implemented the REAVER analysis tool to quantify multiple blood vessel properties such as length, density, and diameter. We also manually quantified the length of higher-order branches. Custom written code was also used to quantify regional density of GFAP across wholemount retinas as well as assess radial complexity of the GFAP distribution through Scholl analysis.

Results: Aged GC1-/- mice exhibit peripheral retinal vessel dilation compared to WT (33.1 ± 6.1 μm vs. 28.4 ± 6.3 μm diameter; $p = 0.015$) as well as an increased frequency of shorter capillary branches ($p<0.001$). There is evidence of blood-retinal-barrier (BRB) breakdown and vessel leakage in aged GC1-/- mice that is absent in age-matched WT mice. GC1-/- mice show aberrant isolectin-B4 staining in a debris-like pattern and increased leakage of fluorescein into the retina by fundus imaging. Retinal vessel compromise coincided with an abnormal morphological astrocyte phenotype; focal regions of GC1-/- retina exhibit a highly disorganized distribution of astrocytes, with areas of dense “matted” astrocytic networks surrounding major blood vessels as well as increased global GFAP-positive density across the retina.

Conclusions: Together our results indicate that dysfunctional GC1-cGMP signaling leads to alterations in retinal vessel and astrocyte morphology with age, which may lead to interruption of blood flow to exacerbate or trigger neurodegeneration. Our results suggest that functional cGMP signaling is important for maintaining the BRB and retinal astrocyte morphology.

CONTROL ID: 3714584

SUBMITTER (NAME ONLY): Denis Proshlyakov

TITLE: Correction of diabetic retinopathy by mitochondrial transfer

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Proshlyakov, S.S. Hammer, T.F. Dorweiler, K. Fisher, J.V. Busik, Physiology, Michigan State University, East Lansing, Michigan, UNITED STATES|S. Li Calzi, C.P. Vieira, M.B. Grant, Department of Ophthalmology and Visual Science, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S. Atilano, M. Kenney, Ophthalmology Clinical, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mitochondrial (Mt) damage precedes histopathological abnormalities in diabetic retinopathy (DR). Recent studies show that Mt transfer can rescue cells from bioenergetic abnormalities and cell death. This study in DR cell culture and animal models examines whether i) Mt transfer can normalize bioenergetics of retinal cells and ii) if bone marrow derived mesenchymal stem cells (MSC) represent a source of Mt for transfer to damaged retinal endothelial cells (REC).

Methods: BREC, hMSC, and ARPE19 cells were cultured using established protocols. ARPE19 cells were depleted of mitochondria by culturing in media containing 50 ng/ml ethidium bromide and 50 µg/ml uridine for up to six passages. Mt were labeled using rLV-EF1-EGFP infection. Mt were isolated using differential centrifugation protocols. Mt haplogroups were analyzed at the sequence depth ID 30,000; range 1,000 to 100,000. Respiratory activity was assessed using a custom microfluidic respirometer. Retinal ischemia-reperfusion (I/R) mouse model was used to assess Mt transfer in vivo.

Results: The effect of Mt transfer on bioenergetics was assessed in Mt depleted Rho^o ARPE19 cells. ARPE19 cells have U5 mitochondrial haplogroup with high respiratory activity, however adherent Rho^o ARPE19 cells had no significant respiratory activity (0.2±0.08 pmol O_2/sec/10^6 cells). Overnight incubation of adherent Rho^o ARPE19 cells with Mt isolated from control ARPE19 cells led to progressive increase in the respiratory activity over 10 days up to 3.4±0.7 pmol O_2/sec/10^6 cells, which is equivalent to the activity of the wild type ARPE19 cells at day 10 (4.2±1.7 pmol O_2/sec/10^6 cells). Moreover, normalization of respiratory activity due to Mt transfer improved viability and increased growth rate of Rho^o ARPE19 cells. We next determined if Mt transfer occurs between vascular progenitor cells and REC in DR cell culture and animal models. BREC treated with TNFα (10 ng/ml) for 24 hrs induced tunnelling nanotube (TNT) formation and Mt transfer by non-diabetic hMSC. No Mt transfer was observed in control BREC. 4 days following injection of MSC, TNT formation and Mt transfer was observed using IHC in I/R injured, but not in the uninjured mouse eye when injected with hMSC.

Conclusions: Exogenous Mt incorporate into cellular mitochondrial networks and normalize bioenergetics of damaged retinal cells. Mt transfer is a mechanism that provides paracrine support to damaged retinal vasculature.

CONTROL ID: 3714586

SUBMITTER (NAME ONLY): Peter Koulen

TITLE: Oxidative stress responses and cytoprotection of in vitro models of human retinal pigment epithelium cells

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Koulen, D.T. Hurtado, C.W. Hall, R.S. Duncan, Vision Research Center, Department of Ophthalmology, School of Medicine, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|P. Koulen, Department of Biomedical Sciences, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to determine the effects of oxidative stress on phagocytosis, barrier function and both redox and innate immune signaling in two in vitro models of human retinal pigment epithelium (RPE) cells, human telomerase reverse transcriptase-overexpressing RPE (hTERT-RPE) and induced pluripotent stem cell-derived RPE (iPSC-RPE) cells.

Methods: Cells were grown in Dulbecco's modified Eagle's medium:F-12 + 10% FBS (with non-essential amino acids, 1% B27 supplement, 10ng/ml triiodothyronine and 100µM taurine for iPSC-RPE only) to full confluence for experiments. Cells were exposed to 50µM or 200µM tert-butyl hydroperoxide (tBHP) in media for 24 hours to induce mild or severe oxidative stress, respectively. Fluorescein isothiocyanate (FITC)-conjugated latex beads of 1µm diameter were used in phagocytosis assays to measure cell function. Actin was labeled with phalloidin-Alexa Fluor 594 and immunocytochemistry was performed to detect zonula occludens 1 (ZO-1), nuclear translocation of nuclear factor erythroid 2-related factor 2 (Nrf2) and nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) immunoreactivity. Cells were imaged with confocal microscopy (Leica TCS SP5) and image analysis was performed using ImageJ software. Transepithelial electrical resistance (TEER) measurement was conducted with an Ussing chamber system to determine RPE cell barrier function.

Results: Mild oxidative stress (exposure to 50µM tBHP for 24 hours) had no apparent effect on RPE cell size or morphology as determined by microscopy. Mild oxidative stress also had no effect on phagocytosis, but led to increases in ZO-1, Nrf2 and NFκB immunoreactivity, as well as to a 45% increase in TEER. Higher levels of oxidative stress (exposure to 200µM tBHP for 24 hours) led to changes in cell size and morphology, but did not result in cell death. RPE cells undergoing such severe oxidative stress displayed also impaired phagocytosis, altered and less organized distribution of actin and ZO-1 immunoreactivity and decreased TEER indicative of impaired RPE cell barrier function.

Conclusions: Oxidative stress induces specific structural and functional changes in cellular signaling in in vitro models of human RPE cells. These changes include an altered cellular redox homeostasis and innate immune signaling potentially contributing to adaptive functional responses in RPE cells.

CONTROL ID: 3714587

SUBMITTER (NAME ONLY): Claus Christian Gruber

TITLE: Exploring barriers and solutions to digital inclusion in outpatient Ophthalmology

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ramessur, L. Raja, M. Ting, B. Riley, D. Sim, S. Kang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|C. Gruber, D. Sim, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Ting, Western Eye Hospital, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Whilst teleophthalmology has gained increasing importance during the pandemic by providing a novel way of patient-physician encounter, not all of our patients seem to benefit from this new format of access to eye-care. Exploring user perspectives and perceived barriers is crucial for avoiding digital exclusion. This study investigated patients motivation for and factors preventing them from utilizing teleophthalmology.

Methods: A 15-item questionnaire was distributed to patients attending face-to-face (F2F) appointments or video-consultations (VC) at Moorfields Eye Hospital. Questions explored participants rationale for (not) using VC, digital literacy skills, confidence online, access to technology and potential demand for support. Anonymised responses were collected and analysed.

Results: Responses were obtained from a total of 92 patients (F2F n=63, VC n=29). Key findings revealed an overall 30.4% had low confidence in diagnostic proficiency of VC. Older patients (38.9% of patients aged ≥65y vs. 14.6% of those aged 35-64y vs. 3.8% of those aged ≤34y) were less comfortable navigating online and were more likely to lack access to internet or devices required to join VC (27.8% vs. 4.2% vs. 0.0%). Avoidance of traveling long distances (51.1%), minimization of disruption of daily life (31.5%) and fast access to eye specialists (25.0%) were the main perceived benefits of VC. Younger patients (aged ≤34y) were more likely to use and prefer VC. Participants having encountered VC at least once were generally more positive about VC. 13.0% of all participants were not aware that healthcare services could be accessed remotely.

Participants (19.6%), and particularly older generations (27.8% ≥65y), felt that local community support and technology teaching sessions could bolster engagement with digital healthcare services.

Conclusions: This study found that younger patients and those who have previously used VC are more likely to prefer and benefit from using VC. Lack of digital skills, poor access to technology and low confidence in digital healthcare are factors that must be addressed to ensure that certain patient subgroups do not miss out on the benefits of teleophthalmology. Patients have expressed interest in solutions such as digital skills workshops (delivered in hospital or the community) and schemes to enhance access to the internet and devices.

CONTROL ID: 3714589

SUBMITTER (NAME ONLY): Rob Knight

TITLE: Developing Scalable Purification of Small Extracellular Vesicles Using Size Exclusion Chromatography

SESSION TITLE: Corneal stromal biology, wound healing modulators and regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Knight, B. Le, J.J. Zheng, S.X. Deng, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|P. Neviani, Extracellular Vesicle Core, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our research group has demonstrated beneficial functional responses using extracellular vesicle (EV) EVs isolated using a polymer based technique, however this purification technique is not scalable or cGMP compliant. The purpose of this research is to evaluate size exclusion chromatography (SEC) as an alternative isolation technique for the production of functional EVs.

Methods: EVs were purified from the conditioned medium of CSSC cultures using either a) precipitation using Total Exosome Isolation Reagent (TEI; ThermoFisher) or b) SEC (qEV; Izon). EVs were examined in respect to their size using nanoparticle tracking analysis (NTA, Nanosight; Malvern), morphology by Transition Electron Microscopy (TEM) and tetraspannin expression (CD9, D81 and CD63) using ExoviewR100 (NanoView). Functional testing was carried out in RAW cells by inhibiting their inflammatory response when stimulated with LPS and in inhibiting myofibroblast formation when corneal fibroblasts are stimulated with TGFb1.

Results: EVs were purified using both TEI and qEV purification methods as determined by an increase in the Particle:Protein (P:P) purity ratio. NTA analysis demonstrated an enrichment of particles between 50-130 nm. The size was confirmed using TEM which also demonstrated cup-shaped membrane bound vesicles. TEI purification resulted in a larger modal particle size than that of SEC (85nm vs 73nm, respectively). Both purification techniques demonstrated comparable tetraspannin expression profiles that were similar to the tetraspannin profiles before purification ($P>0.05$). Functionally, it was observed that EVs were capable of inhibiting the inflammatory response of RAW Cells stimulated with LPS by 34% compared to the LPS only control as measured by IL6 and TNFa expression ELISA ($P<0.05$). EVs demonstrated comparable levels of functionality (decrease in IL-6 and TNFa expression) in this assay with no significant difference observed in potency ($P>0.05$). At this same concentration EVs demonstrated comparable potency in reducing aSMA and EDA-FN expression in primary corneal fibroblasts indicating potential inhibition of myofibroblast transdifferentiation.

Conclusions: Both polymer-based centrifugation and SEC techniques are capable of purifying sEVs from CSSC conditioned medium. Both techniques demonstrate no bias in the sEVs population purified. Therefore, SEC could be used for the scale up of sEV purification.

CONTROL ID: 3714591

SUBMITTER (NAME ONLY): Sean Doherty

TITLE: Overexpression of membrane bound Fas ligand accelerates inflammation in response to corneal alkali burns.

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Doherty, W. Su, E. Bilsbury, E. Wood, H. Lin, B. Tian, Ophthalmology, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|W. Su, Ophthalmology, Tianjin Medical University General Hospital, Tianjin, CHINA|S. Sun, Retina, Tianjin Medical University Eye Hospital, Tianjin, CHINA|A. Marshak-Rothstein, Medicine, University of Massachusetts Chan Medical School, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Fas/Fas ligand (FasL) system plays an integral role in the maintenance of corneal immune privilege and regulation of corneal wound healing. Previous research has shown that membrane bound FasL (mFasL) and soluble FasL (sFasL) exert opposing pro- and anti-inflammatory effects respectively in response to corneal injury. This study aims to explore the proinflammatory role of mFasL in the setting of alkali burns in mouse corneas which are sFasL deficient.

Methods: A mouse model with a deleted matrix metalloprotrease cleavage site was established to suppress the expression of sFasL, resulting in increased levels of mFasL expression systemically. To induce injury, the corneas were exposed to alkali burns. The corneas were observed for one month following injury to monitor for corneal neovascularization (CoNV), and then harvested. The collected corneas were stained for macrophage markers F4/80 and CD11b then analyzed and quantified by immunofluorescence.

Results: The mice that overexpressed mFasL showed significantly increased CoNV 14 days after alkali burn treatment compared with wild-type mice. Analysis of the harvested corneas from mFasL mice also showed an approximately 30% increase in F4/80+ and CD11b+ inflammatory cell infiltration at 1 month compared to the control group.

Conclusions: The increased CoNV and inflammatory cell infiltration observed in the corneas of mice that overexpressed mFasL suggests that mFasL plays a proinflammatory role in the cornea after injury. Considering the impact of mFasL on corneal injury and wound healing, it may serve as a potential target for therapy in corneal disease.

CONTROL ID: 3714593

SUBMITTER (NAME ONLY): Milton Hom

TITLE: Comparison of ocular surface disease in patients between two different clinical settings: Preliminary results from the Neurosensory Abnormalities in ocular SurfAce Disease (NASA) study

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Hom, Canyon City Eye Care, Azusa, California, UNITED STATES|S. Cox, P. Hamrah, Department of Ophthalmology, Center for Translational Ocular Immunology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|S. Cox, P. Hamrah, Cornea Service, New England Eye Center, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|L. Szczotka-Flynn, Vision Research Coordinating Center, Department of Ophthalmology and Vision Sciences, School of Medicine, University Hospitals, Cleveland, Ohio, UNITED STATES|L. Szczotka-Flynn, Contact Lens Service, University Hospitals, Cleveland, Ohio, UNITED STATES|N. Gee, New England Eye Center, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The goal of this study is to compare the demographic features and clinical findings of patients who present for initial or follow up evaluation of ocular surface discomfort to a primary care optometric private practices to those who present to a tertiary care hospital-based ophthalmology clinics.

Methods: Patients were prospectively recruited in this multicenter study if they had complaints of or a history of ocular surface discomfort. Demographic information was collected, and patients competed the OSDI and Ocular Pain Assessment Survey (OPAS) and underwent a clinical examination including medical history. For each bilateral clinical measure, the worse measure was used for analysis. Results were compared using the chi square, Mann-Whitney U test, or T-test as appropriate.

Results: The average age of patients at the tertiary care sites was higher (49.8±2.5 years) than that of the private practice site (39.1±2.2; p=0.003). There was no significant difference in male/female distribution (82.4% female for tertiary care vs. 71.4% for private practice; p=0.210). There was no significant difference in the scores of the OSDI or the OPAS 24 hour eye pain intensity, 2 week eye pain intensity, or non-eye pain dimensions between the sites. Patients treated at the tertiary care sites had more medications included in their medical history [8.0 (range: 0-22) vs 0.0 (0-3); p<0.001] and a lower Schirmer's test result [6.0 mm (1-15) vs 15 (3-15); p<0.001]. The private practice sites' patients had a lower tear break-up time [3.8 sec (1.3-6.3) vs. 5.0 (0-15); p=0.006] and a worse meibum grade [1.0 (0-3) vs 0.0 (0-3); p=0.020].

Conclusions: Patients who report to tertiary care and private practice sites have similar symptom profiles. However, those who report to tertiary care clinics are older and have more extensive medical histories to consider. While both samples of patients showed reduced tear film break-up time, it appears that those who presented to the tertiary care clinics are more likely to show features of aqueous deficient dry eye disease while those at the private practice clinic showed features more consistent of meibomian gland dysfunction. As numbers of clinics and sample size increase in the NASA Study, a profile neurosensory abnormalities across this wide representation of dry eye patients will be established.

CONTROL ID: 3714596

SUBMITTER (NAME ONLY): Andrew Berneshawi

TITLE: Feasibility of Glaucoma Home Self Testing Using a Virtual Reality Visual Field Test Combined with Home Tonometry

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.R. Berneshawi, A. Shue, R. Chang, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure: Andrew Berneshawi: Commercial Relationship: Code N (No Commercial Relationship) | Ann Shue: Commercial Relationship: Code N (No Commercial Relationship) | Robert Chang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess completion rate and correlation of virtual reality visual field (vFA) home monitoring in a pilot sample of experienced visual field test takers with glaucoma.

Methods: 9 Adults (mean age 60.6 years) with an established diagnosis of glaucoma were prospectively enrolled in this ongoing pilot study from a single institution. After an in-office training, participants were sent home with the VisuALL Field Analyzer (vFA; Olleyes Inc. Summit, NJ) for perimetry and the iCare Home Rebound Tonometer (TA022, Icare Oy, Vanda, Finland) for intraocular pressure (IOP) measurements. They were instructed to collect 4 IOP measurements per eye per day for 3 days, and 1 perimetry test per day over the same 3 days. The mean deviation (MD) and pattern standard deviation (PSD) values from the 3 at-home vFA tests were averaged and compared to the most recent in-office Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, CA) visual field (HVF) values using SPSS V.28 (IBM SPSS Statistics) to determine the Spearman correlation coefficient. The intraclass correlation (ICC) for MD and PSD values were also calculated for the 3 vFA perimetry tests taken at home. IOP in-clinic and at-home were compared using the Pearson correlation coefficient.

Results: Of 9 participants enrolled, 6 (10 eyes) successfully completed the protocol. 1 participant had difficulty using the devices and 2 were lost to follow-up. The Spearman correlation coefficient of the MD and PSD from vFA relative to the HFA was 0.758 ($p=0.011$) and 0.867 ($p=0.001$), respectively. ICC values for the 3 vFA perimetry tests taken at home were 0.918 ($p<0.001$) for MD and 0.955 ($p<0.001$) for PSD. The average of the last 5 IOP measurements in-clinic compared to the average of all the at-home measurements yielded a Pearson correlation coefficient of 0.954 ($p<0.001$).

Conclusions: Home monitoring with vFA and rebound tonometry is feasible and may provide clinically useful data to help manage glaucoma patients remotely.

CONTROL ID: 3714597

SUBMITTER (NAME ONLY): Sara Memon

TITLE: Introducing the 'Benign Eyelid Lesion Pathway': 1 year experience of hybrid asynchronous-synchronous tele-oculoplastics in a tertiary hospital

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.F. Memon, Department of Medicine, University College London, London, London, UNITED KINGDOM|L. Ah-Kye, S. Kang, Adnexal, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A. Butt, O. Dawe, P. Thomas, D. Sim, D. Ezra, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|P. Thomas, D. Sim, D. Ezra, Biomedical Research Centre for Ophthalmology, National Institute for Health Research, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Sara Memon: Commercial Relationship: Code N (No Commercial Relationship) | Laura Ah-Kye: Commercial Relationship: Code N (No Commercial Relationship) | Anum Butt: Commercial Relationship: Code N (No Commercial Relationship) | Oliver Dawe: Commercial Relationship: Code N (No Commercial Relationship) | Peter Thomas: Commercial Relationship: Code N (No Commercial Relationship) | Dawn Sim: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Ezra: Commercial Relationship: Code N (No Commercial Relationship) | Swan Kang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: As demand for eye services is projected to rise by 30-40% in the next two decades, long-term solutions must be sought to continue to provide quality care. Telemedicine is an option for specialities reliant on history and observation, such as Oculoplastics, of which benign eyelid lesions make up most referrals. We undertook a retrospective analysis of 974 patients referred for benign eyelid lesions to our tele-oculoplastic clinic. By assessing the efficacy of a hybrid synchronous-asynchronous teleconsultation model, we describe a new streamlined approach to our Benign Eye Lesion Pathway (BELP).

Methods: We retrospectively collected data from 'OpenEyes' electronic patient records for patients who went through the BELP service from July 2020 to July 2021. Patients sent from primary care with benign lid lesions were booked to a live video-consultation using 'Attend Anywhere'. Prior to this, they completed an online questionnaire and uploaded a photograph of the lesion. Patients requiring minor surgery were booked in during the video consultation and consented virtually. We assessed time efficiency, accessibility, affordability and theatre utilisation of the BELP service. To analyse safety, 50 discharged patients were monitored in surveillance clinic to ensure correct diagnosis and management.

Results: Of 974 patients, 558 (57.2%) were listed for surgical procedure from virtual assessment, 232 (23.8%) were discharged and 180 (18.5%) required follow up. Of those requiring follow up, 65 (36.1%) were booked face-to-face and the remainder virtually. The DNA rate was 2.57%, compared with an average of 8.7% for first face-to-face outpatient appointments. Theatre utilisation was efficient, with only 36 (5%) of the patients listed for surgery not proceeding on the day. 58.6% of diagnoses made virtually were accurate with histological findings. No cases deemed benign on remote assessment came back atypical or malignant. There was no significant change in management plan in any case.

Conclusions: The BELP service is a safe alternative to face-to face consultation, leading to efficient theatre utilisation, reduced cancellations, and elimination of travel time and cost for the patient. If clinician satisfaction and issues regarding accessibility to digital infrastructure are explored, telemedicine could be an effective service for the non-urgent biopsy pathway.

CONTROL ID: 3714598

SUBMITTER (NAME ONLY): Weisha Liu

TITLE: Edge Detection Percentile Intensity-based Automated Segmentation Algorithm for Measuring Outer-retinal Layer Thickness in OCT scans

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Liu, Y. Cheng, E. Chu, Q. Zhang, H. Zhou, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R.K. Wang, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure: Weisha Liu: Commercial Relationship: Code N (No Commercial Relationship) | Yuxuan Cheng: Commercial Relationship: Code N (No Commercial Relationship) | Erica Chu: Commercial Relationship: Code N (No Commercial Relationship) | Qinqin Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Hao Zhou: Commercial Relationship: Code N (No Commercial Relationship) | Ruikang Wang: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec;Code F (Financial Support):Carl Zeiss Meditec;Code P (Patent):Carl Zeiss Meditec

ABSTRACT BODY:

Purpose: To develop an automated segmentation algorithm for quantifying the outer-retinal layer (ORL) thickness in 3D OCT scans.

Methods: Eyes were imaged with swept-source OCT (SS-OCT, PLEX® Elite 9000; ZEISS, Dublin, CA) using a 6 x 6 mm scan pattern. ORL is defined from the upper boundary of the outer plexiform layer (OPL) to the retinal pigment epithelium (RPE) layer. To segment the ORL, the algorithm was designed to particularly target the region bounded by the internal limiting membrane (ILM) and RPE layers. The ILM was segmented by an edge detection method; and the RPE was identified by the maximum value of the optical attenuation coefficient (OAC) along depth[1]. Then a percentile intensity-based threshold approach was developed to localize the upper/lower OPL boundary. The ORL thickness was then measured from the identified upper OPL boundary to RPE. Mean pixel-wise variation was assessed by comparing the upper boundary of OPL to the manual segmentation by expert graders.

Results: A total of 36 SS-OCT scans from 17 normal eyes and 2 eyes with geographic atrophy (GA) were included in this study. Auto-segmentation results were compared to manual segmentations in B-scans (Fig. 1). In addition to normal cases, the algorithm also achieved successful segmentation on GA cases (Fig. 1D-F). The mean pixel-wise difference between the algorithm and manual segmentation is 0.924 on normal cases, and is 0.38 on GA cases, demonstrating sufficient consistency and accuracy of the developed algorithm. The actual auto-segmentation could be better as the manual segmentation may be prone to errors when manually identifying the upper boundary of the OPL. In GA cases, the variation is smaller due to the limited sample size.

Conclusions: An automated ORL segmentation algorithm is developed for OCT scans, with demonstrated good stability and flexibility in normal and diseased eyes. The algorithm should be clinically useful in the investigations of possible ORL involvement in the AMD development.

1. Chu Z, et al. Am J Ophthalmology. 2022; 236: 249-260.

CONTROL ID: 3714599

SUBMITTER (NAME ONLY): Mark Mackanos

TITLE: A NOVEL TRACKING SCANNING LASER OPTHALMOSCOPE (TSLO) SYSTEM FOR FIXATION AND SACCADE QUANTIFICATION

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mackanos, C. Sheehy, C. Light Technologies, Inc., Delaware, UNITED STATES|J. Karp, D. Gray, Gray Optics LLC, Portland, Maine, UNITED STATES|S. Liddle, N. Luck, Blur Development Group, LLC, Cary, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a commercial-ready scanning laser ophthalmoscope system, the Retitrack, for retinal eye-tracking that can be used to quantify fixational eye motion and voluntary saccade characteristics.

Methods: A manufacturable confocal, lens-based SLO system, was created to record and analyze fixational and saccadic eye responses to a visual stimulus.

The Retitrack has a Head Unit, a Base Unit, and a Head & Chin Rest (Figure 1). The Head Unit is an illumination collection system for the capture of retinal images with eye motion output. A subject's retina is raster scanned, pixel by pixel, with a 5-degree field of view (FOV) containing 640x480 pixels using a 15 kHz resonance scanner and a 30 Hz galvanometer for the x and y-axis, respectively. A focusing lens is used to focus light onto a confocal pinhole and onto an Avalanche Photodiode (APD).

The Base Unit has an FPGA for syncing the timing of the scanners, sampling the APD output, and relaying it to a Nvidia Jetson Nano serving as the computer. Two motorized stages allow the optical scan path and optical fixation path to compensate for refractive error and are driven by the Jetson Nano based on the refractive error spherical equivalent through the software UI.

Results: The commercially viable device has software that records eye motion in standard mode (5-degree FOV) and montage mode (14.5-degree FOV) for fixational stability and visually guided saccades:

a) Fixational stability, including microsaccade and drift characteristics, are quantified and displayed. This can be recorded and analyzed in either Standard or Montage mode, using a stationary cross hair for visual stimuli for 10-second trials.

b) Visually guided saccades up to 7-degree in extent can be recorded and analyzed with Montage mode. Horizontal and vertical saccades are quantified with the presentation of two crosshair targets 5° apart.

Conclusions: The Retitrack device uses a scanning laser ophthalmoscope (SLO) to record, view, measure, and analyze the temporal characteristics of fixation and saccadic responses when viewing a visual stimulus. The detected light is used to generate a digital image with a computer which incorporates real-time, strip-based eye tracking methodologies to measure and report fixation and saccadic responses.

CONTROL ID: 3714601

SUBMITTER (NAME ONLY): Alejandra Bosco

TITLE: Schlemm canal-targeted Tie2 knockdown (SC-Tie2 KD) as mouse model of adult-onset human glaucoma

SESSION TITLE: New Ideas in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Yarishkin, Salk Institute for Biological Studies, La Jolla, California, UNITED STATES|J. Millar, North Texas Eye Research Institute, University of North Texas, Fort Worth, Texas, UNITED STATES|A. Bosco, C.O. Romero, J. Schwakopf, M. Steele, M.L. Vetter, Neurobiology, University of Utah Health, University of Utah Health, Salt Lake City, UT, US, academic/health, Salt Lake City, Utah, UNITED STATES|D. Krizaj, Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiopoietin-Tie2/TEK signaling at the Schlemm's canal (SC) critically regulates aqueous humor outflow (AHO) and intraocular pressure (IOP) in humans and mice. Tie2 receptor loss-of-function mutations associate with primary congenital and open angle glaucoma (POAG), and conditional Tie2 knockout adult mice show SC regression, chronic IOP elevation and glaucomatous degeneration. However, systemic Tie2 deletion reduces choriocapillary flow, causing cone photoreceptor loss. To avoid potential effects on retinal/choroidal or systemic endothelial Tie2, we developed a targeted approach to selectively attenuate Tie2 expression in the SC of adult mice, and report their glaucomatous pathology.

Methods: Adeno-associated virus AAV2, which transduces rodent SC, was used to deliver Cre recombinase (AAV2-Cre) by bi- or unilateral injection into the anterior chamber of Tie2 $^{FL/FL}$ C57BL/6 mice aged 1-1.5 months. Live, we measured in AAV2-Cre vs. AAV2-GFP and naive littermates: weekly IOP (n>20 eyes/group) for 8 to 12 weeks post-injection (wpi), AHO facility 4 wpi (n=6-11 eyes), optomotor reflex and pSTR (n=5-13 mice), and retina/optic nerve head integrity by optic coherence tomography (OCT; n=7 mice) 12 wpi. Postmortem, we analyzed: AAV2 transduction 2-8 wpi (n=3-5 mice), and density of optic nerve axons and retinal ganglion cells immunostained for RBPMS and Brn3a 12 wpi (n=6-13 mice).

Results: AAV2-Cre selectively transduced the SC endothelium, leading to impaired AHO facility 4 wpi, and to significant IOP elevation from 1-4 wpi that persisted to 8 or 12 wpi. Visual acuity and pSTR amplitude were significantly decreased in AAV2-Cre eyes 12 wpi, relative to the controls, whereas ERG a- and b-waves were unaffected. OCT showed intact outer retinal layers, but significant thinning of the inner retina and optic nerve head 12 wpi. RGC analysis showed significant RBPMS+ RGC loss with maximal degeneration localized to the dorsal retina, and significant RGC decline (Brn3a-) preceding loss 12 wpi. Optic nerve analysis detected significant axon density drop, coupled to RGC loss, 12 wpi.

Conclusions: The "SC-Tie2 knockdown" model reproduces a pathogenic mechanism of humans POAG, undergoing chronic ocular hypertension, and progressive glaucomatous optic neuropathy and retinopathy. This model thus offers a robust and reproducible model of POAG, valuable for advancing its treatment.

CONTROL ID: 3714602

SUBMITTER (NAME ONLY): Varsha Alex

TITLE: Microperimetry in foveal sparing late-onset retinal degeneration

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Alex, S. Borooah, Ophthalmology, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|V. Papastavrou, A.C. Browning, Newcastle University, Newcastle upon Tyne, Royal Victoria Infirmary, UNITED KINGDOM|B. Dhillon, S. Borooah, School of clinical sciences, The University of Edinburgh Centre for Clinical Brain Sciences, Edinburgh, Edinburgh, UNITED KINGDOM|

Commercial Relationships Disclosure: Varsha Alex: Commercial Relationship: Code N (No Commercial Relationship) | Vasileois Papastavrou: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Browning: Commercial Relationship: Code N (No Commercial Relationship) | Baljean Dhillon: Commercial Relationship: Code N (No Commercial Relationship) | Shyamanga Borooah: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Late-onset retinal degeneration (L-ORD) is a rare autosomal dominant macular dystrophy caused by mutations in C1QTNF5. Microperimetry changes have been reported previously in L-ORD. The aim of this study is to validate microperimetry as a platform for longitudinal follow up in L-ORD.

Methods: This is a cross sectional clinical study with a subset of cases providing 4-year follow-up data. Patients were enrolled as part of a prospective study at the Princess Alexandra Eye Pavilion, Edinburgh, and the Royal Victoria Infirmary, in Newcastle. Patients were included in this analysis if they had foveal sparing dystrophy. Patients who were unable to do microperimetry were excluded.

Mesopic microperimetry was performed with a Nidek MP-1 microperimeter (NAVIS Software version 1.7.0) (Nidek Technologies, Italy). Following dilation, patients were dark adapted for 10 minutes and tested in 90 test locations using a Goldman size III white stimulus, in a customized test pattern covering the central 40 degrees. Stimulus duration was 200 milliseconds on a white monochromatic background ($1.27cd/m^2$) using a red fixation target and a 4-2 test strategy. The sensitivity of each test location was determined on a scale of 0 dB to 20 dB. The mean sensitivity was measured by taking an average of each location measured in each eye.

Results: A total of 20 eyes from 10 patients had baseline data (58.0 years +/- 4.77, 7 male). A subset of 10 eyes from 5 patients had follow up data. The mean baseline sensitivity was 10.02 dB (+/-5.26). Age was moderately negatively correlated with microperimetric sensitivity (r= -0.663).

For the follow up cohort, baseline mean sensitivity was 7.32 dB (+/- 5.21) at baseline which decreased to 4.69 dB (+/- 4.83) after 4 years of follow up. This approximated to 0.66 dB loss per year. Paired t-test confirmed a significant decrease in mean sensitivity over four year follow up ($p = 0.0008$).

Mean sensitivity was symmetric and was highly correlated between eyes of patients ($r = 0.979$) with no significant difference ($p = 0.054$) between eyes.

Conclusions: Our study demonstrates that microperimetric mean sensitivity is negatively correlated with age in our cohort. Microperimetric findings are symmetric. In addition, 4 year follow up shows a significant reduction in mean sensitivity suggesting that it is likely a useful tool for macular function follow up.

CONTROL ID: 3714604

SUBMITTER (NAME ONLY): Joon-Young Hyon

TITLE: Prediction accuracy of IOL power calculation in patients with a large difference between conventional keratometry and total keratometry

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hyon, Y. Son, Seoul National University Bundang Hospital, Seongnam, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Joon-Young Hyon: Commercial Relationship: Code N (No Commercial Relationship) | Yengwoo Son: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: With the advancement of technology, not only conventional keratometry (K) but also total keratometry (TK) can be measured. In previous papers comparing K and TK, no studies were showing statistical significance when comparing the two. This is because in general, there is no statistically significant difference between the two values. The purpose of this research is to investigate the IOL calculation in the cases where there are large differences between K and TK.

Methods: Study design: retrospective case series

Medical records of 15711 patients (37601 exams) who underwent IOL master 700 optical biometry were reviewed. Of the total, 825 patients (1835 exams) who had previously undergone refractive surgery were excluded. The number of patients with a difference of 0.5 diopter (D) or more in K-TK values was 77 patients (80 eyes), of which 14 patients (14 eyes) were subjected to IOL implantation. A study was conducted on 9 patients (9 eyes) excluding 5 cases undergone scleral fixation.

Results: All 9 patients had underlying diseases, two with a history of DSAEK, two with high myopia, two with corneal opacity, a bullous keratopathy, a Mooren’s ulcer, a history of epikeratophakia, and a pterygium. When using the algorithmic formula selection considering keratometry, anterior chamber depth, and axial length, the absolute prediction errors in K and TK groups were 0.663 ± 0.511 D and 0.349 ± 0.344 D (p-value=0.09). In the two groups, the prediction error within ±0.25 D was 1 eye (11%) and 5 eyes (56%), ±0.5 D was 5 eyes (56%) and 7 eyes (78%), and ±1.0 D was 9 eyes (100%) in both groups (within ±0.25 D vs the rest, p-value=0.102).

Conclusions: In cases of large differences between K and TK, IOL calculation based on TK showed better results.

CONTROL ID: 3714606

SUBMITTER (NAME ONLY): Rémy Marcotte-Collard

TITLE: Montreal experience part 2 : Corneal topographical changes of four orthokeratology lenses and their relationship with axial elongation.

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Marcotte-Collard, P. Simard, L. Michaud, École d'optométrie, Universite de Montreal, Montreal, Quebec, CANADA|M. OUZZANI, Universite d'Oran 1 Ahmed Ben Bella, Oran, ALGERIA|

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ABSTRACT BODY:

Purpose: To investigate the relationship between topographical changes generated with orthokeratology and axial elongation using different orthokeratology lens platform.

Methods: This is a retrospective analysis using the data from the Montreal Experience study. Data were extracted from the file of each patient who consulted between January 2017 and December 2018 and were kept under the same myopia control strategy. The orthokeratology (OK) patients were selected (OK-4 designs, N=140) and corneal topographical analysis were done using the tangential differential maps between baseline and 3 months follow-up, which involved determining the treatment zone diameter (TZD) and the high mid-peripheral convex power. A comparison of the topographical corneal changes on the cornea was done between the four OK designs. Finally, the correlation was estimated between the relative area ratio between the convex zone and the distance zone in the subject pupil and the axial elongation after 1 year.

Results: There were no significant differences in the high peripheral convex power in all quadrant between the four OK designs.

Significant differences were found for the distance treatment zone diameter (DTZD) generated on the cornea between the OK L1 and the other designs, L2, L3 and L4. (horizontal = L1: 3.7 ± 0.45 mm ; L2: 3.00 ± 0.64 mm ; L3: 2.97 ± 0.58 mm; L4: 3.2 ± 0.58 mm).

The relative area ratio between the convex zone and the distance zone in the subject pupil showed a significative negative correlation with axial elongation after 1 year ($r = -0.48$).

Conclusions: In the Montreal orthokeratology patient cohort, it appears that the major difference created on the cornea between the four lenses used was the size of the treatment zone diameter, which appears to be related to the effectiveness in slowing axial elongation after 1 year when related to the subject's pupil. These results confirm the dose-response of the proportion of myopic defocus generative zone in orthokeratology on axial length management and reinforce the importance of analyzing topographic change in clinical and related studies of this method of myopia control.

CONTROL ID: 3714609
SUBMITTER (NAME ONLY): Dirk-Uwe Bartsch
TITLE: Regional variability in OCT Angiography
SESSION TITLE: Multidisciplinary Ophthalmic Imaging
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: D.G. Bartsch, A. Heinke, A. Warter, F.P. Kalaw, C.B. Galang, W.R. Freeman, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|
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ABSTRACT BODY:
Purpose: To study the temporal and spatial variability in OCT-Angiography measurement across the branching order of the vascular network and across instruments.
Methods: We measured 5 normal subjects a total of 10 times within a 30 minute session and recorded the OCT-Angiography scan according to the manufacturer's guidelines. We imaged the subjects in three difference instruments, the Heidelberg Engineering Spectralis OCT, the Optovue AngioVue and the Zeiss Cirrus 5000 Angioplex.
We used the build-in eye tracking feature for each instrument to align the follow-up exam of each scan with the first scan.
To analyze the data, we exported the OCT-Angiogram to ImageJ. In ImageJ we aligned the images to compensate for small variation in image alignment between repeat scans. We calculated the coefficient of variation (COV) for each blood vessel along the vessel tree.
Results: We found that the variability in OCT Angiography measurements is higher in smaller blood vessels and capillaries than in larger blood vessels. The variability was different between the three instruments.
Conclusions: This study compared the temporal and spatial variability in OCT Angiography measurements in normal subjects. The high temporal variability in smaller blood vessels indicates that the significance of OCT Angiography measurements based on a single measurement may be impacted. The reason for the high variability might be the snapshot approach of all OCT Angiography devices that capture only a fraction of the cardiac cycle in each vessel segment. Therefore, the natural variation in bloodflow may not be accurately sampled by a single OCT Angiogram.

CONTROL ID: 3714614

SUBMITTER (NAME ONLY): Jessica Henry

TITLE: Laser-induced Choroidal Neovascularization in pigmented rabbits

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Nguyen, NTT-Hi Tech Institute, Nguyen Tat Thanh University, Ho Chi Minh City, Ho Chi Minh, VIET NAM|J. Henry, V. Nguyen, Y. Li, Y.M. Paulus, Department of Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|Y.M. Paulus, Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Jessica Henry: Commercial Relationship: Code N (No Commercial Relationship) | Van Phuc Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Yanxiu Li: Commercial Relationship: Code N (No Commercial Relationship) | Yannis Paulus: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Choroidal neovascularization (CNV) is a leading cause of visual impairment and vision loss in humans. Therefore, it is important to establish an accurate, rapid, and durable animal model to perform CNV research. This study introduces a novel model involving laser induced CNV in pigmented rabbits in vivo. The model is longitudinally monitored using photoacoustic microscopy (PAM) and OCT to track development and maintenance of CNV.

Methods: CNV models were generated in 6 Dutch Belted Rabbits ages 2-4 months and weighing 1.9 to 3.0 kg. A laser contact lens was coated in Gonak Hypromellose Ophthalmic Demulcent Solution (2.5%) and placed directly on the eye. The eyes were then irradiated at a power of 450 mW with 532 nm laser light Vitra photocoadulator connected to a Zeiss SL 130 slit lamp. The rabbit eyes received 16 laser spots in a 4 x 3 rectangle with a spot size of 300 μm in aerial diameter and a pulse duration of 500 ms/spot. The models were monitored for 28 days, allowing time for CNV to generate and persist at the locations of laser irradiation. Longitudinal visualization of the models was acquired using multimodal PAM and OCT, fundus photography, FA, and ICGA. The rabbits were then euthanized, and histological analysis was performed to determine CNV or ocular damage.

Results: Using the multimodal imaging system, it was demonstrated that all 6 rabbit eyes had successful development and persistence of CNV in some of the laser irradiation sites. CNV developed approximately on day 14. This was deduced from leakage present on FA and ICGA images and 3D PAM and OCT data. In the FA images, the late leakage and hyperfluorescence observed was consistent with CNV. Histological analysis verified focal areas of laser damage. No rabbits had unexpected complications during the procedure or imaging.

Conclusions: The imaging data demonstrates that laser photocoagulation can effectively produce a stable model of CNV in pigmented rabbits. PAM and OCT imaging provide high resolution imaging of the growth of CNV without exogenous contrast agents. FA and ICGA confirmed the presence of CNV leakage.

CONTROL ID: 3714615

SUBMITTER (NAME ONLY): Ajay Kolluru

TITLE: Comparing the efficacy between 0.09% cyclosporine, 0.05% cyclosporine, and 5% lifitegrast in patients with dry eye disease

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kolluru, A. Nguyen, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Ajay Kolluru: Commercial Relationship: Code N (No Commercial Relationship) | Annie Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The prevalence of dry eye disease is estimated to be greater than 30 million adults in the United States. Three topical medications that are currently being prescribed in treatment of dry eye disease are 0.09% cyclosporine ophthalmic emulsion, 0.05% cyclosporine ophthalmic emulsion and 5% lifitegrast. The purpose of this study is to compare the efficacy of 0.09% cyclosporine, 0.05% cyclosporine and 5% lifitegrast by analyzing patient outcomes treated at an academic dry eye clinic, through a retrospective chart review.

Methods: Patients with dry eye disease treated with 0.09% cyclosporine, 0.05% cyclosporine or 5% lifitegrast and had a follow up of at least 3 months were included for analysis in this retrospective chart review. Variables included in the analysis were patient subjective improvement, Schirmer's test, tear osmolarity, and side effects of irritation and burning. A linear mixed-effects (LME) model, was used to study the relationship between treatment and each of the continuous or numeric outcomes of interest which included change in Schirmer test score, and change in tear osmolarity.

Results: A total of 40 patients were analyzed. There was not a significant association between the medication prescribed and 3-month follow-up subjective improvement in the sense of better, versus worse/same (n=28; Fisher exact test P=.820). For Schirmer test score (n=31) there was not a statistically significant association between the eye drop prescribed—0.09% cyclosporine, 0.05% cyclosporine, or 5% lifitegrast. (likelihood ratio test $\chi^2(2)=5.40$; P=.067) There was not a statistically significant relationship overall between the particular eye drop prescribed and the effects of days on tear osmolarity (likelihood ratio test $\chi^2(2)=5.61$; P=.061). There was not a significant association between the medication prescribed and irritation/burning at 3-month follow-up (n=25; Fisher exact test P=.350).

Conclusions: Current topical therapy for dry eye disease includes 0.09% cyclosporine, 0.05% cyclosporine, and 5% lifitegrast. There was no significant difference in efficacy between the different medications in this study. However, further studies are needed given the limitation of the small sample size.

CONTROL ID: 3714616

SUBMITTER (NAME ONLY): Angelo Leite

TITLE: Development of neovascular glaucoma in severe diabetic retinopathy during follow-up treatment with anti-VEGF drugs treated with laser panphotocoagulation

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Leite, Universidade Federal do Para, Belem, PA, BRAZIL|A. Nassaralla, J.J. Nassaralla, Instituto de Olhos de Goiânia, BRAZIL|M.H. Amaro, Instituto de Olhos e Laser de Belém, BRAZIL|M. Motta, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, BRAZIL|C. Muccioli, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|R. Vallory, Espirito Santo Private Practice, BRAZIL|

Commercial Relationships Disclosure: Angelo Leite: Commercial Relationship: Code N (No Commercial Relationship) | Miguel Amaro: Commercial Relationship: Code N (No Commercial Relationship) | Arthur Nassaralla: Commercial Relationship: Code N (No Commercial Relationship) | Mario Motta: Commercial Relationship: Code N (No Commercial Relationship) | Cristina Muccioli: Commercial Relationship: Code N (No Commercial Relationship) | Romar Vallory: Commercial Relationship: Code N (No Commercial Relationship) | Joao Nassaralla: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the occurrence of neovascular glaucoma in patients with severe diabetic retinopathy who were treated solely with anti-VEGF therapy and their treatment afterwards

Methods: We reviewed the outcome of eyes with severe diabetic retinopathy who were treated with anti-VEGFs alone. The patients were in follow-up care for two years, undergoing monthly structural OCTs and biyearly color fundus photography and fluorescein angiography

Results: Forty-five eyes from seventy patients who were treated with anti-VEGFs alone were followed for two years. Seven of these eyes developed neovascular glaucoma over the two-year follow-up. Two of the seven eyes had been treated with ranibizumab; two with bevacizumab; and three with aflibercept

All eyes with neovascular glaucoma were then treated with both panretinal photocoagulation and additional injections of the same anti-VEGF that was initially used. The neovascular glaucoma progression stabilized then. The presenting visual acuity varied between 20/100 to 20/400 prior to the treatment. All patients had worse acuity after treatment (20/400 to count fingers).

Conclusions: Neovascular glaucoma developed in eyes with diabetic retinopathy who are treated with anti VEGFs alone despite close follow-up. The condition responds well to treatment with panretinal ablation and additional anti VEGF injections, but despite the rigorous treatment, the visual outcome is poor

CONTROL ID: 3714619
SUBMITTER (NAME ONLY): Jordan Huang
TITLE: Strabismus post plaque brachytherapy
SESSION TITLE: Strabismus
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: J. Huang, University of Calgary, Calgary, Alberta, CANADA|A. Saleem, E. Liao, P. Campbell, E. Weis, Serac Eye and Skin Care Centre, Alberta, CANADA|
Commercial Relationships Disclosure: Jordan Huang: Commercial Relationship: Code N (No Commercial Relationship) | Aqsa Saleem: Commercial Relationship: Code N (No Commercial Relationship) | Emily Xi Liao: Commercial Relationship: Code N (No Commercial Relationship) | Paige Campbell: Commercial Relationship: Code N (No Commercial Relationship) | Ezekiel Weis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the most common treatment provided to patients with strabismus post plaque brachytherapy for choroidal melanoma. Secondary aims include determination of incidence and type of strabismus post plaque brachytherapy, and extraocular muscle most commonly removed and repositioned for plaque placement.

Methods: This study involved patients diagnosed with choroidal melanomas between October 2011-2020. Demographic data collected included patient age, gender and city. Outcome data included presence of strabismus post-plaque brachytherapy, strabismus treatment received, pre-and-post-operative visual acuity, tumour dimensions, tumour distance from the optic nerve and fovea, duration of follow-up post-plaque surgery, extraocular muscles operated, and primary deviation following treatment. Patients that developed strabismus post surgery underwent strabismus classification into slipped muscle, sensory, decompensated phorias, cranial nerve palsies, restrictive or a combination of the above.

Results: A total of 440 patients underwent plaque brachytherapy. 10/440 (2.27%) patients with treated choroidal melanoma developed strabismus. 7/440 (1.59%) patients were classified as having sensory strabismus, 2/440 (0.45%) slipped muscle, and 1/440 (0.22%) decompensating phoria. Of the 10 patients that developed strabismus, 1/10 (10.00%) is performing convergence insufficiency exercises, 2/10 (20.00%) require Fresnel for diplopia and are considering prism incorporation, 2/10 (20.00%) are awaiting consultation for strabismus surgery, 5/10 (50.00%) underwent strabismus surgery. Four of these patients had sensory exotropia and underwent lateral rectus recessions (1 had Botox prior to surgery). One patient had a combination of sensory exotropia and slipped muscle. Treatment for this patient included exploration and reattachment of the inferior rectus, superior rectus recession and Botox to the lateral rectus. A total of 389 muscles were removed and repositioned for plaque placement. The lateral rectus was the most common (157/389;40.36%), correlating to intraocular tumour location.

Conclusions: The incidence of strabismus post plaque brachytherapy was 2.27% over 10 years. Strabismus surgery was the most common treatment modality, comprising 50% of treatment for strabismus patients. Sensory strabismus was the most common, occurring in 1.59% of patients. The lateral rectus was the most common muscle repositioned during surgery, comprising 40.36% of all muscles repositioned.

CONTROL ID: 3714621

SUBMITTER (NAME ONLY): Maria Iribarne

TITLE: Inflammation modulates regeneration following acute or chronic retinal damage in zebrafish

SESSION TITLE: Neuron/Glia Interactions in Retinal Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Iribarne, D. Hyde, University of Notre Dame, Notre Dame, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Maria Iribarne: Commercial Relationship: Code N (No Commercial Relationship) | David Hyde: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Unlike mammals, zebrafish regenerate in response to retinal damage. Because microglia are activated by retinal damage, we investigated their role during regeneration following acute or chronic damage. How inflammation regulates regeneration in zebrafish would provide important clues towards improving the therapeutic strategies for repairing injured mammalian tissues.

Methods: We used three weeks-post-fertilization (wpf) zebrafish exhibiting either NMDA-induced acute retinal damage or chronic retinal damage due to the cone photoreceptor-specific degeneration mutation gold rush (gosh). Fishes were treated with either dexamethasone to inhibit the immune response or LPS to stimulate the immune response. Immunohistochemistry and transgenic lines were used to monitor the proliferative response and microglia. Pro-inflammatory and anti-inflammatory cytokines were tested by qRT-PCR.

Results: NMDA-induced acute damage or the gosh chronic degeneration mutant displayed reactive microglia and Muuller glia proliferation. Retinas treated to inhibit the immune response lacked reactive microglia and possessed fewer PCNA-positive cells, while LPS treatment increased microglia and PCNA-labeled cells. NMDA-injured retinas upregulated the expression of IL-1β and TNF-α pro-inflammatory cytokine genes, followed by increased expression of IL-10 and Arg1 anti-inflammatory/remodeling cytokine genes. An early and transient TNF-α pro-inflammatory microglia population was identified following acute damage. In contrast, gosh mutant retinas exhibited a mild increase of pro-inflammatory cytokine gene expression concurrent with a major anti-inflammatory/remodeling cytokine gene expression. Few TNF-α pro-inflammatory microglia were observed in the gosh retina.

Conclusions: Acute or chronic retinal damage induces an immune response that modulates the proliferative response in zebrafish larvae. However, acute and chronic damage display different immunological response strategies. While acute damage presents an early and transient proinflammatory response, chronic damage presents a weak pro-inflammatory and a strong anti-inflammatory response simultaneously.

CONTROL ID: 3714623

SUBMITTER (NAME ONLY): Wei Hau Lew

TITLE: Impact of Unequal Contrast on the Range of Disparity Sensitivity (Dmin & Dmax)

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Lew, D.R. Coates, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Wei Hau Lew: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Coates: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In a real-world scenario, disparity sensitivity depends on both the smallest stereo threshold (Dmin) and its upper limit to double vision (Dmax). Studies have shown that Dmin reduces with lower contrast and blur, more strongly in the monocular than in the binocular conditions. However, little is known about the effect of Dmax across different spatial frequencies in a complex task, especially with unequal image properties between the two eyes, such as contrast differences. Here, we assess the effect of contrast on the range of disparity sensitivity function (DSF) in a stereo letter recognition task.

Methods: Previously, we developed a stereo test consists of Sloan letters with crossed disparity embedded in Random dot stereograms, viewed through active-shutter goggles and a 3D monitor. A letter, corresponding to 0.5-2cpd at 10ft, appeared in front of the background RDS (1sec) at different depth planes, and subjects identified the letter seen. Adaptive staircases were used to obtain Dmin and Dmax. Uncorrelated background RDS were used to measure Dmax. With correct responses, the letters in the Dmax staircase are presented closer to the observer until fusion breaks, making the letters unrecognizable. The range of the DSF was determined as the difference between Dmax and Dmin. Three subjects performed the experiment, at high contrast, and with different contrast combinations (100, 32, and 10%) in monocular and binocular conditions. One eye's contrast was fixed at 100% in the monocular condition.

Results: With stereo letters varying in sizes, the Dmin and Dmax curves were lowpass in shape. The range of DSF was more extensive at low SF (~35 to ~4500 arcsec) and condensed at higher SF (~80 to ~1800 arcsec). With lower contrast, Dmin increased while Dmax reduced, resulting in a smaller DSF range (Kruskal-Wallis, p=0.005). Comparing between congruent and incongruent contrast conditions, the range was smaller across the SFs, but was statistically significant only at 10% contrast.

Conclusions: Our result illustrates the shrinkage of the range of functional stereopsis, especially under unequal contrast. With lower contrast, maintaining fusion is more challenging, the range of DSF is smaller, and the probability of seeing double is higher, more so in the unequal condition. One should consider both Dmin and Dmax when the image quality between the two eyes is unequal, such as in the case of monovision or contrast differences.

CONTROL ID: 3714624

SUBMITTER (NAME ONLY): Nguyen Nguyen

TITLE: United States Retina Fellowship Program Characteristics and Trends: 2010 to 2019

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.S. Nguyen, L.S. Jones, S.J. Yousuf, Howard University College of Medicine, Washington, District of Columbia, UNITED STATES|R.C. Guiseppi, A. Allahdina, L.S. Jones, S.J. Yousuf, Department of Ophthalmology, Howard University Hospital, Washington, District of Columbia, UNITED STATES|

Commercial Relationships Disclosure: Nguyen Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Rodney Guiseppi: Commercial Relationship: Code N (No Commercial Relationship) | Ali Allahdina: Commercial Relationship: Code N (No Commercial Relationship) | Leslie Jones: Commercial Relationship: Code N (No Commercial Relationship) | Salman Yousuf: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While some data about the ophthalmology fellowship match has been reported, studies investigating the details and trends in retina fellowship positions are lacking. Therefore, we performed a retrospective study of the San Francisco Match Central Application Service (CAS) database to identify program characteristics and trends for retina fellowships.

Methods: The CAS database was reviewed from 2010 to 2019. The total number of retina fellowship positions were recorded and classified by location, association with an ophthalmology residency, as medical-only or medical/surgical retina, and compliance status set by the Association of University Professors of Ophthalmology - Fellowship Compliance Committee (AUPO-FCC). Programs that did not provide sufficient information to make the above classifications were excluded.

Results: The number of retina fellowship positions offered annually increased 57% (102 to 160) from 2010 to 2019; medical retina-only and medical/surgical fellowship programs increased 257% (7 to 25) and 40% (67 to 94), respectively. In 2019, 59% (95 of 160) of positions offered were compliant with AUPO-FCC standards and 71% (114 of 160) of positions offered were associated with an ophthalmology residency. The state with the greatest number of fellowship positions in 2019 was California (20) and 20 states did not offer any positions. Of the 37 vacant positions in 2019, 78% (29) were not certified by the AUPO-FCC.

Conclusions: The number of retina fellowship positions offered has grown over the last decade. With the increasing prevalence of retinal diseases, further study is needed to determine if the increase in workforce will be commensurate with future needs.

CONTROL ID: 3714625

SUBMITTER (NAME ONLY): Roger Henry

TITLE: Cyclin D1 Expression and Molecular Genetic Findings in Periocular Histiocytic-Dendritic Neoplasms

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Henry, Ophthalmology, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|R. Henry, T. Milman, Ocular Pathology, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|M. Eiger-Moscovich, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|T. Milman, Pathology, Anatomy, and Cell Biology, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Roger Henry: Commercial Relationship: Code N (No Commercial Relationship) | Maya Eiger-Moscovich: Commercial Relationship: Code N (No Commercial Relationship) | Tatyana Milman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Histiocytic-dendritic (HD) neoplasms may involve the eye and other organs resulting in significant morbidity and even mortality. Previous studies of non-periocular HD demonstrated mutations in mitogen-activated protein kinase (MAPK) genes leading to MAPK pathway activation. As a result of MAPK signaling activation, expression of CCND1 (cyclin D1) protein is upregulated. CCND1 immunohistochemical (IHC) stain has been shown to be a useful ancillary diagnostic marker and to correlate with MAPK gene mutations in non-periocular HD neoplasms. Our objective was to determine whether periocular HD neoplasms express CCND1 via IHC and to further characterize their genetic basis.

Methods: We retrospectively searched pathology records for all patients with HD neoplasms diagnosed (years 1995-2020). Select cases with non-specific histiocyte-rich ocular adnexal inflammation served as controls. Immunohistochemistry was performed with CD68, S100, CD1a, and CCND1. A subset of HD Neoplasms was evaluated via next generation sequencing (NGS) and digital droplet PCR (ddPCR).

Results: HD neoplasms were identified in 36 patients: juvenile xanthogranuloma (N=9), adult onset asthma and periocular xanthogranuloma (N=8), Langerhans cell histiocytosis (N=7), Rosai-Dorfman disease (N=5), adult isolated xanthogranuloma (N=5), Erdheim-Chester disease (N=1), and histiocytic sarcoma (N=1). Eleven patients with non-specific histiocyte-rich inflammation were selected as controls. Compared to non-specific inflammation, HD neoplasms demonstrated strong nuclear staining for CCND1 in >50% lesional cells [23/36 (64%) vs. 0/11 (0%), $p<0.001$]. NGS and ddPCR on a subset of 17 histiocytic-dendritic neoplasms demonstrated MAPK gene mutations in all 16 cases with amplifiable DNA.

Conclusions: CCND1 immunohistochemistry is a useful diagnostic marker for periocular HD neoplasms, correlating with underlying mutations in MAPK genes.

CONTROL ID: 3714626

SUBMITTER (NAME ONLY): Wendy Dailey

TITLE: Development of Noregen, a novel regenerative ocular therapeutic medicine

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.A. Dailey, K.P. Mitton, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|W.A. Dailey, M.T. Trese, K.A. Drenser, Caeregen Therapeutics, North Carolina, UNITED STATES|M.T. Trese, K.A. Drenser, Associated Retinal Consultants, Royal Oak, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Wendy Dailey: Commercial Relationship(s);Code E (Employment):Caeregen Therapeutics | Kenneth Mitton: Commercial Relationship: Code N (No Commercial Relationship) | Michael Trese: Commercial Relationship(s);Code O (Owner):Caeregen Therapeutics | Kimberly Drenser: Commercial Relationship(s);Code O (Owner):Caeregen Therapeutics

ABSTRACT BODY:

Purpose: To develop and produce a non-toxic protein therapeutic for the repair and regeneration of the retinal vasculature in eyes affected by ischemic retinopathies, by targeting and stimulating endogenous retinal endothelial cells. A strategy for producing Noregen protein in bacteria, based on the human norrin protein, was developed and tested for toxicity, in vitro activity and in vivo efficacy.

Methods: A method was refined to produce Noregen (human-derived growth factor) protein as inclusion bodies in E. Coli, to meet several milestones. 1) Culturing at least 1,000 mg per Liter of protein. 2) Purifying protein sufficiently for safe intravitreal injection in the rat eye as confirmed by ERG. 3) Refolding Noregen to produce active protein. Activity was measured by a receptor (Frizzled-4) binding assay, RT-PCR to determine alterations in Norrin-target gene expression (AXIN-2 & PLVAP) in primary human retinal endothelial cells and use of a mouse OIR model to evaluate accelerated vascular regrowth in vivo. OIR mice (n=11) were removed from 75% oxygen at post-natal day (P) 12 and received a single injection of either Noregen 40 ng (n=6) or Vehicle (n=5) in the left eye at P14. Eyes were evaluated by retina whole mount and lectin staining at P17.

Results: Production of protein met and then exceeded the desired culture concentrations. Noregen protein was refolded into a biologically active state and achieved sufficient binding to Frizzled-4, matching the binding EC50 of Norrin (30-150 ng/mL). Purification was reached to minimize endotoxin and no toxicity was detected in the Long Evans rat eye based upon analysis with fluorescein angiography, Spectral Domain-Optical Coherence Tomography (SD-OCT), and full-field electroretinogram (ERG) up to 6 weeks following a single intravitreal injection of Noregen 250 ng. Significant vascular regrowth was seen in the Noregen treated eyes compared to vehicle treated eyes (p=0.027). Noregen treatment of primary HRMECs increased AXIN-2 gene expression (Wnt pathway activation) similar to human norrin, increased cell proliferation in a dose dependent fashion, and suppressed PLVAP (marker of transcytosis).

Conclusions: Noregen, a novel protein therapeutic, was successfully produced in E. Coli at sufficient scale, purity and biological activity to enable the continued development of Noregen for future GMP grade manufacturing.

CONTROL ID: 3714627

SUBMITTER (NAME ONLY): Emma Drabbe

TITLE: A Novel Tissue Bioreactor for Retinal Organoid Microenvironmental Control

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Drabbe, D. Pelaez, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|E. Drabbe, T. Arcari, E. Rippes, A. Agarwal, Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|A. Agarwal, D. Pelaez, Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure: Emma Drabbe: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Arcari: Commercial Relationship: Code N (No Commercial Relationship) | Emmanuel Rippes: Commercial Relationship: Code N (No Commercial Relationship) | Ashutosh Agarwal: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Pelaez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In vitro culture systems generally apply homogeneous stimuli and rely on intercellular signaling to guide growth of tissues. However, to derive complex tissue structures such as the human retina, a gradation of certain stimuli is required. The inner retina resides in a hypoxic environment (2% O_2) adjacent to the vitreous cavity. From there, oxygenation levels rapidly increase towards the outer retina (18% O_2) at the choroid. Here we developed a novel tissue bioreactor allowing the maturation of inner and outer retinal cell phenotypes within an O_2 gradient.

Methods: The bioreactor is assembled from a 75x25x3 mm acrylic slide, a PFA film, a cover glass, and double-sided adhesives, which were adjusted with computer numerical control milling and laser cutting (Fig. 1A). The 60 culture wells of 2 mm in diameter and 0.7 mm high each hold one retinal organoid. A nitrogen (N_2) tank provides the bioreactor with 5 mL/min N_2 gas and a dual syringe pump creates a 5 µL/min continuous flow of culture medium though the bioreactor (Fig. 1B). Gas diffusion through the PFA membrane and culture medium was predicted using computational modeling software for atmosphere (20.9% O_2) and incubator (18.6% O_2) conditions. O_2 concentration measurements were performed with O_2 sensors along the z-axis in 50 µm steps in atmospheric conditions.

Results: The gas diffusion throughout the culture medium resulted in an O_2 concentration gradient along the z-axis (Fig 1C). The computational predictions in atmospheric conditions are in accordance with the measurements around the retinal organoid location in the bioreactor (Fig. 1D).

Conclusions: This open-well bioreactor is easily accessible for downstream analysis, establishes a steep O_2 gradient and allows high-throughput retinal organoid culture. It will help retinal organoids mature into the complex structure to use them for disease modeling and drug testing.

CONTROL ID: 3714628
SUBMITTER (NAME ONLY): Haichun Sun
TITLE: Relative Scaling for the Creation of Simulated Phosphene Maps
SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: H. Sun, Neuroscience, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|L. Yang, A. Kartha, G. Dagnelie, Ophthalmology, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|R. Sadeghi, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|
Commercial Relationships Disclosure: Haichun Sun: Commercial Relationship: Code N (No Commercial Relationship) | Liancheng Yang: Commercial Relationship: Code N (No Commercial Relationship) | Arathy Kartha: Commercial Relationship: Code N (No Commercial Relationship) | Roksana Sadeghi: Commercial Relationship: Code N (No Commercial Relationship) | Gislin Dagnelie: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Intracortical visual prostheses (ICVPs) generate a phosphene map in wearers' visual fields. Three modalities, finger pointing, eye movement, and head movement, are tested for reconstructing ICVP patients' phosphene map, but each may have considerable distortion. The distortion may be reduced by scaling the simulated phosphene map obtained from each of the above modalities.
Methods: Normally sighted participants were shown a set of 32 dots ("phosphenes") in the central 35° of the lower-left visual field quadrant, one by one, in a VIVE Pro Eye headset. Participants indicated the location of the phosphene by finger-pointing, eye movement, and head movement. Finger positions were collected in two conditions: finger-eye and finger-head. Each condition was repeated three times. Polhemus G4 trackers recorded finger positions and head movements. Eye movements were recorded using the VIVE Pro Eye built-in tracking feature. Data analysis was performed through shifting and scaling the clusters of obtained dots to equate their centers of mass and dispersions to those of the original phosphenes.
Results: Across all obtained data, the average scaling factor for eye maps, finger maps, and head maps are 0.75(±0.18), 0.41(±0.11), and 0.60(±0.17), respectively. The average distances between scaled dots and original phosphenes in eye, finger, and head maps were 1.56°, 1.71°, and 2.53°, respectively. Thus, similar scaling factors were observed across subjects for all three settings; eye position and finger movement had better accuracy and precision than head movement.
Conclusions: Since the three scaling factors are similar across sighted subjects, we can apply these factors to blind subjects' data. Furthermore, the scaled phosphenes were close to the original ones, so we can expect the scaled phosphenes to be sufficiently accurate for image presentation in blind subjects.

CONTROL ID: 3714630

SUBMITTER (NAME ONLY): Ruchi Sharma

TITLE: iPSC-RPE with CFH Y402H risk variant show higher disease propensity compared to the non-risk CFH variant

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sharma, D. Ortolan, K. Klein, J. Montford, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Nimmagadda, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The alternate complement pathway and age-related macular degeneration (AMD) have been long connected via genetic association studies. The complement factor H (CFH) gene has one of the highest odds ratio for the disease propensity, and dysregulated alternate complement pathway is thought to accelerate the disease phenotype. RPE cells with the highest CFH expression are the likely initiation site for complement attack. Using iPSC-RPE derived from patients with risk(Y402H) and non-risk(H402H) CFH alleles, we aim to decipher the role of CFH in disease propensity under a complement attack and determine genotype to phenotype interaction.

Methods: Four iPSC lines from CFH risk Y402H and three from non-risk H402H variants were differentiated into RPE and confirmed for functionality and maturity. To check if CFH risk-allele containing iPSC-RPE show signs of vulnerability to complement attack, we tested secreted CFH, C3a, and C5a levels, phagocytic ability, monolayer transepithelial resistance (TER) with and without complement serum. In addition, cells were stained with sub-RPE deposit marker-APOE, lipid droplets with Nile red, and BODIPY and complement lytic attack complex to check the AMD phenotype.

Results: CFH risk variant iPSC-RPE showed lower outer segment digestion capacity, and lower TER. CFH high-risk cells also had significantly higher sub-RPE and lipid deposits than CFH non-risk variant iPSC-RPE, suggesting disease vulnerability. The lower CFH secretion and higher C3a and C5a levels in CFH risk variants likely is the downstream mechanism making these RPE cells susceptible to AMD.

Conclusions: iPSC-RPE from the CFH risk variant recapitulated the AMD phenotype at basal levels and under complement attack- creating AMD model in a dish. This study provides a tool to decipher genotype interaction with macular degeneration phenotype and other retinal dystrophies. In addition, this platform can be used to further study interactions between different risk alleles such as ARMS2/HTRA1 and to perform drug screens to discover potential therapeutic agents.

CONTROL ID: 3714631

SUBMITTER (NAME ONLY): Mohammad Khan

TITLE: Machine Learning Quantification of Fluid Volume in Eyes with Retinal Vein Occlusion Undergoing Treatment with Aflibercept: The REVOLT study

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Khan, McMaster University, Hamilton, Ontario, CANADA|S. Sodhi, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|A. Pereira, N. Choudhry, Ophthalmology & Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|J. Golding, A. Dhawan, N. Choudhry, Vitreous Retina Macula Specialists of Toronto, Ontario, CANADA|J.D. Oakley, D. Russakoff, Voxeleron, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vein occlusions (RVOs) are the second leading cause of vascular blindness, where anti-VEGF agents are among the first-line treatment options. Recent developments in artificial intelligence (AI) models have shown promise in OCT fluid segmentation and predictive value in anti-VEGF treatment outcomes. However, there are currently no trials demonstrating AI with swept-source Optical Coherence Tomography (SS-OCT) images in concordance with OCT analysis for RVO patients.

Methods: 49 treatment-naive subject eyes were diagnosed with visual impairment due to RVOs, either central (CRVO) or branch (BRVO). SS-OCT data was used to assess retinal layer thicknesses, as well as quantify intraretinal fluid (IRF), subretinal fluid (SRF), and serous pigment epithelium detachments (PEDs) using a deep learning-based, macular fluid segmentation algorithm. Patients received 3 loading doses of 2 mg intravitreal aflibercept injections (IAI). Image analysis was performed at baseline, month 3 & month 6 follow-up. Baseline OCT morphological features and fluid measurements were correlated using the Pearson correlation coefficient (PCC) to changes in BCVA to determine which features most impacted 6-month change in BCVA. The difference between areas of non-perfusion in OCT-A images treated with and without a denoising algorithm would also be evaluated.

Results: A combined model of thickness in the Outer-Plexiform Layer (OPL), retinal nerve fiber layer (RNFL) and presence of IRF had the strongest overall correlation for CRVO (PCC=0.865, $p < 0.05$); while for BRVO the addition of IRF to the OPL-Inner Nasal model had a strong correlation (PCC=0.803, $p<0.05$). Baseline Ischemic Index in the Deep Capillary Complex (DCP) for CRVO without denoising demonstrated notable correlation with 6-month change in BCVA (PCC=0.7501, $p = 0.079$), and denoising strengthened this correlation (PCC=0.9100, $p = 0.0101$).

Conclusions: A combined model of IRF and thickness, alongside ischemic indices provide the best correlation to BCVA changes. This is clinically consistent given that the DCP supplies the OPL, as macular fluid builds up, these vessels have reduced flexibility to accommodate; thus becoming more occluded, causing further damage to the OPL. Ultimately, an AI approach to analyzing fluid metrics may provide an advantage in personalizing therapy and predicting BCVA outcomes for RVO patients.

CONTROL ID: 3714632
SUBMITTER (NAME ONLY): Eunice You
TITLE: Scleral buckle removal in patients with rhegmatogenous retinal detachment
SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: E. You, M. Hébert, S. Bourgault, M. Caissie, É. Tourville, A. Dirani, Ophtalmologie, CHU de Quebec-Universite Laval, Quebec, Quebec, CANADA|M. Ghasempourabadi, S. Doukkali, Universite Laval, Quebec, Quebec, CANADA|
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ABSTRACT BODY:

Purpose: Scleral buckling (SB) can be used alone or in combination with pars plana vitrectomy (PPV) for the treatment of rhegmatogenous retinal detachment (RRD). In specific cases, buckle removal is necessary due to SB-related complications. The purpose of this study is to investigate the indications of SB removal and the rate of recurrent retinal detachment in these patients.

Methods: This was a retrospective cohort study. The medical records of eyes operated for RRD with SB (simple SB or in combination with PPV) at CHU de Québec – Université Laval (Quebec City) between 2008 and 2020 were reviewed. Exclusion criteria included non-RRD of tractional or traumatic etiology. The indications for all cases of SB removal were reviewed. The primary outcome of interest was recurrence of retinal detachment following SB removal.

Results: Out of 2375 eyes that underwent SB for treatment of RRD, 40 eyes had SB removal (1.7%). The main indication for SB removal was infection, occurring in almost a third of patients (n=13, 32.5%). Pain/intolerance (n=12, 30%), buckle extrusion (n=6, 15%), strabismus and/or diplopia (n=3, 7.5%) and other causes including persistent inflammation and increased intraocular pressure (n=6, 15%) made up the remaining indications. The median time from scleral buckle placement to removal was 11.5 months, but in 25 cases (62.5%), the buckles were removed after less than 6 months, and an additional 37.5% (n=15) of cases after more than 1 year. Patients who had infection as the primary cause of SB removal were likely to have earlier removal of SB (median [Q1, Q3] in months) than those with SB removal for other reasons (infection: 2.8 [1.1, 9.5] vs. other causes: 11.2 [6.3, 25.1]; p=0.012).

After SB removal, recurrent retinal detachment was observed in 7.5% of eyes (n=3), with all recurrences occurring within the first month. All patients underwent PPV without placement of a SB. Re-detachment occurred in all three patients within the first 6 months.

Conclusions: The indications for SB removal are numerous, with infection making up one third of cases and generally necessitating earlier intervention. There is a 7.5% risk of redetachment after SB removal. Additionally, treatment of recurrent RRD post-SB removal is associated with a high rate of failure and should therefore be carefully considered.

CONTROL ID: 3714633

SUBMITTER (NAME ONLY): Karen Hernandez

TITLE: Role of Hyperinsulinemia and Hyperglycemia in Outer Blood Retinal Barrier (BRB) Breakdown

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hernandez, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|K. Hernandez, L. Pollock, B. Anand-Apte, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure: Karen Hernandez: Commercial Relationship: Code N (No Commercial Relationship) | Lana Pollock: Commercial Relationship: Code N (No Commercial Relationship) | Bela Anand-Apte: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of preventable blindness in developed countries. Breakdown of the blood retinal barrier (BRB) leads to macular edema and is one of the earliest events in the development of DR. Previous work from our laboratory suggest that hyperinsulinemia (as seen in type 2 diabetes) may lead to disruption of the outer BRB. The purpose of this study is to explore the effect of hyperglycemia/hyperinsulinemia on the permeability and expression of tight junction proteins (claudin 19, claudin 10, zonula occludens-1 (ZO-1) in primary porcine retinal pigment epithelial (RPE) cells. The proposed study will provide a better understanding of the molecular mechanisms involved in the breakdown of the BRB in DR.

Methods: Impedance spectroscopy was used to evaluate the transepithelial electrical resistance (TEER) as well as capacitance of primary porcine RPE cells grown in media containing 5 mM D-glucose (mimicking physiological conditions) or 25 mM D-glucose (mimicking high glucose as seen in diabetic patients). Once cells reached confluence, the effect of exposure to 100 nM insulin over 2 weeks was evaluated. Expression of tight junction proteins were evaluated by western blotting and the spatial localization of these proteins was evaluated by immunofluorescence.

Results: RPE cells cultured in physiological glucose (5mM) had a lower TEER compared to RPE cells cultured in high glucose (25mM). Insulin induced a significant decrease in TEER in RPE cells only in high glucose (25mM) conditions with no effect on cells cultured in physiological glucose media.

Conclusions: These data suggests that high levels of insulin can induce BRB breakdown under hyperglycemic conditions and may have implications for the development of DR in type 2 diabetes.

CONTROL ID: 3714634

SUBMITTER (NAME ONLY): Nawaf Almutairi

TITLE: Accommodation Microfluctuation is Impaired in Mild Traumatic Brain Injury

SESSION TITLE: Vision assessment and Clinical applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.M. Almutairi, Optometry, Qassim University, Buraidah, Al Qassim, SAUDI ARABIA| N.M. Almutairi, C. Liu, Optometry, Pacific University, Forest Grove, Oregon, UNITED STATES|K. Hampson, Department of Engineering Science, University of Oxford, Oxford, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Individuals with mild traumatic brain injury (mTBI) exhibit significant accommodative abnormalities that can impair their near-work comfort and efficiency. Accommodative insufficiency is widely reported in mTBI patients who show significantly higher accommodative error (AE). Accommodation microfluctuation (AMF) plays an important role in the accommodation steady-state control mechanism. The purpose of this study was to investigate the impact of mTBI on the characteristics of the AMF.

Methods: Monocular static accommodation was recorded continuously for 1 minute from 54 healthy (age 21-30 years) and 30 mTBI subjects (age 18-33 years) using Power Refractor 3 at 5 accommodative stimulus (AS) levels (0 to 5 D). The accommodative response (AR) data were processed using Fast Fourier Transform to determine the amplitude of high (HFC), medium (MFC), and low (LFC) frequency components of the AMF.

Results: Consistent with previous reports, the amplitude of LFC increased as the AS increased in both groups (Fig 1a). However, mTBI subjects showed a significantly lower LFC amplitude than that of the control at higher AS levels (3 D – 5 D) (main effect $F_{(1,78.7)} = 8.56$ ($p < 0.01$). Similar group effect was also observed for the HFC ($F_{(1,77.9)} = 5$ ($p = 0.028$) (Fig 1b). Pairwise comparison revealed that the HFC amplitude was significantly lower in the mTBI than the control group for 2D, 3D, and 4D stimulus levels. There was no significant difference between groups for the amplitude of the MFC. Interestingly, a strong correlation between the AE and the LFC of AMF was revealed for all AS levels (except 0D) in both groups (Fig 2). Lead of accommodation (AE< 0) was associated with higher LFC amplitude, and lag of accommodation (AE > 0) was associated with lower LFC amplitude. No correlation between the AE and MFC or HFC was observed.

Conclusions: Our data is the first to show impairment of AMF in subjects with mTBI. Both the LFC and HFC showed significantly lower AMF amplitude compared to the control group. The magnitude of LFC was correlated with AE in both groups, suggesting that AMF may be influenced primarily by the changes in the motor output properties of the accommodation plant with increasing accommodation response.

CONTROL ID: 3714636

SUBMITTER (NAME ONLY): Youssef Mohamed

TITLE: Modelling and measuring the viscoelastic properties of the in vivo rat eye

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.H. Mohamed, C.L. Passaglia, Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|Y.H. Mohamed, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Goldmann Equation models the eye as a purely resistive element, which is adequate understeady-state conditions but insufficient to quantify the dynamic properties of the eye. We propose a model with both resistive and viscoelastic components that represent the trabecular meshwork and scleral shell, respectively. This study aims to use the model to measure viscoelastic parameters of rat eyes.

Methods: Figure 1 provides a schematic of the viscoelastic eye model and experimental setup, which was simulated in MATLAB. Two 33-gauge needles were advanced into the anterior chamber of anesthetized Brown-Norway rat eyes. The first needle was connected to a pressure transducer to record true intraocular pressure (IOP). The second needle was attached to a stopcock connected with 25-gauge tubing to anotherpressure transducer, a flow meter, and a controllable pump. IOP and flow data were collected at 50Hz. Outflow facility (1/RT) was measured by recording steady-state flow at multiple IOP setpoints. Ocular compliance (CW) was measured by recording IOP responses to bolus injections of varying volumes. To determine corneoscleral resistance (RW), the time constant of the eye was measured by fitting an exponential function to the decay in IOP after a pressure step. RW was calculated from the measured facility, compliance, and decay time as follows: t = CW (RW + RT). To help minimize error, a third needle of small and known resistance RSH was inserted in the eye as a shunt, eliminating uncertainties in RT.

Results: Viscoelastic data were successfully collected from 5 animals. Model simulations accurately described measured pressure and flow dynamics to step changes in IOP of 5 mmHg. $1/R_T$, C_W, and t were measured to be 0.017 ± 0.01 $ml*min^{-1}*mmHg^{-1}$, 0.08 ± 0.05 $ml*mmHg^{-1}$, and 0.18 ± 0.05 min, respectively. Based on these results, R_W averaged 2.22 ± 1.27 $mmHg*min*ul^{-1}$ across animals.

Conclusions: The viscoelastic model captures ocular fluid dynamics of anesthetized rats to pressure and flow steps. The “shunt method” provides a quick and accurate means of estimating Rw. RW is relatively small but may cause overestimation of RT if measurements have not reached steady state.

CONTROL ID: 3714638

SUBMITTER (NAME ONLY): Claude Gagna

TITLE: Multiplex Immunofluorescent Demonstration of B-DNA, Z-DNA and G4-Quadruplex DNA in the Mouse Crystalline Lens: Spatial Genomic Organization of Different DNA Structures, i.e., Genomesorganizomics

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Gagna, Biological and Chemical Sciences, New York Institute of Technology, Old Westbury, New York, UNITED STATES|

Commercial Relationships Disclosure: Claude Gagna: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The lens is an excellent system to investigate molecular biological processes, such as mitosis, cellular quiescence, stem cells, cellular differentiation, and cell death. Our group wanted to demonstrate, for the first time, the presence and distribution of three totally different types of DNA structures in the anterior epithelial cells and nucleated secondary fiber cells of the normal lens. DNA is a dynamic molecule and can adopt many structures, such as canonical right-handed double-stranded (ds-) B-DNA, left-handed ds-Z-DNA, and four-stranded G4-quadruplex DNA. These DNAs have different molecular biological functions in eukaryotic cells.

Methods: Twenty mice (Jax) were sacrificed and histotechnologically processed (Davidson's fixative) to obtain paraffin-embedded tissue section (3.0 μm). Using anti-DNA monoclonal antibodies (MAbs), (i.e., anti-ds-B-DNA, anti-ds-Z-DNA, and anti-G4-quadruplex DNA MAbs), we localized and quantified tissue-bound DNAs in the nucleus of epithelial cells, and nucleated secondary fiber cells undergoing cell death: terminal differentiation, i.e., denucleation. Immunofluorescence (IF) was performed using a confocal microscope and advanced computer analysis software. Cells were counterstained with wheat germ agglutinin. AR enhanced IF of certain DNAs. Both positive and negative controls were used.

Results: Our data shows that all three types of DNA can be identified within the nucleated cells of the epithelium [i.e., central zone, pre-equatorial zone, germinative zone, meridional rows, and differentiating cells], and nucleated secondary fiber cells. IF was highest in the GZ and lowest in the CZ. IF decreased at different rates within denucleating cells depending on type of DNA. No IF was observed in the annucleated secondary and primary fiber cells. AR enhanced IF of certain DNAs.

Conclusions: All three types of DNAs are regulating different roles in the molecular biology of genes and telomeres in the lens. We are applying a novel "omics" method towards the characterization of DNA structure found within the nucleus, i.e., "Spatial Genomic Organization of Different DNA Structures: Genomesorganizomics". Future research will demonstrate how DNA structures specifically influence the biology of lens cells managing proliferation, differentiation and cell death.

CONTROL ID: 3714639

SUBMITTER (NAME ONLY): Rhiya Mittal

TITLE: Assessing the Test-Retest Reproducibility of the Ocular Photosensitivity Analyzer to Quantify Visual Photosensitivity

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Mittal, M.C. Aguilar, A. Gonzalez, V. Graham, K. Leviste, P.A. Sepulveda Beltran, E. Arrieta, B. Maceo Heilman, J. Parel, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Maceo Heilman, B. Hurwitz, Department of Biomedical Engineering, College of Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|W.J. Feuer, B.L. Lam, A. Galor, Anne Bates Leach Eye Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|G. Alvarez, E. Felix, Department of Physical Medicine and Rehabilitation, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Hurwitz, Department of Psychology, University of Miami, Coral Gables, Florida, UNITED STATES|E. Felix, A. Galor, VA Miami Healthcare System, Miami, Florida, UNITED STATES|J. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: As few methods exist to reliably quantify visual photosensitivity, the Ocular Photosensitivity Analyzer (OPA) was devised (Aguilar et al. BOE 2018, 9(11): 5583-5596). This study was conducted to assess the test-retest reproducibility of the OPA to quantify visual photosensitivity thresholds (VPT) in healthy subjects across two visits.

Methods: This IRB-approved study included 25 healthy adults with no history of ocular abnormality. During two in-person visits, subjects were administered study questionnaires (VLSQ-8: Visual Light Sensitivity Questionnaire-8, OSDI: Ocular Surface Disease Index, NPSI-E: Neuropathic Pain Symptom Inventory for the Eye) and filled out a medical history form. VPT was measured with the OPA, an automated device that assesses subjects' responses to multiple light stimuli presented at varying intensities. The test-retest reproducibility for VPT measured at each visit was analyzed by reliability analysis. An Intraclass Correlation Coefficient (ICC) ≥ 0.90 was considered to indicate excellent reliability. Correlation between VPT and study questionnaire responses were assessed via linear regression. An R^2 ≥ 0.7 was considered significant.

Results: The average age of the subjects (n=25) was 32.5±13.3 years, 48.0% self-identified as male, 64.0% as White, and 24.0% as Hispanic. Visit #1 and Visit #2 were conducted 34.1±7.1 days apart. The mean measured VPT in healthy subjects were 2.5±0.8 log lux at Visit #1 and 2.3±0.8 log lux at Visit #2. The test-retest reproducibility for healthy subjects measured during the two in-person visits had excellent reliability (ICC = 0.92). Overall, dry eye and ocular pain scores were low in our healthy population (VLSQ-8 11.3±3.5, OSDI 1.2±1.8, NPSI-E 0.8±1.6). No significant correlations were found between VPT and study questionnaire responses (R^2=0.03 – 0.06, p>0.05).

Conclusions: The data indicate that the OPA is a reliable tool for quantifying visual photosensitivity in individuals without ocular disease. Ongoing studies are being performed to increase our subject population and examine repeatability in subjects with TBI associated visual photosensitivity.

CONTROL ID: 3714641

SUBMITTER (NAME ONLY): Munevver Cicekdal

TITLE: Single-cell transcriptional dynamics and in vivo enhancer assays provide insight into gene regulatory networks of PRDM13 and IRX1 implicated in North Carolina macular dystrophy

SESSION TITLE: Biochemistry and molecular biology of ocular disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.B. Cicekdal, K. Vleminckx, Department of Biomedical Molecular Biology, Ghent University, Universiteit Gent, Ghent, BELGIUM|M.B. Cicekdal, S. Van de Sompele, V. López-Soriano, A. Dueñas Rey, M. Bauwens, K. Vleminckx, E. De Baere, Department of Biomolecular Medicine, Ghent University, Ghent, Belgium & Center for Medical Genetics, Ghent University Hospital, Universiteit Gent, Ghent, BELGIUM|J.J. Tena, J.R. Martinez-Morales, Centro Andaluz de Biología del Desarrollo, Consejo Superior de Investigaciones Científicas and Universidad Pablo de Olavide, Sevilla, SPAIN|

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ABSTRACT BODY:

Purpose: North Carolina macular dystrophy (NCMD) is an autosomal dominant developmental disease, hypothesized to be a retinal enhanceropathy with noncoding variants and duplications overlapping with cis-regulatory elements (CREs) near PRDM13 or IRX1 as genetic cause. We aimed to provide insight into the disease by single-cell (sc) transcriptional dynamics and in vivo enhancer assays.

Methods: Single-nucleus RNA-seq (snRNA-seq) data of embryonic (53, 59, 74, 78, 113 & 132 days) and adult (n=3) human retina (PMID:34788628) was mined for sc expression of PRDM13 and IRX1. Expression matrices from these samples (GSE183684) were imported into R and processed using Seurat. Harmony was used to merge all sc data. Five previously identified candidate CREs (cCREs, 3 for PRDM13, 2 for IRX1) were assessed using enhancer assays in Xenopus (X.) tropicalis and/or albino X. laevis using a fluorescent enhancer detection vector and transgenesis via I-SceI meganuclease.

Results: SnRNA-seq data from all retinal samples was put into ten clusters representing the major retinal cell types. Transcriptional profiling during retinal development showed predominant expression of PRDM13 in amacrine cells, with low expression in retinal progenitor cells (RPCs), horizontal, and retinal ganglion cells (RGCs). IRX1 showed low expression during development, with highest expression in RGCs and weakest in RPCs. The first mutational hotspot of PRDM13 did not drive EGFP reporter expression in X. tadpoles (Nieuwkoop & Faber (NF) stage 42), while the second hotspot region drove EGFP expression in eye and brain. The first tested IRX1 cCRE drove EGFP expression in the neural plate and tube at NF stage 15 and 20. At NF stage 42 and 45 EGFP expression was seen in neural crest derivatives and the eyes, and at stage 55 reporter gene expression was maintained in the eye. The cCRE containing the shared duplicated region of IRX1 showed lower EGFP expression.

Conclusions: A shared developmental expression in amacrine cells and RGCs and to a lesser extent in RPCs has been shown for PRDM13 and IRX1. Genetic defects in both loci may affect CREs that are active in early RGCs. Due to the dominant nature of NCMD a gain-of-function impairing PRDM13 or IRX1 expression can be suspected, perturbing macula-specific synaptic interactions between amacrines and RGCs during retinogenesis.

CONTROL ID: 3714642

SUBMITTER (NAME ONLY): Colin Lemire

TITLE: Intravitreal injection dead volume varies significantly with different forces applied to TB, ranibizumab, and aflibercept syringes

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Lemire, E. Gonzalez, Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|C.A. Lemire, E. Gonzalez, J.J. Raevis, Division of Ophthalmology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Colin Lemire: Commercial Relationship: Code N (No Commercial Relationship) | Efren Gonzalez: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Raevis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The optimal syringe to use for intravitreal injections remains under debate. We investigated the relationship between the force applied to the syringe and volume output.

Methods: Empty pre-filled syringes of aflibercept and ranibizumab as well as 1 mL tuberculin (TB) syringes, used for bevacizumab injections, were filled with 50 µL of deionized water. Syringes were attached to a 32-gauge needle and held in an apparatus with weights being placed in 50 g (0.49 N) increments until the plunger was completely depressed and fluid ceased exiting the needle. Following this equilibrium point, additional weight was added serially to increase the force on the plunger. The mass of water expelled at each force was measured and converted to volume (1 mg water = 1 µL water). Six trials of each syringe were performed, and differences were compared using an ANOVA test. Pairwise differences were calculated with t-tests.

Results: The mean total excess volume with 400 g (3.92 N) being added after equilibrium was reached was 8.58 µL for aflibercept (95% CI: 8.04-9.13), 5.70 µL for ranibizumab (5.13-6.27), and 0.40 µL for the TB syringe (0.14-0.66). One-way ANOVA revealed that the mean total excess output was significantly different between the three syringes ($F = 495.6$, $p = 2e\text{-}14$) and t-tests found significant differences between all syringe pairs ($p < 0.0001$).

Conclusions: Ideally, 50 µL is injected with intravitreal injections, but with only 400 g of extra weight applied to the depressed plunger the output volume increased by 17% from the aflibercept syringe and 11% from the ranibizumab syringe. Under the same conditions, the TB syringe expressed only 0.8% more volume. Design elements of the syringes, including the domed shape, compressibility of the stopper, short push length, and large diameter of the plunger likely account for the differences. Given the small volume of intravitreal injections, the effect of force on syringe output should be minimized to prevent improper dosing of medication.

CONTROL ID: 3714645

SUBMITTER (NAME ONLY): Jacob Wang

TITLE: Posterior vitreous detachment increases macrophage-like cell density

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Wang, J.X. Ong, P.L. Nesper, A.A. Fawzi, J. Lavine, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) imaging has identified mobile, ramified macrophage-like cells (MLCs) at the vitreoretinal interface in human subjects. The identity of MLCs remains unknown and a potential cell type includes vitreal hyalocytes. We performed OCT and OCT angiography (OCT-A) imaging in patients with and without posterior vitreous detachment (PVD) to determine if MLCs exist in the retina or vitreous, and to determine if PVD status changes MLC detection.

Methods: We imaged 21 eyes from 21 subjects, including 11 eyes with no PVD and 10 eyes with PVD. Repeated foveal-centered 3 x 3 mm OCT-A images were obtained (mean: 6.0 repeats, range: 4–10). The images were segmented, registered, and averaged. The OCT slab segmented from 0 to 3 microns above the internal limiting membrane was used to detect MLCs, which were binarized and quantified using our previously published semi-automated method. The distribution of MLCs in relation to vessels in the superficial capillary plexus was investigated, and MLC density was calculated for 3 vascular regions – on vessels, perivascular, and ischemic (>30 microns from the nearest vessel).

Results: MLC density was 1.8-fold greater in the PVD group (13.21 ± 7.29 cells/mm^2) compared to the no PVD group (7.48 ± 4.43 cells/mm^2; P = 0.04). MLCs were increased 1.9-fold on-vessel (P = 0.07), 1.9-fold in the perivascular region (P = 0.12), and 2.2-fold in ischemic areas (P = 0.22).

Conclusions: MLCs were detected in both PVD and no PVD eyes, suggesting that MLCs exist in the retina, although we cannot exclude a remnant of the cortical vitreous on the retinal surface. PVD eyes showed a trend toward more MLCs near vessels than ischemic areas, suggesting that MLCs could be extravasating from the vasculature in response to PVD. However, vitreous separation could merely enhance MLC detection. PVD status is an important parameter to consider in future MLC studies.

CONTROL ID: 3714647

SUBMITTER (NAME ONLY): Leonardo Lando

TITLE: Quantification of long anterior zonules in late-onset retinal degeneration

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lando, University of Toronto, Toronto, Ontario, CANADA|A. Nguyen, McGill University, Montreal, Quebec, CANADA|R. Li, R. Megaw, B. Dhillon, The University of Edinburgh, Edinburgh, Edinburgh, UNITED KINGDOM|S. Borooah, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Late-onset retinal degeneration (L-ORD) is an autosomal dominant macular dystrophy with anterior segment involvement, notably long anterior zonules (LAZs). In this study, we aim to analyze LAZs in a cohort of L-ORD patients.

Methods: This prospective, single-center study included patients with a genetic diagnosis of L-ORD from 2011-2016. Imaging included true-color non-mydriatic anterior segment photographs by slit-lamp retroillumination. LAZs were identified, marked and plotted using Matlab (R2021a) (Figure 1). The zonule-free zone (ZFZ) was calculated using the longest LAZ to the pupillary axis scaled to an average pupil size of 12 mm. The LAZs number and location, ZFZ length, iris transillumination defects, pachymetry, and features on gonioscopy were described. Calculations were performed on SPSS (v. 25; IBM) with $p<0.05$.

Results: Twelve eyes from 6 patients (median age = 60.5 years, range 56-70; 4 males) were included (Figure 2); one case (2 eyes) was excluded due to inadequate imaging. LAZ length measurement showed high inter-rater (ICC=0.98; $p< 0.001$) and test-retest repeatability (ICC=0.97; $p<0.001$). There was marked variability in the number of LAZs in the cohort, with a median of 160 (range: 11-372). LAZ prevalence varied with quadrant: superior (39%), inferior (24%), nasal (19%), and temporal (18%). LAZ was strongly correlated between right and left eye ($r=0.98$, $p=0.001$), with no significant difference between eyes ($p=0.34$). Additionally, LAZ was strongly correlated with pachymetry ($r=0.92$; $p=0.01$) and inversely with age ($r=-0.78$; $p<0.05$). Scaled ZFZ had a median of 2.0mm (range:1.3-5.4), without significant differences in size between eyes of patients ($p=0.34$). ZFZ was correlated with age ($r=0.85$; $p=0.03$) but not with total LAZ number ($r=-0.68$; $p=0.14$).

Conclusions: This study validates a method for measuring and counting LAZ in L-ORD. In our cohort LAZs are most prevalent in the superior quadrant. LAZ number and ZFZ were symmetrical between L-ORD eyes. ZFZ is smaller in L-ORD patients compared to previous studies of LAZ. The reduced LAZ count in older patients and increased ZFZ may suggest a decrease in the number of zonules with time with a primary loss of longer LAZ. The LAZ findings require validation in a larger cohort, planned as part of an ongoing longitudinal study.

CONTROL ID: 3714648

SUBMITTER (NAME ONLY): Saif Hamdan

TITLE: Patient Health Literacy Levels Across Different Ophthalmology Specialty Clinics and Patient Education Levels

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hamdan, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Siktberg, T. Pfister, S. Gangaputra, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Saif Hamdan: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Siktberg: Commercial Relationship: Code N (No Commercial Relationship) | Tyler Pfister: Commercial Relationship: Code N (No Commercial Relationship) | Sapna Gangaputra: Commercial Relationship(s);Code C (Consultant/Contractor):MERITCRO;Code F (Financial Support):NIH/NEI

ABSTRACT BODY:

Purpose: Health Literacy (HL)—the ability to get, understand, and use basic health information and services—is vital to effective care delivery. However, more than 1/4th of US adults are estimated to have inadequate HL, putting them at greater risk for poor health outcomes and high health care costs. This study seeks to quantify health literacy across different ophthalmology clinics and patient education levels.

Methods: In January 2020, routine HL assessment was integrated into the clinic intake performed by ophthalmic technicians in all comprehensive ophthalmology clinics at an academic eye institute as part of a quality improvement initiative. HL was assessed using the Brief Health Literacy Screening (BHLS), an orally administered, validated 3-item survey with each question scored on a five-point Likert scale. A retrospective chart review of adult patients seen at various ophthalmology clinic sites of an academic eye institute from January 2020 to December 2021 was performed. Information collected included basic demographic factors, education level, and HL score. Patients younger than 18 years old were excluded.

Results: A total of 16587 patients qualified for the study. 6.58% of all patients had inadequate HL. Among the individual clinics, Retina (16.13%), Neuro-ophthalmology (11.54%), and Glaucoma (10.15%) had the highest proportion of their patients with inadequate HL. When broken down by patient education level, health literacy was greatest among patients whose highest completed education was less than high school (36.51%) or high school (7.97%) compared to those who completed college (1.96%) or an advanced degree (1.78%). Further details are presented in Table 1.

Conclusions: Over a two-year period at an academic medical center, 6.58% of ophthalmology patients had inadequate health literacy, and inadequate HL was highest among those with less completed formal education.

CONTROL ID: 3714650

SUBMITTER (NAME ONLY): Rajeev Muni

TITLE: Pathophysiology of Outer Retinal Corrugations in Retinal Detachment

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Muni, M. Norouzi Darabad, P. Oquendo, H. Hamli, W. Lee, F. Nagel, A. Bansal, I.M. Melo, Ophtalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|A. Ramachandran, Chemical Engineering, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Outer retinal corrugations (ORCs) in rhegmatogenous retinal detachment (RRD) that do not fully resolve prior to reattachment may lead to the development of outer retinal folds which are associated with worse functional outcomes. The purpose of this study is to investigate the dynamic evolution of outer retinal corrugations (ORC) in vivo with optical coherence tomorgraphy (OCT) imaging.

Methods: Prospective cohort study. Eyes with RRD that underwent RRD repair were assessed longitudinally with multimodal imaging at baseline and at frequent intervals for up to 6 weeks post-operatively. The primary objective was to assess differences between RRD eyes with and without ORCs and to formulate a theory on the pathophysiology of ORCs by carefully observing the evolution and resolution of ORCs in vivo with OCT.

Results:

Fifty-seven eyes in 51 patients were assessed and followed. 34 participants were male with mean age of 60.9 (SD 7.77). 34 participants were phakic with baseline logMar visual acuity of 0.919 (SD=1.05). Mean duration of fovea-off of 6.88 days (SD=6.52) with 2.01 (SD=0.83) detached quadrants. 56.1% (32/57) of eyes had ORCs and 43.9% had no ORCs on presentation. All (100%) eyes with ORCs had complete and acute loss of RPE control with a larger extent of RRD (1 quadrant or more) and for a duration of more than 2 days. Although eyes without ORCs had subretinal fluid, the RPE was still in relative control of the subretinal space or the RRD had a duration of less than 2 days in all (100%) cases. This included 10 eyes with chronic non-progressive localized RRDs, 6 eyes with small localized acute RRDs, 5 eyes with residual displaced fluid following successful PnR or SB, and 4 eyes with larger acute RRDs of less than 2 days duration.

Conclusions: This prospective study describes a novel dynamic RPE-control theory of ORCs in RRD. The study demonstrates that more extensive RRD with loss of RPE-control for more than 2 days are more likely to develop ORCs. Clinical observations suggest that exposure of the outer retina to liquefied vitreous leads to the outer retina being more susceptible to deformation. Regaining RPE control following RRD repair results in a reversal of the ORCs. Understanding the pathophysiology of ORCs could lead to a modification of vitreoretinal surgical approach that allow ORCs to resolve prior to reattachment. The presence of ORCs is also suggestive of an open retinal break and absence of RPE control.

CONTROL ID: 3714651

SUBMITTER (NAME ONLY): Hanna Choi

TITLE: Subretinal drusenoid deposits is associated with increased risk towards the development of iRORA and cRORA

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Choi, D. Lally, New England Retina Consultants, Springfield, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Hanna Choi: Commercial Relationship: Code N (No Commercial Relationship) | David Lally: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The presence of subretinal drusenoid deposits (SDDs) confers increased risk of the development of geographic atrophy. With the recent consensus definition of OCT-defined atrophy, the purpose of this study was to retrospectively investigate the presence of SDD in the development of iRORA and cRORA in non-exudative AMD eyes.

Methods: Retrospective cohort of patients with intermediate dry AMD in one eye, defined as at least 1 large soft druse (≥125 μm), 5 SDDs, or 5 intermediate drusen (>67μm), with at least 5 years of follow-up were examined. SD-OCT biomarkers, including hyperreflective foci, soft drusen, refractile and cuticular drusen, SDD, subretinal hyperreflective material (SHRM), iRORA, and cRORA were recorded at baseline and at year 5. Eyes with baseline cRORA were excluded. Data was analyzed using the Fisher's exact and t test.

Results: Inclusion criteria was met in 122 eyes (84.79±7.40 years old; Female N=79, follow-up 62.90 (±4.78) months), of which 27% (N=33) developed cRORA at 5 years. iRORA developed in 6.56% (N=8). Baseline SDD was independently associated with iRORA or cRORA development (OR=4.45; p=0.0006). In the 45 eyes with SDD at baseline, 11.11% developed iRORA (N=5) and 46.67% developed cRORA (N=21) at 5 years. In comparison, in eyes without SDD at baseline, 3.90% (N=3) developed iRORA and 15.58% (N=12) developed cRORA.[1] Age and baseline hyperreflective foci (OR=5.37) were also indendently associated with iRORA or cRORA development (both $p<0.0001$) while soft drusen was not (OR = 1.56; p=0.32).

Conclusions: Subretinal drusenoid deposits is associated with greater risk of iRORA or cRORA development at 5 years in intermediate AMD eyes; about half developed cRORA by year 5. SDD may be a potential biomarker for the development of iRORA or cRORA. Further investigations are warranted.

CONTROL ID: 3714653

SUBMITTER (NAME ONLY): Sonali Ghosh

TITLE: Evidence for IL-2 signaling in corneal epithelium

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Ghosh, G. Tadvalkar, M. Stepp, Anatomy and Cell Biology, GWU Medical School, Washington DC, District of Columbia, UNITED STATES|W. Kao, Ophthalmology, College of Medicine University of Cincinnati, Cincinnati, Ohio, UNITED STATES|Z. Yu, Y. Kelegere, G. Yazdanpanah, C.S. De Paiva, Ophthalmology, Ocular Surface Center, Houston, Texas, UNITED STATES|V.J. Coulson-Thomas, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: IL-2 signals through its heterotrimeric receptor (IL-2R) consisting of the α (CD25), β, and g chains. We previously reported the gene expression of all three IL-2R chains in the cornea. Our purpose is to investigate the existence of corneal epithelial IL-2 signaling.

Methods: Eyes and adnexa of female C57BL/6 mice were collected, snap-frozen in liquid nitrogen. Cryosections were stained with antibodies anti-CD25, IL-2Rβ, and IL-2Rg and digital images were acquired with laser scanning confocal microscopy. Immortalized human corneal epithelial cells were grown for 24 h in media with increasing concentrations of IL-2 (0, 50, 125, 250, 500, or 1000 IU),fixed, and stained with an antibody against Ki67. The number of Ki67+ cells was quantified within 6 non-overlapping fields per well; 3 wells were assessed per variable; the study was repeated twice. Tet-On $Krt12^{rtTA}$ (Keratin 12-reverse tetracycline-trans-activator knock-in), tet-O-Cre, and $CD25^{flox}$ lines were mated to create ternary $Krt12^{rtTA/rtTA}$/tet-O-Cre/$CD25^{flox/flox}$ ($K12^{r/r}$/TC/$CD25^{f/f}$) in which $CD25^{f/f}$ was ablated in corneal epithelium upon doxycycline induction hereafter named $CD25^{D/DCEpi}$. $K12^{r/r}$/TC/$CD25^{f/f}$ without Dox induction and binary $K12^{r/r}$/$CD25^{f/f}$ with dox induction serve as controls. Both male and female experimental mice were subjected to the corneal barrier function assay at eight weeks of age using Oregon-Green-Dextran (OGD) dye (n = 8-16/condition/sex).

Results: In C57BL/6, CD25, IL-2R-β, and IL-2R-g chains were present in the corneal epithelium. There was a significant increase in Ki67+ cells/field at IL-2 doses of 125 and 250 U/mL followed by a plateau at higher concentrations ($P < 0.05$ and $P < 0.01$, respectively) in human corneal epithelial cells in vitro. A significant increase in corneal OGD levels (indicating corneal barrier disruption) was observed only in the female doxycycline-fed $CD25^{D/DCEpi}$ mice compared to the doxycycline-fed binary $K12^{r/r}$/$CD25^{f/f}$ mice and in non-induced $K2^{r/r}$/tet-O-Cre/$CD25^{f/f}$ mice (regular diet-fed mice).

Conclusions: All three chains of the IL-2R are expressed in the corneal epithelium at the protein level. Our results indicate for the first time that IL-2 regulates corneal epithelial cell proliferation in vitro and that disrupting IL-2 signaling in the cornea leads to dry eye disease in vivo. This effect was only seen in female mice. Future studies are needed to delineate the pathways used by IL-2 signaling to influence cornea homeostasis.

CONTROL ID: 3714654

SUBMITTER (NAME ONLY): Prashant Tailor

TITLE: A Cross-Sectional Prevalence Study of Myopia and High Myopia during COVID-19 Pandemic

SESSION TITLE: Myopia epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tailor, T.W. Olsen, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Prashant Tailor: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Olsen: Commercial Relationship(s);Code O (Owner):Imacular Regeneration LLC

ABSTRACT BODY:

Purpose: The COVID-19 pandemic has caused societal, behavioral changes that have resulted in increased near work and less outdoor time. These changes may influence myopia progression. We performed a retrospective, cross-sectional prevalence study on the population base in Olmsted County, Minnesota to determine if there are short-term changes in myopia.

Methods: Individuals living in Olmsted County who received ophthalmic care at Mayo Clinic Rochester from 2018 to 2021 were analyzed. Exclusion criteria included 1) visually significant cataract, 2) pseudophakia, 3) prior refractive surgery and 4) Age < 6 years. Manifest refractions were converted to spherical equivalent (SE). Patients with a SE ≤ -0.5 D were classified as myopic while SE ≤ -6.0 D were classified with high myopia. Individual age, sex, visual acuity, and lens prescription data were recorded. An algorithm was designed to estimate prevalence for patients without a manifest refraction utilizing their visual acuity, as was used in the NHANES study[1].

Results: We sampled 11,783 invidiual records (8,413 adults; 3,370 children). In adults from 2018 to 2021, the prevalence of myopia was similar at 61% vs 59% (p=0.3887) and high myopia was also similar at 10% vs 9.9% (p=0.5447). In children from 2018 to 2021, the prevalence of both myopia was similar at 21% vs 17% (p=0.2) and high myopia was also similar at 2.6% and 3.8% (p=.37).

Conclusions: From 2018 to 2021, we did not find any trends in myopia development over a relatively brief, 4-year window in either pediatric or adult patients living in Olmsted County, Minnesota.

CONTROL ID: 3714655

SUBMITTER (NAME ONLY): Massood Mohammadi

TITLE: Macular GCL vs. IPL Rates of Change in Eyes with Suspected and Established Glaucoma

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mohammadi, L. Chew, J. Caprioli, K. Nouri-Mahdavi, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|M. Mohammadi, L. Chew, J. Caprioli, K. Nouri-Mahdavi, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|E. Su, R.E. Weiss, Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Massood Mohammadi: Commercial Relationship: Code N (No Commercial Relationship) | Leila Chew: Commercial Relationship: Code N (No Commercial Relationship) | Erica Su: Commercial Relationship: Code N (No Commercial Relationship) | Robert Weiss: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Caprioli: Commercial Relationship: Code N (No Commercial Relationship) | Kouros Nouri-Mahdavi: Commercial Relationship(s);Code F (Financial Support):Heidelberg Engineering;Code F (Financial Support):NIH;Code F (Financial Support):Research to Prevent Blindness

ABSTRACT BODY:

Purpose: Dendrite remodeling may occur in stressed or injured retinal ganglion cells (RGC) before apoptosis. Macular inner plexiform layer (IPL) thickness has been proposed as a biomarker for early glaucomatous damage. We compared ganglion cell layer (GCL) and IPL rates of change (RoC) in two patient cohorts with suspected and established glaucoma to test the hypothesis that RoC of IPL may be superior to GCL for detection of early glaucoma damage.

Methods: 64 eyes (46 patients) with suspected glaucoma (GS) and 112 eyes (112 patients) with moderate to severe visual field damage and ≥2 years of follow-up and ≥3 macular OCT scans were recruited. The GS cohort had suspicious optic discs with normal OCT retinal nerve fiber layer thickness at baseline. GCL and IPL measurements from the central 18° of the macula (36 superpixels, 3°×3° each) were exported. A Bayesian linear hierarchical model with random intercepts, slopes, and random variances was fitted to estimate GCL and IPL RoC at superpixels. RoC were normalized by dividing absolute rates by their SD. Normalized RoC and proportions of superpixels with significantly negative RoC for GCL and IPL were compared within the GS and glaucoma groups.

Results: The average (SD) baseline age, mean (SD) follow-up time, and average (SD) number of OCT scans were 61.3 (13.7) years, 3.5 (0.7) years and 4.2 (1.0) scans, respectively, in the GS group and 66.9 (8.5) years, 3.6 (0.4) years and 7.3 (1.1) scans in the glaucoma group. In the GS group, the mean normalized RoC (averaged across all superpixels) was faster for GCL than IPL (0.66 vs.0.32 SD unit per year). In 24 out of 36 superpixels, average GCL RoC was significantly negative while only 8 out of 36 superpixels showed significant negative IPL RoC ($p=0.003$)(Fig.1). In the glaucoma group, the mean normalized RoC was faster for IPL than GCL (0.46 vs.0.28 SD unit per year). 13 out of 36 and 23 out of 36 superpixels had significant negative RoC for GCL and IPL, respectively ($p=0.006$)(Fig.1).

Conclusions: GCL thickness is more likely to demonstrate significant negative slopes compared to IPL in very early stages of glaucoma. In contrast, in eyes with established glaucoma, the IPL change rates tended to provide more information(Fig.2). These results confirm our prior findings based on cross-sectional data. The sum of GCL and IPL thickness may provide a stronger signal to detect change in the macula.

CONTROL ID: 3714656

SUBMITTER (NAME ONLY): Mark Kleinman

TITLE: Acetyl-histone profiling of degenerating RPE after selective HDAC1/2 inhibition

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Kleinman, R. Dubey, K. jung, A. Davila, S.K. Dubey, Surgery, East Tennessee State University, Johnson City, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Mark Kleinman: Commercial Relationship: Code N (No Commercial Relationship) | Rashmi Dubey: Commercial Relationship: Code N (No Commercial Relationship) | kyung sik jung: Commercial Relationship: Code N (No Commercial Relationship) | Alex Davila: Commercial Relationship: Code N (No Commercial Relationship) | Sushil Dubey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Preliminary data demonstrate significant down-regulation of HDAC1/2 expression in the RPE of eyes with atrophic age-related macular degeneration (AMD). RPE cytotoxicity and patterned inflammatory gene expression were observed after Class I HDAC inhibition in vitro and in vivo. In this study, we investigated the cellular effects of a potent HDAC1/2 inhibitor, romidepsin, on RPE cell viability and interrogated unique signatures of acetyl-histone marks.

Methods: Short term and long-term (>21d) primary human RPE (hRPE) isolates (n=3, Lonza) and ARPE19 cultures were exposed to a dose range of romidepsin (0.1/0.5/1 ng/mL, Selleck). Cell viability was assessed using MTS assay (AQueous One, Promega, measurement of trans-epithelial resistance (TER) and evaluation of tight-junction by ZO-1 immunofluorescence. Levels of histone acetylation (H3Ac/H4Ac) were measured by Western Blotting while specific acetyl-histone marks were evaluated by multiplex assay (EpiGentek). Statistical analyses were performed with ANOVA and Mann-Whitney U test.

Results: Romidepsin induced a dose-dependent loss of RPE cell viability by MTS assay ($P<0.05$) in both short-term and long-term RPE cultures with decreased TER ($P<0.05$) and degradation of ZO-1 tight junctions. Western blotting revealed significantly upgregulated H3ac and H4ac levels after romidepsin treatment (12/24h, $P<0.05$). Multiplex assays identified a specific acetyl-histone signature with elevated levels of H3k14ac, H3k18ac, H4k8ac and H4k16ac.

Conclusions: Class I HDAC expression is critical for RPE homeostasis and cell viability. Targeted inhibition of HDAC1/2 with romidepsin leads to loss of cell viability, decreased TER, disorganized tight junctions in long-term hRPE cultures. There is robust upregulation of acetylated H3/H4 with a specific signature of acetyl-histone marks that may be critical in the epigenetic regulation of RPE cell death. These histone marks may be important in signaling pathways of RPE degeneration that occur during progression of atrophic AMD and may serve as novel targets for AMD therapeutics.

CONTROL ID: 3714657

SUBMITTER (NAME ONLY): Christine Xu

TITLE: Risk factors and outcomes of glaucoma following cataract surgery in infancy for persistent fetal vasculature (PFV)-related cataract

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Xu, Harvard Medical School, Boston, Massachusetts, UNITED STATES|D. Vanderveen, B. Gangwani, I. Oke, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a common complication following cataract surgery in patients with persistent fetal vasculature (PFV). We aim to identify risk factors predisposing to glaucoma in this population and characterize the optic nerve appearance and treatment outcomes.

Methods: This is a retrospective cohort study of patients with PFV-related cataracts at a single tertiary care center. We included all infants who underwent cataract surgery without primary intraocular lens placement before one year of age, with at least five years of follow-up. The primary outcome was a diagnosis of glaucoma or ocular hypertension requiring treatment. Risk factors investigated included age, sex, and the presence of microcornea (horizontal diameter less than 10 mm). Secondary outcomes included type of treatment, optic nerve appearance, and visual acuity. We performed univariate and multivariable regressions and report odds ratios (OR) and 95% confidence intervals (CIs).

Results: 36 eyes from 34 patients were included. The median age at the time of cataract surgery was 1.3 months (Interquartile range [IQR] 1.0-2.2 months). 38% of patients were female and 50% were left eyes. Following surgery, 39% of eyes developed glaucoma or ocular hypertension. The median age of glaucoma diagnosis was 2.5 years (IQR 0.4-6.2 years). The median cup to disc ratio was 0.25 and 50% had visual acuity of 20/200 or worse. All of these patients were treated with topical medication such as timolol, latanoprost, and timolol-dorzolamide. Six of the eyes underwent glaucoma surgery at a median age of 7.5 months (IQR 3.7-45.2 months), most commonly goniotomy and trabeculotomy. Patients who developed glaucoma were more likely to have microcornea (77% vs. 36%, $p = 0.040$) (Table 1). While univariate regression identified microcornea as a significant risk factor for glaucoma in eyes with PFV (OR 4.37, 95% CI 1.08-20.6, $p = 0.046$), after adjusting for age at surgery, microcornea was no longer significant (OR 3.09, 95% CI 0.68-16.0, $p = 0.2$) (Table 2).

Conclusions: Microcornea is frequently observed in the patients with PFV who develop glaucoma or ocular hypertension. A greater understanding of potential risk factors and treatment outcomes can help guide interventions.

CONTROL ID: 3714658

SUBMITTER (NAME ONLY): Timothy Nguyen

TITLE: Quality of Life Analysis in Patients with Retinitis Pigmentosa

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Nguyen, J. So, S.M. Duff, S. Grover, J. Chen, Ophthalmology, University of Florida, Florida, UNITED STATES|Y. Song, Indiana University, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure: Timothy Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Joshua So: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Duff: Commercial Relationship: Code N (No Commercial Relationship) | Yiqing Song: Commercial Relationship: Code N (No Commercial Relationship) | Sandeep Grover: Commercial Relationship: Code N (No Commercial Relationship) | Jinghua Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) is an inherited retinal disease (IRD) with progressive loss of night and peripheral vision. We conducted this survey study to assess the quality of life of patients with RP.

Methods: A questionnaire study was performed on 34 RP patients from the University of Florida Department of Ophthalmology's patient base. Each patient was called over the phone to take part in the survey. Data on education, employment, and medical care status were collected. Each of their responses were then analyzed collectively with other patients' responses.

Results: A total of 34 patients with RP (10 males, 24 females) with a mean age of 55.1 +/- 18.9 were assessed (range, 21-91 years) 76% of patients (26 of 34) noticed visual difficulties under the age of 18. At the time of data collection, one patient was still attending school. Of those who finished school, 33% of patients who graduated (11 of 33) only have a high school diploma, while 58% (19 of 33) have a college degree. Three patients only completed primary education. 11 of the 33 patients reported that they did not finish all the education they had intended to complete. Two of the 11 patients reported that they could not finish their education due to visual difficulties. 42% (14 of 33) of those who were no longer in school were unemployed (9 females, 5 males). Of the 42% who were unemployed, 57% of patients did not have a job due to vision. 33 out of 34 patients (97%) were insured. Of those who were insured, 18% (6 of 33) were not satisfied with their insurance. 29% of patients had financial and visual difficulties obtaining visual aids and only 53% have disability insurance.

Conclusions: The results of our study show that RP may affect the levels of education, employment, and access to medical care. Further studies and statistical analysis, such as obtaining vision, visual field, and optical coherence topography (OCT) data as well as comparing our results to normal population, are required to identify and confirm the contributing factors of the quality of life of patients with RP.

CONTROL ID: 3714659

SUBMITTER (NAME ONLY): Yuniar Ningtiyas

TITLE: Psychometric characteristics and use of 360-degree assessment tool for ophthalmology residents in Indonesia

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.S. Ningtiyas, S. Sutjipto, Y. Primitasari, E. Komaratih, Department of Ophthalmology, Dr. Soetomo Academic General Hospital - Universitas Airlangga, Surabaya, East Java, INDONESIA|

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ABSTRACT BODY:

Purpose: Competency-based medical education requires a robust and multifaceted evaluation system. We performed a cross-sectional study of ophthalmology residents to determine the validity, reliability, and feasibility of 360-degree assessment tool for assessing competency in professionalism, interpersonal and communication skills, and system-based practice.

Methods: A 5-point Likert-type online questionnaire was completed by attendings, nurses and allied health staffs, patients/families, and resident peers after each ophthalmology resident rotation from January 2021 to June 2021. The questionnaire was adapted from the International Council of Ophthalmology (ICO) 360-degree assessment tool. The Indonesian version questionnaire was developed using forward and backward translation.

Results: A total of 534 evaluations were completed for 42 residents. Validity test using Pearson correlation analysis between all combinations of evaluators ranged from 0.51 to 0.94 and all were statistically significant ($p<.01$). The internal consistency reliability of the instrument was a Cronbach's alpha of 0.92, 0.80, 0.86, and 0.93 for attending doctor, nurse and allied health staff, patient/family, and resident peer, respectively. Sixty percent of study participants felt that this assessment contributed positively to the operation of ophthalmology service. All evaluators rated residents highly (mean Likert score range, 3.96 – 4.60). Patient/families rated the resident highest for interpersonal and communication skills (4.54±0.12) and system-based practice (4.60±0.16) among other evaluator groups. Nurse and allied health staff rated resident highest for professionalism (4.58±0.35). Ratings by year of training varied for each competency. No significant differences were found between rating from patient/families and their educational background ($p>.05$).

Conclusions: The 360-degree assessment tool appears to be valid, reliable, and feasible to evaluate ophthalmology residents' competency in professionalism, interpersonal and communication skills, and system-based practice. Information from the assessment may provide multidimensional formative feedback for residents' development and improve residents' performance.

CONTROL ID: 3714661

SUBMITTER (NAME ONLY): Alfonso Iovieno

TITLE: Novel hyaluronic acid-based corneal stromal replacement

SESSION TITLE: Corneal stromal biology, wound healing modulators, and regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Iovieno, S. Yeung, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|R. Ghaemi, V. Yadav, The University of British Columbia, Vancouver, British Columbia, CANADA|

Commercial Relationships Disclosure: Alfonso Iovieno: Commercial Relationship: Code N (No Commercial Relationship) | Roza Ghaemi: Commercial Relationship: Code N (No Commercial Relationship) | Vikramaditya Yadav: Commercial Relationship: Code N (No Commercial Relationship) | Sonia Yeung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To develop a durable, biocompatible, transparent, artificial corneal stromal substitute that would mimic the human corneal stroma in key physical and physiological functions

Methods: a hyaluronic acid (HA)-based 500 μm hydrogel was fabricated and then crosslinked. Compounds ratios as well as crosslinking condition was systematically evaluated by assessing swelling ratio (hydrogel weight after submerging in PBS), mechanical strength (rheometer with cone-and-plate geometry), biodegradability (remaining weight after submerging in an enzyme cocktail), optical transparency (spectrophotometer at UV-Visible wavelengths) and glucose/albumin permeability (glucose and albumin concentration across the hydrogel) of the resulting hydrogels. The hydrogel was then coated with an antiangiogenic compound to prevent neovascularization

Results: all composites were completely clear (>88% transmittance) with refractive index of ~1.3, which is very close to that of the human cornea. Hydrogels were shown to have an equilibrium water content of ~90% with less than 5% degradation in enzymatic solution over 2 months. Tensile strength and maximum elongation of the hydrogels were found to be 1.47 MPa and 8.57% respectively, which are comparable to native cornea. The presence of the specific bonds in the hydrogel structure and the crosslinking of the antiangiogenic compound coating on the walls were confirmed by Fourier Transform Infrared Spectra

Conclusions: We have been able to produce a hyaluronic acid-based co-polymer with optical and mechanical properties similar to the human corneal stroma. Further studies would be needed to test biocompatibility in vitro and in animal models

CONTROL ID: 3714662

SUBMITTER (NAME ONLY): Larry David

TITLE: Creation of a semi-synthetic γS-crystallin to support studies of age-related modifications in cataract

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.L. David, F.I. Valiyaveetil, R. Reddi, K.A. Haverson, U.P. Shinde, Chemical Physiology & Biochemistry, Oregon Health & Science University, Portland, Oregon, UNITED STATES|V.S. Halls, Medicinal Chemistry Shared Resource, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K. Zientek, Proteomics Shared Resource, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K.J. Lampi, Integrative Biosciences, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a semi-synthetic approach using native chemical ligation to introduce specific sites of age-related modifications into crystallins to examine their impact on protein structure and contribution to cataract.

Methods: An N-terminally SUMO tagged human γS-crystallin containing residues 16-177 was expressed containing a Q16C mutation to act as a ligation site. Following removal of the SUMO tag using ulp-1 protease, the resultant γS 16-177 was solubilized in 6M guanidine and ligated to a synthetic γS 1-15 peptide containing a C-terminal peptide thioester using 4-mercaptophenylacetic acid under reducing conditions, followed by dialysis and purification using cation ion exchange chromatography. Full length γS-crystallin was confirmed by mass spectrometry and proper folding of the protein examined by both CD spectroscopy and hydrogen/deuterium exchange to measure the number of surface exposed amides in the whole protein. The ligated product was also compared to full length bacterially expressed γS Q16C, as well as denatured/refolded γS Q16C, and wild type γS.

Results: The semi-synthetic γS crystallin was successfully created and refolded in its native state as supported by an identical CD spectrum and similar numbers of rapidly exchanging amide residues as fully bacterially expressed versions of wild type γS, Q16C γS, and denatured/refolded Q16C γS.

Conclusions: This is the first known successful use of native protein ligation to create a semi-synthetic crystallin in its native state. The methodology will allow introduction of specific isoaspartate residues in γS at residues D12 and N14, two sites containing isoasp modifications in the insoluble protein of human cataractous lenses. Introduction of these age-related modifications in γS will test whether they contribute to cataract or are merely associative. The technique should prove useful to examine other age-related modifications in crystallins and provide more relevant information than previous studies relying on only in-vitro incubation or mutagenesis.

CONTROL ID: 3714663

SUBMITTER (NAME ONLY): Zhaoxia Zhang

TITLE: Subthreshold Photocoagulation Treatment of Recurrent Central Serous Chorioretinopathy with Pachychoroid Pigment Epitheliopathy

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Zhang, B. Sun, J. Xie, G. Hou, Shanxi Eye Hospital, Taiyuan, Shanxi, CHINA|

Commercial Relationships Disclosure: Zhaoxia Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Bin Sun: Commercial Relationship: Code N (No Commercial Relationship) | Juan Xie: Commercial Relationship: Code N (No Commercial Relationship) | Guangping Hou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pachychoroid spectrum disorders are characterized by attenuation of the choriocapillaris overlying dilated choroidal veins, and associated with progressive retinal pigment epithelium dysfunction and neovascularization, including central serous chorioretinopathy (CSC) and pachychoroid pigment epitheliopathy (PPE). Subthreshold laser therapy is known to have RPE function as its main target. In this study, we evaluated subthreshold photocoagulation treatment for patients diagnosed with CSC and PPE.

Methods: Participants in this study were 7 patients (7 eyes; 4 males and 3 females) with CSC and PPE, who underwent enhanced depth imaging optical coherence tomography (EDI-OCT), fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA). Subthreshold photocoagulation was performed to treat pigment epithelial detachment (PED) at site of PPE outside of macular, which was performed with the following parameters: 5% duty cycle, 200 ms pulse duration, 160 μm spot size and 50% power of the barely visible threshold. Best corrected visual acuity (BCVA), the central choroidal thickness (CCT), and choroidal thickness (CT) at the lesion site of PPE were measured during follow-up.

Results: Of 7 eyes with recurrent CSC and PPE (Snellen< 20/40), FFA demonstrated one or multiple focal leaks at the level of RPE in 2 eyes, and multiple indistinct leaks in 5 eyes. ICGA showed multifocal areas of choroidal hyperpermeability as hyperfluorescent patches in the mid phase in all 7 eyes. EDI-OCT revealed macular serous retinal detachment (SRD) and irregular RPE elevation or PED outside of macular, CT increased at the lesion site of SRD and RPE characterized by dilated choroidal vessels in Haller's layer (pachyvessels), accompanied by attenuation of choriocapillaris. After subthreshold photocoagulation at the site of PPE (e.g. PED) outside of macular, with the recovery of SRD and RPE lesion, CCT and CT decreased significantly ($P<0.05$).

Conclusions: In the eyes of recurrent CSC with PPE, subthreshold photocoagulation at the lesion site of PPE can resolve CSC within macular. Simultaneously, pachychoroid at the sites of CSC and PPE also improved. These results may support that PPE and CSC clinically overlap and have a common pathogenic background.

CONTROL ID: 3714664

SUBMITTER (NAME ONLY): Joshua Huang

TITLE: Vision outcomes of a vision screening program amongst schoolchildren in underserved, rural, Zimba, Zambia

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, J. Huang, A. Steeves, P. Huang, K. Huang, S. Huang, W. Astle, J. Huang, P. Huang, University of Calgary, Calgary, Alberta, CANADA|J. Huang, University of Hawai'i at Manoa, Honolulu, Hawaii, UNITED STATES|B. Samoyo, The University of Zambia, ZAMBIA|

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ABSTRACT BODY:

Purpose: To investigate the prevalence of visual acuity impairment and external eye abnormalities in school-aged children in Zimba, Zambia.

Methods: Vision screening was performed in children 5 to 18 years old (grades kindergarten to grade 9) between July-August 2019. The vision screening program involved the assessment of visual acuity, pupil size, colour vision, and reading vision. An external eye examination of the eyelids, orbit, cornea, and iris was also performed. Demographic data collected included patient age and gender. Screening failures were defined as any child presenting with a visual acuity of 20/40 or worse or ≥2-line interocular difference between eyes. Schoolchildren with abnormalities upon external eye examination were also classified as a screening failure. All screening failures were referred to the eye clinic for further assessment.

Results: A total of 676 schoolchildren underwent vision screening. 3.70% (25/676) of schoolchildren did not pass the vision screening program and were referred to the local ophthalmology clinic for further assessment. 1.33% (9/676) of schoolchildren did not pass the vision screening criterion for visual acuity. 2.4% (17/676) did not pass the vision screening criterion based on external eye examination. One student failed both visual acuity and external eye exams. Mild vision impairment (visual acuity between 20/40 to 20/60) was the most common amongst schoolchildren, comprising 55.56% (5/9) of visual acuity failures. Corneal/conjunctival scars were the most common external eye abnormalities amongst schoolchildren, comprising 47.06% (8/17) of external eye exam failures.

Conclusions: Our study is the first to report on visual acuity impairment and external eye abnormalities amongst schoolchildren in rural Zimba, Zambia. A total of 3.70% schoolchildren did not pass the vision screening program and were referred for further ophthalmic assessment. 1.33% of schoolchildren did not pass the vision screening criterion for visual acuity. 2.4% did not pass the vision screening criterion based on external eye examination. Compared to other regions around the world with similar vision screening criterion, a low percentage of schoolchildren failed the visual screening program.

CONTROL ID: 3714665

SUBMITTER (NAME ONLY): Rachel Breliant

TITLE: Effect of low-dose Atropine on Binocular Vision in Children Aged 6 to 17 Years

SESSION TITLE: Myopia: Clinical Interventions and Diagnostics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.E. Breliant, Y. Pang, A. Bandstra, V. Kattouf, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effect of 0.01%, 0.03%, and 0.05% atropine on pupil size and binocular vision function in children aged 6 to 17 years.

Methods: Forty-six children (28 girls and 18 boys) aged 6 to 17 years were randomized into 4 groups: placebo (n= 10), 0.01% (n=13), 0.03% (n= 11), or 0.05% (n= 12) atropine. One drop of atropine was administered into each eye once. The following measurements were collected before applying atropine and 30 minutes, 60 minutes, and 24 hours following application of atropine: pupil size in bright and dim illumination, associated phoria by cover test at distance and near, near point of convergence (NPC) break and recovery, 5 times repeat of NPC (stamina), NPC through red and green glasses (fragility), negative fusional vergence at near, and positive fusional vergence at near. Repeated measures ANOVA with post hoc comparison was performed to determine the effect of 0.01%, 0.03%, and 0.05% atropine eye drops on binocular vision measurement at each time point.

Results: The mean age of participants was 10.73 ±3.01 years. Average spherical equivalence by cycloplegic refraction was -1.70 ± 1.98 D and -1.72 ± 2.10 D, OD and OS respectively. Difference in pupil diameters in bright and dim illumination was statistically significant when comparing all 3 atropine groups to placebo group over time ($P < 0.001$). Atropine eye drops had the most effect on pupil diameter 60 mins after installation ($P<0.001$). Pupil diameter was partially recovered at 24 hours with no statistical significance compared to the 30-minute time point ($P >0.05$), although still significantly different from baseline in the 0.03% atropine group ($P=0.002$). In the 0.01% and 0.05% atropine groups pupil diameter fully recovered after 24 hours with no significant difference from baseline ($Ps>0.05$). There was no significant difference in binocular vision measurements including associated phoria, NPC, NPC stamina and fragility, negative fusional vergence, and positive fusional vergence(all Ps >0.05)

Conclusions: Pupil size was significantly enlarged by 0.01%, 0.03%, and 0.05% atropine in both dim and bright illumination with more effect at 60 minutes after application. However, low dose atropine eye drops have no effect on binocular vision measurements. Thus, in respect to binocular vision, it is relatively safe to use low-dose atropine to treat myopia progression in children aged 6 to 17 years.

CONTROL ID: 3714666

SUBMITTER (NAME ONLY): Jared Moon

TITLE: Program Directors of Accredited Pediatric Ophthalmology Programs: A Descriptive Analysis

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Moon, E. Bowden, E. Crowell, Mitchel and Shannon Wong Eye Institute, The University of Texas at Austin Dell Medical School, Austin, Texas, UNITED STATES|M. Geloneck, Dell Children's Eye Center, Texas, UNITED STATES|

Commercial Relationships Disclosure: Jared Moon: Commercial Relationship: Code N (No Commercial Relationship) | Eileen Bowden: Commercial Relationship: Code N (No Commercial Relationship) | Eric Crowell: Commercial Relationship: Code N (No Commercial Relationship) | Megan Geloneck: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine the academic background, scholarly activity, and demographic characteristics of pediatric ophthalmology program directors (PDs) through cross-sectional analysis.

Methods: All pediatric ophthalmology PDs of fellowship programs that participated in the San Francisco Match in January 2020 were included. Information was collected through online search of publicly available sources from July 7th, 2021 to July 23rd, 2021. Scholarly activity was measured by the number of peer-reviewed articles published as well as the Hirsch index.

Results: Of the 43 pediatric ophthalmology fellowship programs reviewed, 22 (51%) had a male PD, and 21 (49%) had a female PD. The mean age of current PDs was 53.5 ± 8.8 years old. The average age at time of appointment was 39.2 ± 7.7 years old. There was a significant difference between the current age of female PDs (49 ± 7.3) and male PDs (57.8 ± 8; $P < 0.0001$).

Thirty-eight (88%) PDs attended medical school in the United States. Forty-two have an MD (98%) and one (2%) has an MBBCh. Thirty-nine (91%) PDs completed ophthalmology residency in the U.S. Forty-two (98%) completed a fellowship in pediatric ophthalmology in the U.S. Ten (23%) of the PDs were dual fellowship trained.

The average number of peer-reviewed publications published by each pediatric ophthalmology PD was 62 ± 77.4 (median 31, range 3-299). There was a statistically significantly higher Hirsch-index among male PDs (23.9 ± 15.7) than female PDs (10.3 ± 10.1; $P = 0.0017$). There also was a higher number of peer-reviewed publications for male PDs (91 ± 89) than female PDs (31.5 ± 48.6; $P = 0.0099$).

Conclusions: Pediatric ophthalmology fellowship programs have equal representation of male and female program directors. This is unique to this subspecialty as women continue to be underrepresented in ophthalmology. The reasons for higher scholarly output of male versus female PDs is unclear, and further research will be helpful to address this disparity.

CONTROL ID: 3714668

SUBMITTER (NAME ONLY): Acadia Moeyersoms

TITLE: Understanding the role of MYB in LGACC in developed in-vitro model

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.H. Moeyersoms, D. Pelaez, Cancer Biology, University of Miami, Coral Gables, Florida, UNITED STATES|D. Pelaez, Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lacrimal gland adenoid cystic carcinoma (LGACC) is a rare but highly lethal indolent cancer originating in the cells of secretory glands, primarily of the head and neck. With the 10-year survival rate of 20%, the only life extending technique is to remove the eye and surrounding socket contents followed by extensive chemoradiation. Despite radical treatment, LGACC has a poorer prognosis than head and neck adenoid cystic carcinoma (ACC) in part due to its propensity for perineural invasion, and hematogenous and intracranial spread. Extensive genome analysis of adenoid cystic carcinoma (ACC) of the head and neck has uncovered a high mutation rate of MYB that leads to overexpression. This event is thought to be the key driving mutation of ACC that has been well characterized in tissue samples. A pressing issue in the field of ACC research is the loss of MYB expression in cell lines developed from tumor tissue. As MYB overexpression is a key characteristic of ACC, it is important for cell line models to maintain the overexpression. Here, we develop the tools and cell lines essential for the molecular and in vitro characterization of MYB in LGACC.

Methods: We completed RNA sequencing on our 12 LGACC cell lines and identified a loss of MYB expression, consistent with head and neck ACC cell lines. To address this issue, we transduced 3 LGACC and 3 normal lacrimal gland cell lines with a dual vector system that includes tet-inducible MYB expression to reintroduce its overexpression in the LGACC cells. We validated MYB overexpression via RT-qPCR and western blot. We completed RNA sequencing on our newly developed cell lines and have studied the effects of reintroducing MYB expression in migration and proliferation assays.

Results: We developed new LGACC cell lines with inducible MYB expression, essential for downstream in vitro characterization of this key molecular driver underlying cancer progression in patients. We characterized how the overexpression of MYB in normal and LGACC cells changes the proliferation and migration.

Conclusions: To advance the understanding and treatment of LGACC, there is a need for a validated model to be able to LGACC in-vitro. We have developed cell line models that have regained the main driver of ACC. This now allows us to further understand the role of MYB in LGACC progression and have a model to test treatments.

CONTROL ID: 3714669

SUBMITTER (NAME ONLY): Mary Drekh

TITLE: Evaluation of a Novel Targeted-Sequencing Panel for Detection of FZD4 Gene Variants in Subjects with Familial Exudative Vitreo-Retinopathy.

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Drekh, K.P. Mitton, W. Dailey, K.A. Drenser, William Beaumont School of Medicine, Oakland University, Rochester, Michigan, UNITED STATES|M. Drekh, K.P. Mitton, W. Dailey, K.A. Drenser, Eye research institute, Oakland University, Rochester, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Identify potential pathogenic mutations in the Frizzled 4 gene (FZD4) in patients with clinically diagnosed Familial Exudative Vitreo-Retinopathy (FEVR). FEVR is caused by variants impacting several genes including the FZD4 gene. FZD4 is the central cognate receptor for Norrin WNT signaling in the human retinal endothelium. 76 subjects diagnosed with FEVR, and near relatives, were sequenced using a custom Ampliseq panel that includes eight genes related to FEVR/ND and Retinoschisis (NDP, CTNNB1, TSPAN12, KIF11, FZD4, LRP5, ZNF408, RS1).

Methods: A custom Ampliseq targeted panel (180 amplicons) for 8 genes was designed with Illumina's Design Studio. The targeted panel used three pools (PCR reactions) per patient sample for complete coverage of 83 exons with 25 bp of adjacent intron sequence. Targeted Genes were: NDP (ChrX), RS1 (Chr10); CTNNB1 (Chr3); TSPAN12 (Chr7); KIF11 (Chr10), FZD4 (Chr11), LRP5 (Chr11), and ZNF408 (Chr11). Ampliseq libraries were sequenced on the Illumina iSeq-100 platform. Variant impacts and allele frequency data were obtained from ClinVar and The Genome Aggregation Databases (gnomAD).

Results: 33 protein-altering variants were found in six FEVR/Norrie Disease related genes. Of note, 9/33 (27.3%) of the variants were present in the FZD4 gene. The 9 variants included 1 pathogenic, 1 novel pathogenic variant (Cys450Ter) and 3 of uncertain significance. 95.5% of the base reads were > Q30 quality, the percent on-target bases passing filer was 92.2%, and the average sequencing depth coverage for the entire panel was 978.

Conclusions: Our custom targeted-sequencing panel was developed with the intention to detect gene variants associated with FEVR, Norrie Disease and Retinoschisis. The panel’s sequencing coverage was of sufficient depth to detect protein-altering variants in the FZD4 gene and to determine variant zygosity.

CONTROL ID: 3714671

SUBMITTER (NAME ONLY): Kevin Schneider

TITLE: The impact of subconjunctival injections of Humanin-G loaded microspheres on RCS rat model of retinal degeneration

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Schneider, M. Ozgul, V.N. Ianopol, S. Atilano, B. Lin, M.J. Seiler, M. Kenney, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Kevin Schneider: Commercial Relationship: Code N (No Commercial Relationship) | Mustafa Ozgul: Commercial Relationship: Code N (No Commercial Relationship) | Vasilica Ianopol: Commercial Relationship: Code N (No Commercial Relationship) | Shari Atilano: Commercial Relationship: Code N (No Commercial Relationship) | Bin Lin: Commercial Relationship: Code N (No Commercial Relationship) | Magdalene Seiler: Commercial Relationship: Code N (No Commercial Relationship) | M.Cristina Kenney: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mitochondrially Derived Peptides (MDPs) are short peptides encoded off the short open reading frames (sORF) of human mitochondrial DNA. Humanin (HN), a 24 amino acid MDP has both in vitro and in vivo benefits improving cell survival. Humanin-G (HNG) has a serine-to-glycine substitution at position 14, making it a 1000-fold more potent variant. We hypothesized that subconjunctival injection of HNG loaded microspheres (HNG-MS) would improve retinal function and alter gene expression in both RPE and retina of treated RCS rats.

Methods: 21 day old RCS rats received subconjunctival injections in both eyes of (1) 286µg Empty-MS in 100µL Buffered Saline Solution (BSS) (N=6); (2) 286µg HNG-MS in 100µL BSS (N=5); or (3) received no injection (N=6). Functional Analyses. Scotopic & Photopic Threshold Response Electroretinography (ERGs) was performed at 14 and 27 Days After Starting Treatment (DAST). Molecular Analyses. Animals were sacrificed after 4 weeks. One eye was used for immunohistochemistry (IHC), and the other for eye for RNA extraction and gene expression analysis (qRT-PCR). Statistical analysis was performed using Graphpad Prism, using Mann-Whitney U. The significance set at $p<0.05$.

Results: Subconjunctival injections of HNG-MS significantly improved the ERG Scotopic A-wave (166% increase, P=0.0057) compared to the Empty-MS treated RCS rats. The Scotopic B-wave trended towards improvement but did not reach significance (59% increase, P=0.0668). (HNG-MS, n=4; Empty-MS, n=6; NT (n=2). (Fig.1) At 30 DAST with HNG-MS, in neuroretinal cells there was decreased expression of inflammation genes (TNFa 0.53-fold, P=0.032; IL1B, 0.47-fold, P=0.009; CCL2, 0.64-fold, P=0.016) (Fig. 2); In RPE cells, there was decreased expression of apoptosis genes (DDIT3, 0.78-fold, P=0.03; CASP3, 0.7-fold P=0.016; CASP7, 0.77-fold, P=0.029; CASP9, 0.77-fold P=0.016) (Fig. 3), along with antioxidant (SOD2, 0.64-fold P=0.016) and inflammatory genes (TNFa, 0.11-fold, P=0.029; IL1B, 0.25-fold, P=0.004) (Fig. 4). Significance of gene expression values for HNG-MS compared with Empty-MS.

Conclusions: The subconjunctival injection of HNG-MS provides significant improvement in retinal function and beneficial impact on gene expression in RPE and neuroretina of RCS rats. This supports our hypothesis that HNG loaded microspheres can serve as an effective delivery method for HNG in models of retinal degeneration.

CONTROL ID: 3714672

SUBMITTER (NAME ONLY): Roberto Gonzalez-Salinas

TITLE: Comparison of Cumulative dissipated energy using the ABS Mini-Tip vs. the Mini-flared Kelman tip in femtosecond laser-assisted cataract surgery (FLACS).

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gonzalez-Salinas, R. Aguilar-Díaz, G. Fonseca-Aguirre, Anterior Segment Surgery Department, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|A. Peña-Aceves, Oftalmología Profesional, Guadalajara, MEXICO|P. Navarro, Asociacion Medica de Los Andes, Bogota, COLOMBIA|

Commercial Relationships Disclosure: Roberto Gonzalez-Salinas: Commercial Relationship(s);Code C (Consultant/Contractor):LayerBio Inc. | Roberto Aguilar-Díaz: Commercial Relationship: Code N (No Commercial Relationship) | Adolfo Peña-Aceves: Commercial Relationship: Code N (No Commercial Relationship) | Gustavo U. Fonseca-Aguirre: Commercial Relationship: Code N (No Commercial Relationship) | Pedro-Iván Navarro: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This cross-sectional study included patients diagnosed with senile cataracts who underwent FLACS at the Anterior Segment Surgery Department, Asociación para Evitar la Ceguera en México I.A.P., Mexico City, Mexico. Included patients were assigned to two groups for either the Gravity-Fluidics system (Infiniti® Vision System) or Active-Fluidics (Centurion® Vision System) for routine phacoemulsification.

Methods: Lens epithelial cells (LECs) were obtained from the anterior capsule of type-two diabetic patients undergoing phacoemulsification surgery. All subjects were divided into two groups. Group 1 comprised T2DM patients without Proliferative Diabetic Retinopathy (PDR) and Group 2 T2DM patients with mild and moderate PDR. Immunofluorescence determined the expression of TGFß1, TGFß2, IL-1ß, IL-6, and MMP-9.

All values are expressed as means ± SD (Standard Deviation). According to data distribution, the significance between groups was evaluated using a Students-T-test or the Mann-Whitney test. Differences were defined as significant at $P < 0.05$. Gaussian distribution was determined using the D'Agostino-Pearson omnibus normality test for all variables. The SPSS 20.0 evaluated significance and GraphPad Prism 8 was used to generate figures and plots.

Results: A total of 74 eyes underwent cataract removal. Thirty-five patients were in the Gravity-Fluidics System group and thirty-nine in the Active-Fluidics System. We found a median CDE of 4.42 ± 7.92 (IQR) for the Gravity-Fluidics System group. Also, a mean phaco time of 15.88 ± 18.06, 436.3 ± 129.5 mean aspiration time, and estimated fluid of 85.74 ± 25.35. For the Active-Fluidics System group, a median of 4.81 ± 2.26 CDE ($p=0.908$), 70.96±45.19 phaco time ($P <0.001$), 413 ± 176.4 aspiration time ($p= 0.130$), and a 103 ± 52.57 estimated fluid was measured. aspiration time ($P= 0.130$) and estimated fluid ($P= 0.306$)

Conclusions: All main variables were comparable between Gravity-Fluidics and Active-Fluidic systems undergoing FLACS. CDE measurement, aspiration time, and estimated fluid failed to demonstrate statistically significant differences between groups.[MOU1] Moreover, all parameters also evidenced a good level of agreement, showing a narrow-width variability, except for CDE estimates for dense cataracts in the Bland-Altman analysis.

CONTROL ID: 3714673

SUBMITTER (NAME ONLY): Archana Boga

TITLE: EFFECTS OF ELEVATED SERUM OESTROGEN ON DRY EYE IN WOMEN UNDERGOING IN VITRO FERTILISATION

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Boga, F. Stapleton, B. Golebiowski, Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|M. Chapman, St.George's Hospital and School of Women's & Children's Health UNSW Sydney, New South Wales, AUSTRALIA|M. Chapman, IVF Australia, Southern Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Purpose: Altered oestrogen levels may play a role in the pathophysiology of dry eye in women. During IVF (in vitro fertilisation) treatment, circulating oestrogen levels increase 10-50x, providing a platform to observe the effects of systemic oestrogen on dry eye symptoms and signs. This study examined changes in ocular pain and in symptoms and signs of dry eye with IVF treatment and the relationship between sex hormones and ocular symptoms and signs.

Methods: Methods: A 2 visit study of women undergoing antagonist IVF treatment was conducted. The baseline visit was on the first day of menstruation when oestrogen levels are lowest, and the peak oestrogen visit was on day 9-11 of the treatment. Symptoms were examined using the Ocular Surface Disease Index (OSDI), Meibomian Gland Dysfunction specific questionnaire (MGD-14), Instant Ocular Symptoms Score (IOSS) and Ocular Pain Assessment Survey (OPAS). Signs of dry eye including Non-Invasive Breakup Time (NIBUT), Phenol Red Thread (PRT), meibomian gland grading and ocular surface staining were assessed. Serum levels of a panel of sex hormones, their precursors, and metabolites were assessed using mass spectrometry and immunoassay methods. Wilcoxon signed-rank test was used to assess changes in symptoms and signs. Spearman and Pearson correlations were used to evaluate association between sex hormones and symptoms and signs.

Results: Results: 40 women (36.2 ± 4.0 years) completed the study. Baseline oestradiol levels were 28.9 pg/ml (20) (median (IQR)) and peak oestradiol levels were 1360 pg/ml (1276). OPAS and SANDE scores worsened ($p=0.02$ and $p<0.01$) and NIBUT and PRT values decreased ($p=0.005$ and 0.01) at peak oestrogen visit relative to baseline. Higher oestradiol (E2) and lower luteinising hormone (LH) were associated with worsening of OSDI scores (rho = 0.34 $p=0.03$, rho= -0.49 $p=0.001$). A greater oestradiol to testosterone (E2: T) ratio was associated with shorter NIBUT (rho= -0.32, $p=0.04$) and lower progesterone (P4) was associated with greater ocular pain (rho= 0.39, $p=0.01$).

Conclusions: Conclusions: An extreme rise in oestradiol levels and changes in other sex hormones (E2: T, LH, P4) during IVF treatment resulted in increased symptoms of ocular dryness, ocular pain, and tear film alterations analogous to mild dry eye. Ocular surface symptoms and clinical signs were higher at peak oestrogen visit, but the change was not clinically significant.

CONTROL ID: 3714674

SUBMITTER (NAME ONLY): Wonkyu Ju

TITLE: Protective role of AIBP in glaucomatous retinal ganglion cells and their axons

SESSION TITLE: Neuroprotection and Neuroregeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Ju, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure: Wonkyu Ju: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The goal of this study is to investigate the effect of Apolipoprotein A-I binding protein (AIBP; gene name APOAIBP) on retinal ganglion cell survival and central visual pathway preservation in a mouse model of glaucoma

Methods: Human retina tissues sections were obtained from a normal human donor or patients with glaucoma. Five mo-old Pre-glaucomatous DBA/2J (D2) mice eyes were intravitreally transduced with recombinant adeno-associated virus serotype 2 (AAV2) constructs including AAV2-Null or AIBP for 5 months. Each of the 10-mo-old D2 mice used in this study had a single IOP measurement. RGC survival and its axon preservation were assessed by cell counting and RBPMS or NF68 immunohistochemistry. The microglial alteration was measured by IBA1 immunohistochemistry. The preservation of the central visual pathway was assessed in the superior colliculus (SC) by labeling with cholera toxin submit B (CTB).

Results: We found that RGC soma and axons were the primary sites of AIBP expression in the normal retina from a human donor. In contrast, AIBP immunoreactivity was significantly decreased in the RGC somas in glaucomatous human retinas. In 10-mo-old glaucomatous D2 mice, we found that cholesterol content was significantly elevated in the inner retinal layer, and expression of AIBP and ABCA1 was significantly decreased – by half – compared to age-matched control D2-Gpnmb^{+} mice. Based on these data, we overexpressed AIBP in the retina by in vivo delivery of AAV-AIBP. Our results demonstrated that overexpression of AIBP significantly protected RGCs in the middle and peripheral retinas and preserved their axons in the glial lamina of 10-mo-old glaucomatous D2 mice. We also found that overexpression of AIBP significantly increased microglial branch length and the number of endpoints in the middle area of the retina in 10-mo-old glaucomatous D2 mice. However, there were no changes in soma size and number of IBA1-positive microglia. Using CTB labeling, we found that 10-mo-old glaucomatous D2 mice had decreased CTB density in the SC. Surprisingly, we also found that overexpression of AIBP significantly increased CTB density in the SC of 10-mo-old glaucomatous D2 mice.

Conclusions: These findings suggest the possibility that AIBP has a therapeutic potential to treat glaucoma and other optic neuropathies

CONTROL ID: 3714675

SUBMITTER (NAME ONLY): Sean Ogle

TITLE: Agonism of the liver X receptor improves dry eye pathology in vitro and in vivo

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.D. Ogle, W.K. Jones, A.K. Ghosh, eyeNOS, Inc., Forest Park, Illinois, UNITED STATES|S. Kaja, K&P Scientific LLC, Forest Park, Illinois, UNITED STATES|W.K. Jones, Molecular Pharmacology & Neuroscience, Loyola University Chicago, Forest Park, Illinois, UNITED STATES|S. Kaja, A.K. Ghosh, R&D Division, Experimentica Ltd., Forest Park, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate pharmacologic liver X receptor agonism in human corneal epithelial cells and in a murine model for dry eye disease.

Methods: Human corneal epithelial (HCE-T) cells were seeded in 8-chamber slides grown to confluency. Cells were pre-treated with DMSO (vehicle) and or ouabagenin (0.05 µM in DMSO). One hour later, cells were exposed to hyperosmolar conditions by supplementation with a dose-range of NaCl (0 - 75 mM). after 24 h, tight junction organization was quantified by anti-zona occludens 1 (ZO-1) immunostaining. For in vivo studies, the liver X receptor agonist, T-0901317, was encapsulated into poly (lactide-co-glycolide) nanoparticles (PLGA NP). Dry eye disease was induced using the SiccaSystem® desiccating stress environment combined with transdermal administration of scopolamine to inhibit lacrimal gland exocrine function for a period of 14 d. Concomitantly, mice were treated three times daily by topical application (10 µl) with either empty PLGA NP or T-0901317-encapsulating PLGA NP. Corneal fluorescein staining was performed to assess corneal damage.

Results: Hyperosmolar stress resulted in ~30% decreased ZO-1 immunoreactivity ($P < 0.05$) and significantly reduced tight junction organization index (TiJOR). Treatment with ouabagenin fully protected against loss of ZO-1 immunoreactivity and disorganization of cellular tight junctions. Desiccating stress/ scopolamine-induced corneal damage was significantly lower in T-0901317-encapsulating PLGA NP-treated eyes (median score: 1, range 0 – 3) compared with vehicle-treated eyes (median score: 2, range 1 – 4; n= 16; $P < 0.05$).

Conclusions: LXR agonists, oubagenin and T-0901317, improve dry eye disease pathology in vitro and in vivo. These data support feasibility of the ongoing development of LXR agonists for the treatment of dry eye disease.

CONTROL ID: 3714677

SUBMITTER (NAME ONLY): Alessandro Jammal

TITLE: Incidence and risk factors for recurrent visual field progression in glaucoma

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Jammal, T. Estrela, F. Medeiros, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|C.A. Johnson, M. Wall, Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate incidence and clinical characteristics of eyes that exhibit recurrent glaucomatous visual field progression during follow-up.

Methods: This study included 12,402 standard automated perimetry (SAP) tests of 1,070 eyes of 734 subjects from the Duke Glaucoma Registry (DGR). Eyes were followed for at least 5 years with a minimum of 7 reliable SAP 24-2 tests. Progression was determined by event-based analysis using the Guided Progression Analysis (GPA, Carl-Zeiss Meditec). At the time of each event of progression, the baseline visual field tests used for reference were reset and the GPA was subsequently reapplied until the end of follow-up. Similarly, risk factors such as mean and peak intraocular pressure (IOP) were revaluated to reflect each interval leading to the next event or end of follow-up. Survival analysis for recurrent events was used to evaluate risk factors for progression.

Results: Mean follow-up time was 8.5±2.9 years, with an average of 11.6±5.5 (range: 7 to 40) SAP tests per eye. A total of 375 events of progression occurred in the population during follow-up; 279 (26%) eyes had at least 1 event, of which 76 (27%) eyes presented a recurrence and 18 (6%) eyes presented a second recurrence. The cumulative probability of showing recurrent progression at 5 years was 13% and at 10 years was 63%. Eyes with recurrent progression tended to exhibit accelerated rates of progression in the interval leading to recurrence, with average rate of SAP MD of -0.45±0.17dB/year until the first event vs. -0.95±0.81dB/year between the first and the second event ($P<0.001$). Baseline MD (HR: 1.08; 95%CI: 1.05 to 1.12 per 1 dB lower; $P<0.001$), male gender (HR: 1.76; 95%CI: 1.05 to 2.95; $P=0.033$), and age (HR: 1.66; 95%CI 1.30 to 2.11 per decade older; $P<0.001$), were significantly associated with increased risk of recurrence in the multivariable analysis.

Conclusions: In this study with a large clinical population, approximately a quarter of eyes with glaucoma with a previous event of progression presented at least a second event during follow-up. The second episode of progression had, on average, faster rates of visual field loss than the first. Lower baseline MD, male gender, and older age were significant risk factors for recurrent progression.

CONTROL ID: 3714678

SUBMITTER (NAME ONLY): Sofya Gindina

TITLE: The Relationship Between Optic Nerve Cup-to-Disc Ratio and Retinal Nerve Fiber Layer Thickness in Rhesus Macaques

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gindina, J. Danias, Ophthalmology, SUNY Downstate Health Sciences University, Brooklyn, New York, UNITED STATES|A.G. Fernandes, A.D. Melin, Anthropology and Archaeology, University of Calgary, Calgary, Alberta, CANADA|P. Alexopoulos, T. Lee, G. Wollstein, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|A. Burgos-Rodriguez, M.I. Martinez, Caribbean Primate Research Center, Universidad de Puerto Rico, San Juan, PUERTO RICO|J.P. Higham, Anthropology, New York University, New York, New York, UNITED STATES|T. Lee, Department of Population Health, NYU Langone Health, New York, New York, UNITED STATES|A.D. Melin, Alberta Children's Hospital Research Institute, Calgary, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: Increased cupping is a sign of glaucomatous optic neuropathy. It is clinically measured using the cup-to-disc ratio (CDR). Similarly, retinal nerve fiber layer (RNFL) loss is associated with disease severity. Due to the similarities in their visual systems and anatomy to humans, rhesus macaques (Macaca mulatta) often serve as a model in ophthalmology research. The purpose of this study was to evaluate the relationship between RNFL thickness and cupping in adult rhesus macaques.

Methods: A total of 52 adult animals were studied (42 females and 10 males), from all ages (range 3.3 to 25.6 years old), which were part of two social groups with high rates of ocular pathologies previously identified. Animals underwent a comprehensive eye exam, including slit-lamp biomicroscopy, pachymetry, axial length measurement, fundus photography and optical coherence tomography (OCT). CDR was determined independently by two experienced glaucoma specialists in a masked fashion from non-stereoscopic digital fundus images. The circumpapillary global and quadrant RNFL thickness was analyzed using a custom automated segmentation software. Eyes were also grouped into those with low CDR (<0.5) and those with high CDR (≥0.5). The relationship of CDR and RNFL was investigated by multilevel mixed-effects models adjusted for axial length, age, and weight.

Results: CDR ranged from 0.2 to 0.75. No statistically significant effect was detected for axial length (mean 19.57±0.57 mm), age (mean 14.5±3.3 years), weight (mean 10.6±2.9 kg) or CDR on RNFL thickness. When eyes were grouped by their CDR, no significant correlation was detected between CDR and global RNFL thickness. However, a significant correlation between CDR and RNFL thickness in the superior quadrant was found ($r = -0.068$, $p < 0.05$). Similar correlations were not detected for RNFL thickness in the inferior, nasal or temporal quadrants.

Conclusions: Higher cup-to-disc ratio is associated with increased superior RNFL loss in rhesus macaques. The CDR in rhesus macaques is likely smaller than in humans, even in animals with substantial RNFL loss, which should be tested in future studies.

CONTROL ID: 3714679

SUBMITTER (NAME ONLY): Ian Han

TITLE: Choroidal Neovascularization and Associated Structural Features in Best Vitelliform Macular Dystrophy Using Swept-Source Optical Coherence Tomography Angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Han, R.G. Coussa, M. Motlagh, J. Russell, D. Critser, E. Sohn, E.M. Stone, Department of Ophthalmology and Visual Sciences, Institute for Vision Research, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Best vitelliform macular dystrophy (BVMD) is one of the most common causes of inherited macular dystrophy. Although choroidal neovascularization (CNV) is usually associated with advanced stages of the disease, the detection of CNV in the context of a vitelliform lesion can be difficult using older imaging modalities such as fluorescein angiography. In this study, we use swept-source optical coherence tomography angiography (SS-OCTA) to evaluate the presence of CNV and to correlate structural features that may be useful for CNV detection.

Methods: This was an IRB-approved retrospective review of consecutive patients with molecularly-confirmed BVMD imaged with SS-OCTA (PLEX Elite 9000, Carl-Zeiss Meditec Inc, Dublin, California) at the University of Iowa from September 2017 to July 2020. Clinical data including age, gender, best-corrected visual acuity (BCVA), and prior clinical diagnosis of CNV (i.e., determined without SS-OCTA) were recorded. Structural features including the presence of intraretinal fluid, subretinal fluid, nodular subretinal pillar, focal choroidal excavation, or outer retinal atrophy were identified, and the presence of CNV was also assessed using 6 mm x 6 mm fovea-centered scans by expert graders. Structural features were correlated with the presence or absence of CNV on SS-OCTA using Pearson correlation with p-value <0.05 considered statistically significant.

Results: A total of 53 eyes from 27 patients (13 female; 48.1%) were included for analysis. The average age was 45 years old (range 8-79), and the mean LogMAR BCVA was 0.38 (range 0-1). A total of 14 eyes (26.4%) had a clinical diagnosis of CNV, whereas evaluation by SS-OCTA revealed the presence of CNV in 27 eyes (50.9%). Structural features potentially associated with CNV including interstitial fluid (14 eyes; 26.4%), focal choroidal excavation (8 eyes, 15.1%), nodular pillar (8 eyes; 15.1%) and outer retinal atrophy (21 eyes; 39.6%) were seen relatively frequently. Of these, the presence of focal choroidal excavation and nodular pillar were both independently correlated with the presence of CNV on SS-OCTA ($p<0.01$).

Conclusions: CNV is relatively common in eyes of patients with BVMD. SS-OCTA is a useful tool for CNV detection, and the presence of focal choroidal excavation or nodular pillars should heighten clinical suspicion for the presence of CNV.

CONTROL ID: 3714681

SUBMITTER (NAME ONLY): Amanda Miller

TITLE: Periocular melanoma-in-situ treated by Mohs micrographic surgery compared to wide local excision

SESSION TITLE: Oculoplastics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Miller, A.C. Jiang, A. Endicott, M. Ahmad, R. Kersten, B. Winn, R. Vagefi, S.R. Grob, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Amanda Miller: Commercial Relationship: Code N (No Commercial Relationship) | Alice Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Alyson Endicott: Commercial Relationship: Code N (No Commercial Relationship) | Meleha Ahmad: Commercial Relationship: Code N (No Commercial Relationship) | Robert Kersten: Commercial Relationship: Code N (No Commercial Relationship) | Bryan Winn: Commercial Relationship: Code N (No Commercial Relationship) | Reza Vagefi: Commercial Relationship: Code N (No Commercial Relationship) | Seanna Grob: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Standard treatment for melanoma in-situ (MIS) has been wide local excision (WLE). More recently, Mohs micrographic surgery has been utilized as an alternative with the benefits of frozen section margin control and its tissue sparing nature in critical anatomic locations, such as the periocular area. Herein, the authors compare WLE versus Mohs surgery in the treatment of MIS and evaluate clinical and surgical characteristics.

Methods: A retrospective review of 347 patients ≥18 years of age was obtained through a UCSF Research Database Search for patients with periocular MIS treated with WLE or Mohs with reconstruction between 2010 and 2019. On further review, 57 met inclusion criteria. The study excluded patients with purely invasive melanoma, intraocular melanoma, or other cutaneous malignancies. Demographic data, clinical characteristics, surgical treatment including defect size, Mohs or excision technique, reconstruction technique, complications, and recurrence data were obtained.

Results: A total of 57 patients were identified, 52 with periocular MIS and 5 MIS with an invasive component on pathology at initial presentation. Average follow-up time was 62 months. Within 50 patients with purely MIS and known recurrence status, there was a 3.6x increase in recurrence for patients treated first by WLE (57.7%) versus Mohs (12.5%) (p=0.0008, 95%CI[0.220-0.683]). Of 35 patients with measurements available, the average difference between the size of the lesion versus surgical defect for the Mohs group (n=24) was 426.46mm^2, while for the WLE group (n=11) was 1098.18mm^2, representing a 1.6x increase (p=0.295, 95%CI[-2023.69-680.23]), however, the finding was not significant. 79% and 75% of patients required complex repair after Mohs resection and WLE respectively. Complications occurred in 14/26 patients (53.8%) after Mohs and 6/15 (40%) after WLE, this difference was not significant (p=0.393, 95%CI[-0.175-0.452]).

Conclusions: Patients with Mohs for MIS had a lower recurrence rate than those with WLE. Although defect size was smaller for Mohs excision, it was not statistically significant. For either type of resection, complex reconstruction rates were high suggesting importance of involving an oculoplastic surgeon in periocular reconstruction.

CONTROL ID: 3714682

SUBMITTER (NAME ONLY): Karl Csaky

TITLE: Cross-Sectional Study Comparing Cone Function in Participants with Intermediate Age-Related Macular Degeneration (iAMD) and in Participants with iAMD and Non-Foveal Nascent Geographic Atrophy (nGA)

SESSION TITLE: AMD Functional Testing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.G. Csaky, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure: Karl Csaky: Commercial Relationship(s);Code C (Consultant/Contractor):Roche/Genentech, Abbvie/Allergan, Novartis, NGM Biopharmaceuticals, Johnson & Johnson, Allexion, Retrotope, Merck & Co.

ABSTRACT BODY:

Purpose: To compare cone function in participants with drusen only intermediate age-related macular degeneration (iAMD) and those with iAMD and non-foveal nascent geographic atrophy (nGA) to determine if a more advanced stage of iAMD has an effect on cone photoreceptors.

Methods: In this cross-sectional study, 60 eyes from 33 participants - 30 with drusen only (15 participants) and 30 (18 participants) with nGA determined by spectral-domain optical coherence tomography (OCT) underwent testing for visual acuity (VA), low-luminance visual acuity (LLVA), qCSF algorithm (area under log CSF (AULCSF) under both standard photopic (90 cd/m2) and low luminance (2.0 log neutral density filter)(LL AULCSF) conditions. Student's t-test was used to compare differences in LLVA, AULCSF and LL AULCSF. Correlations between VA, AULCSF and LL AULCSF were determined using Pearsons' r.

Results: In the iAMD group VA = 81 letters ± 3 (mean ± standard deviation), LLVA = 65 letters ± 4, AULCSF = 0.99 ± 0.0.5 and LL AULCSF = 0.38 ± 0.04 while in the nGA group VA = 77 letters ± 4, LLVA = 61 letters ± 8, AULCSF = 0.87 ± 23 and LL AULCSF = 0.28 ± 0.15. Student t-test demonstrated a significant difference in LL AULCSF (p= .048) but not in LLVA (p= .048) or AULCSF (p= .048). Correlation analysis demonstrated significant relationships between visual acuity and AULCSF in both iAMD and nGA groups (r = 0.83 (p<10-9); (r = 0.61 (p=0.0004) and between VA and LL AULCSF in the in the iAMD group (0.68 (p<10-5) but did not correlate with AULCSF under low luminance conditions (r = 2.9 (p= 0.13) in the nGA group.

Conclusions: Nascent GA may represent a more advanced form of iAMD that can impact preferentially one measure of low luminance = LL AULCSF. As normal vision does not correlate with this measurement this test should be considered for use in clinical trials of iAMD.

CONTROL ID: 3714683

SUBMITTER (NAME ONLY): Hamidah Mahmud

TITLE: Comparing targeted azithromycin treatment strategies in a trachoma hyperendemic area

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Mahmud, J.D. Keenan, T. Lietman, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|B.A. Haile, Z. Tadesse, S. Gebresillasie, A. Shiferaw, M. Zerihun, The Carter Center, ETHIOPIA|J.D. Keenan, T. Lietman, University of California San Francisco Department of Ophthalmology, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The World Health Organization (WHO) currently recommends annual mass azithromycin distribution to communities with a prevalence of trachomatous infection above 5%. However, after several rounds of annual mass treatment, the majority of treated individuals are not infected. We performed a cluster-randomized control trial to compare two annual targeted treatment strategies: (1) an age-targeted arm of preschool-aged children (6 months-5 years old), (2) a household-targeted arm of households with children with clinically active trachoma.

Methods: 48 communities in the trachoma hyperendemic area of Amhara, Ethiopia who previously received annual mass azithromycin distribution, were randomized to one of four arms for three years: (1) age-targeted, (2) household-targeted, (3) annual mass azithromycin, (4) stop treatment. The primary outcome of interest was PCR prevalence of ocular chlamydia infection and secondary outcome of interest was clinical trachoma (TF), both observed in children 0-9 years old.

Results: 4100 children 0-9 years old were monitored annually for ocular chlamydia and clinical trachoma. When corrected for baseline, there was no significant difference between the two targeted treatment arms for ocular chlamydia (mean difference (MD) 0.0, 95% CI -0.1 to 0.1, P=0.49) nor clinical trachoma (MD 0.0, 95% CI -0.1 to 0.1, P=0.98). Targeted treatment communities had non-significantly less infection and clinical trachoma than communities that stopped treatment (MD 0.0, 95% CI -0.1 to 0.1, P= 0.37) and (MD 0.0, 95% CI -0.1 to 0.1, P=0.78) respectively. However targeted communities also had non-significantly more infection and clinical trachoma than communities that continued WHO recommended community-wide annual mass azithromycin distribution (MD 0.0, 95% CI -0.1 to 0.1, P=0.85) and (MD 0.0, 95% CI -0.1 to 0.1, P=0.99) respectively.

Conclusions: We did not detect a difference between the age-targeted and household-targeted treatment approaches. However, our results suggest that targeted treatment is superior to stopping annual azithromycin treatment. Although targeted treatment was not enough to eliminate infection in this trachoma hyper-endemic region, even WHO guideline annual mass azithromycin distribution may not be sufficient to eliminate the trachoma burden in this area. Thus, targeted treatment strategies may still be beneficial to less trachoma endemic regions facing antibiotic resistance.

CONTROL ID: 3714684

SUBMITTER (NAME ONLY): Samuel Smithers

TITLE: Idiosyncratic Effects of Viewing Direction and Real-World Depth on Treated Strabismus Investigated with a Multi-Depth Plane Display

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Smithers, J. Skerswetat, P.J. Bex, Psychology Department, Northeastern University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Samuel Smithers: Commercial Relationship: Code N (No Commercial Relationship) | Jan Skerswetat: Commercial Relationship(s);Code I (Personal Financial Interest):PerZeption Inc.;Code P (Patent):Northeastern University, Boston, USA | Peter Bex: Commercial Relationship(s);Code I (Personal Financial Interest):PerZeption Inc. ;Code P (Patent):Northeastern University, Boston, USA

ABSTRACT BODY:

Purpose: Strabismus is a developmental visual impairment affecting 3-5% of children that can cause impaired binocular vision and a broad range of educational and social disadvantages. Strabismus assessment and treatment prioritizes near-distance primary gaze. To quantify strabismus at multiple gaze directions and depths, we developed a novel multi-depth plane display consisting of three screens at 0.4m, 1.26m and 4m.

Methods: Ocular deviation was measured in seven adults who reported a strabismus diagnosis during childhood and two typically sighted controls. Subjects were shown 27 targets in random order in a 3x3x3 grid with 10° between adjacent targets. While participants fixated on each target, an automated cover test was performed by occluding OS or OD with a LCD shutter for 2.25 sec. A head mounted eye-tracker recorded eye movements at 200Hz, and ocular deviation was calculated from the change in eye pupil position between OS, OD, and OU viewing. An optometrist also conducted a standard prism cover test (PCT) at 1m and 4m.

Results: For the controls, the overall mean deviation ± standard deviation was 0.91° ± 1.3° across gaze direction and depth, and the PCT detected no tropia. Five strabismics had received vision and/or amblyopia therapy and two had undergone surgery. Three of these subjects manifested deviations in the PCT that were correlated with eye tracker deviations at primary gaze. The overall mean ocular deviation of strabismic eyes (the eye with the larger deviation) across all directions and depths ranged from 0.32° ± 0.22° to 7.6° ± 2.3° in vision therapy subjects, and 1.2° ± 1.7° to 3.4° ± 2.1° in surgery subjects. The effect of depth and gaze direction on ocular deviation was highly idiosyncratic, e.g., for one vision therapy subject, deviations ranged from 15.8° ± 1.3° for the bottom right target at 4m to 1.9° ± 0.18° for the top target at 0.4m. In contrast, deviation was <0.4° in all directions and depths in another vision therapy subject.

Conclusions: Ocular deviations are highly dependent on gaze direction and depth in observers with a history of strabismus. Strabismus may manifest away from primary gaze and depth and may differentially impact binocular visual function. Comprehensive assessment of strabismus therefore requires measurement across multiple directions and depths of gaze and may be performed with an automated system.

CONTROL ID: 3714685

SUBMITTER (NAME ONLY): Maria Vega Garces

TITLE: Telemedicine Vision Threatening Diseases and Wellness Screenings in Uninsured Latino Community During COVID-19

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.I. Vega Garces, P. Tailor, A. Zhu, R. Verma, B. Szirth, A. Khouri, M. Habiel, Ophthalmology, New Jersey Medical School Division of Clinical Sciences, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limited access to eye-care among Latinos can lead to missed Vision Threatening Diseases (VTDs) defined as Age-related Macular Degeneration (AMD), cataracts, Diabetic Retinopathy (DR) and glaucoma. As 50% of the people with VTD's are unaware of their condition made worse during COVID-19, comprehensive eye screenings to assess ocular wellness was implemented using telemedicine, Artificial Intelligence (AI) and robotic consultations.

Methods: State-sponsored screenings were conducted at a church in West New York, NJ (78% Latino, mostly from Colombia) over 3 weekends during the 2021 Pandemic. All participants had received two-dose vaccinations and wore a surgical mask during screenings. Nine first-year medical students and 6 community volunteers took part in the wellness evaluation including: medical history, blood pressure, visual acuity, automated refraction, puff tonometry, 45-degree non-mydriatic retinal photography AI. To confirm findings: 6-micron resolution ocular coherence tomography (OCT) B-scan was performed. Screened subjects had their data reviewed by an onsite ophthalmic grader using a Spanish-speaking interpreter. As 80% of screened subjects are lost to follow-up, remote robotic ophthalmology consultation via HIPAA compliant Wi-Fi was utilized in real-time to connect with an off-site ophthalmologist.

Results: 153 subjects, (71 Female (46%), median age 55) had 127 ocular findings (Table 1) found in 85 (55%) subjects, of which 98% of findings were previously unknown and 40 (47%) classified as VTD. 23(15%) subjects had multiple findings. OCT confirmed 23 cases of AMD and glaucoma. AI referred 39 cases. 36 individuals took part in robotic virtual consults. Findings were: cataracts 70 (45%), glaucoma 32 (20%), and AMD 25(16%). Among those with findings, 82% were uninsured and 90% had >2 years since last eye exam. 32 (32/153) subjects had undertreated or untreated hypertension. 93% were un-familiar with telemedicine.

Conclusions: Latinos without health insurance and ease of access to eyecare may have a higher burden of multi-VTDs. An exception was DR which could be a limitation of population bias. This pilot study supports comprehensive wellness eye screenings that may allow for early detection, confirmation, and referral of single or multiple VTD in high-risk low-income communities. Further studies are needed using larger sample populations.

CONTROL ID: 3714686

SUBMITTER (NAME ONLY): Alec Bernard

TITLE: Seeing New Challenges: The Impact of COVID on a Diverse Sample of Adults with Vision Impairment in SE Michigan

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bernard, S. Weiss, M. Rahman, J.D. Stein, J.R. Ehrlich, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|A. Bernard, J.D. Stein, J.R. Ehrlich, Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, Michigan, UNITED STATES|M. Buck, Henry Ford Center for Vision Rehabilitation & Research, Henry Ford Health System, Detroit, Michigan, UNITED STATES|M. Thomas, P.A. Edwards, Henry Ford Health System Department of Ophthalmology, Detroit, Michigan, UNITED STATES|A. Riddering, Center for Vision and Neuro Rehabilitation & Research, Henry Ford Health System, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The disruption of COVID-19 has caused differential impacts on vulnerable populations. This study tested the hypothesis that persons with visual impairment in Ann Arbor and Detroit, MI faced increased difficulty in their daily lives since summer 2020 during the pandemic compared to normally sighted individuals.

Methods: We administered the Coronavirus Disability Survey (COV-DIS) to assess general and psychological health, isolation, financial and transportation challenges, information access and instrumental activities of daily living. Our study population included 112 adults recruited from the University of Michigan (UM) Health System and 151 adults recruited from the Henry Ford Health System (HF) in Detroit, MI with moderate or worse visual impairment (<20/60 in better-seeing eye), and 160 age/sex-matched controls (C). The COV-DIS was administered via phone or email. The UM IRB approved this study and all participants provided informed consent.

Results: There were no significant site differences in age or visual acuity of participants. Participants with visual impairment at Henry Ford (VIHF) lived in more disadvantaged neighborhoods (higher Area Deprivation Index) compared with UM participants with visual impairment (VIUM) (66 VIHF 52 VIUM; p<.01). All groups reported similar overall health prior to the pandemic. However, a greater proportion of VIHF participants reported somewhat or much worse health than pre-pandemic compared with VIUM or controls (C) (25% VIHF, 10% VIUM, 12% C; p=.003). Participants with visual impairment had more difficulty accessing medical care since the start of the pandemic (13% VI, 6% C; p=.049). One-quarter of participants reported difficulty obtaining trusted information during the pandemic; those with vision impairment were more likely to find the information hard to understand (10% VI, 3% C; p=.01).

Conclusions: COVID-19 and associated mitigation measures had differential effects on populations with visual impairment. Participants with visual impairment in Detroit were more likely to report a negative impact on their health than participants from Ann Arbor, MI. Those with visual impairment in both locations faced greater challenges accessing medical care and trusted and understandable information related to the pandemic. This information may be helpful for shaping health policy to address the barriers faced by individuals with visual impairment.

CONTROL ID: 3714687

SUBMITTER (NAME ONLY): Shereen Chew

TITLE: Timed Notch signaling inhibition drives cone or rod photoreceptor differentiation in human retinal organoids

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.H. Chew, C. Martinez, S. Kandoi, D.A. Lamba, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|K.R. Chirco, Oregon Health & Science University Oregon National Primate Research Center, Beaverton, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Transplanting photoreceptors derived from human induced pluripotent stem cells (hiPSC)-retinal organoids have the potential to reverse vision loss in affected individuals. However, the scarcity of available transplantable photoreceptor cells provides an unmet challenge. Hence the goal of our current study was to accelerate and synchronize photoreceptor differentiation in retinal organoids by inhibiting the Notch signaling pathway using a small molecule, PF-30184014 (PF), at different developmental time-points.

Methods: Human iPSC- and ESC (Embryonic stem cells)-derived retinal organoids were treated with 10μM of PF for three days at day 45 (D45), D60, and D90 of differentiation. PF-treated organoids collected at 2-, 4-, and 6-weeks post-treatment were analyzed for progenitor and photoreceptor markers by immunohistochemistry (IHC; n=3-5 organoids from 3 independent experiments) and bulk RNA-seq (n=3-5 organoids from 3 independent experiments).

Results: PF-treated retinal organoids collected at 2-weeks post-treatment (at all time-points of differentiation), showed a decrease in progenitor markers (KI67, VSX2, PAX6, and LHX2) and an increase in differentiated photoreceptor precursor markers (OTX2 and CRX). PF-treated organoids at D45 and D60 exhibited an increase in cone photoreceptor markers (RCVRN, RXRG, and ARR3). PF-treatment at D90 revealed an increase in rod photoreceptors markers (RCVRN, NRL, and NR2E3). Bulk RNA-seq analysis mirrored the IHC data.

Conclusions: Timing Notch pathway inhibition in human retinal organoids to align with progenitor competency stages can yield a homogenous population of early cone or rod photoreceptors. Future work will focus on the effects of Notch inhibition on other retinal cells such as retinal ganglion cells and bipolar cells.

CONTROL ID: 3714688

SUBMITTER (NAME ONLY): Tirthasree Das

TITLE: Characterization of ubiquitin dynamics in photoreceptors

SESSION TITLE: Photoreceptor Biology, Protection and Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Das, M. NACHURY, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Tirthasree Das: Commercial Relationship: Code N (No Commercial Relationship) | MAXENCE NACHURY: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Biological processes are imperfect and errors in trafficking to the outer segment (OS) of photoreceptors can result in the entry of inner segment proteins into the OS. The correction of such errors has been illuminated by studies of Bardet-Biedl Syndrome (BBS), a mendelian disorder whose cardinal features include retinal degeneration. The BBSome, a complex of BBS proteins, ferries membrane proteins out of cilia and retinal degeneration in BBS is likely caused by defects in the removal of mistargeted proteins from the OS, which is a specialized cilium. To better understand the pathological imbalances that leads to photoreceptor death in BBS, we sought to define the characteristics of proteins that are removed from the OS by the BBSome.

Methods: Past work in cultured cells has shown that ubiquitin (Ub) chains linked at lysine 63 (K63) mark cargoes for BBSome-mediated exit. We stained retinal sections of Bbs4 knockout mice at P15 with pan-Ub and linkage-specific probes. We next biochemically isolated the ubiquitinated proteins that accumulate in $Bbs4^{-/-}$ OSs using Tandem Ubiquitin Binding Entities (TUBEs). Experimental replicates and quantitative mass spectrometry enabled a statistically robust identification of BBSome cargoes in photoreceptors.

Results: Ubiquitin levels in the OS of $Bbs4^{-/-}$ mice are considerably elevated compared to control mice. Specifically, K63Ub chains accumulate in $Bbs4^{-/-}$ OS. Mass spectrometry analyses of K63Ub-associated proteins found 49 proteins statistically enriched ($p < 0.05$) by 1.5-fold in $Bbs4^{-/-}$ OS compared to wildtype OS while only 10 proteins were depleted. The vast majority of proteins linked to K63Ub that accumulate in $Bbs4^{-/-}$ OS are membrane proteins that are known to localize to the inner segment, to synaptic vesicles, or to the synaptic terminal. The identification of Syntaxin 3, a synaptic protein known to mislocalize to the OS in Bbs knockout mice, in this dataset directly validates our approach. The preliminary characterization of hits from our data set suggests the existence of a novel class of BBSome cargoes that may be subject to quality control.

Conclusions: The analysis of our mass spectrometry data set shows that K63Ub chains mark unwanted proteins for clearance from the OS by the BBSome. Our study generalizes the function of BBSome in the clearance of unwanted proteins from the OS and suggests the existence of quality control mechanisms that maintain the proteome of photoreceptor OS.

CONTROL ID: 3714689

SUBMITTER (NAME ONLY): Kirill Larin

TITLE: In vivo Characterization of Corneal Shear Modulus Under Localized Cross-linking Using Confocal Air-coupled Optical Coherence Elastography

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Larin, F. Zvietcovich, A. Nair, M. Singh, S. Aglyamov, M.D. Twa, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recently, the riboflavin/UV-A collagen cross-linking (UV-CXL) clinical technique to treat corneal keratoconus has been applied locally in the cornea for patient-specific treatment. We hypothesize that a confocal air-coupled ultrasonic optical coherence elastography (ACUS-OCE) system can detect local changes of corneal elasticity in vivo under localized and global UV-CXL in rabbits.

Methods: ACUS-OCE measurements were made in four Dutch-Belted rabbits (n = 8 corneas) in the following protocol: (1) the left cornea was measured before (untreated: UT) and after half-treated (HT) UV-CXL; and (2) the right cornea was measured before and after full-treated (FT) UV-CXL. The ACUS-OCE setup includes a spectral-domain optical coherence tomography system coaligned with an air-coupled 1 MHz ultrasonic transducer that produced mechanical excitation (Lamb waves) at the apex of the corneas. Corneal thickness and Lamb wave speed were measured along four meridians: superior, inferior, nasal, and temporal. Finally, a modified Rayleigh-Lamb equation was used to convert wave speed into shear modulus.

Results: Lamb wave speed maps (Fig. 1a) along the inferior-superior direction are shown for the UT, HF, and FT corneas with UV-CXL. The inferior meridian (i.e., UV-CXL treated) in the HT cornea case was stiffer (~7.14 m/s) than its superior (untreated) meridian (~5.88 m/s). Moreover, the speed map for the FT case was symmetric and showed a marked speed elevation (~7.66 m/s) compared to the UT case (~5.31 m/s). There was a significant increase in the shear modulus in the inferior meridian of the left HT corneas ($p < .001$) after localized UV-CXL (Fig. 1b). Similarly, for the right FT corneas, there is a significant increase in shear modulus ($p < .001$) in all meridians after full UV-CXL.

Conclusions: In this work, we have demonstrated that ACUS-OCE can detect localized untreated and UV-CXL treated regions in the same cornea in vivo. This technology shows great potential for the monitoring and customization of patient-specific UV-CXL treatment.

CONTROL ID: 3714690

SUBMITTER (NAME ONLY): John Siano

TITLE:

Prevalence of Ocular Findings in NICU Patients with Suspected Congenital TORCH Infections

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Siano, Ophthalmology, Nassau University Medical Center, East Meadow, New York, UNITED STATES|A. Shusko, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|J. Ha, Ophthalmology, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|P. Shah, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose:

To determine the prevalence of ocular findings during inpatient consultations for suspected neonatal Toxoplasmosis, Other, Rubella, Cytomegalovirus, and Herpesvirus (TORCH) infections. It is hypothesized that the prevalence of positive inpatient ocular examinations for TORCH rule out is low using current screening recommendations.

Methods: A retrospective chart review of neonates who received inpatient dilated ophthalmic exams for suspected TORCH infections while in the neonatal intensive care unit between May 2015 and October 2020 at a single, tertiary, safety-net institution. Birth weight, gestational age, reason for ophthalmology consultation, and associated ocular findings were recorded.

Results: he medical records of 84 patients were evaluated. The reasons for consultation included Small for Gestational Age (SGA, 40%), Intrauterine Growth Restriction (IUGR, 14%), Microcephaly (8%), Hypotonia (6%), Dysmorphic Features (3.5%), Maternal History of TORCH Infection in Previous Pregnancy (3.5%), and Conjunctivitis (3.5%). None of the patients had ocular examination findings consistent with congenital TORCH infection. The most common ocular finding was retinal hemorrhages (12%), however this is likely a consequence of birth trauma. One patient had positive urine IgM for CMV however no ocular findings. Other rare findings include Peters Anomaly, Primary Hyperplastic Persistent Vitreous, and Dacryocystocele

Conclusions: There was a surprisingly low prevalence of ocular findings in neonates receiving inpatient ocular examination for suspected congenital TORCH infections, despite a patient population that is reported to be at a higher risk of infection. The low diagnostic yield may be explained by the lack of a consensus recommendation for which patients with TORCH rule out would benefit from an urgent inpatient examination. It is likely more cost effective to reserve these examinations for an outpatient basis until clearer indications are defined. White we cannot provide specific criteria for examination based on our results, our study does suggest that inpatient neonatal ophthalmic examinations for TORCH rule out are not indicated solely for isolated cases of SGA or IUGR.

CONTROL ID: 3714693

SUBMITTER (NAME ONLY): Darren Schuman

TITLE: Transcorneal Needle Puncture Stimulates Macrophage Recruitment to the Conventional Outflow Pathway

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.M. Schuman, A. Grimsrud, D.R. Saban, W.D. Stamer, K. Liu, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intracameral injections are an effective delivery route to tissues in the conventional outflow tract. One consequence of intracameral injection is a full-thickness corneal puncture and subsequent inflammatory response. This study assesses macrophage number and distribution in the conventional outflow tract after intracameral injection.

Methods: Intracameral injections were performed by a single puncture using beveled glass microneedles. C57Bl/6 mice, aged 3-5 months, received unilateral intracameral injection of 2µl of PBS with the contralateral eyes serving as untreated controls (n=3). In a separate cohort, mice underwent unilateral transcorneal needle puncture to one-half anterior chamber depth (without injection) with untreated contralateral eyes (n=2). Intraocular pressure (IOP) was monitored at baseline and daily after treatment. Mice were sacrificed and eyes enucleated 3 days post-treatment. Eyes were fixed and immunostained to identify macrophages in the conventional outflow tract. Anterior segment whole mounts were imaged by confocal microscopy, and macrophages were quantified from 5-6 non-consecutive 40X magnification images per eye. Statistical analysis was performed by one-way ANOVA and post hoc tests with $p < 0.05$ considered significant.

Results: At 3 days post-treatment, macrophage numbers increased in PBS injected and needle puncture eyes in the trabecular meshwork (TM) (53% with $p < 0.002$ and 40% with $p < 0.03$, respectively) and around distal vessels (DVs) (47% with $p < 0.0001$ and 60% with $p < 0.0001$, respectively) compared with untreated eyes. The number of macrophages in Schlemm's canal (SC) was unchanged with PBS injection or needle puncture ($p = 0.23$) compared with control eyes. There were no significant differences in IOP from baseline in sham injection, needle puncture and untreated groups ($p = 0.25, 0.25, 0.99$, respectively).

Conclusions: Intracameral injection of PBS results in an increased number of macrophages in TM and DVs but not SC, and our results suggest that this effect is due to needle puncture injury.

CONTROL ID: 3714694

SUBMITTER (NAME ONLY): Marc Bloomenstein

TITLE: Effectiveness of TearCare System in Improvement Dry Eye Disease Symptoms in Meibomian Gland Dysfunction

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bloomenstein, Schwartz Laser Eye Center, Scottsdale, Arizona, UNITED STATES|J. Loh, Loh Ophthalmology Associates, Miami, Florida, UNITED STATES|K. Dhamdhere, Sight Sciences Inc, Menlo Park, California, UNITED STATES|

Commercial Relationships Disclosure: Marc Bloomenstein: Commercial Relationship(s);Code C (Consultant/Contractor):SIGHT SCIENCES | Jennifer Loh: Commercial Relationship(s);Code C (Consultant/Contractor):SIGHT SCIENCES | Kavita Dhamdhere: Commercial Relationship(s);Code E (Employment):SIGHT SCIENCES

ABSTRACT BODY:

Purpose: To demonstrate the superiority of the TearCare system in improvement of dry eye disease (DED) symptoms associated with meibomian gland dysfunction (MGD) compared to LipiFlow.

Methods: In this multi-center, masked, randomized-controlled trial, 235 subjects received a single TearCare treatment (n=115) or a single LipiFlow treatment (n=120) and were followed for 1-month post-treatment. DED symptoms were assessed using the Ocular Surface Disease Index (OSDI) Symptom Assessment in Dry Eye (SANDE), and eye dryness (ED) questionnaires at baseline and at 1-month. Subgroup analysis was conducted on subjects with less severe and more severe gland obstruction determined by baseline meibomian gland secretion score (MGSS).

Results: TearCare group and LipiFlow group had similar baseline mean OSDI (51.7 ± 14.79 and 51.7 ± 15.27). The reduction from baseline OSDI was 29.1 ± 1.62 for TearCare and 24.4 ± 1.59 for LipiFlow. The reduction in OSDI achieved with TearCare was significantly greater compared with LipiFlow (29.1 ± 1.62 vs 24.4 ± 1.59, pANCOVA = 0.04). Furthermore, subjects with more severe MGD (MGSS <7) achieved greater symptom-relief with TearCare compared to LipiFlow as shown in OSDI Section A (ocular symptoms), Section B (vision-related functions) and SANDE, $p_{ANCOVA} < 0.05$ for all comparisons.

Conclusions: TearCare provides significant DED symptom relief at 1-month after a single treatment. Outcomes were consistent in OSDI, SANDE, and ED assessments. In subjects with more severe gland dysfunction, TearCare performed significantly better than LipiFlow in improving quality of vision and overall DED symptom frequency determined by OSDI and SANDE.

CONTROL ID: 3714698

SUBMITTER (NAME ONLY): Cynthia Andrews-Pfannkoch

TITLE: MEK inhibition reduces expression of transcription factor early growth response-1 (EGR1) in BRAF mutant and BRAF wild type melanoma

SESSION TITLE: Tumor - Diagnosis, prognosis, and molecular mechanism

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Andrews-Pfannkoch, D.R. Miley, S. Adams, A.D. Marmorstein, L.A. Dalvin, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|J.S. Pulido, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the effects of mitogen activated protein kinase inhibitor (MEKi) treatment on EGR1 expression in BRAF mutant and wild type melanoma in cell culture.

Methods: We used three cell lines to investigate the response of EGR1, a transcription factor, to MEK inhibition. Two cell lines were derived from cutaneous melanoma, MEL888 and MEL624, and harbored the same BRAF mutant, Val600Glu (V600E). YUARGE 13-3064 was generated from a conjunctival melanoma neck lymph node metastasis and was BRAF wild type. After plating and overnight incubation, cells were treated daily for 72 hours with the MEK inhibitor trametinib at 18 nM concentration compared to DMSO vehicle control. At 72 hours, viability was measured using PrestoBlue™. qPCR and simple western assays were used to evaluate changes in EGR1 expression and a panel of genes associated with EGR1 and the MEK pathway. Targeted knockdown of EGR1 was performed to determine whether the observations in the MEK treated cells were a direct result of EGR1 knockdown.

Results: In MEL888, MEL624, and YUARGE 13-3064, treatment with the MEKi trametinib reduced viability and resulted in reduced EGR1 expression at the RNA ($p<0.001$, $p<0.001$, and $p=0.04$, respectively) and protein level ($p=0.03$, $p=0.03$, and $p=0.007$, respectively). Targeted EGR1 knockdown resulted in similar reduction in viability for BRAF mutant melanoma MEL888 compared with trametinib treatment.

Conclusions: MEKi treatment of BRAF mutant and BRAF wild type melanoma resulted in knockdown of EGR1 gene and protein expression in cell culture. Direct EGR1 knockdown resulted in reduced viability for BRAF mutant melanoma, suggesting a key role for EGR1 in the anti-cancer effects of MEKi for melanoma treatment.

CONTROL ID: 3714699

SUBMITTER (NAME ONLY): Yurico Lopez

TITLE: Infectious and sterile keratitis after corneal crosslinking for keratoconus

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lopez, J. Guerrero, A. Ramírez-Miranda, A. Navas-Perez, E.O. Graue-Hernandez, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|V.M. Bautista- de Lucio, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: Collagen crosslinking (CXL) is a proven effective treatment for halting the progression of keratoconus, with a low rate of complications including infection. To recognize risk factors is fundamental. We describe infectious keratitis prevalence and findings after accelerated (Epi-Off) and transepithelial (Epi-On) CXL in a third-level center.

Methods: Descriptive case series of patients who were treated with Epi-Off or Epi-On CXL for progressive keratoconus. We retrospectively reviewed all clinical records for a period of 10 years (2009-2018) of patients who underwent CXL for keratoconus. Keratitis patients were noted and analyzed. Based on clinical findings, they were classified either as sterile or infectious. Microbial cultures and antibiotic susceptibility were recorded when available. We recorded the following features: common risk factors, treatment regimen, detected microorganisms, antibiotic susceptibility, and clinical outcomes.

Results: From 1082 eyes reviewed, a total of 7 eyes developed keratitis (0.64%). Four of the seven cases presented as infectious keratitis (57.14%) and three as sterile keratitis (42.85%). Epi-On was performed in corneas with thinnest corneal point less than 380 um. Two cases developed keratitis in this group (28.57%). The mean time of presentation was 10.8 days postoperatively. The most common pathogen was Staphylococcus aureus (50%) and Staphylococcus epidermidis (75%). One case reported Pseudomonas mendocina culture growth. Preoperative mean best corrected visual acuity (BCVA) was 0.42 (logMAR), mean BCVA at resolution was 0.65 (logMAR). Most common posterior complications were corneal leucomas (71.4%). The use of steroids and soft bandage contact lenses in the immediate postoperative period were reported in 100% of the patients. Five cases were covered with antibiotic therapy in this period (tobramycin 42.85%, ciprofloxacin 14.2%, moxifloxacin 14.2%). History of atopic disease was present in 85.71% of all the cases.

Conclusions: The overall frequency of infectious keratitis after CXL remains low, but the implications can be deleterious. History of atopia could be associated with disturbance of the immunological barriers, predisposing to keratitis. The importance of judicious use of steroids, promptly identification of the condition and a cultured directed antimicrobial therapy when possible, as well as more frecuent check up visits may be highly valuable in these patients.

CONTROL ID: 3714700

SUBMITTER (NAME ONLY): Jie Ding

TITLE: Intrinsic signal optoretinography of dark adaptation abnormality due to rod degeneration

SESSION TITLE: Retinal Degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Ding, T. Kim, X. Yao, Biomedical Engineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Jie Ding: Commercial Relationship: Code N (No Commercial Relationship) | Tae-Hoon Kim: Commercial Relationship: Code N (No Commercial Relationship) | Xincheng Yao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study is to demonstrate optoretinography of dark adaptation abnormality due to rod dysfunction in the retinal degeneration 10 (rd10) mouse model.

Methods: Six WT C57BL/6J and six rd10 mice at postnatal 14 days were used for this study. Optical coherence tomography (OCT) was employed for depth resolved morphological characterization of retinal layers. Time-lapse OCT measurement was used for intrinsic signal optoretinography of dark adaptation. Retinal B-scans were acquired in light condition and during 30 minutes of dark adaptation, with 5 min interval.

Results: Figure 1 shows comparative OCT imaging of the retina under light and dark-adapted conditions, revealing differences primarily within the outer retina part. Further analysis shows that the peak OCT intensity value of inner segment ellipsoid (ISe) band decreased, and the distance between external limiting membrane (ELM) and retinal pigment epithelium (RPE) reduced during the dark adaptation, compared to light condition. It was observed that the relative ISe intensity change was faster and larger in rd10, compared to WT. After 5 min, the relative ISe intensity value has significantly decreased in rd10 compared to the baseline ($p < 0.0001$); while significant ISe intensity decrease in WT was observed after 15 min ($p < 0.05$). Furthermore, the ISe intensity peak is split into a1 (left slope) and a2 (right slope). ISe band width has slightly decreased, while the intensity value of a1 both in WT and rd10 significantly dropped (WT $P<0.001$, Rd10 $P<0.01$, compared to light condition) and a2 also shown overall decrease.

Conclusions: In this study, we found that rd10 retina manifest abnormal outer retinal changes during dark adaptation. During dark adaptation, ISe band thickness was reduced in rd10, and peak intensity rapidly decreased compared to WT group.

CONTROL ID: 3714701

SUBMITTER (NAME ONLY): Younghoon Lee

TITLE: Comparison of retinal layer thickness and microvasculature changes in patients with diabetic retinopathy treated with intravitreous bevacizumab vs panretinal photocoagulation

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lee, M. Lee, Ophthalmology, Konyang University College of Medicine, Daejeon, Daejeon, KOREA (THE REPUBLIC OF)|S. Baek, Nuri eye hospital, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Younghoon Lee: Commercial Relationship: Code N (No Commercial Relationship) | Min-Woo Lee: Commercial Relationship: Code N (No Commercial Relationship) | Seung-Kook Baek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare changes in retinal layers and microvasculature in diabetic retinopathy (DR) patients after bevacizumab therapy and panretinal photocoagulation (PRP)

Methods: This prospective study divided patients into two groups: patients treated with bevacizumab and those treated with PRP. Patients visited our retinal clinic at 1, 3, and 6 months after treatment. Retinal layer thickness and vessel density (VD) using optical coherence tomography angiography were analyzed

Results: 37 eyes in the bevacizumab group and 36 eyes in the PRP group were enrolled. In the bevacizumab group, the parafoveal RNFL, GCL, and IPL thicknesses significantly decreased ($P < 0.001$, $P = 0.013$, and $P = 0.017$, respectively), whereas the thicknesses in the PRP group showed an increasing tendency over time ($P = 0.087$, $P = 0.005$, and $P = 0.003$, respectively). The VD of the superficial capillary plexus (SCP) and deep capillary plexus (DCP) in the bevacizumab group did not show significant changes, whereas the VD in the PRP group significantly increased over time (both $P < 0.001$). Additionally, RNFL ($P = 0.001$) and GCL thicknesses ($P = 0.035$) were significant factors affecting changes in BCVA, whereas the VDs of SCP and DCP did not.

Conclusions: Patients who received bevacizumab therapy did not show a significant change in macular VD, whereas the VD of patients after PRP significantly increased after treatment. The increased macular VD in patients after PRP would be associated with the increased inner retinal layer thickness after treatment, which was significantly related to the impairment in visual acuity.

CONTROL ID: 3714702

SUBMITTER (NAME ONLY): Sara González-Godínez

TITLE: Keratometric influence in ten IOL calculation formulas for long eyes

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. González-Godínez, I. Domínguez Varela, J.E. Valdez, Oftalmologia, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|R. Saucedo-Urdapilleta, M. Mayorquin-Ruiz, C. Velasco-Barona, R. Gonzalez-Salinas, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To compare and determine the best intraocular lens formula in eyes greater than 25mm with normal and keratometries greater than 45D.

Methods: Retrospective comparative study. 119 eyes with axial length 25mm were included and divided into two groups: Ksteep (45D) and Kreg (<45D). Refractive error (RE) was calculated with 10 calculation formulas. Mean absolute error (MAE) and median absolute error (MedAE) of RE were compared. The percentage of eyes was obtained at ±0.50, ±1.00 and ±2.00 diopters, as well as the OR of achieving a refraction at ±0.50D.

Results: For the Ksteep group, the lowest MAE was from Panacea, Kane and Barret U2. The lowest MedAE was Ladas, Panacea and SRKII with the highest percentage in ±0.50D of Panacea and Kane. For the Kreg group the lowest MAE was from Kane and Hill-BRF. The lowest percentage at ±0.50D of Kane, Barret U2 and Haigis. All the formulas except Hill-BRF and Barret U2 presented statistically significant difference in MedAE between both groups.

Conclusions: Kane and Panacea had the best results for long eyes with keratometries greater than 45D. For long eyes with normal keratometries the best formulas were Hill-BRF and Barret U2. The latter can be used in long eyes regardless of keratometry.

CONTROL ID: 3714703

SUBMITTER (NAME ONLY): Carol Cheung

TITLE: Texture-transformer-based deep-learning (DL) network for enhancing image-quality of OCT-angiography images with lower-resolution

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.Y. Cheung, D.G. YANG, Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, HONG KONG|H. Chen, Computer Science and Engineering, The Hong Kong University of Sciences and Technology, HONG KONG|Y. RUAN, Electrical Engineering, City University of Hong Kong, HONG KONG|W. Zhang, Mathematics, The Hong Kong University of Sciences and Technology, HONG KONG|

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ABSTRACT BODY:

Purpose: Despite quantitative diabetic macular ischemia (DMI) assessment using optical coherence tomography-angiography (OCT-A) is gradually recognized, most of OCT-A studies only focus on using small-of-view with high-resolution (HR) scanning protocol to ensure the reliability of measurement. We aim to develop a DL network to reconstruct 6mm×6mm OCT-A images with image-quality enhancement to tackle the issue of “resolution trade-off” between field-of-view, image-quality and scanning time.

Methods: A novel texture-transformer-based DL network was built for reconstruction task for 6mm×6mm (320A-scan/320B-scan) fovea-center OCT-A images (Fig 1) acquired from a swept-source OCT (Triton DRI-OCT, Topcon, Inc., Japan). 296 eyes from 158 individuals with diabetes were used for training and primary validation (8:2) with each eye consists of one 3mmx3mm and one 6mm×6mm fovea-center OCT-A images. Structural similarity index measure (SSIM) and peak signal-to-noise ratio (PSNR) were used to compare the image-quality before and after reconstruction. To test the relationship between OCT-A metrics and diabetic retinopathy (DR) severity on the reconstructed images. We used a non-overlapping dataset (no DR: 22; mild DR:20; moderate DR:18; severe DR or proliferative DR:18) with each eye consists of 5 3mmx3mm (320A-scan/320B-scan, 1 fovea-center and 4 at parafoveal regions) and 1 6mm×6mm (320A-scan/320B-scan, fovea-center) OCT- A images. The 5 3mmx3mm OCTA images were then stitched as montage to provide a HR 6mm×6mm image serving as the “ground-truth” to the reconstructed images.

Results: After image reconstruction, better visibility of retinal capillaries are appreciated (Fig 2). The SSIM ($SSIM_{original}$ = 0.670 vs. $SSIM_{reconstructed}$ = 0.500, $p<0.001$) and PSNR ($PSNR_{original}$=19.71 vs. $PSNR_{reconstructed}$ =17.41, $p< 0.001$) of the reconstructed images was significantly higher than that of the original images. In the non-overlapping dataset, we measured foveal avascular zone (FAZ) area, FAZ circularity, vessel density on both the ground-truth and reconstructed images. We found that the associations of the OCT-A metrics with DR severity between “ground-truth” and reconstructed images were large identical (i.e. similar R^2 values).

Conclusions: The proposed DL network can enhance the image-quality among OCT-A images with lower resolution and maintain the accuracy of quantitative OCT-A measurements.

CONTROL ID: 3714704

SUBMITTER (NAME ONLY): Ou Tan

TITLE: Focal Loss Analysis of Peripapillary Nerve Fiber Layer Reflectance for Glaucoma Diagnosis

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Tan, D. Choi, A. Chen, D. Huang, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D.S. Greenfield, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Francis, Doheny Eye Center, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|R. Varma, Southern California Eyecare and Vision research Institute, Los Angeles, California, UNITED STATES|J.S. Schuman, NYU Langone Health, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Ou Tan: Commercial Relationship(s);Code P (Patent):Optovue | Dongseok Choi: Commercial Relationship: Code N (No Commercial Relationship) | Aiyin Chen: Commercial Relationship: Code N (No Commercial Relationship) | Brian Francis: Commercial Relationship: Code N (No Commercial Relationship) | Joel Schuman: Commercial Relationship: Code N (No Commercial Relationship) | Rohit Varma: Commercial Relationship: Code N (No Commercial Relationship) | David Greenfield: Commercial Relationship: Code N (No Commercial Relationship) | David Huang: Commercial Relationship(s);Code F (Financial Support):Optovue;Code I (Personal Financial Interest):Optovue;Code O (Owner):Optovue;Code P (Patent):Optovue

ABSTRACT BODY:

Purpose: To evaluate nerve fiber layer (NFL) reflectance for glaucoma diagnosis using a large dataset.

Methods: Participants were imaged with 4.9mm ONH scans using spectral-domain optical coherence tomography (OCT). The NFL reflectance map was reconstructed from 13 concentric rings of optic nerve head(ONH) scan, then processed by an azimuthal filter to reduce directional reflectance bias due to variation of beam incidence angle. The peripapillary thickness and reflectance maps were both divided into 96 superpixels. Low-reflectance and low-thickness superpixels were defined as values below the 5th percentile normative reference for that location. Focal reflectance loss was measured by summing loss, relative to the normal reference average, in low-reflectance superpixels. Focal thickness loss was calculated in a similar fashion. The area under receiving characteristic curve (AROC) was used to assess diagnostic accuracy.

Results: Fifty-three normal, 196 pre-perimetric, 132 early perimetric, and 59 moderate and advanced perimetric glaucoma participants were included from the Advanced Imaging for Glaucoma Study. Sixty-seven percent of glaucomatous reflectance maps showed characteristic contiguous wedge or diffuse defects. Focal NFL reflectance loss had significantly higher diagnostic accuracy than the best NFL thickness parameters (both map-based and profile-based): AROC 0.80 v. 0.75 ($p<0.004$) for distinguishing glaucoma eyes from healthy control eyes. The diagnostic sensitivity was also significantly higher at both 99% specificity operating points.

Conclusions: Focal NFL reflectance loss improved glaucoma diagnostic accuracy compared to the standard NFL thickness parameters.

CONTROL ID: 3714706

SUBMITTER (NAME ONLY): Laura Kopplin

TITLE: Persistent Subclinical Photoreceptor Loss in a Patient with Acute Posterior Multifocal Placoid Pigment Epitheliopathy After Reactivation of Symptoms post COVID Vaccine

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.J. Kopplin, K.E. Stepien, N. Stangel, J. Rogers, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|J. Rogers, Morgridge Institute for Research & McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a generally self-limited disease with a good prognosis and resolution of symptoms between 4 weeks and 6 months. Retinal imaging is used to establish the diagnosis; however, the resolution of routine diagnostic imaging to assess changes at the photoreceptor level is limited. Here we explored outer cellular retinal structure of APMPPE lesions in a patient 4 years after initial presentation and 8 months after recurrent scotoma symptoms in the same region as her initial APMPPE scotomas a few days after her first COVID-19 vaccine.

Methods: The subject underwent a complete eye exam and high resolution imaging. Outer retinal structure was assessed using spectral domain optical coherence tomography (SD-OCT), and the photoreceptor mosaic was imaged using both confocal and split detection adaptive optics scanning light ophthalmoscopy (AOSLO).

Results: SD-OCT identified a subtly irregular ellipsoid zone (EZ) band in the area of a previous APMPPE lesion, improved from initial presentation and initial visit after reactivation. Confocal AOSLO (Figure A) revealed an abrupt transition from dense regularly spaced cones to a disrupted photoreceptor mosaic. However, confocal AOSLO signal can be difficult to interpret in the presence of debris or non-waveguiding cones. Split detection AOSLO (Figure B) highlights cone inner segments providing a clearer view of cone distribution even in the absence of waveguiding and revealed reduced photoreceptor density in disrupted areas (Figure A and B '*').

Conclusions: COVID-19 vaccination may induce reactivation of APMPPE symptoms. Despite improved EZ band structure by SD-OCT in the areas of previous APMPPE lesions, AOSLO revealed several focal areas of persistent subclinical photoreceptor loss. Split detection AOSLO allows for more precise assessment of photoreceptor structure and highlights the variability in inner segment changes throughout retina lesions. This demonstrates the potential utility of split-detector AOSLO for assessment of photoreceptor structure alterations in retinal uveitic diseases such as APMPPE.

CONTROL ID: 3714707

SUBMITTER (NAME ONLY): Alexandra Vitale

TITLE: Phenotypic Differences of Punctate Inner Choroidopathy (PIC) and Multifocal Choroiditis (MFC) Utilizing Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO)

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vitale, S. Collon, L. Sauer, P.S. Bernstein, John A. Moran Eye Center, SLC, Utah, UNITED STATES|

Commercial Relationships Disclosure: Alexandra Vitale: Commercial Relationship(s);Code C (Consultant/Contractor):Tesseract | Sean Collon: Commercial Relationship: Code N (No Commercial Relationship) | Lydia Sauer: Commercial Relationship(s);Code C (Consultant/Contractor):Tesseract | Paul Bernstein: Commercial Relationship(s);Code C (Consultant/Contractor):Tesseract;Code S (non-remunerative):Heidelberg Engineering

ABSTRACT BODY:

Purpose: Punctate inner choroidopathy (PIC) and multifocal choroiditis (MFC) are two white dot syndromes that share common clinical features such as choroidal neovascularization (CNVM), cystoid macular edema (CME), intraocular inflammation, and retinal atrophy. This study investigates phenotypic differences between these two inflammatory diseases utilizing fluorescence lifetime imaging ophthalmoscopy (FLIO).

Methods: 8 eyes of 8 patients with PIC and 6 eyes of 6 patients with MFC (mean age 40 ± 18 years) and 14 age-matched healthy subjects were investigated in this study. FLIO images of a 30° retinal field at the foveal center were acquired using a prototype Heidelberg Engineering Spectralis-based FLIO. In all patients, FLIO lifetimes were recorded in short (498-560 nm, SSC) and long (560-720 nm, LSC) spectral wavelength channels, with mean autofluorescence lifetimes (tm) calculated and analyzed. In addition, FLIO lifetimes from PIC and MFC-specific lesions were obtained and compared in both spectral channels.

Results: FLIO can discriminate between PIC and MFC based on phenotypic differences in FLIO lifetimes from both spectral channels. While MFC lesions have consistently prolonged of lifetimes in both channels, PIC lesions show heterogeneity of long and short lifetimes in the SSC and LSC, respectively. Some PIC lesions with long FLIO lifetimes in the SSC emit short FLIO lifetimes in the LSC. Collectively, FLIO lifetimes are prolonged in MFC and PIC compared to age-matched controls in the outer ring of the posterior pole in the LSC (240 ps versus 194 ps, $p<0.05$).

Conclusions: FLIO proves to be a promising imaging modality that offers a possibility to differentiate between PIC and MFC. The lifetime heterogeneity seen in PIC and significantly prolonged lesion lifetimes of MFC patients may provide additional diagnostic tools as well as insight into disease-specific mechanisms, activity, and progression.

CONTROL ID: 3714708

SUBMITTER (NAME ONLY): Maria Yera

TITLE: Measurement of energy metabolism in dissociated mouse retinal rod photoreceptors

SESSION TITLE: Photoreceptors and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.G. Yera, T. McLaughlin, J.J. Wang, S.X. Zhang, Department of Ophthalmology, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York, UNITED STATES| M.G. Yera, J.J. Wang, S.X. Zhang, Neuroscience Program, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure: Maria Yera: Commercial Relationship: Code N (No Commercial Relationship) | Todd McLaughlin: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Wang: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Photoreceptors are metabolically active retinal cells. Disturbance in photoreceptor metabolism leads to neuronal degeneration associated with a broad range of diseases such as age-related macular degeneration, and diabetic retinopathy. Understanding the changes in this process is critical for unraveling disease mechanisms and developing new treatments. The goal of this study is to develop an accurate and reliable approach for the measurement of energy metabolism in isolated mouse retinal photoreceptors.

Methods: Rod photoreceptor cells from dark-adapted mouse retinas were isolated using enzymatic digestion and mechanical dissociation. Cell viability was evaluated using Trypan blue and live-dead assays. Neuronal population and preservation of cell structure were examined by immunofluorescence staining. Cellular bioenergetics were measured by extracellular flux analysis using a Seahorse extracellular flux analyzer. To maintain a high number of metabolically active cells, dark conditions were used throughout the process of dissociation, cell seeding, and metabolic analysis.

Results: Successful isolation of retinal photoreceptors was achieved using as few as one single mouse retina. Immunostaining for multiple retinal neuronal markers revealed that 90% of the dissociated cell population were rod photoreceptors. The majority of photoreceptor cells preserved an intact structure and 93% of them were viable. Reproducible functional data were obtained in oxygen consumption rate (OCR) for mitochondrial respiration and extracellular acidification rate (ECAR) for glycolysis with adjustment of cell densities and titration of substrate concentrations. Compared to analysis using retinal explants, dissociated retinal photoreceptors demonstrated an enhanced response to inhibitors for mitochondrial respiration in metabolic assays.

Conclusions: Our study provided a novel approach for reproducible and accurate measurement of energy metabolism in dissociated mouse retinal rod photoreceptors, which may have a broad application in future studies on retinal degenerative disease.

CONTROL ID: 3714709

SUBMITTER (NAME ONLY): Paige Richards

TITLE: Using Imaging Biomarkers and Anatomic Features To Predict the Success of Macular Hole Repairs

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Richards, J.S. Chang, Department of Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure: Paige Richards: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Chang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Despite growing literature looking at factors that contribute to the closure of full-thickness macular holes, there are still gaps in our knowledge. This study sought to examine the role of preoperative and intraoperative factors in predicting anatomic and visual success of vitrectomy for full-thickness macular holes.

Methods: A retrospective chart review of cases in year 2018-2019 was conducted at the University of Wisconsin. Inclusion criteria included vitrectomy for macular hole and pre- and post-operative imaging. Successful closure was defined as the absence of a full-thickness disruption by imaging. Final statistical analyses are currently underway. Data will be summarized using the median and inter quartile range (IQR; span from 25^{th} to 75^{th} percentile capturing central 50% of the sample) for continuous features or with frequencies and percentages for categorical factors. Risk factors associated with hole closure will be compared between groups using either rank-sum procedures or Fisher's exact tests. Analyses will be performed using R (ver. 4.0.3).

Results: There were 138 subjects who met inclusion criteria and had vitrectomy for macular hole. One had a traumatic injury and was especially young (< 15 years old) at the time of repair; all others were between 42–87 years at time of surgery, with the mean age of 71.5. 69.5% of patients were female. Internal limiting membrane was peeled in all cases. Hole closure was successful for 126 subjects (90.5%); 120 (95%) of these had single surgery success. Age, lens status, prior hole repair, and chronicity (present > 1 year), pathologic myopia or staphyloma were included in data collection, among several other variables of interest. 6 (50%) of the unsuccessful surgeries were highly myopic patients and 11 of the total 17 (64.7%) highly myopic patients achieved successful closure. Mean minimum hole diameter (MHD) was 316.2 uM. A larger mean MHD was found among those who had an unsuccessful repair (598.2 uM). Mean preoperative logMAR visual acuity was 0.81 with mean improvement to 0.52 postoperatively.

Conclusions: The study suggests that factors such as being highly myopic and large MHD may portend a decreased likelihood of a successful macular hole surgery, although final statistical analyses are pending.

CONTROL ID: 3714712

SUBMITTER (NAME ONLY): Aniruddh Srinivasan

TITLE: KCNQ-targeting drugs reveal a possible regulatory role in visual light response

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Srinivasan, P.K. Shahi, S. Afsheen, Department of Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|P.K. Shahi, B.R. Pattnaik, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|B.R. Pattnaik, Department of Pediatrics and Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The effect of KCNQ-targeting drugs on the visual light response (VLR) is unknown. Previous studies have demonstrated the expression of these channels in the retina and retinal pigment epithelium (RPE). Patients note persistent visual disturbances while using the KCNQ-activating anti-epileptic drug Retigabine. Given that KCNQ subunits are also expressed in the retina, we sought to identify how KCNQ modulators alter rodent retinal function.

Methods: VLR was assessed with ex-vivo or full field electroretinograms (exERG, ffERG). For exERGs, retinae were removed from freshly enucleated mice eyes and stimulated using OcuScience's ex-vivo ERG (custom protocol). Baselines were recorded in Ames medium. Retinae were incubated in 10 μM Zinc Pyrithione (ZP), 10 μM RL-648_81 (RL), 10 μM XE-991 (XE), 50 μM L-AP-4 (positive), 0.5% DMSO or 0.1% PBS treated Ames for 20 minutes. Another exERG was then taken, and a final recording after a 20-minute Ames wash. ffERGs were performed on the Espion-E3 system using the ISCEV protocol to assess a and b-waves and a custom c-wave protocol. Recordings consisted of a baseline, ffERG 15 minutes after treatment, and a follow-up after 3 days. Drugs were injected intravitreally for final vitreal concentrations given above. Two-tailed Student's t-test was used for data analysis.

Results: ExERGs revealed b-wave amplitude reductions in ZP treated retina (89 ± 22 μV) compared to baseline, (247 ± 38 μV, $p = 0.01$), which persisted post-wash. b-wave implicit time (IT) increased in ZP treated groups (116 ± 10 ms) relative to baseline (78 ± 6 ms, $p = 0.009$). Amplitude decrease was not observed with concurrent XE and ZP treatment, but IT was still delayed.

For ffERGs, b-wave and c-wave amplitude of ZP treated eyes decreased (233 ± 24, 161 ± 61 μV) compared to baseline (408 ± 31, 523 ± 37 μV, $p = 0.001$, 0.0008). b-wave IT decreased after ZP treatment (66 ± 13 ms) relative to baseline (32 ± 1 ms, $p = 0.03$). Interestingly, RL treatment increased a-wave amplitude (178 ± 17 μV) above baseline (113 ± 19 μV, $p = 0.04$). All mice had normal follow-up ffERGs.

Conclusions: Our results show that KCNQ modulation may alter retinal function. However, differences between the RL and ZP responses suggest non-uniform expression of functional KCNQ subunits in the retina. Exploration of ocular KCNQ distribution and modulation in specific retinal circuits will further elucidate the role of KCNQ channels in VLR.

CONTROL ID: 3714713

SUBMITTER (NAME ONLY): William West

TITLE: Cataract Surgery and One-year History of Vancomycin: A TriNetX Analysis

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. West, D. Kulman, D. Belyea, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|W. West, D. Akinbolue, H. Pakhchanian, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To observe the influence of preoperative vancomycin exposure on cataract surgery outcomes.

Methods: A retrospective cohort study was performed using patients from a national database, TriNetX (Cambridge, MA, USA), which compiles patient data in healthcare records from several large healthcare organizations in the United States. Patients undergoing cataract surgery were identified by CPT code and placed into cohorts based on any history of vancomycin use within one year prior to surgery vs. no history of vancomycin within one year prior to surgery. Patients were matched for age, BMI, sex, hypertension, diabetes, chronic respiratory disease, heart failure, and nicotine dependence. Primary outcomes were: Vitreous Hemorrhage, Choroidal Hemorrhage, Retinal Detachment (RD) or Break, Iridocyclitis, Retinal Edema (RE), Cystoid Macular Degeneration (CMD), Macular Puckering (MP), Toxic Maculopathy, Ischemic Optic Neuropathy (ION), Glaucoma, Strabismus, Hemorrhage of Orbit, Corneal Edema (CE), Dry Eye Syndrome (DES), Central Retinal Vein Occlusion (CRVO), Central Retinal Artery Occlusion (CRAO), Vitreous Opacities, Ptosis, lens dislocation, Endophthalmitis, Retinal Vascular Occlusions (RVO). Outcomes were compared between cohorts after propensity score matching using logistic regression.

Results: 32,716 patients were included in the study, with 16,358 in both the vancomycin-receiving and non-vancomycin-receiving groups. Vancomycin use was associated with higher rates of RE (RR 1.24; 95% CI, 1.04-1.49), CMD (RR 1.23; 95% CI, 1.08-1.4), MP (RR 1.28; 95% CI, 1.1-1.48), ION (RR 2.17; 95% CI, 1.1-4.3), glaucoma (RR 1.23; 95% CI, 1.09-1.4), DES (RR 1.26; 95% CI, 1.14-1.39), ptosis (RR 1.27; 95% CI, 1.06-1.53), endophthalmitis (RR 2.02; 95% CI, 1.47-2.76). Vancomycin use was associated with fewer vitreous opacities (RR 0.77, 95% CI (0.64-0.93). There was no significant difference between rates of vitreous or choroidal hemorrhage, hemorrhage of orbit, RD or retinal break, iridocyclitis, toxic maculopathy, strabismus, CE, lens dislocation, or RVOs such as CRVO or CRAO.

Conclusions: Vancomycin use may be associated with postoperative complications after cataract surgery. Patients who received vancomycin within one year before cataract surgery were more likely to develop RE, CMD, MP, ION, glaucoma, DES, ptosis, and endophthalmitis. The risk of these complications should be considered and discussed when evaluating patients peri-operatively.

CONTROL ID: 3714714

SUBMITTER (NAME ONLY): Yuhua Zhang

TITLE: In vivo characterization of erythrocyte supply in the human retinal capillaries

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhang, X. Wang, B. Gu, Doheny Eye Institute, Pasadena, California, UNITED STATES|Y. Zhang, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Yuhua Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Xiaolin Wang: Commercial Relationship: Code N (No Commercial Relationship) | Boyu Gu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the relationship among the velocity, cell flux, and cell lineal density of the erythrocytes in the human retinal capillaries.

Methods: We imaged the erythrocytes flowing in retinal capillaries of the human subjects in normal ocular and physical health, using a high-speed adaptive optics near-confocal ophthalmoscope at a frame rate of 800 Hz. We measured the erythrocyte velocity, lineal density (defined as the number of cells presenting within a certain length of the capillary), and cell flux (defined as the number of cells per second flowing through a capillary segment) within a cardiac cycle with custom software.

Results: In 29 macular capillaries of 7 eyes of 7 human subjects aged 20-29 years old, the linear density was 59.60 ± 10 cells/mm and cell flux was 60.16 ± 20.18 cells/s. In a single capillary, erythrocyte cell flux showed a distinctive fluctuation associated with the heartbeat, the lineal density of erythrocytes varied over time within a cardiac cycle, but the average lineal density over multiple cycles exhibited a fairly consistent distribution within a cardiac cycle under the normal cardiovascular and respiratory resting state (Figure).

Conclusions: The consistent erythrocyte lineal density over time in a retinal capillary disclosed the essential number of erythrocytes that are needed to provide a constant, uniform flux of oxygen to the local tissue thereby maintaining a normal retinal function. In vivo quantification of erythrocyte lineal density in human retinal capillaries under the natural rheological state may provide a potential useful biological index or a biomarker for assessing vascular function and pathophysiology.

CONTROL ID: 3714715

SUBMITTER (NAME ONLY): Linda Couto

TITLE: Laterally Spreading AAV.SPR-hRS1 Vector for Treatment of XLRS

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The presence of schisis cavities in the central retina has hampered safe and effective delivery of AAV-RS1 to XLRS patients. The novel AAV.SPR capsid laterally spreads well beyond the margins of the subretinal injection (SRI) bleb, providing a means to perform peripheral SRI (without detaching the fovea and avoiding schisis cavities) and effectively deliver RS1 to both the peripheral and central retina. The purpose of this study was to (1) evaluate the efficacy of AAV.SPR-hRS1 in Rs1 knock-out (RS1KO) mice and (2) compare the extent of central retina transduction mediated by AAV.SPR and AAV5 vectors encoding myc-tagged RS1 following peripheral SRI.

Methods: GFP, hRS1 or myc-RS1 were packaged into AAV.SPR and AAV5. RS1KO mice were treated via SRI with 3 different doses of vector, and retinal structure and function were assessed over 6 mo by OCT and ERG, respectively. Cynomolgus macaques were treated via SRI with AAV vectors expressing myc/hRS1 alone or both AAV-GFP and AAV-myc/hRS1. Vectors were delivered in either one or two extrafoveal blebs, and wide field color fundus, cSLO and OCT images were collected for up to 6 wk post-injection. Immunohistochemistry and biodistribution analysis were performed post mortem.

Results: Improvements in both retinal structure (resolution of schisis cavities), and function (scotopic and photopic b-waves) were observed in a dose-dependent manner, and hRS1 expression was observed in PR inner segments of RS1KO mice treated with AAV.SPR-hRS1. GFP and myc/RS1 expression was observed well beyond the bleb margins in NHPs treated with AAV.SPR (but not AAV5) vectors, including the majority of foveal cones, and myc/RS1 expression mimicked that of endogenous NHP RS1. Biodistribution of AAV.SPR compared favorably to AAV5.

Conclusions: A novel AAV vector has been developed for the treatment of XLRS. AAV.SPR delivered therapeutic levels of hRS1 to subretinally injected RS1KO mice, resulting in improvements in both retinal structure and function. In addition, AAV.SPR safely and efficiently mediated hRS1 expression in the central retina of primate eyes following peripheral subretinal injection. Contrary to previous vectors delivered intravitreally, SRI of AAV.SPR represents a safer (avoids surgical manipulation of schisised retina and fovea) and potentially more effective (promotes efficient transduction of photoreceptors) option for the treatment of XLRS.

CONTROL ID: 3714716

SUBMITTER (NAME ONLY): Samarendra Mohanty

TITLE: Double-masked, Randomized, sham-controlled, Multicenter Phase 2b study of Multi-Characteristic Opsin enabled vision restoration in patients with advanced retinitis pigmentosa: Design and Development of novel endpoints

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mohanty, S. Batabyal, A. Ayyagari, J. Rittimann, K. Tchedre, Nanoscope Therapeutics Inc, Bedford, Texas, UNITED STATES|S. Mohanty, S. Batabyal, S. Kim, M. Carlson, K. Tchedre, Nanoscope Technologies LLC, Bedford, Texas, UNITED STATES|S. Kim, M. Carlson, Nanoscope Instruments Inc, Bedford, Texas, UNITED STATES|S.H. Chavala, TCU-UNTHSC School of Medicine, FortWorth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In advanced retinitis pigmentosa, severe photoreceptor degeneration occurs. Optogenetics therapy offers the potential for vision restoration in these patients by photosensitizing higher order neurons. Since this approach focuses on disease phenotype versus a specific genotype deficit, it is applicable to a wide patient population. Existing optogenetic tools utilize opsins that do not generate adequate electrical current in ambient light requiring an external device for stimulation. Further, evaluation of efficacy in such low-vision patients require development of novel endpoints.

Methods: Multi-Characteristic Opsin (MCO) is an engineered opsin that is activated at ambient light levels, thereby avoiding the need for an external amplifying device and associated phototoxicity. Through the delivery of opsin encoding genes, residual retinal neurons take on the photosensitizing function of the photoreceptors. Targeting bipolar cells with MCO allows potential for greater spatial resolution. AAV2 was used to deliver MCO in advanced retinitis pigmentosa subjects. Subjects received prophylactic oral steroids prior to a single intravitreal injection of AAV2-MCO (vMCO). Safety of different intravitreal vMCO doses is evaluated using OCT, slit lamp and indirect ophthalmoscopy. Novel end points such as Y-Mobility Test (YMT) and Low-Vision Multi-Parameter Test (LVMPT) utilizing multiple luminance levels are deployed to evaluate efficacy.

Results: Approximately 50% low-vision subjects at multiple centers passed the screening criterion requiring failing of the YMT at 1 lux. The three-dimensional shape recognition by LVMPT allowed measurement of accuracy in shape recognition at different light intensities. The two different vMCO doses are well tolerated with no reported serious adverse events. Ocular adverse events include inflammation and intraocular pressure rise in few subjects, controlled via medication without requiring any surgery.

Conclusions: The vMCO doses are well tolerated with no serious adverse events. The novel endpoint measurements in low-vision subjects in a randomized and masked manner provide opportunity to evaluate the efficacy of the optogenetic vMCO monotherapy in improving functional vision in advanced RP patients.

CONTROL ID: 3714717

SUBMITTER (NAME ONLY): Sandeep Grover

TITLE: Aqueous Levels of VEGF Decrease After Serial Intravitreal Injections of Anti-VEGF Agents in Patients With Exudative Age-Related Macular Degeneration

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Grover, G. Hamdani, C. Shoup, B. Mynampati, Ophthalmology, University of Florida Health Science Center Jacksonville, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure the levels of VEGF in aqueous of patients with exudative macular degeneration (eAMD) receiving intravitreal anti-VEGF agents and to explore whether this can be used to personalize treatment options for patients.

Methods: The study was approved by the local University IRB. Aqueous samples were collected at the time of paracentesis following each intravitreal injection of an anti-VEGF agent given serially every 4 – 6 weeks in patients with eAMD. These samples were immediately stored in -80^{0} C freezer. At the time of analysis, aqueous samples were thawed at room temperature and VEGF (pg/ml) levels were measured using human premixed multi-analyte kit and magnetic bead assay on Luminex MAGPIX analyzer (Austin, TX, USA).

Results: In 139 samples from 31 eyes, the average VEGF level from the first sample measured in each patient was 34.9 pg/ml. This decreased significantly to an average level of 6.8 pg/ml in the last sample measured from each patient after 2 – 10 injections (average 4.5 injections) of an anti-VEGF agent. The change in VEGF levels correlated with the presence of subretinal fluid on OCT.

Conclusions: Aqueous levels of VEGF can be easily measured at every injection in eAMD patients. Aqueous levels of VEGF were significantly reduced after treatment with anti-VEGF agents. With the ease of obtaining the aqueous sample and measuring the VEGF levels, this parameter maybe a useful parameter in the future, in addition to visual acuity and retinal thickness, to possibly personalize the treatment of eAMD patients.

CONTROL ID: 3714718

SUBMITTER (NAME ONLY): Kailyn Ramirez

TITLE: Social Determinants of Health, Medication Adherence, and Glaucoma in Vulnerable Patients

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.A. Ramirez, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|M.I. Vega Garces, M. Suarez, A. Khouri, Rutgers New Jersey Medical School Institute of Ophthalmology and Visual Science, Newark, New Jersey, UNITED STATES|B. Holland, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is one of the leading causes of irreversible blindness in the United States, affecting nearly 3 million. This number is expected to rise to 6.3 million by the year 2050. We performed a cross-sectional study investigating the interactions between Social Determinants of Health (SDOH), self-reported non-adherence, and Glaucoma Severity (GS) in vulnerable patients.

Methods: Participants that met inclusion criteria of confirmed clinical diagnosis of glaucoma, on medical therapy, at an academic medical center in Newark, NJ serving a widely underserved population (Median Income $20k) were randomly enrolled. All participants completed a structured survey in their preferred language (English or Spanish) consisting of demographic information, self-reported adherence and Short Assessment of Health Literacy (SAHL). Subjects unwilling to complete surveys were excluded. Objective data included Visual Field Mean Defect (MD). Survey scores were correlated with demographic and objective data. Participants were compared based on mild or severe glaucoma severity (MD <-12dB, MD >-12dB, respectively) and high or low health literacy (score: 15-18 and 0-14 correct, respectively). Continuous data was compared using analysis of variance (ANOVA) and t-tests.

Results: 61 participants met inclusion criteria, with a median age of 62 years. The majority of participants were female (65.5%), Black (48%), and had a low education (no diploma or high school only, 57.3%). Participants who classified as severe (N=25) more often reported having high school education or less (60%), greater difficulty accessing medication (60%), and lack of adherence (59%). Severe glaucoma was associated with low-health literacy($P<.05$). Participants lost to follow-up, 75% classified as having low health literacy and no education. The association between glaucomatous severity, education level, and health literacy level was significant ($p<.05$). Average mean defect was calculated for each demographic (Table 1).

Conclusions: Patients with vulnerable demographic risk-factors may have a higher burden of severe glaucoma and difficulty with adherence. This pilot study supports that various SDOH may predict GS and loss to follow-up. Further studies need to be conducted on larger populations to guide appropriate preventative intervention for identified patients.

CONTROL ID: 3714720

SUBMITTER (NAME ONLY): Jacob Granley

TITLE: Effects of Stimulus Parameters on Phosphene Appearance in Epiretinal Prostheses

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Granley, M. Beyeler, Computer Science, University of California Santa Barbara, Santa Barbara, California, UNITED STATES|Y. Hou, T. Bhatia, B. Johnson, M. Beyeler, Psychological and Brain Sciences, University of California Santa Barbara, Santa Barbara, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The shapes of phosphenes elicited by epiretinal prostheses have been shown to depend on stimulus parameters as well as the retinal location of the stimulating electrode. While previous studies have individually documented some of these effects, there is not yet a single model that can predict phosphene appearance across a wide range of electrical stimuli. To fill this gap, we conducted a meta-analysis across multiple modalities of patient data to comprehensively document and model the effects of stimulus amplitude, frequency, and pulse duration on phosphene appearance.

Methods: We first aggregated data from four psychophysical (phosphene drawings, size and brightness ratings) and one electrophysiological study (retinal ganglion cell activation maps) to investigate the effect of stimulus amplitude, frequency, and pulse duration on phosphene size, brightness, and streak length across 7 different Argus I/II users (Second Sight Medical Products) as well as 15 wild-type rat retinas. We then developed a simple phosphene model using a simulated map of retinal nerve fiber bundles combined with a few simple equations constrained by our combined dataset. We evaluated per subject how well the model predicted phosphene area, orientation, and ellipse major/minor axis length on held-out electrodes and compared the results to previous models.

Results: Phosphenes grew brighter ($r=0.64$, $p<0.01$), larger ($r=0.46$, $p<0.001$), and less elongated ($r=-0.14$, $p<0.05$) with increasing amplitude, grew brighter ($r=0.77$, $p<0.001$) with increasing frequency, and grew brighter ($r=0.85$, $p<0.001$), larger ($r=0.85$, $p<0.001$), and less elongated ($r=-0.84$, $p<0.001$) with increasing pulse duration (Table 1). When fit to data from individual patients, the model accurately predicted brightness as a function of amplitude ($R^2=0.91$) and frequency modulation ($R^2=0.97$) as well as size for amplitude ($R^2=0.97$). The model also generalized to brightness ratings from new subjects ($R^2=0.61$).

Conclusions: Through an analysis of psychophysical and electrophysiological data, we modeled the effects of various stimulus parameters on phosphene appearance in epiretinal prostheses. Overall this work is an important step towards predicting visual outcomes across a wide range of stimuli.

CONTROL ID: 3714721

SUBMITTER (NAME ONLY): Vishal Shinde

TITLE: VEGFR1 localization in mouse RPE.

SESSION TITLE: RPE/choroid pathology: oxidative stress, inflammation and neovascularization

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Shinde, D.M. Wu, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|E. Blank, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|D.M. Wu, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: VEGF plays a central role in the physiology of the eye as well as the pathology of AMD. Receptors for VEGF exist in the RPE, but their exact role in the physiology of the RPE is not well characterized. VEGFR1 is a member of the VEGF receptor family that can have contradictory effects on VEGF signaling. It can negatively regulate VEGF-mediated angiogenesis through sequestration of VEGF. At the same time, although it possesses weaker tyrosine kinase activity than VEGFR2, signaling through VEGFR1 has been found to be important in the mediation of inflammation. As inflammation of the RPE is a key component of AMD pathogenesis, we elected to more closely examine the localization of VEGFR1 in the RPE.

Methods: VEGFR1 expression was assessed in RPE cells of adult c57/bl6, cd1, and rd10 mice by immunostaining of RPE flat mounts and cryosections with two different antibodies against VEGFR1. In addition, we examined VEGFR1 expression in primary RPE cell culture from c57/bl6 mice retina. In some cases, we treated the RPE cells with VEGFR1 siRNA or shRNA to further validate VEGFR1 expression.

Results: We found VEGFR1 staining in c57/bl6 and cd1 RPE flat mounts across 3 time points (P30, P50, P70). In contrast, it was significantly reduced in rd10 RPE flat mounts checked at 3 time points (P30, P100 and P750). VEGFR1 staining could be cytoplasmic or nuclear. This was further examined in cryosections of wild type mouse eyes, where nuclear staining co-localized with immunostaining for Otx2, a transcription factor found in RPE nuclei. A blocking peptide eliminated this staining. RPE cells freshly isolated from c57/bl6 mice in primary culture also showed staining for VEGFR1 in the nucleus and cytoplasm, and these levels could be reduced after transfection of either VEGFR1 siRNA or a VEGFR1 miR30 shRNA construct. A scrambled shRNA construct that does not target VEGFR1 RNA did not show a reduction of VEGFR1.

Conclusions: VEGFR1 is expressed in the RPE of wild type mice, and can be found in both the nucleus and the cytoplasm. VEGFR1 is significantly reduced in the rd10 mouse model of retinal degeneration. The interesting pattern of VEGFR1 localization suggests the value of studying the role of VEGFR1 beyond its role in VEGF sequestration.

CONTROL ID: 3714722

SUBMITTER (NAME ONLY): Charles Karrasch

TITLE: CCN2 regulates the extracellular matrix and facilitates retinal ganglion cell maturation in the developing retina

SESSION TITLE: Retinal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Karrasch, G. Mohiuddin, Cell Biology, SUNY Downstate Health Sciences University The School of Graduate Studies, Brooklyn, New York, UNITED STATES|S. Moon, O. Evgrafov, B. Chaqour, Cell Biology, SUNY Downstate Health Sciences University, Brooklyn, New York, UNITED STATES|C. Karrasch, G. Mohiuddin, Ophthalmology, SUNY Downstate Health Sciences University The School of Graduate Studies, Brooklyn, New York, UNITED STATES|S. Moon, B. Chaqour, Ophthalmology, SUNY Downstate Health Sciences University, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Extracellular matrix (ECM) remodeling is a key factor in retinal development. Recent work suggests the ECM protein Cellular Communication Network Factor 2 (CCN2) regulates retinal progenitor cell survival, proliferation, and differentiation. We employed transcriptional profiling of murine embryonic retinas to test the hypothesis that CCN2 regulates the ECM in a cell type-dependent manner and mediates cell fate specification.

Methods: Germline CCN2 deletion was achieved using a $Ccn2^{fl/fl}$; CMV-Cre mouse model. Embryonic day (E)18 $CCN2^{-/-}$ and $CCN2^{+/+}$ littermate control retinas from both sexes were used for bulk RNA sequencing (RNA-seq) (n=3), RT-qPCR (n≥3), and single-cell (sc)RNA-seq (n=2). RNA-seq and scRNA-seq data were interrogated by Gene Set Enrichment Analysis (GSEA).

Results: In $CCN2^{-/-}$ retinas, GSEA of RNA-seq data revealed significant repression of the Core Matrisome gene set (p=0.017, q=0.20), representing the core components of the ECM proteome. New retinas were probed via RT-qPCR for a selection of Core Matrisome genes, which confirmed broad ECM repression. Subsequent scRNA-seq and GSEA were performed with new retinas. Each retinal cell type possessed a unique ECM expression signature, and Ccn2 was specifically expressed by retinal progenitor cells (RPCs). CCN2 deficiency repressed the structural ECM genes Col1a2 (-2.58-fold, p<0.01) and Col5a2 (-1.88-fold, p<0.001) specifically in RPCs. Damaged cells were approximately 3-fold more prevalent in $CCN2^{-/-}$ retinas compared to controls (17.6% vs. 5.76%), suggesting decreased viability following CCN2 deletion. Among retinal ganglion cells (RGCs), $CCN2^{-/-}$ retinas contained a greater proportion of immature RGCs compared to controls (71.2% vs 51.8%). Accordingly, RGCs from $CCN2^{-/-}$ retinas repressed a fetal RGC gene set (p<0.001, q<0.001) and upregulated a fetal RPC gene set (p<0.001, q<0.001). Finally, GSEA of scRNA-seq data revealed cell type-specific regulation of the Core Matrisome, which in $CCN2^{-/-}$ retinas was repressed in RPCs (p=0.017) yet upregulated in RGCs (p=0.021) and horizontal cells (p=0.016).

Conclusions: In the developing retina, CCN2 mediates pan-retinal ECM gene expression, yet differentially regulates the ECM in a cell type-dependent manner. CCN2 is critical for RPC-specific expression of structural collagen genes, retinal cell viability, and RGC specification from RPCs.

CONTROL ID: 3714723

SUBMITTER (NAME ONLY): Anna Paula Nassaralla

TITLE: Central serous chorioretinopathy: a restrospective appraisal of choroidal neovascularization types 1 and 2 in nonconsecutive subjects

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Nassaralla, A. Nassaralla, J.J. Nassaralla, Retina, Instituto de Olhos de Goiânia, Goiânia, GO, BRAZIL|M.H. Amaro, Instituto de Olhos e Laser de Belém, Belém, BRAZIL|J. Mitre, Faculdade de Medicina do ABC, Santo Andre, SP, BRAZIL|T. Aihara, Irmandade da Santa Casa de Misericordia de Sao Paulo, Sao Paulo, SP, BRAZIL|L. Lima, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: To investigate choroidal neovascularization (CNV) types 1 and 2 in non-consecutive cases of central serous chorioretinopathy (CSCR) and its response to the best treatment.

Methods: We retrospectively evaluated 35 non-consecutive cases of CSCR for the presence of CNV types 1 and 2 during a 5-year follow-up. Those which developed CNV were submitted to monthly anti-VEGF applications for six months (either Ranibizumab, Bevacizumab or Aflibercept). Initially, the best corrected visual acuity ranged from 20/40 to 20/60 in the eyes presenting CSCR.

Results: During follow-up, we found three cases with evolving CNV: two were type 1 CNV and one was type 2. Among the eyes that developed CNV, no improve in visual acuity was observed, despite of the rigorous treatment and follow up.

Conclusions: Even though choroidal neovascularization type 1 is the most common reported CNV developed in such cases, CNV type 2 can occur in CSCR, and the outcome may be similar, with worsening in visual acuity prognosis regardless of best treatment.

CONTROL ID: 3714726

SUBMITTER (NAME ONLY): Neil Khatter

TITLE: Utility of UW-based solutions for reducing apoptotic signaling and retinal ganglionic cell death in a whole eye transplantation rodent model

SESSION TITLE: Tissue, drug and genome engineering

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.J. Khatter, C.R. Owens, B. Li, Y. Wang, C. Huang, A. Su, K.M. Washington, Department of Surgery, Division of Plastic and Reconstructive Surgery, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|N.J. Khatter, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|A. Jani, Department of Medicine, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|R.W. Nickells, McPherson Eye Research Institute, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Overcoming retinal ganglionic cell (RGC) death induced by ischemia reperfusion injury and optic nerve transection is necessary for successful whole eye transplantation (WET). Current organ transplants use tissue preservatives like University of Wisconsin (UW) solution. We tested UW and a modified version including $BaCl_2$ and valproic acid (mUW) as RGC preservation solutions in an orthotopic rodent WET.

Methods: Untreated naïve eyes from 14-to-16-week-old male Brown Norway rats (n=32) were harvested and retinas were stained by immunohistochemistry (IHC) for Brn3a to quantify RGC preservation and phospho-c-Jun (PNJ) for apoptotic signaling. Donor eyes were then intravitreally injected with 10 µL of heparinized saline (n=3), UW (n=5), mUW (n=5), or not injected at all (n=3) and hemifacial flaps with donor eyes were harvested for WET. At POD2, transplanted and native (recipient, untreated) eyes were enucleated and retinas were prepared for IHC analysis. Continuous variables are presented as mean (±standard error) and compared using one-way ANOVA and two sample Z tests.

Results: Naïve retinas expressed 102.4±3.2k Brn3a+ RGCs with a 12% background expression of PNJ+ signal. At POD2, native recipient retinas show 107.8±4.0k Brn3a+ RGCs with 9% co-staining for PNJ+. In the untreated WET condition, retinas show 114.6k±5.6k Brn3a+ RGCs with 39% co-staining for PNJ+, a significant increase from the naïve condition ($P<0.05$). In the saline condition, retinas show 90.4±8.8k Brn3a+ RGCs with 21% co-staining for PNJ+, a significant increase from the naïve condition ($P<0.05$). UW treated retinas show 78.7±4.5k Brn3a+ RGCs with 1% co-staining for PNJ+. mUW treated retinas show 88.9±4.9k Brn3a+ RGCs with 2% co-staining for PNJ+. UW and mUW are not statistically different from one another ($P>0.05$) and both provided a significant reduction in RGC apoptosis in the setting of WET at POD2 ($P<0.05$).

Conclusions: We have established a novel system to assess RGC preservation and apoptosis post-WET. Injecting UW-based preservation solutions represents a promising strategy for RGC survival post WET. UW and mUW reduced apoptotic signaling compared to no treatment and saline in donor eyes at POD2 after WET. Future research will include monitoring Brn3a+ and PNJ+ expression at other timepoints and analyzing other apoptotic markers.

CONTROL ID: 3714727

SUBMITTER (NAME ONLY): Winston Lee

TITLE: Identifying critical diagnostic features that distinguish ABCA4 disease from its Mendelian phenocopies

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Lee, Genetics & Development, Columbia University Irving Medical Center, New York, New York, UNITED STATES|W. Lee, J. Zernant, T. Nagasaki, S.H. Tsang, R. Allikmets, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|S.H. Tsang, R. Allikmets, Pathology & Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify the most critical diagnostic features that differentiate ABCA4 disease from its numerous monogenic phenocopying retinal disorders.

Methods: Clinical and demographic features from a large cohort of 407 genetically-confirmed ABCA4 disease patients were compared to 68 patients harboring causal variants in various retinal dystrophy genes known to phenocopy ABCA4. Clinical data analyzed in both groups included detailed clinical and family histories, multimodal retinal imaging (fundus photographs, 488-nm, 521-nm and 787-nm AF, spectral domain-optical coherence tomography) and full-field electroretinogram (ffERG) testing.

Results: We identified 6 predominant phenotypes of ABCA4 disease that exhibit significant clinical overlap with approximately 43 different retinal dystrophy genes. In milder phenotypes such as bull's eye maculopathy (BEM), ABCA4 was most effectively distinguished from genes such as CRX, GUCY2D, RPGR and PROM1 by the age at clinical presentation ($p<0.001$). Age was also a critical factor between ABCA4 and RP1L1-associated occult macular dystrophy (OMD); however, non-retinal features such as the presence of nystagmus were considered for early onset OMD-associated genes like CNGA3 and CNGB3. In the most advanced clinical stages characterized by widespread degeneration across the posterior pole, differential diagnoses extended to non-maculopathy genes such as RPE65 and CERKL. Differentiating factors included identifying degenerative progression patterns and delayed peripapillary atrophy although symptomatic history was singularly most effective ($p<0.001$). Several genes such as PRPH2 and ROM1 phenocopied multiple pathognomonic features of ABCA4 disease and required more in-depth characterization such as fleck morphology and total area of the spared foveal region ($p<0.00001$). With some exceptions, ffERG, visual acuity and family history were the least effective considerations for diagnostic accuracy.

Conclusions: The clinical spectrum of ABCA4 is phenocopied, to varying degrees, by over 40 different retinal dystrophy genes. The list of differential diagnoses changes according to the various clinical stages of ABCA4. In the vast majority of cases, individual demographic considerations such as the age at presentation or symptomatic history are sufficient for making an accurate diagnosis.

CONTROL ID: 3714728

SUBMITTER (NAME ONLY): Anna Howell

TITLE: Improved Protocol for hiPSC-derived Retinal Organoid Generation Increases Yield and Decreases Variability

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Howell, A. Vielle, Y. Park, M. Vergara, N. Mathiyakom, Opthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|A.C. Howell, A. Vielle, Y. Park, M. Vergara, N. Mathiyakom, Opthalmology, CellSight Ocular Stem Cell and Regeneration Program, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal organoids (RO) generated from human induced pluripotent stem cells (hiPSC) constitute important in-vitro tools for retinal disease modeling and therapeutic drug development. However, low organoid yield and variability between batches of RO cultures hinder the use of these models in translational applications that require a high level of reproducibility for quantitative analyses. Likewise, lengthy culture times make the model impractical for drug screening purposes. Therefore, we set out to optimize current protocols to overcome these limitations.

Methods: Two different wild-type hiPSC lines were used for RO generation using the well-established protocol by Zhong et al. (2014). Five different media supplementation regimens of were tested on RO cultures starting at 63 days of differentiation: 1μM retinoic acid (RA), 10μM RA, 1μM 9-cis retinal (9cisRAL), 10μM 9cisRAL, and no supplementation. RO yield and photoreceptor outer segment (OS) length were longitudinally assessed in live organoids from each condition over a 4-month period. Additionally, ROs were collected at various time points, fixed, and their composition was evaluated by immunofluorescent staining and confocal microscopy with image quantification using FIJI software.

Results: Compared to other supplementation conditions, RO cultures that were supplemented with 9cisRAL displayed higher yield, increased OS length, and accelerated photoreceptor differentiation.

Conclusions: In this work we evaluated the performance of 5 different media supplementation regimens on the yield and quality of RO generation, to identify the most robust conditions for quantitative translational applications. We found that even though all tested conditions were able to produce RO with all the different retinal cell types and with photoreceptors displaying outer segment structures, 9cisRAL produced better RO yield than other conditions. Moreover, this condition accelerated OS development by approximately 30 days and produced longer OS.

CONTROL ID: 3714729

SUBMITTER (NAME ONLY): Manjot Grewal

TITLE: Longitudinal changes in visual function parameters in varying severity of age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Grewal, S. Chandra, A. BIRD, G. Jeffery, S. Sivaprasad, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|M.K. Grewal, S. Chandra, S. Sivaprasad, NIHR Moorfields Biomedical Research Centre, London, Greater London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To investigate the progression of visual impairment at 12 months on various visual function tests in dry age-related macular degeneration (AMD).

Methods: Visual function of 44 participants recruited during the baseline study were re-assessed at 12 months. Participants with varying severity were classified into 1) Healthy aging (N=9), 2) intermediate AMD (iAMD) without subretinal drusenoid deposits (SDD) (N=17), 3) iAMD with SDD (N=10) and 4) non-foveal atrophy (N=8). Changes at 12 months in best corrected visual acuity (BCVA), low luminance visual acuity (LLVA), low luminance deficit (LLD), low luminance questionnaire (LLQ), mean scotopic perimetry, rod intercept time (RIT) and photopic ERGs were analysed using paired t-tests or Wilcoxon matched pairs signed rank test.

Results: Compared to baseline, delayed rod recovery in iAMD group without SDD group (p=0.043) was observed at 12 months. Lower composite scores on LLQ questionnaire were noted after 1-year review only in eyes with non-foveal atrophy (p=0.016). A decrease in BCVA of 4.5 ETDRS letters was observed in iAMD with SDD group (p= 0.035) and eyes with atrophic changes (p=0.008) at 12 months. There was no change over time in any other functional tests.

Conclusions: Rod recovery test is able to identify worsening of visual function in eyes with iAMD without SDD by 12 months while deterioration of LLQ score was observed in eyes with non-foveal atrophy only. These changes will inform future clinical trial designs in AMD.

CONTROL ID: 3714731

SUBMITTER (NAME ONLY): Bharani Krishna Mynampati

TITLE: Aqueous Levels of VEGF Decrease After Serial Intravitreal Injections of Anti-VEGF Agents in Patients with Diabetic Retinopathy

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Mynampati, G. Hamdani, K. bell, D. WuDunn, S. Grover, Ophthalmology, University of Florida Health Science Center Jacksonville, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure the levels of VEGF in aqueous before and after treatment in patients with diabetic retinopathy treated with anti-VEGF agents. This was compared to VEGF levels in control eyes

Methods: The study was approved by the local University IRB. Aqueous samples were collected at the time of paracentesis following each intravitreal injection of an anti-VEGF agent given serially every 4 – 6 weeks in patients with proliferative diabetic retinopathy (PDR) or diabetic macular edema (DME). The control eyes consisted of aqueous collected from patients without diabetes or any retinal disease, undergoing cataract surgery. These samples were immediately stored in -80^{0} C freezer. At the time of analysis, aqueous samples were thawed at room temperature and VEGF (pg/ml) levels were measured using human premixed multi-analyte kit and magnetic bead assay on Luminex MAGPIX analyzer (Austin, TX, USA).

Results: In 203 samples from 59 eyes, the average VEGF level from the first sample measured in each eye was 198.3 pg/ml. This decreased significantly to an average level of 26.5 pg/ml in the last sample measured from each eye after 2-9 injections of an anti-VEGF agent (average, 3.4 injections). In 64 control eyes, the average level of VEGF was 34.06 pg/ml. The change in VEGF levels correlated with the retinal thickness on OCT

Conclusions: Aqueous levels of VEGF can be easily measured at every injection in patients with diabetic retinopathy. Aqueous levels of VEGF were significantly reduced after treatment with anti-VEGF agents. With the ease of obtaining the aqueous sample and measuring the VEGF levels, this maybe a useful parameter in the future, in addition to visual acuity and retinal thickness, to possibly personalize the treatment of patients with diabetic retinopathy.

CONTROL ID: 3714732

SUBMITTER (NAME ONLY): Jessie Wang

TITLE: Prompt Primary Cyclophotocoagulation with Subsequent Aqueous Shunt as Needed for Neovascular Glaucoma with Synechial Angle Closure

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, M. Qiu, Ophthalmology and Visual Science, The University of Chicago Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Jessie Wang: Commercial Relationship: Code N (No Commercial Relationship) | Mary Qiu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In acute NVG, implanting an aqueous shunt into eyes with active anterior segment neovascularization (NV) increases bleeding related complications. Prompt anti-VEGF rapidly regresses NV but is ineffective at lowering IOP when the angle is already synechially closed. CPC has historically been reserved for eyes with poor visual potential. The purpose of this case series is to describe a single surgeon's experience utilizing prompt CPC with prior or concurrent anti-VEGF and subsequent aqueous shunt as needed in NVG eyes with synechial angle closure, regardless of visual potential.

Methods: A retrospective chart review was performed for NVG patients with uncontrolled IOP, active anterior segment NV, a synechially closed angle, no contraindications to prompt anti-VEGF, CPC within 3 days of presentation, and at least 6 months of follow-up.

Results: Seven patients (3 male, 4 female, all African American) with mean age 63.9 years were included. Underlying etiologies were PDR (N=3), CRVO (N=3), and chronic RD (N=1). All patients received prompt intravitreal anti-VEGF on the day of acute presentation or within 3 days at the time of CPC. Patients received ongoing anti-VEGF injections and PRP at the discretion of the retina service. Five patients did not require subsequent aqueous shunts through a mean follow-up of 14.8 months; most recent visual acuities ranged from 20/50 to LP, and IOPs ranged from 4-20mmHg on 0-3 IOP-lowering medications. Two patients who required subsequent tubes (1 Ahmed 5 weeks later, 1 Baerveldt-350 11 weeks later) had resolution of active anterior segment NV by the time of surgery, and phaco could be performed to facilitate sulcus tube placement. At most recent follow-up (26 and 7 months), visual acuities were 20/40 and 20/150 with normal IOP. No eyes developed uncontrolled anterior segment inflammation, macular edema, or phthisis.

Conclusions: Prompt primary CPC within 3 days, with prior or concurrent anti-VEGF, is an effective strategy to immediately lower IOP in acute NVG eyes with active anterior segment NV and synechially closed angles, regardless of visual potential. If IOP becomes uncontrolled later, an aqueous shunt can be implanted in a controlled setting after active anterior segment NV has regressed. Further research is needed to compare outcomes of prompt CPC vs aqueous shunt in acute NVG eyes with completely synechially closed angles.

CONTROL ID: 3714733

SUBMITTER (NAME ONLY): Abdullah Sarhan

TITLE: Integrating Machine Learning into Visual Field Analysis to automate glaucoma detection

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sarhan, J. St Amand, RetinaLogik Biotech Inc., Calgary, Alberta, CANADA|A. Sarhan , University of Calgary, Calgary, Alberta, CANADA|A.C. Crichton, Department of Surgery, University of Calgary Cumming School of Medicine, Calgary, Alberta, CANADA|J. St Amand, Kinesiology, University of Calgary, Calgary, Alberta, CANADA|G. Docherty, Department of Opthalmology, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: The visual field (VF) exam, especially the 24-2 or 30-2 version, is commonly used when diagnosing glaucoma. The exam tests patient response to stimuli and summarizes findings in a report. This study evaluates the potential of a machine learning based approach for glaucoma detection using a VF report. This automated approach has the potential to help specialists make better-informed decisions, to optimize screening and to help triage referrals.

Methods: We collected 144 VF exam reports for this study. There were 28 women and 44 men (average 67 years old), and both eyes were examined. Exams were either 24-2 (58%) or 30-2 (42%). A specialist reviewed the patient charts and labelled the reports as glaucomatous (66%) or not (33%). We separated the reports into two datasets, “training” (70%) and “testing” (30%), each with the same distribution of glaucomatous eyes. For every report, we collected the dB values for each data point on the visual sensitivity map, total deviation, and standard deviation grids. The 24-2 exam has fewer grid points than 30-2, so the 24-2 datasets had null values for the corresponding plot points present in the 30-2 but not 24-2. We also recorded the fixation monitor and losses. We then cleaned the data to prepare it for analysis and applied an xgb machine learning model to the “training” dataset. We selected XGBoost because it can be trained on datasets with null values and still produce high-quality results. We then evaluated the model by running our model on the “testing” dataset and measured precision and area under the curve (AUC). We also used cross-validation to avoid overfitting.

Results: We achieved 92% precision (in 92% of cases it will detect a glaucomatous patient) and an AUC score of 82% (in 82% of cases it will accurately classify the patient as glaucomatous or not, indicating minimal false negatives). Out of 239 features, 203 were unnecessary for the prediction to achieve the above results.

Conclusions: We developed a reliable automated glaucoma detection approach that requires only 36 data points from a VF exam. This approach could be used to optimize referrals. Further, combining this model with portable VF exams could improve access to vision screening and hence early detection of glaucoma in rural areas. Further testing on large and diverse samples is needed to validate our findings and to discover additional insights.

CONTROL ID: 3714734

SUBMITTER (NAME ONLY): Ashank Bains

TITLE: Diverse Research Teams Increase Recruitment of Minorities into Ophthalmic Clinical Studies

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bains, M.L. Subramanian, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|C. Chiu, M.G. Fiorello, N. Sanjiv, P. Osathanugrah, M.L. Subramanian, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|H. Cabral, School of Public Health, Boston University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prospective clinical trials in ophthalmology have historically struggled to enroll underrepresented racial and ethnic groups. In this study, we reviewed screening logs documenting consent or refusal to participate in prospective clinical studies. The purpose was to determine if specific patient and research personnel characteristics, such as demographics and languages spoken, influenced recruitment.

Methods: Retrospective cohort study at an urban academic hospital. Screening logs from 8 prospective clinical studies between 2015-2021 with a total of 1290 patients were included; demographics (age, gender, race/ethnicity, primary language, insurance status) were collected via electronic medical record, socioeconomic status (SES) was determined via area-deprivation index scores. Research staff demographics were collected via survey. Variables were analyzed using chi-square tests and odds ratios were calculated by multivariate logistic regressions.

Results: Black patients (OR=0.32, 95% CI 0.24-0.44; p<0.001) and Hispanic/Latino patients (OR=0.30, 95% CI 0.20-0.46; p<0.001) were significantly less likely to consent compared to White patients, even after adjusting for gender, language, SES, and insurance status. Males (OR=1.30, 95% CI 1.01-1.68; p=0.04) and those insured through Medicaid compared to Medicare (OR=1.6, 95% CI 1.30-2.16; p<0.001) were significantly more likely to consent, and patients with lower SES were significantly less likely to consent (OR=0.43, 95% CI 0.33-0.55; p<0.001). Concordance between patient and research staff gender decreased odds of enrollment (OR=0.71, 95% CI 0.54-0.93; p=0.014), while concordance in race and ethnicity (OR=2.98, 95% CI 2.14-4.16; p<0.001) significantly increased odds of enrollment. Patient’s primary language, concordance between patient and research staff language, and study design (interventional vs non-interventional) did not significantly influence the odds of participation.

Conclusions: Patients from racial and ethnic minority groups and low socioeconomic backgrounds were significantly less likely to participate in ophthalmic clinical studies. Notably, concordance of race/ethnicity and gender discordance between patients and research staff significantly increased patient enrollment, despite controlling for language. This study underscores the necessity of diversity in clinical research teams to decrease disparities amongst study subject populations.

CONTROL ID: 3714735

SUBMITTER (NAME ONLY): Andrew Voigt

TITLE: Spectacle: A Platform for Interacting with Over 1.5 Million Single-Cell Expression Profiles from the Eye

SESSION TITLE: Transcriptomics, proteomics, metabolomics and systems biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.P. Voigt, N.D. Lessing, E.M. Stone, B.A. Tucker, R.F. Mullins, T.E. Scheetz, University of Iowa Institute for Vision Research, Iowa City, Iowa, UNITED STATES|A.P. Voigt, N.D. Lessing, E.M. Stone, B.A. Tucker, R.F. Mullins, T.E. Scheetz, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Single-cell RNA sequencing (scRNA-seq) has revolutionized our understanding of ocular gene expression. However, analysis of scRNA-seq data is time consuming and requires a degree of bioinformatic expertise. We developed the free online platform Spectacle to provide rapid, interactive access to scRNA-seq data. Spectacle contains over thirty fully processed datasets that collectively contain 1.5 million cells across the cornea, iris, limbus, trabecular meshwork, retina, retinal organoids, RPE, choroid, and sclera.

Methods: We reprocessed scRNA-seq data from thirty-one previously published ocular scRNA-seq manuscripts with our R package cellcuratoR, which transforms expression matrices into interactive objects within R Shiny. For over 90% of datasets, the exact clustering coordinates have been recaptured, which simplifies comparison with figures from existing manuscripts.

Results: Like other scRNA-seq visualization tools, Spectacle supports interactive exploration of cell clustering and gene expression through dot plots, heatmaps, and violin plots. However, a growing number of scRNA-seq studies compare gene expression across different biological conditions. Spectacle uniquely supports such studies and facilitates sophisticated, biologically driven analyses. For example, Spectacle powers flexible differential expression to identify genes enriched with different biological conditions (e.g., health versus disease) (Figure 1). In addition, cells can be reclustered to search for rare subpopulations of cells with certain biological characteristics. Finally, Spectacle can simultaneously compare gene expression across multiple different data sets, increasing confidence that a gene is expressed in a particular cell type or enriched with a particular biological feature (e.g., enriched in foveal retinal cells). Spectacle is freely accessible online at https://singlecell-eye.org.

Conclusions: Spectacle is a free, interactive resource that powers sophisticated, user-driven biological analyses with a very large collection of ocular scRNA-seq studies.

CONTROL ID: 3714738

SUBMITTER (NAME ONLY): Bikash Pattnaik

TITLE: Functional restoration of Kir7.1 nonsense mutations using engineered tRNA

SESSION TITLE: Development of molecular therapies for inherited ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.R. Pattnaik, Pediatrics Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|B.R. Pattnaik, M. Kabra, P.K. Shahi, E. Akyuz, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|M. Kabra, P.K. Shahi, E. Akyuz, Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|C. Ahern, Molecular Physiology and Biophysics, University of Iowa Carver College of Medicine, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nonsense mutations in eukaryotic biology cause diverse diseases due to the creation of premature termination codon that results in truncated protein products. These diseases are often rare and ultra-rare, with an unmet medical need for therapeutic development. We have reported a KCNJ13 gene homozygous nonsense mutation c.158G>A, p.Trp53*.in a patient, and a c.496C>T, p.Arg166* nonsense mutation was reported earlier that caused Leber Congenital Amaurosis. Inwardly rectifying potassium channel (Kir7.1) is present in retinal pigment epithelial cells encoded by the KCNJ13 gene. This study aims to use engineered tRNA for the nonsense suppressing readthrough to rescue channel function.

Methods: HEK293 cells were co-transfected with a control plasmid (a Mo2RD reporter plasmid with either TAG or TGA codon) and a GFP tagged anticodon-engineered tRNA plasmid (4X Trp TAG 2-1 or 4X Arg TGA 3-1). The cells were imaged using a confocal microscope. The functionality of these plasmids to restore Kir7.1 current was assessed in a heterologous system expressing two GFP tagged nonfunctional nonsense mutation constructs, W53* or R166*. To study this, HEK293 cells were co-transfected with either R166*-eGFP-Kir7.1 plasmid along with 4x-Arg TGA, or W53*-eGFP-Kir7.1 plasmid along with 4x-Trp TAG. 72 hours post-transfection, cells were assayed for Kir7.1 current by whole-cell patch-clamp.

Results: All transfected cells showed red fluorescence indicating PTC correction for either TAG or TGA nonsense mutation with 80% transfection efficiency. Negative control experiments using a scrambled tRNA did not demonstrate any red fluorescence. HEK293 cells expressing W53* plasmid, when co-expressed 4X Trp TAG 2-1, we found expression Kir7.1 protein on the membrane compared to cytoplasmic expressions in the non treated cells. Biophysical properties of the Kir7.1 current like current-voltage plot, blocker sensitivity, and activation by Rb+ persisted in cells treated with 4X Trp TAG 2-1. Evaluation of the functional restoration of R166* mutation is underway.

Conclusions: Expression of red fluorescence after treating with respective tRNA treatment for Mo2 RD carrying nonsense mutation codons indicate normal protein translation by incorporating a wildtype amino acid. The restoration of Kir7.1 protein expression through membrane localization and functional restoration further assures the therapeutic use of engineered tRNA to correct nonsense mutation errors.

CONTROL ID: 3714739

SUBMITTER (NAME ONLY): Thomas Hwang

TITLE: Automated fluid volume detection is associated with 1-year treatment requirements in eyes with diabetic macular edema

SESSION TITLE: Diabetic macular Edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.S. Hwang, K. tsuboi, Y. Guo, J. WANG, C.J. Flaxel, S.T. Bailey, D. Huang, Y. Jia, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the relationship between optical coherence tomography angiography (OCTA) parameters at the baseline and treatment requirements over 1-year in eyes with diabetic macular edema (DME).

Methods: We followed one eye of each patient with DME without treatment in the preceding 12 months prospectively over one year. Participants underwent 3x3-mm OCTA scans centered on the fovea using Avanti (Optovue) at baseline. DME was defined as eyes with any fluid detected by a custom algorithm in a 3x3-mm area. We measured the foveal avascular zone (FAZ) and extrafoveal (excluding the central 1-mm circle) avascular area (EAA) in the superficial vascular complex (SVC), intermediate capillary plexus (ICP), and deep capillary plexus (DCP). Fluid volume (FV) was assessed in the inner nuclear layer (INL) and outer plexus layer (OPL). Patients received treatment for DME per standard of care. The primary outcome measure was the predictive value of baseline OCTA parameters for treatment requirements for one year.

Results: We included 66 eyes (mean 60 years old, 27 female). The mean number of treatments over 1 year was xx (range 0 to 14), and the mean number of visits was 1.4 ± 2.7 (range 0 to 14). Twenty-three eyes (35%) underwent treatment during the follow-up. These eyes were significantly younger ($P = 0.027$) and had greater FV in the INL and OPL ($P = 0.017$ and $P = 0.017$) at the baseline than eyes without treatment over 1 year. Univariate analyses showed significant associations with the number of treatments for age (rho = -0.28, $P = 0.025$), FV in the INL ($R = 0.35$, $P = 0.0083$), FV in the OPL ($R = 0.38$, $P = 0.0003$), and DR severity ($R = 0.30$, $P = 0.016$), but not for FAZ, EAA in all layers, and baseline central subfoveal thickness ($P > 0.05$). In a multivariate linear regression model ($R^2 = 0.36$), FV in the OPL (Standard $\beta = 0.35$, $P = 0.016$) and DR severity (Standard $\beta = 0.36$, $P = 0.0062$) were significant factors.

Conclusions: Greater FV at baseline is a predictor of greater treatment frequency in DME. The vascular metrics at baseline does not predict treatment requirement.

CONTROL ID: 3714740

SUBMITTER (NAME ONLY): Moying Wang

TITLE: Toxic Effect of Extracellular Histones and Their Role in Retinal Diseases.

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wang, H. Liu, J. Sun, X. Zhang, J. Kong, Fourth Affiliated Hospital of China Medical University, Shenyang, Liaoning, CHINA|

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ABSTRACT BODY:

Purpose: To detect released histone in the vitreous space of patients with various retinal diseases, and to identify its role and activity using the retinal degeneration mice model.

Methods: Vitreous samples of patients were collected during vitrectomy and the histone concentration was tested by enzyme-linked immunosorbent assay. And a retinal degeneration mouse disease model was conducted by knocking out the nr2e3 gene. And the released extracellular histone in mice retina was verified by western blot and immunofluorescent staining. Besides, subretinal injection and intravitreal injection were utilized to deliver anti-Histone into the retina of nr2e3 knockout mice. Optical coherence tomography (OCT), fundus photography, fundus fluorescein angiography, and ERG were used to track the morphology changes over time.

Results: Released histones were detected in the vitreous space of patients with different retinal diseases. And in the retina of nr2e3 knockout mice, histone was also observed releasing from the nucleus of dying photoreceptor cells and then acting as damage-associated molecular pattern molecules when they were released into extracellular space. Interestingly, classic rosettes lesions of nr2e3 knockout mice usually appear by 12 days after birth, but the released histone and activated microglial appeared earlier than rosettes. Moreover, histone was also released by microglial cells via extracellular traps. After anti-Histone treatment by subretinal injection and intravitreal injection in postnatal 14 days mice, the number of the rosettes in the treated eyes was significantly less than that of the untreated control eyes at 1 month after injection tracked by fundus photography and OCT.

Conclusions: Our findings suggest that histones can be released from retinas with retinal diseases and the extracellular histone may act as the damage-associated molecular pattern molecules inducing the proinflammatory process thereby cause tissue toxicity.

CONTROL ID: 3714741

SUBMITTER (NAME ONLY): Jiaming Zhou

TITLE: A potential role of cyclic dependent kinase 1 (CDK1) in late stage of retinal degeneration

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zhou, Ophthalmology department, Lunds Universitet, Lund, SWEDEN|

Commercial Relationships Disclosure: Jiaming Zhou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) refers to a group of inherited disorders that lead to the dysfunction and death of photoreceptors, which causes progressive vision loss, and there is in principle no treatment available. The cGMP-PKG system has been suggested as a disease driver in several mouse RP models, although the downstream signaling of this enzyme system has not been clarified. Here we investigate the cGMP-PKG-system with the aim to reveal its potential target(s), that may have a direct detrimental effect during retinal degeneration.

Methods: With the aid of organotypic retinal explant cultures from a mouse-based disease model, i.e. the rd1 mouse, we added cGMP analogues to inhibit PKG in retinal explants from rd1. Mass spectrometry followed by peptide enrichment was then done to study the cGMP-PKG dependent signaling. Via a bioinformatics analysis, we identified downstream targets regulated by this system, and selected cyclin dependent kinase 1 (CDK1) for further validation. The expression of CDK1 within photoreceptors was compared between the rd1 model and its healthy, normal wild-type counterparts. CDK1 expression was also observed after various lengths of pharmacological inhibition of PKG during culturing of rd1 explants, to further assess the association between cGMP-PKG and CDK1. Co-staining with two cell death markers, namely acetylated lysine and TUNEL, was performed to study the possible involvement of CDK1 during photoreceptor degeneration.

Results: We observed that CDK1 was expressed in rd1 photoreceptors while no expression was noticed in the wt peers. With PKG manipulation of rd1 retinal explants, we could not find any alternation of CDK1 expression after 2 hours nor after 2 days of PKG inhibition, respectively, while CDK1 was lower expressed after 4 days treatment, compared to non-treated counterparts. Also, we found a high overlap of CDK1-positive and TUNEL-positive cells, as well as a partial overlap of CDK1-positive and acetylated lysine-negatively cells, according to the data from the co-staining of in vivo retinas.

Conclusions: Our results, particularly the overlap of CDK1 and TUNEL positive cells, suggest that CDK1 could be a downstream effector of the cGMP-PKG system and that it may be directly connected to the cell death process. Further studies of the CDK1 enzyme during retinal degeneration may therefore put it forward as a potential target for neuroprotection.

CONTROL ID: 3714743

SUBMITTER (NAME ONLY): Katherine Leviste

TITLE: Inhibitory Effect of Disodium and Lactone Rose Bengal on the Growth of Candida spp. Isolates In Vitro

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.D. Leviste, H. Durkee, P.A. Sepulveda Beltran, E.C. Alfonso, G. Amescua, D. Miller, J. Parel, Department of Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|K.D. Leviste, H. Durkee, P.A. Sepulveda Beltran, J. Parel, Ophthlamic Biophysics Center, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|B.C. Ferreira, R.M. Leblanc, Department of Chemistry, University of Miami, Coral Gables, Florida, UNITED STATES|D. Miller, Ocular Microbiology Laboratory, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Effective therapies to manage infectious keratitis are limited and rose bengal photodynamic antimicrobial therapy (RB-PDAT) is an emerging adjunct treatment (AJO 2019 PMID: 31493402). However, the antifungal activity of the photosensitizers on yeast species is unknown. We report the in vitro fungicidal effect of research (RB-1) versus clinical grade (RB-2) photosensitizers for RB-PDAT on Candida spp. Growth curve analysis was performed to assess the impact of non-irradiated rose bengal disodium (RBD) and lactone (RBL) on the metabolic activity of Candida spp. prior to photoactivation.

Methods: Candida albicans (CA, n=2) and Candida parapsilosis (CP, n=2) isolates were inoculated in tryptic soy broth (TSB) at 1.5×10^7 CFU/mL then 0.1% RB-1 or 0.1% RB-2 in 0.9% sodium chloride. Aliquots were plated on Sabourad-Dextrose agar in 3 groups: 1) Control (no photosensitizer/no irradiation); 2) Photosensitizer/No Irradiation; 3) Photosensitizer/Irradiation with 525 nm green LED light for 15 minutes at 5.4 J/cm2. After 72 hours of incubation at 37 degrees C, plates were photographed. Subsequently, three groups of 8 Candida spp. isolates (CA n=3, CP n=3, standard strains n=2, ATCC 90028, ATCC 22019) were prepared at 1.5×10^3 CFU/mL and inoculated in 1) TSB only 2) 0.01% RBD and 3) 0.01% RBL. 200µl samples were loaded onto a 96-well plate in triplicate and growth kinetics were measured on a Fluostar Omega instrument over 48 hours.

Results: Fungicidal activity (>95% elimination) was observed in all strains treated with RB-PDAT, whereas organisms that did not receive RB-PDAT grew confluent colonies with zero growth inhibition. Growth curve kinetics of Candida spp. prior to photoactivation showed no differences in ATCC CA, ATCC CP, CP-2 and CP-3 organisms in RBD. CA-2, CA-3, CA-4, and CP-1 in RBD versus RBL, showed increased growth in RBL at the stationary phase.

Conclusions: Candida spp. isolates recovered from patients treated with disodium RB were susceptible to in vitro RB-PDAT irradiation. A comparison of Candida spp. growth curves in non-irradiated RBD versus RBL showed no difference in optical density with either photosensitizer, suggesting that the solutions alone are insufficient to inhibit fungal proliferation.

CONTROL ID: 3714745

SUBMITTER (NAME ONLY): Michelle Hribar

TITLE: Can EHR Data Automatically Calculate Ophthalmic Quality Measures? The Impact of Baselines

SESSION TITLE: Using Technology for Care Delivery and Improvement

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Hribar, DMICE, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|M. Hribar, J.S. Chen, A. Chen, Ophthalmology, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The American Academy of Ophthalmology (AAO) ophthalmic clinical quality measures (QM) define successful clinical outcomes for ophthalmic care. Of the AAO's 30 ophthalmic QMs in 2020, 17 of them use an improvement over baseline as the outcome. Nevertheless, the QM definitions do not provide details about what baseline value to use, which makes automatic calculation of the quality measure difficult and variable.

Methods: We evaluated two QMs using different baselines in two different patient populations: 1) Oregon Health & Science University (OHSU) clinical practices and 2) the IRIS Registry. We analyzed IRIS 39, Glaucoma – Intraocular Pressure Reduction Following Trabeculectomy or an Aqueous Shunt Procedure, and IRIS 59, Regaining Vision after Cataract Surgery using surgeries that occurred between January 1, 2019 and December 31, 2019. Neither measure defined the time frame or rules for selecting which values to use as baseline. We chose to calculate IRIS 39 using the best (lowest) and worst (highest) interocular pressure (IOP) values measured within 1 year prior to surgery as baselines, and chose the best (lowest) and worst (highest) visual acuity (VA) values measured within 30 days prior to surgery for baselines in IRIS 59.The results for the different baselines were compared using Z tests.

Results: The percentage of patients who met each of the measures varied at both OHSU and in the IRIS Registry depending on baseline used (Figures 1 and 2). For both measures and populations, the worst baseline values resulted in higher percentage of patients meeting the measure; in all cases over 70% of patients met the measure (the benchmark for full reimbursement), but the best baseline values achieved this benchmark in only one case (IRIS 39 in IRIS Registry). The difference in the % of patients meeting the measure for different baselines were statistically significant ($p < 0.01$) for both measures in both populations.

Conclusions: This study shows that baseline values have an impact on the number of patients who meet QMs. Careful definition of baselines has important implications for healthcare quality and reimbursement; without these definitions, electronic health records cannot accurately and consistently calculate QMs. Moreover, explicit baseline definitions are crucial for demonstrating effectiveness of treatments in research and clinical trials.

CONTROL ID: 3714746

SUBMITTER (NAME ONLY): Carlos Parra

TITLE: Diffusion tensor imaging of optic nerve integrity in mouse models of E50K optineurin mutation and optineurin deficiency

SESSION TITLE: Neurodegeneration

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mutations in optineurin (OPTN) are associated with familial normal tension glaucoma and other neurodegenerative diseases, yet their contribution to visual impairments remain unclear. Recently, in vivo longitudinal assessments on transgenic mouse models revealed that E50K OPTN was associated with differential age-dependent vision loss, whereas knocking out OPTN appeared to preserve visual function [IOVS 2021; 62(8):2385]. Here, we aimed to determine the role of E50K OPTN on underlying structural integrity in the mouse visual pathway using diffusion tensor imaging (DTI).

Methods: Twenty-eight 24-month-old mice with C57BL/6 background were used: wildtype (WT; n=9), homozygous OPTN knock-out (mOPTN-KO; n=8), hemizygous mouse E50K OPTN knock-in (mE50K het; n=3), homozygous mouse E50K OPTN knock-in (mE50K homoz; n=5), and human E50K OPTN bacterial artificial chromosome overexpression (hE50K BAC; n=3) (PMID: 31076632, 25818176). Ex vivo whole-brain DTI was acquired in 60 directions in a 7-Tesla MRI scanner. DTI parametric maps including fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD), and mean diffusivity (MD) maps were derived, and bilateral regions-of-interests (ROIs) were manually delineated for the optic nerve (ON) and anterior commissure (AC) on each map (Fig. 1). Results were analyzed using ANOVA and post-hoc tests.

Results: Significant group differences were observed in FA, RD, and MD but not AD for ON (ANOVA, $p<0.05$). No significant group difference was observed in either DTI map for AC ($p>0.05$). As shown in Fig. 2, Bonferroni-corrected post-hoc tests for ON revealed significantly lower FA in mE50K het and mE50K homoz relative to WT, along with significantly higher RD and MD in the same mE50K groups. Post-hoc analyses also revealed higher RD in mE50K het relative to hE50K BAC for ON.

Conclusions: The significant DTI differences in ON but not AC between WT and mE50K groups suggest the preferential disruption of structural integrity in the visual pathway upon a toxic gain of function mechanism from E50K OPTN. Such overall integrity loss as indicated by reduced FA appeared to be driven by increases in RD and MD, which are sensitive to glial activity and neuroinflammation. The non-significant differences between mOPTN-KO and WT suggest that suppression of OPTN might help preserve white matter structures from glaucomatous neurodegeneration.

CONTROL ID: 3714747

SUBMITTER (NAME ONLY): Rhys Ishihara

TITLE: Assessing the short term visual and anatomical outcomes in ocular syphilis treated with adjunctive topical or oral steroids

SESSION TITLE: Anti inflammatory agents, antibiotics and antivirals

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ishihara, S. Buscho, P. Gupta, Department of Ophthalmology and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Rhys Ishihara: Commercial Relationship: Code N (No Commercial Relationship) | Seth Buscho: Commercial Relationship: Code N (No Commercial Relationship) | Praveena Gupta: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is very little documented about the use of adjunctive steroids for uveitis associated with ocular syphilis. Because little evidence exists for the route of steroid treatment, we compared the effectiveness between the use of adjunctive topical steroids versus oral steroids. We performed a retrospective, clinical study to learn about the anatomic and visual outcomes in ocular syphilis patients treated with adjunctive topical steroids or oral steroids.

Methods: Nine male patients aged 26 to 72 years old were identified with a diagnosis of ocular syphilis by a positive RPR, positive treponemal IgG/IgM, with associated bilateral anterior or posterior chamber inflammation. All patients were treated with IV penicillin and topical prednisolone acetate or high dose oral prednisone. Six patients were found to be treated with topical prednisolone acetate 1-2 days after starting treatment with penicillin. Three patients were treated with high dose oral prednisone 1-2 days after starting treatment with penicillin. Visual acuity and slit lamp findings (cells and flare) were documented at presentation. Outcomes were visual acuity and slit lamp findings at discharge from the hospital or first clinic follow up after discharge.

Results: Patients in the topical steroids group had an average presenting visual acuity of 20/400. There was improvement to 20/100 at a mean follow up of 16.1 days. Patients in the oral steroids group had an initial visual acuity of 20/100. There was visual improvement to 20/25 at a mean follow up of 8.3 days. Qualitatively, there was significant improvement of ocular inflammation in both groups, but there was swifter improvement in the oral steroids group.

Conclusions: There was a noticeable increase in the rate of improvement of visual and anatomical recovery in ocular syphilis patients treated with oral steroids in the short term. Also, average recovered visual acuity in the oral steroids group was significantly better than the topical group, although, the starting average visual acuity was worse in the topical group. However, this is a small study, and we are looking to expand our sample size to other sites. Furthermore, many of the patients were lost to follow up and more studies need to be performed to assess long term outcome.

CONTROL ID: 3714748

SUBMITTER (NAME ONLY): MD Imam Uddin

TITLE: Inhibition of HIF-1α mRNA could regulate monocyte functions and could inhibit neovascularization in a mouse model of proliferative retinopathy

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Uddin, R. Atalor, Ophthalmology, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|M. Uddin, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bone marrow-derived activated monocytes and progenitor cells migrate to the retina in response to inflammation and neovascularization. Hypoxia-inducible factor-1α (HIF-1α) has been shown to contribute to the pathogenesis of neovascularization. However, contribution of monocyte-derived macrophages to neovascularization is largely unknown. We describe here the synthesis of a new hybrid nanoparticle for targeted delivery and gene silencing in activated monocytes that are associated with pathological neovascularization.

Methods: Single-cell RNAseq data analysis were performed to characterize HIF-1α mRNA expression in activated monocytes in mouse oxygen-induced retinopathy (OIR). HIF-1α targeted AS-shRNA-lipids were synthesized by conjugating diacyl-lipids to anti-sense short hairpin RNA with an anti-sense sequence complimentary to HIF-1α mRNA. The short hairpin RNA compounds were stabilized using 2'-O-methyl-protected ribonucleotides allowing in vivo delivery of AS-shRNA-lipid to the activated monocytes that are associated with neovascularization.

Results: HIF-1α mRNA expression was associated with MRC-1 positive activated monocytes. In addition, HIF-1α mRNA was induced in monocytes by exposing the cells to hypoxia, and the expression was inhibited by AS-HIF-1α-shRNA-lipid. CD14 mRNA expression was significantly elevated in monocytes that were exposed to hypoxia, suggesting monocyte activation. AS-HIF-1α-shRNA-lipid could significantly inhibit this activation. In addition, significant reduction of neovascularization was achieved in mouse OIR after intraperitoneal injection of AS-shRNA-lipids.

Conclusions: Inflammation and hypoxia could activate monocyte functions and inhibition of HIF-1α mRNA could recover these cells from activation. In summary, we have developed a novel method for targeted delivery and inhibit HIF-1α mRNA in activated monocytes in living ocular tissues using diacyl-lipid-conjugates of antisense short hairpin RNA (AS-shRNA-lipid) designed to target HIF-1α mRNA. These conjugates are readily internalized by activated monocytes that are associated with neovascularization in the living retina. These findings may provide a framework for a novel strategy to inhibit retinal neovascularization.

Keywords: targeted delivery, activated monocytes, gene therapy, short-hairpin RNA, neovascularization.

CONTROL ID: 3714749

SUBMITTER (NAME ONLY): Siyun Liu

TITLE: Does Optic Flow Enhance Depth Perception in the Presence of Artificial Acuity Reduction?

SESSION TITLE: Visual Function: perception, adaptation, spatial, visual acuity and binocular vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Liu, G.E. Legge, Psychology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optic flow induced by self-motion can enhance depth perception in 3D space. For observers with reduced acuity and contrast sensitivity, motion cues might be helpful when pictorial and binocular depth cues are unreliable. Motion-related depth cues can be categorized as optical expansion when the observer approaches the fixated object, and motion parallax when the observer's motion is orthogonal. Is there a difference in the accuracy of depth perception with these two types of observer motion under conditions of blur? If yes, is the benefit due to the difference in starting and ending viewpoints, or does it require continuous motion?

Methods: We created a virtual 3D room containing a target cube on the floor and a reference sign. Two-second-long videos were rendered in five types: a single static view, optical expansion from continuous forward motion or the corresponding first and last static views, and motion parallax from continuous orthogonal motion or the corresponding first and last static views. Videos were prepared with three levels of calibrated blur—Moderate, Severe, and Profound with corresponding logMAR values of 0.95, 1.15, and 1.55. Ten normally sighted observers viewed the videos on a computer monitor. They judged how far the target cube was in front or behind the reference sign in feet by moving an on-screen slider.

Results: Averaged across the three blur levels, motion parallax reduced depth estimation errors by 47% and optical expansion by 10% compared to a single static view. The difference in performance between continuous motion and conditions with start-ending views was only significant in the Moderate blur condition ($p<.001$). In the Severe and Profound blur conditions, the difference between continuous motion and start-and-end static views was not significant.

Conclusions: Motion parallax yielded greater benefits in judging object depth than did optical expansion. Except in the Moderate blur condition, continuous motion was no more effective than static views at the beginning and end of the motion sequence. Together, these results indicate that motion cues are beneficial in judging object depth for conditions of artificial acuity reduction.

CONTROL ID: 3714750

SUBMITTER (NAME ONLY): Aseef Ahmed

TITLE: Outcomes of pre-operative corticosteroid use in glaucoma surgery

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ahmed, W. West, D. Belyea, Ophthalmology, The George Washington University Department of Ophthalmology, Washington, District of Columbia, UNITED STATES|A. Ahmed, H. Pakhchanian, W. West, D. Belyea, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|C. DeYoung, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the post-operative outcomes of corticosteroid use prior to glaucoma surgery in the treatment of primary open angle glaucoma (POAG).

Methods: A retrospective cohort study was conducted using the TriNetX (Cambridge, MA, USA) electronic health records research network to identify patients who underwent glaucoma surgery for POAG, identified by ICD-10 and CPT code. Cases were stratified into two cohorts based on history of corticosteroid therapy of any kind for up to one year preceding surgery. Cohorts were matched for age, gender, and medical comorbidities (essential hypertension, diabetes mellitus, chronic lower respiratory disease, heart failure, nicotine dependence, alcohol related disorders, and body mass index). The primary outcomes were as follows: development of secondary glaucoma, ocular hypotony, hyphema, vitreous hemorrhage, choroidal hemorrhage, retinal detachment (RD) or tear (RT), iridocyclitis, macular edema (ME), cystoid macular degeneration (CMD), cataract, strabismus, secondary corneal edema, dry eye syndrome (DES), central retinal artery occlusion (CRAO), central retinal vein occlusion (CRVO), vitreous hemorrhage (VH), and revision of the aqueous shunt. Outcomes were compared between the cohorts after propensity score matching using logistic regression and greedy nearest-neighbor matching algorithm. The risk ratio (RR) was obtained, with a p-value <0.05 being considered as significant.

Results: A total of 6,494 eyes were included in the analysis with 3,247 cases in each of the cohorts. Cases with a history of steroid use had increased risk ($p<0.05$) for hypotony (RR 1.73, 95% CI 1.31-2.30), ME (RR 2.11, 95% 1.54-2.88), CMD (RR 1.88, 95% CI 1.43-2.47), choroidal hemorrhage (RR 1.79, 95% CI 1.0-3.18), cataract (RR 1.31, 95% CI 1.10-1.56), strabismus (RR 1.55, 95% CI 1.03-2.32), DES (RR 1.41, 95% CI 1.11-1.79), and need for aqueous shunt revision (RR 1.34, 95% CI 1.08-1.65). Lack of steroid use increased risk ($p<0.05$) for developing secondary glaucoma (RR 0.64, 95% CI 0.51-0.82). No significant difference was found in all other primary outcome measures.

Conclusions: History of any corticosteroid use is an important consideration for post-operative complications following glaucoma surgery. Limitations of this study included lack of data indicating route of corticosteroid administration and stratification based on type of glaucoma surgery (i.e., trabeculectomy versus aqueous drainage device).

CONTROL ID: 3714754

SUBMITTER (NAME ONLY): Anne Hanneken

TITLE: Revival of In Vivo-like ERG A- and B-waves in Ex Vivo Human Organ Donor Eyes

SESSION TITLE: Electroretinography and disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.M. Hanneken, Molecular Medicine, The Scripps Research Institute, La Jolla, California, UNITED STATES|A.M. Hanneken, Retina Consultants San Diego, Poway, California, UNITED STATES|F. Abbas, F. Vinberg, John A. Moran Eye Center, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many blinding diseases and aging impact specific geographic regions of the human retina, including the macula, the area responsible for our high-acuity color vision. Significant gaps in our knowledge about human vision exist due to technical barriers for studying phototransduction and light signal transmission specifically in the human macula. We aimed to establish criteria and methods for generating functionally viable peripheral and central human retina patches obtained from donor human eyes using ex vivo Electroretinography (ERG).

Methods: Eye bank autopsy eyes were recovered within 2-5 hours of death; organ donor eyes within 45 min - 2 hours following cardiac death (DCD), or 1 – 20 mins following circulatory arrest in brain dead donors (DBD), and within 5 mins of death from macaques. Eyes were transported to the laboratory in oxygenated Ames medium. Retinal punches were taken from the macula and periphery and perfused with Ames media at 35-37^{O}C in a custom ex vivo ERG device to measure light-induced electrical responses.

Results: We recorded ex vivo ERG a-waves from macular samples in autopsy eyes and in DCD eyes up to 5 hours postmortem. Photoresponse amplitudes in the DCD maculae were not different from those recorded from freshly dissected macaque maculae ($p=0.61$, n=3/5 human and macaque biological/technical replicates) but declined with increasing enucleation delay (decay time constant = 74 mins). ERG b-waves were not normally present in these donors (n=20), with one exception, where we could record ERG b-waves in the peripheral samples from a research donor who died of stroke (>2 hours enucleation delay). Using DBD eyes, we were able to consistently revive ERG b-waves when enucleation delay was under 20 mins (n=5/10 biological/technical replicates). DL-AP4, known to block mGluR signaling from photoreceptors to ON bipolar cells, abolished the b-wave both in peripheral and macular samples.

Conclusions: We established a method and distinct criteria for revival of ERG a- and b-waves in the human retina. We recorded the first ex vivo light responses from the human macula and used pharmacology to demonstrate that ERG b-wave in the human periphery and macula is mediated by photoreceptor-ON bipolar cell transmission. This approach enables future studies to advance our understanding of human vision, vision disorders and visual rehabilitation.

CONTROL ID: 3714756

SUBMITTER (NAME ONLY): Gengxi Lu

TITLE: Non-invasive ultrasound retinal stimulation for vision restoration and its frequency-dependent efficiency

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Lu, X. Qian, R. Li, Y. Zeng, B. Thomas, M.S. Humayun, Q. Zhou, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current treatment strategy for blindness caused by retina degeneration is to use invasive retinal prostheses based on electric stimulation. We hypothesize that ultrasound stimulation can be a promising non-invasive retinal prosthesis by observing the ultrasound-evoked neuron activities in cortical visual circuits of retina degenerated rats. The relationships between the ultrasound center frequency and the stimulation efficiency is also investigated.

Methods: In vivo experiments were conducted on both normal rats and RCS retina degenerated rats. Self-designed transducers with different center frequencies were mounted on a 5-axis precision stage and were placed in front of the rat eye. For electrophysiological recording, a small craniotomy was made based on stereotactic coordinates to expose the superior colliculus or primary visual cortex, then the multi-electrode array was advanced. Experiments were conducted on 10 normal rats and 16 blind rats.

Results: We show that direct ultrasound retina stimulation can evoke neuron activities from the visual centers in normal and retinal degenerated blind rats (Fig. 1). The neuron activities induced by the focused 3.1-MHz transducer have shown a spatial resolution of 250±50 μm. Ultrasound frequencies ranging from 2 MHz to 8 MHz were tested. Higher frequencies are more efficient for neuron stimulation. Mechanical index (MI) to evoke neuron activities is lower at higher frequencies.

Conclusions: Our findings demonstrate that ultrasound stimulation of the retina in vivo can evoke neuron activities. Higher ultrasound frequency leads to a lower stimulation threshold. Ultrasound stimulation is a promising technology as a novel and non-invasive visual prosthesis for translational applications in blind patients.

CONTROL ID: 3714759

SUBMITTER (NAME ONLY): Sameera Nadimpalli

TITLE: Proptosis secondary to poor ocular tethering from congenital aplasia / hypoplasia of multiple extraocular muscles

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Nadimpalli, J. Yu, L. Prasov, P. Williams, A. Jacobson, Ophthalmology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe a case of an infant with unilateral proptosis and bilateral asymmetric extraocular muscle (EOM) aplasia / hypoplasia in the setting of bilateral posterior embryotoxon.

Methods: Observational case report

Results: A full-term newborn was consulted for evaluation of a wide nasal bridge and anisocoria. Birth history was significant for anti-phospholipid antibody syndrome in the mother. Family history revealed hypertelorism in the brother with limited negative work-up, bilateral congenital cataracts in the mother, and congenital cardiac abnormalities in the brother and mother. Newborn screen was normal and the newborn evaluation was notable for a large atrial septal defect. Ophthalmology exam showed blink to light vision OU, anisocoria symmetric in light and dark without an APD, abduction deficits OS > OD, adduction deficit OS, corneal haze OU, posterior embryotoxon OU, and normal remainder of exam. She was noted to have left eye buphthalmos versus proptosis and underwent exam under anesthesia (EUA) with MRI head / neck at 5 months. EUA revealed IOP 21 OD and 24 OS, corneal haze OU, megalocornea OU, gonioscopy with peripheral anterior synechiae to posterior embryotoxon OU, pachymetry 670s OU, and axial lengths of 20.24 OD and 20.73 OS. Fundus exam OU showed normal nerves with 0.1 cup to disc ratio, blunted foveal light reflex and was otherwise normal. MRI revealed right lateral rectus and left medial rectus hypoplasia and left lateral rectus aplasia and was otherwise unremarkable. Given the constellation of findings, genetic testing was recommended but deferred by parents other than testing for mucopolysaccaridoses, which was negative.

Conclusions: In this patient, left eye proptosis was mistaken for congenital glaucoma-related buphthalmos from an anterior segment dysgenesis syndrome. Proptosis in this case is likely related to poor ocular tethering from EOM hypoplasia / aplasia. The latter could be related to a primary neurocristopathy resulting in anterior segment dysgenesis and associated EOM abnormalities as previous studies have suggested that neural crest migration is required for EOM development. Alternatively and less likely, this may be a case of a congenital cranial disinnervation disorder with incidental posterior embryotoxon. While genetic testing would be useful, the parents have elected to defer further work-up at this time.

CONTROL ID: 3714760
SUBMITTER (NAME ONLY): Cristos Ifantides
TITLE: Experimental study of the effect of heat on intraocular lens PMMA haptics
SESSION TITLE: Cataract surgery II
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: C. Ifantides, Ophthalmology, sue anschutz-rodgers eye center, University of Colorado, Aurora, Colorado, UNITED STATES|C. Ifantides, M. Johnson De Tora, R. Shandas, J. Wagner, School of Bioengineering, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|
Commercial Relationships Disclosure: Cristos Ifantides: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon;Code F (Financial Support):Johnson and Johnson;Code F (Financial Support):New World Medical;Code P (Patent):University of Colorado;Code P (Patent):New World Medical;Code C (Consultant/Contractor):Centricity Vision;Code C (Consultant/Contractor):Acufocus | Mari Johnson De Tora: Commercial Relationship: Code N (No Commercial Relationship) | Robin Shandas: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Wagner: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Poly(methyl methacrylate) (PMMA) three-piece intraocular lenses (IOLs) have poor durability for manipulation, resulting in haptic fracture or permanent bending. This study evaluates the mechanical properties of PMMA IOL haptics through stress-strain analysis and bend testing before and after applying heat to the material to enhance the durability and flexibility.

Methods: PMMA haptic material is heat treated by a water bath, for clinical relevance, at 8 different temperatures, and mechanically tested in tension, compression, and bending procedures. This method is then applied to 20, three-piece intraocular lenses, of the same manufacture.

Results: Preliminary data from this study indicates that after heat was applied to the PMMA haptics, the Young's Modulus was decreased by approximately 10%, and the average load force was decreased by approximately 25%. Experimental results show that at bending angles of 75 degrees and more acute, there is progressive deformation of the PMMA haptics at room temperature. Heating the haptics from 40°C to 45°C, for five minutes, showed minimal deformation immediately after bending that resolved after 20 minutes. Heating the haptics at any temperature above 35°C for 10 minutes led to increased deformation, when compared to five minutes, that did not resolve after 20 minutes. When heated from 50°C to 55°C, the haptic deformation improved, but did not completely resolve after 20 minutes. When heated past 60°C for five minutes, the haptic material undergoes permanent plastic deformation before performing the bending procedures. The data collected from experimental bending procedures showed a trend that the PMMA haptic material did not permanently deform when heated for five minutes between 40-45° C. When heated past 50°C for five minutes, the haptic material undergoes permanent plastic deformation with loss of elastic memory after bending procedures.

Conclusions: Pre-heating of PMMA IOLs within particular temperature ranges decreases their stiffness, enhances their flexibility, and reduces capacity for permanent plastic deformation. Such treatments may allow increased use of conventional PMMA IOLs for surgeries where haptic manipulation is expected (i.e. scleral fixation) by reducing the risk of plastic deformation due to haptic bending.

CONTROL ID: 3714761

SUBMITTER (NAME ONLY): Colin Flowers

TITLE: Letter-based perimetry: Initial findings

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Flowers, G.E. Legge, S. Engel, Department of Psychology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|C. Larson, E.J. Van Kuijk, Department of Ophthalmology and Visual Neurosciences, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|A.G. Erdman, Department of Mechanical Engineering, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|A.G. Erdman, Earl E. Bakken Medical Devices Center, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: People with central field loss rely on peripheral vision to read. We introduce a letter-based perimetry method to assess letter recognition over the central region of the visual field (13.5° x 14.9°). Performance is compared with microperimetry (Macular Integrity Assessment; MAIA). We expect that letter-based perimetry can accurately map the scotoma. Reading is influenced by other processes not needed in light detection (e.g., crowding, letter recognition) and letter-based perimetry may be useful in predicting peripheral reading ability.

Methods: We report data from one participant with macular degeneration that completed letter-based perimetry and microperimetry monocularly with their better functioning eye (left). Fixation stability was 'stable' (95% BCEA = $1.8°^2$) with a preferred retinal locus below and to the left of the scotoma (approx. 8° in diameter). For letter perimetry, strings of three randomly chosen letters were presented briefly (200 ms) at controlled locations (n = 117) on a computer. Fixation was confirmed to be at the center of the screen using an eye tracker (Tobii Spectrum Pro; 300 Hz). The participant verbally reported any detected letters. Correct and incorrect responses were summed for each letter location and accuracy was computed. The participant chose a comfortable letter size for reading. For microperimetry, a 10-2 Cartesian grid was used with a 4-2 threshold strategy to obtain light sensitivity thresholds; 60 of these locations overlapped with the tested letter locations. Mean letter recognition accuracy was computed for each of the 60 locations by averaging the recognition accuracies of overlapping letters.

Results: To test how well letter-based perimetry was able to map the scotoma, the letter recognition accuracy for MAIA grid locations with low light sensitivity (<= 13 dB; n = 22 locations; mean = 3.05 dB) were compared to those areas with high light sensitivity (>= 17 dB; n = 38 locations; mean = 21.79 dB). Locations with low light sensitivity had significantly lower letter recognition accuracy (9.1%) than locations with high light sensitivity (41.0%; $T(58) = -6.62$; $p < 0.01$).

Conclusions: We introduce a letter-based perimetry task where letter recognition is assessed across the central visual field. Letter recognition for areas with low light sensitivity as measured with microperimetry was significantly lower than areas with high light sensitivity demonstrating that letter-based perimetry is useful to detect scotomas.

CONTROL ID: 3714762

SUBMITTER (NAME ONLY): Haojie Fu

TITLE: Thrombospondin-1 p.R1034 missense alleles cause congenital glaucoma with variable expressivity by inducing extracellular protein aggregation

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Siggs, L. Knight, J. Craig, Department of Ophthalmology, Flinders University, Adelaide, South Australia, AUSTRALIA|O. Siggs, Garvan Institute of Medical Research, Darlinghurst, New South Wales, AUSTRALIA|H. Fu, A.E. Birsner, R.J. D'Amato, Department of Surgery, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|H. Fu, E. Collantes, J.L. Wiggs, R.J. D'Amato, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S.E. Staffieri, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|J.B. Ruddle, Department of Ophthalmology, Royal Children's Hospital, Parkville, Victoria, AUSTRALIA|E. Collantes, J.L. Wiggs, Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S.E. Staffieri, Department of Surgery, University of Melbourne, Parkville, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Few genes are known to cause early-onset glaucoma, a severe disease affecting children and young adults. The overall purpose of this work is to identify novel early-onset glaucoma genes.

Methods: Whole-exome sequencing (WES) was conducted to identify variants in glaucoma families. A CRISPR-mediated mouse germline knock-in strategy was used to create a mutation equivalent to THBS1 R1034C. Mutant mice were evaluated for intraocular pressure (IOP), outflow facility, anterior segment histology and RGCs counts. The force field program-FoldX was used to determine the protein folding energy changes related to different mutations. The effect of mutations on extracellular matrix (ECM) was studied by site directed mutagenesis and in vitro expression.

Results: We identified novel heterozygous THBS1 missense alleles altering p.Arg1034, a highly conserved amino acid, in 3 unrelated and ethnically diverse families affected by congenital glaucoma with variable expressivity (two families with R1034C and one with R1034S). Both heterozygous and homozygous $Thbs1^{R1034C}$ mice exhibited elevated IOP (ANOVA, $P<0.001$), decreased aqueous outflow facility (43.3% and 40.5%, respectively), and RGCs loss (15.9% reduction in central retina and 22.2% in the peripheral), compared to wild type controls. Histology and electron microscopy revealed an aberrant accumulation of THBS1 in the TM ECM. FoldX suggested that the missense alleles destabilize the THBS1 structure causing protein aggregation by misfolding. Analysis using a mutagenesis series at Arg1034, including R1034C and R1034S, showed that the extent of THBS1 aggregation in ECM is correlated with the extent of mutation-related free unfolding energy. Structural ECM components, especially fibronectin, were also recruited to THBS1 depositions.

Conclusions: Our study suggests that missense variants altering THBS1 p.Arg1034 can elevate IOP through a mechanism involving aberrant TM extracellular THBS1 aggregation with compromised outflow. The role of THBS1 in the regulation of aqueous humor dynamics provides new opportunities for genetic testing and therapeutic intervention.

CONTROL ID: 3714763

SUBMITTER (NAME ONLY): Huey Cai

TITLE: iPSC-derived RPE cells from AMD patients display altered mitochondrial function and gene expression on an in vitro model of aged Bruch's membrane

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Cai, J. Gong, L. Del Priore, M.A. Fields, Ophthalmology & Visual Science, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure: Huey Cai: Commercial Relationship: Code N (No Commercial Relationship) | Jie Gong: Commercial Relationship: Code N (No Commercial Relationship) | Lucian Del Priore: Commercial Relationship: Code N (No Commercial Relationship) | Mark Fields: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mitochondrial dysfunction of retinal pigment epithelial (RPE) cells plays a key role in age-related macular degeneration (AMD) pathogenesis. We have previously shown that RPE cells derived from AMD donors have a distinct mitochondrial gene expression profile as well as distinct phenotype when compared to age-matched controls. Here, we analyze the mitochondrial gene expression and function of these lines cultured on nitrite-modified extracellular matrix (ECM), an in vitro aged Bruch's membrane model, to investigate whether a nitrite-modified ECM alters mitochondrial function and gene expression in AMD-derived RPE.

Methods: iPSCs were generated from fibroblasts isolated from four AMD patients (2 atrophic and 2 exudative). RPE derived from iPSCs were generated using established protocols and analyzed by morphology, cell type specific marker expression, transepithelial resistance (TER), and phagocytosis of rod photoreceptor outer segments. Cells were cultured on nitrite ECM for two weeks and subject to cell viability and mitochondrial function analysis using the Seahorse platform. DNA microarray with 23,000 well annotated genes, including mitochondrial structure and function-related genes.

Results: iPSCs and differentiated RPE displayed cell-type-specific morphology, markers, TER, and phagocytic capacity. Cell viability and mitochondrial respiration were reduced in AMD-derived RPE cells on nitrite ECM, compared to cells cultured on unmodified ECM; mitochondrial related genes such as ATPase Cu++ transporting beta polypeptide (ATP7B), cytochrome P450 family 24 subfamily A polypeptide 1 (CYP24A1) and glutaminase 2 (GLS2) display a distinct expression pattern in AMD-derived RPE when cultured on nitrite-modified ECM compared to AMD-derived lines cultured on unmodified ECM.

Conclusions: Here, we provide evidence that nitrite modification of the ECM affect cell viability and mitochondrial function in iPSC-derived from AMD patients. Further exploration of the mitochondrial genes affected in this model may pave the way for novel treatments for AMD.

CONTROL ID: 3714764

SUBMITTER (NAME ONLY): Mona Camacci

TITLE: Sex Differences in Scholarly Productivity, Academic Rank, and NIH Funding of US Academic Uveitis Specialists

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Camacci, W.F. Hu, V. Gullapalli, OPHTHALMOLOGY, University of Rochester, Rochester, New York, UNITED STATES|M. Chiam, M. Rizk, Ophthalmology, The Pennsylvania State University, University Park, Pennsylvania, UNITED STATES|E. Lehman, Department of Public Health Sciences, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Mona Camacci: Commercial Relationship: Code N (No Commercial Relationship) | Mckenzee Chiam: Commercial Relationship: Code N (No Commercial Relationship) | Monica Rizk: Commercial Relationship: Code N (No Commercial Relationship) | Erik Lehman: Commercial Relationship: Code N (No Commercial Relationship) | Wen Hu: Commercial Relationship: Code N (No Commercial Relationship) | Vamsi Gullapalli: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveitis specialists represent a small group of subspecialists among academic ophthalmologists. To our knowledge, this is the first study to investigate sex differences in scholarly productivity, academic rank, and NIH funding among uveitis specialists.

Methods: This study was a cross-sectional study of academic uveitis specialists of 113 US ophthalmology programs. Using institutional websites, data on sex, residency graduation year, and academic rank were collected. The Scopus database was used to obtain each faculty's h-index, which is a measurement of publication productivity and citation impact, and m-quotient, which adjusts for a faculty's career duration. The NIH Research Portfolio Online Reporting Tool database was queried for data on NIH funding. Chi-square testing was used to analyze categorical values and Wilcoxon Rank Sum testing was used for continuous variables.

Results: A total of 106 academic uveitis specialists were identified, of whom 44 (41.5%) were female and 62 (58.5%) were male. A greater proportion of females vs. males were assistant professors [30 (68.2%) vs. 22 (35.5%); p=0.011] and a smaller proportion of females were full professors [4 (9.1%) vs. 24 (38.7%); p=0.008]. No significance difference was found among associate professors [female: 10 (22.7%) vs. male: 16 (25.8%); p=1.000]. Females had significantly lower median h-indices compared to their male counterparts (5.5 vs. 14.0; p=0.036), but similar median m-quotients (0.5 vs 0.5; p=1.000). Females had a shorter median career duration based on their residency graduation year compared to males (8.0 vs 19.0 years; p <0.001). Among the 22 uveitis specialists who received NIH funding for research, of whom 7 (41.5%) were female and 15 (58.5%) were male, females had a median grant funding of $1.2M compared to $2.5M for males (p=1.000).

Conclusions: Female academic uveitis specialists are overrepresented among assistant professors and underrepresented among full professors. Although females had lower h-indices than male, there was no difference in m-quotients between sexes, which controlled for the specialists' career durations. These differences in scholarly productivity are therefore due to the difference in career duration between female and male specialists and indicates that women are equally as academically productive as their male counterparts.

CONTROL ID: 3714766

SUBMITTER (NAME ONLY): Roshun Sangani

TITLE: Use of Resident Tele-Ophthalmic Diagnosis to Aid in Management of Vision-Compromising Retinal Pathology

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sangani, R. Henry, M.K. Shah, B. Szirth, N. Bhagat, Department of Ophthalmology & Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure: Roshun Sangani: Commercial Relationship(s);Code F (Financial Support):Purchase of the Topcon 3D OCT-1 Maestro Unit was supported by a NJ Health Foundation Grant (#181-21RE) | Roger Henry: Commercial Relationship: Code N (No Commercial Relationship) | Megh Shah: Commercial Relationship: Code N (No Commercial Relationship) | Bernard Szirth: Commercial Relationship: Code N (No Commercial Relationship) | Neelakshi Bhagat: Commercial Relationship(s);Code F (Financial Support):Purchase of the Topcon 3D OCT-1 Maestro Unit was supported by a NJ Health Foundation Grant (#181-21RE)

ABSTRACT BODY:

Purpose: In recent years, innovations in tele-ophthalmology have shown promise in providing quality ophthalmic care to patients in low-access settings and high-risk environments such as the COVID-19 pandemic. Emergency departments and urgent centers may benefit from tele-ophthalmology applications; the tele-images can be sent to the covering ophthalmologist or, to another ED for evaluation of images prior to transferring the patient. In this study, we aimed to assess the ability of resident physicians to identify features of posterior-pole retinal pathology using tele-ophthalmology.

Methods: Retrospective study on 16 patients (32 eyes; 30 with retinal pathology and 2 controls) who presented to a retina clinic at an academic medical center. Automated OCT-B images with 3D topographic maps and fundus photographs of the posterior pole using a Topcon Maestro 3D OCT-1 unit were taken. Images were transmitted remotely to a resident physician who attempted to identify retina pathology using fundus photography and OCT. The same images were consequently evaluated by a retina specialist for grading. We then tested the concordance between diagnoses rendered via tele-OCT by the resident physician and the gold standard clinical examination (performed by the retina specialist) using Cohen's Kappa statistic (κ).

Results: An overall average of 79.9% concordance for 69 potential findings was obtained between the retina attending's diagnosis with clinical examination and the resident physician's diagnosis using tele-OCT/fundus images based on Cohen's Kappa statistic (κ). The concordance was lower in eyes with vitreous hemorrhage most likely due to the inferior quality fundus and OCT-B images. The resident exam also identified the presence of any macular pathology in all 30 eyes with macular pathology and correctly identified the controls, indicating 100% sensitivity for identifying abnormal findings using tele OCT/fundus images.

Conclusions: This study verifies the utility of resident screening of tele-OCT fundus and OCT-B images to identify retinal pathology. Tele-ophthalmology likely has a useful role in triaging retinal pathology whose outcomes could be affected by timely intervention. Many unnecessary emergency transfers may be avoided if the on-call ophthalmology residents are able to review the fundus and OCT images before hand.

CONTROL ID: 3714767

SUBMITTER (NAME ONLY): Vincent Raymond

TITLE: Characterization of unequivocal haplotypes that encode the 20q13 modifier for variable ages-at-onset of primary open-angle glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Dubois, S. Desjardins, Endocrinology-Nephrology, CHU de Quebec-Universite Laval, Quebec, Quebec, CANADA|P. Belleau, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, UNITED STATES|V. Raymond, R. Arseneault, P. Laplante, E. Shink, Neurosciences, CHU de Quebec-Universite Laval, Quebec, Quebec, CANADA|V. Raymond, Médecine Moléculaire, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|J. Anctil, G. Côté, Ophthalmology, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|M. Amyot, Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|M.A. Walter, Medical Genetics, University of Alberta Faculty of Medicine & Dentistry, Edmonton, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) is caused by gene-gene interactions. In 10 % of cases, POAG also segregates as an autosomal dominant (AD) trait that can show wide phenotypic variability. We hypothesize that this variability is caused by modifier genes that interact with AD disease genes. To detect significant gene-gene interactions, we designed a novel unbiased pedigree-based strategy that identifies double-mutants who harbor an AD disease mutation and simultaneously carry haplotypes encoding the modifier.

Methods: We studied a French-Canadian AD glaucoma pedigree in which 154 heterozygotes (HTZ) carry the MYOC ^{K423E} mutation. Diagnoses ranged from juvenile OAG to late adult-onset POAG. Ages-at-onset (AAO), defined as age at which intra-ocular pressure ≥ 22mm Hg, ranged from 7 to > 60 y old. Several asymptomatic HTZ aged > 55 y old were also observed. Using the pedigree, we mapped a modifier locus for extreme variability of AAO at 20q13. It was named Modifier of Glaucoma 1, MOG1. To find reliable gene-gene interactions in humans, we developed a novel unbiased pedigree-based strategy. It was named DIGGI for Double-mutants that participate In Gene-Gene Interactions.

Results: DIGGI is a two-stage algorithm that exploits datasets obtained with diverse types of markers that can be coded, like microsatellites, VNTRs, SNPs and CNVs. The 1^{st} stage is the identification of MOG1 alleles, or marker haplotypes, associated with the modifier. The 2^{nd} stage is the identification of double-mutants who simultaneously carry the primary disease mutation and show higher contrasting ages at onset when compared to the AAO of individuals who are within their neighborhood (kinship coefficient defined as $\Phi(X,Y) \geq 0.0625$ where X and Y are people closer or equal to first degree cousins) and carry the myocilin K423E mutation. Robust double-mutants are positioned at the extremes of the extremes contrast distribution of the AAOs within their neighborhood. Simulation and statistical studies show that DIGGI is reliable at selecting unequivocal double-mutants that participate in gene-gene interactions.

Conclusions: We successfully applied to the case of glaucoma modifier gene a powerful strategy to identify family members who share common modifier haplotypes associated with specific endophenotypes for quantitative traits. These double-mutants will be used to characterize the MOG1 modifier.

CONTROL ID: 3714768

SUBMITTER (NAME ONLY): Zhuangjun Si

TITLE: Effectiveness and Safety of Resident-Performed Simultaneous Bilateral Selective Laser Trabeculoplasty in Patients With Open-Angle Glaucoma

SESSION TITLE: IOP and laser therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Si, M. Qiu, Ophthalmology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|J. Xiao, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Zhuangjun Si: Commercial Relationship: Code N (No Commercial Relationship) | Jason Xiao: Commercial Relationship: Code N (No Commercial Relationship) | Mary Qiu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While its pathophysiology is not fully understood, there are a number of genetic and clinical risk factors associated with glaucoma; the primary risk factor is elevated intraocular pressure (IOP). Laser trabeculoplasty is a widely-used treatment method for glaucoma because it effectively reduces IOP without bearing the greater risks of invasive surgery. Selective laser trabeculoplasty (SLT) is a core competency skill that ophthalmology residents learn; however, competency in SLT is not well-defined, as experience in glaucoma procedures is variable by program. SLT is typically performed one eye at a time. During the COVID-19 pandemic, in-office visits were minimized and surgeries were limited to only the most vision-threatening at the University of Chicago. Bilateral SLT on the same day was used to keep IOP controlled during this period, while patients could not be monitored as frequently and surgeries were postponed. The goal of this study is to assess the effectiveness and safety of same-day bilateral resident-performed SLT in comparison to reported statistics of attending-performed SLT in the literature.

Methods: A retrospective chart review of patients who underwent simultaneous bilateral SLT between January 2019-May 2021 was performed to quantify the effectiveness and safety of the procedure compared to published rates in the literature. Specifically, we examined the intraocular pressure (IOP) at the visits before and after the SLT procedure, type of glaucoma diagnosis, Age, Sex, and complications (IOP elevation, iritis, macular edema).

Results: Preliminary data included a total of 51 patients (of which 32 were female) and 108 eyes (3 patients underwent SLT twice). Average age was 66. Average IOP was 18.7 mmHg (SD 5.0) on visit prior to SLT and 17.6 (SD 6.5) on day of SLT with the average IOP decreasing to 15.9 (SD 5.0) and 15.7 (SD 4.5) on the first and second follow-up. There were 2 patients in whom we documented IOP spikes on the visit after SLT was performed, one of whom had documented compliance issues on multiple visits. No macular edema or iritis was noted.

Conclusions: We found a similar rate of decrease in IOP after bilateral SLT by residents compared to prior studies by attending physicians with very few complications. Resident-performed simultaneous bilateral SLT appears to be an effective and safe option for IOP-lowering.

CONTROL ID: 3714770

SUBMITTER (NAME ONLY): Owen Siggs

TITLE: A polygenic risk score predicts functional progression in early primary open-angle glaucoma

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Siggs, A. Qassim, H. Marshall, S. Mullany, E. Souzeau, J. Landers, J. Craig, Flinders University, Adelaide, South Australia, AUSTRALIA|O. Siggs, Garvan Institute of Medical Research, Darlinghurst, New South Wales, AUSTRALIA|X. Han, S. MacGregor, QIMR Berghofer Medical Research Institute, Herston, Queensland, AUSTRALIA|A.W. Hewitt, University of Tasmania, Hobart, Tasmania, AUSTRALIA|A. Agar, University of New South Wales, Sydney, New South Wales, AUSTRALIA|A. Galanopoulos, R. Casson, The University of Adelaide, Adelaide, South Australia, AUSTRALIA|P. Healey, WMI Centre for Vision Research, Westmead, New South Wales, AUSTRALIA|S.L. Graham, Macquarie University, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Irreversible vision loss from primary open-angle glaucoma (POAG) can be prevented through timely diagnosis and treatment, although definitive diagnosis can be difficult in early-stage disease. As a consequence, large numbers of glaucoma suspects require regular monitoring, even though many low-risk suspects may never develop disease, and other high-risk suspects may have delayed or inadequate treatment. Given that POAG is one of the most heritable common diseases, unique opportunities exist to employ genetic instruments in risk-stratified screening, diagnosis and treatment of early glaucoma.

Methods: Here we assessed the impact of glaucoma polygenic risk on early glaucoma progression, using clinical and genetic data from a prospective longitudinal cohort study in individuals of predominantly European ancestry (PROGRESSA). A total of 1,605 eyes from 829 early manifest glaucoma cases or glaucoma suspects had sufficient data for visual field progression analyses using serial 24-2 Humphrey visual fields, with a glaucoma polygenic risk score (PRS) derived from genotyping array data on all 829 participants.

Results: Individuals in the top 5% glaucoma PRS risk group were at a higher risk of visual field progression compared to the remaining 95% after 5 years (HR 1.5, 95%CI 1.13–1.97, P=.005). Conversely, those in the bottom 20% PRS risk group were at a lower risk of visual field progression compared to an intermediate risk group over 3 years (HR 0.52, 95% CI 0.28–0.96, P=.038).

Conclusions: High polygenic risk was associated with more rapid visual field progression in early manifest glaucoma cases and glaucoma suspects. A PRS may serve as a valuable adjunct to identify individuals who stand to benefit the most from more frequent surveillance, and earlier or more intensive treatment.

CONTROL ID: 3714772

SUBMITTER (NAME ONLY): Tharindu de silva

TITLE: Learning-based modelling for longitudinal prediction of geographic atrophy growth rate

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. de silva, T.D. Keenan, E.Y. Chew, C. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Models that can quantify and predict geographic atrophy (GA) growth would provide valuable insights to the design and efficacy of clinical trials. This work aims to develop learning-based prediction models for accurate GA estimation at variable timepoints using patient demographic and image-based variables.

Methods: As part of the Age-Related Eye Disease Study 2 (AREDS2) clinical trial, data was collected from 890 participants (comprising 1215 eyes and 3411 study visits, spanning 1-4 yrs) who exhibited prevalent or incident GA. Color fundus photographs were graded for GA area, involvement and proximity to center, and GA configuration. Patient demographic information (i.e., age, race, gender, smoking status) was also collected. Random forest (RF) regression models were developed to predict GA growth rates using demographic and image-based predictor variables. Predictions were made for growth rates computed at 1 year (3296 pairs), 2 year (2215 pairs), 3 year (1361 pairs), and 4 year time intervals (719 pairs) and after combining data from all time spans. The performance was quantified using RMSE and correlation coefficient (R^2) in a ten-fold cross-validation setting.

Results: Growth rates measured using GA areas at different timespans were (mean ± stdev) 0.31 ± 0.43 mm/yr over 1 year, 0.29 ± 0.28 mm/yr over 2 years, 0.28 ± 0.22 mm/yr over 3 years, and 0.27 ± 0.19 mm/yr over 4 years. The average growth rate measured using all time intervals was 0.29 ± 0.33 mm/yr. The RF prediction model estimated growth rates with RMSE = 0.43 mm/yr (R^2=-0.01) over 1 year, 0.26 mm/yr (R^2=0.09) over 2 years, 0.20 mm/yr (R^2 =0.15) over 3 years, and 0.18 mm/yr (R^2=0.10) over 4 years. After combining growth rates measured across different time spans, the RF model exhibited RMSE = 0.30 mm/yr (R^2=0.05). Both measured growth rates and errors of the prediction models decreased with increasing measurement time-intervals.

Conclusions: At longer time-spans, both GA growth rate variability and learning-based prediction accuracy worsened gradually. At shorter time-spans, measurement error could constitute a larger portion of the growth rate and could result in higher variability and more challenging estimation by prediction models. Future work investigates additional automated image-derived metrics to improve the prediction accuracy.

CONTROL ID: 3714773

SUBMITTER (NAME ONLY): Luciano Custo Greig

TITLE: Transcription factor Myt1L promotes neuronal fate acquisition in the developing retina

SESSION TITLE: Retinal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Custo Greig, M. Woodworth, J.L. Goldberg, S. Wang, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure: Luciano Custo Greig: Commercial Relationship: Code N (No Commercial Relationship) | Mollie Woodworth: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Goldberg: Commercial Relationship: Code N (No Commercial Relationship) | Sui Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Myt1L is a zinc finger transcription factor expressed by a variety of neuron types. In the cerebral cortex, Myt1L counteracts Notch signaling to promote differentiation of neural progenitors and repress non-neuronal fates. Interestingly, it is one of three transcription factors, in combination with Brn2 and Ascl1, capable of inducing reprogramming of fibroblasts into functional neurons. Here we investigate possible functions of Myt1L in retinal development, which have not been previously reported.

Methods: Tissue was collected from CD1 mice at the indicated developmental time points, and retinas were stained with a MYT1L guinea pig polyclonal antibody (Guoqiang Gu, Vanderbilt University). GFAP-Cre and R26 reporter mice were obtained from JAX. The indicated plasmids were injected subretinally into CD1 mouse pups at P1, electroporated with 5x80V pulses, and retinas were collected for analysis at P21. Imaging was performed on a Zeiss LSM700 confocal microscope.

Results: We find that MYT1L is absent from progenitors, but is present in postmitotic neurons starting as early as E15.5, and well into adulthood (Figure 1A-F). It is most highly expressed by retinal ganglion cells, but is also detected at lower levels in amacrine and bipolar cells, based on co-localization with BRN3A, PAX6 and CHX10 (data not shown). In contrast, Müller glial cells do not express Myt1L, as demonstrated by lack of overlap with GFAP-Cre;R26-tdTom (Figure 1G-K). Interestingly, overexpression of Myt1L in postnatal retinal progenitors was sufficient to strongly repress generation of Müller glia. In control experiments, 56.5% ± 8.4% of electroporated cells in the INL were SOX9-positive Müller glia (Figure 1L-O), compared to only 20.9% ± 3.0% in Myt1L overexpression experiments ($p < 0.01$).

Conclusions: Taken together, our results indicate that Myt1L is expressed by retinal ganglion cells, amacrine cells, and bipolar cells during development, and that it can strongly repress generation of Müller glia by postnatal retinal progenitors.

CONTROL ID: 3714775

SUBMITTER (NAME ONLY): Tristan Hormel

TITLE: A Comparison of OCT Angiography Non-Perfusion Area Measurements Made With a Rules-Based Approach and Artificial Intelligence

SESSION TITLE: AI in Retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Hormel, Y. Guo, T.S. Hwang, D. Huang, Y. Jia, Oregon Health & Science University, Portland, Oregon, UNITED STATES|J. Wang, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Tristan Hormel: Commercial Relationship: Code N (No Commercial Relationship) | Jie Wang: Commercial Relationship(s);Code P (Patent):Optovue | Yukun Guo: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Hwang: Commercial Relationship: Code N (No Commercial Relationship) | David Huang: Commercial Relationship(s);Code F (Financial Support):Optovue;Code P (Patent):Optovue;Code R (Recipient):Optovue | Yali Jia: Commercial Relationship(s);Code F (Financial Support):Optovue;Code P (Patent):Optovue, Optos

ABSTRACT BODY:

Purpose: To compare optical coherence tomography angiography (OCTA) non-perfusion area (NPA) measurements made using artificial intelligence (AI) and a traditional rules-based approach.

Methods: NPA measurements were performed on eyes with diabetic retinopathy (DR), with severity determined by a central reading center based on 7-field color fundus photography using the early treatment of diabetic retinopathy (ETDRS) scale (referable ≥ 35; vision-threatening ≥ 53). We assessed the accuracy of DR diagnosis based on NPA measurements made with each approach by calculating the area under receiver operating characteristic curve, and the robustness of each method by measuring repeatability and the effect of signal strength. Measurements were assessed using 959 OCTA scans of eyes diagnosed with DR (2 non-referable; 670 referable/non-vision threatening; 287 vision threatening). The source of the data is the DRCR Retina Network, but the analyses, content and conclusions presented herein are solely the responsibility of the authors and have not been reviewed or approved by DRCR Retina Network. 15 repeat scans in this dataset were used to test repeatability. Since the DRCR dataset did not contain healthy controls, 128 healthy eyes imaged at Oregon Health & Science University (OHSU) were added to assess NPA-based diagnostic accuracy. The two methods considered here are 1) a rules-based approach that determined NPA using a vessel distance map, and 2) an AI-based approach that used a U-net-like architecture (Fig. 1). Both approaches quantified NPA in the superficial vascular complex and inner retinal slab. The AI model was trained with a separate dataset from OHSU containing 492 scans of eyes with varying degrees of DR.

Results: The AI approach had better diagnostic performance than the rules-based method for referable vs. non-referable DR (Fig. 2). The AI-based NPA measurements were also less correlated with signal strength in the SVC (R^2 = 0.121 rules-based vs. R^2 = 0.002 AI-based). The rules based approach achieved slightly higher repeatability in the SVC (intraclass correlation coefficient = 0.945 rules-based vs. = 0.923 AI-based methods).

Conclusions: NPA measurements made on a clinical dataset using an AI-based approach have a higher diagnostic accuracy for diagnosing referable DR and are more robust with respect to scan quality than NPA measurements from a rules-based approach.

CONTROL ID: 3714777

SUBMITTER (NAME ONLY): Milan Gautam

TITLE: Novel lipid nanoparticle variants for in-vivo mRNA delivery to photoreceptors

SESSION TITLE: Gene Therapy and Gene Editing for Ocular Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gautam, G. Sahay, Department of Pharmaceutical Sciences, College of Pharmacy, Oregon State University, Portland, Oregon, UNITED STATES|R.C. Ryals, G. Sahay, Department of Ophthalmology, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Milan Gautam: Commercial Relationship: Code N (No Commercial Relationship) | Renee Ryals: Commercial Relationship: Code N (No Commercial Relationship) | Gaurav Sahay: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although lipid nanoparticles (LNPs) effectively deliver genes to the retina, most of the gene expression is still limited to the retinal pigmented epithelium (RPE) and Müller glia. This study tested the hypothesis that modifications to LNPs can steer LNP delivery of mRNA to the photoreceptors. Successful gene delivery to RPE, Müller glia, and photoreceptors expands the utility of LNPs for treating inherited retinal degenerations.

Methods: LNP variants were prepared via rapid microfluidic mixing of an organic phase containing lipids and an aqueous phase containing mRNA. The organic phase, consisting of ionizable lipid, DSPC, sterols, DMG-PEG, and PEGs at different molar ratios, was rapidly mixed with the aqueous phase having Cre or mCherry mRNA in the citrate buffer pH 4.0. LNPs were characterized for hydrodynamic radius and polydispersity index (PDI) using dynamic light scattering (DLS) and mRNA encapsulation efficiency using a modified Quant-iT RiboGreen RNA reagent. First, LNPs were evaluated for transfection efficiency in multiple cell lines. Then, Cre or mCherry mRNA (300 ng) was delivered via subretinal injections in both Ai9 and NRL-GFP mice. Live in-vivo retinal imaging and immunohistochemistry (IHC) of retinal sections were performed to characterize the intracellular gene expression.

Results: Novel LNPs had a diameter of < 80 nm with a < 0.13 PDI. The zeta potential (ZP) of the particle varied depending on the functional PEG. The ZP of LNPs without functional PEG was -0.95±0.6. In all cases, encapsulation efficiency was higher than 96% with a spherical shape in morphology. LNP variant had significantly higher transfection efficiencies compared to standard LNPs in photoreceptor cell lines. After delivery of LNP variants in Ai9 mice, robust and selective tdTomato expression was observed using fundus imaging. IHC confirmed expression in the photoreceptors and RPE. With the addition of b-sitosterol, expression was observed in Müller glia as well. At 48 h post-injection, mCherry protein expression was localized to the RPE and Müller glia in NRL-GFP mice, further strengthening our observation.

Conclusions: LNP-based mRNA delivery has largely been restricted to the RPE. We have now demonstrated that LNP variants can deliver genes to the photoreceptors, and the RPE, thus opening the scope for treatments against inherited retinal degenerations.

CONTROL ID: 3714778

SUBMITTER (NAME ONLY): Genevieve James

TITLE: Retinal incorporation and turnover of bis-allylic deuterated docosahexaenoic acid (D-DHA) - a new dry AMD drug candidate: a comprehensive tissue uptake and elimination survey and comparison between murine ocular and related body tissues

SESSION TITLE: AMD and diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. James, Nutritional Sciences, The University of Texas at Austin, Austin, Texas, UNITED STATES|

Commercial Relationships Disclosure: Genevieve James: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retina and surrounding tissues are vulnerable to oxidative damage due to a unique combination of direct light exposure, their high rate of oxidative metabolism, and the high content of the fatty acid DHA. Deuteration at the bis allylic positions dramatically increases the resilience of DHA in vitro and in vivo. We studied the increase and washout kinetics of orally consumed D-DHA in mice over several months to understand how it is incorporated and removed from target tissues.

Methods: At 12 weeks of age, mice were placed on a diet with 0.5% D-DHA for 78 days, then switched to an identical diet with normal H-DHA. Animals were sacrificed periodically, and tissues were collected. Lipids were extracted, converted to fatty acid methyl esters, and analyzed by high-resolution gas chromatography chemical ionization mass spectrometry to quantify the relative proportions of D-DHA and H-DHA, expressed at D-DHA as a % of total DHA in the relevant pool, the key figure of merit for drug efficacy. Doubling time and half-lives were calculated by least-squares fitting to single exponential models.

Results: D-DHA rose more rapidly in RPE-choroid/Sclera than in the neural retina or optic nerve. By day 78 D-DHA was over 90% in all tissues. RPE-choroid/Sclera and retina had more similar washout curves. Doubling times and half-lives were 20-22 days for both retina and optic nerve. Doubling time for RPE-choroid/Sclera and liver were similar at about 9 days, while half-lives were 18 and 14 days, respectively, for these two tissues.

Conclusions: The therapeutic threshold for D-DHA efficacy is considered to be about 20%. Retina reached that level by 8 days of feeding. The vascularized RPE-choroid doubling time was at about 40% D-DHA by 8 days similar to the liver. We conclude that D-DHA rapidly crosses the blood-retina-barrier and enters visually active tissues just as its natural DHA parent and may offer protection against oxidative lipid peroxidation.

CONTROL ID: 3714779

SUBMITTER (NAME ONLY): Alexis Malkin

TITLE: Factors related to proficiency following training to use new visual-assistive smartphone apps in seniors with low vision

SESSION TITLE: Assistive Devices, Visual Function Assessment, and Vision Restoration Therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.G. Malkin, M. Knizak, B. Peterson, C. Idman-Rait, J.K. Ho, N. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|A.K. Bittner, M. Estabrook, M. Chun, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Alexis Malkin: Commercial Relationship(s);Code R (Recipient):Eschenbach Optik, Humanware, GoCheck Kids;Code S (non-remunerative):GoCheck Kids (medical advisory board) | Ava Bittner: Commercial Relationship: Code N (No Commercial Relationship) | Meghan Knizak: Commercial Relationship: Code N (No Commercial Relationship) | Bridget Peterson: Commercial Relationship: Code N (No Commercial Relationship) | Max Estabrook: Commercial Relationship: Code N (No Commercial Relationship) | Cecilia Idman-Rait: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Ho: Commercial Relationship: Code N (No Commercial Relationship) | Melissa Chun: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Ross: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Seniors with low vision underutilize mobile applications (apps) for visual assistance despite their use of smartphones and/or tablet devices. Mobile apps can be a low cost, accessible form of visual assistive equipment for this population, but training is indicated for most to learn to use such apps. We explored which low vision subjects were proficient with these technologies following training.

Methods: 50 adults aged 55+ (mean 72 years; SD ±10; range 55-92) with low vision (VA 20/40-20/800 or legally blind due to visual field) who were naïve to three visual assistive apps (SuperVision+, Seeing AI, Aira) were randomized to receive one-on-one training with one app on a loaner iPhone SE as part of the Community Access through Remote Eyesight (CARE) clinical trial. Subjects' proficiency with the smartphone and app was assessed by the study team after the 1st training session and again at 2-weeks. Multivariable logistic regressions examined potential predictors of app proficiency at the end of the 1st and 2nd sessions. Subjects' race was primarily white (64%), 44% were female, most had macular degeneration (30%) and their own smartphone (84%).

Results: Mean training time was 0.95 hours (SD± 0.44) for the 1st session and 0.43 hours (SD± 0.81) for the 2nd. 48% of subjects were not proficient at the end of the 1st training session, while 39% still lacked proficiency at 2-weeks. Age was a significant predictor of app proficiency, as older subjects were significantly less likely to be proficient after training one (OR: 0.92, 95% CI: 0.85-0.99, p=0.02) and training two (OR: 0.87, 95% CI: .77-.98, p=0.02). Other factors (binocular logMAR visual acuity, randomized app, and duration of the training session) were not significantly related to app proficiency (all p>0.10).

Conclusions: Many older adults with low vision required multiple, lengthy training sessions to become adept at using a new visual assistive app. This suggests that those working in low vision rehabilitation may need to plan for several visits to enable this population to become successful with smartphone apps, especially for the oldest patients.

CONTROL ID: 3714780

SUBMITTER (NAME ONLY): Jeffrey Jamison

TITLE: Efficacy of tandospirone and cytokine production in the mouse blue light damage model of dry AMD.

SESSION TITLE: Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Jamison, A.K. Ghosh, S.D. Ogle, N.E. Pappenhagen, M. Bacellar-Galdino, S. Kaja, R&D Division, Experimentica Ltd., Forest Park, Illinois, UNITED STATES|S. Kaja, Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Jeffrey Jamison: Commercial Relationship(s);Code E (Employment):Experimentica Ltd;Code O (Owner):AcuiSee LLC;Code O (Owner):ONL Therapeutics;Code P (Patent):AcuiSee LLC | Anita Ghosh: Commercial Relationship(s);Code I (Personal Financial Interest):eyeNOS Inc;Code E (Employment):Experimentica Ltd;Code C (Consultant/Contractor):Experimentica Ltd., K&P Scientific LLC;Code P (Patent):eyeNOS Inc;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code S (non-remunerative):Experimentica Ltd., eyeNOS Inc. | Sean Ogle: Commercial Relationship(s);Code E (Employment):Experimentica Ltd.;Code C (Consultant/Contractor):eyeNOS, Inc. | Nathaniel Pappenhagen: Commercial Relationship(s);Code E (Employment):Experimentica, Ltd | Marianna Bacellar-Galdino: Commercial Relationship(s);Code E (Employment):Experimentica Ltd. ;Code C (Consultant/Contractor):AcuiSee LLC | Simon Kaja: Commercial Relationship(s);Code F (Financial Support):Experimentica Ltd., K&P Scientific LLC;Code I (Personal Financial Interest):Experimentica Ltd., K&P Scientific LLC;Code C (Consultant/Contractor):Experimentica Ltd.;Code P (Patent):eyeNOS Inc.;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code S (non-remunerative):Experimentica Ltd., K&P Scientific LLC;Code E (Employment):Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Maywood, IL, USA

ABSTRACT BODY:

Purpose: Blue light induced photooxidative stress (BLD) is an established model of advanced geographic atrophy observed in patients with dry AMD. 5-HT1A agonists have demonstrated neuroprotection in rat BLD studies and other mouse CNS injury models. The purpose of this work was to evaluate the 5-HT1A agonist tandospirone (tando) to provide protection in the mouse BLD model, and to measure cytokine production in the Balb/C mouse retina at 1-7 days after light exposure.

Methods: Male, 10-14 week old Balb/C mice: Group 1 daily subcutaneous injections of vehicle, 5 or 10 mg/kg tando on Day -2 to Day 2, N=5. Group 2 no treatment and were sacrificed at 1, 3 and 7 days post light exposure. N=6. Group 3 no treatment no light exposure, N=6. Group 1 and 2 animals were dark adapted overnight and on Day 0 exposed to 19-21 klux of spectrally filtered blue light for 4 hours. Prior to sacrifice all animals received electroretinograms (ERGs) to assess retinal function, and retinal damage was evaluated with OCT imaging. Eyes were collected from Group 2 and 3 and the cytokines IFNg, IL-1b, IL-2, -4, -5, -6, -10, -12p70, KC/GRO and TNFa were measured using the Mesoscale Discovery system.

Results: ERG amplitudes and retinal thickness was significantly reduced 50-70% in vehicle and the 5 mg/kg tando treated animals compared to Group 3. Animals treated with 10 mg/kg had a ~30% decrease in ERG amplitude and retinal thickness which were significantly better than vehicle treated. IL -2, -4, -12p70 and IFNg were below the lowest limit of quantification. Compared to Group 3, there was a non-significant increase of IL-5 from 1.4 to 1.7, IL-6 from 89.8 to 261.4, KC/GRO from 90.6 to 284.1 and TNFa from 62.5 to 102.7 pg/ml at Day 7 post light exposure and little change at Day 1 or Day 3. There was a non-significant decrease of IL-10 from 2.1 to 0.6 pg/ml at Day 3 post light exposure and little change at Day 1 or Day 7. There was a significant increase of IL-1b from 6.9 to 36.5 pg/ml at Day 7 post light exposure and little change at Day 1 or Day 3.

Conclusions: The 5HT1a agonist tandospirone is a viable positive control for drug discovery at 10 mg / kg in Balb/C mice. Up to 7 days post exposure the cytokines measured are insignificant other than IL-1b, which has been demonstrated to be upregulated in other models of retinal pigmented epithelial cells and photoreceptor cells damage.

CONTROL ID: 3714782

SUBMITTER (NAME ONLY): Ozcan Ozdamar

TITLE: Simultaneously extracted Pattern ERG and VEP responses to visual hemifields using bideconvolution averaging (BiCLAD)

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Ozdamar, J. Bohorquez, Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|H. Korkusuz, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|J. Toft-Nielsen, JORVEC, Florida, UNITED STATES|

Commercial Relationships Disclosure: Ozcan Ozdamar: Commercial Relationship(s);Code I (Personal Financial Interest):JORVEC | Jonathon Toft-Nielsen: Commercial Relationship(s);Code E (Employment):JORVEC | Hazal Korkusuz: Commercial Relationship: Code N (No Commercial Relationship) | Jorge Bohorquez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The Continuous Loop Averaging Deconvolution (CLAD) technique is used to extract "per-stimulus" responses at stimulation rates that normally produce steady-state (SS) responses with conventional methods. This is accomplished by presenting specially designed narrow jitter stimulation sequences (Ozdamar et al., 2014, Toft-Nielsen et al., 2014). In this study, a new bideconvolution (BiCLAD) method employing two temporally jittered biorthogonal sequences to stimulate two visual fields and allow the extraction of independent responses from each hemifield was used.

Methods: Transient (TR) and quasi-steady-state (QSS) pattern PERG-VEPs were recorded at two reversal rates (2.5, 12.5rps) from normal subjects under monocular and binocular conditions. Pattern stimuli were delivered on a rectangular field (28°x14°) made of 2 separate LED based displays. Stimuli were composed of 6 horizontal cycles (99% contrast). Subjects were asked to fixate along the center horizontal line on one of five fixation points. Display subunits were driven either synchronously (monofield) or asyncronously (bifield) with similar mean rates. Conventional TR and BiCLAD deconvolved PERG (N35, P50; N95) and VEP (P60; N75; P100; N135) components were analyzed using latency/amplitude measures.

Results: Both reversal rates produced clearly distinquishable PERG and VEP waveforms with conventional components at all different gaze fixation and eye stimulation conditions. In both monocular and binocular conditions, nasal and temporal PERG responses showed small and consistent differences in amplitude and morphology. Nasal responses resembled a conventional PERG response, while temporal responses exhibited slightly bifurcated and smaller peaks. In the 12.5 rps VEP, the early positive peak (P60) was more prominent and showed binocular summation characteristics and the P100 component was of smaller amplitude. In bifield mode both PERG and VEP components showed lateralization with respect to eye fixation.

Conclusions: Hemifield testing using BiCLAD reveals differences in temporal and nasal morphology and will help in exploring retinal topography and enhancing the diagnostic utility of the PERG in retinal disorders. Simultaneuous VEP testing will further clarify contributions of the visual pathway and cortical areas, helping in stroke and other disorders involving localized trauma to specific cortical regions.

CONTROL ID: 3714784

SUBMITTER (NAME ONLY): Ruy Felippe Missaka

TITLE: Bacillary layer detachment in Vogt-Koyanagi-Harada disease: a biomarker with prognostic value

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Missaka, M. Goldbaum, C.G. Machado, F. Silveira Souto, P.F. Nóbrega, M.M. Lavezzo, M.K. Oyamada, C.E. Hirata, J.H. Yamamoto, Ophthalmology, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|V.M. Sakata, Ophthalmology, Universidade Federal do Parana, Curitiba, PR, BRAZIL|

Commercial Relationships Disclosure: Ruy Felippe Missaka: Commercial Relationship: Code N (No Commercial Relationship) | Mauro Goldbaum: Commercial Relationship: Code N (No Commercial Relationship) | Cleide Machado: Commercial Relationship: Code N (No Commercial Relationship) | Fernanda Maria Silveira Souto: Commercial Relationship: Code N (No Commercial Relationship) | Priscilla Nóbrega: Commercial Relationship: Code N (No Commercial Relationship) | Marcelo Lavezzo: Commercial Relationship: Code N (No Commercial Relationship) | Viviane Sakata: Commercial Relationship: Code N (No Commercial Relationship) | Maria Oyamada: Commercial Relationship: Code N (No Commercial Relationship) | Carlos Hirata: Commercial Relationship: Code N (No Commercial Relationship) | Joyce Yamamoto: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the frequency of bacillary layer detachment (BLD) and its associations with clinical and visual function outcomes of patients with Vogt-Koyanagi-Harada disease (VKHD).

Methods: Retrospective analysis of 33 patients with VKHD followed for a minimum one year since the acute disease onset with systematic clinical, multimodal imaging and visual function evaluations. All patients were treated with high-dose systemic corticosteroid; 23 patients had additional oral azathioprine. Three independent retina specialists read the images obtained in the spectral domain-OCT (Heidelberg Engineering, Heidelberg, Germany) at baseline (M0) and at the 1^{st}, 3^{rd}, 6^{th}, 9^{th} and 12^{th} months. Frequency of BLD was analysed for its association with other OCT findings, clinical and visual outcomes. Generalized estimating equations (GEE) of binomial distribution and logit link function with interchangeable correlation between eyes and moments were carried out. This study was approved by Institutional Ethics Committee and followed Helsinki declaration.

Results: Included patients (29 female/ 4 male) had a median age of 33 years (15 to 67 years) with a median disease duration of 67 months (27 to 121 months). The median initial visual acuity (VA) was 1.8 logMAR (0 to 2.3 logMAR), 0.2 logMAR (0 to 2 logMAR) at M1 and 0 logMAR (0 to 0.7 logMAR) at M12. Sunset glow fundus (SGF) was seen in 42 eyes (63%) and subnormal full-field electroretinogram (ffERG) was seen in 76% of eyes (47/62) in M12. BLD was present in 87.5% (49/56) of eyes at M0 and in 3% (2/66) at M6 and M9. BLD resolution time was longer compared to serous retinal detachment (SRD) with medians of 1 month (0 to 12 months) and 0 month (0 to 9 months), respectively (Figure). Significant associations were observed between BLD in M1 with worse VA in M0 (median 1.8 vs 1 logMAR; p=0.016); worse VA (median 0.25 vs 0.05 logMAR; p=0.014), worse fluorescein angiography scores (9 vs 5; p=0.002) and indocyanine green angiography scores (15 vs 10.5p= 0.007) in M1; severe fundus (p=0.008), SGF (p=0.006), fibrosis (p=0.005), chorioretinal atrophy (p=0.008), and subnormal ffERG (p=0.045) in M12, as well as longer elipsoid zone resolution time (median 12 vs 3 months; p=0.006) (Table).

Conclusions: Our data pointed out the presence of BLD in M1 as a potential biomarker of a worse prognosis in VKHD, as evidenced by changes in fundus and visual function at 12 months.

CONTROL ID: 3714786

SUBMITTER (NAME ONLY): Peiqi Wu

TITLE: OLT1177 (Dapansutrile) Attenuates Retinal Neovascularization by Inhibiting NLRP3 Inflammasome Activation

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Wu, X. Tang, K. Cui, P. Wu, X. Liang, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Peiqi Wu: Commercial Relationship: Code N (No Commercial Relationship) | Xiaoyu Tang: Commercial Relationship: Code N (No Commercial Relationship) | Kaixuan Cui: Commercial Relationship: Code N (No Commercial Relationship) | Peiqi Wu: Commercial Relationship: Code N (No Commercial Relationship) | Xiaoling Liang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: OLT1177 (Dapansutrile) is an effective inhibitor targeted nucleotide-binding domain leucine-rich repeat and pyrin domain containing receptor 3 (NLRP3) inflammasome. Here we aimed to explore therapeutic effect of OLT1177 in oxygen-induced retinopathy (OIR) model and its potential mechanism.

Methods: OIR model was induced in C57BL/6J newborn mice and OLT1177 was delivered to pups through intraperitoneal injection at P12. Flat mount immunofluorescence and hematoxylin and eosin staining were used to evaluate retinal pathological neovascularization. Western blot and real time PCR were performed to quantify the levels of NLRP3 and inflammatory factors, including IL-1β and TNF-α. Cell counting kit-8 assay was used to evaluate the proliferation of BV2 cells and HUVECs under the hypoxia condition. Meanwhile, EdU incorporation assay, wound-healing assay, transwell assay and matrigel assay are applied to evaluate the proliferation, migration and tube formation of HUVECs.

Results: OLT1177 administration (100μM) significantly attenuated pathological neovascularization ($p<0.01$) and reduced 30% of avascular area ($P<0.005$). Moreover, OLT1177 reduced aggregation and activation of microglia and leakage of retinal vessels. No significant change was found in the expression of NLRP3，whereas the expression of cleaved caspase-1, IL-1β and TNF-α were differentially decreased. Meanwhile, Immunofluorescence analysis showed NLRP3 co-located with both microglia and endothelial cell. OLT1177 inhibited the proliferation of BV2 cells and HUVECs. And the migration and tube formation of hypoxia-induced HUVECs were inhibited after OLT1177 intervention.

Conclusions: Our study showed that OLT1177 exhibited highly antiangiogenic effects through inhibiting the NLRP3-dependent pathway, suggesting an alternative treatment for RNV.

CONTROL ID: 3714787

SUBMITTER (NAME ONLY): Joshua Chazaro

TITLE: Comparing Phenotype of Subretinal Drusenoid Deposits in Age Related Macular Degeneration (AMD) with ARMS2 Risk Alleles versus High Risk Vascular Disease

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chazaro, R. Thomson, A. Coughlin, Y. Tong, K. Tai, O. Otero, H. Lloyd, R. Smith, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|J. Chazaro, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Subretinal drusenoid deposits (SDD) are currently considered a morphological change to the retina commonly associated with AMD. An association has been made with ARMS2 rs10490924 gene polymorphism and the presence of SDD in AMD. 1 The presence of SDD have also been linked to the high risk vascular diseases (HRVD) of carotid artery stenosis, cardiac valve defect, and cardiac pump defect, possibly due to hypoperfusion of the choroid. 2 These groups have never been compared and our goal is to detect possible phenotype differences to better understand the mechanism and improve management.

Methods: Volume spectral-domain optical coherence tomography (SD-OCT) scans, health history questionnaire, genetic testing and serum samples containing lipid values were obtained for 61 subjects with SDD. Images were categorized into atrophic vs exudative and early vs advanced. We compared 2 subgroups: 1) subjects homozygous for ARMS2 risk alleles (TT) and 2) subjects with HRVD without homozygous ARMS2 risk alleles. Univariate statistics used were chi square for categorical variables and two-tailed t-test for continuous variables.

Results: Of the 61 subjects with SDD, 11 were in ARMS2 group and 24 in HRVD group. Age of presentation for subjects in ARMS2 group was 78.1 yo vs. HRVD group was 83.4 yo (p=0.033). Exudative AMD was found in 3/11 (27%) of ARMS2 group and 0/24 (0%) of HRVD group (p=0.007); geographic atrophy was found in 5/11 (45%) of ARMS2 group vs 7/24 (29%) of HRVD group (p=0.34). Advanced AMD in 8/11 (73%) in ARMS2 Group and 7/24 (29%) in HRVD group (p=0.016). There were no statistically significant differences in subfoveal choroidal thickness (CTh), health history questionnaire and serum lipid levels between the groups.

Conclusions: Our small study suggests that ARMS2 Homozygous risk allele carriers have a different disease profile than SDD phenotype non-carriers. These risk allele carriers develop a more aggressive phenotype at a younger age with exudative AMD and advanced AMD being more common in this group. This suggests subjects with ARMS2 associated SDD have a different natural history and prognosis than those with systemic vasculopathy associated SDD.

CONTROL ID: 3714788

SUBMITTER (NAME ONLY): Zain Khera

TITLE: Relationships between the Optic Nerve Head in Optical Coherence Tomography and Optic Nerve Volume in Magnetic Resonance Imaging in Glaucoma

SESSION TITLE: OCT Clinical Applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep learning of optical coherence tomography (OCT) may help discriminate glaucomatous eyes from healthy controls. However, the underlying decision making processes remain unclear. Recently, through computing class activation maps, our feature agnostic artificial intelligence of OCT images using a 3D convolutional neural network identified the optic nerve head (ONH) and its surrounding regions as structures significantly associated with glaucoma classification (PMID: 31260494). To pursue their contributions further, here we analyzed the optic nerve morphology from OCT and magnetic resonance imaging (MRI) in a subset of glaucoma and healthy subjects.

Methods: Nine early glaucoma, 12 advanced glaucoma, and 4 healthy control subjects underwent spectral-domain OCT at 30x30x2 μm^3 and 3-Tesla anatomical MRI at 1x1x1mm^3. Maximum intensity projection was applied to en-face OCT scans at the ONH (Fig. 1). The areas of the ONH [inner regions of interest, (ROI)] and surrounding regions (outer ROIs) visible in OCT were measured using global thresholding in ImageJ. One-way ANOVAs with post-hoc Tukey's tests were performed on the inner and outer ROIs between the 3 groups. Also, a Pearson correlation analysis was performed between the ROI areas in OCT and optic nerve volume extracted from MRI between the eye and optic chiasm.

Results: For OCT of the ONH, significant group effect was observed for the areas in the inner ROIs (ANOVA: F= 7.823, p=0.00133). Post-hoc analyses revealed a significant difference between healthy controls and advanced glaucoma (p=0.0082) and between early and advanced glaucoma (p=0.0057) but no significance between healthy controls and early glaucoma (p=0.80) (Fig. 2A). No significant group effect was observed in the outer ROIs (ANOVA: F=0.004, p=0.996) (Fig. 2B). There was a negative correlation between the inner ROI area in OCT and optic nerve volume in MRI (R=-0.47, p=0.0011) (Fig. 2C).

Conclusions: The ONH tissues visible on OCT appeared to contribute more than their surrounding regions to distinguishing between glaucomatous eyes and healthy eyes. The negative correlation between ONH area in OCT and optic nerve volume in MRI suggested the need to further understand the interactions between ONH and deeper brain structures in glaucoma.

CONTROL ID: 3714790

SUBMITTER (NAME ONLY): Colin Korlesky

TITLE: Wearable Light Isolating Medical Device to Perform Electroretinography

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Korlesky, B.R. Pattnaik, Department of Pediatrics, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|J.N. Ver Hoeve, B.R. Pattnaik, Department of Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|J.N. Ver Hoeve, McPherson Eye Research Institute, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Electroretinography (ERG) remains an underutilized clinical diagnostic tool due to high device cost, complex testing procedures, and strict facility requirements. We performed a proof of concept study to explore the feasibility of a wearable medical device that isolates each eye independently while performing clinical grade ERG testing with the goal of decreasing per-procedure cost, time, and facility requirements in order to expand access to ERG testing.

Methods: Device components were designed virtually using Computer Aided Design (CAD) software and 3D printed with black polylactic acid (PLA) thermoplastic polyester. Eye-pieces were made of polyurethane foam and designed for independent eye isolation from all environmental light. Red, green, blue, white, and infrared (IR) LEDs stimulate the retina and illuminate the IR camera. Light intensity is controlled via current and voltage regulators as well as pulse width modulation (PWM). Light stimulus duration is controlled via LED drivers. IR cameras dynamically measure pupil diameter and digitally adjust light intensity using PWM. A phototransistor measures the light stimulus being presented to each eye. EasyEDA and JLCPCB were used for printed circuit board (PCB) design and manufacturing. User interface, testing procedures, and image processing were programmed using a Raspberry Pi 4 and Python. Light intensity calibration was performed using a factory calibrated Internation Light Technologies 2400 Optical Meter. Pupil measurement calibration was performed using known diameter standards and validated on members of the research team.

Results: See attached photos of prototype goggle device with attached LED control board as well as IR picture of eye with pupil measurements. The pupil measurement software was accurate within 2.5% relative to standard controls ranging from 4-26 mm. The estimated cost of this device, not including labor or excess materials, is $450.

Conclusions: This rudimentary prototype is a preliminary proof-of-concept for a wearable ERG-device that reduces the cost, time and facility burdens associated with clinical ERG testing. Such a device would be particularly useful for early detection and monitoring of chronic disease states, such as diabetic retinopathy. Future directions include device fit optimization and incorporating skin electrodes and appropriate electrical amplifiers to measure the retinal response to light stimulation.

CONTROL ID: 3714791

SUBMITTER (NAME ONLY): Jonathan Luisi

TITLE: Longitudinal Imaging Reveals Patterns of Neurodegenerative Inflammation in Rotenone-Induced Retinal Neurotoxicity

SESSION TITLE: New drugs, mechanisms of action and ocular toxicology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rotenone is a mitochondrial toxicant known to induce neurodegeneration, however, the neuroinflammatory progression has not yet been clearly characterized. As resident immune cells of the central nervous system, microglia are known to enhance the neurotoxicity of rotenone. We postulated that non-invasive imaging of the retina can reveal neurotoxic effects intravitreal injection of rotenone and correlate the phases of the neuroinflammatory progression.

Methods: We monitored the spatial and temporal changes in retina inflammation and neurotoxicity following direct exposure to rotenone by intravitreal injection, by combining imaging techniques including optical coherence tomography (OCT) and confocal scanning-laser funduscopic (cSLO). To visualize microglia activation, we used $Cx3Cr1^{eGFP}$ transgenic mice in which macrophages express green fluorescent protein. Accordingly, we utilized a non-invasive imaging protocol to assess neurotoxicity longitudinally, without an invasive biopsy (Fig1). The OCT images were processed to characterize and quantify rotenone-induced changes in retinal morphology.

Results: We found that a 0.3µL of a 10mM concentration of rotenone caused retinal thinning and neurodegeneration, during the late phase of inflammation. Retinal thinning at day 7 correlated to the first appearance of hyper-florescent puncta in the photoreceptor layer. Furthermore, the puncta proliferated at day 14, indicating lipid peroxidation. The Cx3Cr1 microglia, at day 7 post treatment (Fig 2), were aligned with the nerve fiber tracts (arrow). Before 7 days, microglia activation in the inner portion of retina was not detected. Based on the OCT findings, neurodegeneration was 7-14 days post-injury, and photoreceptor loss was not evident until day 14.

Conclusions: These studies showed a predominantly M1 verses M2 microglia phenotype at 7 days, suggesting transition into chronic inflammation rather than a resolving phase. These studies also indicated that a low dose of rotenone can facilitate development of a neurodegenerative pathology over time, and that the late phase M1 microglia activation may be the driving force of the delayed response and subsequent neurodegeneration. Furthermore, we believe that the non-invasive imaging used in the current study provides a novel approach for characterizing the inflammatory progression of neurotoxicity.

CONTROL ID: 3714792

SUBMITTER (NAME ONLY): Bjørn Fabian-Jessing

TITLE: Increasing downstream protein expression of a double Dicer-independent shRNA-containing cassette for multi-targeting gene therapy in neovascular age-related macular degeneration

SESSION TITLE: Developing Molecular Therapies for Inherited Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.K. Fabian-Jessing, S. Alsing, L. Aagaard, T.J. Corydon, Department of Biomedicine, Aarhus University, Aarhus C, DENMARK|B.K. Fabian-Jessing, A. Askou, T. Bek, T.J. Corydon, Department of Ophthalmology, Aarhus University Hospital, Aarhus N, DENMARK|T. Bek, Department of Clinical Medicine, Aarhus University, Aarhus C, DENMARK|

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ABSTRACT BODY:

Purpose: Repeated intravitreal injections with vascular endothelial growth factor (VEGF) inhibitors constitute current standard treatment for neovascular age-related macular degeneration (nAMD). However, two thirds of patients are either partial or non-responders to standard treatment, and new treatment modalities harbouring the potential to target multiple pathways are needed.

We have designed multigenic vectors incorporating intron-embedded double Dicer-independent short hairpin RNA (agshRNA) with potent VEGF knockdown followed by an antiangiogenic gene. However, analysis has revealed mis-splicing leading to low expression of the downstream gene. By eliminating potential competing splice sites, we hypothesized that downstream gene expression could be significantly increased.

Accordingly, this study aimed to eliminate mis-splicing by designing intron-embedded agshRNAs without potentially competing splice sites and to increase downstream gene expression in vitro.

Methods: Using the NetGene2 server for splice site prediction and mFold for RNA secondary structure prediction, we designed new constructs predicted to eliminate problematic splice sites. For easy validation, green fluorescent protein (GFP) was inserted downstream of the agshRNA-containing cassette, and fluorescent microscopy, flow cytometry and RT-PCR with sequencing of amplicons were used to investigate splicing of the agshRNA construct and GFP expression. All experiments were performed in HEK-293 cell lines.

Results: Fluorescent microscopy and flow cytometry showed a significant increase in downstream GFP expression, and RT-PCR with amplicon sequencing confirmed correct splicing.

Conclusions: By eliminating predicted aberrant splice sites in our agshRNA-containing cassette, we corrected splicing and thereby increased downstream GFP expression, paving the way for inserting therapeutic proteins with the aim of developing efficient and persisting therapy for patients with nAMD.

CONTROL ID: 3714794

SUBMITTER (NAME ONLY): Daniel Brock

TITLE: Nrf2 Knockout Mice Exhibit High Glycemic Index Diet Associated Transcriptomic Alterations in Liver and Retina

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.C. Brock, M. English, A. Swaroop, National Eye Institute, Bethesda, Maryland, UNITED STATES|S. Rowan, A. Taylor, Tufts University, Boston, Massachusetts, UNITED STATES|A.K. Mondal, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dietary glycemic index (GI) indicates how fast glucose from dietary carbohydrates enters the bloodstream after consuming a food item. Dietary GI has been found as a risk factor for developing blinding diseases, such as age-related macular degeneration and cataracts. The retinas of mice fed a high GI diet for 12 months show photoreceptor loss, which is accelerated in Nrf2 knockout mice. To assess the molecular consequences of GI in WT and $Nrf2^{-/-}$ mice, we have evaluated transcriptomic changes in the retinas and livers after exposure to a high (HGI) or low glycemic (LGI) diet.

Methods: C57BL/6 (WT) and $Nrf2^{-/-}$ mice were aged from 6 to 18 months while feeding on an LGI diet of 70% amylose + 30% amylopectin or an HGI diet of 100% amylopectin. RNA from retinas and livers was used for RNA-seq. Bioinformatic analyses involved the Bioconductor pipeline of edgeR and limma. Differential analysis was set at two fold change and p-value of 0.05, before pathway annotation with gProfiler.

Results: Principal component analysis showed distinct genotype-based clustering among WT and $Nrf2^{-/-}$ livers. WT HGI mice displayed higher expression of glutathione pathway genes, such as glutathione S-transferase, relative to LGI. Notably, glutathione genes were reduced by 2-6 fold in $Nrf2^{-/-}$ livers, regardless of GI, indicating gene-diet interactions. The expression of retinol metabolism genes, including aldehyde dehydrogenase and UDP glucuronosyltransferase, were also reduced in $Nrf2^{-/-}$ livers. Mitochondrial OXPHOS genes, involved in complexes 1 and 5, as well as late endosomal/lysosomal autophagy genes, were upregulated in WT HGI livers but did not show any response to GI in $Nrf2^{-/-}$ livers. Retinal transcriptome analysis is in progress.

Conclusions: The interaction between genetics and dietary GI in WT and $Nrf2^{-/-}$ mice can help explain the differences in phenotype and disease susceptibility. We reason that $Nrf2^{-/-}$ animals experience reduced ability to respond to glycemia-induced stress due to attenuated antioxidant response systems. This leads to a lowered ability to sanitize the cell of damaging molecules. Retinal transcriptomic analysis would reveal a pathmechanistic relationship between GI, genotype, and retinal degeneration.

CONTROL ID: 3714797

SUBMITTER (NAME ONLY): Leonid Zukin

TITLE: Emergency Ophthalmology Consultations at a Large Tertiary Care Hospital: One-Year Results during the COVID-19 Pandemic in Los Angeles County

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zukin, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Across all medical and surgical specialties, the COVID-19 pandemic has had a massive and likely lasting impact on the practice patterns of providers and the behaviors of patients. In ophthalmology, many new technologies, protocols, and recommendations have emerged, including altered triaging patterns and resource allocation. To provide addition data to such quality improvement efforts, this retrospective study examines one year's worth of data on the volume and nature of emergent ophthalmic consultations at one of the largest and busiest hospitals in one of the largest counties in the United States.

Methods: The timing and nature of every new, daily consultation to the ophthalmology service placed from the emergency department at a large tertiary hospital in Los Angeles County was recorded from July 2020 until June 2021. Of note, this data did not include inpatient consultations, outpatient referrals made by other providers, or consults made from the urgent care clinic. Additional data on COVID-19 cases, hospitalizations, and deaths were obtained from resources publicly available online.

Results: During the study period, the ophthalmology service received 4,149 new consults from the emergency department, approximately 12 new consultations daily on average. Interestingly, we found that this volume dropped from October 2020 through February 2021 (down to 8 daily consults in January), coinciding with a peak of COVID-19 cases, hospitalizations, and deaths reported in Los Angeles County over the same timeframe. Further analysis into the consult reason and the urgency of the consults was also performed.

Conclusions: This study utilizes a large ophthalmic data set obtained through the most severe COVID-19 surge in the United States to date. We identified a decrease in consultation volume during a COVID-19 surge and characterized changes in the nature of these emergent ophthalmic referrals during this time.

CONTROL ID: 3714801

SUBMITTER (NAME ONLY): Jared Nielsen

TITLE: Preliminary Results from a First-in-human Phase I/II Gene Therapy Study (FOCUS) of Subretinally Delivered GT005, an Investigational AAV2 Vector, in Patients with Geographic Atrophy Secondary to Age-related Macular Degeneration

SESSION TITLE: AMD and Geographic Atrophy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate safety and dose response of subretinally delivered GT005, an investigational recombinant adeno-associated viral (AAV2) vector encoding Complement Factor I (CFI), for treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Methods: FOCUS (NCT03846193) is an open-label multicenter study consisting of 4 parts: dose-escalation of GT005 delivered via transvitreal subretinal injection (TVSI), dose-expansion with TVSI, dose-escalation of GT005 delivered using the Orbit subretinal delivery system (Orbit SDS), dose-expansion with the Orbit SDS. All patients had bilateral GA at baseline and received a single subretinal administration of GT005 in the study eye. Primary endpoint is safety of GT005 over 48 weeks, with secondary endpoints including anatomical/functional outcomes and changes in complement protein expression in the vitreous humor. Part 1 explored 3 GT005 dose levels (2E10, 5E10 and 2E11 vector genomes [vg]) delivered via TVSI, Part 2 further explored dose-levels that were shown to be safe and tolerable in Part 1. Interim data from the TVSI cohorts are presented herein

Results: On December 2021, enrolment was complete for Parts 1 and 2 and 31 patients had received GT005 via TVSI, 11 in Part 1 and 20 in Part 2, with a mean follow-up of 51.8 weeks (range: 2.3 to 144.3). At baseline, the mean age was 80.3 years (68 to 93), 71.0% (22/31) were women, and 96.8% (30/31) were white. All 3 dose levels of GT005 delivered via TVSI were well-tolerated, with no dose-related trends in the frequency and type of reported adverse

events (AEs) to date. Of the 48 treatment-emergent ocular AEs in 21 patients, 29 occurred in the study eye only and 10 were bilateral. From the AEs affecting the study eye, majority were mild (30/39) and considered unrelated to GT005 (37/39). From the moderate AEs affecting the study eye (9/39), 5 were related to worsening of cataracts, and 1 described the conversion to choroidal neovascularization. No severe or serious ocular AEs were reported. There were no signs of GT005-related inflammation. Biomarker analysis of vitreous including complement factors at baseline and follow-up will be presented.

Conclusions: GT005 had a positive safety profile at 2E10 to 2E11vg with no signs of GT005-related inflammation.

CONTROL ID: 3714806

SUBMITTER (NAME ONLY): Kirsten Lampi

TITLE: Deamidation in human gammaS-crystallin increases susceptibility to glutathione induced oxidation and aggregation

SESSION TITLE: Lens proteins: normal and pathogenic biochemistry

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.J. Lampi, K. Zientek, S.G. Wheeler, D. Anderson, U.P. Shinde, L.L. David, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether deamidation of γS-crystallin increases the susceptibility of its 7 cysteines to glutathionylation and disulfide bond formation.

Methods: Recombinantly expressed wild type (WT) human γS-crystallin and a triple mutant (TM) containing D14, D76, and D143 (sites undergoing extensive deamidation in cataractous lenses) were incubated under anaerobic conditions for 5 days in either 5 mM reduced glutathione (GSH), or 2.5 mM oxidized glutathione (GSSG). The overall amount of glutathionylation and disulfide bond formation was determined by whole mass measurement. Trypsin digestions were then performed to support parallel reaction monitoring (PRM) and Skyline software analysis to detect specific sites of modification. Aggregation was detected by measuring dynamic light scattering.

Results: Following incubation, WT γS underwent little glutathionylation and only a single disulfide was detected in 18% of the protein. In contrast, 3% of TM γS contained one disulfide + one glutathionylation, 37% one disulfide, 34% two disulfides, and 4% three disulfides. The PRM analysis of tryptic digests of WT and TM indicated that only the TM contained peptide 19-34 (the peptide containing C22, C24, and C26) with both a disulfide bond and a site of glutathionylation. TM furhter contained increased disulfide bonding between peptide 19-34 and the two peptides containing C36 and C129. Further increased disulfide formation occurred in TM between C36-C114, C82-C114, and C114-C129 compared to WT. PRM analysis indicated that the major oxidized form of WT containing a single disulfide was due to a mixture of one disulfide between C22 and C26, and another between C24 and C36. Dynamic light scattering measured larger aggregates in TM than WT initially with sample loss after 5-day incubation in the TM.

Conclusions: Deamidation increased the susceptibility of γS to oxidation through disulfide exchange reaction with GSSG. This presumable was due to increased conformational dynamics allowing increased exposure and proximity of normally buried cysteines. The locking of TM γS into non-native confirmations due to the resultant disulfide bonds may contribute to increased light scatter. The results support that deamidation and elevation of GSSG in aged lenses may act synergistically to cause cataracts.

CONTROL ID: 3714807

SUBMITTER (NAME ONLY): Yu-Chieh Ko

TITLE: Deep learning assisted prediction of long-term visual outcome after 3 monthly anti-vascular endothelial growth factor injections in patients with central-involved diabetic macular edema

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ko, S. Chen, Taipei Veterans General Hospital Department of Ophthalmology, Taipei, TAIWAN|Y. Ko, S. Chen, National Yang Ming Chiao Tung University School of Medicine, Taipei, TAIWAN|C. Peng, H. Ho, C. Lee, Electronics Engineering, National Yang Ming Chiao Tung University, HsinChu, TAIWAN|S. Chiu, Medical research, Taipei Veterans General Hospital, TAIWAN|

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ABSTRACT BODY:

Purpose: Anti-vascular endothelial growth factor (anti-VEGF) injection is now the first-line therapy for central-involved Diabetic macular edema (DME). However, the response to anti-VEGF treatment is not predictable. Alternative treatments should be offered to the non-responders as soon as possible to gain earlier and better visual improvement. We developed a temporal convolutional network (TCN) model to predict the change of visual acuity (VA) at one year after 3 monthly anti-VEGF injections using optical coherence tomography (OCT) images at baseline, one- and three-month follow-up visits.

Methods: Serial OCT images from 317 patients who received at least 3 monthly anti-VEGF treatments, had serial OCT images and completed 12-month follow-up at Taipei Veterans General Hospital were retrospectively collected. The treatment effect was defined by the change of VA at 12-month follow-up (final VA) compared with baseline VA. The improved group refers to patients whose final VA improved for over 2 lines at the Snellen chart compared with baseline. The other patients were classified as non-responders. The image dataset was divided into training and testing datasets at a ratio of 5:1. To apply the TCN on image data, a pre-trained model ResNet50 was used to extract the image features, and then fine-tuned by the training dataset. (Figure)

Results: A total of 101 patients were classified as the improved group. Owing to imbalanced data distribution, data augmentation was performed specifically in the improved group. If 3 OCT images concatenated in the channel dimension were used to predict treatment outcome using ResNet50, the predictive accuracy, specificity and sensitivity were 69.04%, 70.37%, and 68.05% respectively. However, if TCN was applied to catch time-series information of the OCT images, the predictive accuracy improved to 81.25%, with a specificity of 74.40% and sensitivity of 92.07%.

Conclusions: Applying TCN to extract serial features of OCT images following anti-VEGF treatment may be a workable architecture to predict visual outcomes following anti-VEGF treatment in DME patients. This approach may help us to identify unresponsive patients who may benefit by switching to steroid treatment or surgical intervention to avoid unnecessary continual anti-VEGF injection.

CONTROL ID: 3714808

SUBMITTER (NAME ONLY): Dara Baker

TITLE: Using Minimum Test Tradeoff to Assess the Value of OCTA for Predicting Moderate to Severe NPDR in Patients with Diabetes Mellitus

SESSION TITLE: Diabetic retinopathy epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Baker, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Dara Baker: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A recent study utilized machine learning (ML) to diagnose nonproliferative diabetic retinopathy (NPDR) based on optical coherence tomography (OCT) alone, OCT in combination with OCT angiography (OCTA), and OCT/OCTA with clinical factors in classifying diabetic retinopathy. The results demonstrated an increase in area under the curve (AUC)s with OCT/OCTA vs OCT with the addition of image analysis and clinical data. The study failed to consider the costs of data acquisition to improve the model. We therefore questioned whether the addition of the OCT/OCTA was worthwhile to improve risk prediction.

Methods: We used decision analysis to compare models based on clinical factors vs those including image analysis. The methodology is based on recent work by Baker, who developed a useful decision-analytic metric, the test tradeoff, and a simple approximation of its minimum value. For a given ratio of the benefit of a true positive to the cost of a false positive, the test tradeoff is the minimum number of data collections per true positive to yield a positive net benefit. We used Baker's formula applied to model comparisons to compute an approximate minimum test tradeoff (over benefit-cost ratios) for an added predictor, MTT.

Results: Inputs included AUCs for ML models using OCT alone (75.6%) versus OCT in combination with OCTA (92.2%). The formula also requires rates of outcome prevalence in the population, which is 14% for moderate and 6% for severe NPDR in patients with known DM. As a baseline for OCT alone, we found MTT = 42 OCTs per true positive prediction of moderate NDPR and MTT= 10 OCTs per true positive prediction of severe NDPR. For OCTA to be worthwhile when added to OCT, we found MTT=54 OCTAs for 1 true positive prediction of moderate NPDR or MTT= 23 OCTAs for 1 true positive prediction of severe NPDR.

Conclusions: Fundoscopic examination remains a vital component of classification and prognosis of diabetic retinopathy to assess for NPDR. Our findings suggest that the addition of OCTA imaging to OCT imaging alone does not yield a net benefit for the additional cost required to diagnose moderate or severe NPDR in a patient with diabetes. Although the monetary cost for adding OCTA per patient may be moderate, the benefit of improved accuracy in diagnosis remains equivocal, as moderate and severe NPDR are often managed conservatively.

CONTROL ID: 3714809

SUBMITTER (NAME ONLY): Abid Haseeb

TITLE: Evaluation of the association between trachoma and vision-related quality of life using the Pediatric Eye Questionnaire

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Haseeb, A.R. Djalilian, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|T. Eleiwa, I.A. Elsaadani, R.H. ElSheikh, Department of Ophthalmology, Benha University, Benha, EGYPT|A. Elhusseiny, Department of Ophthalmology, University of Arkansas System, Little Rock, Arkansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the association between trachoma and vision-related quality of life (VR-QOL) in children and their families using the Pediatric Eye Questionnaire (PedEyeQ).

Methods: A prospective case-control study including children less than 18 years of age. Participants comprised 113 children with trachoma and their parents versus 75 healthy age-, gender-, residence-matched children who served as controls and their parents. The trachoma was categorized into follicular trachoma (TF), trachoma intense (TI) and trachomatous scarring (TS).

Results: Of 113 participants with trachoma, 53.1% were boys and 58.4% had rural residence. Child PedEyeQ domain scores were lower with trachoma versus controls and the greatest mean difference was in functional vision (10.3 points; P <0.001). Proxy PedEyeQ domain scores were lower with trachoma with the greatest difference in bothered by Eyes/Vision (14.3 points; P <0.001). Parent PedEyeQ domain scores were lower with trachoma; the greatest difference was in worry about child's eye condition (9.1 points; P <0.001). Subgroup analysis showed that the reduction in PedEyeQ domain scores was more severe in TS followed by TI (P<0.001). Stepwise linear regression analysis revealed that 44 % of the PedEyeQ score could be predicted by the clinical grade of trachoma (P < 0.001). In the trachoma group, a higher clinical grade was associated with lower PedEyeQ domain scores in children, parents, and proxy (P<0.001). The parents' PedEyeQ scores were correlated with their children's PedEyeQ scores (R = 0.6; P<0.001).

Conclusions: These findings suggest trachoma has a negative impact on VR-QOL for children and their parents, especially in children with TI/TS grading.

CONTROL ID: 3714810

SUBMITTER (NAME ONLY): Jamie Craig

TITLE: Intraoperative Intravitreal Bevacizumab Prolongs Survival of Trabeculectomy Blebs at 12 months: The Avastin in Trabeculectomy Study

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Craig, S. Mullany, J. Landers, Ophthalmology, Flinders Univeristy, Adelaide, South Australia, AUSTRALIA|

Commercial Relationships Disclosure: Jamie Craig: Commercial Relationship: Code N (No Commercial Relationship) | Sean Mullany: Commercial Relationship: Code N (No Commercial Relationship) | John Landers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the effect of adjunctive intraoperative intravitreal bevacizumab injection on trabeculectomy bleb function and structure during the first postoperative 12 months.

Methods: Single centre double-blinded randomised, placebo-controlled trial on 131 patients with glaucoma requiring trabeculectomy.

Intervention: Patients were subjected to a standardised trabeculectomy procedure augmented with onlay MMC 0.04%, and standardised follow-up protocol. Subjects were randomised to receive intraoperative intravitreal injection of either bevacizumab (1.25mg in 0.05ml) or placebo (balanced salt solution; BSS, 0.05ml).

The primary outcome was defined as ‘complete success’ if intraocular pressure (IOP) remained less than a predefined target IOP without the requirement of topical IOP lowering medication, or ‘qualified success’ if additional topical IOP lowering medication was required to meet the predefined target IOP threshold. Secondary outcomes included IOP, requirement for subsequent bleb needling, number of IOP lowering medications, and bleb morphology based on assessment of the trabeculectomy bleb using the Moorfields Bleb Grading Scheme.

Results: Of 131 patients randomised to bevacizumab (n=65) or placebo (n=66), 128 patients completed 12 months of follow up. At one year, 6% of the bevacizumab group failed the definition of complete success, compared with 17% of those in the placebo group (P=0.015). In addition, 2% of the bevacizumab group failed the definition of qualified success, compared with 10% of those in the placebo group (P=0.033). Within the placebo group, IOP and the requirement for bleb needling was higher at one month (P<0.05). Usage of IOP lowering medication was higher at 6-months (P<0.05) and 12-months (P<0.05). Blebs in the bevacizumab group were larger in the central extent (P<0.001), total extent (P<0.01) and height (P<0.001) at one month compared with the placebo group. There was no significant difference in complications between the bevacizumab and placebo groups.

Conclusions: Bevacizumab given as a single intravitreal dose during trabeculectomy surgery results in improved surgical success as 12 months, with a significant reduction in the need for additional medication and bleb needling to achieve target IOP. Furthermore, this intervention results in blebs which are larger and less inflamed.

CONTROL ID: 3714814

SUBMITTER (NAME ONLY): Arturo Ramirez-Miranda

TITLE: Corneal Biomechanical and Biometric changes after Femtosecond Small Incision Lenticule Extraction (SMILE) refractive procedure at different treatment depths.

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ramirez-Miranda, S. Mangwani-Mordani, J.Y. Arteaga-Rivera, A. Navas, E.O. Graue-Hernandez, cornea and refractive surgery, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|J. Valdez-Garcia, Ophthalmology, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To compare the changes of biomechanical properties, endothelial cell density (ECD), higher-order aberrations, and posterior corneal elevation (PCE) of Femtosecond Small Incision Lenticule Extraction (SMILE) at depths of 100 um, 120um, 140um and 160um

Methods: This retrospective, comparative case series was designed to assess outcomes following SMILE procedures performed at a large surgical center by cornea specialists between May 1, 2020 and September 30, 2021. Four cap depth settings were compared: 100 um, 120um, 140um and 160um. Preoperative corneal biomechanical properties, posterior corneal elevation (PCE), total high-order aberrations (THOA), and endothelial cell density (ECD) by Scheimpflug Tomography (Pentacam AXL) , Dynamic Scheimpflug analyzer (Corvis ST) and specular microscopy (Konan SP 9000-LC) respectively, were measured preoperatively and on days 1, 7, 30 and 90 postoperative.
PCE changes by Pentacam were calculated at the corneal apex. Three parameters including deformation amplitude (DA), first applanation time (A1T), and second applanation time (A2T) were chosen for analysis, and then the ECD was automatically calculated by the computer software.

Results: A total of 140 patients (280 eyes) met the inclusion criteria: 70 eyes in 100nm cap depth SMILE group, 700 eyes in 120nm cap depth SMILE group, 70 eyes in 140nm cap depth SMILE group and 700 eyes in 160nm cap depth SMILE group.
Neither deformation amplitude (DA) nor the first applanation time (A1T) were significantly different between the groups. The second applanation time (A2T) was similar between the groups on days 1, 7, 30 with the exception of 90 days after surgery (22.52±0.18 ms in the 160-cap group versus 22.02 ±0.23 ms in the 140-cap group versus 21.84 ±0.24 ms in the 120-cap group versus 21.34 ±0.34 ms in the 100-cap group, p = 0.004). DA curve depth(μm) was steeper in the 100um depth cap, and the curve will be reduced as the SMILE has a deeper cap. AT2 will be significantly shorter in the 100um depth cap SMILE than in the 160um depth cap. No statistically significant differences were found between the different depth groups regarding THOA, ECD, CV and HEX.

Conclusions: A deeper cap while performing SMILE (140-160um) has less biomechanical effect in the cornea than SMILE with a cap created at 100-120 um.

CONTROL ID: 3714815

SUBMITTER (NAME ONLY): Vishal Govindahari

TITLE: Transscleral Optical Imaging (TOI) in Central Serous Chorioretinopathy – A novel imaging tool in retinal pigment epithelium visualization

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Govindahari, Vitreoretina, Pushpagiri Vitreo Retina Institute, Secunderabad, Telangana, INDIA|L. Kowalczuk, C. Moser, Ecole Polytechnique Federale de Lausanne, Lausanne, VD, SWITZERLAND|L. Kowalczuk, A. Iskandar, Z. Misutkova, A. Gryczka, A. Navarro, F. Jeunet, I. Mantel, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|A. Iskandar, Z. Misutkova, A. Gryczka, A. Navarro, F. Jeunet, I. Mantel, Biology and Medicine, University of Laussane, Laussane, SWITZERLAND|F.F. Behar-Cohen, INSERM, Paris, Île-de-France, FRANCE|F.F. Behar-Cohen, Institut Cochin, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Imaging of the retinal pigment epithelium (RPE) monolayer in various retinal diseases poses a challenge considering the limited lateral resolution of commercially available devices and high reflectivity of the overlying photoreceptor layer in adaptive optics (AO) based imaging systems. We performed a prospective observational study to image the RPE using transscleral optical imaging (TOI) (Cellularis®, prototype), in patients with a clinical diagnosis of central serous chorioretinopathy (CSCR).

Methods: Twelve patients (mean age 43.3±4 years; 3 females, 9 males) with a clinical diagnosis of CSCR, in one or both eyes, underwent a comprehensive eye exam which included best corrected visual acuity, refractive error spherical equivalent and axial length. Demographic data included age and gender of the patient. A trained operator captured six 5.04° x 5.04° high resolution RPE images at different locations of each eye. All patients also underwent clinical imaging with color and autofluorescence fundus imaging as well as optical coherence tomography (OCT).

Results: TOI was successfully performed on 21 eyes with CSCR and one normal contralateral eye. Resolved CSCR eyes (N=15)showed an altered pattern of RPE mosaic in regions with RPE changes. Eyes with active CSCR (N=6) showed poor resolution of TOI imaging in regions with retinal detachment. TOI images revealed hyperreflective dots corresponding to areas of RPE hyperplasia or RPE detachments with hyperreflective content, and dark dots in some areas. Interestingly altered foveal RPE patterns were seen in some cases, even when the retinal morphology was normal on OCT.

Conclusions: TOI circumvents the drawbacks of conventional transpupillary AO imaging to perform cellular level imaging of RPE in CSCR. Various qualitative features such as altered mosaic pattern and hyperreflective dots help define sequelae at the level of RPE and inner choroid. Further understanding of the various qualitative signs on TOI and their correlation with multimodal imaging in CSCR is needed to explore the role of TOI in diagnosis, prognostication and treatment of various retinal conditions such as CSCR.

CONTROL ID: 3714816

SUBMITTER (NAME ONLY): Jesus Arreola-Martinez

TITLE: Triple Therapy efficacy for evaporative dry eye evaluated through the Keratograph 5M.

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Arreola-Martinez, D. Loya-Garcia, J.R. Arreola-Martinez, A. Castillo, J.C. Hernandez-Camarena, J.E. Valdez, Ophthalmology, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: Describe and analyze the effectiveness of triple palpebral therapy in signs and symptoms of evaporative dry eye using dynamic-keratograph parameters.

Methods: Retrospective study of patients with evaporative dry eye disease referred to palpebral therapy sessions from January 2019 to November 2021. Such therapy consisted of 3 sessions once a week during which patients underwent debridement- scaling of the lid margin, followed by moist-heat therapy with Blephasteam® for 10 minutes and meibomian gland manual expression (“Triple therapy”). Ocular Surface Disease Index (OSDI) questionnaire, noninvasive tear break-up time (NITBUT), recorded as the time to first rupture (NITBUTf) and the average time for rupture (NITBUTav), ocular redness, tear meniscus height (TMH) and meibography score were measured before and after the therapy using the OCULUS Keratograph® 5M. Paired t-test and chi-square analysis were used, and the level of statistical significance was taken as $p<0.05$.

Results: A total of 280 eyes (140 patients) were included, 71% were female. The mean age was 52.32±17.79 years. Meibomian gland abnormalities (grade 2-3) were found in 59.64% of cases, being the lower eyelid the most affected (71.43%). Pre-treatment TMH (millimeters), NITBUTf (seconds), NITBUTav (seconds), ocular redness and OSDI score were 0.22±0.16, 4.48±2.61, 7.03±3.51, 1.56±0.59 and 33.38±24.69, respectively. Post-treatment statistically significant improvement was found in TMH, NITBUTf, NITBUTav, ocular redness, and OSDI score with 0.34±0.20, 8.32±4.51, 11.08±4.77, 1.07±0.47, and 13.60±14.66, respectively ($p<.001$). Meibography scores had a non-significant statistical change ($p=.35$). Conjunctival chalasis was only found in 3.93% of cases. Ocular surface diseases other than primary evaporative dry eye disease were present in 10.7% of the eyes. No adverse effects were observed.

Conclusions: Triple therapy showed a significant improvement in evaporative dry eye signs and symptoms after the three-week sessions and appears to be an effective option for these patients. Studies to evaluate the long-term effect of the treatment may be necessary.

CONTROL ID: 3714818

SUBMITTER (NAME ONLY): Aditya Bansal

TITLE: Retinal Displacement On Fundus Autofluorescence Imaging: Only The Tip Of the Iceberg

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bansal, R.H. Muni, St Michael's Hospital, Toronto, Ontario, CANADA|E. Roditi, K. Brosh, Shaare Zedek Medical Center, Jerusalem, Jerusalem, ISRAEL|

Commercial Relationships Disclosure: Aditya Bansal: Commercial Relationship: Code N (No Commercial Relationship) | Eudardo Roditi: Commercial Relationship: Code N (No Commercial Relationship) | Koby Brosh: Commercial Relationship: Code N (No Commercial Relationship) | Rajeev Muni: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal displacement leads to worse functional outcomes following rhegmatogenous retinal detachment (RRD) repair. Although fundus autofluorescence (FAF) imaging can detect retinal displacement, there is a concern regarding its sensitivity & specificity. This study compares the accuracy with which FAF detects the presence and extent of retinal displacement.

Methods: A retrospective study of all patients with infrared (IR) images available before the occurrence of RRD and after RRD repair. At least 4 corresponding RPE and choroidal landmarks were marked on pre-RRD & post-RRD IR images extracted from the Heidelberg optical coherence tomography (OCT) software. Overlay of IR images based on the marked landmarks utilized a computer code in Python to compute the homography and then align the two images. The same procedure was carried out in the contralateral normal eyes to validate the technique. Two masked graders analyzed both the post-operative FAF and the IR overlay images to detect the presence and extent of retinal displacement.

Results: 14 eyes had both a pre-RRD & post-RRD repair OCT and a post-RRD FAF. In 8 patients, the contralateral eye had no other pathology or history of RRD. Homography was able to perfectly align the contralateral eye IR images in 100% (8/8) of cases (Fig 1). Retinal displacement was detected in 64.3% (9/14) of FAF images and in 92.8% (13/14) of IR overlay images respectively. The extent of retinal displacement was far greater as observed on the IR overlay images with a mean number of displaced vessels of 1.1 ± 0.88 in the FAF group and 2.9 ± 1.05 in the IR overlay group ($p=0.00004$). Qualitatively, the IR overlay method was superior at demonstrating both the presence and extent of retinal displacement compared to FAF (Fig 2). The IR overlay showed more extensive displacement in 92.8% (13/14) of cases.

Conclusions: FAF does not demonstrate the full extent of retinal displacement that is present and reveals only the “tip of the iceberg”. When available, overlay of pre-RRD & post-RRD repair IR images generated by OCT provides a better assessment of retinal displacement.

CONTROL ID: 3714819

SUBMITTER (NAME ONLY): Na-Kyung Ryoo

TITLE: Evaluation of foveal avascular zone associated with foveal pit restoration after idiopathic epiretinal membrane surgery

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ryoo, B. Bae, Y. Choi, Ophthalmology, Veterans Health Service Medical Center, Seoul, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure: Na-Kyung Ryoo: Commercial Relationship: Code N (No Commercial Relationship) | Byung-jin Bae: Commercial Relationship: Code N (No Commercial Relationship) | Young-Jae Choi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the relationship between ophthalmic parameters—including OCT and OCTA findings—and foveal pit restoration in eyes that had undergone vitrectomy for idiopathic epiretinal membrane (iERM) removal.

Methods: This study retrospectively analyzed data of patients who underwent 25-gauge pars planar vitrectomy (PPV) for the removal of ERM. Only eyes with iERM above stage 2 with a follow-up over 6 months were included. Baseline data and changes in ophthalmic parameters and their values were analyzed from 3 months before surgery to 12 months after the ERM surgery. Additionally, we stratified iERM patients into two groups (foveal pit restoration and no restoration group). Longitudinal comparison analyses between the two groups were done with the pre-and postoperative best-corrected visual acuity (BCVA), central foveal thickness (CFT), and superficial foveal avascular zone (FAZ) areas measurements using swept-source optical coherence tomography (SS-OCT) and optical coherence tomography angiography (OCTA).

Results: Overall, 43 patients with a mean age of 75± 5 years were enrolled in this study. After surgery, BCVA, FAZ, and CFT showed statistically significant improvements over time (all p-value <0.002). Thirty-one patients were designated into the foveal pit restoration (R) group and 12 patients into the no restoration (NR) group. Differences in BCVA and FAZ areas in both groups existed for up to 6 months. However, BCVA improved (R group: 0.12 ± 0.11 vs. NR group: 0.12 ± 0.07) and FAZ expanded (R: 0.20 ± 0.05 vs. NR: 0.18 ± 0.04) in both groups showing no statistical difference 12 months post-surgery. The CFT continuously decreased in both groups after removal of ERM, but the restoration group was thinner at every point compared to the no restoration group (all p-values < 0.05)

Conclusions: The removal of epiretinal membrane in PPV significantly improves BCVA, decreases the CFT and expands the superficial FAZ. Foveal pit restoration improves BCVA, CFT and FAZ area possibly at a faster rate in the early months but long-term improvements could be achieved regardless of the status of foveal pit restoration.

CONTROL ID: 3714820

SUBMITTER (NAME ONLY): Simon Mogendi

TITLE: Correlation of Social Determinants of Health with Outcomes of Pediatric Uveitis

SESSION TITLE: Clinical Uveitis and Scleritis: Therapies and Outcomes

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mogendi, G. O'Keefe, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

Commercial Relationships Disclosure: Simon Mogendi: Commercial Relationship: Code N (No Commercial Relationship) | Ghazala O'Keefe: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Considering the devastating visual consequences of uveitis in the pediatric population, it is important to understand the social determinates of health (SDOH) that contribute to the visual outcomes these patients. We performed a retrospective observational study and cross-sectional survey to evaluate the relationship between SDOH and the visual outcomes of pediatric patients diagnosed with uveitis.

Methods: We conducted a survey and interview of 31 pediatric patients diagnosed with uveitis. We collected quantitative data to determine the social needs of patients and qualitative data about specific barriers or difficulties to see a uveitis specialist at the Emory Eye Center. We collected demographic and clinical information from the electronic medical record of these patients. Patients under the age of 18 with a diagnosis of uveitis were included in this study. The primary outcome of interest was final visual acuity. We utilized MAXQDA 2020 to analyze the qualitative data we collected in the survey.

Results: Of the 31 patients/parents surveyed, regarding barriers when seeking care, 35% stated they experienced no difficulty seeing a uveitis specialist, 26% mentioned a long driving distance, 19% mentioned difficulty with scheduling an appointment, 6% mentioned difficulty with payment/insurance issues, 6% had difficulties related to the uncertainty of the illness before their child was diagnosed, 3% had difficulty with referrals, and 3% experienced difficulty with taking time off work. The mean time from symptom onset to seeking care was 30.58 days and the median was 3 days. 39% of patient's first visited a pediatrician, 26% first went to an ophthalmologist, 16% went to an optometrist, 13% went to an urgent care, and 6% went to an ER. The average time of symptom onset to the first visit with a uveitis specialist was 356.23 days with a median of 94 days. On average the patients saw 2.1 other providers before being referred to Emory with a median 2. 52% (16/31) of the patients surveyed lived with both parents, 45% live with their mother, and 3% live with their father. Regarding final visual acuity, 48% of patients had vision >20/50, 32% were 20/50-20/200, and 19% were >20/200.

Conclusions: The main barriers to see a uveitis specialist were related to appointment scheduling issues, travel distance/time, and the difficulty of waiting for long periods of time in a waiting room with a child.

CONTROL ID: 3714821

SUBMITTER (NAME ONLY): Thomas Koch

TITLE: Comparison between Drusen Volume Calculations on Heidelberg OCT using Automated vs Manually Adjusted Segmentation for Intermediate AMD and Its Association with Retinal Pigment Epithelium Bruch's Membrane Thickness

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Koch, A. Nigalye, G. Tsougranis, R. Katz, I. Garg, H. Wescott, D. Husain, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T. Koch, A. Nigalye, R. Katz, I. Garg, H. Wescott, J.B. Miller, Harvard Retina Imaging Lab, Boston, Massachusetts, UNITED STATES|S. Pundlik, Department of Ophthalmology Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Drusen burden is a key indicator of age-related macular degeneration (AMD) severity. Real time manual measurement of drusen volume (DV) by clinicians is not practical and automated estimates with inbuilt software save time, but are not readily available. Existing work on DV has shown variation between OCT devices and with automated vs. manually adjusted segmentation. We further examined this variation.

Methods: Retrospective, cross-sectional study of intermediate AMD eyes imaged with macula centered 97 line enhanced depth imaging OCT (Spectralis, Heidelberg). Volume scans were processed for automated segmentation of the RPE and BM to generate the drusen volume. To manually adjust segmentation, RPE and BM were fit to demarcation in each B-scan prior to calculating DV. The average retinal thickness (RT) and DV, and highest retinal pigment epithelium/Bruch's Membrane thickness (RPEBMt) were measured in all 9 ETDRS grid sectors. Multi-level linear regression models, accounting for participant and eye-in-participant levels, were used to associate the log RT and log DV measurements with the processing method (automated vs. manual), RPEBMt(continuous measure), and their interaction.

Results: We included 10 eyes of 5 participants. Over entire ETDRS grid, the mean difference between manual and automated processing for RT and DV was 7.9±21.1 μm and 0.015±0.04 mm^3, respectively. Larger differences between manual and automated methods were observed for inner grid segments (GS) and the center than the outer GS for both RT (Inner: 12.3±26.6 μm; Outer: 2.5±8.4 μm) and DV (Inner: 0.017±0.037 mm^3; Outer: 0.012±0.044 mm^3). The mean±SD of RPEBMt parameter was 85.3±51.9μ. Significant interaction seen between RPEBMt and processing method for both RT (β=0.006, $p<0.001$) and DV (β=0.007, $p<0.001$), meaning the variation between manual and automated processing became larger as the RPEBMt increased.

Conclusions: Presence of large drusen affected the automated segmentation resulting in larger deviations, as measured by significant association between RPEBMt and DV and RT, compared to the manual segmentation. In eyes with large drusen, the current automated segmentation does not reliably measure these parameters, and there is a need for manual review to mitigate the effects of segmentation compromise.

CONTROL ID: 3714825

SUBMITTER (NAME ONLY): Emily Xi Liao

TITLE: Plaque Brachytherapy Outcomes for Large Choroidal Melanomas

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Liao, J. Huang, A. Saleem, M. Laroque, G. Menon, A. Murtha, P. Campbell, E. Weis, University of Calgary, Calgary, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: Large choroidal melanomas are still a common presentation. Treatment with plaque brachytherapy (PB) has historically demonstrated poor outcomes including increased risk of local failure and severe vision loss. The purpose of our study is to report on the outcomes for large choroidal melanomas treated with PB and prophylactic adjuvant bevacizumab.

Methods: A prospective consecutive case series of patients with large choroidal melanomas treated with I-125 (^{125}I) PB. Outcomes included local tumor failure, survival, secondary enucleation and visual acuity.

Results: In total, 87 patients with a large choroidal melanoma were identified. 54 (62.1%) patients were treated with PB and 33 (37.9%) were treated with primary enucleation. A large choroidal melanoma was defined as having a maximum tumor diameter of >16.0 mm or an apex height >10.0 mm regardless of diameter. Of the 33 primary enucleation patients, the mean tumor apex height was 11.1 ± 2.8 mm (3.5 mm – 14.9 mm) and the mean maximal basal diameter was 16.6 ± 3.2 mm (10.5 mm – 23.0 mm). Of the 54 PB patients, the mean tumor apex height was 9.3 ± 3.0 mm (2.0 mm – 14.8 mm) and the mean maximal basal diameter was 16.7 ± 2.2 mm (9.2 mm – 20.5 mm). Of the 54 PB patients, the overall survival rate was 35/54 (64.8%) with a mean follow-up time was 3.6 ± 95% confidence interval of 2.5 years. The local failure rate was 0/54 (0.0%) and the secondary enucleation rate was 3/54 (5.6%). Visual acuity was better than 20/200 in 40% of the patients at a mean follow-up time of 3.6 ± 2.5 years.

Conclusions: Plaque brachytherapy provides excellent local tumor control, an eye preservation rate of 94.4%, and a 65% overall survival rate with a mean follow-up of 3.5 years. Visual acuity was better than 20/200 in 40% of the patients.

CONTROL ID: 3714826

SUBMITTER (NAME ONLY): Samantha Madala

TITLE: RIPLs, an optical coherence tomography marker of occult cardiovascular disease

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cardiovascular disease is the number one cause of death in the world, and frequently goes unnoticed until the occurrence of serious events such as heart attack or stroke. Therefore, early detection of occult cardiovascular disease, prior to catastrophic illness, is critical. We sought to determine whether retinal ischemic perivascular lesions (RIPLs), which are anatomical biomarkers of subclinical microvascular ischemia in the retina, can be used to detect occult cardiovascular disease.

Methods: We identified individuals with no significant retinal pathologies and who had RIPLs detected on spectral domain optical coherence tomography (SD-OCT) scans during routine retinal examination in our clinic. We excluded individuals with pre-existing cardiovascular disease, diabetes, and those who did not have a follow-up medical visit. Additionally, we excluded patients with any retinal pathology including diabetic retinopathy. We reviewed the medical chart and present the medical outcome of subjects who had subsequent cardiovascular workup prompted by RIPLs detection.

Results: We identified thirty-six patients, with incidental RIPL identification on SD-OCT at the time of examination. A total of 25 patients were excluded. Of the 11 subjects that were included, 5 were males and 6 were females. Ages ranged from 44 to 80 years. The eleven subjects with no prior history of cardiovascular disease, other than essential HTN, followed up with their primary care physician or cardiologist for age-appropriate cardiovascular work-up. Of these, newly diagnosed cardiovascular disease was identified in 8 individuals (72.7%), including three-vessel CAD, significant carotid artery stenosis, soft carotid plaque, reduced cardiac ejection fraction, patent foramen ovale, cerebral infarction, subclavian steal syndrome and undiagnosed or uncontrolled HTN. Two patients subsequently underwent invasive procedures including coronary artery bypass grafting (CABG) and carotid artery stent placement. Three patients were started on new medical therapy for their conditions, and two were advised to undergo periodic follow up.

Conclusions: Our findings indicate that presence of RIPLs, which are anatomical markers of prior retinal ischemic infarcts, may indicate the need for cardiovascular referral which in some cases can lead to important interventional management.

CONTROL ID: 3714827

SUBMITTER (NAME ONLY): Rachel Munzar

TITLE: Engagement of Patients with Diabetic Retinopathy by Telehealth Extenders Improves Follow Up

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Munzar, C. Lasalle, S. Roh, D.J. Ramsey, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|R. Munzar, C. Lasalle, S. Roh, D.J. Ramsey, Lahey Hospital and Medical Center, Burlington, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effectiveness of telehealth (TH) services delivered by a health extender in promoting patients with diabetic retinopathy (DR) who are overdue for care to schedule and/or return for in-clinic eye examinations.

Methods: Established patients with DR who had not been seen within the last year were identified by a retrospective review of the EMR using a reporting tool. Patients who had not returned for follow-up care were contacted by phone by a TH extender. Each patient was offered screening for acute eye problems by means of a symptom-based screening script. Those patients who raised concerns about vision-related issues were offered transfer to a physician for triage. Finally, patients were offered assistance in scheduling an in-person clinic visit.

Results: 159 patients with DR potentially overdue for care were contacted by phone. 43% of calls reached patients; 52% of calls went to patient voicemail (VM) where instructions were left for appointment-booking; 5.0% of patients were unreachable, and 2.9% of patients contacted were identified to be deceased. Of the 67 patients reached by phone, 39% reported that they had transferred/declined further care. Of the remaining 41 patients, 77% agreed to take the symptom survey, and out of those 91% went on to book a booked an appointment, including one patient who required transfer to physician triage and was brought into the clinic the next day for management of proliferative retinopathy. By contrast, the 3 patients who chose not to book an appointment after the symptom survey all reported no symptoms. A further 3 patients scheduled despite declining the symptom survey. Finally, 5 patients (12%) requested to be called back later and 3 patients (7.3%) to call back themselves. In total, 27% of patients contacted through the program ultimately booked an appointment, including 12% who were left a VM and 1 patient who was called back by a scheduler. This rate of appointment booking was more than twice that of a larger cohort of patients who were overdue for care but not engaged by the program (27% vs. 11%, X^2=9.561; P=0.002).

Conclusions: Nearly one-third of patients with DR identified as being overdue for eye care and contacted by a TH extender made follow-up appointments. This study adds to the growing body of research that TH, even when delivered by a non-provider, can help improve the rate at which patients with DR access eye care.

CONTROL ID: 3714830

SUBMITTER (NAME ONLY): Benjamin Backus

TITLE: Clinically practical measurement of standard error in bundled visual field tests

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.T. Backus, J. Blaha, Vivid Vision Inc, San Francisco, California, UNITED STATES|M. Deiner, Z. Chia, M.L. Turner, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|B. Damato, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The reliability of a scientific measurement is usually estimated from variability across repeated measurements, with standard error (SE) estimating variability in the mean. However, conventional visual field tests are labor intensive, so it is not practical to collect repeated measurements. New at-home tests with redesigned psychophysical procedures have recently made it practical for patients to undertake a “bundle” of 10 tests at home within a period of 5-14 days (Deiner, Damato, & Ou, 2020. Ophthalmology 127:1258) for which a mean and SE can be computed.

Methods: Patients from the UCSF Glaucoma Clinic were provided a mobile VR headset (Oculus Go, Facebook Inc) running Vivid Vision Perimetry (VVP) software (Vivid Vision Inc, San Francisco, CA). Patients received virtual training while at home and were then asked to perform VVP 10 times within a two-week period at intervals of approximately four months. Tested field locations were arrayed in the Humphrey 24-2 layout. Each location was tested four times per test with a fixed-contrast stimulus chosen to be close to threshold at locations having a sensitivity of 15 dB in conventional HVFA. Percent seen was the dependent variable.

Results: Between April 2020 and October 2021, 24 patients took 1472 tests in 142 bundles, each containing 5 to 15 tests apiece (mean 10.3, SD 1.9). Percent seen varied from 0% to 100% depending on sensitivity at the location, corresponding to a dynamic range of approximately 5 to 25 dB (HVFA). Mean sensitivity (MS) for each of the 1472 tests was percent seen across 52 locations, not including near the blind spot. Bundle SE was 1.2% on average (std dev 0.9%), corresponding to a test-retest variability of 0.24 dB in HVFA units for the bundle, which compares favorably with the test-retest variability of HVFA in glaucomatous eyes, usually estimated between 0.5 and 1.0 dB. 21 of the bundles contained an outlier (interquartile test); it was generally worse, not better, than the bundle mean. Data review suggested that a change in MS of > 2 SE be used to detect changes in vision.

Conclusions: The SE for a bundle of visual field tests provides a clinically practical objective measure of test reliability. It quantifies the statistical difference between test epochs when monitoring progressive field loss in diseases like glaucoma.

CONTROL ID: 3714831

SUBMITTER (NAME ONLY): Daniel Liebman

TITLE: Primary Care Provider Familiarity with Preferred Practice Patterns for Comprehensive Eye Examinations

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.L. Liebman, A. Lorch, R. Vasan, Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|G.A. Moustafa, Ophthalmology, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|S. Crawford, Family and Preventive Medicine, The University of Oklahoma College of Medicine, Oklahoma City, Oklahoma, UNITED STATES|S. Crawford, Family and Preventive Medicine, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|D.L. Liebman, A. Lorch, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L. Samal, N. Osman, Medicine, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|C. Kloek, Ophthalmology, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|C. Kloek, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: The American Academy of Ophthalmology (AAO) developed Preferred Practice Pattern (PPP) guidelines to standardize the frequency of comprehensive eye exams (CEEs) for specific patient groups. These guidelines may benefit Primary Care Provider (PCPs), who often serve as patients' only touchpoints with the healthcare system. However, PCPs' familiarity with these guidelines is unclear. We surveyed PCPs' familiarity and compliance with CEE guidelines, and whether these patterns varied according to practitioner training level, length of experience, or state.

Methods: We surveyed PCPs, primary care residents, physician assistants (PA), and nurse practitioners (NP) affiliated with two academic medical centers in Boston, MA, and Oklahoma City, OK, as well as a sample of private practice PCPs in Oklahoma. Respondents were given five clinical vignettes and asked to indicate when the patient should be referred for a CEE. Additional questions assessed participants' familiarity with PPPs for CEEs, attitudes toward CEE guidelines, and perceived barriers to utilizing such guidelines. Groups were compared using chi-squared or Fisher's exact tests.

Results: The response rate was 216/336 (64.3%). Around half of PCPs (48.1%) reported "usually" counseling patients regarding CEEs; 15.4% reported "always" doing so, while 36.5% reported "seldom" or "never". Few PCPs (10.6%) were able to accurately describe specific guidelines, whereas two-thirds (63.9%) were unaware of their existence. OK-based PCPs reported greater familiarity with PPP guidelines than MA PCPs ($p=0.02$). Alignment with disease-specific PPPs varied considerably; a strong majority of PCPs (90.7%) correctly referred a type II diabetic at their time of diagnosis, but a similar majority (77.8%) inappropriately referred a newly-diagnosed type I diabetic. 13.4% of PCPs would not refer a young patient with family history of glaucoma until they developed visual symptoms. Compared to other providers, NPs/PAs were more likely to recommend unnecessary CEEs for low risk young adults ($p=0.04$), while residents counseled patients less frequently ($p<0.01$), were less likely to be aware of PPP guidelines ($p=0.03$), and less likely to properly recommend baseline exams.

Conclusions: PCPs' familiarity with CEE guidelines is suboptimal. Targeted efforts to improve PCP guideline awareness may be especially well suited for residents and mid-level practitioners.

CONTROL ID: 3714832

SUBMITTER (NAME ONLY): Aravind Sankaramoorthy

TITLE: Targeting High Glucose-Induced Mitochondrial Fragmentation: Implications for diabetic retinopathy

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sankaramoorthy, S. Roy, Boston University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy is characterized by loss of vascular endothelial cells as a result of apoptosis. During apoptosis mitochondria undergo fragmentation, which is sustained/orchestrated at least in part by the action of dynamin-related protein 1 (Drp1) protein, a regulator of mitochondrial fission. In this study, we determined whether downregulation of high glucose (HG)-induced increased mitochondrial fragmentation could be prevented by targeting Drp1 overexpression and thereby inhibiting apoptosis in rat retinal endothelial cells (RRECs).

Methods: RRECs were grown in normal (N; 5mM glucose) or HG (30mM glucose) media for 7 days; in parallel, RRECs were grown in HG medium and transfected with Drp1 siRNA, or exposed to Mdivi-1, a Drp1 inhibitor. To determine Drp1 levels in these cells, total protein was isolated and subjected to Western blot (WB) analysis. The extent of mitochondrial fragmentation was assessed using live cell confocal imaging after staining with MitoTracker Red and analysed for form factor (FF) and aspect ratio (AR). TUNEL assay was performed, to determine the effect of reducing mitochondrial fission on apoptosis.

Results: WB analysis showed significant Drp1 upregulation in cells grown in HG compared to those grown in N medium (143±17% of normal, $p=0.0004$); cells grown in HG medium transfected with Drp1 siRNA showed significant Drp1 downregulation (97±35% of HG, $p=0.003$). Live cell imaging using confocal microscopy revealed that cells grown in HG medium showed significant mitochondrial fragmentation (FF = 1.91, $p=0.001$; AR = 1.98, $p=0.001$). Interestingly, cells grown in HG medium and transfected with Drp1 siRNA or exposed to Mdivi-1 showed a significant decrease in mitochondrial fragmentation (FF = 3.68, AR = 2.46 $p=0.001$; FF = 3.63, AR = 2.57 $p=0.001$, respectively). In addition, cells grown in HG exhibited increased number of TUNEL positive cells (231±8% of normal $p<0.05$) compared to cells grown in N medium. Importantly, when cells grown in HG were transfected with Drp1 siRNA, this resulted in a significant decrease in the number of TUNEL positive cells (125±12% of HG $p<0.05$).

Conclusions: Findings from this study indicate that targeting HG-induced Drp1 overexpression may have beneficial effects in protecting against HG-induced mitochondrial fission and apoptotic cell loss associated with the pathogenesis of diabetic retinopathy.

CONTROL ID: 3714833

SUBMITTER (NAME ONLY): Nazia Alam

TITLE: Improvement of eye-tracking based metrics in children with arteriovenous malformation rupture

SESSION TITLE: Eye movements and nystagmus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.M. Alam, S.W. Mooney, G.T. Prusky, Center for Vision Restoraton, Burke Neurological Institute, White Plains, New York, UNITED STATES|N.M. Alam, S.W. Mooney, Blythedale Children's Hospital, Valhalla, New York, UNITED STATES|G.T. Prusky, Physiology and Biophysics, Weill Cornell Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual impairments in children with brain injury, such as from spontaneous arteriovenous malformation (AVM) rupture, are difficult to assess through conventional methods due to their co-occurrence with communicative and cognitive disabilities. As a consequence, impairments are often only determined through subjective evaluations of gaze-based reactions to different forms and movements. We recently developed a system to grade visual health based on eye movements and evidence from gaze-based tracking behaviors that can be used in communicative and non- communicative children alike. We use this approach here to assess visual impairment and recovery of function following AVM rupture.

Methods: Our approach, the "Visual Ladder" efficiently produces gaze-based metrics that grade a participant’s saccades, pursuits, visual field responsiveness, and spatial visual function from tracking responses to static and moving stimuli. We used the Visual Ladder to periodically assess five children aged 7-18 while hospitalized at a children’s rehabilitation hospital after being treated for an AVM rupture in the brain. Children in the study were verbal and had no known medical problems prior to injury. After reparative surgery and admission to a rehabilitation hospital, however, the children became non-communicative and had limited mobility. While at the hospital we measured the speed and directional biases of their eye movements, pathological nystagmus, visual field asymmetries, and contrast sensitivity deficits.

Results: Children were tested periodically until discharge and they all five showed improvement in their eye-movement-based metrics using the Visual Ladder, as well as their communication, cognitive, and physical abilities as assessed by hospital therapists as part of their routine standard of care. Fig. 1 depicts an example of one child's mean saccades and pursuits 1 month post treatment for AVM rupture (A and B respectively) and 8 months post recovery (C and D). The distributions at 8 months are far from normative.

Conclusions: Our findings indicate that eye-tracking-based tasks enable the measurement of visual metrics in young and impaired individuals. Quantitative assessments in these clinical populations would aid in a much-needed objective diagnostic tool and therapy tool for non-communicative and/or brain injured populations.

CONTROL ID: 3714835

SUBMITTER (NAME ONLY): Alicia Goyeneche

TITLE: Effect of artificial sunlight spectrum on keratinocytes and fibroblasts and the consequences of ultraviolet radiation blockage

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Goyeneche, E. Youhnovska, M. Abdouh, J.V. Burnier, M.N. Burnier, Pathology, McGill University Health Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Sunlight wavelengths of different energy are key environmental factors in the development of skin photo-damage, photoaging, and carcinogenesis. High-energy wavelengths of ultraviolet radiation zone (UVR) are known etiologic agents in the pathogenesis of basal cell carcinoma (BCC) and contributes to photodamage in dermal layers of the skin. Clinical data from our laboratory shows that lower eyelid BCC tends to develop under moderate-to-severe elastosis. In this study, we evaluated the acute effect of different artificial sunlight exposures in keratinocytes and fibroblasts, and assessed the consequences of partial-to-full UVR blockage.

Methods: Four human cell types were used: two normal primary epidermal keratinocytes, and two normal fibroblasts. Cells were exposed to one sun by a Tri-Sol solar simulator (300-1800 nm). Exposure conditions included full sun (FS), exposure to long path filters that partially or completely blocked UVR, and a non-sun light exposure block (B). Following solar stimulation, we evaluated the cells' metabolic capacity and total reactive oxygen species (ROS) production in the presence or absence of antioxidant N-acetyl Cysteine (NAC).

Results: The primary keratinocytes' metabolic capacity was unaffected when exposed to FS, similarly as B. The FS significantly decreased the metabolic capacity of the fibroblasts. When wavelengths below 360 nm were blocked, both cell types experienced a significant decrease in their metabolic capacity. Co-incubation with NAC during exposure prevented a decrease in metabolic capacity of both keratinocytes and fibroblasts, particularly with filtered UVR. In both cells, FS exposure induced a significant increase in total ROS when compared to B exposure. In fibroblasts, unlike keratinocytes, blockage of UVR resulted in higher levels of ROS when compared to FS exposure.

Conclusions: Exposure to FS induces different acute effects in keratinocytes and fibroblasts. Filtered UVR causes a significant decrease in the metabolic capacity in both cell types, which is prevented by NAC. ROS levels increase when cells are exposed to FS; fibroblasts, contrary to keratinocytes, show higher ROS levels when UVR is blocked. Our data suggest that the decrease in cellular metabolic activity caused by complete UVR blockage could be due to increased ROS levels as it was rescued by NAC.

CONTROL ID: 3714837

SUBMITTER (NAME ONLY): Hamed Hatami-Marbini

TITLE: Does sclera deform under electric field?

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Hatami-Marbini, J. Arash Mehr, Mechanical Engineering, University of Illinois at Chicago College of Engineering, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test the hypothesis that the sclera is an electroactive hydrogel and determine its electromechanical properties.

Methods: Scleral strips were dissected from the area close to the optic nerve head in the superior-inferior direction from porcine eyeballs. After measuring the thickness of the strips using a pachymeter, they were mounted at the center of a custom-designed container between two carbon electrodes. The scleral samples were fixed from one side and their other end was free to move. After filling chamber with NaCl solution, the two carbon electrodes were connected to a DC current power supply and the strips were subjected to 5, 10, and 15 volts for 60 seconds. The deformation of strips was recorded by a digital microscope camera as a function of time during the experiments.

Results: The average thickness of porcine posterior sclera samples was found to be 1.3 mm at the beginning of the experiments. No difference in the thickness of the samples was observed after they were removed from the custom-made container. Upon applying the electric voltage, the strips started to bend towards the cathode, Figure 1. The amount of bending of the scleral strips gradually increased with time and its magnitude was a function of the applied voltage. The maximum bending angle of scleral strips was 2.6±0.5, 11.4±1.0, and 22.4±1.6 at 5, 10, and 15 V, respectively.

Conclusions: It was found that the sclera is an electroactive tissue that mechanically deforms when subjected to DC electric voltage. The amount of deformation depends on the strength of the electric field and the duration of the application of the electric voltage. These findings are important for both biomechanical and biochemical characterizations of the sclera and have important implications for the future efforts to characterize the electromechanical properties of ocular tissues.

CONTROL ID: 3714839

SUBMITTER (NAME ONLY): Fargol Mostofian

TITLE: Pilot study to evaluate the impact of exogenous cannabinoids on the human visual system

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Mostofian, R. Karanjia, University of Ottawa, Ottawa, Ontario, CANADA|M.R. Lalonde, H. Nguyen, S.G. Coupland, R. Karanjia, Ottawa Hospital, Ottawa, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Cannabis is a widely consumed hallucinogenic substance and has previously been linked to central neurotransmission abnormalities. Its chronic use is a public health concern due to reported risk of neurotoxicity which could affect visual processing and neurological development. The purpose of this study is to establish the impact of chronic and acute cannabis use on various levels of visual processing in a population of regular cannabis users.

Methods: Six regular cannabis users, and 7 control non-users underwent complete ophthalmological examination including electrophysiological testing: Visual Evoked Potential (VEP) and electroretinogram (ERG). The testing was repeated twice in regular users: 24 hours [chronic use] and 2.5 hours [acute] following cannabis consumption.

Results: There was no difference between groups in terms of age ($p=0.81$), sex ($p = 0.99$), co-occurrent alcohol and smoking ($p=0.78$ and 0.36). Ophthalmological and electrophysiological testing were within normal limits for both cohorts. No significant difference in the cohorts was found when comparing full field ERG, pattern ERG, and VEP results. A difference was noted in a-wave amplitudes, (Figure 1), which were lowest for acute users and highest for controls at different light intensities, but this failed to meet clinical significance.

Conclusions: Current data suggest that there is no significant impact on visual processing despite chronic or acute use of cannabis. However, there is a possible trend toward diminished photoreceptor function in cannabis use that warrants further higher powered studies. Data collection is ongoing.

CONTROL ID: 3714844

SUBMITTER (NAME ONLY): Anh Bui

TITLE: Transcriptome changes in the aqueous humor of diabetic patients

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Bui, D. Yang, J. Wu, J. Chen, R. Lamy, J.M. Stewart, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|A.D. Bui, D. Yang, J. Wu, J. Chen, R. Lamy, J.M. Stewart, Ophthalmology, Zuckerberg San Francisco General Hospital and Trauma Center, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the changes in the exogenous RNA transcriptome of the aqueous humor in patients with diabetes mellitus without diabetic retinopathy or with proliferative diabetic retinopathy, and to screen for genes linked with diabetic retinopathy progression.

Methods: Aqueous humor (100 ul) was collected in case-control cohorts of 15 healthy controls, 14 diabetic patients without diabetic retinopathy, 12 patients with nonproliferative diabetic retinopathy, and 14 patients with proliferative diabetic retinopathy. We were able to obtain total RNA sequencing results from 14 healthy controls, 5 patients with diabetes without diabetic retinopathy, and 7 patients with proliferative diabetic retinopathy. Genes differentially expressed between patients with or without diabetes as well as diabetic patients with or without diabetic retinopathy were identified using DESeq2.

Results: Three hundred thirty-eight genes were found to be differentially abundant in the aqueous humor (False Discovery Rate < 0.1) of diabetic patients without retinopathy vs controls, and 44 genes in diabetic patients without diabetic retinopathy vs with diabetic retinopathy. CACNB2 and CACNG8, two voltage-gated calcium channel proteins highly expressed in retinal cells and linked to VEGF signaling, and SLC22A11, a glucose transporter, were the top three up-regulated gene in the proliferative diabetic retinopathy cohort.

Conclusions: We were able to discern differences in the RNA composition of the aqueous humor of patients with diabetes with or without diabetic retinopathy compared to healthy controls. Our top candidate, CACNB2, has been previously associated with VEGF regulation in GWAS studies and confirms the role of VEGF signaling in diabetic retinopathy. Aqueous humor is a relatively easy to obtain biofluid, and our results reveals it contains a diverse transcriptome which has potential for disease progression monitoring and discovery of disease-associated gene networks.

CONTROL ID: 3714845

SUBMITTER (NAME ONLY): Akua Frimpong

TITLE: Sex Differences in Scholarly Productivity, Academic Rank, and NIH Funding of US Academic Neuro-ophthalmologists

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is a significant gender disparity in ophthalmology, with 22.7% of the workforce consisting of women. Differences in research funding and support may contribute to the disparities, so we sought to identify factors where these disparities in research support and productivity currently exist within the field of neuro-ophthalmology. To our knowledge, this is the first study to investigate sex differences in scholarly productivity, academic rank, and NIH funding among neuro-ophthalmologists.

Methods: This study was a cross-sectional study of academic neuro-ophthalmologists of all 113 US ophthalmology programs. Using institutional websites, data on sex, residency graduation year, and academic rank were collected. Scopus database was used to obtain each faculty's h-index, and m-quotient was calculated based on each faculty members h-index/career duration. The NIH Research Portfolio Online Reporting Tool database was queried for data on NIH funding. Chi-square testing was used to analyze categorical values and Wilcoxon Rank Sum testing was used for continuous variables.

Results: A total of 210 academic neuro-ophthalmologists were identified, of whom 64 (30.5%) were female and 146 (69.5%) were male. A significantly greater proportion of females vs. males were assistant professors [37 (57.8%) vs. 48 (32.9%); p=0.008]. Although not statistically significant, a smaller proportion of females were full professors [14 (21.9%) vs. 62 (69.5%); p=0.051]. No significance difference was found among associate professors [female: 13 (20.3%) vs. male: 35 (24.0%); p=1.000]. One female neuro-ophthalmologist held the departmental chair position, while nine positions were held by male counterparts [1 (1.6%) vs. 9 (6.5%); p = 1.000]. Females had similar median h-indices compared to their male counterparts (6.0 vs. 10.5; p=0.124) as well as similar median m-quotients (0.5 vs 0.6; p=1.000). Females had a shorter median career duration based on their residency graduation year compared to males (15.0 vs 28.0 years; p <0.001). Among the 43 neuro-ophthalmologists who received NIH funding for research, of whom 13 (30.2%) were female and 30 (69.8%) were male, females had a median grant funding of $1.1M compared to $574K for males (p=1.000).

Conclusions: Females had similar h-indices compared to males. There was no difference in m-quotients between sexes, which controlled for the specialists' career durations.

CONTROL ID: 3714847

SUBMITTER (NAME ONLY): Pamela Martin

TITLE: Regulation of retinal endothelial cell barrier function by the hydroxycarboxylic acid receptor 2 (HCAR2)/GPR109A

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.M. Martin, A. Abdelrahman, F.L. Powell, M. Jones, R. Jadeja, Biochemistry and Molecular Biology, Augusta University, Augusta, Georgia, UNITED STATES|P.M. Martin, M. Thounaojam, M. Bartoli, Ophthalmology and Culver Vision Discovery Institute, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Loss of barrier integrity due to endothelial cell damage or dysfunction is common in retinal microvascular diseases such as diabetic retinopathy. We reported previously, the expression of the beta-hydroxybutyrate (BHB) receptor HCAR2/GPR109A in retina where it localizes robustly to the basolateral membrane of the retinal pigment epithelium (RPE) and regulates outer retinal barrier integrity. Our recent work confirms receptor expression also in retinal endothelial cells. However, its functional relevance in these cells is not well understood. Here, we examined relevance of receptor expression to endothelial cell dependent (inner)-blood retinal barrier integrity.

Methods: DasiRNA technology was used to modulate HCAR2/GPR109A expression in primary human retinal endothelial cells (HRECs). Scrambled control and Hcar2/Gpr109a-knockdown HRECs were grown on transwell filters for 4-6 weeks. qPCR was used to monitor HCAR2/GPR109A expression and electrical cell impedance sensing (ECIS) technology to evaluate barrier function. To investigate the relevance of HCAR2/GPR109A expression to barrier function in vivo, retinal inflammation was induced in wildtype and HCAR2/knockout mice using LPS (4 mg/kg). Single cell suspensions prepared from retinal homogenates obtained mice injected intraperitoneally LPS or PBS (control) +/- HCAR2/GPR109A agonist BHB were assessed by flow cytometry to monitor immune cell infiltration.

Results: Absence (KO) or reduction (siRNA) of HCAR2/GPR109A expression impaired barrier function (ECIS) significantly contributing to the increased infiltration of pro-inflammatory immune cells in retina as indicated by flow studies. BHB treatment preserved retinal barrier integrity and prevented increased immune cell infiltration in retina even in the presence of a pro-inflammatory stimulus (LPS), an effect that was receptor (HCAR2/GPR109A)-dependent.

Conclusions: Collectively, these data establish a role for HCAR2/GPR109A in regulating retinal endothelial cell barrier function in normal and inflammatory conditions. Thus, highlighting the therapeutic potential that targeting the receptor holds with respect to prevention and treatment of degenerative retinal diseases like diabetic retinopathy in which compromised barrier function is paramount.

CONTROL ID: 3714848

SUBMITTER (NAME ONLY): Nicholas Pfahler

TITLE: Response of Drusen Volume to Curcumin is Correlated with Risk Alleles for Age-Related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pfahler, I. Bielskus, P.A. Knepper, Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|N.J. Volpe, S. Aman, Z. Zaparackas, P.A. Knepper, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a multifactorial disease with known genetic associations. The ability to forecast morphological changes and treatment response based on genetic and clinical risk factors would be a valuable tool for clinicians. This study evaluated the association between the number of risk alleles for AMD and drusen volume change over two years in a group of AMD subjects taking curcumin.

Methods: Participants were recruited from the office of Zaparackas and Knepper, Ltd. in Chicago, IL after IRB approval and informed consent. All participants (n=17) had drusen ≥63 μm without geographic atrophy or choroidal neovascularization. Participants took oral curcumin (2.66 g/day) and were imaged using OCT for a period of two years. Drusen were categorized by width as 63-124 μm, 125-249 μm, and ≥250 μm. Genetic samples were analyzed by Arctic Medical Laboratories (Grand Rapids, MI). AMD risk alleles evaluated included C2, C3, CFB, CFH (rs412852, rs3766405, rs1048663), CFI, ABCA1, APOE, ARMS2, CETP, COL8A1, LIPC, and TIMP3. Drusen volume was measured in mm^3. Pearson's correlations were used to assess the associations between number of AMD risk alleles and change in drusen volume during the study.

Results: A lower number of overall risk alleles (r=0.65, p=0.009) and of complement system risk alleles (r=0.68, p=0.005) was correlated with a larger decrease in drusen volume after two years. Individually, a lower number of ARMS2 (r=0.55, p=0.04) and CFH rs3766405 (r=0.61, p=0.02) risk alleles was correlated with a larger decrease in volume. A high-risk genetic profile composed of the number of risk alleles for ARMS2, CFH rs412852, CFH rs3766405, C3, and CFI significantly predicted smaller changes in volume over time (r=0.75, p=0.001). The number of risk alleles overall, in complement system genes, and in ARMS2 and CFH were correlated with volume change in drusen 125-249 μm and ≥250 μm but not in drusen 63-124 μm.

Conclusions: The response of drusen to curcumin supplementation is associated with the genetic profile of the patient. A higher number of certain risk alleles is associated with a worse response to curcumin. This explains the variable responses of AMD patients to supplementation with other antioxidants such as AREDS.

CONTROL ID: 3714851

SUBMITTER (NAME ONLY): Sidra Zafar

TITLE: Sex and racial/ethnic diversity among ophthalmology fellowship applicants.

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zafar, M. Ali, F. Woreta, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M. Menard, Meharry Medical College, Nashville, Tennessee, UNITED STATES|B.K. Williams, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: There remains a dearth of literature on sex and racial/ethnic diversity trends among ophthalmology fellowship applicants. Our study purpose was to investigate the proportion of female and under-represented minorities (URMs) among ophthalmology fellowship match applicants.

Methods: De-identifed San Francisco (SF) matching data for ophthalmology fellowship applicants in the U.S. for 2019 and 2010 was analyzed.

Results: Between 2019 and 2020, there were a total 698 ophthalmology fellowship applicants. Of these, 283 (40.5%) were males, 200 (28.7%) females and 215 (30.8%) did not disclose their gender. In terms of race/ethnicity, only 51 (7.7%) identified as URMs, and 213 (32.1%) did not disclose their race. There were significant differences in the mean number of distributions and mean number of interviews completed between URMs and non-URMs (<0.001). The proportion of matched male and female applicants among cornea, glaucoma, retina, and pediatric ophthalmology was: 34.9% vs 30.1%, 43.7% vs 29.1%, 47.2% vs 19.9% and 32.5% and 47%. Among males, the most popular subspecialties were: retina (41%), glaucoma (24.4%), cornea (20.5%) and pediatric ophthalmology (9.5%). Among females, the most popular subspecialities were: cornea (25%), retina (24.5%), glaucoma (23%) and pediatric ophthalmology (19.5%). There was no association between sex and race/ethnicity and match outcomes.

Conclusions: The percentage of URMs applying for fellowship in ophthalmology remains low, and the number of interviews they receive is significantly less than non-URMs. The percentage of females in all subspecialities of ophthalmology except pediatrics remains low. More efforts are needed to collect data on gender and race/ethnicity and improve representation in ophthalmology.

CONTROL ID: 3714853

SUBMITTER (NAME ONLY): Matthew Tran

TITLE: Increased ciliary length of oligodendrocytes in anterior optic nerve with ageing

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tran, K. Ning, T. Kowal, R. Majumder, Q. WANG, Y. Hu, Y.J. Liao, Y. Sun, Spencer Center for Vision Research, Byers Eye Institute, School of Medicine, Stanford University, California, UNITED STATES|T. Kowal, R. Majumder, Y. Sun, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Little is known regarding the role of primary cilia, in aged oligodendrocytes (OLGs), which tend to be dysfunctional in neurodegenerative diseases. To investigate if primary cilia in aged OLGs might be involved in the age-related degeneration of vision, we examined the length and frequency of OLG primary cilia in the optic nerves of young and aged C57BL/6 wild-type mice.

Methods: Cryosections of the optic nerve and optic chiasm were prepared from the eyes of 8 young and aged C57BL/6 mice (3 and 20 months). Samples were immunostained with anti-Arl13b, anti-Oligo2, and anti-MBP to visualize primary cilia and OLGs, and imaged by confocal microscopy. Images of the anterior and posterior optic nerve and optic chiasm were examined, and statistical analysis was performed using the One-way ANOVA and Student's t-test.

Results: The ciliation of Oligo2-positive OLGs in the anterior optic nerve was 8.6 ± 5.9% and 7.7 ± 4.1% in young and aged mice, respectively. The ciliation of Oligo2-positive OLGs in the optic chiasm was 5.4 ± 4.5% and 5.6 ± 3.8% in young and aged mice, respectively. There were no significant changes in ciliation between the young and aged groups. In 3-month-old mice, the mean ciliary length of Oligo-2-positive OLGs was similar in the anterior and posterior optic nerve (1.12 ± 0.80 um and 1.25 ± 1.06 um, respectively). In 20-month-old mice, the mean ciliary length was significantly greater in the anterior optic nerve than in the posterior optic nerve (1.73 ± 1.26 μm and 1.00 ± 0.38 μm, $P<0.05$, respectively).

Conclusions: We reported a novel regional difference in OLG primary cilia length in the optic nerves of aged mice, suggesting that primary cilia may play a role in OLGs and myelination disorders.

CONTROL ID: 3714855

SUBMITTER (NAME ONLY): Sarah Coomson

TITLE: The role of the RNA-binding protein Elavl1 in lens development

SESSION TITLE: Lens Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Coomson, S. Aryal, S.A. Lachke, Department of Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|S.A. Lachke, Center for Bioinformatics and Computational Biology, University of Delaware, Newark, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Analogous to DNA-binding proteins called transcription factors (TFs) that bind DNA and mediate transcriptional control, RNA-binding proteins (RBPs) bind RNA and control its post-transcriptional fate, such as splicing, transport, localization, stability and translation into protein. While there are more genes in the human genome that encode RBPs compared to DNA-binding proteins, the former class of proteins are grossly less studied compared to the latter, especially in the context of eye development. To address this knowledge-gap, efforts over the past decade have identified several RBPs (e.g. Caprin2, Celf1, Rbm24, Tdrd7, among others) that are required for proper lens development and whose deficiency causes lens defects and/or cataracts (Lachke (2022) PMID: 34906599). To further advance the role of RBPs in the lens, we used iSyTE to identify Elavl1 (ELAV (embryonic lethal, abnormal vision)-like 1; also called HuR (Hu antigen R) as a high-priority candidate and analyzed its relevance to lens development.

Methods: Elavl1 expression in mouse lens was analyzed by RT-PCR, Western Blotting and immunofluorescence staining (IF). Elavl1 lens-specific conditional knockout ($Elavl1^{cKO}$) mice were generated by crossing mice containing Elavl1 floxed alleles and the Pax6GFPCre mouse line. RNA-IP (RIP) using Elavl1 antibody was performed on wild-type post-natal day (P) 15 mouse lens lysates Elavl1.

Results: Using the systems-based tool for eye gene discovery, iSyTE, we predicted Elavl1 to be robustly expressed in the lens. RT-PCR, WB and IF independently validated Elavl1 expression in embryonic and postnatal lens. Further, Elavl1 protein was detected in both anterior epithelium of the lens and fiber cells. $Elavl1^{cKO}$ mice exhibit microphthalmia and/or lens defects and cataract that progress with age. Initial studies suggest that several lens markers are misexpressed in the $Elavl1^{cKO}$ lens. Further, RIP assays demonstrate that Elavl1 protein binds Pax6 and Prox1 mRNA in lens cells. These findings suggest that Elavl1 may be involved in post-transcriptionally controling these TFs in the lens.

Conclusions: These data demonstrate that Elavl1 is robustly expressed on both RNA and protein levels in lens development. Elavl1 binds to mRNAs encoding key TFs in the lens and its knockout in mice results in eye and lens defects. Together, these findings indicate that Elavl1 plays an important role the development and maintenance of the lens.

CONTROL ID: 3714856

SUBMITTER (NAME ONLY): Tejabhiram Yadavalli

TITLE: Safety, efficacy and delivery of multiple nucleoside analogs via drug encapsulated carbon (DECON) based sustained drug release platform.

SESSION TITLE: Antimicrobial and Immunomodulator Therapeutics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Yadavalli, J. Ames, D. Wu, N. Bellamkonda, D. Shukla, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|J. Ames, D. Shukla, Microbiology and Immunology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|B. Ramirez, Nuclear Magnetic Resonance Core, Research Resources Center, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Herpes simplex virus type-1 (HSV-1) is the leading cause of infectious blindness in the developed world. The current established method of treatment via nucleoside analog acyclovir (ACV) shows significant and effective viral suppression. Trifluridine needs to be administered up to 9 times daily to ensure effective ocular retention of the drug. We have previously uncovered use of drug-encapsulated carbon (DECON) as a sustained drug delivery platform. We have also yet to elucidate the drug loading and release profile and deduce the toxicity of the platform when translated to a living model.

Methods: Activated carbon was pre-weighed and UV sterilized overnight prior to making a 10 mg/mL sterile stock solution in PBS. ACV, PCV, GCV and FCV stock solutions were prepared in DMSO. Drug loading studies were performed in triplicate to assess the deviation between replicates. These samples were analyzed using Mass spectrometry, NMR. ACV loaded carbons were dropped on murine eyes for a period of 4 weeks, once everyday. Murine eyes treated with ACV, carbon, ACV loaded carbon or mock samples were evaluated every week for any signs of toxicity.

Results: In this study, we have evaluated the ability of activated carbon particles to load and sustainably release ACV and 3 other nucleoside analogues using MS. The carbon particles loaded with the drug, termed as DECON were also able to show excellent antiviral activity even when dosed therapeutically at 0.025 mg/mL. Furthermore, we showed that sustained administration of 0.1 mg/mL DECON particles to the eyes and vaginal tissue is very well tolerated and does not cause any unforeseen toxicity. In this regard, we conclude that DECON is a safe, efficacious and cost effective addition to the list of agents for topical delivery of antiviral agents to the ocular tissue.

Conclusions: Carbon-based technologies show promise in the area of targeted drug release in response to certain stimuli. Further research into the ability of DECON's ability to permeate beyond the cornea for release into other ocular tissues may reveal it’s ability to treat pathogens that travel beyond the routes taken by HSV-1 infection.

CONTROL ID: 3714858

SUBMITTER (NAME ONLY): Min Gao

TITLE: Identification and characterization of microaneurysm in OCT and OCT angiography

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gao, T. Hormel, Y. Guo, S.T. Bailey, C.J. Flaxel, D. Huang, T.S. Hwang, Y. Jia, Casey eye institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify microaneurysms (MA) in optical coherence tomography (OCT) and OCT angiography (OCTA) and explore the relationship between MAs and retinal fluid.

Methods: We obtained four 3×3-mm OCT and OCTA scans with a 400×400 sampling density on one eye of each participant with diabetic retinopathy with a commercial 120-kHz spectral-domain OCT system (Solix; Optovue, Inc.). A projection-resolved algorithm suppressed projection artifacts. A subset of participants also underwent multimodal imaging with color fundus photography and fluorescein angiography, used to identify features of MAs in OCT B-scans and OCT/OCTA en face images. MAs were manually segmented in the OCT and OCTA en face images. We classified MAs as active vs. inactive based on the presence of flow signal within the MA. We compared the amount of fluid in the 0.4mm-diameter circular area including the whole thickness of the retina surrounding the active vs. inactive MAs. A deep learning-based method automatically quantified the fluid volume.

Results: Based on features identified on five eyes that underwent multimodal imaging, [Fig .1], we identified 173 MAs in 35 eyes. MAs were very bright round or irregular spots on OCT en face images [Fig .2 (A)]. Located mainly between the inner nuclear layer and outer plexiform layer, MAs show a strongly reflective wall in OCT B-scans [Fig .2 (C)]. MAs in OCT en face images (2.94±3.20 mm^2) appear larger than in OCTA (1.33±1.15 mm^2, Mann-Whitney U test, $P<0.001$) [Fig .2 (D)]. Seventy-five of 173 had a strong flow signal in OCTA [Fig .2 (B)] and were classified as active. Active MAs had a significantly higher probability of having retinal fluid nearby compared to inactive MA (57/75, 76.00% vs. 59/98, 60.20%, Z test, $P=0.013$). The mean fluid volume near the active MAs (3.63±4.94 mm^3) compared to the inactive MAs (1.09 ±2.46 mm^3) was significantly larger (Mann-Whitney U test, $P<0.001$).

Conclusions: MAs have distinct features on OCT and OCTA images that correlate with observations on multimodal imaging. MAs with flow signals on OCTA are more likely to have associated retinal fluid than those without, suggesting OCTA may identify MAs associated with more leakage.

CONTROL ID: 3714859

SUBMITTER (NAME ONLY): Chu Wang Yee

TITLE: The protective effect of Nicotinamide Riboside on corneal epithelial-stromal injury

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wang Yee, Y. Chan, K.C. Shih, Y. Bu, H. Mak, J. Yung, Ophthalmology Department, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Corneal epithelial-stromal injuries caused by abrasions or surgical complications deteriorate visual acuity and impede quality of life. Yet, current topical treatments, including Mitomycin-C and corticosteroids, have questionable clinical efficacy and severe side-effects. Nicotinamide Riboside (NR), a precursor to Nicotinamide adenine dinucleotide (NAD+), has been shown to promote wound healing in diabetic mice. We therefore hypothesize that NR serves as a promising novel therapeutic agent to accelerate corneal wound healing by utilizing an experimental pre-treatment mice model of alkali-induced corneal injury.

Methods: C57Bl/6J wild-type female mice 8 weeks of age were topically pre-treated with 500 μM NR on right eye for 7 consecutive days before corneal injury in the experimental group, while phosphate-buffered saline was used for control group. Then, alkali injury was induced on right cornea with NaOH-soaked filter paper with mice under anesthesia, followed by rinsing with filtered water. The left eye was uninjured. Fluorescein staining was used to visualize corneal epithelial-stromal damage with slit-lamp microscopy every 48 hours until Day 6. Stained area was measured with ImageJ and percentage of area healed was calculated. Immunohistochemistry (IHC) of pro-inflammatory and fibrotic markers was also conducted on Day 6.

Results: Based on current data, fluorescein staining showed diffuse epithelial damage after alkali injury in all mice. On Day 2, NR pre-treated corneal epithelium healed by 68.2% (n=3), compared to only 21.7% in control group (n=2). However, opacification was not observed and all corneas achieved full re-epithelialization on Day 4. IHC investigation on Day 6 revealed absence of pro-inflammatory and fibrotic markers Interleukin 1 beta and alpha-smooth muscle actin respectively in both groups.

Conclusions: We have demonstrated NR pre-treatment’s efficacy in accelerating corneal wound healing after alkali injury in the short term, but no difference was found in the long term compared to control. This finding accentuates the potential clinical application of NR pre-treatment in protection against corneal damage. Further investigations with larger sample size are needed to establish a more comprehensive correlation. NR post-treatment after injury is another focus for future investigations.

CONTROL ID: 3714863

SUBMITTER (NAME ONLY): Kevin Keppel

TITLE: Effect of Fluocinolone Acetonide Intravitreal Implant on Corneal Astigmatism

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Keppel, K. Baynes, S.K. Srivastava, J. Goshe, C. See, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The fluocinolone acetonide intravitreal implant has important benefits over systemic corticosteroids and immunosuppression for the treatment of non-infectious uveitis. Its benefits and risks have been well-documented, but recent clinical encounters have potentially revealed a new adverse effect of the implant: surgically induced corneal astigmatism. The purpose of this research is to identify and quantify the degree of corneal astigmatism induced by fluocinolone acetonide intravitreal implantation.

Methods: This was a small retrospective cohort study of 7 patients (8 eyes) that underwent surgical implantation of the fluocinolone acetonide device in the last 10 years. Pre- and post-operative corneal astigmatism values were compared using corneal topographic or keratometric studies that were obtained as part of routine care. For mathematical and statistical comparison, astigmatic magnitudes and axes were converted into power vectors representing both with-the-rule/against-the-rule (WTR/ATR) and oblique components (J_0 and J_{45}, respectively). A third power vector, J_{FA}, calculated the component of corneal steepening in the axis of the implant, assuming standard inferotemporal placement (225°/45° in the right eye and 315°/135° in the left eye).

Results: The mean pre-operative right eye corneal astigmatism was 0.81 D at 51°, while the mean post-operative astigmatism was 1.3 D at 45°. The mean pre-operative left eye corneal astigmatism was 2.9 D at 96°, while the mean post-operative astigmatism was 4.6 D at 103°. J_{FA}, the component of corneal steepening in the axis of the implant, increased perioperatively by an average magnitude across all eyes of 0.60 (P = 0.21). Secondary analysis revealed a non-statistically significant decrease in corneal power (0.8 D, P = 0.06) and increase in astigmatic magnitude (1.7 D, P = 0.08). Of note, there were two outliers in the group that had perioperative cylinder changes of 6.3 D and 4.0 D.

Conclusions: While this study was limited statistically by small sample size, the results still showed notable perioperative corneal changes. It remains to be seen if the eyes with more drastic changes were simply outliers, or if expansion of the sample size will eventually reveal real, statistically significant effects of the surgery on corneal astigmatism. The conclusion of this research may ultimately describe a previously uncharacterized adverse effect of the fluocinolone acetonide implant.

CONTROL ID: 3714864

SUBMITTER (NAME ONLY): Jesus Guerrero

TITLE: Herpetic keratitis following penetrating keratoplasty: clinical and microbiological features

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Guerrero, D. Jimenez-Collado, D. Chavez Velazquez, N. Macriz-Romero, F. Anaya Barragán, C.A. Muller Morales, A. Navas, A. Ramirez-Miranda, E.O. Graue-Hernandez, Cornea, External Diseases and Refractive Surgery, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: The present study aims to describe clinical outcomes after infectious keratitis following penetrating keratoplasty (PKP)

Methods: Retrospective consecutive clinical case series study carried out from 2001 to 2018. Clinical records were reviewed in which subjects with herpetic keratitis with previous PKP were identified. Diagnosis was done following clinical characteristics. Analyzed variables were previous ocular surgeries and medications and ocular surface disease were recorded. Treatment characteristics, indications for surgery and clinical outcomes were also noted. Descriptive statistics, means, and SD were used for continuous variables; percentages were used to describe categorical variables. P, 0.05 was regarded as evidence of significance. All analyses were done with STATA v.10 software.

Results: A total of 22 cases were recorded. Mean age was 43.04 years, 14 patients (63.63%) were male. Mean time of herpetic keratitis after PKP was 35.59 months (2.96 years). Of the 22 cases 19 (86.36%) had just one PKP, 3 patients (13.63%) had 2 or more PKP's. 15 patients (68.18%) had history of herpetic keratitis before the PKP. The main indication for PKP among patients with history of herpetic keratitis were: stromal keratitis in 14 patients (93.33%) and just one case of endothelial keratitis (6.66%). Of the 15 patients who presented herpetic keratitis previous to the PKP only 3 (20%) were on antiviral suppression therapy. Of the 22 patients who presented herpetic keratitis, 17 (77.27%) presented epithelial form and 5 patients (22.72%) presented herpetic keratouveitis .Of the 22 patients, 13 (59.09%) had clear grafts, the remaining 9 grafts were already in failure (40%). 8 (61.53%) remained clear after the event, 5 (38.46%) resulted in marked inflammation, leading to graft failure. Before the infectious event 18 patients (81%) were active steroid users, 4 patients (17.39%) were on prostaglandin analogues and at the time of the event all the patients were treated with: acyclovir 800mg 5 times daily and lubricant drops.

Conclusions: Herpetic infectious keratitis following PKP is an important cause of graft failure. Patients with PKP require close monitoring to identify risk factors for developing infectious keratitis and posterior graft failure. Patients whose transplant was for a herpetic cause, require close monitoring and prompt identification of any visual or graft changes to start appropriate treatment.

CONTROL ID: 3714865

SUBMITTER (NAME ONLY): Adrian Tsang

TITLE: Evaluating the Qualitative Features of Occular Surface Dry Eye Disease using a Novel Confocal Microscopy Imaging Protocol

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Tsang, J. Nortey, S.E. Lopez, J.A. Gonzales, J.D. Keenan, Francis. I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure: Adrian Tsang: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Nortey: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Lopez: Commercial Relationship: Code N (No Commercial Relationship) | John Gonzales: Commercial Relationship: Code N (No Commercial Relationship) | Jeremy Keenan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To examine differences of the corneal sub-basal nerve plexus between participants from the Sjogren's International Collaborative Clinical Alliance (SICCA) and healthy controls based on qualitative features of nerve tortuosity, and the presence of nerve sprouts and dendritic cells.

Methods: Cross-sectional study in which participants from SICCA were recalled for follow-up and age-matched healthy controls were recruited. All participants had in vivo confocal microscopy (Heidelberg Rostock, Heidelberg, Germany) of the central sub-basal nerve plexus centered about the central vortex, yielding a montage image comprised of 30 images. Each image was then assessed by 3 masked graders for 3 features: presence of nerve tortuosity, presence of neuromas, and number of dendritic cells.The majority consensus grade between the 3 graders was calculated for each image, and then the fraction of images per eye with the finding was calculated as a score indicating the proportion of images per eye displaying the given feature.

Results: A total of 774 confocal images from 26 eyes (15 from SICCA participants and 11 control eyes) were reviewed by the 3 graders, with each eye contributing between 25-30 scans. The mean tortuosity score was 40 (SD 27) in the SICCA participant group and 2 (SD 2) in the control group ($P<0.001$, Wilcoxon rank sum test); the mean nerve sprout score was 18 (SD 15) in the SICCA participant group and 2 (SD 2) in the control group ($P=0.04$); and the mean dendritic cell score was 44 (SD 29) in the SICCA participant group and 32 (SD 27) in the control group ($P=0.30$).

Conclusions: The presence of tortuosity and nerve sprouts on in vivo corneal confocal microscopy were significantly different between SICCA participants and healthy controls. There was no significant difference in the amount of dendritic cells between SICCA participants and healthy controls. Our novel imaging protocol can be used to standardize the qualitative evaluation of the corneal sub-basal nerve plexus and the presence of tortuosity and nerve sprouts may be used to differentiate between patients with and without Sjogren's dry eye. Standardized evaluation of the corneal sub-basal nerve plexus may have future applications in the diagnostic criteria for Sjogren's disease and help bring clarity in both the research realm and in the direct care of these patients.

CONTROL ID: 3714867

SUBMITTER (NAME ONLY): Pranati Ahuja

TITLE: Impact of Fear of Falling in Adults with Low Vision During the Task of Gait Initiation

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Ahuja, P. Gupta, G. Brusola, T. Chao, R. Welsh, M.E. Schmitz-Brown, M. Ko, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Pranati Ahuja: Commercial Relationship: Code N (No Commercial Relationship) | Praveena Gupta: Commercial Relationship: Code N (No Commercial Relationship) | Gregory Brusola: Commercial Relationship: Code N (No Commercial Relationship) | Tony Chao: Commercial Relationship: Code N (No Commercial Relationship) | Rodney Welsh: Commercial Relationship: Code N (No Commercial Relationship) | Mary Schmitz-Brown: Commercial Relationship: Code N (No Commercial Relationship) | Mansoo Ko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: 1. Quantify severity of fear of falling (FOF) by comparing temporal characteristics of postural control during the task of Gait Initiation (GI) in healthy adults under the conditions of normal vision, low vision sight simulator (SS), and virtual reality (VR) environment.

2. Assess association of low vision (LV) with changes in postural control during GI.

Methods: 8 adults with LV (mean age 63.3 ± 11.2 y), and 8 age-gender matched healthy adults (mean age 68.1 ± 9.72 yrs) were recruited. All participants performed the task of GI barefoot under normal conditions with 5 trials on a Tekscan™ High Resolution Floor Mat System. Healthy participants performed trials under 2 more conditions: GI with SS, and GI with VR headset (HTC VIVE Cosmos Elite 3D VR system and the Richie's Plank VR experience were used to induce FOF). Absolute temporal events of foot position were obtained from the vertical ground reaction forces corresponding to the swing and stance limbs during GI. To normalize temporal parameters of GI, time from onset of movement to stance limb toe-off was defined as 100% of the GI cycle. The temporal events measured were: 1) time from onset of movement to swing limb toe-off (Anticipatory Postural Adjustment: APA) and 2) time from swing limb heel strike to stance limb toe-off (Double Support Time: DST).

Results: Table 1 and Graph 1 (image) show absolute and normalized temporal data means. Normalized APA during GI with VR headset (47.36% ± 6.50) was similar to GI with SS (46.08% ± 3.11) and normal GI conditions (44.52% ± 4.74) in healthy patients. Normalized APA during GI in LV patients (55.04% ± 5.69) exceeded that for all 3 conditions in healthy patients. Normalized DST during GI with VR headset (32.39% ± 11.74) had much longer duration than GI with SS (23.35% ± 8.93) and normal GI conditions (20.60% ± 2.96) in healthy patients. Normalized DST during GI for LV patients (17.95% ± 3.78) was shorter than that for all 3 conditions in healthy patients.

Conclusions: Both APA and DST for securing the weight shift necessary to execute the first step from a static standing position can be used as objective biomarkers to quantify the severity of FOF. APA values demonstrate that low vision has a similar impact on postural control as VR use in healthy adults, and prolonged DST is observed in healthy adults with induced new-onset FOF during GI.

CONTROL ID: 3714869

SUBMITTER (NAME ONLY): Xi Dai

TITLE: Topical Recombinant Human Nerve Growth Factor for Management of Refractory Epithelial Keratopathy

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Dai, X. Zhu, S. Karakus, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure: Xi Dai: Commercial Relationship: Code N (No Commercial Relationship) | Xi Zhu: Commercial Relationship: Code N (No Commercial Relationship) | Sezen Karakus: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the effect of topical application of recombinant human nerve growth factor (rhNGF) eye drops in the management of refractory epithelial keratopathy.

Methods: A retrospective chart review was conducted on patients treated with topical rhNGF for a diagnosis of refractory epithelial keratopathy due to neurotrophic keratitis (NK). Patients with epithelial defects or ulcers due to stage II and stage III NK were not included. Data regarding demographics and ocular/systemic past medical history was extracted from patient charts. Visual acuity, corneal, and conjunctival staining scores were recorded at baseline and subsequent follow-up visits along with side effects from treatment as reported by patients. The primary outcome measure was the change from baseline in corneal staining score upon completion of treatment with treatment success defined as complete resolution of corneal staining or near-complete resolution (corneal staining score ≤1).

Results: We included 26 eyes of 14 patients with refractory epitheliopathy due to stage I NK treated with topical rhNGF. After an 8-week course of treatment, the median corneal staining score in the worse eye decreased from 4 to 1 (p=0.001). All patients showed at least one-grade improvement in corneal staining with complete or near-complete resolution in at least one eye of 13 patients, sustained in 6 patients at three months. A better response was observed in eyes with post-radiation NK, LASIK-induced NK, Sjogren's syndrome, and well-controlled diabetes mellitus. Those with chronic use of other topical treatments (such as anti-glaucoma medications with preservatives) and uncontrolled diabetes mellitus demonstrated incomplete responses. Ten patients (71%) reported mild to moderate ocular discomfort from drop application that all resolved after completion of treatment.

Conclusions: Topical rhNGF application for 8 weeks was effective and tolerable in treating refractory epithelial keratopathy due to stage I NK in our small cohort, although the effect was sustained only in patients with certain underlying etiologies at three months. Further studies are needed to determine the optimum treatment dose and duration based on underlying etiology.

CONTROL ID: 3714870

SUBMITTER (NAME ONLY): parastou pakravan

TITLE: Adverse Events Following Intravitreal Brolucizumab for Exudative Age-Related Macular Degeneration

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. pakravan, A. Shaheen, V. Chau, J. Lai, V. Patel, N. Yannuzzi, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Following its approval by the Food and Drug Administration (FDA) for the treatment of exudative age-related macular degeneration (AMD), brolucizumab has been associated with post-injection intraocular inflammation (IOI) and retinal vasculitis in select cases. We aimed to evaluate clinical outcomes and adverse events (AE) following intravitreal brolucizumab administration at a university-based practice.

Methods: The clinical records of all eyes that received intravitreal brolucizumab at Bascom Palmer Eye Institute between December 1, 2019, and April 1, 2021, were reviewed.

Results: 345 eyes of 278 patients received 801 brolucizumab injections, resulting in 20 eyes of 17 patients who developed an AE. The mean visual acuity (VA) of the entire cohort before brolucizumab injection was 20/51. In patients who developed an AE, baseline VA was 20/43, while VA at initial presentation of the AE was 20/76, representing a loss of approximately 3 lines. Of eyes experiencing an AE, the mean number of injections was 2.3, and the interval between the last brolucizumab injection and presentation with the AE was 24.2 days. The most common presenting symptoms in eyes experiencing an AE were blurry vision (60%) and floaters (50%). Intraocular inflammation was the most common AE (75% of all AEs). Of those eyes with inflammation, 29% had iritis, 50% had vitritis, and 21% had both. No eyes were noted to develop retinitis or choroiditis. Ten percent of eyes with IOI also developed epiretinal membrane. Additionally, there were cases of conjunctivitis (5%), venous occlusion (5%), optic neuropathy (5%), and RPE tear (5%). There was no case of retinal vasculitis. In eyes with IOI, treatment included topical steroids (45%), topical and oral steroids (25%), and observation (30%). Of eyes experiencing IOI, the mean VA at last follow-up was 20/59, representing a loss of 1.5 lines. All eyes with IOI had resolution of inflammation by last follow-up examination.

Conclusions: An adverse event was observed in 5.8% of eyes treated with brolucizumab in this university-based practice. The average symptom onset was 24 days after the last injection. Most symptoms resolved after treatment but mean VA in this cohort decreased on average approximately 1.5 Snellen lines from baseline.

CONTROL ID: 3714872

SUBMITTER (NAME ONLY): Jimena Carreno-Galeano

TITLE: Therapeutic effect of topical autologous serum on ocular graft-versus-host disease associated dry eyes

SESSION TITLE: Dry Eye, Clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.T. Carreno-Galeano, L. Johns, J. Yin, R. Dana, Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) is the most common manifestation of ocular graft-versus-host disease (oGVHD) associated with significant morbidity and reduced quality of life. Persons with oGVHD have been shown to have abnormal corneal sub-basal nerves, which may play a role in the development of the disease. Autologous serum drops (ASD) are used to treat severe refractory DED due to oGVHD; however, no studies to date have investigated the effect of ASD in corneal nerves in patients with oGVHD. In this prospective observational study, we evaluate the changes in symptoms, signs and corneal sub-basal nerve density in patients with oGVHD after the use of ASD.

Methods: We studied patients with moderate-to-severe DED due to oGVHD who had failed to respond to previous treatment including lubrication, anti-inflammatory medications, and punctal occlusion. A comprehensive evaluation was done at 6 and 12 weeks after initiating ASD, including: VFQ-25, SANDE I & II, OSDI, TBUT, Corneal staining, Conjunctival staining, Schirmer Test, IVCM, and Corneal sensation. Exclusion criteria included active ocular allergies, any change in anti-inflammatory or anti-glaucoma regimen, history of contact lens wear or prosthetic replacement of the ocular surface ecosystem (PROSE), and intraocular surgery or ocular laser surgery in the three months prior to enrollment. Repeated measures analysis of variance (ANOVA) were done to test for the significance of changes. Data are reported as mean ± SD.

Results: Twenty patients with moderate-to-severe oGVHD associated DED who initiated ASD were studied. The average age was 63.4 ± 11.2 years. Twelve were female (60%) and eight (40%) male. SANDE I score was lower at 6 weeks (38.4 ± 7.6) and 12 weeks (37.8 ± 8.2) compare to baseline (67 ± 5.3, p=0.001). There were no other significant differences in dry eye symptoms or signs. The corneal sensitivity increased at 6 week (5 ± 1.3) and 12 week (5.3 ± 0.9) follow-up, compared to baseline (3.8 ± 2.1, p= 0.01). There was also a significant difference in SNFL at 6 weeks (11,264.2 ± 5768.5) and 12 weeks (12,028.1± 5,245.8) compare to baseline (10,117.5 ± 5,927.1 mm/mm^2 , p=0.007).

Conclusions: Patients with severe refractory DED due to oGVHD treated with ASD had an increase of corneal sub-basal nerve density after 6 and 12 weeks of treatment as well as improvement of corneal sensitivity and lower frequency and severity of symptoms of DED.

CONTROL ID: 3714873

SUBMITTER (NAME ONLY): Karen Chen

TITLE: Integration of Artificial Intelligence into a Telemedicine-Based Diabetic Retinopathy Screening Program

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chen, E.R. Dow, N.C. Khan, C. Perera, D.V. Do, V.B. Mahajan, P. Mruthyunjaya, K. Mishra, T. Leng, D. Myung, Stanford Medicine, Stanford, California, UNITED STATES|M. Levine, A. Phadke, J. Dang, K. Weng, Stanford Health Care, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Annual diabetic retinopathy (DR) screenings are critical for preventing blindness in patients with diabetes. Our goal was to successfully integrate artificial intelligence-based image interpretation software into a telemedicine-based diabetic retinopathy screening program at primary care clinics.

Methods: The Byers Eye Institute at Stanford (BEIS) partnered with University HealthCare Alliance (UHA) to integrate IDx-DR, an FDA-cleared AI diagnostic system that autonomously detects diabetic retinopathy (DR) in fundus images, into a pre-existing teleophthalmology workflow. Patients without a prior DR diagnosis or a DR exam in the past year were offered the opportunity to have retinal photographs taken at the end of their primary care visit. The AI-human hybrid workflow involves interpretation by the IDx system. Images deemed ungradable by the AI software were then sent for interpretation by a retina specialist at the BEIS reading center. Patients were referred for in-person exam if either the AI or the human reader detected more than mild DR (mtmDR) in the images.

Results: From April 2021 to December 2021, a total of 550 patients with diabetes at four primary care sites opted for DR screening using the AI-human hybrid workflow. Of these, 72 patients screened positive for mild or worse DR (13%) and 425 patients screened negative (77%). Average gradeability ranged by site from between 80% and 90%.

At each site, the percentage of the diabetic patient population up-to-date with recommended eye exams was measured in accordance with the HEDIS measure specification for Comprehensive Diabetes Care (CDC). A target of 67.89% was chosen, reflecting the 90th percentile HEDIS national benchmark. The percentage of patients adherent with annual diabetic eye exams reached a peak of 71.1% across the four sites after integration of AI into the telemedicine workflow. These outcomes demonstrate that integration of the AI-human hybrid workflow resulted in increased patient adherence with annual diabetic eye exams.

Conclusions: An AI-human hybrid workflow for detecting referral-warranted DR was successfully implemented in the primary care setting and resulted in improved patient adherence and quality measures associated with annual diabetic eye exams.

CONTROL ID: 3714874

SUBMITTER (NAME ONLY): Bushra Usmani

TITLE: Epidemiology of Contact Lens-Related Corneal Disorders in Emergency Room: Data from Nationwide Emergency Department Sample (NEDS)

SESSION TITLE: Vision Impairment, Visual Function, and Quality of Life

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dayananda, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|B. Usmani, S.A. Shah, V. Jhanji, Ophthalmology, UPMC, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: Bushra Usmani: Commercial Relationship: Code N (No Commercial Relationship) | Sanjana Dayananda: Commercial Relationship: Code N (No Commercial Relationship) | Syed Mahmood Shah: Commercial Relationship: Code N (No Commercial Relationship) | Vishal Jhanji: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the epidemiology of visits to the emergency room with contact lens-related corneal disorders at a national level and to identify high-risk groups.

Methods: This is a retrospective longitudinal cohort study. National Emergency Department (ED) Sample, a representative sample of all US EDs, was used to determine the incidence and characteristics of corneal disorders in contact lens users presenting to the ED from 2006 to 2017. ICD-9-CM and ICD-10-CM codes for corneal disorder due to contact lens use (371.82 and H1882) were used to identify patients. Incidence was calculated using US National Census Data. Descriptive statistics were calculated, and multivariate regression was used to estimate the changes in incidence and to compare the demographics between patients with and without contact lens-related corneal disorders.

Results: A total of 149,716 ED visits were recorded with a diagnosis of corneal disorder due to contact lens use. The incidence of ED visits with contact lens-related corneal disorder declined steadily from 2010 (6.10 per 100,000 US population) to 2016 (3.51 per 100,000 US population) with most visits consisting of female patients (67%), adult age-groups (68.9%, p-value 0.05), and patients carrying private insurance (56.3%). The most common discharge diagnosis was eye discharge or redness (10.9%), followed by corneal ulcer (3.6%). Patients belonging to the highest income quartiles were more likely to present to the ED with contact-lens-related corneal disorders (adjusted Odds Ratio, 1.21, 95% CI 1.15-1.27) compared to the low-income quartile. Among those who were discharged from the ED, the average charge per patient was $1051.4 (Standard Deviation [SD]= 795.4).

Conclusions: Women, young adults, and patients with low socioeconomic status were found to have a higher incidence of contact lens-related corneal ED visits. Identification of high-risk groups is important for both optometrists and ophthalmologists when prescribing and referring for contact lenses, and devise additional strategies for prevention of further corneal complications and the associated vision loss.

CONTROL ID: 3714876

SUBMITTER (NAME ONLY): casey smith

TITLE: Referral patterns and visual sequelae in children with newly diagnosed primary brain tumors

SESSION TITLE: Pediatric ophthalmology and imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. smith, L.C. Mehner, Ophthalmology, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus in Aurora, Colorado., Denver, Colorado, UNITED STATES|

Commercial Relationships Disclosure: casey smith: Commercial Relationship: Code N (No Commercial Relationship) | Lauren Mehner: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is well established that tumors such as optic pathway gliomas and suprasellar tumors have high rates of associated visual impairment and are often symptomatic. The potential visual sequelae associated with tumors in other areas of the brain, however, have received little attention to date. The purpose of this study was to better understand current referral patterns among patients with newly diagnosed brain tumors and further categorize any associated visual impairment. This will serve as a baseline as we initiate a new ophthalmic screening protocol for these patients at our institution.

Methods: This was a retrospective cohort study of all children with primary brain tumors diagnosed at our tertiary care facility from January - December 2019. Charts were reviewed for oncologic data as well as ophthalmic data if an evaluation was performed in either the inpatient or outpatient setting. Patients who were initially diagnosed at our institution but received their oncologic care elsewhere were excluded.

Results: Seventy-one patients were diagnosed with a new primary brain tumor and received at least some portion of their oncologic care within the study period. The mean age at diagnosis was 9.24 years. The distribution of pathologic diagnosis is illustrated in Figure 1. An ophthalmology referral was sent for 45 of these patients (63%), and 41 of these were evaluated by an ophthalmologist [11 inpatient only (27%) vs 15 outpatient only (36%) vs inpatient + outpatient (36%)]. Thirty of the 41 patients had some form of visual impairment (73%), including optic nerve abnormalities (41%), decreased visual acuity to <20/40 (10%), abnormal eye movements (strabismus/nystagmus/motility disorders, 48%), decreased color vision (5%), visual field deficits (15%), abnormal pupils (12%), and eyelid/anterior segment abnormalities (17%). One patient underwent strabismus surgery during the study period. Only one patient was referred to low vision services.

Conclusions: The prevalence of visual impairment among patients with primary brain tumors is high, however, referral rates for ophthalmology evaluation remain low. We plan to address this gap in care by instituting a formal ophthalmology referral and screening protocol at our institution.

CONTROL ID: 3714877

SUBMITTER (NAME ONLY): Mohit Parekh

TITLE: Effect of ROCK inhibitor on cell migration in Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal Cell and Molecular Biology | Corneal Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Parekh, A. Miall, N. Deshpande, U.V. Jurkunas, Dept. of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Mohit Parekh: Commercial Relationship(s);Code F (Financial Support):Kowa Pharma Development Company | Annie Miall: Commercial Relationship(s);Code F (Financial Support):Kowa Pharma Development Company | Neha Deshpande: Commercial Relationship(s);Code F (Financial Support):Kowa Pharma Development Company | Ula Jurkunas: Commercial Relationship(s);Code F (Financial Support):Kowa Pharma Development Company

ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is a progressive loss of corneal endothelial cells (CECs) that are post-mitotically arrested with limited proliferative capacity. Therefore, wound healing is mainly achieved through cell enlargement and migration. Inhibition of Rho-kinase, a key regulator of cytoskeletal reorganization has been shown to promote cellular migration. The purpose of this study was therefore to investigate the effect of a novel Rho-associated coiled-coil-containing protein kinase (ROCK) inhibitor, ripasudil (K-115) in promoting CEC cell migration on Descemet's membrane in FECD ex vivo.

Methods: Normal and FECD Descemet's membrane-CEC tissues were obtained from cadaveric corneas or patients undergoing Descemet's membrane endothelial keratoplasty (DMEK) surgeries. The tissues were preserved in Optisol-GS and after washing in PBS were stained with Hoechst 33342 for 30 sec and attached to the plastic plates by air drying for 3 min with the endothelial cell side facing up. The tissues were treated with 1uM of K-115 drug and monitored using live cell imaging microscope (Leica DMi8) for 5 hours. Controls were treated with Chen's media without the drug. The images from three biological and three technical replicates were collected per group, and the velocity and displacement of the cells were analyzed using the TrackMate plugin in ImageJ. Mann-Whitney and one-way Anova tests were used for statistical analysis with $p<0.05$ being statistically significantly different.

Results: Mean velocity (pixels/hour±SD) of CECs without the drug was 0.45±0.11 in normal and 0.64±0.21 in FECD tissues; and increased to 0.65±0.20 ($p<0.05$) and 0.82±0.39 ($p<0.001$) with K-115, respectively. Mean displacement (pixels/hour±SD) of the cells from the normal and FECD tissues without the drug was 4.33±2.19 and 6.63±5.8, which increased to 13.49±10.32 ($p<0.001$) and 15.02±13.10 ($p<0.001$) respectively with K-115. Although the fold change in mean displacement between normal and FECD cells did not change significantly following the treatment with K-115, a significantly higher mean velocity ($p<0.01$) was observed in FECD compared to normal cells.

Conclusions: FECD cells migrate faster on the Descemet's membrane following the treatment with K-115 compared to the normal cells, which further provides a promising therapeutic approach for the treatment of FECD using ripasudil after Descemetorhexis without endothelial keratoplasty (DWEK).

CONTROL ID: 3714878

SUBMITTER (NAME ONLY): Linda Musil

TITLE: TGFβ overcomes FGF-induced transinhibition of EGFR in lens cells to facilitate fibrotic posterior capsule opacification

SESSION TITLE: Lens epithelial cell stress and function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Musil, CHEMICAL PHYSIOLOGY & BIOCHEMISTRY, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure: Linda Musil: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In order to cause vision-disrupting fibrotic PCO, lens epithelial cells that survive cataract surgery must migrate to the posterior of the lens capsule and differentiate into myofibroblasts. During this process, the cells become exposed to the FGF that diffuses out of the vitreous body. In vivo and in vitro studies have established that such relatively high levels of FGF induce lens epithelial cells to differentiate into lens fiber cells during normal development. It has been a mystery as to how epithelial cells could instead undergo a mutually exclusive cell fate, namely epithelial to myofibroblast transition (EMyT), in the FGF-rich environment of the posterior capsule.

Methods: Western blotting and immunofluorescent microscopy were used to assess the expression of markers of lens cell EMyT in serum-free primary cultures of embryonic chick lens epithelial cells (DCDMLs) grown in the absence or presence of TGFβ and/or FGF. The effect of growth factors on the activation state of ErbBs, AKT, and ERK was assessed using phospho-specific antibodies.

Results: We have previously shown that the ability of TGFβ to induce lens cell fibrosis requires the activity of endogenous ErbBs. We show here that lens fiber-promoting levels of FGF induce desensitization of the ErbB EGFR1 that involves its phosphorylation on T669 mediated by ERK activity. Transinhibition of EGFR1 by FGF is overcome by a time-dependent increase in expression of total and cell surface EGFR1 induced by TGFβ, the active levels of which are increased after cataract surgery.

Conclusions: Together, our studies show how a novel integration of TGFβ, FGF, and ErbB signaling pathways can direct EMyT of lens cells under physiologically relevant conditions. They also provide a rationale for why TGFβ upregulates EGFR1 in these cells, and further support the receptor as a therapeutic target for PCO.

CONTROL ID: 3714879

SUBMITTER (NAME ONLY): Achuth Nair

TITLE: Multimodal optical elastography assessment of a murine collagen XII knockout

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nair, Y. Ambekar, C. Zevallos-Delgado, M. Singh, F. Zvietcovich, T. Mekonnen, K. Larin, Department of Biomedical Engineering, University of Houston, Houston, Texas, UNITED STATES|S. Aglyamov, Department of Mechanical Engineering, University of Houston, Houston, Texas, UNITED STATES|M. Koch, University of Cologne Center for Molecular Medicine Cologne, Cologne, Nordrhein-Westfalen, GERMANY|E.M. Espana, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|K. Larin, Department of Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Measuring the biomechanical properties of the eye can be useful for understanding structure and assessing ocular health. In particular, the organization of the corneal stroma's extracellular matrix is essential for vision. The presence of Collagen XII in the corneal stroma affects the corneal structure and has been hypothesized to affect biomechanical properties. Here, we use a multimodal optical elastography approach to measure the effect of Collagen XII on the biomechanical properties of the cornea.

Methods: The measurements were performed within 24 hours of eye enucleation (after overnight shipment from Tampa to Houston in corneal preservation media). Age and gender-matched wild type (WT) and collagen XII insufficient corneas were dissected with scleral ring intact and mounted on a closed loop intraocular pressure (IOP) control system. Measurements were taken from 10 mmHg to 25 mmHg in 5 mmHg increments. Figure 1 shows the air coupled ultrasound elastography (ACUS-OCE), heartbeat OCE (Hb-OCE), and Brillouin microscopy systems used to assess the mechanical properties of five corneas of each group. The corresponding Brillouin frequency shift, Lamb wave speed, and compressive strain measured from each technique respectively characterize the mechanical properties of the tissue.

Results: Results of the optical elastography measurements are shown in Figure 2. All measurement techniques show a distinct decrease in stiffness due to collagen XII insufficiency. Furthermore, both OCE techniques show an expected increase in stiffness as a function of IOP; however, this trend was absent in the Brillouin measurements.

Conclusions: Optical elastography can be used to measure the stiffness of the cornea as a function of IOP. Furthermore, measurements suggest that the presence of Collagen XII increases the stiffness of the corneal stroma. Future work will be geared towards the quantification of tissue biomechanical properties, as well as the investigation of tissue anisotropy.

CONTROL ID: 3714880

SUBMITTER (NAME ONLY): Viha Vig

TITLE: Biomarkers for Alzheimer's Disease & Chronic Traumatic Encephalopathy in Postmortem Vitreous Humor Correlate with Pathological Diagnosis and Cortical Brain Tissue

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Vig, J. Xu, M.L. Subramanian, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|F. Tuz-Zahra, Y. Tripodis, W. Xia, T.D. Stein, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|G. Meng, T.D. Stein, VA Boston Health Care System Jamaica Plain Campus, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The eye provides a direct window to display neuro-retinal disease and the interconnections between the eye and brain may elucidate common features of both neurological and eye diseases. This exploratory, validation clinical study sought to examine vitreous levels of neurodegeneration biomarkers in postmortem eyes and brains of those with Alzheimer's Disease (AD), Chronic Traumatic Encephalopathy (CTE), other tauopathies, and healthy controls.

Methods: We examined 43 donated postmortem eyes and corresponding brains, with the diagnosis of AD, CTE, both AD + CTE, other tauopathies, and healthy controls by Meso Scale Discovery immunoassay to quantitatively measure amyloid-beta (Aβ), total and phosphorylated tau (tTau, pTau), neurofilament light chain (NfL), and eotaxin-1. Kruskall-Wallis Rank sum test and Wilcoxon rank tests were used to determine if vitreous biomarker levels were significantly associated with pathological diagnosis, ADNC, and CTE Staging. Spearman's rank correlation was used to compare biomarker levels in vitreous and cortical tissue.

Results: Vitreous levels of tTau ($p=1.6x10^{-}2$), pTau-181 ($p=6.4x10^{-3}$), and pTau-231 ($p=4.2x10^{-2}$) were significantly associated with pathological brain diagnoses. In pairwise comparisons, significance was found for tTau in AD+CTE (n=9) vs CTE (n=15) ($p=4.8x10^{-2}$) and AD+CTE vs AD (n=7) ($p=4.8x10^{-2}$). NfL ($p=1.7x10^{-2}$, n=33) in the vitreous was significantly associated with CTE Staging. When comparing vitreous levels to corresponding levels of the same biomarkers in cortical tissue, eotaxin-1 ($p=1.3x10^{-2}$, n=32, r=-0.45) and t-Tau ($p=1.0x10^{-4}$, n= 39, r=0.61) were significantly correlated.

Conclusions: Vitreous tTau, pTau-181, and pTau-231 in postmortem eyes significantly correlate with AD and CTE pathology in post-mortem brains, while vitreous NfL was correlated with CTE staging. Additionally, vitreous and cortical tissue levels of tTau and eotaxin-1 were significantly correlated. This study validates prior reports by our group and lends further credence that the eye may serve as a potential source of diagnosis and prognosis of neurodegenerative diseases.

CONTROL ID: 3714882

SUBMITTER (NAME ONLY): Hunter Aliff

TITLE: Inexpensive LED light box for modeling light-induced retinal degeneration in pigmented C57Black mice

SESSION TITLE: Modeling inherited retinal degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Aliff, O. Tseytlin, V. Ramamurthy, Biochemistry and Molecular Biology, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|J.M. Nickerson, J. Boatright, M. Chrenek, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Light-Induced Retinal Degeneration (LIRD) is a powerful method to assess the response of photoreceptors to damage. Traditionally performed using fluorescent lamps on albino animals, this tool is unsuitable for pigmented animals. We wanted to model LIRD in commonly used C57Black mice that carry a hypomorphic RPE65 allele. We came across a previously developed method using LED lamps and mouse cages to create small, inexpensive light damage boxes and have successfully implemented this method to achieve LIRD in C57Black animals.

Methods:

We obtained LED lights to reproduce the >60k lux light intensity reported by a previous study. We adapted them with a 3-D printed fitted lid to securely attach the lights to the mouse cages. The light intensity was adjustable from 5,000 to 63,000 lux with the adjustment of a dimmer switch. Low-noise fans had to be equipped to the boxes. These allowed the boxes to maintain an acceptable temperature range of (25-27°C) while lights were in operation with little disturbance to the mouse. Mice used were C57Black, and 129/Sv reared in cyclic lighting conditions. The eyes were dilated with Tropicamide 1% and Phenylephrine Hydrochloride 2.5% (in a ratio 1:1) 10 minutes before light damage. The light damage was performed between 7-11 pm, at varying light intensities ranging from 20-60k lux after 24hr dark adaptation. The mice were returned to dark for 24hrs following light damage and then were returned to the animal facility and maintained with cyclic light conditions. Electroretinography (ERG) was performed at 24hrs and one week post light damage to evaluate visual function.

Results:

We were able to build light boxes for about $200-300 per box, depending on the prices of LED studio lights, fans, and plastic filament. The lightbox was powerful enough to induce a significant reduction in visual function in C57Black mice following four hours and 129/Sv after only 1 hour of exposure at >60000 lux. The results also indicate that visual function is significantly reduced by 24 hrs and remains reduced at seven days.

Conclusions:

This method allows for a rapid assessment of mice models such as the C57Black or 129/Sv background. In addition, most labs can quickly build the light damage box, which can alleviate some of the barriers to studying retinal disease mice models under light stress conditions.

CONTROL ID: 3714884

SUBMITTER (NAME ONLY): Dean VanNasdale

TITLE: Mathematical Modeling of Geographic Disparities in Vision Impairment and Machine Learning Predictive Capabilities Using National Health Surveillance Data

SESSION TITLE: Public Health II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. VanNasdale, E. Shelton, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|C.A. Clark, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|J. Crews, Independent Contractor, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To mathematically model the frequency distribution of county-level vision impairment (VI) prevalence estimates between 2015 and 2019 and assess for geographic disparities. To use machine learning algorithms to test the feasibility of predictive modeling of VI prevalence estimates.

Methods: American Community Survey (ACS) data were used to estimate the county-level prevalence of adult VI in 3220 counties and county-equivalents in the United States for each year between 2015 and 2019. The VI prevalence frequency distribution was assessed for normalcy using the chi-square goodness of fit test. Kurtosis of the frequency distribution was calculated for each year. Machine learning decision tree software was developed in Matlab (IBM, Natick, MA) with a training data set of VI prevalence estimates stratified by age for 2,720 counties from 2014. The training set was used to develop an algorithm to predict the change in vision impairment from 2014-2019 and tested against data from 500 randomized counties held in reserve.

Results: The frequency distribution of vision impairment was not normally distributed for any of the 5 years assessed ($p<0.001$ for each year). Kurtosis ranged from 15.2 to 20.4. Linear regression showed the machine learning algorithm predicted change in VI compared to the actual VI prevalence change with an R^2 coefficient of 0.244. The biggest predictors of change in VI based on the model were the prevalence of VI in the 65 and older age cohort from 2014 and the prevalence of VI in the 18-64 age cohort.

Conclusions: National health surveillance data demonstrate skewed frequency distributions for VI prevalence, indicating vision impairment disparities at the county-level in the United States. This analysis allows identification of locations with disproportionately high VI prevalence and capabilities to monitor changes to that distribution over time. Preliminary machine learning algorithms suggest that predictive capabilities of VI with limited training data are possible.

CONTROL ID: 3714885

SUBMITTER (NAME ONLY): Daeun Jeong

TITLE: Evaluation of a Novel Targeted-Sequencing Panel for Orphan Pediatric Retinal Diseases for detection of LRP5 Gene Variants.

SESSION TITLE: Genetic variants in human ocular disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Jeong, K.P. Mitton, W.A. Dailey, K.A. Drenser, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|D. Jeong, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|K.P. Mitton, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|K.A. Drenser, Associated Retinal Consultants LLC, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test the custom orphan pediatric retinal disease panel for its detection in variants in the LRP5 gene. Familial Exudative Vitreo Retinopathy (FEVR) is due to variants that affect various genes including the LRP5 gene. LRP5 (LDL Receptor Related Protein 5) is an essential coreceptor, along with TSPAN12 and FZD4, which makes retinal endothelial cells uniquely responsive to Norrin WNT-signaling. 76 subjects diagnosed with FEVR, and near relatives were sequenced through a custom Ampliseq panel that includes eight genes related to FEVR/Norrie Disease and Retinoschisis (NDP, CTNNB1, TSPAN12, KIF11, FZD4, LRP5, ZNF408, RS1).

Methods:

8 genes were run through a custom Ampliseq targeted panel (180 amplicons) which was designed with the Illumina's DesignStudio Sequencing Assay Designer. The targeted panel was put into three pools (PCR reactions) per patient sample for complete coverage of 83 exons with 25 bp adjacent intron sequence. The targeted genes included: NDP (ChrX), RS1 (Chr10); CTNNB1 (Chr3); TSPAN12 (Chr7); KIF11 (Chr10), FZD4 (Chr11), LRP5 (Chr11), and ZNF408 (Chr11). Then the Ampliseq libraries were sequenced on the Illumina iSeq-100 platform. Through the use of ClinVar and The Genome Aggregation Databases (gnomAD), the variant impacts and allele frequency data was collected.

Results: 33 protein-altering variants were found in six FEVR/ND related genes. Of note, 13/33 (39.4%) of the variants were present in the LRP5 gene. The LRP5 gene is involved in the Wnt signaling pathway associated with FEVR with mutations showing a lack of vascularization to the retina. For the variants, two are found to be pathogenic, 1 novel likely pathogenic and 1 novel variant of unknown significance. 95.5% of the base reads were > Q30 quality, the percent on-target bases passing filer was 92.2%, and the average sequencing depth coverage was 978.

Conclusions: Our custom targeted-sequencing panel was developed in order to detect variants in seven FEVR / Norrie Disease genes. We conclude that this panel provides sufficient depth of sequencing to detect variants in the LRP5 gene (exons and splice sites) and to determine zygosity of variants.

CONTROL ID: 3714889

SUBMITTER (NAME ONLY): Guoqiang Li

TITLE: Continuously tunable attenuator for vision care with unprecedented contrast ratio

SESSION TITLE: Optics: Accommodation, Lens and Ocular Biometry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Li, T. Dai, Y. Sun, Zhejiang Lab, Hangzhou, Zhejiang, CHINA|

Commercial Relationships Disclosure: Guoqiang Li: Commercial Relationship: Code N (No Commercial Relationship) | Tiantian Dai: Commercial Relationship: Code N (No Commercial Relationship) | Yongqiang Sun: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Attenuators are basic ophthalmic optical elements. They have wide applications such as sunglasses, treatment of amblyopia, ophthalmic imaging systems, etc. The majority of the attenuators has a fixed transmission coefficient and they are usually made of dielectric, semiconductor, or metallic coatings based on optical interference or absorption effects. Variation of the transmission requires use of different coatings. Photochromic materials can change the transmission based on the light condition of the environment, but it is slow as it may take a couple minutes to change the transmission from bright to dark light conditions. Electrochromic materials can be used to change the transmission continuously. However, its contrast ratio (the ratio of the highest transmission to the lowest transmission) is limited to about 10. The purpose of this study is to investigate a new technique that can continuously tune the transmission with a contrast ratio much higher than 100 while keeping the device transparent and also with high speed.

Methods: In order to achieve the above goal, we have made a liquid crystal device with large tunability of the transmission. A liquid crystal mixture including nematic liquid crystal, chiral dopant, and dichroic dye is sandwiched between two glasses each coated with transparent conductive thin film. The thickness of the liquid crystal mixture is only about 20 mm. An electrical field is applied to the device by applying a voltage less than 20 Vrms. The variable transmission is due to change of scattering and absorption affected by the orientations of the liquid crystals and the dye, which are tailored by the applied electric field.

Results: The transmission of the new electro-optic device can be tuned across a very large range, and a contrast over 200 has been achieved, much higher than the concurrent technologies. The spectrum in the whole visible range is almost flat, which is good. The response time is fast and it is around 200 milliseconds. The device is polarization-independent, i.e., it responds equally to the light with any polarization and it is suitable for vision care.

Conclusions: A tunable optical device with the highest contrast ratio while maintaining its transparency has been reported. It is promising for a lot of ophthalmic applications, including treatment of amblyopia, sunglass, imaging, etc.

CONTROL ID: 3714890

SUBMITTER (NAME ONLY): Sarkis Soukiasian

TITLE: Iris dysfunction following uncomplicated cataract extraction by phacoemulsification

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.H. Soukiasian, A. Alwreikat, B.M. Howerter, A.D. Long, D.J. Ramsey, Ophthalomology, Lahey Hospital and Medical Center, Burlington, Massachusetts, UNITED STATES|S.H. Soukiasian, D.J. Ramsey, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|A.D. Long, Tufts University, Medford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Atonic pupil has been reported as a rare complication following cataract surgery. We had clinically observed significant decrease in the maximum pupil dilatation following uneventful cataract surgery in patients. The purpose of our study was to prospectively assess if uncomplicated cataract surgery may result in iris dysfunction with reduced or poor dilation and changes in dynamic pupillary response.

Methods: Prospective, single center, IRB approved observational study of pupillary function (using a Colvard pupillometer). Pupil size was measured in ambient room light, under scotopic conditions, and following standard mydriasis prior to and three or more weeks after uneventful cataract extraction by phacoemulsification using an Alcon Infinity unit. Demographics, cataract type and grade, iris color, and cumulative dissipated energy (CDE) was evaluated. Subjects with preexisting conditions predisposing to pupillary dysfunction were excluded.

Results: 75 eyes from 52 subjects were included in the study. 50% of participants were female. The mean age was 71.9 ± 9.7 years (range of 44-92 years). There was a significant reduction in mean mydriatic pupillary dilation post-surgery (-0.73mm±1.12 mm and 10±14%, p=0.030) and a correlation to the CDE (r=0.258, p=0.040). There was up to a 40% reduction in some cases. There was no association with iris color, nuclear cataract density, or age. Analysis of dynamic pupil response data is ongoing.

Conclusions: There can be a prolonged and significant decrease in pupillary dilation following uncomplicated cataract extraction. Poor dilation (<6 mm) or pupillary disfunction can impact examination of the posterior segment and could also possibly impact performance of some multifocal intraocular lenses. The mechanism for pupillary dysfunction is yet unclear, but investigation is ongoing and will be discussed.

CONTROL ID: 3714892

SUBMITTER (NAME ONLY): Aqsa Saleem

TITLE: Title: Incidence rate of strabismus post plaque brachytherapy

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saleem, J. Huang, E. Liao, C. Solarte, E. Weis, P. Campbell, Ophthalmology, Alberta Health Services, Calgary, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: To determine the incidence of strabismus post plaque brachytherapy and to categorize the type of strabismus into slipped muscle, sensory strabismus, decompensated phorias, cranial nerve palsies, restrictive muscles, or a combination.

Methods: A prospective consecutive case Sseries of patients who were diagnosed with choroidal melanomas between February 2012 and May 2021 were included. Primary outcome data was to identify the incidence rate of strabismus post plaque brachytherapy, and then to classify the type of strabismus. Demographic data included patient age, gender and residing city. Other variables included pre-and-post-operative visual acuity, tumor height, tumor distance from optic nerve and fovea, number of extraocular muscles operated, primary deviation, classifying the type of strabismus into slipped, restrictive, cranial nerve palsy, or sensory strabismus and duration of follow-up post plaque.

Results: 400 patients underwent plaque brachytherapy, and 10/400 (2.50%) were identified to have strabismus. Our results indicated that the most common type of strabismus post plaque was sensory strabismus with 7/400 (1.75%) patients being affected. All 7 patients with sensory strabismus had an exotropia. Slipped muscle was the second most common with 2/400 (0.50%) patients, 1 patient had a hypertropia and the other patient had a hypotropia both corelating directly with the muscle that was removed. Decompensating phoria was the least common type of strabismus with only 1/400 (0.25%) patient being affected, and this patient had a decompensation of the superior oblique.

Conclusions: Incidence of strabismus post plaque is uncommon. Of the 2.50% of patients identified to have strabismus, only 0.50 % were directly related to surgical complications. Others were related to secondary vision loss from plaque brachytherapy. These results match previous studies in the few numbers of patients who end up with strabismus post plaque. Even though multiple extra ocular muscles may be removed for the insertion and removal of plaque, surgery itself is an uncommon cause of strabismus.

CONTROL ID: 3714896

SUBMITTER (NAME ONLY): An-Jey Su

TITLE: Immunological Response Following Whole Eye Transplantation In A Rat Model

SESSION TITLE: Immunobiology: Ocular Surface, Glaucoma and Retinal Degeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Su, B. Li, Y. Wang, C.R. Owens, N.J. Khatter, A.D. Lee, D. Mathes, C. Huang, K.M. Washington, Department of Surgery, Division of Plastic and Reconstructive Surgery, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|T. Banaee, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|E. Farkash, Pathology, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|C.T. Chu, Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure: An-Jey Su: Commercial Relationship: Code N (No Commercial Relationship) | Bing Li: Commercial Relationship: Code N (No Commercial Relationship) | Yong Wang: Commercial Relationship: Code N (No Commercial Relationship) | Charles Owens: Commercial Relationship: Code N (No Commercial Relationship) | Touka Banaee: Commercial Relationship: Code N (No Commercial Relationship) | Neil Khatter: Commercial Relationship: Code N (No Commercial Relationship) | Anna Lee: Commercial Relationship: Code N (No Commercial Relationship) | David Mathes: Commercial Relationship: Code N (No Commercial Relationship) | Evan Farkash: Commercial Relationship: Code N (No Commercial Relationship) | Charleen Chu: Commercial Relationship: Code N (No Commercial Relationship) | Christene Huang: Commercial Relationship: Code N (No Commercial Relationship) | Kia Washington: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Distinct from other vascularized composite allotransplantation (VCA), whole eye transplantation (WET) potentially disrupts the blood ocular barrier which could result in increased ocular immunogenicity and associated pathogenesis. We performed orthotopic rodent WET without immunosuppression to assess the immune reaction and rejection response following WET.

Methods: Male 14-16-week-old Lewis (LEW) Allogeneic or Brown Norway (BN) Syngeneic recipients received hemiface/eye grafts from donor BN rats. Changes in graft skin, eye appearance, serum cytokines, ocular tissue gene expression, and histology (Allo=36, Syn=21) were assessed at cross sectional time-points. Longitudinal assessment (Allo=5, Syn=5) was done for corneal thickness by ocular coherence tomography and serum anti-donor specific antibodies (DSA) by flow cytometry. Skin and cornea rejection grades were assigned using the modified Banff VCA scoring system and clinical corneal transplantation scoring. Eyes were stained with hematoxylin and eosin (H&E) and CD3+ T cells were stained by immunohistochemistry. Serum chemokine levels were measured by Luminex and anti-donor antibody responses were detected by flow cytometry.

Results: Corneal rejection scores were higher in Allo vs. Syn group at POD4 ($P<0.01$). Corneal thickness in the Allo group was 2-fold greater ($P<0.01$) than the Syn group on POD6. H&E revealed Allo lymphocyte infiltrate increased with time in the eye, suggesting graded rejection. qPCR revealed significant upregulation of transplant rejection-associated genes, mirroring the observed infiltration in histology. Allo serum CXCL10 significantly increased by POD4. IFN-γ increased on POD5. Comparing DSA before and after WET showed that Allo eyes increased in IgM on POD4 ($P<0.05$) with a peak at POD5 ($P<0.0001$); IgG appeared at POD6 ($P<0.05$), increasing until POD8. Banff scores showed a difference between Allo and Syn skin at POD5 ($P=0.02$).

Conclusions: Our results suggest that allogeneic WET rejection occurs rapidly without immunosuppression, despite the immune privilege potential of the eye. Corneal transparency and serum CXCL10 level increases are early signs of rejection. IFN-γ and Anti-donor IgM increase reflected ongoing rejection. Skin rejection following WET was consistent with other skin containing VCA models. Since the cornea rejects before the skin, it should receive priority as a diagnostic indicator for WET rejection.

CONTROL ID: 3714897

SUBMITTER (NAME ONLY): Jacob Bear

TITLE: Clinical Efficacy of Multiple Small Incision Sub-Tenon Ab Interno Xen Implantation in Patients with Primary Open-Angle Glaucoma (POAG)

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bear, M. Baum, A. Roschke, B. Graham, J. Lee, Clinic, Colorado Eye Institute, Colorado Springs, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Jacob Bear: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Baum: Commercial Relationship: Code N (No Commercial Relationship) | Aaron Roschke: Commercial Relationship: Code N (No Commercial Relationship) | Brianna Graham: Commercial Relationship: Code N (No Commercial Relationship) | James Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study aims to determine the clinical efficacy of performing multiple Xen stent implantations in patients with POAG as determined by intraocular pressure (IOP) reduction and number of IOP-lowering medications needed after surgery.

Methods: 17 subjects (20 eyes) underwent multiple small-incision sub-Tenon ab interno Xen implantation procedures during a period from 2017 to 2022. Outcome measures monitored were IOP and current number of IOP-lowering medications. Data was taken at the preoperative appointment before each Xen implantation and again at all subsequent post-operative appointments. IOP was attained via Goldman applanation tonometry (GAT). All IOP measurements and procedures were performed by a single surgeon.

Results: Average study participant age was 76.66±9.64 years. At preoperative visits mean IOP was 21.02±8.08mmHg. No eyes recorded an IOP of lower than 10mmHg, 6% recorded an IOP ≤12mmHg, 17% of eyes recorded an IOP ≤15mmHg, 36% recorded an IOP of lower than 17mmHg, and 57% of patients recorded an IOP of 20mmHg or higher. At postoperative visits, mean IOP was 12.37±3.56mmHg. All eyes had an IOP under 20mmHg, 89% of eyes recorded an IOP of 17 or lower, 84% recorded an IOP of 15 or lower, 53% recorded an IOP of 12 or lower, and 26% recorded an IOP of 10 or lower. At preoperative visits, 47% of patients were on 2 or fewer IOP-lowering medications, with an average of 2.53±1.41. At most recent postoperative appointments, 84% of patients were on 2 or fewer medications, with an average of 1.89±1.97. Patients most recent visits ranged from 5-49 months with the mean being 22.5±13.94 months.

Conclusions: IOP-lowering effects were still seen for an average of 22.5 months after most recent Xen implantation. After initial ab interno Xen failure, repeating sub-Tenon ab interno Xen placements is likely a viable option for POAG patients based on IOP-reduction and number of continued drops post-procedurally. These effects have been demonstrated 41 months and longer after procedure in some cases, showing the long-term efficacy of repeating the sub-Tenon ab interno Xen insertion surgery.

CONTROL ID: 3714898

SUBMITTER (NAME ONLY): Robert Bhisitkul

TITLE: UBX1325, A Novel Senolytic Treatment for Patients with Advanced DME or wet AMD: 24-Week Results of a Phase 1 Study

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Bhisitkul, University of California San Francisco, San Francisco, California, UNITED STATES|S. Klier, P. Tsuruda, B. Xie, L. Masaki, J. Bautista, A. Khan, J. Dananberg, UNITY Biotechnology, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cellular senescence is implicated in retinal microvascular pathology that drives disease in DME and wet AMD. UBX1325, a novel small molecule Bcl-xL inhibitor, is a potent senolytic agent. This prospective study assessed the safety, tolerability, and disease-relevant activity of a single intravitreal (IVT) injection of UBX1325 in patients with advanced DME and wet AMD.

Methods: A phase 1, open-label, single ascending dose study (www.clinicaltrials.gov NCT04537884) was conducted in 4 cohorts at 0.5, 1, 5, and 10 µg, respectively. 12 patients, 2 with DME and 1 with wet AMD in each cohort, were enrolled. 7 additional patients with wet AMD were enrolled in the 10 µg cohort. Patients with DME or wet AMD meeting best corrected visual acuity (BCVA) criteria, no anti-VEGF for ≥90 days prior to Day 1, and with macular fluid or, for AMD, subretinal (SR) and/or intraretinal (IR) fluid were eligible to be enrolled. Patients received UBX1325 IVT once and followed through 24 weeks. Safety, change from baseline in BCVA and CST through study end were analyzed.

Results: UBX1325 was well tolerated with a favorable safety profile throughout. No dose-limiting toxicities or evidence of inflammation, infection, hemorrhage, or increase in intraocular pressure were observed.

Amongst 8 patients with DME, BCVA improved in 6 at Week 12, and in 5 at Week 24. At Week 24, 62.5% of patients gained ≥5 letters and 50% gained ≥10 letters. CST remained stable through 24 weeks in most patients with DME. Through 24 weeks, 62.5% of patients did not meet rescue criteria (≥75 µm CST increase from trough or ≥10 ETDRS letters decrease from peak) after UBX1325.

Amongst 10 evaluable patients (of 11) with wet AMD, visual acuity was improved in 7 at 4 weeks and in 5 at Week 12 and CST remained stable through 12 weeks. 80% of patients did not meet rescue criteria through 12 weeks. Reduction in SR and IR fluid was also observed. Additional 24-week data will be available for presentation.

Conclusions: A single IVT injection of UBX1325 up to 10 µg was safe and well tolerated in patients with advanced DME or wet AMD, through 24 weeks. Disease-relevant improvements in BCVA, CST, and IR and SR fluid, were observed in treated subjects. These data support further development of UBX1325, a novel senolytic small molecule, for DME and wet AMD.

CONTROL ID: 3714899

SUBMITTER (NAME ONLY): HARI KUMAR PEGUDA

TITLE: Anti-amoebic activity of RK-7 peptide mimic against Acanthamoeba spp trophozoites.

SESSION TITLE: Antimicrobial Resistance, Epidemiology and New Antimicrobials

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. PEGUDA, R. Kuppusamy, M.D. Willcox, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|R. Kuppusamy, N. Kumar, School of Chemistry, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure: HARI KUMAR PEGUDA: Commercial Relationship: Code N (No Commercial Relationship) | Rajesh Kuppusamy: Commercial Relationship: Code N (No Commercial Relationship) | Naresh Kumar: Commercial Relationship: Code N (No Commercial Relationship) | Mark Willcox: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the anti-amoebic activity of the antimicrobial peptide mimic RK-7 against Acanthamoeba trophozoites (infective form) in comparison with chlorhexidine.

Methods: Acanthamoeba amoebicidal, amoebistatic and encystation assays were performed using protocols described in literature. The activity of peptide mimic RK-7 was compared with chlorohexidine against the Acanthamoeba castellanii 044 with concentrations of both ranging from 125μM to 7.81μM. All experiments are performed in duplicate with three independent replicates. Data was represented as mean ± SE and analysed using two sample t-test and two tailed distributions. $p < 0.05$ is considered as statistically significant.

Results: In amoebicidal assays, both RK-7 and chlorhexidine reduced the numbers of trophozoites by 50% at concentrations ranging from 125 to 15.6 μM, with no difference between activities ($p>0.05$). Similarly,amoebistatic assays showed concentrations between 125 to 7.81 μM prevented the growth of trophozoites by between 100-82% for RK-7 and 100-97% for chlorhexidine ($p>0.05$). In the encystment assay, both RK-7 and chlorhexidine inhibited cyst formation by 70% at the lowest test concentration i.e., 7.81 μM. Inhibition of cyst formation at concentrations 62.5 μM and 15.6 μM by chlorhexidine (97% and 86% reduction) was greater ($p=0.025$ and $p=0.04$) than RK-7 (84% and 71% reduction).

Conclusions: RK-7 peptide mimic showed excellent anti-amoebic activity against Acanthamoeba castellanii 044. Future experiments will evaluate the activity of peptide mimic coated onto contact lens against Acanthamoeba spp.

CONTROL ID: 3714900

SUBMITTER (NAME ONLY): Martin Chan

TITLE: EB3 inhibitor prevents AMD via widespread opening of chromatin

SESSION TITLE: AMD: Clinical and translational research/AMD therapies (excluding anti-VEGF)

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chan, J. Le, Y. Komarova, Pharmacology and Regenerative Medicine, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|M. Maienschein-Cline, Research Informatics Core, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current treatments for wet age-related macular degeneration (AMD) involve regular anti-VEGF intravitreal injections; thus, far less invasive treatment is desired. We developed an inhibitor of microtubule-associated End Binding Protein 3 named EBIN which inhibits pathological calcium releases in endothelial cells and prevents choroidal neovascularization (CNV) in both mouse and non-human primate models of AMD. Since previous work demonstrated progressive decreases in chromatin accessibility in patients with late-stage of AMD, here we analyze the effects of EBIN in chromatin accessibility of different retinal cell types using single nuclei-assay for transposase-accessible chromatin (snATAC) sequencing in non-human primates.

Methods: CNV was induced via laser photocoagulation in monkey eyes. Monkeys then received 30 µL topical formulations of EBIN or vehicle in each eye after laser-induced CNV twice daily for 7 days and once a day for another 14 days. Then monkey retina/choroid were subjected to nuclei isolation used for snRNA- and snATAC- sequencing. Lastly, further bioinformatic analysis and validations of the sequencing data were performed using immunofluorescent staining of CNV lesions.

Results: Using snATAC-seq transcriptome data, we detected 22 distinct clusters corresponding to different retinal cell types characterized via well-known markers. Unknown ATAC clusters were manually characterized by Pearson Correlation using our snRNA-seq data. Analysis of differential peaks within each cluster revealed a widespread opening of chromatin characterized by an increase in promoter peaks in all cell types detected. The change in chromatin accessibility was associated with increased acetylation of lysine 27 of histone 3 (H3K27ac) nuclear signals ($p<0.0001$, $n=4$) but not histone 4 lysine 8 ($p=0.0956$, $n=4$) assessed with immunofluorescent staining of choroidal neovascular lesions. Additional comparison of our snATAC-seq transcriptome data against a published AMD GWAS dataset showed that EBIN does not open chromatin of genes involved in AMD progression (Spearman Correlation = -0.06).

Conclusions: EBIN induces a widespread increase of chromatin accessibility in cells comprising CNV lesions including metabolically active endothelial cells by increasing the acetylation of H3K27. Testing EBIN in clinical trials could provide AMD patients with an alternative non-invasive (topical) treatment.

CONTROL ID: 3714901

SUBMITTER (NAME ONLY): Benjamin Lin

TITLE: Evaluating a Smartphone-Based Optic Nerve Imaging Device as a Glaucoma Screening Tool in an Outpatient Clinic Setting

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lin, Z. Markatia, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Mittal, V. Sanchez, N. Patel, R. Robles, R. Blake, S. Iyer, M.B. Sherwood, Ophthalmology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ideally, population based eye screening could be performed by a layperson with minimal training at low cost with image interpretation occurring at telemedicine grading centers. This would be particularly useful in underserved communities in order to identify high risk individuals and best optimize delivery of ophthalmic care. This study aims to evaluate a smartphone-based ophthalmoscope, D-EYE, as a potential screening device for glaucoma.

Methods: Patients presenting to university based primary care and glaucoma clinics were recruited for this study. Clinical charts were reviewed to determine glaucoma status for each eye of every recruited patient. Without pupillary dilation, bilateral optic nerve videos were captured in 30-second-long clips with the D-EYE portable smartphone attachment for fundus photography. Videos were later independently graded by four ophthalmology residents and an ophthalmology intern in a blinded fashion. Grading criteria included the ability to visualize the optic nerve (yes or no), subjective image quality (5 point Likert scale [1 = minimal visibility of optic nerve head, 5 = optimal visibility of optic nerve head]), cup to disc ratio (0.01 to 0.99), and likelihood of referring patients for additional glaucoma care (5 point Likert scale [1 = very unlikely to refer, 5 = very likely to refer]).

Results: Optic nerve video capture was attempted on a total of 236 eyes (210 normal, 26 glaucomatous). A total of 186 of the 236 videos (78.8%) were of sufficient quality to visualize the nerve (163 normal, 23 glaucomatous). The mean image quality score was 3.11 out of 5. The average cup to disc ratio of normal and glaucomatous eyes was 0.299 and 0.420, respectively (intraclass correlation coefficient [ICC] = 0.436). The likelihood of referral of normal and glaucomatous eyes was 1.671 and 2.565, respectively (ICC = 0.509).

Conclusions: This pilot study used a smartphone-based photography system in undilated eyes which minimizes cost and facilitates ease of adoption. There was a moderate degree of inter-grader agreement for videos and, overall, glaucomatous eyes were more likely to be referred for further workup compared to healthy eyes. Agreement between raters and accurate likelihood of referral for glaucomatous eyes may be increased with dilated imaging and more experienced graders.

CONTROL ID: 3714902

SUBMITTER (NAME ONLY): Carolina Susanna

TITLE: Prospective Cross-sectional Study to Assess the Association between the Time of Peak Intraocular Pressure Occurs in the Water Drinking Test and the Severity of Glaucoma

SESSION TITLE: Aqueous humor dynamics and Trabecular Meshwork

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Susanna, B. Susanna, R. Susanna Jr, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|C. Susanna, B. Susanna, M.A. Ribeiro, R. Mota, V. Lima, Faculdade de Medicina do ABC, Santo Andre, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: This study's primary objective was to prospectively investigate the association between glaucoma severity and time IOP peaks occur during WDT. The secondary objective of the study was to assess the association between glaucoma severity and the value of peak IOP in WDT.

Methods: A prospective cross-sectional study lasting 6 months, including patients with bilateral primary open-angle glaucoma (POAG) with no ocular hypotensive medications, being followed up in the Ophthalmology sector of Faculdade de Medicina do ABC. The WDT was performed in all patients on the day of the first attendance. The test is characterized by the ingestion of 800 mL of water right after the first IOP measurement (basal) and after the water intake, 3 more measurements are taken every 15 minutes, with a total of 4 IOP measurements in 45 minutes. The peak IOP corresponds to the highest IOP measured in those 45 minutes.

Results: A total of 46 eyes from 23 participants were included in the present study. The mean age of patients was 67.17±9.22 (SD) years and 60.86% were male. Visual Field severity (MD) and retinal nerve fiber layer (RNFL) global thickness showed no statistically significant association with IOP peak time ($p=0.180$). However, there was a significant association between the severity of glaucoma and the value of peak IOP ($p<0.001$), in which every 1 mmHg increase in the maximum value of IOP resulted in a decrease in MD of 1.18 dB and of 1.51 Micra in the of retinal nerve fiber layer (RNFL) global thickness in OCT

Conclusions: The peak IOP value, but not the time it occurs in WDT, was shown to be related to the severity of glaucoma in POAG patients with no history of ocular medications.

CONTROL ID: 3714903

SUBMITTER (NAME ONLY): Saleh Alfuraih

TITLE: Effect of fluorometholone acetate, an ophthalmic steroid-ester, on ocular surface mucins

SESSION TITLE: Aqueous humor dynamics, IOP, corneal disease, cytokines and growth factors

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Alfuraih, C. Ross, A. Sharma, School of Pharmacy, Chapman University, Irvine, California, UNITED STATES|S. Alfuraih, School of Pharmacy, Nova Eastern University, Florida, UNITED STATES|

Commercial Relationships Disclosure: Saleh Alfuraih: Commercial Relationship(s);Code R (Recipient):Santen Pharmaceuticals | Christopher Ross: Commercial Relationship(s);Code R (Recipient):Santen Pharmaceuticals | Ajay Sharma: Commercial Relationship(s);Code R (Recipient):Santen Pharmaceuticals

ABSTRACT BODY:

Purpose: We have previously reported that corticosteroids can modulate ocular surface mucins gene expression. Fluorometholone acetate is potent lipophilic steroid ester with enhanced cellular and ocular surface penetration. Short-term topical application of ophthalmic fluorometholone acetate is indicated for many inflammatory conditions involving conjunctiva and cornea. Both corneal and conjunctival epithelial cells express membrane-tethered mucins. Since mucin genes have been shown to contain steroid responsive elements, the present study was designed to test whether fluorometholone acetate can modulate ocular surface mucins levels.

Methods: Stratified cultures of human conjunctival and corneal epithelial cells were used. Conjunctival epithelial cells were grown in serum-free low calcium F12/DMEM medium then switched to serum-containing keratinocyte medium for stratification. Corneal epithelial cells were grown on transwell membrane inserts using growth factor-supplemented keratinocyte medium. The cells were exposed to 100nM and 250nM fluorometholone acetate for 24h, 48 h and 72 h. The effect of fluorometholone acetate on mucin 1, 4, and 16 protein levels was quantified using commercially available ELISA kits.

Results: Fluorometholone acetate treatment resulted in a significant increase in mucin 1 levels in stratified human corneal epithelial cells after 24 hours exposure. However, neither the 100 nor 250nM dose cause any notable change in mucin 4 and 16 protein levels in human corneal epithelial cells at any of the tested time points. Furthermore, fluorometholone acetate treatment did not affect protein levels of mucin 1, 4 or 16 in cultured stratified human conjunctival epithelial cells.

Conclusions: Fluorometholone acetate causes a moderate increase in mucin 1 levels in human corneal epithelial cells but does not modulate mucin 4 or 16 protein levels in human corneal and conjunctival epithelial cells.

CONTROL ID: 3714904

SUBMITTER (NAME ONLY): Chi-wai Do

TITLE: Using a smartphone camera in detecting refractive error among schoolchildren: a simple model to address cost-related barriers for refractive error detection

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Do, L. Chan, O. Kwok, L. Lai, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|C. Do, Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Hong Kong, HONG KONG|P. Lee, Department of Health Sciences, University of Leicester College of Life Sciences, Leicester, Leicester, UNITED KINGDOM|G. Ngai, H. Leong, Department of Computing, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Uncorrected refractive error such as myopia is a global healthcare burden. If detected early, it is a treatable condition, ultimately preventing amblyopia and reducing the risk of severe ocular complications. The inherent smartphone-camera-lens, with built-in flash presents as an affordable and convenient photorefraction device for large-scale vision screening programs. This study evaluated the application of smartphone photorefraction for pediatric vision screening compared against the autorefraction technique, before and after cycloplegia (pupil dilation).

Methods: A total of 141 Chinese schoolchildren (ages 7 to 14 years old) were recruited in this study. Participants' refractive errors were measured by an optometrist using auto-refraction and the smartphone technique under non-cycloplegic (dry) and cycloplegic (wet) conditions. The smartphone camera was employed to capture eye images at different orientations by rotating the smartphone around four distinct meridians (at vertical 90^{o}, oblique 45^{o}/135^{o}, and horizontal 180^{o} orientations). Refractive error was calculated based on pupil diameter size and crescent image width using conventional theory-based approach. A cross comparison of the transcribed autorefractor reading with photorefraction results was made.

Results: The refractive error measured by autorefractor (ranging from +0.50 D to -12.00 D) were compared among photorefraction results along the four meridians. The correlation r were 0.88 and 0.80 for non-cycloplegic and cycloplegic photorefraction, respectively. The overall mean absolute error (MAE) was smaller under non-cycloplegic conditions (0.65 D vs. 0.84 D). In addition, for dry photorefraction, 79.2% fell within a MAE of +/- 1.00 D compared to 70% for wet photorefraction. Both methods demonstrated an overall sensitivity of >97% in estimating myopic values greater than -1.50 D while the specificity was higher in dry photorefraction (dry: 78% vs wet: 72%).

Conclusions: Our results suggest that smartphone photorefraction has good correlation with auto-refraction, particularly under non-cycloplegic condition. The smartphone method yields as reliable and sensitive measures to detect myopic refractive errors compared with the autorefraction, thereby offering a promising low-cost option for refractive error screenings in poverty-ridden areas of the world.

CONTROL ID: 3714905

SUBMITTER (NAME ONLY): Eleanor Burton

TITLE: Gender Representation Among Presenters in Ophthalmology Subspecialties in 2019: A Retrospective Review

SESSION TITLE: Vision care training and education

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Burton, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|A. Jebaraj, D. Eddington, B. Brintz, R. Simpson, J. Pettey, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe gender representation at eight national ophthalmology conferences, stratified by role, session category, and sub-specialty.

Methods: Design: Retrospective cross-sectional study.

Study Population: 3,053 presenters at the 2019 American Academy of Ophthalmology subspecialty days, American Society of Cataract and Refractive Surgery, American Glaucoma Society, American Society of Retina Specialists, American Society of Ophthalmic Plastic and Reconstructive Surgery, American Association for Pediatric Ophthalmology and Strabismus, North American Neuro-Ophthalmology Society, and American Uveitis Society meetings.

Main Outcome Measures: Gender of presenters in seven sub-specialties stratified by category and role.

Results: The proportion of female presenters was lower than the ABO-estimated proportion of women in their respective fields in cornea (24.4% vs. expected 26.0%), glaucoma (28.0% vs. 39.8%), neuro-ophthalmology (35.6% vs. 45.3%), and pediatrics (41.9% vs. 53.3%) and greater than expected in oculoplastics (36.7% vs. 34.7%), retina (24.3% vs. 19.8%), and uveitis (59.1% vs. 49.1%). For clinical sub-specialty sessions, the proportion of female leaders exceeded the overall proportion of female leaders in the respective sub-specialty in cornea (35.1%, 95% CI: [30.3%, 40.1%] vs. 24.4% all sessions), glaucoma (38.5% [29.6%, 48.1%] vs. 28.0%), pediatrics (63.9% [55.4%, 71.6%] vs. 41.9%), and uveitis (74.2% [56.2%, 86.5%] vs. 59.1%). Females represented fewer than the expected number leaders of surgical sessions in cornea (21.6% [19.6%, 23.9%] vs. 24.4%), glaucoma (18.0% [13.1%, 24.1%] vs. 28.0%), oculoplastics (35.2% [26.7%, 44.8%] vs. 36.7%), pediatrics (22.0% [14.3%, 32.2%] vs. 41.9%), retina (17.7% [13.3%, 23.1%] vs. 24.3%), and uveitis (40% [10.0%, 80.0%] vs. 59.1%). These findings were not statistically significant for retina or uveitis.

Conclusions: Gender representation varied, with fewer than expected female presenters in cornea, glaucoma, neuro-ophthalmology, and pediatrics. Females led relatively more clinical sessions, but were vastly underrepresented in surgical sessions, in all sub-specialties.

CONTROL ID: 3714906

SUBMITTER (NAME ONLY): Sadaf Abed

TITLE: Tbr2 regulates melanopsin expression in adult ipRGCs and influences their survival after optic nerve crush

SESSION TITLE: Retinal ganglion cells

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Abed, D. Feldheim, Molecular, Cell, and Developmental Biology, University of California Santa Cruz, Santa Cruz, California, UNITED STATES|

Commercial Relationships Disclosure: Sadaf Abed: Commercial Relationship: Code N (No Commercial Relationship) | David Feldheim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The transcription factor Tbr2 is expressed in intrinsically photosensitive retinal ganglion cells (ipRGCs) and is required during development for their viability, however its role in adult ipRGCs is not clear. Additionally, ipRGCs survive better than conventional RGCs (cRGCs) after optic nerve injury for reasons that are not well understood. We tested the following hypotheses: 1) Tbr2 is required for the maintenance of ipRGCs, 2) Tbr2 can induce expression of ipRGC-specific proteins (the photopigment melanopsin) in cRGCs, 3) Tbr2 is necessary for ipRGC survival after optic nerve injury.

Methods: 1) We administered tamoxifen to adult $Tbr2^{CreER/flox};R26^{tdTomato}$ mice to remove Tbr2 from $Tbr2^{+}$ RGCs while simultaneously labeling their somas, dendrites, and axons with tdTomato. Controls are littermates lacking the floxed Tbr2 allele ($Tbr2^{CreER/+};R26^{tdTomato}$). We analyzed brains (coronal sections) and retinas (flatmounts and sections) >30 days after tamoxifen administration.

2) We injected one eye intravitreally with a virus containing Tbr2 and GFP, and the contralateral control eye with a virus containing GFP alone in wildtype, Tbr2-CKO, $Tbr2^{CreER/flox};R26^{tdTomato}$, and $Tbr2^{CreER/+};R26^{tdTomato}$ mice and analyzed their retinas 2-5 weeks later.

3) We performed the optic nerve crush (ONC) procedure in adult tamoxifen-induced $Tbr2^{CreER/flox};R26^{tdTomato}$ and control mice and analyzed their retinas 2 weeks later.

Three or more mice were used per experimental condition. Images were taken with an Olympus BX51 microscope. 4-8 fields of view (446.15 µm x 333.33 µm) per retina were imaged for quantification. Cells were manually counted in FIJI. Statistical analyses (Student's t-test or two-way ANOVA) and graph generation were performed using GraphPad's Prism9 software.

Results: Loss of Tbr2 in adult $Tbr2^{+}$ RGCs does not affect their viability but results in loss of melanopsin expression (23.5±10 vs. 95.8±6 cells/mm^2, $P<0.001$). Tbr2 is able to induce melanopsin expression in Tbr2 RGCs ($P=0.0156$) but not in Tbr2-deficient RGCs ($P=0.2651$). We find that there is decreased survival of Tbr2-deficient RGCs relative to $Tbr2^{+}$ RGCs after optic nerve crush ($P=0.0153$), however, Tbr2-deficient RGC survival is still greater than the survival of cRGCs ($P=0.007$).

Conclusions: Our findings demonstrate important roles for Tbr2: its regulation of melanopsin expression and its involvement in RGC survival after ONC.

CONTROL ID: 3714913

SUBMITTER (NAME ONLY): Bikram Adhikari

TITLE: Extracellular Matrix Remodeling of Human Trabecular Meshwork Cells in Static and Dynamic Biopolymer Scaffolds

SESSION TITLE: Pharmacology / Cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Adhikari, M. Krebs, Quantitative Biosciences and Engineering, Colorado School of Mines, Golden, Colorado, UNITED STATES|M.B. Pantcheva, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|M. Krebs, Chemical and Biological Engineering, Colorado School of Mines, Golden, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Bikram Adhikari: Commercial Relationship: Code N (No Commercial Relationship) | Melissa Krebs: Commercial Relationship: Code N (No Commercial Relationship) | Mina Pantcheva: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the effect of GAGs on the ECM expression and deposition of hTM cells cultured on 3D natural biopolymer scaffolds and the role of Dex on its remodeling under static and dynamic conditions.

Methods: Anisotropic porous scaffolds were fabricated from natural biopolymers present in the TM extracellular matrix, specifically collagen and a variety of glycosaminoglycans (GAGs), to allow the study of hTM cells' response to extracellular environment composition. 100,000 hTM cells were seeded on the scaffolds and cultured for up to 2 weeks in the presence and absence of 100 nM dexamethasone (Dex). Dynamic 3D cell culture was performed on scaffolds housed in a perfusion chamber connected to a peristaltic pump. mRNA expression levels of elastin, laminin, and MMP-2 were quantified using qPCR. ECM protein deposition was visualized using confocal microscopy. Pressure changes were measured using pressure transducers connected to the dynamic cell culture constructs.

Results: hTM cells cultured on the collagen-only (CO) scaffolds expressed significantly higher amounts of mRNA for the studied ECM proteins compared to hTM cells seeded on tissue culture dishes. The expression of these ECM proteins was also impacted by the composition of those scaffolds. In particular, the addition of chondroitin sulfate (CS) increased the expression of these proteins by up to 8-fold when compared to CO. Dex increased the expression of elastin and decreased expression of laminin and MMP-2 after two weeks of culture in scaffolds. The morphology of elastin and laminin proteins was also impacted as a result of dexamethasone addition. Pressure measured across the scaffolds was higher in cells cultured in the presence of Dex as compared to non-treated controls.

Conclusions: Extracellular matrix remodeling has been shown to play an important role in the IOP homeostasis, increasing the aqueous humor outflow resistance of the TM. Our results show collagen and GAGs are important in providing signals to the cells for the expression of important ECM proteins. CS can potentially be responsible for the promotion of elastin fiber formation. Our results suggest that the presence of GAGs decreases the expression of laminin likely via the integrin pathway when cells are cultured in the presence of Dex. Increased pressure across scaffolds is a result of decreased MMP-2 expression and its effect on ECM protein degradation.

CONTROL ID: 3714914

SUBMITTER (NAME ONLY): Jin Mo Koo

TITLE: Risuteganib-directed staining localizes in the Retinal Pigment Epithelium of Retinal Tissue from Aged, but not Young, Mice

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Koo, D. Zhou, J.A. Kornfield, Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California, UNITED STATES|C. Call, Chemical Engineering, Stanford University, Stanford, California, UNITED STATES|J. Park, H. Karageozian, V.H. Karageozian, Z. Shao, Allegro Ophthalmics LLC, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Risuteganib (RSG) is a therapeutic peptide in clinical trials for various retinopathies. A Phase II trial in dry age-related macular degeneration (AMD) reported therapeutic effects with no drug-related adverse events [1]. In the oxygen-induced retinopathy (OIR) mouse model, RSG mitigated neovascularization and lowered mRNA of angiogenic and inflammatory processes [2]. In human cell studies, RSG protects Retinal Pigment Epithelium (RPE) cells from dysfunction under oxidative stress [3-5]. Here, we report RSG binds preferentially to the RPE in the retina of an aged (14 mo), but not a young (7 mo), BALB/c mouse.

Methods: Sulfonated-Cy5 was used as it gives lower nonspecific staining in murine retinal tissue sections than TAMRA, Cy5 and AlexaFluor 555. Sulf-Cy5 was conjugated with two different peptides: RSG and a negative control, denoted RGE, similar to RSG in size, hydrophilicity and charge. Two aspects of the staining protocol were tested: staining environment and peptide-dye concentration. Three staining environments were compared: DI water, PBS with Ca^{2+} and Mg^{2+}, and homogenized porcine vitreous humor (HVH). In each of these, 5mM and 20mM solutions were prepared for dye-RSG and dye-RGE. The twelve resulting solutions were used to stain 10mm-thick retina sections of BALB/cJ mouse, either 7 mo or 14 mo old (comparable to 20-30 or 50-60 yr old human, respectively).

Results: Among three different staining environments tested, HVH minimized non-specific staining. Mouse age showed a significant effect: retinal sections from a 14-mo-old mouse consistently showed RSG-specific staining at the RPE at 5μM in HVH (n = 2-3 sections). At 20μM, sulf-Cy5-RSG stained RPE and photoreceptor (PR) layers. Some retinal tissue sections of a 7-mo-old mouse were preferentially stained at the RPE, but not consistently nor peptide-specifically (n = 2-3).

Conclusions: The results show an age-related specific interaction of RSG with the RPE. These findings are consistent with the hypothesis that RSG supports RPE function, which may underlie its therapeutic effects.

CONTROL ID: 3714915

SUBMITTER (NAME ONLY): Andrew Barton

TITLE:

A Novel Study of the Extraocular Recti Muscle Degree Orientation: A Cadaveric Approach

SESSION TITLE: Mechanisms of Refractive Error and Eye Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Barton, E. Kim, J. Tanzer, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|V. Rana, J. Schaefer, Department of Ophthalmology, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|

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ABSTRACT BODY:

Purpose:

The anatomy of the extraocular rectus muscle insertions are clinically relevant in the field of ophthalmology. This descriptive cadaveric study determines relative degree orientation of the superior, lateral, and inferior recti with respect to the medial rectus, as well as investigating the distances between the rectus muscle insertions.

Methods:

30 cadavers (50% female, mean age = 81.86 years, SD 12.16) were included for a total of 60 eyes. For each eye, a lateral canthotomy with superior and inferior cantholysis was performed followed by a peritomy. Muscle hooks were then used to access and isolate the recti muscles. The degree orientation was determined by marking the muscle midpoints at insertion, using the center of the cornea as the vertex, and measuring the angle with the Angle Meter app (Fig. 1). The distances between recti were measured from the same muscle midpoints at insertion using calipers.

Results:

The degree orientations with respect to the medial rectus are displayed in Figure 2, and were as follows: superior rectus (mean = 93.14, SD = 3.04, min. 82.3, max. 100.3), lateral rectus (mean = 180.21, SD = 5.65, min. 170.5, max. 190.6), and inferior rectus (mean = 90.57, SD = 4.47, min. 84.0, max. 98.9). The distances (measured in mm) between recti muscle midpoints at insertion included medial rectus to inferior rectus (mean = 13.64, SD = 0.54), inferior rectus to lateral rectus (mean = 13.79, SD = 0.75), lateral rectus to superior rectus (mean =13.54, SD = 0.63), and superior rectus to medial rectus (mean = 13.83, SD = 0.75).

Conclusions:

This is a novel study of the extraocular muscle degree orientation performed with an innovative measuring approach. We found the recti degree orientation to approximate right angles between each muscle, however, there was wide variability. The mean distance between rectus muscle insertions were nearly uniform.The degree orientation of the insertions relative to the medial rectus have not been previously reported and may have surgical application in the field of ophthalmology.

CONTROL ID: 3714918

SUBMITTER (NAME ONLY): Trent Jarin

TITLE: Distribution Of Primary Cilia In hESC-Derived Retinal Organoid

SESSION TITLE: Stem cells and organoids

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.M. Jarin, K. Ning, Z. Luo, T. Kowal, B. Li, Y. Hu, A.Y. Wu, J.L. Goldberg, Y. Sun, Spencer Center for Vision Research, Byers Eye Institute, School of Medicine, Stanford University, California, UNITED STATES|T. Kowal, Y. Sun, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary cilia are microtubule-based organelles that are found on differentiated cell types throughout the body. Proper cilia formation is critical during eye development in humans and rodents; ciliary dysfunction can result in wide-ranging ocular diseases. Our previous papers support both amacrine and retinal ganglion cells (RGC) harbor primary cilia in primate and mouse retina. However, whether primary cilia patterning changes during retinal development remains unknown. The purpose of this study is to describe the primary cilia distribution in hESC (human Embryonic Stem Cell)-derived retinal organoids.

Methods: Retinal organoids were differentiated from the Brn3b-Tdtomato hESC line and collected at different developmental stages (w6-w38) and immunostained for the presence of cilia. Three ciliary markers, including Arl13b, AC3 and Centrin3 were used to identify primary cilia. Chx10, PKC2a, Prox1, GFAP, AP2a GAD67, Calretinin antibodies were used to determine retinal cell types. Arl13b stained the axoneme while Centrin3 marked the basal body. Statistical analysis was performed using One-way ANOVA and Student t-test.

Results: A group of ciliated cells localized in the inner aspects of retinal organoids cultured w7 to w34 (n=3-5 per time point). At w38, the number of primary cilia among non-photoreceptor retinal cell was significantly decreased compared to w13 (n=5, $p<0.001$). Furthermore, there were very few ciliated Prox1-positive horizontal, GFAP-positive astrocytes and PKC2a-positive rod-bipolar cells at w38 or w25. For AP2a-positive amacrine cells, we found ciliation was stable among all stages of retinal organoids (n=3 per timepoint). Ciliation significantly decreased for Brn3b-positive RGCs at later timepoints (n=5). Additionally, AC3-positive ciliation in non-RGC retinal cells at w25 significantly decreased as compared to w9. AC3-positive ciliation in Brn3b-RGCs decreased by w25.

Conclusions: These novel findings indicate amacrine cells incorporate stable ciliation whereas the RGC ciliation decreased along retinal organoid development, suggesting primary cilia potentially play significant roles for RGC survival in the retinal organoid.

CONTROL ID: 3714919

SUBMITTER (NAME ONLY): Chandani Patel

TITLE: Surgical outcomes of trabeculectomy in eyes with low to lownormal baseline intraocular pressure.

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Patel, J. Wong, Rowan University School of Osteopathic Medicine, Stratford, New Jersey, UNITED STATES|J. Wong, S. Hallaj, R. Razeghinejad, A. Shukla, N.N. Kolomeyer, J.S. Myers, D. Lee, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R. Razeghinejad, A. Shukla, N.N. Kolomeyer, J.S. Myers, D. Lee, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine surgical outcomes of trabeculectomy for patients with low preoperative intraocular pressure.

Methods: The retrospective cohort study included patients requiring trabeculectomy(TB) with mitomycin C with preoperative intraocular pressures(IOP) less than 15mmHg from March2006 to May2017. Patients with at least 1 year follow-up in the post-operative period were included. Demographic and clinical data were collected at the preoperative visit and post-operative visits for up to 7 years. Surgical failures were defined as eyes that required reoperation or progressed to no light perception.

Results: Forty eyes of 31 patients met inclusion criteria. Mean patient age was 75.2±9.3 years old and mean follow-up duration was 61.2±23.0 months(range: 14-93). 6(15%) eyes experienced surgical complications:2(5%) bleb leak,4(10%) scarred/encapsulated trabeculectomy blebs. 4 eyes developed IOP less than 6mmHg; however, none developed hypotony related complications.10(25%) eyes were documented to have failed TB with a mean duration of 29.5±28.2 months prior to failure. All failure(100%) were due to the need for reoperation secondary to inadequate IOP control: 8(20%) tube shunt, 2(5%) repeat TB,1(2.5%) CyPass microstent.1(2.5%) eye required 2 reoperations including a repeat TB followed by CyPass microstent. Mean IOP between preoperative and each post-operative visit was not significantly different, which was 12.7±2.7 preoperatively and ranged from 11.4±3.3 to 12.2±4.3 mmHg postoperatively for up to 5 years($p>0.05$ for all). Humphrey 24-2 visual field(VF) mean deviations(n=11) were not significantly different at -12.9±7.2 and -12.9±8.2($p=1$) during the most recent preoperative and postoperative visits, respectively. 24-2 mean slopes were significantly different at -1.3±1.8 and 1.4±3.8($p=0.012$) during the preoperative and postoperative periods, respectively. Octopus 30-2 VF mean defects(n=9) were not significantly different at 11.1±7.1 and 12.6±9.9($p=0.385$) at the most recent preoperative and postoperative visits, respectively. 30-2 mean slopes were not different at 1.4±2.0 and 0.45±2.1($p=0.445$) during the preoperative and postoperative periods, respectively.

Conclusions: Although the IOP was not significantly lower than low-normal preoperative IOP, there was no significant progression on VF. Mean deviation/defect remained stable and 24-2 mean slope even showed possible slowing of glaucomatous VF progression.

CONTROL ID: 3714920

SUBMITTER (NAME ONLY): Kentaro Nishida

TITLE: Morphologic changes and sensitivity of the retina after photocoagulation with various levels of autofluorescence

SESSION TITLE: Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Nishida, T. Fujikado, K. Nishida, Osaka Daigaku Daigakuin Igakukei Kenkyuka Igakubu Igaku Senko, Suita, Osaka, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the correlation between the morphology, autofluorescence and sensitivity of photocoagulated lesions in patients with proliferative diabetic retinopathy (PDR) with good vision.

Methods: Patients with PDR (n=17) who visited Osaka University Hospital from April 2019 to October 2021 and underwent panretinal photocoagulation more than one year ago (BCVA≧0.8) were included. Maintenance of the circulation of photocoagulation scars was confirmed by optical coherence tomography (OCT) angiography (Angioplex Elite 9000), while autofluorescence of photocoagulated lesions were evaluated using ultra-widefield retinal imaging (Optos: TX-200). The scars were then classified according to levels of autofluorescence—group A for those with no autofluorescence, group B for those with remaining autofluorescence, and group C as control. OCT (Spectralis) was used to evaluate the ellipsoid zone (EZ) lines of the photocoagulated lesions.

Results: The retinal sensitivities of photocoagulated lesions were 3.3±5.0dB, 15.3±4.4dB and 21.8±2.4dB for groups A (n=35), B (n=37) and C (n=32), respectively, while the percentages of remaining EZ lines were 5.7%, 81.1% and 100%, respectively. There are significant statistical differences ($P < 0.05$) in both the retinal sensitivities of photocoagulated lesions and the percentages of remaining EZ lines.

Conclusions: The photoreceptors in photocoagulated lesions with autofluorescence retain morphology and some function.

CONTROL ID: 3714921

SUBMITTER (NAME ONLY): Joy Li

TITLE: Volumetric Analysis of Orbital Soft Tissues in Thyroid Eye Disease: Correlations With Clinical Characteristics

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Li, S. Li, J. Lee, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|A. Rajamohan, J. Acharya, A. Lerner, V. Patel, USC Department of Radiology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|K. Gokoffski, S. Zhang-Nunes, J. Chang, USC Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|V. Patel, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using a novel atlas-based segmentation method, we aimed to identify whether specific orbital soft tissue volumes in patients with thyroid eye disease (TED) correlated with patient and clinical characteristics.

Methods: A retrospective chart review was performed to identify patients with a diagnosis of TED who had been evaluated clinically by an oculoplastic surgeon and had a CT scan of the orbits. Patient characteristics included age, sex, race, smoking status, and body mass index (BMI). Clinical characteristics including Clinical Activity Score (CAS) and strabismus were evaluated with respect to soft tissue volume measurements for each extraocular muscle (EOM) and orbital fat. Statistical analyses were performed using R software (version 4.0.3). Multiple regression analysis and Pearson's correlation were used to evaluate data. Significance was defined as $p<0.05$.

Results: 37 patients were evaluated (22 female, 15 male). CAS ranged from 0-5, and 7 patients had documented strabismus. There was no statistically significant correlation between orbital EOM volumes and age (p=0.382), sex (p=0.808), race (p=0.623), smoking status (p=0.684), or BMI (p=0.744). Furthermore, there was no statistically significant correlation between orbital fat volume and age (p=0.520), sex (p=0.934), race (p=0.640), smoking status (p=0.695), or BMI (p=0.700). Overall, EOM and orbital fat volumes showed high correlation with each other (Table 1). However, there was no statistically significant correlation between EOM volumes and CAS (p=0.483) or strabismus (p=0.174); there was also no statistically significant correlation between fat volume and CAS (p=0.514) or strabismus (p=0.163).

Conclusions: There is no significant correlation between orbital soft tissue volumes and patient characteristics (age, sex, race, BMI), and surprisingly no correlation with smoking status (a known risk factor for TED) among patients in our TED cohort. While orbital soft tissue volumes show high correlation with each other, they collectively do not correlate significantly with clinical characteristics such as CAS and strabismus. For CAS, this finding is not entirely unexpected as CAS is a measure of activity rather than severity; for strabismus, this implies there may be qualities other than orbital soft tissue volume which are important in determining strabismus.

CONTROL ID: 3714922

SUBMITTER (NAME ONLY): NITHIN KIRAN

TITLE: Rescue of Lysyl Oxidase levels by Batimastat and Trehalose treatment in human corneal stromal tissue and cell models: implications for Keratoconus therapy

SESSION TITLE: Keratoconus and corneal biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. KIRAN, A. Ghosh, Grow research Lab, Narayana Nethralaya Foundation, Bangalore, karanataka, INDIA|R. Shetty, P. Khamar, Cornea and Refractive surgery, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: Purpose: Keratoconus(KC) is a progressive, corneal, ectatic disorder characterized by increased MMP9 and reduced Lysyl oxidase(LOX) in patients. To rescue LOX expression and inhibit inflammatory signaling, we tested an MMP inhibitor Batimastat(BST) and the inflammation regulator Trehalose(TRE).

Methods: Methodology: Corneal stromal lenticules from donors undergoing SMILE refractive surgeries were treated with TRE and BST for 3 weeks and assessed for expression of LOX, MMP9 and Collagens under chronic inflammatory stress. Primary fibroblasts(HCF) derived from control and KC corneas were analyzed for gene/protein expression and collagen gel contractility when treated with BST/TRE. Human corneal epithelial cells(HCE-T) under chronic inflammation with and without BST/TRE treatment were assessed for LOX, Collagens, MMP9 and phosphorylated MAPK(p38), NFκB(p65) and AKT by immunoblotting.

Results: Results: Inflammatory stimuli significantly enhanced MMP9 and reduced LOX levels in ex-vivo donor stromal lenticules and well as corneal cell types. TRE and BST treatment significantly reduced MMP9 levels which consequently increased LOX and Collagen expression in lenticules under basal and inflammatory stress. Donor control HCF and KC-HCF treated with BST significantly increased LOX levels as well as collagen gel contraction. TRE and BST treatment reduced phosphorylation of p65 and p38 under chronic inflammatory stress in HCE-T cells leading to significantly enhanced LOX and Collagen expression.

Conclusions: Conclusion: Chronic inflammatory signalling including excess MMP9 production transcriptionally suppresses LOX production in corneal stroma. Since TRE and BST rescued LOX and Collagen expression while inhibiting MMP9 via p38 and p65 pathways, they may be a novel therapeutic modality for KC.

CONTROL ID: 3714923

SUBMITTER (NAME ONLY): ZIHE XU

TITLE: Association between a myopia-susceptibility locus within CNGB3 and retinal electrophysiological responses

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. XU, X. Jiang, C.J. Hammond, O.A. Mahroo, P.G. Hysi, King's College London Section of Ophthalmology, London, London, UNITED KINGDOM|Z. XU, C.J. Hammond, P.G. Hysi, King's College London Department of Twin Research and Genetic Epidemiology, London, London, UNITED KINGDOM|X. Jiang, O.A. Mahroo, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinal signalling appears to be important in the process of emmetropisation. A large number of genetic loci associated with myopia risk have now been identified. We explored associations between myopia-risk polymorphisms and light-adapted flicker electroretinogram (ERG) responses recorded in healthy adult twins.

Methods: This study analysed light-adapted 30 Hz flicker ERG peak times recorded in two non-overlapping cohorts recruited from the TwinsUK registry. Cohort 1 comprised 786 genotyped subjects who had undergone non-mydriatic ERG recording with skin electrodes (RETeval system, LKC technologies, Gaithersburg, MD) to stimuli designed to deliver retinal illuminance equivalent to the international standard 30 Hz ERG. Cohort 2 comprised 185 twins who had undergone conventional standard mydriatic 30 Hz ERG recording (Colordome, Diagnosys LLC, Lowell, MA) with conductive fibre electrodes following mydriasis and at least 10 min light adaptation to the standard light-adapting background. Phenotypes were normalised and standardised. Linear mixed models, adjusting for age, sex and familiar relatedness were used to test associations between 334 myopia risk loci and ERG peak times (Cohort 1). Associations of interest were then tested specifically in Cohort 2. We pooled the results from each through a fixed-effect inverse variance meta-analysis.

Results: No genetic associations reached statistical significance after correction for multiple testing in Cohort 1. However, one of the loci reaching nominal significance was rs13268738 (p=0.0148) which is within the CNGB3 gene, encoding one of the subunits of the outer segment cation channel which underlies the cone photoreceptor electrical response to light. This single association was tested in ERGs from Cohort 2 and found to be significant (p=0.00526). The direction of associations was consistent, and it became more statistically significant after a meta-analysis.

Conclusions: Although the association was only nominally significant in Cohort 1, the replication in Cohort 2 strengthens the evidence that this locus is associated with retinal cone-driven flicker responses in healthy individuals. The findings are consistent with alterations in cone-driven signals playing a role in myopia development.

CONTROL ID: 3714925

SUBMITTER (NAME ONLY): Lesley Everett

TITLE: Commercially available, unmodified Octopus perimeters can characterize rod-photoreceptor function in two-color dark-adapted perimetry

SESSION TITLE: Fundamental and Applied Psychophysics and Color Vision

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Everett, A.D. Igelman, P. Yang, M.E. Pennesi, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|J.C. Park, R.A. Hyde, J. McAnany, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Two-color dark-adapted perimetry (2cDAP) is an emerging clinical tool for characterizing the pattern of rod versus cone-dependent deficits across a patient's visual field; 2cDAP has become important in gene-therapy clinical trials given its ability to localize and quantify changes in rod-driven responses. However, custom modifications of static perimeters are often made, limiting their widespread use and comparability across clinical sites. This observational clinical study tested the hypothesis that a commercially available, unmodified Octopus 900-Pro perimeter can characterize rod function by detecting a 2 log-unit difference in retinal sensitivities in healthy subjects between blue and red (450 nm and 610 nm wavelength) stimuli, as expected based upon validated spectral sensitivity curves.

Methods: Ten healthy volunteers with no retinal pathology participated in this IRB-approved study (23-60 years old; 3 females). Subjects were tested with standard (unmodified) Octopus 900-Pro perimeters at the Casey Eye Institute (CEI, n=4) and the Illinois Eye and Ear Infirmary (IEEI, n=6). Testing of the right eye with appropriate refractive correction for measurements within the central 20-degrees of the visual field was performed (left eyes were patched). Fifteen locations from 45^{o} nasal to 60^{o} temporal were tested along the horizontal meridian of the visual field using a Goldmann III stimulus. Testing parameters and statistical analysis were performed as previously described.

Results: An unmodified Octopus 900-Pro perimeter utilized at two clinical sites successfully detected an approximately 2-log difference in threshold values for blue compared to red stimuli outside of the fovea in healthy subjects (Figure 1), which corresponds to the expected difference for rod sensitivity to blue vs red stimuli based on spectral sensitivity curves. In the rod-free fovea, red and blue thresholds were equivalent, consistent with the cone-pathway mediating foveal sensitivity.

Conclusions: Commercially available, unmodified Octopus 900-Pro perimeters may be used to reliably measure rod-photoreceptor function. Thus, custom device modifications are likely not necessary for most clinical and research evaluations of retinal degeneration patients, including potentially for monitoring disease progression and response to gene-based therapies.

CONTROL ID: 3714926

SUBMITTER (NAME ONLY): Ulisse Bocchero

TITLE: Phototranduction noise in rods controlling visual detection threshold.

SESSION TITLE: Photoreceptors and the OPL

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Bocchero, L. Levy, J. Pahlberg, NEI, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The intrinsic noise of the sensory transduction cascade sets fundamental limits for signal detection in sensory neurons. Indeed, the rod phototransduction cascade displays two forms of dark noise called discrete and continuous noise. Thediscrete noise is thought to originate from spontaneous activation of rhodopsin (Rh). Continuous noise has been proposed to be generated in the downstream signaling cascade. Both types of noise have been proposed to limit some aspects of single photon detection in rod photoreceptors. However, it is not clear which form of noise ultimately limits visual perception.

Methods: In our study, we used several mouse strains that express altered concentration of key phototransduction proteins, namely Rh, Transducin (Tr) and phosphodiesterase (PDE6), or a modulatory protein of PDE activity (GARP2 KO mice). We recorded discrete and continuous noise in rods using the single cell patch clamp technique. In the same mice, we analyzed how the synaptic transmission between rods and rod bipolar cells (RBCs) is altered by these manipulations, using the perforated patch technique.

Results:

Rh heterozygous rods indeed express half the amount of Rh, resulting in a reduction of the discrete noise events by half. No alterations of continuous noise were detected in these rods, or in Tr heterozygous mice. On the other hand, halving PDE concentration leads to a significant change in continuous noise. Interestingly, our preliminary results suggest that GARP2 KO mice show a reduction in dark noise, demonstrating the importance of controlling the activity of spontaneous PDE activity for proper single photon detection.

Conclusions: Our results suggest that spontaneous thermal activation of rhodopsin indeed is the source of the discrete noise. Moreover, we demonstrate that continuous noise originates in spontaneous activation of PDE and the cGMP turnover rate. Our mouse models will serve as a critical tool to determine the limiting noise that sets detection threshold in the retina near the absolute limits for vision, currently under investigation.

CONTROL ID: 3714927

SUBMITTER (NAME ONLY): Durga Borkar

TITLE: An EHR-Based Predictive Model to Understand Lost-to-Follow-Up Risk in Patients with Diabetic Retinopathy

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.S. Borkar, M. Hadziahmetovic, Duke University Eye Center, North Carolina, UNITED STATES|C. Xu, B. Goldstein, Duke University, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: Durga Borkar: Commercial Relationship(s);Code C (Consultant/Contractor):Verana Health | Chun Xu: Commercial Relationship: Code N (No Commercial Relationship) | Majda Hadziahmetovic: Commercial Relationship: Code N (No Commercial Relationship) | Benjamin Goldstein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Prior studies have shown that patients with diabetic retinopathy, particularly proliferative diabetic retinopathy, have high rates of becoming lost-to-follow-up (LTFU), as well as worse clinical outcomes after inadvertent treatment lapses. The purpose of this study was to create a predictive model for risk of becoming LTFU after a clinical encounter for diabetic retinopathy using electronic health record (EHR) data.

Methods: EHR data were extracted for all diabetic retinopathy clinical encounters at an academic medical center in Durham, NC from January 1, 2014 to March 15, 2020. Specifically, data on healthcare utilization, demographic factors, and ophthalmic clinical parameters were collected. Information on imaging and therapeutic procedures (i.e. anti-VEGF injection or panretinal photocoagulation) was included. LTFU was determined by diabetic retinopathy stage based on ICD coding and the recommended follow up interval in the AAO Preferred Practice Pattern for diabetic retinopathy. LASSO and random forest models were constructed using LTFU as the outcome using (1) only data available prior to the clinical encounter and (2) data collected during the ophthalmic clinical encounter.

Results: Data for 25,576 clinical encounters for 7,948 patients were extracted. Of these, 12,971 encounters (50.7%) were for proliferative diabetic retinopathy. LASSO and random forest models were created using pre-encounter data, including healthcare utilization and demographic data. Both models had an area under the curve (AUC) of 0.72. A LASSO model utilizing these parameters, as well as ophthalmic factors, had an AUC of 0.74 while the random forest model had an AUC of 0.75. Additional analyses were performed to construct a LASSO model for LTFU by race. While there was some variation, the AUC for all models for racial subgroups were between 0.70 and 0.80.

Conclusions: High performing EHR models for health services utilization typically have an AUC of 0.70 to 0.80. This EHR-based study using structured data fields presents a high performing predictive model to understand risk of becoming lost-to-follow-up for diabetic retinopathy patients. Models involving ophthalmic clinical factors perform slightly better than models considering healthcare utilization and demographic data alone. This study provides further opportunities for direct implementation into clinical care to understand LTFU risk in real time.

CONTROL ID: 3714928

SUBMITTER (NAME ONLY): LUIS F HERNANDEZ

TITLE: Effect of high glucose levels on N-truncated beta amyloid peptides production in the lens capsule of cataract diabetic patients

SESSION TITLE: Lens proteins and cataracts

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. HERNANDEZ, C. Tlapanco, E. Ramirez Hernandez, E. Ucharima, E. Ferreyra, R. Gonzalez Salinas, X. Martínez Santiago, C. Maciel Arias, Research, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|L. HERNANDEZ, Optometria, Universidad Nacional Autonoma de Mexico Escuela Nacional de Estudios Superiores Unidad Leon, Leon, Guanajuato, MEXICO|E. Ramirez Hernandez, School of Medicine, UNAM, Universidad Nacional Autonoma de Mexico, Ciudad de Mexico, Ciudad de México, MEXICO|

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ABSTRACT BODY:

Purpose: To determine the effect of hyperglicemia on the production of N-truncated beta amyloid peptides in the anterior lens capsule from cataracts of diabetic patients

Methods: Informed consent was obtained from all patients. Samples were collected from 40 age-related cortical cataract and diabetic patients over 50 years of age with LOCS II score of nuclear color ≥4 along with 40 age-related cortical cataracts from nondiabetic patients subjects after phacoemulsification surgeries. Lens capsules were processed for immunofluorescence, western blot, immunoprecipitation and ELISA to determine the localization and concentration of Aβ-42, Aβ3-42, and Aβ11-42 peptides in DP and compare them with control cases (non diabetic patients).

Results: The results show the intracellular presence of Aβ-42, Aβ3 -42and Aβ11-42 peptides in cells of the anterior lens capsule, prinncipally from cataracts from DP. Surprisingly, there is a major accumulation and production of Aβ3-42 in capsule lens cells from ARC from DP. These peptides accumulates in the external membrane probably causing mitochondrial damage and it could be related to the development and progression of ARC. Western blot and ELISA assays also shows the presence of Aβ-42, Aβ3 -42and Aβ11-42 peptides. Aβ3 -42and Aβ11-42 peptides concentratioon values demonstrate that there is a statistically differences between ND and DP ($p= 0.017$). Additionally, we detected an increase in the production of pro-inflammatory citokines in cells from ARC from DP.

Conclusions: We show for first time the presence of Aβ42, Aβ3-42, Aβ11-42 peptides in mitochondria and the activation of inflammatory cytokines from tissues affected by the development of ARC from diabetic patients. These AD markers are present in the cells of the anterior lens capsule from ARC of diabetic patients. These markers could be related to the development and progression of ARC an it could be used as an early marker of cognitive imparmeint in aging.

CONTROL ID: 3714931

SUBMITTER (NAME ONLY): Yuvitxa Justiniano-Becerra

TITLE: Retinopathy of Prematurity: 5 years and 715 patients, an Epidemiological Analysis

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.G. Justiniano-Becerra, F. Ramirez-Solis, K. Aguilar-Morales, M. Garcia-Roa, V. Romero-Morales, J.F. Perez-Perez, M. Vazquez, P. Ramirez-Neria, Y. Villalpando-Gomez, Retina, Instituto Mexicano de Oftalmologia I.A.P., Queretaro, Queretaro, MEXICO|

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ABSTRACT BODY:

Purpose: Worldwide 15 million premature infants are born each year, one in ten will develop ROP and Latin America has 40% of cases of childhood blindness. Therefore, epidemiological knowledge is important to implement prevention and screening programs. The purpose of this study is to evaluate the epidemiological characteristics in patients with ROP in a referral ophthalmology center, from January 2016 to December 2021.

Methods: A retrospective, descriptive and observational study was done according to the Screening Guidelines for ROP in Mexico, so patients with a history of gestational age inferior to 34 weeks and/or birth weight lower than 1750g were included; data was collected from an electronic file of The Mexican Institute of Ophthalmology I.A.P. (IMO) in Queretaro, Mexico. The study included infants who received ophthalmologic screening for ROP between January 1, 2016, to December 31, 2021.

Gestational age, birth weight, perinatal history, supplementary oxygen use, maternal history, and staging of ROP were analyzed. incomplete medical records were excluded.

Statistical analysis was performed using the Pearson Statistical Correlation in SPSS IBM 24.0 for windows 10.

Results: 715 patients with a mean gestational age of 35.70 weeks (min 30 max 65, SD 3.80) were included, and mean birth weight of 1595.03gr (min 740 max 2195, SD 330.76), the ROP patients have mature retina in 16.1% and it was immature in 83.9%. The most prevalent ROP stage was 1 with 56.2%, followed by stage 2 with 29.6%, stage 3 with 11.6%, there was only 1.3% for both stage 4A and 4B, and there were no cases in stage 5. The most common zone was 2A in 42.8%. The Pearson test results was a positive correlation in all categories compared with ROP Stage and a negative correlation in all categories compared with the ROP zone.

Conclusions: Currently, the population studied in our institute is in the third wave of ROP, as in India, since we are finding premature babies with higher weight and gestational age and with more retinopathy of prematurity, contrary to what happened in our previous study. It was also found that the lower the gestational age, the more immature retina. It is thought that there are not so advanced stages due to the timely screening we are carrying out and those with a higher stage are because they are referred from other hospitals or private pediatricians. We conclude that screening allows early control and treatment for our population.

CONTROL ID: 3714934
SUBMITTER (NAME ONLY): Mae Gordon
TITLE: Pre- and Post-POAG Rate of Visual Field Progression in the Ocular Hypertension Treatment (OHTS) Study
SESSION TITLE: Clinical studies and trials
SESSION TYPE: Paper Session
AUTHORS/INSTITUTIONS: M.E. Gordon, Opthalmology/Biostatistics, Washington University in St Louis, St Louis, Missouri, UNITED STATES|J.D. Brandt, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|R.K. Parrish II, University of Miami School of Medicine, Miami, Florida, UNITED STATES|C.A. Johnson, University of Iowa, Iowa, UNITED STATES|M.A. Kass, Ophthalmology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|D.K. Heuer, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|E.J. higginbotham, Office of Inclusion and Diversity, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|J. Huecker, Ophthalmology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|J.L. Keltner, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: To compare the rate of visual field (VF) loss (mean deviation dB/year) before and after POAG diagnosis
Methods: 282 participants developed POAG in OHTS 1 and 2. VF tests (30-2 and 24-2 test strategies) HFA were completed every 6 months for 12 years in OHTS 1 and 2 and at 20-year visit in OHTS 3. Diagnosis of POAG required: 1. Reproducible optic disc deterioration and/or VF abnormality as determined by Reading Centers. 2. Attribution of change to POAG by a masked Endpoint Committee. Calculation of pre-POAG slope required at least 3 VF's over 3 years prior to POAG. Calculation of post-POAG slope required at least 3 VF's over 3 years after POAG. Slope coefficient (MD dB/year) was calculated for each eye separately using simple linear regression.
Results: 83% (1,354 of 1,636) of the participants did not develop POAG in either eye in OHTS 1 or 2. The slope of MD from baseline to last f/up visit was -0.07 dB/yr among these participants. 360 eyes of 282 participants developed POAG in OHTS 1 or 2. The mean (SD) age of participants at the time of POAG diagnosis was 66 (10 SD) years, median (range) time to POAG from baseline was 7.0 (0.6 to 14) years and median follow-up after the diagnosis of POAG was 8 years.

66% of 179 participants developed unilateral VF POAG and 34% were bilateral. Mean post-POAG slopes were markedly greater than pre-POAG slopes (Table 1). Mean post-POAG slopes were linear through 20 years of f/up. 41% of the eyes that developed VF POAG progressed at a rate of -0.5 dB/year or more and 23% of these eyes progressed at a rate of -1.0 dB/year or more.
Conclusions: Among eyes that developed POAG, the rate of change in MD dB/year increased substantially after the diagnosis of POAG. The slope of VF loss after the diagnosis of POAG was linear through 20 years.

CONTROL ID: 3714936

SUBMITTER (NAME ONLY): Mary Qiu

TITLE: Dual Blade Goniotomy in Addition to Usual Fenestrating Slits to Enhance Early Intraocular Pressure Lowering in Non-Valved Aqueous Shunt Surgery for Primary Open Angle Glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Qiu, S. Khanna, Z. Si, C. theophanous, Ophthalmology and Visual Sciences, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|C. theophanous, Palo Alto Medical Foundation, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe a single surgeon's experience with dual blade goniotomy in addition to usual fenestrating slits to enhance early IOP lowering in non-valved aqueous shunt (tube) surgery in eyes with primary open angle glaucoma (POAG).

Methods: A retrospective chart review was conducted of all consecutive non-valved tubes with usual fenestrating slits with additional dual blade goniotomy performed by a single surgeon (MQ) between 10/1/2019-10/1/2021 in eyes with POAG. Eyes with prior traditional glaucoma surgery or cyclophotocoagulation were excluded. Three patients were excluded due to missing POW4 data. All cases were Baerveldt-350s and stented with a 3-0 Prolene ripcord, ligated with 7-0 Polysorb, and fenestrated 3 times with a spatulated SE-160-8 needle. This analysis focuses on the early post-operative period between POD1 and POW6 (when the ligature dissolves).

Results: Eleven eyes from 11 patients were included; mean age was 69.2 years, 5/11 were female, 11/11 were African American, 11/11 had severe stage POAG, 6/11 had prior SLT, and 2/11 had prior vitrectomy. Concurrent cataract surgery was performed in 7/11 eyes, the other 4/11 were already pseudophakic. Mean pre-op IOP was 22.2 on 3.9 meds. Mean IOP on POD1 was 17.1 mmHg, mean IOP on POW1 was 16.5 mmHg on 4.0 meds, mean IOP on POW4 was 15.5 mmHg on 4.0 meds. After the ligature dissolved at POW6, mean IOP was 11.2 mmHg on 4.0 meds. Two eyes had hyphemas <=1.0mm at POD1 which resolved by POW1, and there were no reflux hyphemas at POW6 when the ligature dissolved. One eye had IOP spike >30mmHg at POD1 and a different eye had IOP spike at POW1; there were no IOP spikes at POW4 or POW6. No eyes had shallow AC or other hypotony associated complications at any time point.

Conclusions: Excessively large fenestrating slits and/or early ripcord removal in non-valved tubes may carry a risk of hypotony associated complications. We demonstrate our novel surgical strategy of performing a goniotomy at the time of non-valved tubes, in addition to usual small fenestrations, to enhance IOP-lowering in the early postoperative period (POD1-POW6) before the ligature dissolves. The additional goniotomy enhances IOP lowering without risk of hypotony-associated complications, since the additional aqueous outflow from the goniotomy is via the physiologic outflow pathway.

CONTROL ID: 3714937

SUBMITTER (NAME ONLY): Fuyun Bian

TITLE: Functional dissection of Vsx2 cis-regulatory elements during retinal development

SESSION TITLE: Retina Development and Regeneration

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Bian, M. Daghsni, F. lu, J.M. Gross, I. Al Diri, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|S. Liu, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vsx2 is an important and highly conserved transcription factor during retinal development process and its mutations lead to microphthalmia in humans and mice. During early development, Vsx2 is expressed in retinal progenitor cells (RPCs) while later it is exclusively expressed in bipolar neurons and at low levels in Müller glia. How is this precise temporal and spatial pattern of expression achieved during retinal development remains poorly understood. We hypothesized that enhancers should playing an important role in achieving the precise expression of Vsx2.

Methods: Enhancers were tested for their ability to activate expression of reporter genes in developing mouse retinas, using electroporation into retinal explants. We deleted one promising enhancer in mouse using CRISPR/CAS9 technology to examine the functionality of it. Retinas at E14.5 and adult stages were then collected for immunostaining or RNA-seq study.

Results: We identified Vsx2 elements that drive robust reporter expression within the developing retina. Genetic deletion of a Vsx2 enhancer element leads to microphthalmia, recapitulating retinal defects observed in Vsx2-null mutant mice. However, different from Vsx2-null mutant mice, these knock out mice still have bipolar cells. RNA-seq results from E14.5 samples showed that cell proliferation process was affected in the knock-out mice. And these results were further confirmed by immunostaining of EdU and Ki67.

Conclusions: Taken together, our results revealed a cell specific cis-regulatory element which is responsible for the expression of Vsx2 and proliferation of retinal progenitor cells in retinal development. Thus, providing insights onto gene regulatory networks that govern Vsx2 expression during retinal development.

CONTROL ID: 3714938

SUBMITTER (NAME ONLY): Bianca S Gerendas

TITLE: Comparison of diabetic retinopathy severity scores and landmark measurements from ultra-widefield cameras to the gold standard of 7-field color fundus photography

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Gerendas, A. Matakova, F. Goldbach, U. Schmidt-Erfurth, Vienna Reading Center, Department of Ophthalmology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|A. Jakob, U. Schmidt-Erfurth, Vienna Clinical Trial Center, Department of Ophthalmology, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|J. Brugger, Center for Medical Statistics, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

Commercial Relationships Disclosure: Bianca S Gerendas: Commercial Relationship(s);Code C (Consultant/Contractor):Roche, Novartis, Bayer;Code F (Financial Support):Digital Diagnostics | Anastasia Matakova: Commercial Relationship: Code N (No Commercial Relationship) | Felix Goldbach: Commercial Relationship: Code N (No Commercial Relationship) | Astrid Jakob: Commercial Relationship: Code N (No Commercial Relationship) | Jonas Brugger: Commercial Relationship: Code N (No Commercial Relationship) | Ursula Schmidt-Erfurth: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate whether ETDRS DRSS and lesion measurements evaluated in a reading center setting on 4-widefield (WF) and different ultra-widefield (UWF) color fundus photography (CF) images differ from the current gold standard of 7-field CF images.

Methods: Patients with all stages of DR were imaged by an experienced photographer in randomized order according to standardized protocols of the Vienna Reading Center (VRC) with 7-field and 4-WF imaging (Zeiss FF450, mono+stereo) and UWF imaging (Optos California, Zeiss Clarus 700 2-WF protocol and UWF protocol). 6 retina specialists trained for ETDRS DRSS grading at the VRC evaluated the images (with a 7-field mask on each image) in random order. In addition, a different experienced CF grader measured distances of two landmarks seen on images of all modalities of each patient. All final scores were grouped into no/questionable (1), mild (2), moderate (3), severe (4) and proliferative (5) DR (DRSS-G). A logistic regression model with the DRSS-G as the dependent and the camera as the explanatory variable was fitted to investigate whether the grouped score differed from the gold standard and a linear mixed model was calculated to compare measurements.

Results: DRSS-G were distributed as follows: 23%(1); 6%(2); 26%(3); 31%(4); 10%(5). In the logistic regression model, no significant differences between the gold standard and other CF images for the DRSS-G were detected. Landmark distances were 1500-3000µm in size. Statistically significant differences between measurements in the 7-field CF images could be found for different subfields of each UWF camera, but no significant differences were found for 4-WF CF images. The delta of these differences was 5.4-14.5%, lowest in the macula (5.4-5.9%), highest in the superior nasal subfield (12.1-14.5%).

Conclusions: For DRSS-G grading the compared camera models can be used interchangeably in multicenter trials. Landmark measurements of 7-field and 4-WF images are fully comparable, whereas measurements on UWF images must be set into context with the intergrader variability of each landmark. However, it is not recommended to use different camera models for landmark measurements within one patient. Within a multicenter clinical trial using different CF models for different patients, differences may not be clinically relevant in any of the subfields.

CONTROL ID: 3714939

SUBMITTER (NAME ONLY): Matthew Ohr

TITLE: Barriers to Follow-Up After Teleretinal Screening for Diabetic Retinopathy at a Primary Care Site in an Academic Setting

SESSION TITLE: Telehealth

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.P. Ohr, M. Adeli, K. Begley, K. Kopechek, M. Cefalu, N. Challa, M. Whitmeyer, E. Matsa, J. Fulton, K. Hatala, Z. Hanson, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teleretinal screening for diabetic retinopathy has been proven to increase compliance with annual screening. However, appropriate follow-up is needed in patients with abnormal screens in order to ensure treatment of vision-threatening diabetic eye disease and preservation of vision. Few studies have identified patient-specific barriers to follow-up after abnormal screening. This study aims to identify barriers to follow-up beginning at the time of the abnormal screen result through completion of the follow-up visit.

Methods: 184 patients underwent teleretinal screening for diabetic retinopathy during a nine-month period between 2019 and 2020 at a single primary care site at The Ohio State University Wexner Medical Center. These charts were retrospectively reviewed to determine whether a referral to ophthalmology was placed by the ordering physician, an ophthalmology visit was scheduled after referral to ophthalmology was placed, and if the visit was completed for those with ophthalmology visits scheduled.

Results: Of the 184 patients who underwent screening, 80 patients had abnormal screens with recommendations to refer to ophthalmology. Abnormal screens included diabetic retinopathy, as well as other pathology requiring follow-up including retinal tear, choroidal nevus, glaucoma suspect, etc. Of these 80 patients, 60 were referred to ophthalmology. 45 of 60 (75%) patients scheduled appointments. Factors identified as barriers in scheduling appointments include inability to successfully contact patient and patient declining to schedule when contacted. Of the 45 who scheduled appointments, 23 appointments were completed. 17 patients cancelled and 5 patients failed to show for their scheduled appointments.

Conclusions: Overall completion rate of follow-up visit after abnormal teleretinal screen in this study was 29%. While patient factors including lack of clarity in process following screening and cost have been previously identified as barriers to follow-up after teleretinal screening, other factors that impact follow-up include placement of referrals by the ordering physicians, ability to contact patients to schedule appointments, and patients declining to schedule appointments. Further research is necessary to elucidate barriers in placement of referrals, as well as ability to contact patients and successfully schedule appointments after abnormal teleretinal screen.

CONTROL ID: 3714941

SUBMITTER (NAME ONLY): Kristen Kwan

TITLE: Retina-lens detachment: a matrix-mediated step of vertebrate eye development

SESSION TITLE: Retinal Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Kwan, M. Casey, C. Bryan, J. Brown, Human Genetics, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: During eye formation, cells and tissues undergo dramatic movements to generate the precise 3-dimensional structure that is crucial for visual function. We lack a comprehensive understanding of the dynamic cell and tissue interactions governing eye morphogenesis, which have implications for structural malformations underlying vision impairment disorders. To uncover new genetic loci and processes shaping the eye, we carried out a haploid forward genetic screen in zebrafish for eye morphogenesis mutants.

Methods: A zebrafish haploid forward genetic screen was carried out in which the shutdown corner (sco) mutant was isolated. 4D imaging datasets were acquired via confocal microscopy, and cell tracking performed using our LongTracker software. Antibody staining was used to visualize extracellular matrix (ECM). CRISPR mutagenesis was used to screen genes in the deletion interval for their ability to phenocopy the sco phenotype.

Results: In a haploid screen, we isolated shutdown corner (sco), which exhibits an intriguing novel eye morphogenesis defect: the retina and lens make initial contact normally, but then fail to detach, abolishing the space between the retina and lens. Contact between the prospective retina and lens is necessary for reciprocal signaling and coordinated invagination, but how these tissues detach is unknown. The retina-lens space is where the hyaloid vasculature forms: in sco, the hyaloid vasculature exhibits delayed abnormal development. 4D cell tracking of sco mutants reveals that neighboring cells in the retina and lens move normally. ECM molecule deposition (e.g. laminin and hyaluronic acid binding protein) is altered, however, and preliminary transmission election microscopy suggests aberrant features at the retina-lens interface. Subsequent retinal development is impaired. RNAseq analysis revealed a 10 Mb deletion (~100 genes) in sco. Using CRISPR screening in the deletion interval, we identified the causative gene: the chondroitin sulfate proteoglycan versican a (vcana).

Conclusions: The shutdown corner (sco) mutant uncovers a previously unappreciated, genetically regulated step of eye morphogenesis: retina-lens detachment, which is necessary for proper retina and hyaloid vasculature development. The chondroitin sulfate proteoglycan versican is the causative gene, and we are now working to determine the molecular mechanism by which versican facilitates retina-lens detachment.

CONTROL ID: 3714942

SUBMITTER (NAME ONLY): Ravi Parikh

TITLE: Utilization of Crowdfunding for Cataract and Refractive Surgery

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Parikh, Manhattan Retina and Eye Consultants/NYU, New York, UNITED STATES|A. Luu, Touro College, New York, New York, UNITED STATES|D. Vail, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|S.A. Patil, New York University Grossman School of Medicine, New York, New York, UNITED STATES|

Commercial Relationships Disclosure: Ravi Parikh: Commercial Relationship(s);Code C (Consultant/Contractor):Anthem Blue Cross Blue Shield | Amanda Luu: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Vail: Commercial Relationship: Code N (No Commercial Relationship) | Sachi Patil: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the nature of crowdfunding campaigns for common ophthalmologic procedures.

Methods: Out study is a cross sectional, retrospective study of campaigns on GoFundMe.com from January 1st, 2021 to July 31st, 2021. We included all domestic and international campaigns referring to cataract and intraocular lens placement or LASIK procedures, excluding those with non-ophthalmologic conditions or campaigns for multiple conditions. Descriptive analysis of campaigns including condition, country of origin of patient, total and median value raised, total and median value sought, age of the patient, funding goal met, and insurance status when possible.

Results: 137 campaigns were identified, 67.9% (93/137) were for cataract and 32.1% (44/137) were for LASIK. 13.1% (18/137) of campaigns were international. 7.3% (10/137) campaigns were successful at reaching their funding goal. Of the successful campaigns, 70.0% (7/10) were for cataract and 30.0% (3/10) were for LASIK. Total value raised (in USD) was $131,763, where $106,593 was for cataract and $25,170 was for LASIK. The median value sought overall was $5,000, where the median sought for cataract procedures was $5,000 and the median for LASIK was $4,000. The median value raised was $395. 5.8% (8/137) of campaigns mentioned minors. 12.5% (1/8) of campaigns for children or minors were successful at reaching their funding goal, compared to 7.0% (9/129) adult campaigns. The total funds raised for children or minors was $9,224 with a goal of $41,050. The total funds raised for adults was $122,539 out of a goal of $775,617. 14.6% (20/137) campaigns mentioned insurance coverage, of which 85% (17/20) were for cataract and 15.0% (3/20) were for LASIK. Premium lenses (toric, multifocal, etc) were mentioned in 1.1% of campaigns (1/93) as being cost prohibitive.

Conclusions: Crowdfunding is ineffective as a means for patients to raise funds for cataract surgery and LASIK. The broad range of financial requests for cataract surgery, an insurance covered procedure, indicates a large patient knowledge gap in cost for procedures.

CONTROL ID: 3714945

SUBMITTER (NAME ONLY): Vicki Chen

TITLE: In Vivo Confocal Microscopic Evaluation of Patients with Epidermolysis Bullosa to Demonstrate Severe Corneal Nerve Loss: A Case Series

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Chen, L. Yavuz Saricay, S. Galinko, P. Hamrah, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|V. Chen, L. Yavuz Saricay, S. Galinko, P. Hamrah, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Epidermolysis bullosa (EB) is a disease characterized by blistering, scarring, recurrent corneal erosions, and refractory corneal ulcers. Additionally, it presents with early-onset pain and irritation, which is not a usual presentation of disease with severe corneal nerve loss, such as neurotrophic keratopathy. Our aim is to illustrate severe corneal nerve loss using quantitative analysis by in vivo confocal microscopy (IVCM) images in EB patients

Methods: Case reports of five EB patients (ten eyes) who presented with ocular and systemic features of the disease, as confirmed by systemic evaluation and ocular examination. Records of best-corrected visual acuity (BCVA), ocular and periocular involvement, and comprehensive slit-lamp biomicroscopic evaluation, were summarized alongside IVCM findings

Results: The mean age of the patients were 13±3.08 (range 11-18) years. The mean total, main and branch corneal nerve density were 2,201.47 ±3,015.26 (range 0-8,646.64) $\mu m/mm^2$, 965.39 ±1,388.38 (range 0-3,104.53) $\mu m/mm^2$, and 1,236.09±1,893.41(range 0-5,542.11) $\mu m/mm^2$ respectively. This degree of corneal nerve loss is consistent with repeated abrasions and ulcers, which is both the primary factor in EB and a risk factor for neurotrophic keratopathy.

Conclusions: Epidermolysis bullosa is a painful and vision-threatening condition, which causes a significant decline in both quantity and density of corneal nerves. The repeated cycle of abrasion and scarring could play a role in progressive corneal nerve loss, as seen in early-onset EB, but may also be part of the pathogenesis of the disease..

CONTROL ID: 3714946

SUBMITTER (NAME ONLY): Sundaram Natarajan

TITLE: Using Offline Artificial Intelligence in a Smart Phone by a semi skilled workers for screening of Diabetic Retinopathy

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Natarajan, A. Iyer, Vitreo Retinal Surgery, Aditya Jyot Eye Hospital Pvt Ltd, Mumbai, Maharashtra, INDIA|

Commercial Relationships Disclosure: Sundaram Natarajan: Commercial Relationship: Code N (No Commercial Relationship) | Aishwarya Iyer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of the study was to analyse the reliability of an offline artificial intelligence (AI) algorithm for community screening of diabetic retinopathy.

Methods: A total of 1378 patients with diabetes visiting public dispensaries under the administration of the Municipal Corporation of Greater Mumbai between August 2018 and September 2019 were enrolled for the study. Fundus images were captured by non-specialist operators using a smartphone-based camera covering the posterior pole, including the disc and macula, and the nasal and temporal fields. The offline AI algorithm on the smartphone marked the images as referable diabetic retinopathy (RDR) or non-RDR, which were then compared against the grading by two vitreoretinal surgeons to derive upon the sensitivity and specificity of the algorithm.

Results: Out of 1378 patients, gradable fundus images were obtained and analysed for 1294 patients. The sensitivity and specificity of diagnosing RDR were 100% (95% CI: 94.72-100.00%) and 89.55% (95% CI: 87.76-91.16%), respectively; the same values for any diabetic retinopathy (DR) were 89.13% (95% CI: 82.71-93.79%) and 94.43% (95% CI: 91.89-94.74%), respectively, with no false-negative results.

Conclusions: CONCLUSION

The Innovation –

Use of smartphone to take good quality fundus photographs

Portable, Sustainable and cost effective equipment for screening a large population.

Training unskilled workers to make them semi skilled and generating employment among the uneducated youth of India, preventing them from being a burden on society.

Generating semi skilled manpower to screen diabetics in villages. There are 6,64,369 villages in India – screening the population of these villages can be made easy with this model.

Early prevention of diabetic blindness – Screening and early detection of RDR (Referrable DR) by offline AI model can prevent diabetic blindness especially in young or undiagnosed diabetics, who may be the sole breadwinners in the family.

Sustainable model which does not require electricity or internet connectivity to work – best for rural areas.

Equipment can be transported on motorbikes and two wheelers easily.

The robustness of the offline AI algorithm was established in this study making it a reliable tool for community-based DR screening.

CONTROL ID: 3714947
SUBMITTER (NAME ONLY): Yizhen Tang
TITLE: Gut-microglia communication mediates glaucoma neurodegeneration
SESSION TITLE: Neurodegeneration
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: Y. Tang, MEEI, Harvard Medical School, Boston, Massachusetts, UNITED STATES|
Commercial Relationships Disclosure: Yizhen Tang: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Glaucoma neurodegeneration is reported to be associated with microbiota related retinal immune response. While how microbiota regulate the retinal immune response is still unclear.
Methods: Germ-free (GF) mice, specific pathogen free (SPF) mice and microbead-induced glaucoma mouse models were used to study the changes of retinal immune responses following elevated intraocular pressure. Moreover, primary microglia were isolated and stimulated by Lipopolysaccharide (LPS) for 24 h in culture. The cytokine arrays and RNA-seq analysis were performed to characterize the inflammatory responses and gene expression changes of microglia derived from GF and SPF mice.
Results: Retinal microglia of GF mice exhibited much reduced inflammatory responses and neurodegeneration under continuous elevation of intraocular pressure compared to those from SPF mice. LPS-stimulated primary microglia isolated from GF mice also displayed different gene expression profile, showing enriched angiogenesis, cell morphogenesis, and ameboidal-type cell migration-related genes by KEGG terms, when compared with those taken from SPF mice.
Conclusions: These results support that microbiota effect on retinal microglia and glaucomatous neurodegeneration by affecting retinal immune responses. This study provided novel insights and potential therapeutic targets for glaucoma.

CONTROL ID: 3714948
SUBMITTER (NAME ONLY): Hugang Ren
TITLE: Foreground-background registration for angiography fundus images
SESSION TITLE: Machine Learning and Image Processing
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: H. Ren, S. Su, A. Kolli, N. D'Souza, N. Manivannan, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|
Commercial Relationships Disclosure: Hugang Ren: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Susan Su: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Archana Kolli: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Neil D'Souza: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc. | Niranchana Manivannan: Commercial Relationship(s);Code E (Employment):Carl Zeiss Meditec, Inc.

ABSTRACT BODY:

Purpose: The predominant descriptive features of fundus images are the retinal vessels. The performance of a registration algorithm when applied to the fundus angiography images is often not optimal due to the poor contrast of retinal vessels in the early stages of angiography. In this research, we propose a weighted foreground-background registration (FBR) method to improve the performance.

Methods: The workflow of the proposed method is shown in Figure 1. Retinal vessels images (RVI) are detected using first-order derivative of the Gaussian filter in image pairs. Registration is applied in two steps. 1) Coarse registration: Harris corner detection is applied to RVI pairs followed by non-maximal suppression. Feature point matching is done between the RVI pairs and the transformation is applied to form a coarse registered image. 2) Fine registration: Retinal background image (RBI) is computed for the coarse registered image pairs by eliminating the retinal vessels and applying contrast limited adaptive histogram equalization (CLAHE) for simultaneous noise reduction and contrast enhancement. Feature point matching is done between the RBI pairs and the transformation is applied to form a fine registered image.

Fluorescein angiography image sequences from 22 eyes (5 healthy and 17 subjects with various retinal pathologies) were acquired using CLARUS^{TM} 700 (ZEISS, Dublin, CA). Three image pairs from each of the eyes were randomly selected (1 image pair each from early, mid, and late phases) and six landmarks were labeled for each pair of the images [1]. The angular distance between the landmarks in the registered images should be minimal for ideal registration. The mean angular distance (MAD) with and without FBR was calculated for the quantitative evaluation.

Results: Table 1 shows the MAD for image pairs from different angiography phases. With FBR, the performance of the registration is improved by 9.5% in early phase and 7.1% in late phase. In the mid phase, the performance doesn’t show any improvement with FBR.

Conclusions: The proposed FBR algorithm may improve the registration in early and late phase angiography images by augmenting the feature point matching of retinal vessels with histogram equalized background information.

Reference:
[1] Manivannan et al. IOVS 2021; 62(8):1794.

CONTROL ID: 3714949

SUBMITTER (NAME ONLY): Shirley Li

TITLE: Volumetric analysis of orbital fat and extraocular muscles in TED patients vs. normal controls using a novel fully automated atlas-based segmentation method.

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Li, J. Li, J. Lee, A. Rajamohan, J. Acharya, A. Lerner, K. Gokoffski, S. Zhang-Nunes, V. Patel, J. Chang, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|A. Rajamohan, J. Acharya, A. Lerner, V. Patel, USC Department of Radiology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|K. Gokoffski, S. Zhang-Nunes, J. Chang, USC Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|V. Patel, Gavin Herbert Eye Institute, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure: Shirley Li: Commercial Relationship: Code N (No Commercial Relationship) | Joy Li: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Lee: Commercial Relationship: Code N (No Commercial Relationship) | Anandh Rajamohan: Commercial Relationship: Code N (No Commercial Relationship) | Jay Acharya: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Lerner: Commercial Relationship: Code N (No Commercial Relationship) | Kimberly Gokoffski: Commercial Relationship: Code N (No Commercial Relationship) | Vivek Patel: Commercial Relationship: Code N (No Commercial Relationship) | Sandy Zhang-Nunes: Commercial Relationship: Code N (No Commercial Relationship) | Vishal Patel: Commercial Relationship: Code N (No Commercial Relationship) | Jessica Chang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We aim to demonstrate the use of a novel atlas-based segmentation method for orbital soft tissues on normal and thyroid eye disease (TED) patients, and to characterize differences between normal and TED orbits using this method.

Methods: A novel consensus orbital soft tissue atlas was created by iteratively aligning 32 normal individual orbit CT scans with a variety of nonlinear registration protocols and then manually refined. The atlas was then used to identify soft tissue components of normal and TED orbits using a nonlinear registration process. Manual segmentation was used to assess accuracy. T-test was used to compare the two cohorts for each extraocular muscle and orbital fat compartment volumes, as well as to compare the ratio of fat to EOM volume for TED and normal control patients.

Results: Accuracy as determined by the Jaccard index (Intersection over Union, IoU) varied between 0.705 and 0.918 while the mean Dice coefficient ranged from 0.801 to 0.952. Orbit volumes based on 32 normal orbit CT scans and 37 TED orbit scans are summarized in Table 1.

TED orbits demonstrated significantly higher fat ($p = 0.00013$) and total EOM volume ($p = 0.00021$) compared to normal orbits. The ratio of fat to EOM volume was calculated for TED and normal control patients, and the distribution plotted on Figure 1. T-test was used to compare the two cohorts. Of 32 normal orbits compared to 63 TED orbits, the fat to EOM ratio measured 3.37 and 3.36, respectively ($p = 0.82$).

Conclusions: This automated atlas-based process produces accurate segmentation of orbital soft tissue compartments in normal and TED patients. This is the first fully automated segmentation of orbital soft tissue components, allowing for rapid determination of specific soft tissue compartment volume and density on CT, which has many potential clinical and research applications.

There does not seem to be a bimodal distribution of fat to EOM ratio, in contrast to previous publications which have suggested that there are subtypes of TED with primarily fat hypertrophy or primarily muscle hypertrophy. While there may be outliers on either end of the spectrum, the majority of TED patients in our cohort have a similar degree of fat and muscle volume expansion, and a similar ratio compared to normal controls.

CONTROL ID: 3714950

SUBMITTER (NAME ONLY): Michael Puente, Jr.

TITLE: Comparison of delay in diagnosis of congenital cataracts between ethnic groups

SESSION TITLE: Pediatric Ophthalmology Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Puente, Jr., T. Lien, H.V. Neves da Silva, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Michael Puente, Jr.: Commercial Relationship: Code N (No Commercial Relationship) | Tiffany Lien: Commercial Relationship: Code N (No Commercial Relationship) | Helio Neves da Silva: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Congenital cataracts should be removed within the first 6-10 weeks of life to reduce the risk of permanent visual impairment from deprivation amblyopia. However, congenital cataracts are often not diagnosed until a child is months or even years old. Given that racial and ethnic healthcare disparities are known throughout medicine and ophthalmology, we sought to determine whether there was a significant difference in the timeliness of diagnosis of congenital cataracts between ethnic groups at our institution.

Methods: We retrospectively reviewed records of all patients who underwent cataract surgery by a pediatric ophthalmologist at Children's Hospital Colorado from May 2009 to April 2020. We identified children whose cataracts were considered congenital by the diagnosing ophthalmologist and recorded the age at which they were first evaluated by a pediatric ophthalmologist. Using racial and ethnic information provided by each child's family in their medical record, we categorized children into the two categories of non-Hispanic White (NHW) and Racial/Ethnic Minority (REM). We then performed a two-tailed Mann-Whitney U Test to compare the age of diagnosis between the two groups.

Results: A total of 328 cataracts were extracted from 223 children during the study period, with 94 children having been diagnosed with congenital cataracts. Of those 94 children, 43 were non-Hispanic white, 48 were from other racial/ethnic groups, and 3 were of unknown race/ethnicity. The NHW children had a median age at diagnosis of 90 days and a mean age of 583 days, while the REM children had a median age at diagnosis of 159 days and a mean age of 709 days. This difference was not found to be statistically significant by a two-tailed Mann-Whitney U Test (p-value 0.30772).

Conclusions: The majority of children in our study were not referred to a pediatric ophthalmologist until they were already older than the ideal age for cataract surgery, regardless of their race or ethnicity. There was no significant difference in this delay between non-Hispanic white children and children of other racial or ethnic backgrounds. Though our study was limited by its small sample size, it highlights the crucial need to investigate and address the underlying reasons for delayed diagnosis of congenital cataracts. Such efforts should consider disparities in access to healthcare for children from different racial and ethnic backgrounds.

CONTROL ID: 3714952

SUBMITTER (NAME ONLY): Rashmi Dubey

TITLE: CCL26 expression is elevated in the retinal pigment epithelium in atrophic AMD

SESSION TITLE: Microglia in AMD and other immune factors in Retinal Degenerative Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Dubey, S.K. Dubey, K. jung, K. Mohan, M.E. Kleinman, Surgery, East Tennessee State University, Johnson City, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Rashmi Dubey: Commercial Relationship: Code N (No Commercial Relationship) | Sushil Dubey: Commercial Relationship: Code N (No Commercial Relationship) | kyung sik jung: Commercial Relationship: Code N (No Commercial Relationship) | Kabhilan Mohan: Commercial Relationship: Code N (No Commercial Relationship) | Mark Kleinman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age related macular degeneration (AMD) is a degenerative disease of the central retina and the leading cause of irreversible blindness worldwide. We previously reported that CCL26 (eotaxin-3), an inflammatory chemokine, is epigenetically regulated by histone deacetylase-1/2 (HDAC1/2) in human retinal pigment epithelium (hRPE). In this study, we evaluated the expression of CCL11/24/26 (eotaxins-1/2/3) in eyes with atrophic AMD compared to age-matched controls and examined epigenetic regulation of CCL26 in targeted knockout (KO) models of HDAC1/2.

Methods: CCL11/24/26 levels in RPE/choroid tissues of advanced dry AMD patients (n=5) and age-matched controls (n=5) were determined using qPCR and immunohistochemistry (IHC). Viability of hRPE cells (n=3) was evaluated after treatment with different doses of recombinant CCL26 (10, 100, and 1000 ng/ml) for 48h followed by SYTOX staining. RNA samples and cell lysates of HDAC1/2 KO hRPE models generated using short-interfering RNA (siRNA) and CRISPR/Cas9 based approaches were analyzed using qPCR and multiplex bead arrays. HDAC1/2 interaction with the CCL26 promoter was observed using chromatin immunoprecipitation assay. Statistical testing was done (p-value <0.05) using the Mann-Whitney U test.

Results: Posterior segment showed high expression of CCL26, followed by CCL24 and low levels of CCL11. CCL26 mRNA was significantly increased in RPE/choroid (~7-fold change) in atrophic AMD patients compared to controls. IHC in whole eye sections revealed moderate CCL26 expression in the ganglion cell layer (GCL), inner nuclear layer (INL), outer nuclear layer (ONL) in both control and atrophic AMD eyes. However, in atrophic AMD eyes, elevated CCL26 deposition localized to RPE/Bruch's membrane. Human RPE cells treated with CCL26 demonstrated dose-dependent cytotoxicity. HDAC1/2 KO models showed increased CCL26 expression compared to controls. ChIP assay revealed enhanced binding of HDAC1/2 to CCL26 promoter which was blocked by a pan-HDAC inhibitor, valproic acid.

Conclusions: CCL26 expression in RPE/choroid is significantly elevated in atrophic AMD eyes compared to controls and is epigenetically regulated by HDAC1/2. Our results suggest that CCL26 may play a crucial role in the RPE cell death process observed in atrophic AMD. Collectively, our data suggest that selective neutralization of CCL26 may be therapeutically effective in the treatment of atrophic AMD.

CONTROL ID: 3714953

SUBMITTER (NAME ONLY): Vidhya Rao

TITLE: Pooled human immune globulins protect against neutrophil activation

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Mun, S. Jain, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|S. Kaja, R&D Division, Experimentica Ltd, Forest Park, Illinois, UNITED STATES|S. Kaja, Departments of Ophthalmology and Molecular Pharmacology & Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|V. Rao, Department of Ophthalmology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Vidhya Rao: Commercial Relationship: Code N (No Commercial Relationship) | Christine Mun: Commercial Relationship: Code N (No Commercial Relationship) | Sandeep Jain: Commercial Relationship(s);Code C (Consultant/Contractor):Neutrolis Inc, Ocugen Inc, Roche, GlaxoSmithKline;Code O (Owner)::Advaite Inc, Selagine Inc;Code P (Patent):PCT/US19/60566 | Simon Kaja: Commercial Relationship(s);Code C (Consultant/Contractor):Experimentica Ltd;Code P (Patent):eyeNOS, Inc.;Code F (Financial Support)::Experimentica Ltd., K&P Scientific LLC;Code I (Personal Financial Interest):Experimentica Ltd., K&P Scientific LLC;Code R (Recipient):Experimentica Ltd., K&P Scientific LLC;Code S (non-remunerative):Experimentica Ltd., K&P Scientific LLC

ABSTRACT BODY:

Purpose: Our previous studies have demonstrated the presence of anti-citrullinated protein autoantibodies (ACPA) in ocular surface washes from patients with autoimmune dry eye disease (DED). Moreover, autoimmune DED was responsive to treatment with pooled human immune globulin (pooled IgG) eye drops. The purpose of this study was to develop a plate reader-based in vitro assay to evaluate therapeutics targeting neutrophil activation and neutrophil extracellular traps formation (NETosis). Specifically, the efficacy of pooled IgG in preventing neutrophil activation and NETosis were assessed.

Methods: Primary human neutrophils (HemaCare) were maintained in phenol red-free RPMI1640 media supplemented with 10% fetal bovine serum. 1×10^5 neutrophils were seeded into black/ clear bottom 96-well plates (FIAv plates, Greiner Bio) and stained with 1 µM SYTOX green (S7020, Thermo Fisher Scientific), a fluorescent dye that is impermeant to live cells and has a high affinity to nucleic acid. Subsequently, cells were allowed to settle for 20 min and subsequently stimulated with either phorbol 12-myristate 13-acetate (PMA; 100 nM; 79346, Sigma-Aldrich), or anti-histone 4 R3 ACPA (H4R3 ACPA; 100 ng/mL; Abcam, #ab81797). Fluorescence of extracellular NET-bound SYTOX Green (excitation λ: 488 nm, emission λ: 510 nm) was measured every 30 min for a period of 72 h using a microplate reader (Cytation 5, Biotek Instruments) at 37°C. Dose-responses (0.001 – 4%) of pooled human IgG diluted in saline (Flebogamma) were tested for the ability to inhibit NETosis.

Results: H4R3 ACPA resulted in ~2-fold increased SYTOX Green fluorescence over a 72 h period indicating neutrophil activation and NETosis. The level of NETosis elicited by H4R3 ACPA was similar to activation by PMA. Pooled IgG resulted in a dose-dependent decrease in SYTOX Green fluorescence that could be fitted with a fourth parameter non-linear regression ($R^2 = 0.95$). 1% pooled IgG reduced SYTOX Green fluorescence to 115.4 ± 10.9% (mean ± S.D.) of control for H4R3 ACPA-induced NETosis and 99.6 ± 9.1 % (mean ± S.D.) for PMA-induced NETosis.

Conclusions: The plate reader-based SYTOX Green assay provides a standardized platform for testing NETosis-targeted therapeutics. Pooled IgG exert potent protection against ACPA-induced NETosis in vitro. Our findings confirm observations from our previous studies that have shown improvement of ocular surface pathology following Pooled IgG administration.

CONTROL ID: 3714954

SUBMITTER (NAME ONLY): Dibyendu Pusti

TITLE: Localized peripheral choroidal response to signed defocus with and without native aberration

SESSION TITLE: Myopia and refractive error development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Pusti, G. Yoon, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure: Dibyendu Pusti: Commercial Relationship: Code N (No Commercial Relationship) | Geunyoung Yoon: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Unlike the defocus-dominated central retina, peripheral ocular optics are affected further by astigmatism and complex higher-order aberrations that cause apparent directional blur in an image formed on the retina. The peripheral choroidal response to defocus may differ from the fovea. Hence, we aim to evaluate peripheral choroidal response to short exposure of defocus signals with and without the presence of peripheral native aberrations.

Methods: The temporal 15° retina was exposed for 30 min with a video stimulus (±4° horizontal & ±3° vertical visual field), providing a wide range of time-varying spatial frequency and contrast without exposing the foveal region. The fellow eye was used to fixate at the eccentric fixation target. We used a custom-built adaptive optics (AO) visual simulator to induce pure defocus with and without correcting peripheral ocular aberrations. Four subjects with cycloplegia underwent four separate sessions: AO-controlled myopic defocus (AO-Myo), AO-controlled hyperopic defocus (AO-Hyp), myopic defocus without AO (NoAO-Myo), & hyperopic defocus without AO (NoAO-Hyp). The choroidal thickness (ChT) was measured using Heidelberg Spectralis OCT. ChT in the peripheral retina exposed to the defocus and at the fovea was captured at 0, 10, 20, & 30min exposure time points. The response is represented by the averaged ChT change from baseline measurement.

Results: All tested optical conditions showed a bi-directional ChT alteration at the peripheral exposed ocular region, in which myopic and hyperopic defocus caused choroidal thickening and thinning, respectively. On average, AO-controlled conditions showed more significant ChT change from the baseline (AO-Myo: 10.67±9.89μm, AO-Hyp: -9.77±6.58μm) compared to those without AO (NoAO-Myo: 5.53±6.88μm, NoAO-Hyp: -0.55±5.26μm). The highest ChT alteration was seen at 20min (7.53% thickening) & 30min (-6.97% thinning) under AO-Myo and AO-Hyp conditions respectively. The unexposed foveal region showed insignificant thickness alteration under all test conditions.

Conclusions: Peripheral complex blur signals due to astigmatism and higher-order aberrations reduced the choroidal response to both signs of defocus compared to the pure defocus exposure with AO. The choroidal response remains localized to the defocus exposed region.

CONTROL ID: 3714956

SUBMITTER (NAME ONLY): Allen Ho

TITLE: Safety and Efficacy of a Phase 1/2a Clinical Trial of Transplanted Allogeneic Retinal Pigmented Epithelium (RPE, OpRegen) Cells in Advanced Dry Age-Related Macular Degeneration (AMD)

SESSION TITLE: Retinal Prostheses and Transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.C. Ho, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|A.C. Ho, Mid Atlantic Retina, Philadelphia, Pennsylvania, UNITED STATES|E. Banin, T. Jaouni, Hadassah Medical Center Department of Ophthalmology, Jerusalem, Jerusalem, ISRAEL|A. Barak, Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|D.S. Boyer, Retina Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|R. Ehrlich, Rabin Medical Center Ophthalmology Division - Beilinson and Hasharon, Petah Tikva, Central, ISRAEL|H. MacDonald, West Coast Retina Group, San Francisco, California, UNITED STATES|C.D. Riemann, Cincinnati Eye Institute, Cincinnati, Ohio, UNITED STATES|D. Telander, Retinal Consultants Medical Group, Sacramento, California, UNITED STATES|J. Mones, Ophthalmology, Institut de la Màcula, Barcelona, SPAIN|J. Mones, Barcelona Macula Foundation, Barcelona, SPAIN|A.B. Shabat, Lineage Cell Therapeutics, Inc (Cell Cure Neurosciences), Jerusalem, ISRAEL|G.S. Hogge, Lineage Cell Therapeutics, Inc., Carlsbad, California, UNITED STATES|B. Reubinoff, Center for Embryonic Stem Cells and the Department of Gynecology and Obstetrics, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|

Commercial Relationships Disclosure: Allen Ho: Commercial Relationship(s);Code C (Consultant/Contractor):Adverum, Aerie, AGTC, Alcon Laboratories Inc, Aldeyra, Allergan, Apellis, Asclepix, Atsena, Beaver-Visitec International Inc, Chengdu Kanghong Biotechnology, Clearside, Dompe, Eyevensys, Genentech, Graybug, Gyroscope Therapeutics Ltd, Iveric, Janssen/Johnson & Johnson, Kiora, Lineage Cell Therapeutics Inc, Notal, Ocular Therapeutics, ONL, Oxular, Regeneron Pharmaceutics Inc, RegenXBio ;Code F (Financial Support):Adverum, Aerie, AGTC, Alcon Laboratories, Aldeyra, Allergan, Apellis, Asclepix, Atsena, Chengdu Kanghong Biotechnology, Genentech, Graybug, Gyroscope Therapeutics Ltd, Iveric, Janssen/Johnson & Johnson, Kiora, Lineage Cell Therapeutics Inc, Lumithera, National Eye Institute, Notal, Novartis, ProQR, Regeneron Pharmaceutics Inc, RegenXBio;Code O (Owner):Covalent Medical LLC, Gyroscope Therapeutics Ltd, Kiora, ONL, | Eyal Banin: Commercial Relationship(s);Code C (Consultant/Contractor):Lineage Cell Therapeutics, Cell Cure Neurosciences;Code F (Financial Support):Lineage Cell Therapeutics, Cell Cure Neurosciences;Code P (Patent):Lineage Cell Therapeutics, Cell Cure Neurosciences | Adiel Barak: Commercial Relationship(s);Code F (Financial Support):Lineage Cell Therapeutics Inc, Cell Cure Neurosciences | David Boyer: Commercial Relationship(s);Code C (Consultant/Contractor):Lineage Cell Therapeutics Inc;Code F (Financial Support):Lineage Cell Therapeutics Inc | Rita Ehrlich: Commercial Relationship(s);Code F (Financial Support):Lineage Cell Therapeutics Inc, Cell Cure Neurosciences | Tareq Jaouni: Commercial Relationship(s);Code F (Financial Support):Lineage Cell Therapeutics Inc, Cell Cure Neurosciences | H Richard MacDonald: Commercial Relationship(s);Code F (Financial Support):Lineage Cell Therapeutics Inc | Christopher Riemann: Commercial Relationship(s);Code C (Consultant/Contractor):Lineage Cell Therapeutics Inc;Code F (Financial Support):Lineage Cell Therapeutics Inc | David Telander: Commercial Relationship(s);Code F (Financial Support):Lineage Cell Therapeutics Inc | Jordi Mones: Commercial Relationship(s);Code C (Consultant/Contractor):Lineage Cell Therapeutics Inc and Cell Cure Neurosciences | Avi Shabat: Commercial Relationship(s);Code E (Employment):Lineage Cell Therapeutics Inc, Cell Cure Neurosciences | Gary Hogge: Commercial Relationship(s);Code E (Employment):Lineage Cell Therapeutics Inc | Benjamin Reubinoff: Commercial Relationship(s);Code F (Financial Support):Lineage Cell Therapeutics Inc, Cell Cure Neurosciences;Code P (Patent):Lineage Cell Therapeutics Inc, Cell Cure Neurosciences;Code C (Consultant/Contractor):Lineage Cell Therapeutics, Cell Cure Neurosciences

ABSTRACT BODY:

Purpose: Transplanted healthy RPE cells may benefit AMD patients. We created allogenic RPE cells (OpRegen) using directed differentiation. Safety and tolerability of OpRegen is being evaluated in a Phase 1/2a clinical study in patients with dry AMD and geographic atrophy (GA) (NCT02286089). We report safety and imaging data from the primary endpoint for all patients (N=24).

Methods: Subretinal transplantation of 50-200k OpRegen cells in suspension were delivered to the worse vision eye via pars plana vitrectomy (PPV) and retinotomy (n=17) or via a suprachoroidal route (n=7). Short course, perioperative systemic immunosuppression was used. Endpoints include systemic/ocular safety and retinal structure/function.
Results: Patients in cohorts 1-3 (<20/200) have completed (4/12), entered long-term follow-up (F/U) (6/12; 3-5 yrs) or withdrawn (2/12). Cohort 4 patients (<20/64) continue in F/U (11/12; 1-3 yrs, 1 withdrawal). OpRegen has been well tolerated to date, with no unexpected adverse events (AEs). Using PPV, the most common ocular AEs were mild to moderate epiretinal membranes (ERM) (15/17; 88%); 3 (18%) severe ERM required surgical peeling. Two PPV-treated patients (2/17; 12%) developed retinal detachments, which were successfully treated. In patients treated via a suprachoroidal route, 3 mild AEs of CNV were reported; one successfully treated with a single anti-VEGF injection; 2 responsive to regular administration. Disease in cohorts 1-3 typically progressed as expected in advanced GA. However, in cohort 4 patients, improvement or maintenance of baseline visual acuity has been noted in 9/12 (75%) (-2 to +24 letters). Treatment effects, including alterations in drusen appearance, subretinal pigmentation and hyper-reflective areas, suggest persistence of transplanted OpRegen. Patients with atrophic areas extensively covered by the subretinal surgical bleb containing the cell suspension (4/12) have potential signs of outer retinal restoration and reduction in GA area based on OCT analyses of the periphery of the GA compared to baseline imaging.
Conclusions: Subretinal transplantation of OpRegen cells in dry AMD and GA patients appears well tolerated. Imaging findings suggest presence of transplanted cells in the subretinal space. Encouraging structural and clinical changes observed in some patients are being followed.

CONTROL ID: 3714957

SUBMITTER (NAME ONLY): Roya Garakani

TITLE: Comparing outcomes of photoablative refractive surgery in patients evaluated by ophthalmology residents, cornea-refractive fellows, and attending surgeons

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Garakani, L. Tran, S. Dawood, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|R. Haddadin, Ophthalmology, Northwestern University Department of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Roya Garakani: Commercial Relationship: Code N (No Commercial Relationship) | Lillian Tran: Commercial Relationship: Code N (No Commercial Relationship) | Sherif Dawood: Commercial Relationship: Code N (No Commercial Relationship) | Ramez Haddadin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate postoperative visual outcomes in patients treated with photoablative refractive surgery, including photorefractive keratectomy (PRK) and laser-assisted in situ keratomileusis (LASIK), at a teaching institution with trainee involvement in preoperative planning.

Methods: This is a retrospective chart review of patients (age 22 to 57) treated with photoablative refractive surgery, including PRK and LASIK, from 11/2/2018 to 3/29/2021 at Cook County Health. Preoperative evaluation, surgery, and postoperative visits were conducted for each patient. All cases with trainee involvement were supervised by an attending surgeon. Follow-up examinations were performed at 1 day, 1 week, 1 month, and 3 months or greater postoperatively. The primary outcome measure is final postoperative visual acuity at 3 months or greater.

Results: 147 eyes of 74 patients were evaluated. 89 eyes were treated with PRK and 58 eyes were treated with LASIK. Average preoperative spherical equivalent was -3.63D (range -8.75D to +5.50D). Final postoperative uncorrected visual acuity (UCVA) of 20/25 or better was seen in 90.48% of eyes (133 of 147 total eyes). UCVA of 20/25 or better was achieved in 93.18%, 89.47%, and 89.13% of eyes that were preoperatively evaluated by resident trainees (RES), cornea-refractive fellow trainees (FEL), and attending surgeons (ATT), respectively. When separated by type of procedure, eyes that were preoperatively evaluated by the RES group achieved UCVA of 20/25 or better in 93.94% and 90.91% in the PRK and LASIK groups, respectively. Five eyes required postoperative enhancements - 3 out of 44 from the RES group, 0 out of 57 from the FEL group, and 2 out of 46 from the ATT group. No patients had significant postoperative complications.

Conclusions: Residents and fellows can safely and effectively be involved in preoperative planning for photoablative refractive surgery with excellent outcomes, comparable to that of attendings.

CONTROL ID: 3714958

SUBMITTER (NAME ONLY): Yevgeniy Sazhnyev

TITLE: Choroidal Changes in Rhesus Macaques in Aging and Age-Related Drusen

SESSION TITLE: AMD - Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Sazhnyev, A. Ma, E. Chang, L. Huynh, S. Park, K. Choy, S. Farsiu, A. Moshiri, S.M. Thomasy, G. Yiu, Department of Ophthalmology & Vision Science, University of California Davis, Davis, California, UNITED STATES|Y. Sazhnyev, A. Ma, Department of Ophthalmology, California Northstate University College of Medicine, Elk Grove, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Choroidal vascular changes occur with normal aging and may also be associated with retinal diseases such as age-related macular degeneration (AMD). Here, we evaluate choroidal thickness and vascularity in rhesus macaques across their adult lifespan, and in animals that exhibit soft drusen, to determine the potential role of the choroid in the pathogenesis of this nonhuman primate model of AMD.

Methods: We analyzed spectral domain-optical coherence tomography (SD-OCT) images of 234 eyes from 117 rhesus macaques (range 4 - 32 years of age). Sub-foveal choroidal thickness (CT) measurements were performed using the Heidelberg Explorer software, while choroidal vascularity was measured by binarization using Niblack's auto-local threshold to measure total choroidal area (TCA) and luminal area (LA), and to calculate stromal area (SA) and choroidal vascular index (CVI). Regression analyses were used to determine the relationship between CT and CVI with age, while Student's t-tests were used to detect differences in CT and CVI in the presence or absence of soft drusen.

Results: Sub-foveal CT decreases with age at 3.2 μm/year (R^2 = 0.481, P < 0.001), while CVI also decreases over time at 0.67% per year (R^2 = 0.275, P < 0.001). Eyes with soft drusen exhibited thicker choroid (171.5 μm ± 12.2 μm vs. 137.4 μm ± 12.2 μm, P < 0.001) and higher CVI (0.606 ± 0.041 vs. 0.459 ± 0.107, P < 0.001) than age-matched control animals. In eyes with drusen, neither CT or CVI appear to be associated with drusen number, size, or volume.

Conclusions: Changes in choroidal vascular architecture in rhesus macaques resemble choroidal changes in human aging, although the relationship with age-related soft drusen in these animals appears less clear when compared to AMD in humans. The relative contribution of the choroid to drusen pathogenesis in monkeys may be different from its role in human AMD.

CONTROL ID: 3714960

SUBMITTER (NAME ONLY): Jennings Luu

TITLE: Absence of PP2A accelerates retinal degeneration in GRK1- and Arr1-deficient mice

SESSION TITLE: Retinal metabolism and physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Luu, H. Jin, Pharmacology, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|J. Luu, A. Kolesnikov, K. Palczewski, V.J. Kefalov, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A critical, yet often-overlooked, step enabling efficient perception of light is the dephosphorylation of rhodopsin, mediated by protein phosphatase 2A (PP2A). PP2A deficiency has been reported to impair rhodopsin regeneration after phosphorylation by rhodopsin kinase (GRK1) and arrestin (Arr1), thereby delaying rod dark adaptation, although its effects on the viability of photoreceptors in the absence of GRK1 and Arr1 remain unclear. Here, we investigate the effects of PP2A deficiency in the absence of GRK1 or Arr1, both of which have been implicated in Oguchi disease, a form of night blindness.

Methods: We utilized a rod-specific mouse line lacking the predominant catalytic Cα-subunit of PP2A, which was crossed with $Grk1^{-/-}$ or $Arr1^{-/-}$ strains to obtain corresponding double knockout lines. To evaluate rod function, mice were dark adapted overnight for ex-vivo transretinal electroretinography (ERG). To assess rod photoreceptor viability, histological cross-sections of retina were stained with hematoxylin and eosin, and spider plots were generated by manual counting of photoreceptor nuclei in the outer nuclear layer at fixed distances from the optic nerve head.

Results: PP2A deficiency alone did not impair photoreceptor viability up to 12 months of age. Ex-vivo ERG revealed rod function in $Arr1^{-/-}$ mice was reduced by approximately 80% at 3 months, and this effect was exacerbated by an additional ~10% with concomitant PP2A deficiency. $Arr1^{-/-}$ mice exhibited mild retinal degeneration of approximately 10-15% relative to age-matched controls, and concomitant PP2A deficiency accelerated degeneration by an additional 10% at 6 months but not at 3 or 12 months of age. Histological and spider plot analyses in $Grk1^{-/-}$ mice revealed retinal degeneration of approximately 20% relative to age-matched controls at each time point, which was exacerbated up to an additional 10% with concomitant PP2A deficiency.

Conclusions: Our results demonstrate that deficiency of PP2A in the absence of Arr1 results in further suppression of rod responses. Moreover, while PP2A is not required for survival of rod photoreceptors, its deletion accelerates the degeneration induced by inefficient inactivation of rhodopsin in the absence of either GRK1 or Arr1. Further mechanistic studies will be required to delineate the pathways involving protein dephosphorylation by PP2A pertinent to retinal degenerative diseases causing blindness.

CONTROL ID: 3714961

SUBMITTER (NAME ONLY): Reena Bapputty

TITLE: High glucose modulates thyroid hormone levels in mouse retinal cells

SESSION TITLE: Biochemistry and Molecular Mechanisms of Diabetic Retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Bapputty, R.A. Gubitosi-Klug, Pediatric Endocrinology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|H. Sapa, Nephrology and Hypertension, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|M. Miyagi, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior investigations demonstrated that iodothyronine deiodinase (Dio2) gene expression, the enzyme that converts thyroxine (T4) to triiodothyronine (T3), is decreased in the mouse retina during diabetes. As well, exogenous T3 supplementation of primary mouse retinal endothelial cells (mREC) in culture prevented high-glucose induced cell death. Yet, investigations of Dio2 function in mREC under high glucose conditions and the mechanism underlying thyroid hormone effects on the retinal microvasculature have not been studied.

Methods: T4 and T3 were simultaneously quantified by liquid chromatography-tandem mass spectrometry. mREC were cultured in physiologic (5 mM) or high glucose (30 mM). Cell lysates were analyzed after five days in culture for T4 and T3 concentrations. Endothelial nitric oxide synthase (eNOS) was detected in cell lysates by western blotting.

Results: When mREC were grown in the presence of high glucose, intracellular production of T3 decreased and T4 increased leading to a significantly increased T4/T3 ratio (P=0.007) when compared to cells grown in physiologic glucose. Supplementation of cells with T3, but not T4, increased T3 in mREC (P=0.007), consistent with suppressed Dio2 function under high glucose. Similarly, T3, but not T4, supplementation prevented the high glucose-induced rise in eNOS level (P=0.03).

Conclusions: Our study indicates that high glucose during diabetes may cause decreased intracellular T3 concentrations in retinal cells and that may lead to alterations in vascular tone and function, thereby contributing to the pathogenesis of diabetic retinopathy.

CONTROL ID: 3714962

SUBMITTER (NAME ONLY): Arkasubhra Ghosh

TITLE: Regulation of epithelial to mesenchymal transition (EMT) and chemoresistance in advanced Retinoblastoma tumors by miR-181a

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ghosh, V. babu, Narayana Nethralaya Foundation, Bangalore, INDIA|

Commercial Relationships Disclosure: Arkasubhra Ghosh: Commercial Relationship: Code N (No Commercial Relationship) | Vishnu babu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Advanced retinoblastoma (Rb) tumors, if neglected can metastasize through the optic nerves to distant tissues and cause potent threat to vision and life. Since tumor metastasis by the epithelial to mesenchymal transition(EMT) also confers chemotherapy resistance, it is critical to understand this process in Rb tumors.

Methods: Transcriptomic analyses were performed on Rb tumor samples (n=9) & paediatric control retina (n=2) to identify EMT specific genes and microRNAs. Q-PCR & western blot was performed on WERI-Rb1 cells, under RB1 null & RB1 over expression, to assess EMT related miRNAs, genes & protein expression. Validation was performed by immunochemistry in tumor sections. Functions of miR-181a on tumor pathways were assessed using mimics and antagomirs.

Results: We found EMT and drug resistance genes to be differentially regulated in advanced and non-advanced Rb tumors compared to healthy pediatric controls ($P<0.05$, $FC>2$). EMT transcription factors ZEB1, SNAI2, Twist and drug resistance genes MDR1, CTSL were significantly upregulated in advanced tumors. ZEB1, SNAI2, MDR1 protein expression was higher in Rb tumor tissues. Reduced miR-181a observed in advanced Rb tumors inversely correlated with EMT and drug resistance genes. RB1 overexpression or miR-181a mimics significantly reduced cancer and EMT hallmarks. MiR-181a mimic enhanced chemosensitivity and reduced proliferative capacity of Rb null lines.

Conclusions: EMT and chemoresistance in advanced Rb tumors is characterised by higher expression of ZEB1, SNAI2, MDR1, CTSL, etc which mediate invasion and metastasis. MiR-181a transcriptionally controls the EMT program, reducing proliferation/invasion and enhances chemosensitivity, highlighting its potential for therapeutic applications.

CONTROL ID: 3714963

SUBMITTER (NAME ONLY): Irene Santiago Tierno

TITLE: Impaired neovascularization by choroidal endothelial cells from a monkey model of early age-related macular degeneration

SESSION TITLE: Vascular Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chandrakumar, M. Agarwal, K. Ghosh, Doheny Eye Institute, Pasadena, California, UNITED STATES|I. Santiago Tierno, S. Chandrakumar, M. Agarwal, K. Ghosh, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|I. Santiago Tierno , Molecular, Cellular, and Integrative Physiology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The early stage of age-related macular degeneration (AMD) is marked by loss of choriocapillaris and choroidal vessels, which leads to outer retinal hypoxia and subsequent pathological choroidal neovascularization (wet AMD). In health, endothelial cells (ECs) efficiently form new vessels to replace those lost to injury. Thus, here we investigated whether choroidal ECs from early AMD eyes lose their neovascularization potential and, if so, what potential mechanisms might underlie this impaired functional response.

Methods: Choroidal ECs were isolated from young normal (YN; 6 yrs old), old normal (ON; 20 yrs old), and old-drusen-laden (AMD; 19 yrs old) eyes of rhesus monkeys and plated at 20,000 cells/cm^2 on the surface of regular or type 2 (higher stiffness) Cultrex® basement membrane (10 mg/mL) in starvation medium composed of basal medium supplemented with 0.5% fetal bovine serum and antibiotics. Further, choroidal ECs isolated from the peripheral regions of AMD eyes were also compared with their corresponding macular counterparts. Images of capillary-like structures were obtained at 12h using a Zeiss Axio Observer 7 epifluorescence microscope, and total chord length per unit area was quantified using ImageJ.

Results: Our findings revealed that, of the three groups of choroidal ECs, those from AMD eyes exhibited the lowest neovascularization potential, which was 15% ($P<0.05$) or 48% ($P<0.05$) lower than their YN or age-matched ON counterparts, respectively. Notably, peripheral ECs from AMD eyes formed significantly (~1.6-fold; $P<0.05$) longer chord structures than their macular counterparts. Interestingly, the superior chord formation ability of YN ECs was substantially reduced on basement membrane of lower stiffness.

Conclusions: These studies show that choroidal ECs from early AMD eyes, and specifically those from the macula, exhibit poor neovascularization potential, which may explain their inability to replace the degenerating choroidal vessels in early AMD. Further, the observation that chord formation was impaired on softer basement membrane indicates a potential role of mechanotransduction in the observed differences in chord formation. Ongoing studies are aimed at further elucidating the molecular mechanisms underlying these spatial (macular vs peripheral) and temporal (young vs AMD) differences in neovascularization potential.

CONTROL ID: 3714964

SUBMITTER (NAME ONLY): Shyamanga Borooah

TITLE: Characterization of Danon disease human induced pluripotent stem cell derived retinal pigment epithelial cells

SESSION TITLE: Stem cells and disease modeling in vitro

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Borooah, K. Huffman, Ophthalmology, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|P. Bushway, J. Fong, Y. Yacoubian, E. Adler, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Danon disease (DD) is a rare X-linked syndromic disorder resulting from mutations in the gene LAMP2 leading to dysfunctional autophagy. The exact contribution of lysosome-associated membrane protein 2 (LAMP2) deficiency to retinal degeneration in human DD remains unclear. We performed a phenotypic and functional characterization of human-induced pluripotent cell (hiPSC) derived RPE (hiPSC-RPE) cells possessing harboring a frameshift insertion in exon 2 of LAMP2 to better understand the pathogenesis of retinopathy in DD.

Methods: HiPSCs were generated using Sendai virus expression of Yamanaka factors in donor cells from an affected male patient with DD and unaffected control patient. The hiPSCs were differentiated to hiPSC-RPE using our in house protocol. We performed basic hiPSC-RPE characterization using immunostaining, electron microscopy (EM), rod outer segments (ROS) phagocytosis and autophagy analyses by performing LC3-II immunostaining and western blot as well as qPCR for LAMP2 isoforms

Results: Both DD and control hiPSC-RPE demonstrated expression of ZO-1, MITF, Bestrophin-1 and CRALBP RPE markers. Control hiPSC-RPE demonstrated a significantly greater expression of LAMP2A ($p<0.001$) and 2B ($p<0.001$) isoforms compared with 2C (Fig 1).

Phagocytosis of ROS in Danon hiPSC-RPE cells at 6 hours (21.4±18.9 ROS) was significantly greater ($p<0.05$) compared to control hiPSC-RPE cells (45.7±6.6 ROS) Western blot found no significant difference in LC3-II expression between the DD line and control line under normal conditions but did find a significant difference under conditions promoting autophagy including serum starvation ($p<0.05$) and under conditions blocking fusion of the autophagsomes and lysosome with the addition of hydroxychloroquine ($p<0.01$)(Fig 2).

Conclusions: Functional hiPSC-RPE were successfully differentiated from both a DD and control hiPSC line. Our findings suggest that there is a cell specific isoform expression signature in RPE. In addition, autophagic flux is impaired in DD hiPSC-RPE under stress, likely resulting in autophagosome accumulation and our finding of increased ROS preservation. These disease-relevant in vitro phenotypic markers will assist testing of approaches aimed at treating DD and other diseases in which LAMP2 deficiency is implicated. Further studies, with additional lines will be helpful to confirm these early findings.

CONTROL ID: 3714965

SUBMITTER (NAME ONLY): swathi somisetty

TITLE: OCT angiography to assess outcomes of type 1 macular neovascularization in eyes with treatment naïve exudative AMD

SESSION TITLE: Anti-VEGF in AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. somisetty, E. Bousquet, A. Santina, V. Romero Morales, N. Abraham, D. Sarraf, Retinal Disorders and Ophthalmic Genetics Division, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|D. Sarraf, Greater Los Angeles VA Healthcare Center, Los Angeles, California, UNITED STATES|E. Bousquet, Department of Ophthalmology, Ophtalmopôle, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, AP-HP, Université Paris 5, Sorbonne Paris Cité, Paris, FRANCE|V. Romero Morales, Instituto Mexicano de Oftalmologia I.A.P., MEXICO|

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ABSTRACT BODY:

Purpose: OCT angiography is a very important tool to detect macular neovascularization (MNV) but its value would be further strengthened by providing prognostic information. The aim of this study was to evaluate the outcomes of eyes with treatment naïve exudative age-related macular degeneration (AMD) based on baseline OCT angiography (OCT-A) morphology of type 1 MNV.

Methods: This was a retrospective study of treatment naïve AMD patients that developed exudative disease. MNV was classified as “distinct” or “indistinct/absent” in each patient at baseline with OCT-A and the kappa coefficient was calculated. Clinical and imaging data were reviewed at baseline and after 12 months of anti-VEGF therapy. Markers such as best-corrected visual acuity (BCVA), central macular thickness (CMT), subretinal fluid (SRF), intraretinal fluid (IRF), subretinal hyper-reflective material (SHRM), and retinal pigment epithelial (RPE) atrophy were evaluated using spectral-domain OCT.

Results: Twenty-six eyes of 26 patients were included in this study. Seven eyes displayed “distinct” MNV and 19 eyes displayed “indistinct” MNV. Kappa coefficient for classifying MNV among the graders was calculated to be 76% ($p<0.05$).

At baseline, there was no statistically significant difference in age, gender, and BCVA between both groups. The central macular thickness was lower in patients with distinct MNV (218 ± 68.7 vs 314.2 ± 48; p=0.002). RPE atrophy was more prevalent in the distinct MNV group (71.4% vs 15.8%; p=0.014). There was no statistically significant difference in percentage of subretinal fluid, intraretinal fluid, and SHRM between both groups at baseline.

One year after anti-VEGF therapy, signs of persistent exudation (SRF, IRF, or SHRM) were detected in 5 eyes (71.3%) in the distinct MNV group and 6 eyes (31.6%) in the indistinct MNV group (p=0.09). The number of anti-VEGF injections between both groups was not different (6.9± 3.1 vs 7.8± 3.1; p=0.69).

Conclusions: This study suggests that AMD patients with distinct type 1 MNV on OCT-A at baseline have greater central macular thinning and RPE atrophy compared to those with indistinct MNV. The distinct MNV group may be less responsive to anti-VEGF therapy after 1 year. Further studies with a larger sample size are mandatory to confirm these results.

CONTROL ID: 3714966

SUBMITTER (NAME ONLY): PEI-YIN SU

TITLE: Vitelliform foveomacular lesions in ABCA4 disease: A phenotypic expansion and longitudinal study

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. SU, W. Lee, J. Zernant, T. Nagasaki, S.H. Tsang, R. Allikmets, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|W. Lee, Genetics & Development, Columbia University Irving Medical Center, New York, New York, UNITED STATES|S.H. Tsang, R. Allikmets, Pathology & Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the transient development and resolution of foveomacular vitelliform lesions in ABCA4 disease.

Methods: Patients were identified from a database of genetically confirmed biallelic ABCA4 disease (n=407). Longitudinal clinical data analysis included short-wavelength (SW-AF, 488-nm), and near-infrared (NIR-AF, 787-nm), spectral domain-optical coherence tomography (SD-OCT), OCT angiography (OCTA), electrooculogram and full-field electroretinogram (ffERG) recordings. Thickness of total retina, total receptor+ (TREC+), outer segment+ (OS+) and retinal pigment epithelium (RPE) layers were measured on horizontal SD-OCT scans and en face slabs of the inner segment ellipsoid (ISe) and RPE layers were derived from 97 raster scans.

Results: Three patients (mean age 24.3 years) presented with moderate bilateral central vision loss. The common feature of ABCA4 genotypes in all three cases was the p.(Gly1961Glu) allele. SD-OCT showed focal disruptions of the ISe at the fovea resulting in a concave displacement of the overlying outer nuclear layer, resembling optical gap lesions. Large intraretinal hyperreflective foci (IHF) directly above the lesions, corresponding to yellow deposits on fundoscopy, were observed in P2 and P3. At initial presentation, the base of the optical gap lesions in P1 were filled with a dense, egg yolk-like, autofluorescent fluid. Resolution of the vitelliform fluid occurred in 3 months after which similarly-appearing IHF were detected on SD-OCT. EOG recordings were within normal limits (Arden ratio >1.8) and no generalized dysfunction was detected on ffERG. OCTA of the choriocapillaris revealed subfoveal visibility of large choroidal vessels. Total retina and RPE thicknesses were within the 95% confidence interval of healthy control eyes; significant thinning of TREC+ was observed within and in a 1 mm perimeter around the lesion. This abnormality spatially corresponded to a halo of abnormal reflectance in the ISe layer (en face OCT) and a homogeneously bright elliptical region on NIR-AF. Vitelliform material and IHF were no longer visible in the retina after 2 years in all eyes.

Conclusions: Vitelliform lesions are rare, transient events associated with the p.(Gly1961Glu) allele of ABCA4. Early deterioration of the underlying choriocapillaris and formation of IHF may be contributing factors in the rapid resolution and rare incidence of vitelliform lesions in ABCA4 disease.

CONTROL ID: 3714967

SUBMITTER (NAME ONLY): Matthew Baum

TITLE: Small incision sub-Tenon ab interno Xen implantation comparison to iStent, Trabeculectomy, and Tube shunt

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Baum, J. Bear, A. Roschke, B. Graham, J. Lee, Colorado Eye Institute, Colorado Springs, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare small incision sub-Tenon ab interno Xen implantation with iStent, Trabeculectomy, and Ahmed tube shunt visual acuity (VA) changes and efficacy in treating primary open angle glaucoma.

Methods: Xen was implanted by a single surgeon using small incision sub-Tenon ab interno technique. 11 eyes from the start of 2020 until September 28th, 2021, were recorded. Each subject had their VA checked via computer Snellen chart, intraocular pressure (IOP) by applanation tonometer, silt lamp exam was performed to determine bleb avascularity, and glaucoma medications were checked at each visit. Data was taken from pre-implantation, 1-day post-implantation, and 6 months post-implantation. T-Test was performed for statistical significance. IStent, Ahmed tube shunt, and trabeculectomy data were compiled from previous studies

Results: The average age of subjects receiving Xen was 70 ± 10.79. Mean IOP at 6 months was 13.17 ± 1.64 ($p=0.003$, 12-17), median IOP was 12.5. Of these, 100% of subjects had IOP of 17 or below, 91% were 15 or below, and 55% of 12 or below. IStent mean IOP at 6 months was 15.8 ± 3.0 ($p<0.001$). Ahmed tube shunt had a mean IOP at 6 months of 12± 4.6 ($p<0.001$). Trabeculectomy IOP at 6 months was 13.4 ± 4.2 ($p<0.001$, 6-32) No eyes receiving Xen developed an avascular bleb due to the procedure.

Xen mean decrease of medications was 1.58 ± 1.31 at 6 months. IStent mean decrease in medications was 1 ± 0.8 ($p<0.001$). Ahmed tube shunt mean number of medications went from 2.97 ± 2.03 to 1.05 ± 1.15. Trabeculectomy medications went from 3.6 ± 0.9 (1-5) to 0.37 ± 0.9 (0-4).

Xen mean VA recovery time to return to normal was 1 week. IStent VA is neutral following surgery. Ahmed tube shunt worst VA occurred at 1 week postoperatively and mean VA returned to preoperative levels by 3 months. Trabeculectomy mean VA returned to preoperative levels in 88 days (6-720 days).

Conclusions: Xen had a lower IOP at 6 months than iStent with a similar decrease in medications, while mean visual acuity returned to baseline one week after. Xen had similar IOP at 6 months with Ahmed tube shunt and trabeculectomy, similar decrease in medications with Ahmed tube shunt, and faster return to preoperative VA. Since no eyes receiving Xen developed an avascular bleb, the tissue is still viable for possible additional procedures.

CONTROL ID: 3714969

SUBMITTER (NAME ONLY): Jibril Hirbo

TITLE: Extensive genetic interactions between POAG loci add another layer of complexity in disease etiology

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hirbo, E. Gamazon, N. Cox, Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure: Jibril Hirbo: Commercial Relationship: Code N (No Commercial Relationship) | Eric Gamazon: Commercial Relationship: Code N (No Commercial Relationship) | Nancy Cox: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is disparity in POAG prevalence, clinical presentations and outcomes across ancestries. Our previous Global Biobank Meta-analysis Initiative (GBMI) POAG meta-analysis, the largest and most diverse to date, from ~1.48 million individuals from six ancestries identified a total of 109 GWAS loci, 18 of which were novel. Ten of the GWAS loci are ancestry-specific. Additionally, we show heterogeneity in effects for 14 loci across ancestries and sexes. Considering genetic interactions may contribute to phenotypic complexity, we hypothesize that ancestry specific genetic interaction in POAG underlie observed disparity. In GBMI analysis we found evidence of a significant interaction between multi-ancestry SIX6 rs33912345 and causal variants in CDKN2B-AS1 locus, with concomitant effect on expression of CDKN2A, and CDKN2B.

Methods: We tested for genetic interactions in BioVU data for a subset of 65 lead SNPs that represent just over half of the overall loci identified in our GBMI study. We determined interaction using wtest in 49,034 European and 3573 African American BioVU patients. We further checked the effect of the loci i) that show interaction in both ancestries, and ii) with the highest number of significant pairwise interaction with other POAG loci in European patients, by checking the differences in the measured gene expressions of genes in a target locus in GTEx skeletal muscle tissues (N=716) between the haplotype background that has the reference and derived alleles. Statistical difference in expression was determined using ANOVA.

Results: We identified a total of 187 and 126 pairwise interactions in European and African American patients, respectively ($p<0.05$). These interactions are mainly due to 18 core loci with ≥5 pairwise interactions with other loci across the two ancestries: 6 common to both ancestry and 6 unique to each ancestry. Four core loci unique to African BioVu patients are African-specific. Chr3_rs62250629_CADM2 locus has pairwise interactions with 27 and 9 other loci in European and African American patients, respectively. The lead variant in the locus has significant trans effect on NEAT1 ($p= 0.006$) gene in chr11_ rs12789028 locus and interact with local GTEx eQTL to alter its expression pattern.

Conclusions: Our findings, if replicated (in other GBMI biobanks), point to genetic interactions as additional contributor to observed disparities in POAG.

CONTROL ID: 3714970

SUBMITTER (NAME ONLY): Jamie Anderson

TITLE: Neurodevelopmental outcomes in patients screened for retinopathy of prematurity.

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Campbell, Ophthalmology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|P. Blasco, Oregon Health & Science University Child Development and Rehabilitation Center, Portland, Oregon, UNITED STATES|J.E. Anderson, A.S. Coyner, P. Campbell, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the relationships between low birthweight (LBW), gestational age (GA) and subsequent neurodevelopmental outcomes in premature children who were screened for retinopathy of prematurity (ROP). Recent attention has been focused on potential impact on neurodevelopmental outcomes from ROP treatment, but there is a gap in knowledge as to the baseline outcomes in this population, independent of ROP.

Methods: Forty children from a population of infants screened for ROP (26 diagnosed; 7 treated) at Oregon Health & Science University (born less than gestational age (GA) of 31 weeks or with a birthweight (BW) less than 1500 grams) were recruited for neurodevelopmental testing. The mean ± standard deviation (SD) BW was 1000.0 ± 355.7 grams and mean ± SD GA was 27.8 ± 2.3 weeks. Mean ± SD age was 6.0 years ± 1.1 years (range 4 – 7.6) at time of testing. The Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV) performance-based assessment was used to provide Scale IQ (FSIQ), Verbal Comprehension (VCI) and Visual-Spatial (VSI) composite scores. Global Executive Composite (GEC) scores were assessed by having parents complete either the Behavior Rating Inventory of Executive Function for preschool children <5 years (BRIEF-P) or the BRIEF-2 for children >5 years. The Vineland-3 Domain-Level Parent/Caregiver Form provided motor skills scores (MOT). Univariate and multivariate linear regression was used to investigate whether there were correlations between BW, GA, or BW and GA and FSIQ, VCI, VSI, GEC, and MOT. Interactions between BW and GA were accounted for.

Results: In this cohort, LBW was a significant predictor of FSIQ (R^2: 0.38), VCI (R^2: 0.24), VSI (R^2: 0.26) and MOT (R^2: 0.41). GA was a significant predictor of FSIQ (R^2: 0.17), VSI (R^2: 0.13), GEC (R^2: 0.15) and MOT (R^2: 0.31). Together, BW and GA (and their interaction) were significant predictors of VSI (R^2: 0.38).

Conclusions: BW and GA have significant correlations with neurodevelopmental outcomes. Studies that evaluate neurodevelopmental outcomes as a result of ROP treatment need to account for potential confounding by prematurity, and other comorbidities of premature birth.

CONTROL ID: 3714971

SUBMITTER (NAME ONLY): jacqueline ohmura

TITLE: Soft clustering analysis of primary open angle glaucoma loci and their association with multiple endophenotypes uncovers pathophysiological and cellular mechanisms of disease

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.F. ohmura, A.R. Hamel, A. mcadams, J.L. Wiggs, A.V. Segre, Ocular Genomics Institute and Department of Ophthalmology, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES| J.F. ohmura, Harvard-MIT Division of Health Sciences and Technology Program, Harvard Medical School, Boston, Massachusetts, UNITED STATES|C. Kim, M. udler, Center for Genomic Research, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|C. Kim, A.R. Hamel, M. udler, J.L. Wiggs, A.V. Segre, Broad Institute, Cambridge, Massachusetts, UNITED STATES|T.A. van Zyl, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|T.A. van Zyl, Department of Ophthalmology and Visual Sciences, Yale School of Medicine, New Haven, Connecticut, UNITED STATES|W. yan, A. mcadams, A. Monavarfeshani, J.R. Sanes, Department of Molecular and Cellular Biology and Center for Brain Science, Harvard University, Cambridge, Massachusetts, UNITED STATES|Q. Liang, R. Chen, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary open angle glaucoma (POAG) is a heterogeneous disease for which the underlying molecular mechanisms and their associated traits are not well defined. We applied a soft clustering method, Bayesian nonnegative matrix factorization (bNMF), to genome-wide association study (GWAS) data to identify novel sets of known POAG genetic loci that cluster with endophenotypes potentially significant to POAG. Such clusters propose different mechanistic pathways and traits that could be causal to POAG, which we further investigated for gene enrichment in ocular cell types and biological pathways.

Methods: bNMF clustering emulates physiological relevance as individual genes can belong to more than one pathway, and accounts for trait direction of effect on POAG risk in the prepared standardized association matrix. bNMF was performed using 133 independent POAG variants from the largest European and cross-ancestry genome-wide association study (GWAS) meta-analyses of POAG. Endophenotypes were selected based on known or putative pathogenic mechanisms of POAG, and available GWAS summary statistics. Genes were mapped to POAG loci via e/sQTL colocalization analysis, and tested for single cell expression enrichment in anterior segment (AS), optic nerve head and retina, and enrichment in biological processes.

Results: Of 100 POAG-related traits identified, 33 met the inclusion criteria. bNMF identified 4 clusters with 5 to 39 POAG variants each (converging to N=4, 83.8% of 1000 iterations). Each cluster was represented by unique trait and direction of effect combinations. The strongest effects on POAG risk resulted from decreased plateletcrit, diastolic blood pressure and urate serum levels (cluster 2), and increased intraocular pressure and decreased corneal hysteresis (cluster 3). Genes in POAG loci of each cluster showed significant enrichment (FDR<0.1) in specific cell types and pathways, e.g. pericyte (AS) and Müller glia (retina) (cluster 2), and ciliary and iris fibroblasts (AS) and retinal astrocytes (cluster 3).

Conclusions: Soft clustering identified several trait clusters and cell types associated with POAG risk, suggesting functionally distinct disease subtypes and offering a genetically-informed path towards personalized diagnosis and treatment.

CONTROL ID: 3714975

SUBMITTER (NAME ONLY): Fahmeeda Murtaza

TITLE: Safety and Effectiveness of MicroPulse Transscleral Laser Therapy in Non-Incisional Eyes with Ocular Hypertension and Primary Open Angle Glaucoma

SESSION TITLE: Clinical studies and trials

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is limited evidence on the use of MicroPulse transscleral laser therapy (TLT) in non-incisional eyes. This study evaluates and compares the safety and effectiveness of MicroPulse TLT in non-incisional eyes with ocular hypertension (OHT), early and moderate primary open angle glaucoma (POAG).

Methods: All consecutive eyes with OHT, early and moderate POAG that underwent MicroPulse TLT from May 2016 to March 2018 at a single outpatient clinic in Ontario, Canada were included. The Canadian Ophthalmological Society guidelines were used for staging glaucoma. Eyes were excluded if an incisional glaucoma procedure was performed prior to MicroPulse TLT. Laser settings were maintained at 80 seconds per hemisphere, 160 seconds per eye with a duty cycle of 31.3% and power range of 900-2800 mW. The primary outcomes included mean IOP reduction ≥20% from baseline, adverse events, and change in logMAR best corrected visual acuity (BCVA) from baseline. Secondary outcomes included change in topical medications from baseline, number of retreatments, and escalation to incisional glaucoma procedures during follow-up.

Results: A total of 150 eyes from 96 patients were included: 35 had OHT, 68 had early POAG, and 47 had moderate POAG. All cohorts experienced a significant mean IOP reduction at 1, 3, 6 and 12-month follow-ups ($p<0.05$). By 12-months, 71.4% of eyes with OHT, 69.7% with early POAG, and 48.3% with moderate POAG achieved an IOP reduction ≥20% from baseline. There were no cases of persistent inflammation, persistent hypotony, phthisis bulbi or sympathetic ophthalmia. At 12-months, the mean BCVA in the total cohort was unchanged from baseline (mean difference [MD]=0.01 ± 0.01, p=0.51). At 12-months, the mean number of topical glaucoma medications in the total cohort was unchanged from baseline (MD=0.30 ± 0.01, p=0.09). Sixteen eyes (10.7%) required retreatment within 4.5 ± 4.3 months of the initial laser treatment. Retreatment provided an additional 1.0 ± 7.0 mmHg of IOP reduction (p=0.155). By final follow-up, 4 eyes (2.7%) required escalation to incisional procedures.

Conclusions: MicroPulse TLT is a safe and effective adjunctive IOP-lowering treatment in non-incisional eyes with OHT, early and moderate POAG. Our results suggest that MicroPulse TLT may be used earlier in the treatment paradigm.

CONTROL ID: 3714976

SUBMITTER (NAME ONLY): Angelica Scanzera

TITLE: Risk factors and Contact Lens Modality in Patients with Acanthamoeba Keratitis

SESSION TITLE: Contact lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Scanzera, H.H. Yoon, E. Shorter, E. Tu, Ophthalmology and Visual Sciences, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acanthamoeba keratitis (AK) is a rare but potentially visually devastating ocular infection. Diagnosis can be challenging, often resulting in misdiagnosis with delayed treatment. Individuals with history of contact lens use and improper lens handling including exposure to water or corneal trauma are at higher risk of infection.
The purpose of this study was to describe patient demographics, time from symptom onset to diagnosis, time from presentation to clinic to diagnosis and risk factors in patients diagnosed with AK at a tertiary care center.

Methods: Medical records of all patients evaluated at the Illinois Eye and Ear Infirmary (IEEI) between 2015 and 2020 with a diagnosis of AK were reviewed. Patients with a new diagnosis of AK during the study period were included. This study was approved by the University of Illinois at Chicago Institutional Review Board.

Results: There were 58 patients identified with AK including 5 patients (8.6%) with bilateral disease. Mean age was 38.7 years (range 12 to 80) with 55.2% females. The majority (94.8%) were contact lens wearers using soft lenses (65.5%) followed by corneal gas permeable (21.8%), hybrid (5.5%), and scleral lenses (1.8%). There was documented exposure to water including rinsing lenses in water, swimming in pools, lakes, hot tub use and showering in almost half of the patients (48.3%). Overnight lens use was documented in 29.3% including three orthokeratology lens users. Mean time from symptom onset was 44 days ± 51, and mean time from presentation at IEEI to diagnosis was 3 days ± 8. Confocal microscopy was performed on 48 patients and cysts consistent with acanthamoeba were present in 41 of those patients (93.2%) while cultures were positive in only 17 of 38 patients (44.7%).

Conclusions: In this case series, 35.5% of contact lens related AK cases were in rigid and hybrid lens users. Previous epidemiologic studies found that 85-88% of contact lens related AK infections are in soft lens users, and among U.S. contact lens prescribers, soft lenses consist of 95% of lens fits. This data suggests that the risk of AK in rigid and hybrid lens users may be increasing. A future well-designed case-control study may assist in evaluating the relationship between AK and different lens modalities.

CONTROL ID: 3714977

SUBMITTER (NAME ONLY): Jennifer Tran

TITLE: Microvascular Changes in Sickle Cell Retinopathy (SCR) using Wide-Field Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA)

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Tran, I. Garg, H. Wescott, M. Duich, Y. Cui, J.B. Miller, Harvard Retinal Imaging Lab, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Cui, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|J.A. Tran, I. Garg, H. Wescott, J.B. Miller, Retina Service, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sickle cell disease encompasses a spectrum of inherited hemoglobinopathies that have various ophthalmic manifestations, including SCR. WF SS-OCTA is a valuable tool to assess the extra-macular region compared to traditional OCTA. Herein, we aim to study the utility of WF SS-OCTA in SCR.

Methods: We conducted a single-institution observational study using WF SS-OCTA to obtain 3x3mm, 6x6mm, and 12x12mm scans centered on the fovea. The ARI Network (Zeiss Portal) was used to quantify vascular metrics such as vessel density (VD), vessel skeletonized density (VSD) in superficial (SCP), deep capillary plexus (DCP) and whole retina; and foveal avascular zone (FAZ) area, circularity and perimeter. Mixed-effects multiple regression models adjusting for age were used for statistical analysis.

Results: The median age was 59 (46-63.3) years. We analyzed 38 control eyes of 20 patients and 20 eyes of 11 patients with SCR: proliferative SCR (PSCR, n=5), non-proliferative SCR (NPSCR, n=9), and no SCR (NSCR, n=6). On 3x3mm scans, the PSCR group had decreased FAZ circularity vs the control (β=-0.15), NSCR (β=-0.15), and NPSCR (β=-0.11) groups ($p<0.05$). Importantly, the NSCR group had greater FAZ area vs controls (β=0.27, $p=0.04$). On 6x6mm scans, there was reduced SCP VD (NSCR β=-0.05; NPSCR β=-0.05, PSCR β=-0.04, all $p<0.05$) and VSD (NSCR β=-2.67; NPSCR β=-2.53, PSCR β=-2.41, all $p<0.05$) and whole retina VD (NSCR β=-0.04; NPSCR β=-0.04, PSCR β=-0.03, all $p<0.05$) and VSD (NSCR β=-2.09; NPSCR β=-2.18, PSCR β=-1.96, all $p<0.05$) for all groups compared to controls. NPSCR eyes also demonstrated reduced DCP VSD (β=-3.66) and VD (β=-0.07) vs controls ($p<0.05$). There was increased FAZ perimeter for NPSCR (β=1.64) and PSCR (β=1.06) vs controls ($p<0.05$). FAZ area was also increased for NSCR (β=0.28), NPSCR (β=0.36) vs controls, and NPSCR (β=0.17) vs the PSCR group (all $p<0.05$). On 12x12 scans, there was increased FAZ area for the NSCR group (β=0.31, $p=0.02$) vs controls.

Conclusions: Our results show that in patients with no evidence of SCR, there is an increased FAZ area vs control, suggesting a subclinical disease featuring early retinal capillary dropout. This study demonstrates reduction in VD/VSD and hence the potential benefits of utilizing WF SS-OCTA in SCR. In future, we aim to investigate changes in the periphery and its clinical significance using this imaging technology.

CONTROL ID: 3714980

SUBMITTER (NAME ONLY): Bin Lin

TITLE: Effect of immunosuppression on transplants of hESC-derived retina organoids to retinal degenerate rats

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lin, R. Sims, R.T. Fouda, J. Delgado, M.J. Seiler, Stem Cell Research Center, University of California Irvine, Irvine, California, UNITED STATES|B. McLelland, G. Nistor, H. Keirstead, AIVITA Biomedical, Irvine, California, UNITED STATES|M.J. Seiler, PM&R, Ophthalmology, Anatomy & Neurobiology, University of California at Irvine, Irvine, California, UNITED STATES|Y. Xue, Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|A. Browne, Biomedical Engineering, Ophthalmology, Gavin Herbert Eye Institute, Institute for Clinical and Translational Science, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The effect of immunosuppression on the survival of human embryonic stem cell (hESC) derived retina organoids (ROs) produced by a scalable cGMP compatible process was studied after transplantation to the subretinal space of Rho S334ter-3 retinal degeneration (RD) rats, and in vitro.

Methods: A Working Cell Bank (WCB) of CSC-14 hESCs (NIH 0284) was established using a scalable cGMP compatible process. RO sheets differentiated from hESCs were transplanted to 3 groups of rats: 1. Immunodeficient (nude) RD rats; 2. Immunocompetent RD rats; 3. Immunocompetent RD rats with immunosuppression. The survival of the transplants was monitored by Optical Coherence Tomography (OCT). Immunosuppressants (Tacrolimus [TAC] pellet implant and oral mycophenolate mofetil [MMF]) were applied to the rats in group 3. TAC levels in blood were determined by LC-MS and MMF/cytokine levels were monitored by Elisa. Cytostatic effects on target lymphocyte populations were evaluated by flow cytometry. Sections through transplants were stained with hematoxylin & eosin (H&E) and immunohistochemistry (IHC) with different markers. The effect of TAC and MPA on RO was tested by fluorescence lifetime imaging (FLIM) after exposure for 1 and 4 weeks. Visual function was tested by optokinetic testing (OKT).

Results: A WCB of hESCs was established from the MCB. In vitro immunogenicity tests showed that ROs are not likely to induce an immune response. IHC of ROs shows early lamination and development of retinal cell progenitors. No significant difference was found between ROs exposed to immunosuppressants and controls. The transplants developed different retinal cells including photoreceptors; integrated with the host retina; and survived for more than 6 months in immunocompromised rats. CD8 T-cells obliterated donor cells in immune competent rats without immunosuppression after 2 months post-surgery. Therapeutic levels of immunosuppressant remained in the blood and helped transplants survive in the host for 6 months. OKT showed improvement of visual function in transplanted rats compared to non-surgery controls.

Conclusions:

Retina organoids matured, developed photoreceptors, and improved visual acuity after transplantation. Suppression of host CD8 T-cells may be necessary for transplant long term survival. Activity of microglia and macrophages alone may not be detrimental to transplant survival.

CONTROL ID: 3714981

SUBMITTER (NAME ONLY): Krishna Shanmugam

TITLE: Investigating the The Role of Neoplastic Disorders in the Development of Open-Angle Glaucoma: A Big Data Approach

SESSION TITLE: Data science, machine learning, and AI

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.P. Shanmugam, A. Tadjali, Texas A&M University Health Sciences Center, Bryan, Texas, UNITED STATES|C. Murugesan, M. Raju, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Open-angle glaucomas are challenging and usually silent disease processes that often present with advanced optic nerve damage and visual field defects. In the current study, we present a novel population-based data mining analysis to gain a deeper
understanding of glaucoma risk factors through innovations in big data science. This study aims to more clearly define whether there is a correlation between neoplastic conditions and other assorted demographic variables on the development of open-angle glaucoma.

Methods: Using deidentified electronic health records (EHR) from the vast i2b2 database from the University of Missouri, ICD (International Classification of Disease) codes based on inclusion and exclusion criteria of the specific study cohorts were examined. Cumulatively, 14,212 patient records were analyzed. We applied a Pearson correlation analysis and stepwise regression analysis to find a possible association between glaucoma and selected study variables.

Results: This study specifically found that neoplasms of skeletal and connective tissue have an increased association ($p<0.05$) with open-angle glaucomas as compared to any other neoplastic processes. No other oncologic conditions appeared to show a similar association. Similarly, in our cohort, there is an association ($p<0.01$) between glaucoma and lifelong non-smoking status and patients with any previous history of smoking. This is particularly interesting, as patients who were current smokers were not associated with an increased glaucoma risk. Lastly, this study found that African American individuals have an incredibly statistically significant ($p<0.01$) risk of glaucoma development versus other study populations.

Conclusions: In our analysis of a large subset of patients in a vast database, glaucoma was associated with neoplasms of the connective tissue and bone more than any other neoplastic process. A possible explanation for this could be the fact that there is a common ectodermal embryology between these structures. Furthermore, African Americans and nonsmokers/former smokers have been associated with an increased risk for glaucoma, when compared with current smokers, and these facts should be examined in larger scale studies. Without a doubt, this study demonstrates the vast potential of applying data mining methods for risk assessments using large-scaled EHR data.

CONTROL ID: 3714988

SUBMITTER (NAME ONLY): Mario Cale

TITLE: The Effect of Teprotumumab on Ocular Surface Symptoms in Thyroid Eye Disease

SESSION TITLE: Thyroid eye disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Cale, E. Osias, P. Singh, D. Rootman, Orbital and Ophthalmic Plastic Surgery, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Mario Cale: Commercial Relationship: Code N (No Commercial Relationship) | Ethan Osias: Commercial Relationship: Code N (No Commercial Relationship) | Pallavi Singh: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Rootman: Commercial Relationship(s);Code C (Consultant/Contractor):Horizon Pharmaceuticals

ABSTRACT BODY:

Purpose: Dry eye syndrome occurs in up to 85% of patients with thyroid eye disease (TED), and it is unclear how teprotumumab affects this symptomatology. We tested the hypothesis that treatment with teprotumumab would significantly reduce both subjective and objective ocular surface disease symptoms in TED patients.

Methods:

This was a retrospective cohort study of adult patients with thyroid eye disease treated at the University of California, Los Angeles since 2014. We assessed the effect of teprotumumab therapy on subjective ocular surface symptoms as measured by the Ocular Surface Disease Index (OSDI), a previously validated questionnaire for dry eye syndrome. The degree of change from baseline OSDI score was compared between patients that received teprotumab and baseline score-matched control patients that never received it. Change in objective dry eye manifestations like punctate epithelial erosions and superior limbic keratopathy were also studied. Statistical analysis was performed using an independent two-tailed t test with an alpha level of 0.05.

Results: We identified 18 patients (14 females, 4 males) treated with teprotumumab with a mean age of 53.5 (SD=14.9), and 18 controls (15 females, 3 males) with a mean age of 49.8 (SD=13.3). The average time from baseline OSDI to the next patient visit was 5.3 months (SD=3.0). Patients treated with teprotumumab experienced a statistically significant decrease of 15.4 (SEM=3.6) in their OSDI score compared to the controls (p=0.002). The change in severity of punctate epithelial erosions or superior limbic keratoconjunctivitis did not differ between groups.

Conclusions: Teprotumumab was effective in significantly mitigating clinical ocular surface symptoms, although the effect on objective physical exam findings was negligible. Given the complexity of dry eye syndrome and the importance of the subjective experience of disease, our findings illustrate a possible benefit of this therapy.

CONTROL ID: 3714989

SUBMITTER (NAME ONLY): Jiakai Lyu

TITLE: Quadrifocal diffractive lens design for presbyopia correction

SESSION TITLE: Crystalline lens and IOLs

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Yoon, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|S. Bang, Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|J. Lyu, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although bifocal and trifocal diffractive intraocular lenses are effective in correcting presbyopia, the fact that retinal image quality is significantly degraded between the designed foci remains a limitation. One potential solution can be to generate more foci, resulting in improved through-focus image quality. The goal of this study is to evaluate a new method to design a quadrifocal diffractive presbyopia-correcting ophthalmic lens.

Methods: To design a quadrifocal lens with focal points at 0, 1, 2 and 3 diopters (D), two bifocal diffractive lenses, one for 0 and 2D and the other for 1 and 3D, are radially cut into rings based on a threshold value in wavefront phase (one below and one above). The rings are combined to be a quadrifocal lens. To validate the performance of the quadrifocal lens, an optical bench testing system equipped with a spatial light modulator generating the diffractive design was constructed. The quadrifocal lens was compared against a typical trifocal diffractive design (foci at 0, 1.5 and 3D) for a 4mm pupil with 579nm monochromatic light. An image quality metric, area under modulation transfer function (areaMTF) calculated from the collected images of a letter E chart through the lens designs, was used to quantify retinal image quality at various object distances ranging from 0 to 3D.

Results: Both simulation and bench testing showed that the quadrifocal lens created peak image quality at the designed foci. The quadrifocal design provided significantly better image quality at 1 and 2D than the trifocal design at the cost of slight image quality degradation at 0 and 3D. As expected, image quality at 1.5D was significantly better with the trifocal lens. Both diffractive designs showed similar overall through-focus image quality represented by the sum of the areaMTF values between 0 and 3D. Additional simulation demonstrated that by controlling the relative phase and ring width between the two bifocal designs, the relative image quality at the four foci could be manipulated as needed.

Conclusions: A newly designed quadrifocal diffractive lens for presbyopia correction was proposed. The results demonstrated that generating more than 3 foci was feasible, without sacrificing overall through-focus image quality.

CONTROL ID: 3714990

SUBMITTER (NAME ONLY): Amr Elsawy

TITLE: Detecting Cataract from Color Fundus Photographs Using Explainable Deep Learning

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Elsawy, Q. Chen, Z. Lu, National Center of Biotechnology Information, National Library of Medicine, Bethesda, Maryland, UNITED STATES|T.D. Keenan, A. Thavikulwat, S. Bhandari, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diagnosing cataract usually requires in-person evaluation by an ophthalmologist. However, many individuals undergo color fundus photography (CFP) outside ophthalmology clinics, which represents an opportunity towards more accessible diagnosis by developing automated cataract detection methods. Therefore, the purpose of this study was to develop an explainable deep learning network that can detect cataract from color fundus photographs (CFPs) obtained from the Age-Related Eye Diseases Study 2 (AREDS2).

Methods: A dataset of 17, 514 CFPs was obtained from 2,573 AREDS2 participants. The dataset comprised 8,681 CFPs from eyes with cataract and 8,833 CFPs from eyes without cataract. The ground truth labels were transferred from slit lamp exams of nuclear cataracts conducted by ophthalmologists and from reading center gradings of the anterior segment photos (red reflex photos) for evaluating cortical and posterior subcapsular cataracts. The dataset was divided into training, validation, and testing datasets (70%, 20%, and 10% participants, respectively). A deep learning network was developed using separable convolutions and residual connections. The network performance was compared to that of three ophthalmologists. The network was visualized using Gradient Class Activation Maps (Grad-CAMs) where areas of high signal correspond to the CFP pixels that contributed most to the network decision.

Results: The network achieved performance scores (with 95% CI) of 0.6683 (0.6531, 0.6838), 0.6691 (0.6536, 0.685), 0.6686 (0.6533, 0.6842), 0.6686 (0.6533, 0.6842) compared to that of the combined ophthalmologists of 0.6025 (0.5100, 0.7000), 0.6119 (0.5085, 0.7123), 0.5988 (0.5074, 0.6895), and 0.5988 (0.5074, 0.6895) for accuracy, precision, recall, and AUC, respectively. Qualitative analysis of the Grad-CAMs, of correctly graded CFPs, showed that areas of high signal in CFPs without cataract and areas of low signal in CFPs with cataract corresponded to retinal blood vessels, as shown in Fig. 1.

Conclusions: The proposed network outperformed three ophthalmologists in the detection of cataract from CFP, which may increase the accessibility of cataract diagnosis. The detections were generally explainable where the retinal blood vessels seemed to be an important diagnostic feature.

CONTROL ID: 3714991

SUBMITTER (NAME ONLY): Lydia Sauer

TITLE: The Sensitivity and Specificity of FLIO (Fluorescence Lifetime Imaging Ophthalmoscopy) when Imaging Patients with MacTel

SESSION TITLE: Macular Diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Sauer, A. Vitale, P.S. Bernstein, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure: Lydia Sauer: Commercial Relationship(s);Code C (Consultant/Contractor):Tesseract | Alexandra Vitale: Commercial Relationship(s);Code C (Consultant/Contractor):Tesseract | Paul Bernstein: Commercial Relationship(s);Code C (Consultant/Contractor):Tesseract;Code S (non-remunerative):Heidelberg Engineering

ABSTRACT BODY:

Purpose: Macular telangiectasia type 2 (MacTel) is a retinal disease that leads to central visual distortions such as metamorphopsia and central scotomas in affected individuals. The clinical diagnosis of MacTel can be challenging, and the use of multimodal imaging approaches improves diagnostic potential. Fluorescence lifetime imaging ophthalmoscopy (FLIO) has proven to be a useful tool in diagnosing this condition. The aim of this study is to investigate all suspected MacTel patients that received FLIO imaging in order to determine sensitivity and specificity of FLIO in our clinical practice.

Methods: From March 2018 until January 2022, 161 patients were referred for FLIO imaging at the Moran Eye Center to be evaluated for MacTel. A prototype Heidelberg Engineering FLIO was used to obtain autofluorescence lifetimes in short (SSC, 498-560 nm) and long (LSC, 560-720 nm) spectral channels. All patients received a comprehensive ophthalmologic exam and most patients received standard clinical imaging including optical coherence tomography (OCT).

Results: 119 patients had characteristic patterns of MacTel on FLIO imaging and the diagnosis of MacTel was clinically confirmed. Images of 5 patients were inconclusive on FLIO imaging, due to severe cataracts (3 cases) or poor image quality (2 cases). All of these 124 patients were clinically diagnosed with MacTel. The remaining 37 patients did not show characteristic signs of MacTel in FLIO imaging. None of these patients were diagnosed with MacTel, and further testing revealed the presence of other retinal diseases, such as cone dystrophy, tamoxifen retinopathy, hydroxychloroquine toxicity, or age-related macular degeneration.

Conclusions: The ability of FLIO to detect disease related changes in patients with MacTel has proven to be diagnostically advantageous in clinical practice. In our cohort of 161 patients evaluated for MacTel, FLIO has a high sensitivity (96%) and specificity (100%) when determining if a patient has MacTel or not.

CONTROL ID: 3714992

SUBMITTER (NAME ONLY): Ziyu Yu

TITLE: TNF-α stimulation enhances the neuroprotective effects of gingival MSCs derived exosomes in retinal ischemia-reperfusion injury via the MEG3/miR-21a-5p axis

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Yu, Y. Zhuo, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

Commercial Relationships Disclosure: Ziyu Yu: Commercial Relationship: Code N (No Commercial Relationship) | Yehong Zhuo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We examined TNF-α-stimulated gingival MSC (GMSC)-exosomes for their neuroprotective and anti-inflammatory effects in retinal IRI. We further aim to explore the crucial factors and pathways involved in protective mechanisms of GMSC-derived exosomes.

Methods: In this study, exosomes from the CM of GMSCs were isolated by ultracentrifugation. Exosomes from conditioned culture medium (CM) of MSCs stimulated by TNF-α were injected to cell and the vitreous of mouse model. The effects of TNF-α-stimulated gingival MSC (GMSC)-exosomes (TG-exos), in modulating inflammatory microglia and alleviating apoptosis was detected by PCR, western blot analysis, immunofluorescence staining assay.

Results: The results showed that intraocular injection of TG-exos into mice with IRI notably reduced inflammation and cell loss than that with G-exos (GMSC-exosomes). Similar results were observed in vitro. Additionally, with the microRNA (miR) arrays, it was found that miR-21-5p acted as a crucial factor in TG-exos for neuroprotection and anti-inflammation. Following target prediction and dual luciferase assay suggested that miR-21-5p played a role by combining with programmed cell death 4 (PDCD4), which was regulated by the long non-coding RNA (lncRNA) maternally expressed gene 3 (MEG3) as a competing endogenous RNA (ceRNA).

Conclusions: This study demonstrates a new therapeutic pathway for neuroprotection against IRI by delivering miR-21-5p-enriched exosomes through MEG3/miR-21- 5p/PDCD4 axis and paves the way for the establishment of a cell-free therapeuticapproach for glaucoma.

CONTROL ID: 3714993

SUBMITTER (NAME ONLY): Shresta Patangay

TITLE: Signal Quality and Repeatability of Two Corneal Electrodes Used with a Handheld Electroretinogram System

SESSION TITLE: Electroretinography: basic mechanisms and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Patangay, J.R. Hetling, Bioengineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|J.R. Hetling, Ophthalmology and Visual Science, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Shresta Patangay: Commercial Relationship(s);Code E (Employment):Retmap, Inc. | John Hetling: Commercial Relationship(s);Code S (non-remunerative):Retmap Inc;Code P (Patent):RetMap, Inc. US 10,952,630 B2;Code I (Personal Financial Interest):Retmap Inc

ABSTRACT BODY:

Purpose: This study evaluated the performance of two corneal electroretinogram (ERG) sensors when used with a hand-held ERG system. Conductive thread-type sensors (DTL Plus, Diagnosys LLC) and prototype disposable contact lens sensors (RM Electrode, provided by RetMap Inc.) were used. The hypotheses were that the RM sensor, which makes electrical contact with the cornea only, would provide signals of higher signal to noise ratio (SNR) and improved repeatability (responses within a test, and across repeated tests) when compared to the DTL sensor, which makes electrical contact with the cornea and other nearby tissues.

Methods: Three normally-sighted subjects (six eyes) participated. Following administration of a corneal numbing agent the DTL was installed in one eye and the RM in the other eye (randomly assigned). Using the handheld RETeval system (LKC Technologies) the “ISCEV 6 Step Dark First Td” protocol (no pupil dilation) was followed, with 10 min dark- and light-adaptation periods. After the protocol was complete the sensors were removed, new sensors of the opposite type were installed in each eye, and the protocol was repeated. The entire procedure was carried out on two consecutive days. Repeatability was quantified as the root mean squared error (RMSE) over a 150 ms post-stimulus interval. RMSE was calculated between responses to repeated stimuli within a test, and between averaged waveforms obtained in tests performed on consecutive days.

Results: For the 3.0 dark-adapted stimulus (85 Troland seconds), RMSE values for repeated tests were lower in 67% of eyes with the RM sensor, with an average reduction of 40% compared to values obtained with DTL sensors. RMSE values for repeated stimuli within a test were lower in 100% of eyes with the RM sensor, with an average reduction of 59% compared to values obtained with DTL sensors. SNR values for individual responses in eyes with the RM sensor were increased by 128% (4.28 dB), on average, compared to values obtained with DTL sensors.

Conclusions: A disposable sensor designed to improve the consistency and location of corneal contact (RM) can improve repeatability of responses compared to thread-type ERG sensors. Improved repeatability has the potential to shorten ERG test times and narrow reference ranges used for diagnosis and monitoring.

CONTROL ID: 3714995

SUBMITTER (NAME ONLY): James Tian

TITLE: Evaluating the outcomes of dried vs cryopreserved amniotic membrane grafting in the treatment of corneal epithelial defects

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tian, C. Wisely, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure: James Tian: Commercial Relationship: Code N (No Commercial Relationship) | Clayton Wisely: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Amniotic membrane grafts (AMGs) have been used to provide nutritious and anti-inflammatory scaffolding to the cornea surface to promote epithelial wound healing. While initial AMGs were first prepared with cryotherapy, there are logistical advantages of using dried AMGs that can be stored at room temperature. However, there is insufficient clinical data on the outcomes of amniotic membrane grafting between dried vs cryopreserved AMGs for specific indications. Thus, we aim to compare the resolution rate of corneal epithelial defects when treated with a dried vs cryopreserved AMGs.

Methods: A search for CPT codes for AMG placement was performed in our institution's electronic health record, and the corresponding charts were reviewed to isolate patients who received an AMG for a corneal epithelial defect. The type of (dried vs cryopreserved) AMG, presenting best-corrected visual acuity (BCVA), indications for AMG, and anterior segment exam data were collected. Patients were separated into a "fully healed", "partially healed", or "no improvement" based on clinical documentation. Statistics were computed with Chi-square and Student's t-test.

Results: A total of 43 charts were reviewed of patients who underwent AMG placement for corneal epithelial defects. 32 patients underwent dried AMG placement, 11 underwent cryopreserved AMG placement. The indications ranged from persistent epithelial defects after corneal transplantation or superficial keratectomy to herpetic neurotrophic keratitis or ocular cicatricial pemphigoid. The mean age of the dried AMG group was 68 and the mean age of the cryopreserved group was 64. The mean presenting BCVA was higher in the dried AMG group (20/160-20/200) than in the cryopreserved AMG group (20/400-20/600). The rate of full or partial epithelial healing was 94% (30/32) for the dried AMG group and 91% (10/11) for the cryopreserved AMG group (p=0.75).

Conclusions: The logistically simpler dried AMG and the cryopreserved AMG showed similar outcomes when used to treat corneal epithelial defects.

CONTROL ID: 3714996

SUBMITTER (NAME ONLY): Michael Larsen

TITLE: Heritability and risk factors of incident early drusen in the Copenhagen Twin Cohort Eye Study: a 20-year follow-up

SESSION TITLE: Retina epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Larsen, S. Dabbah, S. Rothenbuehler, M. Belmouhand, Ophthalmology, Rigshospitalet, Kobenhavn, DENMARK|I. Munch, J. Bjerager, Bispebjerg and Frederiksberg Hospital, Centre for Clinical Research and Prevention, Frederiksberg, DENMARK|J. Hjelmborg, Statistics, Univerity of Southern Denmark, Odense, DENMARK|C. Dalgård, Faculty of Health Sciences, University of Southern Denmark, Odense, DENMARK| M. Larsen, Faculty of Health and Medical Sciences, Kobenhavns Universitet, Kobenhavn, DENMARK|

Commercial Relationships Disclosure: Michael Larsen: Commercial Relationship(s);Code C (Consultant/Contractor):Roche Genentech;Code C (Consultant/Contractor):Novartis;Code C (Consultant/Contractor):Bayer;Code C (Consultant/Contractor):Stoke;Code C (Consultant/Contractor):Novo Nordisk;Code C (Consultant/Contractor):Lundbeck | Jacob Hjelmborg: Commercial Relationship: Code N (No Commercial Relationship) | Inger Christine Munch: Commercial Relationship: Code N (No Commercial Relationship) | Sami Dabbah: Commercial Relationship: Code N (No Commercial Relationship) | Jakob Bjerager: Commercial Relationship: Code N (No Commercial Relationship) | Simon Rothenbuehler: Commercial Relationship: Code N (No Commercial Relationship) | Christine Dalgård: Commercial Relationship: Code N (No Commercial Relationship) | Mohamed Belmouhand: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The transition from normality to early drusen (≥ 20 small hard drusen or drusen ≥ 63 µm in diameter) has received little attention. As hypothesized by some researchers, small hard drusen precede the development of large drusen. Consequently, they should share similar genetic and environmental associations. The purpose was to research, by examining lesion-by-lesion, the genetic and environmental factors associated with the 20-year incidence of early drusen and whether small hard drusen are associated with large drusen.

Methods: A single-center, 20-year follow-up cohort study comprising 138 twins at the Department of Ophthalmology, Rigshospitalet. Examinations included biometry, fundus optical coherence tomography, and fundus photography. Each macula was classified, at baseline and follow-up, as having 1) < 20 small hard drusen, 2) ≥ 20 small hard drusen, 3) drusen ≥ 63 µm, and 4) ≥ 20 small hard drusen combined with drusen ≥ 63 µm.

Results: The median age was 59 (range 41 - 66) years. Of 25 (18.1%) incident cases, 7 had developed ≥ 20 small hard drusen, 18 had developed drusen ≥ 63 µm, whereas none had developed the combination of the two traits. Smoking was associated with incident ≥ 20 small hard drusen ($p = 0.04$) and with incident drusen ≥ 63 µm ($p = 0.003$). At baseline, having≥ 20 small hard drusen was associated with incident drusen ≥ 63 µm at follow-up ($p = 0.02$). Development of drusen ≥ 63 µm was attributable to 49% genetic effects and 51% environmental effects.

Conclusions: Incident cases with ≥ 20 small hard drusen or drusen ≥ 63 µm were strongly associated with smoking and genetic predisposition. Having ≥ 20 small hard drusen at baseline was associated with having developed incident drusen ≥ 63 µm after 20 years.

CONTROL ID: 3714997

SUBMITTER (NAME ONLY): Mark Kravitz

TITLE: Functional profiles of wild-type and nob retinal ganglion cell populations

SESSION TITLE: Retinal and central processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kravitz, B. Borghuis, R.G. Gregg, University of Louisville, Louisville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure: Mark Kravitz: Commercial Relationship: Code N (No Commercial Relationship) | Bart Borghuis: Commercial Relationship: Code N (No Commercial Relationship) | Ronald Gregg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Congenital stationary night blindness 1 (CSNB1) is caused by a mutation in the NYX gene, which encodes for nyctalopin, a protein located on the dendrites of bipolar cells that is critical in phototransduction. This mutation results in severe dysfunction within the ON visual pathway while the integrity of the OFF pathway remains relatively intact. While the cause and effect of this mutation are known, how the dysfunction is represented at the level of the retinal ganglion cell (RGC) population remains unclear.

Methods: We crossed nob knockout mice with Thy1-GCaMP6f mice, which label a subset of RGCs with the calcium indicator GCaMP6f. Using two-photon microscopy, we recorded calcium responses of wild-type Thy1-GCaMP6f and Nob/Thy1-GCaMP6f RGCs while presenting the retina with a variety of visual stimuli. These responses were processed and analyzed using MATLAB.

Results: Of the cells labeled by GCaMP6f, there are approximately half as many light-responsive RGCs in the nob retina compared to the wild-type. In the wild-type RGC population, there is a mix of ON, OFF, and ON-OFF cells, while the nob population is composed almost entirely of OFF cells. Unlike in the wild-type retina, when ON responses are present in nob RGCs, they are significantly delayed. The receptive fields of the nob RGCs are slightly smaller on average than wild-type RGCs. There appears to be a greater degree of direction selectivity in the nob RGC population than the wild-type population. Finally, there is a significant number of non-light evoked responses present in the nob population that is not seen in the wild-type.

Conclusions: There are significant functional differences between the nob and wild-type RGC populations in terms of polarity, receptive field, direction selectivity, and responsiveness to light stimuli.

CONTROL ID: 3714998

SUBMITTER (NAME ONLY): Brian Wollocko

TITLE: Validation of an Advanced Keratography Unit to Measure Dry Eye Disease in an Animal Model - Implications for Clinical Use

SESSION TITLE: Dry eye regulators: lacrimal gland, Meibomian gland, basic mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Huang, K. Tourmouzis, B. Rigas, R. Honkanen, Department of Ophthalmology, Stony Brook University Hospital, Stony Brook, New York, UNITED STATES|W. Huang, Department of Ophthalmology, Second Xiangya Hospital, Changsha, Hunan, CHINA|B. Rigas, Department of Family, Population, and Preventive Medicine, Stony Brook University Hospital, Stony Brook, New York, UNITED STATES|B. Wollocko, M. Wolek, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|L. Huang, Department of Medicine, Stony Brook University Hospital, Stony Brook, New York, UNITED STATES|K. Tourmouzis, Barts and The London School of Medicine and Dentistry, London, UNITED KINGDOM|

Commercial Relationships Disclosure: Brian Wollocko: Commercial Relationship: Code N (No Commercial Relationship) | Michael Wolek: Commercial Relationship: Code N (No Commercial Relationship) | Liqun Huang: Commercial Relationship: Code N (No Commercial Relationship) | Wei Huang: Commercial Relationship: Code N (No Commercial Relationship) | Konstantinos Tourmouzis: Commercial Relationship: Code N (No Commercial Relationship) | Basil Rigas: Commercial Relationship: Code N (No Commercial Relationship) | Robert Honkanen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Dry Eye Disease (DED) is a common condition whose pathophysiology and treatment are still actively being researched. Absence of a universally accepted animal model for DED research poses a barrier to further development of our understanding. All animal models have limitations in how they translate to the human condition in both disease physiology and assessment. Here we show the ability of an advanced keratography unit (AKU) already used in clinical practice to effectively measure DED status in rabbits.

Methods: Numerous measures of DED using an advanced keratography unit (AKU) were made before and after DED was induced in 15 New Zealand White (NZW) and 4 Dutch Belted (DB) rabbits with concanavalin A. Standard DED measures included first and average non-invasive keratographic break-up time (NIKBUT), tear meniscus height (TMH), meibomography, and Tearfilm dynamic (TFD). Other measures included palpebral fissure height (PFH), temporal angle size (TAS), and corneal irregularity (CI). A normative dataset for parameters in each species was created.

Results: First and average NIKBUT, PFH, and TAS (9.14±5.48, 17.14±2.94, 10.7±1.0, 122 ± 10 respectively) significantly decreased following DED induction (4.54±2.63, 12.93±3.33, 7.1±3.0, 81±32 respectively; all $p<0.001$). TMH (0.21±0.03) and CI (0.021± 0.008) both increased (0.27±0.09, 0.040±0.017 respectively; both $p<0.003$) after DED induction. The data were similar if looking at DB and NZW groups separately. Meibomography and TFD were not useful discriminating DED.

Conclusions: We present normative data values for a panel of DED and other metrics collected with an AKU. Statistically significant changes in the expected direction were observed for NIKBUT, PFH, TAS and CI following induction of DED. The significant change in TMH was in the wrong direction suggesting other compensatory responses are occurring. The results indicate this AKU (Oculus Keratograph 5M) can measure DED status in this rabbit model. AKU technology has potential to improve diagnostic capability in DED research using rabbit models. This non-invasive, objective quantification of DED can improve translational research allowing for improved fidelity between methods of DED assessment in rabbit and human DED. Such benefits may be especially useful in studies new pharmacologic treatments for DED.

CONTROL ID: 3714999

SUBMITTER (NAME ONLY): Emily Witsberger

TITLE: Graft Suture Fixation in High Risk Descemet Stripping Endothelial Keratoplasty

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Witsberger, K.A. Oyemade, S. Patel, B. Keith, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

Commercial Relationships Disclosure: Emily Witsberger: Commercial Relationship: Code N (No Commercial Relationship) | Kafayat Oyemade: Commercial Relationship: Code N (No Commercial Relationship) | Sanjay Patel: Commercial Relationship: Code N (No Commercial Relationship) | Baratz Keith: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the efficacy of radial full-thickness fixation sutures in DSEK among patients considered at high risk for graft dislocation.

Methods: A retrospective chart review was performed to identify patients who underwent DSEK at Mayo Clinic between January 2015 and January 2021. Cases at high risk of graft dislocation were defined as eyes that had prior trabeculectomy, glaucoma drainage devices, absence of lens capsule, vitrectomy, or penetrating keratoplasty. The primary outcome was graft dislocation rate (defined as the need for rebubble) among eyes that had graft fixation with four radial full-thickness 11-0 nylon sutures versus no fixation sutures.

Results: Three hundred fifty-seven DSEK surgeries occurring among 323 eyes of 242 patients were reviewed, and 181 were considered high risk. Of the high risk cases, 66 had graft suture fixation and 115 were unsutured. Baseline demographics and ocular comorbidities were comparable. Sutured DSEKs had a graft dislocation rate of 5% (n=3), versus 14% (n=16) of unsutured grafts ($p<0.05$). In the sutured group, one case of dislocation also had primary graft failure which may have contributed to failure to attach.

Conclusions: DSEK is a useful graft procedure for patients with corneal endothelial failure and complicated anatomy. We showed that intraoperative suture fixation of the graft reduces graft dislocation rates in these high-risk eyes.

CONTROL ID: 3715000

SUBMITTER (NAME ONLY): Hovhannes Gukasyan

TITLE: Ophthalmic Biopharmaceutics Classification System (oBCS): in vitro in silico relationship (IVISR) for comparability risk assessment in topical eye drop formulations

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.J. Gukasyan, I. Haworth, Pharmacology and Pharmaceutical Sciences, University of Southern California, Los Angeles, California, UNITED STATES|X. Faraj, M. Martinez, University of Southern California, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Hovhannes Gukasyan: Commercial Relationship: Code N (No Commercial Relationship) | Xavier Faraj: Commercial Relationship: Code N (No Commercial Relationship) | Melissa Martinez: Commercial Relationship: Code N (No Commercial Relationship) | Ian S Haworth: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Perform composite parameter sensitivity analysis, elucidate relative contribution of two parallel drug penetration pathways into eye from topically applied drops, towards establishing an oBCS and refining its framework.

Methods: Experimentally determined intrinsic solubility values of drug substances found in commercially available eye drops were compiled. A subset of forty drugs with available in vitro corneal (Cr) and conjunctival (Cj) tissue permeability (Papp) data, expressed as CrPapp/CjPapp, were used to plot sensitivity surfaces as a function of total topical ophthalmic dose (Do). Extent of aqueous humor (AqH), iris-ciliary body (ICB) and systemic exposure was calculated 0-20 minutes (e.g. $AUC_{0\text{-}20min}$) using OCAT™ simulated topical ophthalmic dosing as a function of corneal vs. conjunctival penetration access, and nasolacrimal drainage. Do and CrPapp/CjPapp parameter sensitivity analysis (PSA) were performed on 40 drugs to assess influence of corneal/conjunctival permeability, dose/solubility ratios on extent of absorption into eye vs. systemic.

Results: Contribution of the corneal route of absorption was dominant at nearly 90% fraction of dose reaching AqH for all compounds, while relatively low corneal permeability ones displayed up to 90% dependence of their ICB exposure on conjunctival access. Similarly, Do displayed up to 40% dependence on ICB access via conjunctival absorption, however was insensitive towards AqH access via corneal route of penetration. Contribution of nasolacrimal drainage towards systemic exposure displayed up to 15% dependence specifically on compounds with corneal penetration route preference as a function of increasing Do, while the opposite was true for compounds with conjunctival penetration route preference.

Conclusions: A oBCS is proposed in FIGURE. Pragmatic limitations in ocular bioanalysis result in challenges for bioequivalence establishment between different topical ophthalmic formulations of the same drug substance. There is potential value for computational model integrated biopharmaceutics in formulation design, optimization, and performance prediction.

CONTROL ID: 3715003

SUBMITTER (NAME ONLY): Daisuke Shiba

TITLE: Agreement of glaucoma progression diagnosis between optic disc and macular retinal structure change in a 3-year prospective observational study

SESSION TITLE: Structure-Function Relationship

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Shiba, S. Adachi, K. Yuki, K. Negishi, Ophthalmology, Keio University School of Medicine, JAPAN|

Commercial Relationships Disclosure: Daisuke Shiba: Commercial Relationship(s);Code R (Recipient):Santen, Senju Pharmaceutical, Glaukos Japan, Kowa, Otsuka Pharmaceutical, Novartis Japan, Nidek, SEED, Nitto Medic;Code F (Financial Support):Santen, Senju Pharmaceutical, Kowa, Otsuka Pharmaceutical, Nidek | Sayaka Adachi: Commercial Relationship: Code N (No Commercial Relationship) | Kenya Yuki: Commercial Relationship: Code N (No Commercial Relationship) | Kazuno Negishi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate agreement of glaucoma progression diagnosis between optic disc and macula by regression analysis of retinal structures measured with spectral-domain optical coherence tomography (SD-OCT) in a prospective observational cohort study.

Methods: Primary open angle glaucoma patients with visual field defect above -18dB of mean deviation value were included in this prospective study. Exclusion criteria were eyes with ocular diseases including cataract, abnormality history of intraocular surgery except successful glaucoma surgery, and the onset of other ocular diseases during study period that may influence the SD-OCT measurement. The circum-papillary retinal nerve fiber layer (cpRNFL) thickness and macular ganglion cell complex (GCC) thickness were measured using SD-OCT (NIDEK RS-3000 Advance) during three years with arbitrary intervals less than six months. Linear regression analysis of cpRNFL thicknesses in temporal, superior, nasal and inferior quadrants and GCC thicknesses in superior macula and inferior macula were performed with build-in software of the SD-OCT. A statistically significant thinnings in any area were defined as glaucoma progression ($P < 0.05$).

Results: 48 eyes of 48 glaucoma patients were included. Age and mean deviation at baseline visit were 61 ± 8.7 (mean ± standard deviation) years old and -5.7 ± 4.8dB. cpRNFL thinning rates (thickness at baseline) in temporal, superior, nasal and inferior quadrants were -0.38 ± 1.21 μm/y (57.9 ± 17.5 μm) , –1.49 ± 2.07 μm/y (90.3 ± 21.2 μm), 0.0 ± 1.4 μm/y (74.3 ± 14.4 μm) and -0.21 ± 1.63 μm/y (.2 ± 27.8 μm), respectively. GCC thinning rates (thickness at baseline) in suprerior and inferior macula were -0.18 ± 0.84 μm/y (84.6 ± 11.8 μm) and -0.07 ± 0.83 μm/y (74.7 ± 15.5 μm). Twenty four and 17 eyes were diagnosed as glaucoma progression by by cpRNFL and GCC, respectively, those were overlapped in 11 eyes. Kappa value was 0.21.

Conclusions: Agreement of glaucoma progression diagnosis was fair between cpRNFL thinning and macular GCC thinning.

CONTROL ID: 3715005

SUBMITTER (NAME ONLY): LINA CHEN

TITLE: Decreased cone density in circular retinal regions at the outer edge of full thickness macular hole edema in adaptive optics imaging

SESSION TITLE: Multidisciplinary Ophthalmic Imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. CHEN, Ophthalmology and vision sciences, University of Toronto, Toronto, Ontario, CANADA|L. CHEN, Kensington eye institute, University of Toronto, Toronto, Ontario, CANADA|

Commercial Relationships Disclosure: LINA CHEN: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Purpose: To introduce a method for analyzing adaptive optics (AO) imaging data on the full thickness macular hole (FTMH) and compare the cone density at the corresponding retinal regions surrounding the outer edge of para-macular hole edema (OEME) between the eyes with the FTMH versus the contralateral non-pathological eye within individual patients.

Methods: Method: Twenty-two patients (n=22) between the ages 53 and 73 years were recruited at the Kensington Eye Institute, Toronto. Each patient had one eye diagnosed with FTMH and the contralateral eye with no pathology. The AO images from 44 eyes were captured using rxt1 AO retinal camera. Nine images of each retina was overlapped covering 8°X8° central retina. The raw fragments of 4°X4° images were aligned to create a montage with developer-provided software. ImageJ was used for creating a grid. On the FTMH montage, a circle outlining OEME, and two perpendicular lines from diagonal meridians by 45° crossing the center of the macular hole were drawn. On the montage of the contralateral eye, a circle delineating the foveal avascular zone (FAZ), two lines with the same features as those on FTMH montage crossing the center of FAZ were drawn. The grid was created by overlaying the two lines from each montage. The created grid was overlaid on each montage. And the region of interest (ROIs) were sampled and compared with the guidance of the grid.

Results: Results: Of raw images from 22 eyes with FTMH, montage creation failed in 15 eyes (15/22, 68%), which was remarkably higher than contralateral eyes (P=0.01). The shifted fragment images were found in 38.8 % of total images taken from the eyes with FTMH, which was significantly higher than contralateral eyes (7.7%) (P=0.001). The cone density in 4 quadrants by OEME was decreased significantly than the contralateral corresponding retina (p=0.0004). Furthermore, the negative correlation between cone density and spacing at same regions was found in FTMH. (r=0.553, CI 95% [-0.79,-0.16], P=0.009).

Conclusions: Conclusion: The method of grid overlaying on the montage image was applicable to analyzing the AO imaging acquired from eyes with FTMH. Utilizing the grid, we found the cone density in circular retinal regions at the outer edge of ME was significantly decreased in adaptive optics imaging, which indicated that disturbance of the cones may occur outside OEME.

CONTROL ID: 3715006

SUBMITTER (NAME ONLY): Jesse Jung

TITLE: Level of Diabetic Retinopathy Severity Correlates to Degree of Quadrant Asymmetry in OCTA Metrics

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Jung, East Bay Retina Consultants, Inc, California, UNITED STATES|J.J. Jung, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|Q.V. Hoang, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|S. Lim, X. Chan, Q.V. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS Medical School, Singapore, SINGAPORE|

Commercial Relationships Disclosure: Jesse Jung: Commercial Relationship(s);Code C (Consultant/Contractor):Carl Zeiss Meditec, Inc. | Shen Yi Lim: Commercial Relationship: Code N (No Commercial Relationship) | Xavier Chan: Commercial Relationship: Code N (No Commercial Relationship) | Quan Hoang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Asymmetry among the ETDRS quadrants on en-face OCTA metrics (superficial [SRL] and deep retinal layer [DRL] perfusion density [PD] and vessel density [VD]) allows for intra-eye comparisons and possibly mitigates inter-eye variabilities such as refractive error, age, axial length, and magnification. Herein, we assess the effect of the level of diabetic retinopathy (DR) on quadrant asymmetry (QA) with en-face OCTA

Methods: 90 eyes (60 patients) [27 non-diabetic (noDM); 12 diabetics without DR (noDR); 11 mild, 10 moderate (mod) and 7 severe (sev) non-proliferative DR (NPDR); and 23 proliferative DR (PDR)] underwent 3x3mm OCTA scans (signal >7, fovea-centered and auto-segmented for SRL/DRL). QA was defined as the max-min value among 4 ETDRS quadrants for a given eye in terms of OCTA metrics for the SRL and DRL and was compared to DR severity by linear regression including fixed effects for each individual eye

Results: Mean age was 55.5 years (range 24-88) with 60% male. QA for SRL VD was 1.87, 1.95, 1.69, 2.37, 2.38 and 3.13 for noDM, noDR, mild, mod, sev and PDR, respectively. QA for SRL PD was 0.028, 0.035, 0.028, 0.046, 0.045 and 0.061, for DRL VD was 2.17, 1.76, 1.78, 2.38, 2.90 and 3.25, and for DRL PD was 0.037, 0.036, 0.033, 0.056, 0.071 and 0.069 for noDM, noDR, mild, mod, sev and PDR, respectively. Linear regression demonstrated for every step increase in DR severity, there was a 0.34 increase in QA ($p<0.001$) for SRL VD, +0.008 SRL PD ($p<0.001$), +0.41 DRL VD ($p<0.001$), and +0.010 DRL PD ($p<0.001$). QA for both SRL VD and PD were significantly higher in eyes with sev or PDR when compared to noDM or noDR eyes (+0.23 and +0.004, $p<0.001$). QA for both DRL VD and PD were significantly higher in eyes with mild or mod when compared to noDM or noDR eyes (+0.15, $p=0.04$ and +0.003, $p=0.02$)

Conclusions: DR severity affects PD and VD more asymmetrically across the 4 ETDRS quadrants with a linear increase in QA for each worsening level of DR. Clinically significant increase in QA occurs when eyes are worse than mod NPDR in the SRL and > mild NPDR in the DRL. Individual intra-eye metrics such as QA can be utilized to quantify DR severity without concerns for inter-eye variabilities that could affect the reproducibility and reliability of OCTA quantification

CONTROL ID: 3715010

SUBMITTER (NAME ONLY): Naveen Ambati

TITLE: Are perioperative blood pressure & blood glucose risk factors for poor surgical outcomes after 27-gauge vitrectomy for diabetic tractional detachments?

SESSION TITLE: Vitreoretinal surgery/VR Interface/PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ambati, X. Cai, R. Duong, Y. Shildkrot MD, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure: Naveen Ambati: Commercial Relationship: Code N (No Commercial Relationship) | Xiaoyu Cai: Commercial Relationship: Code N (No Commercial Relationship) | Ryan Duong: Commercial Relationship: Code N (No Commercial Relationship) | Yevgeniy Shildkrot MD: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Extremes in perioperative blood pressure and blood glucose are known risk factors for adverse outcomes after general surgical interventions. In the field of ophthalmology, there is little literature studying these parameters as risk factors. We performed a retrospective case series analysis to determine whether blood pressure and blood glucose on the day of surgery are associated with adverse outcomes in the postoperative period after 27-gauge (27g) vitrectomy for diabetic tractional retinal detachments (DM-TRD).

Methods: Data including peri/intraoperative blood pressure, fasting blood glucose (FBS), and postoperative visual and anatomic outcomes of 110 eyes that underwent 27g vitrectomy for repair of DM-TRD from 2013-2020 were evaluated. Logistic regression was performed to determine risk factors.

Results: Average age of the patient population was 45.33±12.07 years. Intraoperative complications included two cases of choroidal detachments. Of the patients who followed up on postoperative month six, 91.3% had an attached retina. Re-detachment was seen in 10.9% of cases, most often by postoperative month one. Pre-operatively, 80.2% of patients were legally blind compared to 56.3% at postoperative month 6 ($p<.001$). Higher maximum intraoperative mean arterial pressure (MAP) was associated with legal blindness at postoperative month six ($p = 0.010$). Though borderline, higher perioperative MAP was associated with fewer Snellen lines of improvement by postoperative month six ($p = 0.040$). Perioperative and intraoperative blood pressures were not a risk factor for poor anatomic outcomes in the postoperative period. Further, perioperative FBS was not a risk factor for poor visual and anatomic outcomes in the postoperative period.

Conclusions: Increased maximum intraoperative MAP is associated with worse visual outcomes. Blood pressure on the day of surgery was not a risk factor for poor anatomic outcomes. Perioperative FBS was not a risk factor for poor visual and anatomic outcomes. Further research is necessary to further elucidate the association between blood pressure and visual recovery after vitrectomy surgery.

CONTROL ID: 3715012

SUBMITTER (NAME ONLY): Diane Sayah

TITLE: Characterizing Macular Neovascularization in Myopic Macular Degeneration and Age-related Macular Degeneration using Swept Source OCT Angiography

SESSION TITLE: Imaging of posterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.N. Sayah, I. Garg, R. Katz, Y. Zhu, Y. Cui, R. Zeng, R. Tandias, J.Y. Moon, F. Vingopoulos, H. Wescott, G. Baldwin, N.A. Patel, J.B. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|D.N. Sayah, I. Garg, R. Katz, R. Zeng, R. Tandias, J.Y. Moon, F. Vingopoulos, H. Wescott, G. Baldwin, N.A. Patel, J.B. Miller, Retina Service, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|Y. Zhu, Eye Center, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|Y. Cui, Guangdong Eye Institute, Guangdong Provincial People's Hospital Department of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To describe and compare macular neovascularization (MNV) associated with myopic macular degeneration (MMD) and age-related macular degeneration (AMD) using swept-source optical coherence tomography angiography (SS-OCTA).

Methods: Adult patients with documented MNV were recruited in this cross-sectional study and imaged using 6 x 6 mm angiograms on SS-OCTA. Several qualitative and quantitative features of MNV were assessed, including the MNV area and vessel density (VD). Descriptive statistics and linear regression analyses were carried out.

Results: A total of 75 eyes with MNV, including 30 eyes with MMD-MNV and 45 eyes with AMD-MNV, were considered in this study. Mean subjects' age in each group was 55 ± 19 years and 75 ± 8 years respectively. The MMD-MNV group exhibited three-fold smaller sized MNV ($p=0.001$), lower greatest linear dimension (GLD) ($p=0.009$) and greatest vascular caliber (GVC) ($p<0.001$) compared to AMD-MNVs, and had a higher prevalence of tree-in-bud pattern. Eyes with AMD showed a higher prevalence of type 1 MNVs with medusa pattern, and tended to have better defined margins with the presence of peripheral loops. There was no difference in the location of the MNV, the shape's regularity, the presence of a core vessel, a capillary fringe or a perilesional dark halo between both conditions (all $p>0.05$). MMD-MNV presented a significantly high proportion (59%) of non-discernable MNV on SS-OCTA in our cohort. After adjustment, decreased MNV area and increased VD were associated with the tree-in-bud pattern, whereas the diagnosis did not significantly influence those parameters.

Conclusions: This study is the first to describe and compare MMD-MNV and AMD-MNV using SS-OCTA, providing relevant insight on MNV secondary to MMD and AMD, and further validating OCTA as a powerful tool to detect and characterize MNV non-invasively.

CONTROL ID: 3715014

SUBMITTER (NAME ONLY): Luis Rodríguez

TITLE: Richmond HRR and quality of life results in patients with color blindness wearing faded red tinted lenses

SESSION TITLE: Quality of Life Outcomes, Rehabilitation and Training Programs

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Rodríguez, I. Domínguez Varela, M. Hernandez, Y. Macias, Oftalmologia, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

Commercial Relationships Disclosure: Luis Rodríguez: Commercial Relationship: Code N (No Commercial Relationship) | Irving Armando Domínguez Varela: Commercial Relationship: Code N (No Commercial Relationship) | Miguel Hernandez: Commercial Relationship: Code N (No Commercial Relationship) | Yolanda Macias: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the effect of faded red filter lenses on the degree of severity of the Richmond HRR test scores in color blind people, the type of dyschromatopsia and its severity were classified, the results of a quality of life questionnaire was evaluated before and after the use of the glasses

Methods: Observational, descriptive and comparative study, in patients with color blindness in a Mexican population wearing faded chromatic lenses. Inclusion criteria comprised patients older than 6 years of age, who failed an Ishihara test, and had HRR Richmond tests performed before and after wearing the tinted lenses for more than 2 hours daily for 2 months.

Results: Fifty-one individuals with a diagnosis of dyschromatopsia were included. Fifty (98%) were men and 1 was female (2%). The mean age was 27.1 years (range 6-64y). When classifying the type of color blindness, the deutan group constituted 66.7% of the population, and 31.4% were classified as protans. Most subjects were classified as a severe grade of color blindness in (59.2%), followed by the moderate group (28.6%). The average percentage of incorrect answers in the Richmond HRR test prior to wearing the lenses was 45%, after using the lenses, an average percentage of incorrect answers of 26% was obtained. Subjects referred an improvement in the quality of life questionnaire scores from 13.74 points before using the glasses, to 9.61 points after wearing the tinted lenses.

Conclusions: Color blindness is a common condition affecting almost 1 in 12 men. This condition can have an effect on the quality of life these subjects because of the difficulty to perceive certain colors. In our study, almost all of the subjects were male, classified as severe deutans. Richmond HRR results improved with the use of the tinted lenses. After wearing the faded red tinted glasses the majority of subjects who were initially classified with a severe degree of dyschromatopsia, were classified with a mild degree of color blindness. These subjects also referred a subjective improvement in their quality of life. Further studies are needed to understand the effect of tinted glasses on the quality of life of subjects with color blindness.

CONTROL ID: 3715016

SUBMITTER (NAME ONLY): John Miller

TITLE: Surgical outcomes of scleral buckling for rhegmatogenous retinal detachment using the NGENUITY three-dimensional visualization system with a guarded light pipe

SESSION TITLE: Vitreoretinal Surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Miller, J. Sokol, C.A. Ludwig, G. Baldwin, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: John Miller: Commercial Relationship(s);Code C (Consultant/Contractor):Alcon;Code C (Consultant/Contractor):Allergan;Code C (Consultant/Contractor):Genentech;Code C (Consultant/Contractor):Carl Zeiss;Code C (Consultant/Contractor):Sunovion | Jared Sokol: Commercial Relationship: Code N (No Commercial Relationship) | Cassie Ludwig: Commercial Relationship: Code N (No Commercial Relationship) | Grace Baldwin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the surgical outcomes of traditional scleral buckling (SB) under indirect ophthalmoscopy (ID) for primary rhegmatogenous retinal detachment (RRD) repair to a new SB technique that utilizes the NGENUITY heads-up three-dimensional visualization system with a guarded light pipe (3DGLP).

Methods: A retrospective comparative study of 47 eyes that underwent SB for primary RRD by a single surgeon was performed. Electronic medical records of the ID group (n = 31) and the 3DGLP group (n = 16) were evaluated. In the 3DGLP group, the scleral buckle was attached to the eye in the traditional manor, but the retina was visualized with the NGENUITY 3D visualization system and a guarded light pipe. The guarded light pipe was created by sliding a trimmed Watzke-Allen sleeve onto the shaft of a light pipe as a guard to prevent insertion into the vitreous past the internal os of a single 25 or 27-gauge trocar cannula. The primary outcome of the study was single surgery anatomic success and secondary outcomes included final anatomic success, visual acuity, operative time, and intra and post-operative complications.

Results: The single surgery anatomic success rate was 87.0% in the ID group and 87.5% in the 3DGLP group ($p = 1.00$). The final anatomic success rate was 100% in both groups. The mean post-operative logMAR was 0.206 in the ID group and 0.339 in the 3DGLP group ($p = 0.4339$). The mean operative time was 110.3±24.9 minutes in the ID group and 101.0±16.4 minutes in the 3DGLP group ($p = 0.2533$). Among eyes that underwent subretinal fluid drainage, the operative time was significantly longer in the ID group compared to the 3DGLP group. There were no post-operative complications in the ID group and one episode of self-resolving vitreous hemorrhage in the 3DGLP group ($p = 0.3404$).

Conclusions: Compared to traditional SB surgery for the treatment of RRD, SB surgery utilizing NGENUITY three-dimensional visualization with a guarded light pipe results in similar anatomical, visual, and peri-operative outcomes and may result in a shorter surgical times with subretinal fluid drainage. This new technique allows for all participating surgeons, including trainees, to view critical procedural steps simultaneously while using the familiar light pipe tool for illumination.

CONTROL ID: 3715017

SUBMITTER (NAME ONLY): Ryan Gallo

TITLE: Müller glia-specific Notch signaling knockout mitigates reactive gliosis after ischemia-reperfusion injury

SESSION TITLE: Neuroprotection, blood flow and ischemia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Gallo, G. Dvoriantchikova, H. Wang, A.H. Moeyersoms, K. Pino, D. Pelaez, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Notch signaling pathway has various roles during retinal development and is involved in the pathological changes that occur after retinal injury and disease. Notch signaling activation in Müller glia (MG) enhances reactive gliosis, neural death, and fibrosis after retinal injury. In mammals, four different Notch receptors (Notch1-4) have been identified. Yet, the specific roles of each receptor in the retina are not yet fully elucidated. We have generated transgenic animals to characterize the roles of Notch1 and Notch2 during MG gliosis. Given the activation of Notch1 signaling during retinal injury, we hypothesize that directly blocking Notch1 will mitigate reactive gliosis and subsequent neuropathic progression.

Methods: Retinal ischemia-reperfusion (IR) injury was induced in one eye of adult mice (8 to 12-weeks-old) by increasing intraocular pressure to 120 mmHg with normal saline for 1 hour. Ischemia was confirmed by fundus whitening. C57BL/6J mice were sacrificed and retinas isolated at various timepoints after injury for Western blot and staining. To determine how Notch signaling contributes to MG gliosis, we deleted Notch1 and Notch2 in MG via an inducible Cre/LoxP system driven by the MG-specific GLAST promoter (GLAST-CreERT; $Notch1^{fl/fl}$/$Notch2^{fl/fl}$). These transgenic mice received daily intraperitoneal injections of tamoxifen for 5 days prior to retinal IR injury. They were sacrificed 3 and 7 days after injury and their retinas were isolated for Western blot, staining, and RNA-Seq. Tamoxifen-treated GLAST-CreERT mice served as controls.

Results: Notch1 signaling is activated upon retinal IR injury in a time-dependent manner as confirmed by increases in Notch1 and cleaved Notch1 intracellular domain (NICD) expression on Western blot. MG-specific Notch1/2 knockout mitigates the gliotic response 7 days after IR injury as demonstrated by decreased GFAP expression on Western blot and immunofluorescence staining and reduced MG hypertrophy. RNA-Seq after IR injury on Notch1/2 KO and control mice retinas is ongoing. In addition, ChIP-Seq for the activated NICD on wild-type mice is underway to identify the genes Notch1 regulates directly during gliosis.

Conclusions: Notch1 signaling is activated after IR-mediated gliosis, and its direct blockage is a potential therapeutic strategy for retinal injury or disease.

CONTROL ID: 3715020

SUBMITTER (NAME ONLY): Usman Baqai

TITLE: Multi-omics profiling shows BAP1 loss is associated with upregulated cell adhesion molecules in uveal melanoma

SESSION TITLE: Intraocular tumors - Uveal melanoma and retinoblastoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Baqai, T.J. Purwin, V. Chua, N. Bechtel, A.E. Aplin, Department of Cancer Biology, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|A. Han, Department of Food Science and Human Nutrition, Jeonbuk National University, Jeollabuk-do, KOREA (THE REPUBLIC OF)|E.J. Hartsough, Department of Pharmacology and Physiology, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|J. Harbour, Department of Ophthalmology, The University of Texas Southwestern Medical Center Medical School, Dallas, Texas, UNITED STATES|J. Kuznetsoff, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: BRCA1-associated protein 1 (BAP1) is a tumor suppressor gene that is mutated in cancer, including uveal melanoma. Given that the loss of BAP1 is detected frequently in high-risk metastatic uveal melanoma cases, we sought to study molecular differences that could explain disease progression. In certain contexts, upregulation of cell-cell adhesion proteins is involved with collective migration and metastatic seeding of cancer cells.

Methods: We analyzed publicly available RNA sequencing data from 80 primary uveal melanoma cases in The Cancer Genome Atlas (TCGA), separated into BAP1 mutant (n=40) and wild-type (n=40) groups. We also analyzed single cell RNA sequencing data from BAP1 mutant and wild-type patient tumors, RNA sequencing from a panel of six BAP1 mutant (MM28, MP38, MP46, MP65, WM3618F and PDX4) and two BAP1 wild-type cell lines (92.1 and MM66), and RNA sequencing from a BAP1 mutant vs BAP1 re-expressing cell line (UM22). We used targeted knockdown of CDH1 and CADM1 to determine the functional role of cell adhesion molecules (CAMs) in BAP1 mutant uveal melanoma.

Results: We show that BAP1 loss in uveal melanoma patient samples is associated with an upregulated gene expression profile of multiple CAMs, including E-cadherin (CDH1), cell adhesion molecule 1 (CADM1), and syndecan-2 (SDC2). Similar findings were observed in uveal melanoma cell lines and single cell RNA sequencing data from patient samples. BAP1 re-expression in uveal melanoma cells reduced E-cadherin and CADM1 levels. Functionally, knockdown of E-cadherin decreased spheroid cluster formation and knockdown of CADM1 decreased growth of BAP1 mutant uveal melanoma cells.

Conclusions: Our findings demonstrate that BAP1 regulates the expression of CAMs which may regulate metastatic traits.

CONTROL ID: 3715021

SUBMITTER (NAME ONLY): Seth Fortmann

TITLE: Retinal Ischemia Induces Rapid and Reversible Histone Hypermethylation

SESSION TITLE: Cell biology of retinal diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Fortmann, M.B. Grant, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure: Seth Fortmann: Commercial Relationship: Code N (No Commercial Relationship) | Maria Grant: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Hypoxia-induced VEGF expression is a well-characterized disease mechanism that underlies ischemic retinopathies and requires stabilization of hypoxia-inducible factors (HIFs). However, less is known about HIF-independent hypoxia-sensitive pathways, which may alter the epigenetic landscape of hypoxic retinal cells and thereby promote the transcriptional activity of HIFs.

Methods: The oxygen-induced retinopathy (OIR) mouse model (75% O2 from P7-P12) was used to investigate histone modifications during acute retinal ischemia following hyperoxia exposure. Immunofluorescence (IF) and western blotting (WB) were performed at various timepoints in OIR mice (time post-hyperoxia exposure: 0 hours (h; baseline), 2h, 4h, 1 day (d), 3d, and 5d) to probe the spatiotemporal modifications that occur on histones following acute retinal ischemia, including H3K4me3, H3K9me3, H3K27me3, H3K36me2, and H3K36me3. The dynamicity of hypoxia-induced histone hypermethylation was examined using reoxygenation experiments in the OIR mouse model, where mice were removed from hyperoxia for 2h and then returned to hyperoxia (reoxygenation) for 2h or 4h. Lastly, IF, WB, and single-cell RNA-sequencing data (scRNA-seq) were used to examine the retina for expression of the hypoxia-sensitive histone demethylases, KDM5A and KDM6A.

Results: WB on whole retinal lysates showed that the hypoxia-sensitive histone demethylases, KDM5A and KDM6A, were strongly expressed in the mouse retina. IF and scRNA-seq showed that KDM5A and KDM6A were globally expressed in the retina, with the strongest expression in inner nuclear layer cells. WB on whole retinal lysates from OIR mice showed that H3K4me3 was induced as early as 2 hours following the onset of hypoxia, which mirrored the simultaneous stabilization of HIF1α. Reoxygenation experiments in OIR mice showed that the induction of H3K4me3 was rapidly reversible and that H3K4me3 levels returned to baseline within 2 hours of reoxygenation.

Conclusions: These findings reveal a novel, rapidly induced, and reversible hypoxia sensitive pathway in the ischemic retina that acts on histone modifications. H3K4me3 is a promoter-specific histone modification that influences transcription factor docking and thus, may play a role in instructing the genomic binding of HIFs during retinal ischemia.

CONTROL ID: 3715024

SUBMITTER (NAME ONLY): Allie Lee

TITLE: Ocular Graft-Versus-Host-Disease and Vision-related Quality of Life following Allogeneic Haematopoietic Stem Cell Transplantation in Hong Kong

SESSION TITLE: Corneal epithelial biology and repair mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lee, T. Cao, P. Lam, The University of Hong Kong, Hong Kong, HONG KONG|

Commercial Relationships Disclosure: Allie Lee: Commercial Relationship: Code N (No Commercial Relationship) | Tianyi Cao: Commercial Relationship: Code N (No Commercial Relationship) | Pui Ming Lam: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Allogeneic hematopoietic stem cell transplantation (HSCT) is an effective treatment for all array of haematological disorders, rendering improved disease prognosis and long-term survival rate. However, ocular graft-versus-host-disease (oGVHD) as a chronic complication of allogeneic HSCT affects patients' ocular health and their daily living. Vision-related quality of life (QOL) and its association with oGVHD were examined.

Methods: 134 patients who received allogeneic HSCT between year 2000 to 2010, and aged 18 or above at the time of transplant were recruited. oGVHD related ocular surface and adnexa changes were assessed by various ophthalmological examinations: Schirmer test without anaesthesia, measurement of tear meniscus height (TMH), non-invasive tear break-up time (NIBUT), conjunctival injection, corneal fluorescein staining, subconjunctival fibrosis (SCF) and meibomian gland dysfunction. Infrared meibographs were taken to assess meibomian gland dropout percentage by ImageJ software. Diagnosis of oGVHD was made based on both the National Institutes of Health (NIH) consensus criteria and the scoring system of International Chronic Ocular Graft-vs-Host-Disease Consensus Group (ICC). Ocular Surface Disease Index (OSDI) and National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ25) were used for measurement of vision-related QOL.

Results: Of the 130 patients included in analysis (4 excluded as they had two or more allogeneic HSCT), 72 (55.3%) of them were male. Age at the year of BMT was 19-60 (s.d.= 10.9) and follow-up months since BMT was 133-262 months (s.d.= 39.5). With NIH dignosis criteria, 61.5% had oGVHD, with 43.1% having grade 1 severity and 18.5% having grade 2 severity. Diagnosis by ICC criteria showed 56.2% oGVHD in worst eye, with 27.7% having probable oGVHD and 28.5% having definite oGVHD. Mean MG atrophy in oGVHD patients by NIH criteria was 37.9% (s.d.=14.1) and non-oGVHD patients had 36.3% (s.d.=14.2) MG atrophy. OSDI in oGVHD and non-oGVHD patients by NIH criteria was 26.0 (s.d.=21.9) and 20.4 (s.d.=18.8) respectively.

Conclusions: Although MG atrophy did not show significant difference between oGVHD and non-oGVHD patients in this study, with oGVHD becoming more prevalent as allogenic HSCT advances, further studies are needed to correlate clinical findings and patient perceived QOL.

CONTROL ID: 3715025

SUBMITTER (NAME ONLY): Margaret Runner

TITLE: Outbreak of Acute and Subacute Post-Injection Endophthalmitis caused by Pseudomonas aeruginosa

SESSION TITLE: Endophthalmitis/ trauma/Intravitreal/periocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Runner, T. Begaj, D. Scoles, M. Trese, J. Park, K.A. Drenser, G.A. Williams, S. Randhawa, A.J. Ruby, Vitreoretinal Surgery - Associated Retinal Consultants, Beaumont Health, Royal Oak, Michigan, UNITED STATES|

Commercial Relationships Disclosure: Margaret Runner: Commercial Relationship: Code N (No Commercial Relationship) | Tedi Begaj: Commercial Relationship: Code N (No Commercial Relationship) | Drew Scoles: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Trese: Commercial Relationship: Code N (No Commercial Relationship) | Jong Park: Commercial Relationship: Code N (No Commercial Relationship) | Kimberly Drenser: Commercial Relationship: Code N (No Commercial Relationship) | George Williams: Commercial Relationship: Code N (No Commercial Relationship) | Sandeep Randhawa: Commercial Relationship: Code N (No Commercial Relationship) | Alan Ruby: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the atypical presentation, clinical course, and visual outcomes associated with post-injection endophthalmitis (PIE) caused by Pseudomonas aeruginosa.

Methods: A detailed retrospective review was conducted of four cases of Pseudomonas aeruginosa PIE who presented from May – September, 2021 to different ophthalmology practices in Michigan.

Results: Four patients undergoing treatment for age-related macular degeneration (n=3) or diabetic macular edema (n=1) received right eye intravitreal injections of aflibercept (n=1), ranibizumab (n=1), bevacizumab (n=1), or dexamethasone implant (n=1) at two separate ophthalmic practices by three different providers on four separate dates. All patients were pseudophakic with a baseline vision of 20/20 to 20/50. Each patient subsequently developed rapid vision loss to hand motion (n=3) or light perception (n=1) and diagnosed with Pseudomonas aeruginosa endophthalmitis by aqueous fluid culture. Onset of endophthalmitis post-injection varied significantly with two patients presenting at the typical acute time frame (3 and 10 days post-injection) and the other two patients presenting during the subacute period (27 and 36 days post-injection). All patients received intravitreal vancomycin and ceftazidime and aqueous fluid biopsy on day of presentation, followed by a vitrectomy, vitreal biopsy, and repeat intravitreal antibiotics within 1-3 days after presentation. Despite all Pseudomonas strains being pansusceptible, these eyes continued to remain Pseudomonas culture positive on subsequent biopsies despite repeated intravitreal ceftazidime injections. There was a high incidence of post-vitrectomy choroidals and retinal detachment (n=3) which was associated with worse visual outcomes.

Conclusions: As far as the authors are aware, this is the first series of PIE caused by Pseudomonas aeruginosa. Important insights can be made into the atypical presentation and disease course to help guide future management. Unlike other cases of bacterial PIE, Pseudomonas persists within the eye despite intravitreal antibiotic injections with adequate coverage. In addition, a high rate of post-operative choroidals and retinal detachment were observed. Therefore, early vitrectomy, repeat antibiotic injections, and placement of silicone oil should be considered in these patients.

CONTROL ID: 3715030

SUBMITTER (NAME ONLY): Clifford Jin

TITLE: Physiologically Based Dissolution Modeling for Topical Ophthalmic Suspensions

SESSION TITLE: Drug delivery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Jin, Sage Hill School, Newport Coast, California, UNITED STATES|H.J. Gukasyan, Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Clifford Jin: Commercial Relationship: Code N (No Commercial Relationship) | Hovhannes Gukasyan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The quality of an ophthalmic suspension is crucial to its clinical effectiveness and understanding formulation attributes is important for successful product development. This study aims to demonstrate the effect of physicochemical properties including solubility, pK_a (for ionizable molecules), and particle size with morphology/shape on in situ drug dissolution rate (e.g. release within tear following topical instillation). Such descriptors and relationships of simulated in vitro release tests (IVRT) can be used as input parameters for predictive optimization of sensitive product design parameters impacting drug absorption and disposition from complex topical ophthalmic suspensions.

Methods: DDDPlus™ and Ocular Compartmental Absorption & Transit (OCAT) v3, a module in GastroPlus™ (Simulations Plus, Inc.) were used to simulate drug dissolution (vs IVRT) and biodistribution (vs rabbit pharmacokinetics, PK) in aqueous humor (AH) and iris ciliary body (ICB) as target compartments. Measured or empirically estimated input parameters for drugs found in commercial topical ophthalmic suspensions were obtained from experimental literature. The simulation results were compared to IVRT, and then used for global optimization of physiologically based PK models. All referenced data were extracted from original publications using GetData Graph Digitizer®.

Results: DDDPlus™ simulations enabled fabrication of dissolution profiles similar to experimentally determined ones from IVRT. Between sets of dissolution predictions variations on mixing rate (e.g. blinking), USP simulated tear fluid (STF) composition, and molecular structure based vs. physicochemical property support files use were successfully evaluated. Without sensitive parameter identification and optimization DDDPlus™ tended to underpredict dissolution of studied drug particle examples. OCAT v3 simulated ocular exposures produced expected results and trends in rabbit AH and ICB from topical ophthalmic suspensions.

Conclusions: DDDPlus™ can serve as an initial assessment tool to build in vitro correlations with STF dissolution models, which can subsequently be relayed to OCAT v3 for ocular pharmacokinetic predictions. This is a novel tool being developed and promoted by the FDA for in silico approaches for establishment of bioequivalence in complex drug products, such as topical ophthalmic suspensions.

CONTROL ID: 3715031

SUBMITTER (NAME ONLY): Aaron Roschke

TITLE: Long Term Efficacy of Intraoperative Mitomycin-C in Novel Approach Small Incision Sub-tenon Ab-Interno XEN® Gel Stent Implantation

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Roschke, Colorado Eye Institute, Colorado Springs, Colorado, UNITED STATES|

Commercial Relationships Disclosure: Aaron Roschke: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the long term efficacy of the intraoperative use of sub-tenon Mitomycin C in a novel approach sub-tenon ab-interno XEN® Gel Stent implantation IOP versus baseline intraocular pressure prior to surgery.

Methods: The study group consists of approximately 44 eyes with uncontrolled primary open-angle glaucoma without previous glaucoma surgery and with uncontrolled intraocular pressure, documented glaucoma progression, and/or intolerance to IOP-lowering therapy. All patients underwent Mitomycin C application via small incision sub-tenon Ab-Interno XEN® Gel Stent Implantation as a stand-alone procedure by a single surgeon. Recovery included tapering postoperative steroid drops through 4 weeks following surgery and adjusting topical glaucoma drops based on intended target intraocular pressure. Postoperative visits were conducted for all patients at regular intervals through 12 months. Surgical outcome tracking assessed through IOP measurement via calibrated Goldmann Applanation Tonometry by a single surgeon.

Results: Of the 44 subject eyes at 6 month interval, 100% of the population had IOP below 17mmHg, 91% of the population 15mmHg or below, and 55% of the patient population of 12mmHg or lower. The mean decrease in topical glaucoma medications was 1.95 ± 1.31 at 6 month postoperative period. The mean IOP was 13.13 ± 1.64 ($p=0.003$) at 6 month postoperative period. At the 12 month postoperative interval, 3 subjects were lost to follow-up, 90.2% of the patient population had an IOP 17mmHg or lower, 70.7% of the patient population 15mmHg or lower, and 51.2% of the patient population 13mmHg or lower. The mean IOP after the 12 month postoperative period was 14.07mmHg ± 3.80.

Conclusions: Application of Mitomycin C in a novel approach sub-tenon ab-interno XEN® Gel Stent implantation appears to demonstrate high efficacy for the reduction in intraocular pressure (IOP) in patients with uncontrolled primary open-angle glaucoma.

CONTROL ID: 3715032

SUBMITTER (NAME ONLY): David Thorn

TITLE: Structure and stability of domain-swapped mutant γ-crystallins: implications for lens cataract and βγ-crystallin evolution

SESSION TITLE: Molecular and Biochemical Mechanisms of Ocular Disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.C. Thorn, E. Serebryany, E. Shakhnovich, Harvard University Faculty of Arts and Sciences, Cambridge, Massachusetts, UNITED STATES|G. Birrane, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Kaya, Argonne National Laboratory Advanced Photon Source, Lemont, Illinois, UNITED STATES|

Commercial Relationships Disclosure: David Thorn: Commercial Relationship: Code N (No Commercial Relationship) | Eugene Serebryany: Commercial Relationship: Code N (No Commercial Relationship) | Gabriel Birrane: Commercial Relationship: Code N (No Commercial Relationship) | Ali Kaya: Commercial Relationship: Code N (No Commercial Relationship) | Eugene Shakhnovich: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Vertebrate βγ-crystallins adopt two homologous domains connected via a linking peptide which is considered a key determinant of their tertiary and quaternary arrangements. In vitro, γ-crystallins are monomeric whereas β-crystallins form mainly dimers that are thought to associate further via domain-swapping to form larger oligomers. This study aims to better understand the oligomeric preferences of βγ-crystallins.

Methods: The propensity to form domain-swapped dimers in mutant γ-crystallins was predicted with AlphaFold Multimer and initially assessed by Superdex-75 column size-exclusion chromatography. The dimeric structure was determined by X-ray crystallography. Aggregation propensity was assessed by turbidimetry. Thermal stability was measured by circular dichroism and differential scanning calorimetry.

Results: Several γ-crystallin mutants adopted non-covalently associated dimers in solution under both reducing and non-reducing conditions. The crystal structure of one select mutant shows a domain-swapped dimer, distinct from the compact ‘face en face’ dimeric structure of β-crystallin in solution. The domain structures show no structural perturbation and the conserved interface between the N- and C-terminal domains is preserved. The domain-swapped dimers of γ-crystallin are not markedly aggregation-prone at physiological temperature relative to their wildtype monomeric counterparts; however, they exhibit reduced thermodynamic stability.

Conclusions: Domain-swapped dimers of vertebrate βγ-crystallins are less stable and are unfavorable in an aging lens where the risk of protein misfolding and aggregation is pronounced due to cumulative post-translational modifications. The long-lived crystallin proteins have therefore been engineered to avoid domain-swapped dimerization in order to retain their soluble, folded conformations throughout adulthood and avoid diseases of the lens such as cataract.

CONTROL ID: 3715033

SUBMITTER (NAME ONLY): Pradeep Ramulu

TITLE: Patient features associated with a higher sibling risk of angle closure disease

SESSION TITLE: Glaucoma Genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.Y. Ramulu, S. Mudalegundi, A. Mihailovic, Ophthalmology, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|R. Venkatesh, K. Srinivasan, Aravind Eye Institute, Pondicherry, INDIA|N. Zebardast, Massachusetts Eye and Ear Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure: Pradeep Ramulu: Commercial Relationship(s);Code C (Consultant/Contractor):Ivantis, W.L. Gore, Heru, Roche;Code R (Recipient):Perfuse Therapeutics | Shwetha Mudalegundi: Commercial Relationship: Code N (No Commercial Relationship) | Aleksandra Mihailovic: Commercial Relationship: Code N (No Commercial Relationship) | Nazlee Zebardast: Commercial Relationship: Code N (No Commercial Relationship) | Rengaraj Venkatesh: Commercial Relationship: Code N (No Commercial Relationship) | Kavitha Srinivasan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess if specific findings gathered during an examination of patients with a known angle closure diagnosis (probands) could better determine the risk of angle closure in the patient's sibling.

Methods: Patients 30 years and older with suspect primary angle closure (PACS) or primary angle closure/primary angle closure glaucoma (PAC/G) seen at the Aravind Eye Hospital in Pondicherry, Tamil Nadu, and a biological sibling above age 30 years, were recruited as 'probands' and 'siblings' (n=346 pairs). Demographics, ocular history, and an ophthalmic examination with Anterior Segment Optical Coherence Tomography (ASOCT) were obtained. Siblings were classified as having open angles (OA), PACS, or PAC/G per ISGEO criteria. Models were created to analyze the contribution of specific proband factors in predicting sibling angle closure diagnosis.

Results: When predicting (1) any sibling angle closure (PACS or PAC/G) vs. open angles, (2) sibling PAC/G vs PACS or OA, or (3) PAC/G vs. PACS amongst siblings with angle closure, models incorporating proband ASOCT data outperformed models including proband diagnosis alone or proband diagnosis plus demographic (age/gender) and exam metrics (gonioscopy, optic nerve exam, visual acuity, and intraocular pressure). For example, in the prediction of PAC/G vs. PACS amongst siblings with angle closure, the model using only proband diagnosis had the lowest explained variability (0.64%). Adding proband demographics and ocular exam metrics improved model accuracy to a limited extent (1.99% of variability explained), while adding ASOCT Metrics created a significant improvement (17% of variability explained, $p<.0001$ vs other models). The model incorporating ASOCT metrics resulted in the lowest Bayesian Information Criterion (101.9 vs. 123.6 for the diagnosis-only model and 119.7 for the diagnosis + demographics + exam metrics model).

Conclusions: Utilizing ASOCT information from angle closure patients can help better predict sibling angle closure status, leading to more efficient and cost-effective screening of family members.

CONTROL ID: 3715035

SUBMITTER (NAME ONLY): Carla Berkowitz

TITLE: Utility of Intraoperative Optical Coherence Tomography In Optimizing Air Fill for Endothelial Keratoplasty

SESSION TITLE: Corneal Imaging and Corneal Nerves

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Berkowitz, A. Ramaprasad, M. Tseng, S. Basti, Northwestern Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Carla Berkowitz: Commercial Relationship: Code N (No Commercial Relationship) | Abhijit Ramaprasad: Commercial Relationship: Code N (No Commercial Relationship) | Michael Tseng: Commercial Relationship: Code N (No Commercial Relationship) | Surendra Basti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A full air fill and sufficiently high intraocular pressure (IOP) are crucial to ensure optimal graft adhesion during endothelial keratoplasty. While air fill and IOP can be approximated on the operating table, it is difficult to quantify if the air fill will provide an adequate IOP. The purpose of this study is to evaluate how the air fill in the anterior chamber anterior chamber (AC) correlates with IOP, AC depth, and the iris configuration.

Methods: Cadaveric human eyes were mounted on a microscope with intraoperative optical coherence tomography (OCT). Inclusion criteria for the eyes included pseudophakia and harvest time within 48-72 hours. Three categories were used: baseline, an air fill that just spanned limbus to limbus (“limbus to limbus”), and an air fill that maximally filled the entire AC (“max fill”). IOP was measured by taking the average of 3 Tono-pen (Reichert, Buffalo, New York) measurements. OCT images were obtained in the operating room and analyzed using ImageJ software. ImageJ was used to measure the distance from the posterior cornea to the anterior iris to determine AC depth, and to measure the angle between the iris and the cornea to determine iris configuration.

Results: Preliminary data has shown that at baseline the IOP was 14.33, AC depth was 3.067, and an irido-corneal angle of 37.33°. Limbus to limbus fill had an IOP of 14.33, an AC depth of 2.968, and an irido-corneal angle of 36.25°. Max fill had an IOP of 17.33, an AC depth of 3.37, and an irido-corneal angle of 44.09°. Finalized data will be based on a total of 10 eyes to power this study, assuming an 80% power, a p-value of <0.05, an R-squared of 0.50, and a single variable model.

Conclusions: Early data has indicated a correlation of IOP with AC depth as perceived on intraoperative OCT. In addition, while an air bubble may appear to fill the AC, as demonstrated by the “limbus to limbus” category, it’s IOP may not be sufficiently high to optimize graft adherence. Finally, a concave iris contour on OCT may be a reliable surrogate to suggest an adequate anterior chamber fill.

CONTROL ID: 3715046

SUBMITTER (NAME ONLY): Sailaja Manda

TITLE: Estimating Pedestrian Detection with peripheral prisms in Homonymous Hemianopia

SESSION TITLE: Mobility, Reading and Driving with Vision Impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Manda, A.D. Hwang, J. Jung, E. Peli, Opthalmology, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|N.M. Kurukuti, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

Commercial Relationships Disclosure: Sailaja Manda: Commercial Relationship: Code N (No Commercial Relationship) | Nish Kurukuti: Commercial Relationship: Code N (No Commercial Relationship) | Alex Hwang: Commercial Relationship: Code N (No Commercial Relationship) | Jae-Hyun Jung: Commercial Relationship: Code N (No Commercial Relationship) | Eli Peli: Commercial Relationship(s);Code P (Patent):Chadwick Optical

ABSTRACT BODY:

Purpose: Fresnel(F, 57PD) and Multiperiscopic(M, 100PD) prisms are peripheral prisms designed to expand the visual field for persons with Homonymous Hemianopia (HH). Prism segments are placed above(U) and below(L) the pupil in a horizontal(H) or oblique(O) configuration. We constructed a mathematic model to simulate pedestrians walking toward a patient wearing any combination(U/L/Both(U&L)) of (F/M) prisms to compare detection rates and estimate if wearing single prism(U/L) is as good as both(U&L).

Methods: The dataset simulated 6-second events of a patient wearing F/M looking straight ahead without eye movement and walking toward a collision point. A pedestrian approached at 0°-90° to this point (at 1° intervals). We modelled 6 pedestrian forms based on physical anthropometry measurements. Each form used 80 data-points to model patient and pedestrian attributes such as walking speed, height, torso, arm/leg width and span. A pedestrian was categorized detected if the height/width of the pedestrian's image within the prism was >3°(based on experiment data collected from 4 HH patients). Detection rates were computed for 540 events per HH model wearing a U/L/U&L prism combination of F/M prisms. Differences in detection rates were analyzed using a 2(F/M) x 2(H/O) x 3 (U/L/U&L) ANOVA.

Results: The detection rate with any prism(F:0.40±0.38, M:0.62±0.32) was better than without prisms(0.05±0.2). There were significant main effects(all ps<0.001) of the type of prism design(F vs M), configuration(H: 0.62±0.4, O: 0.37±0.27) and number of segments(U:0.15±0.03, L: 0.67±0.33, U&L:0.71±0.33). All interactions between these variables were significant(all ps<0.001). The LH configuration(LHF:0.82±0.01, LHM:1) had the best detection rates and these were not significantly different from three of the U&L prisms performance(U&L HF:0.824±0.01, U&L HM:1±0, U&L OM: 0.782±0.02).

Conclusions: A mathematic model was used to simulate if a single prism supported detection as well as dual peripheral prism configurations in the absence of observer head tilt or eye movement. Use of a single prism configuration would provide reduced cost and better cosmesis for patients. Mathematic modeling to estimate detection can combine real world physical measurements with theoretical prism expansion calculation. Further analyses with head and gaze shift modelling could be a useful tool to support design of peripheral prisms and aid clinical decision making.

CONTROL ID: 3715047

SUBMITTER (NAME ONLY): Paige Campbell

TITLE: Patient satisfaction with teleophthalmology in ocular oncology.

SESSION TITLE: Eyecare delivery and economics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Campbell, T. Crump, E. Weis, University of Calgary, Calgary, Alberta, CANADA|E. Weis, University of Alberta, Edmonton, Alberta, CANADA|

Commercial Relationships Disclosure: Paige Campbell: Commercial Relationship: Code N (No Commercial Relationship) | Trafford Crump: Commercial Relationship: Code N (No Commercial Relationship) | Ezekiel Weis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Teleophthalmology decreases barriers to accessing highly specialized care, such as ocular oncology. However, there is a dearth of research into patients' perceptions of having care delivered through this modality. The purpose of this study is to evaluate patients' satisfaction with a teleophthalmology program for ocular oncology and whether it addressed their healthcare needs.

Methods: The teleophthalmology program includes diagnostic imaging, remote physician assessment, and a follow-up phone call from a member of the healthcare team to relay results to patients. Patients who had received care from this program were contacted and asked to participate in this study. Those that agreed were surveyed using an adapted version of the Telehealth Satisfaction Scale (TeSS) and four open-ended questions pertaining to their healthcare needs. The TeSS is scored out 32, with higher scores indicating greater satisfaction.

Results: To-date, 15 of patients were contacted, and 13 agreed to be surveyed (response rate = 87%). On average, participants had received care from the teleophthalmology program 3 to 4 weeks from the time they were surveyed. The median TeSS score was 32 (SD = 1.57), ranging from 28 to 32, indicating high satisfaction with the program. 44% (n = 4) of participants lived in a rural community, where they would otherwise have had to travel between 27 to 110 kilometers to receive specialized ophthalmic care in-person. Overall, patients responded positively to open-ended questions stating the convenience and lack of waiting times was preferred to in-person appointments. Four patients advocated for further use of technology in additional modalities as they appreciated regular communication with their healthcare providers.

Conclusions: The analysis demonstrates that patients of an ocular oncology clinic are highly satisfied with a teleophthalmology program. The delivery of this kind of specialized care mitigates the access barriers to rural patients while still meeting patients' needs and perceptions.

CONTROL ID: 3715051

SUBMITTER (NAME ONLY): Cinthia Kim

TITLE: Ocular surface changes in the early stage of post allogeneic hematopoietic stem cell transplantation

SESSION TITLE: Ocular surface health and conjunctiva

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kim, Y. Shi, O.L. Lee, ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|Y. Shi, Doheny Eye Institute Doheny Image Reading Center, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Cinthia Kim: Commercial Relationship: Code N (No Commercial Relationship) | Yue Shi: Commercial Relationship: Code N (No Commercial Relationship) | Olivia Lee: Commercial Relationship(s);Code C (Consultant/Contractor):Cloudbreak Therapeutics

ABSTRACT BODY:

Purpose: This study aims to characterize anatomical and functional changes in the ocular surface after allogeneic hematopoietic stem cell transplantation in the absence of GVHD.

Methods: A total of 8 eyes of 4 patients with hematologic malignancies requiring HSCT were prospectively recruited for this pilot study. All patients underwent a full ophthalmic examination before and 3 months after transplantation. Examinations performed on all subjects included OSDI survey, tear matrix metalloproteinase (MMP)-9 test, tear break-up time (TBUT), corneal fluorescein staining (Oxford scale), lower lid meibomian gland dysfunction score and lower lid meibography. In addition, in vivo confocal microscopy (IVCM) imaging of the central cornea was used to evaluate morphological changes of the corneal epithelial layers, corneal nerves and presence of dendritic cells (DCs).

Results: The mean age of patients was 42.75 ± 19.8 years, and mean follow-up was 91.25 ± 25.7 days after allo-HSCT. Four eyes of two patients patients exhibited positive results for MMP-9 test after transpantation despite all 8 eyes having tested negative for MMP-9 at baseline.

In the early-stage post transplantation, no statistically significant differences were found in the following variables when compared to baseline: OSDI score (P=0.067), TBUT (P=0.181), Schirmer's test (P=0.059), corneal fluorescein staining score (P=0.085), meiboscore (P=0.142) and meibography (P=0.5).

IVCM images obtained from 4 eyes of 2 patients at baseline and post allo-HSCT were analyzed. There were no significant differences in epithelial wing cell density (P=0.281), epithelial basal cell density (P=0.089), subbasal nerve density (P = 0.468) and DC density (P=0.093).

Conclusions: In our study, significant changes were not observed in the ocular surface parameters prior to and after all-HSCT. However, MMP-9 was detected in tears of 50% of eyes after transplantation in the absence of any ocular surface symptoms or clinical changes.

Although many patients are asymptomatic, severe dry eyes is a common finding after allo-HSCT in the context of oGVHD. The risk of oGVHD development is elevated in the first year of transplant, and there is substantial evidence that the ocular surface and meibomian glands are damaged in patients with this condition. Further study is required to determine what role, if any, the presence of MMP-9 plays in early detection of oGVHD.

CONTROL ID: 3715058

SUBMITTER (NAME ONLY): Luis Sanchez

TITLE: TIME-COURSE ANALYSIS OF HUMAN TRABECULAR MESHWORK SINGLE CELL CONTRACTION AFTER A 5-DAY DEXAMETHASONE TREATMENT

SESSION TITLE: Glaucoma: biochemistry, biomechanics and omics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.U. Sanchez, J.J. Zheng, C. Zhang, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure: Luis Sanchez: Commercial Relationship: Code N (No Commercial Relationship) | Jie Zheng: Commercial Relationship: Code N (No Commercial Relationship) | Chi Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glucocorticoids, such as dexamethasone (Dex), are speculated to alter the contractile properties of human trabecular meshwork (HTM) cells. However, there are no definitive studies showing that dexamethasone treatment modulates the contractile forces exerted by HTM cells in vitro. Because cellular contraction is a dynamic process, it is important to quantify changes in contractile force generation over time. Additionally, observed heterogeneity in primary HTM cell cultures call for single cell contraction measurements.

Methods: In order to measure HTM cell contraction at the single cell level, primary HTM cells from 4 different donors were cultured for 5 days in the presence of DMSO vehicle, or 0.1μM Dex. After 5 days, primary HTM cells from each condition were harvested, dissociated to single cells, and seeded into the wells of the fluorescently labeled elastomeric contractible surfaces (FLECS) assay for single cell contraction measurements. Data were collected every 2 hours over a period of 16 hours and analyzed using computational algorithms.

Results: Interestingly, a single large population of weakly contractile cells and smaller subpopulations of strongly contractile cells were identified across both conditions. The strongly contractile subpopulations remained smaller compared to the single weakly contractile cell population throughout the course of 16 hrs. Furthermore, the strongly contractile cell subpopulations became increasingly prominent in the DMSO vehicle condition throughout the course of 16 hrs. Dex treated cells also displayed small subpopulations of strongly contractile cells. However, these subpopulations were smaller compared to DMSO vehicle, and remained mostly unchanged throughout the course of 16 hrs.

Conclusions:

Based on our findings, Dex treatment appeared to reduce the ability of a population of primary HTM cells to exert strong contractile forces.

CONTROL ID: 3715064

SUBMITTER (NAME ONLY): Lynn Hassman

TITLE: Antigen-driven immune responses distinguish uveitis subtypes.

SESSION TITLE: Uveitis: Human and Murine Experimental Medicine Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Hassman, Department of Ophthalmology and Visual Science, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

Commercial Relationships Disclosure: Lynn Hassman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Non-infectious uveitis is a heterogeneous group of blinding ocular inflammatory diseases whose pathophysiologic mechanisms are poorly understood. This results in empiric treatments that are ineffective for many patients. We therefore set out to identify immunologic mechanisms that would differentiate uveitis subtypes and reveal therapeutic targets.

Methods: We performed single-cell V(D)J sequencing to identify clonally expanded lymphocytes, an indication of antigen-driven immune responses, in parallel with single-cell RNA sequencing in order 1)identify antigen-expanded lymphocytes and 2) characterize the gene expression of aqueous fluid and peripheral blood immune cells from 18 patients with diverse types of uveitis.

Results: We identified clonal CD4 T cell expansion in aqueous samples from a subset of patients with uveitis, suggesting that these ocular immune cells had responded to an antigen. Furthermore, we found that patients with robust CD4 clonal expansion tended to have granulomatous features and prolonged disease courses. Furthermore, these patients' CD4 T cells were enriched in expression of genes associated with the effector memory cell state, a group of antigen-experienced T cells that drive chronic or recurrent inflammatory disease. These patients also had more type 1 conventional dendritic cells (DC1s) enriched in expression of genes required for activating T effector memory cells, and fewer type 2 conventional dendritic cells (DC2s).

Conclusions: This suggests that antigen-driven immune responses may be a distinguishing feature in uveitis patients with granulomatous features and prolonged disease courses. Furthermore, the correlation between increased frequencies of DC1s and CD4 clonal expansion suggests that DC1s may activate CD4 T effector memory cells to drive chronic granulomatous uveitis.

CONTROL ID: 3715074

SUBMITTER (NAME ONLY): Michal Laron

TITLE: Evaluation of Epithelial Cell Remodeling After a Lenticule Removal Procedure with a New Femtosecond Laser System

SESSION TITLE: Refractive and non-refractive corneal surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Laron, B. Schwam, A.P. Voorhees, H. Fu, Y. Wang, L. Vargas, Clinical Research, Johnson & Johnson Surgical Vision Inc, Santa Ana, California, UNITED STATES|R. Shetty, P. Khamar, S. Nagaraj, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

Commercial Relationships Disclosure: Michal Laron: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision | Rohit Shetty: Commercial Relationship: Code N (No Commercial Relationship) | Brian Schwam: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision | Pooja Khamar: Commercial Relationship: Code N (No Commercial Relationship) | Sri Harsha Nagaraj: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Voorhees: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision | Hong Fu: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision | Ying Wang: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision | Luis Vargas: Commercial Relationship(s);Code E (Employment):Johnson & Johnson Surgical Vision

ABSTRACT BODY:

Purpose: To assess epithelial cell remodeling after myopic laser vision correction with a new femtosecond laser for the correction of myopia and astigmatism through intrastromal lenticule removal procedure.

Methods: A prospective clinical study in myopic subjects ≥18 years is ongoing. 48 eyes of 24 myopic subjects were treated binocularly at 1 site for vision correction using a new femtosecond laser. Mean pre-operative Manifest Refraction Spherical Equivalent (MRSE) was -4.04 D and ranged from -2.00 D to -6.25 D (SD: 1.17 D). A lenticule removal procedure was used. The RTVue anterior segment Pachymetry + Cpwr scan (SW Ver. 6.11.0.12) was used to generate epithelial thickness maps comprised of 17 sectors over a 6 mm diameter circle. One central 2 mm diameter circular sector, 8 sectors within an annulus 2-5 mm diameter (ring-1), and 8 sectors within an annulus 5-6 mm diameter (ring-2). ANOVA with Tukey pairwise comparison was used to evaluate change in total epithelial thickness and change in superior versus inferior thickness from pre-operatively (44 eyes) to 1-day (42 eyes), 1-week (44 eyes), 1-mo (44 eyes), and 3-mo (17 eyes) post-operatively. A correlation between pre-operative MRSE and change in epithelial thickness was also evaluated.

Results: No significant change in epithelial thickness was found in the central sector at all time points. In ring-1, there was variability with significant thickening (1.47 μm) from pre-op to 1-day post-op followed by a significant thinning of 1.41 μm at 1-week and then continuous thickening at 1- and 3-mo post-op of 2.37 and 0.22 μm, respectively ($p = 0.0001$). In ring-2 there was a continuous thickening at 1- and 3-mo post-op of 1.47 and 1.08 μm, respectively ($p = 0.0001$). No significant change was observed between the superior vs. inferior sectors, and no correlation was found between pre-op MRSE and change in epithelial thickness ($R^2 = 0.07, 0.05$ for 1 and 3-mo post-op).

Conclusions: Significant change in epithelial thickness after lenticule removal with the new femtosecond laser was observed in rings 1 and 2. This thickening may be attributed to epithelial remodeling and is apparent at 1- and 3-mo post-op. No difference between superior and inferior change in thickness implies no effect of the lenticule entry cut on remodeling.

CONTROL ID: 3715076

SUBMITTER (NAME ONLY): Tetsuju Sekiryu

TITLE: Evaluation of choroidal vascular morphology in retinal degenerative diseases by using 3D models

SESSION TITLE: New improvements in imaging and development of biomarkers

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sekiryu, Y. Sugano, Y. Kato, Ophthalmology, Fukushima Kenritsu Ika Daigaku Igakubu, Fukushima, Fukushima, JAPAN|

Commercial Relationships Disclosure: Tetsuju Sekiryu: Commercial Relationship: Code N (No Commercial Relationship) | Yukinori Sugano: Commercial Relationship: Code N (No Commercial Relationship) | Yutaka Kato: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate choroidal blood vessels in retinal degenerative diseases using a novel biomarker calculated from a three-dimensional (3D) model of the choroid.

Methods: The subjects were crystallin retinopathy (CR) 6 eyes of 4 patients, retinitis pigmentosa (RP) 23 eyes of 13 patients. Controls were healthy eyes with no age difference 51 cases 51 eyes. Swept Source optical interference tomography A 3D model was created from the (OCT) image (6 x 6 mm) based on the previous report. The foveal choroid thickness (CT) was measured with an OCT tomographic image. From the 3D model, choroidal blood vessel volume (CVV), blood vessel surface area/volume ratio (S / V) as an index of the size of blood vessel structure, blood vessel diameter index (blood vessel diameter index) and blood vessel length per unit volume (blood vessel length index)) was calculated.

Results: The average value of CT (μm), CVV (mm^3), S / V (mm^{-1}), vessel diameter index (mm), vessel length index (mm^{-1}) is 117, 0.42, 124, 0.031, 62 for CR, 164, 0.68, 94, 0.042, 53 for RP, and 255, 1.27, 86, 0.042, 49 for control. In CR and RP, CT, CVV, and blood vessel diameter index were smaller and S / V was larger than in the control (all $P < 0.05$). The vessel length index was large in CR ($P = 0.043$) and was not different from the control in RP ($P = 0.162$).

Conclusions: Both CR and RP have smaller CT and CVV than healthy eyes. From the decrease in the blood vessel diameter index, it is considered that the decrease in the blood vessel diameter has an effect on both diseases. CR has a high vessel length index, and the choroidal parenchyma may be more severely impaired. New biomarkers using 3D models can evaluate choroidal vascular morphology.

CONTROL ID: 3715085
SUBMITTER (NAME ONLY): Sarah Hull
TITLE: Lamination of the outer plexiform layer in dominant Wolfram disease
SESSION TITLE: Genetic variants in human ocular disease
SESSION TYPE: Poster Session
AUTHORS/INSTITUTIONS: S. Hull, A.L. Vincent, Ophthalmology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|
Commercial Relationships Disclosure: Sarah Hull: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Vincent: Commercial Relationship: Code N (No Commercial Relationship)
ABSTRACT BODY:
Purpose: Heterozygous variants in WFS1 are associated with a Wolfram- like syndrome characterised by sensorineural hearing loss, optic atrophy and diabetes mellitus. A previous study described outer plexiform layer (OPL) lamination in dominant WFS1 disease. In this report two further patients are described.
Methods: This was a retrospective case study of two probands from two families with detailed clinical phenotyping including ophthalmic examination, optic nerve and retinal imaging, and neuroimaging. Molecular investigations included targeted Sanger sequencing and next generation gene panel sequencing.
Results: Two female patients with a background of congenital, severe sensorineural hearing loss, were incidentally found aged 10 years and 16 years to have optic disc pallor, with slightly reduced visual acuity (0.2-0.3 logMAR) and reduced color vision. Optical coherence tomography (OCT) of the nerve fiber layer identified severe generalised thinning. OCT of the macula demonstrated a linear splitting abnormality of the OPL within the central macula. Neuroimaging confirmed no intracranial cause of optic neuropathy.

In both probands, heterozygous variants were found in WFS1, specifically c.937T>C (p.His313Tyr) and c.2590G>A (p.Glu864Lys), both previously reported in affected patients. After identification of the optic neuropathy, diabetic screening was performed confirming diabetes mellitus in one proband.
Conclusions: In optic atrophy, OCT macula may reveal a pathognomonic OPL lamination that is associated with dominant WFS1 variants.

CONTROL ID: 3715090

SUBMITTER (NAME ONLY): Hirotaka Tanabe

TITLE: Comparison of Visual Performance between Non-tinted and Yellow-tinted Monofocal Intraocular Lenses of the Same Material and Basic Design

SESSION TITLE: Cataract surgery II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Tanabe, T. Shojo, K. Takase, T. Yamauchi, H. Tabuchi, Ophthalmology, Tsukazaki Hospital, Himeji, Hyogo, JAPAN|

Commercial Relationships Disclosure: Hirotaka Tanabe: Commercial Relationship: Code N (No Commercial Relationship) | Tomohiro Shojo: Commercial Relationship: Code N (No Commercial Relationship) | Kosuke Takase: Commercial Relationship: Code N (No Commercial Relationship) | Tomofusa Yamauchi: Commercial Relationship: Code N (No Commercial Relationship) | Hitoshi Tabuchi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the visual performance of a non-tinted monofocal intraocular lens (IOL) (ZCB00) and a yellow-tinted monofocal IOL (ZCB00V) of the same material and basic design.

Methods: We evaluated postoperative parameters at 10 weeks after the last surgery in cataract patients who underwent bilateral ZCB00 or ZCB00V implantation from January 4, 2011, to November 19, 2020, with the right and left lenses implanted within 3 months of each other. The study enrolled 2278 eyes of 1139 patients. A linear mixed-effects model using data for both eyes, with strict adjustments for sex, age, subjective refraction spherical equivalent, subjective refraction cylinder, corneal astigmatism, axial length, corneal higher-order aberrations, and pupil diameter, ensured statistical validity.

Results: Contrast sensitivity with glare (6.3/4.0/0.7 degrees) were significantly better in the yellow-tinted group ($p<0.00068$, Wald test), and contrast sensitivity (4.0/2.5/1.6 degrees), contrast sensitivity with glare (2.5/1.6/1.0 degrees), the 25-item National Eye Institute Visual Function Questionnaire (VFQ-25) score for general health, and near spectacle independence were likely better in the yellow-tinted group ($p<0.05$, Wald test). Uncorrected intermediate/near visual acuity (UIVA/UNVA), corrected near visual acuity (CNVA), higher-order aberration (internal, scaled to a pupil size of 6 mm) (WF_6_post_I_Trefoil), the VFQ-25 scores for Role_Limitation, Mental_Health, Social_Function, Distance_Vision, Color_Vision, were likely better in the non-tinted group ($p<0.05$, Wald test).

Conclusions: The two IOL groups had different characteristics in terms of UIVA/UNVA/CNVA, contrast sensitivity, contrast sensitivity with glare, the VFQ-25 scores, higher-order aberration, and near spectacle independence.

CONTROL ID: 3715106

SUBMITTER (NAME ONLY): Timothy Lai

TITLE: Association of fundus autofluorescence changes and pachydrusen in central serous chorioretinopathy and polypoidal choroidal vasculopathy

SESSION TITLE: Macular diseases/Macular edema/Functional testing/evaluation/Laser

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.Y. Lai, Z. Tang, C. Cheung, Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|T.Y. Lai, A.C. Lai, R.Y. Lai, 2010 Retina & Macula Centre, Kowloon, HONG KONG|

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ABSTRACT BODY:

Purpose: To evaluate the association between pachydrusen and changes in fundus autofluorescence (FAF) in eyes with central serous chorioretinopathy (CSC) and polypoidal choroidal vasculopathy (PCV).

Methods: Retrospective review of 75 eyes with CSC and 33 eyes with PCV. Color fundus photo, FAF and optical coherence tomography (OCT) were evaluated to assess for pachydrusen, changes in FAF and OCT subfoveal choroidal thickness (SFCT).

Results: Pachydrusen were found in 18.7% of CSC eyes and 63.6% of PCV eyes. The mean age of patients with eyes having pachydrusen was significantly older than those without pachydrusen in both CSC and PCV ($P<0.001$ and $P=0.003$, respectively). No significant difference was found in the mean SFCT in both CSC and PCV eyes with or without pachydrusen. More extensive area of FAF abnormalities was found to be associated with eyes with pachydrusen ($P=0.041$).

Conclusions: Pachydrusen are more prevalent in eyes with PCV than CSC. Pachydrusen are associated with increasing age and more extensive retinal pigment epithelial abnormalities as shown by the FAF changes.

CONTROL ID: 3715126

SUBMITTER (NAME ONLY): Marie-Helene Errera

TITLE: ADAPTIVE OPTICS AND MULTIMODAL IMAGING FOR INFLAMMATORY VITREORETINAL INTERFACE ABNORMALITIES

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Errera, E. Satcho, V. Snyder, K.K. Dansingani, I. AHMAD, A. THOMPSON A, N. KEDIA, J. Chhablani, J.A. Sahel, E.A. Rossi, Ophthalmology, UPMC Eye Center, University of Pittsburgh, Pittsburgh, PA, USA, Pittsburgh, Pennsylvania, UNITED STATES|M. Paques, Ophthalmology, 1Quinze-Vingts hospital, INSERM-DHOS CIC 1423, Paris, F-75012 France, Sorbonne Universités, UPMC Univ Paris 06, France 2DHU ViewRestore, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: To investigate the changes of the vitreoretinal interface as seen on multimodal adaptive optics imaging of eyes with uveitis.

Methods: Four eyes (4 patients) affected by fovea-attached (subtype 1A) or fovea sparing epiretinal membranes (ERM) on spectral domain optical coherence tomography (SD-OCT) or visible internal limiting membrane (ILM) on Infrared fundus imaging were recruited in this pilot study.

The microstructure of the vitreoretinal interface was imaged using flood-illumination adaptive optics (FIAO) and images were compared to the cross-sectional SD-OCT data.

Two eyes from 2 additional patients with Gunn's dots identified by FIAO had their FIAO images compared with the microstructures seen associated with ILM.

Results: Adaptive optics images revealed multiple abnormalities of the vitreoretinal interface, such as deep linear striae in ERM, and hyperreflective microstructures at the location of ERMs (picture 1) and ILMs.

The Gunn's dots were morphologically different from the hyperreflective microstructures or spots associated with the ILM and ERM.

Conclusions: FIAO imaging can identify specific patterns associated with ERMs and ILMs.

FIAO imaging of the vitreomacular interface and its correlation to FIOA imaging of outer retinal structures to discerne structural alterations can be valuable to understand the cause of significant macular dysfunction associated to ERM.

CONTROL ID: 3715176

SUBMITTER (NAME ONLY): Lea Bennett

TITLE: Patients diagnosed with autosomal dominant macular or pattern dystrophy who harbor the mutation p.Pro210Arg in PRPH2 have clinical abnormalities in both rod and cone photoreceptors

SESSION TITLE: Retinal Degenerations, Gene Therapy, Transplantation, and Prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.D. Bennett, N. Al Kadhem, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|D.G. Birch, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in PRPH2 are among the leading genetic causes of inherited retinal diseases (IRD). More than 200 different mutations in PRPH2 have been associated with multiple subtypes of IRD including retinitis pigmentosa and cone or macular diseases. The molecular mechanism associated with the mutation p.Pro210Arg (P210R) in PRPH2 has not been evaluated and little is known about the clinical presentation of patients with this particular genetic defect. The purpose of this research was to understand how this mutation affects visual function and retinal structure as well as gain insight into the mechanism driving the clinical features observed in these patients.

Methods: Eleven patients from seven families had clinical assessments including best corrected visual acuity (BCVA), static (spot size V) perimetry (Octopus 900) and dark-adapted chromatic (DAC; Medmont; spot size V) perimetry. Images were acquired with the Optos ultra-wide field camera and spectral-domain optical coherence tomography (SD-OCT).

Results: Patients who were previously determined to harbor the P210R mutation in PRPH2 had BCVA (Snellen) that ranged from 20/15 to 20/80. Perimetry exams showed an overall reduction in sensitivity. Scotomas were identified that corresponded to atrophic lesions on the retina. Imaging revealed drusen, hyper-fluorescent flecks, migrating RPE, interruptions in the inner/outer-segment junction, and foveal sparing.

Conclusions: Rod and cone sensitivity was decreased in subjects with the P210R mutation in PRPH2. However absolute vision loss occurred within the macula and likely secondary to drusen formation. This suggests that although rod and cone photoreceptors are dependent on PRPH2, preventing blindness in this specific subgroup of patients should involve therapeutics to impede drusen formation.

CONTROL ID: 3715181

SUBMITTER (NAME ONLY): Syed Ahmed

TITLE: The eyePlate-300 implant: Results in refractory glaucoma

SESSION TITLE: Surgery & Wound Healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ahmed, S. Virdee, A. Al-nahrawy, A. Mazrouaa, F. Ahmed, Western Eye Hospital, London, London, UNITED KINGDOM|S. Ahmed, S. Virdee, A. Al-nahrawy, A. Mazrouaa, F. Ahmed, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The eyePlate glaucoma drainage implant (eyePlate, Rheon Medical SA) is a novel non-valved drainage device constructed entirely out of medical grade silicone. This study evaluates the 6-month efficacy and safety of the eyePlate-300 implant in cases of uncontrolled glaucoma. To our knowledge this is the first report of this novel glaucoma drainage implant device.

Methods: A retrospective, non-comparative study of 16 consecutive eyes treated with the eyePlate-300 glaucoma drainage implant at the Western Eye Hospital, London between March 2020 and April 2021 was performed.The patients were followed up for 6 months. For all patients, care was overseen by the same glaucoma consultant who performed all the surgeries under local anaesthesia. The Kolmogorov-Smirnov and Shapiro-Wilk tests established normality of results. The paired t-test was used to assess statistical significance of the results.

Results: A total of 15 patients (16 eyes) were included. The mean age was 59.7 (15.8) years. The most common diagnosis was primary open angle glaucoma (37.5%). Previous procedures included trabeculectomy (31.25%), micropulse diode laser trabeculoplasty (56.25%), iStent (12.5%) and cyclodiode laser (12.5%). Mean pre-treatment IOP was 31.5 (mmHg. There was a significant reduction ($p<0.05$) in IOP at 1 month to 11.8 (4.2) mmHg (62.6% reduction), at 3 months to 16.25 (2.3) mmHg (51.6% reduction) and at 6 months to 15.4 (2.2) mmHg (51.1% reduction). The requirement of topical treatment significantly reduced ($p<0.0.5$) from a baseline of 3.44 (1.09), to 2.06 (0.42) at 1 month, 2.0 (0.47) at 3 months and 2 (0.46) at 6 months. There was no statistically significant drop in visual acuity or increase in central retinal thickness found. Two patients (12.5%) experienced prolonged uveitis requiring extended steroid treatment for resolution. Three patients (18.75%) had post-op hypotony with choroidal effusions but showed an improved VA at 6 months. None of the patients required any further surgery.

Conclusions: The above results have shown the eyePlate-300 to be significantly effective in reducing IOP and need for topical treatment in patients with refractory glaucoma within a 6-month period following surgery. Further long-term data is needed to confirm efficacy and comparability to current commonly used procedures.

CONTROL ID: 3715193

SUBMITTER (NAME ONLY): Irmela Mantel

TITLE: Transscleral optical imaging in non-neovascular age-related macular degeneration.

SESSION TITLE: Applications of adaptive optics and advanced imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Mantel, L. Solomos, Z. Misutkova, A. Iskandar, A. Gryczka, A. Navarro, F. Jeunet, L. Kowalczuk, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|L. Kowalczuk, R. Dormier, C. Moser, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, SWITZERLAND|F.F. Behar-Cohen, Centre de Recherche des Cordeliers, Inserm, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) cells have been shown to be primary affected in age-related macular degeneration (AMD). We report here the results of transscleral optical imaging (TOI) in AMD patients. This image modality has been developed for in vivo visualization of RPE cellular structure in human retina.

Methods: 25 non-neovascular AMD cases with clear optic media and good fixation were recruited for TOI, associated with conventional imaging: spectral domain optical coherence tomography (OCT), autofluorescence, color and infrared fundus imaging. Five zones of 5.04x5.04 degrees were acquired with TOI: one was foveal, four were localized in the macular quadrants at 3.8° eccentricity. The resulting TOI images were optimized for contrast and confronted with information from conventional multimodal imaging.

Results: Included were 31 eyes of 25 AMD patients (mean age 71.8 years, 56% females). Prominent features on the TOI images were the reticular pattern of the choriocapillaris, particularly well contrasted on areas of geographic atrophy and RPE hypopigmentation, and the presence of additional dark spots irregularly distributed (Fig. 1C). These dark spots, with size varying from 1 time to approximately 15 times the mean RPE cell size, were located on the low reflectance areas of the choriocapillaris, and particularly present in the border area around atrophic zones and in areas of visible RPE changes. A subgroup of these cells, showing a bright halo around them, correlated well with drusenoid deformation of the RPE line on SD-OCT. Dark spots were particularly frequent in eyes with reticular pseudodrusen. Drusen were also observed in a particular pattern of hyporeflective center with hyperreflective edges. An example of TOI images is given in the figure, including correlation with clinical fundus autofluoresence (FIG 1A) and OCT (FIG 1B).

Conclusions: TOI performed in 25 AMD patients revealed different patterns of altered tissue in the RPE layer. Upon confirmation of these results, TOI might become a relevant tool in the evaluation of retinal diseases such as AMD.

CONTROL ID: 3715227

SUBMITTER (NAME ONLY): Hari Jayaram

TITLE: Home Visual Field Monitoring with the Melbourne Rapid Fields: Test-Retest Variability and Agreement with the Humphrey Visual Field Analyzer

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Jayaram, G. Montesano, N. Nathwani, J. Yu, G. Gazzard, Glaucoma Service, NIHR Moorfields Biomedical Research Centre, London, Greater London, UNITED KINGDOM|G. Montesano, Optometry and Visual Science, City University of London, London, London, UNITED KINGDOM|J. Yu, Glaucoma Service, Manchester Royal Eye Hospital, Manchester, Manchester, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To compare the agreement and repeatability between the Melbourne Rapid Fields home monitoring platform (MRF-HM) and the Humphrey Field Analyzer (HFA, Zeiss Meditec) in patients with glaucoma

Methods: One hundred patients at Moorfields Eye Hospital who have previously participated in the LiGHT trial, who have previously demonstrated stable and reliable hospital-based HVF tests in one eye, were recruited and stratified to two groups according to the severity of visual field loss. Participants were asked to perform two visual field (VF) tests with the MRF-HM using their home computer over a month. HFA data were obtained from the two most recent tests performed in the clinic. A false positive rate < 15% was the only metric used to assess reliability of the test. Test-retest variability was quantified with Bland-Altman (BA) plots and 95% Limits-of-Repeatability (LoR), calculated as the 2.5% and 97.5% quantiles of the test-retest difference, and the 95%-LoR range. Calculations were performed for pointwise sensitivity and total deviation (TD) and on the Mean Total Deviation (MTD) using the 52 locations of the 24-2 grid, excluding the two blind-spot locations. 95%-Confidence Intervals (CIs) and p-values were calculated via paired bootstrap sampling. BA plots and 95%-Limits of Agreement (LoAs) were also used to assess the agreement between all four possible MRF-HM and HFA test pairs, accounting for proportional bias.

Results: Ninety-nine patients had four reliable tests and were analyzed. The interval between the two repeat tests was 6.2 [4.4, 9.0] months for HFA and 2.14 [1.42, 3.78] weeks for MRF (Median [Interquartile range]). The 95%-LoRs and corresponding CIs are reported in Figure 1 with the BA plots. The MRF-HM had a significantly larger 95%-LoR range for all metrics compared to HFA (all $p < 0.001$). The agreement and the 95%-LoAs are shown in Figure 2. There was a significant proportional bias for all metrics (all $p < 0.001$), with the estimates from the MRF being systematically lower than HFA for more damaged VFs.

Conclusions: MRF-HM is a useful tool for home monitoring in glaucoma patients, but has a larger test-retest variability compared to HFA and the two tests are not directly interchangeable. The possibility of more frequent testing could overcome the larger test-retest variability of MRF-HM.

CONTROL ID: 3715636

SUBMITTER (NAME ONLY): Mathew Palakkamanil

TITLE: The Effect of Gingko Biloba Extract (GBE) on Optic Nerve Head Perfusion Examined Using Ocular Coherence Tomography Angiography (OCT-A): A Prospective Study

SESSION TITLE: OCT Angiography Clinical Applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Palakkamanil, A. Zhang, C.A. Smith, O. Dyachok, L. Shuba, Ophthalmology and Visual Sciences, Dalhousie University, Halifax, Nova Scotia, CANADA|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the effect of gingko biloba extract (GBE) on optic nerve head perfusion examined using ocular coherence tomography angiography (OCT-A).

Methods: Six patients with a diagnosis of mild primary open angle glaucoma (POAG) were included in this study. POAG diagnosis was based on the clinical assessment, optical coherence tomography (OCT), and visual field defects using the Humphrey Field Analyzer. Patients were included if they had a mean deviation (MD) better than -10 dB, and a best corrected visual acuity (BCVA) better than or equal to 0.3 logMAR. Patients with other ocular diseases, high refractive errors, and history of glaucoma surgery were excluded. Additionally, patients with seizure disorders, on anticoagulation therapy, or on medications with possible interactions with GBE were excluded. The participants received GBE supplementation (a 120 mg soft gel twice a day) for a four-month period. All participants had baseline OCT-A optic nerve head and macula imaging performed on both eyes prior to initiation of GBE. Repeat imaging was performed after completion of the four-month course of GBE. The primary outcome of interest was the difference in perfusion density of the superficial vascular plexus of the macula and the optic nerve head annulus (adjusted by optic nerve head dimensions) before and after GBE supplementation. This study was approved by the institutional research ethic boards and was registered with ww.clinicaltrials.gov (NCT04846179).

Results: Six patients were included in the analysis which were composed of two females and four males. The average age of the participants was 69.3 years. The average baseline BCVA was 0.08 LogMAR. In post-consumption measurements, macular and optic nerve head annulus superficial vascular plexus perfusion density were not statistically significantly higher than pre-consumption measurements ($p = 0.3$ and $p = 0.5$, respectively). No significant difference was observed in post-consumption BCVA compared to baseline measurements.

Conclusions: Our study suggests that four-month supplementation with gingko biloba does not result in a significant increase in perfusion density of the macula and optic nerve head. Larger, comparative studies are needed to demonstrate the effects of GBE supplementation on ocular vascular density and glaucoma disease course.

CONTROL ID: 3715760

SUBMITTER (NAME ONLY): Jonghwa Kim

TITLE: Automated processing of images obtained by anterior segment fluorescence imaging device: evaluating dry eye

SESSION TITLE: Machine Learning and Image Processing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kim, H. YOON, K. Yoon, Ophthalmology, Chonnam National University Hospital, Gwangju, Gwangju, KOREA (THE REPUBLIC OF)|T. Eom, E. Park, Advanced Photonics Research Institute, Gwangju Institute of Science and Technology, Gwangju, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Clinical examination of dry eye patients may yield different results according to the examiners. We aimed to invent a fluorescence anterior segment imaging device using blue light LED (490 nm wavelength) light source and automated image processing system that analyzes acquired video images so that we can obtain a diagnostic index for dry eye by measuring the temporal change of the fluorescence signal.

Methods: We developed an anterior segment fluorescence imaging device consisting of an LED light source of 490 nm wavelength and a filter that selectively transmits only the fluorescence signal to measure the fluorescence signal change in the corneal lesion and tear film after topically applying fluorescein sodium.

In order to measure the change in the tear meniscus height (TMH), a fixed region of interest independent of eye movement was chosen and the height of tear meniscus in the region was measured.

In order to measure the tear film break-up time (TBUT), we obtained changes in fluorescence signal area in the cornea between blinking and processed the video images automatically. The point of tear film break-up was provisionally set as the point at which non-fluorescence area increased by 0.5%.

In order to measure the corneal staining score (CSS), the punctate points in the cornea that did not change in fluorescence temporally were extracted. The scoring was done according to the Oxford grading scale.

To test the reliability of the device, TMH, TBUT and CSS of 80 eyes of volunteers were measured by Keratograph 5M (OCULUS Inc., Wetzlar, Germany) and by slit-lamp biomicroscopy examined by a cornea expert.

Results: The images obtained with the newly developed device showed tear film break-up pattern, TBUT, TMH, and CSS similar to the images obtained with a video capture system in a slit-lamp biomicroscopy using cobalt-blue filter and the images obtained with keratograph 5M. The correlation coefficient showed highly reliable results for TBUT, TMH and CSS (all>0.8)

Conclusions: The LED-based anterior segment fluorescence imaging device with automatic analysis program is a useful tool for measuring dry eye indices and can yield precise results. By further applying a deep learning system, the program would even be able suggest treatment strategies.